Stephen Hawking, theoretical physicist and best-selling author, visits his Caltech collaborators once every year or so. During his stay he traditionally gives a public lecture, which invariably overflows Beckman Auditorium. This time, some hardy undergrads showed up in the middle of the night in order to be sure of being first in line for the free tickets required for admission. It's as close as Caltech gets to hosting a rock star—when the box office opened later that morning, the ticket line wrapped all the way around the Gene Pool and extended nearly to Del Mar Boulevard.

You Light Up My Mice

Specially prepared HIV-derived viruses stripped of their disease-causing potential have been harnessed to introduce foreign DNA into animals in a method that could have wide-ranging applications in biotechnology and experimental biology. David Baltimore, professor of biology and president of Caltech, and his team have infected single-celled mouse embryos with the virus, leaving a new gene from a jellyfish permanently deposited into their genomes.

The resulting mice carried at least one copy of the gene in 80 percent of the cases, and 90 percent of these showed high levels of the jellyfish protein. Furthermore, their offspring inherited the gene and made the new protein. (The mice were given the jellyfish gene for Green Fluorescent Protein, which makes the cells containing it glow green under an ultraviolet light—an easy way to verify that the gene had been transferred in good working order.) Such animals that carry and pass on a foreign gene are called transgenic.

"It's surprising how well it works," says Baltimore, whose Nobel Prize-winning research on the genetic mechanisms of viruses 30 years ago is central to the new technique. "This technique is much easier and more efficient than the procedure now commonly in use, and the results suggest that it can be used to generate other transgenic animal species." The current method involves injecting the new gene into the nucleus of an egg cell before it is fertilized.

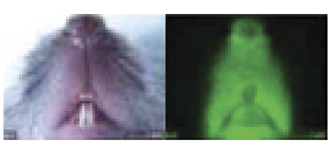
The new technique uses HIV-like viruses known as lentiviruses, which can infect both dividing and non-dividing cells, to insert new genes into the cell's existing genome. Unlike HIV, the lentivirus is rendered incapable of causing AIDS. Baltimore and his team developed two ways of introducing the lentivirus into cells: microinjection of virus under the layer that protects recently fertilized eggs, or incubation of denuded fertilized eggs in a concentrated solution of the virus. The latter method is easier, although less efficient.

Transgenics holds promise to biotechnology and experimental biology because the techniques can be used to "engineer" new, desirable traits in plants and animals, provided the trait can be identified and localized in another organism's genome. A transgenic cow, for example, might be engineered

Right: Warts on a fingertip? No. Craters on Mars? Wrong again. The ripples on this slab of sandstone were left on a shallow seafloor more than 500 million years ago. The rings mark the last resting places of a school of jellyfish.

to produce milk containing therapeutic human proteins, or a transgenic chicken might produce eggs low in cholesterol. In experimental biology, transgenics are valuable laboratory animals for fundamental research. A cat with an altered visual system, for example, might better accommodate fundamental studies of the nature of vision.

According to Baltimore, the procedure works on rats as well as mice. This is a huge advantage to experimentalists because of the number of laboratory applications in which rats are preferable, he says. The paper appeared in the February 1 issue of *Science*. The other authors of the paper are postdoc Carlos Lois; undergrad Elizabeth Hong, a senior this year; Shirley Pease, a Member of the Professional Staff; and postdoc Eric Brown. □—*RT*



Like a Grateful Dead poster under a black light, this transgenic mouse glows in the dark.

Jellyfish in the Sands of Time

And speaking of jellyfish, postdoc James Hagadorn has found an armada of them in a flagstone quarry in Wisconsin. Finding a fossil impression of a soft-bodied creature in a coarse-grained deposit is rare; finding hundreds of them in one spot is almost unheard-of. In fact, this is only the second mass stranding of jellyfish ever found.

Jellyfish (more properly, scyphozoan medusae) used to run aground all the time, of course, just as they do now. "The only reason these were preserved is that there were no higher organisms in this setting," says Hagadorn. "If they washed up on the beach today, the birds would eat them. Or your dog. Or if they did get buried, a burrowing horseshoe crab would churn up the impression. These fossils are from the end of the Cambrian era, about 510 million years ago, just before land animals appeared. So it's not that something caused them to be preserved, but the lack of something that was destroying them."

It's precisely because these jellyfish were at the top of the food chain that makes them so interesting. If they behaved like their modern counterparts, they were free-swimming predators. Yet because they lack the hard body parts that typically make good fossils, they have been sorely underrepresented in previous studies of who was eating whom in the Cambrian world. This has proven to be a big omission. Literally—the few previous finds had been about the size of demitasse saucers, while these guys averaged as big as dinner plates (about par for their descendants today), and some were up to 70 centimeters (about 27 inches) in diameter.

Back in the Cambrian, Wisconsin was just south of the equator, and most of it lay beneath a tropical sea. In fact, this quarry near Mosinee was already famous among fossil hunters for the spectacular jeep-tire-sized tracks left there by giant molluscs. In Cambrian times, it was probably the bottom of a shallow lagoon or bay. The jellyfish were most likely blown in by a storm whose ebb left them high and dry, only to be buried by fresh sediment in succeeding tides.

Hagadorn, who starts as a professor at Amherst this fall, found the fossils purely by accident. His real field is the Precambrian, where he works with Professor of Geobiology Joseph Kirschvink (BS, MS '75) and Kenneth Nealson, head of JPL's astrobiology group. The Precambrian contains the first fossils of creatures that are more than mere agglomerations of cells such as algal mats. But the fossils are very rare. For example, the Ediacarans, the subject of Hagadorn's PhD thesis at USC, are known only from a handful of impressions that their soft bodies left in some exceptionally well-preserved sand- and mudstones. Late in 1999, Kevin Peterson, a postdoc in Chandler Professor of Biology Eric Davidson's lab with an interest in fossils, noticed Ediacarans for sale in a fossil catalog. "He knew I had

worked on them, so he suggested I call the company," recalls Hagadorn. "So I spoke to Dan Damrow, who supplied the fossils, and asked him to send me some pictures. It turned out that they weren't Ediacaran fossils, but some of the photos included things that looked like jellyfish. So after I picked my jaw up off the floor, I called him back and said, 'Do you have any idea how rare those things are? Stop digging!' And then I called Bob Dott, of the University of Wisconsin-Madison, who is the godfather of Cambrian sediments in the midwest. We went out to the quarry in the summer of 2000, and now Bob and Dan are coauthors on the paper," which appeared in the February 2002 issue of *Geology*. □—*DS*

Top: Three jellyfish impressions and part of a fourth. Notice the second set of ripples within one impression, indicating that it was resubmerged under a calmer tide. (The broader the ripples, the more energetic the water that made them.)

Inset: The ridges radiating out from the center of this fossil are sediment-filled cracks that opened in the dead jellyfish as it dried out, so this one was clearly exposed to the air for some time.

DEFINITELY AN "E-TICKET"

The prelaunch configuration of GRACE's twin orbiters, which were nicknamed Tom and Jerry, looked like a Borg telephone booth.

Twin satellites took off on the ultimate roller-coaster ride on March 17, when the GRACE (Gravity Recovery and Climate Experiment) blasted into a polar orbit from Russia's Plesetsk Cosmodrome. Like cars on a roller coaster, GRACE will speed up on the "downhill" stretches where concentrations of mass make Earth's gravitational field stronger. The lead spacecraft will feel the effect first, and pull slightly away from the trailing one. And, when the lead spacecraft passes over a lower-mass region later on, it will be the first to slow down as it coasts back "uphill." (The effect is incredibly subtle, of

THE CIRCLE OF LIGHT

A spherical glass bead, no thicker than this page, makes a highly efficient laser that could be a boon to the telecommunications industry. Professor of Applied Physics Kerry Vahala (BS '80, MS '81, PhD '85) and grad students Sean Spillane and Tobias Kippenberg (MS '00) melted a standard fiber-optic wire to make the bead, which they mated to another fiber-optic wire stretched thin. The laser is especially efficient—1,000 times more so than previous devices—because of the way it stores light inside the microsphere, or resonator, as well as the manner in which the wire permits efficient coupling of light into the sphere.

The light travels around the sphere in a ring-shaped orbit and, over hundreds of thousands of orbits, an extreme concentration of optical power can accumulate. In this way, very weak signals applied to the sphere from the fiber-optic wire can build to enormous intensities within the sphere itself. At these power levels, the atomic arrangements within the glass are distorted, resulting in a process called Raman emission and lasing. Because Raman lasers require enormous intensities to function, they are usually power-hungry devices. Normal Raman lasers turn on "with a shout"—these new devices require "only a whisper."

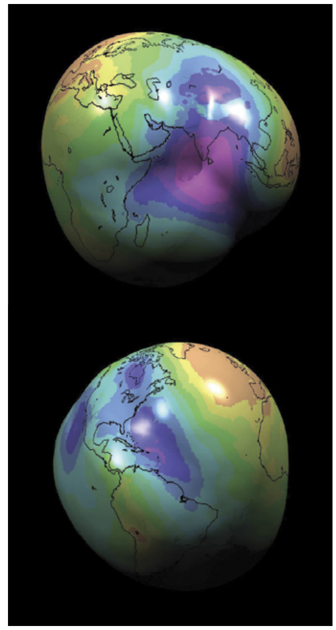
RIDE

course: picture measuring the change in distance between two cars on the 405, one in San Diego and one in L.A., to the accuracy of the diameter of a soot particle from a tailpipe.) The spacecraft do this with JPL-built microwave-based range-finding systems and Global Positioning System (GPS) sensors that will improve existing global gravity maps a hundredfold.

Over GRACE's five-year mission, it will help track melting glaciers in Antarctica, map deep ocean currents, and even measure the seasonal changes in the amount of water stored in underground aquifers. And, of course, it will keep an eye on the flow of molten rock in Earth's mantle, giving us a better insight into the "conveyor belts" that are ramming India into Asia while ripping California apart.

GRACE is a joint project of NASA and DLR, the German space agency. JPL manages the U.S. portion of the project. JPL, the University of Texas, and Germany's Earth Research Center (GFZ) are processing the data. For more info, see http://www.csr.utexas.edu/grace. □—*DS*

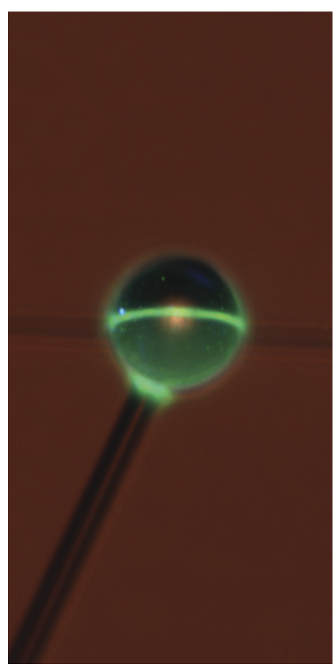
Below: Earth's geoid—the imaginary surface on which the pull of gravity is equal everywhere—resembles a stress-busting squeeze toy.



Central to this breakthrough was the ability to couple directly to the ring orbits, or whispering-gallery modes, of the sphere while preserving its exquisite perfection in terms of its ability to store and concentrate light. The tapered optical fiber achieved near-perfect coupling efficiencies, with negligible loss, both to and from the sphere.

Because Raman lasers and amplifiers can operate over a very broad range of wavelengths, they allow other lasers to reach previously inaccessible wavelength bands. For example, Raman amplifiers are now used widely in commercial long-distance fiber communications systems because of this wavelength flexibility. And, through a process called cascading, one Raman laser can pump another to generate a whole series of wavelengths in a kind of domino effect. More generally, cascading can be used to extend the wavelength range of other lasers into difficult-to-access wavelength bands for sensing or other purposes.

The work appeared in the February 7 issue of *Nature*, and can be found online at www.its.caltech.edu/~vahalagr. □—*RT*



Right: A green laser beam whizzes around a microsphere's equator.

MINDING YOUR POLYP'S AND Q'S

Huntington's disease is a cruel disorder, destroying nerve cells in the brain and, over time, robbing an individual of the ability to walk, talk, and eat. As yet, there is no cure or effective treatment for this hereditary condition. The end result, then, is death, caused by such complications as infection or heart failure. But now Professor of Biology Paul Patterson, postdoc Ali Khoshnan, and research assistant Jan Ko have come one step closer to understanding how Huntington's disease develops and how it can be stopped. In a paper published in the January 22 issue of the *Proceedings of the National Academy of Sciences*, they describe how they used antibodies to block the effects of the disease in cultured cells.

Huntington's disease is caused by a mutation in a protein called huntingtin, or htt, in which a site known as polyQ on the htt protein gets expanded. This mutation normally kills the afflicted cell. Khoshnan and his colleagues made an antibody that binds to the polyQ site, along with another antibody that binds to a different site, called polyP. The idea was to block either of these sites and see whether the toxic effects of mutant htt, which kills nerve cells in the brain, could be blocked.

"We knew that the polyQ site was critical because when it is expanded by mutation it causes Huntington's," says Patterson. "It was also known that the polyP site on htt might be important for interfering with the functions of other proteins." The investigators produced a modified version of the antibodies that would allow them to be produced inside cells that also carry the toxic, mutant htt. They found that cells producing the antibody against the polyP site were unaffected by the mutant protein. In striking contrast, when cells were induced to produce the antibody against the polyQ site, htt's toxicity was enhanced and the cells died even faster.

It may be that the polyQ antibody stabilizes a shape of the mutant htt protein in its most deadly form. Most important, though, says Patterson, is that the survival of the polyP-antibody-producing cells may indicate that it is the polyP site that actually gives mutant htt its cell-killing ability, so covering the site with a molecular Band-Aid saves the cell. "Or, an alternative interpretation is that the binding of the antibody preserves the protein in a non-toxic shape," he says.

The researchers have two goals in mind with their work: elucidating the mechanism of neuronal death caused by mutant htt, and devising molecular strategies for blocking its toxic effects. "Potentially, this knowledge could be useful in designing a therapeutic drug, one that covers up that part of the mutant protein that kills healthy cells," says Patterson. "The next stage of the work will be to deliver this antibody into the brains of mice that carry the human mutant gene and that have developed motor symptoms that are related to the disease. We want to see if this antibody can rescue these mice, even after they show signs of the disease. These experiments are, however, just beginning." □—*MW*

¡Uvas, No; Libros, Sí!

In this, the centenary year of Steinbeck's birth, the California Council for the Humanities, chaired by Associate Professor of History William Deverell, is urging everyone in the state to read and reflect on *The Grapes of Wrath*. The project kicks off in June so that people will be ready to participate in the discussions, screenings, and so on at the Huntington and other libraries statewide come October. "It promises to be great fun and illuminating at the same time," says Deverell.

The Cause of Many Effects

Ray Feeney (BS '75) has five Academy Awards sitting on his desk. You remember his work from *Terminator 2*, right? And *Independence Day*? You don't? Well, that's not surprising. Four are Scientific and Engineering Awards for advances in visual-effects technology, and the fifth is the John A. Bonner Medal of Commendation for his body of work, presented to him this March. He's a little leery of calling the Bonner medal a lifetime achievement award, as he's the youngest person to receive it by a good 20 years or so. But it does give some idea of where the industry would be without him.

When Feeney started working in Hollywood, the art of creating flying saucers hadn't evolved that much beyond hanging scale models on fishing line. The paint jobs were getting more sophisticated, of course, but the models still had to be photographed frame by frame, and the models and the camera manually repositioned between each exposure. So for his summer job in 1974, he and fellow Techer Bill Holland (BS '77) built a motion-control camera system for special-effects wizard Robert Abel. A basic

In other Hollywood news, on March 20 the Museum of Television and Radio hosted a panel, organized by the Sloane Foundation and the American Film Institute, to discuss the manner in which science and scientists are portrayed on film these days. From left are: Brian Greene, author of *The Elegant Universe*; James V. Hart, screenwriter for *Contact*; Caltech president David Baltimore; actor Dustin Hoffman (*Outbreak*, *Rain Man*); moderator Jean Oppenheimer, film critic; Jared Diamond, professor of physiology at UCLA and Pulitzer Prize-winning author of *Guns, Germs, and Steel: the Fates of Human Societies*; Sylvia Nasar, author of *A Beautiful Mind*; Jonah Nolan, author of *Memento*; Sarah Bottjer, professor of neurobiology at USC; and Simon Wells, director of *The Time Machine*.

motion-control system steers the camera along a very reproducible path so that you can make multiple passes with it, each time photographing different elements. When the film is put together, it will look as if everything was shot in a single pass. More elaborate systems coordinate the movements of scale models, two-dimensional art, and the camera—enabling it to fly, for example, through the midst of a fleet of starships orbiting a planet. (Not that the system they built was ever used for that purpose, says Feeney. "In the early days, the primary applications were commercials. Budgets on commercials were $600,000 to $1,000,000 for 30 seconds, whereas movie budgets couldn't sustain that many dollars per frame.") The computer revolution was just getting under way, and Feeney and Holland thought it would be a good challenge to try to use a computer to drive the system. "We were horrified at what they were doing by hand," Feeney recalls. "They had automated the precision and repeatability, but were figuring out all the numbers on a mechanical calculator and writing them down. Obviously computers were ideal for enhancing the process." One thing led to another, and by the next summer they had built two more systems, including one of the first to be entirely controlled by a minicomputer—gotten as surplus from a bankrupt manufacturer called Redcor in Chatsworth. Feeney, Holland, and 10 other people shared an Academy Award in 1988 "for their individual contributions and the collective advancements… in the field of motion control technology."

Holland went to work for Hewlett-Packard after graduation, while Feeney stayed on with Abel. Feeney had always had a career in Hollywood as his goal—

Feeney as an undergrad with one of his and Holland's computer-controlled camera stands. This one was used for animating logos for commercials. The camera (visible at far right over Feeney's shoulder) points at an illuminated glass table, on which artwork and colored gels were placed to be photographed.

Feeney in the conference room at RFX. Posters (this one signed by Arnold) are common souvenirs in the movie business, but all good Techers prefer toys! Every one of these action figures owes its existence to special effects.

"When I was at Caltech I was a photographer for the yearbook and the newspaper, and discovered when I wanted to work in Hollywood that anyone interested in photography started as an intern or a driver, just trying to get in, and I also discovered at Caltech that as an engineering major I got paid very little to work over the summer for a professor. So when I tried to get going in Hollywood, I came in as an engineer, and when I was trying to work around Caltech, I would work as a photographer."

Star Wars came out in 1977, and motion-control technology entered its heyday. At the same time, computer graphics, or CGI, was taking its first significant steps. *Tron* would come out in 1982, and Robert Abel would provide some of the effects for it. Feeney, however, had gone on to found his own company, RFX, Inc., in 1978. "A lot of the work was being done on VAX-sized computers, but in 1983 Silicon Graphics came out with their first workstation, and we got involved with them. They were primarily designing and building equipment for scientific and engineering uses—universities and government projects—and RFX was pretty much responsible for their adoption into the motion-picture industry."

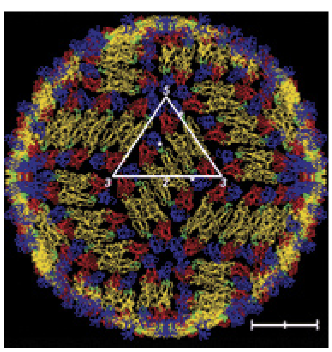
Now people could "sweeten" space battles with digital laser beams, and even create an entire object in the computer. But special-effects scenes were still assembled photochemically in an optical printer. Many strips of film, each containing one or more elements, would be run through the printer in the proper order to create the final composite. So to be able to get that blaster ray out of the computer and into the bad guy's chest, RFX helped to develop the Solitaire Film Recorder, which converted digital data into image frames and then output them on film stock. This resulted in Feeney's second award, shared with Richard Keeney and Richard Lundell of Management Graphics, Inc., in 1991.

Computers, of course, kept getting faster and better, and by the late '80s it was possible to compose an entire scene in silicon rather than on film. This led to the converse problem: now you had to get the live actor, or at least the image thereof, into the machine. This was really two problems, with the second being how to separate the live actor from the live background. The first problem was licked by scanning the film frame-by-frame into the computer, using CCD arrays like those that would become standard in today's digital cameras. In 1994, this netted Feeney his third award, along with Will McCown (BS '77, MS '78) and Bill Bishop of RFX, and with Les Dittert of Pacific Data Images. The second problem was solved by radically expanding the bluescreen technology used to place a weather map behind your favorite meteorologist. The resulting software package, christened Cinefusion, also won in '94, with the Academy honoring Bishop, Feeney, and three people from Ultimatte, the company that originally developed the video bluescreen system.

"We helped to build the computer-graphics department at Lucasfilms for *The Abyss* and *Terminator 2*," says Feeney. "The CGI elements for *The Abyss* were composited in a traditional optical printer. *T2* was entirely digitally composited. It was at that moment that the technology came of age. You could take your favorite producer to that movie and say, 'See, whatever you can imagine, we can do.' Stories that had been languishing on the shelf, because there was just no practical way to visualize them, could now be made. All the rules changed.

"Another watershed event was *Independence Day*. The other projects had one 'key element'—the water snake in *The Abyss*; the silver, molten guy in *T2*; the photo-real dinosaurs in *Jurassic Park*. But in *ID4*, what was different was the sheer number of elements, the complexity. It was like telling the story of the Battle of Britain without actually hiring a bunch of Spitfires. *ID4* was one of the first major movies to use a software package we wrote called Chalice, which was later used on *Titanic* and is the forerunner of some of the compositing tools in use today. Starting at *ID4*, I would say, it became less about the hardware and more about software. *T2* was mainly about hardware problems to be solved—film scanning, film recording. In *ID4* it was more about software tools to manage complexity.

"I find it fascinating to try to follow the evolution of science and technology in other industries, and to try to figure out how those tech-nologies can be brought over to the motion-picture indus-try. Being a technically oriented but motion-picture-driven person, this is the best career for me. The work you do is seen by millions of people; they've never heard of you, but one or two people can change how movies are made." □—*DS*



The glycoproteins on the dengue virus's exterior are arranged in an icosahedral symmetry (white). The scale bar is 100 Ångstroms, or one hundred-millionth of a meter.

MAPPING THE ENVELOPE

Scientists at Caltech and Purdue University have determined the fine-detail structure of the virus that causes dengue fever. This could lead to newer and more focused strategies for devising a vaccine to protect the world against an illness that causes 20,000 deaths each year.

In the March 8 issue of *Cell*, James Strauss (PhD '67), the Bowles Professor of Biology; Richard Kuhn of Purdue, the lead author and a former postdoc in Strauss's lab; and Purdue's Michael Rossman and Timothy Baker describe the viral structure they obtained with a cryoelectron microscope. The detailed electron-density map shows the inner RNA core of the virus as well as the other spherical layers that cover it. At the surface is the glycoprotein scaffolding whose projections are thought to allow the virus to interact with a receptor and invade a host cell.

This is the first time the structure of one of the flaviviruses has been described, Strauss says. The flaviviruses include the yellow fever, West Nile, tick-borne encephalitis, and Japanese encephalitis viruses. All are enclosed with a glycoprotein outer layer. "Most viruses that cause serious illness are enveloped, including influenza, hantaviruses, West Nile virus, smallpox, and herpes—though not polio," Strauss says.

The dengue fever virus's glycoproteins are arranged in a very unusual manner. Details from the computer-generated images show a highly variegated structure of glycoprotein molecules that are evenly dispersed, but in a surprisingly complex pattern. "The proteins in the envelope are surrounded by their neighbors in more than one way. In most viruses with icosahedral symmetry, each protein always has the same arrangement of neighbors," Strauss explains.

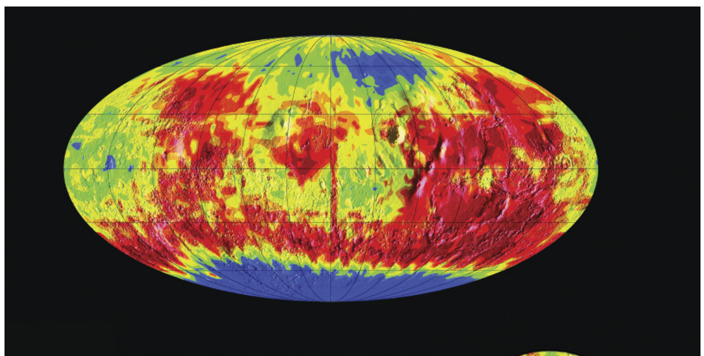
Strauss says it's still unclear what the odd symmetry will ultimately mean for future research aimed at controlling the disease, because the precise function of the glycoproteins' different structural domains are still unknown. Those that have been false-colored blue in the rendering at left are thought to be involved in receptor binding, and thus responsible for the virus's entry into a cell. The yellow structures are an elongated domain thought to be responsible for holding the scaffolding together; the red ones' function is not yet known.

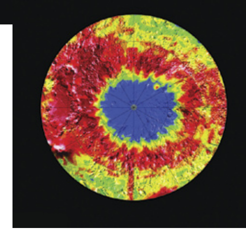
But a more detailed view of these structures is the beginning of a more informed strategy for a focused medical or pharmaceutical attack, Strauss says. "You can think of the protease inhibitors for HIV. Those in large part came from knowing the structure of the HIV enzymes you were trying to interfere with." Thus, the new work could lead to drugs that will bind to the virus to prevent it from entering the cell, or perhaps from reassembling once it is already inside the cell.

Dengue fever is a mosquito-spread disease that has been known for centuries, but was first isolated in the 1940s after it became a significant health concern for American forces in the Pacific theater. A worldwide problem, the disease is found throughout Latin America, the Caribbean, Southeast Asia, and India, and is currently at epidemic levels in Hawaii. Especially serious is a complication of dengue infection called dengue hemorrhagic fever, which is responsible for most of the deaths. The disease is a leading cause of infant mortality in Thailand, where there is an especially vigorous program to find an effective vaccine. □—*RT*

Hello, Rubipy Tuesday

The next time you stop by the Ath, try a Rubipy (pronounced roo-bippy, as in "bet your"). Named in honor of Harry Gray, Beckman Professor of Chemistry, it's a brilliant red organic compound of vodka, Cointreau, watermelon schnapps, and Midori. "Rubipy" is the Gray group's pet name for tris(2,2´-bipyridine) ruthenium(II), an electron-transfer molecule used in their research on artificial photosynthesis. What better way to get lit?





The Mars Odyssey's mapping mission is off to a flying start. Within days of its beginning routine data collection, a press conference was held at JPL to announce that ice probably permeates the Martian subsurface to a depth of at least one meter over a vast area extending from about 60° south latitude all the way down to the pole. Such an enormous reservoir of water ups the chances that life may have existed on Mars. The discovery was made with the Gamma Ray Spectrometer package, which found high levels of hydrogen (shown in blue above) in the soil. Meanwhile, an infrared camera called the Thermal EMission Imaging Sytem (THEMIS), was taking the first "night vision" pictures of Mars. The view at right shows a portion of the Hydaspsis Chaos (2° N, 29° W), which is believed to have formed by the sudden withdrawal of subsurface ice or water, causing the ground above to collapse. The chaos's outflow system encompasses Mars Pathfinder's landing site. In this image, fine-textured dust loses its heat more quickly after sunset and appears dark, while larger rocks hold their heat and appear bright. The mesas and plateaus are covered in dust while the rocks on their flanks are relatively dust-free, which may indicate they are still moving downslope. The inflow channel at the bottom of the image is about seven kilometers wide and 280 meters deep.