1993 JAPAN PRIZE COMMEMORATIVE LECTURES

In commemorating the 1993 Japan Prize, the two laureates Drs. Frank Press and Kary B. Mullis delivered public lectures which were attended by many scholars, researchers and other guests in Tokyo.

Date: Friday, April 30, 1993
Place: The Hall, Science Council of Japan, Roppongi

Opening Remarks by Dr. Masami Ito, Chairman
The Science and Technology Foundation of Japan
Introduction of the Laureate by Dr. Yoshiaki Iwasa, Professor Emeritus, Kyoto University
Lecture: "Science, Serendipity and Society" by Dr. Frank Press

Introduction of the Laureate by Prof. Kumao Toyoshima, Director, Professor, Research Institute for Microbial Diseases, Osaka University
Lecture: "Nucleic Acids: The Long Stringy Information Bearing Molecules of Life" by Dr. Kary B. Mullis

SCIENCE, SERENDIPITY AND SOCIETY

Dr. Frank Press
President of the U.S. National Academy of Sciences

I want to begin by thanking The Science and Technology Foundation of Japan and its Selection Committee for awarding me one of the two Japan Prizes for 1993. I know that this high honor would not have been possible without the support of colleagues in many countries. And I am grateful to all of these friends for their efforts in my behalf. Albert Einstein said "In science...the work of the individual is so bound up with that of his scientific predecessors and contemporaries that it appears almost as an impersonal product of his generation." The Japan Prize is unique in that it honors individuals for the social contributions of their researches. In Einstein's meaning it also calls attention to the efforts of a generation of scientists and engineers who have labored to apply the new knowledge their researches have uncovered to better the human condition. Scientists of my generation in Japan, the United States, and in many other countries have worked to reduce the toll of natural disasters, to create a green revolution that eliminated recurrent famines in many countries, to conquer many of the diseases of humankind, to create jobs and wealth through new technologies and industries, to foster arms control and reduction, and much more.

In this talk, I plan to briefly describe the development of American science over the past 40 years in terms of my own experience. This period has been described as a "Golden Age" of science. I will also characterize the unprecedented use of the new knowledge generated in this period for the betterment of the human condition.

Before the 1940's, America could be characterized as strong in technology and dominance in industrial production and relatively weak in science compared to Western Europe. Most of the basic research was carried out in universities (supported by philanthropy) and a few industrial laboratories. The government's involvement in the support of basic science was secondary to the private sector. Some have said that the United States was the Japan of this period.

The role of American scientists in determining the outcome of World War II had its rewards. They assumed positions of influence to the government. Their vision of science as a force for economic growth and national security was accepted as a rationale for the federal government to assume the primary responsibility for the support of science. With this support, the period between the end of World War II and the present became the Golden Age of science - characterized by explosive growth in numbers of scientists at work and fueled by seemingly unlimited expansion in the level of government financial support. The American research university system flourished, and times ensued of extraordinary creativity and discovery spanning almost every scientific field. The United States rapidly assumed a world leadership position in science.

My own career reflects this history. My earliest researches were supported by private sources such as the National Geographic Society and the Geological Society of America. With growing government involvement, private sources were replaced by federal agencies such as the Office on Naval Research and the new National Science Foundation. The largesse of the federal government made it possible for me to use advanced equipment. I could secure arrays of detectors to explore the sea floor and the continental crust using elastic waves generated by explosions and earthquakes. In this way, I could obtain geophysical data of a quality and amount that enabled more detailed exploration of the Earth's interior than hitherto possible. This was a period when just about every qualified American scientist with a creative idea could receive a research grant. It enabled a young scientist like me to work as an independent investigator pursuing my own ideas, to design and field new instruments, to acquire the new computers that were just becoming available. I was able to support technicians, graduate students and post-doctoral fellows, all of whom became my partners in research. I was able to engage in joint research with scientists from Japan and Russia. All of this served to increase my own productivity as a scientist. Tens of thousands of American scientists can describe their own careers in these terms. This is the essence of the Golden Age of American Science. But it also was a golden age for the applications of science to human betterment.

A great nation has among its obligations the support of science as a cultural endeavor, as an intellectual quest for new knowledge. However, history shows that the collateral and often serendipitous beneficial fallout from research more than pays for the initial investment in basic science and engineering. This can be measured in economic terms such as improved productivity or the creation of new industries, and in human terms such as improved health, better understanding of the environment and of natural hazards, or developing countries becoming self sufficient in food. Together with many scientists I found that my work in the basic geophysical sciences had important social consequences. The team exploring the seafloor led by Maurice Ewing, in which I participated as a young scientist, pioneered the technology of offshore oil exploration. The arrays of detectors which I and others used to explore the continental crust and mantle became the basic technology for detecting violations of a nuclear test ban treaty. And what I and others learned about earthquakes and volcanoes using the methodologies of our science led to the proposal for the International Decade of Natural Hazard Reduction, perhaps my most important accomplishment. Some examples of the contributions of fundamental science and engineering to society will now be discussed in greater detail.

Contributions to industrial development. The following are representative examples of new technologies with commercial importance that flowed from fundamental scientific and engineering research. To a large extent this research was carried out in American research universities:

modern agricultural products such as: hybrid crops,
mechanical harvesters, and computerized data bases on crop yields
biotechnology
designer drugs
magnetic resonance imaging systems (MRIs)
penicillin and many other antibiotics
many important industrial catalysts
computer numerically controlled machine tools
digital signal processing (used in communications, exploration for oil, compact discs)
the stored program computer (the basis for all modern computers)
Frequency Modulation (FM)
masers and lasers
ion implantation (in the manufacture of semiconductor devices)
computer work stations
plasma etching
reduced instruction set computing (RISC)
artificial intelligence and neural networks
compilers
word processing
image processing
instrument landing system, loran, inertial guidance
nuclear energy

Other Contributions of Science and Technology. Examples of contributions to the conquest of disease, the understanding of the environment, and the production of food will be given.

Contribution to Natural Hazard Mitigation. The year 1992 was one of the worst years for natural disasters in the United States.

Property damage was large, but very few lives were lost. Our country learned many lessons about improving standards for construction, but did well in minimizing casualties by providing warnings, evacuating populations at risk, and providing post disaster relief.

But it is the poor countries of the world, where two-thirds of the world's population lives, that bear 95 percent of all disaster casualties. Over the past few decades we have witnessed events of devastating proportions in these countries. Single disasters have set back economic progress by as much as five years. The "Decade" can do much to reduce these losses. For instance, by the year 2000 all countries could have national assessments of disaster risks, plans for prevention and preparedness, and access to global, regional, and local warning systems. Design parameters exist about how much ground motion structures must accommodate. The development of advanced radar technology has greatly advanced our ability to predict tornadoes and other weather-related hazards. Computer modeling of watersheds has led to more accurate flood alerts. Modern fire codes, dam safety standards, seismic codes, and other technologies exist and can help. Training could be provided and these technologies could be transferred to countries that need help.

There is no higher calling than for scientists and engineers to use their talents on behalf of humanity.

NUCLEIC ACIDS: THE LONG STRINGY INFORMATION BEARING MOLECULES OF LIFE

Dr. Kary B. Mullis
Founder and Vice President, Research of Atomic Tags, Inc.

Life on the Earth, as we know it in this century is always associated with these very long stringy molecules which we call by the rather unfortunate name nucleic acid. The term was coined in 1899 long before the structure or the function of the nucleic acids was understood, and it sounds like something you wouldn't want to spill on your hand, much less have in all of your cells. It turned out of be a bad name. Inside of every living cell on the planet as far as we know there are nucleic acids, and remarkably every structural detail of every living creature arises from easy to read instructions on these long stringy molecules. And as if that weren't enough, there is a lot of information on these molecules which isn't currently being used by the creature bearing it. It belongs in a way to the creature's past, like old trunks in the attic. A more fitting name for nucleic acid might have been magnesium archivate or informationate or something like that, but the concept of informational molecules was not appreciated until late in the 1950s.

The threads of our modern understanding of life and it's informational molecules began to be woven somewhere around 1930. Irwin Schroedinger, one of the brilliant physicists who created quantum mechanics, wrote a little book called "What is Life?" and he puzzled in that book over the notion, "how like begat like?" The subject had been broached in the Old Testament of the Bible but no mechanistic details were offered. There had been a few thinkers, people like Charles Babbage, John von Neumann, and Alan Turing who had already imagined computing machines with evolutionary capabilities which could operate from ordered lists of coded instructions. For these few the notion of long stringy molecules bearing symbolic information from generation to generation would not have been too bizarre to take seriously but these men were not biologists. Most biologists were of the opinion that "how like begat like" was an impossible question, not likely to be answered in their lifetime. The details appeared in the 1950s starting with Oswald Avery who demonstrated that at least in one case the hereditary material was nucleic acids.

Not a lot of people were ready to accept that because no one knew then that nucleic acids were not just what the name implied, acids from the nucleus. No one knew they were the most beautiful, complex, long stringy molecules to be found on earth. The very satisfying answer arrived when Francis Crick and James Watson postulated a structure for deoxyribonucleic and which had two very remarkable qualities. The molecule seemed capable of encoding a great deal of information and it could serve as a template for its own replication. It could bear children. In its structure was the answer to the old question of begetting and indeed, the very essence of life. Watson and Crick noted this in their 1953 paper in Nature in a statement that must rank as the most cautious understatement of an earthshaking discovery in the scientific literature. They wrote, "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

Today we are completely surrounded even in the privacy of our own homes, with mechanical devices that regularly and dependably record and dispense long strings of information converying everything from mathematical descriptions of theoretical objects to high fidelity recordings of Eric Clapton playing his guitar and singing about some woman. We are accustomed to this now. Most of us know that floppy disks and CD's and tape recordings and old 78 records even are mechanical devices that allow us to assemble a long string of information into a convenient coil, where it can be stored and retrieved.

Long stringy information bearing molecules make perfect sense to us now, but our curiosity about them goes further than just knowing that they exist. We want to know what they say and some of us want to be able to manipulate them, repair broken ones, make new ones, fool around with them.

But very long stringy molecules are not so easy to work with. They break up into little irregular pieces, and if you want to examine a particular region of human DNA, for example, the gene which encodes insulin, you are looking for something in the presence of about a million other things which look very much like it. For a long time after the discovery of the structure of DNA, detailed information about it came out only very slowly. Then came molecular cloning. With this technique molecular biologists could isolate particular DNA sequences and produce them and their encoded proteins in large amounts. Biology became very exciting and biotechnology emerged as a new industry. Still it was a long, tedious process to isolate a particular DNA sequence, and the manipulations one could perform were limited.

In 1983 I was driving my Honda Civic from San Francisco to Mendocino County, which is to the north in the mountains by the coast. It was spring and the California buckeyes were in full bloom. The moist still air was saturated with their perfume. I was imagining experiments which I thought I might do in the coming weeks. It was late at night and my thoughts were very loose, almost like dreams, as the road curved right and left through the mountains. Suddenly almost by accident I had assembled in my mind the elements of what I later named the polymerase chain reaction. I was in the mood to think new thoughts, to discover new possibilities in the combination of familiar elements. I had not been looking for PCR, but I was ready to find it. I stopped the Honda. Within a minute or two I realized that I had discovered something fantastic. I tried to wake up my girlfriend, but she had heard wild new ideas from me before and most of them evaporated in the scrutiny of daylight. It could wait for morning. But I was up all night, and in the morning PCR had not evaporated.

After a few months in the laboratory it was working.

Now almost ten years have passed. PCR is a standard tool without which most biochemists would cry in their sake. It has done for DNA chemistry what the word processor did for writing. Out of long stringy molecules, complex and annoying to work with, PCR can make little, orderly, well-behaved pieces of DNA in whatever size and amount is convenient. It can splice them together, cut them apart, add something here, delete something there.

DNA has been tamed, and all the information it contains is in our hands. Our human DNA, our genome, has as many letters as a thousand long books, a fair sized library. It is our story. Each of us carries it around in our cells. Some of it is personal, some of it is public, the same in everyone. It will tell us about our health and our diseases. In it we can find traces of our past, and if we can use it wisely it will help us direct our future toward peace and prosperity for all mankind.