expected to benefit, as the law requires. The newspaper reported that Steiner, in his presentation at the AACAP meeting and in a recent interview with the *Times*, said he chose a dose so low as to have no effect. If that is true, it might be considered a placebo, which would generally be seen as not providing subjects with a reasonable chance to benefit.

Steiner vigorously denies designing a sneak-placebo, although he says a placebo would have made the analysis more powerful. But even the low-dose arm could well have had a therapeutic effect, he says, citing the experience with other psychoactive drugs, including Haldol and commonly used antidepressants, which were found to be effective at levels much lower than what had once been given. Psychiatric experts will weigh those arguments during the state's review.

The use of a low-dose arm as a placebo "would certainly fail to meet the intent of the regulations," says bioethicist Jeffrey Kahn, director of the University of Minnesota Center for Bioethics. But Kahn says that juvenile inmates can also lose out if the laws protecting them are so strict as to prohibit potentially beneficial research from being done. One could argue, he says, that juvenile and adult prisoners are no more compromised in their ability to make informed choices than seriously ill hospital patients who routinely serve as study subjects, and that inmates are selectively being denied "the benefits of research participation … because of the current law."

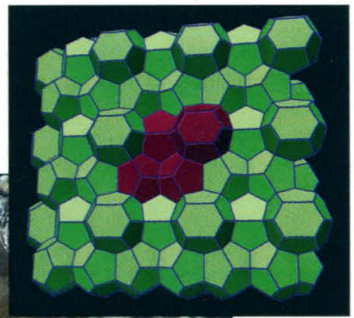
Larry Stone, executive medical director of Laurel Ridge Hospital in San Antonio, Texas, and a past president of the AACAP, supports that view. "Certainly prisons are the places where … we should be experimenting with a number of things for rehabilitation," including medications, he says. "My concern is that good, solid researchers who are trying to do that do not get persecuted and tried in the media because of some quirk in the system."

–MARCIA BARINAGA

MATHEMATICS

## Proving the Perfection Of the Honeycomb

Why do bees build their honeycombs out of hexagonal cells? As early as the first century B.C., Marius Terentius Varro—Rome's answer to Isaac Asimov, the most prolific science writer of his day—speculated that it had to do with the economy, rather than the symmetry, of the design. From Varro to the present, scientists have assumed that a hexagonal lattice allows bees to store the most honey in a single layer of equal-sized cells, while using the least beeswax to separate them. Until this summer, however, no one could prove that a honeycomb was the sweetest solution. Now, a mathematician has removed all doubt: Bees do it best. The result also confirms the intuition of human engineers, who have relied on honeycomb composite materials made of paper, graphite, or aluminum to reduce the weight of components for cars, planes, and spacecraft with little sacrifice in strength.



**Perfect and near-perfect.** Bees use optimal construction for a two-dimensional foam; Weaire and Phelan's foam (*inset*) remains unbeaten in three dimensions but is not known to be optimal.

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Last month, at the Turán Workshop in Mathematics, Convex and Discrete Geometry in Budapest, Thomas Hales of the University of Michigan, Ann Arbor, presented his proof that a hexagonal honeycomb has walls with the shortest total length, per unit area, of any design that divides a plane into equal-sized cells. (The proof has also been available on the Web since June.) Hales says that he began working on the honeycomb conjecture just last year, after solving a similar conjecture on the packing of spheres (*Science*, 28 August 1998, p. 1267). That problem, called the Kepler conjecture, stated that the densest packing of spheres is a face-centered cubic lattice, the pattern a grocer makes when he stacks apples. The proof had taken years. "After the Kepler conjecture, I expected every problem to be very difficult," Hales says. "In this case, I feel as if I won the lottery."

Both questions, Hales explains, can be viewed as versions of the same physical problem: how bubbles of equal volume are distributed in foams. "In a really wet foam, the faces of each cell are not surfaces but have thickness," Hales says. Because a sphere uses the smallest possible surface area to hold a given volume, the bubbles acquire a spherical shape, with the foam material filling up the interstices. Minimizing the amount of extra foam translates to maximizing the number of spherical bubbles per unit volume—the problem Hales solved last year.

A honeycomb is more like a dry foam. "In a dry foam, the walls have zero thickness," Hales explains. With no space between them, the bubbles in a dry foam affect one another's shape and thus can't all be spheres. And although Hales showed that a wet foam of equal-sized bubbles will form a regular lattice, with all its cells the same shape, no one knew whether the same is true for a dry foam. In 1994, Denis Weaire and Robert Phelan of Trinity College in Dublin had found an arrangement of bubbles with equal volume but different shapes, which used 0.3% less wall area than the best known single-shape arrangement.

Weaire and Phelan's discovery led to renewed scrutiny of the honeycomb—in effect, a two-dimensional foam, because bees build just a single layer of cells. Mathematicians realized they still didn't have an adequate explanation for why the cells in a honeycomb had the same shape. Could an optimal honeycomb, like Weaire and Phelan's foam, have cells of different shapes, with some being pentagons or heptagons, say, or having curved sides?

Any individual bubble can improve its perimeter-to-area ratio by rounding its sides out to circular arcs, or by adding more sides (because a heptagon is rounder than a hexagon). But that improvement comes at a cost to its neighbors. As mathematicians have long known, the topology of the plane forces the average number of sides to be six, so any heptagon must be balanced, for example, by a less efficient pentagon somewhere else. Similarly, one bubble's outward-curving arc will curve inward to the adjacent bubble and make its perimeter-to-area ratio too large. The question was how to calculate these trade-offs to find out whether one bubble's gain outweighs its neighbor's loss, making the overall arrangement more efficient.

"Hales's bright idea was that no single

cell can do better than a hexagon if appropriately penalized for having more than six sides or outward curves," says John Sullivan of the University of Illinois, Urbana-Champaign. Although other mathematicians, including Weaire, had discovered a penalty for the number of sides, Hales is the first to find the right penalty for the curvature of the sides and to combine both penalty terms.

Other geometers seem quite pleased with the proof. Unlike Hales's proof of the Kepler conjecture, which involved thousands of elaborate computer calculations, the proof of the honeycomb conjecture does not require a computer at all. "The overall idea just seems right," Sullivan says. "There should be an easy reason for a pattern this simple, and I think Hales has found it." –**DANA MACKENZIE**

Dana Mackenzie is a writer in Santa Cruz, California.

DEVELOPMENTAL BIOLOGY

## Selenium's Role in Infertility Explained

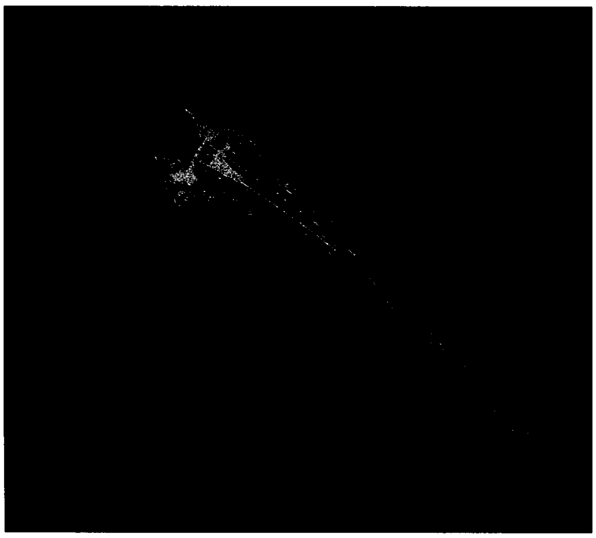
Many proteins lead multiple lives, depending on environmental conditions or on the presence of particular partners. It's rare, however, for a protein to change its stripes completely, acting as a soluble enzyme under some circumstances and an insoluble structural component under others. But that's what new research suggests for a particular selenium-containing protein of sperm—a discovery that may help explain the long-standing mystery of why selenium deficiency in lab and domestic animals leads to male sterility.

On page 1393, biochemists Leopold Flohé of the Technical University of Braunschweig in Germany, Fulvio Ursini of the University of Padova in Italy, and their colleagues report that the protein, previously identified as an enzyme that helps rid developing sperm of dangerous reactive oxygen molecules, moonlights as part of the glue that holds together mature sperm. "This is a new function for a selenoprotein—to form a structure, not just to carry out a reaction," says Raymond Burk, a selenium expert at Vanderbilt University in Nashville, Tennessee.

Although selenium deficiency is rarely a problem for humans, who get the element from common foods such as seafood, liver, lean red meat, and grains grown in soil that is rich in selenium, scientists showed decades ago that animals fed selenium-deficient diets produce sperm that break in the middle and can therefore no longer fertilize eggs. Beyond demonstrating that selenium is concentrated in the midpiece, the region between the head and tail, of normal sperm, scientists made little headway in explaining this effect. Several years ago, they thought they had an answer: The selenium deficiency might be interfering with another protein they had identified in the mitochondrial capsule, a structure that holds the energy-producing mitochondria in the sperm midpiece.

But that idea dropped out when sequence analysis of the corresponding gene revealed that in some perfectly normal animals it doesn't encode the amino acid that carries selenium—evidence that the element isn't required for the protein's function. "There's been a question of whether there is such a thing as a real structural selenoprotein in sperm," says Thressa Stadtman, a selenium biochemist at the National Heart, Lung, and Blood Institute in Bethesda, Maryland.

Flohé and his colleagues have now shown that there likely is, by studying a known selenoprotein called phospholipid hydroperoxide glutathione peroxidase (PHGPx). The enzyme, which likely protects the developing sperm cell against damage by converting toxic peroxides to harmless alcohols, climbs to extremely high levels in testes. Because the levels are much higher than would be expected for protection against the amounts of peroxides probably present in that tissue, Flohé describes the situation as "kind of strange." About 2 years ago, however, his team's work began pointing to a structural role for the protein. Their analysis of the mitochondrial capsule showed that PHGPx is its most abundant component, accounting for about 50% of the capsule material.



**Sperm aid.** A selenoprotein known as PHGPx may help keep normal sperm, such as this one, from breaking apart.

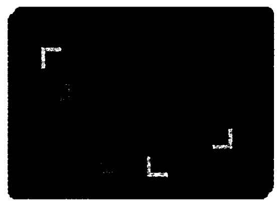
But even though it constitutes such a large proportion of the capsule, tests revealed that the protein from mature sperm had lost its enzymatic activity, apparently because the protein molecules had become linked together in an inactive form. Based on these findings, the researchers propose that PHGPx acts as a soluble enzyme early in sperm development and later polymerizes into a protein mesh that contributes to the structural integrity of the midpiece. If so, says Burk, "this [work] may explain the head-to-tail separation seen in sperm of selenium-deficient animals."

In addition, the result opens the door to a better understanding of the mechanisms underlying normal sperm development, presumably in humans as well as in animals, say experts. Currently, Stadtman notes, the triggers for the switch from active enzyme to inactive structural protein are not known. "The next step is to work out the signals that tell the sperm to undergo this developmental change," she says. Indeed, as anyone who has juggled identities knows, timing is one key to success. –**EVELYN STRAUSS**

NEUROBIOLOGY

## New Role Found for The Hippocampus

When you remember a friend, your first day of work, or your address, you're fully aware of what you're remembering. But memory has another guise: nonconscious skills like riding a bicycle or knowing how to tie your shoes. Subjectively, the two kinds of memory seem very different, and the brain structures responsible for them are different as well. Results reported in this month's issue of *Nature Neuroscience* suggest, however, that the hippocampus, a twist of tissue deep in the brain long believed to help form only conscious memories, also serves certain memories that don't rise to the level of awareness.



**T is for target.** Without a healthy hippocampus, subjects couldn't learn from seeing the same complex pattern twice.

The report comes from psychologists Marvin Chun of Vanderbilt University in Nashville, Tennessee, and Elizabeth Phelps of New York University. Chun and Phelps compared how normal people and those with anterograde amnesia, a memory defect caused by damage to the hippocampus, respond to certain complex patterns. They found that the normal subjects, but not the amnesiacs, could learn to remember repeated patterns they weren't consciously aware of. "What they've con-

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