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.

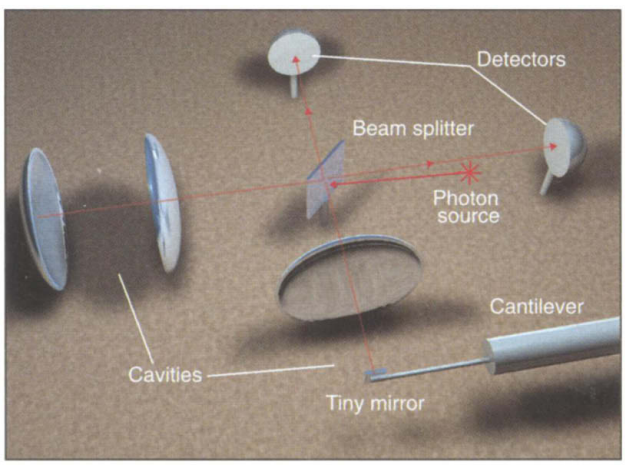
The work explores the concept of superposition, a quantum object's ability to be two opposite things at the same time, like a switch that is at once both on and off. Physicists have long wondered why superposition works with small objects such as photons but not with large ones such as cats. To find 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

the mirror is in the "did move" state, the "did not move" state, or a superposition of the two, and they can measure how long the superposition lasts.

If the experiment actually puts a mirror into superposition, it will suggest that there is nothing fundamental about large things that makes them behave like classical objects rather than quantum ones. "If quantum mechanics hasn't gone wrong at the size of a cell," Tegmark says, "it probably won't go wrong with something the size of a mouse or a human." Bouwmeester's team is already testing components that will go into the lab setup, which requires very high vacuums, very cold temperatures, and very precise measuring equipment. Should the team overcome those formidable hurdles, Schrödinger's hypothetical tabby might become more than a pet notion. **–CHARLES SEIFE**

SWITZERLAND

Compromise Allows Transgenic Trials

BERN—Swiss biologists believe they have won a decisive victory in a 9-year battle with campaigners opposed to genetically modified (GM) organisms. After 11 hours of rancorous debate, the National Council, the lower house of the Swiss parliament, voted last week to accept watered-down legislation governing gene technology. To the relief of researchers, the council deleted measures that would restrict research and impose a 5-year moratorium on commercial release of GM organisms. The new version is "a good sign for young scientists to stay in the field," says Heidi Diggelmann, president of the Swiss National Science Foundation's Research Council.

Don't eat this. Swiss officials have approved field tests of wheat engineered to resist the stinking smut fungus, which smells and apparently also tastes "just like rotten fish."

Anti-GM groups first aired the Gene-Protection Initiative in 1993 to ban all research on GM animals and patenting of any GM organism. Researchers went on the offensive, attempting to convey to the public the importance of their research. In 1996 a bill was put forward as a compromise, plugging gaps in existing law without aggressively curbing GM research. The initiative was decisively defeated in a national referendum (*Science*, 12 June 1998, p. 1685).

However, under pressure from anti-GM groups, the bill was modified to include provisions such as limiting releases of GM organisms to biosafety experiments that could be guaranteed to be 100% risk free and could not be performed with conventional means. These were poison pills to many scientists, who argued that the terms would amount to a de facto ban on basic transgenic research. The proposed legislation would also have banned antibiotic resistance genes in deliberately released GM organisms and would have held producers of GM products liable for damages for up to 30 years, even for nondefective, grossly misused products.

Some members of parliament rallied against these measures, and last-minute negotiations succeeded in defanging the bill. Under the approved measures, there will be no commercial moratorium, and restrictions on the release of GM organisms for research will be eased. In addition, antibiotic resistance genes in released GM organisms will be allowed until 2008, and in general, producers of GM products will be liable only for defective products. The legislation still has to go to the upper chamber of parliament for final revisions, but a moratorium looks unlikely.

Although many scientists are satisfied with the outcome, they are not dancing in the streets. Gottfried Schatz, president of the Swiss Science and Technology Council, a government advisory group, says that the approved measures were "the best that could be hoped for given the current climate of mistrust." Daniel Ammann, director of the Swiss Gene-Technology Working Group, an anti-GM umbrella organization, confirms that the group plans to continue its fight by seeking a ban on any commercial release of GM organisms.

The modifications dispel a cloud of uncertainty that had been hanging over Switzerland's first-ever field trial of GM plants. On 13 September, Moritz Leuenberger, head of Switzerland's Department of Environment, Transport, Energy, and Communications, approved the trial of wheat engineered to make a protein toxic to a crop pest called stinking smut fungus. Regulatory authorities had rejected the proposed experiment last year on the grounds that the transgenic plants contain an antibiotic resistance gene (*Science*, 7 December 2001, p. 2067). Leuenberger approved the trial "solely for legal reasons," as current laws do not require such an experiment to exclude all possible safety risks. Final approval is expected in a few months. **–MIN KU**

Min Ku is a writer in Bern, Switzerland.

ScienceScope

A Pox on Polygraphs In the first major U.S. government report on polygraphs since 1983, a panel of the National Academy of Sciences this week said the government should not use the so-called lie detectors to see if an employee poses a security risk. The study, commissioned by the Department of Energy (DOE) in the wake of the Wen Ho Lee affair (*Science*, 15 September 2000, p. 1851), says that although the devices can be a help to criminal investigators, they are too crude to screen out possible spies.

The panel, led by statistician Stephen Fienberg of Carnegie Mellon University in Pittsburgh, Pennsylvania, notes that lie detection research "has not progressed ... in the manner of a typical scientific field." It calls for expanded tests of the polygraph and other "indicators of deception."

The panel has briefed DOE and other agencies that now test thousands of employees. Fienberg didn't say if any was planning a change in policy, but polygraph critics say the course is clear. Physicist Alan Zelicoff of DOE's Sandia National Laboratories in Albuquerque, New Mexico, says the panel has come to a "very strong conclusion. ... As a screening test, [the polygraph] has now been tossed onto the ash heap of history."

Hatchet Buried After years of wrangling, Russia and the World Health Organization (WHO) have agreed to cooperate in attacking the country's tuberculosis (TB) crisis. The deal, reached late last month, will funnel up to $150 million in World Bank loans into a revitalized TB monitoring and treatment system.

TB has soared to epidemic levels in Russia, and the disease now claims 30,000 lives annually. But many Russian specialists rejected WHO's insistence on tying aid to the use of Western anti-TB strategies, such as microscopy for detection, saying that homegrown methods, such as mass x-ray screening, worked fine (*Science*, 12 July, p. 170). New results from 18 projects that integrate Russian and WHO methods, however, helped end the standoff. The projects, begun in 1994, have boosted detection and lowered incidence rates, officials say.

"Five years ago ... we couldn't find common ground," Anatoly Vialkov, a deputy health minister, said in announcing the deal. "Today we understand each other." The World Bank must still approve the loan.

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