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- **Universities and Federal Science Policies**

In distributing federal support more widely, we will retain the criteria responsible for our present success.

Donald F. Hornig

The relationship between the federal government and the universities has been a developing partnership in the public service, a partnership which has proved extraordinarily fruitful for the universities, for the government, for science, and, above all, for the nation we serve. I would like to take stock of the benefits as well as some liabilities arising from this partnership, and to look ahead at its future development.

In historical perspective it is clear that overall progress in science is marked here and there by peaks of achievement, true breakthroughs in sometimes unsuspected directions. These peaks rest on a broad and expanding base of solid growth. The central problem in fostering scientific progress, therefore, is how best to encourage the breakthroughs while maintaining the greatest possible rate of growth, in both quality and quantity, at the base. Even in the most abstract

terms such considerations revolve ultimately, so far as the federal government is concerned, around the problem of financial support. In the first instance, we as a nation must decide how much of our funds to allocate to science; in the second, how to allocate them; and in the third, by what specific mechanisms to distribute the funds in order to best accomplish the goals we have set.

Such reasoning clearly implies that the future shape of science and the directions of its progress will be determined not only by the scientific community but by the nation as a whole. As in all human affairs, the people who foot the bills are entitled to decide how they want to spend their money.

Let us take a closer look at some of these problems. This relationship between science and the public, or more directly between the universities and the federal government, first became intimate during World War II and has since grown to very substantial proportions. About three-fourths of all university research, one-third of all graduate students in science, and substantially all Ph.D. candidates are

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now supported by the federal government, and federal funds pay for about one-third of the cost of all new science facilities. Recently this support has been extended by various new programs of the National Science Foundation to bring training and participation in research to college teachers and undergraduates. The many federal programs of support for science involve about 400 colleges and univerincluding substantially all sities, Ph.D.-granting institutions in all parts of the country.

When these programs are compared with those of any other country in the world, one notes one very striking difference. Except for those of the Department of Agriculture, they have not provided for the allotment of funds by formula, either of population or geography. They have not provided for distribution of funds by institution, as in the British university grant system. By and large they have rested on the identification of talented, promising individuals and groups of individuals, on the identification of worthwhile, creative, original, and significant researches, in large measure proposed by the individuals. In short, we have attempted to operate a system based on talent and on merit of individuals. Naturally, judgments of merit are hard to make. The evaluations of proposals have in some cases, such as in the National Institutes of Health and NSF, been carried out by study sections or panels of scientists. Such judgment by peers has been widely commended in every study which has been undertaken. I note particularly that of the National Academy of Sciences Committee on Science and Public Policy, "Federal Support of Basic Research in Institutions of Higher Learning," and the Wooldridge study of the NIH, which was undertaken

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for the President. However, other agencies have sought to achieve a similar goal through the use of internal consultants or staff judgments. Whether the approach was consistently correct in its judgments or not, it was basically sound in that it focused attention on excellence and merit wherever they were found, in whatever state or whatever institution, and in that way it avoided many of the difficult questions posed by institutional choices. I want to say most emphatically that I consider this approach a major invention in government support of science and one that is in no small measure responsible for the success we have had.

The Advisory System

Another invention of great significance has been the network of advisory panels, groups, committees, and boards established to provide advice on the award of federal grants and contracts. The primary function of these groups is to provide scientifically competent and unbiased advice to the federal agencies. They have performed this function well. But they have done much more. The advisory groups have involved scientists in large numbers from many universities in the making of decisions. This wide participation has played a large part in preventing the kind of split between universities and the federal government which many feared after the end of World War II. In addition, these advisory groups have been, in a significant but unanticipated way, a major means of strengthening informal communication among scientists.

The advisory system inevitably generates problems, such as the possibility of lack of objectivity. But on the whole, the entire structure has contributed in an important way to the health of the existing federal system for the support of research.

This way of doing things, this emphasis on merit and excellence, this concentration on the individual and on the proposed research rather than on the institution, has raised some problems to which I will allude later. But please do not mistake me. It has been the backbone of our system. It has provided a degree of freedom for the individual research worker and scientist, particularly for younger men,

a freedom from administrative restraints both within the university and within the government that is in my mind unmatched anywhere. It has brought great vitality and energy to our scientific enterprise. It has held out the prospect of support to all capable individuals no matter where in the country they are located. There will be changes, but I am sure that this primary emphasis on quality and on the individual must and will remain the backbone of our government relations with the universities.

Now I do not believe I can demonstrate that either the quantity or the mode of federal support is wholly responsible for the extraordinary progress of American science in the last two decades. Nevertheless, the fact that science has flourished is unquestioned. This period has seen the interpretation of living systems in terms of chemical reactions and structure of molecules take hold in a way which promises to place biology on a theoretical and experimental foundation as secure as that of chemistry and physics in the past. It has seen elementary particle physics step out into an unknown realm which makes the revolution of physical understanding of the 1920's only a prelude to much more fundamental problems toward which we can only grope. That ancient science, astronomy, has burst forward with a new vigor as both radio and optical astronomers discover new and fantastic objects on the outermost borders of space. The advent of space astronomy has already given us a new knowledge of x-ray sources and promises to open up spectral regions heretofore closed to us. Earth scientists have begun to investigate the entire atmosphere of the earth as a system and to study the structure and dynamics of the entire globe so that the pace of our understanding advances by leaps and bounds.

Problems of Success

Why, then, if things are going so well, isn't the right approach simply to continue doing what has been successful? Many scientists feel precisely this way, particularly those who have profited from this approach, and they are very concerned at the prospect of change. But there will be change, because our very success and growth

have changed the situation. The progress of science has accelerated the development of the society which science serves. For example, one of the most striking characteristics of the university scene today is the growth of new, strong centers of scholarship and research. In the fields I know, quite aside from statistical data, there are many more good schools than there were two decades ago. What is even more striking is the growth of the ambition to be excellent, the ambition to be strong. All over the country there are schools which in the past awarded no advanced degrees, or at best a few, and whose faculties were little concerned with scholarship, which are now on the road to academic excellence, which have recruited or are recruiting stronger faculties and building new facilities, and which aspire to compete on their own terms with the established centers of strength. These schools want help and deserve help and, if given the support they need, will in many cases achieve the kind of excellence which has been realized by the best of the older institutions. They will eventually compete for their share of research support on the traditional terms, but they may need some investment before they reach that happy state.

Another factor which has caused some concern is that as federal dollars become a considerable part of the budget of an institution, their effect may be to distort the structure of universities as educational institutions. I am worried that, having freed the creative and talented investigator from the petty bureaucracy of the departmental tyrant, we have also helped remove him from the university as a whole and have turned the science departments into a collection of feudal fiefs rather than organic wholes. And then there is the concern over the effect of our great research programs on undergraduate education. Curiously, these arguments take two quite different forms. On the one hand, it is felt that good undergraduate education can only be given in institutions where creative minds are at work and scholarly activity goes forward, where the students can sense the pulse and thrust of important enterprise in motion. It is argued that institutions which do not carry on enough research cannot recruit the faculties to provide a first-class education. On the other hand, it is sometimes argued that within institutions in which advanced education and research are active, the faculties lose all interest in undergraduates and leave them to junior members of the faculty. Surely, both cannot be true, or if they are, we should be able to devise a better way of doing things.

Training the Talented

In my view the situation is something like this. We set out two decades ago, realizing that scientific and technological advances were the foundation for the nation's health, for its economy, for its secure defense, and for many other purposes, to strengthen the scientific foundations of the country. This is still our conviction, so one of our big jobs is to strengthen and workers and institutions develop that can advance our knowledge and understanding and carry on researches at the very forefront of man's knowledge. The accomplishment of this goal with finite resources requires that we find the most able and talented students, give them the very best teachers, and provide them with tools which can accomplish the job. This inevitably means that for this purpose we must select and concentrate our most talented students at the institutions at which we can find the inspired teachers and researchers with whom they might study, and where we can build up the necessary facilities and experimental equipment. This is the historical method by which the spires of supreme scientific achievement were erected and which was the pattern that continued to be followed in the early days of federal support. What is more, I would assert that for the purpose of producing the very best science, for the purpose of penetrating the frontiers of ignorance, such pinnacles of achievement are a proper and necessary part of the scene and will be in the future.

To put the matter more clearly, I will use an analogy. This nation wants deeply to have its share of Olympic gold medals. We want to win a majority of the events. Now, to produce Olympic athletes, no amount of running little boys around the block will suffice. We won't do it even by running Academy members around the block. We have to find those with

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real talent and concentrate the care of our best coaches upon them. We must concentrate the best education to develop the mental gymnasts as well.

But there is another side to this coin. To follow my analogy, we could not hope to recruit the skilled athletes without a national physical fitness program to build up the skills of all the children so that the potential champions can be selected for intensive training. Similarly, in the intellectual sphere it is important, if we are to identify the most able and best qualified, that there be academic strength throughout the country. For this purpose we must not only maintain and increase the pinnacles of outstanding achievement, but we must build a strong base of strength. This is a philosophy the President has repeatedly proclaimed and is surely the key to the future, at least for this administration!

These fine generalities are all very well, but I'd like to look a little deeper into the guides we can find for the directions in which we are going and ought to go to achieve the best balance between these factors. When science was a small enterprise it was easy to think in terms of selecting a few gifted individuals and backing them. But it has now become a very large enterprise. The nation invests several billion dollars a year on research, \$1.3 billion of that in the universities proper, not counting the accelerator laboratories and other attached institutions. As a consequence, the shape of science and the directions of scientific progress are no longer a matter for the scientific community alone; they have become part of the public enterprise. We had better face the fact that now and in the future the Congress and the public, who respectively appropriate the money which supports us and pay the bill, expect to be heard as we set our course for the future. And this is quite properly so.

Expectations of the Public

This has led me to ask why the American public is in fact willing to spend so much on scientific research and on scientific education. Part of the reason is the expectation of future benefits. Certainly the appropriations for research in the biomedical sciences, no matter how abstract, are supported in the public mind in the expectation of future improvements to health, cures for disease, longer and more fruitful life, and so forth. The rapid expansion of support and the big proportion of our efforts which go in this direction reflect only in part the judgment of the scientific community that this is a fruitful area of understanding, ripe for great progress. We should realize that the rapid growth came about in the 1950's through the action of the Congress, particularly Senator Hill and Congressman Fogarty, who insisted on appropriating more funds than the executive branch and many scientists thought wise. I think that it shows the conservatism of many scientists that a later study of a representative sample of projects by a distinguished panel indicated that the funds had been extremely well spent. This is clearly one case where the public was right.

The public has come to accept the argument that progress flows from basic science and that material and social benefits in the future derive from the most abstract investigations today. It has come to accept the belief that the health and intellectual tone of a community or region is improved by the presence of strong, alive, and vigorous universities. Beyond the expectation of practical results, there is the very sincere and general conviction, which has been expressed so often by the President, that the 20th century is a century of science and technology and that the progress of applied science depends on the constant replenishment of its sources of new ideas. I think the public well understands that we have no idea from what obscure basis the critical new discoveries may come. And this may be the reason that, much as in my analogy of the Olympic games, we find a very general determination that we should be first, or at least in the forefront, of every field of science, from mathematics to space, to high-energy physics, and so forth. It would be wrong to underestimate the public interest in the pure intellectual achievements of science. I am constantly struck by the fact that pronouncements on science policy or promises of new practical benefits often attract only the slightest attention in the press, but that the measurement of the occultation of the

crab nebula by the moon for the purpose of discovering whether the x-ray source there is a point source or diffused throughout the nebula can occupy two columns of the Washington papers, which are not normally much aware of science.

Institutions Set the Tone

I have rambled somewhat, but to summarize, the situation is this. We have a number, perhaps something like 20, really outstanding institutions which set the tone and standard for the whole enterprise. This number will grow, but we will always look to a limited number of institutions to perform this function. Our scientific support has been concentrated in the direction of those institutions, but as science becomes increasingly a public matter, there is a spreading desire by all parts of the country to share in the material and intellectual benefits which spring from strong science and strong universities. Now, where does this leave us and where are we going? There are a variety of winds blowing, but I don't doubt that the dominating philosophy I have mentioned will persist and that all our policies will be directed to two things: first, that we want to be at the forefront of every major field of scientific advance, and second, that the whole nation wants to participate in the process.

For the present the first goal has been achieved. But this is a competitive world, and I have no doubt that to maintain the excellence of our science we will continue to back the best brains wherever we find them. We will surely continue, as the President said at Brown University, to support those institutions which provide the superior training for the teachers and researchers who go from them to the aspiring institutions and who will provide the core around which the new institutions will grow.

We are less satisfied with our progress toward the second objective, which is to provide the best possible advanced education in enough institutions so that able American children from all backgrounds and from all parts of the country have an opportunity to participate in the best that science and the modern world have to offer. It is clear, therefore, that there will be a major emphasis on improving education as well as science. It was with this in mind that the President sent a memorandum to the heads of all departments and agencies in the government, most of which spend their funds for the primary purpose of producing scientific advance in those areas of science of primary concern in achieving their goals. The memorandum, "Strengthening Academic Capability for Science throughout the Nation," is an instruction that in the course of spending money for those purposes, all the agencies should, recognizing the impact that their expenditures have on the higher educational system for the country, also keep in mind this educational impact and so adjust their practices as to do the most possible for higher education. Specifically, I would like to quote from some of the President's instructions.

Our policies and attitudes in regard to science cannot satisfactorily be related solely to achievement of goals and ends we set for our research. Our vision in this regard is limited at best. We must, I believe, devote ourselves purposefully to developing and diffusing—throughout the nation—a strong and solid scientific capability, especially in our many centers of advanced education.

And later,

To the fullest extent compatible with their primary interests in specific fields of science, their basic statutes, and their needs for research results of high quality, all Federal agencies should act so as to:

a) Encourage the maintenance of outstanding quality in science and science education in those universities where it exists:

b) Provide research funds to academic institutions under conditions affording them the opportunity to improve and extend their programs for research and science education and to develop the potentialities for high quality research of groups and individuals, including capable younger faculty members;

c) Contribute to the improvement of potentially strong universities through measures such as:

—Giving consideration, where research capability of comparable quality exists, to awarding grants and contracts to institutions not now heavily engaged in Federal research programs;

—Assisting such institutions or parts of institutions in strengthening themselves while performing research relevant to agency missions, by such means as establishing university-administered programs in specialized areas relevant to the missions of the agencies.

The President has asked, therefore, that the 1.3 billion dollars we spend in universities directly and the half billion dollars a year we spend on research institutes attached to universities be used to improve higher education and the higher educational system of the country in the course of procuring research. You may well ask what practical impact this is likely to have on the universities. This question is not easy to answer definitely yet. A committee of the Federal Council for Science and Technology, under the chairmanship of Leland Haworth, is reviewing the practices of the various agencies and will make recommendations for steps to implement the President's instructions.

Still, certain things seem clear. In the first place, we do not intend to abandon either the merit system, our general concern for the quality of what is undertaken, or our use of the project system as a base for supporting scientific research. Nevertheless, it seems very likely that more funds will be expended in ways which increase the flexibility of administration, at least in those institutions where capable scientific administration has been developed. I have in mind such programs as the sustaining university grants of the National Aeronautics and Space Administration, the variety of training grants, area grants, and programmatic grants of the NIH, and the institutional grants of the NSF. Some other mechanisms for flexibility may be developed, including perhaps transfers of funds between projects within reasonable limits, or the use of project funds to support central services, for example. Still another effect will be a more conscious effort to encourage developing institutions, developing departments within institutions, or strong research groups in institutions not yet strong, to grow in areas of the country which are not so well served by advanced educational institutions as others. Of course, the planning and the initiative for development must come from the universities themselves. Federal money cannot create or buy excellence. It can back excellence with funds and increasingly it can assist institutions with sound plans on the way to excellence. Certainly the quality of the educational institutions in the Research Triangle area of North Carolina was a large factor in persuading the government to establish the Environmental Health Center there.

More and more often, too, the directions of university development will be affected by the location of research facilities and equipment. Since one of the characteristics of many areas in modern scientific advance is the necessity to provide bigger and more expensive special equipment if work is to be undertaken at all, it becomes increasingly impossible to provide such equipment at all the universities of the country. It seems likely that the day when every university can aspire to be at the forefront of all the fields of modern science is nearly at an end. I think, therefore, we will see the development of a variety of cooperative arrangements to cope with this problem. In high-energy physics this problem has been attacked through the concept of user groups by which national facilities are available to groups all over the country who carry out the analysis of records and their interpretation at their home sites but either perform experiments at the national centers or receive the raw material from experiments there for work. More generally, I suspect that additional associations of universities which are geographically proximate will be formed in which each can contribute to the strength of the other by maintaining special facilities which are available to all of the associating universities. Several such groups are now being formed, and the process is certainly a good one.

One problem to which I must make reference, but for which I cannot make predictions, is that everywhere there is concern with the plight of the small college and its role in the future. The problems are clear: the small colleges have difficulties recruiting faculties in the sciences; they have difficulties in providing the kind of facilities and the awareness of current change in science which is important if they are to continue to play the strong role they have in the past. There are some indications that their role is declining. I am sure that increased federal attention will be placed in this area through programs in various agencies, but I cannot now predict their form.

I have mentioned earlier the trend toward more general-purpose support. Examples of such programs in science might include the traineeship programs of the NIH and NSF, the various facilities programs and equipment programs, the general research support grants of the NIH for medical schools, and the institutional grants of the NSF. What is new is the assistance being provided to universities in all fields of study by the Office of Education as a result of several recent acts. These include facilities, fellowships, scholarships, loan funds, assistance for libraries, and so on. It seems very likely to me that there will be more.

In closing I want to return to my original theme. The close association of the federal government and the universities in performing many public functions is here to stay. The successful experience we have had so far gives me the greatest confidence that we will continue to develop that association in a way which responds to the needs of all parts of our country and all segments of our population, which places greater responsibility on the university as an institution to plot its course and determine its destiny, and which preserves the freedom of the individual scientist to pursue understanding according to his own insights.

Biological Feedback Control at the Molecular Level

Interaction between metabolite-modulated enzymes seems to be a major factor in metabolic regulation.

Daniel E. Atkinson

A living cell consists in large part of a concentrated mixture of hundreds of different enzymes, each a highly effective catalyst for one or more chemical reactions involving other components of the cell. The paradox of intense and highly diverse chemical activity on the one hand and strongly poised chemical stability (biological homeostasis) on the other is one of

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the most challenging problems of biology.

The first clear demonstrations of metabolic regulation at the molecular level by mechanisms other than mass action came in connection with biosynthetic sequences. This area has been adequately reviewed (1). In a short paper that already may be considered a classic, Umbarger (2) supplied the conceptual foundation for the operation of regulatory controls through specific interaction of the synthetic pro-

duct with an enzyme early in its synthesis and also furnished an experimental demonstration of such control by showing that in extracts of disrupted cells, isoleucine strongly and specifically inhibits threonine dehydrase, the first enzyme unique to its synthesis. He pointed out the apparent advantages for the organism of such regulation at the molecular level and suggested a comparison with technological negative feedback-control devices. Another example of the same type of regulation was recognized at about the same time by Yates and Pardee (3), who discovered product feedback control in the biosynthesis of pyrimidines.

Enzyme-Effector Interaction

Although they are often used, in this article and elsewhere, for reasons of convenience, the terms "stimulation" and "inhibition" do not adequately describe the action of the regulatory metabolite (termed effector, modifier, or modulator) on the enzyme. The effector typically modifies the affinity of the enzyme for its substrates and frequently also for other reaction components. The terms positive and nega-

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