Infection and Immunity

Reforming Science: Methodological and Cultural Reforms

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Reforming Science: Methodological and Cultural Reforms

Contemporary science has brought about technological advances and an unprecedented understanding of the natural world. However, there are signs of dysfunction in the scientific community as well as threats from diverse antiscience and political forces. Incentives in the current system place scientists under tremendous stress, discourage cooperation, encourage poor scientific practices, and deter new talent from entering the field. It is time for a discussion of how the scientific enterprise can be reformed to become more effective and robust. Serious reform will require more consistent methodological rigor and a transformation of the current hypercompetitive scientific culture.

"All but foolish men know, that the only solid, though a far slower reformation, is what each begins and perfects on himself."—Thomas Carlyle (4)

"There is no more delicate matter to take in hand, nor more dangerous to conduct, nor more doubtful in its success, than to set up as a leader in the introduction of changes. For he who innovates will have for enemies all those who are well off under the existing order of things, and only lukewarm supporters in those who may be better off under the new."—Niccolò Machiavelli (27)

It can be argued that the scientific revolution has been the single greatest transformative event for humanity since the harnessing of fire. Science has cured disease, unleashed the green revolution, taken us into space, and shrunk the world through rapid transportation and instant communication. However, science has also brought devastating weaponry and planetary degradation from natural resource extraction, pollution, and climate change. Regardless of one's stance on the benefits and liabilities of the scientific revolution, science remains humanity's best hope for solving some of its most vexing problems, from feeding a burgeoning population to finding alternative sources of energy to protecting our world against planet-killing meteorites. And yet, notwithstanding the importance of the scientific enterprise, only a tiny fraction of the human population is directly involved in scientific discovery. It is therefore crucial for society to nurture and sustain the fragile scientific enterprise and optimize its functioning to ensure the continuing survival and prosperity of mankind.

Since eclipsing theology as a framework for understanding the natural world and freeing itself from philosophy as an intellectual discipline, science has reigned as the supreme arbiter for certain types of knowledge for almost 2 centuries. The association of science with technology and national power has led to considerable public and governmental funding support. Looking back, the progress of science may appear inexorable, but there are increasing signs that this great human enterprise could benefit from some introspection and retooling. Today's science finds itself increasingly besieged, and some of its disciplines are in outright crisis. Threats to science come from both within and outside of the scientific enterprise. External threats include increasing antiscientific attitudes expressed by the general public and politicians, skepticism about the scientific community's conclusions (the global warming debate is but one current example), inadequate funding, and increasing regulation. These external threats are exacerbated by inadequate efforts by scientists to educate and engage the public in a clear discussion of the benefits and limitations of scientific findings. Internal threats include dissatisfaction of scientists with many aspects of the business of science as it is performed today (including but certainly not limited to peer review and incessant pressure to obtain grants and publications) and the corrosive impact of research errors and misconduct, as reflected by an increasing number of retracted publications.

History teaches us that most, if not all, great human enterprises must undergo periodic cycles of self-examination and renewal to maintain their vigor. Examples of great reforms include Marius' revamping of the legion system that allowed the Roman Empire to survive for centuries, the abandonment of scholasticism during the early Enlightenment that ushered in the scientific revolution, and Flexner's creation of the modern medical school curriculum. Reforms are nearly always catalyzed by crisis and discontent, and perhaps we are approaching a time when fundamental reforms are needed for the scientific enterprise. However, history also tells us that reforms are usually bitterly resisted by the establishment, and any attempt at reforming science is likely to encounter strong headwinds.

Any movement to reform science must consider the problems and suggest solutions. In our view there are changes that can be made entirely within the scientific enterprise (methodological and cultural), whereas others must engage societal and political processes (structural). This article will focus on methodological and cultural reforms, and the accompanying paper (15) will address structural problems.

PROBLEMS WITH CONTEMPORARY SCIENCE

By many measures, contemporary science has been a resounding success, particularly when one considers the impressive advances in technology and biomedicine. Yet this progress has come at a price, and one may still ask whether the scientific enterprise is healthy. A romantic ideal depicts scientists as intrepid and objective explorers in the relentless pursuit of truth (26). Although many, if not most, scientists are drawn into the business of science by curiosity about nature and a desire to improve the human condition through the accrual and application of knowledge, the

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realities of science can be quite different. To be successful, today's scientists must often be self-promoting entrepreneurs whose work is driven not only by curiosity but by personal ambition, political concerns, and quests for funding. Individual scientists intensively compete with other scientists for resources, and many scientists are dependent on grant funding to provide part or all of their salaries. Although scientists would prefer to follow wherever their data may lead, research funding is often restricted to specific topics believed to represent the most urgent social priorities. Scientists are expected to demonstrate consistent productivity in terms of manuscripts, on which their future funding, promotion, and tenure depend. The greatest value is placed on journals with high "impact" (and commensurately high rejection rates, as an indication of selectivity), and most of the glory goes to the first and last authors of a publication. In this environment, we see several problems with contemporary science.

A workforce imbalance. One major concern is the imbalance among members of the research workforce and the funding currently available to sustain that workforce. In some respects the current scientific workforce resembles a pyramid scheme with a small number of principal investigators presiding over an army of research scientists, postdocs, students, and technicians who have little autonomy and increasingly uncertain career prospects. Despite efforts to foster the career development of young and female investigators, senior researchers remain disproportionately male and increasingly senior.

Publish and still perish. The well-known "publish or perish" mentality can drive some scientists to write papers whether or not they have anything new and important to say. The result is an unwieldy scientific literature in which the most highly cited papers are concentrated in a small number of journals (19) while a large proportion of papers are cited infrequently or not at all (2). Jinha has estimated that 50 million scholarly articles have been published since 1665, when the first modern journal appeared, with more than half of these published during just the last 25 years (21). Much of the recent scientific literature is repetitive, unimportant, poorly conceived or executed, and oversold; perhaps deservingly, much of it is ignored. However, the sheer number of papers generates an enormous burden on the peer review system (9). As the pool of qualified peer reviewers is inadequate to meet demand, the critical role of peer review in screening and correcting manuscripts prior to publication cannot properly function. These factors, as well as the difficulty publishing negative results (publication bias), serve to undermine the reliability of the scientific literature (13, 18).

Survival of the fittest. A Darwinian struggle for existence can produce multiple behaviors, including competition, aggression, reciprocity, altruism, cooperation, and sometimes, unfortunately, cheating. Each of these behaviors may be readily observed among contemporary scientists. Competition can be beneficial when it provides a motivation for resourcefulness and innovation. However, competition in excess can be a compelling incentive for scientific misconduct ranging from egregious fraud to more subtle transgressions, such as selective reporting of results (12). The need to distinguish one's work from that of competitors can induce scientists to exaggerate the importance of their findings or downplay potential caveats (20). While this may seem relatively innocuous in the short run, the cumulative effect can be the erosion of public confidence in the scientific method (10). Another casualty of the competitive environment is timely communication. Scien-

tists often keep valuable information to themselves for fear of being "scooped" by competitors, and attempts to place work in the most highly selective journals may delay publication for months or years. The entire shape of the research effort is distorted as researchers scramble to conform their work to targeted funding opportunities and steer away from risky lines of inquiry or projects requiring a lengthy time investment. Unfortunately, in science risk and reward often go hand in hand (24), so a focus on conservative projects means that opportunities to make revolutionary breakthroughs will be missed.

Winner takes all. The current scientific enterprise is a highly competitive environment with a winner-takes-all system in which the greatest rewards are given to individuals who excel in scientific discovery, publication prestige and quantity, and grant funding. Since its inception, science has operated with the priority rule, which means that when different scientists work on the same problem, the credit goes to the one who provides the answer first (33a). Furthermore, success in science tends to beget more success, in a phenomenon that Merton called the "Matthew effect" after the Gospel of Matthew: "For whosoever hath, to him shall be given" (27a). The benefits of scientific success even appear to translate into better health, as recipients of Nobel Prizes live longer than those who are only nominated (30a). In any human endeavor, competition can be healthy when it promotes ingenuity and creativity and harnesses primal human energies. Thus, it has been argued that the priority rule in science is beneficial to society (33a). However, a winner-takes-all system has inherent dangers, including a greater likelihood of cheating by participants. In this regard, scientific fraud is a form of cheating that can lead to publications (as well as retractions). Fraudulent publications that affect public perception and policy, such as the 1998 Lancet article that linked autism to the measles vaccine (11), can be destructive to society. Despite occasional high-profile instances of fraud that adversely affect public opinion, society at this time continues to have an overwhelmingly positive view of science and scientists (22). Nevertheless, this trust is precious and must not be taken for granted, as illustrated by the rapid loss of trust in climate science and scientists that has followed the release of emails and computer files in the incident known as "climategate" (25).

The priority rule. The priority rule means that credit and its associated rewards go to the first individual or group of individuals who announce a discovery irrespective of the number of scientists who have contributed to the solution of the problem. How did the priority rule become the dominant economic system in science for assigning rewards? Why do scientists accept this economic system? There are no simple answers to these questions, but the priority rule was in place long before science became a major human enterprise. For example, Newton and Leibnitz quarreled in the 17th century about priority in the invention of calculus. A list of scientific priority disputes is maintained by Wikipedia (36). In the early days of the scientific revolution, most inquiry was carried out by individuals with sufficient means and leisure to devote to thinking, experimentation, and the publication of books. In a system that began without prizes, salaries, or grant applications, priority may have been the only source of prestige among a small number of colleagues. However, the priority rule probably contributes to many of the current maladies in science. The effort to get there first and grab the largest share of the credit undoubtedly contributes to such practices as citation bias, secrecy, and the appropriation of others' ideas and data. The competitive

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environment created by the priority rule is vividly apparent in Watson's unauthorized inspection of Rosalind Franklin's X-ray diffraction data as described in the *The Double Helix* (35). A more recent example is provided by the dispute over priority in the discovery of HIV (34). The race to be first encourages risk taking that can lead to scientific breakthroughs that benefit society while at the same time creating conditions that are detrimental to science. Hence, it may be worth reconsidering the priority rule and whether it is the best reward system for science.

Science as a team sport. Although the edifice of scientific understanding is sometimes envisaged as an accumulation of individual discoveries, in reality science is a community effort comprising innumerable interdependent contributions. Credit is disproportionately awarded to principal investigators for what is truly the product of teamwork, and nearly all scientific contributions are heavily dependent on knowledge obtained earlier. As Newton famously remarked, he was able to see further by standing on the shoulders of giants. In the spirit of an Amish barn-raising, a celebration of the collective achievement of science should subsume individual achievement.

THE SIGNIFICANCE OF RETRACTIONS

Recently we reviewed the problem of retracted publications in science (14). Trends in the numbers of retracted publications can be viewed as an indicator of the failure rate of the scientific process. Retracted publications represent wasted resources and can erode public confidence in science, which can translate into cynicism and reduced support. There is a general consensus that retracted publications are the proverbial "tip of the iceberg," signifying a much larger body of poor-quality scientific work that has made its way into the published literature. If that is the case, then a significant proportion of the scientific literature is incorrect. Although scientists have always comforted themselves with the thought that science is self-correcting, the immediacy and rapidity with which knowledge disseminates today means that incorrect information can have a profound impact before any corrective process can take place. For example, the aforementioned fraudulent Lancet paper was not retracted until 12 years later (16), consequently raising considerable false alarm among the public regarding the wisdom of vaccination. It has also become sadly apparent that misinformation can be as effectively disseminated as valid information via modern technology (28). Thus, even retracted papers continue to be cited and used as evidence to buttress false claims (23). Although concerns about the relationship between pressure to publish and research fraud are not new (38), the frequency of retracted papers is increasing (32). The accelerating rate of retractions should be regarded as a serious indicator of trouble in the scientific enterprise. Even though retractions for misconduct constitute a tiny fraction of all research publications, they risk discrediting science as a whole. Retractions in areas of great public interest, such as medicine and global warming, are particularly dangerous because they undermine confidence in scientifically grounded policy recommendations. Hence, bad science is bad for society.

Retracted papers tend to fall into two general categories: those retracted because of scientific misconduct and those retracted because of errors in methodology, conclusions, or approach. One might refer to these as "dishonest" and "honest" retractions, respectively. Although each has a different cause, and the consequences to authors are very different, their immediate effects are

the same in that they undermine the credibility of science. A recent study analyzed the cause of retraction for 788 retracted papers and found that error and fraud were responsible for 545 (69%) and 197 (25%) cases, respectively, while the cause was unknown in 46 (5.8%) cases (31). Although the majority of papers were retracted for honest errors, it behooves scientists and journals to establish standardized approaches for dealing with each problem.

Honest retractions. Honest retractions may occur as a result of errors of methodology, conclusions, or approach. We call them "honest" because no malicious intent is involved. This category accounts for the majority of retractions (12). To reduce honest retractions would require implementing reforms that would reduce the number of such errors, and here we would make a few general suggestions under the category of methodological reforms.

Dishonest retractions. Dishonest retractions occur when the deliberate manipulation or fabrication of results is discovered, prompting a retraction of the published work. Reducing dishonest retractions might be achieved either by increasing the penalties or reducing the incentives for misconduct. Severe penalties ranging from the loss of reputation to criminal charges of fraud are already in place, raising doubts about whether further penalties would be effective. The adoption of uniform standards for reporting retractions and perhaps the institution of a centralized database for documenting scientific misconduct might help to ensure that individuals guilty of misconduct are recognized. Scientists are conscious of reputation, and unflattering notoriety remains a potent disincentive for cheating. Nevertheless, there is a limited role for sanctions. Although it is important for misconduct to have consequences, unequivocal instances of misconduct are uncommon and represent only a portion of undesirable behavior. Therefore, we would focus efforts on reducing the incentives for dishonest actions by scientists.

METHODOLOGICAL REFORMS

Revising criteria for promotion. As the Guinness Book of World Records shows, the desire to be first, whether in science or in the consumption of hot dogs at one sitting, is human nature and as such unlikely to change. Scientists will continue to race to be the first to achieve a goal, and journals will continue to vie for original reports. Perhaps the best place for a methodological reform to replace the priority rule is at the level of academic promotion and in the awarding of symbolic rewards, such as scientific prizes. In the present system, promotion decisions typically depend upon performance review by other faculty members who have a limited understanding of an investigator's work, which increases reliance on surrogate measures of quality, such as grant dollars, bibliometric analysis, and journal impact factor (8). A reform of the promotion process based on careful peer evaluations of scientific quality and the specific contributions of the authors might help to reduce the present emphasis on priority. Furthermore, increasing the value of collaborative publications when considering promotion could provide important incentives for greater cooperation between scientists.

Reembracing philosophy. Science traces its ancestry to natural philosophy, which in turn emerged from philosophy. Many early scientists were fully grounded in the philosophical fields of their time and contributed to both disciplines. Descartes separated philosophy from theology while making seminal contributions to mathematics and physics. Leibnitz discovered the calculus

while at the same time proposing the metaphysical theory of monads. In this regard it is worth remembering that Ph.D. degrees granted in the natural sciences are actually Doctorates of Philosophy. However, scientific training today does not include significant instruction in philosophy despite the critical importance of the philosophical branches of logic, epistemology, and ethics to science. In fact, there are numerous instances in which philosophical thought has greatly influenced scientific discovery and vice versa. Einstein credited the philosopher Immanuel Kant with inspiration that led to the theory of relativity, and Einstein's scientific contributions have in turn influenced philosophy (29).

Philosophy is currently regarded as including four branches: epistemology, logic, ethics, and metaphysics. We believe that the knowledge found in each of these branches can contribute significantly to improving the scientific enterprise. Formal training in logic and epistemology could reduce the number of errors by scientists. One common error in science is the attempt to make positive inferences from negative data (e.g., ruling out a mechanism or cause and effect from negative experimental data). Errors in logical thought can lead to dogma and affect the direction of entire fields of study. For example, the conclusion that humoral immunity had no role in protection against many intracellular pathogens was based on an inability to demonstrate the efficacy of antibody with the methodology used (7). This conclusion evolved into dogma and greatly affected the direction of research, including the development of vaccines. However, this constituted a logical error because a possible protective role of antibody could not be excluded by experiments that showed no protection. The original conclusion was eventually shown to be faulty when hybridoma technology allowed the generation of protective monoclonal antibodies. A stronger foundation in epistemology, supplemented by an awareness of philosophical issues involving language, might also avoid some of the problems created in science from the misuse of such terms as "descriptive" (5) and "mechanistic" (6) in the categorization of projects and papers. Ethics, or "moral philosophy," has already returned to scientific training as students are increasingly taught formal ethical principles in science, but much more could be done in this realm with the goal of reducing the number of dishonest retractions. Metaphysics, or the study of reality, is perhaps the most problematic branch of philosophy for scientists who regard it as a domain outside scientific pursuit. However, metaphysics is the antecedent of natural philosophy and is thus in the ancestral line of the scientific enterprise. Knowledge of metaphysical questions could help scientists to frame problems and perhaps approach the boundary without crossing it.

Enhanced training in probability and statistics. In science, certainty is often defined in probabilistic terms. Knowledge of probability and statistics is essential for the design, execution, and interpretation of many scientific experiments. Although most scientists have some knowledge of probability and statistics and can calculate "P values" using statistical software, the level of statistical expertise varies greatly among individuals. In fact, much deeper knowledge of the foundations of these disciplines is needed. For example, a recent paper in *Science* was retracted because the authors assumed that two correlated variables were independent while these variables were in fact additive and dependent (30). As the late statistician Stephen Lagakos observed, "Sure, you can lie with statistics . . . but it's a lot easier to lie without them" (R. Schooley, personal communication).

Use of checklists. There is conclusive evidence that the use of

TABLE 1 Sample checklist for an observation in which a stimulus elicits an effect

Checklist

Does an increase or decrease in the magnitude of the stimulus translate into a commensurate effect? (e.g., a dose-response relationship)

Does the effect ever occur without a stimulus? (e.g., false-positive rate)

Does the stimulus ever fail to elicit an effect? (e.g., false-negative rate)

What is the temporal relationship between stimulus and effect? (temporal

causality)
Is the effect reproducible? (reproducibility)
Can the effect be measured by an independent technique? (validation through independent methodology)

checklists can reduce errors in human activities ranging from aviation to surgery (17). Science should be no exception. An increased use of checklists in the conduct of scientific experimentation and publication could conceivably reduce scientific errors and consequently improve productivity, reduce waste, and prevent retractions. Clearly, different types of checklists would be needed for different occasions. For example, a simple checklist can be constructed for a scientific result in which a stimulus appears to cause an effect (Table 1), which if followed would enhance conceptual rigor and reduce the likelihood of a false conclusion.

CULTURAL REFORMS

Is science too masculine? The reward system in science will be difficult to reform. However, any attempt to reduce the incentives for cheating will have to address structural issues in the payoffs for scientists. Winner-take-all strategies have been proposed to be male evolutionary strategies that disproportionally reward risk taking in the production of offspring (33). Hence, it might be argued on more than one level that science is too "masculine." A reform to the payoff system may also have other benefits in addition to reducing the incentives for cheating. Given the increasing connectivity between fields and specialties of science, there is an increasing need for collaboration, yet a system of winner-takes-all is inherently unfair to collaborators. A different reward system could promote team science and thus promote the overall progress of the scientific enterprise. A less "masculine" scientific culture could be a fairer, more honest, more cooperative, and more successful enterprise. In this regard, we note that efforts are already ongoing to promote and recognize collaboration and team science that provide guidance for communication, sharing credit, and handling conflict (3).

Nobody here but us chickens. Such a culture would place a greater emphasis on the derivative and collaborative nature of scientific advances, along with a reduced emphasis on rewarding hypercompetitive behavior and the cult of the "rock star" investigator. The evolutionary biologist David Sloan Wilson has recounted an attempt to improve the productivity of egg-laying hens by Purdue researcher William Muir (37). The approach of selecting the most productive individual hens from each group to breed the next generation was compared with selecting the most productive groups of hens. Unexpectedly, the latter approach was most successful because the individuals within successful groups had learned to function cooperatively, and the happier hens laid more eggs. Productivity plummeted when the star performers were grouped together, and all but three hens in this group were dead by the end of the experiment. After a lecture describing these

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TABLE 2 Retraction problems and some suggested solutions

Problem	Reform	Suggested solutions
Honest retractions	Methodological	Embracing philosophy with formal training in logic, epistemology, and metaphysics Rigorous training in probability and
		statistics
		Increased use of checklists
Dishonest retractions	Cultural	Development of new reward systems with an emphasis on quality and a recognition of team science
		Reconsideration of the priority rule
		Establishment of a centralized database of scientific misconduct
		Enhanced focus on ethics

results, a professor in the audience exclaimed, "That describes my department! I have names for those three chickens!" In fact, we all know who those chickens are.

A vision of a healthier scientific culture. Science functions best when scientists are motivated by the joy of discovery and a desire to improve society rather than by wealth, recognition, and professional standing. In spite of current pressures, it is perhaps remarkable that many scientists continue to engage in selfless activities such as teaching and reviewing, decline to publish work that doesn't meet stringent standards for quality and importance, freely share reagents and knowledge without worrying about who gets the credit, and take genuine pleasure in supporting the efforts of other investigators. Such individuals should be recognized and emulated.

How to build a motivated research community. The systems biologist Uri Alon has written a thought-provoking essay on how to build a motivated research group (1). He concludes that individuals need to be matched with projects appropriate for their talents and passions and that they require both autonomy and connectedness with other members of the group. The research group is but a microcosm of the entire research community. A healthy scientific environment is one in which the freedom to do what one wants is complemented by support and stimulation from a community. This will enhance productivity and innovation.

CONCLUDING REMARKS

The question is not whether science is failing, but rather, whether the current scientific enterprise is as healthy as it should be. Our answer is that, in many respects, it is not, and we point to the growing problem of retractions as a symptom. What we propose is nothing less than a comprehensive reform of scientific methodology and culture. However, the dialogue can begin by addressing specific problems in science. For example, some possible solutions to the problem of honest and dishonest retractions are listed in Table 2.

Science has been so successful over the past 3 centuries that it should now be sufficiently secure to return to its philosophical roots. Embracing this central field of the humanities could also help scientists to be better communicators in their engagement with the public at large. Science can become methodologically

more rigorous by adherence to the principles of epistemology and logic, which in turn could reduce the number of errors in scientific work. A better appreciation of ethics could also reduce the problem of dishonest retractions. An emphasis on probability and statistics in the graduate curriculum should be noncontroversial given its importance in experimental design and interpretation. The use of checklists is a simple pragmatic suggestion that could be expanded to incorporate principles of epistemology and logic.

We call for a cultural change in which scientists rediscover what drew them to science in the first place. In the end, it is not the number of high-impact-factor papers, prizes, or grant dollars that matters most, but the joys of discovery and the innumerable contributions both large and small that one makes through contact with other scientists. For many of us, old habits may be too deeply entrenched to change, but we can start to foster a more cooperative scientific culture in our trainees. It would be naive to believe that competition and personal ambition could or should be eliminated from science. Nevertheless, it is reasonable to ask whether the current scientific culture is allowing science to be as fruitful as it could be, particularly when the present system provides such potent incentives for behaviors that are detrimental to science and scientists. Only science can provide solutions to many of the most urgent needs of contemporary society. A conversation on how to reform science should begin now.

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