HOW TARGETED SHOULD RESEARCH AND HIGHER EDUCATION BE?

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Abstract—The education and research system in the biomedical sciences is tremendously vital. But the scientific community must exert more leadership if this vitality is to continue, for both science education and research are prone to a common villain: inertia. For example, in the education arena, why do medical schools require two semesters of organic chemistry but no cell biology, when the center of biomedical research has shifted to cell biology? And why do so many graduate schools continue to send a strong message to their science students that there is only one really successful career path—the one leading to academia—when most of our PhD students cannot expect to become professors? Inertia in research can be seen in the trend for cell biologists to train researchers just like themselves, which means that the many opportunities to use new cell biological techniques to address important problems in tissue biology are likely to be missed. A solution to such problems is to design funding mechanisms that promote more adventuresome research. As a bottom line, our research system must support the independence of our best young scientists and encourage them to take the risks inherent in highly creative endeavors. *Acad. Med.* 69(1994):180–184.

I come from a background of academic research and teaching: ten years at Princeton followed by 17 years at the University of California, San Francisco (UCSF). I am fortunate in having had support for my research from R01-type grants for this entire time, and I am a strong believer in the value of investigator-initiated, peer-reviewed research funding mechanisms. I have also spent 27 years teaching courses in chemistry and biology. During much of this time, I played a major role on departmental committees that designed—and each year redesigned—the programs and curricula leading to undergraduate and graduate degrees. Obviously, I believe in the creativity and spirit that emanate from such a situation, which allows the faculty in each department to custom-design the experiences that, added together, will constitute the education of their students.

But my aim is not simply to praise the present systems of research and higher education in the United States. I would be wasting your time if this were my theme. Instead, I focus on what is less than perfect in both these systems, to encourage those of us involved in research and higher education to think about what we can do as a community to avoid some of the pitfalls of the past. I start by discussing our system of higher education in the sciences, and then proceed to the system of biomedical and biological research as I know it. With such a broad sweep, it is impossible for me to do more than to touch very lightly on a few major points, and I apologize in advance for the superficial treatment that I give to my topics.

My major points are that (1) Both of these systems—education and research—seem to need much more leadership and guidance than they are presently receiving, and (2) Most of this guidance—or to use a more pejorative word, this targeting—can be much more effectively designed by the scientific and biomedical community itself than by government.

A COMMON VILLAIN

A common villain accounts for most of the imperfections I address here. That villain is inherent to all human systems: *inertia.* I first learned this word in an early science class, when we were taught that a body will continue moving in the same direction and at the same speed if left unperturbed. Not until about 30 years later did I come to realize that there is much more inertia in human systems than there is in any moving object. A moving object, no matter how large, will adjust its trajectory appropriately in response to each small perturbation. Human systems, in contrast, almost always contain a restoring force that allows them to respond only very transiently to any attempt to change them. Thus, over the long run, our systems can remain absolutely unchanged despite even huge perturbations. One obvious example is the rapid retreat of our nation's precollege science curriculum to boring and mindless textbooks, once the exciting post-Sputnik reforms of the 1960s ran out of federal funding. Another example, more central to academic medicine, is the failure of past efforts to increase the proportion of primary care physicians being produced by our medical schools.

It is important to analyze the reasons that make human systems so difficult to change. Clearly, there are many causes. But I want to mention three.

First, most humans seem to be much more comfortable with the known, no matter how imperfect, than with unknown territory. This makes them automatically fearful of anything that perturbs the present system. We are seeing this in spades in the nation's present response to President Clinton's health care plans. It has been said that if humans had been present at the moment of Creation, when Order was created out of Chaos, a clear majority would have voted for Chaos!

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Second, there is a fundamental law in physics and chemistry that also applies to human society: If left alone, a system will decay toward its state of lowest energy. It is this law, I believe, that best explains our country's return in the 1970s to boring fill-in-the-blanks, high school science textbooks — once the outside perturbations of the post-Sputnik reformers were removed.

Third, much of the resistance of human systems to change stems from the existence of positive feedback loops. I define *positive feedback* as a system whose product induces the production of more of itself. This principle presumably helps to explain why it has been so difficult to produce more primary care physicians. Put most simply, if most of the mentors and teachers whom our students are exposed to in our medical schools are specialists, the students will tend to absorb the values that surround them and want to become specialists too.

INERTIA IN SCIENCE EDUCATION

This analysis leads naturally into a discussion of the inertia in college and graduate school education in the sciences. Many of you may be asking yourselves: what in the world is he talking about? As I did 30 years ago, you may think of universities as one of the few refuges for rational thought in a world full of irrationality — as places where an irrational situation that originates from inertia could not survive for more than a millisecond. For those of you who have still managed to retain such a wonderful state of innocence, consider the following question: Why do medical schools require two semesters of organic chemistry but no cell biology? This is a question that I have asked many people. The answer, I believe, stems from a period, about 50 years ago, when organic chemistry lay at the heart of biomedical research, which centered on the metabolic interconversions of small molecules — that is, the unraveling of metabolic pathways. Fifty years later, not only has the center of biomedical research shifted to cell biology, but the field of organic chemistry has changed profoundly — so that the central thrust of this discipline is now largely irrelevant to medicine. One semester of organic chemistry is certainly enough. Inertia is the only possible explanation for the continuation of a course requirement for two semesters that found my son, a few years ago, memorizing the names and pathways of hundreds of arcane organometallic reactions as part of his required premedical curriculum. I may be biased, but I could not help but think at the time how wasteful it was for us to be forcing untold thousands of young Americans like him through this initiation rite, when for the same effort they could be gaining an understanding of cellular structure and chemistry that would both excite them about science and given them a real foundation for their future careers in medicine.

The problem is not confined to undergraduate education. Many, if not most, of our graduate schools have a problem that is analogous to the one I mentioned earlier for medical schools: we are producing too many young scientists who want to be only like ourselves. Figure 1 presents the most extreme view of this problem. We are allowing our students who do not become professors to think that they have failed. Again we have the famous positive feedback loop in operation. Should we allow our PhD-program students to believe that, in our opinion, the only real success is in becoming exactly like us? Whether consciously or unconsciously, we tend to give a strong message to our graduate students that there is only one really successful career path — the one leading to an academic career.

What is the answer here? I was struck by a recent chance juxtaposition of articles in *Scientist*: the headline for one was "Job Market for Researchers Will Remain Sluggish in Both Academia and Industry, Observers Predict," while the other headline read "NSF Study Finds Many Teachers Unprepared for Instructing Children in the Sciences." We seem to have an excess of talented, scientifically trained people in some fields — while at the same time we have an enormous need for people with similar talents as teachers in K–12 education. If the United States is to have any chance of becoming outstanding in science and math education by the year 2000, as is said to be our national goal, the only hope is to induce an enormous movement of young people away from academic careers into teaching careers.

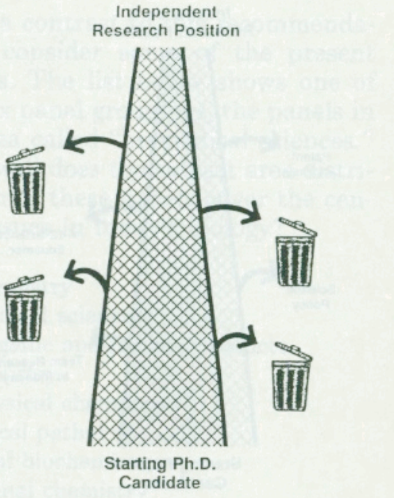

Figure 1. **Representation of a leaky educational pipeline for students with PhD degrees. This wasteful process is encouraged when graduate schools allow students to think they have failed if they do not become professors or independent researchers.**

We have to wake up to the fact that our universities are on the verge of a crisis. We can choose to educate fewer PhD students. But a much better outcome would be for us to increase the options that we present to these outstanding young people during graduate school, both by providing them with an intimate exposure to outstanding individuals in other scientifically-based careers, and — just as important — by showing our students that we ourselves honestly value these other career options. Our aim should be the creation of a very different type of pipeline than the one mentioned previously — that illustrated in Figure 2.

This pipeline is not going to be generated without a targeted effort. First, professors will have to make a con-

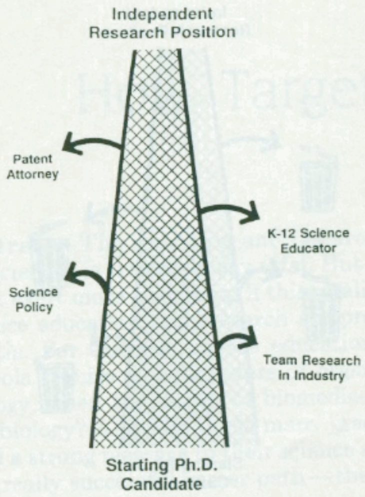

Figure 2. **Representation of a productive pipeline for PhD candidates. This process will be facilitated if graduate schools make a concerted effort to acquaint students with a variety of options for scientific careers, making it clear that these careers are valued by the faculty.**

scious attempt to broaden their own outlooks by getting to know and respect individuals in relevant careers. To give one example, my daughter was a biochemistry major at Berkeley. When she decided in her junior year to become a high school science teacher, she could find no one on that large campus to advise her on such a career path. Moreover, the professors in the department (many of them my friends) made it clear that they were disappointed and that none of them were prepared to help someone who wanted to "desert science." I was once guilty of the same type of ignorance myself, since I was a professor at UCSF for ten years before I got to know a single science teacher from the San Francisco public schools. In later years, I redeemed myself by helping to found our Science and Health Education Partnership. This partnership was originally designed to provide volunteer help to the San Francisco public schools. But just as importantly, it has permeated the university with large numbers of outstanding local science teachers whom we now view as our colleagues. As one healthy but unintended result, this exposure to teachers has served to validate K–12 teaching as a career for our postdocs and students, and a number of our outstanding young scientists have decided to enter this field.

INERTIA IN RESEARCH

So much for science education. What about research? Why isn't it enough to merely sit back and let investigator-initiated research take its natural course? What are the important sources of inertia that need attention in our present, highly successful research system?

To begin, it is very clear to me that the natural world is much too subtle and complicated for top-down management of most scientific investigations. Too much central planning is deadly in biological research for the same reason that the world seems to have given up on planned economies. In a "free market" approach to government-supported science, individual scientists are able to aggressively seek out problems in need of solutions and then offer their services in a marketplace of ideas. These ideas are marketed in the form of written research proposals. The selection of the most promising of these ideas by expert peer-group panels encourages the survival of the best scientists, and it allows us to exploit the fact that the most important new breakthroughs in biology will always be unexpected—and therefore impossible to plan.

As all of us learned when we studied American history, major distortions tend to occur in economic free markets when they are left unsupervised, and as our nation has matured we have actively intervened in our market economy in an attempt to improve its performance.

The question I want to address here concerns the type of free market that we have today in biomedical research: does the market work well in its present form, or is some more active stewardship required to optimize the large public investments being made? This is not just a theoretical question: it is the same question that is being addressed by Congress when it targets

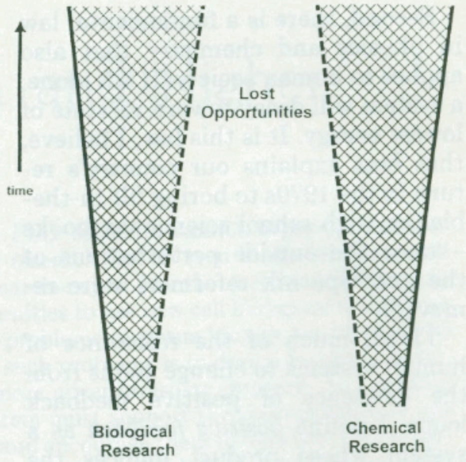

Figure 3. **Representation of a well-recognized problem in scientific training: chemists train more chemists to do research, and biologists train more biologists. As a result, research opportunities that demand sophisticated knowledge of both fields are likely to be ignored.**

research funding to specific diseases or to so-called strategic research fields.

There is at least one well-recognized form of inertia in the system that has already been actively addressed by the National Science Foundation (NSF) and others. This particular distortion in the free market of ideas is diagrammed in Figure 3. Chemists train more chemists to do research, and biologists train more biologists. As a result, opportunities in research that use new sophisticated chemistry to address important biological problems are likely to be missed—very few chemists will understand biology well enough to see the unsolved problems there that their skills could address, and biologists are unlikely to understand the new chemistry well enough to see how it can be applied to their concerns. A solution is to use education and funding mechanisms to promote interdisciplinary research, as is increasingly being done in universities through special graduate programs or research centers that, in the long run, are likely to make many of our present departmental structures irrelevant.

But the problem of inertia in re-

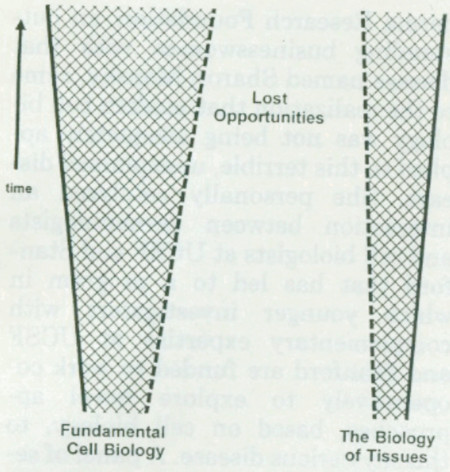

***Figure 4*. Representation of an unappreciated problem in training biological researchers: cell biologists train more cell biologists, and tissue biologists train more tissue biologists. As a result, research opportunities that demand sophisticated knowledge of both fields are likely to be ignored.**

search fields is much more pervasive than shown here. Let us confine ourselves to just one discipline, biology, and look at a diagram of this research stream in Figure 4. Here we are getting very close to home. On the left we have my field, cell biology, which is in a period of explosive progress — with new techniques, large numbers of talented energetic students entering the field, and startling new fundamental insights appearing every month. On the right we have a more traditional field that is even more relevant to human health, which for the lack of a better name I have called tissue biology. By this I mean the study of how individual cells cooperate and communicate with each other to form and maintain tissues, such as liver or bone. Now that we understand so much about how cells work, we are ready to attack this problem with new approaches and new tools. There are tremendous opportunities for students like mine in such fields, but for the most part these opportunities are not being adequately exploited anywhere. The reason is much the same as the one I gave earlier: my students tend to go on and do the same kind of work that I do, and they see too much risk in starting a new type of research project with no obvious prototype. Meanwhile, the students of those scientists who have been working on tissues for their entire careers do not have a deep enough feeling for the new cell biology to deviate markedly from the traditional approaches in their field.

There is another important reason for the inherently conservative choice of research fields. This reason is clearly structural and within our control, because it originates from the nature of the peer review groups established at the National Institutes of Health (NIH). This problem was identified during 1992's NIH strategic planning process by a committee that I co-chaired with Eugene Braunwald that was specifically charged with future planning for peer review. The committee members represented many different types of biomedical fields — from basic to clinical research. Most of them had served at one time or another as a leader for an NIH peer review group. The committee members looked at the present distribution of 80 review panels and unanimously recommended the following major changes:

> A reorganization of the NIH review process will be based on the following principles:
>
> - Each review panel will deal with grants in a reasonably broad subject area of long-term significance to the mission of the NIH, since the biomedical sciences are changing rapidly.
> - In most cases, review panels will not correspond to a particular technique. Rather, they will be broad-based, representing a variety of approaches to particular subjects.
>
> As a general rule, nearly all grant applications will be reviewed by a chartered Division of Research Grants (DRG) review panel. Ad hoc review groups with highly specialized expertise will be avoided as much as possible. The type of reorganization described above should greatly facilitate this aim, since the broader review groups will provide a more complete coverage of the entire spectrum of biomedical research.

As a contrast to this recommendation, consider some of the present panels. The list below shows one of the six panel groupings, the panels in an area called "biomedical sciences." How well does the subject area distribution of these panels cover the central issues in today's biology?

Biochemistry
Biomedical sciences
Bio-organic and natural products chemistry
Biophysical chemistry
Chemical pathology
Medical biochemistry
Medicinal chemistry
Metabolism
Metallobiochemistry
Molecular and cellular biophysics
Pathobiochemistry
Physical biochemistry
Physiological chemistry
Radiation

Our committee decided that the rapid pace of change in biomedical research means that major adjustments to the panels will be needed on an ongoing basis. We therefore recommended a vigorous mechanism, based on a regular outside overview by expert committees, to monitor the distribution and quality of the review panels. To date, this recommendation has not been implemented.

It is important to always keep our eye on the bottom line: what is it that we want most in our research system? My personal answer is that our research system should support the independence of our best young scientists and encourage them to take the risks inherent in highly creative endeavors.

Of course we want to encourage creativity in more mature researchers also. But we have a serious problem today in this respect. Because of the nature of our present NIH review panels — and the fact that it will always be more risky to try new things than to follow in well-respected, proven paths — there are severe disincentives to the pursuit of adventuresome research. Consider, for example, my own scientific career, which is schematically mapped out in

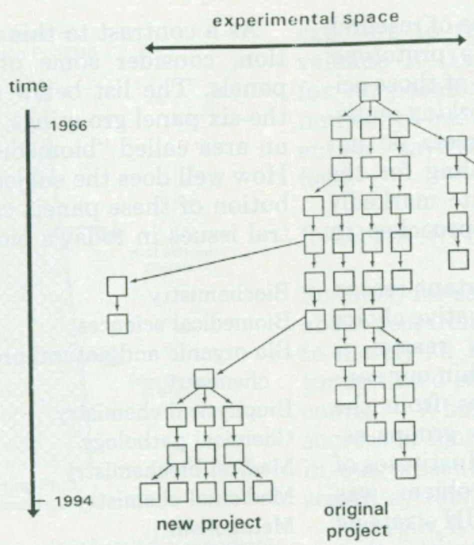

***Figure 5.* Representation of a career in science, where *time* has been plotted against an imaginary variable called *experimental space.* The greater the distance along the experimental-space axis, the greater the leap to a new approach or new subject. The present funding system for research strongly discourages large leaps or changes in the direction of research, yet such adventures are crucial for both the vitality of a scientific career and the productivity of the entire scientific enterprise.**

Figure 5. In this schematic diagram, I have plotted time against an imaginary variable that I have entitled "experimental space": the greater the distance along that axis, the greater the leap to a new approach or new subject. Each box in this figure represents one or two graduate students or postdoctorate fellows who have worked together on a focused aspect of my laboratory's research. Periodically, I have started a new research project in my laboratory by finding an interested young person who is willing to be more adventuresome than his or her colleagues. Sometimes the project ends when the individual leaves my laboratory. Occasionally, these forays into the unknown have led to projects that have taken over most of my laboratory.

Our present funding system for research strongly discourages such large changes in direction, and yet such adventures are very important, both for the vitality of a scientific career and for the productivity of the entire scientific enterprise. How can we optimize scientific exploration by facilitating such hops? This needs careful thought. I just want to stress here that there definitely are ways to encourage, rather than discourage, creativity.

One way is to offer two-year grants at a level of, say, $50,000 per year for innovative, exploratory research that would require no previous data and only a five-page application. A small program of just this sort was suggested in the 1993 Institute of Medicine report to the U.S. Army on strategies for managing the $200 million in their breast cancer research program. I am not aware of its present status.

Another way is represented by a recent experiment that I have been a part of. The founder of the Scleroderma Research Foundation, an outstanding businesswoman with that disease named Sharon Monsky, came to the realization that modern cell biology was not being adequately applied to this terrible, unexplained disease. She personally catalyzed an interaction between dermatologists and cell biologists at UCSF and Stanford that has led to a program in which younger investigators with complementary expertise at UCSF and Stanford are funded to work cooperatively to explore novel approaches, based on cell biology, to this mysterious disease. A panel of senior advisors, on which I serve, meets with this group every six months to help connect them to resources and to cheer on their cooperative efforts. I can only report that this has been fun for me, and that Sharon is now about to establish a second experiment of the same kind in the Baltimore area.

CONCLUSION

In the biomedical sciences, we presently have a tremendously vital system of education and research. This system must be preserved. A highly competitive process selects out the very best of our young people for independent scientific careers. And it keeps the rest of us in education and research working 80 hours per week at our jobs! But the progress in biology has accelerated to such an extent that much of the exciting research of five years ago has now become mundane. In part for this reason, the entire system of education and research needs active management. More and more in recent years, government has been stepping in to play this role. A much better alternative is for the scientific community to step forward more boldly to address the inertia ourselves. This will take real leadership. We need to convince all of our colleagues that they should be bold and choose order over chaos. Let us begin.