RESEARCH FUNDING

Structural Disequilibria in Biomedical Research

Many current problems for U.S. biomedical research can be attributed to fundamental structural elements of the NIH funding system.

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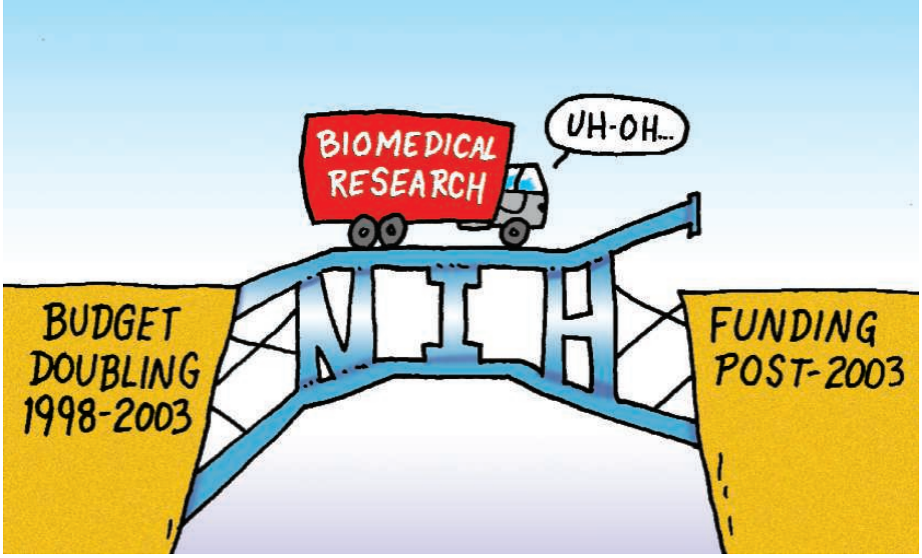
Many are calling for large increases in the budget for the National Institutes of Health (NIH) to address the damaging effects on biomedical research resulting from recent flat funding levels. Yet politicians respond with skepticism, as the NIH budget is already very large and was doubled over the 5-year period 1998 to 2003 (*1*). What is often left unsaid is that the fundamental problems are structural in nature—biomedical research funding is both erratic and subject to positive-feedback loops (*2*, *3*) that together drive the system ineluctably toward damaging instability. It may be possible to create broad political support for large annual NIH funding increases into the indefinite future. But if not, objective analyses of systemic instabilities, followed by incremental adjustments, would be strongly in the interest of maintaining the quality of U.S. biomedical research.

Concerns about crises and discouragement resulting from flat funding levels for the National Institutes of Health (NIH) over the last 5 years (*4*) are valid and widely shared. Special worries are being expressed by NIH leadership about "the impact of this difficult situation on junior scientists, and on the ability of established investigators to maintain their laboratories" (*5*).



Crisis Despite the Doubling

NIH research funding is more difficult to get now than it was before the NIH budget doubled, especially for early-career researchers. In 1998, about 32% of NIH competing Research Project Grant (RPG) applications were successful; by 2007 the comparable success rate had declined to 21% (*6*). The percentage of NIH awardees aged 40 or under, already less than 23% in 1998, declined to just over 15% by 2005 (*7*).

Some of the reasons are well understood: First, adjusting for inflation, the value of the NIH budget has declined by about 13% from its peak in 2003 (*8*). Second, the rapid annual increases from 1998 to 2003 were followed by 5 years of small annual decreases (*7*). The inflation-adjusted budget today is not much higher than it would have been had smaller NIH budget increases, common before 1998, been sustained from 1998 to 2008 (*9–11*). Third, the number of applications for new and competing NIH research grants nearly doubled, from about 24,000 in 1998 to more than 47,000 in 2007. This was due primarily to a near-doubling of grant applicants, many of whom were trained under NIH research funding—from nearly 20,000 in 1998 to nearly 39,000 in 2007. In addition, the number of applications per applicant also increased somewhat (*12*).

Problems Fundamentally Structural

What is too often left unsaid is that these trends are fundamentally structural. This makes sustainable solutions exceptionally difficult to find. In the absence of careful adjustments to the current structure, these problems are unlikely to be solved by increases in NIH funding over the coming decades.

Symptoms of structural malaise were amply reported well before the NIH budget doubling began in 1998 (*13*). Indeed, the 1998 to 2003 budget doubling was intended in part to mitigate some of these symptoms. Rapid increases in research funding initially did have such effects, but only temporarily. A 2002 *Science* article (*10*) was prescient in concluding that biomedical research had become dependent on at least 6% annual budget increases. As if on cue, damaging crises emerged when the increases from 2003 onward proved to be smaller than 6%.

The harsh impacts of these structural problems now are being felt by research institutions and individual biomedical researchers. Yet, none of these institutions or individuals has it within their power to modify the key structural elements of the system in which they find themselves. These can be addressed only at the level of policy and administrative practice by the Congress and NIH itself.

Positive Feedback in the System

For NIH, more research funding does produce increased research output, as intended. Yet, because the system as currently structured employs graduate and postdoctoral research assistants to do much of the laboratory work, increased research funding also produces (after a multiyear lag) additional Ph.D.-level applicants for NIH grants. No effective mechanisms are in place to align these increased numbers with expanding career opportunities (*14*).

In theory, the resulting chilly job markets for recent biomedical Ph.D.'s should generate negative feedback that would tend toward more stable equilibria. In a closed system, and one with full information available to prospec-

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tive graduate students, some fraction of undergraduates who might otherwise consider becoming Ph.D. students and postdocs would correctly perceive the difficult career paths and would pursue other options.

In practice, however, the system is not closed. Given increased research funding, additional graduate students and postdocs can be readily recruited from large potential pools in countries with fewer such opportunities—precisely what took place as the NIH budget was rapidly doubled (*15*). Nor is there anything even approximating full information about career prospects available to prospective entrants, whether domestic or foreign.

The employment and career implications of such a positive-feedback structure were modeled during the 1990s (*16*). One simulation (for mathematics) assumed a 2% real increase in annual research funding for 5 years, followed by stabilization. The result was short-term improvement in employment prospects for recent mathematics Ph.D.'s, followed by deteriorating career prospects that ended up worse than before the funding increases began, even with the assumption of a permanent 10% increase in real research funding (*16*).

The 1998 to 2003 budget doubling resulted in other kinds of positive feedback. In particular, it offered incentives for expansion by U.S. academic medical centers, many of which encouraged their faculty to recover more of their compensation from external sources (*17*). Academic biomedical research facilities also were expanded, in expectation of overhead payments from increased research grant funding: Facilities investments rose from a predoubling average of about $348 million per year to $760 million per year during 1998 to 2003, to $1.1 billion per year from 2003 to 2007 (all figures in constant 1990 dollars) (*18*). Much of the expansion capital apparently was borrowed, in part because federal rules allow inclusion of debt service in NIH grant overhead calculations while excluding overhead claims for the imputed value of equity. In financial terms, one might say that the system became more highly leveraged, rendering it more vulnerable to unanticipated downward deflection of the increase in federal research funds.

What Can and Should Be Done?

Strong lobbying for increases in the NIH budget is under way. Yet, if current and prospective federal fiscal constraints preclude sustained budget increases of 6% or more, the system needs to be guided toward more stable equilibria. More stability would be in the interest of research institutions and established researchers, would facilitate medical progress and, over time, might make biomedical research careers more attractive to U.S. students.

This is, of course, far easier said than done. The current system has evolved over decades, has produced outstanding research and valuable returns to the world, and has served the interests of research institutions and senior researchers.

NIH's Office of Extramural Research could help greatly by convening a strong advisory committee of biomedical researchers and analysts of the NIH research and training system. Its charge would be to identify elements of the current structure that render it prone to instability and to suggest prudent sustainability strategies that would reduce the system's vulnerability to destructive booms, busts, and funding crises. Adjustments warranting assessment include the following:

» Ways to attenuate the currently strong positive feedback between research funding and financial support for additional graduate students and postdocs,

More support for NIH's Ph.D. "training" functions (*19*), with proportionately less for graduate students and postdocs financed under NIH research grants—long discussed, but not yet implemented (*20*).

» New mechanisms to better align the Ph.D.-postdoc systems with demand in the labor market for their graduates, e.g.,

a. Providing more current data on biomedical labor market conditions to prospective domestic and foreign entrants;

b. Allowing increases in NIH research funds to support career-path biomedical research positions (e.g., professional staff scientist positions) at research institutions rather than depending on temporary students and/or trainees.

c. Reconsidering the goals and career impacts of unlimited numbers of temporary visas for Ph.D. students and postdocs financed by NIH research funding.

» Assessment of possible mechanisms for NIH funding increases that would be less destabilizing than the budget doubling, e.g.,

a. Avoiding rapid acceleration and deceleration of NIH budget increases, aiming instead at sustained increases in excess of inflation and keyed to gross domestic product growth (*11*).

b. Limiting the percentage of a faculty members' salary that can be paid by NIH research grants (*17*);

c. Adjusting overhead rules regarding debt service for research facilities;

d. Designing creative financial mechanisms to stabilize or buffer erratic annual federal budget decisions. One suggestion worthy of analysis is an extra "stabilization overhead" that grantee institutions would reserve to provide bridge funding for biomedical researchers facing funding gaps (*11*).

References and Notes

1. The current FY 2008 budget for NIH is $29.457 billion, up by about $2.2 billion and 8% from the 2003 level; http://officeofbudget.od.nih.gov/ui/2008/Summary%20of%20FY%202009%20BudgetPress%20Release.pdf.
2. The concepts of positive and negative feedback are commonly associated with the work of Norbert Weiner (*3*).
3. Norbert Weiner, *Cybernetics: Or the Control and Communication in the Animal and the Machine* (MIT Press, Cambridge, MA, 1948).
4. "A broken pipeline? Flat funding of NIH puts a generation of science at risk," from a collaborative consisting of Brown University, Duke University, Harvard University, Ohio State University, Partners Healthcare, University of California at Los Angeles, and Vanderbilt University, March 2008; www.BrokenPipeline.org.
5. E. A. Zerhouni, *Science* **314**, 1088 (2006).
6. National Institutes of Health, "Success rates," at *NIH External Data Book 2007* (NIH, Bethesda, MD, 2007); slide 25 http://grants2.nih.gov/grants/award/Research_Training_Investment/Research_Training_Investment.cfm.
7. National Institutes of Health, Office of External Research, presentation to Association of Independent Research Institutes, Phoenix, AZ, 3 October 2006, slide 25; http://grants.nih.gov/grants/award/trends/airi2006.ppt.
8. The real value of the budget was based on the Biomedical Research and Development Price Index (BRDPI), the standard price index for biomedical research. Both increases and declines are "real," i.e., adjusted for biomedical cost inflation using the BRDPI. See http:// officeofbudget.od.nih.gov/UI/GDP_FromGenBudget.htm. The BRDPI measure has a number of acknowledged imperfections, e.g., that it adjusts for the costs of research inputs but not for the cost of outputs.
9. S. J. Heinig, J. Y. Krakower, H. B. Dickler, D. Korn, *N. Engl. J. Med.* **357**, 1042, fig. 1 (2007).
10. D. Korn *et al*., *Science* **296**, 1401 (2002).
11. R. Freeman, J. Van Reenen, "What if Congress doubled R&D spending on the physical sciences?" presented at the National Bureau of Economic Research Conference on *Innovation Policy and the Economy*, Washington, DC, 15 April 2008.
12. NIH, "Research project grants," at *NIH External Data Book 2007*, http://grants2.nih.gov/grants/award/Research_Training_Investment/Research_Training_Investment.cfm.
13. National Research Council, *Trends in the Early Careers of Life Scientists* (National Academy Press, Washington, DC, 1998).
14. Some see solutions in special funding programs focused on young investigators. While these may have a place, they cannot preempt negative countermessages conveyed by career crises being faced by more senior researchers.
15. National Science Board (NSB), *Science and Engineering Indicators 2008* (NSB 08-01; NSB 08-01A, National Science Foundation, Arlington, VA, 2008), figs. 2-12 and 2-32.
16. C. A. Goldman, W. E. Massy, *The PhD Factory: Training and Employment of Science and Engineering Doctorates in the United States* (Anker, Bolton, MA, 2000).
17. S. A. Bunton, W. T. Mallon, *Acad. Med.* **82**, 282 (2007).
18. S. J. Heinig, J. Y. Krakower, H. B. Dickler, D. Korn, *N. Engl. J. Med.* **357**, 1042 (2007).
19. Under the Ruth L. Kirschstein National Research Service Award program.
20. National Research Council, *Addressing the Nation's Changing Needs for Biomedical and Behavioral Scientists* (National Academy Press, Washington, DC, 2000).

10.1126/science.1160272