transfer, Maria Freire. They signed the papers in August.

Their agreement says that NIH scientists are free to share cre-lox mice with other nonprofit research labs, provided they sign a simple transfer agreement indicating the recipient won't give the material to anyone else and that DuPont keeps commercial rights. DuPont is not asking to preview publications, nor does it claim extensive "reach-through" property rights on second generation discoveries, as in the past. However, the company does insist that commercial uses of the technology must be covered by a license. DuPont also plans to retain strict control of the use of cre-lox genetic modifications in agricultural research and in the production of mouse embryonic and stem cells. The most significant aspect of the agreement, according to a Jackson Lab staffer, may be its universality: DuPont has said that all researchers who receive federal funding—not just those who work at NIH—will be covered by the liberal rules, effectively freeing up the nonprofit world.

–ELIOT MARSHALL

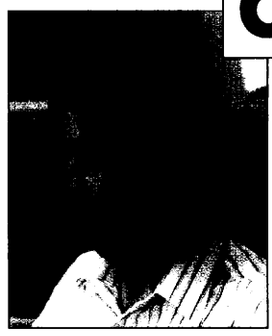
TECHNOLOGY TRANSFER

## Small Businesses Get Extra Boost From NSF

Twenty years ago, the National Science Foundation (NSF) had the then-radical idea of providing federal funds to help budding scientist-entrepreneurs turn research findings into products. The idea grew into the government-wide Small Business Innovation Research (SBIR) program, now a billion-dollar operation spread across 10 agencies, that provides small companies with two rounds of federal support before they must stand or fall on their own. This month, NSF gave its portion of the program a new twist, adding a third round of funding for companies that aren't quite ready to cut the federal cord. The move is likely to rekindle debate over just how well the program is working in generating an economic payoff from federally funded research.

Congress created SBIR in 1982 and modeled it after the original NSF experiment. The program—which is funded by a controversial 2.5% "tax" on the R&D budgets of all major research agencies (*Science*, 17 May 1996, p. 942)—awards up to $100,000 for a feasibility study of a potential product, called Phase 1, and up to $750,000 for additional research on a prototype, called Phase 2. The law stipulates that Phase 3, the company's entry into the marketplace, must occur without the help of government funding. Now, NSF has tinkered with those rules by adding a component, dubbed Phase 2b, that allocates an additional $100,000 for 12 more months to companies that have lined up investors willing to put up at least $200,000. NSF, which currently limits Phase 2 awards to $400,000, is testing the idea with four companies this year and plans to expand it to more than 100 next year using money from its existing SBIR pot.

The rationale, say NSF officials, comes from a survey that found most fledgling companies aren't ready for the free market after only 2 years of federal support, and that a small percentage of the companies aided by SBIR generate most of the jobs and revenue. "SBIR is not working as well as it should," says Kesh Narayanan, head of NSF's industrial innovation division, who conceived the extended funding idea. "We wanted to find ways to encourage more companies to take the next step [toward commercialization]."



**Green for green.** New award helps Alan Kinnersley run field tests of Auxein's plant metabolite.

AUXEIN CORP.

SBIR's supporters generally regard NSF's new twist as fine-tuning an already worthy activity. "Our commercialization rate is much higher than most university technology transfer programs," says Dan Hill of the Small Business Administration, which coordinates the government-wide program and approved NSF's experiment. "I don't see the additional federal support as a crutch, but rather as a way for a company to do more R&D while it lines up investors. And since NSF is buying more research, it's a win-win situation for both parties," adds Hill.

However, others say that NSF may be giving the companies a little too much nurturing. "It's extremely tricky to find the right balance between federal incentives and the commercial sector," says Tom Moss, head of the Government-Industry-University Research Roundtable at the National Academy of Sciences. And Harvard University economist Josh Lerner says that successful companies tend to use SBIR as seed money to attract private investors and that "it's not healthy for companies to avoid the need to go out into the market."

One company participating in NSF's pilot program, Polatomic Inc. of Richardson, Texas, is also looking at the government as a primary customer. The company received $100,000 from NSF based on money it has lined up from NASA's Jet Propulsion Laboratory in Pasadena, California, to help it develop an instrument called a vector/scalar laser magnetometer, which can measure a planet's magnetic field from orbit. "We didn't want to restrict the source of their outside funding," says Narayanan. "As long as it's for the benefit of the federal consumer, what does it matter who's putting up the money?"

Polatomic's chairman, industrial physicist Bob Slocum, says that the company hopes someday to have customers besides NASA and the Navy, which is interested in using it on submarines. Slocum adds that a modified version of the device should also appeal to private companies, who could use it to identify mineral and oil deposits, locate toxic waste sites, and detect buried explosives. But geophysicist John Connerney of NASA's Goddard Space Flight Center in suburban Maryland, which builds a different type of magnetometer for space observations, sees the new injection of federal funding as a sign that the company hasn't really built a better mousetrap. "If Polatomic was truly a commercial business, I would think they would have identified paying customers by the end of Phase 2," says Connerney, who in the past has reviewed SBIR proposals for NSF.

Another grantee, Auxein Corp. of Lansing, Michigan, says it needs the additional funding to conduct more field trials of a plant growth stimulant based on the natural hormone gamma aminobutyric acid, which acts as a neurotransmitter in animals. Chief scientist Alan Kinnersley says the company has lined up $2 million from three investors and found another company interested in becoming the exclusive distributor for its use in horticulture. But sales have fallen short of projected levels. "We have faced an uphill battle educating people about what AuxiGro can do," he explains, "including a 30-year history of biostimulants that have failed to live up to their promise."

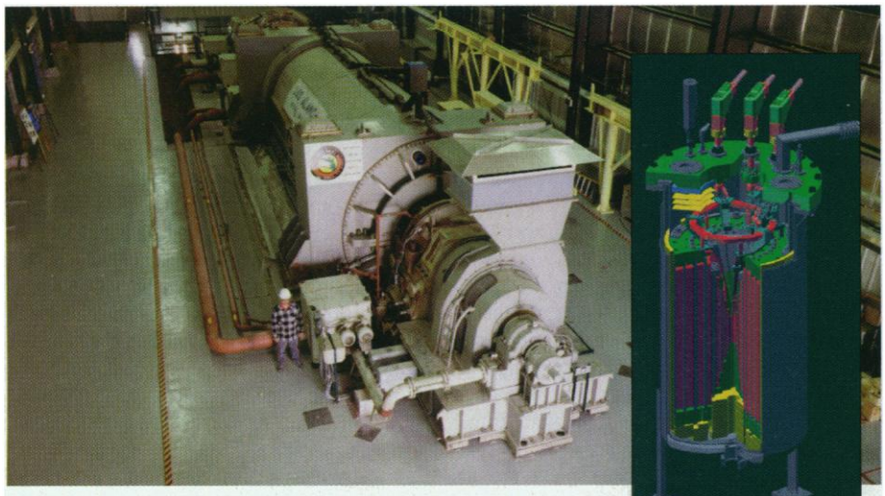
Narayanan says he doesn't expect dramatic results from Phase 2b. But he says the SBIR program needed a boost. "We had two choices," he says. "We could sit back and hope for the best. Or we could try something new."

–JEFFREY MERVIS

MAGNETIC RESEARCH

## Los Alamos Magnet Leads the Field

It shrieks like Godzilla, harnesses the power of 80 diesel locomotives, exerts a force strong enough to crumple the strongest reinforced steel beams, and now it's open for business. Today, officials at the Los Alamos National Laboratory in New Mexico are scheduled to cut the ribbon on a new magnet



J. FLOWER, CIC9/LOS ALAMOS; *FAR RIGHT:* J. R. SIMS, J. B. SCHILLIG, J. VAN ANNE/LOS ALAMOS

**Brute force.** A 1000-ton generator sends current to a refrigerator-sized magnet *(inset)*, its coils separated by channels for liquid nitrogen coolant.

capable of generating fields of 60 tesla, about 1 million times stronger than the Earth's own magnetic field.

The new magnet isn't the first to reach such high fields, but what it does have is staying power. The best existing machines create roughly the same field but can hold it for only about 1 millisecond. The new magnet, with a 1000-ton generator capable of powering a modest-sized city, sustains that field for about 100 times longer.

"It's a unique facility that will allow experiments that are impossible to do elsewhere," says Simon Foner, a high-field magnet expert at the Massachusetts Institute of Technology in Cambridge. The magnet is expected to be most useful for looking at the electronic and magnetic behaviors of a variety of materials, such as semiconductors, high-temperature superconductors, and the layered magnetic materials used to make computer disk drives.

In high-temperature superconductors, for example, free-flowing electric current and magnetic field are like oil and water: They don't mix. Hence, researchers can use the new magnet to wipe out the superconductivity of the materials at temperatures at which they would normally work, thereby allowing them to study the transition between the superconducting and nonsuperconducting states.

Los Alamos physicist Scott Crooker and his colleagues became acquainted with the magnet's capabilities this spring, during its testing phase. The researchers looked at the behavior of layered semiconductor materials designed to confine large numbers of electrons in a thin sheet within the device. Crooker and his team are still analyzing the results, but it was instantly clear that the new machine made life easier. "The beauty of the long-pulse magnet is that we have 100 times longer to collect data and get meaningful results," he says. "The machine is a real tour de force."

The brute behind that force is a building-sized generator that arrived at its present role via a circuitous route. It was built in 1980 to convert energy from a steam turbine in a Tennessee nuclear power plant into electricity. When plans for the power plant were scrapped, Los Alamos picked up the generator to power the high-field magnets needed to confine the energetic plasma in a planned nuclear fusion reactor. But when the fusion reactor itself was later cancelled, the pulsed-magnet builders snagged the homeless generator.

Today, the machine has been reengineered to act first as a motor, which slowly takes power from the grid to crank up a giant spinning shaft, and then as a generator to convert that mechanical energy back into an enormous pulse of electricity.

But the magnet designers did a lot more than simply apply an electrical sledgehammer. "From an engineering point of view, it's quite an accomplishment," says Foner. The generator provides some 1.4 billion watts of power, much of which is dumped straight into the metal coils of the refrigerator-sized magnet. That huge amount of current puts an enormous strain on the coils. The magnetic forces essentially try to squash the magnet into a pancake, and the energy dissipating in the coils generates heat that would also melt the metals in seconds if allowed to stick around.

To prevent an implosion of the coils, the magnet's designers made them out of reinforced copper laced with aluminum oxide, surrounded by specially coiled stainless steel supports, says James Sims, a mechanical engineer at Los Alamos and the magnet's chief engineer. And to prevent a meltdown, the researchers take two main precautions. First, they shunt the power out of the magnet as quickly as possible after the pulse has finished to minimize heating in the coils.

Second, Sims and his colleagues designed the magnet with nine separate sets of

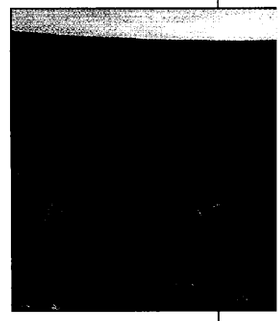
## ScienceScope

### MARS MAPPER GETS THE HICCUPS

Scientists may have to wait 9 months longer than planned for the Mars Global Surveyor spacecraft, currently orbiting the red planet, to begin delivering an uninterrupted map of the surface.

On 10 August, NASA officials announced that they may need the extra time to fix a potential flaw in a 2-meter-long communications antenna, which was supposed to be deployed in March 1999. But air bubbles in a hydraulic shock absorber could cause the unfolding arm to swing wildly and perhaps break.

The 9-month delay "would reduce the flow of imagery and science data somewhat," says NASA's Glenn Cunningham, because Surveyor won't be able to scan the planet's surface and send data home simultaneously. Instead, the spacecraft will store information, then pivot away from Mars to transmit data back to Earth. The pauses will produce gaps in the Mars maps Surveyor is assembling, but NASA officials hope to fill them in after the problem is solved.



NASA

**Mars surface**

### PAYDAY IN CANADA

Some of Canada's young scientists will soon be sprucing up their labs. On 13 August, the federal government handed out the first 214 checks—totaling $23.4 million—from a long-awaited 5-year, $520 million initiative to improve aging research facilities (*Science*, 13 February, p. 979). The grants to 26 universities are intended to help launch the careers of more than 400 young researchers.

While 71% of applicants in this first competition were successful, grant seekers shouldn't expect such high odds in the main funding round this fall, says Canada Foundation for Innovation (CFI) president Denis Gagnon. Institutions have flooded the CFI with 465 requests totaling $735 million to bring workbenches up to snuff and create new national laboratories, but the foundation will dish out less than $260 million.

**David Malakoff, Pallava Bagla, and Wayne Kondro**

coils that nest within one another like Russian dolls. The coils are kept cool by ultracold liquid nitrogen, circulating through channels between them. Just before an experiment, the researchers drain the coolant to prevent it from vaporizing, fire up the magnet, and then flood the coolant back in.

Even with its improved design, the new 60-tesla magnet may not top the high-field heap for long. Researchers at the Los Alamos branch of the National High Magnetic Field Laboratory already have designs on the drawing board for a 100-tesla pulsed magnet. A prototype of the new machine is expected next year and the full 100-tesla device is scheduled to be built by 2002.

–ROBERT F. SERVICE

NEUROBIOLOGY

## A New Route to Treating Schizophrenia?

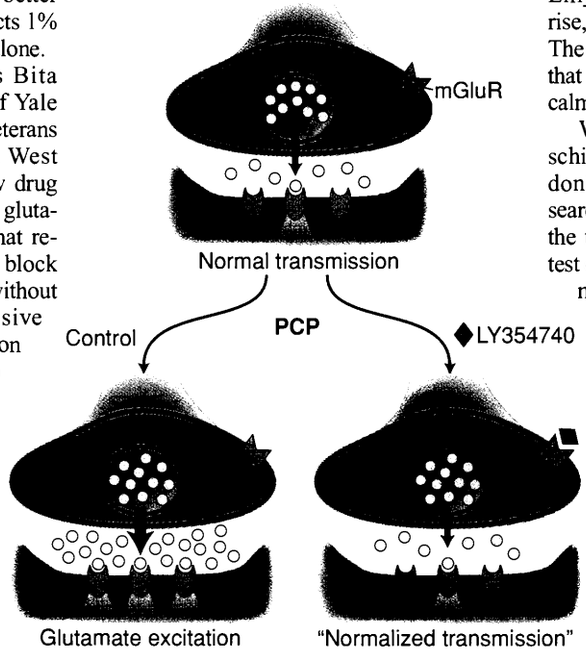
Last month's shootings of two Capitol Hill police officers were a sad reminder of how far we are from a cure for schizophrenia, the debilitating mental illness that plagues the alleged murderer. But work described in this issue suggests a new approach to schizophrenia drugs that may someday lead to better therapies for the condition, which afflicts 1% of the population of the United States alone.

On page 1349, neuroscientists Bita Moghaddam and Barbara Adams of Yale University School of Medicine and Veterans Administration Medical Center in West Haven, Connecticut, report that a new drug that lowers brain levels of the chemical glutamate—one of the neurotransmitters that relay messages between neurons—can block schizophrenia-like symptoms in rats, without apparent side effects. "It's impressive work," says schizophrenia researcher Jon Horvitz of Columbia University in New York City. "This is a promising avenue for a drug that attenuates schizophrenic symptoms."

Such drugs are badly needed. Current schizophrenia medications, known as neuroleptics, work by blocking the action of another neurotransmitter, dopamine, and they are far from ideal. While patients who take them often see reductions in paranoia and hallucinations, the drugs offer little relief from other symptoms, such as poor attention spans, jumbled thoughts, and difficulty interacting with other people. What's more, the neuroleptics often cause troubling side effects, including uncontrollable tremors similar to those in Parkinson's patients. "We are desperate for compounds that might treat psychosis that are not primarily dopaminergic," says schizophrenia specialist David Pickar of the National Institute of Mental Health (NIMH) in Bethesda, Maryland.

The psychoactive drug phencyclidine, or PCP, offered tantalizing hints that a different approach might work. Researchers have known for many years that PCP—"angel dust"—induces schizophrenia-like symptoms in healthy people, an effect that's been attributed to its ability to block the *N*-methyl-D-aspartate (NMDA) receptor, one of a number of receptors in the brain through which glutamate exerts its effects. That finding led scientists to hypothesize that a depression of glutamate transmission in the brain might contribute to schizophrenia. Efforts to treat schizophrenia with drugs that rev up the NMDA receptor didn't pan out, however, largely because the agents can cause serious side effects such as seizures. Meanwhile, scientists and drug developers focused on dopamine, as evidence accumulated that the effectiveness of neuroleptics is proportional to their ability to block dopamine transmission in the brain.

But the Yale workers took a new look at glutamate, using rats treated with PCP, which develop symptoms, such as frantic running and incessant head-turning, thought to parallel psychotic symptoms in humans. As expected from previous work, the drug raised dopamine concentrations in the rats' brains. But much to the surprise of the researchers, for reasons as yet unknown, PCP also caused a surge in brain glutamate levels. This suggests that abnormally high, rather than low, glutamate activity might underlie the rats' reactions to PCP. Moghaddam then speculated, she recalls, that "if we block glutamate activation, maybe we can block these behavioral effects."




**A calming influence.** By binding to a metabotropic glutamate receptor (mGluR), LY354740 prevents the PCP-induced surge in glutamate excitation.

K. SUTLIFF, ADAPTED FROM D. SCHOEPP

To avoid side effects, Moghaddam and Adams wanted to block glutamate activity only in those parts of the brain where it might be elevated. So, they turned to a drug called LY354740 that is under development at Eli Lilly & Co. in Indianapolis for other psychiatric disorders such as anxiety. LY354740 stimulates a subgroup of the so-called metabotropic glutamate receptors, which sit on the terminals of glutamate-releasing neurons and act as regulators of glutamate levels: As shown in rat experiments by Lilly's Darryle Schoepp and colleagues, LY354740 dampens output of the neurotransmitter when its levels get too high but doesn't interfere with normal levels. By stimulating these receptors, Moghaddam and Adams hoped, they could selectively lower glutamate levels in their PCP-treated rats.

The plan worked. In seven control rats, PCP caused glutamate levels to rise more than twofold in the prefrontal cortex, one of the brain regions that goes haywire in schizophrenia, but the six animals given the Lilly drug experienced no such glutamate rise, although their dopamine levels surged. The treated rats also escaped the symptoms that PCP induced in the controls. They stayed calm and showed little head-shaking behavior.

What's more, the drug might even act on schizophrenia symptoms that neuroleptics don't relieve. With food rewards, the researchers trained other rats to alternately visit the two arms of a T-shaped maze. This is a test of working memory, a type of short-term memory used to make decisions or draw conclusions that is often severely impaired in schizophrenia. Control rats treated with water and PCP suffered memory lapses, choosing the wrong arm about half the time under certain conditions. But rats pretreated with LY354740 made a wrong choice just 30% to 40% of the time, about the same rate as normal rats. This suggests that the drug reduces this PCP-induced cognitive deficit.

Of course, many a drug that has looked promising in animals has failed in human trials. Researchers worry, for example, that PCP-induced symptoms in rats do not accurately reflect schizophrenia in humans. Lilly will not say whether the company plans to test LY354740 in schizophrenia patients, but it has conducted early clinical trials of the drug for other diseases, including anxiety and nicotine withdrawal. "It's a very exciting approach to a number of psychiatric disorders," says Steven Paul, the head of Eli Lilly's re-