NIH Plans Bioengineering Initiative

The National Institutes of Health, the bastion of hypothesis-driven research, plans to increase its support for an engineering approach to solving biomedical problems

There's a new buzzword these days on the National Institutes of Health (NIH) campus in Bethesda, Maryland: "bioengineering." It's the term NIH leaders are using as they promise to focus more attention on technology in 1999, a departure for the government's biggest basic science agency.

NIH director Harold Varmus and other NIH officials held a symposium in February to identify engineering ideas worth supporting, and over the next few months they will be trumpeting a new drive to accelerate bioengineering research. NIH's plans are still at a preliminary stage, but the effort will span a broad area, from using engineering principles to help decipher the intricacies of cell signaling to developing new imaging technologies (see sidebar). Varmus and other top NIH brass say the goal is to bring together engineers, computer scientists, mathematicians, physicists, and biologists to work on biological problems that are becoming increasingly multidisciplinary in nature. "Biology is not just for biologists," Varmus said earlier this year. Wendy Baldwin, deputy director for extramural research, who chairs a special NIH-wide committee charged with coordinating bioengineering research, adds: "There's an awareness that this is a really ripe area."

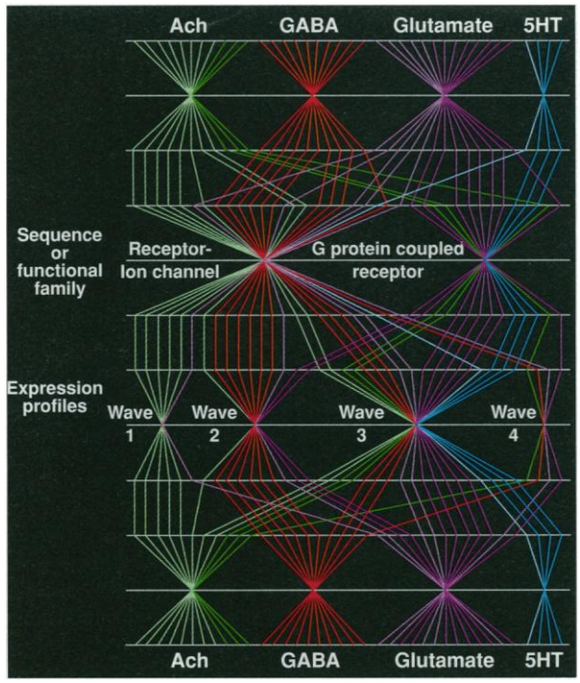
There's also an awareness in Bethesda that this is an area with a lot of political thrust behind it. Senator Bill Frist (R–TN), a former heart surgeon who chairs a subcommittee that oversees NIH, has proposed establishing a new center for bioengineering at NIH. Senior academic engineers, who complain that most NIH officials and peer-review study sections don't understand them, are also pressing NIH to give bioengineering a higher profile—and even to create a bioengineering institute.

Many bioengineers seem to believe, however, that NIH is offering them more buzz than honey. "To a large extent, NIH really hasn't been responsive," charges Robert Nerem, director of the Parker H. Petit Institute for Bioengineering and Bioscience at the Georgia Institute of Technology in Atlanta. Nerem chaired a consultants' group that in 1995 urged the creation of "a central focus for basic bioengineering research ... at the highest level" at NIH. But "we're still, as a community, waiting to see what NIH is going to do," Nerem says. This summer, NIH will begin to show its hand.

Growth spurt

"The field already has started to grow at a greater rate than the overall NIH budget," Varmus says, "and I see that continuing for a while." In fact, Baldwin says, NIH funding of bioengineering-related research projects, including biomaterials, prosthetic devices, and artificial organs, jumped 37% between fiscal years 1993 and 1996, to a total of $417 million in FY 1996, the latest year for which figures are available. Every institute and center supports some applied work. More than half of NIH's often-overlooked Small Business Innovation Research and Small Business Technology Transfer grants—which are expected to total more than $260 million this fiscal year—fund bioengineering projects.

NIH's first concrete step in the new initiative will be the imminent release of a report summing up the 27 to 28 February symposium on bioengineering that gathered several hundred researchers on the NIH campus and identified more than 70 fruitful areas for funding. (It will be posted at www.nih.gov/grants/becon/becon.htm) "We have to lay out a rich array of things that highlight the fact that we really are receptive to these grant applications, that we really do have a plan for how we're going to peer review them, and that the institutes welcome them," Baldwin says. Then, Baldwin's interinstitute committee—known as the Bioengineering Consortium (BECON)—will try to identify one or two research areas for more specific program announcements, allocating healthy funding for push-the-envelope collaborations in which biologists and engineers join hands.



R. SOMOGYI / NIH

Bioengineer's map. An illustration of shifting waves of neurotransmitter receptor expression in a rat spinal cord, showing stages in development from top to bottom.

No decision has been made yet on which research areas to highlight. Nor has a solution been found for the peer-review problem that bioengineers have long complained about. They say that hypothesis-driven scientists on NIH study sections are rarely wowed by hardware-development projects, which leads to low success rates in the funding competition. "A serious effort" to put more bioengineers on study sections "could actually go a long way toward addressing the complaints people have about the system," says Martha Gray, co-director of the Harvard–Massachusetts Institute of Technology (MIT) Division of Health Sciences and Technology in Cambridge, Massachusetts.

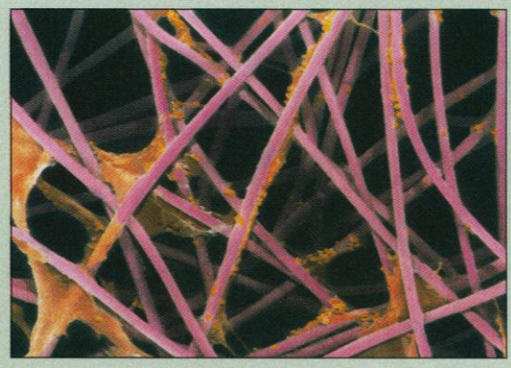
NIH officials acknowledge that the problem exists and have begun internal discussions on how to fix it. Finally, Baldwin says no funding is likely to flow under the new program announcements until late next year, because she wants to give researchers several months to plan projects and work out collaborations. NIH will also need several months to peer review them. Says Baldwin: "We don't want people just to pull out of the desk drawer that application that didn't get funded" and resubmit it.

NIH funding will be flowing at an increased rate this year for existing programs, however. The National Institute of General Medical Sciences (NIGMS), for example, is inviting researchers with current grants to apply for supplemental funding to expand their research by building collaborations with "physicists, engineers, mathematicians, and other experts with quantitative skills" to help them analyze

Biology by Design: From Software to Skin

Because bioengineering overlaps virtually every field of biological research, bioengineers' views of which research areas are the most promising might be expected to be all over the lot. But bioengineers and officials at the National Institutes of Health (NIH) consistently named three areas as the most significant: computational science (including bioinformatics), imaging, and tissue engineering. They also seem likely to get attention in NIH's new bioengineering initiative.

Computing. As the Human Genome Project churns out more and more gene sequences and the spotlight turns to functional genomics—how genes are turned on and off, how proteins interact—researchers will need more than diagrams in lab notebooks to help them understand these intricate systems. "The complexities of protein-protein interactions have now reached the point where most of us are flummoxed about the best way to be asking questions," says NIH director Harold Varmus. But if computing is to fulfill its promise, data have to be presented in a consistent format that researchers can understand readily, systems analysts can manipulate, and databases can exchange.



D. MOONEY / PHOTO RESEARCHERS

Cultured collagen. New techniques are being used to engineer human tissue.

Imaging. "We need cutting-edge technologies, imaging technologies, that help us get information as close to the molecular level as possible," says Judith Vaitukaitis, director of NIH's National Center for Research Resources. "We're far from that currently." A panel at a 27 to 28 February NIH symposium on bioengineering said that among other research goals, new approaches are needed to improve three-dimensional imaging in the size range between x-ray crystallography and conventional microscopy—as well as to track the fourth dimension, movement over time.

Tissue engineering. "From biology we've learned a lot about the molecular regulation of cell behavior, and now engineers are figuring out ways to design that sort of molecular regulation into ... polymeric materials," says Douglas Lauffenburger, director of the Massachusetts Institute of Technology's Center for Biomedical Engineering. Possible applications range from gene therapy (embedding gene sequences in microcapsules designed to enter specific cells) to artificial organs. At the University of Washington, Seattle, researchers are trying to develop new materials to thwart the body's protective response of encapsulating foreign objects. "The proposed answer is to create a surface on the foreign material which is in fact biological and appears to be biological and is recognized as such by the surrounding tissue," says Provost Lee Huntsman. This work hints at a way to build artificial organs. "If you could overcome the encapsulation reaction," Huntsman says, "who knows what might be possible?" –B.A.

complex biological systems. NIGMS also expects soon to issue program announcements aimed at spurring collaborations in the areas of complex biological processes and the genetic architecture of complex traits.

"Understanding complex systems is something that engineers are trained to do," says NIGMS director Marvin Cassman. An example of the complex kind of data that is already taxing the system was presented last month at a meeting on functional genomics in Boston by developmental biologist Roland Somogyi, a former NIH staffer who now heads up neurobiology at Incyte Pharmaceuticals Inc. of Palo Alto, California. Somogyi and his NIH team have been studying genes that control the growth of the rat's central nervous system (see image on p. 1516). Somogyi's computer displays, which illustrate genes interacting over time, can be viewed on NIH's Web site (rsb.info.nih.gov/mol-physiol/homepage.html#SlidePresentations). Such a system, says Cassman, is "not a pathway, it's a network. It's a complex, interacting network of proteins, ligands, receptors. I think understanding that is a bioengineering problem—or at least, bioengineering skills could be applied to understanding that."

The National Center for Research Resources (NCRR) also is in the bioengineering game in a big way. NCRR, which received the highest percentage increase of any NIH institute or center in the Administration's proposed 1999 budget, plans to spend at least $35 million next year on shared instrumentation grants to groups of NIH-supported researchers who get together to buy high-end research devices (compared with $28 million this year). It also plans to increase its nearly $1.5 million in new technology-development pilot projects or proof-of-principle grants next year—perhaps dramatically, if Congress significantly increases NIH's appropriation.

NIH's growing enthusiasm for bioengineering follows a trail blazed by the 23-year-old Whitaker Foundation in Rosslyn, Virginia, which awarded $41 million in bioengineering research grants last year. Whitaker is now emphasizing efforts to foster new academic bioengineering programs—and it intends to spend down its endowment of more than $450 million over the next 8 years. That will produce a lot more bioengineering programs, which will turn out a lot more bioengineers, who will be writing a lot more NIH grant applications.

The academic production line for bioengineers is, in fact, already humming. Bioengineering is the fastest growing specialty at engineering schools that offer such programs, and the "bio" side is getting more and more attention in the curriculum, according to the heads of several bioengineering departments. Moreover, "a substantial portion" of students attracted to bioengineering "are the very best, the most talented" of their class, says Roger Barr, head of the bioengineering department at Duke University. NIH, too, is accelerating its bioengineering training. Varmus points to a new agreement with the National Science Foundation that will bring NSF-funded engineering scientists to the NIH campus for collaborative training and research efforts. NIGMS plans new efforts to promote its predoctoral training programs for bioengineering students and is about to launch postdoctoral bioengineering fellowships and workshops to train biologists in computational science and statistics.

Bioengineering dreams

Will all this satisfy bioengineers who, like Georgia Tech's Nerem, believe that NIH has been slighting their discipline for years? Probably not.

"A large fraction of our community" favors the creation of a bioengineering institute,

says Murray Sachs, chair of the bioengineering department at The Johns Hopkins University in Baltimore. Barr says NIH has supported "a lot of good [bioengineering] work," but because the individual institutes are organized by disease and organ systems, "they haven't found a way to support bioengineering projects in their own right."

Support for a bioengineering institute isn't unanimous, however. Sachs says he is "of mixed mind" because of the possibility that the disease-oriented institutes might reduce their bioengineering support. "I would not want my own research [on the neurophysiology of hearing] anywhere but in the deafness institute," he says. Even more firmly opposed to creating a new fiefdom is Douglas Lauffenburger, director of MIT's Center for Biomedical Engineering. He says a separate institute would take the field a step in the wrong direction. What's needed instead, he says, is "to bring engineering and fundamental biology into more intimate contact and collaboration. That's where the advances will come from." And the place to forge such collaboration, he adds, is in the existing NIH structure.

Senator Frist, chair of the Public Health and Safety Subcommittee of the Senate Labor and Human Resources Committee, believes bioengineering should have a home of its own at NIH. Frist, a former NIH grant recipient, last year introduced legislation to create a National Center for Bioengineering Research within the National Heart, Lung, and Blood Institute. He plans to include the idea in an overall NIH Reauthorization bill this summer—although passage this year is doubtful.

Varmus rejects the idea of a separate institute or center: "I'm always a little concerned about ghettoizing an area by institutionalizing it." Noting that every institute has a stake in bioengineering, he adds, "You run a risk if you say we're going to put bioengineering in one office or center."

Nerem retorts that by that rationale, NIH should scrap NIGMS, because every NIH institute also does basic research. In fact, Nerem contends that everything NIH has been doing to highlight bioengineering—such as the creation of BECON and the "flag-waving" of the February symposium—is simply a response to pressure from Frist: "My gut-level feeling is that if Frist stopped pushing, everything would grind to a halt."

The big question, of course, is how much money is NIH willing to put behind its bioengineering thrust. It's a question Varmus won't answer—at least not precisely. "I never try to predetermine this," he says. The best way to proceed "is to bring a lot of forward-seeing people together, let them propose some ideas, test some of them out with pilot grants, and see what's productive," says Varmus. "But I do think we're prepared to place more emphasis in this area."

Frist, Nerem, and other supporters of bioengineering will be watching NIH closely over the next year to see what happens.

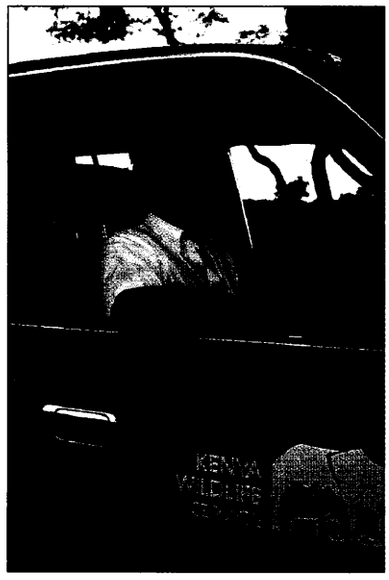
–Bruce Agnew

Bruce Agnew is a writer in Bethesda, Maryland.

CONSERVATION

Ousted Kenya Parks Head Gets Job Back

David Western, the conservation biologist who was sacked on 21 May as head of the Kenya Wildlife Service (KWS), was reinstated 6 days later for a 9-month term by Kenya President Daniel arap Moi. "Exhausted" by his roller-coaster ride in Kenyan politics, Western says he now hopes to be able to complete the restructuring of the cash-strapped agency, which runs Kenya's national parks and other protected areas. He believes he was dismissed in large part for refusing to allow mining concessions on park lands, so he sees a positive side to the week of turmoil: His reinstatement "sends a very clear message that KWS lands are not up for grabs."



W. STONE / GAMMA LIAISON

This "sends a very clear message that KWS lands are not up for grabs."

—David Western

Western, who is highly regarded by the international conservation community, took over KWS in 1994 from anthropologist Richard Leakey. Although Leakey had focused on rehabilitating the parks and guarding them from poaching, Western has also been trying to involve communities outside the park system in conservation. But he has faced a financial crisis as tourist revenues—the backbone of KWS support—dropped drastically owing to bad weather and political strife (*Science*, 24 April, p. 510). Things "have been really extremely tough" over the past year, he says.

In a telephone interview with *Science* last week, Western said that in recent months he had sensed that his support within the government was waning because he was resisting pressure by officials to open up some parks to mining operations. He had also been taking a drubbing from opponents in Kenya, including Leakey, who complained that he was a poor manager and criticized his community conservation strategy. Western says these criticisms may have given his opponents a pretext for ousting him: "I think what has happened is this rather futile debate [over whether conservation efforts should focus on the parks or outside them] ... was simply used as an excuse for other political interests to take over."

The reaction to Western's dismissal (*Science*, 29 May, p. 1335) in Kenya and abroad was swift and vehement. Fearing for the future of Kenya's parks and wildlife, conservationists wrote letters (see p. 1507) and the European Union (EU) froze some $3 million in operating funds that it had just approved for KWS.

Western says that he requested a 27 May meeting with the president to clarify what was happening at KWS, and discovered at the meeting that Moi "wasn't fully au fait with events." He says Moi was particularly concerned that the civil service had violated its own procedures by breaking Western's contract, which had been renewed early this year and reaffirmed on 20 April at a KWS board meeting, but—ominously—had never been recorded in the government *Gazette*. Western also says Moi recognized the toll that the ouster could take on tourism and international support. Indeed, he says, in the fight to keep mining concessions out of the parks, "the biggest supporter I had in this had actually been the president himself."

Western is now trying to "consolidate the direction" of KWS. The agency is reducing its staff from 4100 to 2600 employees and closing 51 field stations. Earlier this month it outlined a "minimum conservation area" strategy that should save