the natural gels, which are found in secretory granules, sacs that ferry substances like neurotransmitters, growth factors, and hormones to the cell surface, where they are expelled in a process called exocytosis. "Our expectation was that the result would be very uninteresting, just a number," says Fernandez. As a test case, they chose certain easily studied granules found in mast cells, immune-system cells that play a role in allergic reactions by releasing their cargo of histamine.

Researchers already knew that another component of the granules, a crosslinked network of a polymer called heparin, plays a role in the release. The heparin mesh expands several-fold when a secretory granule fuses with the cell membrane, allowing ions from outside the cell to rush in. Current theory holds that the swelling results because incoming sodium ions are less efficient than histamine or calcium—another granule component—at shielding the negatively charged strands of heparin from one another. When enough sodium enters, the strands repel each other and the matrix swells, absorbing more water and allowing its contents to diffuse out.

Nanavati and Fernandez's work, however, suggests that the ion exchange might not be the only swelling mechanism at work. They isolated mast cell matrices and placed them in a glass pipette to which they could apply varying voltage. At positive voltage, the granule matrices were condensed, opaque, and poorly conducting. But when the voltage was negative, the matrices swelled in milliseconds, becoming transparent and highly conducting. Fernandez speculates that such voltage-stimulated swelling may also occur during exocytosis, triggered by a voltage that may be generated when a granule first opens to the extracellular space.

Others aren't sure the laboratory results say anything about processes in the living cell. "I think it may have a physical significance but not a physiological one," says cell biologist Michael Curran at Baylor College of Medicine. Indeed, the arresting properties of the heparin matrix do make it seem destined for roles on a larger stage. The Mayo Clinic certainly thinks so; it has filed a patent covering several possible uses of the gel.

Because its conductance varies with voltage, for example, the matrix might serve as a biocompatible electrical diode for implantable mechanisms. The patent also suggests that the electrically induced optical properties of these matrices might give them a role in display technology. And because the gel is strong as well as sensitive, exerting a force equivalent to a few hundred pounds per square inch as it swells, it could drive gears in micromachines, says Fernandez. All those possibilities may mean that human technologists will once again be taking their lessons from nature.

–John Travis

MEETING BRIEFS

Mathematicians Gather to Play the Numbers Game

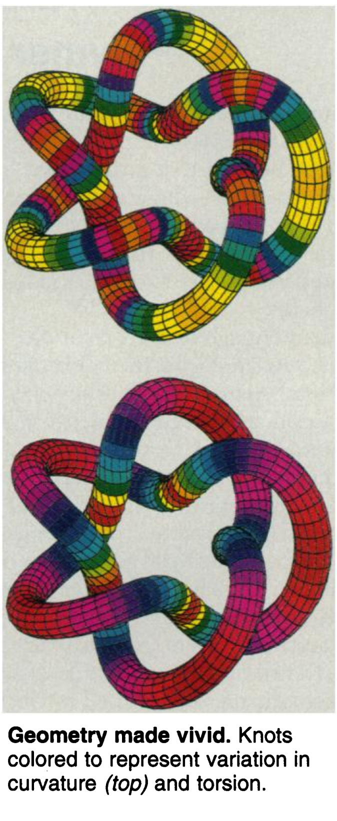
The Riverwalk area in San Antonio was crawling with mathematicians for a week in January, when the American Mathematical Society and the Mathematical Association of America held their joint annual meetings. Among the topics that kept the bars, halls, and lecture rooms abuzz from 11–16 January were the latest results on some venerable problems in the field and the effect of a brand-new technology, computer graphics, on the process of mathematical discovery.

Abstract Expressionism In Math

Mathematicians often talk about the beauty of a theorem or proof, but that beauty is rarely apparent to nonmathematicians. Now, however, computer graphics is helping to change that. Increasing power and decreasing costs have turned even the least artistically talented mathematician into a Rembrandt with a laser printer. But to mathematicians, the resulting images are more than just a vivid way to advertise their work to the public. In some cases, in fact, the computer's capacity for graphics is changing the direction of mathematical research.

Alfred Gray of the University of Maryland, who drew the twin "torus" knots at right using the computer algebra system *Mathematica*, thinks graphics is driving such a change in differential geometry. Loosely defined as the study of curvature, differential geometry has found applications in fields as disparate as Einstein's theory of general relativity and molecular biology, where researchers have become interested in what it has to say about such things as the supercoiling of DNA.

In recent years, though, mathematicians' explorations of the subject have begun to turn increasingly abstract, with algebraic symbols playing a bigger role than geometric shapes. But now that tide is beginning to flow in the other direction, thanks to the accurate, three-dimensional images that computers can spew forth with ease. "People are looking at more concrete things [now]," Gray says. And as graphics technology gets into more hands, that trend is likely to continue. "The revolution is only in its beginning stages," he adds, but already it's aided mathematicians in such things as the discovery, in the mid-1980s, of an entire new class of "minimal" surfaces.



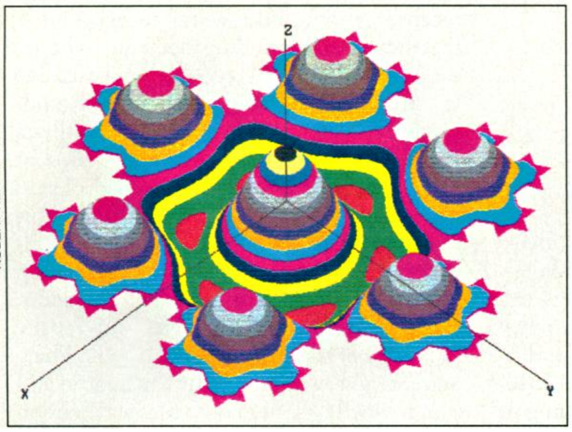
ALFRED GRAY

Geometry made vivid. Knots colored to represent variation in curvature *(top)* and torsion.

Differential geometry is not the only place where pictures help. Michel Lapidus of the University of California, Riverside, is looking to computer graphics to gain extra insight into analytical theories he's been developing over the past several years. Lapidus is interested in the reverberations of mathematical "drums" with fractal boundaries (*Science*, 13 December 1991, p. 1593). The interaction of wave phenomena and fractals is an important aspect of scattering theory for applications such as radar ranging, Lapidus points out, but it also contains many problems of purely mathematical interest.

Recently, Lapidus has begun analyzing the waveforms produced when the fractal drums reverberate. For help, he turned to Robert Renka and John W. Neuberger at the University of North Texas, who wrote programs to produce pictures of standing waves on a fractal shape known as the Koch snowflake. The picture on the next page shows how the "energy" of a waveform is concentrated at a relatively few peaks, Neuberger notes. That image isn't breaking new ground—it confirms what the researchers already knew—but it does give them confidence in their numerical methods. And their next steps in computer artistry may well break new mathematical ground. Lapidus is particularly interested in exploring what the standing wave looks like close to the fractal drum's infinitely crinkled

ROBERT RENKA AND JOHN NEUBERGER



Trapped in a fractal. Energy peaks on a fractal drum.

boundary. That's unknown territory, he says—turf where both graphics and theory are in "very preliminary stages."

Gaps in a Sphere-Packing Proof?

In mathematics, the most obvious "truths" can be the hardest to prove. Take the experience of Wu-Yi Hsiang of the University of California, Berkeley. Three years ago, Hsiang announced a solution to a centuries-old problem in solid geometry: proving that the densest possible packing of spheres is the "face-centered" cubic arrangement often seen in stacks of oranges. But Hsiang's proof has still not won acceptance by other experts in the field: Doubters think his reasoning is flawed at some points and unclear at others. At the meeting, he unveiled a shorter version of his proof, which he thinks will satisfy the critics.

The problem Hsiang claims to have solved is known as the sphere-packing problem (*Science*, 1 March 1991, p. 1028). In 1611, Johannes Kepler stated—without proof—that the face-centered cubic arrangement, which fills slightly more than 74% of space ($\pi/\sqrt{18}$, to be exact), gives the densest possible packing. Kepler's statement has vexed mathematicians for more than 380 years: It's "obviously" true, but no one has been able to offer a mathematically satisfactory proof. Not surprisingly, Hsiang's attempt has attracted intense interest and careful scrutiny.

Common to both versions of Hsiang's proof is an approach that combines spherical geometry with calculus and vector algebra to obtain estimates of the "local density" of various sphere packings, then converts these estimates into "global" densities. The global densities can then be compared to test Kepler's conjecture. Sphere-packing experts who looked at Hsiang's earlier proof agree the approach is sensible, but some think he has unjustifiably dismissed certain cases.

"A lot of people think it's a legitimate approach, but an approach is not a proof," says Tom Hales of the University of Chicago, who has also worked on the problem. Hsiang's original proof, says Hales, "had so many flaws that were so obvious that many people threw it into the corner in disgust."

Hsiang admits the original proof omitted details and was "not as clean-cut" as he wanted. He claims the new version corrects those errors. Strangely, his new proof is also a good deal shorter: a svelte 98 pages, compared to the nearly 200-page original, which should make it easier for other mathematicians to reach a verdict. And some of them, Jon Reed of the University of Oslo, for example, are already convinced. Reed spent 2 months last fall poring over the details of Hsiang's revised proof. "I believe it's correct and complete," he says.

Others are reserving judgment. "There are still some things that make me uneasy about the proof," says Doug Muder of the Mitre Corp. in Bedford, Massachusetts, who owns the best previous results on the sphere-packing problem: In 1988, he proved that no sphere-packing can fill more than 77.836% of space. Muder thinks Hsiang's argument contains too many unsupported claims—statements that are most likely true but need shoring up with rigorous proof.

But Hsiang is confident that in time, other people's geometric understanding of the problem will catch up with his own. "In the end, this whole thing will be resolved by clean-cut logic," he says. He regards the controversy over his proof as a dispute about subjective standards of how much detail a properly written mathematical proof has to contain. It "has nothing to do with me," says Hsiang, "and it has nothing to do with sphere packing."

A New Step for Fermat's Last Theorem

Another obvious "truth" that has posed a long-standing problem for mathematicians is Fermat's Last Theorem—the famous assertion that the equation $x^n + y^n = z^n$ has no solution in positive integers x, y, and z if the exponent n is greater than 2. The theorem, which is nearly as old as Kepler's sphere-packing conjecture, still has not been proved in general. But researchers are slowly extending the mathematical territory within which it is known to be true. At the San Antonio meeting, number theorists were talking about the latest milestone: Fermat's Last Theorem is now known to be true for all exponents up to 4 million, up from 1 million 2 years ago and a mere 150,000 just 6 years ago.

This territorial expansion results from a monumental computational effort carried out late last year by Joe Buhler at Reed College in Portland, Oregon, and Richard Crandall at NeXT Computer Inc., in Redwood City, California, with help from mathematicians Tauno Metsänkylä and Reijo Ernvall at the University of Turku in Finland. The work does more than verify Fermat's Last Theorem in a broader domain. Along the way, it has yielded other insights into number theory and provided a rigorous test of new computational techniques.

The latest work extends a 1991 computation by Buhler, Crandall, and Richard Sompolski at Oakton Community College in Des Plaines, Illinois, which verified Fermat's Last Theorem for exponents up to 1 million. The trio did so by calculating and testing what number theorists call "irregular" primes—primes that divide the numerator of one or more associated fractions known as Bernoulli numbers—up to 1 million. Fermat's Last Theorem has already been shown to be true for all "regular" primes and the composite numbers of which they are factors, so only irregular primes and the associated composite numbers are in doubt.

In their new calculations showing that the theorem holds for irregular primes up to 4 million, Buhler and his colleagues in effect gave it a double boost. Mathematicians have had to reckon with the possibility that the number of regular primes, for which the theorem is known to hold, is finite—in contrast to the irregular primes, which are known to be infinite. The current computations, however, support an earlier claim that regular primes actually outnumber irregular primes, in a ratio of roughly 3 to 2.

To cope with the vast amount of computation these results entailed, the researchers made use of a relatively new practice called distributed computing, in which large numbers of machines contribute toward a large-scale effort, sort of like a computational quilting bee. The calculations of irregular primes were spread over about 100 NeXT workstations, which did the estimated 10^{15} operations required. "This is about as big a computation as you tend to find," Buhler notes.

Keeping the computation even that small was hard work, requiring algorithms for doing exact arithmetic with enormously large polynomials. Pushing the verification of Fermat's Last Theorem further isn't out of the question, but researchers won't get much past 4 million without developing new computational techniques, Buhler predicts. That's part of the reason for trying, he adds: "So far every jump has required a genuinely new idea."

And the jumps so far haven't just shed light on Fermat's Last Theorem. In an unrelated bonus, the calculations also supported Vandiver's conjecture, a somewhat arcane statement about prime numbers that is key to certain areas of number theory. That result is especially welcome, says Buhler, because even though no one doubts Fermat's Last Theorem, Vandiver's conjecture is still a tossup.

–Barry Cipra