Japanese Technology Evaluation Center

JTEC

JTEC Panel Report on

Japan's ERATO and PRESTO Basic Research Programs

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September 1996

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JTEC PANEL ON JAPAN'S ERATO AND PRESTO PROGRAMS

Sponsored by the National Science Foundation and the Department of Commerce of the United States Government

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INTERNATIONAL TECHNOLOGY RESEARCH INSTITUTE
WTEC PROGRAM

The World Technology Evaluation Center (WTEC) at Loyola College (previously known as the Japanese Technology Evaluation Center, JTEC) provides assessments of foreign research and development in selected technologies under a cooperative agreement with the National Science Foundation (NSF). Loyola's International Technology Research Institute (ITRI), R.D. Shelton Director, is the umbrella organization for WTEC. Paul Herer, Senior Advisor for Planning and Technology Evaluation at NSF's Engineering Directorate, is NSF Program Director for WTEC. Other U.S. government agencies that provide support for the program include the National Aeronautics and Space Administration, the Department of Energy, the Department of Commerce, and the Department of Defense.

WTEC's mission is to inform U.S. policy makers, strategic planners, and managers of the state of selected technologies in foreign countries in comparison to the United States. WTEC assessments cover basic research, advanced development, applications, and commercialization. Small panels of about six technical experts conduct WTEC assessments. Panelists are leading authorities in their field, technically active, and knowledgeable about U.S. and foreign research programs. As part of the assessment process, panels visit and carry out extensive discussions with foreign scientists and engineers in universities and in industry and government labs.

The ITRI staff at Loyola College helps select topics, recruits expert panelists, arranges study visits to foreign laboratories, organizes workshop presentations, and finally, edits and disseminates the final reports.

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<u>FINAL REPORT</u>

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ABSTRACT

This report is a review of two basic research programs funded by the Research Development Corporation of Japan (JRDC). The primary focus of the report is on the Exploratory Research for Advanced Technology (ERATO) program, as an update of a 1988 JTEC report on the same subject. The current panel found that the ERATO program has been quite successful as a catalyst for changing the Japanese system of supporting and performing research, and that research performed under ERATO is of high quality, with several projects leading to the development of world-class research. At least in one case, an ERATO project created a new scientific field. The panel also concluded that the ERATO process has unique characteristics that can be applied in the United States, particularly in encouraging the development of closer ties between academic, national laboratory, and industrial researchers. The report also briefly reviews a newer JRDC program entitled Precursory Research for Embryonic Science and Technology (PRESTO). Its process and mode of funding are more like traditional U.S. procedures than is the case with ERATO, although its objective is more focused and designed to help researchers embark upon new lines of work. The panel found that, while PRESTO is too new to be fully evaluated, early indications suggest good results. Information sources for this study included a literature review, visits to JRDC-funded laboratories, and interviews with numerous past and present ERATO and PRESTO researchers.

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FOREWORD

The National Science Foundation (NSF) has been involved in funding technology assessments comparing the United States and foreign countries since 1983. A sizable proportion of this activity has been in the Japanese Technology Evaluation Center (JTEC) and World Technology Evaluation Center (WTEC) programs. NSF has supported more than thirty JTEC and WTEC studies over a wide range of technical topics.

As U.S. technological leadership is challenged in areas of previous dominance such as aeronautics, space, and nuclear power, many governmental and private organizations seek to set policies that will help maintain U.S. strengths. To do this effectively requires an understanding of the relative position of the United States and its competitors. The purpose of the JTEC/WTEC program is to assess research and development efforts in other countries in specific areas of technology, to compare these efforts and their results to U.S. research in the same areas, and to identify opportunities for international collaboration in precompetitive research.

Many U.S. organizations support substantial data gathering and analysis efforts directed at nations such as Japan. But often the results of these studies are not widely available. At the same time, government and privately sponsored studies that are in the public domain tend to be "input" studies; that is, they provide enumeration of inputs to the research and development process, such as monetary expenditures, personnel data, and facilities, but do not provide an assessment of the quality or quantity of the outputs obtained.

Studies of the outputs of the research and development process are more difficult to perform because they require a subjective analysis performed by individuals who are experts in the relevant technical fields. The NSF staff includes professionals with expertise in a wide range of disciplines. These individuals provide the technical expertise needed to assemble panels of experts that can perform competent, unbiased, technical reviews of research and development activities.

Specific technologies, such as telecommunications, biotechnology, microelectro-mechanical systems, and advanced materials, are selected for study by government agencies that have an interest in obtaining the results of an assessment and are able to contribute to its funding. A typical assessment is sponsored by two to four agencies. In the first few years of the program, most of the studies focused on Japan, reflecting concern over Japan's growing economic prowess. Studies were largely defined by a few federal mission agencies that contributed most of the funding, such as the Department of Commerce, the Department of Defense, and the Department of Energy.

The early JTEC methodology involved assembling a team of U.S. experts (usually six people from universities, industry, and government), reviewing the extant literature, and writing a final report. Within a few years, the program began to evolve. First we added site visits. Panels traveled to Japan for a week and visited twenty to thirty industrial and research sites. Then, as interest in Japan increased, a larger number of agencies became involved as cosponsors of studies. Over the ten-year history of the program, fifteen separate branches in six agencies of the federal government (including NSF) have supported JTEC and WTEC studies.

Beginning in 1990, we began to broaden the geographic focus of the studies. As interest in the European Community (now the European Union) grew, we added Europe as an area of study. With the breakup of the former Soviet Union, we began organizing visits to previously restricted research sites opening up there. These most recent WTEC studies have focused on identifying opportunities for cooperation with researchers and institutes in Russia, the Ukraine, and Belarus, rather than on assessing them from a competitive viewpoint.

In the past several years, we also have begun to substantially expand our efforts to disseminate information. Attendance at JTEC/WTEC workshops (in which panels present preliminary findings) has increased, especially industry participation. Representatives of U.S. industry now routinely number 50 percent or more of the total attendance, with a broad cross section of government and academic representatives making up the remainder. JTEC and WTEC studies have also started to generate increased interest beyond the science and technology community, with more workshop participation by policy makers and better exposure in the general press (e.g., *Wall Street Journal*, *New York Times*). Publications by JTEC and WTEC panel members based on our studies have increased, as have the number of presentations by panelists at professional society meetings.

The JTEC/WTEC program will continue to evolve in response to changing conditions in the years to come. NSF recently has authorized new JTEC/WTEC initiatives aimed at the following objectives:

- Disseminating the results of JTEC/WTEC studies via the Internet. Fourteen of the most recent JTEC/WTEC final reports are now available on the World Wide Web (http://itri.loyola.edu) or via anonymous FTP (ftp.wtec.loyola.edu/pub/). Viewgraphs from several recent workshops are also on the Web server.
- Expanding opportunities for the larger science and technology community to help define and organize studies.
- Increasing industry sponsorship of JTEC and WTEC studies.

The latter two objectives are now being served under the recently inaugurated JTEC/WTEC Community-Initiated State-of-the-Art Reviews (CISAR) initiative. As of this writing, JTEC/WTEC has formed partnerships with university-industry teams, with partial funding from industry, to carry out three CISAR studies. These cover the Korean semiconductor industry, electronics final assembly technologies in Pacific Rim countries, and civil infrastructure technologies in Pacific Rim countries, respectively. Several other topics are under consideration. Further information on the CISAR initiative is available on the JTEC/WTEC WWW server (http://itri.loyola.edu /cisar.htm) or by contacting the JTEC/WTEC office.

In the end, all government-funded programs must answer the question, *How has the program benefited the nation?* A few of the benefits of the JTEC/WTEC program follow:

- JTEC studies have contributed significantly to U.S. benchmarking of the growing prowess of Japan's technological enterprise. Some have estimated that JTEC has been responsible for over half the major Japanese technology benchmarking studies conducted in the United States in the past decade. JTEC reports have also been widely cited in various competitiveness studies.
- These studies have provided important input to policy makers in federal mission agencies. JTEC and WTEC panel chairs have given special briefings to senior officials of the Department of Energy, to the National Aeronautics and Space Administration (NASA) Administrator, and even to the President's Science Advisor.
- Studies have been of keen interest to U.S. industry, providing managers with a sense of the competitive environment internationally. Members of the recently completed study on satellite communications have been involved in preliminary discussions concerning the establishment of two separate industry/university consortia aimed at correcting the technological imbalances identified by the panel in its report.
- Information from JTEC and WTEC studies also has been valuable to both U.S. and foreign researchers, suggesting a potential for new research topics and approaches, as well as opportunities for international cooperation. One JTEC panelist was recently told by his Japanese hosts that, as a result of his observations and suggestions, they have recently made significant new advances in their research.
- Not the least important is the educational benefit of the studies. Since 1983 over 200 scientists and engineers from all walks of life have participated as panelists in the studies. As a result of their experiences, many have changed their viewpoints on the significance and originality of foreign research. Some have also developed lasting relationships and ongoing exchanges of information with their foreign hosts as a result of their participation in these studies.

As we seek to refine the JTEC/WTEC program in the coming years, improving the methodology and enhancing the impact, program organizers and participants will continue to operate from the same basic premise that has been behind the program from its inception: the United States can benefit from a better understanding of cutting-edge research that is being conducted outside its borders. Improved awareness of international developments can significantly enhance the scope and effectiveness of international collaboration and thus benefit all of the United States' international partners in collaborative research and development efforts.

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The National Science Foundation (NSF) and the Department of Commerce commissioned a panel of U.S. experts to study and evaluate two Japanese basic research programs administered by the Research Development Corporation of Japan (JRDC): Exploratory Research for Advanced Technology (ERATO) was started in 1981, and Precursory Research for Embryonic Science and Technology (PRESTO) in 1991.

This study grew out of the U.S. technical community's need to better understand Japanese efforts in promulgating basic research, to see whether the execution of these programs provides any insights for the United States, and to identify opportunities for future U.S. participation or cooperation. This study follows a similar study performed by the Japanese Technology Evaluation Center in 1988.

The panel's principal conclusions are

- **The ERATO program has been quite successful as a catalyst for changing the Japanese system of supporting and performing research.** ERATO directly and indirectly spawned more than fourteen new research programs in Japan, affected the scientific infrastructure there, and started the expansion of overseas operations. Within JRDC alone, ERATO's success has spawned three complementary programs. One of these, Precursory Research for Embryonic Science and Technology (PRESTO), is discussed in this report. The second, the International Joint Research Projects (IJRP) initiative, is focused on improving international collaboration between Japanese and overseas researchers. The newest JRDC program, Core Research for Evolutional Science and Technology (CREST), was created after this JTEC panel's visit to Japan. The CREST program for the first time enables university researchers to build a research project and hire additional staff and contrasts sharply with the way Japanese university science typically has been funded in the past — small grants awarded to individual senior professors. In spite of severe economic problems in Japan, JRDC's budget has nearly doubled recently.

- **The research performed under ERATO is of high quality, with several projects leading to the development of world-class research, and at least in one case, a project created a scientific field.** Examples of the excellent research resulting from ERATO projects are too numerous to be listed here. Examples include the development of the high-vacuum and high-resolution electron microscope; the use of electron holography to image and measure magnetic flux, e.g., vortices in superconductors; the development of a dual laser interferometer with one nanometer resolution; the creation of the world-class Japan Marine Science Technology Center as a result of the Superbugs project; and a spin-off project involving transgenic swine.
- **The ERATO process has unique characteristics that can be applied in the United States, particularly to develop closer bonds between academic, national laboratory, and industrial researchers.** The unique characteristics of ERATO, not found in any U.S. programs, include single-source funding for joint industry, national laboratory, and university teams managed under one umbrella; five-year-long, unrenewable projects started from the very beginning; and the creation of real, life-long bonds among team members. All current U.S. research project grants go to institutions, whose main objective is to continue them and to expand. While such efforts have been and will continue to be the backbone of U.S. research programs, there might be value in experimenting with small ERATO-type programs. A possible ERATO-type effort in the United States might give the grant to a professional association — one perhaps similar to the Royal Society in the United Kingdom — which in turn could help manage the project for the duration of the funding. That way, researchers could be recruited from all sectors to work on the projects and then return to their institutions upon termination of the project. Donor organizations would need to have liberal unpaid leave policies to ensure top researchers would be available to work on such projects.
- **PRESTO is too new to be fully evaluated, but early indications suggest good results.** Its process and mode of funding are more like traditional U.S. procedures, although its objective is more focused and designed to help the researcher embark upon a new line of work.

DISCUSSION

ERATO's impact on the Japanese scientific infrastructure is quite extraordinary given its modest size of three to four new projects per year, each funded at a level of approximately $3 million (U.S.) per year. Fewer than a thousand researchers divided among forty-five projects have participated or are currently in the program. When it began in 1981, ERATO was quite controversial because its purpose was to try to break long-held traditions dealing with the support and performance of basic research in Japan. The program was designed to support unfettered basic research and to break the traditional hierarchical structure that exists in almost all sectors in Japan. Its sociological results have been quite amazing; ERATO achieved its goals. About 20% of the researchers are from abroad, and ERATO has moved off-shore, with some of the projects being set up in the United States and elsewhere.

For each ERATO project, the ERATO administrators choose an emerging researcher who is attractive to young scientists to be project director and ask him to organize an effort along some previously agreed upon line of basic research. He then organizes three research groups, not necessarily located in the same facility or even the same city. Projects begin from the beginning: the project director must find laboratory space and order equipment. He must also put together a team of researchers from industry, national laboratories, universities, and/or foreign organizations. They all must begin to work as a group in a totally new environment and structure. As participants, team members are expected to be loyal to ERATO, not to their parent organization, and get paid by ERATO.

Each project is managed according to the project director's wishes with some rules that apply across all projects. The rules are as follows:

- *Funding is fixed for each year, and the project director must manage within this annual budget.*
- *The project can run for only five years, with no exceptions. A project's administrative office continues for six months after the project to complete publications or other administrative chores, but that is all. In the almost fifteen-year history of ERATO, no exceptions have been made to continue a project.*
- *The management structure of each project is similar: a project director, a technical manager, an administrative manager, and often three group leaders. Everyone on the project, with the exception of the project director, works full-time on the project and is an ERATO employee.*
- *An entire research staff is recruited for each project, although on many occasions, the project director has brought a few researchers from his parent organization.*
- *Research projects are focused on high-risk/high-payoff, cross-disciplinary research topics which usually would not be supported within the Japanese university system.*
- *Projects are implemented by highly diverse groups comprised primarily of young researchers (around 30 years old) from Japanese industry, government, and academia, as well as from overseas.*
- *Once a project is initiated, the project director has almost complete freedom over such aspects as research direction, staffing, and distribution of funds. There is no pressure for results or evaluation, a feature unusual anywhere in the world.*
- *The selection of a project is a total reversal of the typical proposal review process. JRDC accepts neither proposals nor applications for projects. Armed with advice from select groups of public- and private-sector scientists, JRDC officials search for appropriate candidates whom they then invite to develop and lead a project.*

PRESTO is a relatively new program whose impact is still too new to be fully appreciated. It funds three-year projects, in much the same way that individual investigators are funded in the United States. Unlike ERATO, which does not have a formal application process, PRESTO is a formal, very competitive program to which researchers submit peer-reviewed research proposals. Fewer than 8% of the applicants receive funding. Sometimes PRESTO funds have been used to extend certain aspects of research developed under ERATO, but more often, the funds have been used to promote pioneering and embryonic research for the future. Many researchers use PRESTO as a stepping stone to their next positions.

BACKGROUND

The United States leads the world in basic research and has developed a science and technology infrastructure that is admired by other countries. Japan has been known for its strength in technology and more importantly for its ability to change ideas into viable commercial products. Japan has not been known for its basic research programs. In part, Japan's culture and organizational structure has inhibited scientists' freedom to think along nontraditional lines and to participate in groups of researchers from different organizations and backgrounds. Furthermore, young Japanese scientists are rarely in a position to make important decisions. ERATO was designed to try to break that mold and to help Japan compete in basic research.

The NSF commissioned a study to look at ERATO in 1988. While the 1988 study indicated the research was of high quality, the program itself was still too new to be appreciated fully, and its cultural impact had not yet been seen even in Japan. This present study, however, clearly demonstrates that ERATO has had a very positive impact on Japan, and its success has been felt even on the international scene. Although ERATO was designed to affect Japanese science, its success clearly has demonstrated that there are lessons to be learned even by the United States. No program like ERATO exists in the United States. The unique feature all the projects share is the formation of a team of researchers, drawn from industry, national laboratories, and universities, who work together, get paid by a single organization, and for five years have professional ties only to the funding organization.

To date, JRDC has sponsored forty-five ERATO projects. The projects fall into two general technical categories: biosciences and physical sciences. Twenty-one projects have been completed, some as early as 1986. The JTEC panel's strategy was to sample a number of projects from each scientific area, choosing from among the following categories as well: those completed some time ago, some that are nearly complete or are just being completed, and some that are in the process of being formed. The panel also chose a geographical range for its sample, visiting projects in Tokyo as well as outside the capital. In total the study team had contact with at least half of the forty-five projects and were able to obtain a very good picture of the ERATO program and its impact on the Japanese science community; on the interest of the Japanese industrial community; on government science and technology establishments; and on the international science community.

Designed to nurture young, innovative researchers, PRESTO provides funds and mentors for projects that would be considered risky in more traditional sectors of Japanese science.

Although the program is still too new to be evaluated, its potential impact on the Japanese university system for funding science could be enormous: PRESTO researchers have more of the time and resources needed to conduct innovative research than do university scientists operating in more traditional funding modes. Early indications are that the science in PRESTO projects has been impressive. However, there are also some signs that the PRESTO process and mode of funding, which are somewhat similar to U.S. procedures, also have the potential to create a cohort of post-PRESTO researchers who move from project to project without a clear career path to permanent employment.

The most conspicuous difference between ERATO and PRESTO is their structures. While an ERATO project is conducted under the general supervision of the project director in groups headed by a group leader usually at the same site, PRESTO researchers work alone, independently, at a place of their choice. The PRESTO process is similar to that found in the United States, although the application process is much simpler, and there appears to be much less oversight. Funding for an ERATO project is about ¥1.8 billion, or $17 million (U.S.) for five years, while PRESTO projects are funded at ¥30 million, or about $300,000 (U.S.) for a three-year period.

CHAPTER 1

INTRODUCTION

George Gamota

In 1988 a team of U.S. scientists commissioned by the National Science Foundation (NSF) went to Japan to study an unusual Japanese research program called ERATO (Exploratory Research for Advanced Technology), which had been in operation since the early 1980s but was just beginning to be noticed outside Japan. Although ERATO is funded by the Japanese government, the program's scientists are free to conduct their own research with little, if any, interference or oversight. Seven years after the first study, another panel of experts from the Japanese Technology Evaluation Center (JTEC), including some who served on the first panel, returned to Japan to reexamine ERATO and also to study a newer project, Precursory Research for Embryonic Science and Technology (PRESTO). The primary charge of the JTEC panel was to study the ERATO concept and process, especially its impact on science and researchers, rather than just to evaluate the details of the large number of technical projects that have been funded under ERATO. During this study, based on an intensive ten-day visit which began on September 1 and ended on September 10, 1995, the JTEC panel interviewed representatives of more than half the forty-five ERATO projects (past and current).

PURPOSE OF THE STUDY

In 1981 the Japanese government approved funding for a very unusual (in the Japanese context) basic research program designed to support unfettered basic research in Japan and to break the traditional hierarchical structure that exists in almost all sectors in Japan. Because of the program's bold objectives and its acceptance and continuing strong support within the Japanese government and science and technology community, the JTEC team wanted to achieve the following:

- increase U.S. understanding of this program
- provide insights useful for the U.S. technical community
- identify future opportunities for U.S. participation or cooperation

Specifically, the JTEC panel was looking at the overall ERATO program, not just at the technical results. In addition, many of the panel's questions, while originally directed at ERATO projects, applied to PRESTO projects as well. Some of the specific questions the panel addressed were as follows:

- What is the overall scientific quality of the program? Does this program foster high-risk, leading-edge research?
- Has the research achieved an international standing?
- Is the research important, i.e., published in peer-reviewed journals?
- Has the research stimulated new lines of research?
- How scientifically sophisticated are the research teams?
- How well does the program train young researchers?
- Does the program encourage independent thinking?
- What value can and does the program have for Japanese industry?
- How much of the research has been continued in other settings, primarily in industry or universities?
- What are the advantages and disadvantages of the ERATO process?
- Does this process foster the success of projects? If so, in what ways?
- Does the program attract top people as directors and research staff?

There was also a set of secondary questions, more related to broad sociological and cultural issues, that the panel wanted to answer. Some of these were the following:

- How successful has the program been in internationalizing Japanese science?
- How successful has the program been in changing cultural attitudes in Japan?
- Are these changes viewed as positive or negative by the "establishment" in Japan?
- What has happened to researchers as a result of being involved with ERATO projects?
- Can the program be scaled up in funding and in numbers without lowering the quality of the research?

STUDY TEAM

Most JTEC panels are asked to evaluate specific technologies, each panel being chosen according to the technical expertise needed to understand and evaluate certain areas. This study, however, needed a group that could cross disciplines and, in addition to being technical, understand research policies and detect subtle sociological and cultural changes. The JTEC team was composed of senior experts, a mix of scientists, engineers, and policy-makers.

The chairman of the panel is Dr. George Gamota, who has been involved with JTEC since its inception in 1983. A physicist and an expert on foreign and domestic research assessments, he has been tracking changes in Japanese science and technology policies for over two decades. Two panelists had served on the earlier ERATO study team in 1988: Drs. John Rowell and Rita Colwell. Rowell, a noted materials expert, is also a technical manager with industrial experience. Colwell, a well-known bioscientist, is President of the University of Maryland Biotechnology Institute. By revisiting ERATO after seven years, they were better able to assess the long-term effects of the program. They were also able to revisit some of the people they met on their earlier trip.[1]

Mr. Paul Herer is Senior Advisor for Planning and Technology Evaluation at NSF. Besides being a senior policy maker in the U.S. government, he brings a unique perspective to the panel. In 1989, he was a Science and Technology Agency (STA) fellow in Japan working at the Research Development Corporation of Japan (JRDC) when ERATO policies were still being formulated. He thus has seen policies being developed and can now observe their impact. Drs. Leo Young and William Bentley are new to ERATO, but each has been able to bring important perspectives. As a former director of defense research, Young brings important knowledge of science policy as well as expertise in electronics and the physical sciences. Bentley is a chemical engineer at the University of Maryland and an expert in biosciences research. The panel also included Drs. David Kahaner, Jay Lee, and Tamami Kusuda. The first two were living in Japan during the JTEC panel's visit, and were able to help not only during this trip but also in preparing information and following up after the visit. Kahaner, a well-known Japan watcher, is an expert on electronics and computers. He is currently director of the Asian Technology Information Program (ATIP). Lee, a mechanical engineer, was an STA fellow in Japan. Kusuda has often traveled to Japan and has been particularly interested in the PRESTO program, an offshoot of ERATO begun in 1991. He recently retired from a senior position at the Asia/Pacific Technology Program in the Department of Commerce, and is now serving as a consultant. In addition, Dr. Alan Engel helped us with planning this study and participated in the visit. Currently ERATO's Overseas Representative, he brought the perspective of a foreigner who has been involved in ERATO projects. Engel was one of

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[1] Dr. Rita Colwell was unable to make the trip with the rest of the panel due to a last-minute scheduling conflict, but she visited Japan several weeks later and was able to report on her findings. These are covered in Chapter 5.

the first foreign researchers to join ERATO and has since continued to consult for JRDC on ERATO matters.

CONDUCT OF STUDY

This JTEC study was formally initiated by a request in a letter from Paul Herer to Mr. Genya Chiba of the JRDC. Mr. Chiba is a Vice President of JRDC, and the person most responsible for developing ERATO and overseeing it over the past fifteen years. The letter sought permission to visit JRDC and to study the impact the ERATO program has had on the Japanese technical community. Chiba replied enthusiastically, and plans began to be made to form the panel and set up a schedule for the planned trip and associated meetings. The kick-off meeting occurred on July 17, 1995, in Washington. At this meeting the scope of the study was discussed, and a strategy was delineated for carrying it out. Unlike other JTEC studies, where a certain technical area has been covered, this study examined the effects of both the science and the program, covering a very wide swath of technical and sociological topics.

JRDC has sponsored forty-five ERATO projects since its inception. These projects fall into two general technical categories: biosciences and physical sciences**.** A complete list of current and past projects, including brief project descriptions, is included in Appendix B. Twenty-one projects have been completed, some as early as 1986, so the panel's strategy was to sample a number of projects from each scientific area, choosing from among the following categories as well: those completed some time ago, some that are nearly complete or are just being completed, and some that are in the process of being formed. This panel chose not to speak with anyone from the newest 1995-2000 group since they were in the very earliest stages. The panel also chose a geographical range for its sample, visiting projects in Tokyo as well as outside the capital, and one offshore in the United States.

Although the JTEC panel hoped to sample almost all the projects, it was able only to make contact with people associated with about half of them due to time limitations. Table 1.1 lists JRDC, ERATO, and PRESTO people that this panel interviewed, including information on their project affiliations. By choosing to sample a few projects from each category, the panel felt it could best examine the changes that are taking place within ERATO and within the Japanese scientific community, assess the effect ERATO has had on the scientific and technical fields, and try to follow the career paths of those involved. To accomplish all these tasks, we divided the panel into two teams, maintaining an interdisciplinary mix to make sure that each team covered all perspectives. To evaluate the biosciences projects, Bentley, Young, and on occasion Lee and Herer made on-site visits and interviewed researchers. Gamota, Rowell, and Kahaner evaluated the physical science projects**.**

Table 1.1
Persons Interviewed by the JTEC ERATO Panel

PERSON	POSITION AT TIME OF JTEC VISIT	ROLE IN ERATO or JRDC
(Tokyo)		
Naoya Ogata	Professor, Sophia University	Project Director, Ogata Project (former)
Eiichi Goto	Professor, Kanagawa University	Project Director, Goto Project (former)
Mitsuru Furusawa	Advisor, Daichi Pharmaceutical Co., Ltd.	Project Director, Furusawa Project (former)
Toyoki Kunitake	Professor, Kyushu University	Project Director, Kunitake Project (former)
Joh-E Ikeda	Professor, Tokai University	Project Director, Ikeda Project (former)
Nobuhiro Fusetani	Project Director, Fusetani Biofouling Project	
Daisuke Yamamoto	Project Director, Yamamoto Behavior Genes Project	
Shoichiro Yoshida	Executive Vice President, NIKON Corp.	Project Dir., Yoshida Project (former)
Kiyoshi Iizuka	Director, Tsukuba Research Laboratories, NIKON	Technical Manager, Yoshida Project (former)
Hiroyuki Sakaki	Codirector, IRJP Quantum Transition Project	Project Director, Sakaki Project (former)
Keiji Kawachi	Project Director, Kawachi Millibioflight Project	
Takeshi Ohnuki	Technical Manager, Kawachi Millibioflight Project	
Hiroto Okayama	Project Director, Okayama Cell Switching Project	
Seiji Shinkai	Project Director, Shinkai Chemirecognics Project	
Shinichi Aizawa	Associate Professor, Teikyo University	Researcher, Hotani Project (former)
Masaaki Oda	Vacuum Metallurgical Co., Ltd.	Researcher, Hayashi Project (former)
Noboru Kitamura	Professor, Hokkaido University	Researcher, Masuhara Project (former)
Kazutaka Terashima	Professor, Shonan Institute of Technology	Technical Manager, Kimura Project (former)
Quingzin Ru	Researcher, Takayanagi Particle Surface Project	
Nobuaki Kawamura	Professor, Yamanashi University	Researcher, Japan-UK Joint Research (former)
Hiroshi Harada	Head of Laboratory, National Research Institute for Metals	Researcher, Japan-UK Joint Research (former)
Koji Izunome	Toshiba Ceramics	Technical Manager, Kimura Project (former)
Akira Taomoto	Technical Manager, Yoshimura p-Electron Materials Project	
Satoshi Ebina	Technical Manager, Nagayama Protein Arrays Project	
Misako Takezawa	Technical Manager, Torii Nutrient-Stasis Project	
Gerhard Fasol	Researcher, PRESTO	
Michiyuki Matsuda	Researcher, PRESTO	
Masaaki Fujii	Researcher, PRESTO	
Yasunori Inoue	Researcher, PRESTO	
Shuji Hasegawa	Researcher, PRESTO	
Shigeru Suetomo	Researcher, Arakawa Chemical Industries	Sent researcher to Shinkai Project
Yasutsugu Kida	Director, Tokuyama Tsukuba Research Labs	Sent researcher to Shinkai Project
Haruhiko Umeda	Chairman, Komatsu Electronic Metals	Sent researcher to Kimura Project
Kenji Shinoyama	Nippon Steel, Advanced Technology Research Lab.	Sent researcher to Kimura Project

PERSON	POSITION AT TIME OF JTEC VISIT	ROLE IN ERATO or JRDC
Takuo Takeshita	General Manager, Mitsubishi Materials Materials Technology Lab	Sent researcher to Kimura Project
Masuo Sugie	Vice President, Toshiba Ceramics	Sent researcher to Kimura Project
Makoto Fujimoto	Sumitomo Sitix Silicon Process Technology Center	Sent researcher to Kimura Project
(Tsukuba)		
Shigeyuki Kimura	Project Director, Kimura Metamelt Project	
Robert Lewis	Managing Director, Tsukuba Research Consortium	Researcher, Kuroda Project (former)
Hideki Toyotama	Director, Stanley Electric, Tsukuba Research Lab	Researcher, Hayashi Project (former)
Souji Komiya	Vice President, Tsukuba Research Consortium	Rents labs to ERATO & PRESTO
Yoshinobu Mitsuhashi	General Manager, Nippon Sheet Glass	Sent researcher to Hirao Project
Ken Koizumi	Advisor, Nippon Sheet Glass	Sent researcher to Hirao Project
Masaru Goto	Advisor, Nippon Sheet Glass	Sent researcher to Hirao Project
Sumio Iijima	Research Fellow, NEC	Researcher, Hayashi Project (former)
Eichi Osawa	Air Liquide Laboratories	Researcher, Hayashi Project (former)
Hitoshi Nejo	National Research Institute for Metals	Researcher, Aono Project (former)
Hiroshi Miyamoto	National Institute for Bioscience and Human Technology	Researcher, Hayashi Project (former)
Kyo Wakasa	National Agriculture Research Center	Technical Manager, Ikeda Project (former)
Takatoshi Seto	Researcher, PRESTO	
Seishi Kudo	Yaskawa Electric	Researcher, PRESTO (former)
Chikako Noro	Researcher, PRESTO	
Koichi Koyama	Researcher, PRESTO	
Akitoshi Ishizaka	Tokyo University	Researcher, PRESTO (former)
Takashi Hiraga	Electrotechnical Laboratory	Researcher, PRESTO (former)
Masahiro Tosa	National Research Institute for Metals	Researcher, PRESTO (former)
(Kanagawa)		
Yoshihiro Takiguchi	Technical Manager, Yamamoto Quantum Fluctuation Project	
Huang De-Huan	Researcher, Yamamoto Quantum Fluctuation Project	
Toya Hiroshima	Researcher, Yamamoto Quantum Fluctuation Project	
Yoshiharu Horigoe	NTT Materials Properties Research Section	Sent researcher to Yamamoto Project
Masaaki Kawase	NTT Research Planning	Sent researcher to Yamamoto Project
Takaaki Mukai	NTT Materials Properties Research Section	Sent researcher to Yamamoto Project
Masato Miyoshi	NTT R&D Advancement Dept.	Sent researcher to Yamamoto Project
(Saitama)		
Masakazu Aono	Institute for Physical and Chemical Research (RIKEN)	Project Director, Aono Project (former)
Akira Tonomura	Research Director, Hitachi Advanced Research Laboratories	Project Director, Tonomura Project (former)
Katsumi Miyauchi	Vice Director, Hitachi Advanced Research Laboratories	Site of Tonomura Project (former)
Yasuo Wada	Researcher, Hitachi Advanced Research Laboratories	Technical Manager, Goto Project (former)
Junji Endo	Researcher, Hitachi Advanced Research Laboratories	Technical Manager, Tonomura Project (former)

PERSON	POSITION AT TIME OF JTEC VISIT	ROLE IN ERATO or JRDC
Toshiaki Kudo	Researcher, RIKEN	Researcher, Japan-U.S. IJRP
Katsuhiro Omiya	Researcher, RIKEN	Researcher, PRESTO (former)
Jun Otomi	Researcher, PRESTO	
(Osaka, Kyoto)		
Osamu Hayaishi	Director, Osaka Bioscience Institute	Project Director, Hayaishi Project (former)
Yasuyoshi Watanabe	Codirector, IJRP Subfemtomole Project	
Toshio Yanagida	Project Director, Yanagida Biomotron Project	
Yoshiharu Ishii	Technical Manager, Yanagida Biomotron Project	
Hirokazu Hotani	Professor, Nagoya University	Project Director, Hotani Project (former)
Takeji Hashimoto	Project Director, Hashimoto Polymer Phasing Project	
Kentaro Hiraga	Technical Manager, Okayama Cell Switching Project	
Tomoko Ishihara	Researcher, Okayama Cell Switching Project	
Fumio Osawa	Mentor, PRESTO, Cell and Information Project	
Keiichi Namba	Research Director, Matsushita Electric International Institute for Advanced Research	Researcher, Hotani Project (former)
Noriko Oda	Researcher, Matsushita Electric International Institute for Advanced Research	Researcher, Hayaishi Project (former)
Ichiro Yamashita	Researcher, Matsushita Electric International Institute for Advanced Research	Researcher, Hotani Project (former)
Nobunori Kamiike	Osaka Industrial Research Institute	Researcher, PRESTO (former)
(JRDC Headquarters)		
Hiromichi Matsudaira	President, JRDC	
Masahiro Kawasaki	Senior Vice President, JRDC	
Genya Chiba	Vice President, JRDC	
Noboru Fujikawa	Director, ERATO	
Yukihiro Sugaya	Manager, ERATO General Activities	
Tomonori Sato	Manager, ERATO Research Activities	
(ERATO Overseas Representative)		
Alan Engel	International Science & Technology Associates, Inc. ERATO Overseas Representative	Researcher, Ogata Project (former)

Source: A. Engel, JRDC

To help manage the logistics of covering such a large number of projects and people who are geographically dispersed throughout Japan, the panel was fortunate to have had assistance and support from the JRDC and ERATO project offices. Without their help, this effort would have taken far more time, and the sample would have been far less representative than it was. For ongoing projects, the panel visited the laboratories; for completed projects, it interviewed past directors or researchers and representatives from a sample of Japanese companies who had had direct contact with the projects; and for projects nearing completion, it was fortunate to have its visit coincide with final symposia being held for the Shinkai Chemirecognics and the Kimura Metamelt projects.

Most of the panel members also had an opportunity to visit some of the PRESTO researchers briefly; Dr. Kusuda spent a whole week visiting these researchers and their laboratories.

1988 ERATO/JTECH[2] STUDY

Soon after the first group of ERATO projects was completed, the NSF commissioned the first ERATO study (JTECH 1988), co-chaired by Dr. William Brinkman from AT&T Bell Laboratories and Dr. Dale Oxender. Their team included Colwell and Rowell, who are also members of the present study. Additional members included Drs. Joseph Demuth, Richard Skalak, and Edward Wolf. Since there were then far fewer projects and since only a few had been completed, the 1988 panel was able to assess the quality of the research but could not evaluate the program's sociological or political impact.

The 1988 panel rated the scientific quality of the overall program as high, but found considerable variation from project to project. The panel cited two examples of ERATO successes: one where the work achieved international recognition for the group, and another where the work enhanced an existing but strong program that had been only marginally funded before. The panel also mentioned at least a couple of political successes: (1) the program had been renewed for seven continuous years, and (2) other institutions were copying the ERATO model.

Finally, the panel noted that ERATO was a small program, and members were somewhat skeptical about its eventual payoff since ERATO could not be compared to much more visible projects like the Very Large Scale Integration (VLSI) project, for example.

In contrast, the 1995 panel found ERATO research to be of very high quality and disagreed with the earlier panel on ERATO's impact. This panel believes that ERATO has had a major impact on Japan, even more significant than some of Japan's bigger projects, since it has been able to change the culture. By 1995, ERATO had become a very well-known program in Japan and had gained international recognition and respect. Its biggest former skeptics are now supporters of the concept: the Ministry of International Trade and Industry (MITI), the Ministry of Education, Science, and Culture (Monbusho), and other Japanese ministries are implementing similar programs, and the government is nearly doubling JRDC's basic research funding for 1996.

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[2] Until 1989, the Japanese Technology Evaluation Program was managed by Science Applications International Corporation (SAIC), and it was referred to as JTECH.

ERATO AND PRESTO OVERVIEW

The ERATO research program is funded by the Japanese government. It is administered by one of the government-run public companies, JRDC, which under the STA, reports directly to the prime minister's office. There appear to be no similar programs in the United States. Each year the program selects four directors to run projects of their own choosing for five years with an annual budget of about ¥370 million (U.S. $3.6 million). Each director, with the help of the ERATO project office, organizes his effort from the beginning, namely, finding space to lease, recruiting staff and ordering equipment. Usually projects have been located near a university, company, or government laboratory. The ERATO process has changed very little from its inception, and its objectives today are the same as they were in 1981.

Typically, a project director, who works only part time on an ERATO project, organizes three groups, not necessarily located in same facility or even the same city. Each group then is headed by a group leader. While each project is managed according to the project director's wishes, common rules apply across all projects:

- *Funding is fixed for each year, and the project director must manage within this budget.*
- *The project can run for only five years, with no exceptions. A project's administrative office continues for six months after the project to get things in order, but that is all. In the almost fifteen-year history of ERATO, no exceptions have been made to continue a project. Projects occasionally have been continued by the project director when he has returned to his organization full time, but in most cases research has continued at a reduced funding level and scale and has been funded by the company itself.*
- *The management structure of each project is common to all: a project director, a technical manager, an administrative manager, and often three group leaders. Everyone on the project, with the exception of the project director, works full time on the project and is an ERATO employee.*
- *The entire research staff is recruited for each project, although on many occasions, the project director might bring a few researchers from his parent organization. This is particularly true if the project director comes from a company.*

ERATO PROGRAM OBJECTIVES

ERATO was created by the Japanese government "for the purpose of fostering the creation of advanced technologies while stimulating future interdisciplinary scientific activities and searching for better systems to carry out basic research" (JRDC 1995). This objective, first written in 1981, still applies today. Within this stated objective, however, there are many other goals, some of which are unique to Japan, although others could be applied to the United States as well. Before ERATO, real interdisciplinary teams, particularly those cutting across age, company, government, organization, and disciplinary barriers, were nearly impossible to form within Japanese society.

ERATO was created in part to help remove such barriers, to show the rest of the country that there is value to working together and that creative young people, in particular, work best when given the freedom to pursue their own interests. ERATO was also designed to help recruit foreign researchers to come to Japan and work on projects. While today almost everyone in Japan believes that ERATO has been a great success, in 1981 it was a bold gamble to "sell" this idea to a very conservative government and technical community.

PRESTO, a relatively new program, was begun in 1991. It funds three-year research projects, somewhat similar to the U.S. program for funding individual investigators. Unlike ERATO, which does not have a formal open competition, PRESTO is a formally competitive program where researchers submit peer-reviewed research proposals. Less than 8% of the applicants receive funding (see Table 7.1, p. 64). Sometimes PRESTO funds have been used to extend certain aspects of research developed under ERATO, but they have more often been used to fund preliminary research that later could lead to an ERATO project.

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CHAPTER 2

JAPANESE SCIENCE

George Gamota
David K. Kahaner

OVERVIEW OF JAPANESE SCIENCE

This report makes no attempt to duplicate the many surveys of Japanese science. A partial list of these may be found in *Science* (Kinoshita 1994, 266: 1169-90). This summary is brief, designed only to orient readers and to place the Exploratory Research for Advanced Technology (ERATO) and Precursory Research for Embryonic Science and Technology (PRESTO) programs in the context of overall science policy in Japan. In addition, see Gamota and Frieman (1988), Shelton (1994), and Holdridge (1994) for reviews of this topic.

Japanese government science policy (and funding) is primarily determined by government ministries. Several of the key organizations are listed below, ranked by decreasing size of budget:

- Ministry of Education, Science and Culture (Monbusho), ¥1,100 billion
- Science and Technology Agency (STA), ¥605 billion
- Ministry of International Trade and Industry (MITI), ¥283 billion
- Japan Defense Agency (JDA), ¥140 billion
- Ministry of Posts and Telecommunications (MPT), ¥35 billion.

The STA is part of the prime minister's office and functions as the coordinating and overall policy-making organization for government funding of science in Japan, with two major exceptions: industrial research and development is funded by MITI, and research and development in universities is handled and funded by Monbusho.[1] The STA also controls Japan's "big" science projects, e.g., its space and nuclear programs. The STA, like a ministry, runs laboratories including the National Aerospace Lab, the National Research Lab for Metals, and several others. The STA has also created several public corporations funded by the Japanese government. The four most notable examples are the Japan Atomic Energy Research Institute, the Institute of Physical and Chemical Research, the Japan Information Center of Science and Technology, and the Research Development Corporation of Japan (JRDC).[2] Figure 2.1 is an organization chart showing STA's role in the context of the overall government R&D funding structure.

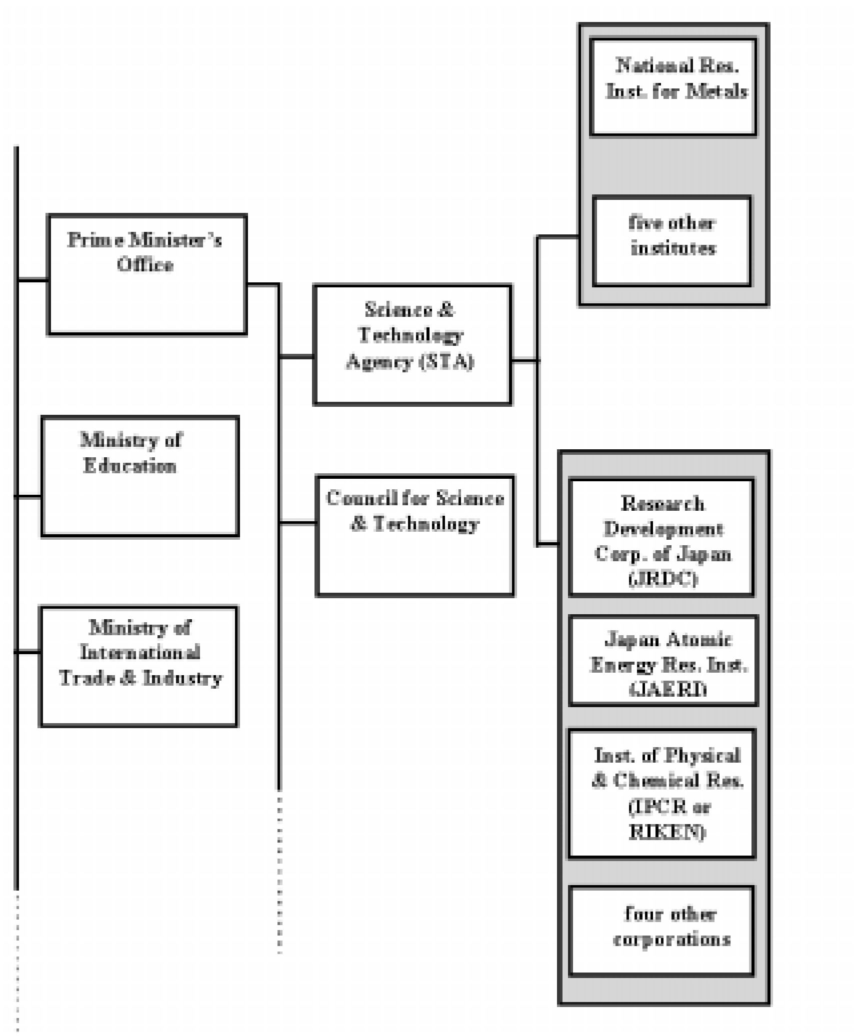

Fig. 2.1. Administrative structure of science and technology in Japan (JRDC 1995, 2).

[1] Since the JTEC panel's visit, the policy has been modified in a major new program called "CREST," funded by STA, which is now available for support of professors conducting university research. MITI has also begun to fund some academic research in targeted project areas.

[2] JRDC and the Japan Information Center for Science and Technology (JICST) will merge in October 1996 to become the Japan Science and Technology Corporation (JST).

In budgetary terms, Monbusho administers about half the Japanese government's science and technology budget, mostly because of its responsibilities for funding many universities, including all the associated costs of teaching, research, and infrastructure. The STA with its smaller budget, however, has had the greatest impact on basic research in Japan by implementing new and often innovative programs such as ERATO. MITI’s impact, of course, must be viewed not by its small budget, but by its enormous impact on industrial research and development and on technology. Its role in stimulating new technologies, commercializing the resultant products, and spawning new industries is also well documented. See, for example, previous JTEC studies by Brandin (1984), Elkus (1991), and Tannas and Glenn (1992).

Japanese government policy, at least since the mid-1940s, has been focused as follows (Kawasaki 1994):

1945-1955: Development of industrial structure after war-related destruction

1956-1969: Integration of science and technology policy with economic growth, based on the theory that investment invites further investment

1970-1980: Shift from economic growth to social welfare

1980s: Globalization of science and technology

1990s: Increase of world knowledge base by increasing support for basic research

Since the early 1990s, Japanese policy has placed a much higher emphasis on the growth of basic research and on Japan's role and obligation to increase the world's stock of knowledge. Although programs and policies have been moving in this direction for many years, especially through university research funded by Monbusho, the desire and ability to contribute is currently at the highest level ever seen. For example, one specific priority listed in a March 1992 major cabinet decision was to double government funding for research and development "as soon as possible." More recently, *Science* magazine (1995, 1207) has reported that the Japanese government has told its ministries to set aside an additional ¥140 billion to support research and infrastructure. The increase was designed to be a response to cuts made in the private sector that are due to economic problems. This new policy has been very sorely needed in Japan as government research funding for the country's universities and national laboratories had stagnated through the 1980s. As Japan has begun to pull out of the economic recession of the early 1990s, additional government funding increments for science and technology have been announced, including a new JRDC program for funding large, long-term research projects that is slated to grow to an annual budget of $500 million per year (*Science* 1996, 272:645).

The government's role in pushing basic science comes at the same time that there is a reduction in all but highly focused research within most Japanese corporations, even large well-known ones. Research and development expenditures by all major Japanese industry sectors have been at best flat and have been decreasing regularly since the early 1990s (NSF 1995).

It should be noted, however, that while Japan's ratio of research and development to domestic gross product is the highest in the world, its ratio of government funded research and development is lowest in the developed countries (Hayashida 1996).

Westerners frequently characterize the best Japanese science and technology as occurring primarily in industrial laboratories, rather than in the universities or public institutes. This has certainly been the observation of many past JTEC panels. However, the two trends mentioned above are changing the situation rapidly. The following trends are also affecting Japanese science at a time when it is only now beginning to make itself known:

- reduced industrial funding for research and development
- much stronger government funding and innovative programs for basic research in industry, universities, and national laboratories
- improvements in the public infrastructure such as computers and lab equipment needed to support this
- integration of international scientists into Japanese research programs

It should be noted that the shift from industry- to government-funded research in industrial laboratories is changing research from very applied and directed to more basic and unfettered projects. The long-term effect of this shift remains unclear.

In the meantime, the basic research community in Japan is enjoying a resurgence of government interest. The 1996 fiscal year, which began on April 1, gives a 7% boost to research and development (*Science* 1996, 271:22). Some selected programs that will benefit are listed in Table 2.1 below. The postdoctoral program is particularly timely since a growing number of such researchers will now find support to continue their work. However, as we have found in the United States, those postdoctoral positions will eventually have to become "real" jobs in industry or academia. If they do not, a class of perpetual postdoctors will continue to hunt for nonexistent jobs.

Table 2.1
Selected Programs with Major Increases for 1996

Program	**(Ministry)**	**Funding (U.S.--in millions)**	**Change from 1995**
Centers of Excellence	(Monbusho)	114	+24%
Grants-in-Aid for Research	(Monbusho)	1,018	+10%
Postdoctoral positions	(Monbusho & STA)	905	+42%
Computer research networks	(STA)	121	+57%
Earthquake-related research	(STA)	134	+96%
Oceanographic research	(STA)	199	+19%

JRDC

One of the major administrative arms of the STA is the Research Development Corporation of Japan (JRDC). JRDC implements STA policies by performing three major support functions: support for basic research, technology transfer, and international research cooperation (JRDC 1996).

JRDC was founded in 1961 and had a fiscal year (FY) 1995 budget of ¥22.8 billion (approximately $230 million) and about 100 employees. JRDC's total budget has risen dramatically — to ¥38 billion for FY 1996 (year ending March 31, 1997). This increase may be due in part to the announcement of the new CREST program (see Executive Summary) and may also have something to do with a planned merger with the Japan Information Center of Science and Technology (JICST), which maintains a database on science and technology as well as providing network and Internet services to academic institutions in Japan. The proposed merger will result in a larger organization with a new name, the Japan Science and Technology Corporation (JST) and will take place by October 1996. Currently, JRDC has an attractive World Wide Web (WWW) homepage (URL= http://www.jrdc.go.jp).

JRDC's FY 1995 budget allocations are shown in Table 2.2 below:

Table 2.2
JRDC's 1995 Budget Allocations

JRDC Activity	Budget
Support for basic research	¥11 billion
Technology transfer activities	¥5.8 billion
Research cooperation programs	¥4.6 billion
Other activities	¥1.5 billion

Basic Research Programs

The basic research programs that JRDC runs are ERATO (¥8.7 billion, FY 1995), PRESTO (¥2.3 billion), and the International Joint Research Projects (IJRP) (¥1.6 billion). It is not clear yet whether the CREST program will fall under the "basic research" category in JRDC's budget, which alone will account for ¥24.3 billion in FY 1996. Information available at the time of this publication indicates that both ERATO and IJRP will experience small budget decreases for FY 1996 (to ¥7.83 billion and ¥1.45 billion, respectively).

ERATO was established in 1981 and is the oldest of JRDC's research programs. As discussed in Chapter 1, it was a remarkable program then and remains so today. Aside from the previous JTECH study (Brinkman and Oxender 1988), ERATO has been written about extensively (e.g., *Science* 1994, 266:1169-90 and 1996, 272:645; and also Kusunoki

1993). The program was motivated by the perceived need to develop new models for research and development, rather than merely add money to existing programs. ERATO has allowed Japanese researchers to break out of a highly structured system that makes it difficult, organizationally and financially, for young scientists to embark on their own projects. ERATO has been in a sense more a social than a technical experiment in a country that prides itself on structure, conformity, and unquestioned respect for elders.

IJRP was established in 1989. It is an international version of ERATO (not to be confused with ERATO projects that have project groups off-shore). IJRP sets up cooperative basic research projects between JRDC and foreign research organizations based on the principle of equal sharing of costs and facilities. Several such projects exist in the United States, for example, the Microbial Evolution project at Michigan State University and the Quantum Transition project at the University of California, Santa Barbara. IJRP funding like ERATO's is for five years, and the total cost per project is ¥2 billion (¥1 billion from JRDC and the other billion from the foreign partner). Costs for U.S. partners to date have been funded by the National Science Foundation (NSF). Researchers travel freely between the two sites (one in Japan and one in the host country), and all results are open to the public. Patents are co-owned, an issue that sometimes causes problems in negotiating agreements with U.S. universities.

PRESTO, a more recent JRDC program, was started in 1991. It provides individual investigators with opportunities to conduct precursory research which cannot be easily carried out within conventional organizations. The newest program, Core Research for Evolutional Science and Technology (CREST), was created in 1996. CREST for the first time enables university researchers to build a research project and hire the additional staff to carry it out.

Technology Transfer Programs

JRDC began its technology transfer program soon after its establishment in 1961. Its mission is to take research results developed from various research programs (e.g., ERATO, PRESTO, national laboratories, and universities) to industry. Three processes are available for this transfer: cooperative technology development, technology transfer facilitation, and exploitation and application study.

Cooperative technology development and technology transfer facilitation have been JRDC activities since 1961. Through cooperative technology development, JRDC promotes research results that are commercially promising but are too high-risk for industry to develop on its own. JRDC reduces the risk by providing interest-free funding which is repaid only if the project becomes successful commercially. If a company can bear the costs of developing the technology, then through the Technology Transfer Program, JRDC acts as a transfer facilitator between the researcher and the company. JRDC also sometimes forms high-tech consortia.

In 1986, JRDC established the Exploitation and Application Study program to help develop results from ERATO, national laboratories, and universities. However, because ERATO is a basic research program, few results have been picked up by industry. Overall, JRDC earned only ¥19 million in direct royalties from ERATO results between 1986 and 1995.

JRDC receives royalties from many of its other investments. Industry has to date paid JRDC ¥574 million from the Cooperative Technology Development program and ¥118 million from other programs. In turn JRDC has paid researchers (inventors) ¥150 million from cooperative technology development and ¥106 million from other programs. Figure 2.2 shows a typical yearly flow chart of activities carried out by the JRDC Technology Transfer Office.

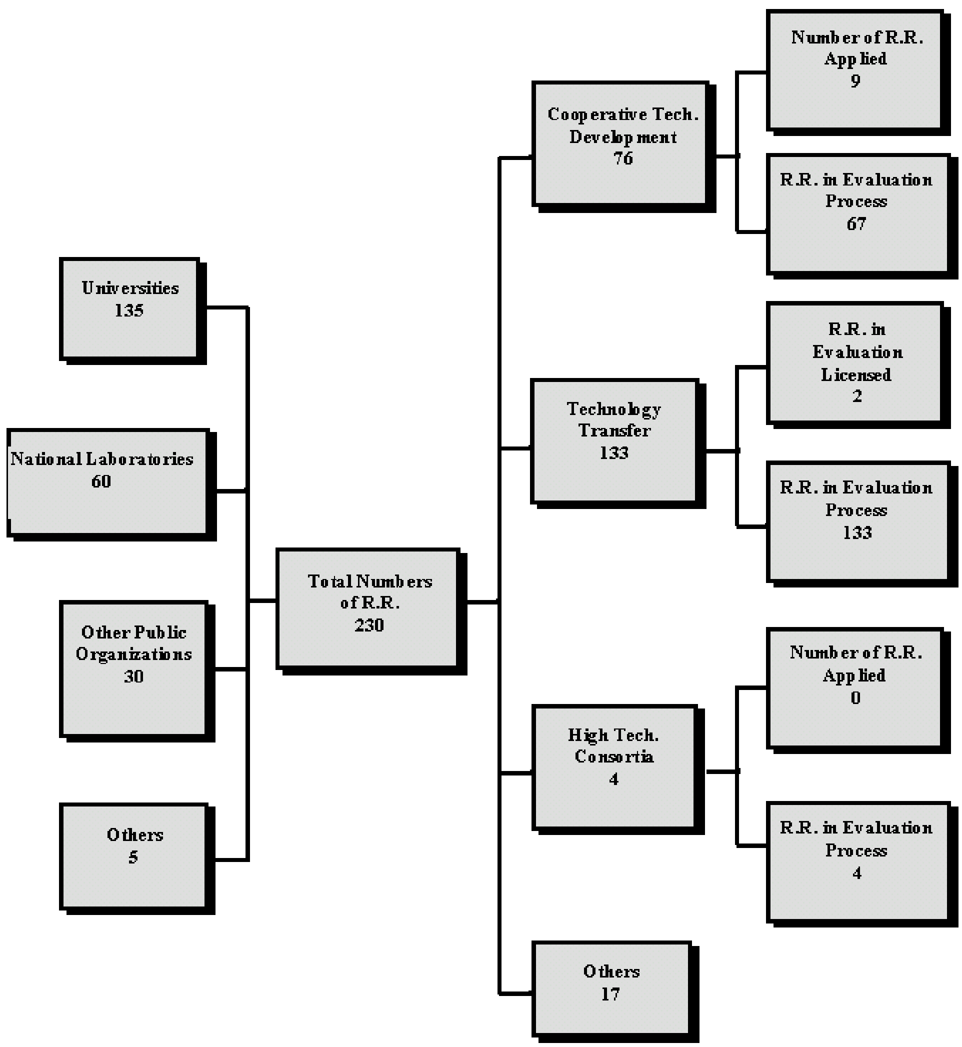

Fig. 2.2. Flowchart of research results (patents) — April 1994 - March 1995 (JRDC).

Research Cooperation Programs

JRDC's research cooperation programs began in 1989 with the introduction of STA fellowships. These provide opportunities for foreign researchers to conduct research at Japan's national laboratories and other organizations. In 1994 there were 235 foreign fellows in Japan. JRDC provides housing and living information for all successful applicants to make it easier for them to come to Japan. One of the panel members, Dr. Jay Lee, has just returned from a six-month STA fellowship and was living in Japan with his family during the time of the JTEC panel visit. Mr. Paul Herer was a fellow in 1989 and also stayed for six months. He worked at JRDC headquarters.

JRDC also has a program to send Japanese researchers to foreign countries. However, this program, the Research Cooperation Promotion program, is much smaller. Only twenty researchers have been sent abroad. Australia has received the largest number — eight. In 1993 JRDC started other programs — postdoctoral fellowships, regional joint research, and researchers' fora — to promote interdisciplinary research efforts. These small grant programs aim at exploring research fields not covered by other, more established programs. In 1994 JRDC started yet another program called Preresearch for New Fields to consolidate this effort further.

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CHAPTER 3

ERATO PROGRAM ANALYSIS

Paul J. Herer

OVERVIEW

Established in 1981, the Exploratory Research for Advanced Technology (ERATO) program was one of several initiatives undertaken to counter criticism both at home and abroad that Japan was not contributing enough to the world's store of basic knowledge. ERATO's stated purpose is to foster "the creation of advanced technologies while stimulating future interdisciplinary scientific activities and searching for better systems by which to carry out basic research" (ERATO 1995a, 1). In many ways, ERATO is intended as a great social experiment which seeks to chart new ways of doing basic research and to breathe change into the rigid, bureaucratic structures which characterize many of Japan's formal research systems. Compared to many research systems worldwide, the ERATO model can be considered quite radical. Let's look at some of its most distinguishing features:

- Research projects are focused on high-risk/high-payoff, cross-disciplinary research topics which usually would not be supported within the university system. And since the research topics provide only starting points without goal-oriented restrictions, a broad spectra of disciplines can participate in any project.
- Projects are implemented by highly diverse groups comprised primarily of young researchers (around 25-35 years old) from Japanese industry, government, and academia, as well as from overseas. Unlike those in university and government laboratories, ERATO researchers work within a performance-based system in which there is a high degree of job mobility.
- There are no permanent research facilities and, without exception, every project is concluded and dispersed within five years. Compared to university research, ERATO

projects are generously funded, with each project receiving about –1.8 billion ($17 million) over the five-year project life.

- Once the project is initiated, the project director has almost complete freedom over such aspects as research direction, staffing, and distribution of funds. There is minimal pressure from the sponsors for research results or evaluation, unusual anywhere in the world.
- Selection of projects is a total reversal of the typical proposal review process. The Research Development Corporation of Japan (JRDC) does not accept proposals or applications for projects. Armed with advice from select groups of public- and private-sector scientists, JRDC officials basically hunt down appropriate candidates whom they then invite to develop and lead research projects.

Perhaps the spirit of ERATO is best expressed by Genya Chiba, one of its founders and longtime director of the program. He sees basic research as an art form, perhaps most like the theater. Within the ERATO program JRDC acts as a *producer* in selecting innovative, scientifically-versed, key individuals — *directors* — each with an assortment of open-ended themes. These "motifs" are explored by heterogeneous teams of talented young sci-tech *performers*. The concept is that of an "individual-centered" research structure, where a highly capable project director is called upon to nurture and bring out the creative talents of these young researchers.

PROJECT MANAGEMENT

In Figure 3.1 we see the basic management structure of an ERATO project. Each project involves between fifteen and twenty researchers. Participants are further divided into an average of three groups, composed of five or six researchers each, with one person in each group designated the group leader. There is also a "project office" composed of a research manager and an administrative manager, who help with many of the day-to-day details of managing the project, including ordering the equipment, managing the finances, doing the paperwork, and interfacing with ERATO headquarters. Including supporting staff, most projects involve about twenty-five persons.

The 1995 JTEC panelists found surprisingly little variation in this basic structure in the projects they visited. However, within this structure, there was unusual variability in project management styles, team composition and skill mix, and budget utilization. In some projects, especially those with higher numbers of doctoral researchers and loosely defined project themes, the researchers work almost independently of one another. In such cases, group leaders were more experienced researchers who functioned chiefly as coaches or facilitators. In other projects, especially where there were many inexperienced researchers, the JTEC panel found more structure and hierarchy and consequently, more control of the project by the director and group leaders. No matter what the management style, once their projects were defined, ERATO researchers were given sufficient freedom to explore interesting avenues of research within their chosen areas.

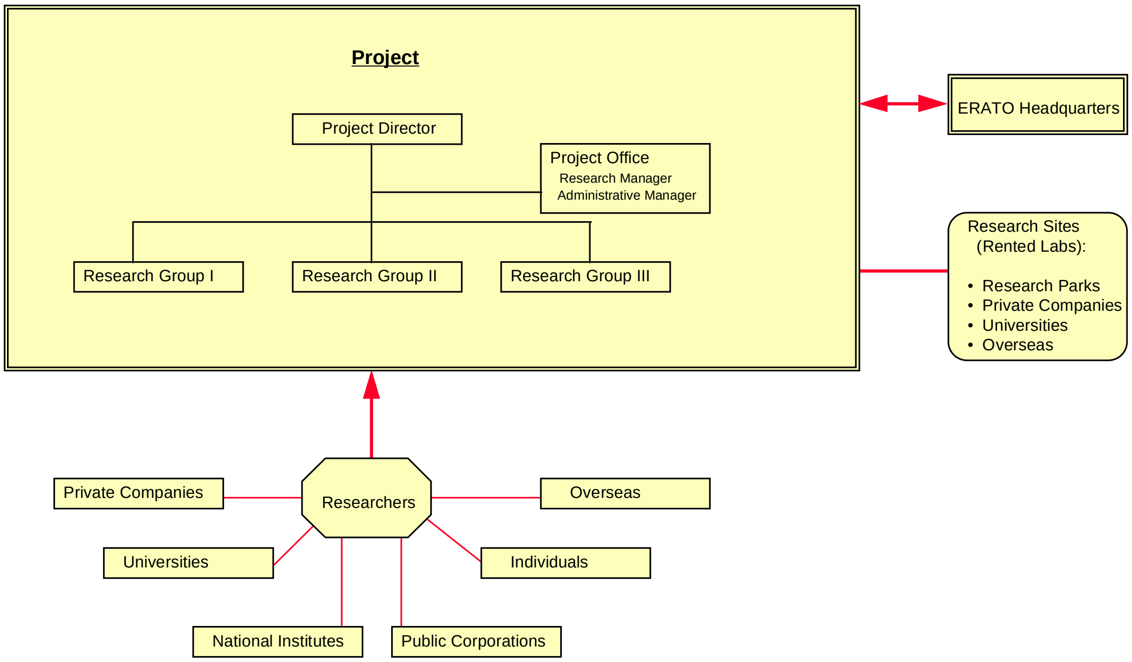

Fig. 3.1. ERATO organizational chart.

Most likely, such variability exists because of the extremely broad discretionary power vested in the project director. Within the basic ERATO framework, the director has almost complete freedom to determine the scope, staffing, and management of the project. In fact, the director must fulfill just three obligations: to conduct the research within budget, to present progress reports at annual conferences, and to submit a final report after the project is completed.

With some variation, the project director usually hires all the researchers and negotiates salaries and terms of employment (within the limits set by JRDC). However, he usually plays a minimal role in the day-to-day execution of the project. Per agreement with his home university or company, he is usually limited to 20% time on the project, or about one day per week. However, he typically spends considerably more time than this just thinking about and planning the project.

The ERATO system is designed to enhance individual-oriented research activities as well as organizational flexibility and fluidity. For example, a particular research theme is assigned to each researcher in accordance with his or her own research interests. In each project, allocation of research funds is the responsibility of the project director or group leaders.

However, researchers also work together as a team and usually meet at least once a week to discuss their work. There is some evidence that group peer pressure is significant. In some cases, researchers from Western countries have encountered problems in coping with the Japanese group dynamics. For example, several researchers (from different projects) encountered significant "conflict" because they failed to obtain the consensus of their group before starting new lines of research. In other instances, foreign researchers encountered some resistance in the group to openly discussing and criticizing each other's research ideas and findings.

PROJECT LIFE CYCLE

Figure 3.2 illustrates the life cycle of a typical project. As previously mentioned, a unique feature of ERATO is that all projects are time-limited and are automatically finished and dispersed without exception after five years. This policy prevents funded projects from becoming "entrenched bureaucracies," so common to other Japanese research programs. It also fosters considerable personnel mobility and invigorates the system by creating the resources to start three or four new projects every year.

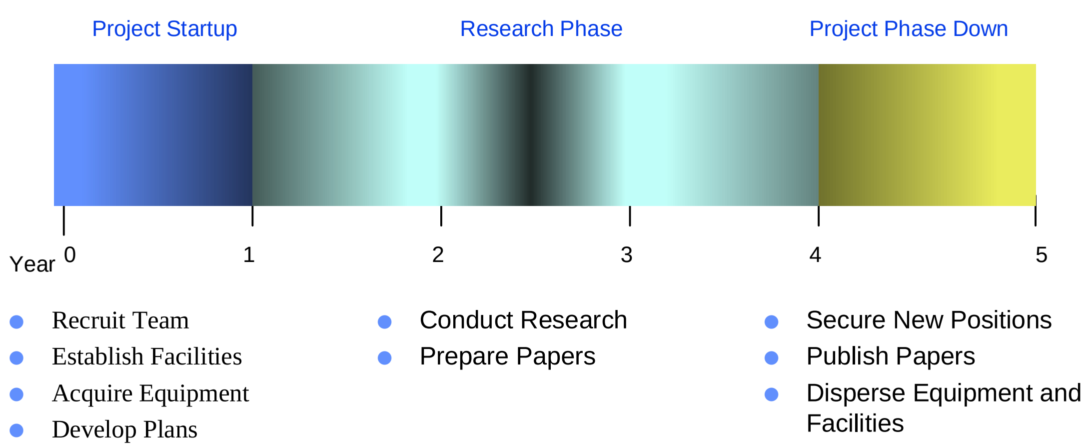

Fig. 3.2. Life cycle of an ERATO project.

However, the fixed project lifetime sometimes results in research and personnel discontinuities. For example, up to a year may be needed to obtain the equipment, facilities, and personnel to actually begin the research project. The typical method of obtaining equipment ensures a long waiting time; i.e., it is roughly sketched out by the researchers and then contracted out to industry to design and construct. Likewise, by the time the project enters its fifth year, the independent researchers are concentrating on closing down the project, publishing papers, and finding suitable employment elsewhere.

This leaves about three years for the researchers to do most of the research, adequate time for most research projects but not all. Sometimes a discovery in the third or fourth year will open up an exciting new research direction, which then cannot be pursued.

Several ERATO project directors this panel interviewed were critical of the “five-year rule” and suggested that ERATO should be more flexible. One suggested that ERATO should not start the clock until the research laboratories are fully operational. While the JTEC panelists understand these views, they believe that there are more disadvantages than benefits to changing the current policy.

For one thing, all project directors and staff are made aware of the “five-year rule” early enough to incorporate it into their project, research, and career planning. If the project life cycle were more flexible, project directors would likely find all sorts of reasons for continuing projects, and perhaps would even engage in political lobbying in an effort to win project extensions. Furthermore, having a standard life cycle provides the ERATO program with a regular source of funds with which to start new projects.

As previously mentioned, JRDC has no facilities of its own; thus, research is carried out in rented laboratories, sometimes at several scattered locations. The flexibility may make ending a project easier, but then research equipment, much of it expensive and state-of-the-art, may remain. At the project’s end, JRDC retains title to all equipment and dispenses it in a common-sense way. In some cases, equipment is transferred to other ongoing ERATO projects or stored for future use. Sometimes it is left with the former ERATO researchers who may be continuing the same line of research at their home institutions.

The use of independent researchers also may be problematic. Since they quit whatever jobs they had when they joined an ERATO project, they must find employment again when their projects end. In the past, most researchers have found other suitable positions relatively easily, many at universities (mostly at the assistant professor level). This ability to find positions reflected both the high quality of the ERATO researchers themselves and the reputations they built as a result of their participation in the program. However, with the recent spiraling down of Japan’s economy, an increasing number of researchers are encountering difficulties in locating positions. Others who have recently joined ERATO projects are quite worried about the prospective job environment. Consistent with Japan’s culture, the project director bears a heavy burden in seeing to it that his researchers are well placed.

PROJECT DIRECTOR SELECTION

Because a project director has such extraordinary influence over the project, the selection of project directors is one of ERATO management’s most important functions. The selection process is highly unusual for research funding programs. Basically, JRDC officials hunt down appropriate candidates whom they then invite to lead a project. The

JRDC and the prospective project director then jointly decide on a research theme, a total reversal of typical research-grant procedure in which the investigator must submit a lengthy grant application, which is then evaluated through a merit review process. The process for selecting topics and project directors involve the following steps, as depicted in Figure 3.3.

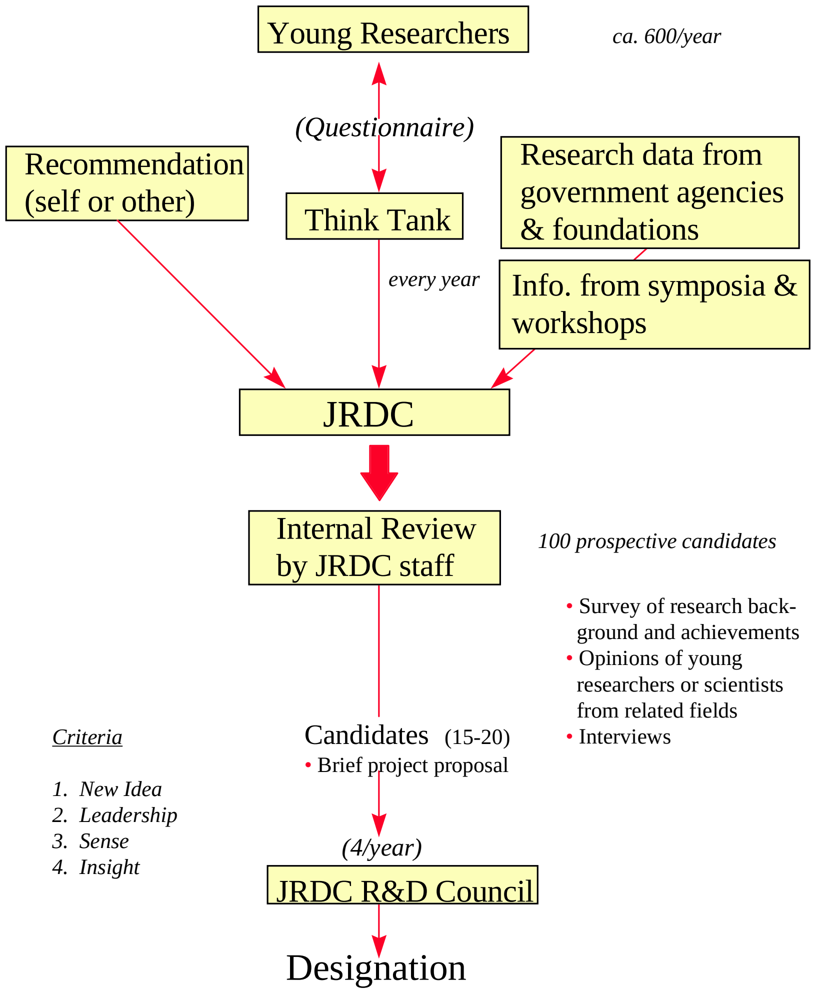

Fig. 3.3. Designation process of ERATO's project leader and research field.

1. Throughout the year, JRDC staff members attend conferences and meetings in a variety of fields to gather information about prospective directors. They consult a wide range of knowledgeable people in each field, including researchers who have participated in past ERATO projects. They also interview hundreds of promising young researchers, usually at the post-doctorate level. In these interviews, the researchers are asked, "*Who are the people for whom you would like to work for five years?*" Through these efforts a list of about 100 likely candidates is compiled.

2. This initial list is then narrowed down by the ERATO staff to about fifteen to twenty candidates through contacts with the candidates themselves, their colleagues, and young postdoctorates. Genya Chiba says that the JRDC looks for two basic qualities when scouting prospective project directors: scientific and technological vision and leadership. Since a primary aim of the program is to plant the seeds for future research ideas in the minds of budding young researchers, the project directors chosen must not only be involved in interesting, leading-edge work, but must also be charismatic and capable of attracting younger people to their team.
3. The 15-20 prospective project directors are visited and interviewed by the manager of ERATO's Research Management Group and a young, technically trained administrator from that group who will be responsible for liaison between ERATO and the project. This is the first formal contact between ERATO and the prospective project directors. In these interviews, ERATO seeks to confirm two points within the context of discussing prospective research: (1) that the prospective director likes the ERATO system and is willing to work with it and, most importantly, and (2) if the prospective project director is attractive to younger scientists.
4. Brief written proposals are invited from perhaps ten of these, and five or six candidates are invited to JRDC headquarters for more in-depth discussions. Finally, four candidates are selected for ERATO's budget proposal to STA. These steps are completed by June, about sixteen months before the projects will actually start. If ERATO's budget proposal containing the four new projects is approved by STA, by the Ministry of Finance, and finally by the National Diet, the projects undergo a final review and approval by the JRDC Research and Development Council the following May and June. If they receive approval, the new projects commence the next October.

The more recently selected project directors are fairly young, between 35 and 45, so that there will not be too great a generation gap with the young researchers. Most of the directors this panel interviewed were astute, dynamic, often charismatic individuals, and all were well versed in English. This is a must if one is to recruit, maintain, and direct an internationally-oriented team of researchers.

In general, the project topics or fields must be focused on leading-edge, fundamental science so Japan can collaborate internationally. They must involve high-risk, "blue sky" research but have significant potential applications as well, because ties with industry are crucial. Other important considerations are avoiding overlap with other agencies and weighing the chances of getting approval from the Science and Technology Agency (STA) and the Ministry of Finance (MOF). To date, most of the projects have been focused on basic aspects of the biological and physical sciences. Surprisingly, no projects have focused on computer and information science or on social, behavioral, and economic sciences. When asked why this is so, ERATO officials explained that, in Japan, these fields are considered "softer" science and consequently, more difficult to directly link to industry interests. This view appears to be changing as Japan's interest and presence in the software industry grows.

SELECTION/COMPOSITION OF ERATO PERSONNEL

Data on current and past personnel appear in Table 3.1. Of the past 919 researchers (aggregate) who have participated in ERATO, 368 (about 40%) came from industry. Most of these researchers are sent from companies to join ERATO as "the delegated researchers." They do not resign from their companies, and they can return to those companies after finishing their research on the ERATO project. These assignments typically are one to three years in duration.

Table 3.1
ERATO Researchers
As of 8/1/95

	Industry	Academia	National Institutes	Others	Independent	Foreign	Total
Current Researchers (Aggregate)*	75 (368)	2 (12)	1 (9)	0 (18)	140 (359)	45 (153)	263 (919)
Home Organizations (Aggregate)*	57 (169)	2 (11)	1 (4)	0 (6)		16 countries (29 countries)	

*Aggregate = Current + Former

Of researchers currently involved in ERATO projects, 140 (53%) are independent, as compared to only 359 (39%) throughout the thirteen-year course of the program. JRDC explains this by pointing to the fact that, unlike earlier projects, current projects are focusing on more "basic" research topics so there is less industry participation.

According to JRDC, the larger number of independents include post-doctors, researchers who have returned to Japan from abroad, and researchers who have resigned positions at universities and companies. Researchers who are employed on full-time contracts with ERATO cannot hold posts in other organizations concurrently. When asked during recruitment why they wish to join ERATO, these researchers give such responses as "there is more intellectual freedom" or "ERATO gives me a chance to do things I'm not presently able to do at the university."

The average age of ERATO research team members, excluding project directors, is about 31. A little more than 18% of the staff are technicians; the rest are researchers. About 40% of the researchers have doctorates. These are generally postdoctoral scientists with fewer than five years' research experience. The personnel who are borrowed from industry tend to have master's degrees, with some intending to obtain doctorates, based on their ERATO work.

Very few ERATO researchers are on loan from universities. Likewise, there are very few university graduate students working on ERATO projects. This is most likely due to the inflexibility of the university system and to rivalry between the STA and the Ministry of Culture and Education (Monbusho). Whatever the reason, the ERATO program may be missing a major opportunity to impact the next generation of researchers by not involving more students in its projects.

Securing a researcher position in ERATO is very competitive. This is because there is a clear perception of its good points, i.e., higher pay, more intellectual freedom, and better project funding. Researchers are extensively recruited through public advertisements, including use of the Internet. Those who desire to join ERATO are directly and intensively interviewed by the project director. In the screening processes, project directors consider applicants' future research plans, as well as their past achievements, career backgrounds, and academic records. Attention is given to ensuring that the researchers are as heterogeneous as possible, because there is a strong likelihood that new ideas will emerge from the interaction among people with different values and perspectives.

Very few ERATO researchers and no project directors have been women. ERATO project directors attributed this to the very small applicant pool. This observation indicates that there are still very limited opportunities in Japan for women in science. In keeping with its vision as a "social experimenter," ERATO may, in the future, choose to recruit more women scientists and have at least one female project director.

INTERNATIONAL COOPERATION

As has been pointed out, the ERATO program requires that its research staff be heterogeneous collections of individuals. A particularly important element of the program is its opening doors to individuals from overseas. Of researchers currently involved in ERATO projects, 45 (17%) are foreign. This is roughly the same percentage as the aggregate for the thirteen-year course of the program, with present and former project members representing some twenty-nine countries.

According to Table 3.2 below, the greatest number of these researchers have come from the United States, Canada, and Western Europe. This is not by accident. Japan has long admired the Western system of basic research, with its many accomplishments, as measured by major discoveries and Nobel prizes garnered. In particular, many Japanese believe that Western culture encourages individual thinking, competitiveness, and creativity while the Japanese system encourages group accomplishment and teamwork. It is presumed that by increasing interaction with Western laboratories and researchers, an exchange of research cultures and philosophy will occur, benefiting both parties.

Individual ERATO projects vary considerably with respect to foreign participation, with some projects obtaining one-third of their researchers from abroad, while others get few or none. The number of foreign researchers involved in a given project is heavily influenced not only by the type of research being pursued but also by the extent to which the project director has established an international network of personal contacts.

Table 3.2
Origins of Non-Japanese Researchers
As of 8/1/95

	Current Researchers	**Former Researchers**	**Total**	**% of Total**
U.S./Canada (2)	8	32	40	26
CIS + Eastern Europe (6)	5	14	19	12
Western Europe (10)	11	31	42	28
Other Asian (6)	9	18	27	18
China, PR (1)	11	9	20	13
Other (4)	1	4	5	3
Totals (29)	**45**	**108**	**153**	100%
	30%	70%	100%	

( ) = number of countries represented

An interesting group dynamic occurs when foreigners are introduced into ERATO laboratories. This panel has been told that a certain "critical mass" of foreigners — usually about four researchers — is needed to change the group culture in the laboratory. For example, labs with fewer than that number tend to communicate primarily in Japanese, but when at least four foreign researchers are working in a laboratory, most conversations occur in English.

Currently, with the relatively high cost of living in Japan, it is more difficult to attract good people from the United States or Western Europe. ERATO's policy is to hire researchers on contract for the long term (two to five years), and there is not yet a mechanism to enable foreigners to visit for short periods of time under fellowships and grants.

In recent years, the ERATO program has received considerable international attention and even acclaim. For example, the 1988 JTECH study of ERATO was viewed as very positive by the Japanese government. Such international attention is furthering the development of the ERATO program, resulting in what Chiba calls "the internationalization of ERATO."

A number of ERATO projects have established laboratories overseas. For example, in a new project, headed by Dr. Daisuke Yamamoto, the Behavior Genes project, one of the research groups is being established at University of Hawaii under the direction of Dr. Ken Kaneshiro. The principal reason for this site is that the research project requires good established colonies of Drosophila subspecies, and subspeciation of these flies is unparalleled in Hawaii. The project is in its first year, and the primary effort is directed toward assembling the team and developing the laboratory facilities.

In an interview, Kaneshiro said that initial negotiations with the University of Hawaii and JRDC were very time-consuming because of issues concerning project management and patent rights. The agreement finally reached provides for a project that is well integrated with the university in terms of post-doctors, students, equipment, and facilities. To date, such agreements have not occurred with Japanese universities. Kaneshiro also reports some difficult administrative problems arising from differences between the U.S. and the Japanese systems; for example, there is too much time and paperwork involved in ordering new equipment. However, he is very excited about the ERATO project, stating that it allows him to pursue high-risk research that the normal U.S. peer-review system might discourage.

For the first time, as well, an ERATO project is now being led by a scientist based outside Japan. Yoshihisa Yamamoto, a Japanese national formerly with the Nippon Telegraph and Telephone research laboratories and now a professor at Stanford University in California, was selected in 1993 to lead a project in quantum fluctuations in nanometer-scale semiconductor devices, research focused on devices that will go into the computers of the future.

Greater international cooperation is the guiding principle behind another JRDC program, the International Joint Research Program (IJRP), informally known as the "International ERATO." Started in 1989, this program fosters collaborative research on a single theme across international borders. JRDC supports the Japanese side of the research; a foreign governmental organization supports the research in its own country; and the two sides exchange researchers. The fifth project is now underway, involving Hiroyuki Sakaki, a professor at the University of Tokyo's Research Center for Advanced Science and Technology, and a University of California, Santa Barbara group supported by the National Science Foundation.

MOBILITY OF RESEARCHERS

Compared to other industrialized nations, Japan has a rigid employment sector based on lifetime employment. However, this appears to be slowly changing. In the 1980s job mobility in Japan increased as a whole but particularly in the industrial sector. ERATO has contributed to increasing the mobility of young researchers though its own programs and its interaction with various programs with similarities to ERATO.

Two studies undertaken by the ERATO headquarters illuminates this accelerating trend. For example, a survey of 121 researchers who participated in the first five projects reveals that, of the 72 people sent from private companies, 68 (or 95%) returned to their original employers after completing their project (Kusunoki 1995). However, in a follow-on survey of 116 researchers participating in the next six projects, only 39 out of 52 industry researchers (or 75%) returned to their companies. The others went to a wide variety of institutions (ERATO 1995b).

Moreover, of the 37 researchers who came from academia (many held untenured postdoctoral positions) 33 (or 89%) changed jobs following the completion of their projects. These researchers went to the following types of institutions:

to their original university	4
to a different university	14
to a company	5
to a national laboratory	3
to another JRDC project	4
to other organizations	7

A follow-on study of their career paths would be very useful in evaluating the unique “training” that the ERATO experience is assumed to impart to its participants.

DISSEMINATION OF RESULTS

Publications

ERATO encourages its researchers to publish actively in distinguished international journals and to present papers at international meetings. ERATO provided data to the JTEC panel indicating that, of the projects completed thus far, the number of published papers has averaged between twenty-five and fifty per project.

Patents

Although not the primary aim, a large number of patents have resulted from ERATO-sponsored research. Any patent right which has resulted from a project may be shared in an agreed-upon manner — by JRDC (50%) and the researchers who are directly responsible for the invention for which the patent has been granted (50%). The portions of the patent rights belonging to members can be transferred to their home institutions upon termination of the project.

According to data provided by ERATO, up to the present time, ERATO researchers have applied for 849 Japanese and 157 foreign patents. Eight licenses were granted to companies interested in using research results from the following six projects: Ultra-fine Particle, Perfect Crystal, Fine Polymer, Solid Surface, Quantum Magneto Flux Logic, and Chemirecognics. Subsequent to licenses being granted, twenty-one patents were filed.

Four projects had six research results that were transferred through JRDC's Cooperative Technology Development program. These projects were Ultra-fine Particle, Superbugs, Fine Polymer (three results), and Perfect Crystal.

Royalties have also been obtained from ERATO results. From 1986 (the end of the first set of projects) until 1995, ¥19,437,000 (approximately $194,000) was received.

Research Follow-On

Most ERATO projects are focused on basic knowledge rather than being oriented toward achieving utilitarian results. While it is important for the projects themselves to bear fruit, a second consideration is whether or not project results lead to further research and development. Continuing the research at universities and national research institutes has proven difficult. However, there are a number of cases where ERATO research has led to some rather large research programs outside JRDC. In one case, a former group leader of an ERATO biosciences project was subsequently funded by Matsushita Electrical Industrial Co, Ltd.. for about $10 million per year to continue basically the same line of research. Below are several examples of ERATO projects that were subsequently funded by Japan's Key Technologies program in cooperation with private companies:[1]

1. <u>Masumoto Amorphous and Intercalation Compounds Project (1981-1986)</u>
   Performer: Amorphous Magnetic Device Laboratory (KK)
   Term: March 1988 - March 1994
   Sponsor: Japan KeyTec Center with 28 companies
   Funding: ¥2.3 billion

2. <u>Nishizawa Perfect Crystal Project (1981-1986)</u>
   Performer: Small Power Communications Systems Research Laboratories (KK)
   Term: March 1988 - March 1993
   Sponsor: Japan KeyTec Center with 26 companies
   Funding: ¥2.0 billion

3. <u>Inaba Biophoton Project (1986-1991)</u>
   Performer: Biophotonics Information Laboratories
   Term: March 1993 - 1999
   Sponsor: Japan KeyTec Center with 19 companies
   Funding: ¥3.45 billion

Symposia and Workshops

ERATO holds two sets of annual symposia that are open to the public and aimed primarily at corporate and governmental research managers. At these symposia, new ERATO projects are introduced, and projects in their third, fourth, and fifth years present their

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[1] [See also Chapter 5 for a discussion of follow-on activities at JAMSTEC based on work initiated by the ERATO Horikoshi Superbugs project.]

results for the previous year. Approximately 1,300 persons attend the symposia. At the end of its five-year term, each project presents a one-day symposium that is open to the public and aimed primarily at researchers active in the field. If the project is located outside the Tokyo/Kanto region, the symposium is held twice, once in the project's home region and a second time in Tokyo. Attendance at the Tokyo symposia averages about 240. ERATO also holds one or two international symposia each year in Europe, the United States, Canada, and Japan to focus on selected key fields in which ERATO projects are participating.

PROGRAM SPIN-OFFS

Since ERATO is intended to be a catalyst for change within the larger Japanese research system, it is fair to ask what changes have occurred as a result of ERATO.

In response to this question, JRDC provided the panel with a list of ERATO-inspired programs dedicated to promoting a new, more flexible and integrative style of basic research (see Table 3.3 below). While the panel did not seek to document ERATO's influence in each and every case, there is considerable anecdotal evidence suggesting that ERATO did indeed influence many of these important research projects.

The success of the ERATO program helped launch three important new programs within JRDC: the International Joint Research Program (IJRP) in 1989, the Precursory Research for Embryonic Science and Technology (PRESTO) in 1991, and the Core Research for Evolutional Science and Technology (CREST) in 1996. PRESTO is aimed at young, individual researchers: it supports and stimulates their embryonic research for three-year periods. Eight new projects are added each year. CREST for the first time enables university researchers to hire staff and build research projects. The IJRP is an international version of the ERATO program which is conducting five-year co-sponsored joint research projects involving public organizations located in both Japan and abroad on a 50-50 cooperative basis. In this program, international borders do not separate the laboratories, and JRDC serves in both implementing and funding capacities.

PROGRAM EVOLUTION AND FUTURE TRENDS

The establishment of ERATO did not sit well with some government officials, who preferred the traditional way of doing things. Knowing that it would have to counter early and strong criticism and present some early successes, JRDC initially selected ERATO topics that were applied/materials-oriented and project directors who were well established and had close ties to industry. The first five projects are examples of this strategy.

Table 3.3
Basic Research Programs Established Since ERATO's Founding

Year	Program	Agency or Ministry
1981	ERATO	JRDC (STA)
1981	Research and Development Program of Basic Technologies for Future Industries	Ministry of International Trade and Industry
1985	Japan Key Technology Center	Ministry of International Trade and Industry
1986	Frontier Research Program	Institute for Physical and Chemical Research
1986	Bio-oriented Technology Research Advancement Institute (BRAIN)	Ministry of Agriculture, Forestry and Fisheries
1987	Drug Fund for Adverse Reaction Relief and Research Promotion	Ministry of Health and Welfare
1989	International Joint Research Program	JRDC
1989	Kanagawa Academy of Science and Technology	Kanagawa Prefecture
1990	Grants-in-Aid for Creative Basic Research	Ministry of Education, Science and Culture
1990	Joint Research Utilizing Science and Technology Potential in Regions	Science and Technology Agency
1991	Precursory Research for Embryonic Science (PRESTO)	JRDC (STA)
1992	Telecommunication Advancement Organization of Japan (TAO)	Ministry of Posts and Telecommunications
1993	National Institute for Advanced Interdisciplinary Research	Ministry of International Trade and Industry
1993	Industrial Science and Technology Frontier Program	Ministry of International Trade and Industry
1994	International Institute for Advanced Research	Matsushita Electric

After seven or eight years, however, the program achieved a certain level of acceptance by senior government and industry officials. JRDC began expanding the number of projects initiated each year, and these new projects were more oriented toward fundamental science and the discovery of basic knowledge. Many of the new projects were focused on the biosciences, as Japan sought to strengthen its position in this area. Also, JRDC sought to recruit younger project directors who could establish more contemporary relationships with young researchers.

More recently, as Japan has sought more influence in international science and technology, and workforce mobility has become more accepted within Japanese society, JRDC has sought more international connections — within ERATO, with its offshore groups, and by expanding the number of overseas IJRP groups. This trend is likely to continue.

During this panel's visit to Japan, some panel members had the opportunity to meet with very high-level officials within the STA, including one who was on loan from MITI. Without exception, these officials viewed ERATO as a very valuable and successful program that is helping to change the Japanese R&D culture. They also expressed the view that, after more than a decade of experience, perhaps ERATO needed to be reinvented, and that something might be on the horizon that would be even bigger and better than ERATO.

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CHAPTER 4

ERATO PROJECT ANALYSIS X PHYSICAL SCIENCES

John Rowell

OVERVIEW

As described earlier, the Exploratory Research for Advanced Technology (ERATO) projects, as created by the Research Development Corporation of Japan (JRDC), represent an unusual way to fund research, unique in this panel's experience. But has the unusual method of funding resulted in unusual or novel science?

The unusual features of the mode of funding are as follows: The project director receives five years of funding for a team of fifteen to twenty people. The director has to create the team from scratch, drawing his personnel from universities, industry, and government laboratories. The team is generally divided into three groups, which can work at geographically dispersed sites. Often, laboratory and office space has to be found for the project in locations which are unfamiliar to most of the project members. During the five-year project, a director has considerable freedom to pursue the broadly defined area of research and is not required to give frequent reports and reviews. No renewal is possible, so the scientists can concentrate on their research to the end and do not have to prepare a renewal proposal. Some of the staff, however, often do have to search for jobs during the last year of the project. Above all, fundamental long-term research is encouraged, without any constraints as far as the JTEC panel could tell, to have the work in strategically important research fields.

While many U.S. scientists would view some aspects of ERATO funding with envy, in particular the high level of funding guaranteed for five years and the minimal requirements for reporting to the funding agency, the unusual features of ERATO funding do impose some constraints. For example, a well-established university group of similar size would have much more continuity in personnel, in space, in equipment, and in the research topics themselves. Ideas from one graduate student or postdoctorate researcher might flourish in the hands of a subsequent student. In an ERATO project, once the first year has been spent establishing the project personnel in their laboratory space, and the last year is taken somewhat by job searches, research work has to be started, carried out, and finished in three or four years. It has to be largely self-contained in that time span. Thus there can be little evolution of the project, at most one change of emphasis or one chance to follow a new direction that might be uncovered. In some cases the work has continued at a reduced level after the end of the project, either in the laboratory of the director or picked up by industry, but the message was strong that the projects truly end with the fifth year.

The well-defined lifetime of the projects might also have an effect on the choice of topics and style of research. Although there is remarkably little formal pressure to succeed, i.e., no specific measures of performance and success, the directors and staff naturally want to show impressive results within the project's lifetime. Therefore, projects that have some chance of being completed in about four years are chosen. This five-year limit might explain the observation that a number of the projects have been on more applied topics than the freedom of choice associated with the funding itself might have required. How strongly JRDC itself influences the scientific emphasis of the program, through its choices of directors and topics, also is not clear.

The projects in the physical sciences that have been supported to date by JRDC under ERATO funding fall, very roughly speaking, into four broad areas: materials growth, the properties of small physical structures, probes to create or study such small structures, and high-speed devices. Viewed in this way, the projects are as follows (dates given are the final year of each five-year project):

Materials Growth

- Masumoto — Amorphous and Intercalation Compounds — 1986
- Kuroda — Solid Surface — 1990
- Kimura — Metamelt — 1995
- Yoshimura — Pi Electron Materials — 1996
- Tanaka — Solid Junction — 1998

Small Structures

- Hayashi — Ultra-Fine Particle — 1986
- Sakaki — Quantum Wave — 1993
- Aono — Atomcraft — 1994
- Yamamoto — Quantum Fluctuation — 1998

Probes for Small Structure Creation and Analysis

- Yoshida — Nano-Mechanism — 1990
- Tonomura — Electron Wavefront — 1994

High-Speed Devices

- Nishizawa — Perfect Crystal — 1986
- Goto — Quantum Magneto Flux Logic — 1991
- Nishizawa — Terahertz — 1992

Given the considerable freedom that can be exercised by both the project directors and JRDC to choose topics of study, one might ask whether these projects represent a cross-section of the most exciting and important research in the physical sciences worldwide over the past fourteen years. However, it should also be noted that it has not been the intent of JRDC to cover all such fields. In fact JRDC indicated that certain popular and “hot” fields were avoided, presuming that such areas would be well funded from other sources. Given that objective, it is perhaps surprising to see the number of ERATO projects that have been focused on the physics of semiconducting materials, a field which receives more research and development funds across academic and industrial laboratories worldwide than any other.

ERATO funding is also designed to encourage work that is long-term and fundamental. Given this enlightened policy, it is reasonable to ask whether the topics have been as aggressively forward-looking as possible. Some projects were speculative and long-term, but others have probably been more “applied” than might have been expected. This panel has speculated earlier that the four-year working life, out of the five years of the project’s funding, might be a factor governing such choices.

OUTCOMES

During the JTECH visit to Japan in 1988, when only a few ERATO projects were complete and ongoing, it was possible to review the scientific activities in some detail. In 1995, this was not possible, and at most only some general impressions could be obtained, with a few specific details for a small number of projects. ERATO had simply grown too large, in those seven years, for all the past and present projects to be carefully reviewed in one week for technical accomplishments and impact. It is therefore with reservation that members of this panel attempt to make any detailed comments on the ERATO projects in the physical sciences.

Clearly ERATO has supported research that is respected and widely referenced in the worldwide scientific community. In some cases, i.e., for some of the projects, the work appears to be regarded as the most important, or among the most important, in the field. In at least one case, the project can be viewed as having created the field. Without in any way trying to be comprehensive, a few highlights can be mentioned.

One of the first projects (1981-1986), the Hayashi Ultra-Fine Particle project, has had both commercial and scientific success. This project was quite extensively reviewed in the 1988 JTECH report, which makes interesting reading in hindsight. Film Deposition Systems, using the methods pursued in the project, have been developed and sold. As with most ERATO projects, there is an interesting story about the effect of the project on the careers of the participants. In this case, Dr. Sumio Iijima joined the project from a position at Arizona State University, a center of activity in electron microscopy. Under the ERATO project, he developed a high-vacuum and high-resolution electron microscope, which allowed him to image for the first time the growth and restructuring of small gold particles. In 1987, Iijima joined NEC, where he continued both microscopy research and the development of the microscopes. In 1991, he discovered carbon nanotubes, a discovery of major scientific importance. While this discovery was not made under ERATO funding, Iijima has stated that he owes his career in Japan to the opportunity to do fundamental research in the Hayashi ERATO project. He also illustrated a difficulty in the early projects, which has been addressed since, in that he was not able to take his custom microscope from the project to NEC. This loss of equipment was one outcome of fixed-term funding, in that his work was disrupted at the end of the project.[1]

It has been argued that the Goto Quantum Magneto Flux Logic Project (1986-1991) did not result in technology that was widely adopted, which is true. But for an ERATO project, this is surely the wrong judgment. The project did successfully explore the limits of an alternative high-speed digital device technology. After the formal end of the project, work continued at Hitachi, where a 36 GHz circuit was demonstrated. Using the same technology, HP and Conductus in the United States built a “stop watch” with a timing resolution of 300 femtoseconds. In terms of expanding the envelope of knowledge, the project succeeded. Five books, the proceedings of annual conferences, were published; and 34 Japanese and 14 foreign patents were filed, “one of which has made some money.” Most of the superconducting electronics research worldwide is now based on the manipulation of single flux quanta, following either the ideas of the Goto project or those of the work of Likharev and his group in the Soviet Union. The human interest story in this project is that Professor Goto is now working, at least part of his time, on the engineering issues associated with design of low-cost refrigerators. Such refrigerators are a necessity if superconducting circuits are to be widely used.

A project to explore X-ray lithography technology that was anticipated to be needed in ten years or so was the Yoshida Nano-Mechanism project (1985-1990). Dr. Yoshida was the Managing Director of Nikon and is now Executive Vice President. One can only wonder how many similarly placed executives in the United States could be an ERATO project

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[1] Partly due to Iijima’s experience, the policy on continued use of research equipment has been modified, and JRDC permits the post ERATO continued use of research equipment by the researchers upon request.

director. The project, which included groups studying analysis and tools such as the scanning tunneling microscope (STM), controlled positioning systems, and processing of multilayers for X-ray optics, resulted in the development of a dual laser interferometer with 1 nanometer resolution. Dr. Yoshida stated that there was no research activity in X-ray techniques at Nikon before the ERATO funding. At the end of the project, a joint seminar with the United Kingdom nanotechnology group was held at Warwick University, United Kingdom, which attracted over one hundred attendees.

Relatively few projects fall outside the areas of the physical sciences or biology. One such example, however, is the ongoing Kawachi Millibioflight project (1992-1997), which could perhaps be called an aeronautical engineering basic research project. From his experience in fluid dynamics, Prof. Kawachi and his team, which includes a research manager from the National Aerospace Laboratory, are studying the mechanisms of flight used by insects. The study appears to be an interesting departure from the more traditional fields of study of the majority of the physical sciences projects, but it is too early to judge its effect on the field.

In most projects, the research followed the initially defined directions reasonably closely. However, the Kimura Metamelt project (1990-1995) began as a study of phenomena occurring in both liquids and solids during the growth from the melt of crystals of optical materials such as lithium niobate. During the first year, with some encouragement from the companies that had sent participants, the project was reoriented towards similar studies of silicon crystal growth. It is interesting to note that research into silicon is a very well-supported field worldwide.

A number of projects illustrate an important aspect of ERATO funding, namely that it has made possible an accelerated program after an initial idea has been conceived or after early observations looked promising. Clearly JRDC has demonstrated agility in identifying and funding such fields at their early stages.

One such example is the Aono Atomcraft project (1989-1994), which developed methods to detect, displace, extract, and deposit single atoms on surfaces using STM techniques. This project had a five-person international advisory board, which included Dr. Rohrer of IBM, Zurich, who with Binnig invented the STM. Before the ERATO funding, Dr. Aono's research at the Institute for Physical and Chemical Research (RIKEN) was limited by equipment and personnel. The project allowed two or three instruments to be built, and two to be purchased, and made possible the participation of theorists and industrial scientists. Aono clearly saw it as a turning point in his research career. He did comment, however, along with some other directors, that the project members were really making great progress in their fifth year, and even greater things could have been done if the project had been longer. In fact, following the end of the Atomcraft project, a high-technology consortium between JRDC and industry has continued some of the work for two years, and STA will be funding an Atomic Scale Sciengineering group at RIKEN from 1995 to 1999.

Another example of ERATO quickly expanding work around an early discovery is the Tonomura Electron Wavefront project (1989-1994). Dr. Tonomura, at Hitachi Laboratories, had for some years attempted to observe interference between electron beams. Not until the development of the field emission tip as the electron source were the beams sufficiently coherent for such experiments to be possible. ERATO funding allowed his group to grow in an area that even the most basic of the Hitachi labs regarded as risky. The work, which includes the observation by electron holography of vortices in superconductors, is now internationally renowned. The end of the project was marked by a joint conference at the Oak Ridge National Laboratory.

A number of ERATO projects have strong international linkages or have led to such collaborations. After the end of the Sakaki Quantum Wave project (1988-1993), which was at the forefront of research into dimensionally confined structures made by the growth of III-V semiconductor samples on nonplanar substrates, an International Joint Research Program (IJRP) was funded by JRDC to extend from 1994 to 1999. Under this program, entitled Quantum Transition, similar work on III-V quantum structures is being carried out at both the University of Tokyo and the University of California, Santa Barbara.

The Yamamoto Quantum Fluctuation project (1993-1998) was international in scope from the beginning of ERATO funding in that groups are located at Stanford University, where Professor Yamamoto has taken an appointment, and at the NTT Basic Research Laboratory, where he holds a joint position and visits every two months or so.

CHAPTER 5

ERATO PROJECT ANALYSIS — BIOLOGICAL SCIENCES

William Bentley
Rita Colwell

OVERVIEW

Although the nature of this study was more to evaluate the processes and outcomes of ERATO as a program designed to influence the manner in which people work rather than to evaluate, in detail, the scientific content of the work, nonetheless, an evaluation of the science and engineering contributions is necessary since they are the foundation upon which ERATO is built. The "biosciences" subpanel consisted of Drs. Bentley, Lee, and Young, and Mr. Herer, who visited individuals and laboratories in Tokyo, Osaka, and Kyoto over a four-day period. The projects the JTEC panel visited included some previously completed, ongoing, and just underway. Specifically, the panel visited the following projects in chronological order: Furusawa MorphoGenes, Doi Bioasymmetry, Ikeda Genosphere, Yamamoto Behavior Genes, Shinkai Chemirecognics, Hayaishi Bioinformation Transfer, Watanabe Subfemtomole Biorecognition (an International Joint Research Project), Yanagida Biomotron, Hotani Molecular Dynamic Assembly, Hashimoto Polymer Phasing, Okayama Cell Switching, and Horikoshi Superbugs.

SCIENTIFIC CONTRIBUTIONS

In general, the quality of science was very high. Most of the scientists viewed publication as the primary indicator of quality and recognition and, with few exceptions, sought publications in top peer-reviewed scientific journals. A sampling of the journals include *Science*, *Nature*, *Proceedings of the National Academy of Sciences* (USA), *Journal of Molecular Biology*, *Cell*, *Journal of Biological Chemistry*, *EMBO Journal*, *Journal of Theoretical Biology*, and *Developmental Biology*, among others. It was also apparent that the investigators viewed participation at international conferences and symposia as a primary means for disseminating their results to the international scientific community. Most project directors were either quite aware of their international competition or, in many cases, were in partnership with their international colleagues.

FOCUS OF WORK

It is the intent of the ERATO program to focus on basic research, and several of the projects were deeply involved in the most fundamental pursuit of knowledge. However, many of the projects performed what we will refer to as “targeted” research, where the focus was on discovering a protein or cellular factor that influenced a certain behavior. In these projects, the techniques employed were standard techniques, common among modern molecular biology laboratories, and a specific target was sought. Where a researcher engaged in more basic research might ask why or how a given technique works, a common question in some ERATO projects is, how can I use an existing technique to identify something I predict should be found there?

It is important to underscore, however, the academic freedom that exists for the project directors and their scientists. This intellectual freedom is at the heart of the ERATO program. It was obvious and very appealing scientifically that the project directors were given full autonomy to choose the questions they wanted to ask and the research directions they wanted to pursue. Such freedom allows scientists to ask very basic and fundamental questions. If the questions actually asked are of a more applied or targeted nature, then the process of implementing ERATO, not the basis for ERATO, might be examined so as to strengthen the fundamental component of the research. For example, since the academic and financial freedom exists for each project director to perform basic research, if basic research is not being performed, an evaluation as to why might be beneficial. Are the proposed research directions given sufficient weight in determining the project directors? Are the scientists added to the group the best, given the research directions? Are there other mechanisms (i.e., international collaborations) that would enhance the basic research?

In summary, the quality of science in the biosciences area was impressive. A question of basic versus applied research had been asked during JTECH’s previous visit. Indeed, the composition of projects has moved significantly to the basic side during the past seven years. That this panel found no publications in biotechnology or bioengineering journals suggests the intent of the work was uniformly of a basic nature. Instead, it used the term "targeted" basic research in this report. The quantity of scientific output was not addressed by this study. Some communication with Japanese scientists outside ERATO revealed concern regarding the quantity of science produced during ERATO projects. The data this panel has gathered is presented in Chapter 3. It shows that the average number of pages published per project averaged from 25 to 50.

REVIEW OF SELECTED INDIVIDUAL PROJECTS

Furusawa MorphoGenes Project

Dr. Mitsuru Furusawa asked why DNA was double-stranded and came up with the theory of asymmetric evolution. Results were published in *the Journal of Theoretical Biology* and in *Proceedings of the National Aacademy of Sciences*. This project successfully demonstrated that creative and fundamental questions could be answered by ERATO projects. The Furasawa team was multidisciplinary, including theoreticians and experimentalists in molecular biology and cell biology. Two of the scientists were non-Japanese, one has since joined Wayne State University as a faculty member. There was also an industrial component on this project: two individuals from Daiichi Pharmaceutical. Interestingly, Furusawa recruited Dr. Doi, who will start a new project next year.

Yamamoto Behavior Genes Project

Because there is substantial Drosophila subspeciation in Hawaii and a good established fly colony or set of colonies at University of Hawaii, Dr. Daisuke Yamamoto will start an interactive project there. The project is in its first year, and the primary effort is directed at assembling the team, which thus far consists of a researcher from Germany (Dr. Kei) and one from China (Dr. Xu), and five Japanese scientists. Yamamoto will recruit molecular biologists from various places. The overall team will include two Hungarians, an American (not from the Hawaii group), a French female (who is not an ERATO employee, but will study the behavior of the scientists), and a Japanese. Dr. Yamamoto has no female scientists except technicians and attributes this to the applicant pool and the apparent poor quality of the female candidates.

Ikeda Genosphere Project

An interesting spin-off of this project has been the continuation of work by the Ministry of Agriculture and Forestry involving transgenic swine. Dr. Joh-E Ikeda, the project director, expressed some concern about (1) the duration of the projects, (2) the lack of ERATO laboratory facilities, and (3) the lack of core research outside Japan. He suggested that a seven-year duration for ERATO projects would be better and that an ERATO home laboratory would be advantageous, since at present, each project undergoes a year start-up, which he felt was unnecessary. Ikeda also recommended that there be some core research outside Japan so that the individuals in ERATO could learn Western philosophy, particularly the way American scientists conceptualize research.

Shinkai Chemirecognics Project

Dr. Seiji Shinkai, the director, commented that three items were indispensable for ERATO projects: (1) money, (2) equipment and materials, and (3) the facility. A university has manpower and laboratories but very little money, which is tightly regulated when available.

When one has a research idea, he can get resources but must carry out the research as specified. There is little flexibility for investigating new directions. This is the opposite of the ERATO program.

Shinkai was critical of a lack of communication and understanding that can occur between the Ministry of Education (Monbusho) and the Science and Technology Agency (STA). He noted that Monbusho allowed him to work only one day per week on the project, and he was unable to work on the research after the ERATO project at the same level in terms of funding and facilities available at the university. He noted that in ERATO, if a postdoctoral researcher does well, he can actually progress careerwise in the scientific community. If one does not make full use of the resources and flexibility, however, then the doors will not open later. Such performance-oriented evaluation is new in Japan and is a positive outcome of ERATO.

Finally, he presented an image that describes the influence and importance of ERATO projects well: he likened ERATO to being able to draw on a completely blank sheet of white paper, whereas with Monbusho, one primarily fills in between the lines, as in a child's coloring book. The JTEC panel was impressed with his candor and his opinions, given the importance of the day, the Final Symposium on the Chemirecognics project, for his own career.

Yanagida Biomotron Project

Industrial researchers were not involved in the Biomotron project. Most of the researchers came from universities. Osaka University, for example, is the home of the project director. This panel’s guess was that if he could, Dr. Yanagida would employ more students. Typically, he utilizes 80% physicists and 20% biologists.

The project did not include foreign researchers, primarily because of the additional time that would be needed for adequate training. Instead many established foreign scientists in the field visited and stayed at the project for a couple of months to one year to collaborate with them as visiting researchers. This project is an example of excellent basic research, noted worldwide for its quality. Another impressive aspect of this project was the fact that the space was a converted warehouse, with no prior laboratory facilities, let alone equipment. ERATO helped to secure the space and convert it into a state-of-the-art laboratory.

Okayama Cell Switching Project

The project was divided into three subgroups, typical of all ERATO projects. The JTEC panel was very impressed with Dr. Ishihara, who was the single female scientist to present her work. It is likely she will pursue opportunities overseas upon project completion.

Hayaishi Bioinformation Transfer Project

Discussion centered around the Osaka Bioscience Institute (OBI) and the conversations Dr. Osamu Hayaishi had early on with Mr. Chiba over the formation of ERATO. Hayaishi helped formulate the ERATO policy that considers the person's personality, vision, and insight when choosing project directors. His work at ERATO was conducted entirely at OBI, which in turn, he had initiated with the mayor of Osaka. Of the twenty-seven researchers, eight continued on at OBI after the project ended. Ten went back to the universities from whence they came, half of these to the same position. The JTEC panel felt this was rare. In addition, Dr. Watanabe worked with Hayaishi originally and now has his own IJRP project.

Horikoshi Superbugs Project

The panel's interview was with Dr. Koda, a staff scientist from the Institute of Physical and Chemical Research (RIKEN). The Superbugs project ended in 1989. Dr. Koda now has an IJRP project with Michigan State University on microbial evolution. More than other projects, this work has attracted the interest of many companies. Two postdoctoral researchers from Michigan State, resident in the RIKEN labs during our visit, expressed concern about the flexibility of laboratory procurement procedures. Furthermore, they felt that group meetings were formal, which inhibited their making significant progress. They suggested that four foreign people in a laboratory might change interpersonal dynamics so that the conversation would revert to English.

Follow-on Work at JAMSTEC Based on the Superbugs Project

During a recent visit to Japan, Rita Colwell had an opportunity to visit researchers at the Japan Marine Science and Technology Center (JAMSTEC) who are carrying on and expanding some of the work pioneered in the ERATO Superbugs project. Her observations offer a perspective on what happens at the conclusion of an ERATO program. ERATO's Superbug project ran from 1984 to 1989. Its director was Dr. Koki Horikoshi, very much a traditional leader in that he was older and more established. His project was to look at unusual microorganisms, particularly bacteria that grow at very high pH (12, 14, close to absolute basic pH), like alkalophilic bacteria that grow in solvents. Horikoshi actually isolated a bacterium that grew in practically full-strength toluene, for example. It was an interesting feat that took two or three years. The 1988 JTECH review panel concluded that the work that was done, however, wasn't truly innovative in the sense of being high-risk. Then Horikoshi's focus of interest became extremophiles.

The Superbug project was a reasonably successful ERATO project, in that some new, young scientists had been trained and several successful patents had come out of the project. For example, the bacteria that were capable of operating at very high pH and had a proteolytic activity were utilized in a very popular detergent in Japan. So there were successful applications of this ERATO program.

What is interesting is that, subsequently, Horikoshi was selected to lead a Superbug continuation project in Yokosuka through JAMSTEC. Five scientists were recently asked to carry out a review of that program: Dr. Harlan Helderson from the University of Massachusetts, Dr. Ian Dundis from the Bergen Rienvow Tech Center in Norway, Dr. Rita Colwell from the University of Maryland Biotechnology Institute, and two researchers from Japan: Dr. Koichi Oada, who heads the Ocean Sciences Research Institute of the University of Tokyo Marine Microbiology Group, which is itself converting to marine technology, and Dr. Tadashi Matsunaga of the Tokyo University of Agriculture and Technology. This team reviewed Horikoshi's JAMSTEC project on November 9-10, 1995.

The program at Yokosuka turns out to be rather extraordinary in that $5-20 million a year has been expended since 1991. At this JAMSTEC project there are 29 researchers working on deep sea research; and from 1992-1995 there were also 21 researchers from six countries who came in to work with them. Engineers and scientists at this project spent two years constructing an incredible facility that allows them to collect microorganisms under deep sea hydrostatic pressure and grow them continuously in culture, transferring them constantly under pressure. These scientists also have developed the capability of working at very high temperatures, to better preserve and study deep sea hydrothermal vent bacteria.

Researchers at the Yokosuka JAMSTEC program, called "Deep Star," have built two submersibles. In addition to the Shinkai 2000, which allowed them to go to 2,000 meters, they have built the Shinkai 6500, which will allow manned (human-operated) descent to the deepest trenches of the world's oceans, to a depth of 6,500 meters, which will be the world record as soon as that has been accomplished. (It either already has been done in one of the dives or will be very soon.) They are also developing another submersible, a "tethered" vehicle that will, by remote operation, allow them to collect samples in the deep sea.

The Deep Star project is unique in that it targets only deep sea areas and microorganisms in that environment. It is an extension of Horikoshi's Superbug project; but it goes into its focus very extensively, to the very deep part of the ocean. This has necessitated the development of a considerable amount of expensive and unique hardware.

Five groups in the JAMSTEC Deep Star project are focused on organic, solvent-tolerant microorganisms. This is the extension of Horikoshi's original ERATO project, with the addition of hyperthermophiles, bacteria that grow at temperatures of 110-140 or 150^{o}C under high pressure; psychrophiles, bacteria that grow at very low temperatures (this, of course, is a characteristic of the deep sea); and barophiles, bacteria that grow only with hydrostatic pressure. JAMSTEC researchers have succeeded in isolating two obligately barophilic bacteria that function only with high pressure. They are doing some work on preservation and culture collection and have started some research on the genetics of these marine bacteria.

Basically, the Deep Star program has developed a very unique set of engineering skills for construction of submersibles and of isolation and incubation chambers for research. These engineering capabilities are not matched anywhere else in the world. It is clear that the next phase of the creative basic research work that spun off from ERATO provides a capability and commitment for much longer support — 15 years — and this has enabled the group to devise an apparatus for very precise sampling of microorganisms and the capability of studying the properties of microorganisms under natural conditions.

The Deep Star project was possible only because of Horikoshi's previous experience and equipment; but as the new facilities are now available, expansion into molecular techniques has been introduced. This expansion represents a next phase and an opportunity for young scientists. One of the very strong recommendations made by the review team is that in the next round, the next five years, leadership be initiated by Horikoshi, but that one of the "young tigers" aged 35 to 40 be groomed to take over. Unfortunately, there isn't anybody on site among the younger workers who can take on this leadership. That seems to be a shortcoming, and it may well be a shortcoming of the ERATO projects in general, at least of the older ones, not to have a capacity for cultivating the next head or director from within the group.

The JAMSTEC Yokosuka facility is the premier center for this kind of research in the world. The only other related programs are Ifremer in France and Wood's Hole in the United States. But these are secondary; they really do not have the capacity, the skills, and the breadth of the JAMSTEC Deep Star program. Some institutions are beginning such studies. The University of Maryland Biotechnology Institute is doing such studies in Baltimore — but the engineering side, as invested in by JAMSTEC, is unique.

The five-year-old Deep Star project has obtained good results. For example, new selective procedures have resulted in the isolation of a number of solvent-tolerant strains in mutants. The mutants are the next step, since solvent-tolerant strains came out of the ERATO technology. JAMSTEC researchers are beginning now to look at the fundamental mechanisms of membrane proteins for tolerance, and they are also looking for commercial use in bioconversion applications. What are particularly interesting are the barophiles that have been isolated, adding to the very meager knowledge of these organisms, and the molecular-genetic studies of baro-tolerance, especially in the identification of a very specific protein that appears to be correlated with the capacity to grow under pressure. The Deep Sea staff have begun studies of the psycrophiles, the bacteria capable of growing at very low temperatures, around 0-10 degrees, and they are looking at the interrelationships of temperature, salinity, pressure, and other environmental parameters. The results are in a very early stage but constitute a sound basis for launching this major research program on systematics, biodiversity, and preservation methods.

Horikoshi has provided strong leadership. He has brought in scientists from within Japan and from other countries. The key factors have been the flexibility and recruitment aspects of the program. The publication record has been very good. The Deep Star program researchers published 24 original papers by 1994. By the end of 1995 they had published about 56 papers total, and these paper have been published in very good journals. Researchers at the Deep Star program have also made 132 presentations around the world.

At this stage of development of the program, the review committee concluded that a very healthy beginning has been made for Deep Star, but that in the next phase several factors will be critical. Every effort, this panel believes, must increase collaboration with universities and other research centers in Japan and abroad; must increase communication with the disciplines that are involved — engineering, molecular biology, protein chemistry, and so forth; and must maximize opportunities to interact with related basic sciences.

One of the interesting aspects of the Deep Star program is that it brought in external peer review. The panel believes that this is a characteristic brought forward through the experience of Horikoshi, not only from working with overseas scientists, but from working within the ERATO program.

One of the JAMSTEC program's shortcomings, however, is its inability to fund scientists from abroad and from other universities to come to work at Deep Star. The program depends on the ability of scientists to bring in their own money, and that is a bit unrealistic.

Deep Star provides a very interesting example of an extension of an ERATO program. It shows the influence of some of the characteristics that George Gamota was referring to in the Introduction that are unique to ERATO, and it demonstrates the influence of ERATO to extend a research area into an entirely new, broader area, in this case, to extend deep sea research into the fields of deep sea molecular biology and biotechnology.

CHAPTER 6

CONCLUSIONS REGARDING ERATO

George Gamota
William Bentley
Rita Colwell
Jay Lee
John Rowell
Leo Young

IMPACT ON SCIENCE/DISCIPLINES

Discussions with the scientists who have been involved in Exploratory Research for Advanced Technology (ERATO) projects have indicated that the major effects of its method of funding have been on the culture of scientific research, on the modes of doing research, and on the careers of the involved scientists, rather than on the scientific fields themselves. This is not to say that ERATO-supported science has not been important. The descriptions of just some of the projects, outlined in chapters 4 and 5 above (see also Appendix B), illustrate the very high quality of the work and its impact internationally in many cases. But in almost every interview, the discussion uncovered an impact that went beyond science. Some examples follow.

In all projects, scientists from universities and industry were brought together, often with group members from a government laboratory. In cases where the project director was from a university, exposure to the needs of industry and the objectives of industrial research was generally a new and broadening experience. The "management structure" of ERATO projects, with separate groups, a technical manager, and group leaders, represented a new style of research for those who had only been in a university environment before. Often at least one of the groups in the project was carrying out research which had not previously been the specialty of the project director. Thus interdisciplinary research was introduced to the universities. A loose comparison could perhaps be made with NSF-supported Materials Research Labs and Materials Research Groups (now Materials Research Science and Engineering Centers), but it should be emphasized that the deliberate inclusion of industry researchers into the projects funded directly by ERATO from their beginning implies a much stronger university-industry coupling than in any NSF-funded centers, where the NSF requires cofunding but does not require that industry researchers be on site, and where industry involvement is not supported by NSF through the center budget. There are U.S. government programs that fund industrial researchers, such as the Small Business Innovation Research (SBIR) program, the Small Business Technology Transfer (STTR) program, the Advanced Technology Program (ATP), and the Technology Research Program (TRP), but none do it in a way to ensure that the team members all work for the same employer, which is the case with ERATO.

Before ERATO, research funding in universities came almost exclusively from the Ministry of Education (Monbusho) and was predominantly for a professor and a small number of students. ERATO has caused two changes: first, multiagency support of university research is growing;[1] and second, both Monbusho and the Ministry of International Trade and Industry (MITI) are starting "ERATO-like" projects in universities (i.e., projects that are carried on by larger teams, including postdoctoral researchers) that are more interdisciplinary. Increasingly, university facilities and equipment are becoming available to nonuniversity scientists through such projects.

From many of the project leaders, the JTEC panel heard the comment that ERATO funding "represented an unusual opportunity to expand the size and scope of the work," i.e., that ERATO made possible, for the first time in Japanese universities, a working group that could exceed the capabilities of one professor and a small number of students.

IMPACT ON POSTDOCTORAL ACADEMIC RESEARCH SYSTEM

Most Japanese basic research organizations, especially universities, can be characterized as bureaucratic organizations which primarily pursue stability and continuity of research activities. Traditionally, the Japanese academic system has been somewhat rigid under Monbusho. The fundamental unit of the research organization in Japanese national universities is the chair (*Koza).* Chairs are grouped for administrative, teaching, and research purposes into departments. A typical chair might consist of one professor, one associate professor, two assistant professors, and several graduate students. The career growth of young researchers is pretty much limited by the *Koza* system, since the research direction is set by the professor.

ERATO has made a large contribution towards increasing the mobility of young researchers, in particular postdoctoral students, in Japan. It gives young researchers extraordinary flexibility for exploring ambitious ideas. Typically, an entirely new project

[1] See discussion of the new JRDC program, CREST, in the Executive Summary (p. xi).

starts when various researchers including those in companies are gathered together around a single research theme. Then, after five years, the project is disbanded. Most researchers are able to return to their parent companies or to find new positions in universities at the end of the ERATO project. However, there are still a number of researchers who have difficulties in making the transition to a career in a university or in industry. As a result, postdoctors are beginning to be concerned about exploring opportunities with ERATO projects.

Over 50% of the team members in ERATO projects were from industry. For them, the typical length of stay in an ERATO project is between two and three years. The majority of the industrial participants indicated that the company's lab did not have enough flexibility and freedom for young researchers to attempt challenging research projects. On the other hand, a few industrial researchers were able to continue their research projects in their parent companies after they returned. One young researcher from the Hotani Molecular Dynamic Assembly project was recruited by Matsushita's Institute for Advanced Research after his tenure with the ERATO project. He transferred the project both physically and in spirit and formed an ERATO-like research team in Matsushita's Advanced Research Laboratory in Kyoto. Another Matsushita researcher in the Ogata Fine Polymer project transplanted the research equipment and activities to his parent company and developed new products. The company then paid the royalty to the Research Development Corporation of Japan (JRDC) for using its technology.

IMPACT ON RESEARCHERS' CAREERS

It was clear to the JTEC panel that most researchers involved in ERATO projects were quite satisfied with their experience. The evidence gathered by the JTEC panel was largely anecdotal, but this panel was fortunate to receive a recent study performed by Professor Ken Kusunoki from Hitosubashi University. His study, entitled "Report on a Survey of Research Participant Attitudes toward ERATO," summarizes the results of polling 319 former project participants. The questionnaire was mailed only to Japanese participants who have been out of ERATO at least one year (the average was five years). He received 168 responses. The current age of respondents was slightly over 40, most having been in their early thirties when they began their ERATO experience. Of the respondents, 165 were male and three were female. Kusunoki's objective was to analyze any differences between researchers who came from industry (company-sponsored) and those classified as independent. As we shall see, most independents actually came from universities, but because employees of Monbusho are already government employees, researchers actually had to resign from their university positions in order to accept ERATO funding. Some independents also came from industry but were categorized as independents because their company was not interested in their joining ERATO, so they resigned in order to work on an ERATO project.

Kusunoki's findings were consistent with those of the JTEC panel: the vast majority would take part in other ERATO-style research projects if given a chance. His findings also confirmed this panel's notion that most of the Japanese researchers were selected rather than recruited by open advertisement. Foreign researchers, the panel believes from its own discussions, were mostly recruited. (Presently foreign recruiting in the United States and in Europe is being handled by Dr. Alan Engel. As a former ERATO participant he is able to recruit people from abroad and discuss any concerns potential researchers might have.)

Kusunoki's report identifies interesting differences between those who are company-sponsored and independents. The company-sponsored people generally have an abrupt change in their work upon coming to ERATO. Upon leaving, they again most likely will change their work. From the panel's discussions with former participants, it was quite clear that many did not like this abrupt change, and in fact many changed their company affiliation or went to a university. Independents, on the other hand, generally found ERATO research to be somewhat in line with what they had been doing before, and statistics show that they then continued along the same line after leaving ERATO.

Kusunoki uses the words "unusual experience ... relatively discontinuous with respect to their careers as a whole" for company-sponsored researchers. This JTEC panel's findings differed somewhat since while it is true that the experience was discontinuous, the panel found numerous examples that the research done under ERATO was in fact continued at the company sponsoring the individual. In one case, Nikon, the home company of the project director, began investigating a new line of potential business — X-ray lithography — based on the results of the project.

Kusunoki's report shows that applications-oriented research did not play a great role in deciding whether to join ERATO sponsorship. Some of the companies this panel interviewed verified this observation by saying that their interest in ERATO was basically twofold: (1) to provide their people an opportunity to pursue research (viewed almost as a perquisite) and (2) to benefit from the networking that their people develop with other industrial and university researchers. On this latter point, this panel questioned them about possible concerns that such networking might lead to "loss of corporate secrets." They answered that they were aware of the potential liability, but they considered networking to be much more important and were willing to take the risk.

The level of education also differed between the independents and company-sponsored researchers. Kusunoki's study found that about 50% of the respondents had doctorates, 37% had master's degrees, and 13% had bachelor's degrees. It also found that the average stay on an ERATO project was 37 months. This was also observed by the JTEC panel. Most independent researchers already had doctorates, stayed the full five-year term of the project, and went on to work in a similar research field. Company-sponsored researchers, on the other hand, generally came for two to three years at most. Many earned their doctorates or master's degrees while on the project, and some have stated that their main interest in ERATO was to obtain an advanced degree.

The JTEC panel also observed much more anxiety from independent researchers as compared to the company-sponsored people. This observation was verified by Kusunoki. In discussions, the panel found this anxiety was even greater at the time of its September 1995 visit than it had been in earlier years since, as in the United States, fewer and fewer research positions were opening up. Ultimately, researchers have to be able to find real positions in industry, government, or universities; otherwise, a perpetual group of aging postdocs will be created — a situation that currently exists in the United States.

In general, participating in ERATO enhances career potential. The development of new scientific knowledge is career-enabling: researchers acquire skills such as developing and executing a research plan, preparing and submitting research manuscripts, and in several cases, presenting their results at scientific symposia. Most researchers in the biosciences area were postdoctoral researchers who had come from university laboratories. Some were participants from industry who usually stayed with an ERATO project for a shorter term (two or three years). If they had stayed longer, they might have lost the advantages linked to seniority. Consequently for scientists from companies, ERATO provides a training program where one or two staff scientists or engineers can learn new techniques and strengthen their skills. For those coming from universities, the ERATO project is typically a stepping stone to a university position, to an industry position (infrequently), or to another postdoctoral appointment abroad. A number of researchers resigned academic appointments at universities to join ERATO projects. Often, after the project, they relocated to new university positions, and in some specific cases, have done much better at their new locations.

IMPACT ON TECHNOLOGY AND INNOVATION

A stated goal of JRDC in creating ERATO was to support basic research. There is no pressure to create technology or to be innovative in an applied sense. So large observable impacts on technology and innovation might not be expected. Yet ERATO seems to have had its fair share of such impact, and JRDC has established the means for carrying applications forward, if they appear likely during a project, although entrepreneurial high-tech small companies are still a rarity in Japan.

One way technology transfer is encouraged is through high-tech consortia, begun by JRDC in 1986. The potential of a novel concept, for example from ERATO but not exclusively so, is investigated across a number of applications by funding a consortium of noncompeting companies, each one carrying out applied research in its own area. Funding, partially provided by JRDC, is rather modest and extends for a maximum of two years. At present, ERATO results are receiving priority in high-tech consortia activities; furthermore, a recent trend is making the program increasingly regional so small companies are becoming more important.

Industrial researchers, and particularly directors, have tended to choose projects that are more closely aligned with potential applications, and in a number of cases continued the work at their home institutions after the expiration of ERATO funding. As noted earlier (see Chapter 4), a good example is that of Dr. Yoshida's work in X-ray lithography.

IMPACT ON INDUSTRY

The benefits of having industry employees participate in an ERATO project appeared to vary enormously. In some companies, the employee gave his company little feedback about the research activities of the project. In other cases, the company took participation much more seriously, selecting the employee and the project carefully so both employee and company would benefit. In addition, the level of interaction between the employee and his home company, during his participation in the project, also appeared to vary from minimal to an ongoing discussion.

In a relatively small number of cases, company management was so impressed by the results of the project that they continued part of it, with some matching JRDC funding, in their own laboratory. A more general benefit was access, through the participating employees, to the patents generated by the ERATO project, which in a few cases totaled 30-40. Although it is a basic research program, ERATO (particularly in recent projects) has generated a large number patents as well as publications.

ERATO has also encouraged interactions among scientists from different companies. Scientists from different industrial laboratories were, often for the first time, working together, sometimes in a laboratory that was located in a third company. Surprisingly, this did not seem to create difficulties for the host company, in that proprietary information seemed to be respected by the visitors and generally the visitors were not from directly competing companies.

Comments from companies having ERATO participants were generally positive. A frequent message from industry was that ERATO projects had a very different style of research from industry, where research is carried out by teams that are rather tightly organized. A few quotes illustrating this industry view of the ERATO research style, recollected from notes and memory, are as follows: "A two- or three-year stay [on an ERATO project] is best, otherwise the employee becomes very scientifically oriented." "ERATO is strange, in that it has so little preplanning and control of people and budgets." "ERATO introduced individualism into the research and development culture." "ERATO introduced flexibility, which is good." "I learned a 'do something new' attitude from ERATO." "Team members from universities needed training in the industrial research style." "It gave me experience outside [my company], which has a very conservative style." These quotes indicate that the effects of ERATO's research style were on everyone's mind.

A theme that emerged during this visit, in contrast to the 1988 study, concerns ERATO's role in the support of basic research in industry in Japan. During the period between 1985 and 1990, the robust economy allowed Japanese companies to expand their research programs to include an increasing fraction for basic research. In discussions with high-level managers at NTT, NEC, Hitachi and other companies, the JTEC panel learned that the support for basic research in industry is still seen as very desirable. This is in stark contrast to the United States today. In fact these discussions were reminiscent of the United States in the 1960s and early 1970s. (It was almost a shock to hear the phrase "basic research" used openly in a corporate dining room.) But the downturn in the Japanese economy has caused increasing concern, also expressed in these discussions, that companies will not be able to support that level of basic research without the help of government funding. On a number of occasions, ERATO and other government funding was cited as a way to retain top researchers during these more difficult times and as a way to share the costs of basic research.

Interestingly, no small companies have been created as a result of ERATO projects. This, of course, is not specific to ERATO, as very few companies are created in such a way in Japan. Given the unique nature of ERATO projects, perhaps eventually this will change also.

ERATO AS A POSTDOCTORAL PROGRAM

As noted above, for the majority of the bioscience projects, ERATO is a postdoctoral program. New Ph.D.s gain valuable experience that enables them to compete for permanent positions in academia or industry. It is thus very attractive to young, ambitious scientists. This panel was left with the impression that positions in ERATO, from project director to researcher, were highly sought. Indeed, the panel interacted with a few individuals who sought future project directorships. Since securing ERATO positions is very competitive, a clear perception was that the ERATO program has many good points: increased funding, increased interaction with leading scientists, increased visibility, and better facilities. There are a few negative points, as noted earlier: there may be insufficient time in some cases to develop solid research results; projects that are more applied than basic in nature may be proposed and selected; and the continuation of projects is more difficult than under other funding programs, or may even be impossible. If one does not define a research plan with these constraints in mind, an individual could be left in an uncomfortable position when looking for employment beyond ERATO. Some ERATO scientists have moved from one project to another, in most cases because they excelled and were sought by new project directors, but in a few cases because they were helped by ERATO administration.

GENDER BALANCE AMONG ERATO RESEARCHERS

Women participants are infrequent. There is still very limited opportunity in Japan for women in science. In one project, Okayama Cell Switching, there were proportionally more women. This project was unusual. There was no rigid "group leader" structure. All scientists were equal and knew that their success would be based on their work. This structure was likely due to the influence of the project director, who had spent a significant period of his career at the U.S. National Institutes of Health (NIH). (Even the laboratory layout, including equipment and desk space, was similar to the labs at NIH.)

At this project the members of this panel were very impressed with Dr. Ishihara, who summarized the overall project for the group. She is the only female so far who has taken a leading role in an ERATO project. Several other ERATO projects include women, but in most of them the women serve primarily as technicians. The panel's impression is that women scientists in Japan feel there was little opportunity for growth beyond postdoctoral positions like those in ERATO projects, so presumably they would most likely need to go abroad to continue their scientific careers.

COMPARISON WITH NSF'S ENGINEERING RESEARCH CENTER PROGRAM

An intrinsic value of the ERATO project is training postdoctors for team-oriented exploratory research. The mixture of industrial researchers and academic researchers stimulates new interactions in research strategies and thought. In contrast to the postdoctoral system in the United States, ERATO projects provide postdoctors with sufficient funds and equipment for a period of five years. Thus, postdoctors have opportunities to help build a research facility from scratch as well as participate in the organization of a research team. The research atmosphere of the ERATO project is challenging and stimulating, key factors in attracting postdoctors to ERATO projects.

ERATO heavily emphasizes publications and is interested in patents. Typically 25-50 publications and 20-30 patents are produced from each ERATO project during its five-year existence. Furthermore, patents and publications are key criteria for evaluating ERATO's outcomes.

In addition, ERATO projects are heavily dependent on instruments and equipment. As a result, data analysis and evaluation are two major research activities across all ERATO projects. It is fair to say that ERATO projects are more experiment-oriented than theory-oriented.

In general, the first year of an ERATO project is mostly spent acquiring research instruments and developing research facilities. The major part of the project director's time is spent recruiting researchers from academia and industry. Undergraduate and graduate students normally are not involved in ERATO projects, thus there is no emphasis on curricular development or on the educational system. As a result, ERATO has had little impact on Japanese academic infrastructure.

The Engineering Research Centers (ERC) program in the United States was initiated by NSF in 1985 with the goal of addressing both intellectual and academic infrastructure challenges. ERCs and their industrial partners jointly develop strategic research planning for fundamental research through cross-disciplinary teams. A long-term goal of the ERC program has been to integrate research and alternative educational cultures for both undergraduates and graduates. Postdoctors are involved in the ERCs to develop test beds for proof-of-concept research. ERCs provide postdoctors with opportunities to develop leadership skills for seeking academic and industrial career opportunities. Throughout these efforts the ERCs have produced a new cadre of academic leaders and managers in addition to advancing knowledge in the fields of engineering. Curricular reform is as important as the patents and publications for researchers within ERCs. Most ERCs base the development of their research teams on existing research facilities and equipment by leveraging funding from NSF and from industry. This is completely opposite from ERATO, where staff, facilities, and equipment are all new.

This latter point illustrates two key differences between ERATO and the ERC program:

1. In the U.S. program, industry is expected to pay its way (and its people) in joint projects. In the ERATO model, industry scientists are paid directly by ERATO to join in the project — and use ERATO facilities as the focus of their ERATO work, though they may also conduct some work in their company labs.
2. In the United States, the programs are continued for a long time, and staff and laboratories are built up and are in need of funding. In contrast, an ERATO project is set up for a specific purpose and then terminated at the end of the five-year term. Thus the director and the ERATO staff spend no time in continuously writing proposals or participating in reviews to ensure funding for their research.

CHAPTER 7

PRESTO PROJECT ANALYSIS

Tamami Kusuda

INTRODUCTION

Like the Exploratory Research for Advanced Technology (ERATO) program, the Precursory Research for Embryonic Science and Technology (PRESTO) program is a social experiment by the Japanese government to see whether it is possible, given sufficient opportunities, abundant financial support, and technological resources, to stimulate resourceful individual researchers to explore new areas of science and technology on Japanese soil.

The significance of this undertaking must be viewed in the context of the traditional Japanese research environment. As has been mentioned in previous sections of this report, young Japanese researchers in universities and in national research institutes *(Kokken)*, and in many respects company research institutes, have never had opportunities to explore new and innovative ideas of their own unless these were directly in line with the overall research goals of superiors or parent organizations. Research funding in Japan is directly and tightly controlled and very much limited depending upon the interests of superiors. It is well known in the *Koza* system of the universities, that anyone under the rank of *jokyoju* (associate professor) is essentially a serf to his *kyoju* (professor). It has been practically impossible to convince a *kyoju* or a *shitsucho* (principal researcher) to divert some of the research funds to pursue projects originated by the research staff. This is especially true since the total research support that a professor receives from the Ministry of Education (Monbusho) for basic research is also limited. The situation has been acute in the bioscience area, and it is the reason why many talented Japanese researchers are found in overseas laboratories like the National Institutes of Health and the Scripps Oceanographic Laboratory in the United States, or at universities like Cambridge University in the United

Kingdom. In fact, many PRESTO researchers are returnees from these foreign research institutions.

Similar situations may have arisen in the United States, given the current decline of research freedom resulting from the general shortage of research funds, however the degree of freedom and opportunity and financial support that the U.S. researchers enjoy is vastly superior to Japan’s. Clearly there is a larger quantity of innovative basic research coming out of U.S. universities and national laboratories than from the Japanese universities and *Kokken*. Many senior officials of the Science and Technology Agency (STA), especially the senior officials of the Research Development Corporation of Japan (JRDC), like Mr. Genya Chiba, who have worked in U.S. laboratories, have long recognized the Japanese problems and have been examining ways to change the traditional methods of supporting Japanese basic research.

In addition, the senior management of JRDC wanted to change the commonly held notion of "Japan's technology free ride," the reputation Japanese company researchers have of taking advantage of U.S. generated ideas and/or technology for quick commercialization. By talking to young researchers, JRDC has recognized that many innovative ideas remain buried in Japan because its suffocating academic and research structure obstructs the germination of these new ideas. JRDC management wanted to show the world that Japan can contribute new ideas.

PRESTO VS. ERATO

In 1981 JRDC established the ERATO system in which promising research themes and well-established senior researchers heading these projects were first identified. (It should be noted that since 1986, ERATO has shifted from the selection of well-established senior researchers as heads to the selection of emerging young researchers who may become well-established as the result of their ERATO projects.) The senior researchers were then asked to form research teams to explore several innovative ideas under these specific research themes. In an ERATO project, the project director has complete freedom to choose his group through one-on-one interviews with promising individual researchers who are willing to work on his project. ERATO is a team-based research activity to explore creative ideas. It has been a resounding success in terms of generating new information and training a new breed of young research leaders. Yet JRDC officials noted that it is not suitable for nurturing individual, independent-minded researchers who like to pursue their own ideas by themselves and who may not fit into a group-oriented research environment like ERATO’s.

In l991 JRDC initiated a new program for individual researchers called “*Kojin Kenkyu-Sakigake 21*” which is known as PRESTO in English, although it is not the direct translation, to promote pioneering and embryonic research for the 21st century. The most conspicuous difference between ERATO and PRESTO is their structures. While an

ERATO project is conducted in groups headed by a group leader under the general supervision of the project director usually at the same site, PRESTO researchers work alone, independently, at a place of their choice.

Unlike ERATO, PRESTO is not a program to train young researchers. Instead, it is used as a haven for professional postdoctors and for ERATO graduates to continue their research.

IMPLEMENTATION OF PRESTO

JRDC first identifies an area of research, develops a broad, general work statement of the specific program, and appoints its mentor, based upon painstaking consultations with many researchers and research communities in selected areas. The mentor is then asked to choose eight or nine “associate mentors” from academia, industry, and government. This group then constitutes the researcher selection committee which reviews the applications which have been openly solicited through announcements in about 30 scientific journals and through the Internet. (JRDC has an attractive World Wide Web homepage at URL=http://www.jrdc.go.jp).

Most striking is the brevity of applications or proposals that JRDC requires for PRESTO grant applications. Compared to the bulky and very comprehensive research proposals that U.S. government funding agencies such as NSF receive, an application for PRESTO grants is simplicity itself. It is a brief document which includes biographical data, a technical proposal of up to five pages, a desired research site, a list of required equipment including the list of equipment which might already be available for PRESTO research, the type of participation (full- or part-time), support from other organizations, references, publications during the previous five years, and specific requests if there are any. The application deadline is usually around June.

Each proposal is reviewed by two members of the selection committee to decide whether it merits further consideration. This screening process results in a list of twice as many candidates as there are openings for each research area for that year. These candidates are then interviewed by a committee consisting of mentors, associate mentors, and JRDC management for 10-30 minutes before final selections are made and the chosen researchers are notified.

For each program, JRDC requested approval of funds for 24 research projects in each of three areas in l991: “Structure and Functional Property” (Mentor: Prof. Kazutake Kora, president of the Tsukuba Institute of Science and Technology), “Light and Material” (Mentor: Prof. Ken-ichi Honda of the Tokyo Institute of Polytechnics), and “Cell and Information” (Mentor: Prof. Fumio Osawa of the Aichi Institute of Technology).

Three more programs were added in l994: “Inheritance and Variation” (Mentor: Dr. Kumao Toyoshima of the Osaka Medical Center for Cancer and Cardiovascular Diseases), “Intelligence and Synthesis” (Mentor: Prof. Ryoji Suzuki of the Kanazawa

Institute of Technology), and “Fields and Reaction” (Mentor: Prof. Akio Yoshimori of the Okayama University of Science).

It should be noted that these titles clearly imply the interdisciplinary nature of PRESTO research. For example, the "Cell and Information" program seeks research covering the interaction of cell biology and information science, i.e., from subjects broadly scattered in the two-dimensional plane defined by two coordinate axes representing "cell biology" and "information science."

JRDC’s budgetary strategy means that JRDC has decided not to select all twenty-four researchers at once. For example, in l991 only twelve researchers were chosen for each of the three research areas mentioned above, which have been followed by four in l992 and eight in l993. For each of the research areas, the committee received approximately ten to twenty times more proposals than the number allotted for funding, and this competition rate has been steadily increasing. Table 7.1 is an overview of the number of grant applicants and recipients in the various research areas in recent years.

Table 7.1
Applications and Success Rate of PRESTO Proposals
1991-1995

Research Area	Number of Applicants	Number of Grant Recipients
Structure and Functional Property	246	24
Light and Material	193	24
Cell and Information	466	24
Inheritance and Variation	313	20
Intelligence and Synthesis	192	20
Fields and Reactions	305	20
Total as of Sept. 1995	**1715**	**132**

Source: JRDC

PRIVILEGES OF PRESTO RESEARCHERS

When selected, each individual PRESTO researcher receives ¥30 million (approximately $300,000) in research funds over the next three years in addition to their salary, laboratory rental, insurance, and administrative costs, which are borne by JRDC (the total budget for each project averages $600,000). For a typical Japanese researcher, a PRESTO budget is ten times larger than an otherwise normal research allowance. For three years, he can pursue the research on his own initiative, unfettered by tradition-bound bureaucratic constraints, free to travel to attend conferences overseas, with a substantial amount of funds. This is very attractive indeed, even when compared to U.S. standards for single individual grants given to university faculty who hold teaching positions.

The principal qualifications for the application are that the researcher reside in Japan and that he be able to conduct research in a Japanese environment. No consideration is given to age, sex, nationality, religion, beliefs, parent organization, or educational background. Although most PRESTO researchers appear to be in their late thirties, the panel was told that some are over sixty.

Unlike their counterparts in U.S. universities, Japanese university researchers, even assistants, instructors, and assistant professors, are tenured employees of the universities. Many stay at the same institution, getting old without attaining the coveted titles of *kyoju* (professor) and *jokyoju* (associate professor). Many researchers, under the rank of *jokyoju* in the universities, who have wanted to pursue their own area of research interest but were long limited by their superiors, have even proposed to resign from their tenured positions to accept PRESTO assignments. They are willing to move out of their familiar research environments into completely new sites, thus starting from scratch to build entirely new laboratories.

Some industry researchers, hired during the bubble days of the Japanese economy when many companies set up research laboratories, mostly for cosmetic purposes, to encourage any basic research remotely connected to company products, have been feeling a dramatic cooling of company interest in their research in the recent economic recession. They have jumped at the opportunity to continue their research offered by PRESTO. The situation is even true in some national research institutes where research focus has shifted.

But the majority of proposals from universities and national research institutes are for researchers to explore, on a part-time basis, new areas of research either by improving their existing research capability or by adding new equipment such as mass spectrometers, scanning tunneling microscopes (STMs), atomic force microscopes (AFMs), micro-beam reflective high energy electron diffraction (μRHEED) systems, or polymerase chain reaction (PCR) systems, each costing as much as $100,000, well beyond traditional funding levels.

In order to facilitate the program and assist these selected researchers, JRDC sets up a research field office consisting of a research manager, an administrative manager, and clerical staff, the expense of which is supported separately by JRDC. The specific function of the field office is to assist in procuring laboratory equipment, solving space rental problems, submitting patent applications, organizing meetings and the annual plenary conventions, and making travel plans.

While the mentor plays an important role — providing researchers with general scientific guidance as well as indirect or psychological assistance, visiting each of them once or twice a year for face-to-face meetings — the most vital role is played by the research manager. He maintains constant, very close touch with researchers via visits, telephone, and e-mail. In fact many PRESTO researchers have attributed the success of their research to good research managers. These research managers are usually retired personnel directors of large corporations who are very relaxed and kind, intimately familiar with the day-to-day problems of researchers.

OBSERVATIONS

PRESTO scientists have been very productive. According to data provided by JRDC as of September l995, the total number of researchers-participants in six PRESTO programs is 132. They have produced 328 technical papers (mostly in international journals) and 41 patent applications.

Of these 132 researchers, 14 (5 under "Structure and Functional Property, 4 under "Light and Materials," 4 under "Cell and Information," and 1 under "Fields and Reactions") were interviewed by a member of the JTEC panel, and 11 of their laboratories were visited. Their laboratories are usually small by U.S. standards, covering approximately 400 square feet of floor area, congested with standard lab furniture and equipment, including many shiny instruments, wall-high bookshelves, and computers and peripherals that scarcely leave room to walk about. Yet compared to typical Japanese university laboratories, all PRESTO laboratories are cleaner, better equipped, and more spacious.

The titles of the many PRESTO research projects that this JTEC member visited are basic — "Interaction Dynamics of Excited States of a Highly Condensed Dispersion System," "Signal Transduction Mediated by Tyrosine Kinases," "Ion Selectivity and Pumping Mechanisms of Bacterial Rhodopsins," the “Molecular Nature of 'Weak' Cell-Cell Interaction during Development," "Functional Analysis of Flagellar Motor." The names may not excite many U.S. research managers or technology gatekeepers since they will see no immediate applications; however, the work may be more significant than the titles might imply to a layman.

JTEC has found all PRESTO researchers to be very excited, enthusiastic and deeply appreciative of the opportunities provided them. They are generally very happy except for some difficulties in procuring equipment and hiring assistants. What they like most in PRESTO are: (1) the ease of preparing a proposal to obtain a significant sum of research funds; (2) the freedom of research, procurement, publication, travel, and communication; (3) no formal review process; (4) very little paperwork; and (5) solid assistance from the research field office for miscellaneous chores involving laboratory maintenance, procurement, patents, and so on.

One of the major complaints is the manner in which research funds are dispensed. Instead of letting researchers have complete freedom to use their $300,000, JRDC has limited expenses to $100,000 per year, which has prohibited researchers from procuring expensive items at the outset of the project. Relaxation of this restriction could affect the type of research and the amount of research actually accomplished.

The majority felt that the research period should be extended beyond three years since at least one year is needed before a laboratory can become productive.

Although PRESTO is designed for individual researchers, a talented and ambitious researcher needs assistant(s) who can help assemble laboratory apparatus, prepare specimens, run computer programs, and take data when the researcher is attending a conference. Many researchers who lack affiliation with a university (where student assistants are available) complained about the difficulties in hiring suitable laboratory assistants. There are not many qualified laboratory assistants or technicians available in Japan who are willing to work for low wages for a period of three years. If such a person were available, he would be very expensive. Moreover, the researcher has to worry about how to discharge the assistant when his services are no longer needed.

Types of PRESTO Researchers

The JTEC review found that there are four types of PRESTO researchers.

The first group consists of those part-time researchers who use the PRESTO funds to enhance their ongoing research programs or to start new laboratories, and whose PRESTO work is in harmony with the activities of their parent organizations, especially in those whose superiors encouraged them to apply for PRESTO support from the outset. These researchers have succeeded in producing tangible results in terms of publications and patents or else have improved the images of the parent organizations.

The most successful example has been Associate Professor Shuji Hasegawa of the University of Tokyo, perhaps one of the happiest and luckiest of the PRESTO researchers. PRESTO has provided a tremendous opportunity for his professional growth: he has received career advancement, more equipment, an improved laboratory, and a dramatic increase in research funding.

Prior to PRESTO, Prof. Hasegawa was a struggling *joshu* (research associate) in a crowded laboratory assisting Professor S. Ino on semiconductor surface structure. Hasegawa proposed to PRESTO to study the surface structure and conductance of epitaxially grown films of gold (Ag) and silver (Au) on silicon (Si) substrate. With PRESTO funding he was able to acquire a new µRHEED system for $50,000 and a monochromatic light illumination system for $100,000. With this newly acquired equipment he was able to show a strong dependence of the conductance on the substrate-surface and epitaxial growth styles at the early stages of Ag and Au deposition on Si (111) surfaces at room temperature. When the PRESTO project was completed, he was promoted to associate professor, was allowed to establish his own laboratory, and received funding of approximately $1 million from the Monbusho to equip his laboratory with an STM and two µRHEED systems. The

Hasegawa laboratory is currently staffed by a graduate student and four undergraduate students. The recent government decision to boost science and technology research at the university level has created a situation where MITI’s New Energy Development Organization (NEDO) program is offering him $2 million to expand his laboratory capability further so that the research on surface structure and conductance can lead to improved semiconductor circuits.

Although not as spectacular as Hasegawa, six of the fourteen PRESTO researchers JTEC interviewed fall into this category.

The second group is made up of independent full-time researchers who have no affiliations or who have resigned from their parent organizations to pursue their own research interests without giving due consideration to the immediate applications of their findings. After all, these are precisely the types of researchers for whom the PRESTO program was intended. Many of the researchers have gone through previous postdoctoral programs, or even ERATO, and have enjoyed the freedom and generous funding afforded by PRESTO. Yet they have begun to worry about what to do when their PRESTO project is completed. They want university positions but are afraid they are already overqualified for many available positions and know that to assume a professorship in a Japanese university from the outside is very difficult. They also know that U.S. university and research institutions are short of research funds, and that competition is very high because of the overabundance of researchers created during the 1970s and 1980s. They consider Japan still to be the best place to find research opportunities, especially in view of the recent special economic stimulus package of $300 million approved by the Ministry of Finance to conduct basic research at the Monbusho, at STA, particularly under JRDC, and at MITI under its NEDO program.

The third group consists of very strong-minded and articulate individuals who are convinced that their research will lead to other programs or to future industrial support for good applications. They assume PRESTO research will enhance that potential. These are very resourceful individuals, full of entrepreneurial spirit even in circumventing JRDC rules on procurement, on hiring, and on getting collaborative research from the outside. They are also very enthusiastic, and their results and activities are already well publicized in Japanese news media.

Associate Professor Gerhard Fasol represents the epitome of this type of researcher. He is an extremely talented, energetic, and prolific 40-year-old researcher at the Institute of Industrial Science (IIS) of the University of Tokyo, a native of Austria who has come to IIS by way of the Max Planck Institute, Cambridge University, and Hitachi's Cambridge Laboratory. He had significant and impressive accomplishments before PRESTO. He has been very productive (80 papers and four patent applications) and is the second foreign researcher that PRESTO has ever employed (the first one being Ronald O. Scott, who completed a PRESTO project on the "Statistical Properties of Biological Photoluminescence Measurement and Analysis" and has been with the University of

Arkansas since PRESTO). Foreign researchers are accepted into PRESTO as long as they can conduct research in Japan and are able to work in a Japanese research environment (language capability is a major factor).

Prior to joining PRESTO, Fasol had an impressive research record. He was the laboratory manager at the Hitachi Cambridge Laboratory before joining IIS. At the Cavendish Laboratory of Cambridge University, he led a team of researchers involved in the construction of a Raman laboratory ($400,000) and a femtosecond laboratory under a grant from the Science and Engineering Research Council (SERC) of the United Kingdom. At these research organizations he was able to supervise several research assistants and had complete freedom to purchase any equipment as long as he could manage within his allotted grant. But he had to work hard to get the grant by spending considerable time writing the proposal. Hitachi offered him the job of laboratory manager at its U.K. lab, an offer attractive enough for Fasol to quit prestigious Cambridge. He left Hitachi when the company venture did not work out as promised. At IIS, he discovered the spin polarization effect in semiconductor microstructure resulting from an analysis of electron-electron scattering and proposed a solution to the polarization control problem of surface-emitting microcavity lasers. He invented a new class of devices based on semiconductor/magnetic atomically thin superlattice in collaboration with M. Tanaka of the department of electrical engineering at the University of Tokyo. Based on these proposals, Fasol applied to PRESTO in order to supplement his funding from IIS (the University of Tokyo, l994 Shinsei-Kenkyu project) to develop new magneto-electronic and magneto-optic devices. The specific objective is the design and fabrication of these devices using CAD, optical lithography, selective etching, and a new simulation method. (Already he has made four patent applications.)

Dr. Fasol has been extremely happy that he can pursue independent research in the Japanese environment under PRESTO and is very optimistic about the future even when PRESTO is finished. He plans to set up a research laboratory in Japan where he can commercialize the results of his PRESTO research and use his experience in several European countries and Japan to help further technological cooperation among European, U.S., and Japanese industries.

The last group of PRESTO researchers consists of industrial researchers who were hired during the bubble days of the Japanese economy to pursue innovative research, and then found company support for basic research suddenly declining because of Japan’s recent economic difficulties. PRESTO has been a salvation for them to continue basic research in a rather depressed company research environment. Unless they shift their research themes to make them more in line with company goals, these researchers see no future in their parent organizations after PRESTO and worry privately about their futures.

Another small group of researchers JTEC has not interviewed are older, retired researchers who have innovative ideas which they have had no opportunity to pursue as long as they were working for companies or at national laboratories. Generous retirement funds from their previous employers allow them to be free from worry in pursuing research beyond PRESTO. They are happily devoting their energy to their investigations.

Emphasis on Experimental Research

As far as JTEC's interviews of researchers and published literature indicate, PRESTO projects appear to emphasize experimental research. Purely theoretical research involving advanced mathematical analyses, computer simulation, or large-scale software development is not apparent in the program listing. Of course, there are cases in which advanced software was developed during this experimental research. A good example is the development of a simulation program for quantum transport in semiconductor microstructures by Fasol, which was awarded a prize in the Japanese Computer Visualization Contest for its graphical presentation. We do not know whether this emphasis on experimental research is by design or due to the structural orientation of the JRDC philosophy.

Communication

Most researchers JTEC interviewed have access to the Internet and have a good use of on-line databases and e-mail. According to Dr. Ishizaka, researchers engaged in similar or related fields constantly get in touch with each other through e-mail to form a virtual laboratory consisting of a group of approximately ten people. In addition, people belonging to this virtual group even get together once or twice a year at a resort hotel for a two nights/three-day type camp workshop to make informal presentations. Since this is a meeting of researchers who are strongly bonded and share common interests and experiences, discussions that take place during these overnighters are so intense, frank, and productive that all participants come out refreshed, sometimes with new ideas. Professor Kohra, the mentor for "Structure and Functional Property," says, "The communication among researchers in [his program] is much more than expected. Their casual meetings strongly contrast with formal academic meetings controlled by university professors." This comment indicates a strong need for isolated individual researchers to communicate with each other.

Use of Computers

All laboratories visited are equipped with advanced workstations or high-power PCs loaded with advanced software for data analysis and connected to experimental systems as well as to graphic display terminals for preparing technical papers and colorful demonstration exhibits. All researchers appear to be thoroughly familiar with the use of advanced software commonly found in the United States.

Evaluation

Anyone familiar with the U.S. research funding system will be dumbfounded when told that PRESTO research is never formally evaluated. Except for the quarterly progress reports and encouragement of publication in international journals, there is no formal evaluation system for PRESTO projects. In fact, Chiba is adamant that premature evaluation of embryonic research by outsiders who do not fully comprehend the particular subject does more harm than good. Many researchers have never even prepared project summaries in English, although every researcher has prepared attractive posters to describe the objective, scope, and progress of the research to be explained to visitors. PRESTO researchers are completely free to explore whatever they are doing. They do not have to worry about being criticized or proving that PRESTO money is well spent.

Ishizaka, for example, spent an entire three years and nearly $400,000 of PRESTO funds assisted by partial support from his parent company, Hitachi, on assembling a special-purpose µRHEED system for an STM investigation of semiconductor crystal growth during the epitaxial process. Although he produced only two papers under PRESTO, JRDC made an exception and allowed him to take his µRHEED system with him for an additional two years in order to continue his research at the prestigious Joint Research for Atom Technology laboratory located within the National Institute for Advanced Interdisciplinary Research in Tsukuba, Japan’s most modern research center for atom technology based on the use of the STM. Ishizaka discovered that the transition temperature between high- and low-temperature growth models in molecular beam epitaxial systems is equal to one-half of the melting point of semiconductors. His work is well publicized, and the µRHEED system he assembled during his PRESTO research is expected to provide microstructural verification of his theory at crystal surfaces of many different semiconductors.

PRESTO Spin-Offs

Since PRESTO is new, started only four years ago, it is difficult to find tangible technical spin-offs to credit to the projects, except that some universities and national research institutes have become better equipped and that there are potentially important technologies in the applications of electron spin devices, bacteriorhodopsin films, flagellar motors, nanotechnology, and so on. It all depends on whether these research results will be discovered by industry in the near future and on how PRESTO researchers will fare after their projects are over. The databases and networks developed during the projects should play a vital role.

The short-term spin-offs may be more in the area of intangible benefits. PRESTO gives talented individual researchers the joys and frustrations of conducting research all by themselves under a finite timeframe. There will be a number of innovative researchers who have become toughened to withstand and survive the harsh economic realities of independent research. They are taught to become self-reliant in building up new laboratories, much more self-reliant than in the more traditional laboratory environment. They have been forced to worry about finding sponsors for their research in their post-PRESTO period.

The close communication networks developed among talented, innovative, and entrepreneurial researchers from different fields of science and technology appear to be strong and long-lasting and should definitely provide ample opportunities for future collaboration. These networks are expected to play a vital role for some innovative research finding its way into important technical innovations.

CONCLUSIONS

The JTEC team came to Japan to learn the impact as well as the effectiveness of social experiments like PRESTO in terms of the following areas:

Generating and Nurturing Embryonic Research

PRESTO appears to be very effective in identifying numerous innovative research topics with exotic titles. PRESTO research has resulted in finding basic functions of materials, genetic and biochemical behaviors of cells, mechanisms of bioluminescence and bacterial motion, ion pumping, atomic scale structure of semiconductors, spin-polarized electron behavior, and so on. All researchers are very enthusiastic, extolling the uniqueness or innovation of their research. They have produced numerous papers in international journals, as well as an impressive number of patents.

Enhancing Research Opportunities

Some mechanism might be created to continue or expand the embryonic research germinated during PRESTO. Knowledge acquired, techniques developed, and instruments constructed during this research must be utilized by other and/or future researchers.

Improving Future Opportunities for Individual Researchers

There is no question that the majority of researchers have used PRESTO for their professional and/or academic advancement. Yet some researchers risked lifelong employment security for PRESTO with its somewhat uncertain future. They moved their families to new locations where they have had to adapt to new environments. The opportunities will depend upon Japan's economic situation at the time their PRESTO projects near completion. Although one hopes every PRESTO researcher will find a suitable opportunity to keep pursuing his or her research, there is no guarantee. Lifetime employment and the seniority system is anathema to the very concept of PRESTO. Yet one cannot help but be sensitive to what will happen to the researchers who eventually lose their productive capability.

Improving the Technological Competitiveness of Parent Organizations

Through the innovative proposals to combine the existing capabilities and research structures with refreshing research ideas, many universities and national labs definitely have improved their research capabilities by acquiring equipment otherwise too expensive for them to buy alone. These laboratories should be able to start new programs to further improve their research potential for securing future funding opportunities.

Improving Scientific and Technical Databases to be Useful in Future

PRESTO projects have generated a great many useful data: data for crystal structures, genetic manipulation, material constants, experimental techniques, cell-cell interaction, learning mechanisms, brain functions, protein chemistry, and others. These data must be critically evaluated and stored in electronic databases readily accessible to future researchers. Otherwise the impact of the entire PRESTO effort will be diminished.

ACKNOWLEDGMENTS

The JTEC panel wishes to extend sincere appreciation to all PRESTO researchers who generously spent valuable time showing their laboratories and responding to many questions. Special appreciation must go to Mr. Kenji Kaneko of JRDC for preparing valuable information on PRESTO's accomplishments and for making appointments and assisting with travel for interviews.

CHAPTER 8

IMPLICATIONS FOR THE UNITED STATES

William Bentley
Rita Colwell
George Gamota
Leo Young

OVERVIEW

The attractiveness of the ERATO and to some extent the PRESTO programs stems from the amount and duration of funding and from flexibility. Additionally, these programs require only short research proposals.

ERATO projects differ from U.S. research projects funded by federal agencies in at least two ways: the complete freedom given to a project leader to carry on a large research project without review or interference for a relatively long period of time (five years), and the ability for a team of interdisciplinary researchers from universities, industry, and national labs to work together under one roof with responsibility only to ERATO. Since not all research projects can be like that, then how many should be? If some projects should be conducted in this or a similar manner, then how much funding would be appropriate? How should the topics and the leaders be selected?

These questions do not lend themselves to easy answers, but ERATO deals with the last question in an interesting way. ERATO attempts to attract top-quality researchers by actively searching out top-quality leaders. Not only must such a leader be a scientist or engineer with a proven record in research, but he (or she) must also be able to communicate and inspire others. To find such a person, ERATO does not advertise U.S.-fashion but goes about (somewhat undemocratically by U.S. standards) seeking out such persons and going after them, for years if necessary, and inviting them to submit ideas (short proposals). ERATO officials say that they find these leaders by taking a kind of informal survey among young researchers (such as might have participated in previous ERATO projects). It was not made clear to us just how this is done; rather we got the impression that it is a deliberately informal process. ERATO officials then invite unusual or high-risk proposals from these potential project directors. The one hundred or so short proposals received are narrowed down to about twenty by the JRDC staff. The authors are then invited for an interview with an advisory council which includes outside experts. The experts are given the opportunity to interview but do not pick the winners, since in most cases the winners are selected by JRDC. Some experts expressed a desire to be able to select the interviewees from a larger pool of candidates. This process is repeated annually.

ERATO projects are organized into three groups that are sometimes closely and sometimes loosely coupled, depending on the project director. Research is typically performed in three locations, and these may be quite far apart. As the project leader is usually in great demand, he (we never heard a “she”) is always part-time on the project, devoting perhaps 10% or 20% of his time to it. He must give direction and cohesiveness to the project, but he also needs to select a good deputy to manage the science or engineering efforts on a day-to-day basis and he must have a dependable financial officer. The project leader is responsible for hiring these two critical people and the other dozen or more key personnel. As it may take one year, sometimes more, to find and rent a suitable location and fix it up for research, and furthermore, as much of the fifth and last year is taken up by winding down research, disposing of equipment, preparing to move out of the rented facility, and by job hunting for many (it could be one half) of the team members, it follows that the most productive years may be limited to three out of five. Thus ERATO projects are not only temporary research efforts, but, in contrast with U.S. projects, are also temporary stand-alone entities, not embedded in or reporting to organizations like universities or industrial corporations that existed before the project and continue after it is terminated.

ERATO was designed to allow Japanese researchers to work under conditions more like those in the United States, but it does have unique features that vary from the United States (i.e., challenging conditions without job security). Its success is evidenced by the fact that its budget will be increased as part of an economic stimulus package to revive the country's economy. Although designed to meet Japanese conditions and shortcomings in its research programs, the ERATO model has lessons to teach the United States. Here are some suggestions:

Reduce Proposal Writing Efforts

Research is recognized as an investment in the country's future, not as an entitlement. Such investment opportunities abound, but funds are limited. In the United States the frantic need to compete has caused U.S. researchers to spend more and more time on proposal writing, time that is taken away from the research itself. In contrast, in Japan historically there has been too little competition for research funding, a situation that ERATO has gone some way to correct. To alleviate burdensome competition in the United States, some federal agencies are limiting proposal lengths, but due to shrinking research budgets, the competition has become fierce. Thus the two systems are converging in a small way. Other measures could be taken; for example, very short pre-proposals could be used to select qualified researchers, somewhat along the lines of ERATO.

Appoint Part-time Project Leaders

An intriguing possibility is the selection of outstanding, part-time leaders, particularly from industry, to direct and guide even very large research projects. These leaders would have to be very carefully selected and provided with competent full-time deputies to manage the project. University restrictions on the use of outside help for thesis directors and part-time research faculty would have to be eased to stimulate this possibility.

Encourage More Risk-Taking

The idea of giving a few large projects to strong independent leaders without review or interference from the funding agency for a relatively long period (like ERATO's five years) would be novel in the United States, where accountability is emphasized. Accountability favors caution over risk-taking. It is appropriate where quantitative measures apply to predictable outcomes at the conclusion of the work, but progress in research depends on risk-taking; "safe" research that always pans out is not necessarily good research. Success may not be judged for years to come. Risk-taking by responsible, qualified individuals should not only be allowed, it should be encouraged. That is what ERATO aims to do. It does so by limiting the ERATO project leader's accountability to JRDC to fiscal matters, while his scientific "accountability" is left to his peers through his publications and their assessment of his scientific contributions.

Cast a Wider Net

Develop multidisciplinary groups from diverse fields, even when they seem far apart (e.g., medicine and engineering) to cross-fertilize ideas and to form networking that may be productive for a lifetime. (Such groups may be thought of as a form of lateral technology transfer.) The same trend — the formation of multidisciplinary teams from ever more diverse fields — has also been purported to be encouraged in the United States, especially by government agencies, but very few projects actually exist. This would seem to be particularly worthwhile when it involves advanced information technologies (software and communications), in which the United States leads the world.

Create a Real Industry-University-Government Team

Create a few interdisciplinary research projects composed of researchers from industry, universities, and government working together under one umbrella for a specified time period. The umbrella organization could be a professional society or consortium to assure that no single member organization would attempt to control the project and steer it in its own direction. All researchers would be employed for the duration of the project by the umbrella organization. Upon completion, the projects would be disbanded. Liberal unpaid leave policies or sabbaticals would be needed from researchers' home institutions to ensure the success of such a program.

OPPORTUNITIES TO PROMOTE SCIENTIFIC COLLABORATION

At least two project directors specifically noted the need to incorporate Western research philosophy and thought into the Japanese scientific community. This would expose Japanese scientists to individuals who more routinely ask fundamental questions in their research. As noted previously, ERATO provides complete flexibility in research direction, yet the research questions being asked in many labs were not basic but targeted questions. By increasing the interaction with Western labs, an exchange of research philosophy could be enhanced. Thus, perhaps ERATO projects could involve more partnerships with U.S. laboratories.

The JTEC panelists found Japanese officials and researchers connected with ERATO projects very open and genuinely interested in cooperating with foreign researchers, especially from the United States. This should not surprise anyone, as it benefits Japanese science. But such cooperation works both ways, benefiting all nationals who participate, and U.S. scientists should be encouraged to participate. The flow of scientists in and out of Japan is fairly well balanced overall, but unbalanced in detail; i.e., overall about as many Japanese scientists go abroad to do research as foreign scientists come to Japan, but the exchange by country is unbalanced. More Japanese come to the United States than the other way around, whereas more scientists from China and other "learning" countries go to Japan than Japanese go to those countries.

The United States is still the leading country in scientific research overall. However, where Japan makes a determined effort to excel, it is capable of doing so. Areas of emphasis will shift from time to time, sometimes through government policy, sometimes through company strategy, and sometimes through the appearance of a strong individual with special interests. U.S. scientists and engineers need to pay special attention to those shifting areas.

Cooperation with Japan must take local conditions into account. Until now, Japanese universities have been hampered in several ways. They lack adequate funding, they lack facilities, and they lack equipment as compared with Japanese industrial labs. They also lack flexibility because of an antiquated system concentrating power in the hands of the senior professor and because job security and funding are disconnected from performance. These limitations which separate academic and industrial research do not encourage creativity. Yet professorial chairs at Tokyo, Osaka, Kyoto, Tohoku, Kyushu, and other prestigious universities are occupied by outstanding individuals with the freedom and connections to influence research directions. No country has a monopoly on brain power, and it is important for the United States to remain “plugged in” wherever frontier research is carried on.

Japanese industrial labs have more money and better equipment than do universities, but may be less accessible to foreigners. Language is a major problem, although the JTEC panel was told that if three or four foreigners join an ERATO project, all members switch to English as their common language. Nevertheless it is difficult to see how or why a preponderance of Japanese researchers should force themselves to speak English (which is likely to be a foreign tongue even to most foreigners in their midst). ERATO provides a three-month course in the Japanese language to all foreigners at the beginning of their research. Perhaps the piecemeal exchange of individuals could be augmented by limited cooperation among organizations, such as university-to-university, lab-to-lab, etc., wherever teams have common research objectives and perceive the exchange of selected team members as beneficial to their research objectives. JRDC's small International Joint Research Program serves such a purpose and might well be expanded by both Japan and the United States.

Specific ERATO research areas for more cooperation might include materials science, electron holography, nanomechanics, genetic engineering, bioprocessing, cell biology, and others. In Japan as in the United States, the JTEC panel detected a gradual trend for research to move more into the life sciences, even into the hard sciences or engineering disciplines — e.g., many life science projects in ERATO are performed by electrical engineers. Some of this trend is driven by environmental considerations, and is likely to result in new industrial products, such as biodegradable materials, with substantial world markets. Wherever science leads, Japanese industry is sure to follow.

APPENDICES

APPENDIX A. PROFESSIONAL EXPERIENCE OF PANEL MEMBERS

George Gamota (Panel Chair)

George Gamota is President of Science and Technology Management Associates, a technology consulting firm specializing in technology assessments, research and technology policy, and small business development. Dr. Gamota also serves as Co-Principal Investigator to the JTEC/WTEC program, which assesses trends in international science and technology for the National Science Foundation (NSF), the Department of Commerce, the National Aeronautics and Space Administration, and various agencies of the Department of Defense. Dr. Gamota played a key role in the founding of the JTEC program in 1983 and has been involved in its management ever since.

Dr. Gamota previously served as the director of the Mitre Institute, Chief Scientist of the Mitre Corporation's Bedford Group, President of Thermo Electron Technologies Corporation, Professor of Physics and Director of the Institute of Science and Technology at the University of Michigan, Director for Research in the Office of the Secretary of Defense, Special Assistant to the President of Bell Laboratories, and member of the staff (MTS). He has also served as a consultant to Science Applications International Corporation (SAIC), Thermo Electron Corporation, the JMAR Technology Corporation, and the National Academy of Sciences Committee on International Security and Arms Control. He was the 1995 national chairman for the National Conference on the Advancement of Research, and served as its program chair in 1993.

Dr. Gamota holds a Ph.D. in physics from the University of Michigan (1966) and an M.S. (1963) and B.S. (1961) from the University of Minnesota.

Among the recognitions and awards Dr. Gamota has received are the Meritorious Civilian Service Award from the Department of Defense, a Certificate of Appreciation from the Presidential Management Interns, the Minority Technology Council of Michigan, the American Legion Award, Fellow of the American Association for the Advancement of Science (AAAS), Fellow of the American Physical Society (APS), and senior member of the IEEE. He is the author of over 100 articles and the author or contributor to six books.

William E. Bentley

William Bentley is Director, Bioprocess Scaleup Facility, and Manager, Biotechnology Program, at the University of Maryland’s Engineering Research Center. Dr. Bentley is also

Associate Professor of Chemical Engineering at the University of Maryland, College Park; and in addition, is Associate Professor at the Center for Agricultural Biotechnology of the University's Biotechnology Institute. His research interests include metabolic engineering, structured metabolic modeling and bioreactor optimization, biodegradation, insect cell/baculovirus protein expression systems, and cellular stress responses.

Prior to his appointment at the University of Maryland, Dr. Bentley was with the International Paper Company, where he worked on alternative fuels and recovery process improvement.

Dr. Bentley holds a Ph.D. in chemical engineering from the University of Colorado at Boulder (1989), and M.Eng. (1983) and B.S. (1982) degrees (both in chemical engineering) from Cornell University.

The recognitions and awards received by Dr. Bentley include Dow Outstanding New Faculty Award from the American Society for Engineering Education (1995); 1993 Best Abstract Award (with D.M. Ramirez), Society of Industrial Microbiology; and Research Initiation Award (1990), National Science Foundation.

Dr. Bentley is the author or joint author of numerous articles in refereed publications, as well as conference proceedings and other non-refereed publications.

Professional activities include, among others, Member, NSF Small Business Innovation Research Panel, Division of Environmental Biology, NSF; Member, Executive Committee, Biochemical Technology Division, American Chemical Society; Advisory Board, *CHEMTECH*, published by the American Chemical Society; Session Chair, Biochemical Technology Division Poster Session, American Chemical Society Spring National Meeting, Anaheim, California, March 1995.

Rita R. Colwell

Prof. Colwell is currently President of the University of Maryland Biotechnology Institute. She is also a Professor of Microbiology at the University. Her research interests include biotechnology, microbial biodiversity, marine and estuarine microbial ecology, microbial systematics, marine microbiology (ecology, physiology, genetics, and fine structure of marine and estuarine bacteria), temperature and high-pressure effects on marine bacteria, microbial degradation, applications of computers in biology and medicine, and release of genetically engineered microorganisms.

Dr. Colwell has served the University of Maryland previously as Director of the Center of Marine Biotechnology, Director of the Maryland Biotechnology Institute, Vice President for Academic Affairs, Acting Director of the Center for Environmental and Estuarine Studies, and Director of the University of Maryland Sea Grant College. Before coming to the University of Maryland in 1972, Professor Colwell was at Georgetown University (Associate Professor of Biology with tenure, 1966-72; Assistant Professor of Biology, 1964-66), the National Research Council of Canada (Guest Scientist, 1961-63), and the University of Washington (Assistant Research Professor, 1961-64; Predoctoral Associate, 1959-60; and Research Assistant, 1957-58). Dr. Colwell served as a Member of the National Science Board of the National Science Foundation (a Presidential appointment) from 1984 to 1990 and from 1993 to 1994. She has also served on various special advisory panels for NSF, the Food and Drug Administration, the Environmental Protection Agency, the National Institutes of Health, the Department of Defense, and the United Nations.

Dr. Colwell received a Ph.D. from the University of Washington (1961), and an M.S. in Genetics (1958) and a B.S. (with Distinction) in Bacteriology (1956) from Purdue University. She has also received the following honorary degrees: Professor Extraordinario, Universidad Catolica de Valparaiso, Chile, 1976; D.Sc. (Hon.), Heriot-Watt University, Edinburgh, Scotland, 1987; Honorary Professor, The University of Queensland, Queensland, Australia, 1988; D.Sc. (Hon.), Hood College, Frederick, Maryland, 1991; D.Sc. (Hon.), Purdue University, West Lafayette, Indiana, 1993; and LL.D. (Hon.), College of Notre Dame of Maryland, 1994.

Prof. Colwell is a Member of Phi Beta Kappa, Sigma Delta Epsilon, and the Washington Academy of Sciences. She is currently Chairman of the Board of the AAAS (and served as its President in 1995), and is a Fellow of AAAS, the American Academy of Microbiology and the Canadian College of Microbiologists. She served on the Board of Governors of the Society for Industrial Microbiology (1976-79), the Board of Managers of the Washington Academy of Sciences (1976-79), and as Member (1970-85) and Chair (1980-81) of the Board of Trustees of the American Type Culture Collection. She was a Member of the Governing Boards of the American Institute of Biological Sciences (1987-82) and the Marine Technology Society (1980-86). She has served on the Editorial Boards of *Microbial Ecology* (1972-1990), *Applied and Environmental Microbiology* (1969-81), and *Estuaries*. She has also served in various editorial capacities with the *Canadian Journal of Microbiology*, the *Journal of Microbiology and Biotechnology*, *Microbial Ecology*, *Applied and Environmental Microbiology*, and the *World Journal of Microbiology and Biotechnology*. She was a member of the National Academy of Sciences Committee on Field Testing Genetically Modified Organisms (1989). She has been Chair of the U.S. National Committee of the International Union of Biological Sciences and Member of the General Committee and President of the International Congress of Systematic and Evolutionary Biology. She has held several offices in the International Union of Microbiological Societies (IUMS), including Secretary-Treasurer, Vice Chairman and Chairman of Bacteriology Division, and President. She is currently a member of the Executive Board of the International Council of Scientific Unions (ICSU), and has also been President of the American Society for Microbiology (ASM).

Dr. Colwell has received many awards, including the ASM Fisher Award, the ASM Alice Evans Award, the Alpha Chi Sigma Professional Service Award, the Society for

Experimental Biology and Medicine Distinguished Scientist and Lecturer Award, and the National Commercial Company Research Award. She is author or editor of 16 books, has produced an award-winning film (*Invisible Seas*), and is author or coauthor of more than 400 papers and articles and approximately 400 published chapters, reports, and abstracts.

Paul J. Herer

Paul Herer currently serves as Senior Advisor for Planning and Technology Evaluation for the Directorate for Engineering at the National Science Foundation. He coordinates strategic and long-range planning, program development, budget preparation and defense, and R&D policy formulation. Mr. Herer also oversees an NSF program focused on assessing science, engineering and technology, which includes the Japanese Technology Evaluation Center (JTEC) and the Critical Technologies Institute, which supports White House science and technology policy analysis.

Mr. Herer previously worked as a program analyst for the Strategic Systems Projects Office of the Department of the Navy. He has been a Department of Commerce Science and Technology Fellow and has served on long-term assignments to the White House Office of Management and Budget (OMB) and the Research Development Corporation of Japan (JRDC).

Mr. Herer holds a B.A. degree in psychology and an M.B.A. degree from the University of Maine. He has written articles in several science and technology journals, most recently in *IEEE Engineering in Medicine and Biology*, July/August 1995. He has frequently served on government and private committees, panels and working groups.

He is the recipient of numerous awards and honors. In June of 1995 he was awarded NSF's Meritorious Service Medal in recognition of his distinguished contributions in the areas of strategic planning and technology evaluation, which have significantly impacted the evolution and success of NSF's engineering programs.

David Kahaner

Dr. David K. Kahaner is the founder of the Asian Technology Information Program and is its Director. He was formerly the Associate Director of the U.S. Office of Naval Research Asia (ONR). Since 1979 he has also been co-employed at the U.S. National Institute of Standards and Technology (NIST) (formerly the National Bureau of Standards)

Dr. Kahaner has been examining information-rich technologies in Asia for a number of years. His analyses are circulated worldwide to thousands in industry, government, and academia. They are reprinted in many journals as well as often quoted in major news media, and he consults and lectures frequently on those topics both in and outside of the region. In 1993 he was awarded the title of "Mr. Asia" by *Computerworld*. He was the Asian Chair for Supercomputing 90–94 and is the International Relations Chair for Supercomputing 95. He was the originator and one of the organizers of the first HPC-Asia, held in Taipei in September 1995.

One of Dr. Kahaner's goals is to develop a technology-based information service focused on activities in the Asian region that will be of strategic and business value to both Westerners and Asians.

Dr. Kahaner obtained his Ph.D. in applied mathematics from Stevens Institute of Technology in 1968. From 1968 until 1979 he was at Los Alamos National Laboratory, and became responsible for mathematical software activities and library development as well as applications consulting. At NIST he was responsible for scientific software on both large and small computers. Many of the applications he and his group developed are used in scientific computing centers worldwide, and he has received several national awards for this work. Dr. Kahaner is the author of two well-known books and more than 50 refereed research papers. He has edited a column on scientific applications of computers for the Society of Industrial and Applied Mathematics, and has held numerous journal editorial and associate editorial positions in publications ranging from *IEEE Micro*, *IEEE Computer Science and Engineering*, the *MIT Journal of Supercomputer Applications*, and others. He has had visiting professorships at major universities in the United States, Austria, Italy, and Switzerland, where he has taken extensive sabbaticals and still maintains significant associations.

Tamami Kusuda

Dr. Tamami Kusuda is a private consultant in Japanese technology. Previously he served as consultant to the Japan Technology Program in the Technology Administration of the U.S. Department of Commerce. In this role, he assisted the director of the Japan Technology Program in carrying out the mandates of the Japanese Technical Literature Act of l986 to improve the availability of Japanese science and engineering literature in the United States. The Act calls for (1) monitoring Japanese technical activities and development, (2) consulting with business, professional societies and libraries, (3) acquiring and translating selected Japanese technical reports and documents, and (4) coordinating with other agencies and departments of the Federal Government that are engaged in acquiring and disseminating Japanese technical information to avoid duplication.

Using his engineering and research background and language skills, Dr. Kusuda was involved in all phases of these activities since the inception of the program in l987. He routinely reviewed selected reports of the Japanese government, Japanese technical newspapers, newsletters and technical reports published by the national laboratories and major companies. The information thus obtained was placed into the databases at NTIS

(National Technical Information Service) and at the Japan Technology Program Office. Some noteworthy information was translated and published through the *Japanese Technical Literature Bulletin*, a quarterly publication of which Dr. Kusuda was the editor.

In addition, Dr. Kusuda consults with researchers and policymakers in federal agencies and the private sector seeking Japanese technical and scientific information by utilizing the information provided by the various databases of JICST (Japan Information Center for Science and Technology), NTIS, NK-Media, COMLINE, and others.

Previously, Dr. Kusuda worked at the Center for Building Technology of the National Bureau of Standards (currently the Building and Fire Research Laboratory at the National Institute of Standards and Technology) since l962 and retired in l986 as Chief of the Building Physics Division. He has published over 100 technical papers in the area of building environmental design and energy conservation and received the Silver (1972) and Gold (1980) medals of the U.S. Department of Commerce for his contribution to building energy analysis. He was a staff engineer at the Worthington Air-Conditioning Company during l955-1962, engaged in the development of advanced heat pumps.

Dr. Kusuda is a Fellow of the American Society of Heating, Refrigeration and Air-Conditioning Engineers and has received several awards, such as the William Holladay Distinguished Fellow Award in l987.

Dr. Kusuda is a graduate of the University of Tokyo (1947) and received his Ph.D. in mechanical engineering from the University of Minnesota in l955.

Jay Lee

Dr. Jay Lee is Program Director of the Engineering Education and Centers Division at the National Science Foundation (NSF). He jointly manages fifty Industry/University Cooperative Research Centers (I/UCRC) in fourteen different technological areas and three Engineering Research Centers (ERCs) in the manufacturing area. He also serves as a Program Director for the Division of Design, Manufacture, and Industrial Innovation. He recently returned from a six-month tour of duty in Japan as an STA Fellow, where he worked at MITI's Mechanical Engineering Lab in Tsukuba.

Before joining the NSF, Dr. Lee was Program Director, Office of Advanced Technology, at the U.S. Postal Service. He directed and managed R&D in the areas of material handling automation system, adaptive robotics, high-speed sorting machines, intelligent diagnostics, machine vision, high-speed image processing, neural networks, simulation, and computer-integrated factory technologies through contracted research programs with the University of Pennsylvania, Purdue University, SRI, GE/RCA, David Sarnoff Lab., IBM, AT&T, Westinghouse, Hughes, ERIM, and other firms.

Prior to joining the USPS, he was program manager, precision motion systems, at ANORAD Corporation (a company invested by the Ford Motor Co.). He led a group and developed several revolutionary motion control technologies including hybrid linear/rotary drive spindle for high-speed drilling of engine blocks for Ford (Ford's Factory of the Future Project), a piezo-based compensation device for positioning table in semiconductor manufacturing for IBM, and an optical turbine blade inspection technique for GE. From 1984 to 1987, he was robotics group leader for Robotics Vision Systems, Inc. (RVSI) — an automation R&D and system integration company invested by General Motors. Prior to this, he was N/C engineer for Fenn Manufacturing Co., the aerospace division of AMCA International. He worked with a variety of CNC machine tools and was involved in the installation of an adaptive control system for tool wear monitoring.

Dr. Lee received his B.S. in Taiwan and holds an M.S. degree in Mechanical Engineering from the University of Wisconsin-Madison, an M.S. degree in Industrial Management from the State University of New York at Stony Brook, and a D.Sc. degree in Mechanical Engineering from the George Washington University. During 1986-87, he served as part-time lecturer for the State University of New York at Stony Brook, the Polytechnic University of New York and the New York Institute of Technology. Currently, he is an adjunct professor at the Johns Hopkins University–Applied Physics Lab.

Dr. Lee pioneered several robotics technologies and holds three patents in the area of automation. He has over fifty publications (40 single-authored papers) in international journals, magazines, conference proceedings, and book chapters. In addition, he serves as editor or coeditor for a number of international journals and books. He is a certified manufacturing engineer and a licensed professional engineer. In 1992, he received the Outstanding Young Manufacturing Engineer Award from the Society of Manufacturing Engineers (SME). He served as the Chairman of the Material Handling Engineering Division of ASME during 1992-1994 and is a member of the executive committee of the Production Engineering Division (1995-2000) of ASME. His current research work is focused on the neural networks-based intelligent manufacturing system and remote manufacturing methodology.

John M. Rowell

Dr. John M. Rowell is a consultant to the superconductivity industry. He was until recently Vice President and Chief Technical Officer of Conductus, Inc., of Sunnyvale, California.

He has over 30 years of experience in physics, materials, and superconductivity research carried out in the laboratories of the Bell System and at Conductus. He joined Bell Laboratories in 1961 and soon afterwards (with P.W. Anderson) made the first observation of the Josephson effect and demonstrated the magnetic field sensitivity of the Josephson current. He holds the first patent granted for an application of the Josephson effect, in which he proposed both magnetic field and current-induced switching for digital applications. With W.L. McMillan, he developed superconducting tunneling spectroscopy, a measurement technique that determines in detail the electron-phonon interaction that causes superconductivity, at least in low-T_c materials. His work on superlattices of Nb and Al with J. Geerk led him to suggest that a thin Al layer on thick Nb would create a good tunnel junction. This was demonstrated with M. Gurvitch and M. Washington and is now the basic trilayer process of all low-T_c Josephson electronics and instrumentation.

Dr. Rowell held a series of management positions at Bell Laboratories, and became Director of the Chemical Physics Laboratory in 1981. Shortly before the divestiture of AT&T in 1984, he joined Bell Communications Research (Bellcore) as Assistant Vice President for Solid State Science and Technology. He was responsible for guiding the growth of this laboratory from scratch, with respect to both personnel and facilities. The technical programs of the laboratory included materials research, optoelectronics, optical switching, high-speed electronics, and the high-T_c superconductivity program that contributed at the forefront of the field in the years following 1986.

Dr. Rowell holds a Ph.D. (1961), an M.A. (1961), and a B.A. (1957) in physics from Oxford University.

Dr. Rowell received the Fritz London Memorial Low-Temperature Physics Prize in 1978 for his work in tunneling and superconductivity. He is a Fellow of the American Physical Society and was elected Fellow of the Royal Society in 1989. He was elected a member of the National Academy of Sciences in 1994 and a member of the National Academy of Engineering in 1995. He is author or coauthor of over 90 publications and holds 6 patents.

Leo Young

Dr. Leo Young has served as Consultant to the Director for Defense Research and Engineering (DDR&E) of the U.S. Department of Defense since retiring from DDR&E in February 1994. He also is a Member of the Board of Directors of Filtronic-Comtek, Ltd. (U.K.). Previously, Dr. Young served as Staff Specialist and Director for Research and Laboratory Management at ODDR&E. In this capacity, he was responsible for preparing the Congressionally-mandated Department of Defense Critical Technologies Plan and served as DOD representative on interagency committees tasked with preparing the National Critical Technologies Report for the Office of Science and Technology Policy in the Executive Office of the President. Prior to that, Dr. Young served as Associate Superintendent of the Electronics Division of the U.S. Naval Research Laboratory, as Program Manager and Senior Scientist at the Stanford Research Institute (SRI), and as Advisory Engineer at Westinghouse Electric Corporation. He chaired NSF's first Engineering Advisory Committee. While at SRI he consulted for many companies on microwave engineering topics. He has served on advisory boards of the University of California, the Johns Hopkins University, and MIT.

Dr. Young holds a doctorate in engineering from the Johns Hopkins University (1959) as well as an M.A. (1950), a B.A. in physics (1947), and a B.A. in mathematics (1945) from Cambridge University, England.

He served as a member of the U.S. National Committee of the International Union of Radio Science (URSI) and of several URSI scientific committees. He was twice Distinguished Lecturer at a summer course at Leeds University; visiting professor at the Israel Institute of Technology; and NATO/AGARD lecturer at the Marconi Institute, Bologna University.

Dr. Young is a Fellow of the Institute of Electrical and Electronic Engineers (IEEE). Among the many IEEE awards he has received are the Microwave Prize (1963), the Citation of Honor (1978), the Distinguished Service Award (1979), the Centennial Award (1984), and the Microwave Career Award (1988). He has been elected to numerous IEEE offices, among them: President of the Microwave Society (1969), Member of the Board of Directors (four times), and President and Chairman of the Board (1980). Dr. Young received the Naval Research Laboratory Outstanding Performance Award (1977), a Letter of Appreciation from Secretary of Defense Caspar Weinberger (1984), and Senior Executive Service Bonus Awards (1984, 1989, 1990). He became Fellow (1980) and Patron (1994) of the AAAS and served on the Board of Governors of the American Association of Engineering Societies (1980). Dr. Young is a founding member of the National Academy of Sciences/National Academy of Engineering Government-University-Industry Research Roundtable. He has published more than 100 technical papers, holds 22 patents, and has authored or edited 14 books, one of which he coauthored with his wife.

APPENDIX B. DESCRIPTIONS OF ERATO PROJECTS

[Editor's note: the following is a compilation of the ERATO project descriptions that were available on the JRDC World Wide Web server (http://www.jrdc.go.jp) as of April 1996. This material is reproduced herein by permission of JRDC.]

TAKAYANAGI PARTICLE SURFACE 1994-1999

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Background

Cleave a crystal. When you do so, many bonds are broken, electrons exposed, and a raw, high energy surface results. To reduce this high energy, the surface of the crystal will reconstruct itself. In the case of silicon, some atoms are ejected from the surface layer, a fault is introduced, and atoms add back to a new outer layer. The resulting surface is a regular repeating pattern of unit cells much like linoleum tiles on a floor, and with an atomic structure and energy states which are quite different from those of the bulk crystal under it.

Now shrink the crystal to nanometer scale, until it contains tens, hundreds, or a few thousand atoms. At this size, the surface dominates. In a particle of a thousand atoms, more than half of the atoms are on the surface. Yet, until now, research on these ultra fine particles has viewed them as though the surface atoms are identical to the underlying bulk atoms. To be sure, many important results came out of that research. For example, metal clusters are stable only if they contain certain numbers of atoms; this number is called the magic number. Quantum effects have also been measured. Nevertheless, this research has not distinguished between surface atoms and bulk atoms.

Recent research has found that the surfaces of these mesoscopic particles indeed differ from their insides. Mesoscopic particles form surface shells and the particle can be viewed as a capsule. The mesoscopic crystal has facets, the surfaces of which have structures identical to the unit cells of macroscopic surfaces. However, as the crystal's size becomes smaller than a surface unit cell, the structure of the surface unit cell changes in a way that is not yet understood.

Research Strategy

The Takayanagi Particle Surface Project will focus on the surfaces of mesoscopic particles and research their structures and properties in relationship to their nanoscale sizes.

The Takayanagi Particle Surface Project will divide its research into three areas. The first area will be the basic structure of particle surfaces. The project will use real-time electron microscopy to determine the rules that govern their surface structures, atomic makeup, and electron distributions.

The second area of research will focus on quantum properties associated with the surface including light emission and chemical reactivity. This research will particularly try to uncover how particle surfaces reconstruct to form capsules.

The third area of research will direct itself at the design and synthesis of mesoscopic particles using cluster beams and other methods. As mesoscopic particles are currently synthesized and studied in ultrahigh vacuum, researchers will experiment with particles which can exist outside a vacuum in more practical media.

The Takayanagi Particle Surface Project started October 1, 1994, and will run for five years with a projected total budget of ¥1.5 to ¥1.8 billion ($13-16 million).

HIRAO ACTIVE GLASS 1994-1999

Project Director: Dr. Kazuyuki Hirao
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Background

Glass is an extremely important material in science, being used in a wide variety of ways: from lenses, mirrors and fiber optics to filters and substrates for active materials. Yet, in all of these well-known applications glass is only a passive medium, not an active type capable of amplifying, switching, storing or changing light in some way.

The reason that glass has traditionally been used only for passive applications is that its atomic arrangement has no asymmetry; rather, it is ambiguously amorphous. Active applications require that symmetry be broken, as in crystalline electro-optical materials.

Still, glass has a valuable characteristic in that any element can be dissolved in it to some limited amount. It has recently been found that if this capability is combined with a pulsed laser light or high electric fields, the glass center of symmetry can be broken, thus liberating glass from its previously conceived limit to only passive roles.

For instance, Kazuyuki Hirao found three years ago that if a high voltage is applied across a slightly rare-earth-doped SiO_2 plate at a high temperature (280°C) and the material is subsequently cooled, the resulting glass is capable of converting infrared laser light up to visible yellow, green, and even blue laser light. So far, a blue laser diode has not been realized at room temperature (limited to infrared light). However, by stimulating specially treated glass, stable up-converted laser light is produced that is both coherent and stable. Though the physical process of how the field changes the electronic structure of glass is not known, the modified glass somehow combines the energy of two photons into one photon. Almost nothing is known about the implied virtual energy states of glass or the related “hot electron.” Room-temperature short-wavelength blue light will greatly increase the information-storage capabilities in CDs and other materials.

It has also recently been found that photochemical hole-burning materials which are stable at room temperature can be made from glass. In this process narrow bands of color are selectively burned out of reflecting coatings. The storage capacity of the coating is multiplied by the number of colors that can be selectively removed and detected — about 100. It may be possible to multiply this storage capacity another 100-fold by applying electric voltages to the materials. This type of nonlinear behavior has the possibility of being applied to switches operating in the picosecond, or even femtosecond, region, compared to the billionth second time scale of ordinary switches. Possible applications include replacing the currently used semiconductor switches in optical computers. For this to be realized the reliability and speed of these glass-type switches need to be increased.

As another important application of activated glass, Hirao has found that it is possible to store much information within a very small (0.5 cm^3) piece of glass by using the multiplexed frequency, where one frequency corresponds to one picture. Each image is contained within the whole glass and at low temperature (77K). Ten thousand such pictures can be stored in one piece of glass. This is just like a hologram. However, in this case, the element of time is added to that of space by scanning the wavelength while applying a Fourier transform (wavelength multiplexing), resulting in a movie, rather than just an image. Thirty video tapes can be compressed to just one piece of small glass.

Research Strategy

The Hirao Active Glass Project is taking the view that understanding the effects of electromagnetic and other fields on glass is a key to making greatly value-added optical computing elements. This project is researching glass under applied fields from the most basic physics to experiments on applications practical to optical computing. The research is divided into three main areas.

The first area involves understanding the basic electronic structures induced by applying an external field to doped glass. The second is learning to make new induced structures by applying external fields to glass, including electric and magnetic fields, pulsed laser light, ultrasound and electron beams. The third is computer simulations of new active and passive glass structures under applied electromagnetic fields and temperatures in order to provide both an understanding of the basic physics and chemistry as well as practical design tools for making practical optical-computing elements.

The Hirao Active Glass Project started October 1, 1994, and will run for five years with a projected total budget of ¥1.5 to ¥1.8 billion ($13-16 million).

TAKAI BIOTIMER 1994-1999

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Background

ATP, adenosine triphosphate, mainly determines the energy of life. This has been known for decades and every biology student learns about ATP. ATP's sister, GTP, guanosine triphosphate, may mainly determine the timing of life. This is not well known and is the focus of ERATO's Takai Biotimer Project.

The precise timing of cellular events is crucial. This is well illustrated by the white blood cell's suicidal defense of the body against invading bacteria. The presence of bacteria sets off a sequence of actions leading ultimately to the white blood cell's death while killing as many bacteria as possible. After it first detects bacteria, the white blood cell migrates to where the concentration of bacteria is highest. It will not waste itself on small numbers of bacteria, so only when the concentration of bacteria reaches a minimum level, will the white blood cell then engulf as many bacteria as it can by a mechanism called phagocytosis. After the cell engulfs the bacteria into vesicles, it injects superoxide into the vesicles to kill the bacteria. At the same time, it secretes proteases into the surrounding medium to kill neighboring bacteria. Finally, the white blood cell dies.

These precisely timed events are set in motion by the attachment of bacteria and bacterial products to the cell surface and the transduction of the resulting signal to various parts of the cell. There are several mechanisms for signal transduction. In the above example, signal transduction for the key events of cell migration, phagocytosis, superoxide formation, and protease secretion involve GTP-binding proteins (G-proteins) which bind GTP and GDP, guanosine diphosphate. These proteins are active when binding GTP and inactive when binding GDP. This binding of GTP and GDP appears to be part of a timing mechanism which determines the beginning and duration of processes.

The example of white blood cells is good for illustrating the various roles of G-proteins. But there are medically more important processes that involve G-proteins in timing functions. One such process is the secretion of neurotransmitters by presynapses of nerves with possible relationships to dementia and other memory-related diseases. Another is smooth muscle contraction with possible relationships to hypertension. A third is the migration of smooth muscle cells from the outside of arteries to the inside with relationship to arteriosclerosis. And a fourth is the rampant cell proliferation and metastasis in cancer. All appear to be related to timing mechanisms involving G-proteins.

Research Strategy

The Takai Biotimer Project will research the G-proteins and their related proteins, the genes that code for them, and their functions in search for a biological timing mechanism. Research will be divided among three subgroups. One group will research the G-proteins and related proteins, and the genes that code for them. They will clone these genes in order to analyze their structures. A second group will research the expression of these genes and their resulting proteins as they function in their lease of neurotransmitters in synapses, in the various functions of white blood cells, in smooth muscle contraction and motility, and in cancer cell proliferation and metastasis.

The ultimate goal of the project is in the third group which will research the timing mechanisms involving G-proteins and ways to control timing by introducing related genes into cells and observing effects on timing mechanisms.

The Takai Biotimer Project started October 1, 1994, and will run for five years with a projected total budget of ¥1.5 to ¥1.8 billion ($13-16 million).

YAMAMOTO BEHAVIOR GENES 1994-1999

Project Director: Dr. Daisuke Yamamoto
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Background

Darwin's theory of evolution postulated that there are two fundamental drives: survival and the selection of male mates by females. In regard to the second, evolution has produced striking anatomical features and behaviors which make males attractive to females, one of the most outlandish being the plumage of the peacock: it has no function in survival and exists only for attracting females.

A good example of sex-oriented behavior is the lek system of certain insects, birds, and mammals. In this mating system, males form territories called leks. The females move from lek to lek until they select a mate. A lek contains no food or anything else useful for the female's survival, only the male. This behavior exists solely for the purpose of mate selection.

Thus, when studying the relationships between genes and behavior, a good place to start is with sexual behavior, similarities of which extend across all species of animals. One of the best organisms for studying sexual behavior is the fruit fly, Drosophila. An important benefit is its relatively short lifetime: from egg to adult takes ten days, after which the mature fruit fly lives for only a month or so. Not only is it easy to quickly observe the lifetime behavior over a short time period, but it is also easy to generate mutations. Mutations and their related phenotypes, physical expressions, provide a powerful way to identify the genes related to behavior. Drosophila generally have only several chromosomes; out of the around 10,000 or so genes, perhaps 1000 have already been cloned and sequenced.

The mating behavior of Drosophila with age has already been observed and documented, showing a variety of patterns. Interestingly, during copulation the male uses various physical mechanisms to produce a variety of love songs. Each song has its own frequency characteristics that confer an aphrodisiac action for conspecific partners of the opposite sex onto the song.

Research Strategy

Since mating behavior is so closely tied to evolution, a similar set of genes should be general to behavior in many animal species. This project is thus using mating behavior as a good starting point for researching the genetics of behavior.

Research is concentrating on the fruit fly Drosophila melanogaster. A few mating behavior mutants of Drosophila are already known. In the spinster mutation, females very strongly reject courting males. The satori mutation produces homosexual males. Bisexuality is also induced by different types of mutations in the same genetic locus as that of satori. Croaker males produce aberrant courtship songs. These mutants are but the starting point in this project's search for the genetics of behavior.

An early goal is to increase the number of known behavioral mutants in Drosophila, especially those in which the original mutation is suppressed or enhanced. These can be used to make a map of the behavior genes on the genome, then to clone the relevant cDNAs. From the clones one can learn about those proteins coded by behavior genes.

Also, the anatomy of behavior gene expression is being studied. Genetic mosaics are being used to identify the critical cells in which the gene products play crucial roles in controlling mating behavior. For example, the gene related to the satori mutation is selectively expressed in a subset of cells in the brain. By replacing wild type cells with mutant counterparts and examining the individual mosaics for their mating behavior, it will be possible to specify single cells that determine the fly's sexual orientation. The biochemical basis for the gene's action in these cells is also being studied.

To demonstrate the link between single genes and behavioral phenotypes, cloned wild-type genes are being introduced into the relevant mutants to cure their behavioral abnormality. This type of gene therapy has already been accomplished for the spinster. It should be possible to change the homosexual orientation displayed by the satori males into heterosexual or bisexual as well.

Finally, the evolution of these genes, starting with related Drosophila species, is being studied. There are over 2400 species of Drosophila and in some groups the species can be traced to a single ancestor. Yet, within these groups there is a wide range of mating behaviors. For example, some species use the lek system while many do not. Traceable to a single ancestor, this wide range of behaviors is probably due to a relatively small number of mutations. By identifying behavior genes in Drosophila melanogaster, the project can then explore the similarities and differences in the genes which cause this wide range of behaviors. One sub-team is located in Hawaii, the home of picture-winged Drosophila. As the research target, using these species is effective not only because of their large size, advantageous for physiological experiments, but also for their peculiar sexual habits, including a tendency to form leks.

Though this project is quite basic, potential applications include therapy for human behavioral abnormalities, psychological as well as genetic, for which the research may help to identify the responsible genes. Another possibility includes agricultural fields, such as the genetic control of pest populations.

The Yamamoto Behavior Genes Project started October 1, 1994, and will run for five years with a projected total budget of ¥1.5 to ¥1.8 billion ($13-16 million).

Dr. Daisuke Yamamoto (Dah-ee-suu-keh Yah-mah-moh-toh) joined the Mitsubishi Kasai Institute of Life Sciences after receiving his Masters degree from Tokyo University of Agriculture and Technology in 1978. He received his Ph.D. degree in 1981 and thereafter conducted postdoctoral research at Northwestern University. Dr. Yamamoto has been a guest scientist at Cambridge University, Autonoma University of Madrid, and Cold Spring Harbor Laboratory.

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YAMAMOTO QUANTUM FLUCTUATION 1993-1998

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Background

One of the major events of 20th-century physics has been the founding and subsequent evolution of quantum mechanics. At first a strange curiosity that went strongly against intuition and caused decades of debate that straddled both fundamental physics and philosophy, quantum mechanics eventually became a powerful force in our understanding of the nature of atomic and sub-atomic physics, as well as a potent tool in the development of new technology.

At the heart of quantum mechanics is the Heisenberg uncertainty principle, which puts strong limits on quantum systems as well as what can actually be observed: the limits to simultaneously measure both the position and momentum, or energy and time. However, according to Yoshihisa Yamamoto, the time has come in which the uncertainty principle can be better understood, and even manipulated as a tool in our development of solid state systems as well as new technologies based on this understanding.

One field where this is especially true is in quantum electronics, where electrons and light are manipulated to make functional devices, such as a semiconductor laser. In this case, light can be confined within a very small cavity. Another such system is a high density of light pulses “squeezed” into a very short time duration in optical fibers.

However, although laser light approaches perfection regarding the uniformity of its intensity and phase coherence, the fundamental laws of quantum physics state that laser light cannot be perfectly uniform in intensity nor in phase. There will always be some fluctuation (noise) in the rates (intensity) and the phases of photon emission. The Heisenberg uncertainty principle of quantum physics states that the product of the intensity noise and the phase noise cannot fall below a minimum value.

Recent research, however, has found that this noise is “malleable”: the intensity noise can be reduced if the phase noise is allowed to increase. Likewise, the phase noise can be reduced if the intensity noise is allowed to increase. In other words, light can be squeezed. The concept of squeezed light is one result of recent research on semiconductor lasers and optical fibers.

Considering another aspect of quantum mechanics, one myth has held that a quantum system cannot be measured without destroying the system itself. However, more than sixty years ago, a prediction was made that nondestructive measurements are possible under certain conditions. Recent research has confirmed this prediction in the case of measuring the intensities of solitons in optical fibers. The key is in a trade-off between the measurement error in intensity and the back action noise in the phase.

Yamamoto believes that squeezed light and nondestructive measurements are novel results of research on quantum optics, and that as the sizes of the features in semiconductor devices become smaller, quantum effects become more important. He also believes that it is now possible to observe the effects of single electrons in semiconductors and that it will soon be possible to observe single photons emitted by these single electrons.

Research Strategy

The Yamamoto Quantum Fluctuation project is pursuing greater understanding of the uncertainty principle of quantum mechanics while developing much more sophisticated technologies for creating and manipulating electrons and photons within semiconductor cavities.

One part of this research involves the suppression of quantum fluctuations of photons and electrons and the manipulation of electron-photon interactions in semiconductors at the quantum limit. Research includes studying the principles and underlying physics of the artificial manipulation of the photonic quantum state while focusing on the control of spontaneous emission. The artificial manipulation of electron quantum states while emphasizing the quantum fluctuations of electron transport in mesoscopic and macroscopic systems, the suppression of quantum fluctuations and applications to nanostructure devices are also being pursued. Further, control of vacuum field fluctuations and spontaneous emission by semiconductor microcavity structures is being investigated.

A second theme involves quantum nondestructive (QND) measurements. Techniques using optical soliton and electron interferometry while extending experimental research to wave compression and quantum interferometry are being explored. Efforts include the construction of QND measurement devices, the demonstration of information readout at the quantum limit, and suppression of the free evolution of the quantum system.

Finally, the project is seeking to control the injection of single electrons into mesoscopic semiconductor junctions and is thus conducting research towards the production and control of single photons emitted from these junctions. Efforts are being made to include an estimation of a micro-pn-junction, the measurement of regulated single electron-hole injection and single photon emission, as well as theoretical analyses of these systems.

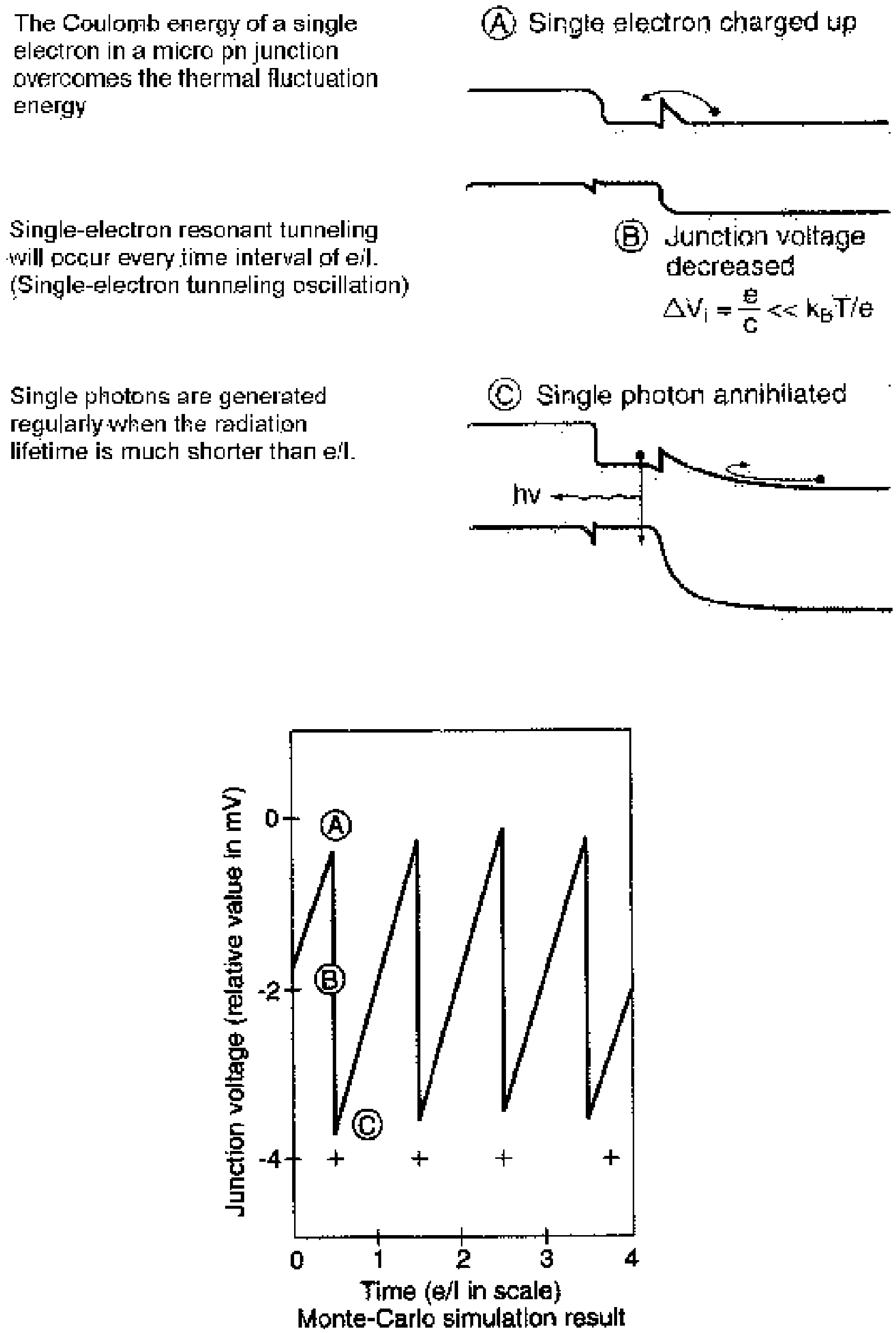

Fig. Yamamoto.1. Figures illustrating the dynamic operation of the Coulomb blockade and resonant tunneling in a semiconductor micro pn junction at low temperature as well as its Monte-Carlo simulation results in the time domain.

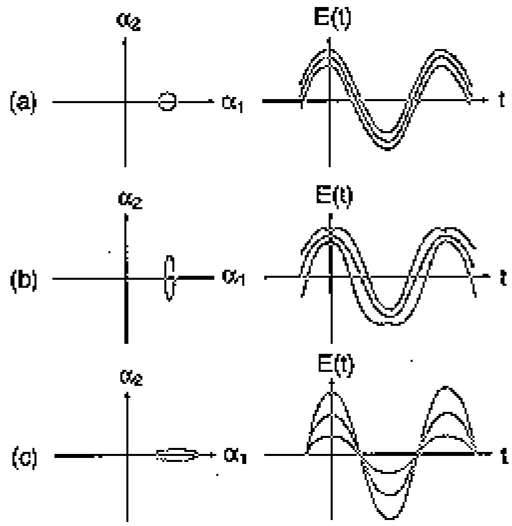

Fig. Yamamoto.2. Figure (a) shows the quantum fluctuation of ordinary electromagnetic fields, indicating two orthogonal amplitude components and E(t) in the time domain. Figure (b) shows the α_1 squeezed state where the fluctuation of α_1 is suppressed. Figure (c) depicts the α_2 squeezed state in which the fluctuation of α_2 is suppressed.

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TANAKA SOLID JUNCTION 1993-1998

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Background

A major part of human evolution has been ever-expanding technological sophistication. From earliest times the trial-and-error mixing of metals impacted greatly on history. The very same process, but with much greater sophistication, has continued through to the present. Only now, materials are needed to withstand the high stress and temperature during faster and higher flight, to produce better energy efficiency at higher temperatures and to realize faster computing through materials that can rapidly dissipate heat.

A key factor for success in achieving these technologies might well be an understanding of more clever ways to fabricate composite materials which involve a wide variety of shapes and characteristics. A ceramic portion, for instance, could be exposed to high temperature and corrosive conditions that a metal part could not withstand. However, a metal portion could be kept away from the most extreme conditions while providing strength. Some newly developed composite materials have metallic fibers imbedded in a ceramic material to provide reinforcement.

However, the most outstanding aspects of composites and the joining of various materials is the complexity involved. Even for very simple flat interfaces, at the atomic-scale behavior is very complex: dissolving, diffusion, the development of a solid solution and finally precipitation. Other factors that must be contended with are grain boundaries, filler/matrix, deposited films, and brazed joints. Induced stress distribution and lattice defects affect the mechanical properties of an interface. The list goes on.

Although great efforts have been made to better understand the many phenomena involved using electron and other microscopies, the very important interface formation and bonding mechanisms are still little understood on the atomic scale. And although simple-shaped interfaces have been observed, many unobserved complex mechanisms involving multistep physical and chemical reactions may have led to them. Thus, to further develop the technology of composite materials, a much better scientific understanding of the very wide variety of factors involved must be achieved.

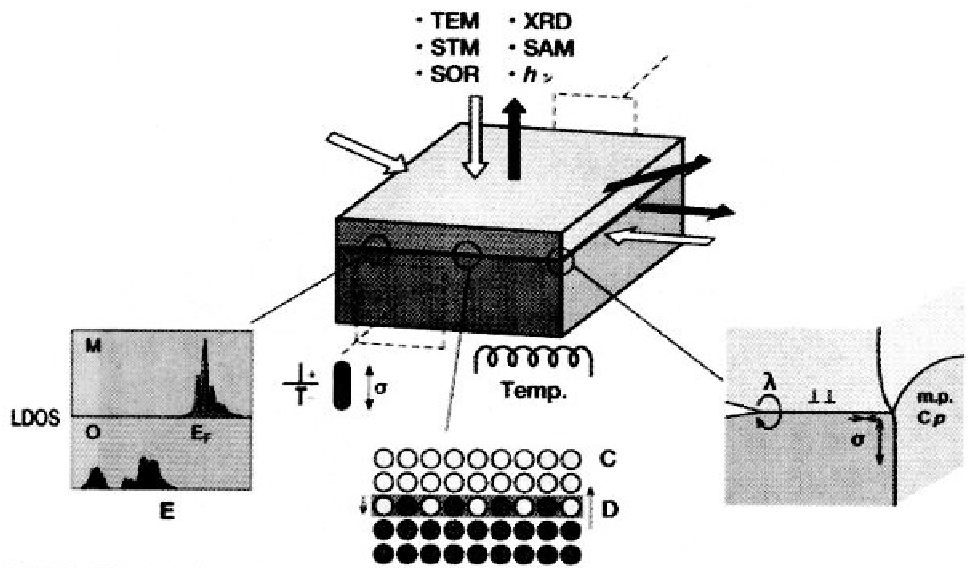

Fig. Tanaka.1. Phenomena around a hetero-interface and their control.

Research Strategy

The Tanaka Solid Junction Project is exploring the nature and science of hetero-interface formation from the viewpoints of elementary atom dynamics in and around interfaces while pursuing the possibility of actually designing them.

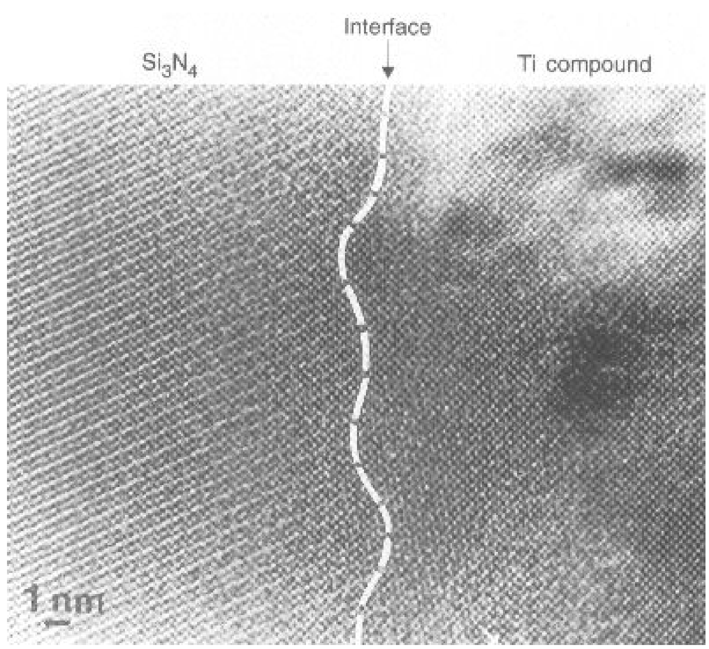

Fig. Tanaka.2. Lattice image of a ceramic/metal brazed interface (51K).

Concerning interface dynamics, research is pursuing the elementary atomic processes which occur when solids are joined together, while looking for the nature and controlling factors of hetero-interface formation. How atoms dissolve, diffuse, and otherwise rearrange themselves during an interfacial reaction is being examined. Nucleation/growth theory is also being checked. Both bulky reactions and thin-film deposition are being pursued. The tools being used to facilitate these efforts include high-resolution transmission electron microscopy, scanning tunneling microscopy, and the use of high-energy X-rays. Ways to control an interface using applied stresses and electric and magnetic fields are also being investigated.

Regarding interface properties, an effort is being made to quantitatively understand the various lattice defects and residual stresses which exist around a hetero-interface, which arise during bonding or deposition, and to determine the stress values around interfaces using collimated X-rays along with scanning acoustic microscopy and micro-Raman scattering. Another aim is to characterize any lattice defects induced at or around the interface. Singularities in the interfacial properties are also being investigated with reference to the mechanical, electrical, and thermal properties of their systems. All of the processes around the interfaces must be calculated, including the atmosphere.

Interfaces are also being treated theoretically, using computer calculations to better understand the physical and mechanical natures that exist during bonding or deposition. With a new understanding, attempts will be made to simulate the process of hetero-interface formation and thereby begin the microscopic design of interfaces. Both simulations and experimental checking will hopefully eventually be carried out simultaneously.

Thus, the main objectives of this project are to find ways to understand both the multistep functions and physical states at and around interfaces and eventually to control the interface reactions and properties. The subtitle of this project is therefore the atom dynamics of complex material solutions, since many different materials with many different characteristics and properties must interact. By thoroughly researching the nature and the science of hetero-interface formation, this project will hopefully contribute to the design and fabrication of new materials and components.

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HASHIMOTO POLYMER PHASING 1993-1998

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Background

Nature tends to self-organize towards equilibrium, the driving forces being the tendencies of any system to minimize its energy while maximizing entropy. If one of these forces dominates, simple phase behavior is observed. Entropy favors complete mixing at the molecular level (one-phase behavior); an unfavorable interaction energy favors complete phase separation (two-phase behavior), as when oil floats on water. Even for small molecules, a delicate balance between these two forces can lead to a rich variety of phase behavior on the mesoscopic scale (1 nm - 1 µm); when a detergent is added to oil and water, the oil molecules disperse into the water as mesoscopic spheres, cylinders, or even lamellae.

In a similar fashion, most differing polymers separate. Even if one could manipulate them so that they become miscible with each other to form a single phase at a given temperature, there might occur phase separations if the temperature of the system changes. For polymers, the analogues of detergents are block copolymers, chains of two differing polymers that are coupled end-to-end. However, while oil in most cases disperses in water in the form of spheres, the phase behavior of polymer systems containing long-chain block copolymers exhibits a rich variety of different shapes, including cylinders and lamellae; there are also tetrapod networks, meshes, and struts. Of special interest are microphase-separated systems in which the phases form bicontinuous domain structures.

What makes the polymer phase particularly interesting is the dynamics of the phase separation process. Though for small molecules this process is too fast to be observed in detail, for polymers the time scale can be on the order of days. This makes it possible to both observe and control the process. Though it is known that the time evolution involves a non-linear, non-equilibrium process, little is known about the kinds of intermediate structures appearing on the pathway between the one- and two-phase regions.

It has become a significant theoretical challenge to solve the self-organization process in these systems and its implications for natural processes, such as those occurring in proteins. Hashimoto believes that if polymers can be used as model systems, it might become possible to study these complicated non-equilibrium processes very precisely. He is also aware that, from a practical point of view, it should be possible to pin the non-equilibrium structures and then use them to create new technology.

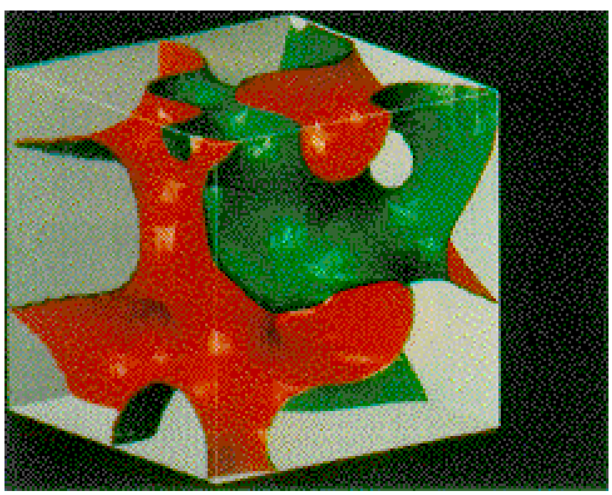

Fig. Hashimoto.1. Interfaces developed by phase separation via spinodal decomposition between the two coexisting phases in binary fluid mixtures. The two bicontinuous phases exist in both sides of interfaces colored by red and green. The interfaces have a negative Gaussian curvature, and the two phases have equilibrium compositions. The pattern is obtained by a computer simulation using the time-dependent Ginzburg-Landau equation.

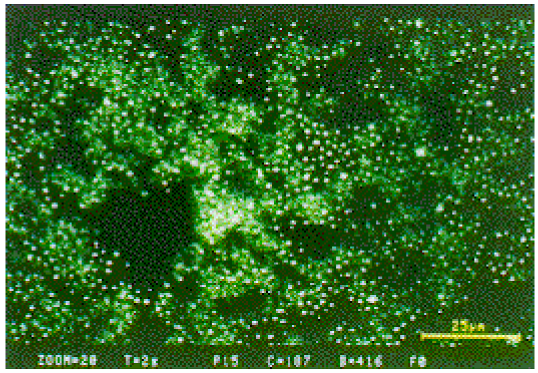

Fig. Hashimoto.2. "Void" structure in dilute aqueous colloidal dispersions observed by a confocal laser scanning microscope. The coexistence of a spherical-dense region and a less dense region is observed. This self-organized structure represents provocative analogies to the bicontinuous structure shown in the figure above. Sphere diameter: 0.96 micrometer, sphere concentration: 2.0 vol%.

Research Strategy

The phrase "polymer phasing" was coined to suggest mesoscopic pattern formation via phase transitions and separation in multiphase polymer systems, as a model for complex fluids. Thus, the main research goal of this project is to elucidate basic knowledge concerning the phase transitions in complex fluids, which would allow the design of novel materials by manipulating phase-separated structures formed in the self-organization process.

The first step must be to design and synthesize polymers that self-organize on the mesoscopic scale, then to watch them on the space-time self-organization process level of multi-component mixtures of these molecules. Unique structures occurring as a consequence of phase transitions are of special interest. High molecular-weight polymers are being heavily used, providing extremely good model systems for understanding non-linear and non-equilibrium problems, because the fundamental length and time scales are large and long. The block copolymers also have interesting features with respect to equilibrium statistical mechanics, forming various phase-separated domain structures with nanometer periodicities, the so-called nano-patterns.

A major theme involves investigating self-organized structures that evolve over wide spatial and temporal ranges, using various real-space and reciprocal-space methods of structure analysis. The combination of real-space analysis by microscopy and reciprocal-space analysis by scattering methods is very important. Although scattering methods are good for analyzing statistical properties and convenient for *in situ* measurements, it is necessary to understand structural details by microscopy. The dynamical evolution of the self-organized structures are also being studied by both methods and analyzed both theoretically and numerically in order to unveil the laws governing the non-linear and non-equilibrium phenomena.

Another emphasis of the project is to explore methods for controlling the self-organized structures while developing interesting structures having novel properties. This involves the synthesis and characterization of unique monomers and polymers, incorporating isotopic labels, photochromic moieties, and other functional groups responsive to electromagnetic fields. These are important both in pinning intermediate structures and investigating structure formation under applied fields. Determining the way in which electromagnetic, stress, and other external fields influence the structure is another important aspect of the research being carried out.

Although this project might well uncover new functional semiconductor and bicontinuous structures with combined functionalities, its basic aim is to provide fundamental knowledge on the subtle interplay of the energy and entropy terms that are the basis for their formation and to understand the self-organization process itself.

HIROHASHI CELL-CONFIGURATION 1993-1998

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Background

The cell is the most basic unit of life. Interestingly, during the course of evolution from single-cell to multi-cell organisms involving many types of specialized cells functioning as an interrelated and holistic whole, both the cell shape and binding among cells have become extremely important regarding the state of the organism.

Setsuo Hirohashi, a pathologist and M.D. in the fields of cancer diagnosis and research on the mechanism of carcinogenesis, has come to think that the cell shape and binding are interactive elements in what can be considered a “cell society.” These elements not only arise from the genetic material found within each individual cell, but are also influenced by contact with surrounding cells and other elements in their environment.

For instance, it has long been known that in certain types of cancers cells lose their shape and become detached from their tissues. They then spread cancer to other tissues, occult metastases, a major factor in limiting the ability of medical science to control cancer by treating only the localized tumors.

Cancer thus provides a window on the cell society, just as a scandal provides a window on the human society that gives rise to it. However, understanding the cell society requires research that goes beyond cancer to examine the society on its own terms. Pathologists are thus constantly concerned with the morphological features of cancer cells, which provide an enormous amount of information. Shape and function and their molecular bases are very closely associated. Cancerous cells have many different sizes: the nucleus is larger and cell polarity is lost.

A very important question is why do cancer cells become disassociated. Recent research has uncovered proteins that bind cells to each other and give cells their shape. Proteins called cadherins bridge the gap between cells. Other proteins called catenins are thought to anchor the cadherins to the cytoskeleton found under the cell surface. For some types of cancer, for example, one of the cadherins is not expressed or mutated and the cells cannot bind to each other. However, if genes for the cadherin are introduced into the cancer cells, the cells can bind to each other.

Hirohashi believes that many molecules involved in the formation and maintenance of cell shape and cell society remain to be discovered. He also believes that the window on cell society provided initially by cancer will open additional windows to provide basic knowledge concerning the architectures and workings of tissues.

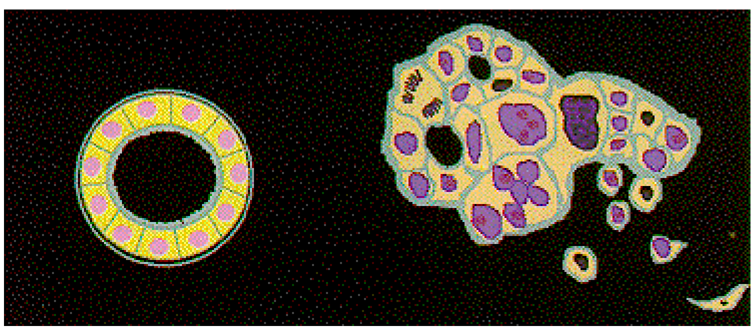

Fig. Hirohashi.1. Apparent differences of the cell adhesion and the cell polarity are shown between a normal epithelial cell (left) and a cancer cell (right).

Research Strategy

The Hirohashi Cell-Configuration Project aims to uncover the architectures and workings of the cell society. Research is focusing on the shapes of cells as expressions of their genetics and the influences of surrounding cells and inter-cellular environment as well as cell-to-cell interactions. By doing so it might be possible to understand why cells have their particular shapes and functions and why they are built up with particular molecules.

One area of research is concentrating on the genes which are related to shape and binding, while locating, isolating and sequencing them. It is also concentrating on the establishment of *in vitro* tissue reconstruction models and dynamics, as well as fine morphological image analysis. Further, an effort is being made to understand how these genes give rise to binding and related functions. To do this, selected genes that are possibly related to tissue formation are being destroyed or reintroduced; the effects on the cell shape and binding are then examined. At the same time, the means by which the genes and functions that they code for cell shape are being considered, as well as how cell shape is influenced by the surroundings.

An effort is also being made to develop a microscope by which it will hopefully become possible to look more closely at the dynamic changes which take place in cells as well as three-dimensional *in vitro* reconstituting.

This project is not just concentrating on cancerous cells but is also very much concerned with the factors that determine the shapes and binding of normal cells. It is also hoped that a system can be established by which it will become easy to determine the mechanism which determines cell shape. If tissue reconstitution can be understood and a means of transferring genes to cells to make their shapes non-cancerous can be determined, a sophisticated cancer-treatment method might well be in the making.

KAWACHI MILLIBIOFLIGHT 1992-1997

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Background

Every microorganism, plant and its seeds, insect, fish, bird, and animal has evolved so as to be critically adapted to the circumstances of its environment. The act of effective and efficient motion in various media is a part of this scheme of nature. Thus every shape and moving mechanism of an organism is closely coordinated with the characteristics of the fluid in which it moves. Yet, the state-of-knowledge today is such that although it is possible to make a rocket-plane like the space shuttle which can blast into space and then glide back to Earth, the aerodynamics of a mosquito, pollen, seeds, or a spider's web are still very little understood.

Interestingly, the hummingbird's flight mechanism is based on the same principle as that of a helicopter or a 350-ton Boeing 747: the phenomenon of lift, utilizing a wing with a rounded leading edge and a sharp trailing edge. Small insects, however, such as the dragonfly, housefly, or mosquito, use both lift and drag. Because the ratio of the inertial-to-viscous forces — the Reynolds number — is much different, the fluid dynamics of objects in gaseous and liquid media change abruptly at the millimeter level. The dragonfly, for instance, uses wings that are very thin and rough, which are operated at a low Reynolds number. Other insects are known to fly using additional forces generated by making vortices which remain behind in their wake.

The mathematical foundation of fluid dynamics was stimulated by the desire to design ships, land vehicles, and aeroplanes — human-size objects — so that they could pass through their respective fluids with greater speed and efficiency. Until now, the movement of organisms has generally been studied by life scientists who often little understood fluid dynamics or stability control. Today, however, interdisciplinary basic research is being aimed at micro-machines and understanding the motions of organisms and objects on scales from millimeter on down.

Because just shrinking big machines to small machines does not work, the Kawachi Millibioflight Project is taking a very wide-ranging look at the millimeter-to-nanometer region. In doing so the basic science of fluid dynamics on this scale closely interplays with many fields of science and technology.

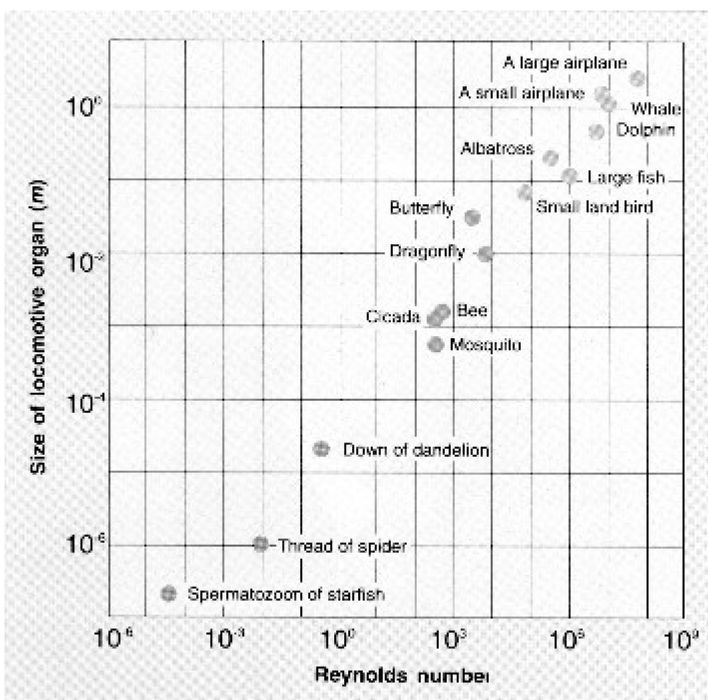

Fig. Kawachi.1. Relation between the size of a locomotive organ and the Reynolds number.

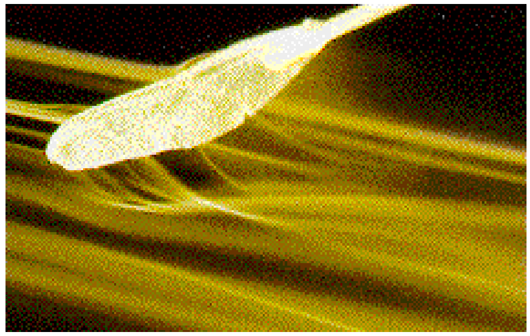

Fig. Kawachi.2. Flow around a dragonfly wing.

Research Strategy

Keiji Kawachi's background includes helicopter rotor-blade aerodynamics using supercomputers. He has already applied this knowledge to the analysis of hummingbird flight and is now blending such interdisciplinary fields as biologic mechanics and flow visualization while focusing on situations in which both drag and lift are aerodynamically important.

As a major part of this attempt, fluid dynamics is being considered while carefully observing and analyzing the propulsion mechanisms in flying and swimming. To this end, high-speed observational instruments, such as the streak camera, are being developed and used. Wind tunnel and water-tank tests are also being conducted to analyze various models under controlled situations. By these means it should be possible to carefully analyze how the wings, bodies, tails, and other appendages of organisms operate during motion. Interlinking all of the experimental procedures are sophisticated computer simulations.

The biodynamics and control mechanisms of organisms moving through a fluid are also important. For instance, the housefly has vibrating bars on its body which act as gyroscopes to help stabilize flight by providing feedback to the wings. Research in this field involves the various sensory and feedback mechanisms, including wing elastic deformation and beating motions. An effort is also being made to clarify the information systems inside an insect's body, such as the neurons which carry electrical signals, thus helping to develop new types of control systems.

Another important area of this project is bioenergetics. This field involves such questions as how energy consumption is regulated during flight and swimming. The energy supplied by an organism is being compared on a real-time basis with the energy required for propulsion. One important element is to determine how to produce power by using muscle or by changing the rate of gas flow.

Though this is a very basic research project, in today's movement to elucidate and utilize molecular-level processes and machines, any information obtained will surely be valuable.

And though this project is starting out by analyzing organisms on the millimeter level, it could well set its sights at the level of bacteria and smaller, where the fluid dynamics involve situations on the scale of the mean free path of molecules and are almost completely different and unknown.

ITAYA ELECTROCHEMISCOPY 1992-1997

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Background

In a physical universe comprising the solid, liquid, gaseous, and plasma states of matter, it is natural that many important phenomena take place at the interfaces of these states. Concerning the interfaces between solids and liquids, some very common examples include the corrosion of metals, the charging and discharging of a storage battery, and the wet processing of semiconductor devices. Many such processes involve electrochemical oxidation-reduction reactions.

Although these and related phenomena have long been studied, until recently knowledge concerning the atomic and molecular processes that occur at the interfaces have depended on indirect experiments. One of the major reasons for this is that there has been no good observational technique that could work in a liquid. Thus, most previous information resulted from observations made in a high vacuum after removing a solid sample from a liquid. During this process irreversible reactions, such as surface oxidation and contamination often occur, thus complicating the analysis of surface structures.

Recently, however, techniques involving scanning tunneling microscopy (STM) and atomic force microscopy (AFM) have been extended to observations of solid samples immersed in liquids, thus allowing direct observation of the solid/liquid interface in its reacting state. One of the most important advancements in this field is a system called electrochemical STM developed by Kingo Itaya. In this system which has a four-electrode configuration, the electrode potentials of the substrate and the tip can be independently controlled relative to a reference electrode. This apparatus thus offers new possibilities for complete *in situ* observations of electrochemical reactions under potentiostatic conditions, since the tip can be continuously scanned over a surface, even while electrochemical reactions are occurring at the working electrode.

The Itaya Electrochemiscopy Project is using these new techniques to examine electrochemistry at the atomic and molecular levels. The project is treating the solid/liquid interface as a reaction site in order to uncover the mechanisms of surface reactions while pursuing the precise control of these reactions. Analysis is focusing particularly on the reactivity and structure of solid surfaces in the presence of adsorbed ions and solvent layers.

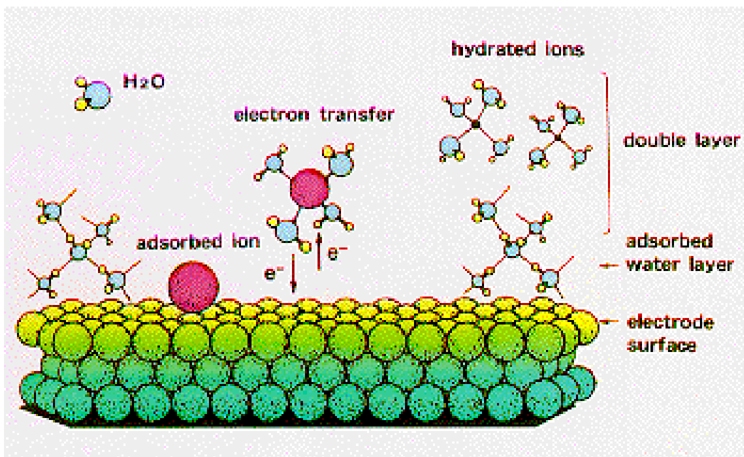

Fig. Itaya.1. Schematic model of atomic/molecular interactions at solid/liquid interfaces.

Research Strategy

In order to understand interface structure an effort is being made to establish methods to form well-defined solid/liquid interfaces. This is being done by using many types of single-crystal surfaces along with both aqueous and nonaqueous solvents. Research is also focusing on new ways to make measurements and to control surfaces using *in situ* scanning probe microscopes, such as STM and AFM. In addition, the use of ultrahigh-vacuum surface-analysis techniques is being pursued. As part of this pursuit, special multi-chamber vacuum systems are being developed in which solid samples can be removed from a liquid and then analyzed without experiencing oxidation or contamination.

Regarding interface formation, work is concentrating on the bond-formation reactions which occur at the solid/liquid interface. For example, the mechanisms by which metal and semiconductor surfaces are electrochemically formed and dissolved, thin-film crystal growth processes, as well as the adsorption and orientation of ions and molecules are being pursued. In addition, the formation of modified surfaces and new methods for making thin films using knowledge gained about reactions at the solid/liquid interface is being studied.

Another area of concentration concerns interface fabrication, while concentrating on reactions that break bonds at the solid/liquid interface. The processes involved in chemical and electrochemical etching as well as in dissolving adsorbed molecular layers should hopefully be clarified. To this end, the electrochemical energy and optical energy necessary to control reactions at the solid/liquid interface are being applied. A search for technology to control metal and semiconductor surfaces at the atomic and molecular levels is also being conducted.

YANAGIDA BIOMOTRON 1992-1997

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Background

One of the great mysteries of science is how such a large organism as the human being with billions of individual cells and their sub-components can move with smoothness and energy efficiency as a unified whole. And it does this regardless of the speed of action or the forces involved. These characteristics exist all the way from the large-scale whole to the sub-cellular.

The heart of most investigations on muscle contraction has been within the muscle cell. There, huge numbers of nanometer-size bio-motors — called biomotrons — are involved in the most basic aspects of motion. Each biomotron is a complex formed by the act of a myosin protein head attaching to, and pulling on, a 7-nanometer thick actin filament. Biomotrons convert chemical energy into mechanical kinetic energy with up to 90% efficiency; and they operate with little friction while adapting to their circumstances, even by easily aggregating to form large muscle systems.

The flexibility and efficiency of the biomotron stands in sharp contrast to the situation of man-made machines, in which efficiency requires high-rigidity and -energy inputs to overcome interfering thermal vibration. Precession requires large external frames to hold the parts in alignment. The biomotron operates without these requirements due to unknown principles of engineering.

Recent seminal research carried out by Toshio Yanagida on biomotrons is consistent with the existence of such unknown principles, such as that involved in energy transduction and action. The former common wisdom was that a single attach-move-detach cycle of the myosin-actin complex in a biomotron is accompanied by the hydrolysis of one ATP molecule. In reality, the biomotron can spread the released energy across several attach-move-detach cycles.

Another interesting aspect is that compared to a man-made chip, for instance, the biomotor needs no special isolation from the environment to maintain good communication, even at a very low signal-to-noise ratio. Further, a huge number of biomotrons can exist within a cell and operate efficiently at body temperature. The molecular motor therefore seems to be very skillful at communicating within its network. It is thus becoming clear that a considerable degree of control occurs within the biomotron without direct control by the higher nervous system. In this sense the elements of the molecular machine have "intelligence" to sense what is happening around it.

Yanagida never liked the standard model of muscle operation, since it was too similar to the operation of man-made machines. The Yanagida Biomotron Project thus aims to uncover the uniquely biological operations and structure of the biomotron.

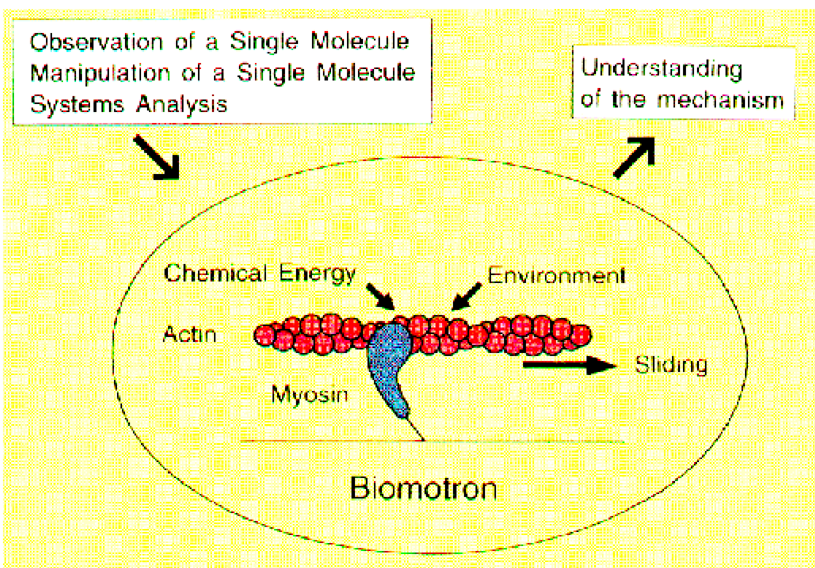

Fig. Yanagida.1. "Biomotron" and the goal of the project.

Research Strategy

The traditional method to observe biomotors is to stain them within cells with a fluorescent material. Optical microscopy reveals their motions and interrelationships. The actin is usually bound to a glass surface where ATP energy is added. To increase the dynamic observational capability in a liquid medium, various instrumentation having nanometer resolution and a millisecond time scale is being sought, such as evanescent laser optics (PSTM) as well as STM and AFM in high-speed imaging and low-level light detection.

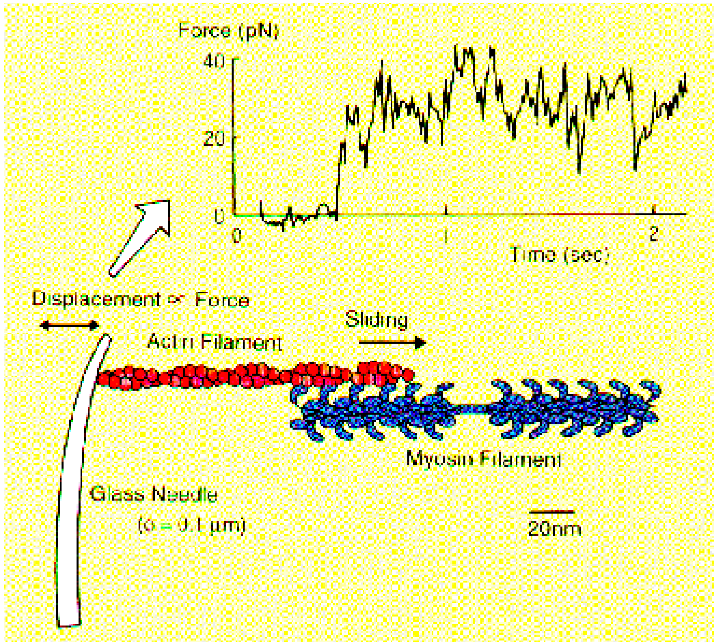

Fig. Yanagida.2. Measurements of the force fluctuation of a biomotron.

Yanagida has already developed a delicate technique in which a specially coated glass microneedle is manipulated by a piezo-actuator to catch and attach to an actin filament fixed to a glass surface. In this procedure both the nanometer movement and pico-Newton forces involved in the actin-myosin molecular-motor reaction can be measured on a 0.1 millisecond time scale while being observed in a liquid medium by fluorescent optical microscopy.

Instrumentation is also being developed for real-time tracking and measuring of the chemical reactions which occur in biomotrons in order to formulate chemical-kinetic energy transduction theories explaining how the biomotors run so efficiently and under ambient noise conditions and under varying loads. Since during one ATP interaction this motor produces many impulses, not just one, an important question is how a biomotron can control the rate of chemical energy release.

Structural analysis, which involves both the static and dynamic structures of the proteins that make up a biomotron, is also being carried out. The interface and interactions between molecules are being studied as well as how the molecular-level actions of biomotrons are translated into macroscopic motions.

Since it is impossible to connect each biomotron individually to the brain by a neuron, a systems analysis of the higher-level motion systems from many biomotrons is being conducted. Interacting biomotrons and the interfaces between the parts of biomotrons are also being studied, as well as reconstituted systems and intermolecular cooperation and information transmission in these systems.

YOSHIZATO MORPHOMATRIX 1992-1997

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Background

One of the most intriguing questions in biology is how starting from a single microscopic cell a macroscopic entity comprising billions of cells and having complex functions and shape that far transcend the characteristics of the original cell can grow through repeated division and differentiation. And all of this is done based on a single set of rules existing in the DNA of the original fertilized egg. Further, throughout its life each organism can heal injuries, and in some cases, such as frogs, can even undergo dramatic transformations, called metamorphosis.

Although much is known about the bio-molecular mechanisms by which cells divide and differentiate, the processes by which they arrange themselves to give the body shape and wholeness are little understood. Perhaps this situation exists because most previous research focused on cells rather than on what is called the extracellular matrix (ECM). In plants the ECM is the wood which binds the plant’s cells. In animals, it comprises a complex combination of several kinds of proteins including at least 17 types of collagen as well as laminin, fibronectin, and proteoglycans. The proteoglycans can also hold other control molecules, such as growth factors and hormones.

Normal animal cells require some substances to which to adhere; otherwise, they cannot express normal functions. Connecting is just one function of the ECM. Another important function is to provide locations for adhesion. When ECM components and cells are mixed they recognize each other and can thus combine together to self-organize tissues and organs. The orientation of cells is also an important phenomenon. One possibility is that orientation occurs when one cell adheres to the ECM and the cell membrane becomes polarized. This type of difference in the cell surface is also important for expressing normal function and specific form.

Katsutoshi Yoshizato believes that one of the most important ingredients for understanding the ECM, its components, and related metamorphosis is to take a very eclectic view. Just as looking only at cell biochemistry has failed to reveal the strategy for making a whole organism, anything but taking a wide view of all of the factors involved is insufficient. It is the overall picture — the cells in combination with the ECM — that is important.

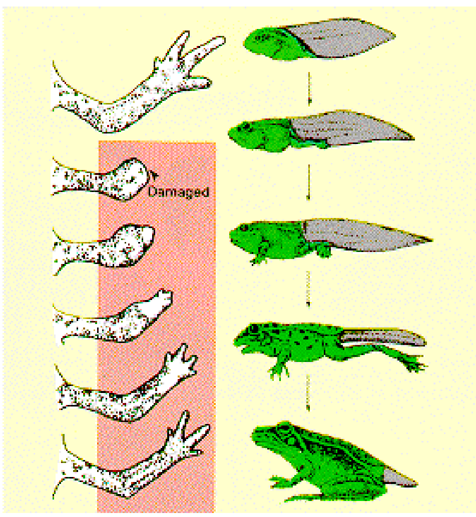

Fig. Yoshizato.1. Regeneration and Metamorphosis - Newts regenerate their limbs when damaged (left). Anuran tadpoles transform into frogs (right). These are representative of the reconstitution of the animal body shape.

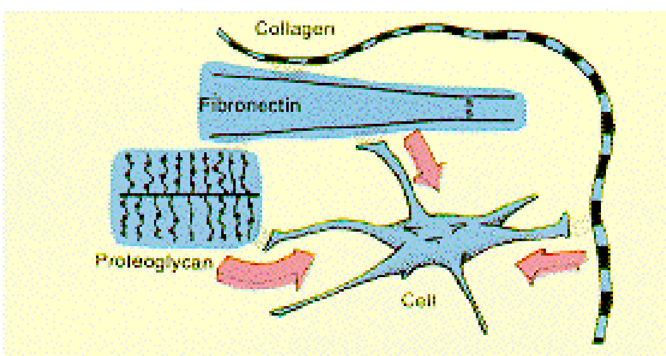

Fig. Yoshizato.2. Cells and ECMs.

Research Strategy

The Yoshizato Morphomatrix project is seeking to uncover the mechanisms for higher order organization and structure formation in animals by taking regeneration and transformation as the reconstituting of animal bodies and researching the role of the ECM in them. This project is a biological version of chemical self-organization: the self-organization of biological polymers and cells.

A major theme in this project is to observe the regeneration and transformation mechanisms of organisms. Emphasis is being placed on the frog and newt due to their outstanding regenerative and metamorphic abilities. Research includes investigating the molecular mechanisms which determine transformations in the head and tail regions, while focusing on the expression of homeotic genes as well as the genes for ECM molecules. Thus, the regeneration mechanism of the tail region, as influenced by thyroid hormones and retinoic acid, should be elucidated. In addition, the chemical entity of the mesenchymal factor which determines the region-specific differentiation of epidermal cells is being studied as well as the role of the ECM as a structural information molecule which controls regeneration and transformation.

The bearer of information for regeneration of tissues and organs in response to injury, and the factor which controls structural transformation, is either ECM itself, or something closely related to it. By clarifying this factor, it should become possible to investigate the role of ECM as a structure-information molecule as well as the mechanism by which signals from ECM are transferred into genes.

Using the cells and ECM which participate in the regeneration and transformation of tissues and organs, a search is being made for ways to reconstitute in-vitro the three-dimensional structure of tissues and organs. In order to construct an artificial model of this process, a search is being made for ways to analyze and reconstitute higher order structures (tissues and organs) by using the self-organizing properties of cells and biological polymers.

In addition to developing basic concepts related to the formation of structure in animals, this project is expected to provide the basic advances which will contribute to medical technology in the areas of artificial organs, such as tissue transplantation and the treatment of trauma.

YOSHIMURA π-ELECTRON MATERIALS 1991-1996

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Background

All of nature's plants, animals, and minerals contain molecules with two kinds of electron orbitals: sigma (σ) and pi (π). The σ electron structure holds nature together, providing strength. The π-electron structure, comprising clouds extending from normal to the bond axis between atoms, allows electrons to be mobile, resulting in bright green and red coloration of plants, as well as the absorption of the light necessary for photosynthesis.

Although the π-electron cloud is a fundamental reaction field for organic and biological materials, such as photo charge-transfer reactions, the π-electrons in these compounds cannot migrate freely without running into "barriers." In contrast, delocalized π-electrons can move widely throughout an inorganic crystal or molecule — graphite, for example — without distorting it. Such materials comprising them thus have many interesting characteristics, including low effective mass, extremely high electron mobility and superpolarization — π-electrons migrating over long distances when placed in electric fields.

Susumu Yoshimura, while being a group leader in the Ogata fine polymer ERATO project, discovered how to make graphite materials that are large single crystals — called "super graphite" — while studying the electrical properties of organic polymers. The electrons in graphite can move faster than the electrons in gallium arsenide high electron mobility transistors (HEMTs) that are being developed for the newest generation of supercomputers. Under the right conditions they may even become superconducting.

Little is known, however, about the roles of π-electrons in solid surface states or the quantum effects in two-dimensional conductors. Typical π-electron materials are low-dimensional graphites made in the forms of fibers and blocks having physical properties almost identical to those of single crystals. Carbon clusters, such as C_{60} and C_{70} — Bucky balls — can now be processed in large quantity. Although they are probably not a form of graphite, they can be made from graphite, and supergraphite materials are a good starting point for studying them.

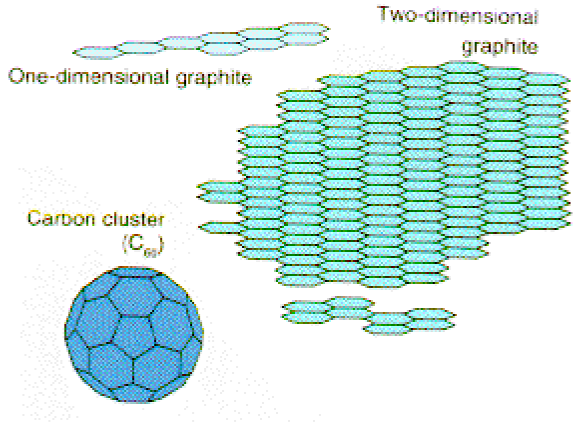

Fig. Yoshimura.1. Various forms of π-electron materials.

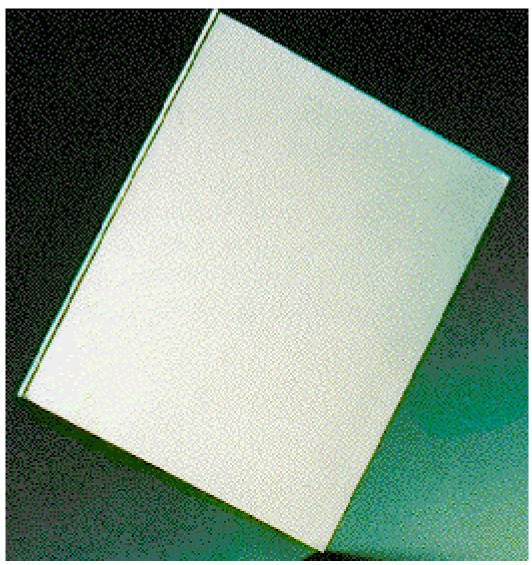

Fig. Yoshimura.2. High-quality graphite crystal (material with extended π-electron system).

Research Strategy

This project aims to study the large space occupied by freely-moving π-electrons as domains of electron motion and material transformation while elucidating the unique physical, chemical, and biological phenomena which result from these domains. In order to achieve these goals, synthetic methods are being developed for new materials with extended π-electron systems, which show high crystallinity. The mechanisms of superpolarization, high electron mobility, and nonlinear phenomena are also being elucidated while studying chemical reactions and electronic functions.

One part of this project is to create new synthetic methods for both organic and inorganic π-electron materials. In one-dimensional graphite, for example, benzene rings can be made to extend in only one direction, whereas ordinary graphite has benzene rings in two dimensions. Carbon clusters which contain benzene rings, or π-electrons condensed in a cluster, are also being sought.

Chemical and biological reactions are being designed on the surfaces of π-electron materials, such as graphite, Bucky balls, and silicon. There is much interest in the biological activities made available by π-electrons, such as proliferation or mutation. If there is a sudden change in the form of the character of a biological cell, as a basic property or structure, it probably involves some reaction involving π-electrons.

Graphite can be synthesized at very low temperatures (200°C, rather than the usual 3000°C) by controlling the structural order of the starting materials. In making graphite to be incorporated in semiconductor devices, low-temperature preparation is much more convenient. Further, the electronic states of π-electron materials are being studied using various equipment, such as the STM. More understanding should allow basic concepts to be developed for devices based on graphite and other π-electron materials.

A materials science based on π-electrons should enrich our knowledge concerning the optical, electronic, magnetic, chemical, and biological properties of π-electron materials, leading to new higher speed electron devices. Superpolarizability may lead to new nonlinear — red light in, blue light out — optical devices, which are essential for computers based on light. Biocompatibility might allow new materials for fabricating artificial organs. Bioactivity might result in new stocks or mutants.

NOYORI MOLECULAR CATALYSIS 1991-1996

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Background

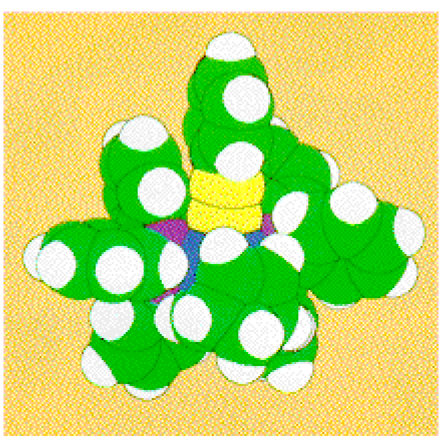
A perfect chemical reaction would produce only the desired product, with no waste of either raw material or energy. This would allow chemists to construct molecules of exactly the desired shape, including chirality.

Ryoji Noyori's research interests have been primarily in the exploitation of new synthetic methodologies — particularly those based on organometallic chemistry — and their applications. In 1966 he reported the first example of a homogeneous asymmetric reaction catalyzed by a transition-metal complex; in 1991 he received the prestigious John Gamble Kirkwood Award for his work in asymmetric synthesis and catalysis. He has also developed many practical catalysts for a wide variety of asymmetric transformations, with optical yields of over 90%, or even close to 100%, frequently being obtained.

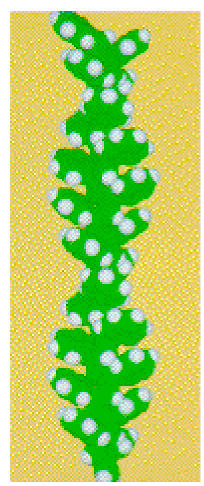
Noyori's strategy involves synthesizing well-shaped organic compounds, then attaching them to a central metal; it is thus possible to control the reactivity of the central metal through such a coordination of the organic ligand. Particularly important is regulation of the stereochemical outcome of the reaction, especially differentiation of right- and left-handedness. This technique must play a key role in science and technology at the molecular structural level.

In certain cases, the efficiency of artificial metal complexes rivals that of natural enzymes, allowing the production of large amounts of chiral compounds having both natural and unnatural configurations with the use of only a very small amount of chiral source. Some of them are applied to commercial production of significant compounds of extremely high enantiomeric purity. Until 15-20 years ago, the major way to obtain optically active compounds was resolution, because many synthetic chemicals are a 50/50 mixture of right- and left-handed molecules.

Noyori is particularly noted for his initiation of BINAP-transition metal chemistry (BINAP = phosphorus-based chiral organic ligand) which opened the tremendous potential to synthetic chemistry. His original research concerning homogeneous catalysis contributed to the development of an industrial process yielding (-)-menthol, a very useful fragrance.



Organorhodium catalyst



Poly (phenylacetylene) having a helical structure

Fig. Noyori.1a & b. Stereospecific polymerization with a well-designed molecular catalyst.

The industrial synthesis of beta-lactam antibiotics, a penicillin analogue, using Noyori's asymmetric hydrogenation technique, has just started.

Research Strategy

The Noyori molecular catalysis project will utilize a modern organometallic strategy. The basic principle, "molecular catalysis," relies on four-dimensional chemistry in which high efficiency is only attainable through a combination of both the ideal three dimensions (x,y,z), and appropriate kinetics (time). Well-designed metal complexes possessing chiral organic molecules as ligands are used not only to accelerate repeated chemical reactions, but also to precisely control the stereochemical outcome in a desired manner. Thanks to the diverse reactivities of the central metal atoms or ions, as well as unlimited structural permutability of organic ligands, this chemistry presents a general principle for the multiplication of chirality. "From ready-made to tailor-made catalysts" is a major theme of the project.

This project is focusing mainly on efficient reactions which can make both right- and left-handed molecules, either large or small, with high enentiometric purity. The project is also examining catalysts for the synthesis of stereo-regular polymers in which all of the chains are the same length. Catalysts with molecular exactness which approach perfection in catalyzing reactions that nature cannot perform are being studied.

Even though the design of catalysts is still empirical, the computer can be used to make models of chemical reactions. Strong emphasis is also being placed on the efficient synthesis of bio-active compounds. Important in biological science is the fact that many sites interact with molecules through molecular recognition, where matching of chirality plays a key role.

Further, high purity at the molecular level provides a new power to create new functions and materials. A typical example is liquid crystals. Many compounds and advanced materials (optics, magnetics, and electronics) need some appropriate molecular assembly, requiring a strict matching of chirality. Very pure, optically active compounds can make nice molecular assemblies. This will be the most important theme required to make advanced materials.

A strictly controlled synthesis of polymers having the same molecular weight and stereochemistry should provide a very powerful tool, particularly in the area of material science. The bulk properties of macromolecules, either natural or artificial, which are highly stereo-regulated in an absolute sense, are very different from those of stereo-random polymers. Synthetic polymers, which are purely left- or right-handed, may lead to unique, advanced materials. Since the evaluation of new polymers is very important, work in this field is also being carried out.

FUSETANI BIOFOULING 1991-1996

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Background

To the many existing species of biological organisms evolution has provided sophisticated chemical systems for communications. These are used for internal regulation, communication among members of the same species and protection from competing species. Such systems are found not only among terrestrial organisms, but more copiously among marine plants and animals. Regarding sea organisms — such as sponges, corals, mussels, barnacles, and tunicates — very little is known in this relatively specialized field. This is partly due to the fact that research has been fairly scattered among disciplines as well as target species. Further, whereas terrestrial organisms can be touched and observed directly, sea organisms are much more remote.

A barnacle larva upon hatching from its eggs, moults several times, and swims for a while before embarking on a “search” for a place to settle and grow. Carried by ocean currents, it floats and swims, while bumping into rocks, plants, fish, and a multitude of other organisms that influence each other. Organisms already growing in some ecological niche have chemical control mechanisms for preventing the settlement of other, competing larvae. Eventually, the larva comes into contact with unique chemical signals that indicate a satisfactory location for its particular species. The larva soon binds tightly to its new ecological niche, metamorphoses, and begins to make its shell and grow.

The biofouling process includes a very wide variety of phenomena, from the attachment and metamorphosis of marine organisms within their natural habitat, to chemical communication among organisms and chemical defense. It also involves the pathways and decisions that facilitate these functions. Once a larva touches the right place and receives a signal to stop and grow, many processes take place. Transmissions within the organism of information provided by these chemical substances can be understood to be due to the binding of chemical signals to receptors and the subsequent action of secondary messengers, similar to nerve transmitters and hormones. This project has some similarities with two other ERATO projects, the Mizutani plant ecochemicals project and the Torii nutrient-stasis project, since the communications systems of animals and plants on land or in the ocean might be quite similar.

Research Strategy

The Fusetani biofouling project is studying how marine larvae know when and how to stop, attach, and grow, paying special attention to barnacles, mussels, hydroids, and bryozoans. In order to understand settlement it is not only necessary to search for the chemical substances involved, but to carry out broad investigations of the structure, function, and characteristics of the receptors, as well as the functions of secondary messengers.

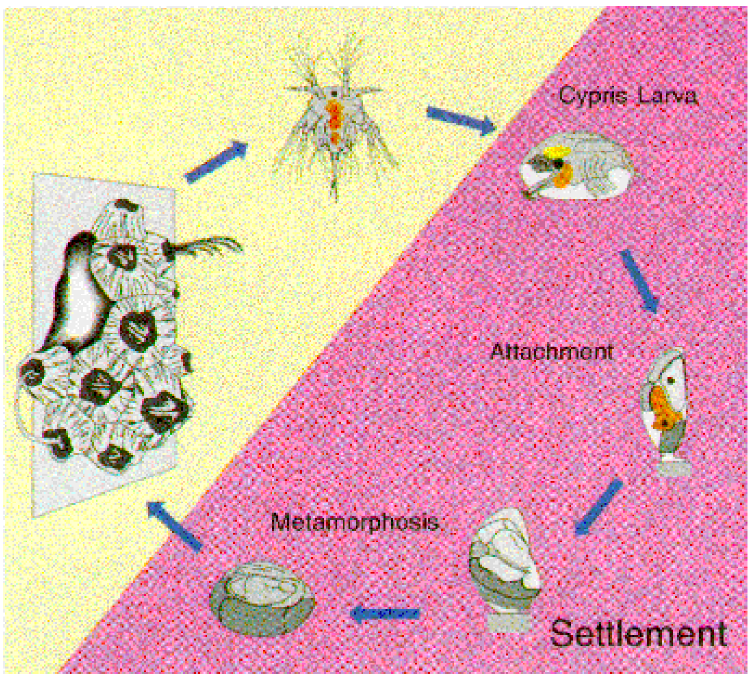

Fig. Fusetani.1. Life cycle of barnacle.

Although the biggest challenge of this project is to learn how to test chemical signals and settlement in the laboratory, even before this is done, the isolation and characterization of possible signal chemicals are being pursued while researching the basic physiology of larvae in order to determine what pathways exist for signal flow. Once this is achieved attempts will be made to determine the chemical signals that trigger the settlement of larvae, while describing the signal transmission and changes that occur within the larvae.

More specifically, the project is searching for settlement-promoting and -inhibiting compounds using highly sensitive bioassays, such as the electrophysiological type. It is also studying the characteristics, structure, as well as distribution of receptors and the expression of function by secondary messengers in order to determine the roles of chemical signals in settlement. Attempts are being made to attach microelectrode probes to the chemoreceptors of the above-mentioned organisms in order to pick up actual signals and to understand the many neurotransmitters, which may act directly on the nervous system.

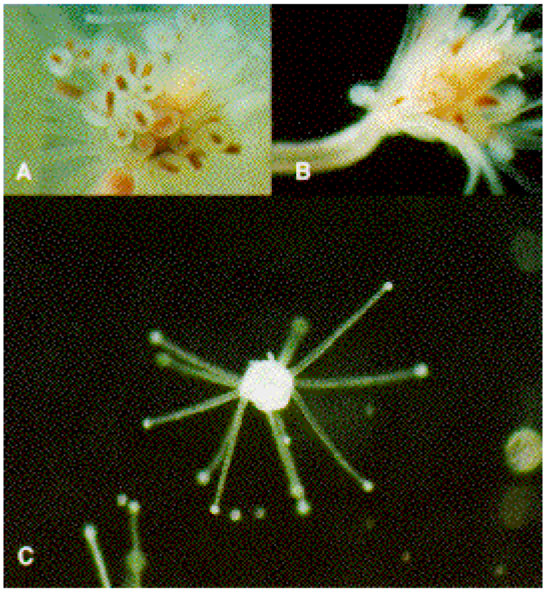

Fig. Fusetani.2. Marine hydrozoan *Tubularia mesembryanthemum*:
A) Polyp (male); B) Polyp (female); C) Actinula larva.

This research should not only contribute to our understanding of various life forms in the ocean but should also provide basic knowledge which can be applied to protecting marine environment and culture. From this research better ways might be found for controlling harmful marine organisms, thus helping to solve problems that have plagued humans for millennia, such as barnacle growth on ships, on fishing facilities, as well as on a wide variety of other man-made objects in the oceans. Better ways to cultivate oysters, abalones, and other marine organisms for food might also be found while perhaps also producing valuable pharmaceutical products.

OKAYAMA CELL SWITCHING 1991-1996

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Background

The various parts of an organism are formed by cells differentiating into new cells which stably express specialized functions. The cells of higher life forms — yeasts, plants and animals — grow and divide in a repeating four-step cycle: dividing, growing (G1), copying their genes, and growing more (G2). Because this process is crucial, the simple cycle has been left almost untouched by the ravages of time and evolution: for instance, the genes that control growth in human cells also function if put into yeast.

G1 growth immediately after division is the most crucial time, since some uncertainty exists as to whether the cell will actually copy its genes, divide, produce sperm and egg cells, change form, or lose control, becoming cancer. The cell's fate is determined by events which occur during G1. Thus, a cell's aging or becoming cancer can be considered to be a type of differentiation. Approaching cell switching based on gene expression and control may uncover a master switch deeply related to the existence of living organisms.

Research Strategy

This very basic project is utilizing a wide array of recently developed tools in order to unravel the secrets of G1 and how to regulate it. Although each human cell contains more than 100,000 genes, only a fraction has been identified regarding structure and function. Very little is known — such as where or how far apart — about the genes that are involved in actually controlling cell switching.

One tool for understanding the G1 process is a specially designed gene library containing DNA cloned from cells, perhaps human muscle. In the millions of volumes there may be many duplicates as well as missing "pages" or "chapters." This library also contains genes engineered to function in a wide variety of cells, from yeast to human, in order to search these libraries for the genes that control G1.

One search is being carried out with fission yeast mutants which have G1 defects. Efforts are being made to locate the human gene that corrects this defect. If it can be decoded — determine the structure of the protein that is made from it — from the protein's structure clues can be found as to its role in G1. To express mammalian, even human, genes in yeast, simply cutting out the gene and putting it into yeast doesn't work.

This is because the gene structure, especially the promoter, is different. However, since the protein coding region is quite similar, it can be expressed in yeast. To do this a promoter must be provided which works in yeast, necessitating the construction of some special construction vector. After making a cDNA library and putting all of the cDNA into this vector, a cDNA library will exist which can be introduced to yeast. Any yeast cell that acquires the gene corresponding to the defective gene is cured and can grow, thus duplicating the basic concept for selecting human counterparts.

By investigating the functions of individual genes and the mutual interactions of gene functions, it should be possible to uncover the control mechanisms for gene clusters. By introducing and substituting genes, a mammalian master switch can be constructed in yeast which can be used to explore ways to artificially control differentiation.

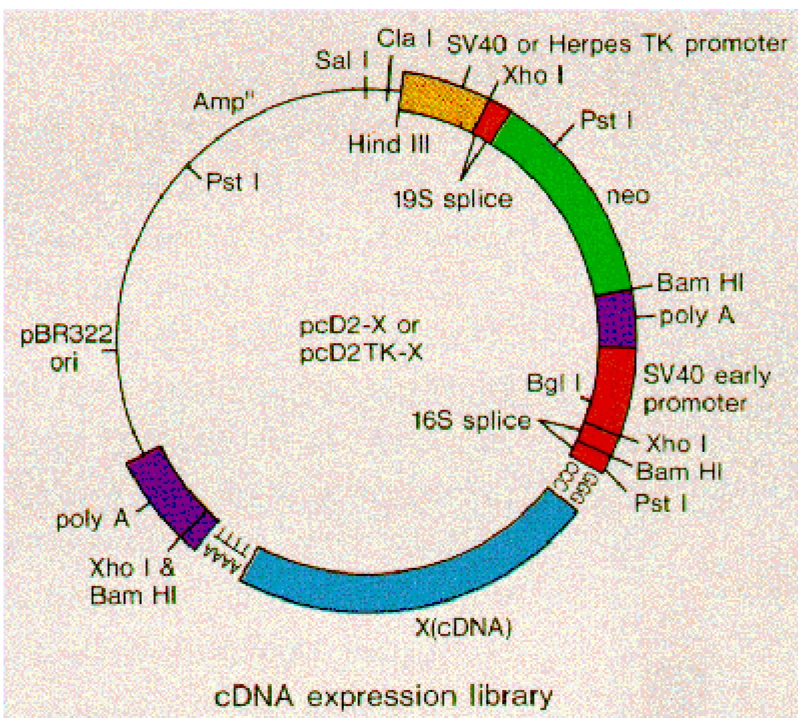

Fig. Okayama.1. Construction of cDNA libraries in a mammalian and yeast cell dual expression vector.

Another search is being carried out using a special kind of rat kidney cell: it becomes cancerous if exposed to growth factors. If the growth factors are taken away, the cancer stops and the cell returns to normal. The cancer can thus be turned on and off. Several mutants have this rat kidney cell, from which it has been learned that there are switches in G1. A search of the human gene library for genes that can correct the defects in these rat cell mutants is being made. Using these genes, it should be possible to learn about switches that turn on cancer in humans — and, perhaps, clues as to how to turn them off.

Efforts are also being made to reconstitute the control system, particularly the mammalian control system, in yeast. To artificially control this cell switching at a given organism is being pursued. Information concerning the universal control mechanisms for cell propagation and differentiation will hopefully yield clues to molecular mechanisms of cell aging, immortality, and oncogenesis.

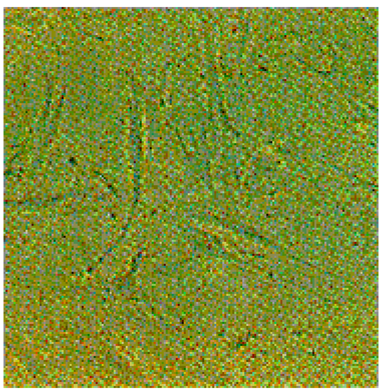

Fig. Okayama.2. Genetic complementation of mammalian cell mutant.

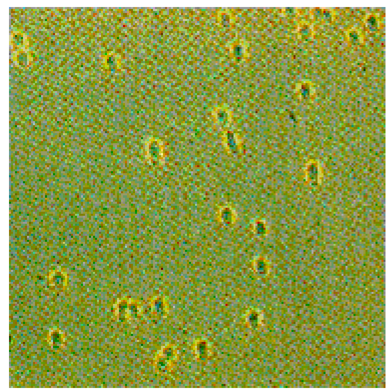

Fig. Okayama.3. Genetic complementation of S. pombe mutant.

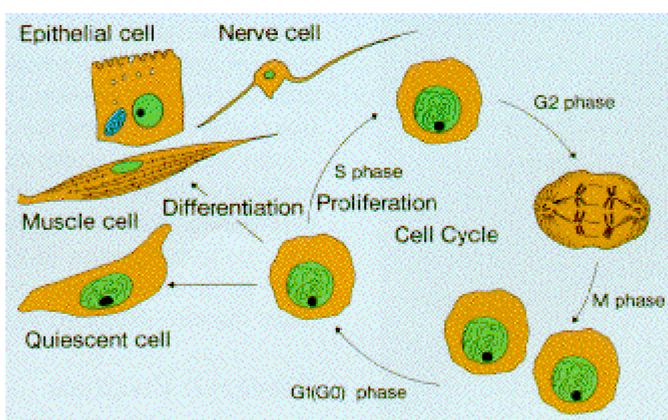

Fig. Okayama 4. Cell growth and differentiation.

KIMURA METAMELT 1990-1995

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Background

Even though many man-made products are solids which evolve from melts — glass, steel, aluminum, copper wire, plastics, and semiconductors — very little is presently understood about the processes involved. Sometimes literature data vary by an order of magnitude, a situation that is very different to that regarding solid state materials. Researchers are therefore searching for a clearer vision of the details concerning the many physical changes that take place during a melt which critically affect the final product.

Since the densities and inter-atomic distances of a melt are close to those of a solid, the attraction between molecules is much stronger than in a gas, suggesting that there must be some form of structure. Shigeyuki Kimura is a crystal grower who has experienced more than a few anomalies over the years regarding the melt process and has come to believe that nanometer-size clusters comprising several hundred atoms with some sort of microscopic structure are continuously moving while changing position with respect to each other. The metamelt project is attempting to elucidate the very basic mechanisms — "equilibration processes" — concerning the dynamics and processes of melts.

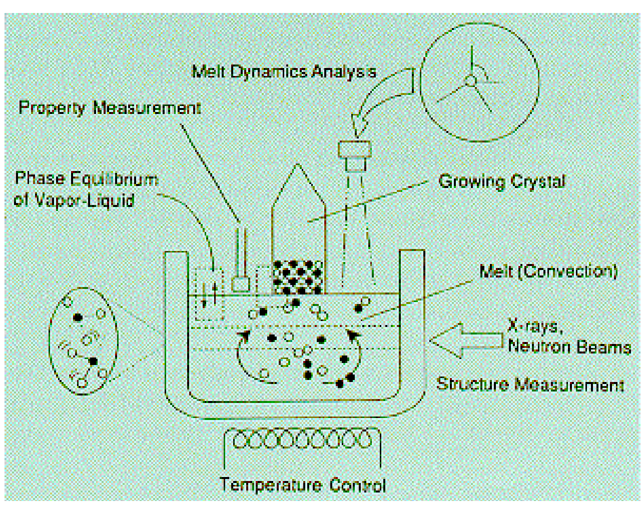

Fig. Kimura.1. Metamelt concept.

Figures Kimura.2 and Kimura.3 illustrate molecular dynamics simulation of silicon solid-liquid interface. The solid-liquid interface of silicon was simulated by molecular dynamics using the Stillinger-Weber potential. The liquid region was obtained by heating up a part of the periodic 1024-atom system to above the melting temperature. The color of the atom indicates three-fold (yellow), four-fold (white), and more than five-fold (red) silicon.

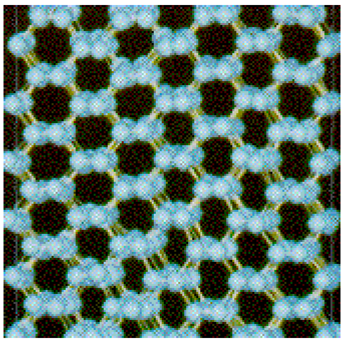

Fig. Kimura.2. Before melting (300K in solid phase, 700K in liquid phase).

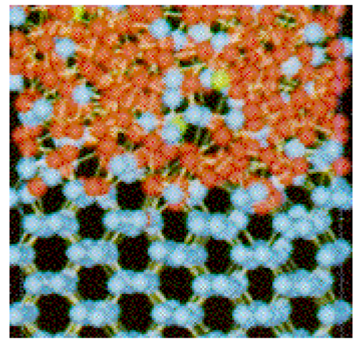

Fig. Kimura.3. After melting (300K in solid phase, 2200K in liquid phase).

Research Strategy

This project is focusing on the changes which occur in melts over time, while analyzing them regarding both structure and behavior. Of special interest are the melts of silicon.

As a key investigative tool, the possibility of using high-intensity X-ray beams to obtain scattering and small-angle diffraction of liquid melts is being explored. Another technique that is being developed involves non-linear laser spectroscopy. These and other techniques are being used to study such relaxation phenomena as viscosity, density, surface tension, and thermal diffusive characteristics. Direct observations of flow patterns in melts combined with simultaneous computer modeling are also being carried out.

An increased understanding of the microstructure and ordering of melts should lead to new materials and new processing technology. It is also hoped that the information gained through this project will allow crystals to be “grown in a computer” before actually carrying out production, as is done in the creation of large integrated circuits. This would allow custom designed optimum furnaces and growth conditions.

Research Progress

- In a study of how impurities behave in the molten state with silicon, antimony was investigated, since it is often used in high concentrations. By using a computerized investigative technique based on a combination of solubility and evaporation measurements it was found that antimony interacts with oxygen produced by the

Czochralski crystal-formation process to form Sb_2O molecules, a very unexpected and unique result. This new method is now being used to investigate other impurities in silicon. By using this technique it has become possible to predict what is going on at the interface of the molten and crystalline states, a point of longtime interest.

- Opposed to the common wisdom, it has been found that the density of a silicon melt as a function of temperature is not linear. A series of tests using various unique techniques has shown that there are at least three specific regions. In each region there is a different thermal coefficient, one of the most important factors when making a computer simulation. If it is high the tendency for convective currents is also high.

- It has been believed that a molten material once melted does not change. However, it has been shown that changes continued to take place even after 500 minutes. This study is being extended to longer time intervals. Such information is important regarding the final characteristics and quality of a crystalline material after being produced through a melt.

- When employing the Czochralski method for crystal formation a standard procedure is to use the rotation speed to control the amount of oxygen impurity in the crystal, believing that oxygen from the sides of the SiO_2 crucible is increased with rotation speed due to friction and other factors. However, both experiments using X-rays and tracer comprising tungsten coated with carbon as well as simulations have shown that increased rotation speed causes the oxygen to evaporate from the surface after complex circulation patterns, though oxygen coming from the bottom of the crucible does enter the crystal with increasing rotation speed.

- A new X-ray energy-dispersive analysis technique has been developed by which the situation surrounding individual atoms in a melt as a function of the temperature and other factors can be determined for the first time. The change as a function of temperature is believed to be related to the (above-mentioned) finding that the density is a non-linear function of the temperature.

NAGAYAMA PROTEIN ARRAY 1990-1995

Project Director: Dr. Kuniaki Nagayama
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University of Tokyo

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Background

Life in the universe as we know it is based upon systems of cells: from single-cell bacteria to trillions of complexly interacting cells — an organism. It is sometimes instructive to consider these cellular units as being “factories” containing various molecular machines consuming energy and material while carrying out complex processes and manufacturing new materials. Interestingly, many of the components of cells — amino acids to proteins to protein complexes (supramolecules) to cellular organelle — are formed by self-assembly under the instructions of DNA. These cells also produce all of the proteins and supramolecules necessary to form tissue and ultimately organisms that are a million times larger than the original simple protein.

If humans are to connect the manufacturing carried out at the bottom level of life with their future technology, it will be necessary to both understand and harness the self-assembly abilities of protein molecules — mesoscopic hands for human use. Until recently it has been generally believed that proteins are structurally weak, and thus unsuitable to join silicon, gallium arsenide, and the other materials that form the backbone of human technology. Kuniaki Nagayama, however believes that proteins are far tougher than ever imagined and that once their self-assembly abilities are understood and co-opted, much interesting and natural technology will become available.

Research Strategy

The Nagayama protein array project is dedicated to finding techniques by which proteins can be coerced to self-assemble into a wide variety of two-dimensional assemblies with unique features. To achieve this goal, not only do the protein-protein interactions and self-assembling processes need to be elucidated, but suitable substrates, or fields of space, must be perfected. Rather than using biomembranes, like those found in nature, an attempt is being made to utilize mobile fluid layers made on very clean substrate surfaces.

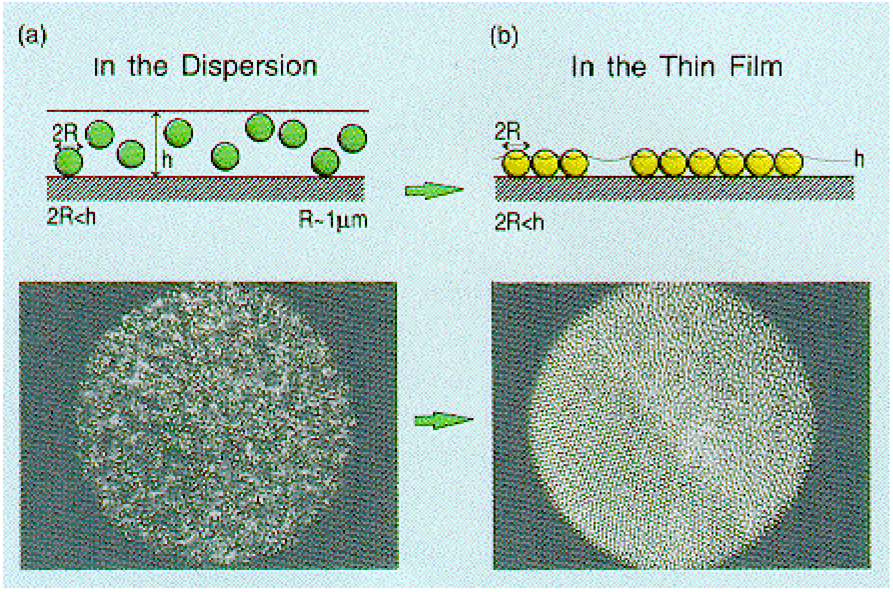
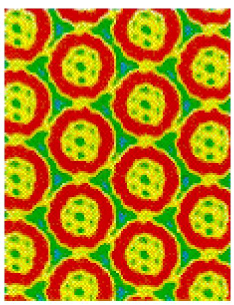
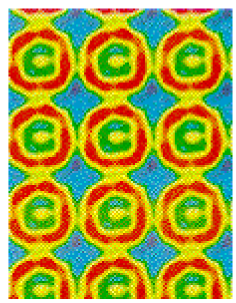


Fig. Nagayama.1. Fabrication of two-dimensional protein arrays.



Ferritin hexagonal lattice



Ferritin square lattice

Fig. Nagayama.2.a & b. Control of crystal form in protein arrays (computer-aided image).

Six years ago Nagayama developed a technique to spread proteins on mercury, which provides a very clean, flat surface. The present project is now generalizing this concept. It is also developing techniques by which assembled protein crystalline films can be transferred to the surface of a carbon or other substrate in such a way that the ordering of protein crystals can be preserved.

Further, an attempt is being made to maintain the original function of proteins while controlling their manner of integration on a substrate surface. By doing this it might be possible to design protein arrays having critical catalytic sites at optimum positions and orientations on the surface. To prepare a protein array with such desired two-dimensional patterns, the properties of protein-protein interactions are being changed by chemically modifying and genetically mutating amino acids on the protein surface and reshuffling domains using genetic engineering.

Research Progress

- The nucleation process in the assembly of proteins has been theoretically and numerically analyzed, and the local structural changes associated with mutagenesis calculated. Also, the surface charge contribution in relation to the effect of the surrounding ionic strength of the crystal stability has been investigated for ferritin using dielectric models. Hexagonally and squarely packed ferritin arrays have been prepared by controlling the inter-molecular attractive forces. Transmission, scanning electron, and atomic force microscopies were used to define the structures.

- The dynamics of the two-dimensional array formation of latex particles have been observed on a solid substrate by means of optical microscopy. The observations suggest a two-stage mechanism of two-dimensional crystallization of small particles: (1) nucleus formation, governed by attractive capillary forces appearing between particles partially immersed in a liquid layer; (2) crystal growth through convective particle flux caused by water evaporation from the already ordered array. This is a very general technique which can be applied to a wide variety of fine particles, including proteins. The new term "convective assembly" has been coined to describe this self-assembling crystallization process.

- Many recombinant proteins with modified surfaces have been made using genetic engineering. Convective assemblies prefer to use large and globular protein elements in the assembly process. By taking this as a "golden rule," large structural "artificial supramolecules" are being designed and made from the recombinant proteins and then assembled. The structural sophistication is in accord with the strategy used by nature, "biological hierarchy." In these attempts, however, an attempt is also being made to employ carbohydrate engineering, and even organic chemistry, as well as genetic engineering.

- It has been found that fluorinated oil (used as artificial blood), having twice the density of water, is an excellent fluid subphase upon which a two-dimensional protein can be made. Further, being quite volatile, it quickly evaporates, allowing the array to naturally lower onto a solid-surface substrate. It has further been found that even an aqueous solution, when it has a higher density than normal water, can be used as a flat subphase.

TORII NUTRIENT-STASIS 1990-1995

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Background

Even though nutrition and its biological mechanisms are extremely important, these subjects have not generally been a part of mainstream basic science. It was only recently that both scientists and the medical profession have come to realize that not only do the quality and quantity of food intake play a wide variety of critical roles in the health of any animal, but so do the condition of the internal mechanisms that regulate nutritional desire, biochemically as well as physiologically.

Along with a growing understanding of DNA, it has been learned that many times those susceptible to such diseases as hypertension have some accumulation of genetic defects. One type causes an extreme desire for salt, leading to hypertension. Many other diseases probably result from breakdowns at the basic level of the DNA and/or parts of the complex physiological systems that constantly monitor and regulate nutrition and metabolism.

Kunio Torii has long been concerned with what he calls “nutrient-stasis” — the ability of animals to subconsciously seek out those nutrients which are necessary for good health but are missing in their diet. In this process the animal’s cellular, especially neural metabolism is continuously changing in an attempt to maintain an optimum balance of internally available nutrients.

Research Strategy

The Torii nutrient-stasis project is studying the mechanisms by which animals change their diet in response to changes which occur both externally and internally. To this end, diets with varying degrees of nutrient balance are provided to animals while being observed externally by video and automatic monitoring of feeding devices. Internally, they are observed by monitoring body fluids in the alimentary canals, blood vessels, and brain, which indicate changes in hormone levels and growth factors.

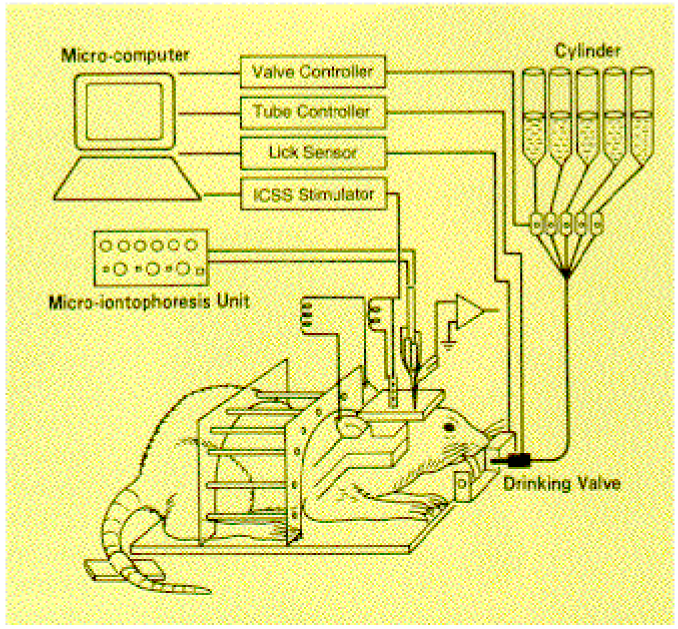

Fig. Torii.1. Neuron response in the brain to a specific nutrient.

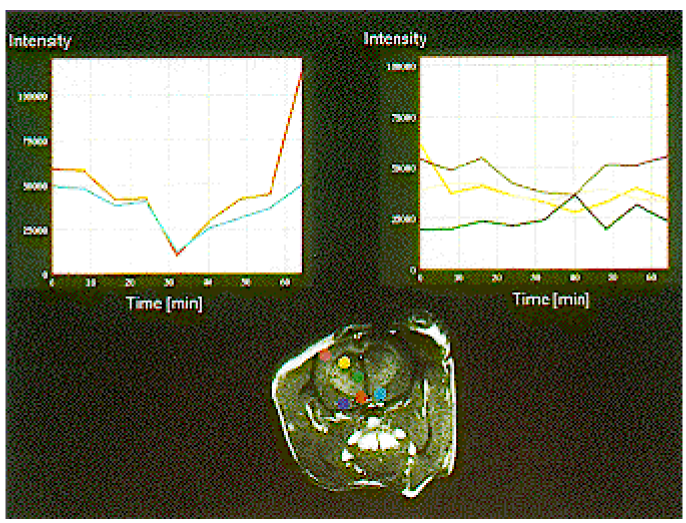

Fig. Torii.2. Brain function of a lys-deficient rat revealed by an MRI method.

Another important aspect of this project is to define the brain's "nutritional headquarters." To this end, magnetic resonance spectroscopy and imaging (MRSI) is being carried out. By performing brain and organ scanning it is possible to observe such chemical activity as the metabolism of animals after being fed various diets. It is hoped that these observations will allow a categorization of ATP use and how animals choose food. An outline of the chronology of the regulatory system before and after meals is also being pursued.

Further, by inserting very small probes into the critical regions of the brain related to nutritional behavior and metabolism, it is possible to continuously record the brain function in each neuron of a particular area without the use of anesthesia. Hormones and growth factors, including neurotrophic factors, are being applied directly to selected parts of the brain while following changes in both the feeding behavior and metabolism. In other experiments the desires of animals suffering from such metabolic diseases as diabetes and senile dementia as well as renal and hepatic failure are being continuously observed while isolated from external contamination.

The composite knowledge gained from this research will hopefully give a better understanding of the basic biochemistry and physiology by which animals maintain themselves through diet. This information might well lead to the prevention of metabolic failure in humans with the advance of age as well as other nutrition-related diseases while providing heightened health.

Research Progress

- An operant behavioral test system was developed by which the behavior of rats fed a nutrient-deficient diet can be analyzed. Specifically, rats which were fed an L-lysine (Lys)-deficient diet selected a Lys solution over a variety of others. Further, direct infusion of Lys into the lateral hypothalamic area of the brain removed the desire of the rat to select this nutrient but did not for the other amino acids. Thus, neuroplasticity in the hypothalamic area was established. Also, it was found that information seems to travel from the oblongata to the hypothalamus and that the brain cortex integrates information between the hypothalamus and other areas.

- Possible neurotrophic factors in serum from rats with and without deficiency of either protein or Lys were assayed. An increase in serum inhibin and activin A was observed in rats fed Lys-sufficient and nonprotein diets, respectively. However, serum activin A-like activity was severely suppressed under Lys deficiency. Further, immunohistochemical distribution of activin A in the brain was observed in addition to the finding that Lys-deficient and nonprotein diet caused a change in the serum levels of activin A as a possible neurotrophic factor. This release may elicit plasticity in the sensitivity for deficient amino acids of neurons in the brain nuclei that could selectively drive ingestive behavior for particular amino acids to maintain amino acid homeostasis.

- An exceptional MRI analysis system has been developed as a sophisticated observational tool. Its characteristics include a 4.7 tesla magnet with a bore size of 40 cm., providing a large (sufficient for a monkey’s head) and stable magnetic field in the bore. Further, the computer systems have been improved and new probes involving copper and plastic wires and tubes developed, which should allow for discrete imaging of neural activity in specific brain regions in response to changes of nutrient status.

SHINKAI CHEMIRECOGNICS 1990-1995

Project Director: Dr. Seiji Shinkai
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Background

In any organism millions of biochemical reactions are continuously taking place. Many of these occur due to very specific lock-and-key interactions: oxygen carried in a special receptor site of hemoglobin; cells held together by inter-cell proteins; enzymes that stimulate highly efficient, specific reactions; antigen-antibody interactions which accurately distinguish targets.

One of the most interesting species of molecules which undergoes host-guest-type specific relationships has a ring-shaped structure. The first such inclusion compound known was cyclodexterin, which has the ability to recognize and bind to organic molecules. The second comprised the crown ethers: hydrocarbons and oxygens which electrolytically bind to various guest metal ions, depending on the size of a fairly flexible ring.

Even more interesting is calixarene. Since it is in the shape of a bowl — "calix" means crater — rather than a simple ring, it can interact with guest molecules in a much more specific and strong way. The word "arene" indicates aromatic compounds, like benzene. According to Seiji Shinkai, these molecules are especially useful as hosts to metal cations and organic molecules. They do this through the intricate combination of hydrogen bonds, coordination bonds, hydrophobic bonds, electrostatic interactions, CH-π interactions, and others.

Through various possible simultaneous interactions as well as the ability to modify the number of the OH contact points with the cavity — generally between 3 and 8 — it is possible to design host sites that can accept a wide variety of three-dimensional metal ions and organic guest structures with both high selectivity and strength. Shinkai calls this process "chemirecognics."

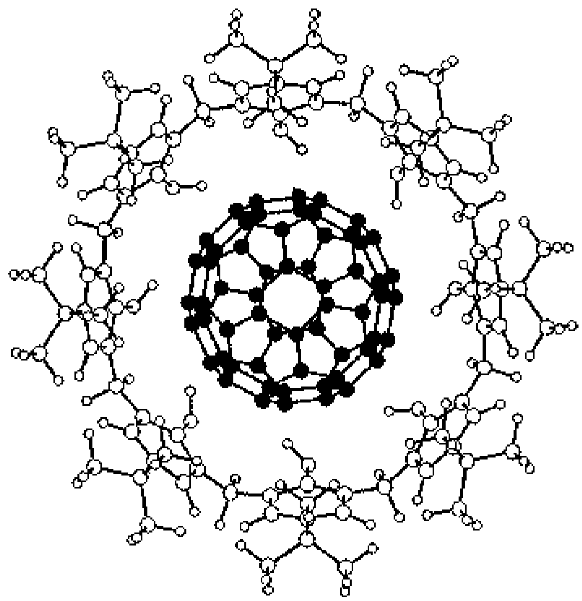

Fig. Shinkai.1. A top view of C_{60} included in calix[8]arene.

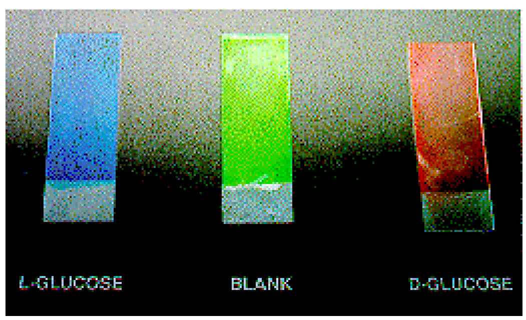

Fig. Shinkai.2. An intelligent liquid crystal to read out saccharide structure as color change.

Research Strategy

This project is exploring the basic relationships between the molecular structures of hosts — calixarene and other intelligent compounds — and their recognition properties. Through modifications, an attempt is also being made to design "artificial" recognition systems with very high recognition of and selectivity towards alkaline and rare earth metal ions and organic molecules. Sugars are especially challenging and important organic molecules. These efforts are not being limited to particular hosts, like those found in nature, but include entirely new recognition mechanisms as well as recognition targets, while also aiming to control (switch) the activity of the receptors.

This project is thus studying calixarenes and other compounds with the aim of establishing a high-precision chemirecognition system by introducing into these compounds: (1) an interface for binding with a specific guest atom or molecule, (2) a transducer for the information transduction, and (3) a stimulation receptor for "on-off" controlling the interface and transducer. Theoretical computer calculations are being made to support the design of such recognition systems. By establishing methodologies for designing recognition, superior molecular sensors and artificial enzymes with high selectivity, environmental resistance, and utility may be produced — all in artificial systems.

Research Progress

- Calixarene was modified in such a way that allowed an extraordinary quantum jump in selectivity (from about 103 to 105) of Na with respect to K. The success of this method was to reverse a clever method of nature. Since the only way to discriminate between physically similar alkaline metals is by size, in nature the antibiotic valinomycin can recognize Na against K by using a bigger ionophore which also fits to Rb. Though the affinity to K is slightly reduced, the affinity towards Na is only slightly decreased, but the selectivity is greatly increased. Thus, by designing a very small cavity as the "interface" — with a size between that of Li and Na — using calixarene capped with a 4-oxygen crown-type loop, a cavity with a very large affinity towards Na was obtained.

- It has been found that the C_{60} fullerene can be separated from other fullerenes in a carbon-powder soot using calixarene. Interestingly, calixarene is the third ring-type supramolecule and C_{60} is the third type carbon cluster, after diamond and graphite. This method produces a 1-to-1 complex of C_{60} and calix[8]arene. Surprisingly, when C_{60} enters the cavity of calix[8]arene it disrupts the intermolecular hydrogen bonding of the OH groups, causing the host to suddenly change from soluble to insoluble in such a solvent as toluene. By collecting the precipitated C_{60} calix[8]arene complex and then putting it into chloroform, which has an even higher affinity to the host, it replaces the C_{60} which is precipitated in 70% yield and 99.8% purity. This new method has greatly reduced the separation costs by possibly 1/50 or so while making the standard method, chromatography, obsolete.

- Other than calixarenes, cholesterol and boronic-acid moieties could be used as platforms of "intelligent" recognition. Since cholesterol forms a helical structure, the stability and related aggregation structure could be controlled by introducing certain substitutes and changing the C-3 position. It was also found that the cholesterol boronic-acid derivative can be applied to the recognition and optical resolution of saccharides (sugars). A saccharide and a cholesterol boronic acid compound form a 1:2 complex with a different steric structure, depending on the type of saccharide used. Upon the addition of such a complex to a cholesteric liquid crystal, the stability of the helical structure of the liquid crystal is differently affected by the structure of the complex, as a "transducer," thus producing a different color change depending on the type of saccharide of the complex.

YOSHIDA NANO-MECHANISM PROJECT 1985-1990

Project Director, Mr. Shoichiro Yoshida
Managing Director
Nikon Corporation

Background

High-precision measurement capabilities are at the heart of scientific research and are synergistic with technological development, especially with regards to the present trend towards miniaturization and "nano-engineering." This project focused on the physical actions and mechanical properties of material in the nanometer region, while investigating new measuring and processing methods.

Research Results

- **Scanning tunneling microscopes:** Several types of scanning tunneling microscopes (STM) were designed: an STM contained within the chamber of a standard scanning electron microscope (SEM), an industrial-type STM for viewing samples from long distances in air, a computer-controlled industrial-type STM, and a device comprising a twin-probe STM controlled by a complex mechanism of PZTs and a hinge.

- **X-ray microscopy:** While placing emphasis on the use of both Fresnel zone plates and phase zone plates, X-rays of 1–4-nm wavelength were found to be selectively absorbed by biological specimens, making high-resolution X-ray microscope images possible.

- **Nanometer position-control system:** A one-axis stage-positioning mechanism was developed using an actuator, newly designed AC synchronous linear motor, and a rolling ball guide which acts like a spring. This system provides an outstanding resolution of 1 nm and a maximum speed of 200 mm/s.

- **Small-distance positioning systems:** A new device employing an ultrasonic linear motor was developed which uses a segmented PZT bimolf which is 90 degrees out phase.

- **Nanometer measurement system:** A two-wavelength (488 and 244 nm) laser beam interferometer which can eliminate errors caused by air turbulence was developed.

- **X-ray multilayer mirror fabrication:** Since multilayer coatings are necessary for reflecting X-rays in normal-incidence optical systems, the reflectiveness of multilayers made from a wide range of materials were calculated using the Fresnel equation for 1-5 nm wavelengths.

- **Beam processing to make ultra-smooth surfaces:** Low-energy (50 eV) Ar-ion/atom beam sputter etching was used to produce atomically smooth surfaces which are applicable as substrates for X-ray multilayer mirrors. This type of processing causes less damage to processed surfaces, making it possible to polish the surface of each layer of X-ray multilayers.

KURODA SOLID SURFACE PROJECT 1985-1990

Project Director: Dr. Haruo Kuroda
Professor, Faculty of Science
University of Tokyo

Background

This project investigated various chemical processes to modify silicon surfaces and to fabricate organic multi-layers using reactions with surface functional groups. Both chemical and photochemical processes were exploited in order to attach metal clusters to silica surfaces as well as to the surfaces of silicon single crystals. This effort was aimed at establishing fabricating methods for specified metal clusters on surfaces. Investigations were also carried out on the formation of new material systems, such as bimetallic artificial superlattices, using molecular beam epitaxy.

Research Results

- **New detector for SEXAFS:** A small UHV-compatible X-ray detector was developed for soft-X-ray spectroscopy using synchrotron radiation. This device has greatly expanded the possibilities of applying both surface EXAFS and soft-X-ray standing-wave techniques to investigations of adsorbed layer structures on surfaces. The structures of S and Cl layers adsorbed on metal single crystal surfaces were extensively investigated using these techniques.

- **Superlattices with unique magnetic properties:** Bimetallic artificial superlattices (Eu/Mn, Eu/Yb, Sm/Yb and Dy/Yb) were synthesized using MBE. It was also found that rare-earth metal layers with structures that are normally unstable could be grown by utilizing the epitaxial relation with the substrate.

- **Photochemical grafting of metal clusters:** It was found that a variety of new types of metal clusters can be selectively fixed on a silica surface by utilizing photochemical processes.

- **Hydrogen passivation of a silicon surface:** A new method called “UV/HF cleaning” was developed for obtaining passivated clean silicon surfaces. On a silicon (100) surface treated by this technique dangling bonds were found to be completely terminated with hydrogen.

- **Chemical modification of silicon surface:** A new method was developed for terminating the dangling bonds on a silicon surface using fluorine atoms. The Si-F bonds on a thus-fluorinated surface were found to be completely converted to Si-OH bonds, producing an OH-covered surface when treated with ultra-pure water.

- **New molecular beam source for organic MBE:** A special type of K-cell was developed for depositing an organic material using a molecular beam technique under UHV conditions.

HORIKOSHI SUPERBUGS PROJECT 1984-1989

Project Director: Dr. Koki Horikoshi
Professor, Faculty of Engineering
Tokyo Institute of Technology

Background

The Horikoshi superbugs project conducted a world-wide search for bacteria that thrive under extreme conditions of pH, salinity, and temperature. Interesting specimens found during this search were studied regarding their DNA, RNA, proteins, lipids, and polysaccharides as well as tolerance mechanisms, metabolic pathways, and gene expressions.

Research Results

- **Unique triangular bacterium:** A very unique microorganism was discovered living in Japanese saltern soil at a temperature of 37°C and a salinity eight times that of sea water. This extremely halophilic archaebacterium — Haloarcula japonicus — is triangular in shape and moves using flagella.

- **Solvent-tolerant bacterium:** A variant strain of Pseudomonas putida (IH-2000), an aerobic gram-negative rod, was discovered which is capable of growing in culture media containing more than 50% (v/v) toluene or high concentrations of cyclohexane, xylene, styrene, and heptanol.

- **Thermophilic bacteria:** A number of novel thermophilic bacteria were isolated from Japanese hot springs and surrounding soils. Thermostable enzymes recovered from such strains including ß-glucosidase, trehalase, pullulanase, heparinase, and chondroitinase were characterized and developed for commercial use. In many cases, the genes encoding these enzymes were cloned in E. coli and their complete nucleotide sequence was determined.

- **Alkalophilic bacteria:** Several new alkalophilic bacteria were isolated, including two selenium-resistant strains capable of growth in a highly alkaline medium containing more than 1% selenite.

- **Methanogenic archaebacteria:** Several new species of halo-, alkalo-, and thermophilic and psychrotolerant methanogenic archaecbacteria were isolated and characterized.

- **Basic analysis of genes:** The ori regions of the DNA of several species of bacteria have shown a new consensus sequence in bacterial plasmids and in the phage lambda.

- **Thermal properties of superbacteria:** The thermal properties of superbacteria have been studied using heat leakage scanning calorimetry, a useful technique for studying the structures, stabilities, and conformational changes of macromolecules without separations into each constituent fraction.

- **Magnetite-producing bacteria:** A better understanding of how small (150-250 nm) magnetic particles are produced by magnetotactic bacteria has been obtained by simulating magnetite synthesis *in vitro* using the enzyme urease.

HAYAISHI BIOINFORMATION TRANSFER PROJECT 1983-1988

Project Director: Dr. Osamu Hayaishi
Director, Osaka Bioscience Institute

Background

The project was aimed at elucidating the mechanism of intercellular and intracellular information transfer through studies of prostaglandin (PG) neuroactive actions and to apply basic-principle type concepts to medical problems as well as information technology.

Research Results

- **Basic biochemical understanding of prostaglandins:** Results clearly showed the importance of PGs in the central nervous system as well as in many other tissues.

- **Regulation of autonomic body functions:** It was found that PGD_2 in the brain is involved in the regulation of such autonomic functions as temperature and ocular pressure as well as the states of sleep and wakefulness through attachment to special receptor sites.

- **Transmission of bodily information:** It was demonstrated that PGD_2 plays an important role in the transmission of pain and the sense of smell. It also seems to have a significant effect on such emotions as depression.

- **Distribution of receptors in the brain:** Using computer-assisted image analysis of autoradiographs and positron emission tomography (PET) scanning techniques, the distribution of receptors for prostaglandins in rat and monkey brains was mapped.

- **Enzymology of prostaglandin biosynthesis:** An understanding was obtained of the biochemistry and enzymology of the biosynthesis and interconversion of the various members of the PG family.

- **New mechanism of biotransmitter release:** It was found that there are PG E_2 receptors in the adrenal medulla which can induce catecholamine release from chromaffin cells.

- **Morphological and biochemical differentiation:** PGD_2 was found to act as an intercellular mediator, a bio-transmitter, as well as an intercellular regulator in the development of the brain.

- **Sensitive immunoassay method:** A new method of highly sensitive solid-phase enzyme immunoassay (EIA) was developed for the determination of prostaglandins in various tissues, particularly in the brain.

- **Prostaglandins in development and aging:** Immunohisto chemical studies on the localization of PGD2 synthetase in rat brain have shown that the major site changed from neuron to oligodendroglia with age.

MIZUNO BIOHOLONICS PROJECT 1982-1987

Project Director: Dr. Den'ichi Mizuno
Professor, Faculty of Pharmaceutical Science
Teikyo University

Background

Though science and technology have created elements and systems with fixed functions, such as ICs and computers, the cooperative interactions between individual elements — holons — making up such systems as biological organisms have great need to be explained. This project has shown special cooperative aspects of this type of interaction to be maintained among molecules, cells, tissues, and organs for energy conversion, information processing, and immunology.

Research Results

- **Macrophage priming:** It was shown that human macrophages can be primed by various agents such as vaccines and other biological response modifiers (BRMs) involving lentinan and gamma-interferon so that they can be triggered by agents such as OK432 to produce the tumor necrosis factor (TNF).

- **Endogenous TNF production:** An endogenous production of TNF in mice was demonstrated by a combined use of commercial drugs, such as gamma-IFN and OK-432. This procedure was then shifted to cancer patients in order to confirm their endogenous production of TNF.

- **A new TNF:** A new TNF (TNF-S) was isolated from the supernatant of THP-1 culture cells. The antitumor effect on TNF-S has been remarkable in clinical trials.

- **Atherosclerosis and macrophges:** In order to activate macrophages in atherosclerotic lesions, monoclonal antibodies against lipid laden cells and against extracellular matrix deposited with lipids in Watanabe heritable hyperlipidemic rabbits were developed.

- **Elimination of lipid deposits using macrophages:** Novel monoclonal antibodies against human atherosclerotic lesions (256C) were shown to be useful for activating macrophages in order to accelerate the elimination of lipid deposits.

- **Self-creation of operational information:** The generally understood mechanism for the self-creation of operational information was attacked and clarified. In this process, neuronal holons were studied based on neuronal network dynamics in the brain. A holon computer, holovision, was designed and constructed for pattern recognition based on the clarified mechanism.

- **Autonomic controls of chemo-mechanical energy conversions:** Autonomic controls of chemo-mechanical energy conversions in some biological motions were also studied. It was shown that myosin molecules in muscle as well as dynein molecules in flagellum work cooperatively as holons. Motors with an automatic control, named biomotors, were created by utilizing actin and myosin molecules isolated from rabbit skeletal muscle.

HAYASHI ULTRA-FINE PARTICLE PROJECT 1981-1986

Project Director: Dr. Chikara Hayashi
Chairman, ULVAC Corporation

Background

In this project, ultra-fine particles were produced for the purpose of clarifying the mechanism of nucleation and growth. The physical, chemical and biological properties of ultra-fine particles as well as crystalographic, electromagnetic, optical, thermal, and catalytic properties were also investigated. Studies were advanced in order to develop techniques for controlling particle size and composition as well as applying unique properties.

Research Results

- **Spraying process of ultra-fine particles:** Ultra-fine particles of nickel and titanium nitride, or iron and silver were evenly mixed and compacted by spraying while successfully producing thin films of ultra-fine particles, enabling the manufacturing of various alloys and composite materials which have unconventional properties.

- **Manufacturing of ceramic ultra-fine particles:** gamma-AlO_2O_3, ß-SiC ultra-fine particles of (50 to approximately 200 nanometers) were made by an arc discharge in an argon gas atmosphere using Al and Si electrodes. This process enables the production of high-strength ceramics without a binder.

- **Lattice-shape deposition of ultra-fine particles:** A method for depositing gold ultra-fine particles regularly on a silicon substrate with several tens of angstroms spacing was developed, enabling the manufacturing of high-performance electronic elements and for the production of ultra-high density recording materials and ultra-fine beam machining techniques.

- **Ultra-fine particles of organic compounds:** Organic compounds of anthracene, pyrene, and phai-locyanine could be atomized to ultra-fine particles by evaporation in a gas. Water-insoluable materials which are almost impossible to soak are easily dispersed in water.

- **Single molecular ultra-fine particles:** Isolated ultra-fine particles such as Ni, Fe, Cu, Sn, and Pb could be formed having mean particle diameters of 40-200 Å. This process will enable the manufacture of new isolated ultra-fine particles coated by polymers which have an affinity to living bodies and are useful for medical and biological applications.

- **Ultra-fine particle catalysts of higher selectivity:** It was found that ultra-fine particles of nickel or copper-zinc compounds are excellent catalysts for the selective hydrogenation of organic compounds.

- **Polymer-coated ultra-fine particles:** Vinyl was introduced to the surface of Fe ultra-fine particles, allowing a polymer coating (5-20 nm) to be formed by a radical copolymerization of vinyl monomer and micro-capsules.

MASUMOTO AMORPHOUS & INTERCALATION COMPOUNDS PROJECT 1981-1986

Project Director: Dr. Tsuyoshi Masumoto
Professor, The Research Institute for Iron, Steel and Other Metals
Tohoku University

Background

The aim of this project was to synthesize unique, inorganic, non-equilibrium structures/materials for industrial use by drastically changing the composition, atomic configuration, and electronic structures of various kinds of materials.

Research Results

- **Amorphous metallic fine particles:** Amorphous fine particles 800-1200 Å in diameter could be formed on substrates by sputter-depositing various metals and metal-oxides after ionized-argon gas etching of the substrate. These particles simultaneously display the characteristics of both amorphous materials and fine particles.

- **Amorphous ferromagnetic thin film:** A transparent, perpendicularly magnetized ferromagnetic thin film has been produced by sputtering in the presence of fluorine. Also, a fluoride thin film with nickel and cobalt has been found to be an excellent alloy with transparent and anti-corrosion characteristics.

- **Ferromagnetic amorphous oxide:** An amorphous ferromagnetic oxide has been made by rapid-quenching or by the sputtering method after adding various oxides to antiferromagnetic $FeBiO_3$. This material has good transparency and magneto-optical properties as well as anti-corrosion characteristics

- **Water-soluble amorphous oxides:** A new colloidal oxide thin film has been synthesized by rapidly quenching V_2O_5 based on binary amorphous oxides.

- **Crystalline BN and BN based composite ceramic:** High crystalline rhombohedral BN, hexagonal-based ceramic and B-N-Ti/B-N-Si-based nano-compound ceramic materials have been synthesized by a CVD method at comparatively low temperatures, having excellent heat resistivity, stability, and electric insulation characteristics.

- **Transparent B-N-Si base amorphous ceramics**: Amorphous BN base ceramics containing 20-30 wt% silicon were synthesized by CVD. The addition of silicon improved the moisture resistibility. Being transparent, these materials have applications as heat-resistant and anti-corrosive optical materials and coating materials.

- **Bi-directional optical memory:** Tris (1, 10-phenarthoroline) Rhodium (III) complex ions were intercalated into the interlayer space of montmorillonite, creating a material that allows optical writing and erasing. A very thin film of less than one micron has good contrast and stability for long time periods.

- **Iron oxide based perpendicularly magnetized thin film:** An iron-oxide base (Fe-B-O, Fe-M-O) thin film has been produced by the sputtering method. The thin film is abrasion resistant with anti-corrosion characteristics and is applicable as a material for both floppy and hard discs.

OGATA FINE POLYMER PROJECT 1981-1986

Project Director: Dr. Naoya Ogata
Professor, Faculty of Science and Technology
Sophia University

Background

The major purpose of this project was to work toward the development of a new generation of synthetic condensation-type polymers of high added value by taking as models the sophisticated functional capabilities of such condensation macromolecular polymers as the DNA, proteins, and phosphatides of living organisms.

Research Results

- **Synthesis of graphite film:** A large-area graphite film having the same physical properties as single-crystal graphite was synthesized by the pyrolysis of POD (poly-para-phenyleneoxadiazol) in a high-temperature inactive gas atmosphere.

- **Crystalline Polymer:** Polymethacyclophane, having a rigid, straight molecular chain and highly crystalline characteristics, has been synthesized. This material can be used as heat-resistant fibers or a fibrous electric conduction material.

- **Condensation polymer ultra-thin film:** An aromatic anphiphilic monomer was dispersed on the surface of water and underwent a double-condensation reaction with another monomer added into the water. Thus, a single-molecule layer film of an aromatic condensation product could be synthesized that is heat resistant and stable in such organic solvents as acetone and alcohol.

- **Polymer synthesis under normal temperature and pressure:** Polyester compounds could be synthesized from carbonic acid and glycol base raw materials using a phosphor catalyst. This enables syntheses under normal temperature and pressure as opposed to conventional polyester synthesis under high temperatures (200-300 °C) and high vacuum (less than 1mm Hg).

- **Single molecular particle of polymer:** A polymer solution was dispersed on the surface of water while producing an ultra-fine particle comprising organic polymers. This technique has enabled the investigations of such polymer surface properties as adhesion, wetting, and lubrication.

- **Absorption materials for separation of optical isomers:** By fixing a chiral group of a polymer carrier with a special molecular structure of amino acid bases, a new bead-like material which has the function of material separation, has been made. This enables a complete separation of such optical isomers as D. L-amino acid. It can also function as a catalyst.

- **Synthesized urease:** This is a hollow fine particle having a polyoxyethylene derivative that can selectively absorb and remove urea. It has applications in the construction of artificial kidneys, various sensors, and functional electrode materials.

NISHIZAWA PERFECT CRYSTAL PROJECT 1981-1986

Project Director: Dr. Den-ichi Nishizawa
Professor, Research Institute of Electrical Communication
Tohoku University

Background

This project worked toward developing a new generation of semiconductors by combining silicon and gallium arsenic perfect-crystal formation and static-induction control technologies. Static induction transistors (SIT) and thyristors were developed featuring such characteristics as high operating speeds, low noise, low power consumption, and large-power handling capacities. Furthermore, crystal photoepitaxy by optical irradiation has been developed as a technology which permits the control of crystal growth with minimal energy, while providing valuable data regarding crystal growth.

Research Results

- **Photo-excited molecular layer epitaxial growth:** The growth of epitaxial films which are necessary for making GaAs compounds semiconducting elements has been realized by low-temperature (350°C) and high-precision (2.5Å) crystal control. This method is applicable for making ultra-high-speed switching circuits and new light-emitting elements. In terms of crystallography, new experimental facts have been obtained regarding the control and elucidation of the stoichiometric structures of GaAs single crystals.

- **GaAs single crystal:** By introducing an arsenic pressure-control method, single crystals having very few lattice defects could be realized. This enables the manufacturing of ultra-high-speed switching elements that are two to three orders faster than ordinary silicon single-crystal elements as well as high-efficiency photo-electric transfer elements.

- **Electrostatic-induction type photo-sensor:** Development of an electrostatic induction transistor which can amplify weak light and convert it to an electric signal. This low-power, low-noise element can detect very weak light ($4x10^{-6}$ lux-sec). Super high-performance SITs are produced so thin that disturbances caused by lattice vibrations are virtually insignificant.

- **Double-gate type thyristor:** A basic technique for manufacturing large-power, double-gate, static-induction thyristors has been established. This thyristor has a peak voltage of 1kV, a current capacity of 100 amps and a sub-microsecond switching speed. It enables the miniaturization of electric motors through the use of higher-frequency power supplies.

- **Ultra high-density SIT integrated circuit:** An integrated circuit having a special structure and using a silicone substrate close to a perfect crystal has been manufactured. This IC enables low-power consumption (less than 10-12 joule), ultra-high-speed switching (less than 10^{-9} sec) and ultra-low capacity (less than 2×10^{-12}W). This performance is one order higher than conventional circuits.

SAKAKI QUANTUM WAVE PROJECT 1988-1993

Project Director: Dr. Hiroyuki Sakaki
Professor, Research Center for Advanced Science and Technology
University of Tokyo

Background

This project was aimed at breaking the barrier imposed by a lack of crystal fabrication techniques on the 50-200 Å level. The project's goals were to develop an understanding of microscopic crystal growth, to develop methods to control the wave state, and to prepare wire and dot structures with good size and cleanliness control.

Research Results

- **Sharp ridge-type quantum wire:** An MBE method for controlling the growth of very sharp ridge structures at the nanometer scale was found. Photoluminescence and cathodeliuminescence measurements showed a clear and intense peak of luminescence from the quantum-wire state.

- **Edge-type quantum wire:** In the edge-type quantum wire, electrons in quantum-well structures were pulled to their edge region by an electrostatic potential to form a wire. A 100 nm-wide N-AlGaAs/GaAs edge quantum wire was successfully fabricated by growing a layered facet structure on a patterned substrate and then depositing another overlay.

- **Self-organization of an island-type quantum structure:** It was shown that a novel microscopic process of crystal growth can lead to the formation of dot structures when a small amount of InP is deposited on GaAs. Coagulation automatically gave an InP island structure.

- **Etched V-shaped quantum structure:** To control crystal structure, an effort was made to develop an ultra-clean selective etching technology for the GaAs and related materials.

- **Resonant scattering transistor:** Quantum wave phenomena and devices, including a resonant scattering transistor, were also studied. This structure is almost as simple as the usual field effect transistor in which the flow of electrons through a thin conducting channel is controlled by a gate electrode.

- **Novel turnstile device:** In cooperation with the Technical University of Delft, a novel turnstile structure has been developed to control the transfer of one electron per one cycle of the gate modulation with a failure rate as small as 10^{-4}.

- **Electron relaxation in a quantum dot structure:** In calculating the relaxation rate in a GaAs quantum dot up to the second order in electron-phonon interactions, it was found that a two-phonon (LO+LA, LO-LA) process can give rise to rapid (subnanosecond) relaxation for suitable values of level separation. Based on this finding, prescriptions for highly-efficient quantum dot lasers have been achieved.

MASUHARA MICROPHOTO CONVERSION PROJECT 1988-1993

Project Director: Dr. Hiroshi Masuhara
Professor, Faculty of Engineering
Osaka University

Background

This project was aimed at developing innovative techniques using lasers to convert molecules and materials in the mesoscopic region by controlling various local environmental reaction conditions as a new field of micro-chemistry.

Research Results

- **Development of a time- and space-resolved spectroscopy:** Methods were developed to observe different stages of microchemical reactions within the micrometer region. A reaction-stimulating pulsed subpicosecond (10^{-13} sec) laser combined with an observation picosecond (10^{-12} sec) laser is one example. By using a special confocal, high-resolution microscope that optically transmits UV pulsed laser light, time- and space-resolved spectroscopies were developed.

- **Observation of dynamics in surface layers:** By combining a picosecond laser with total internal reflection, elementary processes taking place in surface layers (thicknesses of a few tens of nanometers) were found to be different from those of the bulk.

- **Holding particles by a "micrometer hand" in a strong beam:** Using a very strong laser beam focused by the objective lens of a microscope, individual and groups of microparticles could be manipulated freely in three-dimensional space, characterized spectroscopically, and fabricated arbitrarily.
- **Microfabrication and microfunctionalization:** Selective chemical vapor deposition technique, scanning electrochemical microscope, and photochemical reactions were developed to fabricate and functionalize the surface of polymers and semiconductors.

- **Micrometer size effect upon relaxation dynamics:** It was shown that hydrogen bonding interactions, cluster formation, and the association/orientation of molecules are responsible for the characteristic submicrometer size effect in solution.

- **Fast response of micrometer diffusion:** It was shown that in a very small volume, chemical phenomena controlled by diffusion come to completion quickly. It has been confirmed that when designing a reaction within a small volume its time scale is extremely short.

- **Enhancement of optical field in a microcavity:** Light-lasing within a single particle has been developed, which should serve as a very convenient movable light source. Furthermore, when light is confined within a small region, the light and molecules resonate so well that photochemistry becomes very efficient.

- **Spatial control of chemical reactions:** Like in a biological cell chemical reactions should be arranged in space. In order to realize this technology, chemical relaxation sites have been established on the μm scale. By changing the distance of the reaction sites, the efficiency of chemical reactions can be highly controlled.

MIZUTANI PLANT ECOCHEMICALS PROJECT 1988-1993

Project Director: Dr. Junya Mizutani
Professor, Faculty of Agriculture
Hokkaido University

Background

During the long course of evolution most wild species of plants developed resistance to both pests and diseases using what are now called allelochemicals. This project focused on such plant ecochemicals, while aiming at elucidating the defence mechanisms by studying the production, role, and eventual fate of the secondary metabolites in the ecosystem.

Research Results

- **New model for a defense system of plant leaves:** A symbiotic interaction between Polymnia sonchifolia and epiphytic bacteria has been found and elucidated for the first time. A gene which coded the hydroxycinnamic acid decarboxylase in the bacteria has been successfully transferred into Escherichia coli.

- **Cytochrome P-450 for the formation of capsidiol:** The importance of cytochrome P-450 was found for the formation of sesquiterpenoid phytoalexin, capsidiol in green pepper. 5-Epi-aristolochene 3-hydroxylase induced by a treatment of arachidonic acid as an elicitor was isolated and identified as aninducible cytochrome P-450 of 59 kDa.

- **New class of allelochemicals:** A disaccharide derivative designated as lepidimoide has been isolated and identified from the mucilage of germinated cress seeds.

- **Chemiluminescence assay for lipid peroxidation:** Regarding an early responses due to stress, the generation of active oxygen and a subsequent lipid peroxidation were for the first time observed using soybean cell suspension seedlings after a treatment with the fungal elicit or by means of a CL (chemiluminescence) assay and the CL-HPLC technique with ultra high sensitivity.

- **Insect micro dialysis system:** The applicability of “micro dialysis” as an advanced sampling technique for the analysis of insect haemolymph has been investigated. This research was available for continuous sampling of Spodoptera litura haemolymph; samples were analyzed by HPLC with a coulometric electrochemical detector for the determination of octopamine and dopamine.

- **N_2-driven particle gun:** Successful delivery of allelochemicals such as lepidimoide, plasmid DNA (which has a GUS gene) and genomic RNA of the sweet clovernecrotic mosaic virus into plant samples *in situ* has been demonstrated by using an improved particle gun driven by controllable compressed nitrogen gas. The results show that this gun technique is efficient for the introduction of biologically active substances, DNA and RNA, into intact plant cells.

NISHIZAWA TERAHERTZ PROJECT 1987-1992

Project Director: Dr. Jun-ichi Nishizawa
President, Tohoku University

Background

The main theme of this project was to fill in the technological gap between the submillimeter and infrared wavelengths — the tetrahertz (10^{12} Hz) region — for the further development of telecommunications and processing. The semiconductor devices and circuits studied in this project will most likely find applications in ultra-high-speed integrated circuits, high-density optical-fiber communication systems, plasma diagnostics, remote sensing, radio astronomy, and molecular spectroscopy.

Research Results

- **Photo-stimulated molecular layer epitaxy (PMLE):** Methods were developed to fabricate ultra-thin epitaxial gallium arsenide layers of device quality, being controlled to crystal monolayer precision. This method was applied as both a tool and for the development of electron devices.

- **Semiconductor Raman laser:** A semiconductor Raman laser was developed having attractive characteristics for demodulation in the terahertz frequency region as well as a radiation source for the far-infrared wavelength region.

- **Ideal static induction transistor (ISIT):** As a further development of the static induction transistor (SIT), the ISIT features a channel length shorter than the mean-free-path of electrons with atoms of the crystal lattice. The estimated cut-off frequency is around 800 GHz.

- **TUNNETT diode:** Molecular layer epitaxy was applied to fabricate TUNNETT diodes for generators oscillating up to 500 GHz with semi-coaxial cavities.

- **Schottky barrier diode (SBD):** While studying GaAs detectors, mixers, quasi-optical multi-element imaging arrays, and frequency multipliers for measurements in the THz region, a fabrication process was developed for low-conversion-loss, low-noise Pt/GaAs Schottky diodes (0.4-0.8 µm diameter).

- **Quasi-optical imaging arrays:** Multi-element, quasi-optical imaging arrays consisting of Yagi antennas and Schottky diodes were developed.

- **Coherent power combiner:** To solve the problem of low power generated at very high frequencies, a coherent power combiner was developed. Together with active elements, such as Gunn diodes or FETs, it is effective at millimeter and shorter wavelengths.

- **Optical waveguide modulators:** Among the important devices used for light transmission, switching, and signal processing are optical waveguide modulators. A traveling-wave optical modulator was developed which has the potential of offering a perfect matching of microwave and optical velocities.

FURUSAWA MORPHOGENES PROJECT 1987-1992

Project Director: Dr. Mitsuru Furusawa
Board Director, Manager of Molecular Biology Research Laboratory
Daiichi Pharmaceutical Co., Ltd

Background

The main themes of this project were to search for the genes that control the fundamental processes of gastrulation and differentiation of primordial germ cells. “MorphoGene” is a general term which describes the genes that control morphogenesis during the process of ontogeny.

Research Results

- **Four new experimental methods developed:** (1) DNA amplification by the “lone-linker” method and RARGIP (random access retrieval of genetic information through

PCR) method to greatly streamline the entire process from RNA to cDNA; (2) an equalized cDNA library for making a complete mRNA catalogue from a given organism; (3) an in-gel competitive reassociation (IGCR) method for recognizing subtle differences in DNA structure in cell types from various tissues and organs; and (4) the establishment of immortalized cell lines which maintain normal characteristics, the division of which can be controlled.

- **Germ plasm in Xenopus:** Concerning a study of germ-cell differentiation, the germ plasm from Xenopus eggs was isolated by differential centrifugation and made specific monoclonal antibodies against the germ plasm, some of which react to both germinal granules and mitochondria.

- **Germ cell specific-mRNA encoding a regulator gene in mice:** cDNA was cloned with a zinc-finger motif, which is specifically expressed in primordial germ cells and gonia in mice, using the lone-linker and RARGIP method. This function was examined.

- **Equalized cDNA library of developing mice:** According to the previously reported principle, an equalized cDNA library was made using materials from fertilized eggs to the prenatal embryos in mice. A line-up filter of the equalized cDNA was also provided.

- **Changes in the primary DNA structure in rat brain:** The testing of several alternative model systems to improve the sensitivity of the IGCR method and cloning differences in DNA structure between the brain and liver in the rat is being carried out.

- **Establishment of immortalized cell lines with normal characteristics:** Transgenic mice with temperature-sensitive oncogenes were made, and several tissues from these mice were transferred to *in vitro* culture systems. Immortalized cell lines which maintained normal characteristics were successfully established.

- **Evolution:** A new evolution theory has been proposed: the “Disparity theory of evolution.”

KUNITAKE MOLECULAR ARCHITECTURE PROJECT 1987-1992

Project Director: Professor Toyoki Kunitake
Professor, Faculty of Engineering
Kyushu University

Background

Synthetic bilayer membranes are promising materials, since molecular design is easy and the molecular structure is diversified. A technology has been developed to manufacture new chemical products with structures precisely arranged and bonded at the molecular scale by combining the unique molecular structure of synthetic bilayer membranes with other materials.

Research Results

- **Molecular recognition and water-surface monomolecular membrane by complementary hydrogen bonding:** Molecular recognition was studied using water-surface monomolecular membranes. The binding behavior of biochemically important water-soluble guests were examined.

- **Elucidation of molecular interaction by direct surface forces measurement:** When the surface of mica was covered with a polymeric monolayer, surfaces separated by as much as 300nm from each other were attracted. The structural change and interaction of poly (methacylic acid) attached to the mica surface were elucidated.

- **Observation of molecular ordering and epitaxial polymerization with a scanning tunneling microscope (STM):** Ring-opening polymerization of cyclic ether, lactone, and lactam as well as radical polymerization of vinylidine chloride were carried out in contact with a graphite surface.

- **Formation of ultrathin silica layers by a molecular template method:** A multi-layer ultrathin membrane was produced in such a way that the starting material was introduced into a gap between the regularly arranged layers of cast films used as the mold and hardened; the mold was then removed.
- **Film formation from ultrafine inorganic particles:** Self-supporting multi-layer films were produced by applying the molecular template method to metal oxides, including TiO_2, Al_2O_3, SnO_2, and CeO_2.

- **Development of totally conjugated LB membrane:** Various oligophenylene vinylene compounds were systematically synthesized. Various polymeric polar LB membranes were produced based on the results.

- **Multi-layer ultrathin polymeric membrane by a molecular template method:** Various multi-layer polymeric membranes were successfully produced. For instance, a multi-layer polymeric film was produced by casting a water dispersion of the bis-acrylic monomer together with a bilayer membrane, making a two-dimensional crosslinking and removing the membrane mold.

- **Two-dimensional polymer network:** A polymer-ion complex was produced from an anionic monomolecular membrane on water with cationic polyallylamine; it was transferred and cross-linked by heating.

GOTO QUANTUM MAGNETO FLUX LOGIC PROJECT 1986-1991

Project Director: Dr. Eiichi Goto
Professor, Faculty of Science
Kanagawa University

Background

This project took a new look at the parametron which was invented by Eiichi Goto over thirty years ago. The parametron uses the Josephson junction but operates on the parametron principle. The magnetic flux generated by a loop current in a superconducting metal at low temperature (approx. - 270^{o}C) is quantized (the smallest unit of magnetic flux generated by a current in a superconducting circuit). This project explored the possibility of realizing an ultra-fast computer using magnetic quanta as units of operation involving data handling.

Research Results

- **Basic understanding of the quantum flux parametron:** The basic operation of a QFP circuit was studied. Good agreement was obtained, confirming the possibility of QFP applications as a very fast switching device.

- **16-Ghz operation of the QFP:** It was demonstrated that QFP circuits can operate at a 16-GHz clock, 4-phase, equivalent to 64 GHz, as compared to 1 GHz of the fastest conventional Josephson junction devices.

- **New-type logic circuit based on quantum flux:** Progress was made in defining a new-type of logic circuit based on quantum flux. Operation was experimentally ascertained on the elementary unit of a larger circuit. Logic design for a 4 x 4 multiplier was established using 64 x 30 (about 2,000) QFPs.

- **Three-dimensional QFP chip arrays:** Theoretical groundwork has been laid for constructing three-dimensional arrays of QFP chips, as opposed to semiconductor devices which can only be built in two dimensions.

- **New architecture for a Josephson computer:** A new computer architecture which is well suited for a Josephson computer, called a Cyclic Pipeline Architecture (CPA) and implementing a MIMD (multiple instruction stream multiple data) architecture, was developed.

- **New view of information theory:** Theoretical calculations involving QFP devices have shown that it is possible to handle information in QFP circuits without heat generation, and therefore entropy, if the circuit is running at a sufficiently slow clock.

- **New refrigerator for the QFP computer:** The construction of a compact and reliable helium refrigerator for a QFP computer was realized.

HOTANI MOLECULAR DYNAMICS ASSEMBLY PROJECT 1986-1991

Project Director: Dr. Hirokazu Hotani
Professor, Faculty of Science and Technology
Teikyo University

Background

A search was made for ways to utilize the characteristics of supramolecules for engineering "intelligent" molecular biosensor and biochip systems capable of sensing, processing, and judging external information. Specifically, by utilizing methods of embedding proteins in membranes and of artificially modifying proteins, attempts were made to endow single supramolecules with multiple functions.

Research Results

- **Orientation of flagellar filaments:** For X-ray diffraction analyses, a method was developed using superconductive magnets to achieve a sufficient orientation of flagellar filaments in high density.

- **Supramolecular structure of flagellar filaments:** The flagellar shape and its three-dimensional structure have been determined by an X-ray fiber diffraction method.

- **Molecular dynamic recognition of flagellin:** X-ray diffraction and other physico-chemical techniques have revealed that flagellin, the basic building block of flagella, is a multi-domained protein. Various techniques have been used to show that the binding domain of a monomer flagellin is flexible, instead of having a solid three-dimensional structure.

- **Formation of flagellar system:** It has been found that in the binding between the spiral-shaped screw part and the hook part of a flagellum, two kinds of binding proteins are involved and that each has different properties.

- **Microtuble assembly within liposomes:** The microtuble assembly within liposomes has been developed. It has also been shown that the polymerization of microtubule causes morphological changes of liposomes, producing a good model for cellular morphogenesis.

- **Control of microtuble formation:** Microtubles function freely in the formation and dissemble of cellular organelles, sometimes even serving as rails for carrying small membrane vesicles. For switching over among the various roles, control of the formation and assembly is indispensable.

- **Direct observation of the rotation speed of a flagellar motor:** Recent improvements in the optical microscope and the utilization of laser technology have permitted direct measurements of the rotation of the flagella motor.

- **Analysis of the molecular assembly of the flagellar motor:** The flagellar motor comprises ten kinds of proteins. Efforts were made to elucidate the functions of each protein. These included both disassembling the motor and genetic engineering to over-produce the proteins and to assemble each part.

INABA BIOPHOTON PROJECT 1986-1991

Project Director: Dr. Humio Inaba
Professor, Research Institute of Electrical Communication
Tohoku University

Background

This project focused on the ultra-weak ($\sim 10^{-17}$W: tens of photons per second) light that is emitted from, transmitted in, and absorbed by biological tissue and cells. These “biophotons” are quite different from known relatively intense bioluminescence emissions which are detectable by the human eye and for which specific substances are known to be responsible. The difference is in the fact that these biophotons originate completely from chemical activity within cells, and not as a response to external light or other stimulation.

Research Results

- **Single-photon counting device:** A highly sensitive and reproducible biophoton emission measurement technique based primarily on single-photon counting has been developed. A second-generation version of this technique has made possible the first measurements of the quantum statistical properties of biophoton fields.

- **PIN/Charge Integrating Amplification (P/CIA):** A PIN/Charge Integrating Amplification (P/CIA) detection technology has been developed that can be used in the detection of very weak light emission in the near-infrared region, within which certain species of oxygen emit.

- **Single-photon images of plant tissue:** Single-photon-counting images of germinating soybeans and other plant tissues have been obtained using only the ultraweak light emitted by the specimen.

- **Transmission spectrophotometer:** A transmission spectrophotometer based on the use of a micro-channel plate has been developed that has the highest resolution in the world for single-photon counting spectroscopy.

- **Fluorescence in spinach chloroplasts:** Well resolved emission spectra of white light-illuminated spinach chloroplasts at room temperature show that delayed fluorescence occurs at 685 nm one second or more after excitation.

- **Light from sea urchin eggs:** Light in the visible region was detected during the fertilization of sea urchin eggs.

- **Ultraweak light from mammalian nucleus:** The first observation of ultraweak light emission from the mammalian nucleus was obtained.

- **Phase transitions in biological membranes:** Studies also provided the first observations of phase transitions in biological membranes without the use of artificial chemical probes or labels.

TONOMURA ELECTRON WAVEFRONT PROJECT 1989-1994

Project Director: Dr. Akira Tonomura
Senior Chief Research Scientist, Advanced Research Laboratory
Hitachi, Ltd.

Background

The origin of electron interferometry can be traced to the invention of electron holography by D. Gabor in 1949. Its original purpose was to improve electron microscope resolution, which had been expected to achieve atomic resolution because of the short wavelength of the electron wave. While electron-microscope technology has greatly advanced during these fifty years, the performance of the newest instruments is still far from this theoretical limit.

In contrast, electron holography has proven its potential not only to improve electron-microscope resolution, but also for electro-magnetic property investigations of materials in the microscopic region. A big advance occurred after it was found that field-emission techniques could produce electrons in very bright, fairly coherent beams. Akira Tonomura took advantage of this fact by using an electron biprism to manipulate coherent electron beams. Electron interference fringes have become easily observable with a field-emission electron beam that can produce as many as 3,000 interference fringes.

Not only is it now possible to directly observe many molecular- and atomic-level phenomena, but this technology is becoming highly useful in fundamental physics. Two outstanding examples are Tonomura's use of electron holography to confirm the Aharonov-Bohm (AB) effect and to directly visualize magnetic fields. Further improvement will make the method a powerful measuring technique in such fields as microelectronics and material and biological sciences.

Early studies of electron holography clarified several problems, such as time-consuming measurement processes, poor accuracy in comparison with laser interferometry, and practical restrictions caused by electron-beam coherence. The Electron Wavefront Project sought to develop new methods for real-time, high-precision, and high-resolution measurement and also to apply them in a practical manner.

Research Results

- **Phase-shifting method:** A phase-shifting method has been developed which enables precise phase detection. In this method, the phase distribution of an electron wave transmitted through a specimen is calculated from a series of interference patterns. The patterns are taken while the interference conditions are changed in steps. The technique was used to measure carbon nanotubes and bacterial flagella. Accuracy to 1/200 of an electron wavelength has been confirmed.

- **Real-time electron holography:** Real-time electron holography has been achieved by using a liquid-crystal panel. An electron interference pattern is displayed on a liquid-crystal panel connected to a laser interferometer through a TV camera. The time sequential phase distribution of the object electron wave was obtained at a television rate. This technique has clarified the dynamic behavior and structure of magnetic properties.

- **Three-dimensional images:** A three-dimensional reconstruction of electric potential and magnetic flux distribution has been accomplished in electron holographic interferometry, based on a concept similar to that used in X-ray CT.

- **High-resolution holography:** High-resolution holography, exceeding the resolution of original microscope images, has been developed. Several problems have to be clarified to achieve this degree of high resolution. The project theoretically investigated such difficulties as the sampling problem in digitizing a hologram, an aberration compensation method, and how to estimate and decrease original aberrations. The results of these investigations were included in later experiments, and the electron microscope resolution limit has been overcome.

- **Electron antibunching measurement:** Due to Fermi statistics electrons are theoretically predicted to repel each other on a statistical basis in addition to the Coulomb charge repulsion. Data obtained using a new measurement technique involving a very fast electron counting system show a deviation from a random distribution. This is based on measuring the arrival time and phase relation of a bunch of electrons. Some new effect seems to be involved.

Other notable results:

- Small atom-clusters and DNA were observed using in-line holography.

- Holography using a convergent electron beam was developed and applied to detect an atomic defect.

- Practical restrictions caused by poor coherence of the electron wave were eliminated by incoherent holography using a crystal thin film as an electron-beam splitter.

Epilogue

When the project began in 1989, electron holography was studied in only a few universities and laboratories throughout the world. In these five years, the number of research scientists in this field has abruptly increased. This past summer, the first international workshop on electron holography ran for three days in the United States. More than 100 people attended from all over the world. This is clear evidence that industrial demand for new measuring techniques in the microscopic region has been gradually increasing and that the pioneering studies made by this project have been favorably received.

Among the summarized results, phase-shifting interferometry, real-time methods, and electron holography CT are extremely effective techniques. These will be widely used for practical measurements. High-resolution holography will be further improved by aiming to reach sub-atomic dimensions. If incoherent holography is further improved, electron holography can be utilized in a conventional electron microscope.

AONO ATOMCRAFT PROJECT 1989-1994

Project Director: Dr. Masakazu Aono
Chief Scientist
RIKEN (Institute of Physical & Chemical Research)

Background

The ultimate dream of materials scientists is to create new functional materials by controlling their atomic arrangements through the manipulation of single atoms. Thus, the word "atomcraft" was coined in order to express a new dimension of atomic-scale science and technology in which single-atom manipulation is effectively used, including the creation of new materials with customized atomic arrangements which exhibit novel properties, and nanometer-scale electrode arrangements which show novel functions as electrolytic devices. Although only a dream a decade ago, this is now a promising field, thanks to the invention of the scanning tunneling microscope (STM), which can be used not only to observe atoms, but to also manipulate them. This project carried out systematic studies in order to investigate the necessary technology and science for manipulating single atoms by the tip of the scanning tunneling microscope (STM) and while additionally carrying out various related studies.

Research Results

- **Single-atom extraction:** A technique has been developed for routinely extracting single atoms from any predetermined atomic positions using an STM tip, as demonstrated for a silicon surface, Si(111)-(7X7).

- **Extraction mechanism:** The physical mechanism of the above-mentioned atom-extraction technique was studied in detail and was found to involve a field effect or field evaporation; current effects were found to be negligible. This mechanism is supported by theoretical studies conducted by this project as well as those of other groups.

- **Binding-energy measurements:** It was found that single-atom extraction can be used to directly measure the binding-energy differences of atoms on a given sample surface, as demonstrated on two silicon surfaces, Si(111)-(7X7) and Si(001)-(2X1).

- **Atom deposition:** Atoms of an STM tip can be deposited onto a sample surface, as demonstrated in the combination of a tungsten tip and a silicon sample; however, it is difficult to deposit atoms one by one by this method.

- **Alternative atom deposition methods:** It has been found that one-by-one atom deposition from an STM tip can be achieved by two alternative methods. One is to pick up atoms on an STM tip from a sample surface and to then deposit them one by one at different places on the sample surface. By using this method, a chain of silicon atoms was created on a Si(111)-(7X7) surface; these silicon atoms were successfully re-removed one by one without disturbing the atomic arrangement of the substrate surface. Also, silicon-atom vacancies previously produced on a Si(111)-(7X7) surface were repaired by depositing one silicon atom into each vacancy. These results suggest that it is possible to both write and erase information using single atoms or vacancies.

- **Continuous atom deposition:** An alternative method to depositing atoms one by one from an STM tip is to supply foreign atoms to the tip continuously and to deposit them one by one onto a sample surface. This method has been demonstrated by supplying hydrogen atoms to a platinum tip continuously and depositing them on the Si(111)-(7X7) surface, with the tip being scanned laterally. In this method the adsorption sites of hydrogen are different from those in usual hydrogen adsorption experiments, suggesting a different chemical process.

- **Atom displacement:** A method has been found to displace a silicon atom deposited on the Si(111)-(7X7) surface from its original position to another position by the influence of an STM tip at room temperature. However, good displacement control has yet to be established.

- **Real-time monitoring system:** For future practical applications of atom extraction and deposition, a technique has been developed to detect/confirm these processes in real time. In this system the vertical position of an STM tip and/or the tunneling current between the STM tip and a sample are precisely monitored.

- **Observation of the Coulomb blockade:** The Coulomb blockade, which is an important phenomenon in constructing future single-electron tunneling devices but has been so far observed only at ultralow temperatures, was observed at room temperature for the first time. This suggests that single-electron tunneling devices working at room temperature can to be constructed in the future.

- **Substrate preparation:** A method has been studied for preparing substrate surfaces that are suitable for the atom manipulation by molecular beam epitaxy.

- **Theoretical studies:** In addition to the above, various theoretical studies have been carried out. These include the calculation of STM images, the prediction of stable atomic positions and the interaction between a tip and a sample.

IKEDA GENOSPHERE PROJECT 1989-1994

Project Director: Dr. Joh-E Ikeda
Laboratory Chief of Molecular Genetics
National Institute of Agrobiological Resources

Background

All of the characteristics of every organism depend on genetic information inscribed in DNA molecules. The totality of the genetic material harbored in a cell's nucleus, the so-called genome, governs not only the syntheses of proteins, enzymes, and hormones, but also the behavior related to various biological activities, including mental. The research conducted in this project was aimed at investigating the genes responsible for the various mental faculties and to explore the spatial arrangement of the human genome, hopefully providing insights into unanswered questions concerning cell functions as well as neural functions.

Research Results

- **Generation of chromosomal DNA clones:** Newly developed methods have enabled chromosomal DNA clones to be generated from undefined regions of chromosomes. The generation of regional human chromosome DNA clones was conducted by laser chromosome microdissection in conjunction with Single Unique Primer-PCR. The microdissection system was used to isolate specific segments of chromosomes for analysis. It comprised a combination of microscope, argon-ion laser, and computer software. Using this fully automated equipment a slide carrying many chromosomes and other materials could be systematically cleared of all large molecules by laser cutting to sub-micron (0.3µm Å) accuracy, leaving the very specific chromosome part to be studied.

- **Isolation of expressed DNA sequences:** A novel approach was developed for isolating expressed DNA sequences (genes) from a defined region of human chromosomes, which relies on the direct screening of cDNA libraries using region-specific human chromosome DNA clones. The isolation of regional chromosome-specific cDNA clones (genes) appears to offer an additional powerful methodology to explore specific genes underlying neurogenetic disorders, including Huntington's disease. This method was applied to the terminal region of the long arm of human chromosome X, on which several causative genes for neurologic and psychomotor diseases have been mapped. It was also applied to the short arm of human chromosome 4 containing the Huntington's disease (HD) locus as well as to the yeast artificial chromosome (YAC) DNA clones which carry the HD region. Hundreds of human brain-specific cDNA clones mapped to the distal region of Xq and HD gene region were obtained, resulting in a high-density transcriptional map. An analysis of those clones was undertaken.

- **Ottawa GenoSPHERE laboratory:** The Ottawa GenoSPHERE laboratory (located at the University of Ottawa, Faculty of Medicine (Canada)) was established as a research group for chromosome function studies. Two main research goals were 1) to generate DNA libraries from microdissected genomic segments of human chromosome 5 and 19 and 2) to isolate the spinal muscular atrophy (SMA) gene region on chromosome 5q13.

  The development of laser-based methods for the identification of the extra chromosomal material, other than "double minutes" was considered. The combination of laser microdissection and fluorescent *in situ* hybridization developed for "double minutes" was applied to investigate chromosomal abnormalities from patient material. These methods complemented current diagnostic protocols used in clinical cytogenetics. A strong candidate gene for SMA has been isolated. Physical and genetic mapping of this clinically significant disorder must be completed. In addition, extensive mutation analysis of affected families will begin.

  This laboratory represented an effective collaboration between the expertise of Japanese and Canadian scientists in the field of human genetics, which allowed these investigators to pursue research goals that would have been considerably more difficult to obtain as an individual efforts.

- **Spatial territory of chromosomes:** It has been established that the nucleus of eukaryotic cells is the major compartment in which such functions as chromosome replication and gene expression take place. In addition, it is thought that each chromosome occupies a distinct spatial territory in the cell and that this arrangement affects the processes of cell-specific gene expression. What remains unclear is where and in what spatial combination such activities take place within the nucleus and cell. However, it is difficult to reconstruct the three-dimensional topography of chromosomes using unconventional microscopy with serial sectioned images superimposed on one another.

- **Three-dimensional topography of chromosomes:** A novel imaging system has been developed based on a digital deconvolution method to reconstruct the three-dimensional topography of chromosomes. This system comprises a fluorescent microscope with an automatic sample stage, a high-performance digital CD camera, and computer software for image processing and system control. This imaging system has been applied to metaphase cells of the marsupial, and used to analyze the spatial arrangement of its chromosomes. As a result it has been suggested that smaller chromosomes are more likely located in the central region of the chromosome array.

- **Novel digital imaging system:** An effort was made to combine the digital imaging system with the fluorescent *in situ* hybridization technique, which can be carried out on human cells with chromosome specific DNA probes. This combination of techniques should reveal the spatial arrangement of chromosomes in detail and may lead to insights concerning unanswered gene functions.

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