It has money, a Nobel laureate, and MIT's prestige, but a new neuroscience institute launched last year is off to a slow start

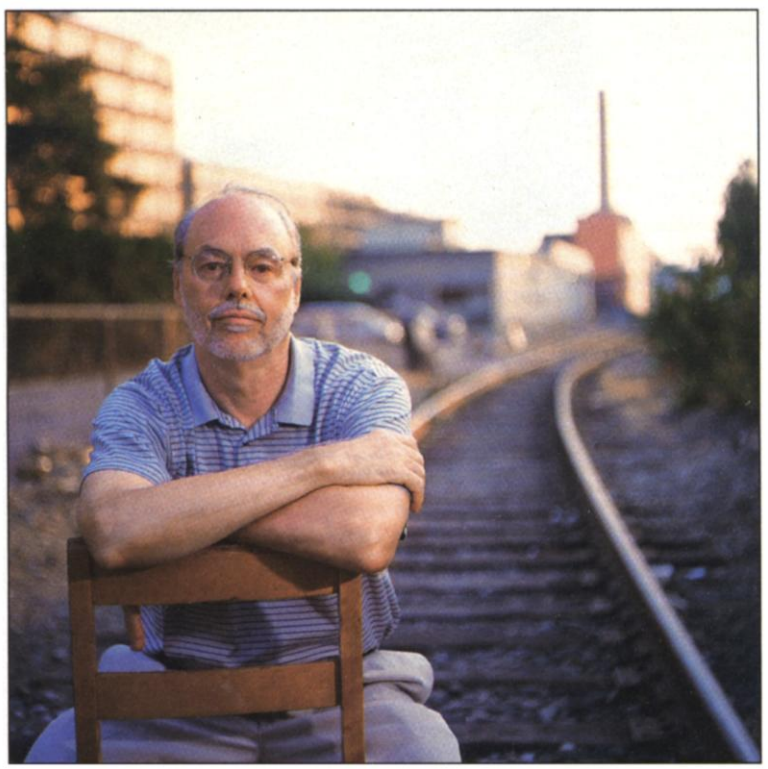
New Brain Institute Struggles for Traction

CAMBRIDGE, MASSACHUSETTS—Can the brain ever understand the brain, much less the mind? Researchers are betting they can, thanks to new tools, large sums of private and public money, and an influx of scientists into neuroscience. Universities around the world are busy launching brain-research programs, with an eye toward winning fame and fortune in the rapidly growing field.

One of the most highly touted efforts is at the Massachusetts Institute of Technology (MIT), which announced in early 2000 a determined initiative to seize the preeminent role in neuroscience. Armed with one of the largest academic gifts in history and a formidable faculty, the McGovern Institute for Brain Research aims to unravel the mysteries of behavior, communication, and perception. But a year and a half into the highly publicized start, the field's researchers say the effort is stalled. The new organization, led by Nobel laureate and MIT molecular biologist Phil Sharp, has yet to define its research direction, attract a senior outside neuroscientist, or find its own niche in a university notorious for its academic rivalries.

Scientists inside and outside the McGovern Institute acknowledge that it is too soon to make definitive judgments about the endeavor's success. But the troubles highlight the difficulties—despite money, smarts, and power—of creating a dynamic research enterprise at the cutting edge, particularly in this unruly interdisciplinary field where competition to hire the best and the brightest is fierce. Other universities, including Harvard just down the street (see sidebar, p. 1419), are aggressively organizing their own ambitious programs.

The competition stems in large part from new tools for molecular biology and medical imaging, which are enabling researchers to begin approaching the enormous complexities of the brain and behavior in a comprehensive way. The effort spans a wide spectrum. At one end are molecular and cellular biology, which examine single neurons. At the other end are cognitive studies that examine learning, memory, emotions, and other higher order brain functions. In between is systems neuroscience, which aims to understand the behavior of aggregates of neurons. But this interdisciplinary reality challenges a university system subdivided into disciplines and subdisciplines.



On track? Neuroscientists say the new institute led by Phil Sharp, here at the site of MIT's planned neuroscience complex, lacks clear direction.

MIT hopes to pull together a variety of researchers in a single campus complex, with Sharp's institute at the center. But the bureaucratic, financial, and research challenges are formidable, and outsiders are watching closely. "There is no model on how to do this," says William Newsome, a neuroscientist at Stanford University, "and that's why the McGovern Institute is so important."

Powering the new institute is a $350 million gift received in March 2000—the largest in history at that time—from International Data Group founder Pat McGovern and his wife, entrepreneur Lore Harp McGovern. Pat McGovern, an MIT alumnus, says that the new institute's mission is to create "a world-class center for the study of how the brain affects human behavior, communications, and perception."

The gift will be dispensed gradually, at $5 million a year, with an endowment of approximately $250 million in the 20th year. MIT will roughly match those funds, primarily by constructing a massive 13,000-square-meter building on the northern edge of campus. The new complex will house not just the institute's 16 researchers (including 10 hired from outside MIT) and its total staff of 300 people, but the many other pieces of MIT's varied neuroscience and cognitive research effort.

Inside job

The leader of the McGovern Institute, a consummate MIT insider, is the former head of MIT's biology department and cancer center (see sidebar, p. 1420). But although Sharp has outstanding credentials in his field of molecular biology (including the 1993 Nobel Prize in physiology or medicine), he has no track record in neuroscience or cognitive studies.

Thus neuroscientists greeted Sharp's appointment with surprise, to say the least, particularly because McGovern and MIT president Charles Vest emphasized that the

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Nearby Rival Takes Quieter Course

The Massachusetts Institute of Technology (MIT) announced its neuroscience initiative last year with a bang: a cascade of media events and press packets filled with glowing profiles of the donors. Longtime neighbor and rival Harvard University is taking a different approach. Harvard has quietly committed $50 million and created 15 new positions to boost its standing in neuroscience. The university also plans to construct a new campus building for the burgeoning field. "Fewer press releases, more recruitment," is how one Harvard scientist sums up the strategy.

Some researchers around the country think that Harvard will prove to be the tortoise to MIT's hare. "Harvard is already a molecular and biomedical juggernaut, and it has one of the best cognitive programs in the country," an MIT professor acknowledges. Even now, the two universities are competing for the field's stars. Before MIT's McGovern Institute for Brain Research could arrange an interview with David Tank, a neuroscientist at Lucent Technologies in Murray Hill, New Jersey, Harvard had made him an offer to lead its initiative. Tank, however, turned that down a few weeks ago for a job at Princeton, and Harvard's search is back on.

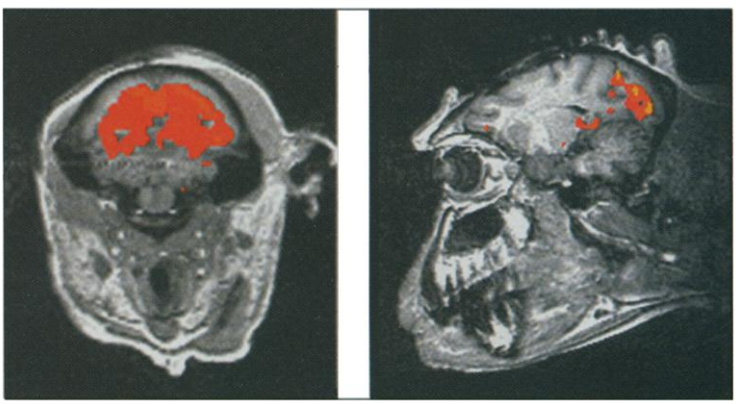
Researchers recall that in the 1960s, Steven Kuffler of Harvard Medical School in Boston created the first proper neuroscience program in the United States, providing a strong interdisciplinary vision in that nascent field. Since then, some of the luster has worn off; the university is now seen as lagging in neuroscience. "Somewhat belatedly, Harvard has realized this is a major area," says Max Cowan, former chief scientist at Howard Hughes Medical Institute in Chevy Chase, Maryland.

Harvard's new initiative will focus on systems neuroscience, with an emphasis on the functioning of the larger nervous system rather than on the molecular level, says Harvard neurobiologist Markus Meister. That requires marshaling a wide variety of researchers and giving them the chance to work closely together. "We don't have to cook up collaboration," he adds, noting that physicists and engineers are already wandering into his lab.

The new building—on the northern tier of its Harvard Square campus in Cambridge—should help heat that interdisciplinary interaction. "Harvard has, for the most part, had buildings divided along disciplinary lines," Meister says. "So this is a somewhat revolutionary proposal." As at MIT, the building is likely a long-term project, requiring up to 4 years for completion. "But it also could be under way very, very quickly," says Harvard biologist John Dowling. "The genome center was built in 2 years."

And whereas MIT plans to wait until its building is complete to hire the bulk of outside researchers, Harvard plans to provide interim space for new faculty members. "We are limited just by who we can find and convince to come here," says Meister. This approach gives Harvard more flexibility than MIT in luring new hires.

Harvard also faces two hurdles that MIT does not. First, Harvard's medical school already has a well-established neuroscience effort. "It's hard to know where the competition is stronger—with MIT or with the med school," says one outside neuroscientist. "We're not trying to compete with the medical school," responds Dowling, merely complement it. "They have a big push in neurodegeneracy and other such areas" that focus more on the medical aspects of neuroscience. As evidence of this coordination, Meister notes that Carla Shatz, who chairs the neuroscience program at the medical school, is also on the steering committee for the new program.



Monkey mind. Visual areas of a rhesus's brain light up in this fMRI scan.

Second, conducting research on monkeys is a critical aspect of neuroscience—but a sensitive topic in Cambridge. Whereas MIT plans to do extensive monkey research, Harvard officials worry about community opposition. Although a small amount of work with monkeys is already being done at the university, the bulk of it is across the river in Boston at the medical school. Still, Dowling says, the steering committee has agreed that banning monkey research on its main campus would be a mistake. "We're trying to prepare the groundwork for this, and we are doing this with great care," one Harvard official adds.

In any case, outside researchers say that Harvard will surely give MIT and other institutions a run for their money. "We will be a major player," promises Dowling. Down the street, Sharp says he isn't worried: "Healthy intellectual competition will be good for the field." **–A.L.**

new institute would study the higher end brain functions. "It was seen as an exceedingly odd choice," says Charles Gallistel, a neuropsychologist at Rutgers University in Piscataway, New Jersey, and a member of an advisory panel for MIT's brain and cognitive sciences department. Adds Charles Stevens, a researcher at the Salk Institute for Biological Studies in La Jolla, California: "Most neurobiologists feel Phil isn't the optimal person to set the research direction for the new institute."

Sharp says he has no illusions "that I understand the deepest aspects of neuroscience." He strongly courted Stanford's Newsome to serve as his right-hand man in navigating the complex terrain of the field. Newsome is a highly respected pioneer in using imaging technologies to investigate brain activity in awake monkeys—research that provides vital clues to the connections between brain activity and behavior. Hiring him might have muted the criticism. "Bill would have been a fantastic hire," says Gallistel, "because he is one of the few bridges between neuroscience and cognition."

But Newsome ultimately declined the offer because of his wife's career in California, and Sharp, noting that there are "a lot of good people right here at MIT," now

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>
> —William Newsome

CREDIT: L. STEFANACCI *ET AL.*, *NEURON*

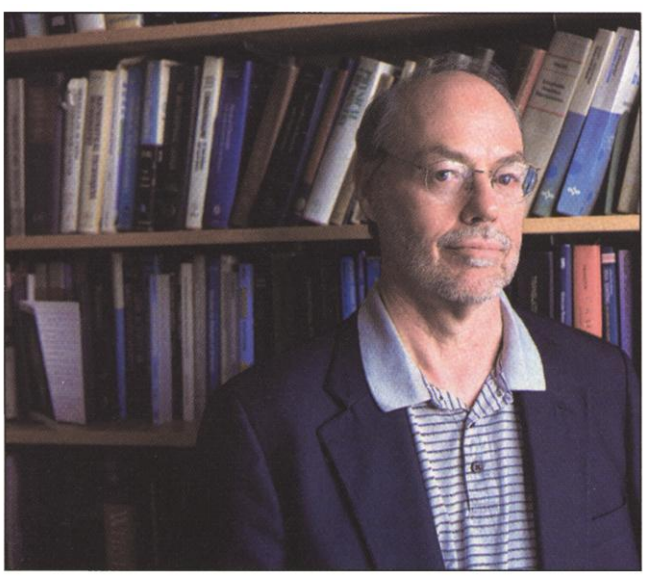
says he has no immediate plans to hire a senior outside researcher. In recent months he has named six current faculty members—and only one outsider, a research associate at Houston's Baylor College of Medicine—to work at the McGovern Institute. That has raised eyebrows in the community. Only one of the six works solely on issues of human cognition; the others tend toward the molecular and cellular end of the neuroscience spectrum.

Thus researchers interested in higher order functions are nervous. "The direction is toward systems and molecular neurosciences, not as much toward cognition—toward understanding emotion, language, and thinking," says Steven Pinker, an MIT psychologist advising the new institute. "There should be more focus on humans in order to distinguish it from the hundreds of other research programs in neuroscience."

The basic problem with the McGovern Institute, Pinker says, is its play-it-safe approach. An emphasis on molecular neuro-

Sharp Edges Into New Terrain

Once you've been offered the presidency of a major university, started a roaringly successful company, and won the Nobel Prize, what else is there to do? For Phil Sharp, the answer is to jump into the thick of a young and burgeoning field. The 57-year-old molecular biologist at the Massachusetts Institute of Technology (MIT) is at the tiller of one of the world's most ambitious efforts to understand the brain and behavior. And he is being closely watched by neuroscientists—many of whom view him as an outsider—to see whether he can match his earlier successes.



Head man. Sharp says his lack of experience with neuroscience may prove a boon for the new institute.

The son of poor Kentucky farmers, Sharp raised cattle and grew tobacco to pay his college tuition. He received his Ph.D. in 1969 from the University of Illinois, Urbana-Champaign, and after working at the California Institute of Technology joined MIT's faculty in 1974. Three years later, he discovered that genes in most cells are split rather than arranged in continuous strands—a finding that earned him a Nobel Prize in 1993. A year after that landmark discovery, Sharp and several U.S. and European colleagues founded Paris-based Biogen, a biotech company that posted $261 million in revenues last quarter. In 1989, he accepted the MIT presidency, only to stun the community by then declining the job, saying he preferred to stick with teaching and research. Through the 1990s, he chaired MIT's prestigious biology department.

Sharp has an almost shy demeanor. "He doesn't like to press the flesh," says one MIT professor. And some colleagues note that along with his natural reserve comes a penchant for administrative control. Those traits, combined with his lack of neuroscience experience, could hamper his acceptance in the community and his ability to draw top-notch researchers, they suggest.

But Sharp's old friends don't buy that. He is a quick study, a precise and detail-oriented researcher, and an able administrator, says MIT biologist Nancy Hopkins: "He sees the cutting edge instantly, and young people flock to him." Adds Robert Birgeneau, former MIT dean of science and now University of Toronto president: "It's easy to take shots at a Nobel Prize winner coming in from [another field]. But I'm confident in the long run that Phil will succeed."

Science recently spoke with Sharp in his cramped office in MIT's biology department, where he was busy planning the building that will house the university's new neuroscience effort. An edited interview follows:

Q: Why did you get involved in neuroscience?

A: I came into science in 1966 as a chemist, and by 1969 I wanted to make a move into molecular biology because I wanted to understand its fundamental processes. I think the biological sciences are now ready for a wonderful expansion in neuroscience; it's a frontier that is exciting a lot of people. So when I was given this opportunity, I said yes. I thought it would be fun.

Q: What do you think will be at the forefront of the field in the next 5 to 10 years?

A: There's a great deal of excitement in bringing molecular and cellular approaches to the nervous system. There are advances in imaging, where clearly there is a lot more to be done. And advances are being made in systems neuroscience. The big challenge is how to integrate molecular and cellular systems with higher order systems.

Q: How important is it to advance brain imaging?

A: Increased resolution, both temporal and spatial, is critical to bridging the gaps between cognitive science and the more physiological aspects of neuroscience. A lot of people here at MIT know how to process such information, and it would be advantageous for the neuroscience community to find a way to interface with them in an effective way.

Q: Have you attended any neuroscience meetings in the last year?

A: I'm just beginning to do that. I've been mostly working with the neuroscience community here at MIT. I certainly will go to neuroscience meetings in the fall.

Q: How do you define consciousness?

A: [Laughs] Oh my goodness, don't ask me that! [Pause] I can't offer an answer.

Q: Many neuroscientists worry that you are not familiar enough with the field.

A: I'm aware of that. I will have to depend on my colleagues to help me work through the issues. But there is some advantage to having a little distance from the specific field: It helps get people to work together and ask how we can do something new. Having that distance, and a commitment to working with my colleagues, will enable us to put together something exciting, important, and at the forefront of the field. **–A.L.**

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sciences is most likely to yield grant support, corporate funding, and Nobel Prizes. Cognitive work, by contrast, involves controversial issues such as consciousness and provides few citations in major journals and few dollars from pharmaceutical companies, he adds.

Others, including at least one McGovern Institute professor, share Pinker's concerns. Nancy Kanwisher, the institute researcher who focuses primarily on human cognition, says that "to realize the institute's stated mission of understanding the higher level functions of the human mind, it will be important to appoint more faculty who work on human cognition." Members of an MIT visiting committee this spring shared that concern, recommending that the word "cognition" be carved into the neuroscience building's facade to ensure that this area is not overlooked.

McGovern, who served on the visiting committee and is active in the new institute's affairs, dismisses the concerns about an overemphasis on biology. He says that 25% to 30% of outside hires will be cognitive scientists. And he adds that systems-neuroscience research will provide the basis for understanding higher functions.

Building up

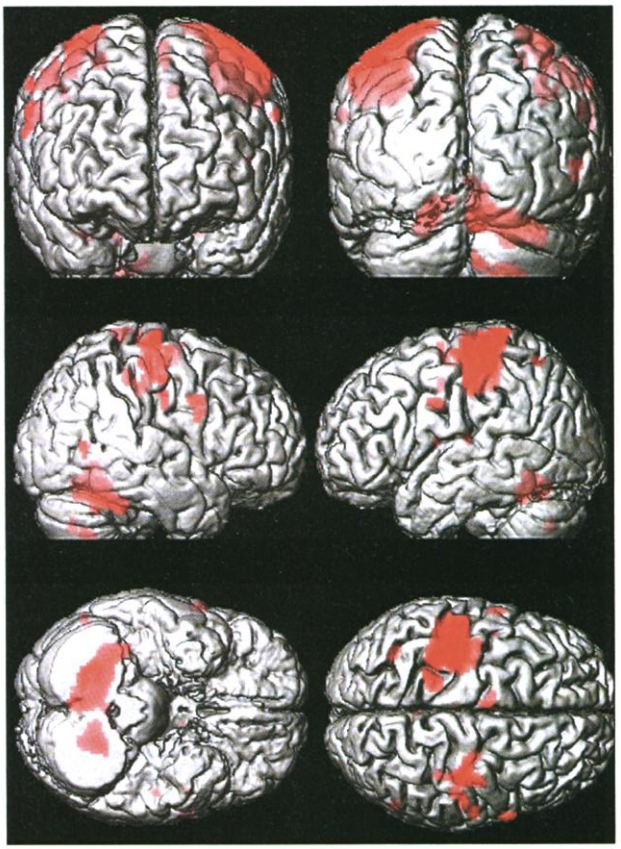
Newsome advises that the new institute make its mark by taking a broad and inclusive view of systems neuroscience. "If you focus on the neurological basis of the higher brain functions, you could be a unique force intellectually," he says. That entails recognizing the limits of biology. "A Palm Pilot and a Cray computer may have the same components, but they are not the same—it's all about organization and complexity." A host of brain-and-behavior–related issues, such as attention, "don't reduce to the molecular level."

Other neuroscientists warn that molecular biologists like Sharp, heady with their decades of research triumphs and formidable arsenal of tools, may underestimate the complexity of this field. "Molecular biologists want to bring our cut-and-dried approach to neuroscience," concedes MIT biologist Nancy Hopkins.

Sharp must also contend with MIT's checkered history in hiring new neuroscience talent and determining a clear research direction. Several now-prominent researchers left MIT in the past after failing to receive tenure, and the administration's support for the field since the 1960s has waxed and waned. The university also has a reputation as a place of competing fiefdoms. "MIT is a notoriously fragmented place; everyone has their own empire," says Anthony Movshon, a New York University researcher who specializes in visual systems.

Sharp says his primary constraint in hiring outsiders and launching an extensive research program is space. Until at least the end of 2004, when the new building is expected to be ready, he has limited room for new faculty members. And the building will present its own scientific challenges: Straddling railroad tracks, it will require pylons sunk deep into the bedrock to minimize vibrations in the labs above. "It's one hell of an undertaking," says Gallistel, who reviewed the plan while on the advisory committee.

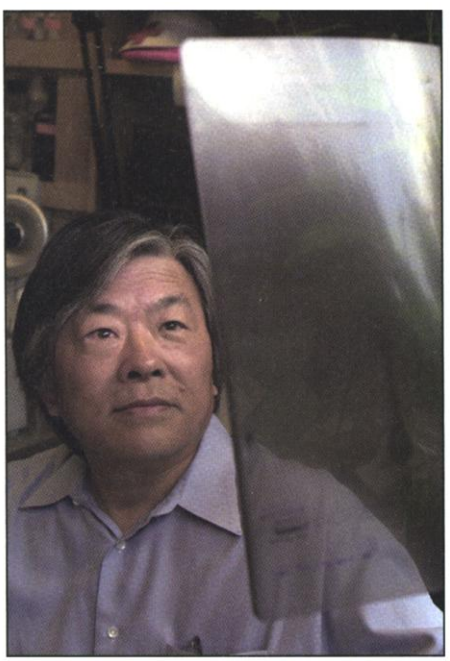
But while the building plans are being drawn up, other U.S. universities like Harvard, Stanford, and the California Institute of Technology are moving quickly to expand their own neuroscience efforts. At least one senior neuroscientist—David Tank of Lucent Technologies in Murray Hill, New Jersey—slipped from MIT's grasp after Harvard and Princeton each made him an offer. Tank will go to Princeton. "There are other programs out there snapping up people," notes Max Cowan, retired chief scientist for the Howard Hughes Medical Institute in Chevy Chase, Maryland. "MIT risks losing momentum by waiting until a building is built," adds another researcher familiar with the McGovern.



Hand out. In this fMRI scan, the left brain reacts to the opening and closing of a volunteer's right hand.

Sharp and his team won't be alone in the new building. Bringing together the myriad pieces of MIT neuroscience in one complex, he says, is the university's central strategy for creating an interdisciplinary environment. But just how well—or if—those pieces will fit together remains uncertain. Just this week, MIT's 7-year-old Center for Learning and Memory, run by Nobel Prize–winner Susumu Tonegawa, won a $50 million gift from the Picower Foundation. The money will enable Tonegawa to add three or four more researchers to his current faculty of nine, increase the center's endowment, and pay for its portion of the new complex, which will be called the Picower Center for Learning and Memory. Tonegawa says he's actively recruiting: "We have our own vision and territory."

The brain and cognitive sciences department, which will also be housed in the complex, intends to continue its work on a broad spectrum of research, says chair Mriganka Sur. Tonegawa's and Sharp's



Alter ego? Susumu Tonegawa's learning and memory effort just reaped a $50 million grant, adding muscle to his MIT institute.

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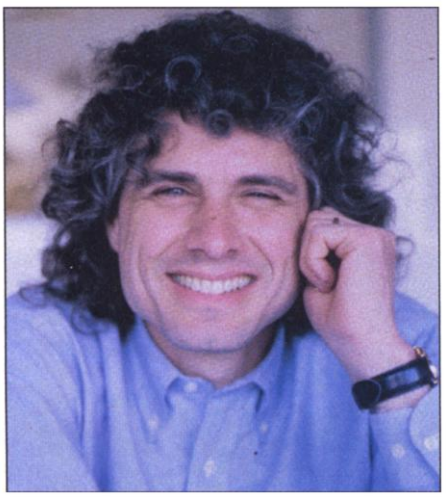

Bio bias. Steven Pinker worries that the new institute lacks focus on human cognition.

centers complement that, he adds, by providing insight into specific issues—such as molecular and cellular mechanisms for learning and memory in the case of the Picower, and possibly systems-level work on vision and movement systems in the case of the McGovern. Center researchers have joint appointments with the department. "We want multiple approaches," Sur adds. The Martino Imaging Center, which develops imaging techniques, will also be part of the complex.

But whereas Tonegawa, Sur, and the Martino Center will build on their existing efforts and reputation, Sharp must build from the ground up. And although he wants the McGovern to do for brain and behavior what the Whitehead Institute has done for molecular biology in the last decade, he faces constraints that Whitehead founders, including David Baltimore, did not. "The Whitehead is off-campus and fantastically endowed," acknowledges Sharp. By contrast, the McGovern must depend on MIT for its building allotment, and it will receive only a restricted annual sum from its donor for the first 2 decades. Sharp anticipates that the McGovern will begin to pull in more money and resources as it matures, providing additional autonomy.

Building up the institute's endowment, as well as its credibility, will take several years, Sharp and McGovern point out. And the current criticism is to be expected, says McGovern, as it reflects the usual cycle of raised expectations and disappointment that follows the start of any project of this magnitude: "This [institute] had a lot of publicity, and everyone thought it would boom immediately. But things are going pretty much according to the original plan."

Many academics agree that it's too early to judge, given the inevitable inertia when large sums of money, a major university, and prominent researchers are involved. "There are concerns in the neuroscience community," says Tonegawa, "but I want to be patient. Adds Newsome: "It's much more important that this be done well rather than quickly."

Still, the community will be watching closely to see if MIT and the McGovern Institute can pull off a program that founders hope will be a model for 21st century neuroscience. **–ANDREW LAWLER**

DNA FORENSICS

Laying Ghosts to Rest In Bosnia

Scientists are embarking on a major effort to identify the remains of as many as 30,000 missing persons

TUZLA, BOSNIA-HERZEGOVINA—Exactly 4419 white nylon bags are stacked on bare metal shelves, row after row, in a chilly, dimly lit room. Inside the duffel-sized bags are the remains of anonymous victims of the worst massacre in Europe since World War II: Bosnian Muslims slaughtered when Serb forces overran Srebrenica in 1995.

This month, the biggest project ever to use DNA testing to identify human remains shifts into high gear here in Bosnia. Using techniques pioneered by the Armed Forces DNA Identification Laboratory in Rockville, Maryland, scientists plan to compare DNA from victims and survivors to try to bring closure to thousands of grieving relatives. "This is the first time this has been done on a scale this large," says the project's leader, Ed Huffine, former head of the mitochondrial DNA (mtDNA) program at the Armed Forces lab.

The plan is to sequence nuclear and mtDNA to identify an estimated 30,000 people missing since the Dayton peace accord brought Bosnia's three-and-a-half-year war to an end in 1995. About 10% to 20% of the victims are expected to be Serbs and Croats. So far, the International Commission on Missing Persons in the former Yugoslavia (ICMP), created at the G-7 summit in France in 1996, has carried out limited DNA testing on war victims, shipping samples to labs in the United States and Poland where costs run up to $5000 per sample. Operating two Bosnian labs—joined by a third later this year at Banja Luka in the Republika Srpska, the Serb-controlled portion of Bosnia—will lower the cost to $300 to $350 per body. That savings, along with donated equipment, free rent, and lower salaries in the war-ravaged country, is expected to hold the overall price tag to no more than $25 million.

Despite the grisly nature of the work, Bosnia offers advantages over other war-torn regions. For example, in Rwanda, where more than half a million people were killed during 3 months of civil war in 1994, the warm, moist climate and widely scattered remains would make such an effort impossible. That doesn't mean the Bosnian project will be easy: Technicians must work meticulously to ensure that the bone samples, in particular, aren't contaminated with other DNA. "If I was asked to do it, I think it would be close to my vision of a nightmare," says the father of DNA fingerprinting, Alec Jeffreys of the University of Leicester, U.K. Nonetheless, he says, "there are plenty of precedents in terms of this type of analysis for mass disasters. [The technique] does work."

Traditional forensics can't begin to tack-

Bone-chilling. Researchers may soon be able to put names to remains of Srebrenica's victims.

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