"Bioinformatics experts want fast access" so they can run follow-up experiments, says John Norvell, who heads the structural genomics program at the National Institute of General Medical Sciences in Bethesda, Maryland. But "experimentalists want time to check the data."

The issue boils down to how protein structures are gleaned and checked before release, says Wayne Hendrickson, a structural biologist at Columbia University. Computer programs, fed data from x-ray crystallography and NMR experiments, generate the likeliest set of three-dimensional coordinates for all of a protein's atoms. Bioinformatics experts initially wanted guidelines that mandate the release of those computer predictions the instant they are produced. Such a policy would be similar to the way sequence data from the publicly funded human genome project are posted daily on the Web.

"That did not fly," says Tom Terwilliger, an x-ray crystallographer at Los Alamos National Laboratory in New Mexico. Experimentalists maintain that protein structure analysis is more complex than spitting out raw genome sequence data. Each modeling prediction must be vetted, Hendrickson says. Several participants, he says, felt there's "no need to abandon the current standards of investigators making the decision" on when data are ripe for release.

But although structural biologists will still make the call on when data are solid, they won't be allowed to withhold a structure for the sake of determining its function. That means changing the status quo. When a protein structure is submitted to a journal today, Hendrickson says, it's almost always accompanied by findings—from experiments that alter key amino acids in the protein, for instance—that allow scientists to make educated guesses about how the protein works. But with a high-speed approach to solving protein structures, says Norvell, "publishing will have to be done in a different way."

NIH and other agencies that plan to pour money into the structural genomics centers don't want to freeze out biologists not associated with the centers. According to Hendrickson, "everyone agreed that the concept should not give those groups a privileged status."

As a compromise, researchers will be asked to publish their results—most likely in electronic format or as a brief summary in a specialist journal—within 2 to 4 weeks of finishing a structure, says Stephen Burley, a structural biologist at The Rockefeller University in New York City. "The moment the paper is posted on the Web," he says, "the coordinates would be placed in the Protein Data Bank," which is freely available to all researchers. The burden will be primarily on funders to enforce the timelines. They're accustomed to that, Burley says: Agencies regularly use their leverage over purse strings to ensure that structural biologists submit coordinates to the Protein Data Bank as soon as findings are published.

As an additional prod, structural biologists plan to add a little peer pressure. Hendrickson and others say the new guidelines call on each structural genomics center to keep a log on the Web of which structures they are attempting to solve. They would chart milestones such as cloning, isolating, and purifying a protein, and coaxing it to form a crystal. This will not only help to prevent several groups from working on the same projects, says Hendrickson, but "it will put internal pressure on the groups that they wouldn't be able to hold something forever."

–ROBERT F. SERVICE

With reporting by Michael Hagmann in Cambridge, U.K.

GLOBAL WARMING

## Some Coral Bouncing Back From El Niño

Coral reefs in the Indian and Pacific oceans seem to be recovering more quickly than expected from a recent devastating "bleaching" caused by high ocean temperatures. New research suggests that the nascent recoveries may be partly due to the unexpected survival of juvenile coral that somehow avoided the brunt of the environmental assault. "It may indicate that reefs are more resilient than we had thought," says Terry Done, a senior research scientist at the Australian Institute of Marine Science in Cape Ferguson who studies reefs in the Indian Ocean. However, the coral would not be able to mature and recover from the repeated bleaching forecast to accompany projected global warming, he adds.

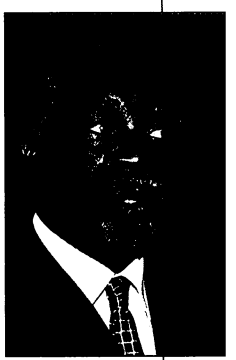
**Resilient reefs.** There may be hope for some areas hard hit by extensive coral bleaching after 1997–98 El Niño event.

Coral stressed by heat or disease expel zooxanthellae, the symbiotic algae that give the white

CREDITS: (TOP TO BOTTOM) MICHEL EULER/AP; PROVIDED BY GREOGOR HODGSON

## ScienceScope

**Unconventional Committee** South African President Thabo Mbeki's controversial AIDS advisory panel found little common ground this week and ended up establishing a four-person committee to devise tests of fringe ideas about what causes the disease. Mbeki outraged many mainstream AIDS researchers last month when he questioned whether HIV causes AIDS and named leading skeptic Peter Duesberg of the University of California, Berkeley, to a deeply divided 33-member panel that will recommend ways South Africa should fight the disease (*Science*, 28 April, p. 590).



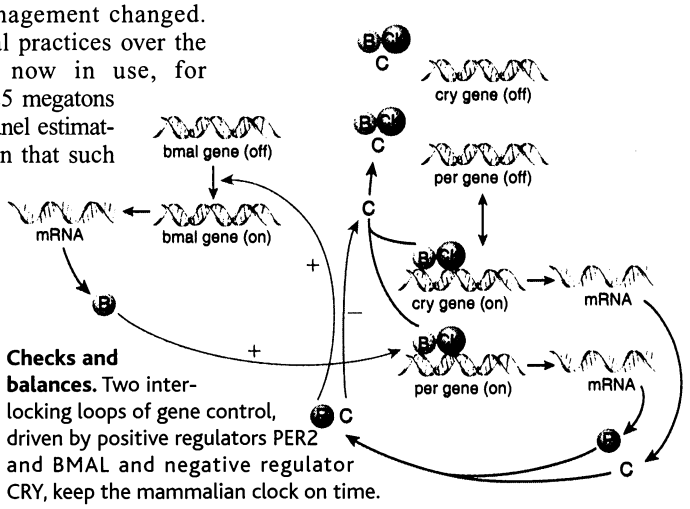
The panel, which met on 6 and 7 May in Pretoria, appointed two researchers from each camp to work on formulating experiments that could test theories about HIV's role in AIDS, which threatens more than 10% of South Africa's 42 million people. The four—Duesberg, William Makgoba of South Africa's Medical Research Council, Helene Gayle of the Centers for Disease Control and Prevention in the United States, and Harvey Baily, a Mexico-based AIDS researcher—plan to confer by Internet over the next 6 weeks. They will return to South Africa to present their ideas before the 7 July opening of the 13th World Conference on AIDS.

Critics call the exercise a waste of time and money. But Mbeki told the panel he is keeping an open mind: "You can't respond to a catastrophe merely by saying 'I will do what is routine.' "

**Eyes on the Finnish** Searching for new ways to battle type I diabetes, the Juvenile Diabetes Foundation (JDF) is turning to the country with the world's highest incidence of the disease. Last week, JDF signed off on two 5-year contracts, together worth over $4 million, to support Finnish researchers.

A joint venture with the Academy of Finland and the Sigrid Juselius Foundation will focus on new treatments, such as using stem cells to replace lost pancreas cells. The other program, run by Turku University since 1995, aims to test 20% of Finnish newborns for genetic susceptibility, then follow at-risk children in a bid to pinpoint what triggers the disease. Says JDF chief science officer Bob Goldstein: "It's a fabulous chance to do long-term epidemiology."

makes a vague reference to sequestering carbon through these "additional activities"; the IPCC panel ended up with the tough task of clarifying this option. First, scientists had to agree on how much of a particular land type exists globally, and then how much carbon it might hold if its management changed. Improving agricultural practices over the 1300 megahectares now in use, for instance, could save 125 megatons of carbon a year, the panel estimated. But experts caution that such estimates are optimistic and difficult to verify. Compared to forests, which "are pretty easy to see from space," tracking carbon soaked up by fields is "a lot harder," says panelist Richard Houghton of the Woods Hole Research Center in Massachusetts.




**Checks and balances.** Two interlocking loops of gene control, driven by positive regulators PER2 and BMAL and negative regulator CRY, keep the mammalian clock on time.

The report also discusses the feasibility of allowing developed countries to offset emissions by planting, protecting, or managing forests in developing countries (*Science*, 24 July 1998, p. 504). Such mechanisms can have "benefits," says the report, but there are risks, for instance, that displaced people will deforest lands elsewhere. Some European countries want to limit such offsets, maintaining that developed countries should reduce their own use of fossil fuels instead.

Now that this report has laid out carbon accounting options, countries must decide which ones to pursue before the next major meeting of Kyoto parties in November to finalize the treaty. **–JOCELYN KAISER**

CIRCADIAN RHYTHMS

## Two Feedback Loops Run Mammalian Clock

As a grandfather clock keeps time with an oscillating pendulum, the 24-hour rhythm of the biological clock is also maintained by oscillations—in this case by oscillating levels of proteins. But the biological clock has two oscillations moving in counterpoint; the levels of one set of proteins cresting while the others are low, and vice versa. Results described on page 1013 now show how the mammalian form of the biological clock keeps those opposed oscillations in sync.

A team led by Steven Reppert of Harvard Medical School in Boston reports that the key to this regulation seems to be a pair of proteins that enter the cell nucleus together but then apparently split their duties. One, called CRYPTOCHROME (CRY), turns off a set of genes, while the other, PERIOD2 (PER2), turns on a key gene. The work "explains how genes can be activated in two opposite phases," says clock researcher Paul Hardin of the University of Houston, whose group recently made a similar discovery about the clock of fruit flies.

Researchers are excited by the way the new work clarifies the role of CRY in the mammalian clock. In fruit flies, CRY, which absorbs light, helps reset the clock in response to light (*Science*, 23 July 1999, p. 506). But the mammalian clock, deep in the brain, doesn't receive direct light input, so researchers wondered what function CRY could be serving there. Reppert's team has now "firmly established" that CRY is a central component of the clockworks, where it turns off key clock genes, says circadian rhythm researcher Steve Kay of the Scripps Research Institute in La Jolla, California. What's more, it seems able to do this alone, without the aid of PER2, the protein previously thought to do the job.

The Reppert team's findings build on work on the fruit fly clock, which features a negative feedback loop similar to the one in which CRY participates. In flies, the feedback is accomplished by PER together with a protein called TIMELESS (TIM). The *per* and *tim* genes turn on in the morning, and the two proteins accumulate in the cytoplasm during the day. By evening, when they reach a critical concentration, they pair up and go to the nucleus to shut down their own genes. This feedback helps keep PER and TIM protein levels oscillating up and down every 24 hours.

But that is only half of the story. A protein called CLK oscillates in counterpoint with PER and TIM; its levels rise as theirs fall and vice versa. CLK is a positive regulator that pairs with a protein called CYC to turn the *per* and *tim* genes on. Indeed, PER and TIM shut their genes off by binding to and inactivating CLK and CYC.

Mammalian clocks use many of these same proteins, although mammals have three

## ScienceScope

**Not-So-Small Doubts** The National Science Foundation (NSF) is looking for a giant-sized, 124% increase in nanotechnology research to lead the Administration's half-billion-dollar initiative (*Science*, 11 February, p. 952). But even legislators impressed with nanoscience's potential aren't sure that NSF is up to the job of overseeing five other agency efforts.

"Powerful bureaucracies usually win out over science," Senator Barbara Mikulski (D–MD) said last week during a hearing on NSF's 2001 budget request, worrying that the foundation could be pushed around by the program's bigger partners. "NSF may be trying to take on more than it can handle," added Senator Kit Bond (R–MO), the panel's chair, noting that it is already responsible for directing the Administration's information technology initiative.

No problem, responded presidential science adviser Neal Lane. A small coordinating office housed at NSF, he said, will help keep the troops in line and marching smoothly. But an army must also be fed. "We can't do it without the money," says NSF engineering chief Eugene Wong.

**Chimpanzee Transfer** The National Institutes of Health (NIH) has assumed ownership of 288 chimpanzees at the New Mexico–based Coulston Foundation. Details were still being worked out as *Science* went to press, but the arrangement "establishes a permanent home for the chimpanzees, with guaranteed support," says Coulston spokesperson Don McKinney. The animals have all been exposed to either HIV or hepatitis B as part of research protocols, and they will continue to be available for research.

Coulston has been under fire from animal rights groups and is the subject of an ongoing investigation by the U.S. Department of Agriculture's (USDA's) of animal welfare office (*Science*, 12 November 1999, p. 1269). As part of a 1999 settlement with the USDA, Coulston agreed to surrender up to 300 of its chimpanzees by January 2002, and McKinney says the 288 chimps, plus 21 animals slated to move elsewhere, would bring Coulston into compliance with that agreement.

For now, Coulston will continue to care for the chimps at Holloman Air Force base near Alamogordo, New Mexico, with funds from NIH. But NIH deputy director Wendy Baldwin says it is not yet clear where the animals will live for the long term. Holloman isn't an ideal spot for a research lab, she says, but its chimp facilities are the best available quarters.

**Contributors: David Malakoff, Martin Enserink, Jeffrey Mervis, Gretchen Vogel**