Federal R & D and Industrial Policy

G. A. Keyworth, II

Summary. Long-term U.S. economic growth requires better use of R & D resources and closer interaction of the academic, government, and industrial research communities. The federal government has proposed to increase support for university research as a key means of addressing national needs for new knowledge in fields important to industrial development and for training of technical personnel. But continuing growth in support for basic research depends on how well the science community can agree on what research investments will have the greatest impact in producing new knowledge.

Over the past year the vitality of U.S. industry has emerged as a major new public policy issue. After decades—literally whole lifetimes for most Americans—of dominance in the world's marketplaces, we suddenly find our industrial leadership and, it seems, our future challenged by aggressive new foreign competition.

Increasingly, we in the Administration hear the question: "What is the federal government's industrial technology policy?" But I am afraid that in asking the question that way, most people are hoping for an answer we cannot give. They want to hear about a detailed federal plan for some kind of moon-landing-like program of industrial rejuvenation.

I wish it were that straightforward to address, but the problems of America's industrial competitiveness have been developing over a decade or longer. They are not going to be solved by a few swift waves of a high-technology wand and a diversion of tax dollars into flashy new federal programs. There are no quick fixes—but there are reliable long-term approaches that build on our strength.

Strengthening American Industry

Many people think of the Science Advisor as dealing only with such specialized things as where to build new accelerators, where to send new space probes, or how many new amino acid sequencers can be put in universities. But for much of the past year I have joined my White House colleagues in looking at far more important issues: the mechanisms and incentives to enable our economy to sustain long-term growth—growth that does not require constant federal intervention or subsidization of the marketplace. We are determined to strengthen our free-enterprise system so that American industry can compete aggressively in the international marketplace, and so that it can create the jobs and profits that we expect from a healthy economic system.

International competition—especially in high-technology industries and in the industries that depend on technology—has been an obvious focus of our attention. The situation today is unsettling, though probably not as alarming as some people suggest. We may have overreacted to recent business downturns. Sometimes we have failed to distinguish between industrial slumping due to general economic sluggishness and loss of market due to foreign competition. In fact, most American industry is very strong and highly productive, and we should see reassuring evidence of that as economic demand picks up this year.

Still, we would be foolish to ignore the trends. Foreign industries are becoming more competent and efficient in the same high-technology fields that we look to for our own prosperity. But the problem of real concern is not what is going to happen in the next year or so but where U.S. industry may be a decade down the road.

Here I want to insert a strong caution against a rising undercurrent of protectionism in this country. We cannot solve trade problems by isolating domestic industries from the international marketplace. We would seriously damage long-term American productivity if we were to shrink from competition, as various protectionist proposals would have us do.

As the President has pointed out, protectionism eliminates as many American jobs in one sector as it purports to save in another. Moreover, it virtually ensures a continuing decline in competitiveness for a protected industry. That approach mortgages the future and prices those industries out of international markets—hardly a farsighted policy in today's world.

Need for Science and Technology Personnel

This issue of trade policy has been heavily debated in the White House Cabinet councils, where the broad issues of both near-term and long-term industrial health have occupied a great deal of the President's time in the past year. At his insistence, we have been weighing a variety of issues and problems that bear on our industrial competitiveness. As might be expected, in addition to trade these include capital formation, antitrust, patent revisions, regulatory relief, and tax policy. The number of ways suggested for approaching industrial problems confirms both their complexity and their importance.

There has been one aspect of these discussions that I found fascinating. All the possible approaches to improving industrial competitiveness had one element in common. It does not matter what combination of actions the federal government or the private sector takes; tomorrow's industrial growth will depend on the availability of skilled technical personnel.

Moreover, virtually all the economic scenarios predict a heavy demand for technical personnel before the end of this decade. In all likelihood we face a situation in which our absolute rate of economic growth may depend directly on the supply of skilled personnel across the board—Ph.D.'s and technicians in industry, researchers in laboratories, teachers in schools.

So, very early in our discussions, the President assigned high priority to

The author is the President's Science Advisor and is Director of the White House Office of Science and Technology Policy, Executive Office of the President, Washington, D.C. 20500. This article is adapted from remarks prepared for the AAAS Colloquium on R & D Policy, 24 March 1983.

strengthening our national base of scientific and technical personnel. That included immediate emphasis on training people in the areas of science and technology that were likely to have the greatest impact on both industrial growth and national defense.

Emphasis on University Research

We realized that the most direct and effective way to meet those needs would be to take advantage of an existing mechanism that we know works well: the participation of students in university-based research as an integral part of their training. Because of that unique mechanism, American universities have a central role in ensuring the nation's long-term economic health.

In fact, that role is going to be increased as a result of a heavy and unaccustomed worldly burden we are proposing to put on academia. This shows up in a number of ways, but it is most evident in the very large increases in funding planned for basic research in universities.

This turned out to be a fairly obvious way to respond to the long-term economic goals we identified. There is no question that we are building on strength rather than trying to invent new mechanisms. As a group, American research universities are the best in the world, both in terms of producing the new knowledge that stimulates technology and in terms of producing the people who drive the innovative process in society.

That unique dual function explains our tremendous emphasis on university research. No other research institutions—federal laboratories, nonprofit organizations, or industrial laboratories—give so much return on investment in the long term. No other institutions produce both knowledge and people.

This mechanism will go a long way toward increasing the supply of highly skilled technical personnel. But we also know that some pressing personnel problems will not be adequately addressed by these increases in research support. We have therefore proposed several additional ways to address what we believe are critical problems: the inadequate supply of new junior engineering and science faculty in universities and the shortage of qualified secondary school science and mathematics teachers.

Without going into detail about these programs, I emphasize that we expect the new Presidential Young Investigator Awards to attract to university research recent Ph.D.'s who might otherwise pursue nonteaching careers in industry. Several other programs should improve the supply of qualified science and mathematics teachers in secondary schools. Because these education programs concentrate resources where they are most needed—on good faculty—we anticipate substantial long-term benefits.

Better Use of R & D Resources

At the same time that we are working on the problem of scientific and technical personnel, we are struggling to make better use of our existing R & D resources. The fact is that some of our major federal efforts in R & D are still largely missing the boat. Think for a moment about our most pressing national needs. Then consider that there are institutions claiming a large portion of our federal R & D resources that do not contribute significantly to training scientific personnel, to industrial competitiveness, or to national defense. What, then, are they doing that is so important? Given the pressures on our federal budget, that situation strikes me as indefensible, though I know many of the institutions involved feel quite comfortable—if not righteous—following their own outdated agendas.

I have not tried to hide my strong feelings on that subject. In February I wrote an editorial (*1*) in which I addressed the notion that federal support for R & D is an entitlement, that it is going to come off the top of the budget independent of economic pressures or national priorities. If my message in that editorial seemed harsh, it is because I see that attitude as being destructive for science and for the nation. The research community has an important role to play in this country's future, but it has to come to grips with the realities of the 1980's.

For example, I emphasize that the increases in support for basic research are not a reward for all the fine things the universities have been doing. Rather, they are a challenge to the universities to assume a greater role in helping us regain our momentum in world technological leadership.

Likewise, we are turning to other research institutions and demanding innovative responses from them. There is no question that the United States has the world's best research capability—not only in our universities but also in our federal laboratories and in much of our industry. How can we do a better job of taking advantage of that capability? Naturally, I do not want to play down the size of the federal budget increases in support for basic research, but it is important to bear in mind that our real concern is for quality of research, not quantity. Larger numbers of projects, or even larger numbers of scientists and engineers, do not automatically produce leadership. After all, we began to lose the overwhelming technological lead we enjoyed for so many years during the same years when we were expanding the amount of activity in our research establishment. Maybe that was a lesson we could not have anticipated then, but it is certainly one we cannot ignore after the fact. Good intentions and keeping busy do not count; results do.

For that reason, our first priority now is to permit the best research to be more fully supported so that its influence can be extended. This is the time to do a job with the best tools we have, not a time to dissipate our resources by parceling them out in response to popular demand.

New Interactions

I have explained how our concern for industrial competitiveness led to today's emphases on basic research and training opportunities. There is another outcome too. American technological progress suffers badly from the artificial barriers between industry and the bulk of the basic research establishment. Most academic and federal scientists still operate in virtual isolation from the expertise of industry and from the experience and guidance of the marketplace. One can make a convincing case that this separation is a root cause of our sluggishness—compared to some of our more energetic competitors—in turning research into products.

I am always puzzled that so much of the academic research community has failed to notice how successful and mutually beneficial those industrial interactions have proved to be. Only a handful of universities have demonstrated how academic research can both achieve the highest levels of quality and be linked to the industrial world for great economic and intellectual benefit. Places such as the Massachusetts Institute of Technology or Stanford University should be beacons for the community. The proliferation of new, technically oriented industries along Route 128 outside Boston is no coincidence, nor is the prosperity of Silicon Valley. Both were stimulated by alert academic communities, and both have returned that stimulation to the universities.

This potential for innovation in the interaction between industrial scientists and engineers and university faculty has been clearly demonstrated, and the example is now being followed in other parts of the country. Maybe it is unrealistic to expect success of the magnitude we have seen in Massachusetts and California, but we can take heart that we are beginning to see a broad movement in that direction.

When I stress the need to develop better mechanisms for research, I include interaction of industrial scientists and engineers with their potential colleagues in universities and in federal laboratories. I am particularly concerned about those federal laboratories, and especially the 12 Department of Energy national laboratories, which represent a public research resource of enormous potential. Many of those laboratories, which were established decades ago to deal with highly specific national problems, are no longer focusing on problems of first-line importance. But they are still valuable resources, and we mean to put them to better use.

Trying a New Role for a Federal Laboratory

I admit that is easier to say than to do—and it takes patience, much like changing the course of a huge ocean liner. We started moving the rudder 2 years ago, and we are finally beginning to sense a change of course. One example of what I think is an exciting prospect for a new level of interaction between academic, federal, and industrial scientists is the Advanced Materials Research Center being established at Lawrence Berkeley Laboratory.

New technology is increasingly being built on advances in materials. We are entering an era in which we not only will shift away from reliance on increasingly scarce natural materials but will process common raw materials into exotic new compounds with astounding performance. It is safe to assume that tomorrow's marketplace will be infused with those new materials.

We see a great opportunity here to capitalize on American expertise. Lawrence Berkeley Laboratory, which is a superb research facility located on the University of California campus at Berkeley, has recognized three things. First, science has made enough progress in recent years in a variety of disciplines to approach a new threshold in understanding materials. Second, the potential applications of this knowledge, as it is developed, would spread throughout our high-technology industries. And third, this is an area of basic science in which the United States now holds a decisive world lead—one that can be broadly extended.

Although the initial impetus for this center is largely federal, there is wide industrial interest in working with the facility as it develops. Equally important, this is also a model for a new kind of federal laboratory. We see it as a test-bed—possibly the best we will have for several years—for exploring new means of university-industry-federal laboratory interaction and cooperation.

This is only one of many ways we are trying to break down the barriers between industrial science and the bulk of basic research. We are not hesitant about trying out new ways in which industry can work more closely with the basic research community. The example of Lawrence Berkeley Laboratory, the shared funding of science education programs, the expansion of industrial research at places like the National Synchrotron Light Source, our increasing determination that the management of the national laboratories should reflect greater private sector perspectives—all these are evidence of our intention to better use our massive, and expensive, resources.

However, in spite of industry's increasing spending for its own R & D, we have no illusions that the private sector is going to relieve the federal government of its responsibilities for support of basic research. In the kinds of programs I am describing, money is not the real issue. What we are counting on is the payoffs from new perspectives, from imparting a better sense of the reality and stimulation of the marketplace to a basic research community that has become increasingly isolated from it over the decades.

We are still in the early stages of this process, and many of these efforts are exploratory. But we really need to stimulate some fresh thinking. One thing that is certain, the creativity and innovations are not likely to come from Washington. I cannot—and will not—tell a place like Los Alamos National Laboratory or Caltech or General Motors how to develop cooperative programs or how to link public and private sector interests. At best, the federal government can create a climate to encourage those things, and it can make a commitment to maintaining that climate.

Stable Funding and Excellent Research

I mentioned earlier that an important part of that climate will be ongoing federal support for good basic research. We have heard many concerns in the science community that this year's increases for basic research might last for only 1 year. That has never been our intention. In fact, a 1-year spike might well prove more harmful than useful, because it would introduce new instability into the funding pattern.

There is no question that stable funding for basic research has to be a high priority for all of us. Moreover, that funding should be at a level high enough to take advantage of intellectual opportunities and high enough to ensure the training of enough new scientists and engineers. And it should be predictable enough to permit continuity in long-term projects and planning for critical new facilities.

But how do we achieve that stability? Some people would have us try to claim some percentage of gross national product as a funding level for R & D. Aside from what I predict would be the failure of that mechanism to hold up in the brutal give-and-take of budget-making, I have already indicated my distaste for trying to turn R & D into an entitlement. That attitude is deadly to good science. The first entitlement begets more. Soon we have individual disciplines demanding their guaranteed share of the pie, then regional demands for portions. Next we would be dividing up portions between universities, 4-year colleges, and 2-year colleges. All too soon the only criterion that should count—excellence—is lost in the noise of formula grants, geographic distribution, and set-asides.

Moreover, I predict that in order to sell and maintain such a funding mechanism, one would have to overstate the benefits to be gained from technology. Actually, this is not a prediction of what would happen because we are already hearing it. I am afraid the resulting pressure for tangible results would inevitably divert resources away from basic research and into applied research and development.

I think we have shown this year that government will respond enthusiastically when it is presented with programs, even as esoteric as basic research, with clear relevance and importance to national objectives. But I have to turn the tables on the science community at this point. The Administration's plan to maintain this emphasis on basic research—and to create a structure for a strong federal R & D program that will attract bipartisan support for years to come—is not automatic. It is critically dependent on cooperation and assistance from the science community itself.

I am especially worried about the continued inability—or unwillingness—of the members of the science community to agree among themselves about priorities or to abide by their decisions when they can agree. Considering all the complaints I hear from that community—and I find that the level of complaint is much the same no matter what the R & D budget looks like—I would not think it necessary to remind them that these are tough times. I will add that, for anyone depending on federal funding, they are going to remain tough times for quite a while.

My experience in the past 2 years reinforces my conviction that the disciplines which present well-considered, unified agendas for research have the best chance of getting support for their programs. After all, in the absence of agreed-upon recommendations, what can we expect the nonscientists who allocate funds to base their decisions on?

There are three choices, none of them good. It may be that funding increases will simply be deferred until the community can come to some consensus. Or decisions may be based on such non–scientifically relevant factors as preservation of politically popular facilities. Or disaffected minority viewpoints, when they are the dominant messages transmitted to the decision-makers, may well carry the day. The central point is that the community has to be willing to establish its own priorities and then stand by them in the public arena.

From my perspective, I would say that the coming year could prove very important for the future of American basic research. The Administration's proposals have been very well received so far. There is every reason to expect that we will see broad bipartisan support for most of the elements of the plan. This favorable reception, if it is supported by the science community and by industry, may set a course for a healthy and beneficial new degree of integration of science and technology in American life.

Reference

1. G. A. Keyworth, II, *Science* **219**, 801 (1983).

RESEARCH ARTICLE

Splice Junctions: Association with Variation in Protein Structure

Charles S. Craik, William J. Rutter, Robert Fletterick

Numerous studies have revealed the existence of families of structurally and functionally homologous proteins (*1*). The members of these protein families present fundamentally similar tertiary structures yet can exhibit quite divergent amino acid sequences and can be of quite different size. Small variations in polypeptide length are usually manifest as loops on the protein surface. The structural and functional relationships among the members of protein families imply a kinship among their respective genes. Presumably they are descendents from a single primordial gene by duplication and subsequent divergence. However, the pathway for this diversification is not clear. Point mutations produce amino acid substitutions, but a mechanism for production of deletions or additions of peptides in the internal region of the proteins is not obvious.

Abstract. *A comparison between eukaryotic gene sequences and protein sequences of homologous enzymes from bacterial and mammalian organisms shows that intron-exon junctions frequently coincide with variable surface loops of the protein structures. The altered surface structures can account for functional differences among the members of a family. Sliding of the intron-exon junctions may constitute one mechanism for generating length polymorphisms and divergent sequences found in protein families. Since intron-exon junctions map to protein surfaces, the alterations mediated by sliding of these junctions can be effected without disrupting the stability of the protein core.*

Eukaryotic genes are fragmented; the coding regions (exons) are interrupted by untranslated segments (introns) that are removed by a splicing system. The introns are excised from the initial RNA transcript and the exons are joined prior to translation of the messenger RNA (mRNA) into the protein product. It has been postulated that the exons represent genetic building blocks that code for discrete structural or functional domains of the proteins (*2*). This hypothesis appears tenable for some systems but clearly fails for others (*3*). Particularly intriguing is the fact that the positions of introns in the genetic sequence map to the surface of the protein (*4*). This implies a relation between the intron-exon structure of the gene and the tertiary structure of the gene product. An analysis of gene structure and variation in protein sequence within gene families shows that intron-exon junction positions correspond with length variations within members of the protein family. This leads to the hypothesis that translation of intron-exon junctions along the genetic sequence (intron-exon junctional sliding) may be one mechanism to account for peptide sequence length variability within protein families.

For these studies, gene families were selected in which the gene sequences, amino acid sequences, and protein structures of family members are known. This information is available for a family of mammalian trypsin-like proteolytic enzymes that typically contain serine at the catalytically active site (the serine proteases) (*5*) and for a homologous bacterial proteinase. Similar information exists for a metabolic enzyme dihydrofolate reductase.

A comparison of gene structure and protein structure for these families re-

The authors are members of the Department of Biochemistry and Biophysics, University of California, San Francisco 94143.