

National Laboratories for Biology?

They could develop new research tools that are now conceivable but too costly for existing institutions.

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In the early stages of a science the invention of tools and techniques occurs rather haphazardly, depending mainly upon the ingenuity of individual investigators. But as a field grows up, the work of invention and design and development begins to be anticipated and can be assigned to a development team or contractor, or even to several of them if it is very important not to leave any avenue unexplored.

In the physical sciences, this stage of organized invention was reached in the work of the Office of Scientific Research and Development and in work on atomic energy, in World War II. Today, physics has dozens of governmental and contractor facilities—Los Alamos, the Advanced Research Projects Agency, General Electric, university development laboratories, and the like—where any idea for a new technical device or advance can be assigned to some group for feasibility studies or development work on as large a scale as necessary. This is how high-energy accelerators are brought into being, and also thermonuclear machines, space devices, and so on, sometimes down to the smallest or most academic research improvements. Established facilities for research and development on tools and methods have become an absolute necessity for maintaining leadership in these fields.

Biological research has now reached the stage where it may also be in serious need of similar facilities. At present we have no comparable arrangements or organizations for systematically exploring and developing new devices and

methods for basic biological research, and probably this is already beginning to limit our rate of progress in this field. There are electronics laboratories that could develop some electronics devices with biological applications, but what I have in mind is the need for organizations equipped to work on more basic biologically oriented research tools of several other kinds that are already needed and wanted by research biologists. As several workers have pointed out, development of a number of such new tools may now be possible, based on recent advances in physics and chemistry—tools that could make a difference by orders of magnitude in the ease with which cells and organisms can be studied and that might open up whole new biological areas of study, but that would require more technical development work than any biology laboratory is presently prepared to undertake.

Possible New Tools

At a recent Atomic Energy Commission conference on bioenergetics and radiation biology, for example, the participants listed a dozen possible new spectroscopic tools and methods at the subcellular level that need development (1). In another direction, Feynman has discussed the possibility of developing much smaller micromanipulators, and he has emphasized particularly our failure to explore alternative possibilities in focusing designs for electron-microscope lenses that might conceivably give a resolution of 1 or 2 angstroms and so permit "direct read-out" of chemical structures and sequences at the atomic level (2). Müller's field-ion

microscope already offers a resolution approaching this, but the problem of mounting an organic molecule or biological sample in this instrument has not yet been solved (3). For better chemical analysis of single cells, important results could follow from systematic development work on new vital stains and new electron-microscope "stains" (work stemming, perhaps, from recent advances in molecular complexes); on new methods of using chemostats for obtaining cell synchrony; on methods and materials for microchromatography and microelectrophoresis; and on methods and materials for higher-resolution autoradiography (4).

Or consider quite a different area, that of marine biology. Think what a tremendous growth there could be in our understanding of the rich biology of the oceans if teams of biologists and chemists, physicists and engineers, could be put systematically to work to develop (i) new physical and chemical devices for locating, identifying, and following aquatic creatures or groups; (ii) new chemical, electrical, or sonic methods of attracting or repelling them; (iii) new methods of labeling, selecting, and breeding; (iv) new methods of studying marine diseases and their cure; (v) new oceanic or estuarine fertilizers or suppressors, analogous to those used in terrestrial range control, insect control, and plant control; (vi) new devices for obtaining or analyzing oceanic data at a much higher rate than is now possible; or (vii) better substitutes for sea water, in which marine creatures could be bred and kept alive indefinitely for study at inland laboratories. Probably research men in almost every biological specialty could make similar lists of new tools and methods that they wish they had, but that they do not have the time or technical know-how to develop for themselves.

The point here is not that all such imaginable inventions are actually practicable but that almost certainly a few of them are, and that even a single successful new technical tool can amply repay all the development costs and can change the face of biology—as we all know from such examples as the electron microscope, chromatography, the use of radioactive tracers, and the use of electronic methods in sensory studies. As one well-known electron-microscopist has said: "If we could now develop a microscope with a resolution of under 2 angstroms, it would be like

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a 'sputnik' in its effects on the whole field of molecular biology, molecular genetics and protein chemistry!"

The Microscope Problem

But are we about to develop such a microscope? No.

As of this writing, some 2 years after Feynman's suggestion, there does not seem to be a single contract or project in this country aimed at developing strong-field or other new focusing designs for higher-resolution electron-microscope lenses. By contrast, there are groups in at least six major university and government laboratories working on focusing designs for high-energy particle accelerators.

The reason for the difference is clear. The microscope problem is a middle-sized engineering-design problem, comparable indeed to designing a new synchrotron, perhaps requiring several parallel approaches, with auxiliary studies on sample preparation and mounting and stabilization, including work at liquid-helium temperatures. A development group would have to include biological electron-microscopists, field-ion microscopists, electronics and field-design physicists, and engineers and computers. To explore all the possibilities and to turn the results into a working research instrument for the biologist might take 3 to 5 years of work at a well-equipped installation, with a dozen or more senior scientists working on various aspects and with costs perhaps approaching a million dollars a year. This level of effort may sometimes be found in drug research and in hospital research on new medical devices, but today there is probably no biological research institution that would have a technical development staff remotely capable of doing this kind of electronics-engineering job. Even if there were such an institution, probably no biology department—and probably no electron-microscope manufacturer, either—would be prepared to turn aside from other work to put into such an expensive development gamble, for the service of a small number of laboratories, the amount of effort needed to assure success.

Yet this is the kind of project that is undertaken easily and frequently by physical science groups. And from a national point of view, the attempt to develop a "direct read-out" microscope

would be a project of low cost and of very high value—as compared, say, to many of our smaller development projects in atomic energy or space technology—which could easily be supported if biology had some institution ready to take the initiative and capable of seeing it through.

The microscope problem is a somewhat dramatic example, but quite similar organizational difficulties stand in the way of exploring many of the other possibilities mentioned. Just to screen several hundred molecular complexes in order to find the most discriminating histochemical or electron-microscope stains for different cell constituents might require 2 or 3 years of work by a group of biologists, histochemists, electron-microscopists, quantum chemists, and chemical physicists. And to develop some of the new tools suggested for marine biology would require a very large laboratory staffed by physicists, chemists, biochemists, botanists, zoologists, electronics and high-pressure experts, designers, and engineers, with access to all kinds of small and large underwater equipment and with extensive and close cooperation from the Navy.

New Organizational Arrangements

These are jobs well beyond the capability of the basement inventor. They are too complex and important to be left to the dedicated amateur who has one or two ingenious ideas and who wants to patent something. And they are too large and uncertain for any one graduate student or research man or department to risk alone. I therefore believe that biologists will simply not be able to solve these problems successfully unless they begin to form new organizational arrangements that will bring together inventive minds with first-rate training and experience in several different advanced techniques, with professional development teams big enough and permanent enough and well-enough equipped and financed to have a maximum chance of coming up with the most useful tools possible.

Such arrangements can and should take many forms, of course. The commercial and hospital and biomedical engineering groups that work on the development of new drugs and new medical devices might enlarge their activities to include the development

of new aids for basic research. Many academic biology departments may also build up engineering-development groups, just as physics departments build up cyclotron groups, wherever there is a research man willing to devote himself to directing the work on an invention he especially believes in.

But this is probably not the way to get the most thorough and balanced exploration of all the new possibilities or to get the most rapid development of new tools for biology as a whole. Some more comprehensive organization is also needed, and it may be that the only way to achieve it will be to take a leaf from the physical scientists' book and establish a permanent national biological research and development center, a kind of small-scale Los Alamos for biology—or several of them! Each one might be intimately connected with some of the large university biology departments, but it would need a staff especially picked, and laboratories and shops and facilities especially equipped, for research and development on all kinds of new biological instruments and methods.

Such biological research and development centers might be financed and operated somewhat like the AEC laboratories, perhaps being run by universities under contract with a government agency. The directors would have to be imaginative men with a good deal of experience in real biological research, so that the projects studied would lead to the development of important and usable research tools and would not degenerate into mere technical demonstrations or electronics gadgeteering. The permanent staffs would need to be augmented by exchange staffs and visitors from other biological institutions, so that continuous contact with front-line research problems elsewhere would be guaranteed.

Obviously such centers would be able to afford much better facilities—better machine shops and electronics shops, better high-pressure and low-temperature equipment, better analytical services and design services and computers and libraries—than any single development project could support. They would offer interesting career opportunities, since workers in a field of specialization would be needed on various projects in succession. New ideas and devices from one project could be carried over and combined in others, producing a series of rapid advances.

Such development centers would certainly attract invention-minded biologists as well as many of the physicists, chemists, and engineers who are now turning to the field of biology. They could also be of direct service to research biologists, since their elaborate physical and technical equipment might be made available part of the time for fundamental research studies requiring unusual manipulators or microscopes or other equipment too special or experimental to be readily obtainable elsewhere. Our present research institutions—such as the Institutes of Health, the marine biological and oceanographic laboratories, and the medical and academic biology laboratories—might, therefore, find it extremely valuable to be able to carry out some of their own more technically demanding and ex-

pensive research projects at such centers.

But the main point I wish to emphasize here is that, in properly equipped biological development centers of this kind, many projects for the development of new biological tools could be explored simultaneously, expeditiously, and competently, whereas such exploration would be difficult or laborious with our present organizational arrangements. And what is perhaps more important, in these centers would be development staffs and leaders who would have the funds, the equipment, the interest, and the definite mission to take the lead in generating other technical ideas and in making an active and continuous search for new methods of biological study.

To create such national research and

development centers for biology, to finance and find sites for them, and to staff and equip them properly will require planning and action by biologists, government officials, and others who see what a vital role they can play in our future biological and medical progress. I believe this progress cannot be made at the maximum possible rate unless we begin now to take such steps.

References

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News and Comment

Federal Pay Reform: Congress Shows Little Enthusiasm for Bill Designed To Raise Specialists' Salaries

The Administration bill that includes higher salaries for government scientists and engineers is becalmed in the Senate and the House.

Both chambers face a massive backlog of legislation before they go off to the autumn political campaign, but neither at present displays any sense of urgency. (This is par for the course, and has been likened by one Senate aide to the student who leaves his term papers to the last week.) Primary campaigns have caused a good number of members to be away from their congressional duties; rivalry and friction between the houses have delayed action on some measures, and the Administration has chosen to concentrate its prodding in areas closer to the New Frontier's major legislative goals: tariff and tax reform and medical care for

the aged. These bills unquestionably are aimed at more grievous problems than those assigned lesser priority, but the attention they merit and receive tends to take the heat off other issues, including the pay bill.

The order of priority reflects the view from the administration's upper reaches, where all problems come home to roost. But down below, at the levels specifically concerned with relations between science and technology and the government, there is considerable apprehension about the fate of the pay bill. It appears likely that Congress will deliver some pay increase for federal employees, but the government's science advisers and administrators are concerned that it will be just a pay increase and not the overhaul of pay scales proposed in the Administration bill. The difference is a crucial one, for the Administration is not simply seeking fatter pay checks for federal employees; it wants, basi-

cally, to stretch out the pay scale—to widen the difference between the bottom and the top—and thus toe a difficult line between its anti-inflationary policies and the realities of the manpower marketplace.

At the lower end, the present federal pay scales are fairly competitive with business and industry, but at the upper levels—where scientists and engineers are placed—the government finds itself at an extreme disadvantage. It has periodically raised the salaries of its employees, but the raises have been weighted in favor of the lower-paid workers. As a result, the ratio of the highest to the lowest Civil Service salary dropped from 8.8-to-1 in 1939 to the present 5.8-to-1. Precise comparisons between government and non-government remuneration are difficult to make, but the consensus of several studies is that the government is not able to compete with the going private scales for specialized, experienced personnel.

In 1960, the Department of Labor surveyed 1606 business firms in 60 metropolitan areas to compare federal and private pay scales for attorneys, accountants, personnel managers, engineers, and scientists. It concluded that a federal employee in General Service grade 15, with a salary of \$14,705, would, on the average, receive \$20,175 in private business. A Civil Service Commission survey of 21 national corporations went higher on the executive scale and examined salaries of