

**Clone collector.** Yoshihide Hayashizaki leads the effort to collect full-length cDNA clones of all the mouse genes.

of all the active genes of the mouse genome. In this week's issue of *Nature*, the researchers report that they have sequenced and analyzed more than 20,000 full-length mouse cDNAs—one of the largest such collections for any organism. Because some genes were represented by more than one cDNA, the team estimates that they now have in hand cDNAs for nearly 13,000 different mouse genes—about 20% of the total encoded by the mouse genome. The consortium expects to complete the project by spring 2002.

Hayashizaki says the consortium set out to produce this “mouse gene encyclopedia,” as he calls it, partly to aid in identifying the genes in the human and mouse genome sequences. Current methods of finding genes in genomic sequences, chiefly using computer prediction programs, are proving inadequate, missing genes and incorrectly identifying where gene coding regions start and stop. But having full-length cDNA copies of the genes makes it much easier to spot the genes in the genomic sequences.

This information should be valuable for understanding the human genome sequence as well, because many of the mouse and human genes are likely to be similar. Indeed, the public group sequencing the human genome is interested in collaborating with Hayashizaki in using the mouse cDNA data to identify genes in the human genome. “It is a very important resource,” says Robert Strausberg, director of the Cancer Genomics Office of the U.S. National Cancer Institute in Bethesda, Maryland. “Hayashizaki is really to be congratulated; they are at the forefront of this work.”

In addition to aiding in gene identification efforts, the cDNA clones can also be used to construct the microarrays now coming into widespread use for profiling gene expression patterns and for synthesizing the proteins themselves. “This is exactly what scientists would like to have in their labs: the ability to produce proteins and study their

functional characteristics,” says Strausberg, who is overseeing a U.S. effort to produce cDNA clones.

A number of U.S. university and public sector labs have already acquired mouse cDNA clones from RIKEN. Although RIKEN retains some rights over the material, a researcher at one institution says the usage agreement is similar to the ones at most U.S. universities.

—DENNIS NORMILE

## SWISS SCIENCE

### New Program Draws Praise, Complaints

**BERN**—A major program launched last month to boost the fortunes of a select group of top Swiss labs has ignited a controversy in the scientific community. Whereas the winners say it will provide much-needed opportunities for networking, some observers complain that the program is elitist. And social scientists are unhappy about being excluded from the winner's circle.

Things got off to an auspicious start when 230 research groups across the country submitted preliminary proposals in 1999 to become one of the government's new National Centres of Competence in Research (NCCR). The Swiss National Science Foundation (SNSF), which will administer the grants, chose 18 finalists and submitted the list to the Science and Research Group (SRG), part of the Federal Department of Home Affairs. The SRG chose 10 winners, each of which will receive between \$1.7 million and \$3.1 million a year for the next 3 years (see table). The \$77 million is expected to be supplemented with funding for an additional 5 to 9 years as well as new

money to fund a second round. The new centers, says SRG State Secretary Charles Kleiber, “are an instrument to reshape the Swiss research landscape.”

The grantees were chosen according to several criteria, including scientific merit, their prospects for transferring the technology to industry, and their plans to train young scientists and advance women in the field. The awards are also meant to promote collaborations among Swiss scientists from various disciplines. The projects “provide a formal structure to put together complementary expertise from all over Switzerland,” says computer scientist Gábor Székely of the University of Zürich, leader of an NCCR grant for computer-aided medicine. According to University of Geneva mouse geneticist Denis Duboule, another NCCR grantee, countrywide collaborations are needed in his field. With the advent of genomics and proteomics, he says, “most of the work in the next 15 years cannot be done by small groups.”

But although the grants are meant to pull researchers together, they're sowing plenty of division as well. Critics contend that the NCCR, a successor to a smaller program that funded a handful of research networks, is making the rich richer. Grantees, they say, are already well known and have little trouble obtaining research funds. By rewarding established groups, the NCCR is taking “a big step back in our efforts to give free rein to young researchers,” says Gottfried Schatz, president of the Swiss Science and Technology Council. The program also puts a premium on size, adds Ernst Hunziker, director of the Müller Institute at the University of Bern, whose proposal for an NCCR grant didn't make the final cut. “It discriminates strongly against

#### SWITZERLAND'S NEW ELITE NETWORKS

Topic	Lead institution	Director	3-year funding
<i>Life Sciences</i>			
Molecular oncology	ISREC, Lausanne	Michel Aguet	\$9.4 million
Genetics	U. Geneva	Denis Duboule	\$8.7 million
Molecular life sciences	U. Zurich	Markus Gerhard Grütter	\$6.4 million
Neural plasticity and repair	U. Zurich	Hanns Möhler	\$7.5 million
Plant science	U. Neuchatel	Martine Rahier	\$6.5 million
<i>Information and Communications Technologies</i>			
Medical imaging	ETH Zurich	Gábor Székely	\$7.8 million
<i>Sustainable Development and Environment</i>			
Climate science	U. Bern	Heinz Wanner	\$5.0 million
<i>Other</i>			
Novel electronic materials	U. Geneva	Øystein Fischer	\$8.7 million
Nanoscale science	U. Basel	Hans-Joachim Güntherodt	\$8.8 million
Quantum photonics	EPF Lausanne	Marc Illegems	\$8.3 million

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groups that are small," he says.

Swiss social science and humanities researchers have their own beef with the program. Of the 18 projects recommended by the SNSF to the SRG, three were in the social sciences. None of these was funded, despite the government's previous declaration of social sciences and humanities as one of four priority areas. On 21 December, more than 300 university students, postdocs, and professors sent a letter of protest to Kleiber and his boss, Home Affairs Minister Ruth Dreifuss. The next day, the general secretary of the Swiss Academy of Humanities and Social Sciences, Beat Sitter-Liver, joined two other leaders of Swiss social science organizations in sending another protest letter to Dreifuss. "Social sciences has been relegated to second-class citizenship," contends Keith Krause, a political scientist at the University of Geneva.

Kleiber, also a political scientist by training, says he hopes that parliament will correct that situation this summer by funding four additional centers, one of which is in social sciences. A second (and probably final) call for proposals is expected next year, but some social scientists may pass unless "we are assured that the process will be fair," says University of Geneva sociologist Christian Lalive d'Epinay.

The next time around, Kleiber would like to see a more focused call for proposals and a shorter review process. SNSF Secretary General Hans Peter Hertig acknowledges that there is "certainly room for improvement" in the evaluation procedure, but he disagrees with Schatz's assertion that NCCR will weaken the foundation's support for individual researchers. Individual grants still account for 80% of SNSF's funding.

For Duboule and others involved with the new centers, the program is not just about allocating resources. It's also part of an ongoing effort to improve Swiss science. "We just have to try it and see how it works," Duboule says. "We have to do something; we can't just do nothing."

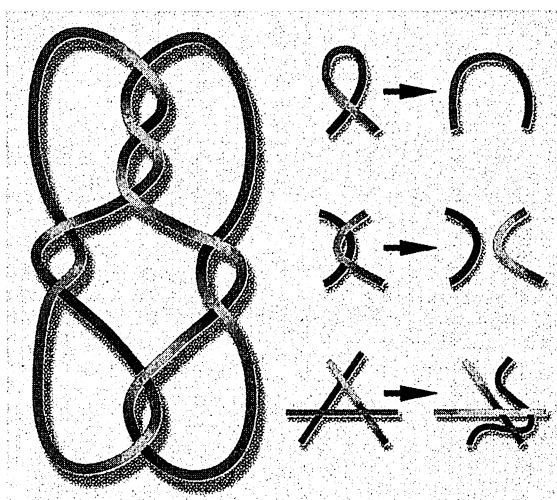
—MIN KU

Min Ku is a science writer based in Bern. With reporting by Robert Koenig.

## KNOT THEORY

### Loopy Solution Brings Infinite Relief

Alexander the Great would sneer. Twenty-three centuries after he slashed through the Gordian knot, mathematicians have finally made their first stab at figuring out how long it takes to untangle a tangle. The unheroic answer, for one key class of knots, is "not forever"—and even that comes with a huge string attached. Still, knot researchers are delighted.



**Circle game.** In time, three basic maneuvers will reduce a tangle like the one at left to a simple loop.

"People have always wondered if [the unknotting process] was unbounded, and people now know that it is bounded," says Joan Birman, a knot theorist at Barnard College in New York City. "It was a very big problem."

For years, knot theory itself has been in such a tangle that even the most fundamental problems in the field still loom large. "If I hand you a knot, you would hope for some method of identifying it," says William Menasco, a knot theorist at the State University of New York, Buffalo. "The classical problem in knots is to have a complete, nonredundant list of knots, and if you give me a knot, I can standardize it and pick out where in the list it lives." Unfortunately, mathematicians aren't certain that they can do that even for the simplest knot of all: a mere loop of string, also known as the unknot.

This isn't to say that knot theorists have made no progress. For instance, as far back as the 1920s, they had figured out that only three types of motion—the so-called Reidemeister moves—are needed to untangle any knot into a standard, recognizable form. But even with that armamentarium, mathematicians didn't see an obvious way to do the unknotting; sometimes the Reidemeister moves made things worse. "They were hoping that the set of moves would make the knot simpler at every step," says Jeffrey Lagarias, a mathematician at AT&T Labs in Florham Park, New Jersey. "The Reidemeister moves do not." As a result, there is no easy way to tell how many moves it would take to untangle a given loop of string—or even whether any finite number could do the job.

Lagarias and Joel Hass of the University of California, Davis, sought to guarantee that unknotting the unknot, at least, does not take forever. Instead of looking at an unknot as a twisted-up loop of string, they treated it as the boundary of a crumpled and distorted disk.

They then performed the disk equivalents of Reidemeister moves and translated the results back into the mathematical language of knots. Their conclusion: The number of Reidemeister moves required to untangle any given twisted-up unknot is finite.

Finite numbers, however, can still be ridiculously large. All Lagarias and Hass guarantee is that if a knot crosses itself  $n$  times, you can untangle it in no more than  $2^{100,000,000,000n}$  Reidemeister moves. In other words, if every atom in the universe were performing a googol googol googol Reidemeister moves a second from the beginning of the universe to the end of the universe, that wouldn't even approach the

number you need to guarantee unknotting a single twist in a rubber band.

"The [bound] is, of course, enormous and hopeless," Lagarias acknowledges. Still, he says, just showing that a limit exists may inspire future researchers to whittle it down to a reasonable size. (Macedonian swordsmen need not apply.)

—CHARLES SEIFE

## ECOLOGY

### Scientists Begin Taming Killer Lake

**CAMBRIDGE, U.K.**—In an unprecedented and potentially risky experiment, scientists this week began venting carbon dioxide-laden water from the bottom of Lake Nyos in Cameroon. The apparatus is intended to prevent a recurrence of a 1986 eruption that claimed 1800 lives.

The carbon dioxide is released from surrounding volcanic sediment and underground springs. Experts say that about 300 million cubic meters of the gas have accumulated in the waters near the lake's bottom, about 200 meters below the surface. In 1986, an estimated 80 million cubic meters of gas escaped from the lake and flowed down the hillside, smothering residents and livestock in what's known as a "limnic eruption."

Hoping to prevent future such disasters, a team headed by Michel Halbwachs of Savoie University in Chambéry, France, has floated a 3-meter-wide raft in the middle of the lake with a 200-meter-long polyethylene pipe running to the lake bottom. As the water travels upward toward the surface, the carbon dioxide comes out of solution. At the surface, 10 liters of carbon dioxide are released for every liter of water. The result is "a jet 40 meters in height, which can continue without any further input of energy," says team member