In 1993, Rohan Pethiyagoda used his own money to found the Wildlife Heritage Trust in Colombo, Sri Lanka. He and his colleagues began a census of Sri Lanka's disappearing wildlife, systematically searching the 750 square kilometers of remaining rain forest, which once covered 15,000 square kilometers. To his surprise, he kept finding frogs he couldn't identify.

Pethiyagoda first showed the animals to frog systematists. They estimated there might be 200 new species, based on the morphology and other characteristics of 1000 specimens. Subsequent genetic studies reduced that number to 120 or so. Claims of a vast number of new species are often greeted with skepticism, but the new data are compelling, say the researchers' colleagues. This work, which combines traditional and molecular approaches, "is right at the forefront of what work in biodiversity should entail," says Roy McDiarmid, a systematist at the U.S. Geological Survey who is based at the Smithsonian National Museum of Natural History in Washington, D.C. Adds Wake, "The molecular data gives a certain validation to the assertion that these things are really different species."

The new species fall into two groups. One consists of just five species, all of which lay eggs in foam nests on leaves, rocks, or branches suspended above water. Once big enough to be out of danger from many aquatic predators, the hatched tadpoles slide off into the stream or pond below. But most of the newfound frogs are "direct developers" whose young never get their feet wet. These eggs incubate individually in leaf litter instead of foam nests, and they hatch as miniature adults, skipping the tadpole stage altogether. This water-free lifestyle "gives species a lot more latitude," McDiarmid explains, and "lends itself to geographic isolation and speciation."

Schneider thinks that these frogs have escaped the fate of other amphibians because disease, ultraviolet light, and other potentially deadly influences appear to be most dangerous to water-based young. "By skipping the aquatic [stage], they may bypass a life stage when they are most vulnerable," he suggests.

But there seem to be some dangers even these direct developers have not escaped. Co-author Kelum Manamendra-Arachchi of the Wildlife Heritage Trust traveled to museums containing specimens similar to the newly discovered ones, looking to confirm his species designations. He found many frogs—perhaps 100 species—that had been collected from Sri Lanka more than 100 years ago that were not among their current finds. "It means a huge number of species must have gone extinct already," says Wake, most likely because so much of the island's rain forest has been lost.

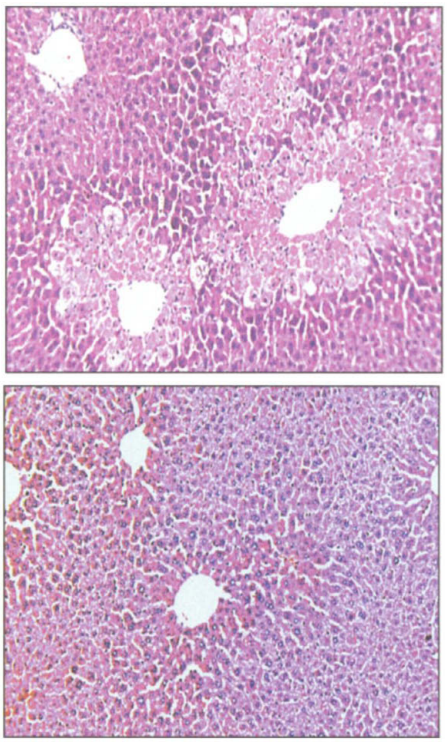
Therein lies the challenge for biodiversity's champions, says Paul Speck, president of the Arlington, Virginia–based Amphibian Conservation Alliance. "We're at a very precarious moment," he says; "there are a lot of species still out there [and] there is the opportunity to save many of them, but we need to act quickly." –ELIZABETH PENNISI

TOXICOLOGY

Protecting Liver From Painkiller's Lethal Dose

Last week a committee of the U.S. Food and Drug Administration recommended that medicines containing acetaminophen, a commonly used painkiller sold under the brand name Tylenol and in many over-the-counter cold and flu remedies, carry stronger warnings about its dangerous side effects. Every year in the United States overdoses of the painkiller cause acute liver failure in as many as 800 people, one-third of whom die as a result. New results help explain just how acetaminophen harms the liver. They may also provide a target for treating liver failure due to overdoses of acetaminophen and perhaps of other drugs as well.

On page 422, a team led by David Moore of Baylor College of Medicine in Houston, Texas, reports that the so-called constitutive androstane receptor (CAR) plays a central role in bringing about the biochemical



Protective effect. Liver cells die (pale areas) when exposed to high doses of acetaminophen (*top*), but a CAR inhibitor protects against such damage (*bottom*).

CREDITS: DAVID MOORE/BAYLOR COLLEGE OF MEDICINE

ScienceScope

Misconduct Aftershocks Bell Laboratories is moving to clear the wreckage created by the misconduct of its one-time nanoscience star, Jan Hendrik Schön. Officials at the Murray Hill, New Jersey, lab said this week that they are withdrawing six patent applications that are based on Schön publications, which an investigating committee has concluded contain fake data (*Science*, 4 October, p. 30). The lab had already asked U.S. and foreign patent offices to put the applications on hold, pending completion of the investigation. Lab parent Lucent Technologies had once hoped the patents, which involve novel transistors and electronic switches, might become cash cows.

Anger in Italy The heads of Italy's 107 research institutes are protesting government plans to cut science budgets and redirect ongoing reforms. Their strongly worded letter last week to Guido Possa, the government's vice minister for research, escalates a controversy that began last summer, when researchers attacked a leaked government plan to revamp Italian science (*Science*, 16 August, p. 1106). Now, they fear that a rumored 10% cut in the National Research Council's $500 million budget would virtually eliminate $50 million for new projects—along with about twice that amount in matching funds from other sources. Possa had not responded to the letter as *Science* went to press, but he told researchers earlier that he would meet with them next month.

Canadian Student Aid Canadian Prime Minister Jean Chrétien's swan song to his country contains an ode to graduate researchers. Last week Chrétien promised to boost spending on graduate studies and research in his first "Speech From the Throne" since this summer's announcement that he would retire in February 2004. His words lend support to a proposal by the nation's three granting councils for a 10-year, $2 billion program to help train young academics, although Industry Minister Allan Rock says that details await the new budget, due out next spring.

"There's a need for more money per student and more students," says Canadian Institutes of Health Research president Alan Bernstein. "There's 25% more people doing research than there were 2 years ago, and they all want good students and postdocs."

Any expansion, however, must find room in a tight government budget. And Chrétien's ability to set the political agenda is also in doubt after a de facto coup by former Finance Minister Paul Martin forced him to declare his pending departure.

changes that underlie acetaminophen toxicity. Moore and his colleagues "have shown clearly that the receptor is important," says Steven Kliewer, a liver toxicity expert at the University of Texas Southwestern Medical Center in Dallas.

The current work is an outgrowth of previous research by Moore's team and others showing that CAR helps the liver eliminate foreign chemicals. Ordinarily, Moore says, this system is protective, but in some cases it has the opposite effect, creating products that are more toxic than the originals.

A clue that CAR might be involved in acetaminophen toxicity came a few years ago. The drug phenobarbital increases susceptibility to acetaminophen damage because it fosters production of two enzymes in the CYP family that convert acetaminophen to a highly toxic compound called NAPQI. The cell normally eliminates NAPQI by tying it up with a detoxifying molecule called glutathione. But if NAPQI production outstrips the glutathione supply, cell damage occurs. "Everything is fine until you run out of glutathione," Moore says. CAR comes into the story because Moore and other researchers found that phenobarbital works through that receptor to enhance CYP enzyme production.

Following up on that observation, Moore and his colleagues now report that CAR is involved even more directly in acetaminophen toxicity. In normal mice, high doses of acetaminophen increased production of the CYP enzymes and also an enzyme called GSTPi that attaches glutathione to NAPQI and other molecules. That could be a double whammy for liver cells, increasing NAPQI production at the same time glutathione supplies are depleted. Indeed, the animals showed signs of severe liver damage, such as patches of dying liver cells. In animals in which the CAR gene had been inactivated, the same doses of acetaminophen did not increase production of CYP or GSTPi enzymes. Although those animals suffered some liver damage, it was much less than that of the normal mice.

Inactivating the human counterpart of the CAR gene before an overdose isn't a likely therapeutic strategy. But Moore's team found that androstanol, a compound that inhibits CAR activity, protected mice against acetaminophen-induced liver damage even after exposure to the painkiller. It provided 100% protection 1 hour later and 50% protection 3 hours later.

Different species can vary significantly in their reactions to foreign chemicals. To determine whether the human CAR receptor responds to acetaminophen the same way the mouse version does, the Baylor group created a line of mice whose liver cells contain only human CAR. When these "humanized mice" were treated with phenobarbital or acetaminophen, their livers showed damage similar to that in normal mice, Moore says.

More work will be needed to show whether CAR inhibitors might be useful treatments for human liver toxicities, however. One problem is that androstanol does not inhibit the human CAR receptor, so researchers would have to develop new inhibitors that do. And any new treatment would also have to outperform the one currently available, a compound that replenishes the liver's glutathione stores; it works well if given within several hours of the toxic painkiller dose. Moore is looking at whether other liver toxins also work through CAR and might be candidates for treatment.

Kliewer, for one, is hopeful that work on CAR might lead to new therapies: "The more we understand about the mechanisms [of liver toxicity], the more opportunities we will have for treatment." –JEAN MARX

PHYSICS

Quantum Experiment Asks 'How Big Is Big?'

Watch out, world: Erwin Schrödinger's infamous cat is straining at its leash. The cat—a seemingly ridiculous example of a familiar object ruled by quantum-mechanical laws—symbolizes the gulf between our world and the world of the very small. Now quantum physicists propose to bridge that gap by creating by far the biggest quantum-mechanical object ever constructed. If they succeed, the experiment might reveal whether the bizarre quantum antics of small things such as atoms and photons can crop up in large things such as cats and bricks—and if not, why not. "Basically, if this works, you've extended the validity of quantum mechanics by nine orders of magnitude," says Max Tegmark, a theorist at the University of Pennsylvania in Philadelphia.

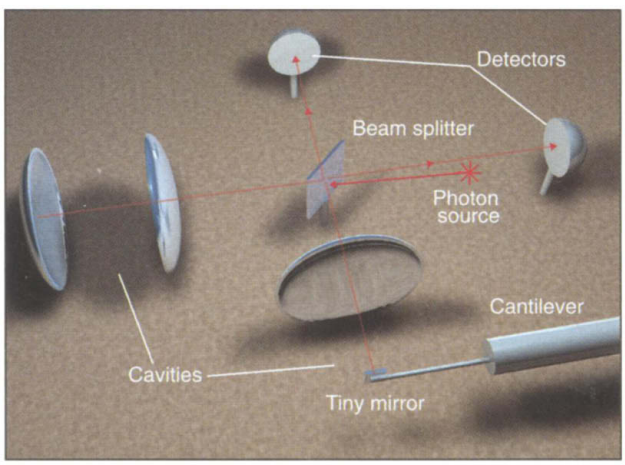
The work explores the concept of superposition, a quantum object's ability to be two opposite things at the same time, like a switch that is at once both on and off. Physicists have long wondered why superposition works with small objects such as photons but not with large ones such as cats. To find out, they have been trying to put increasingly large objects in superposition or teach them other quantum tricks. Anton Zeilinger of the University of Vienna, Austria, for instance, has shown that 70-atom buckyballs, enormous by quantum standards, can still act like quantum objects (*Science,* 25 May 2001, p. 1471).

Now Roger Penrose of Oxford University, U.K., Dik Bouwmeester of the University of California, Santa Barbara, and colleagues have designed a Schrödinger's cat billions of times larger than Zeilinger's record-holding molecules. "It was not clear whether it was feasible at all," says Bouwmeester. "But the more calculations we did, the more it seemed feasible."

The proposed experiment, described in a paper submitted to *Physical Review Letters*, starts with an interferometer. The device is normally used to split a light beam and then, using mirrors, to reroute the two halves so that their waves amplify or cancel one another. Physicists have found that, perversely, a single photon fired into an interferometer behaves the same way: On reaching the beam splitter, it shoots off in two directions at once—a clear case of superposition.

In the Penrose team's device (see graphic), the photon's two-pronged path leads to a pair of mirrored cavities, where the photon bounces around for a while before escaping whence it came. One cavity sports a mirror 10 micrometers wide—about the breadth of a red blood cell—perched at the tip of a cantilever tuned so that the mirror moves if a photon strikes it. That mirror is the "cat." If subatomic particles played by common-sense classical rules, the photon would follow just one of the two paths, either striking the mirror and making it move, or hitting the other cavity and leaving the mirror stationary. But because the photon is in superposition, it both makes the mirror move and leaves it stationary at the same time.

En route back from the cavities, the photon is shunted into detectors that reveal whether the mirror did or did not move. By sending photon after photon through the device, the scientists can learn whether



Bright idea. The proposed experiment would make a lone photon imprint its split personality on a micrometer-scale mirror.

ILLUSTRATION: C. SLAYDEN