PERSPECTIVE

Rescuing US biomedical research from its systemic flaws

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Edited by Inder M. Verma, The Salk Institute for Biological Studies, La Jolla, CA, and approved March 18, 2014 (received for review March 7, 2014)

The long-held but erroneous assumption of never-ending rapid growth in biomedical science has created an unsustainable hypercompetitive system that is discouraging even the most outstanding prospective students from entering our profession—and making it difficult for seasoned investigators to produce their best work. This is a recipe for long-term decline, and the problems cannot be solved with simplistic approaches. Instead, it is time to confront the dangers at hand and rethink some fundamental features of the US biomedical research ecosystem.

graduate education | postdoctoral education | federal funding | peer review

By many measures, the biological and medical sciences are in a golden age. That fact, which we celebrate, makes it all the more difficult to acknowledge that the current system contains systemic flaws that are threatening its future. A central flaw is the long-held assumption that the enterprise will constantly expand. As a result, there is now a severe imbalance between the dollars available for research and the still-growing scientific community in the United States. This imbalance has created a hypercompetitive atmosphere in which scientific productivity is reduced and promising careers are threatened.

In retrospect, the strains have been building for some time, but it has been difficult to recognize them in the midst of so much success. During the last half century, biomedical scientists have discovered many of the fundamental principles that instruct cell behavior in both health and disease, providing a framework for exploring biological systems in great depth: the genetic code, the sequence and organization of many genomes, the cell's growth and division cycle, and the molecules that mediate cell signaling. Many diseases—infectious, hereditary, neoplastic, circulatory, and metabolic—are now approached and often prevented, controlled, or cured with measures based on these and other discoveries.

The American public rightly takes pride in this and has generously supported research efforts through the National Institutes of Health (NIH) and numerous other federal agencies, foundations, advocacy groups, and academic institutions. In return, the remarkable outpouring of innovative research from American laboratories—high-throughput DNA sequencing, sophisticated imaging, structural biology, designer chemistry, and computational biology—has led to impressive advances in medicine and fueled a vibrant pharmaceutical and biotechnology sector.

In the context of such progress, it is remarkable that even the most successful scientists and most promising trainees are increasingly pessimistic about the future of their chosen career. Based on extensive observations and discussions, we believe that these concerns are justified and that the biomedical research enterprise in the United States is on an unsustainable path. In this article, we describe how this situation arose and propose some possible remedies.

Source of the Dilemma

We believe that the root cause of the widespread malaise is a longstanding assumption that the biomedical research system in the United States will expand indefinitely at a substantial rate. We are now faced with the stark realization that this is not the case. Over the last decade, the expansion has stalled and even reversed.

The idea that the research enterprise would expand forever was adopted after World War II, as the numbers and sizes of universities grew to meet the economy's need for more graduates and as the tenets of Vannevar Bush's "Science: The Endless Frontier" encouraged the expansion of federal budgets for research (1). Growth persisted with the coming of age of the baby boom generation in the late 1960s and 1970s and a vibrant US economy.

However, eventually, beginning around 1990 and worsening after 2003, when a rapid doubling of the NIH budget ended, the demands for research dollars grew much faster than the supply. The demands were fueled in large part by incentives for institutional expansion, by the rapid growth of the scientific workforce, and by rising costs of research. Further slowdowns in federal funding, caused by the Great Recession of 2008 and by the budget sequestration that followed in 2013, have significantly exacerbated the problem. (Today, the resources available to the NIH are estimated to be at least 25% less in constant dollars than they were in 2003.) The consequences of this imbalance include dramatic declines in success rates for NIH grant applicants and diminished time for scientists to think and perform productive work.

The mismatch between supply and demand can be partly laid at the feet of the discipline's Malthusian traditions. The great majority of biomedical research is conducted by aspiring trainees: by graduate students and postdoctoral fellows. As a result, most successful biomedical scientists train far more scientists than are needed to replace him- or herself; in the aggregate, the training pipeline produces more scientists than relevant positions in academia, government, and the private sector are capable of absorbing. Consequently a growing number of PhDs are in jobs that do not take advantage of the taxpayers' investment in their lengthy education

Author contributions: B.A., M.W.K., S.T., and H.V. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

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(2). Fundamentally, the current system is in perpetual disequilibrium, because it will inevitably generate an ever-increasing supply of scientists vying for a finite set of research resources and employment opportunities. The resulting strains have diminished the attraction of our profession for many scientists—novice and experienced alike.

Damaging Effects of Hypercompetition

Competition in pursuit of experimental objectives has always been a part of the scientific enterprise, and it can have positive effects. However, hypercompetition for the resources and positions that are required to conduct science suppresses the creativity, cooperation, risk-taking, and original thinking required to make fundamental discoveries.

Now that the percentage of NIH grant applications that can be funded has fallen from around 30% into the low teens, biomedical scientists are spending far too much of their time writing and revising grant applications and far too little thinking about science and conducting experiments. The low success rates have induced conservative, short-term thinking in applicants, reviewers, and funders. The system now favors those who can guarantee results rather than those with potentially path-breaking ideas that, by definition, cannot promise success. Young investigators are discouraged from departing too far from their postdoctoral work, when they should instead be posing new questions and inventing new approaches. Seasoned investigators are inclined to stick to their tried-and-true formulas for success rather than explore new fields.

One manifestation of this shift to short-term thinking is the inflated value that is now accorded to studies that claim a close link to medical practice. Human biology has always been a central part of the US biomedical effort. However, only recently has the term "translational research" been widely, if unofficially, used as a criterion for evaluation. Overvaluing translational research is detracting from an equivalent appreciation of fundamental research of broad applicability, without obvious connections to medicine. Many surprising discoveries, powerful research tools, and important medical benefits have arisen from efforts to decipher complex biological phenomena in model organisms. In a climate that discourages such work by emphasizing short-term goals, scientific progress will inevitably be slowed, and revolutionary findings will be deferred (3).

Traditional standards for the practice of science are also threatened in this environment. Publishing scientific reports, especially in the most prestigious journals, has become increasingly difficult, as competition increases and reviewers and editors demand more and more from each paper. Long appendixes that contain the bulk of the experimental results have become the norm for many journals and accepted practice for most scientists. As competition for jobs and promotions increases, the inflated value given to publishing in a small number of so-called "high impact" journals has put pressure on authors to rush into print, cut corners, exaggerate their findings, and overstate the significance of their work. Such publication practices, abetted by the hypercompetitive grant system and job market, are changing the atmosphere in many laboratories in disturbing ways. The recent worrisome reports of substantial numbers of research publications whose results cannot be replicated are likely symptoms of today's highly pressured environment for research (4–6). If through sloppiness, error, or exaggeration, the scientific community loses the public's trust in the integrity of its work, it cannot expect to maintain public support for science.

Crippling Demands on a Scientist's Time

The development of original ideas that lead to important scientific discoveries takes time for thinking, reading, and talking with peers. Today, time for reflection is a disappearing luxury for the scientific community. In addition to writing and revising grant applications and papers, scientists now contend with expanding regulatory requirements and government reporting on issues such as animal welfare, radiation safety, and human subjects protection. Although these are important aspects of running a safe and ethically grounded laboratory, these administrative tasks are taking up an ever-increasing fraction of the day and present serious obstacles to concentration on the scientific mission itself.

Time pressures are also affecting the quality of peer review, an essential element of a healthy ecosystem for science. Investigators often lack the time to review manuscripts for journals, leaving these tasks to their students and fellows who may lack the experience needed to appreciate the broader context of the work and the provisional nature of truly original findings. Professional editors are increasingly serving in roles played in the past by working scientists and can undermine the enterprise when they base judgments about publication on newsworthiness rather than scientific quality.

The peer review of applications for research grants has also been affected. Historically, study sections that review applications were composed largely of highly respected leaders in the field, and there was widespread trust in the fairness of the system. Today it is less common for senior scientists to serve. Either they are not asked or, when asked, it is more difficult to persuade them to participate because of very low success rates, difficulties of choosing among highly meritorious proposals, and the perception that the quality of evaluation has declined.

Supporting the Next Generation of Scientists

There is a no more worrisome consequence of the hypercompetitive culture of biomedical science than the pall it is casting on early careers of graduate students, postdoctoral fellows, and young investigators. A recent study commissioned by NIH Director Francis Collins documented the rapid growth in the number of biomedical PhDs and postdoctoral fellows trained in the United States, driven most recently by the doubling of the NIH budget that ended a decade ago (2). As those trainees complete their studies, they have come face to face with slowdowns or contractions in the employment sectors—academia, government, and the pharmaceutical and biotech industries—that could and should benefit from their long years of training. This has led to an extended occupancy of training positions, coupled to greatly increased expectations from prospective employers for prior productivity.

Even after they have landed a research position in academia or research institutes, new investigators wait an average of 4–5 y to receive federal funding for their work compared with 1 y in 1980 (2). Two stark statistics tell much of the tale—the average age at which PhD recipients assume their first tenure-track job is 37 y, and they are approaching 42 y when they are awarded their first NIH grant. In 1980, 16% of NIH grant recipients were 36 y of age or younger; today that number is 3% (2). It is no surprise that extraordinarily well-trained and successful young scientists are opting out of academic science in greater and greater numbers; not because they find other opportunities so much more attractive, but because they are discouraged by the nature of their future life in academia.

From the early 1990s, every labor economist who has studied the pipeline for the biomedical workforce has proclaimed it to be broken (2, 7–12). However, little has been done to reform the system, primarily because it continues to benefit more established and hence more influential scientists and because it has undoubtedly produced great science. Economists point out that many labor markets experience expansions and contractions, but biomedical science does not respond to classic market forces. As the demographer

Michael Teitelbaum has observed (9), lower employment prospects for future scientists would normally be expected to lead to a decline in graduate school applicants, as well as to a contraction in the system.

In biomedical research, this does not happen, in part because of a large influx of foreign applicants (2) for whom the prospects in the United States are more attractive than what they face in their own countries, but also because the opportunities for discovering new knowledge and improving human health are inherently so appealing.

Perverse Incentives in Research Funding

The assumption that the biomedical research enterprise will expand continuously at a high rate has powerfully motivated the behavior of large academic medical centers (7–9). Salaries paid by grants are subject to indirect cost reimbursement, creating a strong incentive for universities to enlarge their faculties by seeking as much faculty salary support as possible on government grants. This has led to an enormous growth in "soft money" positions, with stagnation in the ranks of faculty who have institutional support. The government is also indirectly paying for the new buildings to house these scientists by allowing debt service on new construction to be included in its calculations of indirect cost recovery.

These are perverse incentives because they encourage grantee institutions to grow without making sufficient investments in their own faculty and facilities. As a result, thousands of US faculty members now compete intensely not only for research funds but also for their own salaries within a shrinking pool of dollars.

Recommendations for Change

To create a more sustainable enterprise—one that achieves the high goals to which both biomedical scientists and the public aspire—we propose several steps, some of which will need to be gradually implemented over a prolonged period (perhaps as long as 10 y).

Our broad objectives are threefold: (*i*) to advocate for predictable budgets for US funding agencies and for an altered composition of the research workforce, both with the aim of making the research environment sustainable; (*ii*) to rebalance the research portfolio by recognizing the inertia that favors large projects and by improving the peer review system so that more imaginative, long-term proposals are being funded and scientific careers can have a more stable course; and (*iii*) to encourage changes in governmental policies that now have the unintended consequence of promoting excessive, unsustainable growth of the US biomedical research enterprise.

Specific Recommendations

Planning for Predictable and Stable Funding of Science. In this paper, we focused on the structural aspects of the US biomedical enterprise that need attention in an era of limited resources rather than making the case for greater resources. Nevertheless, we strongly believe that increased funding would have great benefits in both the short and long run, that the remarkable opportunities in biomedical science justify enlarged budgets, and that vigorous arguments for such increases should be made. However, our current funding system has no built-in regulator, so budget increases are always rapidly absorbed and create a need for even greater increases.

In allocating federal funds for the research enterprise, greater emphasis should be placed on the predictability and stability of growth. We encourage Congressional appropriators and the executive branch to consider adding a 5-y projected fiscal plan to the current budgetary process. This plan would be updated each year, at the same time that annual appropriation bills are written. This modest addition to the present system, while not creating inflexible mandates, would acknowledge the need for long-term planning for measured growth of the nation's scientific enterprise.

Bringing the Biomedical Enterprise into Sustainable Equilibrium. The goal of the next set of recommendations is to gradually reduce the number of entrants into PhD training in biomedical science—producing a better alignment between the number of entrants and their future opportunities—and to alter the ratio of trainees to staff scientists in research groups. At the same time, we should do more to help transition outstanding young people with scientific training into a broad range of careers that can benefit from their abilities and education. Together those changes will lead to an enterprise that is both more flexible and sustainable.

Educating graduate students. For the last several decades, the numbers of graduate students pursuing careers in biomedical science have grown unchecked because trainees are overwhelmingly supported on research grants (2). In contrast, the number of students who rely on training grants and individual fellowships has remained constant for a long time.

To give federal agencies more control over the number of trainees and the quality of their training, we propose moving gradually to a system in which graduate students are supported with training grants and fellowships and not with research grants. Fellowships have the virtue of providing peer review of the student applicants, and training programs set high standards for selection of students and for the education they receive.

If this recommendation is adopted, it will be essential to change policies that now prohibit the funding of non-US citizens on training grants. Foreign students have contributed enormously to the vibrancy and success of US science, and their continuing contributions are critical to the future of science in the United States.

Broadening the career paths for young scientists. Graduate training in biomedical fields has historically functioned as an apprenticeship, in which students conduct original research with the expectation that they will replace their mentors. With the percentage of recent PhDs in academic positions falling to 20% (2), the training of graduate students needs to diversify to reflect the realities of the job market. A graduate education in the sciences produces individuals with broadly applicable skills in critical thinking and problem-solving, whose expertise could be invaluable in fields such as science policy and administration, the commerce of science, science writing, the law, and science education at all levels. Furthermore, recent surveys reveal that a substantial fraction of today's graduate students in the sciences are interested in pursuing nonresearch careers (13, 14). However, for the most part, neither the faculty nor the students are well enough informed about such careers. Nor are there clear pathways for entry. (One exception is the AAAS Science and Technology Fellowships, which for 40 y have allowed carefully selected scientists and engineers with advanced degrees to work in the US government in Washington, DC, for a year. Historically, approximately half of these Fellows have remained in policy positions, occupying critical positions that greatly benefit the nation. However, such opportunities number in the low hundreds each year, a small fraction of the 8,000 PhDs who graduate annually in the biological sciences alone.)

To make informed decisions, graduate students need opportunities to gain hands-on experience in appropriate career environments. We should aim for a future in which graduate students have opportunities to explore a variety of career paths, with only those seeking careers that demand additional research training taking up postdoctoral research positions. To that end, the NIH has recently announced a new program to encourage diversifying graduate education (15). Moreover, interdisciplinary MS degree programs that combine training in science with leadership, project management, teamwork, and communication skills match well with industry needs (11, 16) and should be expanded with federal support.

Training postdoctoral fellows. There are currently more than 40,000 postdoctoral fellows in the US biomedical research system, and the number has been increasing rapidly in recent years (2, 17). The position has become one in which young scientists spend a significant fraction of their most productive years while being paid salaries that are quite low considering their extensive education. On the one hand, these fellows are pursuing science full time without the distractions that often come with more permanent jobs. On the other hand, for most of them, the holding pattern postpones the time when they are able to explore their own ideas in independent careers.

We offer two suggestions intended to reduce the numbers of postdoctoral fellows and promote a more rapid transit through postdoctoral training:

i) Increase the compensation for all federally funded postdoctoral fellows, regardless of grant mechanisms. This would need to be done gradually over time, with the goal of reaching the compensation levels for staff scientists. This proposal would reduce the total number of fellows that the system could support and eliminate cost considerations when a laboratory head weighs the benefits of choosing between a postdoctoral fellow and a staff scientist (see next section).

ii) Limit the total number of years that a postdoctoral fellow may be supported by federal research grants. Beyond this limit, salaries would be required to rise to that of research staff scientists, as is already the case at some institutions.

Using staff scientists. Historically, staff scientists—usually MSc or PhD recipients who are no longer trainees—have been used sparingly in US research laboratories. Resistance to staff scientists has focused on the greater cost of salaries relative to graduate students and fellows and on the belief that permanent staff may be less creative and hardworking. These arguments ignore the fact that beginning graduate students and fellows are also costly because they often require considerable time to become highly productive.

We believe that staff scientists can and should play increasingly important roles in the biomedical workforce. Within individual laboratories, they can oversee the day-to-day work of the laboratory, taking on some of the administrative burdens that now tend to fall on the shoulders of the laboratory head; orient and train new members of the laboratory; manage large equipment and common facilities; and perform scientific projects independently or in collaboration with other members of the group. Within institutions, they can serve as leaders and technical experts in core laboratories serving multiple investigators and even multiple institutions.

We recommend increasing the ratio of permanent staff positions to trainee positions, both in individual laboratories and in core facilities that serve multiple laboratories. To succeed, universities will need employment policies that provide these individuals with attractive career paths, short of guaranteed employment. Also, granting agencies will need to recognize the value of longer-serving laboratory members. If adopted, this change would help to bring the system closer to equilibrium. There is precedent for such a policy in the intramural NIH research program, which employs many well-trained MSc and PhD graduates as staff scientists to conduct research.

Two of the likely consequences of these changes in graduate and postdoctoral training and employment of staff scientists will be an increase in the unit cost of research and a reduction in the average size of laboratories. We believe that the significant benefits—including brighter prospects for trainees, less pressure to obtain multiple grants to sustain a group's financial viability, increased incentives to collaborate, and more time for investigators to focus on their science—substantially outweigh the limitations.

Grant-Making That Improves Scientific Productivity. To increase support for the best science through federal grants, we recommend that funding agencies take several steps to improve the criteria and mechanisms used to evaluate candidates and their proposals. We also recommend a shift in the kinds of research grants offered. Also, to ensure the highest standards of excellence, we propose that objective outside reviews be commissioned at regular intervals to monitor both the value of established programs and the quality of agency implementations.

Improving the goals and mechanisms for scientific grants. In awarding research grants, recognition of originality is critical for achieving the goal of making scientific advances that promise long-term benefits to society. Providing resources to those scientists who are most likely to make important contributions over the course of their career is essential for the optimal use of research funds.

i) We recommend wider use of grant mechanisms that provide more stable support for outstanding investigators at various career stages, focusing as much (or more) on the overall quality of their science as on their proposed projects. The success of investigators supported by the Howard Hughes Medical Institute (18), which takes this approach, suggests that, with very careful screening by the appropriate reviewers (who must be outstanding scientists themselves), this can be an especially effective way to support and encourage excellent science. This approach is under active discussion among NIH leadership (6).

ii) Inertia and financial dependency favor continuing large research programs, so sunset provisions should be built into all new programs and orchestrated team efforts. To combat the tendency for fields to become parochial, agencies should develop funding mechanisms that encourage the growth of new fields, both by direct support for new science and by a rigorous regular evaluation of existing programs.

iii) Science agencies should significantly increase the numbers and kinds of awards that emphasize originality and risk-taking, especially in new areas of science, without requiring extensive preliminary results. This is particularly critical for beginning independent investigators, who should be encouraged to depart from the work that they carried out as trainees to investigate unexplored problems in new ways. Programs like the NIH Director's New Innovator Award (19) have been designed for this purpose, but there are far too few such awards to affect the way that young scientists currently plan their careers

iv) Agencies should also be sensitive to the total numbers of dollars granted to individual laboratories, recognizing that—although different research activities have different costs—at some point, returns per dollar diminish. For that reason, we applaud the recent decision by the NIH to examine grant portfolios carefully before increasing direct research support for a laboratory beyond one million dollars per year.

Improving evaluation criteria. The peer review panels that evaluate grant proposals require appropriate criteria to guide their work. To this end, we recommend the following:

i) The tools used to judge past performance should be sharpened to identify the strongest candidates for support. The qualitative aspects of each candidate's major scientific achievements should receive more emphasis than the numbers and venues of publications. Evaluation criteria should also put a higher priority on the quality, novelty, and long-term objectives of the project than on technical details.

ii) Review guidelines should be appropriately adjusted for young scientists to promote the funding of thoughtful proposals that reveal ingenuity and promise findings with potentially broad implications. The criteria used to evaluate the NIH Director's New Innovator Award set useful standards.

Strengthening grant review panels. Expert peer review depends on recruiting the most qualified scientists to carry it out.

i) The quality of review groups should be enhanced by taking advantage of the full range of talent in the scientific community. All current grant holders should be expected to serve on such groups if asked and not just once in a career. In addition, federal agencies should diminish the requirement for geographical representation that now limits the choice of panel members. These changes will allow funding agencies to recruit the best scientists of all ages and from all locations to perform this critical service for the scientific community.

ii) Those who plan and assemble review groups should broaden the range of scientific problems judged by each group and include a diversity of fields on each panel. Senior scientists with a wide appreciation for different fields can play important roles by counteracting the tendency of specialists to overvalue work in their own field. When review bodies become too insular, they risk becoming special interest groups for their subfield and may fail to encourage support of the most imaginative science.

Evaluating programs, policies, and their implementation. Even the best policies and processes—whether applied to scientific programs or to the review of applications—require periodic arms-length evaluations, especially in times of fiscal constraint. We urge agencies to continue and expand such evaluations, to make the findings publicly accessible, and to recognize the advantages of having them performed by groups that are independent of the agency being examined. The questions asked should include whether a particular program or policy is being well executed, how it might be improved, what types of data are needed to guide evaluation, and whether the goals might be better met in other ways.

Addressing Policies That Undermine Sustainability. Federal policies regarding indirect cost recovery have the advantage of providing support for facilities and administrative costs only after a merit-based peer review of research proposals. However, they have also enabled academic medical centers and other institutions to expand their faculties and facilities without making corresponding investments of their own, generating some of the perverse incentives discussed earlier.

We recommend that the US government develop a plan to revise these practices gradually over the next decade while providing a discrete timetable. Targets of policy change should include the full reimbursement to amortize loans for new buildings, the payment of indirect costs on faculty salaries, and the provision that allows 100% of faculty salaries to be supported on research grants.

Conclusion and Future Plans

The US research community cannot continue to ignore the warning signs of a system under great stress and at risk for incipient decline. We believe that the American public will continue its strong support for biomedical research and that larger budgets are possible, defensible, and desirable. However, because of structural flaws in the system, such increases can only partially ameliorate a worsening problem.

We are confident that a research system as productive and democratic as ours can correct its vulnerabilities. Some fundamental changes are required because the system cannot expand indefinitely along the current trajectory. The necessary changes are multiple and need to be made in a comprehensive fashion, not piecemeal. Such changes are likely to be difficult and are potentially damaging in the short run; hence, they need to be made with extreme care. Nevertheless, the changes need to begin immediately, because the situation we have described has grown significantly worse in just the last few years. Widespread engagement with these changes is necessary, beginning with immediate debate, strong advocacy for change, and action by individual scientists, the funding agencies, academic institutions, and other entities that control and pay for the conduct of science.

The future world of biomedical science that we envision is not smaller in human talent or financial support or less ambitious in its goals to discover and apply biological principles. Ideally, it will continue to grow. However, it would balance supply and demand in a sustainable fashion, adjust the pipeline that delivers new scientists, moderate the size of laboratories that are now difficult to fund, and restore an environment in which talented trainees and scientists can do their best work.

Our immediate goal has been to stimulate debate of the issues that concern us and the changes we propose. The task cannot be left to a self-appointed subset of senior scientists like ourselves or to the leaders of the NIH who are known to be considering many of these same problems (6). We therefore encourage academic institutions, scientific societies, funding organizations, and other interested parties to organize discussions, national and regional, with a wide range of relevant constituencies.

Some discussions of this type are already planned (20). However, mere discussion will not suffice. Critical action is needed on several fronts by many parties to reform the enterprise. No less than the future vitality of US biomedical science is at stake.

ACKNOWLEDGMENTS. We thank Stefano Bertuzzi, Henry Bourne, Francis Collins, Tony Fauci, Harvey Fineberg, Michael Greenberg, Rush Holt, Tyler Jacks, Elliot Meyerowitz, Tim Mitchison, Dinah Singer, Ron Vale, Rebecca Ward, and Eric Wieschaus for helpful comments on earlier drafts of this manuscript. The views expressed here are personal opinions of the four authors and do not necessarily represent the positions of the academic or governmental organizations for which we work.

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