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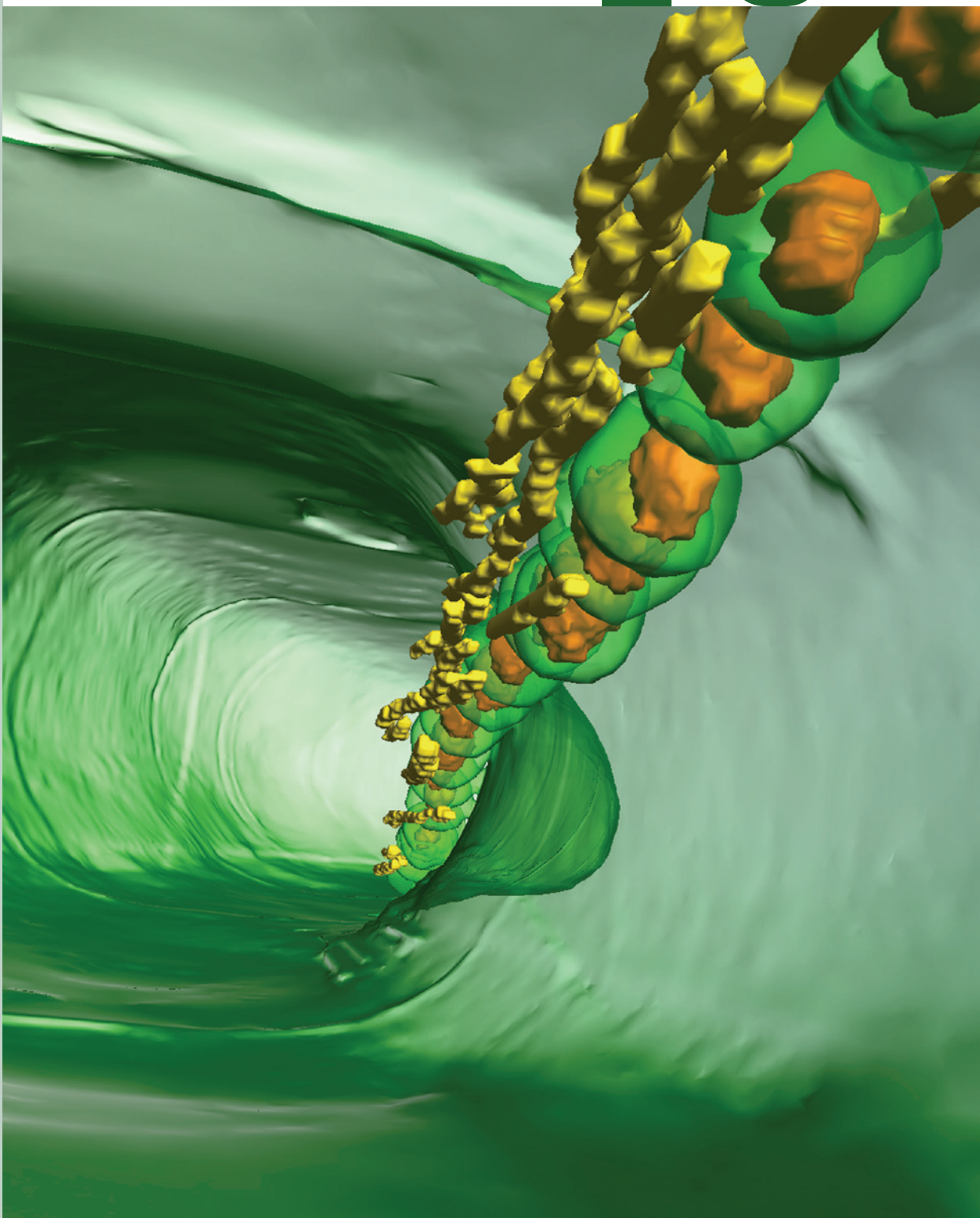

Volume LXIX, Number 2, 2006

IN THIS ISSUE

This isn't a promotional stunt for a summer blockbuster—it's Ditch Day, frosh! When asked if the stack was a tribute to Johnny Depp, Errol Flynn, or Cary Elwes, senior John McNamara replied, "Nah. It's just generic looting and pillaging." Besides flying their colors from Millikan Library, the pirate crew made the Gene Pool next to the Beckman Institute run red with blood in the form of FD&C Red Number 5.

California Institute of Technology

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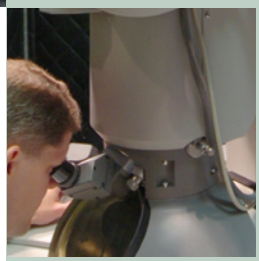

On the cover: If you cut a hole in one end of a bacterium named *M. magneticum* and drained it, this is what you'd see. The semi-transparent green tube is the inner cell membrane. The green bulbs are filled with magnetite (orange) and act as compasses. Caltech researchers have found that these magnetosomes are part of the cell wall—as the wall curves off to the right, you can see the necks where they attach—and discovered a set of protein filaments (yellow) that keep them aligned. See the stories beginning on pages 8 and 25.

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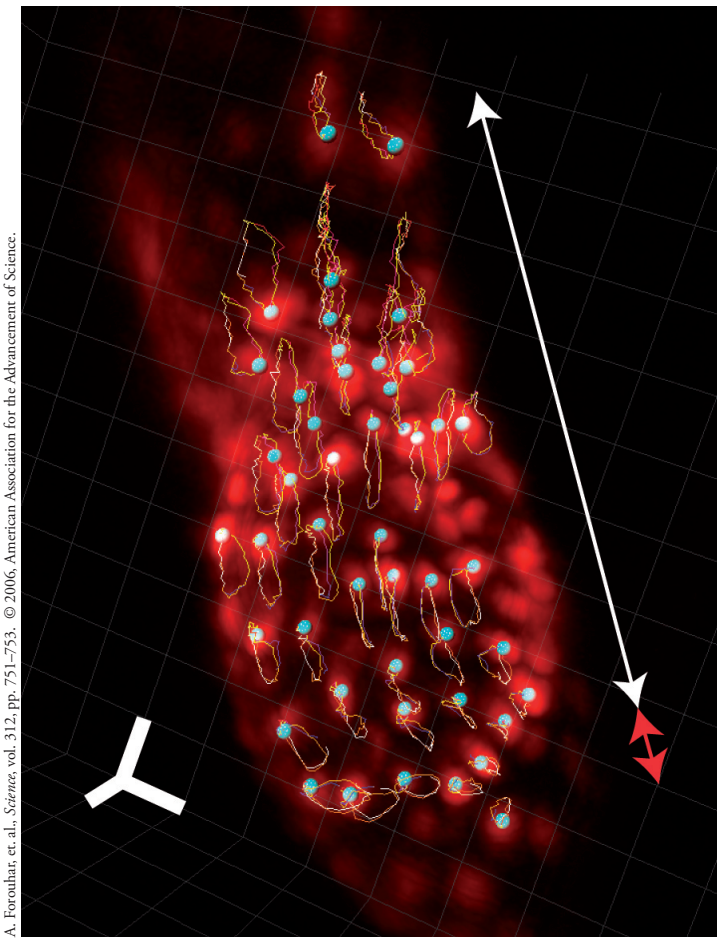
The Heart Is a Suction Pumper



A 3-D reconstruction of a 26-hour-old zebrafish embryo's heart tube. The glowing red cells are the myocytes, and the three-dimensional trajectory traced by the center of each cell (colored dots) over two successive heartbeats has been drawn in as well. The inflow tract is at the bottom, and the red double-headed arrow shows where the "pacemaker" cells are located. The 3-D scale bar at lower left corner is 20 microns, or millionths of a meter, along each leg.

Looking at an adult human heart and an embryo's heart, you'd never guess that the former developed from the latter. While the adult heart is a fist-shaped organ with chambers and valves, the embryo heart is tubular. It's been assumed that the embryonic heart pumps by peristalsis, like your intestines do—a method of action similar to squeezing a tube of toothpaste. But Caltech biologists and engineers leading an international team have shown that the tube is actually a suction pump that works much like the left ventricle in the mature heart.

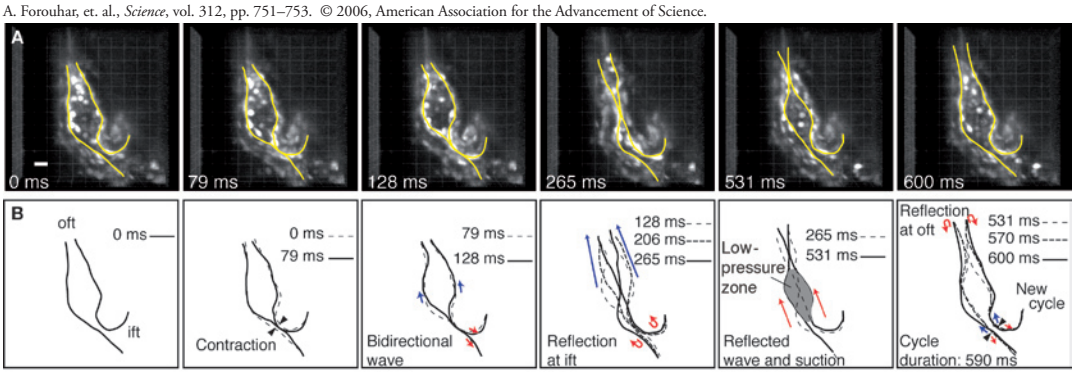
Says Mory Gharib (PhD '83), Caltech's Liepmann Professor of Aeronautics and professor of bioengineering, "Embryonic and adult hearts look like two different engineers designed them separately. But this study shows there is continuity to the pumping mechanism."

Gharib's graduate student Arian Forouhar (PhD '06) and the other researchers used confocal microscopes in the Biological Imaging Resource Center (BIRC) located in Caltech's Beckman Institute to do time-lapse photography of embryonic zebrafish. Zebrafish were chosen because they are essentially transparent, thus allowing for easy viewing, and because they develop completely in only a few days.

Scott Fraser, Caltech's Rosen Professor of Biology and professor of bioengineering and the principal investigator of the BIRC, notes that "this pumping mechanism had not been noticed before because of the limitations of imaging technology. Now we have a device that is 100 times faster than the old microscopes, allowing us to see things that previously would have been a blur. Now we can see the motion of blood and the motions of cardiac walls at very high resolutions."

The time-lapse photography showed that the embryo heart uses a valveless pumping action known as hydroelastic impedance pumping, in which a handful of cells called myocytes, usually situated near the entrance of the heart tube, contract to initiate a series of forward-traveling elastic waves that eventually reflect back from the tube's far end. At a specific range of contraction frequencies, these waves constructively interfere with one another to generate an efficient dynamic-suction region at the tube's outflow tract. This mode of action is also noteworthy because a small number of "pacemaker" cells are sufficient to sustain circulation.

A. Forouhar, et. al., *Science*, vol. 312, pp. 751–753. © 2006, American Association for the Advancement of Science.



"The heart is one of the few things that makes itself while it's working," Fraser says. "It likely begins forming its structures when it's still a tiny tube the diameter of a hair." "This allows us to reconsider how embryonic cardiac mechanics may lead to anomalies in the adult heart, since impairment of diastolic suction is common in congestive heart-failure patients," says Gharib. "One of the most intriguing features of this model is that the mechanical stimuli from only a few contractile cells may guide later stages of heart development," says Forouhar.

According to Gharib, this simplicity of construction could guide the design of devices to gently move blood, drugs, or other biological fluids. The findings could also lead to new treatments of heart diseases that arise from congenital defects, and, says Fraser, demonstrate the promise of advanced biological imaging techniques for the future of medicine.

The work is described in the May 5 issue of *Science*. In addition to Forouhar, Gharib, and Fraser, the authors are Michael Liebling, a postdoc in the BIRC; bioengineering grad students Anna Hickerson (BS '00, PhD '05) and Abbas Nasiraei Moghaddam; Huai-Jen Tsai of National Taiwan University's Institute of Molecular and Cellular Biology; Jay Hove of the University of Cincinnati's Genome Research Institute; and Mary Dickinson of the Baylor College of Medicine. □—*RT*

Above, A: In this set of six 3-D reconstructions during a single heartbeat, the myocytes appear as white blobs, and the yellow lines mark the heart wall, or endocardium. The grid size is 20 microns. B: The red and blue arrows show the paths of the wave fronts as they spread out from the contraction site. Changes in heart-tube diameter and elasticity at the inflow tract (ift) and outflow tract (oft) reflect the waves back on themselves to form the low-pressure zone that pumps the blood. Elapsed times are shown in milliseconds.

The Eyes Have Trees

If a tree falls in the forest and lands next to another one, does a caveman invent the letter L? He might. According to Caltech postdoc Mark Changizi, a theoretical neurobiologist, letters and other commonly used symbols may have their particular shapes because "these are what we are good at seeing."

In essence, he says, the basic elements of the Greek and Roman alphabets, plus the Chinese, Persian, and 96 other writing systems that have been used through the years, are visual repetitions of common sights, just as onomatopoeias such as "bow wow" are aural repetitions of common sounds. "Evolution has shaped our visual system to be good at seeing the structures we commonly encounter in nature, and culture has apparently selected our writing systems and visual signs to have these same shapes," says Changizi, the lead author of a study published in *The American Naturalist*.

Engineers have known for some time that the best way to create a computer-vision system that recognizes objects is to identify where lines meet. In other words, a robot navigating a room sees the conglomeration of contours in a corner by its "Y" shape, and sees a wall because of its "L"

junction with the floor. Says Changizi, "It struck me that these junctions are typically named with letters, such as 'L,' 'T,' 'Y,' 'K,' and 'X,' and that it may not be a coincidence that the shapes of these letters look like the things they really are in nature."

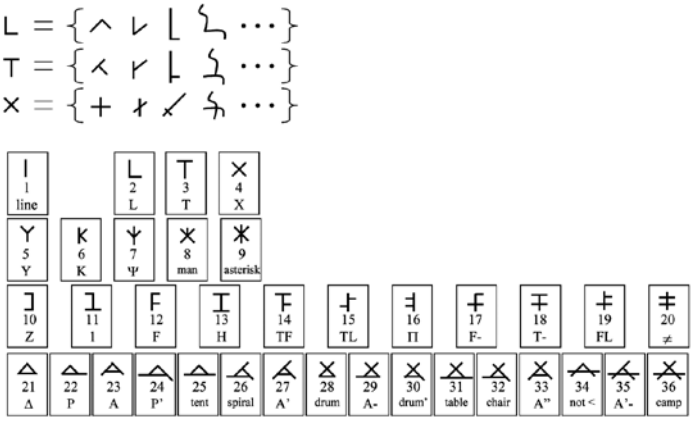
So Changizi used topology to group letter and symbol shapes. An "L" can be turned into a "V," for example, just by bending it, so they are topologically the same. Cutting line segments is not allowed, nor is changing the ways in which they intersect. He ended up with a catalog of 36 shapes made of two or three line segments, which he ranked according to how frequently they occured in three classes of images: pictures of things that ancestral humans would have seen millions of years ago, pictures across many cultures that he culled from *National Geographic*, and computer-generated architectural forms.

It turns out that the common shapes are precisely those that frequently show up in the letters of various writing systems, in company logos, and in symbolic systems such as musical notation. The forms not found as frequently in nature, by contrast, show up less often.

"It's striking that symbols that are intended to be seen have high correlations to natural forms," Changizi says. "Company logos, for example, are meant to be recognized, and we found that logos have a high correlation. Shorthand systems, which are meant to give a note-taker speed at the expense of a commonly recognizable system of symbols, do not. Figures that are intended to be 'read' seem to be selected because they are easy to see rather than easy to write. They're for the eye."

In addition to Changizi, the authors are Professor of Biology Shinsuke Shimojo and undergrads Qiong Zhang and Hao Ye (BS '06). □—*RT*

M. Changizi, et. al., *The American Naturalist*, vol. 167, no. 5. © 2006, University of Chicago Press.



Above: Changizi's periodic table of letter topologies.

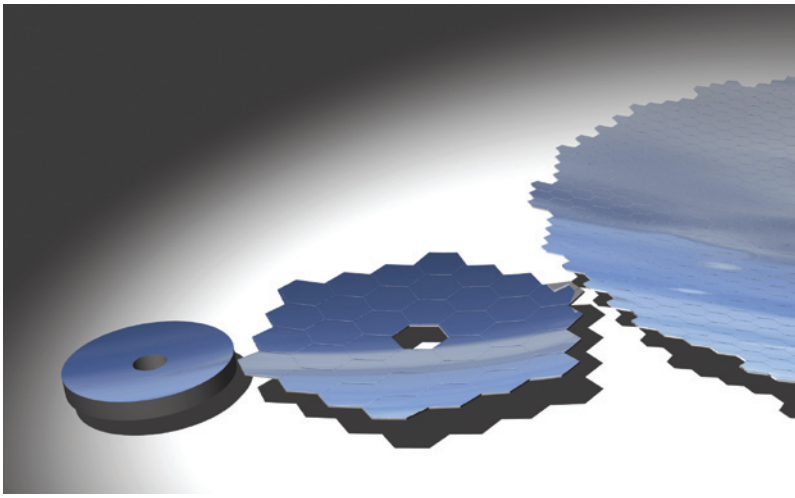
TMT Is A-OK

The Thirty Meter Telescope, or TMT, has passed its conceptual design review by an independent panel of experts. Now in detailed design, the TMT will be the world's largest telescope. It consists of a primary mirror with 738 individual 1.2-meter segments that span 30 meters in total, three times the effective diameter of the current largest telescopes. All of the segments will be under exquisite computer control so that they work together as a single mirror.

The review panel evaluated all aspects of the project, including optical design, telescope structure, control systems, science instrumentation, site testing, and management and cost-estimation procedures. The panel praised in particular the adaptive optics technology that will allow the TMT to reach the "diffraction limit," seeing things the way a telescope in outer space would see them. Much of the TMT's scientific work will be done in the infrared, where the diffraction limit is easier to attain, young stars and galaxies are to be found, and the opportunities for new discoveries are abundant.

TMT's eight scientific instruments, also in the detailed-design phase, are huge in comparison to current astronomical instruments, and equivalently more complex. Each one is the size of a school bus or larger, and they rest on two basketball-court-sized platforms on either side of the telescope. The biggest technical challenges are posed by the Planetary Formation Instrument, which employs "extreme" adaptive optics in an effort to see other planets directly, rather than infer their presence by their effects on their stars, as is currently done.

Says Richard Ellis, Caltech's Steele Family Professor of Astronomy, "We'll decide in mid-2008 where to build the telescope and then plan to start construction in early

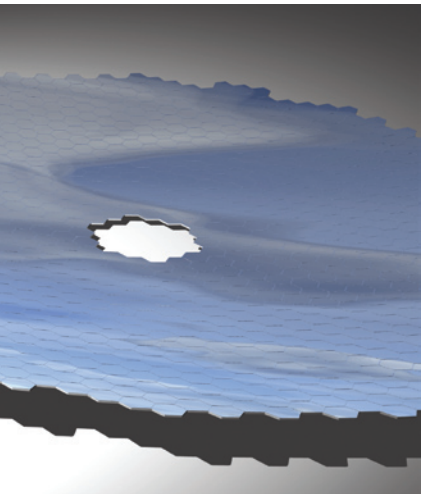


On the road again: The Fleming cannon journeys cross-country from Caltech to That Other Institute of Technology and back again in this commemorative pen, available for $3.95 at the Bookstore. Visit www.bookstore.caltech.edu if you can't stop by in person. And while you're there, pick up the MIT "because not everyone can go to Caltech" T-shirt that started it all.

2009." Science operations are slated to begin in 2016. The TMT project is studying five sites in Chile, Hawaii, and Mexico, and the project's offices are located at CIT^2, formerly St. Luke's Hospital, in Pasadena, where the design review was carried out.

The TMT is a collaboration between Caltech, the University of California, the Association of Universities for Research in Astronomy, Inc. (AURA), and the Association of Canadian Universities for Research in Astronomy (ACURA), with significant instrument-design work being done by industry and by university teams. TMT's design and development phase has a budget of $64 million, including $35 million in private-sector contributions from the Gordon and Betty Moore Foundation. □—*RT*

Below: From left, the five-meter Hale, ten-meter Keck, and Thirty Meter Telescope mirrors to scale.



LEGOs for Biochemists

Figuring out how proteins fold—that is, the way that amino-acid sequences determine the unique structures and functions of protein molecules, which then act as "biology's workhorses"—remains one of the biggest open questions in biology today. One common approach analyzes numerous proteins with similar structures and functions—a protein family—to try to tease out the fundamental interactions responsible for a given property. Now a Caltech team of chemical engineers, chemists, and biochemists has created a huge family of proteins that, even though they have very different sequences, all fold the same way.

Grad student Christopher Otey and his colleagues analyzed three natural protein structures and pinpointed locations at which they could be broken apart and reassembled, like LEGO pieces. The proteins were then broken into eight pieces each and reassembled into all possible eight-piece combinations, creating 3^8, or 6,561, sequences. Nearly half of these constructs were able to fold themselves to constitute an artificial protein family. Says Otey, "In this single experiment, we've been able to make about 3,000 new proteins."

The viable proteins have an average of about 72 sequence changes relative to any known protein. "We can use the new proteins and new sequence information to learn about the original proteins," Otey adds. "For example, we can determine which combinations of amino acids contribute to specific protein properties."

The original proteins belong to a family called the cytochrome P450s, which play critical roles in drug metabolism, hormone synthesis, and the biodegradation of many chemicals. The researchers broke these roughly 460-amino-acid proteins into LEGO blocks of about 60 to 70 amino acids each. It has taken researchers 40 years to collect 4,500 natural P450 sequences, but the Caltech team required only a few months to create their new P450s.

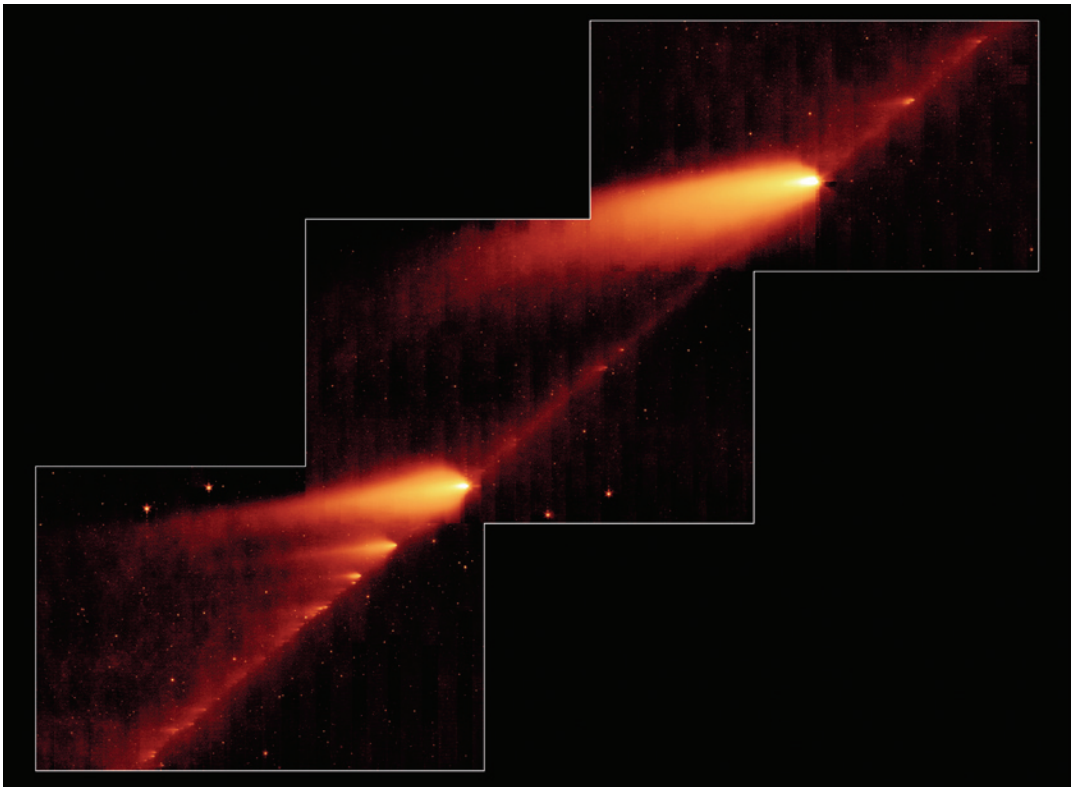
"During evolution, nature conserves protein structure. We do the same thing by shuffling natural proteins with the help of computational tools. By changing protein sequences, we can generate new functions," Otey says. "One of our goals is to be able to create new and possibly useful proteins for pharmaceuticals, to do chemical syntheses, or to be used in sensors or other biotechnology applications."

The paper appeared in the April 10 issue of the *Public Library of Science Biology*. The other authors include Frances Arnold, Caltech's Dickinson Professor of Chemical Engineering and Biochemistry; biochemistry postdoc Marco Landwehr; Jeffrey Endelman, PhD '05 in bioengineering; chemistry grad student Jesse Bloom; and postdoc Kaori Hiraga, now at the New York State Department of Health. □—*RT*

A Nanorod in the Sun

Caltech and BP, the energy company formerly known as British Petroleum, are embarking on an effort to develop cheap, high-efficiency solar cells that will make widespread production of electricity from sunlight a more cost-competitive option. The five-year program will explore ways of growing silicon nanorod arrays to make solar cells, rather than by casting silicon ingots and cutting them into wafers, as is conventionally done. The tightly packed nanorods, small cylinders of silicon some 100 times smaller than a human hair, would be arrayed like bristles in a brush.

A solar cell made up of nanorod arrays would efficiently absorb sunlight along its entire length, offering far more collecting area than a flat, wafer-based cell of equal size. The nanoarray would



Above: Comet 73P/Schwassmann-Wachmann 3 began crumbling two orbits ago, back in 1995. Astronomers speculate that its icy outer crust cracked from thermal stresses upon close approach to the sun, allowing fresh ice in the interior to evaporate, and the pressure from the resulting vapor essentially blew the comet apart. On May 12–28, the comet's 5.4-year orbit brought it some 9,000,000 kilometers from Earth, or about 22 times farther away than the moon, and every telescope on the planet (and aloft!) seems to have been trained on it. This infrared view, from the Spitzer Space Telescope, shows at least 36 identifiable fragments following a trail of millimeter-sized comet-dust particles laid down in previous orbits. Caltech and JPL run the Spitzer for NASA.

Right: The Seismo Lab's remodeled Earthquake Media Center opened for business on June 29, with director Jeroen Tromp, McMillan Professor of Geophysics, presiding. Gone is the wall of drums, a staple of TV coverage but decidedly state-of-the-art 1950s technology. In their place is a nine-panel, 10-by-6-foot video wall that can display any number of simultaneous images, including "ShakeMovies"—2-D animations of seismic waves superimposed on topographic maps—shaking and felt-intensity maps, and the zigzaggy seismic waveforms that the drums used to produce. The Dell Corporation provided the technology behind the wall.

also collect the electricity more efficiently than a conventional solar cell.

The program will be directed by Nate Lewis (BS '77, MS '77), Argyros Professor and professor of chemistry, and Harry Atwater, Hughes Professor and professor of applied physics and materials science. Lewis, an expert in surface chemistry and photochemistry, will use nanotechnology to create designer solar-cell materials, from nanorods to nanowires, and explore their properties to find the optimum ones. Atwater, an expert in electronic and optoelectronic materials and devices, will investigate ways of making the resulting materials and designs using vapor-deposition methods that are scalable to very large areas. "Using nanorods as the active elements opens up radically new approaches to design and low-cost fabrication of high-performance solar cells," says Atwater. Eight grad students and postdocs in Lewis's and Atwater's labs will be funded by the project.

The research contract is part of BP's long-term technology strategy, and partners Caltech with BP Alternative Energy, which was launched in November 2005 to develop low-carbon-emission options for the power industry. Says BP Solar's CEO and president, Lee Edwards, "This program represents a significant commitment by BP to the long-term potential of solar energy. Nanorod technology offers enormous promise. However, like any new technology, challenges remain to be solved to make it commercially viable at scale." □—*RT*

E&S Polishes the Silver

For the second consecutive year, *E&S* has won a silver medal in the Research Magazine category in CASE's annual Circle of Excellence competition. CASE, the Council for Advancement and Support of Education, is the world's largest nonprofit education association in terms of institutional membership, including more than 3,200 colleges, universities, and independent elementary and secondary schools in 55 countries around the world. The Circle of Excellence judges some 40 categories of alumni relations, institute advancement, public and media relations, and student recruitment pieces in print and electronic forms. Not all medals are awarded in all categories—in fact, last year no research-magazine gold was given out, and *E&S* shared the silver with the Woods Hole Oceanographic Institution's *Oceanus*. (This year, the University of North Carolina at Chapel Hill's *Endeavors* took the gold.)

Averse as we are to tooting our own horn, we'd like to share some of the judges' comments from 2005 with you. "The best entrants, not surprisingly, keep their readers in the middle of their radar screens. They know their audiences, and they are slaves to them alone. They feature thoughtful writing, inventive story ideas, and display copy that works." "*Engineering and Science* . . . excels at meeting its mission and serving its unique readership. . . . Their entry succeeds in meeting its stated goals with a compelling lineup of stories with depth. (Such depth was a critical distinction between both of these publications and all the rest.) The stories and writing were very good, . . . [the] topics were compelling and well executed." The comments from this year's competition will be posted starting in late September. □—*DS*

Bacteria Are Beautiful

by Dianne K. Newman

Above: The widespread use of antibacterial chemicals in common household products could be doing more harm than good (*Annals of Internal Medicine*, 2004, 140, 321–329). Below: In contrast to the bacteriophobia of the products above, other grocery-store items advertise that they're chock-full of live bacteria. For example, each capsule in the jar on the right contains half a billion live *Lactobacillus acidophilus* and *Bifidobacter* bacteria.

As a microbiologist, I'm appalled when I go to buy soap or dishwashing detergent, because these days it's very hard to find anything that doesn't say "antibacterial" on it. This is disturbing for a couple of reasons. First, there's absolutely no evidence to suggest that these antibacterial versions in any way help to keep our homes cleaner and us safer from disease—in fact, there's some evidence to suggest these products contribute to the spread of antibiotic resistance. And second, it distresses me to see the public given the perception that bacteria are bad and need to be eradicated.

It's a commonly held fallacy that all bacteria are germs, but it's been estimated that out of more than 30 million microbial species, only 70 are known to be pathogens. That's a trivial number. The vast majority are actually doing remarkable things, both for the quality of our life and for the quality of the planet.

How many of you have a glass of red wine with your dinner or begin your morning with yogurt or cheese? These are all foodstuffs that use lactic-acid bacteria for secondary fermentation.

These bacteria have made our lives more enjoyable, but the cyanobacteria have given us something much more important—the air we breathe. They invented oxygenic photosynthesis, by which I mean the process of taking water and splitting it to generate oxygen and power the conversion of carbon dioxide to carbohydrates and, therefore, biomass.

Over the course of time, these types of cyanobacteria became engulfed by other organisms that then evolved into plants, so the key part of the plant in which the metabolism that generates oxygen occurs, the chloroplast, is nothing more than an ancient cyanobacterium.

Moreover, we can only breathe this oxygen because our mitochondria—the little organelles in our cells that produce energy—are vestigial microorganisms descended from *another* ancient bacterium.

Microbes are very, very old. They've been on our planet for at least 3.8 billion years, appearing just 800 million years after the planet formed. For the first 1.6 billion years or so of their existence, they had the place to themselves, and it was only after the oxygenation of the air and oceans by the cyanobacteria that the forerunners of plants and animals came along.

Some bacteria have even changed the planet's geology. Microbial metabolism(s) most likely catalyzed the formation of the huge iron-ore deposits known as banded iron formations that occur in various parts of the world, such as the 2.5-billion-year-old Hamersley Range in Western Australia. There have been many of these types of deposits throughout the course of Earth's early history, and we're now beginning to appreciate that the earliest types may have been formed by photosynthetic iron-oxidizing bacteria.

Instead of taking water and converting it to oxygen, which is what plants or cyanobacteria do, these bacteria take reduced ferrous iron (Fe^{2+}) and, in the presence of sunlight, convert it to rust (which contains Fe^{3+}). Over millions of years, this rust accreted into deposits that today constitute the world's major sources of iron ore. (You can read more about this in *E&S*, 2005, no. 4, pp. 10–20.)

How many bacteria are there on Earth today? The father of microbiology, Antony van Leeuwenhoek, appreciated back in the 17th century that there were quite a few. "Though my teeth are usually kept very clean, nevertheless when I view them in a magnifying glass I find growing between them a little white matter as thick as wetted flour," he wrote in 1684. "The number of these animals in

the scurf of a man's teeth are so many that I believe they exceed the number of men in a kingdom."

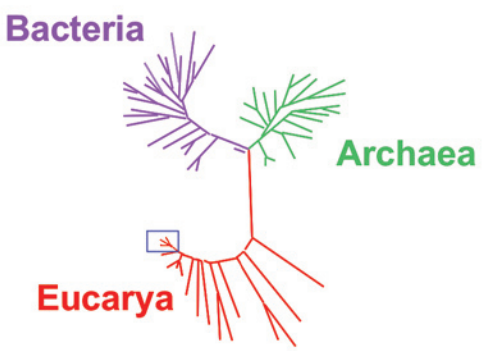
Leeuwenhoek underestimated: Not only do they exceed the number of men and women in a kingdom, they go far beyond that. We have anywhere from 5 million to 50 million bacteria per square inch on our teeth, and over 700 microbial species living in our mouths. Most of them are aiding us in our digestion—as are the 300 billion bacteria living in each gram of our colon. The palms of our hands have between 5,000 and 50,000 organisms per square inch, although that's nothing compared to the skin of our groin and armpit areas, which has at least 5 million per square inch.

The grand total per person is about 70 trillion (70×10^{12}), so we're really walking vats of bacteria. There are 10 times the number of microbial cells in an adult body than there are human cells, and the gut microbiome alone is estimated to contain more than a hundred times the number of genes that we have in our own genome—so there's a remarkable amount of metabolic diversity living within us. We shouldn't be alarmed by this, however, because most of these bacteria are our friends.

It's a commonly held fallacy that all bacteria are germs, but out of more than 30 million microbial species, only 70 are known to be pathogens.

As well as living on and within animals, microbes live in plants, oceans, rivers, lakes, aquatic sediments, soils, subsoils, and air. The total number of microbes on the planet has been estimated at 5×10^{30}, which is an enormous number. If they were all lined up end to end in a chain, it would stretch to the sun and back 200×10^{12} times.

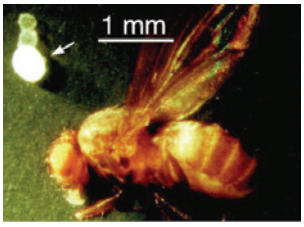
Microbes are not only ancient and present in vast numbers, they're also very diverse. We tend to think of diversity in terms of plants and animals—the beaks of finches, the wings of butterflies, or the flowers of orchids—but in the "family tree" that shows the relatedness of living things, all the examples that capture our imagination as being representative of diversity are in a small section at the top of the eukaryote branch (below). As you can see, that's just a fraction of the life that is out there. The remainder of the tree belongs to the microorganisms (be they bacteria, archaea, or eucarya).



In the universal tree of life based on ribosomal RNA sequences, the organisms we think of as representing diversity of life on Earth—animals, plants, and fungi—occupy the very small area delineated by the blue box. The tree of life is mainly microbial.

Hundreds of thousands of myxobacteria can swarm together to make 3-D "fruiting bodies" whose petal-like capsules are packed full of baby bacteria. This photo of *Chondromyces crocatus* is courtesy of George Barron, University of Guelph, Canada.

Although they're small, it's a fallacy to think of microbes as just a bunch of rods or spheres. *Thiomargarita namibiensis,* the largest bacterial cell, is about three-quarters of a millimeter across, and strings of them can be seen in shallow waters off the Namibian coast. This bacterium owes its large size to a central vacuole filled with nitrate, which acts as an electron acceptor to oxidize sulfur.



H. N. Schulz, et al., *Science*, 1999, 284, 493-495. © 1999, AAAS

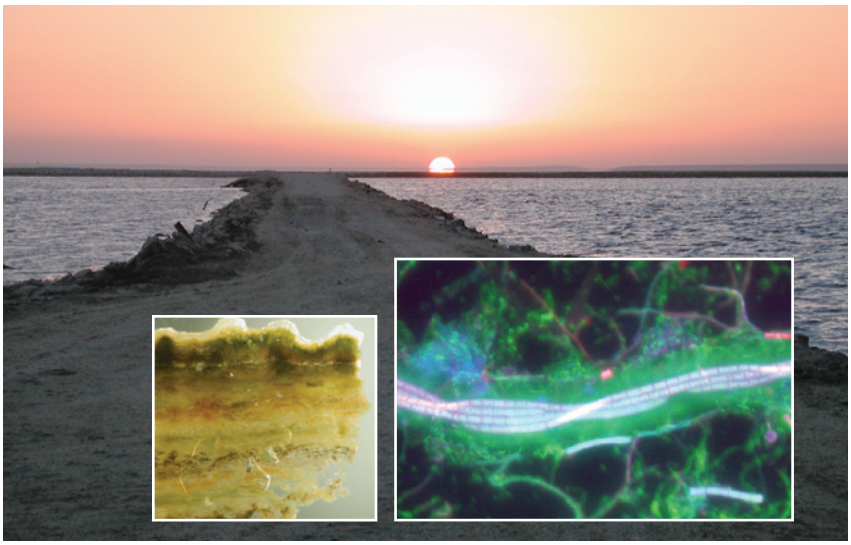
The current record-holder for bacterial size is *Thiomargarita namibiensis*, the sulfur pearl of Namibia. The arrow points to the largest "pearl" in a string of three that is almost the size of the fruit fly's head.

Myxobacteria develop a "fruiting body" when the population reaches a high density, swarming together to form structures such as the one at the top of the page—not an action typically associated with microbial cells.

The bacteria closest to my heart with respect to their structure are the magnetotactic bacteria, which synthesize magnetite particles in organelles called magnetosomes. (Yes, some bacteria do have organelles.) Aligned in a row inside the cell, these magnetic particles act like the needle of a compass to point the bacterium in the direction of the geomagnetic field. Arash Komeili, a former postdoc in my lab who is now an assistant professor at UC Berkeley, has been studying their ultrastructure and development (see p. 29).

Microbes also have some interesting behaviors. *Vibrio fischeri*, for example, can glow in the dark,

Main picture: These seawater evaporation lagoons in Guerrero Negro, Baja California, Mexico, are used for commercial salt production, but below the water, there's a rich biofilm community of salt-tolerant microorganisms attached to the rocks and sand grains. Left inset: A magnified section through a microbial mat shows the fine layering of different species. Right inset: Some intertwined strands of one of these species, the filamentous cyanobacterium *Microcoleus chthonoplastes*.



See also R. Ley, et al., *Applied & Environmental Microbiology*, 2006, 72, 3685–3695.

J. Leadbetter & K. A. Egland, *J. Bacteriology*, 1999, 181, 2667–2668. © 1999 American Society for Microbiology

E. Ruby, et al., *Science*, 2004, 303, 1305–1307. © 2004, AAAS

The ability of some *Vibrio* bacteria to glow in the dark, even in culture dishes (top), is exploited by the tiny Hawaiian bobtail squid (bottom) to make itself invisible to predators at night. (Photo of squid courtesy of M. J. McFall-Ngai, University of Wisconsin-Madison.)

a phenomenon known as bioluminescence, and often lives in a symbiotic association with the Hawaiian bobtail squid *Euprymna scolopes*. This squid has a terrific strategy. It creates a home for these microbes, called a light organ, where they can feed and grow to a density at which they produce light, something that single cells of *Vibrio* swimming around in the ocean can't do. The squid rises at night to feed in the upper parts of the ocean, but this makes it vulnerable to predators swimming below, because they can spot its shadow. To cope, it uses a counterillumination strategy—the bacteria light up the squid's underside to match the light of the surrounding ocean, which makes the squid "invisible" from below. So these bacteria do a very useful thing for their partner squid.

Some bioluminescent bacteria form such large blooms that they're even visible from space. A bloom the size of Connecticut composed of *Vibrio harveyi* in association with the alga *Phaeocystis* was seen by satellites in 1995 just east of the coast of Somalia. It's now thought that the milky seas described by ancient mariners must also have been caused by this phenomenon.

One of the most fascinating behaviors that microbes have is their ability to live in very hostile environments. Extremophiles, as they're called, like to live in extreme cold or heat, in high acidity or alkalinity, or in places like the Dead Sea or Mono Lake, where the salt is so thick that it's coming out as halite. They can even live on toxic substrates like toluene, benzene, or uranium, converting them to less harmful forms. Such bacteria are very useful for cleaning up waste materials in the environment.

The reason we find microbes almost everywhere we look is because, over the billions of years of Earth's history they've been around, they've figured out how to be fantastic chemists. Their needs are quite simple, because all these single-celled organisms really want to do is to divide. In order to do that, they need two things: energy, and carbon for building biomass. I would argue that metabolism can be thought of as a fusion of two separate processes that provide these needs. The part where energy is generated is catabolism, and the part where biomass is made is anabolism. These parts need to be balanced so that the energy that comes from the substrates, or "foods," the cell uses is sufficient to power the conversion of simple molecules into cellular constituents and hence biomass.

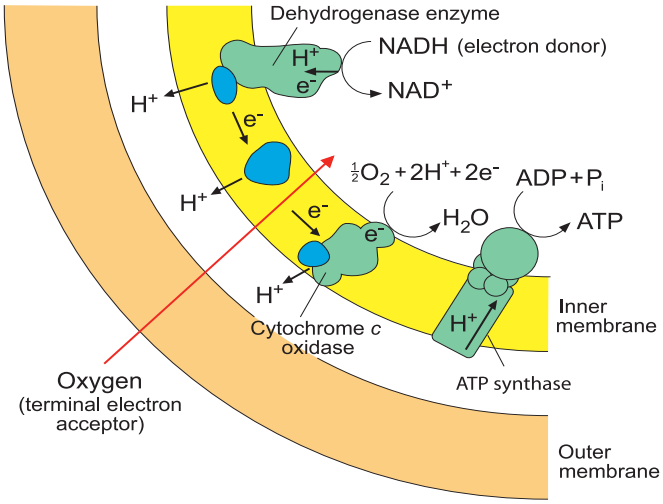
The energy that microbes need can come from many different places. It can come from inorganic chemicals such as hydrogen, hydrogen sulfide, ferrous iron, or ammonium, or from organic chemicals such as glucose or toluene. In addition, energy can come from sunlight. The carbon needed to build biomass can come from inorganic carbon such as CO_2 or from organic carbon.

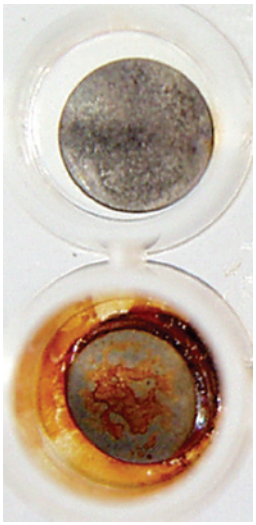
Many microbes can mix and match these different substrates virtually at will as long as the aggregate provides enough energy. They don't need much, because they can operate really close to the thermodynamic limit for metabolism—in fact, some types of fermenting bacteria have been found to grow where the free energy available is only on the order of four kilojoules. Don't worry about what that means, but trust me—it's really skating a very fine line.

One of the topics my research group is investigating is how bacteria survive metabolically when they're in biofilms. A simple definition of a biofilm is that it's a group of microorganisms attached to a surface. Most people think biofilms are the rings around the sink or bathtub, but that's unfortunate, because they can be very beautiful, like those found in the salt lagoons of Baja California, above. (Admittedly, the biofilm that can form on the surface of our teeth is not so attractive.)

Biofilms are everywhere. They form on the surface of still water, on any solid surfaces in contact with moisture such as river rocks (they're the reason immersed rocks are so slippery), and in the soil around the roots of plants. Bacteria such as *Bradyrhizobium japonicum* even live in biofilms in the root nodules of plants, providing their host with

When *Shewanella oneidensis* respires oxygen, NADH is oxidized to NAD^+ by a dehydrogenase enzyme sitting in the inner membrane of the cell. This releases hydrogen ions (protons) that cross into the space between the two membranes, while transferring electrons to a chain of (blue) electron carriers. The carriers pass the electrons to the enzyme cytochrome *c* oxidase, which sends them back inside the cell to the terminal electron acceptor, oxygen. The protons that have accumulated on the "wrong" side of the inner membrane move back into the cell through the enzyme ATP synthase, releasing energy that is used to make ATP from ADP and inorganic phosphorus (P_i).





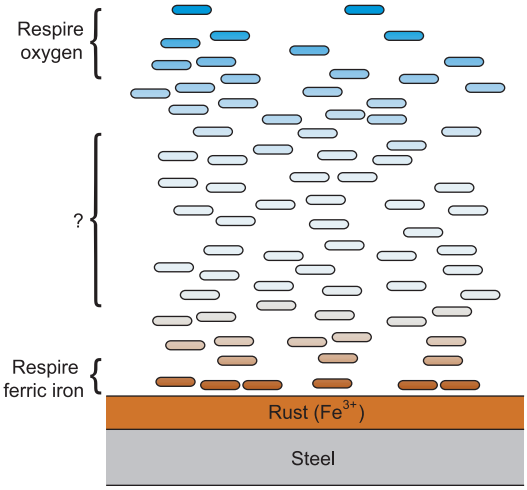
Which of the steel chips above has a biofilm of *S. oneidensis* growing on it—the clean one or the rusty one? Surprisingly, it's the clean one. *Shewanella* removes corrosion because it uses the rust for respiration.

nitrogen they've fixed from the atmosphere.

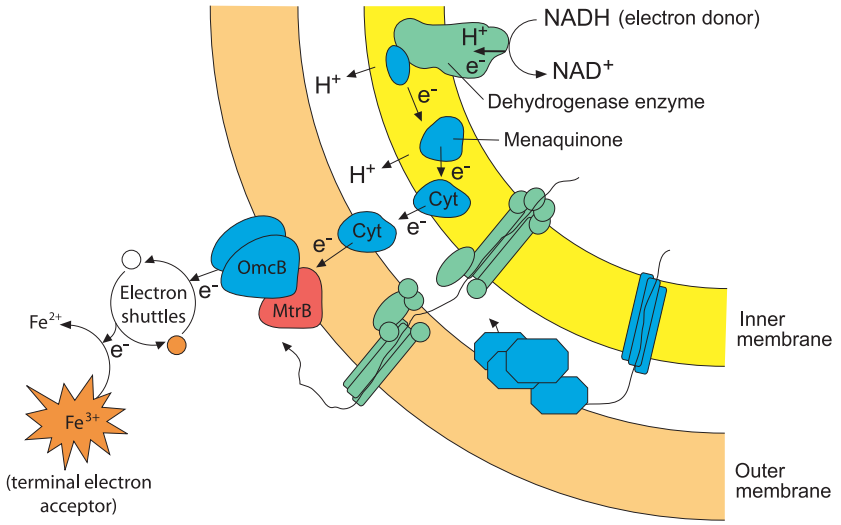
Bacterial biofilms can corrode the hulls of ships, the legs of oil rigs, and the insides of cooling towers, but a biofilm of the bacterium *Shewanella oneidensis* does the opposite—it removes the rust from steel and keeps it shiny (left). Rust, which is mainly iron oxide, Fe_2O_3, is used by *Shewanella* in its metabolism. This is a very challenging thing for any organism to do, because iron oxides are insoluble and can't diffuse into the cell.

Let me first explain how respiration works when there's oxygen available. *Shewanella* has two cell membranes, an inner and an outer one. This is very similar in structure to a mitochondrion—which, you recall, is our cellular powerhouse. A major goal of respiration is to make adenosine triphosphate (ATP), the "energy currency" of all living things. As outlined in the diagram above, the process begins when an electron donor, such as the reduced form of nicotinamide adenine dinucleotide (NADH), releases hydrogen ions (protons) and electrons upon oxidation by a dehydrogenase enzyme spanning the inner membrane. This enzyme is the first in a succession of protein complexes embedded in the inner membrane that form an electron-transport chain, which transfers electrons from carrier to carrier while also moving protons from the inner cell matrix into the space between the inner and outer membranes. The chain ends when the electrons reach an enzyme, such as cytochrome oxidase, that takes oxygen as the electron acceptor. In the course of this electron transfer, the protons that have built up in the intermembrane space move back into the cell interior via an enzyme called ATP synthase, and power the phosphorylation of adenosine diphosphate (ADP) into ATP. The electrons, and a few more protons, combine with oxygen to form water—which is why oxygen is called the terminal electron acceptor. That's respiration in a nutshell.

When *S. oneidensis* MR-1 forms a biofilm on steel, the top few layers of bacteria can use oxygen, but it can't diffuse down to the bacteria at the very bottom of the film. To survive, those cells in contact with the rusty steel convert their metabolism to use ferric iron (Fe^{3+}) as the terminal electron acceptor. But as I said above, iron, unlike oxygen,



In this conceptual drawing of a section through a *Shewanella* biofilm growing on rusty steel, the bacteria at the top (colored blue) respire oxygen, while those at the base (brown) switch their metabolism to respire ferric iron. The bacteria in the middle of the biofilm, starved of both oxygen and iron, have to be more imaginative in their respiration.



Above: When *Shewanella* uses insoluble Fe^{3+} as the electron acceptor, the electrons released by the oxidation of NADH have to be transported out of the bacterial cell and brought in close proximity to the rust. Electron carriers (blue; Cyt, *c*-type cytochromes) take the electrons through both cell membranes until they reach the *c*-type cytochrome OmcB, which transports them to the outside. The electrons either make direct contact with the iron or reach it via small electron-shuttling molecules.

is insoluble and can't diffuse into the cell. So how can it be a terminal electron acceptor? After many, many hours of research both by members of my lab and by others, we think we have now solved the problem, at least at the blueprint level.

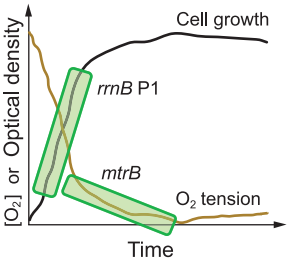
Electrons flowing from NADH pass through the dehydrogenase enzyme as before, then via the electron carrier menaquinone to several cytochromes, some of which are embedded in the inner membrane, while others are in the intermembrane space (above). These cytochromes interact—in a way that is not yet understood—with a complex of proteins in the outer membrane, including one called OmcB, a *c*-type cytochrome with 10 heme groups; each heme contains an iron atom at its center that can do redox chemistry. It's not yet been crystallized, so we don't know whether or not the hemes in this cytochrome come in close enough proximity to the rust for an electron to hop across. Electrons can only hop, or "tunnel," across a very short distance, as Harry Gray, the Beckman Professor of Chemistry, has found.

So we don't yet know whether or not these electrons are transferring directly, but we do know that this protein complex is also capable of transferring electrons to what I'll call electron shuttles—small molecules that can interact with the microbial cell and be reduced by the electrons coming from it to some state that can then interact with ferric iron and reduce it to ferrous (Fe^{2+}). The shuttles cycle back and forth between the cell and the terminal electron acceptor. They leave the cell to dump their electrons, and then they are taken back by the cell in order to be reduced.

The bacteria at the very top of the biofilm use oxygen, those at the very bottom use rust, but the ones in the middle are stuck between a rock and a hard place in terms of their respiration, because they're too far from either electron acceptor. We wanted to know how they solved this problem. Were they even alive?

To find out, grad student Tracy Teal followed the progression of an *S. oneidensis* MR-1 biofilm as it developed from single cells into large multicellular aggregates. She cultured the bacteria on a glass slide inside a flow cell constantly flushed with nutrients and then added live-dead stain, which stains cells red if they're dead and green if they're alive. As you can see in the photos below left, the cells in the middle of Tracy's biofilm stained red, indicating they were dead.

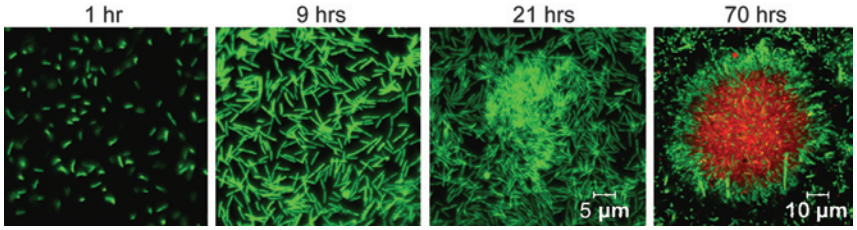
But we had suspicions about the accuracy of this stain, so Tracy went further and developed a way of monitoring metabolism at the single-cell level when the bacteria are swimming freely as single cells, unattached to any surface.



***Shewanella* growing in a free-living culture increase in number very rapidly at first, as measured by optical density. During this time, a gene that indicates growth, *rrnB* P1, is expressed. As oxygen levels fall, the rate of increase in cell numbers levels out, and the *mtrB* gene that encodes a protein necessary for anaerobic metabolism is activated.**

To monitor cell growth, she measured the optical density of the cultures, and you can see from the results in the graph above that initially the density rose rapidly. That's when the bacteria were in an exponential, or logarithmic, growth phase. Later, the growth curve hit a plateau, called the stationary phase, when the bacteria were no longer increasing in number.

To monitor metabolic activity, Tracy followed changes in the expression of two genes. The first, *rrnB* P1, expresses a ribosomal RNA. Ribosomes make proteins, and when bacteria multiply, they need to make more ribosomes, so by monitoring



After *Shewanella* was left to grow on a glass slide for an hour, individual cells started to attach to the base of the slide. After nine hours, they had multiplied and spread over the slide and by 21 hours they were beginning to aggregate into microcolonies. A biofilm had formed after 70 hours. A chemical that stains live cells green and dead cells red suggested that the cells in the middle of this biofilm were dead.

the expression of this gene, we'd find out if the bacteria were growing or not.

To find bacteria that might not be growing, but nevertheless are metabolizing, Tracy looked at a gene that tells us something about what happens as the cultures use up oxygen. As oxygen runs out, a whole suite of genes necessary for anaerobic metabolism is suddenly expressed, including one called *mtrB*, which codes for a protein *Shewanella* has on its surface that is thought to help hold the outer-membrane cytochromes in place.

Tracy labeled her cells with a stable fluorescent protein that was expressed all the time and never faded, but she also used an unstable fluorescent protein that only glowed if the growth gene *rrnB* P1 or the anaerobic gene *mtrB* was turned on. In other words, as long as the bacterium was present, it was red, but if either of those two genes was also active, it turned green.

The results were surprising and exciting. We found that although at this stage the cells in the middle of the biofilm had stopped growing, they were still remarkably metabolically active.

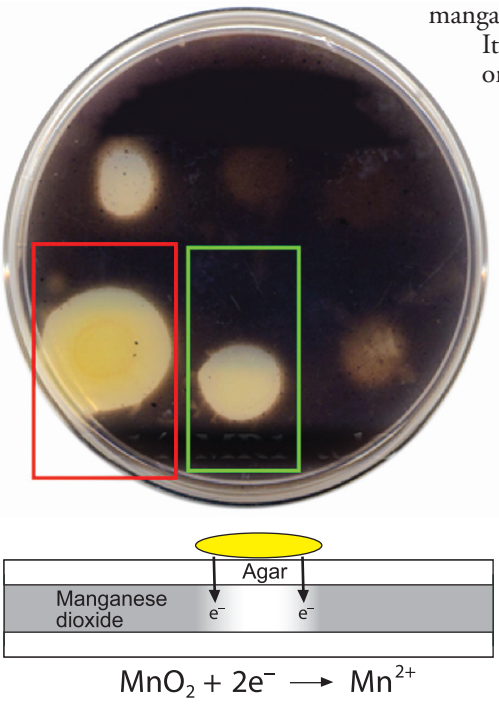
Now we had to find out why the bacteria were expressing these particular genes and their protein products when they were not growing.

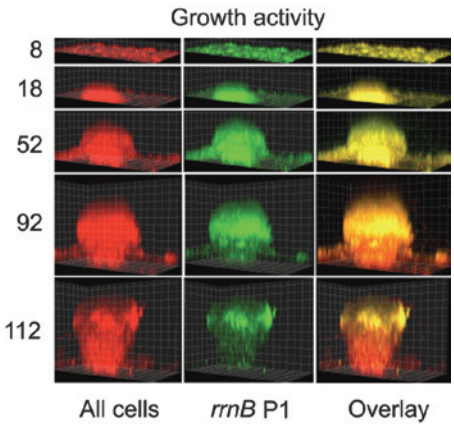
To keep alive, the bacteria have to make ATP, which means they have to keep on doing electron-transfer reactions. So we decided to look for molecules that would indicate that this type of activity was going on. We grew a *Shewanella* biofilm on a clear layer of agar above a black manganese dioxide layer. The agar layer was so thick and dense that none of the bacteria could swim through it, so any changes in the manganese dioxide could only be due to the excretion of some diffusible small molecule that could interact with the manganese.

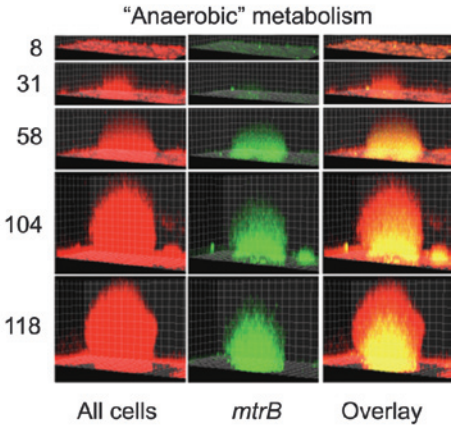
It worked, as you can see on the left. A light-colored patch appeared in the black manganese layer below the biofilm (green box), indicating that *Shewanella* had released a molecule that had transferred two electrons to the black manganese dioxide and reduced it to a clear form. We also grew a biofilm of another bacterium, *Pseudomonas aeruginosa* strain PA14, on the same culture dish, and as you can see from the size of the clear patch in the red box, it produced something even more effective.

This piqued the interest of two other

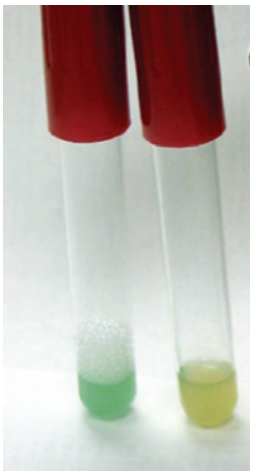
Below: The clear agar in the culture dish has a layer of black manganese dioxide (MnO_2) beneath it. When a biofilm of *S. oneidensis* MR-1 was grown on the agar, it produced a molecule that diffused down to the MnO_2 and reduced it to a clear form, producing the patch in the green box. *Pseudomonas aeruginosa* PA14 growing in another area of the culture dish produced even more of this reducing molecule, judging by the size of the clear patch in the red box.







Biofilms of *Shewanella* fluoresced red at all times, but fluoresced green only when the growth gene *rrnB* P1 or the anaerobic metabolism gene *mtrB* were turned on. The column on the left indicates the thickness in microns (1 micron is 1,000th of a millimeter) of the developing biofilm. Growth activity (top) was initially spread throughout the biofilm, but as the film thickened, there was only growth at the top. The *mtrB* gene was only expressed once the biofilm got thicker (bottom), presumably because the bacteria were switching over to anaerobic metabolism.

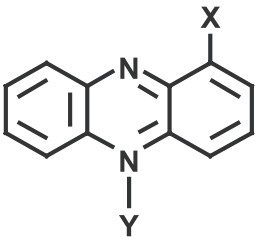


When a colorless culture of *Pseudomonas aeruginosa* was swirled around vigorously to introduce oxygen, the solution turned blue due to the oxidation of phenazine. After the tube was left to stand for several minutes, the solution lost its color again once the oxygen was used up by the respiring bacteria.

members of my lab, grad student Alexa Price-Whelan and postdoc Lars Dietrich. It's been known for over 100 years that pseudomonad species produce beautiful fluorescent molecules called phenazines. Phenazines come in many different forms with different oxidation-reduction (redox) potentials, hydrophobicity (oiliness), and colors. You can see their color very dramatically above. When the phenazine in the colorless culture is oxidized by swirling it around, it turns blue. Left to sit on the benchtop for just a couple of minutes, it will rapidly get reduced by the bacteria and become colorless again. That's redox chemistry in action.

For decades, people have been describing these phenazines as antibiotics because of their ability to react with molecular oxygen to generate free oxygen radicals—a very reactive form of oxygen that attacks and destroys proteins. But in the absence of oxygen, phenazines may be doing something much more interesting. Bacteria lived on Earth long before there was oxygen on the planet—so could these phenazines (or phenazine-like molecules) have played a more fundamental role in those anaerobic days, and do they still, when oxygen is absent, play that role now?

When *Pseudomonas* is grown in a free-swimming culture, phenazines are only produced at the very tail end of exponential growth, at the point at which the bacteria go into the stationary phase. At this point, the bacteria are at a very high density and running low on oxygen, so are they using these phenazines as electron shuttles to power the oxidation of NADH? By coupling the oxidation of NADH to the reduction of phenazines, the cell could be gaining a "last gasp." I've calculated the free energy that would result from the reduction of several phenazines, and it's always well within the limit that seems reasonable to power microbial growth, or at least to keep the microbes going during the stationary phase.



Phenazines are fluorescent molecules that come in a range of beautiful colors such as deep red, lemon yellow, deep blue, and orange, depending on the chemical groups attached to the X and Y positions of the molecule.

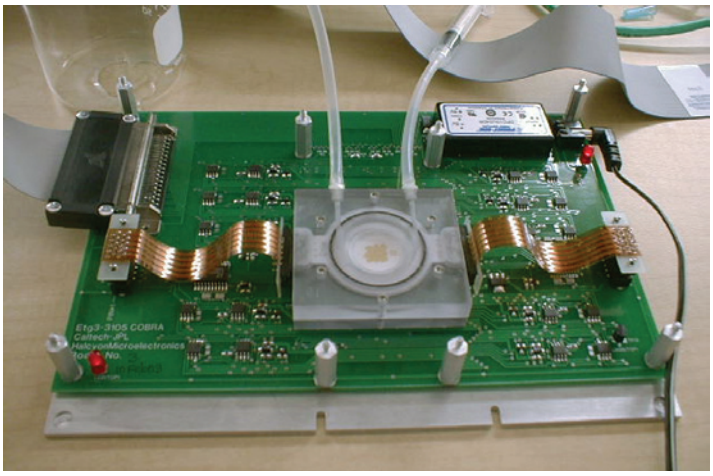
The toxicity of phenazines, and the stationary-phase timing of their production, have long led researchers to malign these compounds in the literature and categorize them as "secondary metabolites." However, phenazines are made as a branch off a metabolic pathway that leads to the production of many other important things for the cell, and their potential roles in central metabolism indicate that actually, they may not be secondary at all.

The next step in our investigation was to find out if phenazines are being made in biofilms. We collaborated with Martin Buehler and Didier Keymeulen at JPL to make a really neat biofilm flow cell that we've called the E-Tongue 3, in which nutrients are fed into the chamber through tubes and flow over a substrate chip that contains an array of nine planar electrodes that analyze the chemicals secreted by the biofilm as it grows. The whole circuit board is so small that it can fit on the stage of a microscope.

Using a technique called cyclic voltammetry, we can look for different phenazines in the chamber, as they have very specific "fingerprints." We focused on one particular phenazine called pyocyanin. When Doug Lies, the senior staff scientist in my lab, grew biofilms of *P. aeruginosa* in the E-Tongue 3, he found that this phenazine was produced only during the late phase of growth, after 144 hours.

We also have some preliminary evidence that the production of these phenazines may play a very important role in the ability of these organisms to aggregate and form a biofilm of significant density. Alexa and Lars made a mutant of *P. aeruginosa* that couldn't make any phenazines and compared its ability to make biofilms with the wild-type strain, PA14. The mutant bacteria didn't aggregate until phenazine was added to the culture, after which they formed a biofilm.

So we're finding that the production and cycling of small molecules such as phenazine antibiotics under times of redox stress—when



The E-Tongue 3 (for electronic tongue) is a state-of-the-art flow cell developed in collaboration with Martin Buehler and Didier Keymeulen at JPL. It enables us to observe the development of biofilms under the microscope (that's senior staff scientist Doug Lies in the photo on the right) while monitoring the chemicals the bacteria use and produce. The cells grow in a culture dish into which nutrients flow in and out over a sophisticated substrate chip that sits in the middle. This chip controls an array of nine planar electrodes that detect chemical changes in the solution.

oxygen is limited and there is no other redox acceptor around—appears to be far more important for microbial metabolism than was previously believed.

Our challenge now is to determine how important this is to microbial survival outside the lab in other areas, such as in our bodies and in the environment, and whether or not these findings apply to any other secondary metabolites. It's going to keep us busy for years to come. □

Dianne Newman joined the geology and planetary sciences division in 2000 as the Clare Booth Luce Assistant Professor of Geobiology and Environmental Science and Engineering, and gained tenure in 2005. She became a professor of geobiology earlier this year, and was also recently appointed a professor of biology. Dianne has carved out a name for herself in the geobiology community with her ground-breaking research into the way in which bacteria have shaped, and continue to shape, the chemistry of their environment, but she didn't start off as a biologist—for her undergraduate degree from Stanford (1993) she majored in German studies and translated descriptions of antiquities into English for the Pergamon Museum in Berlin. She must have decided she needed a complete change from languages, because she then undertook a PhD in civil and environmental engineering at MIT (1997), after which she spent two years as a postdoc at Harvard Medical School working on bacterial genetics. Dianne was named one of the world's top 100 young investigators of 1999 by MIT's Technology Review *magazine, and she has gained an Office of Naval Research Young Investigator Award and a Packard Fellowship, but her greatest honor (so far) was being selected as an Investigator for the Howard Hughes Medical Institute in 2005. She is married to another member of the Caltech faculty, Professor of Chemistry Jonas Peters.*

This article is adapted from a Watson lecture given on April 12, 2006.

The members of the Newman group firmly believe that their bacteria are beautiful. From left to right, back row: Yongqin Jiao, Davin Malasarn, Tracy Teal, Yun Wang, and Nikki Caiazza. Front row: Sky Rashby, Christine Romano, Alexa Price-Whelan, and Lars Dietrich. Not pictured are Doug Lies, Itzel Ramos-Solis, and Mike Tice. Team leader Dianne Newman is on the right.

Plug In, Charge Up, Drive Off

by Douglas L. Smith

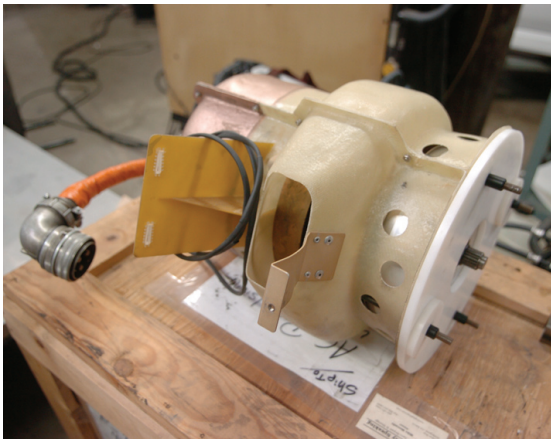
This zippy two-seater goes from zero to 60 in 3.6 seconds, and has a top speed of 100 miles per hour. It's an electric car that, even more remarkably, can drive from Los Angeles to Las Vegas without needing recharging. Designed by Alan Cocconi (BS '80) with some styling tips from Art Center College of Design student Scott Sorbet, who now works for Ford, the t_{ZERO} runs on the same high-energy-density batteries that power your laptop.

Well, here we are 30-odd years after the Great Energy Crisis. We're importing more oil than ever, gasoline prices are once again going through the roof, and there's still turmoil in the Middle East. So what's different this time around? Two things: This time, there really *is* an energy crisis. In *Out of Gas: The End of the Age of Oil* (W. W. Norton, 2004), Caltech vice provost David Goodstein argues that the so-called Hubbert Curve, which tracks global oil production, will peak in the next decade or so and then inexorably decline. After that, he writes, "increasing demand will meet decreasing supply . . . the shortage will not be artificial and it will not be temporary." Since America consumes one-quarter of that production to drive our SUVs (our 5 percent of the planet's population burns 45 percent of the world's gasoline), heat our houses, and manufacture everything from fertilizer to pharmaceuticals to plastic trash cans, the consequences will be profound.

There's one simple, obvious way to help minimize them, says a group of Caltech alums: battery power. Electric cars flopped in the '70s, as the lead-acid batteries that cranked the starters on our station wagons just weren't up to the job. They were (and are) big and heavy, and didn't hold that much juice; much of what they did store was turned into heat by inefficient power controllers. Consequently, electric cars ran like they were powered by tired hamsters. They didn't go very far, and they took an eternity to recharge.

That was then. You can curse all you want at those pinheads whose cell phones ring in theaters, but the explosion in laptops, PDAs, cell phones, pocket GPSes, iPods, and other techno-toys has sparked a revolution in battery technology. In the last couple of years, the lithium batteries that power all your favorite techno-toys have become incredibly small and remarkably powerful, to the point where such batteries would make electric cars practical.

Just a few kilowatt-hours east of Pasadena, a company called AC Propulsion is converting vehicles to run on laptop power. In case you've never disemboweled your Dell, its batteries are roughly the size of rolls of dimes. Six to eight of them let you cruise the information superhighway; driving the L.A. freeways takes 7,000. In 2003, AC Propulsion hand-built a sporty two-seater dubbed the t_{ZERO} that has a 300-mile range. Says



Electric cars never have to shift gears. The t_{ZERO}'s motor puts out up to 240 horsepower in one smooth, continuous whine reminiscent of the sound of the Batmobile.

founder Alan Cocconi (BS '80), who sold the company to a group of investors last December, this "really means you have 250 when you drive without paying any attention to your driving style at all. And we always quote 300 as 'being careful at 65 miles an hour.'" There are no sleep-deprived rodents under this hood—the t_{ZERO} can do zero to 60 in 3.6 seconds and has a top speed of 100 miles per hour. (He knows this from actual experience.) It will out-accelerate a Lamborghini.

"Some of the Lamborghini road tests report that you can do zero to 60 in 3.6 seconds," Cocconi remarks, "but no owner can. We've cost a couple of them some pretty expensive clutches, too. But with electric cars, no big deal. Just jam the pedal and it goes." The t_{ZERO} has a three-phase induction motor that revs to 13,000 rpm at 100 mph. Explains Cocconi, "That's one thing about electric motors. You can push them for extremely high peak power without making the motor much bigger than you need for continuous power. So you can get this fantastic performance with almost no penalty in energy efficiency, size, or weight."

You won't see a t_{ZERO} at Le Mans any time soon, however, as the motor and batteries would overheat in a few laps at full throttle. But for realistic use, or abuse, around town, it's got all the punch you'll ever need. And for people who fantasize about driving in one of those BMW commercials, if "you go on a mountain road, and have fun speeding around the turns, you still use less energy than doing 75 on the freeway," Cocconi says. "You can really hammer it, but your energy per mile is low because at the end of each turn you get it back."

This is the electric car's secret weapon: regenerative braking. Take your foot off the t_{ZERO}'s gas—excuse me, accelerator—pedal and the electric motor gets turned by the wheels instead of turning them. The motor becomes a generator, recharging the battery for free, and the resistance slows the car down. You only need the brake pedal for panic stops caused by sudden red lights or a deer in the road. In general, regenerative braking gives you about a 30 percent increase in driving range in stop-and-go traffic, as opposed to conventional cars where the mpg plunges. And the worse the traffic, the better you do. Says Cocconi, "That's the beauty of electric drive—every time you slow down, you fill your tank a bit." As a bonus, you don't waste fuel idling at stoplights, because the motor only turns when the car is moving.

Speaking of city driving, AC Propulsion is starting to convert Toyota Scion *x*Bs—those squared-off minivans that look like what happened when you sat your G.I. Joe down in a shoebox and called it a Jeep—into electric vehicles for utility-company fleets. "There are none on the market right now," Cocconi says, "and the electric companies really don't like to buy natural-gas vehicles to meet their alternative-fuel-vehicle requirements." The first of five prototypes is rolling out of the garage as *E&S* goes to press, and the company plans to do 100 conversions a year.

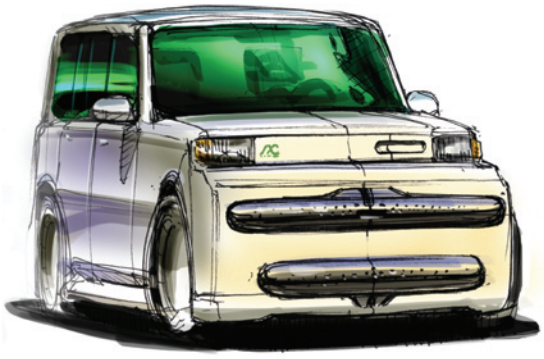


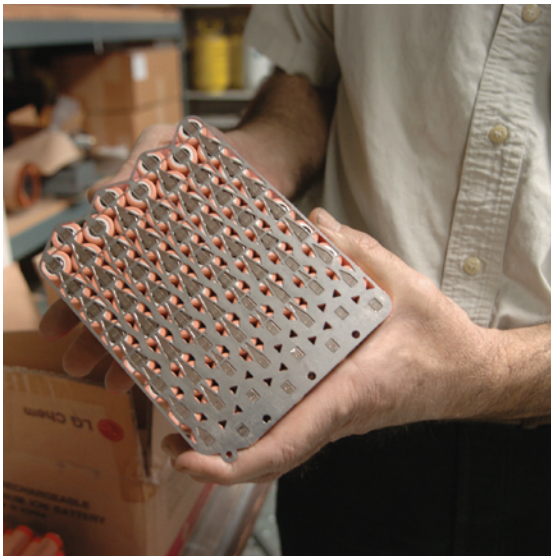
Illustration by Julius Bernardo, Art Center College of Design.

AC Propulsion's electric Scion. Streamlining isn't a big issue in city driving, but minimizing the drag from the frontal area is, so the Scion was chosen for its narrow wheelbase.

"I spend 15 seconds a day recharging my electric car: 10 seconds to plug it in when I get to work, and five seconds to unplug it when I leave."

This first prototype has a 580-pound battery pack and a range of some 180 miles, but an economy version with a smaller battery pack and about half the range is also under development. "It's a tradeoff between cost and range," says Dave Sivertsen (BS '80, PhD '89), AC Propulsion's vice president for research and development. When people first started trying to build electric cars as a commercial venture, one question asked of potential customers was, "How far do you want to go on a full charge?" And people, being used to gasoline, would say, "As far as possible," or "As far as my car does now." But, says Sivertsen, "the question you really want to ask is, 'Here is a car that, as built, will go 100 miles between charges—how much more are you willing to pay to go 200 miles?' Now it becomes a pocketbook issue. Some people would say, 'It's really not worth that much to me. I'll only pay $500.' And others might say, 'Wow! That's great! I'll pay $5,000!' And you can make that economic decision accordingly."

AC Propulsion's lithium-ion battery bricks are especially designed to maximize the air circulation between the individual cells. Charging and discharging the brick produces a good deal of heat, which, without proper ventilation, would lead to unhappy batteries.



Which brings us to the biggest impediment to going electric—laptop batteries aren't cheap. AC Propulsion buys them in bulk from the factories in China and Korea, but not on the same scale that Compaq or even Apple does, and not at the same deep discounts. The company then repackages the batteries into five-and-a-half-pound bricks, 53 in a brick, all hand-assembled and hand-welded by expensively educated people. ("We really want to sell the drive system, motor, and electronics technology," Cocconi says. "We're not in the battery-assembly business, but we do it ourselves because our volume's too low.") When all is said and done, a Scion's worth of battery packs winds up costing him about $25,000. This would fall to under $12,000 or so if the battery packs were made to order at the factory. Says Cocconi, "Right now unless you're building 50,000 cars a year, you don't come *close* to laptops. There are probably four or five major manufacturers in the world, and when we talk to them, they're not very enthusiastic about a new market because they can't meet the present one. It isn't the best situation for us, but on the other hand, it does drive the R&D and the prices. And they're all building new plants. So I hope in two years or so they'll have excess capacity and be looking for more markets."

Meanwhile, the batteries keep improving with no end in sight. "We bought 2.0 amp-hour cells when we built the t_{ZERO}," Cocconi says. "The ones we're working with now are 2.2 amp-hour. We have some 2.4s and 2.6s in stock. We went from 2.0 to 2.6 in two years, so it's more than 10 percent a year. And the cost per cell remains about constant." As has the cell size—18 millimeters in diameter by 65 millimeters long.

But, says AC Propulsion president Tom Gage, the Scion conversions will use 2.0s and 2.2s. "The 2.4s and 2.6s aren't as long-lived," he says. "For cars, low cost and long life are the most important features, but with laptops, it's high energy density. People trade in their laptops every couple of years."

Which brings us to the other problem with lithium-ion batteries: They wear out. The end of their useful life is considered to be 80 percent of their original range, which is about three years at the moment. Cocconi would really like to see batteries with a life of six or seven years, which are probably several years off. It's not just a question of the cell electrochemistry, but of the battery-management electronics and software. Fortunately, Sivertsen's specialty is software design. "With a gas tank, all

AeroVironment's Gossamer Penguin, a three-quarter-scale, solar-powered version of the Gossamer Albatross, takes wing over Rogers Dry Lake bed in the summer of 1980. The Penguin was the prototype for AeroVironment's Solar Challenger and Helios—the latter holding the world altitude record for any steady-flying (as opposed to ballistically climbing) airplane. It soared to 96,863 feet, two miles higher than the SR-71 "Blackbird" it beat.

you need is a fuel gauge," he explains. "But we need to monitor the batteries' temperature, voltage, and current." So the t_{ZERO} has 125 "popcorn" microprocessors, so called because they're very cheap and not too bright, distributed throughout the battery pack. The power-electronics unit, in turn, talks to two slightly more expensive microprocessors in the vehicle-management unit that controls the charge/discharge rates and overall temperature of the system. And that's where the software comes in—being clever in how you shuffle the electrons in and out of your batteries can have a big effect on how long they last. But Sivertsen's job should get easier when battery makers actually begin to cater to the electric-car market. "If the manufacturers just spent another 10 percent up front on better materials, we'd get much better life."

Electric-car buyers pay a stiff premium for the batteries, but get some of it back in lower fuel costs. Says Cocconi, "With gas at $3.75 a gallon, a $12,000 battery pack that lasts 120,000 miles will give about the same operating costs as a conventional car that gets 27 miles to the gallon." Another number to look at is miles per hour of charging: The t_{ZERO} takes three hours to charge fully. This translates to six dollars' worth of electricity for 300 miles' travel at the standard residential rate of 11 cents per kilowatt-hour, compared to $45 for 300 miles' worth of gasoline at 25 miles per gallon and $3.75 a gallon. So as gas prices spiral upward, electricity will look better and better. And an electric car refuels itself overnight—no more waiting in line at the pump!

Says Bart Hibbs (BS '77), "I spend 15 seconds a day recharging my electric car: 10 seconds to plug it in when I get to work, and five seconds to unplug it when I leave." Hibbs is a senior engineer for technology initiatives at AeroVironment in Monrovia, California. Founded in 1971 by Paul MacCready (MS '48, PhD '52), who is probably best known for the Gossamer Albatross, a pedal-powered aircraft that flew across the English Channel in 1979, the company builds tens of millions of dollars' worth annually of lithium-battery-powered drones that weigh 10 pounds or less and can stay in the air for up to four hours. (More prosaically, AeroVironment also makes fast-charging systems for electric forklifts and airport service vehicles.) As the company's name implies, MacCready has an abiding interest in the environment as well as aviation, and along with aerodynamicists he employs a formidable collection of experts on fuel cells, battery packs, solar arrays, and windmills, as well as the control electronics that go with them. Back in 1987, AeroVironment's solar-powered car, the GM Sunraycer, designed and built by a team led by Alec Brooks (MS '77, PhD '81),

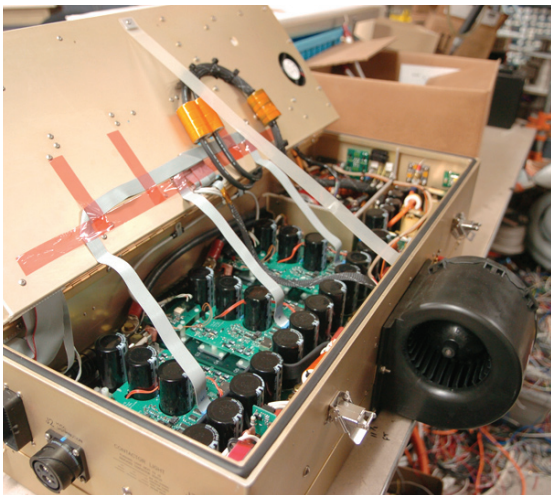
Who Killed the Electric Car?

The saga of the protracted gestation and untimely demise of GM's EV-1, the first production electric car in the United States in nearly a century, has been widely reported. For an inside view of the former, read *The Car that Could: The Inside Story of GM's Revolutionary Electric Vehicle*, by Michael Shnayerson, Random House, 1996. Premiering on June 28 in Los Angeles and New York, the Sony Pictures Classics documentary *Who Killed the Electric Car?* finds plenty of blame to go around for the latter. Like the assassination of Julius Caesar, many hands wielded the daggers, but the fatal blow was struck in April 2003, when the California Air Resources Board, in response to enormous pressure from the automotive and oil industries, essentially rescinded the Zero Emission Vehicle (ZEV) mandate it had passed in September 1990 at least partially in response to the debut of the Impact as a concept car at the Los Angeles Auto Show that January. Intended to combat the Los Angeles basin's worsening smog—41 stage-one alerts in 1990—the ZEV had required that 10 percent of all new cars and light trucks sold in California in 2003 be emissions-free.

Among the on-screen interviewees are Brooks, Cocconi, and Thomas Everhart, General Motors board member from 1989 to 2002 and Caltech president from 1987 to 1997, who had this to say: "I made the case at the General Motors board that the reason for the EV-1 was to give General Motors a very big head start in how you transform electricity into the drive power for the car. . . . But my frustration was they did not capitalize on the lead. And the reason, which was discussed with the board, was that there was not a profit seen to be coming out of either electric cars or hybrids. They could not understand how Toyota could possibly make a profit out of the Prius, for example. They were going to lose their shirt, and as the evidence has shown, I don't think Toyota is losing its shirt. . . . General Motors made a commitment to the Hummer, because they could see the Hummer would make them money. . . . It looks very schizophrenic, but I think when it started, it was, 'we could show the people in California we can meet the zero emission requirements,' and later on, it was, 'do we want to show them that we can?'"

But perhaps the most telling comment came from Wally Rippel (BS '68), a senior design engineer at AeroVironment. As an undergrad, Rippel electrified his '58 VW bus and challenged MIT to a cross-country electric-car race. Caltech won—see *E&S* October '68. At the time of the Impact project he was working for JPL, but he consulted on the design of the motor, electronics, and battery pack. "What the oil companies feared is that the electric vehicle would become successful six years from now. What the automobile companies feared was that they'd be losing money on electric vehicles in the next six months."

For further information, see http://www.sonyclassics.com/whokilledtheelectriccar/



Laptop batteries are DC; three-phase motors are AC. Ordinary inverters work in one direction only, changing DC to AC or vice versa; electric-car inverters have to be reversible in order to harvest the electricity generated when the brakes are applied. Cocconi built his first inverter in his garage; the production model shown here is one-third the size and produces 50 percent more power. About 100 of them have been sold around the world.

now a chief engineer at AeroVironment, trounced the competition in a race across Australia (see *E&S*, Winter '88). On the strength of this, Brooks and MacCready persuaded General Motors to fund the design and construction of the Impact, which became the prototype for General Motors' EV-1. In fact, Cocconi designed the Impact's power electronics as an AeroVironment consultant before leaving to found AC Propulsion in 1991.

While not in the automobile business itself, the company is something of a think tank on transportation and alternative-fuel issues. Some, including Hibbs, see the pure electric vehicle as the way to go, while others feel the so-called plug-in hybrid is the best bet. Like the wildly popular Toyota Prius, a plug-in hybrid has both an electric motor and a conventional gasoline engine. But the Prius's battery can only be charged from its engine, whereas the plug-in, as the name implies, can be recharged from the closest wall outlet.

No car company has announced any plans to start making plug-ins, but in 2004 Ron Gremban (BS '69), the technical lead for the California Cars Initiative (CalCars), converted his own Prius to a plug-in prototype with a lead-acid battery pack. Unlike AC Propulsion's bottom-up approach, integrating the plug-in charger and additional batteries into an existing hybrid called for some reverse engineering. Gremban and CalCars volunteers used a proprietary dashboard-mounted controller from EnergyCS, a builder of battery management systems, to override Toyota's controller, and the

Photo courtesy of CalCars and Set America Free.

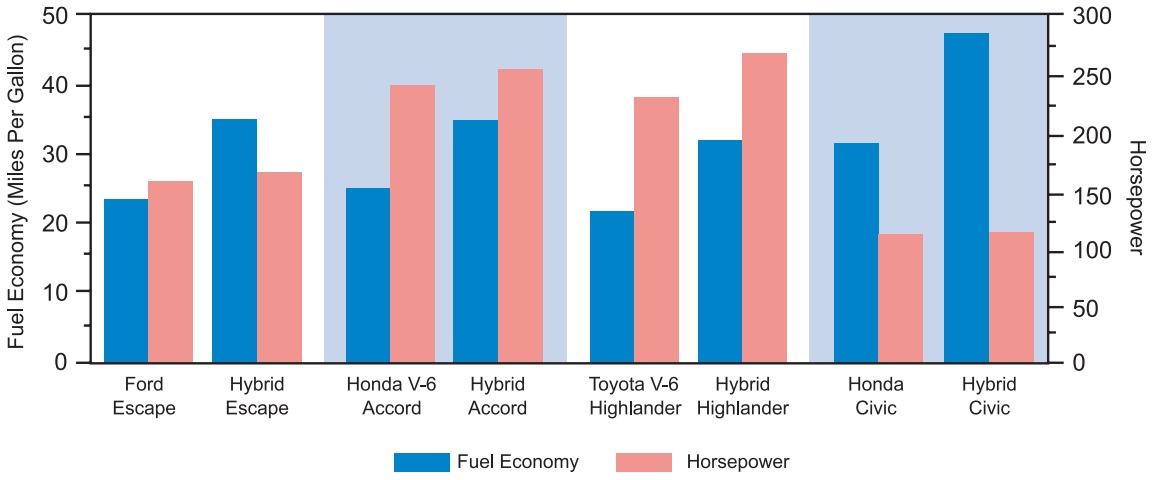
CalCars and the Set America Free coalition, an energy-security advocacy group, hosted a plug-in hybrid "Ride and Drive" for senators and congresspersons in May to coincide with President Bush's meeting with the heads of the Big Three automakers. From left: Gremban; John Davi of CalCars; Andy Frank, inventor of the modern plug-in hybrid; Anne Klein of Set America Free; Kramer; and Set America Free's Gal Luft. The silver Prius was modified by Electro Energy, a Connecticut-based battery manufacturer, for Set America Free.

success of this project has since inspired EnergyCS to form a company called EDrive Systems that plans to sell lithium-battery plug-in Prius conversions. Gremban has since learned how to "spoof" Toyota's system, a tactic he tested on the Prius belonging to CalCars' founder, Felix Kramer. It went so well that Gremban is now working it up into a public-domain conversion procedure.

Gremban recently did the electrical engineering for a Prius plug-in conversion at *Make* magazine's Maker Faire in San Mateo on April 22 and 23. *Make* is the *Popular Mechanics* of the high-tech do-it-yourselfers, and the conversion was done live, in public, from Saturday morning to Sunday afternoon. Well, mostly done, says Gremban. "The circuit boards arrived just barely in advance, and I wound up having to test them at the show, around in the back, while other people were doing the assembly up front. And then we had to finish it in my garage on Monday so that the owner could drive it back up to Seattle, where he lives. It was definitely the skin of our teeth."

A plug-in hybrid gives you the best of both worlds, its advocates argue—you can liberally dilute your gasoline with electricity while tooling around town, but still drive from Pasadena to Las Vegas without trailing a bright orange, 300-mile heavy-duty extension cord after you. Both the gasoline engine and the battery pack can be smaller, as neither has to go it alone. So if you've run the battery flat on the way in to work and your kid's school calls at 10:00 a.m. to say little Sasha is throwing up in the nurse's office and you'd better get over here *now*, no problem. You can afford to burn a few dinosaurs once in a while. A Prius-type hybrid, says Gremban, uses about two-thirds as much gasoline as an ordinary car, while a plug-in or "gas-optional" hybrid can use one-third as much. Says MacCready, "In the short term, let's say the next five years, it seems logical to think of hybrid cars that maybe go 40 to 45 miles" on a battery pack one-sixth the size of the t_{ZERO}'s, "but then when you have to go to San Diego and back in a day, you use the gasoline engine to supplement it. But the battery power would suffice for 80 to 90 percent of the total mileage for typical users." According to the National Household Transportation Survey in the 2000 census, the aver-

The commercially available hybrid versions of existing models not only get better fuel economy, but, surprisingly, increased horsepower, as shown in figure 1-7 of the National Commission on Energy Policy's (NCEP's) 2004 report, *Ending the Energy Stalemate*. This bipartisan commission of heavy hitters from the business world, environmental groups, government, and academia was founded in 2002 to provide real-world solutions to the thorny economic, national security, and environmental issues that entangle debates on energy policy.



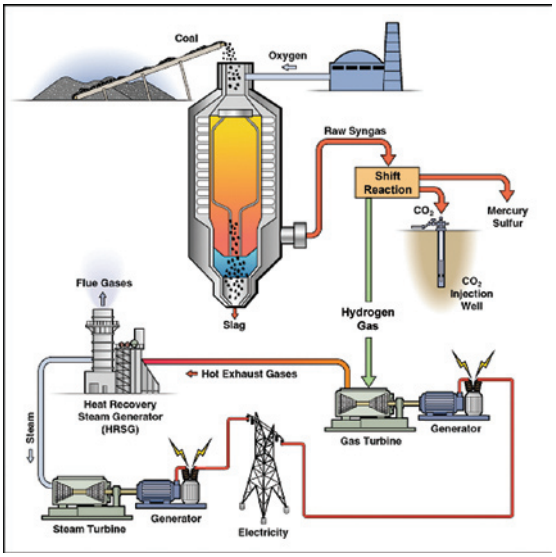
age American round-trip commute in private cars and light trucks was 22 miles in urban areas and, surprisingly, only 28 miles in rural ones. "What we would like to see happen is you go your 40 to 45 miles on battery power and then switch on the engine—gasoline, bioethanol, whatever. The battery and the electric drivetrain would still do all the maneuvering, the accelerations and decelerations, and the engine would just run at a constant output of 20 horsepower to generate electricity for the battery. The battery does everything, and the hybrid system just provides you the energy to go as far as you want. At the moment, that's not the way hybrids are designed, but we hope they will move in that direction."

Now if you have all these cars charging in parking lots all day and garages all night, something really useful can happen. The load on the power grid is always in flux, tracking the aggregate behavior of all the air conditioners, elevator motors, and other devices drawing power from it. This makes the voltage fluctuate, which in turn makes sensitive electronic equipment, like computers—and what doesn't have a computer chip in it these days?—unhappy. So, as Californians learned in the summer of 2000, the grid has a complex load-balancing system. Some power plants ramp their production up and down every few seconds to even things out, and get paid very handsomely for their flexibility. But a huge pool of plugged-in electric-car batteries could do the same job, in the simplest case by allowing the system to ramp up and down your charging rate to balance the load. It's a win-win situation, says AeroVironment's Brooks—you surrender some level of control to the grid operator, and the utility companies would need to induce car owners to participate by selling them discount electricity. Furthermore, most battery charging would happen at night, while drivers are sleeping, and demand (and hence electric rates) is low anyway, so the utilities would benefit by being able to operate their plants at a more even load around the clock. The whole thing could be run over the Internet, using wireless WiFi connections.

Eventually, two-way controllers could be used. "Drivers would specify how much their state of charge would be allowed to vary over the course of a day," Brooks explains. "A lithium battery might have 200 miles' range; allowing the top half to be cycled in and out would still provide 100 miles of available range, enough to get to your sick kid's school." If everyone allowed their batteries to be half drawn down, even such broad, multi-hour demand surges as midafternoon air-conditioning sprees could be handled.

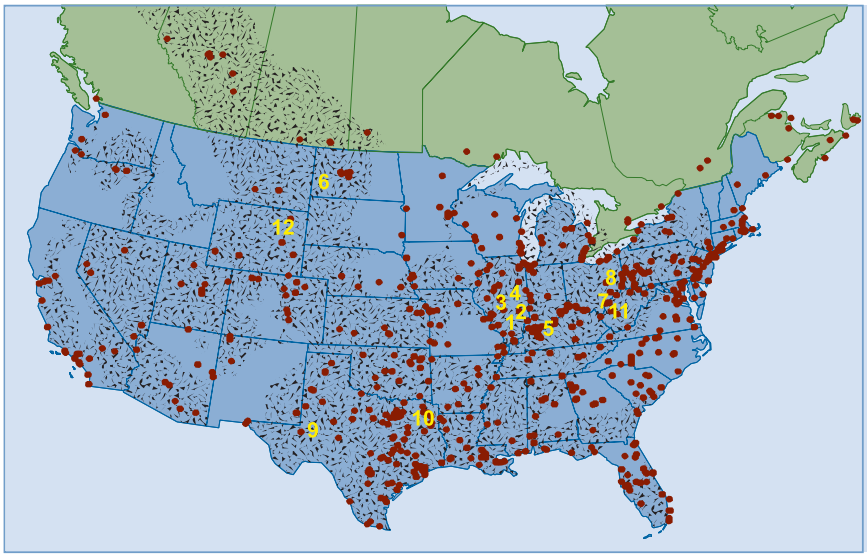
But eventually, as we wean ourselves from gasoline, we're going to need more electricity. And we don't want to solve one problem by exacerbating another. California gets a fair amount of its electricity from "green" sources, but the nation as a whole relies on burning fossil fuels to turn the generators. Says MacCready, climatologists "are in 98 to two agreement that we are getting weather modification, mostly global warming, because of human activities, and CO_2 is a big part of that. But when you hear it discussed on television, they get one person from the two people who think it isn't happening, and one from the 98 who think it is."

In 2004, the last year for which Department of Energy statistics are available, 50 percent of the nation's electricity came from coal, 15 percent from natural gas, and 3 percent from petroleum. That means that 68 percent of our juice came with a side order of CO_2. Coal is dirt cheap, and we've got a jillion tons of it—the largest reserves on the planet—so real-world economics says we're not going to stop using it any time soon. But many of our coal-burning base-load plants, built 20 to 40 years ago, are reaching the ends of their useful lives. Fortunately, a decade-old technology called Integrated Gasification Combined Cycle (IGCC) generation is not only 15 percent more efficient than old-fashioned pulverized-coal power plants, it can reduce pollutants such as sulfur dioxide (acid rain), nitrogen oxides (ozone and haze), particulates, and mercury by over 90 percent. As currently practiced, the process converts coal to synthesis gas—a mixture of carbon monoxide and hydro-



Courtesy of Jim Kopp, Kopp Illustration, Inc. Adapted from *OnEarth*, Fall 2005, p. 29, National Resources Defense Council.

The Integrated Gasification Combined Cycle (IGCC) process, modified for carbon sequestration. Coal is partially oxidized into a mixture of CO and H_2 called synthesis gas, or "syngas," in a common industrial process. An additional set of reactions continues the oxidation of CO to CO_2, which is easy to separate out at this stage—it's about 40 percent of a high-pressure gas stream in a chemical plant, versus some 10 percent of a low-pressure flow up a smokestack. The hydrogen gas goes on to the generating station.



Fossil Power Plants Potential Sequestration Areas

1. Effington, Illinois
2. Marshall, Illinois
3. Mattoon, Illinois
4. Tuscola, Illinois
5. Henderson County, Kentucky
6. Bowman County, North Dakota
7. Meigs County, Ohio
8. Tuscarawas County, Ohio
9. Odessa, Texas
10. Jewett, Texas
11. Point Pleasant, West Virginia
12. Gillette, Wyoming

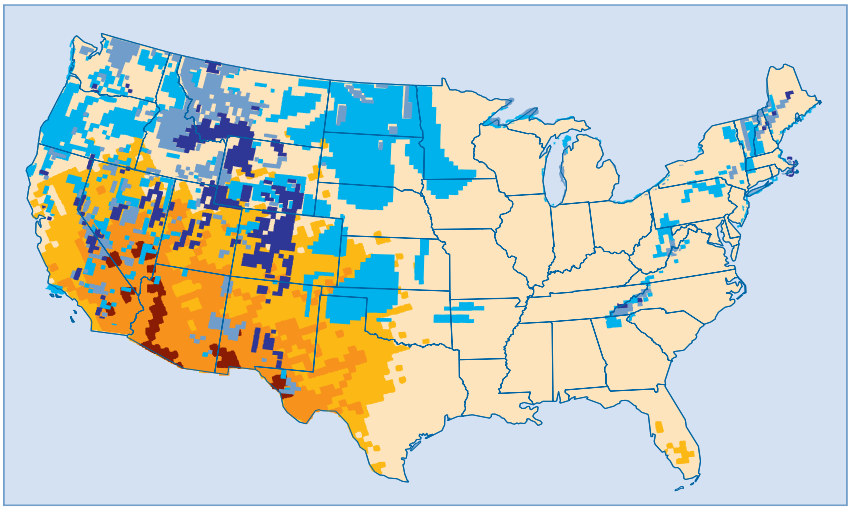
If IGCC catches on, it could be phased in at most of our coal-fired power plants as the aging ones get replaced. The "potential sequestration areas" include saline formations that are geologically similar to oil fields, but wound up containing salt water instead. The 12 sites being considered for the FutureGen plant are also shown. The map was adapted from figure 4-9 of the NCEP report. (The entire three-quarter-inch-thick report can be downloaded from http://www.energycommission.org/site/page.php?report=13.)

gen—before being burned. But adding a "shift reactor" to the gasification process converts all the carbon compounds to CO_2 that can be separated out and pumped deep underground into tapped-out natural-gas or oil wells. Only greenhouse-friendly hydrogen gets burned at the power plant, and only H_2O comes out the smokestack.

The logic to this method of carbon sequestration is that these rock formations have safely held hydrocarbons for hundreds of millions of years, so they can easily store CO_2 for a few million more. A pilot project under way since September 2000 at the Weyburn oil field in Saskatchewan is putting some 2,000,000 metric tons into the ground per year. And FutureGen, a 10-year, $1 billion Department of Energy project to build a 275-megawatt IGCC power plant—enough to charge some 700,000 electric cars, or nearly a million-and-a-half plug-in hybrids—with local CO_2 sequestration is now in the site-selection phase. Twelve sites in seven states are being considered, with the final selection to be made next summer. The plant is expected to sequester over 90 percent, and eventually close to 100 percent, of the coal's carbon content—1,000,000 metric tons of CO_2 per year. Current power-plant turbine designs need a feedstock containing less than about 70 percent hydrogen gas, so high-efficiency hydrogen turbines are among the technologies being demonstrated.

If the nation's entire fleet of 200,000,000 passenger cars and light trucks were all plug-in hybrids, it would take 145 FutureGens, built over several decades, to keep them all humming along. Whether more such plants will be built, however, depends on a number of factors, including the permitting and regulatory agencies—and, ultimately, the amount of pressure from the public they serve. And this would obviously be a *really* good time to start investing seriously in developing solar, wind, and other "green" electricity sources, but that's another article. Says MacCready, "California has more than enough wind-power potential to charge all of California's cars, were they plug-in hybrids. We should be building more wind farms."

You may have noticed that fuel-cell cars and the "hydrogen economy" have not



Average Solar Radiation (kWh/m²/day)
5.5-6.0 Good 6.0-6.5 Better 6.5-7.0 Best

Wind Power Class
4 Good 5 Better 6 Best

Above, left: Figure 4-14 of the NCEP report shows the parts of the country where solar and wind power is just sitting there for the taking on commercial scales, if people were so inclined to build facilities to capture it. Above, right: General Electric Wind Energy built these 3.6-megawatt wind turbines for a wind farm 10 kilometers off the coast of Arklow, Ireland. The rotors sweep out circles 104 meters in diameter.

been mentioned. That's because it will cost a hundred billion dollars or so to build a cross-country network of hydrogen filling stations. (The entire state of California has 16 at the moment, with another 15 planned; Governor Schwarzenegger's California Hydrogen Highway Network's economic team estimates that it will cost $145,000,000 to build 250 of them. But there are some 180,000 or so gas stations nationwide.) And then there is the cluster of undeveloped technologies needed to store and distribute hydrogen safely on that scale. But finally—and this is a point overlooked in most discussions on the subject, says AeroVironment's Brooks—hydrogen is an energy *carrier*, like electricity, not an energy *source*, like a burning lump of coal, a splitting atom, or a turning windmill. Most hydrogen these days is manufactured from natural gas, which is by far the cheapest process. "Green" hydrogen is made by electrolytically splitting water molecules, and that electricity has to come from somewhere. And when the hydrogen recombines with oxygen in a fuel cell to make water and re-release that energy, guess what form it comes out in? Here's a hint: it's not mechanical—fuel-cell cars have no pistons and transmission, no spinning turbine geared to a drive shaft. The energy emerges as electricity; an electric motor turns the car's wheels. So there we are, back where we started . . . with an electric car. And we've already *got* electricity.

"Sometimes you see a sticker on a gas pump that says 'X percent of your cost per gallon goes to local, state, and federal taxes.' I'd like to see another one that says, 'Burning this gallon of gasoline puts more than 19 pounds of CO_2 into the air, where it will remain for hundreds of years, and over 40 cents of the purchase price goes to countries that hate us.' Then people could *really* make informed choices."

Worse, notes Brooks, the process of converting electricity into hydrogen and then back into electricity again is only about 25 percent efficient. Honda's prototype solar-powered electrolyzing station in Torrance, California, takes 32 kilowatt-hours a day to make half a kilogram of hydrogen, the energy equivalent of half a gallon of gasoline. Thus, says Brooks, only eight kilowatt-hours of that harvested sunshine are actually being used for transportation. With the wasted 24, he continues, you could heat the water (in a tankless electric heater) for four showers, use the dishwasher, wash and dry a load of laundry (with a natural-gas dryer), and run the fridge. You could also keep a three-ton central air conditioner, big enough for a 1,200-square-foot house, going for the five hottest hours of the day. That evening, you'd still have enough juice left to surf the net for four hours while the kids watched TV, while leaving 10 compact fluorescent lights burning all over the house for five hours, allowing ample time to get everyone tucked into bed. "So," says Brooks, "You can run your house *and* your car with electricity, or you can just run your car with hydrogen."

But wait a minute—the FutureGen plant will convert coal into "green" hydrogen, so why not siphon some off to run fuel-cell cars? Well, sure, you could do that, says Brooks, but you'd need to burn about one-quarter of that hydrogen right there at the plant to run the compressors needed to fill the cars' storage tanks. Add in the other losses inherent in the system, and the fuel-cell car's mpg equivalent compared to an electric car powered by a hydrogen-fired IGCC power plant plunges to about two-thirds. "Why bother trying to get the hydrogen to the vehicles?" Brooks asks. "It's a lot of trouble, will take much new invention, and you end up with a less efficient result."

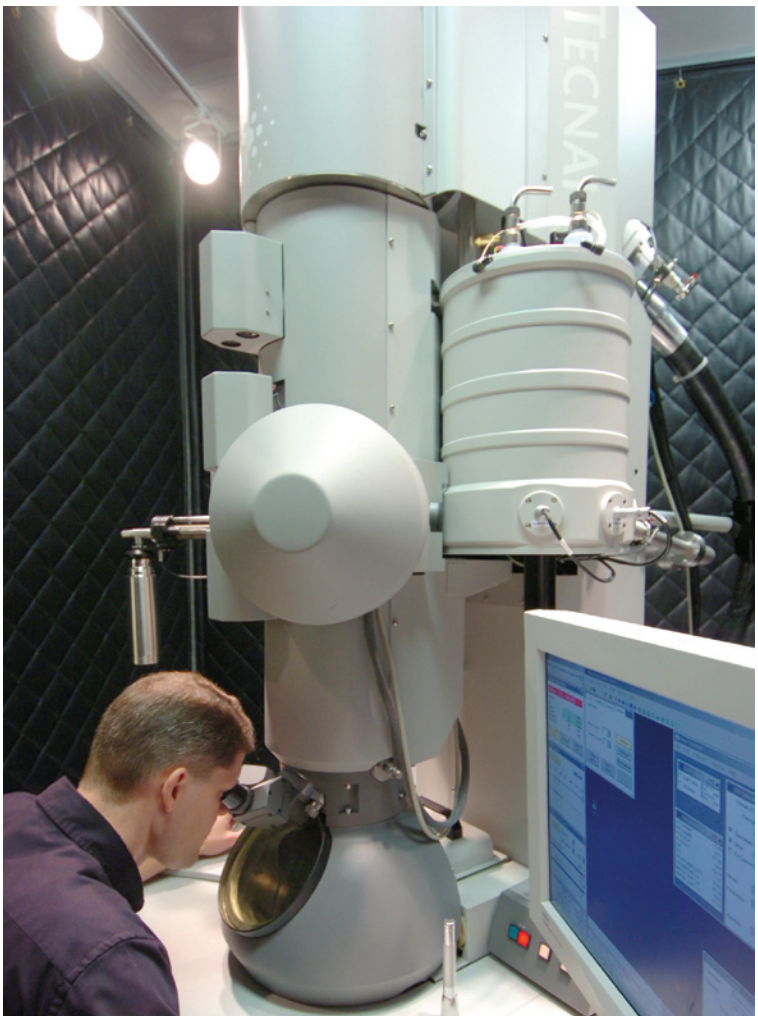
In the end, "it all comes down to the personal economic decisions we all make every day," says MacCready. "Sometimes you see a sticker on a gas pump that says 'X percent of your cost per gallon goes to local, state, and federal taxes.' I'd like to see another one that says, 'Burning this gallon of gasoline puts more than 19 pounds of CO_2 into the air, where it will remain for hundreds of years, and over 40 cents of the purchase price goes to countries that hate us.' Then people could *really* make informed choices."

When it bet on the SUV instead of the EV-1, General Motors lost a golden opportunity to get a jump on building the cars of the new millennium. But, surprisingly, the long-term winner may not be Japan but China. The battery manufacturers are there already, and with an upwardly mobile urban population, few domestic oil reserves, and some of the worst smog on the planet, there's a huge untapped market for electric vehicles of all sorts. The Chinese government plans to have hundreds of electric buses on the streets of Beijing in time for the 2008 Olympics; Chinese-built electric scooters are as close as your local Wal-Mart.

But let's not bury the American automotive industry quite yet. CalCars is working with the R&D folks at Ford on a plug-in version of their hybrid SUV, the Escape. "We've been talking with higher-level executives for six months now to set up a 'qualified vehicle modifier company' to convert Escapes and eventually other cars," says Gremban. "We see a market for 10,000 to 100,000 vehicles, although we're going to start small. We'll build a few in California, let people try them out, get feedback from the field, and then go nationwide." Officially, the Ford Motor Company remains cagey on the subject, although board chairman and chief executive officer Bill Ford Jr. did say at the annual stockholder's meeting on May 11 that they were studying plug-ins. And since great-granddaddy Henry started the firm by building practical, economical vehicles that revolutionized transportation, maybe lightning will strike twice. □

Cellular CAT Scans

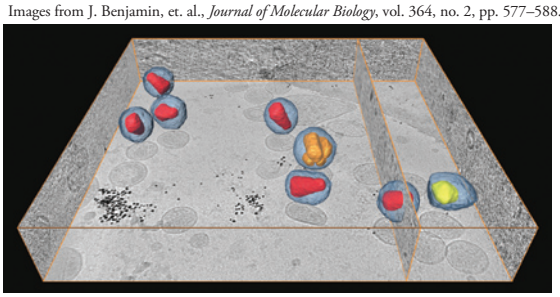
by Douglas L. Smith

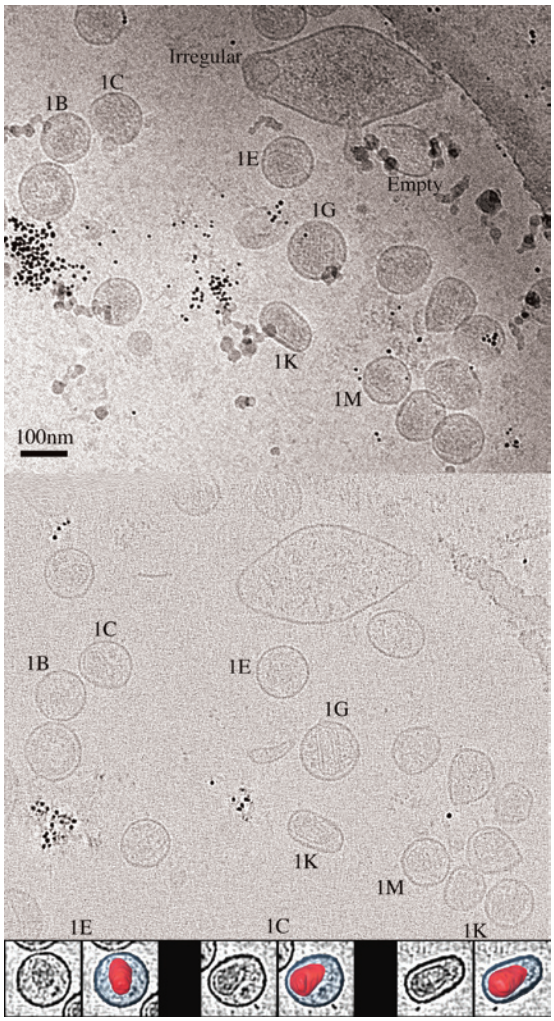


Jensen and the lab's 300-kilo-electron-volt (keV) transmission electron microscope, a liquid-helium-cooled Polara G2. The eyepiece is used for rough positioning of the sample in the vacuum chamber; the actual images will appear on the monitor to his right. The quilted black panels in the background completely surround the apparatus and are part of the airflow-management system.

A cell isn't merely a bag of enzymes sloshing around in a thick soup of cytoplasm. According to Assistant Professor of Biology Grant Jensen, it's more like a multistory factory—a set of interwoven production lines complete with conveyor belts, forklifts, and steel I-beams to hold up the roof. Or, if you prefer, the world's most elaborate Rube Goldberg contraption. The cell's cogs and camshafts, springs and motors, girders and sheet metal (or, in the Rube Goldberg case, gloved hands on sticks, precariously balanced bathtubs, and spring-loaded mallets) are protein molecules. Protein machines conduct the cell's metabolic business; protein motors make muscles contract, amoebas crawl, and paramecia swim. When a cell is preparing to divide, protein diazo machines make a duplicate set of the genetic blueprints, and then protein winches and cables pull the two copies to opposite ends of the cell. Shells of interlocking proteins armor-plate viruses, protein trusswork gives cells their shape, and protein stickers on the protein girders tell the cell which end is front. Jensen's research group wants to photograph each rod, flywheel, and bearing and work out its mechanical interactions with its fellows, in terms as solid as a cast titanium sprocket. As Jensen puts it, "Ultimately, of course, we want to understand how things work at an atomic level—a proton goes here and it causes this atom to move over there, which causes that atom to move over here, and the sum of it all is that the cell swims, or eats, or reproduces itself."

The Jensen lab works in an emerging field called electron cryotomography. Says Jensen, "We're doing a mixture of technology development and basic biological research: trying to answer fundamental cellular questions that are really only answerable by this new technology. How do bacteria maintain their shape? How do they establish polarity? How do they segregate their DNA? How do they cinch off in the middle and divide? And how do they divide asymmetrically, so





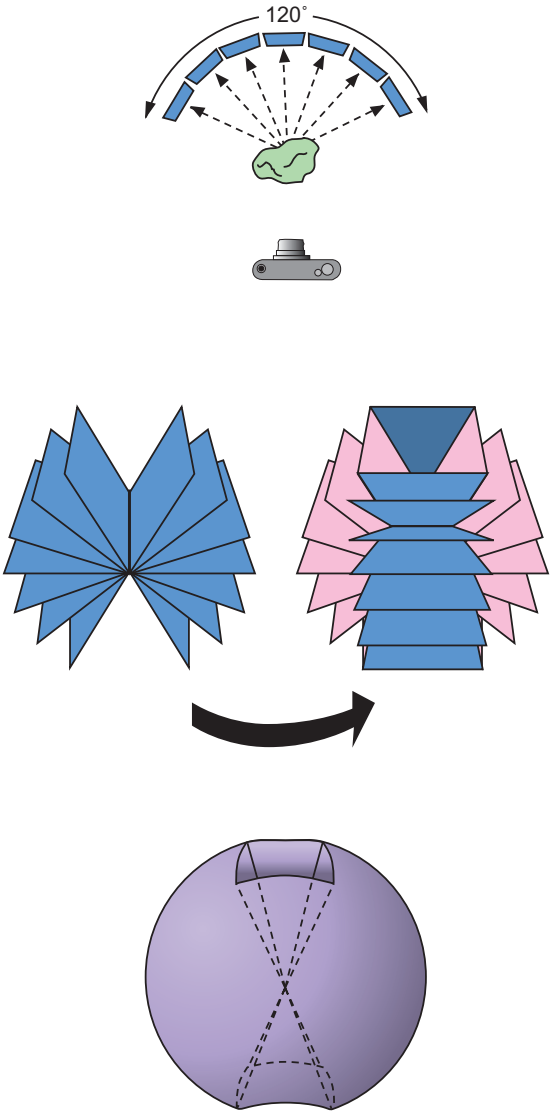
Above: A 3-D rendering of part of a water droplet containing plunge-frozen HIV viruses. The shadows on the aquarium floor, as it were, are viruses above or below the slice. Right, top: One of the raw electron-microscope images on which the rendering was based. The viruses, some of which have been labeled 1B, 1C, and so on, are floating amid other cellular guck. The small black objects that look like buckshot are 10-nanometer-diameter gold spheres used to align the images. Right, center: A slice through the cleaned-up 3-D reconstruction, taken at the same tilt angle as the raw image. Material above and below the image plane is no longer visible. Right, bottom: Three individual virus particles after further processing, rendered in two and three dimensions.

that the 'baby' buds off and swims away, while the 'adult' stays where it is? It's like building a newer and greater telescope—you build a bigger telescope to see deeper into space. We're building a better microscope to see deeper into the smallest cells."

The transmission electron microscope has been around since the 1930s. As the name implies, it uses a beam of electrons rather than a beam of light to look at the very, *very* small. For something to be visible, it must be larger than the wavelength of the radiation you're shining on it. Visible light has wavelengths between 400 to 700 or so nanometers (nm), or billionths of a meter, but individual atoms are 0.1–0.2 nm in diameter, and your average protein molecule runs two to five nanometers in size. The high-energy electrons in a high-end electron microscope have a wavelength of about 0.002 nm. "We accelerate electrons to about 80 percent of the speed of light, so they're really moving, and then we fire them through the sample," says Jensen. When the electrons hit an atom in the sample, they scatter. The scattered electrons interfere with the ones that continue to fly straight and true, and some of each get refocused into a so-called phase-contrast image by a set of electromagnetic coils that act as lenses. In the resulting picture, atoms or regions containing densely packed atoms show up as dark spots. Much of what we know of cellular structure comes from electron microscopy; the key new features that Jensen exploits are the "cryo" and the "tomo."

Like a stop-motion animator, the "cryo" portion freezes living cells in the act of whatever they're doing. Each experiment begins with a droplet of microbe-laden water wicked by surface tension over a set of 2,000-nm-, or two-micron-, diameter holes in a sheet of carbon atoms only 100 nanometers thick. This carbon film, the equivalent of a glass slide in an optical microscope, in turn fits into a three-millimeter-diameter opening in a copper "grid" that acts as the microscope's stage. Ice is less dense than water, which makes life on Earth possible—otherwise the oceans would have frozen solid in the very first Ice Age—but it makes life difficult for electron microscopists. Says Jensen, "When you freeze water gradually, it expands, bursting some cells and distorting the rest and ruining the experiment. But in the late 1980s, people discovered that you could plunge the grid into liquid ethane at about 80 kelvins and freeze the water so fast that the molecules can't bounce around and move apart to form the hydrogen bonds required to make crystalline ice." This amorphous ice, with its molecules caught in random orientations, occupies the same volume as the liquid water it froze from.

The "tomo" part is best known from the medical profession. Says Jensen, "In a CAT scan, Computerized Axial Tomography, they take X-ray pictures of your head through a range of angles and put them together in a computer to get a 3-D model of your skull, your brain, your eyeballs, et cetera. And then you can take a slice through that model



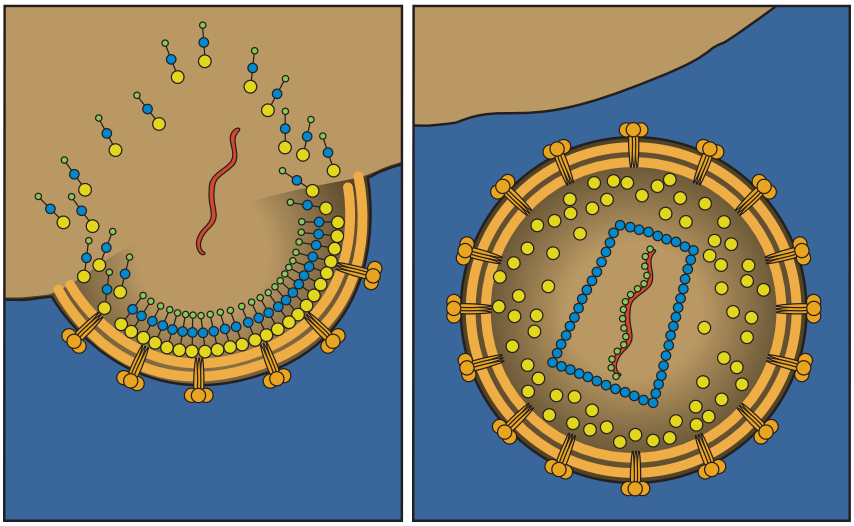
Doing tomography along one arc gives a set of pictures (blue) that don't show the subject from all angles, leading to distortions in the 3-D reconstruction in the wedge where data is missing. Rotating the sample 90 degrees and repeating the scan gives a second set of pictures (pink) that doesn't provide complete coverage either, but fusing the two sets (purple sphere) covers most points of view.

anywhere you want, like cutting through a block of cheese, and see what's in that cross section. We're doing the same thing with bacteria." The microscope automatically tilts the sample grid through about 120 degrees as the series of electron pictures is taken. But, as shown at left, this leaves a wedge of data missing around the north and south poles, as it were, of the 3-D reconstruction. So Jensen's lab bought a prototype device that, at the end of the scan, turns the grid by 90 degrees—without having to remove it from the high-vacuum sample chamber—to do a second scan perpendicular to the first. "Our microscope is exceptional," he says, "because it's the first one that allows us to routinely record a tilt series one way, and then rotate frozen samples and record a second tilt series the other way. This makes the missing wedge turn into a missing pyramid."

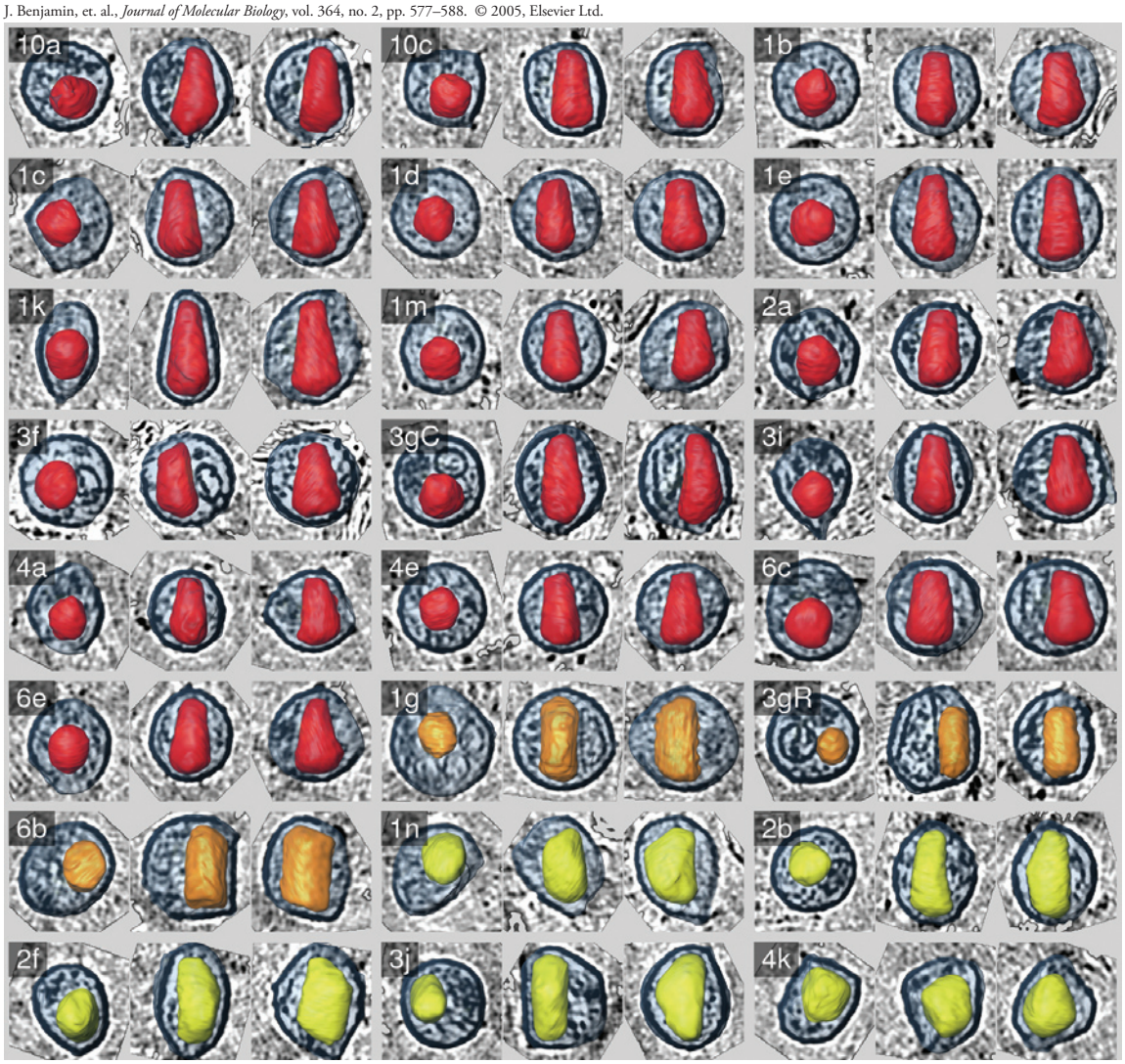
As befits Caltech, it's the world's most automated electron microscope. The scans are recorded on a CCD camera, and a computer using software written by grad student Christian Suloway and a number of collaborators elsewhere interprets the images and tells the microscope where to take the next set of pictures. So once the samples are loaded, six grids at a time, says Jensen, "it operates around the clock, taking tens of gigabytes of data a day without any user intervention. That's kind of cool—a multimillion-dollar, state-of-the-art microscope taking pictures of bacteria all night long for us."

Our factory tour begins by looking at proteins that act as modular steel scaffolding. The mature HIV virus has a spherical skin, a disguise fashioned from the cell membrane of its former host, which encloses a conical shell of protein molecules that contains a wad of protein that swaddles the genetic information, in this case RNA. Says Jensen, "The whole thing can be thought of as a capsule that packages this infective RNA and then sneaks it into a fresh cell, where it causes the cell to build a thousand more copies of itself. Then they all bubble

In an HIV infection, the hijacked cell (brown) produces HIV RNA (red) and a protein called Gag (the linked yellow, blue, and green spheres). The Gag proteins migrate to the cell membrane (orange), sticking to its underside and making it blister up. Gag then gets cut into three smaller proteins—matrix (yellow), capsid (blue), and nucleocapsid (green)—inside the maturing virus.



J. Benjamin, et. al., *Journal of Molecular Biology*, vol. 364, no. 2, pp. 577–588. © 2005, Elsevier Ltd.



A rogue's gallery of 23 HIV viruses, each rendered in three mutually perpendicular views. The capsids are color-coded by shape: conical (red), cylindrical (orange), and other (yellow). To further baffle structural microbiologists, images 3gC and 3gR are actually of the same particle, which contains two capsids and thus a double dose of RNA—something that happens, for unknown reasons, fairly frequently.

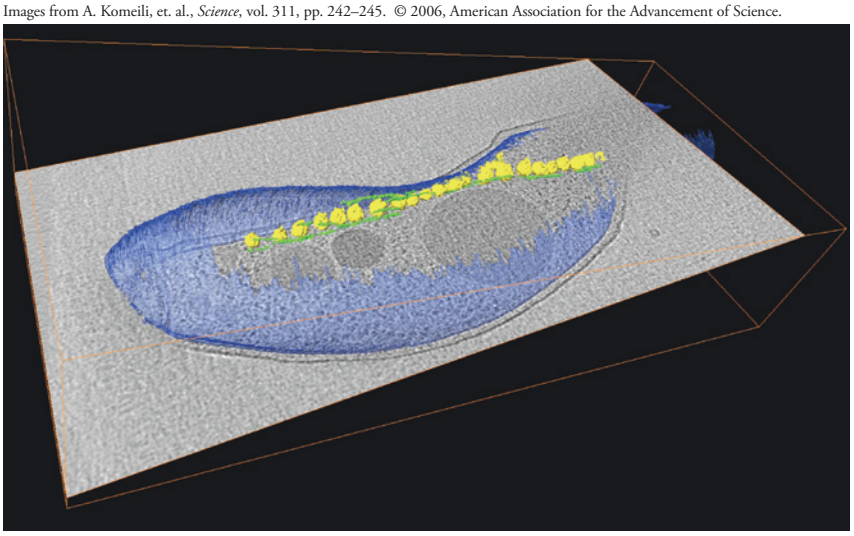
out from the cell surface to go infect more cells."

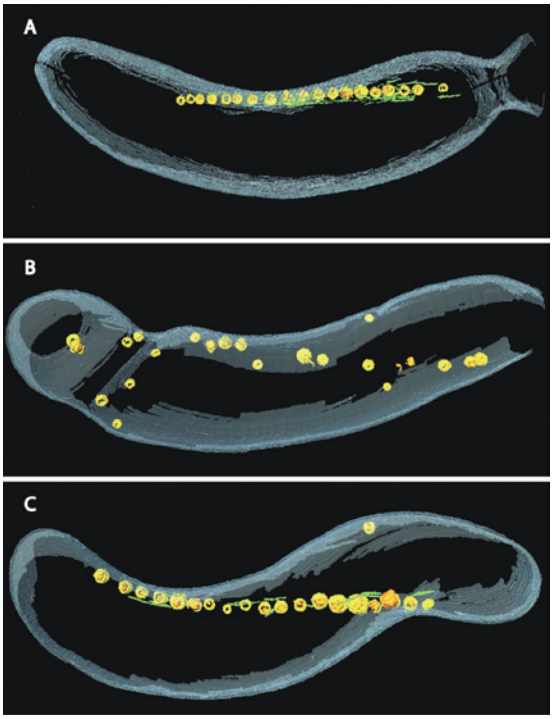
The RNA also forces the infected cell to manufacture a protein called Gag, which is shaped like a wedge of pie. Gag's rounded piecrust binds to the host cell's membrane, and the sides of the slice, where the filling oozes out, stick to the sides of other wedges. So as the wedges lock into place, the membrane starts to curve, forming a bud called the Gag lattice. Once the lattice has grown to become a complete sphere, the bud detaches. The virus finally matures after an enzyme called protease snips the Gag protein into three smaller proteins. (In fact, our best anti-HIV drugs are protease inhibitors, which keep the Gag intact and render the virus noninfective.) The outermost chunk of the Gag protein, the piecrust, having served its purpose, becomes a protein called "matrix" that lets go of the cell membrane and drifts around within the virus. The middle part of the wedge becomes a smaller protein called "capsid" that forms the inner cone containing the RNA, and the little piece at the tip becomes a protein called "nucleocapsid" that coats the RNA.

All this is well known, but teasing out how the individual proteins arrange themselves to form these shells has been confounding because each HIV particle is unique. For one thing, "each virus has a different number of Gag units, so the virus size varies," says Jensen. This alone throws a monkey wrench in the crystallography, and the traditional methods of staining and fixing viruses for microscopy often destroy the Gag structure, so that the workings of the assembly process remain largely hypothetical. But Jensen's grad student Jordan Benjamin and postdoc Elizabeth Wright, collaborating with Wesley Sundquist's group at the University of Utah, have successfully taken pictures of the virus in the immature and mature states and are beginning to discover how the Gags fit together. In the process, they've found that some of the anatomical features that other people had reported were merely artifacts of their sample-preparation methods. The next step will be to try to figure out what interplay of forces locks these three proteins into their proper places, and perhaps—many years from now—figure out some way to stop them.

Let's now consider proteins as I-beams. Protein chains called cytoskeletal filaments give cells their shapes. But Jensen's group has found that there are a *lot* of these filaments. "It's kind of like the first X-rays of humans, when we saw the whole skeletal structure at once. Long before that, we knew about bones from dissections, but X-rays allowed them to be seen in their living context. Similarly,

Images from A. Komeili, et. al., *Science*, vol. 311, pp. 242–245.





Above: A partial 3-D reconstruction of *M. magneticum*. The inner cell membrane is blue, the magnetosomes are yellow, and the filaments are green. Right: In a normal cell (A), the magnetosomes line up along the filaments. In a mutant (B) that does not make the MamK protein, there are no filaments, and the magnetosomes scatter around the cell's periphery. But if you turn the *MamK* gene back on (C), the filaments appear, and the magnetosomes regroup as best they can.

you can get a lot of important information by taking cells apart, but we've taken pictures of intact bacteria and seen more protein filaments than were expected—in their native arrangements."

Most recently, postdoc Zhuo Li, geobiology postdoc Arash Komeili (now an assistant professor of microbiology at UC Berkeley), Professor of Geobiology and Professor of Biology Dianne Newman, and Jensen collaborated on studies of *Magnetospirillum magneticum*. Like other so-called magnetotactic bacteria, *M. magneticum* has little structures called magnetosomes. Each magnetosome is a sack filled with a single crystal of magnetite (Fe_3O_4); when properly aligned, the magnetosomes act as tiny compass needles to help the bacterium orient itself. They tend to be arranged in chains, and in *M. magneticum* they all lie in a line running the length of the cell. Electron cryotomography's close-ups revealed that a protein filament runs like a girder down one side of the magnetosomes and presumably holds them in place. Komeili's fluorescence-labeling studies suggest that the filaments consist of a protein called MamK, and, indeed, in mutants he made that lacked MamK, the magnetosomes were scattered like errant marbles.

Surprisingly, the magnetosomes aren't sealed bubbles within the cell, but are, in fact, pouches—"invaginations" is the technical term—of the cell's inner membrane. This means that magnetosomes are open to the periplasm between the cell's inner and outer membranes, which may help explain how they get filled with magnetite. The dissolved iron destined to become magnetite can probably diffuse across the cell's leaky outer membrane pretty easily, and earlier studies had suggested that the magnetite's precursor, a mineral called ferrihydrite, precipitated out in the periplasm. This solid mineral would then somehow have to get through the cell's inner membrane and, if the magnetosomes had actually been free-floating within the cell, the magnetosome membrane. But this way, a ferrihydrite particle could slowly make its way through the pouch's neck into

the magnetosome, where further chemical reactions would turn it into the magnetite crystal.

Structural members are important, although their job is kind of dull. But proteins with moving parts—now, *that's* cool! Some bacteria propel themselves by long, thin filaments called flagella ("flagellum" is Latin for "little whip") that thrash about and provide thrust. A bacterium known as *Treponema primitia* has two flagella, one on each end, that lie along the bacterium's tubular body between the inner and outer cell membranes. Says Jensen, "The motors that spin bacterial flagella are the quintessential molecular machines—nanoengines that turn an axle. Other people have taken the engine apart and named the pieces, but we don't know how the whole thing fits together. And when the engine is taken apart, some pieces are lost. But because Gavin Murphy, one of my graduate students, is taking pictures of whole cells, we get images of the complete engine, *intact*. If he thawed the cells out, they'd swim away."

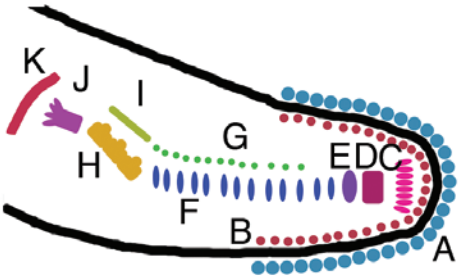
The motors make the flagella spin like a pair of worm gears, which causes the bacterium to spin as well. Like a drywall screw into a 2 x 4, the cell torques itself into the medium ahead of it. "When you're that small, water is like cold tar," Jensen notes.

The engine straddles the inner cell membrane. Embedded in the membrane is a ring-like component called the stator, and nested inside the stator is the moving part, the rotor. "Protons flow through the stator," Jensen explains, "which causes the stator to spin the rotor. It's kind of like a playground merry-go-round, where you have people all around pulling on it to make it spin." The rotor is attached to a rod that leads to the flagellum and causes it to turn. The rod passes through another part, called the P ring. P stands for peptidoglycan, says Jensen, "and the P ring is like a bushing. It greases the rod as it spins through the peptidoglycan layer, which is like the chicken-wire frame that gives the cell its shape." And below the motor, in the cell's cytoplasm, lies a component called the C ring. "Now there's another cool part to this," Jensen says zestfully. "The C ring acts like a transmission. It receives signals from the cell through proteins that dock on its underside and cause the whole motor to either rotate clockwise or counterclockwise. So it's like a forward gear and a reverse gear." It's thought that the C ring and the rotor spin together, as a unit, but that level of detail remains to be seen—as does the actual gear-shifting mechanism.

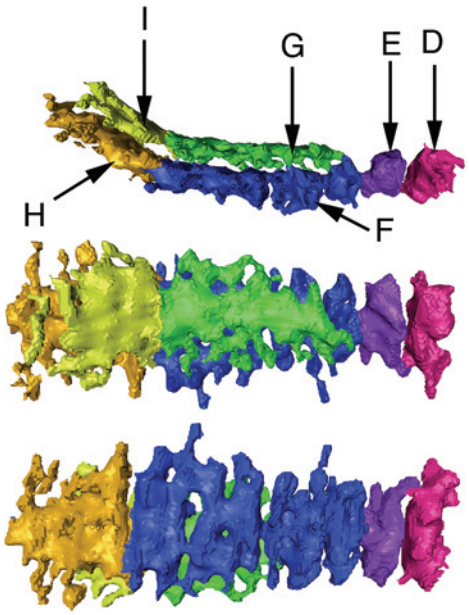
How *T. primitia* gets around also isn't clear, but it's generally assumed that the motors make the flagella spin like a pair of worm gears, which causes the bacterium to spin as well. Like a drywall screw into a 2 x 4, the cell torques itself into the medium ahead of it. "When you're that small, water is like cold tar," Jensen notes. There's a lot of resistance that bigger organisms don't experience. *T. primitia* lives in the guts of termites, swimming through "bits of wood, lots of juice, and thousands of other bugs." The work was done in collaboration with Assistant Professor of Environmental Microbiology Jared Leadbetter, who studies the amazingly elaborate, cellulose-digesting ecosystem that inhabits the termite belly.

But there's more than one way to propel a bacterium. *Mycoplasma pneumoniae*, which causes some types of pneumonia, has a "foot" called the attachment organelle that allows it to stick to surfaces and crawl around inside your lungs. How this works is a mystery, but grad student Greg Henderson's work, in which, says Jensen, "we labeled all the parts and named them, with incredible creativity, A through K" allows for some educated guesses.

In the schematic view on the opposite page, the blue dots labeled A are proteins that coat the outside of the foot, and presumably enable it to stick to the mucus-coated landscape of your lungs. Inside the foot, giving it its shape, are two rodlike



Right: A schematic of the key proteins in *M. pneumoniae*'s attachment organelle.



Below, right: Three 3-D views of the two rod-like structures that act as the motor.

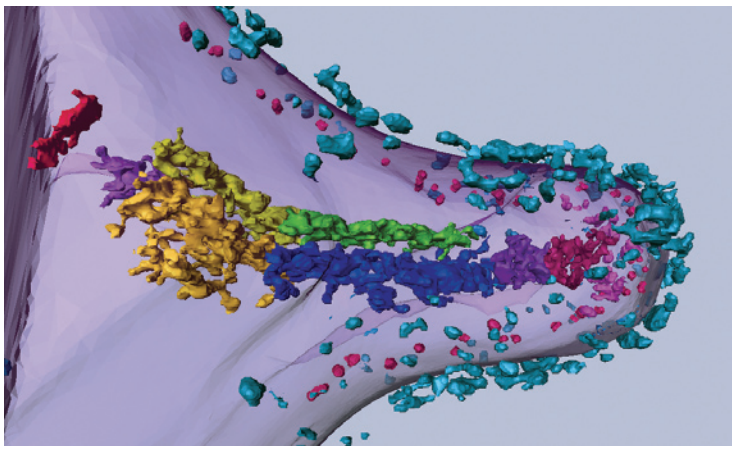
structures—components F and H form the larger, thicker rod, and G and I the shorter, slimmer one—that abut a "terminal button" (C, D, and E) over which the cell membrane is stretched. The base of the rod, where the foot joins the cell body, is attached to a shallow bowl (K) by something that resembles a waiter's hand, fingers splayed, supporting a tray. Since G and F are not solid entities but sets of disconnected segments separated by sizable gaps, says Jensen, "the idea is that the rod contracts and then all of a sudden kicks out. And as it kicks, it's more likely that the front goes forward than that the back goes backwards." Like a paddle against the water, the bowl in the back would meet a lot of resistance as it pushed against the cell's cytoplasm. So the terminal button in the front moves instead, thrusting part of the cell membrane, and the sticky As, ahead. "And then the motor contracts again and kicks, and the cell just rolls forward like the treads on a tank." Once the foot crawls past, the theory goes, the As detach from the lung's surface and diffuse toward the front of the foot again, wading in the cell membrane like an angler waist-deep in a river.

M. pneumoniae may also be a so-called minimal cell. A mere 700 or so genes suffice to build and run this little bug, which is pretty amazing. It also leads to the hope that we could identify each of the 700-odd proteins those genes produce, determine their 3-D structures by X-ray crystallography, and figure out how they all work and fit together. A group led by Sung-hou Kim at UC Berkeley is working on the structures and has gotten well over half of them.

And when you are working on structures, sometimes it does help to look at things in isolation—single-particle analysis, as it's called. Electron cryotomography can do that, too, when the particles are large enough. Among the right-sized particles are complexes where several different proteins form loose associations to perform some task—enzyme A takes a molecule, tweaks it a bit by cutting a bond here or adding an oxygen atom there, and hands it off to enzyme B, and so on, until you wind up with a molecule of, say, fat. In other words, protein complexes are the machines in the cell's assembly lines.

So instead of freezing whole cells, you freeze solutions of the enzymes in the process of doing their thing. What results are pictures of small, blurry blobs, but, says Jensen, "electron cryotomography is the highest-resolution technique currently available to image individual, unique protein

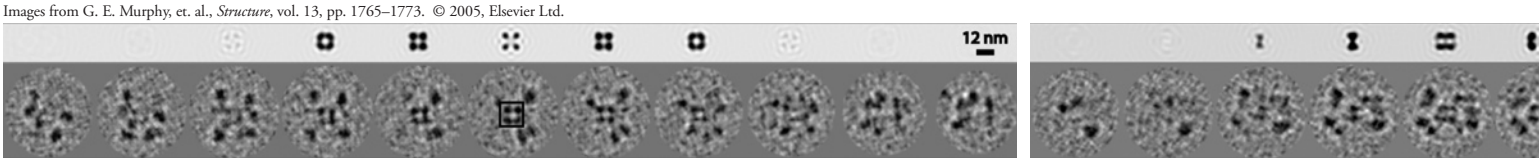
Below: A 3-D reconstruction of the entire foot, coded in the same colors as above right.

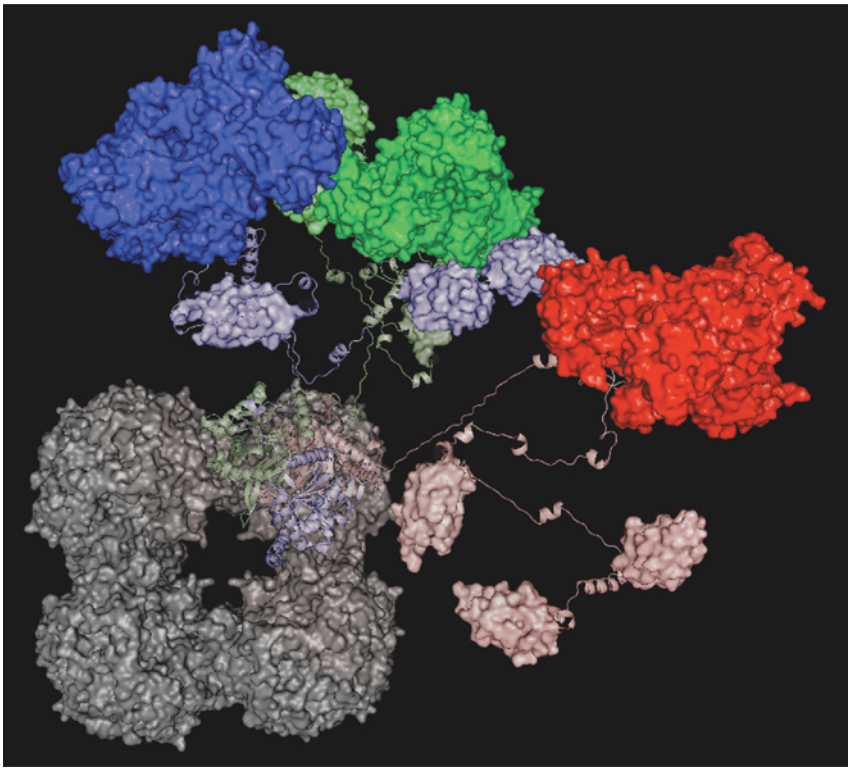


Images from G. P. Henderson, et. al., *Molecular Microbiology*, vol. 60, no. 2, pp. 376–385.

Below: Each of these three strips is a set of slices, taken 2.5 nanometers apart, through an *E. coli* pyruvate dehydrogenase complex. The bottom part is the raw image. The top part shows just the core crystal of enzyme number two. These three complexes were chosen because they happened to be oriented along the crystal's 4-, 2-, and 3-fold axes of symmetry, respectively.

Images from G. E. Murphy, et. al., *Structure*, vol. 13, pp. 1765–1773. © 2005, Elsevier Ltd.



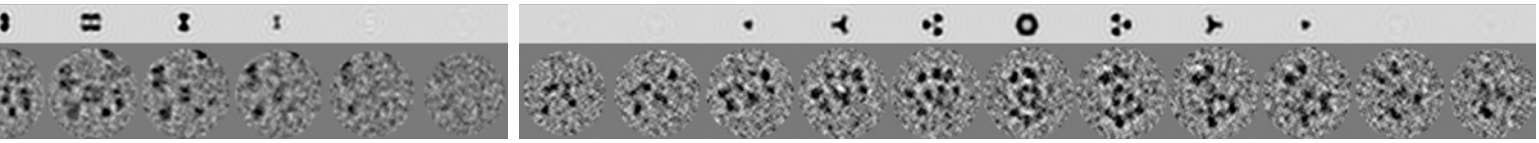


A 3-D model of a core holding three enzyme balloons. The hollow gray square is the central crystal of enzyme number two, with the three specific enzyme molecules holding the balloon strings rendered in light blue, light green, and pink. The corresponding blue, green, and red balloons are all dimers (two molecules bound together) of enzyme number three.

complexes—the other techniques require averaging lots of copies of identical complexes under special conditions." Grad student Murphy has been examining the pyruvate dehydrogenase metabolic pathway, which consists of three enzymes that together catalyze five reactions that burn a simple carbohydrate (called pyruvate, oddly enough) to fuel the cell.

The simplest organisms just let the enzymes in this pathway slosh around in the cytoplasm and wait for lucky collisions to happen in the right order. Sophisticated cells like ours prefer to pack many copies of these enzymes into a near-crystalline machine—a regular icosahedron containing more than 60 copies of each of the three enzymes. "We just pass the substrate from here to there to there to there, and we're done," says Jensen. "It's an efficient pipeline." There are large numbers of metabolic pathways in every cell, and the more sophisticated the cell, the more these pathways tend to get streamlined into such tightly organized structures.

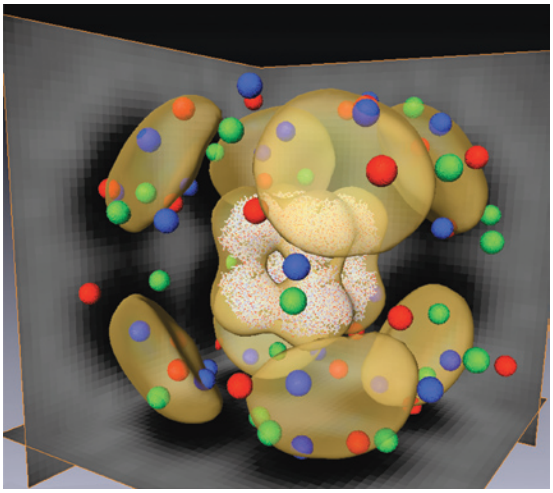
The bacterium *E. coli*, which turns out to lie midway along that scale of sophistication, keeps 24 copies of enzyme number two in a cubelike core, around which many copies of enzymes number one and three drift. Murphy discovered that enzymes one and three are actually tethered to enzyme number two, rather like a child holding a helium-filled balloon on a string in each hand. (The analogy is not quite exact, as the strings are regions of enzyme number two that seek out and attach themselves to handy copies of enzymes one and three.) But picture a classroom of 24 such kids at their desks, their balloons bobbing in the breeze from an open window, and you begin to see why the complete structure had proven unsolvable. But, says Jensen, "Electron cryotomography gave us both the quaternary structure, which means how all the proteins are arranged with respect to each other, and the conformational heterogeneity, which is how free they are to move around."



Combining the 3-D info from single-particle microscopy with all the atomic structures already in protein databases, says Jensen, leads to "another feat that has not been possible before, which is to make a complete map of a whole cell. We see each individual protein molecule, and we can identify some of them by their shapes. So we can actually map out where they are in 3-D, and that's really novel." While the little gray blobs in any individual slice all look pretty much alike to the naked eye, they're quite distinctive to the computer, which reassembles the slices into 3-D images. Imagine a basket full of fresh vegetables: if you took one slice through the basket, a radish and a carrot might show up as two equal-sized circles; but stack several slices together, and their identities are soon revealed.

The vast majority of the cell's proteins are just diffusing through the cytoplasm, but some are bolted to other molecules. And of course the structural members, the girders and I-beams, don't move. Says Jensen, "We'll be able to identify all the big or specifically arranged components, and since we already know how to model the diffusion of smaller proteins, we'll have a nearly complete description of the cell. A lot of what happens in cells depends on where things are. This is the best way to see how all the parts are positioned with respect to each other."

Below: The average structure of 305 pyruvate complexes. The individual atoms in the central crystal of enzyme number two can be seen, while all the copies of enzymes number one and three drift around within the eight brown, jelly-donut-shaped objects surrounding the core. The red, blue, and green spheres mark the specific locations of proteins number one or three in three of the 305 individual pyruvate complexes examined.



It takes a lot of computational horsepower to reassemble all those vegetables from their slices—even in a small cell!—and then rotate and examine them from all possible angles, superimposing them on the collection of reference shapes until a match is found. The Jensen lab is one of the chief users of the Caltech Structural Biology Supercomputer, a 280-unit cluster of dual-processor IBM Power PCs that, when bought in 2005 on a grant from the Parsons Foundation, was one of the Top 500 supercomputers in the world. "We're biologists," says Jensen, "but we use a lot more computers than pipettes."

Jensen is at Caltech thanks to the Biological Sciences Initiative, which also built the Broad Center for the Biological Sciences that houses him. When the initiative was launched, says Jensen, "the faculty got together and asked themselves, 'What are the most exciting new fields we'd like to get into?' One of the areas they identified was cryo EM, and so they started a faculty search that went on for about six years. In the meantime, Caltech built Broad, complete with specially designed rooms for state-of-the-art electron microscopes." The basement facility has two microscope rooms, each with a four-foot-thick, vibrationally isolated concrete mounting slab and a custom-designed air-handling system that bathes the microscope in a stable, laminar flow of air held at a carefully controlled temperature. (If the temperature changes more than a few tenths of a degree, the resistance of the coils of wire that act as electromagnetic lenses changes, and the microscope's focus is thrown off.) The Moore Foundation funded the microscopes—the 300-keV one that is the lab's workhorse and a 120-keV model used for preliminary studies. "A lot of people deserve credit for this. The biology division's vision created this opportunity, and by the time I finished my postdoc, it was an unbeatable offer. *Unbeatable.* They already had the building. They already had the rooms ready, and funds allocated to buy the world's best microscopes. I would have had to be crazy not to come." □

Jean-Lou Chameau Named New President

Jean-Lou Chameau, the provost and vice president for academic affairs at Georgia Tech, has been named Caltech's new president. He succeeds David Baltimore, who is stepping down from the presidency after nearly nine years in the post. Chameau will take office on or before September 1.

Chameau, 53, served as dean of the Georgia Tech College of Engineering for four years before becoming provost and vice president in 2001. As provost, he is responsible for the academic and research programs of the university, including the Georgia Tech Research Institute, and for overseeing the university's education, economic development, and commercialization programs.

Chameau, who is also the Hightower Professor and a Georgia Research Alliance Eminent Scholar, was selected by Caltech's Board of Trustees after a nationwide search conducted by a faculty search committee. "Jean-Lou Chameau impressed us with his intelligence, his vision, his personality, and his extensive administrative and fund-raising experience," said David Stevenson, Van Osdol Professor of Planetary Science and head of the search committee. "We believe that he is well suited to the challenges and opportunities of the Caltech presidency in a time of change in the global environment of science, technology, and education. We expect him to be an engaging and energizing presence in our community of faculty, students, and staff, including JPL."

"Dr. Chameau brings a wealth of managerial experience and a strong commitment to students, faculty, and research," said Kent Kresa, chairman of the Board of Trustees. "He has done a terrific job at Georgia Tech, and I'm positive he will lead Caltech with the same energy, excitement, and wisdom he displayed there."

"As a person who loves science and technology, I cannot imagine a better and more exciting opportunity than to serve Caltech at this point of my career," said Chameau. "Caltech's commitment to and history of excellence are unequaled. It is a privilege to be asked to lead this institution. It is also very humbling. I look forward to working with such an exceptional group of faculty, staff, students, and trustees."

Throughout his 15-year career at Georgia Tech, Chameau worked to make the university a worldwide model for interdisciplinary education and research, innovation, and entrepreneurship, and for the promotion of these activities as a catalyst for economic development.

He played a key role in Georgia Tech's initiative to educate students to understand their role in creating a more prosperous and sustainable society, and led the efforts that established the Institute for Sustainable Technology and Development. He has also fostered the creation of major complexes for bio-environmental materials and nanotechnology, facilities that reflect his vision for "research neighborhoods" in which faculty members from several disciplines are physically located together (something that Caltech also does).

Chameau has enhanced Georgia Tech's international reputation through innovative educational and research programs. There is now a Georgia Tech Lorraine in Metz, France, and a Georgia Tech Singapore, and many research partnerships throughout the world. Nearly one-third of Georgia Tech's students study abroad.

He has placed a strong emphasis on increasing diversity, and has championed programs that contribute to the education of minority students in engineering. His commitment to the recruitment, retention, and promotion of women on the faculty earned him the 2004 Rodney D. Chipp Memorial Award from the Society of Women Engineers.

"Jean-Lou Chameau comes to Caltech with a reputation for deep interest in and effective attention to faculty and student issues," said Henry Lester, chair of the faculty and Bren Professor of Biology. "His vision and energy have led to productive ties with

On May 26, the identity of the new president was finally revealed, and Jean-Lou Chameau was introduced to everyone on campus. At 8:00 a.m. he met the Board of Trustees, at 10:00 a.m. he met the faculty, and at 11:00 a.m. he spoke to the rest of the Caltech community in a packed Beckman Auditorium (and received a standing ovation). He was finally able to relax at an evening barbecue outside Chandler, where he took the opportunity to talk to many of the undergrads (above).

international institutions and with industry. Speaking as a biologist who participates in Caltech's programs in Computation and Neural Systems, in Bioengineering, and in Biochemistry and Molecular Biophysics, I'm delighted by Dr. Chameau's long-standing interdisciplinary interests."

As provost, Chameau led efforts to secure major donations for the university's endowment, and has also been active in state and federal relations and in professional organizations such as the U.S. Council on Competitiveness and the Government-University-Industry Research Roundtable.

A native of Normandy, Chameau received his undergraduate education in France, and his graduate education in civil engineering from Stanford University. In 1980 he joined the civil engineering faculty at Purdue University, where he subsequently became full professor and head of the geotechnical engineering program. He moved to Georgia Tech in 1991 as director of the School of Civil and Environmental Engineering. Between 1994 and 1995, he was president of Golder Associates, Inc., an international geotechnical consulting company. He currently serves on the boards of directors for MTS Systems Corporation, Prime Engineering, and l'École Polytechnique. He is also a trustee and the treasurer of the Georgia Tech Research Corporation, and the president of Georgia Tech Lorraine.

Chameau's technical interests include sustainable technology; environmental geotechnology; soil dynamics; earthquake engineering; and liquefaction of soils. He is the recipient of an NSF Presidential Young Investigator Award and the ASCE A. Casagrande Award.

He is married to Dr. Carol Carmichael, the director of the Institute for Sustainable Technology and Development. A native of Wisconsin, she has been at Georgia Tech for almost 20 years. □—*JP*

New Director for the Keck Observatory

Taft E. Armandroff has been appointed director of the W. M. Keck Observatory, on Mauna Kea, Hawaii, as of July 1. He succeeds Fred Chaffee, who has served as director for the past 10 years. A research astronomer, Armandroff served as associate director at the National Optical Astronomical Observatory in Tucson, Arizona, as well as director of its Gemini Science Center, and he has ties to Hawaii through his work with the Gemini Observatory in Hilo. □—*MF*

New HSS Division Chair

As of July 1, the Division of the Humanities and Social Sciences will be chaired by **Peter Bossaerts**, Hacker Professor of Economics and Management and professor of finance. Bossaerts takes over from Jean Ensminger, who has led the division for the last four years. Widely recognized for his research in several important areas of finance, economics, and econometrics, Bossaerts has also recently joined the interdivisional faculty group in Computation and Neural Systems. □

Honors and Awards

Seymour Benzer, the James Griffin Boswell Professor of Neuroscience, Emeritus (Active), has received the prestigious $500,000 Albany Medical Center Prize in Medicine and Biomedical Research. Benzer is credited with founding the field of neurogenetics, the science of how genes control the development and function of the nervous system and the brain and influence behavior. Prior to pioneering this field, Benzer made his mark with monumental discoveries in molecular biology that bridged the gap between DNA and the fine structure of the gene—work that helped to pave the way for the Human Genome Project. □

Richard Murray (BS '85), the Everhart Professor of Control and Dynamical Systems and director, Information Science and Technology, has been awarded this year's Richard P. Feynman Prize for Excellence in Teaching. The selection committee singled out Murray for his "enthusiasm, responsiveness, and innovation" in the classroom and for his "contribution to the undergraduate experience through teaching outside the conventional classroom." □

Ruben F. Mettler
1924 – 2006

Ruben F. Mettler, a guiding force in the American aerospace program and an advocate of the disadvantaged, died Tuesday, May 23. He was 82.

Mettler was a member of the Caltech Board of Trustees from 1968 to the time of his death, and served as chairman from 1985 to 1993. He was also a life member of the Caltech Associates, the President's Circle, and the Caltech Alumni Association. His many gifts to Caltech included the funding of the Ruben and Donna Mettler Professorship, which is currently held by William L. Johnson.

Born in Shafter, California, on February 23, 1924, Mettler briefly attended Stanford University as a Gamble Scholar before transferring to Caltech, where he earned his bachelor's degree in electrical engineering in 1944. After a stint with the army during World War II, when he specialized in radar systems, he returned to Caltech for his master's and doctoral degrees in 1947 and 1949, respectively.

According to longtime friends and associates at Caltech, Mettler was especially proud of having been a member of the undefeated Caltech football team of 1944. He and other team members had entered Caltech as part of the armed forces' V-12 training program, and their acumen on the football field led to an aggregate point total of 159–0 for the season, against opponents that included USC and UCLA.

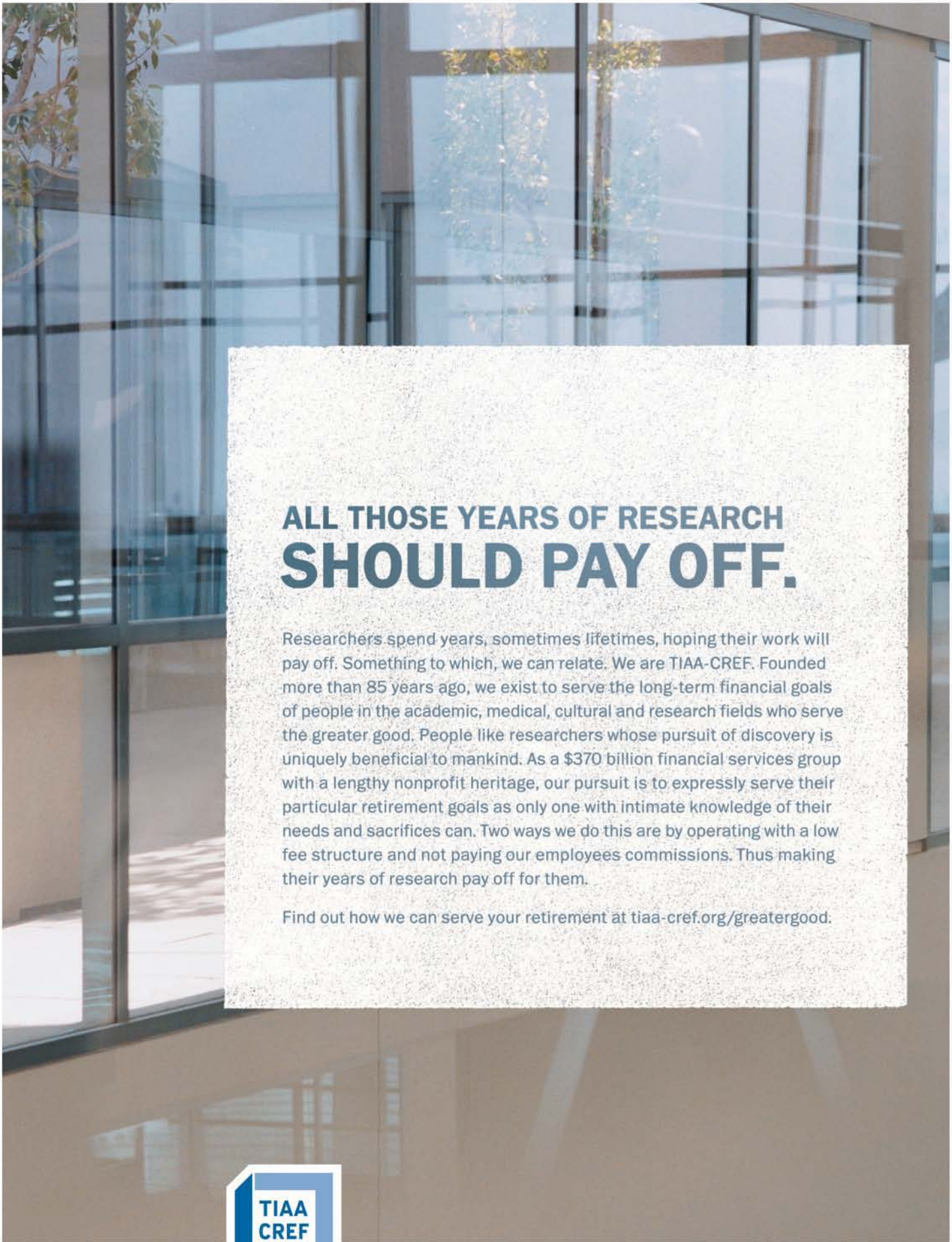
Mettler began his career in the aeronautics industry at Hughes Aircraft as associate systems director for systems research and development. He served as special assistant to the assistant secretary of defense in the Eisenhower administration, then went to work at the Ramo-Wooldridge Corporation, later TRW, where he was responsible for technical supervision of the Atlas, Titan, and Minuteman missile programs and later rose to the positions of chairman, CEO, and director. He was responsible for the Pioneer and the Orbiting Geophysical Observatory satellites, as well as the lunar module descent engine used for the moon landings.

Mettler was also widely known for his advocacy of programs for the disabled. In a 1986 article in *E&S*, he spoke of his experiences with his autistic son Daniel, a musical prodigy who had been unable to speak during early childhood. Mettler's own ability to play the piano led to his initial communication breakthrough with his son, he said.

Mettler also had a keen interest in the welfare of people suffering from the problems associated with economic or ethnic disadvantage. In 1977, he was appointed by President Carter to develop a program to promote the hiring of Vietnam veterans. This program was credited with reducing the unemployment rate of Vietnam vets from 15 percent per year—twice the national average—to less than 8 percent. As chairman of the national campaign for the United Negro College Fund, Mettler was credited with raising $110 million in two years.

His many honors include the National Human Relations Award of the National Conference of Christians and Jews in 1979, the Nation's Most Outstanding Electrical Engineer Award in 1954 from Eta Kappa Nu, the One of Ten Outstanding Young Men of America Award from the U.S. Junior Chamber of Commerce in 1955, the Meritorious Civilian Service Award from the Department of Defense in 1969, and the Roy Wilkins Memorial Award in 1981 from the L.A. Chapter of the NAACP.

He is survived by his wife, Donna Jean Smith, and his sons Matthew Frederick Mettler, an engineer at TRW Inc., and Daniel Frederick Mettler, who resides at the Jay Nolan Center in Canyon Country, California. □—*RT*



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