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.

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.

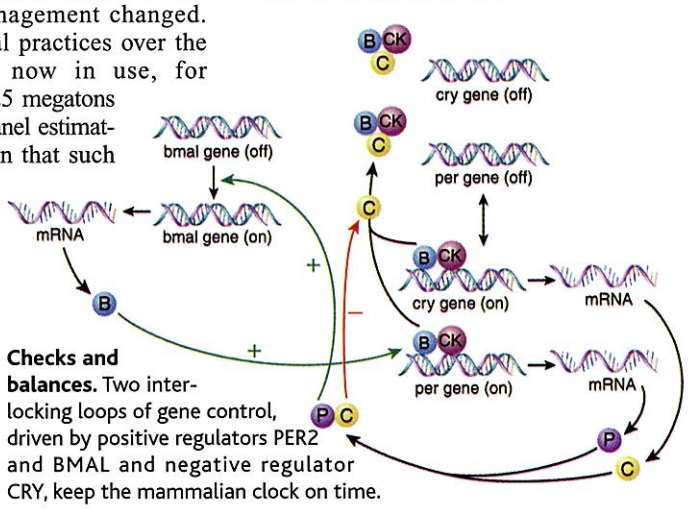
Now that this report has laid out carbon accounting options, countries must decide which ones to pursue before the next major meeting of Kyoto parties in November to finalize the treaty. **–JOCELYN KAISER**

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.



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.

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

PERs and two CRYs, and in some cases—such as that of the CRYs—the proteins play different roles in the two clocks. In mammals, CYC's counterpart is a protein called BMAL, and it is BMAL whose levels cycle in counterpoint to PER's. To get a better fix on how the mammalian cycling works, Reppert collaborated with two research teams that had produced mice with mutant clock genes. Gijsbertus van der Horst of Erasmus University in Rotterdam, the Netherlands, and his co-workers brought to the collaboration a strain of mice that lacks functional *cry* genes, and Cheng Chi Lee of Baylor College of Medicine in Houston contributed mice with a mutant *per2* gene.

Neither strain has a working clock, but the clocks are not identically broken. It's like "hitting a clock with a sledgehammer in different ways," Reppert says. By examining how the clockworks have failed, the researchers gained clues to the function of the protein encoded by the mutant genes. For example, results with mice that have a mutation in the *per2* gene suggest that its protein acts as a positive gene regulator, switching on a key clock gene. Reppert's Harvard colleagues Lauren Shearman and David Weaver deduced that from their observation that, in *per2* mutants, the *bmal* gene is expressed at lower levels than in normal mice, implying that PER2 normally turns *bmal* on.

Work with the *cry* mutants showed that the CRY proteins normally turn off the *per* and *cry* genes. Van der Horst's team had already shown that *per* gene activity is high in the *cry* mutant mice. Now, Sathyanarayanan Sriram, a postdoc with Reppert, has confirmed in cell culture studies that CRY protein alone can turn the genes off, without any help from PER. CRY apparently down-regulates the genes much as PER and TIM do in flies—by binding to CLK and BMAL and taking them out of action.

Experiments with the *cry* mutant mice also suggested a second role for CRY: It seems to stabilize PER2. That conclusion came out of the fact that despite all the *per* gene activity in the clock cells of the mutants, the researchers could find no PER protein there. That suggests PER protein is quickly degraded in the absence of CRY. The *bmal* gene's activity was also low in the mutants, as PER is needed to turn the gene on.

Putting it all together, the team came up with two interlocking loops by which proteins feed back on the expression of their own and other genes. In one loop, PER2 turns on the *bmal* gene. BMAL, after a delay, returns to turn on the *cry* and *per* genes, triggering the second loop. In that loop, CRY and PER proteins accumulate and then pair up and enter the nucleus, where CRY turns off the *cry* and *per* genes and PER2 once again turns on *bmal*. This picture is similar to what Hardin's team found last year in fruit flies, although in the fruit fly clock both PER and its partner, TIM, seem to work together to turn off their own genes and turn on *Clk* (*Science*, 22 October 1999, p. 766).

The paper "is a great move in the right direction," says Scripps's Kay. "It is doing what needs to be done, which is to work out the real mechanics of the clock" in mammals. Many questions remain, such as how PER regulates the *bmal* gene, says Kay, but with the studies moving along like clockwork, those answers are sure to follow soon.

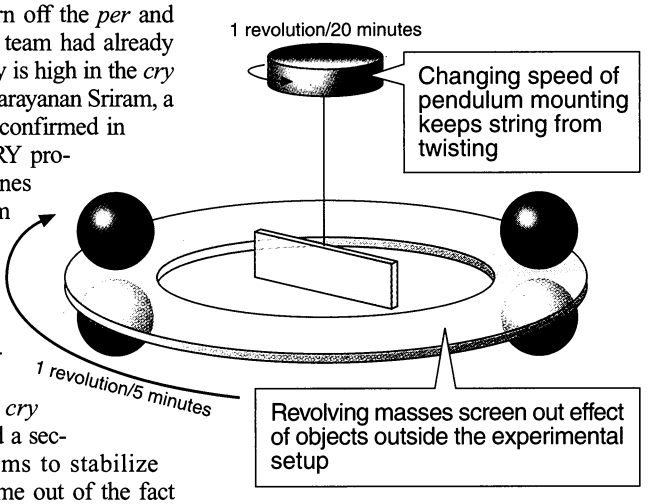
–MARCIA BARINAGA

PHYSICS

A Slow Carousel Ride Gauges Gravity's Pull

Sometimes progress starts with a big step backward. After 14 years of gravitational confusion, physicists at the University of Washington, Seattle, have released the most precise measurement yet of the strength of gravity, thanks to a clever new device.

Although scientists have been studying gravity since the time of Newton, they have had little luck measuring its pull. The strength of gravity, represented by a universal constant nicknamed "big G," is puny; huge amounts of mass exert only a small gravitational attraction. As a result, seismic disturbances, minute electric and magnetic fields, and even the mass of a nearby graduate student can mess up laboratory measurements of G.



Such measurements date back to the end of the 18th century, when the English physicist Henry Cavendish dangled a dumbbell-shaped pendulum from a thread and placed heavy masses nearby. By measuring how much the dumbbell twisted under the attraction of the masses, Cavendish obtained a fairly good measurement of big G. Over the years, Cavendish-like torsion pendulums and other devices yielded better and better values. In 1986, the National Institute of Standards and Technology (NIST) published a value with an uncertainty of only 1.3 parts in 10,000.

Then things started to go downhill. Also in 1986, the PTB, the German equivalent of NIST, performed a technically exquisite experiment that yielded a value 42 standard deviations away from other measurements. "That was quite startling," says NIST's Peter Mohr. "Nobody knows quite what was wrong with it." To make matters worse, in 1995, physicists realized that, because the pendulum wires in Cavendish-style torsion devices are not perfectly elastic, they don't twist in quite the way that scientists had assumed. "[It] should have been obvious," says Randy Newman, a physicist at the University of California, Irvine. "You get a version of G which is too big." NIST hiked its uncertainty about big G by a factor of 12, to a mortifying 15 parts in 10,000.

Enter the big G whizzes of Seattle. At last week's meeting of the American Physical Society,* physicist Jens Gundlach announced that he and his colleagues had eliminated the string-twisting bias and measured big G with an error of a mere 14 parts per million—about 10 times better than previous measurements. The key to the newfound precision was keeping their experimental apparatus in constant motion. Gundlach's team mounted the pendulum's support on a turntable that rotates about once every 20 minutes. As the ends of the pendulum approached the attractor masses—four 8-kilogram steel balls—they felt the increased gravitational force. But whenever the pendulum began to twist, a laser sensor triggered a switch that accelerated the turntable, counteracting the torque. "The torsion fiber hardly gets twisted," says Gundlach. "The gravitational acceleration is transferred to the turntable," getting rid of the string-twisting bias.

Meanwhile, the attractor masses rotated in the opposite direction from the turntable with a period of 5 minutes. That second rotation screened out unaccounted-for gravitational influences from the outside world by turning them into a periodic signal that could easily be subtracted from the data. "You can walk up to this thing, and it won't affect the value," Gundlach says.

The result was a value of G (tentatively $6.67423 \pm 0.00009 \times 10^{-11}$ $m^3/kg \cdot s^2$) far more precise than physicists need for practical purposes. "It's one of the fundamental constants," Gundlach says. "Mankind should just know it. It's a philosophical thing."

–CHARLES SEIFE

* 29 April to 3 May, Long Beach, California.