Biophysical Journal Volume 65 July 1993 2-4

Reflection

The Changing Faces of Research

Arthur Kowalsky
2745 29th Street NW, Apt. 522, Washington DC 20008 USA

Dr. Arthur Kowalsky, Director of the Biophysics Program at the National Science Foundation from 1978 through 1992, had a major impact on the development of modern biophysics and on the careers of many biophysicists. In recognition of this, he was honored by the Distinguished Service Award of the Biophysical Society at its Annual Meeting on February 15, 1993. This paper is the text of his award address.

When I was asked to speak at this session, it seemed that I could have little of interest to say. It has been a number of years since I have been engaged in research, and in the past 10–15 years I have been occupied with the more mundane activities of supervision and administration. All I might contribute would be more or less anecdotal information which might amuse, and possibly inform, this audience. But on thinking it over, it did appear that, having participated in both biophysical research and then in the mechanisms of support of such research, some insights might have been developed through the years which would be worth discussing with you.

I would like to describe not only the various aspects of "The Changing Faces of Research," but also the imperatives for those changes. I also discuss some associated factors: our changing technology and its effects, our general support for research and the difficulties we are experiencing, and the logical (or to some, illogical) directions we might expect to find U.S. research taking. I make no claim for authoritativeness; I merely present my views as colored by my experience.

Although most of us dislike reminiscences that start "When I was a child . . ." or "When I was in research . . .," I think we must remember that there was a time when the research techniques we now take for granted were either in their infancy or actually nonexistent. Let me start with an area of biophysics with which I am most familiar.

Forty years ago NMR spectrometers operated, as archaic as it seems, in the CW mode, at 30 and 40 MHz. FT NMR was unknown, a protein spectrum was strictly one-dimensional, and the use of stable isotopes to clarify or edit a spectrum was virtually unknown. At that time it was possible for an investigator to formulate a problem and carry out the work by himself or herself on his or her own instrument. Today, with the advent of newer and better superconducting magnets, the development of sophisticated and complicated pulse techniques, and the use of faster and more efficient computation, we have 2D and 3D FT spectra at 500 and 600 MHz and we can go even higher. Such studies as 3D NMR of macromolecular structure and dynamics require not only technology and expertise and complex instrumentation for the NMR spectroscopy. They also demand expertise in protein engineering (to obtain adequate amounts of material and to incorporate stable isotopes); practical knowledge of various computer-assisted procedures for calculations and for simulations of structures and dynamics; and, of course, access to adequate computer facilities. Small-scale work by an individual investigator or a very small group is difficult to do when the infrastructure demands are so high.

The situation is similar in a number of other biophysical areas. For example, x-ray diffraction requires protein engineering, extensive computer facilities, allied NMR studies, or the use of synchrotron radiation; while EXAFS and XANES demand synchrotron radiation and require instrumentation far beyond the resources of one, two or even three individual investigators. Along with these comes the horrendous cost of carrying out the work: stipends and tuition for students, salaries for technicians and post-doctoral fellows, the purchase and maintenance of highly sophisticated and complex instrumentation, and the necessity for the home institution to recoup its overhead expenses.

More and more we are finding today that, although our interests and questions can be neatly defined—"How does the proton get across the purple membrane?"; "What gives a spider's thread its extraordinary tensile strength when it is only a peptide chain?"; "How does a DNA molecule package itself inside a virus head and then extrude itself in functional form?"—the solution of these apparently simple questions requires the collaboration of many disparate disciplines and techniques.

From this it is apparent that the individual investigator is an endangered species. To solve the scientific problems we have set for ourselves, e.g., problems of protein structure, dynamics, and function, the requirement seems to be either for a polymath with extensive contacts and facilities, or for a scientist with a large number of collaborators, each proficient in a particular, perhaps narrow discipline. Unfortunately, to many in positions of authority today, the wave of the future is group-directed research on a problem selected by authority, or programmatic attack on a problem set up, orchestrated and overseen by a grand master.

Yet all of us feel, all of us know, that simply orchestrating a multifaceted attack on a problem, an approach which, it must be admitted, has achieved some success in the past (mainly with engineering and technological problems) is not the answer. Appointing a czar of science or a Grand Master of a problem will not solve anything. We all recognize that the truly great advances and discoveries in science have arisen from unique individuals capable of making imaginative and singular leaps and persisting in their efforts against difficult odds and general disbelief.

Parenthetically, one might comment that the famous "two cultures" are not really so alien to each other, if one recognizes that the great constructs of science initially required a willing suspension of disbelief. Examples of the isolated oddball investigator are numerous. We remember the "eccentric" in England trying, of all things, to determine a crystal structure of hemoglobin when everyone knew proteins are much too complicated. And I can also remember chuckling over that cute trick whereby one could visualize, through a proton NMR spectrum, a two-dimensional picture of a tube of benzene held concentric in a tube of water. I am not very proud of my lack of imagination there. Such rare creative individuals must be recognized and supported.

Such startling innovations and advances, even though they come from unique and original minds, are difficult to imagine arising in a scientific vacuum. It is not enough to identify these original minds and support them. They need a nurturing ambiance in which to work, an atmosphere of scientific give and take, challenge, and response. Like any healthy, competitive society, the scientific community, to be viable and productive, needs its own supporting middle class—a praiseworthy, not pejorative, term. The scientific community is really an intellectual ecosystem; and we must all be a part of that interactive environment, whether as giants or merely dedicated workers, if science is to flourish and progress.

One must be careful here. This does not mean indiscriminate support for anyone who can interpret a periodic table or carry out a gel electrophoresis experiment. For science, in another analogy, is a competitive economy of ideas and results; and we must discern and weigh, judge and support those who lay the groundwork for others to build on. The rewards, of course, are not monetary (except for financial support of the research), but rather the immense intellectual gratification on the completion of a piece of work in which the component parts join harmoniously. It is truly, as Wallace Stevens wrote, "the finding of a satisfaction." I sometimes think that scientists are the true masochists of this world, not happy unless they are tormenting and teasing themselves with an as yet unsolved problem. And when that problem is solved, abandoning it and going on to find another problem to tease themselves with.

To carry the analogy of science to society a little further, we should remember, there is a Gresham's Law operating in science as well as in economics. Just as bad money drives out good money, bad science drives out good science. Witness the Lysenko affair in Russia some 30 years ago. And think how much money and effort is wasted on following reports of sloppily designed experiments and fuzzily thought-through data. Despite the complaints against it, our peer review system, imperfect as it is, is the only safeguard for good science. We cannot trust as infallible one man's opinion as to what constitutes a good problem and a reasonable approach to that problem.

So we ask ourselves these questions:

1. What is the future of the individual investigator today? Indeed, does he or she have a future?
2. How can research, either individual or collaborative and integrated, be supported?
3. How can this support be justified and/or correlated with national needs?

Of course, there are no hard and fast answers. I am only giving you my reflections on these difficult points. The second question, for example, is inextricably bound up with the nation's financial difficulties and involves factors far beyond this group's capabilities and expertise. And the question of national needs is a very serious one, for, after all, we are spending the public's money. Scientists do not have an inalienable right to the public's funds simply for their own pleasure. The return on such expenditures must be eventually tangible even if not predictable. We must factor in economic considerations and definitions of national needs.

I might note that the major governmental agencies are undergoing a serious self-examination with respect to these questions. A commission was recently convened to consider: What should be the function of the National Science Foundation? And the DOE is wrestling with the problem: What should be done with the National Laboratories?

In the past, the government's efforts to support research split in two natural directions. There were the mission-oriented agencies, as exemplified by the NIH, DOE, USDA; and the nonmission-oriented agencies of which the major example is the NSF. The function of the NSF has been the support of basic research with no major consideration of its utilitarian or technological value. The justification for such an approach is, of course, what might be called the serendipitous fall-out. There have been notable successes here. It has also to be noted that it is to the credit and vision of the mission-oriented agencies that they have recognized that a solid underpinning of basic research is essential for the ultimate solution of their major problems. They have also carried a large share of support of basic research.

But what makes the situation so confusing and complex today is the interleaving and overlapping of the various scientific disciplines. We recognize that the techniques and development of one discipline can be utilized in other quite distinct areas and may even be required for further progress in those areas. We recognize that the structural biologist needs the x-ray crystallographer, the cell biologist needs the spectroscopist and the electron microscopist and the fluorescence microscopist, and the neuroscientist needs the computer expert; and we know that in a viable and steadily evolving science, new disciplines continually arise from a synthesis of older, classical ones.

Attempts to adjust to these new and disorienting conditions have been made and are continuing. In the NSF, for example, interdisciplinary programs have been set up, and science centers based on a general theme have been established. But these require financial support, which must come out of some budget. This brings up the major confrontation of individual support versus major group or program support.

I feel that in this confrontation between small science and big science there is a case to be made for both, but not with equal weight. I feel the individual investigator, the small scientist, must still be given full and unequivocal support if our basic science effort is to continue to be healthy and productive.

There is, first of all, great danger in the massively coordinated project, danger of concentration of power and funds in the hands of one or two or in a small, self-perpetuating committee.

Beyond this, I feel that some massively coordinated projects are necessary but many are not. To be sure, there are cases where they are absolutely essential, e.g., the use of synchrotron radiation. But this is an extreme. One can make a strong and reasonable argument for a center of, say, primate intelligence. But I am not so sure that, if left to their own devices and given the same pool of funds, individual investigators might not establish their own collaborations and contacts and accomplish as much or more. One can also envision a government agency such as the NSF acting as a catalyst for this; but then one has the ever-present danger of the government setting itself up as arbiter of what is good and what is not. Suppose one set oneself the problem of developing a magnetic resonance imaging microscope, or carrying out time-resolved EXAFS studies, or studying magnetic circular dichroism in the x-ray region. Given the instrumentation and development required, a concerted, directed effort might be justified but only with careful attention to the needs and mechanisms for support of an individual investigator.

There is a delicate balance to be achieved here—involving national needs, funds, effort, manpower, and perceptions of fundamental scientific questions. And in a zero-sum budget game, which is essentially what we are playing these days, if some areas or programs are stressed, it will be at the expense of others. But in all this, I believe the individual must still play a central role; and every effort must be made to insure that he or she is not subordinated to a so-called greater need.

In this tug-of-war between what might almost be called "corporate science" and the individual investigator, substantial efforts must be made by the members of the scientific community to make themselves heard and their needs known: by the Congress, the National Science Board, and the Directors of the NSF. The voices must be not only those of individual investigators, but also of the professional societies which in the past, and in the biological sciences especially, have not been very effective.

One last thought. I have mentioned national needs but have not said anything specific about them. They cannot be disregarded. But it does seem to me that, even with the blurring of the lines between basic science and technology, there are still vast areas where the distinction is clear. It also seems to me that a most reasonable approach to the technological problems facing our society (problems solvable in principle by science or engineering) is to retain the distinction between mission-oriented and nonmission-oriented agencies. Make sure the nonmission-oriented agency is given full support to realize its purpose, recognizing that the best, most productive research is not product-directed. And include a third component of our total research effort: the national laboratories. Define their function as the solution of the major contemporary technological problems, defined not by any individual investigator, but jointly by industry, society, and the scientific community. Such a triumvirate could well be successful beyond our hopes.