On Doing Science in the Modern World

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THE TANNER LECTURES ON HUMAN VALUES

Delivered at

Clare Hall, Cambridge University
March 9 and 10, 1992

David Baltimore was educated at Swarthmore College, and the Massachusetts Institute of Technology, and received a Ph.D. degree in Biology from the Rockefeller University in 1964. That same year he became a research associate at the Salk Institute, and in 1972, a professor of biology at MIT. He was appointed American Cancer Society Research Professor in 1973, the following year joined the staff of the MIT Center for Cancer Research, and in 1982 was named the first director of the Whitehead Institute. He served as President of Rockefeller University from 1990 to 1991, and is currently a member of the faculty of that institution. In 1975 he was awarded the Nobel Prize in Physiology or Medicine, an honor he shared with Howard Temin and Renato Dulbecco for work on the enzyme reverse transcriptase, an enzyme that enables cancer-inducing RNA viruses to replicate within the host organism. Knowledge of this enzyme was also essential to early research on AIDS. He has continued to conduct research on the polio virus and the human immunodeficiency virus (HIV), and was cochairman of a major study of AIDS sponsored by the National Academy of Sciences and the Institute of Medicine. He is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, the Institute of Medicine, the Pontifical Academy of Sciences, and is a Fellow of the Royal Society.

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I have entitled these talks "On Doing Science in the Modern World" because I have the feeling that the societal framework in which science is being done today is different from even that of the recent past. Science is a victim of its own success. It has gone from being the province of gentlemen to being a central force of society; from a financially marginal part of governmental outlays to a significant one; from a minimal part of the academic enterprise to a dominant one. The pivotal role of science has brought it into the political spotlight, which is fundamentally changing the internal workings of the enterprise. In these two lectures I hope to highlight the increasing power of the political dimension in the process and evaluation of science.

Let me start, however, by putting my opportunity to comment on these issues in perspective. First, I am a biomedical scientist and at best a voyeur when it comes to the other sciences. Therefore, my comments will mainly focus on issues of biomedical science. In fact, biomedical science has borne a large share of the politicization of modern science, I believe, because it is the science of life and therefore is of deepest concern to the general population.

Second, I am an American and only know well the political process in America. Therefore, of necessity, my remarks will be placed in an American context. Much of what I will say, however, is, I believe, more widely relevant if for no other reason than that the diseases of America seem to spread quickly to the rest of the world. I assume that what I have to say will be especially relevant to Great Britain, because your political course in recent years has been so parallel to ours.

Finally, although I myself have been caught up in political turmoil during the last few years, I will make only a few comments on my own experience in favor of consideration of events that have not involved me. However, you can assume that all of my attitudes have been colored by my experiences.

Although my personal experiences have led me to think about the changing perception of science in the contemporary world, there are many events on the international scene that might lead one to think along these lines. For instance, there has been a remarkable movement of biomedical research activities out of Switzerland and Germany in the last few years, driven, it would seem, by the unfriendly political environments in those countries. Interestingly, America has been a great beneficiary, with research laboratories of the major pharmaceutical manufacturers of those countries coming to ours. Then we have the incredible charade of adjudicating the discovery of the AIDS virus through investigative reporting, congressional hearings, international lawsuits, and debates over patent rights. Or we might remember how the annual International AIDS Conference has become a political circus. In fact, the AIDS problem has been a focus of political concern from the moment of its appearance, and the spillover into other areas of biomedical research will be with us forever. Finally, I can point to an issue in which I have been centrally involved, the debates over recombinant DNA technology that took place in the middle 1970s and 1980s and involved legislatures around the world. The power of this technology and of all of modern life science is so great, and it touches deep moral and ethical concerns so closely, that this alone is sufficient reason for the politicization of science.

Science in a Political Setting

Science done under government auspices must be seen as part of the political process because anything done by governments is by definition political. Science as it is done today, however, really dates back only to the end of World War II, when the U.S. government committed itself to the massive funding of basic scientific investigation. Before then, science was largely a European affair and was done in the context of the particular organization of the individual countries.

At the end of World War II, President Roosevelt's closest scientific adviser, Dr. Vannevar Bush, wrote a report that established a blueprint for the development of postwar science in the United States. Wartime development work had been very effective, but Bush worried that we had drained the bank of basic knowledge and that it needed to be replenished. In particular, the 1945 report, called "Science—The Endless Frontier," set the future course for funding of scientific research.

Bush had a very pure view of science that fit the idealistic aftermath of the war very well. His plan was to set up the National Science Foundation as the funding agency for science, and he consciously separated it from the other, goal-oriented agencies of the government. Bush also tried to make the NSF as independent as possible from political interference but of course recognized that Congress and the president must have the final say over any governmental agency. The plan worked moderately well in that NSF has been the major source of funds for pure, non-health-related science. Its isolation from political realities, however, has hamstrung its growth, and the National Institutes of Health, which is a goal-oriented agency, now funds much more basic research than NSF.

In today's political world, there is not as much room for pure science as there was in 1945 and what support there is has tended to be strongest for megaprojects like the super-conducting super-collider. The previous director of the NSF was able to get a hefty increase for its budget, but at the expense of turning it toward being an arm of U.S. industrial policy. But let me turn to NIH, because I know more about health-related research and because the most ominous events involve that agency.

NIH developed rapidly and effectively with very little political interference until the late 1960s. Under the supportive eyes of a few key members of Congress, its budget grew while the scientific community largely controlled its policies. In the early 1970s, the War on Cancer was born and the perspective changed. It was Senator Edward Kennedy who initiated the idea of a focused and well-funded attack on the cancer problem, but President Nixon stepped in and took the idea as his own, announcing a Presidential War on Cancer. The bill that provided the funds also gave the president and Congress new powers to appoint the directors of the National Cancer Institute and NIH. The consequence, among others, was that appointments have been much more difficult to make, leading recently to a two-year hiatus in filling the job of NIH director. Nixon did much more to inject politics into scientific decision making. His most egregious act was the abolition of the independent group of scientific advisers that had brought rational considerations on scientific matters to the White House all through the 1960s, an organization known as the President's Science Advisory Committee. This was a clear statement that politics, not rational analysis, should reign in the area of science policy.

Since 1970 there has been an acceleration in the involvement of political considerations in scientific affairs. Probably the most dramatic case was that of the Star Wars missile defense program, which was derided by most knowledgeable scientists and yet became a major drain on resources because of its political support in the Reagan White House.

In 1990 the NSF republished Vannevar Bush's 1945 report and Daniel Kevles wrote a very thoughtful appraisal of the influence of the report as a preface to the new edition. He documented the rise of the political involvement in the conduct of science and eloquently warned that, although it is exactly the danger foreseen by Bush, it is now an unalterable part of the scene. Let me quote from this preface:

> The world —and the structure of R&D —have changed a great deal since Bush wrote his report, but major principles he advanced in it merit reaffirmation. The long-term national in-

> terest still calls for investment in the human and intellectual capital that are essential, ultimately, to national power in the modern world. Science still operates best in an environment of freedom, including freedom from security restrictions. However, Bush's principle of an apolitical science —a system of federally supported research kept comparatively free of the policy controls of democratic government —is no longer viable. . . . Science and technology are so pervasively important in American life as to be irreversibly involved in all parts of the nation's political system. Policy for them is no longer something special but is the product of the normal political interaction among the White House, the bureaucracy, and the Congress. If major principles of *Science —The Endless Frontier,* originally advanced in response to political circumstances, are to prevail, they must be fought for —not least by the basic-research community —in the ordinary rough-and-tumble processes of American governance.

Professor Kevles rightly points to the two sides of the issue. On the one hand, politicization is a tribute to the important role that science plays in the modern world. But basic research flourishes best in the absence of political interference so that politicization can be self-defeating. From the point of view of the public, there should be strong support for leaving scientists to make their own decisions, but the political process dictates that politicians make the decisions and they find it hard, even if they believe the arguments, to allow any entity that they fund —particularly one that absorbs as many resources as are poured into science —to handle its own affairs.

We in the United States have recently had a number of highly publicized cases in which the dominance of the political agenda over science has been writ large. Let me focus on the one that has done the most damage, the hounding of Stanford University over the issue of indirect costs that led to the resignation of its president, Donald Kennedy. Kennedy was the chief spokesman for science in academia, being both articulate and an accomplished biologist. There is no question that both the accounting practices at Stanford and governmental oversight of its procedures had been lax, but the response was wholly out of proportion to the offense. The clear villain here is a U.S. congressman who, in the tradition of Senator Joseph McCarthy, uses his investigative right as a weapon of fear and self-aggrandizement. In the Stanford case, he smelled blood and struck with a vengeance. The hunting metaphor here is appropriate because he is an animal hunter whose greatest pleasure is apparently to shoot ducks and other wild game.

Congress's treatment of Stanford is a classic case of unprincipled exploitation of the political process. Certainly Congress had the right to investigate —the question is how should it respond? If it was sympathetic to the goals and importance of higher education, it could have worked with the university to tighten up procedures. After all, Stanford is a national resource both for education and for research.

At a time when global competitiveness is a phrase on every lip, one would imagine that the Congress would recognize that the universities are the generators of the scientific base on which industry is founded and are therefore critical institutions for economic growth, never mind their important educational and cultural roles. Universities in the United States, and I know this is true in Britain too, are institutions under great financial stress because of lack of government support for so many years. The Congress is now trying to take hundreds of millions of dollars from Stanford, enough to seriously erode its strength, with no evident appreciation for its national importance. It is also trying to extend this sledgehammer approach to other universities, notably MIT.

This is the clearest present case of the government using its funding of research as a tool to gain political advantage by harassment of the recipients of the funding. The Congress argues that it has the right to uncover misuses of government funds and there is no doubt that it does have this right. The problem is that, in classic demagogic tradition, it is using its right to ridicule and undermine the universities with no regard for their importance and fragility. The hearings held by Congress could have been an occasion at which sympathetic members of Congress might have acknowledged the importance of Stanford and the superb job done by Donald Kennedy in running the university for the last ten years, while of course also underlining the need for fiscal responsibility. Rather, our game-hunting congressman took the occasion to demean Dr. Kennedy and to excoriate the university. American higher education took a blow from which it will be a long time recovering. In fact, the relationship between the government and the great research universities of America will never be the same because the level of mutual suspicion and disrespect has risen so high.

It is ironic that one of the few parts of the American economy that is working well, the universities, should be under attack. To some extent, I suppose, they are convenient scapegoats for a deep concern over the declining fortunes of America on the world economic scene. But the fault lies in our inability to translate the fruits of research into competitive products. Our present-day economic system, which has poured money into the pockets of the already-wealthy while the middle and lower socioeconomic groups fall further and further behind, rewards financial manipulation, not effective manufacture or industrial innovation. As people's salaries have declined, they have turned away from progressive forces hoping that conservative approaches will return prosperity. This misreading of the solution explains why the country has turned in the last decade to leadership that has simply stolen their labor and turned it into profits for the rich. I am not exaggerating: a recent report showed that in the booming 1980s 60% of the economic growth went to the richest 1% of American families and all but 6% went to the top 20%. At the same time, the bottom 40% of families had an actual decline in income *(NY Times,* March 5, 1992, p. 1). In such economic circumstances it is easy for unscrupulous politicians to manufacture scapegoats. The shame is that when the research institutions become the scapegoats, future opportunities for building out of the hole become increasingly limited.

For all the discussion in America of the need to upgrade education, the parts of our system that work best, the research universities, are not being publicly supported and, worse, are being hounded. There is no doubt that the present climate is going to bring increasing regulation of science and educational institutions. We will end up spending more on administration and less on matters of substance. We will find students turned off by a more regimented life in science. Scientists will be driven to companies because of the unpleasantness of academic life. While that might actually be beneficial in the short run, it will bring back Vannevar Bush's greatest fear —that we drain the pipeline of ideas and end up falling behind because we have not supported the long-term perspective which can only be taken in universities and research institutes.

Changing Politics

I have argued that the political dimension of science has widened considerably and that part of the changed circumstance is due to the pivotal role that science plays in the modern world. But it is important to realize that changes in politics also have played a critical role. In the United States, at least, our politics has become much more populist in the last decades. By this I mean that we are a truer democracy, with more power in the hands of the voters and less in the hands of powerful individuals. Many influences have brought about this change and it is still coming to equilibrium. One has been increasing access to the ballot box — there is universal suffrage and the impediments to registration and voting have been limited. Another is the increased power and speed of the media. Here the growth of television, bringing Washington into the homes of every American each night, has had a big effect. A particular influence has been the post-Watergate press, which increasingly emphasizes investigative reporting. Politicians are having to answer for every vote they make, every aspect of their private lives. Another influence is the growth of special interest group politics, forcing politicians to pay attention to minority opinions because of the force of their political organizing and the tenacity of their concern. This has had a special importance for biomedical research because of the power of the antiabortion and animal rights groups.

The growth of populism has been so great that the traditional forms of political influence are much less effective today. It used to be that political influence was focused on Washington, but today influence must be exerted through grass-roots education because politicians are paying more attention to the voters and less to the lobbyists who speak to members of Congress directly. In many ways, of course, this is a salutary trend but it has its downside for science, the arts, and higher education because these are aspects of society that have little direct impact on the average voter and are often viewed with suspicion. In fact, in the United States we have a new biomedical support group called Research !America that has as its goal the education of the public about the importance of biomedical research to the health of the nation. In a country of 250 million people spread over the 3,000 miles that separate the Atlantic from the Pacific, sending such a message is difficult and expensive.

Asilomar as an Example of Cooperation

Although President Nixon was particularly responsible for increasing the political involvement in science, it was actually the biomedical research community itself that precipitated the most intense political concern. In the mid-1970s, when the ability to exchange genetic material between organisms was first developed, research scientists raised the question of whether this capability might pose hazards for the general population. We call this new form of experimentation recombinant DNA technology. From the initial questioning there evolved an exemplary process, run largely by the scientific community, that satisfied the political concerns which had been generated by the initial call for caution. The key event was a meeting organized by a group of scientists, of which I was one, in Asilomar, California, in 1975.

The Asilomar meeting was organized to consider whether the recombinant DNA technology was potentially dangerous as a form of biological experimentation. It was the first time in history that the scientific community itself raised in public an issue about the safety of its own activities. The result was a proposed set of guidelines under which many benign forms of the new technology could go forward. There were, however, experiments for which it was recommended that they should only be done with great care and others that at least temporarily should not be done at all. Most importantly, an ongoing mechanism of evaluation was established under the auspices of the government that could monitor the situation as it unfolded and recommend changes in the guidelines that would reflect the changing evaluation of potential hazards.

The process worked very smoothly. In open meetings, covered by the press and attended by critics and supporters, recommendations were made to the director of the National Institutes of Health as to what modifications were appropriate in the guidelines. As it turned out, the feared consequences of the new technology did not materialize and over about ten years the guidelines were systematically liberalized, so that now there is but a vestige of the process left, which is focused solely on the issue of human genetic engineering. One of the experimental protocols that was initially virtually forbidden involved making cloned DNA representations of viruses. I can remember when, at the end of the 1970s, the guidelines were sufficiently liberalized so that such experiments could be performed in ordinary laboratory circumstances. The study of viruses was then my major activity; as much as I supported the guidelines, having been one of their architects, my frustration level was high and the changed regulations allowed me to realize an experimental dream. I mention that because it is important to realize that the biomedical research community had voluntarily put a moratorium on experiments that it very much wanted to do and that individual scientists were prevented from using a technology that could have greatly increased their investigative power.

The regulation of recombinant DNA technology was a model of responsible, effective regulation largely because it was left in the hands of the scientific community. This was not for lack of interest on the part of politicians. They held hearings, carried out investigations, and kept the process very much in view. But they were convinced that the community was handling the problem responsibly. A large number of bills were proposed in Congress to make the guidelines into law, but none was ever enacted because we were able to convince the members of Congress that the situation required flexibility and that laws would be counterproductive. To avoid legislation required that many of us spend long days in the halls of Congress, allaying the fears of the representatives. An important circumstance was that no untoward incident occurred, so that politicians could consider the situation coolly, without the pressure of a highly publicized event. This is somewhat miraculous because although the technology is benign, there are so many practitioners that one might expect someone to charge that he or she had been harmed by a laboratory procedure. To this day, I know of no such charge.

The era of good feelings between the research community and the politicians has not lasted. It seems to me that this is more because of changes on the political side than on the scientific side. But political swings do not occur on their own; they are usually driven by public discontent. It is important to ask where this discontent arose. I want first to argue that failings of the scientific community are at least partly responsible. To make the argument, I am going to go back to the early 1960s, when I was a graduate student tasting the pleasures of experimental science for the first time.

A Life of Science

I grew up in science with a belief that being selfish was what was expected. Science graduate students of the post-Spatnik 1960s thought ourselves to be particularly lucky because we could do only what we enjoyed and still be considered socially useful. We would congratulate ourselves on our good fortune. Entering a life of science is always a joy. Before that one had spent some twenty years growing up, learning facts, developing skills like spelling and mathematics, playing sports, discovering the opposite sex, if you were lucky maybe doing a little traveling and learning a foreign language and doing some rote laboratory work. But nothing had prepared me, at least, for what came next. I can remember when I studied science in college wondering what it meant to do research. It was impossible to formulate a clear idea of where the frontier of knowledge lay. I can remember an inchoate perplexity about what research really was. Now I can diagnose my difficulty —I had no idea how to formulate a problem that could be investigated. Having not had any experience in a research lab, I could not imagine how a problem was posed in research terms. But, of course, not having the experience, I also could not even formulate my concern —it was no more than a vague hole at the center of my being waiting for definition. I suspect it is that way for all young scientists who have not been in a lab. Actually, I'd been lucky in that I'd had a little taste of research in high school. It stayed with me as a memory but, by the end of college, was so disconnected from the book-learning I had absorbed that it stayed as a motivation but not an understanding. Then, in graduate school, the light dawned when I finally had the opportunity to do real experiments. First, the little questions were posed for me, then I saw how to pose them myself, then bigger questions made sense, and within about a year I saw open to me the world of the unknown but the knowable. I began to see how one formulates an answerable question. I assume that such a moment comes for all experimental scientists. Even theoreticians must need to formulate what is studiable so that the frontier becomes evident.

That epiphanal time was to me a realization of what I was meant to do. Not being religious, I do not mean that I was meant by God to do research, but I do suspect that I was meant by my genetic inheritance to do research. Coming to that realization was like putting on a calfskin glove that fit perfectly: it was a warm, enveloping experience. But both my parents had grown up in the depression and my father was from a very poor family. They had worked hard in their lives to earn a living and the idea of a profession being an enjoyment was foreign to my father and something my mother had only found in later life. Did I have a right to indulge my new-found passion? The only way to do research was on government money: could I really make a life spending the government's money to indulge my habit? As I looked to the feedback coming from the outside world in the early 1960s, the answer was a resounding yes. It was clear that the nation had committed itself to greatness in science and that my private passion was a public good. What a relief to me and to a whole generation of scientists who grew up after, but in the shadow of, the Great Depression and World War II: sanctioned self-indulgence.

A Mature Science

But not now. First of all the whole issue of whether scientific investigation is an unconditional good is debated widely. Many people argue that what scientists find is not necessarily good for society. The physicists in the post–atomic bomb era first raised these doubts and now, with Chernobyl and the ozone hole and industrial pollution, the doubts have become a widespread strain of concern. Research has become so much more expensive and so many more resources are going to research that the questions and doubts are multiplying and coming from more places.

But I see another problem. When I entered molecular biology it was in its infancy. We knew so little and, perhaps as importantly, we did not know how we were ever going to decipher the complex problems of human biology. All of that has changed. We now have a powerful, mature science that has a clear idea of how it will answer the problems ahead of it. We have an optimism that any problem is solvable, that the techniques and concepts we have today are sufficient to carry us to the deepest conceivable knowledge of ourselves, and that it is going to get easier as the technologies mature further. It is a heady feeling and those who enter the field feel it and are making themselves into experimental miracle workers.

But with power comes responsibility and that is where the change lies. Because total self-indulgence is not now a stance that all can take. With such power the scientific community has the responsibility to choose the problems it studies with an eye to how it can contribute to the welfare of the world. Does a scientist who can help to learn about AIDS, whose skills provide the ability to contribute to the conquest of this modern plague, have the right to continue investigating an arcane problem of bacterial transposons? I hear the answer from my colleagues as soon as I pose the question: "Maybe," they will say, "the answer will come from work on transposons." Quoting back to me things I might have said once, they will go on, "Head-on research is often the least effective way to get an answer. When we deal with the unknown, answers often come from unexpected quarters."

True, true —because I've made such arguments myself they come easily to my mind and I deeply believe them. But they are not always the right arguments and are not always applicable. Let's remember the Manhattan Project, the American crash program to design an atomic bomb. It was a great success because a group of physicists gave up the self-indulgence of unfettered research and dedicated themselves to making a bomb. The basic underpinnings were there, years of unfettered research had provided the basic understanding —what was needed and provided was research that never lost sight of its goals. It is crucial that the problem was an appropriate one: the basic research knowledge was there. Had the nation chosen in 1970, for instance, to solve the cancer problem that way, no good would have come of it. The basic knowledge of cancer in 1970 was simply not there to build upon. A problem must be ripe for a head-on approach to succeed.

Dedicated Science

But today I fear that too many in the scientific community are unwilling to ask what problems are ripe for a dedicated attack. We are living by the myth that nothing is ripe, that all problems are basic ones. In the infancy of molecular biology, even in 1975, that was certainly the case. There was virtually no human disease that could be seriously attacked by the methods and concepts of molecular biology. It was an infant science, although one with a rapidly increasing sophistication of concept. The last fifteen years have seen a sea change in that perspective. Molecular biology is now a mature science, one with great power to ameliorate human disease.

The best example of the new status of molecular biology is the biotechnology industry. It dates from the late 1970s and saw spectacular growth in the 1980s. It marks the maturity of molecular biology in two ways. One is methodological: there is now a significant segment of the science being done with a direct goal-orientation and it is being successful. The second difference wrought by industrial development is that it is the vehicle for direct contribution to society. Real drugs are on the market as a result of the efforts of the last fifteen years. My favorite example is erythropoietin. Here is a protein made by our bodies in vanishingly small quantities that was a laboratory curiosity fifteen years ago. It is, however, a protein that allows the body to make more red blood cells. For individuals who need more red blood cells, like people on kidney dialysis, this protein can be a literal lifesaver. Today, thanks solely to the efforts of the biotechnology industry, it is available in the local pharmacy. People who need more red blood cells can have them. What better proof can there be of the maturity of molecular biology?

Let me return to the methodological aspect of the biotechnology industry. A scientist in a company can sometimes work in as unfettered a way as he or she can in a university or research institute. But that is very rare. More characteristically, work in a company setting is directed to certain goals. They may be long-term goals or they may be vague goals, but efforts directed outside of their framework is discouraged. The management sets the goals (in the best circumstances with strong input from the scientists) and then those goals establish the pattern of research unless corporate targets change. The willingness of large numbers of molecular biologists to work within the framework of such goals and their success as measured by new products now available, and many more to come soon, shows what can be done by a Manhattan Project mentality allied to the contemporary power of molecular biology.

AIDS, the Genome Project, and Cancer

The question I want to raise here is whether the sophistication of molecular biology, as measured by its ability to produce the goods, should not change the expectations of scientists in the field. We might ask whether applied biological science should not have a higher status in universities than it presently enjoys. Should we not be educating young scientists to think about their newly acquired powers of investigation both as a way to discover new principles and phenomena and as a way to solve societal problems? In a sense, the question is whether genetic engineering, a shorthand phrase that subsumes recombinant DNA technology and other technologies, isn't becoming a real form of engineering. We have chemical engineers alongside chemists and electrical engineers alongside physicists, so why not biological engineers alongside biologists?

There is another opportunity for a more targeted approach to biological research. The pharmaceutical and biotechnology industries mount programs designed to produce defined products that can be sold. Thus, we get agents that can ameliorate heart disease, stimulate red and white blood cell production, fight viral diseases. Sometimes companies even discover the basis of mysterious diseases, like the Chiron Corporation's discovery of the virus that causes hepatitis C. But there is another form of research that companies rarely engage in effectively: research on diseases where the pathology and even the etiology is obscure. My favorite example here is AIDS and I want to discuss it at some length. I'll also comment on cancer research. I could take rheumatoid arthritis or a variety of autoimmune diseases just as well.

My thesis about AIDS is that it is a disease that we should be attacking using an industrial paradigm but that we are attacking it using a basic research paradigm and are therefore wasting time and resources. This position has evolved from my co-chairmanship in 1986 of a committee to advise the country on a response to the AIDS problem appointed by the Institute of Medicine and National Academy of Science in the United States. It seemed to me five years ago and it still does that AIDS is the type of problem one approaches head-on. It is, after all, caused by a small virus and it attacks one of the most accessible systems in the body, the immune system. There are certainly aspects of the AIDS problem we do not understand, and nondirected basic research has to be a part of an attack on the problem, but an organized, preferably worldwide approach could, I believe, accumulate the relevant information much more rapidly than leaving the problem to the whims of the research community. Here, in fact, Great Britain, although devoting only a small fraction of the resources of the United States, has what seems to be a better-coordinated and better-led program that has brought in a very impressive cadre of scientists to study the problem. We seem to be afraid to say that we have identified a national need and we are going to make sure that the best minds put their attention to it. Why not conscript scientists when their skills could avert a disaster? To say that outright would be a drastic change in the relationship of biomedical scientists to their country and one that should only be contemplated in an emergency, but AIDS certainly represents that emergency.

The issue of targeted research versus investigator-initiated research comes up in another context, the genome project. This is a project to map at high resolution the genes of humans and other key species. It has been controversial because it involves diverting resources from the usual intensive, small-science research efforts to one that will require an enormous input of coordinated, repetitive labor and massive data analysis problems, It will give us invaluable information, but acquiring that information might involve new forms of research organization. I have for a long time harbored the hope that the project can be done without giving up the small-science approach, but this is becoming increasingly unlikely. It may be that the only way to actually get the work done is to give the problem to industry because few universities have been willing to undertake anything but minimal aspects. This notion has scared the research community both because it does not want to see large resources going to industry and because of the fear that work done by industry will not be freely available. The issues here go beyond the scope of this discussion.

One other area where targeted research may soon become an issue is cancer research. The progress in understanding cancer over the last fifteen years has been nothing short of miraculous and yet the mortality statistics show only marginal improvements. We hear accusations that cancer scientists are just wasting money and are not really focusing on the problem. It is not a fair charge but it is a reasonable question to ask if the time is not coming for a reassessment of our strategies and a more targeted approach. I am not sure what is the right answer, but it does seem to me that the question should be asked. Patient-advocates are a major force in setting research priorities in AIDS research and I suspect that cancer is soon going to see the same advocacy.

What I am saying is that the discontent of the political world with the activities of the scientific community is partly our own fault. We have not been willing to undertake critical evaluations of our own activities and therefore left ourselves open to the charge of insensitivity, of self-indulgence. While that was not a problem twenty-five years ago —when our science was nascent and the public hungered for achievements in pure science as a way of demonstrating American superiority over the Russians in the post-*Sputnik* era—in the contemporary world, when America is living through a time of diminishing financial expectations, this won't wash. The biomedical research community has to ask itself: how can we contribute best to the alleviation of suffering? How can we demonstrate most directly our importance for the future health and well-being of the people of this earth? If the general population truly believed that me were devoting ourselves to those questions, perhaps our political stock would rise and we would not find ourselves under such political pressure.

I mentioned in passing the notion that America and perhaps other parts of the developed world are living through a period of diminishing expectations. That perception derives from a fascinating book written last year by Paul Krugman, an MIT economist. The book was called *The Age of Diminished Expectations* (MIT Press, 1990) and argues persuasively that the American public has simply given up hoping that things will get better economically and is lowering its sights for the future. To quote Krugman:

> One might have expected that America's economic problems would have come to a head... through the political process. Relative to what almost everyone expected twenty years ago, our economy has done terribly; surely one should have expected a drastic political reaction. I find the lack of protest over our basically dreary economic record the most remarkable fact about America today. . . . it is astonishing how readily Americans have scaled down their expectations.

With real wages having fallen for 40% of the population and the middle class dissolving away, one might think that people would hunger for politicians who could face up to the problems and offer solutions, but Krugman argues, rather, that people are expecting less and are willing to settle for politicians who offer illusory goals like reduced taxes. This may go a long way toward explaining why the political world is so peevish in relation to the arts and sciences. Maybe it is a redirection of frustrations that must be there in a generation undergoing such a radical transformation from the expectations of its parents.

REPRISE

I have covered a lot of territory in this talk so maybe a reprise is in order before we break until tomorrow. I started by asserting that the public has become more skeptical of science leading the political world to take an increasing interest in the activities of scientists. Events on the international scene indicate this as well as events in America. Science that is funded by the government is inevitably under some political scrutiny, but in the post–World War II era, when Vannevar Bush wrote his seminal report, science was relatively independent of political control. Nixon changed the situation dramatically with the War on Cancer and other acts. The situation has escalated recently, with the Stanford situation being the most dangerous because a great institution is in jeopardy. With education and research as the bedrocks of progress, the attack on higher education threatens to undermine the opportunity of the United States to grow out of its present economic problems. It seems that the research universities have become scapegoats for the failures of American economic life.

The increased politicization of science is partly a result of the changing nature of politics. With grass-roots influence high, populism has set in, making it particularly difficult to sell the notion of the importance of science.

The political world's attention was drawn to modern biology by the Asilomar meeting in 1975, which was an example of an effective relationship between politicians and scientists. Relationships deteriorated afterward.

Looking back to my beginnings in science, I can see the change partly as a lack of understanding of the responsibility of a mature science to take societal challenges head-on, as was done so effectively in the Manhattan Project. Molecular biology today is such a mature science, as seen by the power of the biotechnology industry. One problem I believe should be taken on by the molecular biology community in an organized, structured research effort is AIDS. The one project that has been taken on is the genome project. The cancer problem may be ready for such an attack. We could do pure research without being concerned about such problems when the science was nascent and the country was rich, but not now. Today America has so lost its way that even its expectations of improvement have seriously diminished and it is likely that part of the attack on science and education comes from frustration.

Tomorrow I will consider how the issue of political involvement in science forces us to think about the difficult question of what constitutes truth in science. I will also consider whether science doesn't have a natural protection from political interference. Finally, I will discuss some practical remedies that the scientific community can employ to minimize political interference in its activities.

II

Science is a search for provisional truths that provide unitary understanding of disparate observations. Being provisional, and very much a function of just what observations have been made, science is a very personal undertaking. When external political forces begin to impinge on science, the result can be a chilling of the creative force as the scientist tries to satisfy the needs of a political master. Science today still enjoys relative freedom from political dictation. We can compare our situation to that of geneticists in the Soviet Union under Lysenko to understand what political repression can become. But neither is science in the United

States free of political second-guessing, as it was in the period after World War II.

For the last six years I have personally been involved in a controversy that would have been a minor event were it not for the involvement of the political world. You probably know that data gathered in the laboratory of a then-MIT professor, named Theresa Imanishi-Kari, with whom I was collaborating, were challenged and ultimately she was accused of falsification of data. The issue is in the courts and will not be resolved for some time yet, but the discussion of the issue has raised some very fundamental questions about the proper conduct of science and it is these questions on which I want to comment.

Verification in Science

The issue is: how is science verified? How do we know what's right, what's wrong? For the nonscientists in the audience, let me spend a moment on the question before considering the answer. Some outside of science but, I dare say, few within science may think that science progresses from truth to truth. In fact, it might better be said that science progresses from misconception to misconception, from error to error. When a paper is published, the authors generally believe they have made an honest stab at the truth of the situation, but most would agree that putting something into the literature is akin to entering into a ongoing discussion in which the later contributions will alter, refine, and ultimately could invalidate today's contribution. From this process emerge provisional truths, statements that would get wide agreement in the community of scientists and therefore are the truth of their time. They get into textbooks and get taught to students, but rarely with a sufficient warning that this knowledge is provisional, subject to change, may even be invalidated. Thus, in asking how science is verified, we are really asking about the procedures in the scientific community that maintain and underlie the ongoing debate about truth.

REPETITION

A common belief about the process of scientific verification is that truth emerges from repetition, that if others can repeat an experiment that will show the experiment to be a correct one. Repetition is an important form of verification within a laboratory; it is particularly important as a way for a scientist to check on his or her own experiments. But repetition is not really how the ongoing debate in science is maintained. Certain types of experiments, like the isolation of a particular stretch of DNA, are easily repeated; but for complicated experiments, repetition is not commonly attempted by one laboratory to check on another. In a deep sense, there really is no way to repeat an experiment exactly. To appreciate this point, one need only reflect on the fact that time is a variable that can never be repeated — a more mundane level, a laboratory that undertakes a repetition of an experiment in the literature will have different water from the original laboratory, as well as reagents and supplies from a different manufacturer. In fact, given the many variables that differentiate one laboratory environment from another, the inability to repeat a result is not particularly surprising.

In my laboratory, we sometimes want to repeat a published experiment because the methodology would be a valuable one for our own experimental program. Not infrequently, an attempt at repetition fails and a tenacious scientist may call the originating laboratory to see if there are any tricks that might not be obvious in the publication. A long period can ensue in which the experiment may work in one laboratory and not another. I have even sent students to the originating laboratory to watch the experiment firsthand. Finally, some subtle difference may emerge as the culprit. No, for complicated experiments, repetition is not a significant form of verification —it is rather a difficult achievement, rarely undertaken.

Repetition is not frequent for another reason: there are too many interesting questions abroad for many scientists to be willing to repeat an observation with any exactitude. Repetition is just not as exciting as finding something new. In biology, the problem is compounded by an aspect of biological research known as "the system." Each biologist has a system he or she employs; some have a few systems. The system encompasses the organism under study, the level at which it is studied —biochemical or cellular or organismal —and the types of experimental approaches used. Different immunologists, for instance, have favorite organisms and favorite antigenic responses they study. This is not a matter of aesthetics; it takes years to build up the reagents and expertise necessary to study one system and to change involves a major investment. Also, someone who has spent years honing his or her skill at the performance of some set of complicated techniques is going to continue using those techniques rather than change approaches and require new training. There is a built-in technical conservatism that is inevitable in science and is enshrined in the notion of a system. But you see the problem: if each scientist has his or her private range of action, who will repeat the experiments of another when the original experiment came from an individual perspective that may be shared in its details by no one else?

Thus, because of the virtual impossibility of performing a true repetition and because of the desire of scientists to move on to the next question and because of experimental conservatism, verification is rarely accomplished by repetition. What actually happens is, epistemologically speaking, better. A new paper that, let us say, has introduced a new concept causes people working in other systems to try to incorporate the concept into their own work and to test its applicability. Rather than repeating the work of another, they test it by building upon it. If in their systems this concept works, it receives the very strongest form of verification. If it fails, we have a classic problem —is the concept wrong or is it limited to only a range of systems and not universal? As a verifier, I do not care, because if it is inapplicable to my system, I'll go on to things that are applicable and leave the new concept aside. Note that I will not prove it right or wrong, only limit its applicability. If it is an important new idea, others will do the same and ultimately its range of applicability will become evident.

Let us say that no one finds a new concept applicable: how is this information conveyed to the rest of the scientific community? Few people publish negative results, partially because few journals will accept papers that have no positive news. The news does travel, however, mainly through two routes: the grapevine and the literature. The grapevine is quite effective: scientists see each other frequently at meetings and visits. Often the inability to utilize a new idea or method is transmitted in these encounters and experiences are compared. Even though the literature may not include negative results, it carries the message very effectively when no papers appear that carry the concept forward. Lacking any new news, the community comes to the view that the concept was probably of limited value and people go on to think about other things.

RESURRECTION

Meanwhile, what is the epistemological status of the concept enunciated in one paper and not supported further? Is it considered wrong, or just of limited applicability? Could it be that the data on which it was formulated were wrong either for reasons of experimental imperfection or because of conscious misrepresentation? Ordinarily, none of that is ever sorted out. The paper stays in the literature, available to all who wish to peruse it. In fact, the literature has millions of such papers in it, ones that made no positive contribution to the ongoing process of accumulation of knowledge. And one day, maybe a few years after the initial publication, some unsuspecting young student, dutifully examining all of the antecedents to his project, may come across this paper and bring it to his professor and say: Is this right? Should I incorporate this idea into my thinking? What the professor responds depends on many factors. Let us assume that pettiness does not enter into the picture. She is most likely to say that this idea was not productive and therefore has been discarded in most people's thinking. Times may be different however, and she may see that the idea dovetails well with other current ideas and may suggest that it be given a second chance. Or maybe the systems in her laboratory are very close to the original one and she says that it would be foolish to ignore the possibility that this idea is applicable, at least here. Thus, the concept may have a new life. In the real world of science my hypothetical situation comes up all of the time: there is a constant dialogue with history. And it could well happen that this resurrected notion turns out to be applicable and may suddenly gain currency. Other experimental systems may have emerged that now behave in accordance with the notion, showing that it was of general significance but that the systems being studied were just not in a position to incorporate the idea at the time it was first enunciated.

FABRICATION

I glancingly noted one possibility in my analysis: that the original work that provided new data for the literature might have been fabricated. Let us further consider this possibility.

The pertinent issues are what damage is done by conscious data fabrication and how is it detected? The damage is real. Others can be misled and time, money, and careers can be wasted by following up ideas that are false. Fabricated data will not, however, always generate false ideas; in some well-known cases the perpetrator probably had preliminary data that indicated the existence of a new phenomenon and the fabricated data were an approximately correct representation of the truth. This is not to excuse data fabrication — whether it is done in the name of truth or of sheer fantasy, it is anathema to science because it erodes the confidence that science is disinterestedly searching for elusive truths. But fabricated data are actually part of a continuum because nature never speaks to us directly; data are a representation of physical reality, not reality itself. As an example, consider that every time a graph is prepared from numerical data, subtle decisions about the scales and choice of axes can shape the data so that they appear to support a particular interpretation; thus ideas are always shaping the presentation of data, which is perhaps one definition of the word "fabrication." But, from the previous discussion of the power of a new idea to shape research directions, it should be evident that any new idea must be based on honestly accumulated data, if for no other reason than because an idea will shape the activities of others. For the very reason that most science is not verified by repetition, it is imperative that a scientist be able to trust his or her peers. "Trust" is the key word here and it is trust that is undermined by conscious fabrication.

The other question I raised is how data fabrication is detected. One possibility is that it may not be detected, but the power of the ideas it generates to control the work of others will be rapidly diminished as they find it impossible to build upon those ideas. Thus, the normal processes of science will root out ineffective ideas, however they were generated. There is in molecular biology a famous case of many years ago of Mark Spector, who managed to fabricate data on a grand and cynical scale that were relevant to some of the major issues of the day about how growth is controlled in cells. The doubts about him started almost immediately because his data did not fit in with any previous work, but even with doubts about, it was hard to ignore the possibility that he had found a uniquely effective way into a difficult problem, a problem with which we are still wrestling. It took a short time, a few months, for the community to cool on Spector's work and to develop doubts about his veracity. The major reason was that no one could find anything that fit with his data. Also, attempts to get key reagents from him were of no avail. Thus, when a co-worker caught him at his fabrication and he was unmasked, his influence had already waned. But many hours were spent in many laboratories in a fruitless attempt to develop his notions in new directions. I myself was part of the attempt to develop Spector's leads because they related to the field in which I was working and you can be sure that I was furious about his deception.

Dealing with Fabrication

In summary, the publication of false data is morally wrong, disruptive, and eroding of one of the key currencies of science, trust. But its effects are transient and easily absorbed within the ordinary activities of science and, I dare say, most fabrication is probably not unmasked but has little long-term result because the processes of science handle the problem. Thus, what should be done to detect and root out fabrication? Should we unmask it ruthlessly and unrelentingly or should we simply not condone it and shun those who knowingly perpetrate it? The latter approach approximates the behavior of the scientific community up to a few years ago. The ethic was clear and strong — falsity is wrong particularly because of its erosive effect on trust. But because the ethic was so clear, and the shunning of those who participated in fraud was so absolute, the processes for handling fraud were fairly informal and the punishments were meted out in an unobtrusive way.

Now that is changing, at least in the United States. The issue which has brought fraud to a prominent place is money — the U.S. Congress appropriates the money for most American science and it is now insisting that the wasted money due to fraudulent activities be unmasked. Never mind that the cost of discovering fraud is clearly more than the price tag of the fraudulent work, never mind that the process of discovery is erosive of trust and disruptive of the effective course of science. The mind set here is that of the investigator of any governmental activity and seems to have its roots in the notion of prevention by example — if one fraud is detected and punished, it is believed that this will inhibit further frauds.

With the Congress focusing attention on fraud, if I am right and it is not a big problem, why is the scientific community not protesting that the focus is misguided? Why are the institutions of science falling all over themselves to set up commissions and studies, to write reports, and to devise procedures for handling misconduct? To my knowledge, it is not because the elders of science have become convinced that misconduct is more widespread; all of the written documents seem to emphasize that the problem remains rare. Rather, I believe, it is out of fear — fear that funds will be cut unless the whims of Congress are appeased. Long ago Vannevar Bush warned that deep governmental involvement in science could lead to governmental control of the activities of scientists. There is every indication that such a trend is on the rise.

If it is not clear enough, let me state explicitly that I believe that science is best served, and therefore the public is best served, if the doing and evaluation of science is left to the scientists. The criteria that laypeople, especially politicians, might apply to science are likely to be wrongly focused because they will be evaluating science by myths rather than realities. I can illustrate this from another point of view.

It is often said that one crime in science is data selection: that when one selects from a mass of data just those which are supportive of a given notion, and ignores contradictory data, one is misrepresenting reality and is guilty of scientific misconduct. True, one needs in scientific publication to reflect the data honestly. But in saying that one must realize that data are always selectively presented and when data selection becomes fraud science comes to an end. The issue is intent to deceive and it must be distinguished from intent to convince.

I'll give you a recent example from my own laboratory. The other day one of my postdoctoral fellows described an unexpected finding during a meeting of our group. Another of my fellows got excited by this and indicated that it explained an experience of his a few months ago when he had slightly changed the materials he used for an experiment he had done numerous times and suddenly the experiment had not worked in the usual way. He had assumed that something had gone wrong but now saw that the alteration of procedure had been responsible in a way he had not then imagined possible. He had never mentioned what he thought was a failed experiment and had we written up his data for publication the aberrant experiment would not have been part of it. Would that have been misconduct? It was the conscious elimination of an experiment from the record. It would certainly not have been misconduct by any reasonable criterion because, until it was explained, it had no meaning.

One can only publish that which one believes is meaningful. Furthermore, every anomaly that appears in the laboratory cannot be followed up or we would spend our time spinning wheels. Judging what is reliable science is a personal decision made on the basis of experience and on whether the results fit a pattern. Random observations are not science. The reporting of every activity of a laboratory might serve history well but it would not serve science.

Science and the First Amendment

Having considered some of the detrimental aspects of political interference in science that come from my own experiences in research, let me turn to a more general and more speculative point of view. Here I will get into legal issues that are clearly beyond my own areas of direct knowledge and I may get out on a limb and have it sawed off behind me. Nonetheless, after conversations with legal experts, and after reading a number of articles on the subject, I am convinced that there is a deep truth here, even if I can only represent it in imprecise terms. I might say that the writing of Natasha Lisman, a Boston lawyer, has been particularly instructive to me *(Boston Bar Journal,* Nov./Dec. 1991, pp. 4–7).

In American law, the fundamentals of protection of human rights are found in the first ten amendments to the Constitution. They were written by the founding fathers of America in an effort to ensure that government would never become an unduly oppressive force and are known as the Bill of Rights. A key contributor to their formulation was Thomas Jefferson, a man of science. Let us examine whether the First Amendment to the Constitution might be applicable to the issue of what limits there are on the federal government's right to control science.

The First Amendment states that no law shall be made that abrogates free speech. This has been interpreted in a very strong way by the U.S. Supreme Court; it has only allowed the government to make laws that restrict the right to free speech in situations where there is a compelling need. An illustrative restriction is one against shouting "fire" in a crowded room.

Is Science Speech?

Is science speech and therefore does science fall under the First Amendment umbrella ? Commentators for many years have argued that science is speech and is protected. Mainly they have seen that science is embodied in publications, considered nonverbal speech, and therefore fits squarely into the First Amendment. In a more general form, we can see science as an ongoing argument in which the literature of science is a public debate. Just as in political speech or in the gropings of humanists or social scientists, the debate is meant to elicit the truth.

To the public, it may seem odd to argue that the literature of science is a debate because the general view is that science is an amalgam of facts, that it proceeds from discovery to discovery. It would be salutary for nonscientists to sit in on a laboratory discussion where a newly published paper is being analyzed. The first thing you might hear is a hearty judgment of the quality of the research summed up in the classic epithet "bullshit." As tempers cooled, elements of believable data would be sifted out from those that seem inconceivable. The grounds of skepticism could be many: the methods might not be reliable; the data might show only marginal effects; the investigators may have been wrong so often that they are considered a priori unreliable; there may be other data in the literature that are contradictory but accorded more belief because of how the experiment was done or even because of who did it; the implications may be at such variance with accepted theory that the burden of proof is set very high. In any case, these are all issues of judgment, no different from the judgments made in the political or social arena where the arguments are also about logic, personalities, history, and methodology.

One might think that in nonscientific discussions ideology plays a larger role than it does in science, but it is remarkable how much ideological baggage is carried around by the average scientist. As you might guess, this is more characteristic of older scientists and is probably the basis of the often-noted decrease in creativity as scientists age. The ideologies may not fit on the liberal-conservative axis by which political ideologies are gauged, but they are nonetheless fiercely held and can color a scientist's view so completely that no data can sway his or her belief. I know of one investigator who held a particular view of a problem for years in the face of very strong counterevidence, some of it accumulated in his own laboratory, and who therefore played no role in elucidating an important area of study because his ideological preconceptions completely blinded him to the weight of the evidence. But there are many other stories of scientists who held to unpopular beliefs and were vindicated. The work for which I was awarded the Nobel Prize is a good example —the heretical notions were not mine but those of my co-recipient, Howard Temin, but many scientists had to adjust strongly held preconceptions because of the work. As an aside, I have always thought that the speed with which our new perspective was accepted —within days of the first report, confirmation came and new supportive data started flowing —was because not one but two of us simultaneously came across the same phenomenon. This provides a very strong argument for the salutary role played by redundancy in science.

All of this is meant to point out that science is not a cut-and-dried activity. It depends on debate, judgment, hunch, and preconceptions as much as any intellectual activity. It therefore fits within the framework of the most widely accepted theory of the First Amendment: that in a democracy, truth emerges from the marketplace of ideas and that any hindrance to the free flow of ideas is antithetical to democratic process. The notion that the First Amendment protects scientific activity would not be foreign to those who wrote the amendments. As I noted earlier, Thomas Jefferson was himself a scientist and clearly had science in mind in supporting the doctrine. It seems clear that for him governmental control of science would be as wrong as governmental control over any form of expression in the arts or in political life. On a different plane, Jefferson would have realized that science is an important engine moving society forward and that any interference in the progress of science would be counter to the long-range interests of the country.

The notion that there are two cultures, one of science and one of the humanities, is generally accepted and was, as I remember, the basis for C. P. Snow's treatise on "Two Cultures and the Scientific Revolution." For years, the "two cultures" thesis has seemed flawed to me, however plausible it was on the surface, but I was unable to articulate a counterargument. It is certainly evident that in some sense the culture of the laboratory and the culture of the humanist are different, with one emphasizing the agreement with outside reality and the other focused on the purer products of the mind. The First Amendment argument, however, has helped me see that there are clear identities in the searches involved in the two types of enterprises and that the search for truth is a process of successive approximation and vigorous debate, no matter what type of truth is desired.

Experimentation as Speech

It is easily seen that the debates of science and the publications of science are protected activities under the First Amendment. What is less certain to many commentators is that experimentation itself is protected. Some believe it is not, but the more liberal analysts of the Constitution believe that it is. To me it seems clear that it has to be an artificial distinction to separate publication from experimentation. Many have argued that experimentation is an extension of the discussion of science, but it seems to me that it is meaningless to conceive of science without it. Experimentation is so integral to the process of science that to protect publication and not protect experimentation is meaningless. Actually, the discussions of science are a prelude to experiments so that to regulate experimentation limits discussion and therefore is a direct abridgment of freedom of speech.

It may seem odd to argue that laboratory manipulations are a form of speech but the Supreme Court, in other situations, has agreed that actions can form an integral part of speech. As Lisman has said, "the Supreme Court's recent decisions. . . . make clear that. . . . When conduct serves as an important vehicle for a protected activity, or constitutes a form of such activity itself, it falls within the scope of the First Amendment." She continues, "For scientists, freedom of inquiry that does not include the right to engage in experimentation is like freedom to drive without either vehicle or fuel."

This whole issue may seem very theoretical but it has quite practical aspects. In the United States, there are limitations on the use of animals and on the use of fetal tissue that have a clear impact on what experiments can be performed. I know that similar problems exist in Britain. In the early days of recombinant DNA experimentation, when some were afraid of its power, it was argued that such experiments should be banned because humans cannot cope with the consequences. As Lisman has noted, "A bedrock principle of First Amendment law is that speech, whether verbal or in the form of symbolic conduct, cannot be suppressed either because society finds its content offensive or disagreeable or because it fears its potential misuse."

No one has attacked restrictions on scientific activities on First Amendment grounds but I know that such suits are under consideration. If it can be demonstrated that the regulations are a result of particular religious beliefs, they could be easily found in violation of the separation of church and state as well as being in violation of the First Amendment. If they are found to result from moral beliefs, the Supreme Court would have to balance one right against another. In previous times, one could have some hope that the Court would find in favor of the right to research freedom as a form of speech; with the Court having become so conservative, we can be less sure what would happen. Another approach might be to argue that the government, by funding research, does not gain the authority to regulate it in contravention of a constitutionally protected right of freedom of speech. Historically, the doctrine has been accepted that the federal government may not establish such regulations, but that argument was considerably weakened recently by a Court decision upholding the prohibition of abortion counseling as part of federally funded programs. In general, in America, the Court has become so conservative that we fear that many previous precedents extending rights enunciated in the Bill of Rights may fall with new decisions. But the assertion of rights requires many years of litigation and setting the stage through cases brought now may prove important in the future.

IMPROVING SCIENCE'S IMAGE

These lectures have been quite negative in tone because I have emphasized the threats to scientific freedom. It is important to recognize that these comments are made against a background of great successes and that biomedical science, whatever its problems and long-range prospects, is today a vibrant, exciting, and productive science. In the United States, you cannot pick up the daily paper without reading about the elucidation of a new genetic disease or the discovery of a new element of the cancer problem or some other advance in biomedical research. One feels privileged to be in the life sciences today to witness and be part of one of the great revolutions in human knowledge. My comments here are meant to help understand the dangers that come from these successes and to suggest ways to ameliorate the problems before they become too severe.

Science is suffering from something of an image problem and for an enterprise so dependent on public support that could mean trouble ahead. The ambivalence of the public toward science is at least partly because of the recent nuclear and chemical disasters: certainly the fewer Chernobyls and Bhopals we have, the better will be the image of science. The problem is not immense: polls still find that the image of scientists in the general population is quite positive, especially compared to that of politicians. But what can be done to improve the image of science?

I have suggested that part of the problem derives from a general frustration in the population deriving from its inability to see a way to improve its deteriorating economic fortunes. We are seeing today attacks on the freedom of artists, scientists, and institutions of higher learning. It cannot be coincidence alone that has brought these together; it suggests rather that the politicians are seeking to blame the intellectuals for their own failings. It is a resurgence of the anti-intellectualism that often accompanies straitened economic circumstances and there is little the scientific community can do about it except to work, as citizens, for more enlightened government policies that can help return a sense of optimism about the future.

Actions of the Scientific Community

A critical feature of improving science's image is the recognition that some of the problem lies in the scientific community. While the activities of scientists may be apart from the ordinary activities of the general population, we are funded from their labors and we must show ourselves to be responsive to the needs of the population if we are to maintain a healthy relationship. At this juncture of history, it seems to me that we need to carefully assess where our science can help to solve societal problems and to make a conscious effort to organize our efforts so as to have an impact. As I indicated yesterday, this will require us to work in a more coordinated fashion than we are used to, but that is the only way to solve a multifarious problem like that of AIDS.

At the same time, and I cannot overemphasize this distinction, we must insist that there are problems not ripe for solution, where the only hope is maintaining a strong, investigator-initiated, basic research effort. A problem like aging, where the underlying biology is totally obscure — where we still have no idea how the clock works and how it controls the biological phenomena — is a problem whose solution can only be hindered by a head-on attack. Similarly, the nervous system is still obscure enough that it needs the efforts of the whole scientific community — chemists, physicists, mathematicians, and biologists — to uncover its secrets.

In a similar vein, it is important that we be honest in our assessments and not over-promise. I can remember U.S. government officials promising that a vaccine against the AIDS virus would be available soon, at a time when the scientific community knew how unlikely that was. But we heard few voices insisting that a vaccine was far off, if it could be made at all. Now, eight years after the promise was made, we are still a long way from even knowing if a vaccine is possible. Another area where honesty is needed is cancer research. Phenomenal advances in that field have taken place over the last fifteen years, but they have not brought us any closer to finding a magic bullet that would solve the problem. In fact, the discovery of the multiplicity of oncogenes, the realization of how close the genes of cancer are to the normal genes that run our bodies, and the understanding of how easy it is for a cancer cell to develop new oncogenes has made the whole notion of a single or lasting control of cancer cells quite unlikely. There is still debate here, with some asserting that there may be one underlying pathway in the cell that can be controlled, but it is crucial that we not promise what we cannot deliver and that the uncertainty be honestly presented.

SETTING PRIORITIES

As part of the problem of honesty there is one element of science policy that has always eluded the community but which we need to face: the setting of priorities. Today particularly, when high energy physicists, astronomers, space scientists, and biologists all have extraordinary plans that are exceedingly costly, some choices may have to be made among the various opportunities. The scientific community has generally felt that it deserved more funding and that, rather than setting priorities, it should be possible to do everything. There is certainly a point where that is no longer a conceivable argument and that time may be now. Our fear is that if we try to set priorities then we can doom some important projects and that it is best never to say that a given project is of lower priority than another. The difficulty is that we then leave priority-setting up to the politicians. That gets us the space station, which most scientists seem to feel is a waste of precious resources. Sometimes, of course, the politicians have their way no matter what we say, the obvious example being the star wars program.

Along the same lines, the scientific community's approach to politicians is fairly uniformly to approach tin can in hand. We know well how to ask for new money. But I believe that we also have a responsibility to examine closely how the money we have is being spent. Biomedical research in the United States will receive $9 billion next year. That is a phenomenal amount of money and yet the research community will tell you that it is strapped for funds. There is no doubt that the difficulty of acquiring the funds for research is driving good people out of research. It is hurting the image of science and causing young people to make other career choices. This may be reaching crisis proportions. It is easiest to say that the answer lies in more funds, but that is not a politically feasible answer at a time of deep deficits and a shrinking tax base. Even with reduced international tensions, it seems unlikely that there will be a large peace dividend going to the research community. Therefore, for our own direct good as well as that of our image we must look closely at whether savings could be made in existing programs. I must say that in the United States, at least, the bureaucrats often make it difficult for scientists to examine questions of priority and types of expenditures, but we must insist on the need to assess the effectiveness of programs.

PEER REVIEW

There is one area in which there have been calls for reforms where I believe the scientific community should not compromise: peer review. In making decisions about quality or strategy, the scientific community must have autonomy. Because of the very technical and specialized nature of individual scientific disciplines, there is a very small group of people who can understand what represents the highest-quality science. It is particularly hard for politicians to understand this reality because it sounds to them like an irreconcilable conflict of interest. Peer review often does look like all the worst aspects of decision making wrapped together — insider trading, the fox guarding the chicken coop, a license to steal ideas, a total lack of accountability. It is actually so civilized a mode of decision making that politicians have a hard time believing that it can work fairly. Sometimes it breaks down, and it is under particular stress at a time of very limited resources, but it is a necessary form of self-governance.

SCIENTIFIC LITERACY

One problem of which I believe we are all aware is the need for greater scientific literacy in our populations. Both because of the need to function in an increasingly technical world and because those who vote on scientific issues need to understand them, it is of paramount importance that the scientific community devote time to education of nonspecialists. In doing this, we must be aware of the need to meet people at their own level, rather than treating everyone as a neophyte specialist in one's own discipline.

That involves changing one's style from a professional one to a pedagogic one, something that is difficult for scientists and requires conscious effort. Many of the people we must reach are not in school anymore, making the media our only outlet. We need particularly to figure out how to get better science integrated into commercial television, both on news broadcasts and in entertainment shows.

While we are discussing the media, there is another side to our relationship to the press. The press is notably unscientific in its presentation of issues. At the same time, science has become increasingly pervasive in the lives of the public —more drugs are available and used, more synthetic chemicals are in products, computers are increasingly important in all professions and even in the home, prediction of genetic defects is becoming available, bone marrow transplants are becoming a standard part of medical practice, and on and on. But every innovation brings with it decisions about how to employ the new capability, whether and how to regulate it, how to evaluate its strengths and dangers.

It is through the press that the public hears about issues. Newspapers for the decision-makers but television for most of the populace, and magazines to a lesser extent, are the routes through which issues become evident and in which debates take place. For instance, there was recently a long editorial in the *Wall Street Journal* about silicone breast implants (Feb. 8, 1992, p. A24). One issue it raised was whether the silicone causes an autoimmune disease called scleroderma. In the editorial we find the statement that "some incidence of scleroderma would be natural in any group of a million women." This vague assertion is used to raise doubts about the significance of the reported cases of scleroderma among women with breast implants. For anyone with the slightest scientific training it is evident that this is hyperbole, not rational argument. The relevant question is: how does the rate of disease compare in a control group and in a group with implants? A newspaper designed for reading by a literate public should be ashamed to use such an unscientific argument. The *New England Journal of Medicine,* by contrast, has on its staff a group of statistical consultants. The editors know that what appears in the *Journal* affects medical practice and they take this responsibility seriously. Why can't the supposedly responsible segment of the daily press be as careful? It would not have been hard for the *Wall Street Journal* to have found the background rate of scleroderma and it should have a scientific ombudsman who raises such issues. And this is not an isolated case —if you read the papers with an eye to the problem, it is evident that scientists could make a significant contribution to the debates that rage daily about issues of science, medicine, and technology. At the end of the horoscope column in many newspapers it says, "The horoscope is intended for entertainment only. The predictions have no proven scientific basis." I often think that the whole newspaper ought to be read with such a disclaimer in mind.

The process of decision making is one at which scientists are especially adept because they spend their lives evaluating data and drawing conclusions. I'm not arguing that scientists should be *deciding* the issues posed by science —such decisions ultimately must rest with the public. But I am suggesting that scientists should have more input, that the public world should want more rationality in the consideration of public policy issues.

A particular area of concern here is issues of environmental safety where arguments are made with surprisingly little scientific input. In this area, an almost religious reverence for Nature, for the notion of a world without human intervention, seems to control the debate. But the whole world is already altered by human life and the problem is choosing among alternatives, one that is poorly handled by religious absolutism.

An appropriate counterargument here is that many public policy issues have a large moral dimension and that scientists are not better than anyone else at moral judgments. I would go further and say that scientists are often the worst judges of moral issues because they are too ready to believe in their own rationality and generally out of touch with the thinking of the community. But that does not mean that we must entirely give up rationality when we come to difficult choices. A productive dialogue can highlight the moral dimension to a problem and allow for rational discussion of those elements that need such illumination. In particular, scientists can often see where a moral argument is really a question of lack of information and where either some research or a good approximation can keep the discussion moving.

Finally, I want to make a suggestion that is very much in tune with the times — that we privatize science a bit. Here I do not mean that we make science the province of industry — with the present short-range thinking in industry that would be a disaster. Rather, I am suggesting that if we can get more nongovernmental funds into science, we can greatly improve the flexibility of the scientific community to make its own decisions. For instance, in the United States we are prevented from using public funds for certain types of human reproductive and fetal research. The charities and private donors should be encouraged to use their funds for these areas. Private funds can be used more flexibly than public for the purchase of equipment and the support of personnel. In the end, the government controls all parts of society so it can prevent just about anything unless there is constitutional protection, but often the political realities require that the government be stricter about its own funds than about funds from elsewhere.

Concluding Remarks

This is all I wanted to say. To summarize it would take too long and probably not be useful. So I wish to end with thanks. I have greatly appreciated the opportunity to put together my thoughts on these issues in a pair of lectures and I am most grateful to all of you who sat through these two days with not a slide or an overhead. To participate in the remarkable tradition of the Tanner Lectures is a singular honor and an enormous pleasure. I look forward to discussing these issues in the seminar tomorrow and hope that the questions I have raised may engender debate and, might I hope, action in the future on both sides of the Atlantic.

Thank you.