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# Physiological Mini-Reviews

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Physiological Mini-Reviews is a scientific journal, publishing brief reviews on "hot" topics in Physiology. The scope is quite broad, going from "Molecular Physiology" to "Integrated Physiological Systems". As indicated by our title it is not our intention to publish exhaustive and complete reviews. We ask to the authors concise and updated descriptions of the "state of the art" in a specific topic. Innovative and thought-provoking ideas are welcome.

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This Essay was kindly provided by Dr Gerald Pollack, from the University of Washington.
Although it refers to the limitations of the USA system to support breakthrough science, we believe that Pollack´s concepts may apply to our scientific system and to ourselves, as scientists.

The Editorial Board

# Are scientists really doing science? Personal reflections on the NIH grant system

*Gerald H. Pollack, Dept. of Bioengineering, University of Washington, Seattle WA 98195*

This brief essay summarizes some personal thoughts on the NIH grant system. The thoughts arise in part from my experience as a dissenter from scientific orthodoxy, and in part from my experience as a member of several workshops convened to assess and fix problems with the NIH and NSF grant systems.

## 1. Has the scientific enterprise gone awry?

A half-century ago, breakthroughs were fairly common events. They could be counted on to occur on an unpredictable but not infrequent basis. Pioneering such breakthroughs were now-legendary figures such as Linus Pauling, Jonas Salk, Richard Feynman, James Watson, Francis Crick — heroic names familiar even to lay people.

But things have changed. While the past 30 years have brought a great outpouring of scientific results, breakthroughs are less common. Modern equivalents of Pauling, Salk, and Watson-Crick are not easy to identify. Can you name more than a handful of breakthroughs that have emerged during the past three decades? I mean realized breakthroughs such as revelation of the biochemical nature of heredity or a vaccine to eradicate a ravaging affliction, not incipient breakthroughs whose realization always seems just around the corner.

Considering the currently massive investment in science, why are there so few scientific breakthroughs? Why is it that scientific heroes are now so scarce?

Some argue that this settling down is all but inevitable. After all, science today is far more complicated than it has been, often requiring teams of investigators and large groups to pursue effectively. Others argue that there is simply not much more to be discovered — that the breakthroughs have had their heyday and we need content ourselves with merely filling in the gaps. Thus, breakthroughs might not be expected to occur on an everyday basis.

Perhaps some of this is true — but a significant role may also be played by another factor: the growing aversion to risk taking. Although funding agencies have much to be proud of for past achievements, it is broadly perceived that they have become less agile in dealing with proposals that dissent from orthodoxy. Challengers of the *status quo* rarely succeed in today's scientific climate. Hence, the approaches most apt to generate conceptual breakthroughs are frequently throttled before they can emerge from the scientific womb.

The funding agencies are aware of this problem. Both the NSF and the NIH have held recent workshops to deal with the issue, and some measures have been taken over and above existing remedial programs. The term "high risk" now permeates NIH review guidelines. The NIH has established five to ten "Pioneer Awards" each year to encourage novel approaches. And R21 "high risk" grants have been available from many Institutes for some time.

While these responses acknowledge the problem, it is broadly felt that they are nominal. Few dissenters from orthodoxy report any success with the R21 system, and even some NIH administrators admit that these grants do not solve the problem. Admonishing reviewers to be "less conservative" comes with no guarantee that they will be. The Pioneer Awards were given last year to an impressive cohort, but these were not challengers of prevailing orthodoxy; recipients are well-funded mainstream scientists (~$1M mean annual amount), who have enjoyed considerable success within the system. Also, the number of awards, nine last year, makes little dent in the surface of an otherwise tough, pervasive and serious problem. Thus, effective action has yet to be taken.

I am not alone in this view. A recent, highly praised book by Donald Braben, entitled *Pioneering Research: A Risk Worth Taking*, concurs. Braben argues that limiting the ability of scientists to dissent from orthodoxy heralds a line of consequences leading ultimately to societal doom. Only a radical departure from the highly bureaucratic, top-down-managed approach to science, he argues, will solve the problem. In the absence of such a departure, progress will remain incremental, despite a vast pool of talent and an abundant pool of monetary resources. Freedom to dissent is essential.

Thus, the scientific enterprise appears to have gone at least somewhat astray. It has for sure generated a massive number of hugely productive enterprises whose outpouring of results seems to come ever closer to generating the hoped-for conceptual breakthroughs. But those breakthroughs rarely materialize. Always, it seems they are just around the corner. A reason for this mixed track record is that the very approaches that could lead to the desired breakthroughs — those that challenge the current line of thinking with fresh alternatives — have virtually no chance of success.

## 2. Source of the Problem

If this situation seems as antithetical to science to you as it does to me, how could it have arisen? I consider two sources: the scientific culture and the grant system.

### *A. The scientific culture*

Scientists since the time of the ancient Greeks have been dedicated to the pursuit of truth, and the same dedication applies today. We want to find out how the world really works. On the other hand, in response to societal demands for finding cures to diseases and developing technologies to compete effectively in a world growing ever more complex, science has grown from the small cottage industry it once was, into a big business. It consumes money and generates products. Whether the business-like culture spawned by this transformation has brought complicating features that might compromise the noble goal of science is an issue that needs to be considered.

Formerly, science was a modest endeavor. Principals were largely known to one another, and they enjoyed support either from a benefactor, or from having been born into a family of wealth. Scientific pursuit was largely unfettered by the exigencies of everyday life, because it was practiced by a talented and fortunate few.

Today, science has grown to a massive enterprise, not unlike a big business. The business is supported by tax-paying investors, who channel their investments through organizations such as the NSF and NIH. In return, the business generates useful products. These products are mainly conceptual frameworks describing how the universe operates. They are belief systems - theories and hypotheses emerging out of available evidence. Thus, money is invested and belief systems are generated. The presumption is that such belief systems will eventually be useful for advancing technologies, curing afflictions, accruing national prestige, etc.

Investors are patient. Especially with the promise of incipient breakthroughs, the public is remarkably willing to continue its investment, recollecting the incredible scientific and medical breakthroughs of the past and anticipating even more in the future. At least for now, it is axiomatic that scientific and medical research will enjoy continuing (albeit fluctuating levels of) support. Investors will not pull the plug.

It is this implicit confidence that may be the first reason for the existing problem. The scenario is akin to a business that does not need to compete. Ordinary businesses must innovate to beat the competition, but the scientific business suffers little such concern, for so long as the promise of incipient medical breakthroughs continues to be as well advertised as it is now, the public will continue to invest.

Safe and secure, the scientific endeavor presses on. Truth seeking certainly remains high on its agenda — but who is checking to see what fresh and insightful truths have been uncovered? Which investors will demand a list of last year's conceptual breakthroughs? Such breakthroughs are anyway presumed to be beyond the investors' ability to understand, so why even bother. Scientists have become largely insulated from public scrutiny, hidden within the confines of the huge business complex that is today's science.

Breakthroughs are welcome, but certainly not demanded or even expected. Making progress is sufficient.

To illustrate the point, consider the expectations implicit in the typical government-grant proposal. Within the NIH system, applicants are obliged to project annual milestones: What will be accomplished by the end of year 01? Year 02? Even, year 05. Such requirements amount to implicit admission that no breakthroughs are to be anticipated, for any unexpected finding will immediately change the direction of the research and render earlier projections irrelevant. Scientific society has institutionalized its expectation that even modest breakthroughs will not happen, and this expectation is passed onto its scientists.

If not satisfying the expectations of its patrons, what then motivates today's scientists? Is it the pure, noble and unfettered goal of seeking truth, or do extraneous factors come into play?

My take is that the most pressing motivational factor comes not from outside the system, but from within: the competition to survive. To survive, all scientists need funding. The pressure is especially acute when one's salary is at risk, and it is also acute in larger laboratories, where long-term staff akin to family must be supported uninterruptedly. Host universities turn up the pressure further. They count on the indirect costs that come with grants to help pay their bills, and remind you of this when promotion and tenure considerations come around. Thus, obtaining funding has become not just a means of paying for the costs of experimentation, but a relentless pressure in a fiercely competitive arena, which rarely abates. By no means has the motivation to seek for truth been abandoned; but Darwinian survival is an additional motivator of some significance.

How does one ensure survival in so competitive an arena?

Obviously, attention needs to be paid to those determining your fate, and high among those are your grant reviewers. Impressing them is important. Being productive, motivated, and highly professional at all times will go a long way. But the peers reviewing your application are also your competitors, seeking to fortify their own positions, and proposals that threaten to undercut those positions are not likely to be embraced with great warmth. So, one must be ever cautious. The safest bet is to avoid even any hint of serious dissent from orthodoxy. Most every scientist knows it.

In short, the culture has deflected scientists from their singularly noble goal of pursuing truth and challenging orthodox thinking whenever truth-seeking warrants. Just keep it safe, and get your funding. We have evolved into a culture of obedience, bowing to the high priests of orthodoxy in order to secure our own positions.

As you might imagine, this culture generates some unwelcome side effects. Among them are the following:

1. *Truth plays a subsidiary role*: In determining which belief systems prevail, survival-related issues may play a dominant role. Truth may not necessarily be the singular factor.

2. *Crowd Power*. Those on review boards have commanding power, which can be subject to group reinforcement. "Yes, this unorthodox proposal contains brilliant ideas, but, unfortunately…." Colleagues around the review table are relieved, for any threat to the prevailing belief system impacts them, too. The reviewer is applauded for his/her critical insight, and the establishment is sustained.

3. *Narrowness*. Science is broadly conceived as a growing tree of knowledge: The trunk, limbs, and major branches are thought solid and well defined; it is only the most peripheral twigs that remain to be elaborated — and that is the task of today's scientists. Few seem to be paying attention to whether the foundational limbs are really solid. We are all too narrowly preoccupied dealing with the explosion of information to step back from details to rethink the fundamentals. We have defaulted into becoming a culture of believers.

4. *Aggression toward interlopers*. The inner voice repeats: "My colleagues have bestowed ample funding upon me; they seem to think my ideas are all right. Therefore, probably my ideas *are* all right. *Ergo*, challengers are likely to be cranks bent on making unnecessary trouble." Challengers are too often arrogantly ridiculed. Even scientists unfamiliar with the challengers' work seem to take pleasure in demeaning it — many colleagues report this experience.

5. *Misplaced values*. With facts growing at an exponential rate, the growing density of peripheral twigs seems more and more to obscure the core paradigms. From the outside, science looks like a thicket of complexity. The notion of complexity is reinforced by the culture: grant programs provide ample support for large-scale computer models thought to be necessary to make sense out of the seemingly impenetrable minutiae. But, what happened to Occam's Razor? The time-honored approach of replacing complicated belief systems with simpler belief systems that explain more facts, has given way to a resignation that science is too complicated for any one person to comprehend in its entirety. A sense of futility pervades — a sense that formidable problems can no longer be solved through bold approaches and fresh ideas.

In sum, the culture of science is beset with a number of problems. It has produced scientists whose drive to survive can sometimes overshadow their drive to pursue fundamental advances. It accepts growing complexity as a given, and thereby offers limited incentive for scientists to find simplifying truths; those few scientists reckless enough to stray onto paths less traveled are marginalized by the majority of scientists, who are deeply and unquestioningly acculturated in their fields' orthodoxy. Dwelling within this orthodoxy, by contrast, promotes ample rewards. Understandably, this is a culture that is not likely to produce much in the way of breakthrough science.

### *B. The Grant System – Perpetuator of Orthodoxy*

Shortly after the government-grant systems were created a half-century ago, Thomas Kuhn published his now-classic book entitled "The Structure of Scientific Revolutions," arguing that science advances less by accretion of knowledge than by a series of scientific revolutions. These revolutions, as we well know, were referred to as "paradigm shifts." Often, normal science is completely overthrown by the work of some creative scientist who comes upon a finding so completely out of accord with the prevailing view that the latter becomes untenable. Such paradigm shifts, Kuhn argues and many though not all scientists agree, make for the real advances in science.

The NIH grant system was not designed to deal with proposals aimed at promulgating paradigm shifts. Because it was created before Kuhn's ideas became broadly known, the system was implicitly designed around the earlier common-sense principle of accretion of knowledge: Add flesh to the bones of the existing framework, and eventually the universe will be better understood. As knowledge grows, so will understanding. From such a perspective, peer review makes good sense and has produced much new knowledge — for, who better than peers can judge whether a scientific proposal seems sound?

For applications that dissent from orthodoxy, however, the merit of this system is less clear. A fresh idea commonly challenges the *status quo*. Sent to those for whom the *status quo* is a central belief system, the review outcome is more-or-less predictable: too commonly, self-interest will block the application. I do not demean the value of experts, or of knowledge over ignorance, only of the *de facto* power conferred on those who have risen to prominence within today's establishment to dictate the direction of scientific inquiry. It is all too easy for the establishment to deflect unpleasant challenges.

Compare this grant-review system with a court of law. Like the court, the scientific court is set up to adjudicate a matter — the fate of a grant application. In a court of law, the jury is disinterested; it stands to gain or lose nothing whether the prevailing party is the plaintiff or the defendant. In the scientific court a plaintiff makes the case against the defendant — who then turns around and acts as judge. Imagine a court system in which a small auto company's proposed innovation is to be judged by a representative of GM, who has veto power. Situations of such happen, for sure – but is this a reasonable way to judge the merit of the plaintiff's case?

It is difficult to escape the conclusion that the peer review system virtually guarantees that the most far reaching of potential scientific advances will not be supported. Genuine challenges of the *status quo* have little chance, and indeed, scientists broadly acknowledge that submission of proposals that challenge orthodox thinking borders on suicidal. Any such forays are avoided like the plague.

The take-home message? Proper scientific citizens are those who dwell happily within the realms of orthodoxy. The NIH-grant system promotes safe science, not breakthrough science.

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In sum, the scientific endeavor is beset with problems originating both from the culture and from the grant system. One reinforces the other. The result is a proclivity to favor what is safe, and to shun what seems "risky." Einstein's challenge of orthodoxy would probably have failed in today's grant-review system, as would Galileo's – not to mention Watson and Crick, whose coffins of failure would likely have been sealed by the absence of requisite background in nucleic acid biochemistry, and certainly by the absence of any preliminary data. Could these chaps be worth the risk?

It is the focus on safe science that in my estimate is responsible the dearth of conceptual breakthroughs and real (not promised) solutions to medical problems. Left unchecked, the system guarantees that the future is not likely to be any more fruitful than the past.

On the other hand, the issues cited above are not unique to the NIH; they pervade granting agencies worldwide. Understanding their etiology may provide some helpful background through which remedial measures can be taken. With well thought out measures, the NIH stands to become the vanguard for the re-vitalization of science.