

California Institute of Technology

ON THE COVER

Our guts are swarming with trillions of bacteria. Some of those bugs may be important in keeping us healthy, by acting as crucial parts of the immune system. These bacteria influence the behavior of certain immune cells, and in this cross-sectional image of a mouse colon, those cells have been stained to glow green. Read the story on page 35.

LETTER FROM THE EDITOR

It is with profoundly mixed emotions that I write this.

Excitement, on the one hand, as *Engineering & Science* is finally going to get a proper website, one that will take advantage of all that the Web 2.0 has to offer and that will include a searchable archive going all the way back to Volume One, Number One, published in June, 1937. (The *Caltech News* site, too, will get a massive upgrade.) Before we get too deeply into the design, we want to hear from you about this. What features will be most useful to you? What do you want *E&S*'s online presence to be like? How do you foresee yourself using the site?

Which brings me to the other hand. Caltech is not immune to the economic pressures of the outside world. As a consequence, *E&S* and *Caltech News* will suspend print publication at the end of fiscal 2009. Again, we want to know what you, the person holding this magazine, think of this prospect. Are you glad that we will no longer be using 500-year-old technology to bring you news from the future? Or do you see added value in continuing to have a printed publication you can keep on your coffee table? Some readers have asked us why we are still killing trees in this day and age; others have told us that they treasure the sensory experience of reading a physical thing, and won't be reading us any more if we go online only.

Where do you stand?

It's not an either-or proposition—the websites will get an extreme makeover regardless. But whether the paper versions continue is in your hands, and most likely in your checkbooks.

We want to hear from you.

Sincerely,

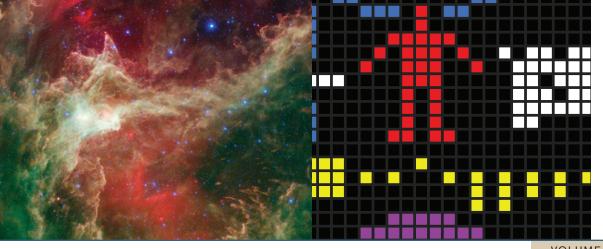
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A PILGRIMAGE TO PRÍNCIPE

Albert Einstein became a worldwide celebrity in 1919 when his outlandish claim that gravity could bend light was proven to be true. Doing so took the efforts of a team of Englishmen led by Arthur Eddington, the Plumian Professor of Astronomy at Cambridge University, and a happy confluence of the stars-literally, in that the sun went into a total eclipse in the midst of the Hyades, a cluster of bright stars in the constellation Taurus; and figuratively, in that World War I had ended just months earlier, making it politically possible for a British astronomer to prove a German physicist's theory.

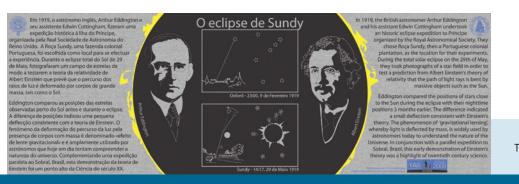
Eddington and E. T. Cottingham sailed to the remote equatorial island of Príncipe off the west coast of Africa, at the time a Portuguese colony. As part of the same expedition, Charles Davidson and A. C. D. Crommelin went to Sobral, Brazil. Both groups took photographs of the Hyades before and during the eclipse, looking for slight changes in the apparent positions of stars near the sun's limb that would indicate that their light had been influenced by the sun's mass. The British astronomers successfully measured the small deflection, 1.75 seconds of arc, predicted by Einstein's theory of general relativity.

Today this phenomenon, called gravitational lensing, is an important astronomical technique. Caltech researchers have exploited it with the W. M. Keck, Hubble, and Spitzer observatories to study some of the most distant galaxies known, make the first 3-D map of the distribution of dark matter in the universe, and trace the mysterious dark energy that pervades the cosmos.

Richard Ellis, the Steele Family Professor of Astronomy, has participated in several of these studies, and was also once the Plumian Professor at Cambridge before moving to Caltech. In September 2008, Ellis undertook what he describes as a "personal pilgrimage" to Príncipe, now part of the democratic republic of São Tomé and Príncipe. (São Tomé is the bigger and by far the more populous island.) Ellis's mission was to find the spot where Eddington took his photographs, and to line up government support to install a commemorative plaque this May-the eclipse's 90th anniversary-as part of the International Year of Astronomy's program of global events marking the 400th year of Galileo's first use of the telescope. The plaque, in Portuguese and English, was designed by Richard Massey of the University of Edinburgh, a collaborator of Ellis's and former Caltech postdoc.

Ellis recounted some of his adventures at a recent lecture in the Hameetman Auditorium in the brandnew Cahill Center for Astronomy and Astrophysics. Eddington arrived with his equipment following a monthlong sea voyage via Lisbon and Madeira; Ellis took a small plane from São Tomé, landing on the tiny Príncipe air-





The plaque.

strip in poor weather—to be greeted by the rusting hulk of an abandoned aircraft in the tall grass just off the runway. Equipped with transcripts of Eddington's letters to his mother, Ellis was able to retrace Eddington's visits to possible observing sites that ultimately led him to Roça Sundy, the now-derelict plantation where the famous photographs were taken.

The arrival of a professional astronomer on this tiny island did not go unnoticed. Ellis was interviewed on national television at the eclipse site-an appearance enlivened by a very aggressive cockerel snapping at his heels-and was subsequently invited to meet the president of the republic, Fradique de Menezes, who graciously offered his support. For meetings at the presidential palace, a dark suit, tie, and black shoes are mandatory. This was a serious problem for an academic who had only packed "Sports Chalet attire," until an obliging former foreign minister loaned him the necessary clothes. The shoes proved to be two sizes too small, but fortunately for Ellis's feet, the meeting was relocated to the president's mountain residence-a more relaxed setting.

Now sponsored by the San Tomean government as well as the International Astronomical Union, the Royal Astronomical Society, and a sympathetic Dutch hotelier and eco-

> Opposite: The Roça Sundy plantation's central square seen from a point close to where Eddington made his observations. Top right: Ellis and o Presidente. Right: Remote Parking Lot A at the Príncipe airport.

tourist developer Rombout Swanborn (who Ellis also met), the plaque's installation will be accompanied by lectures in Portuguese and a poster display. Gisa Weszkalnys, a social anthropologist who studies the islands' economic future, and Pedro Ferreira, a Portuguese cosmologist at Oxford University, are assisting with the project. For further details, see http:// www.1919eclipse.org.



AIDS VACCINES: Y SO HARD?

It's 25 years and counting after the AIDS epidemic began, yet we still don't have a good vaccine against HIV, the virus responsible. A Caltech team thinks that part of the reason may be that our body's natural HIV antibodies simply don't have a long enough reach.

Antibodies, which are Y-shaped, work best when both arms of the Y bind to their target proteins on the virus at more or less the same time. This can increase the antibody's grip strength a hundred- or even a thousandfold. But double-armed binding can be easier said than done. Pamela Bjorkman, the Delbrück Professor of Biology and a Howard Hughes Medical Institute investigator, and grad student Joshua Klein looked at two antibodies that bind to proteins that stick out like spikes from HIV's viral membrane.

"The story really starts to get interesting when we think about what the HIV virus actually looks



like," says Klein, the lead author of a paper published April 16 in the online early edition of the Proceedings of the National Academy of Sciences. Whereas a flu virus's surface is studded with approximately 450 spikes, he explains, the similarly sized HIV may have fewer than 15. With spikes so few and far between, locating two that both fall within an antibody's reach-generally between 12 and 15 nanometers, or billionths of a meterbecomes much more of a challenge. "HIV may have evolved a way to escape one of our immune system's main strategies," he says.

"I consider this a very important paper because it changes the focus of the discussion about why anti-HIV antibodies are so poor," adds virologist David Baltimore, the Millikan Professor of Biology and a Nobel Prize winner. "It brings attention to a long-recognized but often forgotten aspect of antibody attack-that they attack with two hands. What this paper shows is that anti-HIV antibodies are restricted to using one hand at a time and that makes them bind much less well. Responding to this newly recognized challenge will be difficult because it identifies an intrinsic limitation on the effectiveness of almost any natural anti-HIV antibodies."

As well as Bjorkman and Klein, the paper's authors are research technicians Priyanthi Gnanapragasam, Rachel Galimidi, and Christopher Foglesong, and Member of the Professional Staff Anthony West, Jr. (PhD '98). The work was supported by a Bill and Melinda Gates Foundation grant through the Grand Challenges in Global Health Initiative and the Collaboration for AIDS Vaccine Discovery. *—LO*

DR. KOONIN GOES TO WASHINGTON

President Barack Obama has nominated Steven E. Koonin (BS '72), former Caltech provost and professor of theoretical physics, as Under Secretary for Science in the Department of Energy. If confirmed by the Senate, Koonin would oversee the Department of Energy's basic-science portfolio, which includes many of the national laboratories, as well as provide technical advice and coordination across the Department's energy and national-security activities.

Koonin took a leave of absence from Caltech in 2004 to serve as chief scientist for the British energy giant BP, where he guided the company's long-range technology strategy, particularly in alternative and renewable energy sources. He is also a longtime member and past chair of JASON, a semisecret group of advisors to the U.S. government on technical issues associated with national security. He is a member of the Council for Foreign Relations and the Trilateral Commission, and has served on advisory committees for the National Science Foundation, the Department of Energy, and the Department of Defense and its various national laboratories.

Koonin's research interests include theoretical and computational physics, nuclear astrophysics, and global environmental science. He currently holds a position as a visiting associate in physics. *—DW-H*

... AND DR. ZEWAIL GIVES ADVICE

Obama has also named Nobel Laureate Ahmed Zewail, the Pauling Professor of Chemistry and professor of physics, to the President's Council of Advisors on Science and Technology (PCAST). PCAST, which will meet every two months, includes three Nobel laureates, two university presidents, four MacArthur "genius" fellows, and 14 members of the National Academy of Sciences or its Institute of Medicine, the National Academy of Engineering, and the American Academy of Arts and Sciences. In the speech announcing the appointments, Obama said, "I will charge PCAST with advising me about national strategies to nurture and sustain a culture of scientific innovation ... I intend

to work with them closely." PCAST's bailiwick includes energy, education, health, climate change, the environment, security, and the economy.

Zewail won the 1999 Nobel Prize in Chemistry for creating the new field of femtochemistry. A femtosecond is 10⁻¹⁵ seconds—one quadrillionth of a second, the timescale on which atomic bonds break and form. His lab is now developing a technique called four-dimensional microscopy to track atoms in time and space simultaneously to try to understand complex biological reactions.

Zewail serves on many national and international boards, and is involved in promoting science and education in the developing world. —*AB*

FLUID DYNAMICS—FROM MILLIKAN POND TO FORMULA ONE

As amphibious robots engaged in a desperate struggle, hundreds of people—including reporters from NBC, CBS, the *Los Angeles Times* and the *Pasadena Star News*—jostled for a better view from behind yellow caution tape strung around Caltech's Millikan Pond. Eighteen students in a course innocuously titled "ME 72 ab: Engineering Design Laboratory" had been working toward this moment, the final round of their March 10 tournament, for 20 weeks.

Teams of two or three undergrads worked with identical kits of materials to design and build radio-controlled 'bots that could survive a 14-inch fall into the pond, scoop up floating balls, and deposit them into the red or blue team bin on the opposite bank, all within three minutes. (A sandpapercovered ramp allowed the machines to crawl up out of the pond.) Most teams opted to build two boats: a small, nimble attack vehicle and a larger craft to gather as many balls as possible. The class was taught by Joe Shepherd (PhD '81), the Johnson Professor of Aeronautics and professor of mechanical engineering; and Joel Burdick, professor of mechanical engineering and bioengineering.

During this, ME 72's 25th annual double-elimination tournament and its first aquatic challenge, casualties mounted from the moment the vehicles leapt from the bank. One craft plunged into the water upside down twice. One got stuck on the edge with two wheels hanging. But the strategic crux was the ramp. Sumostyle shoving matches broke out in the water at the ramp's foot as teams tried to prevent their opponents from climbing out; whoever gained the high ground usually won.

In the end, team Ramen and Cheesesteaks—named for dietary staples of members Marshall Grinstead and Edmond Wong—faced off in a shoving match with Newt N' Salamander, Marc Sells and Kevin Noertker's team. Nimble Newt raced to the top of the ramp and spun to block its opponent, which was scrabbling tenaciously up the slope. Salamander, the transport craft, attacked from the water. Motors whined, wheels spun, batteries drained—and time ran out.

Sells and Noertker's victory leap into the pond clinched the story for the evening news. But history tells us that their triumph isn't just a geeky human-interest story; it's a portent. However humble the materials, however whimsical the challenge, ME 72 teaches the design process—from concept through building, testing, and refining—that governs engineering everywhere. Many alumni have drawn on similar Caltech preparation to revolutionize entire industries.

Consider Distinguished Alumnus Jim Hall, who, with his wife, just pledged \$2 million to create the Jim and Sandy Hall Fund for Mechanical Engineering.

Armed with the 1957 model of the same BS in mechanical engineering that the ME 72 champions will earn this June, Hall started his own racecar company, Chaparral Racing Cars,



Kevin Noertker (left) and Marc Sells do a victory dance in Millikan Pond after winning the final round of the ME72 contest.

and took on the titans of Formula One racing—Ferrari, Alfa Romeo, Porsche, and Maserati—while still in his twenties. Chaparral drove design innovations on the circuit for two decades, culminating in 1980 when a Chaparral 2K driven by Johnny Rutherford took the pole position at the Indy 500 and then cruised to victory, leading the pack for 118 of the 200 laps. Hall has been on the covers of *Sports Illustrated* and *Newsweek* and is in three motor sports halls of fame.

Hall's Caltech education taught him to see racing as a challenge in aerodynamics. He realized that pressing the car down into the track would improve its cornering speed, and he stunned the racing industry with innovations designed to create such a downforce: spoilers, air dams, movable wings, shaped undersides, skirts, and ducted fans that created a partial vacuum under the car.

The Halls' gift helped kick off a \$20 million ME fund-raising initiative last winter. Their names will grace a conference room planned for the soon-to-be-renovated Thomas Laboratory of Engineering; his name will also adorn the upgraded design and prototyping lab used by students in ME 72 and similar hands-on courses.

The first prototyping lab was built in Hall's senior year. He missed being able to use its mills and lathes by months, and thus had to learn how to apply theory to practice on his own. "When I realized what was happening in the ME 72 course and what those guys were learning, I got excited about it," he says. "When you get to do those things and see how things work and how they're made, it really helps your thought process."

Tom Tombrello, the Kenan Professor and professor of physics, often likens Caltech students to Formula One race cars, hand-crafted through close interactions with faculty. In that sense, Hall is back on the front lines building race cars again. As history repeats itself, perhaps Sells and Noertker will return to Caltech many years hence and dedicate the Newt N' Salamander Laboratory. —AW

OTHER SUNS, OTHER EARTHS

The quest to discover Earth-sized planets orbiting stars at distances such that water could pool on the planet's surface—another step in the search for life on other worlds—kicked into high gear when NASA's Kepler spacecraft roared off the pad at Cape Canaveral aboard a Delta II rocket at 10:49 p.m. EST on Friday, March 6.

The spacecraft has entered a suncentered orbit, and is drifting away from Earth at about one kilometer per second. (The Spitzer Space Telescope, which was launched into the same orbit more than five years ago, is now some 100 million kilometers away.)

From this vantage point, Kepler will watch upwards of 100,000 stars simultaneously, 24/7, for at least three and a half years, looking for a periodic dimming of their light that would be caused by a planet passing between them and Earth.

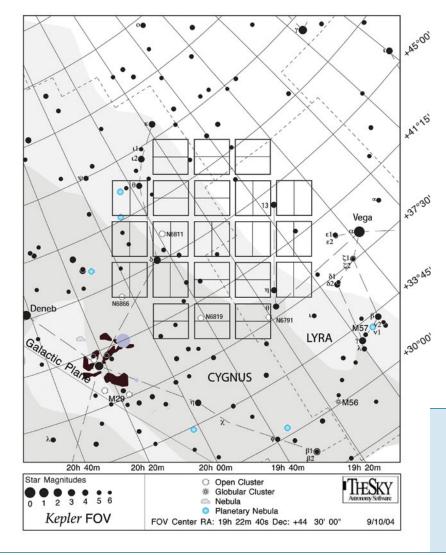
Engineers have now turned on and focused Kepler's single instrument, an 0.95-meter-diameter telescope with a wide-field CCD camera. This 95-megapixel camera, the largest ever launched into space, can detect a change in a star's brightness of 20

While Newt makes a dash for the ramp, Salamander goes bow-to-bow with one of Colin Ely and Kevin Tjho's Professional Ball Handlers, which featured an Archimedes screw to lift balls into the scoring bin without leaving the pond. White balls were worth one point each; orange, three; and blue, minus two.



parts in a million. As soon as the camera is properly calibrated, the search will begin in earnest.

The first planets to catch Kepler's eye are expected to be portly "hot Jupiters"—gas giants that circle close and fast around their stars. Neptunesized planets will most likely be found next, followed by rocky ones as small as Earth. The true Earth analogs ones orbiting stars like our sun at distances where surface water, and possibly life, could exist—will take at least three years to discover, as such planets will have orbital periods similar to Earth. Each planet will have to pass in front of its star at least three times to be discovered—if the time interval between successive pairs of dimmings repeats with high precision, then we can conclude that a planet is responsible. Observations by the Hubble and Spitzer space telescopes will be used to confirm some of



Kepler's discoveries and analyze the planets' atmospheres. Ground-based telescopes will verify some of the finds as well.

In the end, Kepler will give us our first look at the frequency of Earthsized planets in our corner of the Milky Way galaxy, and an idea of the fraction of them that could theoretically be habitable. "Everything about Kepler has been optimized to find Earth-size planets," says James Fanson (MS '82, PhD '87), Kepler's project manager at the Jet Propulsion Lab. "Our images are road maps that will allow us, in a few years, to point to a star and say a world like ours is there."

Kepler is a NASA Discovery mission. The science principal investigator is William Borucki of NASA's Ames Research Center at Moffett Field, California, which is responsible for the ground-system development, mission operations, and science data analysis. JPL manages the Kepler mission development. Ball Aerospace & Technologies of Boulder, Colorado, built the spacecraft. For more information, visit http://www.nasa.gov/kepler. -WC

Kepler's field of view (the rectangles) is aimed along the length of the star-rich Orion Spur, covers 100 square degrees, and includes an estimated 4.5 million stars. Clever pointing maximizes the number of the brightest stars that fall into the gaps between the 42 CCD blocks. The bright starlight would saturate the nearby pixels, blinding the telescope to potential faint flickerings from planets circling dimmer stars nearby.

MOLECULAR MISSILES

A search-and-destroy molecular machine that selectively locks on to cancer cells could make radiation treatments a thing of the past, at least for breast cancers. A team of researchers from Caltech; Technion, the Israel Institute of Technology, in Haifa; and the Cedars-Sinai Medical Center in Los Angeles have joined forces to develop a potentially much less traumatic treatment. tells us that it *does* work."

The team paired the gallium corrole with a carrier protein that binds to human epidermal growth factor receptor 2, or HER2, which is found on about 25 percent of breast-cancer tumor cells and marks them as particularly aggressive and difficult to treat. Preparing this cancer fighter is a breeze the corrole-carrier pairs spontaneously self-assemble in the test tube.

The corrole was simply injected into the bloodstream, where it circulated freely and could hunt down nascent metastatic tumors too small to be seen.

> The method uses a chemical payload called a gallium corrole, mated to a protein carrier that seeks out a cancer-cell marker. Once it binds to the cell, the protein triggers endocytosis, a process in which the cell engulfs the corrole-carrier combo.

Corroles are very similar to the porphyrin molecules used in a cancer treatment called photodynamic therapy, in which they are injected into the body and activated by a laser. This prompts the porphyrins to produce highly reactive, tumor-killing oxygen radicals. But some corroles don't require a laser boost to turn lethal, says Harry Gray, the Beckman Professor of Chemistry. "The striking thing about gallium corroles is that they apparently kill cancer cells in the dark," says Gray. "We don't yet know exactly how this works, but what we've seen so far In trials in mice, the corrole was able to shrink tumors at doses five times lower than doxorubicin, the standard chemotherapeutic agent for HER2-positive tumors. Doxorubicin has to be injected directly into the tumor, because at high doses the drug can cause heart damage. This, of course, also means that you need to be able to actually see the tumor. By contrast, the corrole was simply injected into the bloodstream, where it circulated freely and could hunt down nascent metastatic tumors too small to be seen.

Gallium corroles fluoresce intensely when zapped with a laser, and Gray's lab has been using them for many years to study electron transfer mechanisms. The new application resulted from trying to use the corroles as tracers to track the carrier protein's journey through the body. "We were amazed to see that the tracer itself was killing the tumors," says Gray.

The difficulty in getting to this point, notes Gray, is that corroles were tough to synthesize—until coauthor and Caltech visitor in chemistry Zeev Gross of Technion figured out how to make them in what passes for bulk in a biochemistry lab. "We went from being able to make a couple of milligrams in two years to being able to make two grams in less than a week. It really puts corroles on the map."

The work appeared in the April 14 online edition of the *Proceedings of the National Academy of Sciences*. The paper's lead author is Hasmik Agadjanian of Cedars-Sinai; the other authors are Jun Ma, Altan Rentsendorj, Vinod Valluripalli, Jae Youn Hwang of Cedars-Sinai; Atif Mahammed from Technion; Daniel Farkas, director of Cedar-Sinai's Minimally Invasive Surgical Technologies Institute; Gray; Gross; and Lali Medina-Kauwe, who holds a joint appointment at the David Geffen School of Medicine at UCLA and Cedars-Sinai.

The work was supported by grants from the National Science Foundation, the National Institutes of Health, the U.S. Department of Defense, Susan G. Komen for the Cure, the Donna and Jesse Garber Award, the Gurwin Foundation, the United States–Israel Binational Science Foundation, and by the U.S. Navy Bureau of Medicine and Surgery. *—LO* PCC students Selma Cuya and Russell Lund remove vials of cryopreserved mouse stem cells from a liquid nitrogen tank.

write the grant proposal. PCC's other "Bridges" partners include USC and Children's Hospital of Los Angeles.

Intern Mark Starbird, 28, earned a biotechnology certificate at PCC four years ago, then got his BS at Cal State Long Beach. Now he's back at PCC taking courses that weren't available then. He hopes to pursue a career in biomedical research. "I'm intrigued and enthusiastic about this," he says, "because you can't find this anywhere else. With my earlier training in cell culture at PCC, I'm already ahead of the curve. Now PCC has a stem-cell culture program to go along with it." The biotechnology program was established by Wendie Johnston, Eversole's predecessor, 10 years ago in response to industry requests.

Eversole enjoys the diversity of her students. Many are career professionals seeking to upgrade their skills. Some are mothers returning to the workforce. One is a 17-year-old highschool student whose mother drives him to night classes from South Pasadena. Another is a 30-year-old electrical engineer changing careers.

And the biotech graduates do well. One is employed by Pease and another is working at USC. One is doing graduate work at Cal State Los Angeles. Two have transferred to Berkeley, where both landed undergrad research positions in their first term. Says Eversole, "We tell students, 'You can do more than you think.' And they do it." —LD

CALTECH, PCC'S BIOTECH BRIDGE

This fall, up to 10 Pasadena City College students will work with stem cells at Caltech, thanks to a \$1.7 million grant and the leadership of a former Caltech postdoc. Others will follow in 2010 and 2011. Upon completing the program, they will be fully prepped to work on the frontiers of biomedicine as stem-cell lab techs. PCC is the only two-year college among 11 institutions statewide to win one of these "Bridges to Stem Cell Research" grants from the California Institute for Regenerative Medicine, established in 2005 after the passage of Proposition 71, the California Stem Cell Research and Cures Initiative.

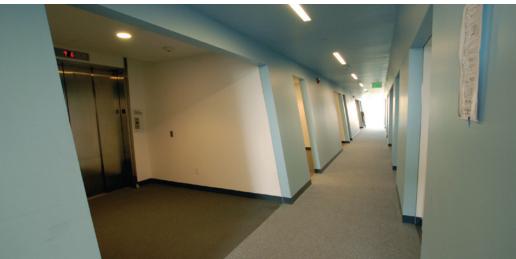
"It's such an incredible opportunity for PCC to partner with Caltech," says professor Pamela Eversole-Cire, director of the biotechnology program at PCC. "We're very excited." It's a homecoming of sorts, as Eversole will once again be working with Shirley Pease, director of Genetically Engineered Mouse services (GEMs) at Caltech, with whom she'd collaborated while a postdoc of Mel Simon, Biaggini Professor of Biological Sciences, Emeritus, and former chair of Caltech's biology department.

Eversole's lab at PCC was once a stockroom. With support from division dean Dave Douglass, equipment donations from private industry, and technical advice from Pease, she turned it into a cell-culture facility. The students grow mouse embryonic stem cells under industry-standard conditions, in incubators heated to body temperature and containing a 5 percent carbon-dioxide atmosphere with 90 percent humidity. The cell cultures are processed in three laminarflow hoods, and a few strides away are a centrifuge, water baths, and a hemocytometer for counting cells. The genetically altered cells are studied under a microscope, and students share their results on an electronic "smart board" contributed by the LA/ OC Biotechnology Center. Most of the equipment was donated by biotech companies such as Amgen, Invitrogen, Biogen-Idec, Cell Biolabs, and Biocatalytics. "Without donations," said Eversole, "this probably would not be possible. The infrastructure is expensive."

Students design their own experimental protocols, prepare solutions, maintain lab equipment, plan research schedules, adapt to schedule changes, and give presentations. They keep meticulous daily notebooks that meet industry standards. When students ask how much detail to include, Eversole replies, "If I can give that notebook to a new student and they can reproduce the experiments in it, then it's properly recorded. If they have questions, it's not." Students even negotiate for their final gradesan exercise intended to prepare them for real-world negotiations, for instance, during annual performance reviews.

At Caltech, interns can work in any of several stem-cell labs, including the GEMs core facility, where Pease has designed a curriculum in advanced stem-cell manipulation techniques for them. The internships are being coordinated by Paul Patterson, the Biaggini Professor of Biological Sciences, who also helped Eversole









MAYNE'S CAHILL: LIGHT DESCENDING A STAIRCASE

Caltech's newest building, the Cahill Center for Astronomy and Astrophysics, was dedicated on January 26. Situated across California Boulevard from the Robinson Laboratory of Astrophysics, the Cahill Center unites the Robinson Lab's former occupants with astronomers and cosmologists who had previously been scattered among several campus buildings.

Designed by Pritzker Prize-winning architect Thom Mayne of Morphosis in Santa Monica, the Cahill's twisted and fractured facade of terra-cotta-colored cement-board panels is intented to harmonize with the Spanish style of the older buildings across the street, while at the same time giving dramatic physical expression to the powerful forces that shape our universe. The Pritzker is sometimes called the Nobel Prize of architecture, and thus Mayne's latest work has attracted considerable attention. Architects and architecture students from across the country have stopped by to have a look—as, apparently, has most of Pasadena.

Ever-changing astronomical images projected on a wall in the lobby can be seen from the street, inviting visitors in. There, once they finish gawking at spacecraft models on display, their eyes will be drawn to the foot of the staircase (left) that is the building's centerpiece. Designed as a medi-

Above, from left: Freshman Jennifer Greco, senior Daniel Walter Rowlands, freshman Samson Chen, sophomore Aliza Malz, and sophomore Jasmine Sears, all members of Blacker House, showed up in *Star Wars* costumes for the Cahill Center dedication.



tation on the optical telescope, the stairwell is all about light. The massive, oddly angled pillars on the ground-floor landing remind one of the piers and supporting trusses of a major telescope like the Hale or the Keck, while the irregularly shaped interior windows and fragments of walls in the upper reaches (right)—a triumph of computer-aided design and fabrication techniques—create a constantly changing interplay of light and shadow as the photons gathered by the skylight at the top of the shaft make their way down the tube to the observer.

On the upper floors, the space warp makes its way indoors. Long hallways are broken into skewed segments, meeting in nooks that encourage people to hang out and chat. And the transverse corridors could have come from a Federation starship.

But another galaxy far, far away was in evidence at the dedication, held beneath the Cahill's overhanging prow. A small procession of Moles dressed as Jawas, plus a silver C-3PO, joined the back of the throng waiting for the ceremony to start. "We're here for the dedication of the giant sandcrawler," they explained.

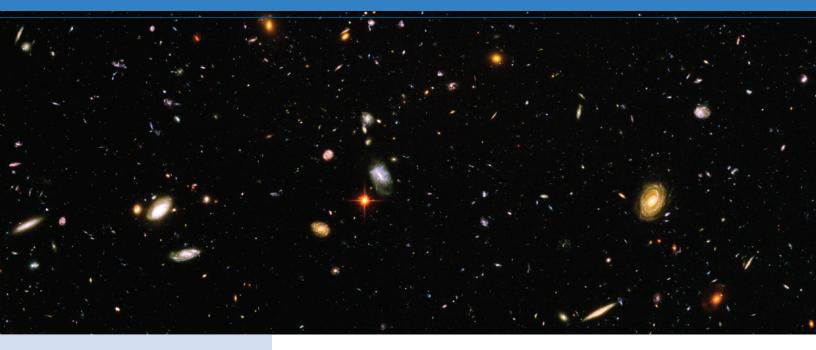
The Cahill Center is named for Charles Cahill and his late wife, Anikó Dér Cahill. Other benefactors include Trustee Fred Hameetman (BS '62) and his wife, Joyce; the Sherman Fairchild, Ahmanson, and Kenneth T. and Eileen L. Norris Foundations; PIN USA, Inc.; and Michael Scott (BS '65). For complete coverage of the dedication ceremony, see *Caltech News*, No. 1, 2009. –*DS*

Right: If our eyes could see a slice of the nearinfrared spectrum beloved of astronomers, the Cahill Center's south side would look like this. Tom Prince, professor of physics, JPL senior research scientist, and director of the W. M. Keck Institute for Space Studies, shot the photo with an 830-nanometer filter.





When Will We Find the Extraterrestrials?



There are a couple of hundred billion stars just in our own Milky Way galaxy, so the odds are good that we are not alone in the universe. On the other hand, if life abounds, why haven't we found any evidence of it and is that about to change?

The dedication ceremonies for the Cahill Center for Astronomy and Astrophysics featured a symposium whose speakers included some of the brightest lights in astronomyall of them former Techers. One of the day's highlights was this talk by Seth Shostak, PhD '72, a senior astronomer at the SETI Institute, where he's been since 1991. But Shostak's interest in extraterrestrials goes much farther back—as a grad student at the Owens Valley Radio Observatory with plenty of time on his hands, he, Robert O'Connell (PhD '70), and friend Jerry Rebold shot such timeless films as The Teenage Monster Blob from Outer Space, Which I Was and The Turkey that Ate St. Louis. The latter can now be seen on YouTube, and is particularly noteworthy for the appearance of

then-department chair Jesse Greenstein as TV newsman Walter Crankcase.

When Shostak isn't listening for aliens, he's talking or writing about them. His weekly radio show, Are We Alone?, is accessible at http:// radio.seti.org. His latest book, Confessions of an Alien Hunter: A Scientist's Search for Extraterrestrial Intelligence, was published by National Geographic in March.

For more information on the SETI Institute, visit www.seti.org.

This article was edited by Douglas L. Smith.



Above: The Hubble Ultra Deep Field is the farthest we have ever peered out into the visible universe. With the exception of one bright, four-pointed, red foreground star, everything you see in this picture is a galaxy. If we're alone in the universe, we are *really* alone. Photo credit: Steven Beckwith (PhD '78) and the Hubble Ultra Deep Field Working Group, STScl, HST, ESA, and NASA. The Terrestrial Planet Finder mission consists of two complementary observatories: a visiblelight coronagraph (right), slated to launch around 2014, and a formation-flying infrared interferometer, intended to launch before 2020.

By Seth Shostak

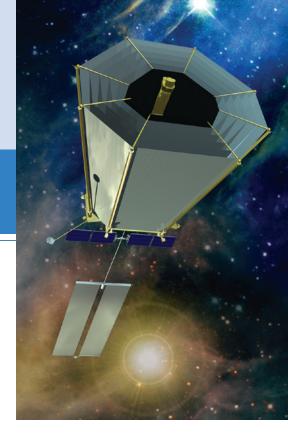
My day job is to look for E.T. I'm a senior astronomer for the SETI Institute, just south of San Francisco in Mountain View, only two miles from Google. SETI stands for the Search for ExtraTerrestrial Intelligence, and our mission is to scan the skies for radio signals that would prove we are not alone in the universe. (Unlike in Europe, in this country the search is entirely privately funded. Your tax dollars have not been at work in this field since Congress pulled the plug on NASA's High Resolution Microwave Survey in 1993.) Everybody who works in SETI eventually gets asked, "So, when are you going to find something?" And everybody has an answer. But I've noticed that the answer is tightly correlated with the number of years until the answerer is expected to retire. These responses probably tell you more about the people you're asking than about E.T., so I'm going to try to give you an answer that you might believe, and as a bonus I'll give you my best guess as to what E.T. might look like.

Why do we think that E.T. is out there in the first place? It's simply a matter of numbers. There are 10²² stars in all the galaxies visible to our telescopes today. That's a 1 followed by 22 zeroes, or 10 *sextillion* stars. Geoff Marcy's team at UC Berkeley has so far found 121 planets around nearby stars, and I recently asked him, "If you had perfect instruments, what fraction of stars would show planets?" His answer was "maybe half or three quarters," which, of course, to an astronomer is the same as "all." And since planets, like kittens, come in bunches, it's likely that the number of planets is an order of magnitude larger, or 10²³, which is the number of grains of sand on all the beaches of Earth. That's a lot of real estate, so if you think that Earth is the only grain of sand where anything interesting is happening, one has to admire your audacity.

That's the basic argument, but there are others. In the picture below you can see some of the oldest and best-preserved sedimentary rock on Earth. Those little lumps in the rock are thought to be the remains of bacterial colonies from three and a half billion years ago. In other words, as soon as Earth was capable of supporting life, almost as soon as the heavy bombardment of our planet by early asteroids had abated, there was life. And that suggests—although it doesn't prove, since the sample size is one—that life is not a miracle, but merely some sort of dirty chemistry that probably occurs in many places.

STUPID LIFE, SMART LIFE

There's a three-way horse race to find compelling evidence of life beyond Earth. I think that each of these methods has, more or less, an equivalent chance of winning. The first approach is to find it nearby perhaps on Mars, or one of the moons of the outer solar system. A JPL mission might do that. The second approach is to build infrared telescope arrays in space, and try to find, for example, methane in the atmosphere of a planet around another star. Methane molecules are destroyed by any of



several processes on a timescale of a few hundred years, so something would have to be creating fresh methane continuously for us to be likely to see it. Much of the methane in this room is produced by what is politely called "bovine flatulence," and also by porcine flatulence, so this technique would at least allow you to find pigs in space. NASA, the European Space Agency, and many universities are collaborating on such projects, which will be built in the next 20 years. In fact, on March 6 NASA's Kepler spacecraft was launched to look for Earth-like planets that could be subjected to closer scrutiny by such telescopes. (See the Random Walk item on page 6.)

Both of these approaches are attempting to find, if you will, stupid life—life that would require a microscope to see—on the not unreasonable assumption that stupid life is far more prevalent than the intelligent variety.

The third approach is to look for intelligent life. What do we mean by "intelligent?" SETI has a very simple operational definition for high IQ, namely: can you build a radio trans-



The business-card-sized lumps in this 3.5-billion-year-old, iron-rich rock from the Pilbara Hills in northwestern Australia are thought to be the remains of ancient bacterial colonies. At age 79, Frank Drake still comes in to work every day at the SETI Institute, where he is the director of the Carl Sagan Center for the Study of Life in the Universe.

FRANK DRAKE AND THE BIRTH OF SETI

Frank Drake, then on staff at the National Radio Astronomy Observatory in Green Bank, West Virginia, did the first radio search for alien civilizations in 1960, Called Project Ozma, for the ruler of the land of Oz, it listened to two nearby, sunlike stars named Tau Ceti and Epsilon Eridani. Drake used a 26-meter dish to scan across 4,000 channels centered on the 21-centimeter emission band of cold hydrogen gas-a frequency popular with radio astronomers that he figured would be a natural choice for a species trying to make itself known. He tape-recorded the data and then printed it out on strip charts, looking for any signals superimposed on the hiss of interstellar static.

In 1961, he and J. Peter Pearman of the National Academy of Sciences organized the first SETI conference, also at Green Bank, where he proposed what is now known as the Drake equation to calculate how many civilizations (N) we might have hope of hearing from:

$$N = R_{\star} \times f_{p} \times n_{e} \times f_{p} \times f_{i} \times f_{c} \times L$$

The equation starts with a very large number, R_{*}, which is the average rate of star formation in the Milky Way, and multiplies it by succession of numbers that represent the probability of critical ocurrances. Thus f is the fraction of stars with planets; n is the average number of planets in those systems that are capable of supporting life; f, is the fraction of planets that eventually develop life; f, is the fraction of species that go on to become intelligent; f is the fraction of intelligent species that invent communication devices, such as radios, that we might detect from Earth; and L is the length of time that such civilizations actually broadcast into space. ess



mitter? If you can, we don't care about the rest. Do you write great literature? Irrelevant. If you can build a radio transmitter, you're in.

This leads to a very contentious and complicated question. Given a million worlds with stupid life on them, what fraction of them will ever develop intelligent life? Consider that if, 65,000,000 years ago, the rock that landed in the Yucatan had whizzed by 20 hours earlier or later, there would be dinosaurs in Pasadena today. Of course, they might have learned to build radio transmitters by now, but I once asked Niles Eldridge, a paleontologist at the American Museum of Natural History, about that. (Niles, by the way, developed the theory of punctuated equilibria with Stephen Jay Gould.) He replied, "Well, Seth-the dinosaurs had 150,000,000 years to get smart and didn't. What would another 65,000,000 have done for them?"

However, there are mechanisms that seem to ratchet up intelligence. Getting smarter can be a weapon on either side of the predator-prey arms race, for example. But a much better driver, at least from the point of view of your next cocktail-party conversation, is called "signaling for fitness." The canonical example is the peacock. The peacocks, the males, gather in groups and display their blue tailfeathers. The peahens cruise by, and the guy with the best display gets to breed. What benefit does that peahen, with her little pea brain, garner from those big blue feathers? After all, they only attract predators. The answer is that a well-patterned tail with a dense collection

of eyespots is a good indicator of a male whose genome has few harmful mutations, so his chicks will be healthy.

Evolutionary psychologist Geoffrey Miller at the University of New Mexico says that a couple of million years ago we were doing the same thing. We didn't have blue feathers, but in a predator-filled world, the mere fact that a male was still walking around was a good sign. It's like those old Clint Eastwood westerns. He rides into town, probably hasn't had a bath in three months, yet all the women turn out for him. Why? The biologists would say, "Well, look, if he made it this far, he *must* be good."

Like the peacock's tail, the human brain is tightly linked to the genome. About half of our genes have some effect on our brains, so if your brain is wired up correctly—if you can tell interesting stories, or sing, or something like that—it shows that you don't have too many bad mutations. Therefore, the best pickup strategy for a man at a party would be to take off his skull and pass his brain around. That's considered a social blunder, so instead the men talk to the women, and the competition to make good conversation ratchets up the size of men's brains.

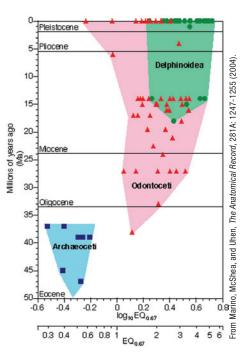
The same holds for women. Miller says that there's a lot of evolutionary pressure on the females to be charismatic in order to hold the guy's interest so he'll help raise their future kids. He says if you doubt this, just look at the couples in a restaurant. If they're just getting to know one another, the guys are doing all the talking to charm the females. But if they've been together for a This plot shows the ratio of brain size to body size (abbreviated as EQ) for the common ancestors of whales and dolphins (Archeaoceti); the modern toothed whales (Odontoceti), which includes the sperm whale; and the Delphinoidea, the dolphins and porpoises. The scale is logarithmic, meaning the dolphins are way smart.

while, the women are doing all the talking to keep the guys from wandering off—at least until they pay the bill.

If this hypothesis is true—which is open to debate—emergent intelligence could be a common evolutionary process that happens on lots of worlds.

Intelligence does appear to increase with time in some cases. Above right is a plot by neuroscientist Lori Marino at Emory University that shows an index computed from the ratio of brain size to body size, the so-called encephalization quotient (EQ), for a bunch of species of dolphins and toothed whales over the last 50,000,000 years. They were all pretty stupid 50,000,000 years ago, but 48,000,000 years later, white-flanked dolphins were the smartest things on the planet. If you go to the local library and look up "Dolphin Literary Criticism," it's all from two million years ago. Once you get to a certain level of complexity, there's a niche market for intelligence, and it may get filled. That's encouraging.

One way to find intelligent life is to look for artifacts. Advanced societies could be doing astroengineering that we might be able to see. For example, a Dyson swarm, which is a grand-scale collection of orbiting solar-power stations, habitats, and whatnot, could surround its star at a radius beyond all the habitable planets. Not much light would get out, but the inevitable waste heat out the backs of all those solar cells would betray their presence in the infrared. Richard Carrigan, a physicist at the Fermi National Accelerator Laboratory, has



been looking for signs of possible Dyson swarms by perusing the Infrared Astronomy Satellite data sets. (IRAS, a joint project of the Americans, British, and Dutch, was launched in 1983, and performed the first all-sky infrared survey. Many Caltech people were instrumental in the project, and the data sets are still housed here on campus, at the Infrared Processing and Analysis Center.)

E.T., PHONE EARTH

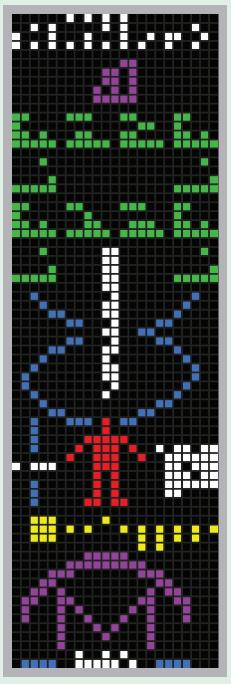
It's much easier to search for signals, and there are a lot of places in the electromagnetic spectrum where we could look. We can, for example, do it in the optical. Berkeley, Lick Observatory, and Princeton all have had projects that look for flashing lights in the sky, but Harvard has the most ambitious program, thanks to physicist Paul Horowitz. There's a lot to be garnered for very little effort, as you can see by the following simple thought experiment.

A typical star like our sun emits some 10⁴⁵ photons per second in all directions, so if you look at it with a one-square-meter mirror

[Dolphins and whales] were all pretty stupid 50,000,000 years ago, but 48,000,000 years later, white-flanked dolphins were the smartest things on the planet. If you go to the local library and look up **"Dolphin Literary** Criticism," it's all from two million years ago.

This guy's encephalization quotient is off the charts. He's going to be very popular as a potential mate.





THE COSMIC WELCOME MAT

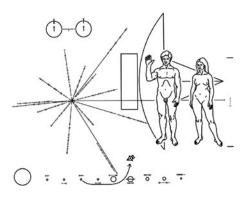
We don't deliberately broadcast into space for the benefit of the aliens, but occasionally it's done as a sort of demo project. The most famous of these efforts was the one-time transmission of an FM (frequency modulated) radio signal at 2,380 megahertz from the 305-meter-diameter antenna at the Arecibo Observatory in Puerto Rico. The broadcast, on November 16, 1974, used the dish's million-watt radar transmitter, normally employed for planetary astronomy, and the message was sent to celebrate a major upgrade to the telescope rather than representing a serious effort at communication. The signal was aimed at a globular star cluster called M13 that is 25,000 lightyears away, so we won't be hearing back from them any time soon.

The message consisted of 1,679 binary digits, sent at the rate of one bit per second. The number 1,679 is the product of two prime numbers, 73 and 23, allowing the recipient to reassemble the rectangular picture they encode in only two possible ways. When correctly displayed as 73 rows by 23 columns, the diagram at left emerges, which attempts to tell any puzzle-loving species everything they need to know about us in a nutshell. (The zeroes are shown in black; the ones have been given various colors for ease of description.) Across the top are the numbers 1 through 10 (white). Next, in the same system of notation, come the atomic numbers of hydrogen, carbon, nitrogen, oxygen, and phosphorus (purple)—the constituents of DNA. The formulas for the backbone

sugars and the nucleotide bases found in DNA are in green—good luck to the aliens trying to figure *them* out!—and below them is a graphic of the DNA double helix itself (blue). Within the helix is the number of base pairs in the human genome (white); below it is a self-portrait (red) of *homo sapiens*. The measuring stick to the left (blue) gives our average height (white) as a multiple of the wavelength of the radio signal. To the right of our likeness is the world's population (white), and below is a map of the solar system (yellow), with us astride an Earth set out of line from the other planets. And finally, on the opposite side of Earth is a cross section of the Arecibo radio dish, along with its dimensions (blue and white, as with the human form). The dish is shown beaming the signal into deep space from its prime focus.

The graphic was designed by Frank Drake, then at Cornell University, with assistance from his colleague Carl Sagan, among others.

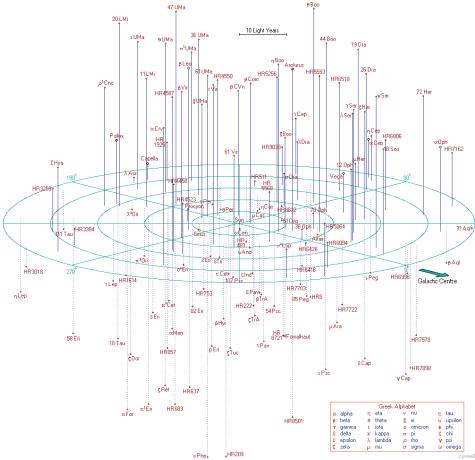
Sagan and Drake also designed the much easier to read six-by-nine-inch gold-anodized plaque (top right) that was mounted on NASA's Pioneer 10 and 11 spacecraft, now on their way out of the solar system. This plaque shows a hydrogen molecule (upper left), our sun's location in relation to 14 pulsars, our solar system, the Pioneer, and us.



Above: The plaque on the Pioneer 10 and 11 spacecraft, which were launched toward Jupiter on March 2, 1972 and April 5, 1973 respectively. Pioneer 11 went on to Saturn, making its plaque inaccurate. Below: Harvard's optical SETI telescope, which sports a 72-inch primary mirror.



From AtlasoftheUniverse.com



from 100 light-years away, you'll get about 100,000,000 photons per second. If you look at it for one nanosecond, one billionth of a second, that's less than one photon. Now, if you work out how many photons per second the biggest lasers we have here on Earth would put into a square meter at a range of 100 light-years-it's only been a half-century since the invention of the laser, so these are perhaps not sophisticated lasers compared to what E.T. might useone could easily produce hundreds or even thousands of photons per square meter. In a nanosecond. It completely swamps the steady photon flux from the star. So to search for such transmissions, all we have to do is put a photomultiplier tube behind a modest telescope and look for nanosecond pulses.

If the aliens used a one-square-meter mirror to point their laser at us from 100 light-years away, the beam would just cover our inner solar system-roughly out to Saturn. But, you ask, why would they be aiming at us? Perhaps they've detected the oxygen in our atmosphere-the spectrographic evidence has been there for two billion years-and concluded that there might be life on Earth, but not necessarily intelligent life. They could be trying a whole lot of potential bio-planets, over and over. It's not that we'd be so special, we'd just be on a very long "ping list." That's pure speculation, but it's not unreasonable, and it doesn't require us to luck out by being in the path of a randomly directed beam.

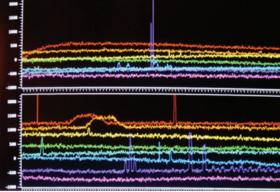
This 3-D map shows 133 naked-eyevisible stars, most of them very similar to the sun, within 50 light-years of Earth. If the sun-like stars have Earthlike planets, as well they might, and if said planets are inhabited by beings with television receivers, those lucky lifeforms may be enjoying *I Love Lucy*, which went on the air for the first time in 1951.

COSMIC EAVESDROPPING

We don't necessarily need to rely on E.T. reaching out to us. At the moment, we are unintentionally announcing our own presence to the universe by emitting copious amounts of television and radar waves. (The radar is more powerful, although not as interesting to listen to.) But those big redand-white TV towers on Mount Wilson are eventually going to go away, as fiber-optic lines come into your house. Our electromagnetic signature as a society, at least in the radio, is going to go down, rather than up. So the question is, would highly advanced societies still be broadcasting willy-nilly into space, or do we have to count on them deliberately trying to signal other civilizations? The opinions on whether we should expect unintentional leakage or deliberate signals seem to change every 10 years, but an intelligent species might always want to have some big radars on the lookout for long-period comets, for example, which if undetected could ruin one's whole day.

Most SETI projects follow Jodie Foster's strategy in the movie *Contact*, where she used the National Radio Astronomy Observatory's Very Large Array, sprawled across the deserts of New Mexico, to look for artificial radio emissions. (The VLA has never been used for this sort of research, by the way, but it's very photogenic.) *Contact* was actually based on our work at the SETI Institute. We were consultants on the film, and I got daily calls from folks at Warner Brothers who would ask questions like, "So, Seth,





real time, and split into frequency channels roughly 1.4 hertz wide and separated by about a hertz. The software then examines all of these channels once per second, recording the amount of power in each. A single observation typically lasts four to five minutes, and once it ends, the computer paws through the data, looking for signals that pulse slowly, say once every few seconds. The software also looks for signals that have slowly drifted up or down the radio dial. This is extremely important. If a signal has zero frequency drift, it means that the transmitter is rotating with Earth, so the source is either bolted to our planet or is in a geosynchronous orbit. The filtering process typically nets us a dozen or so candidates per observation, which are compared to a database of known sources of interference. In general, we can tag a signal as terrestrial or not within 10 minutes or so. Some candidates have endured closer scrutiny for a few hours. In 1997, one lasted even longer than that, but eventually was traced to the NASA/ ESA solar research satellite named SOHO.

So far, we've been using other peoples' telescopes, which is like doing cancer research with borrowed microscopes. Therefore, even though the first radio search was done almost 50 years ago, the total number of stars that we've looked at carefully over a wide range of frequencies is fewer than 1,000. In a galaxy of a couple of hundred

Right: The Allen Telescope Array is near Hat Creek, about 300 miles north of San Francisco. The seemingly random antenna placement gives a near-Gaussian distribution to the spacings between antenna pairs and produces undistorted images of the sky.

Below, right: A tiny piece of a SETI observation at Arecibo in 1998. Each line covers about 1.25 megahertz from left to right across the screen. The sharp peaks are all local signals-from either ground-based transmitters or satellites in Earth orbit-except for the triplet on the purple line that's second from the bottom, which is from Pioneer 10's radio transmitter. The two small, flanking peaks are called sidebands, and show that the signal is amplitude modulatedin other words, the spacecraft was still sending back data.

what does it look like when you fly through a wormhole?" I'd tell them that, relativistically, the whole universe collapses into a bright point of light in front of you and one behind you. But, I added, visually that's not very interesting, so most movies animate the view one would have while flying through a pig's intestine instead. Which is what they did.

People frequently assume that, in trying to recognize E.T., we look for particular patterns in the radio noise-the value of pi, perhaps. We don't. We're not looking for a modulation, just a narrowband signal. The wider the bandwidth, the more noise collected by the receiver. So if the aliens want to be heard, they'd take all their transmitter power and put it into a one-hertz-wide channel or less—as narrow as they can make it. They can't push much information through a channel like that, of course, but at least it tells us that they're on the air. Then they could have lower-power transmitters sending more interesting signals. If we

found that narrowband

signal, we'd go after that spot on the sky for all we were worth, looking for the information channel.

At right is a bit of a spectrum from the National Astronomy and Ionosphere Center's Arecibo Observatory radio telescope, which is run by Cornell. (The whole spectrum covers some 20 megahertz.) You can see several narrowband peaks in there, but they're all local interference, save one-the radio transmitter aboard NASA's Pioneer 10, which at that point was about two times as far away as Pluto. We occasionally listen to a spacecraft, just to make sure that everything is still working. Otherwise, we wouldn't know whether a nonresult means that there's no signal to be seen, or whether it just means that some component in our system has silently quit on us.

Finding E.T.'s signal was very easy for Jodie Foster-she just sat on the hood of a car for about 20 seconds with a pair of earphones. I pointed out to Warner Brothers that we were monitoring 56,000,000 channels, so they should really put 28,000,000 pairs of earphones on her. They said it

Infrared and

would crowd the shot, so they didn't do it. In the real world, looking for a signal takes a lot of computer processing. The incoming stream of cosmic static is Fourier transformed, almost in

All the major SETI projects ever done cover a very small portion of the possible search space. Distances are in lightyears and frequencies are in gigahertz.

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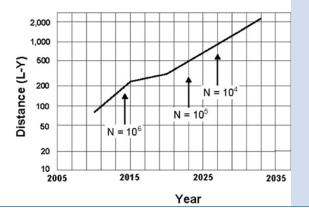
18

Relative depth into space

10

102

Fraction



This graph shows the radius (in light-years) of a sphere centered on Earth versus the year by which we will have listened to all the candidate star systems within that sphere. For each N, or number of civilizations "on the air" out there, the arrow marks the year by which we will have listened to enough stars to have found someone broadcasting.

billion stars, that's nothing. But the situation is about to change.

Our new instrument, the Allen Telescope Array, currently consists of 42 six-meter dishes. It's named for Microsoft cofounder Paul Allen, who gave us and UC Berkeley the money to get started. The array will eventually have 350 antennas, funding permitting. The Berkeley Radio Astronomy Laboratory is already using it, and we'll have two SETI projects under way on it by this summer. We can both use it 24/7—while the Berkeley guys are mapping galaxies, or whatever, we'll be checking the foreground stars in the same field of view for E.T.'s signals.

Each dish has a compact, state-of-theart feed horn that covers the microwave spectrum from 0.5- to 10.5-gigahertz. Most radio-astronomy receivers are only good over a few hundred megahertz, and if you want to switch between different spectral regions you have to physically change out the receiver-feed horn combo. Usually this means sending someone up to the focus with a wrench, although on some big telescopes, like Arecibo, you can just push a button in the control room to rotate the receiver turret. Receiver turrets are big, heavy, and expensive, so they weren't practical for the Allen Array, and changing 350 feed horns by hand is not something I'd want to do. Inside our wide-spectrum feed horn, our receiver is also state-of-the-art-a tiny chip designed here at Caltech by Faculty Associate in Electrical Engineering Sander "Sandy" Weinreb. His chip works over

our entire 10-gigahertz frequency span—a remarkable feat—and together with the feed horn makes a near-perfect low-noise device.

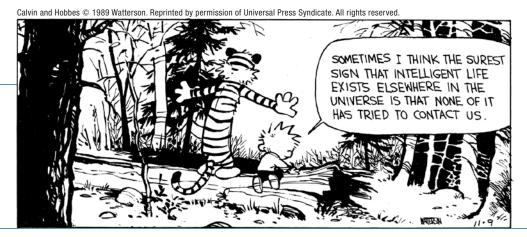
WHEN WILL WE FIND THEM?

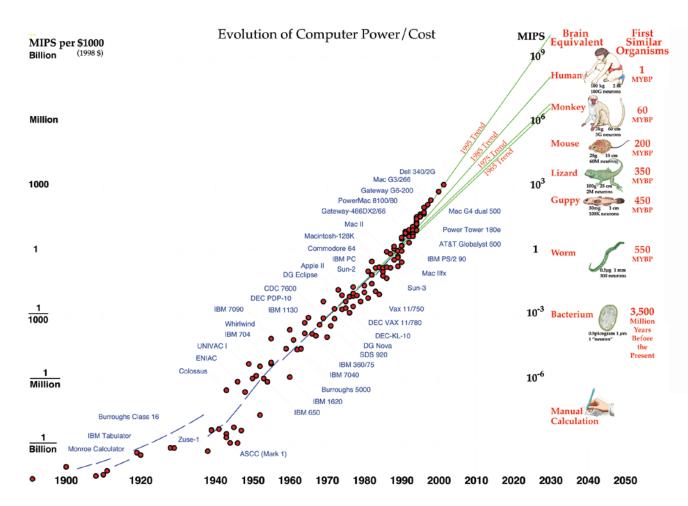
I'm now ready to answer the question I posed in my title: when can we expect success? We're looking for a needle in a haystack; that's the usual metaphor. We know how big the haystack is-it's the galaxy. We don't know how many needles there are, but we can reckon how fast we're going through the hay. SETI's speed doubles, on average, every 18 months, because we use digital electronics that obey Moore's Law. This trend will continue for at least another couple of decades. If we factor in the geometry of the galaxy, we can calculate how far out into space we will have listened to all the interesting star systems by any given year, assuming we relentlessly observe them in order of distance. The Ns in the plot above are guesses by various people as to how many needles are in the havstack. Carl Sagan figured a couple of million, and if he's right we should succeed by 2015. Isaac Asimov figured 670,000, and if he's right, it should take until 2023. Frank Drake is more conservative, with only 10,000 civilizations broadcasting in the galaxy right now, and consequently it takes until 2027-at which

point we will have looked at the nearest million star systems, three orders of magnitude better than we've done so far.

Mind you, all of these numbers could be completely wrong, but it is these guesses that motivate our efforts. The total number of people that work in SETI is fewer than any two rows of audience members in this room, but nonetheless, if that range of estimates is right, we'll find E.T. within two dozen years. I'm so sure of this that I'll bet all of you a cup of Starbucks on it. So either you'll hear news of a detection within two dozen years, or you'll get a cup of coffee in the mail. If we don't find E.T. within a generation, there is something very fundamentally wrong with our assumptions.

There's a counterargument to be made here, which was first posed in the 1950s by physicist Enrico Fermi. The Fermi Paradox runs as follows. The timescale for colonizing the galaxy, even with such primitive technologies as rockets, is not very long. It's on the order of tens of millions of years, which is short compared to the age of the galaxy. Therefore, if there is intelligence out there, the galaxy should have been colonized a long time ago. As Fermi himself is supposed to have put it, "Where is everybody?" Resolving this paradox is a cottage industry in its own right, with explanations running the gamut from "Colonizing the galaxy is





The rapid rise in the number of MIPS (Millions of Instructions Per Second, a measure of computing power) that you can buy for a constant price has rapidly outstripped the evolutionary pace of biological brains. Graph courtesy of Hans Moravec at Carnegie Mellon University's Robotics Institute.

not cost-effective, so they're smart enough not to have bothered" to "They have indeed colonized the galaxy, but we just haven't noticed," in the same way that ants probably don't notice us. I think the so-called paradox is fallacious—a very big extrapolation from a very local observation. Using similar logic, I can go into my backyard and say, "You know, there are no bears here. But they've had plenty of time to arrive. Therefore bears must not exist."

GREEN, GRAY, BORG, AND BEYOND

The SETI community doesn't know what the aliens will look like, but Hollywood does. This is not irrelevant, because our idea of what they may be like determines our search strategy. One hundred years ago we thought that the Martians had a planetwide, canal-based society, and we could find them with large telescopes in Flagstaff. Today we're talking about sending robots to Mars to drill holes to look for bacteria. What you think you're looking for affects how you look for it.

There are a few good Hollywood aliens, like the guys who gave Richard Dreyfuss a joyride in Close Encounters of the Third Kind. You can always tell the good ones; they look like little kids. But most Hollywood aliens are bad, War of the Worlds bad. The ISO standard alien-what UFOlogists call a "gray"—is just a projection of what we think we're going to become as we slowly lose our olfactory sense, our teeth, and so on. And, of course, we'll all be sitting around designing websites, so we'll have big eyes. All of these aliens are very anthropomorphic-soft, squishy quys, just like us. I think that even my colleagues figure, sort of subconsciously, that's what we're going to find. The aliens may not look like this guy, exactly, but they're something like us.

I believe that's wrong, and I'm going to tell you why. We're looking for intelligence, which in our case consists of a three-pound brain that draws about 25 watts of power. When you get an In-N-Out burger, onequarter of the calories go to keep your brain warm, even though it's less than 2 percent of your body weight. Three million years ago we had a one-pound brain. One million years ago we had a two-pound brain. Today we have a three-pound brain. The difference is huge: If you have a two-pound brain, you walk upright and maybe discover fire. If you have a three-pound brain, you can get tenure at Caltech. The assumption is that we'll go on to five-pound brains, ten pounds, and so on, but I think that's unlikely. Women are already having trouble giving birth to babies with heads as big as they are, so they'll go on strike. There are also mechanical problems. If you have a ten-pound brain, you'll twist your head off the first time you turn it.

I think that E.T. will not be flesh and blood, or whatever passes for alien flesh and blood. The artificial-intelligence community predicts that we're going to invent our own successors, and the next dominant life form on the planet will be robotic. If you plot how much computing power you can buy for \$1,000 as a function of time—Moore's Law again—you can see that by 2020 a desktop computer will have as much power as a huThe ISO standard alien—what UFOlogists call a "gray"—is just a projection of what we think we're going to become as we slowly lose our olfactory sense, our teeth, and so on.

man brain. That doesn't mean it will be able to think, but *maybe it can*... if the software guys can keep up. At AI conventions now, they're not talking about whether machines will be able to write the Great American Novel or compose symphonies or teach high-school chemistry; they're discussing whether we'll be able to pull the plug if we need to. Of course, some folks have been trying to build AI for a very long time, but they always point out that we shouldn't confuse the lack of success with a lack of progress.

So if this happens by 2020—or 2050 or 2100, it doesn't matter—then 20 years after that your desktop computer will have as much power as the entire human species. When that happens, I for one am just going to turn the keyboard around and say to my computer, "OK, *you* type." My point is that this is a timescale argument. When Gary Kasparov lost to a chess-playing machine named Deep Blue in 1997, he said his opponent had a kind of "alien intelligence." And that was just a game-playing machine. It didn't think.

The problem is that Darwinian evolution usually proceeds pretty slowly. About 60 million years ago, a horse stood as high as your knee; now, they're the size of, well, horses. I had a home computer in 1977. It ran at one megahertz. My laptop today runs at more than a gigahertz. That's a factor of 1,000 improvement in 30 years. It just blows Darwin away. This is Lamarckian evolutionyou can self-improve. Once we get artificial intelligence evolving, I think we can forget biology. Maybe we'll become the machines' pets, which may not be so bad-at least we'll get to sleep a lot. Yes, humans will try to keep up, of course. We'll put chips in our brains, but that's like putting a four-cylinder engine in a horse-after a certain point you say, let's get rid of the horse and just build a Maserati.

There are soooo many advantages to arti-

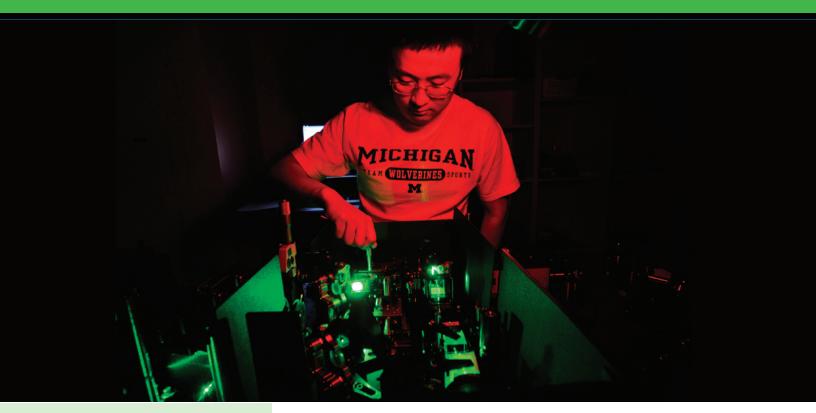
ficial intelligence that I think it will dominate everything. Machines can even operate in interstellar space. We're looking for signals coming from star systems that might have Earth-like planets, and maybe that's the wrong strategy. Maybe we should just look for places that have high concentrations of energy, because in the end that's presumably what the machine wants.

I think that if there's a conscious intelligence out there, it's synthetic. I think we should assume that when we find a signal, it won't be coming from a soft, squishy guy behind a microphone, but from one of the true, deep intellects of the universe. And to prepare for that, we might want to ask ourselves, what would be interesting to machine intelligences? What would keep them busy? Do they just play solitaire endlessly, or *N*-dimensional chess?

NO LOOK

Should we be working on some really compelling PowerPoint presentations to divert their attention while we reprogram them to calculate the exact value of pi? Unless, of course, they've already done that...

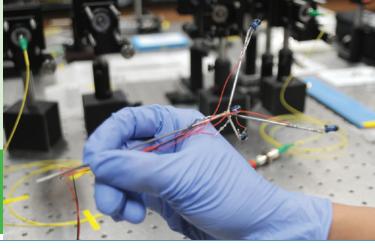
A Toymaker's Lab



Changhuei Yang's lab is filled with clever projects: a system to see through skin and flesh, new kinds of microscopes, and even a device inspired by a video game. But his work's not just fun and games—it may change the way diseases are diagnosed and treated. Changhuei Yang shuttles between workbenches littered with lasers and optics equipment. Yang, an assistant professor of electrical engineering and bioengineering, runs the biophotonics lab at Caltech, and he's showing off one of his latest gadgets a thin, five-inch-long rod with three prongs that could eventually aid doctors in everything from eye surgery to biopsies. This tool, he explains with delight, was inspired by nothing other than the Nintendo Wii, whose remote controller is a motion-sensitive wand. To hit a baseball, for example, you would swing the remote as if you were swinging a bat. Yang's tool doesn't control anything, but uses the same tracking technology so that its precise position is known at all times. The technology could lead to valuable instruments for procedures like prostate exams, in which it's a good idea for doctors to know exactly where they're prodding.

The probe is one of several research projects that are under way in Yang's lab. They are hard to put in a single category, but they all have an element of ingenuity. Biophotonics is the science and technology of using Left: Christmas in the lab? Postdoc Meng Cui shows off an experiment that would allow you to see through skin and flesh.

Right: The four LEDs at the base of the new probe shine in infrared light. A camera connected to the computer follows the LEDs as the probe moves.



By Marcus Y. Woo

light in biology, or as he puts it, "We use optics in clever ways to solve problems." The lab is creating potentially revolutionary new microscopes and developing other methods to see through skin and flesh, possibly changing the way doctors diagnose and treat diseases. All this has landed him on *Discover* magazine's "20 Best Brains Under 40," a list of young, pioneering scientists and engineers from around the country. A colleague once described him as a toymaker, he says, and Yang agrees it's a fair assessment. After all, in how many labs would you find a Nintendo game system on the bench?

With the Wii, a stationary sensor unit tracks the position of two light-emitting diodes (LEDs) embedded in the wand. By measuring the movements of the LEDs and how their sizes change as you move the wand toward or away from the unit, the Wii gauges direction and depth. Yang's probe, being developed by graduate student Jian Ren, looks like a miniature Eiffel Tower with a triangular base and sports four LEDson the bottom of the tower and the foot of each leg. Because the LEDs are at the back end of the probe, they would stick out and remain visible to the tracking camera while the tip is inside the body. As you manipulate the device, a computer follows the positions of each LED, showing the real-time movements on a monitor. The present design is

just a prototype—the tool a doctor would eventually use would likely be smaller and tailored to the specific medical procedure.

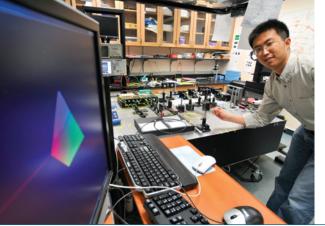
The researchers are now working with doctors to design an instrument for use in eye surgeries. Eye surgeons have to be especially precise, and so must their tools. Many of the probes now have a built-in laser to "see" what's in front of them, Yang says. But these devices have heavy, clunky mechanical parts—not exactly the sort of thing you'd want stuck through your eye. Yang's technology, on the other hand, would make for a light and maneuverable probe. The lab only started developing the device last fall, but the technology is straightforward, and Yang anticipates that doctors will be able to buy the tool in just two to three years.

A MICRO-MICROSCOPE

Another tool of Yang's has already made a splash: a lensless microscope small enough to fit on a microchip. The basic design of the optical microscope—a set of lenses magnifies an object and brings it into focus—hasn't changed in more than 400 years. The space between the lenses dictates that microscopes have to be a minimum size, and when it comes to technology, size often does matter—think ever-shrinking iPods and cell phones. To use the most powerful microscopes, which are too big to lug out into the field, you have to take your samples back to the lab. Yang's solution is the optofluidic microscope, a device that's about the size of George Washington's nose on a quarter.

The principle behind the optofluidic microscope is the same as that of the "floaters" in your eye. When you look at a clear, blue sky, you may notice small shapes floating around, seemingly in midair. Those shapes are shadows cast onto your retinas by debris floating around in the vitreous humor, the gel that fills your eyeballs behind the lens. You see floaters without the aid of lenses-in fact, floaters are just as much in focus whether or not you wear glasses. The particles are so close to the retina that they always appear sharp. In Yang's microscope, the specimen is suspended in a liquid and is drawn through a small channel either with an electric charge or by gravity. The object passes in front of a charge-coupled device (CCD), the "retina" that's the basis for all digital cameras. Some uniform light source-like the sun-then casts the object's shadow onto the CCD, which records the image. However, the resolution is limited by the pixel size, which is about five microns-not much better than conventional microscopes.

Yang's team solved that problem by stacking a metal sheet on top of the

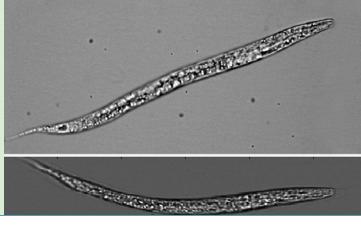




Far left: Graduate student Jian Ren demonstrates the biomedical probe based on the Nintendo Wii. The colorful image on the monitor represents the device, and as Ren moves the probe, the image mirrors the motion.

Left: Yang's probe technology could be used in surgical devices, like this one for the eye.

Images of the roundworm *C. elegans* taken with the optofluidic microscope (bottom) are comparable in quality to those taken with a conventional microscope (top).



CCD. The researchers punched a row of 600-nanometer-diameter holes in a diagonal line across the sheet. The specimen flows across the front of the holes, which operate like pinhole cameras. The holes are spaced five micrometers apart-the same as the pixel size-so that there is one hole per pixel, ensuring that each pixel receives a unique set of photons at a given time. But the key aspect is that the holes are diagonally offset, allowing them to cover the entire specimen while still making sure that each hole corresponds to one pixel. Each hole captures a different part of the object as it flows by, and software then puts the pieces back together to complete the picture. With this approach, the resolution is no longer limited by pixel size; the researchers can increase the resolution just by cutting a row of smaller holes closer together.

While conventional lab microscopes can cost thousands of dollars, the optofluidic microscope can eventually be massproduced for only \$10 a pop. Since it's small enough to put onto iPod-like devices, the microscope could have the biggest impact in developing countries, Yang says. Clinics in rural areas could use the microscopes to diagnose diseases like malaria, test blood and urine samples, and even test for harmful pathogens in food and water. In April, Yang and graduate students Lap Man Lee and Xiquan Cui published a report in Biomedical Microdevices showing that the device could take high-quality pictures of Giardia lamblia, a common water-borne parasite that wreaks havoc on the digestive

system. With some minor tweaking of their microscope, their images of the singlecelled bug were comparable with those from a conventional microscope, even resolving the organism's flagella.

Additionally, medics could keep the optofluidic microscope as part of their tool kits when treating soldiers in the battlefield. Future cell phones might even feature tiny microscopes as a way to protect against bioterrorism by continuously monitoring for harmful substances in the air. The device could also be a boon for biology. Imagine tens or hundreds of tiny scopes all on a small semiconductor chip, working in parallel, boosting the efficiency of researchers who have to make a large number of observations at once. For example, Morgan Professor of Biology Paul Sternberg and postdoc Weiwei Zhong, who are collaborating on the project, study genetic variations in a tiny worm called Caenorhabditis elegans-a process that involves gathering lots of data by watching dozens of individual worms for hours.

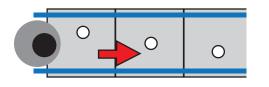
Yang's lab is now working with a semiconductor company to get the microscope mass-produced, and the scope should be commercially available within a couple of years. But although the microscope attracted a lot of media attention when the design was published last summer, Yang says many of his colleagues seem even more excited about a different project of his: finding a way to see through skin and flesh.

THE NO-SCATTERING ZONE

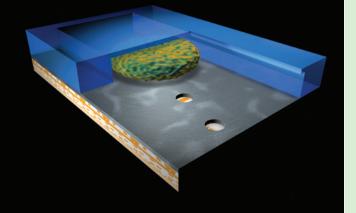
When a photon enters your skin, it bounces around the organelles in your cells, taking a meandering path like a drunkard getting lost in a dense forest. This "scattered" photon never returns to your eyes, so your body appears opaque. "If we can remove the scattering component," Yang says, "I should appear more or less like a jellyfish." But the ability to see through tissue isn't just some weird form of biological voyeurism-it would make treating ailments much less invasive. For instance, diabetics could check their sugar levels without having to prick a finger to test their blood with a glucose monitor-something they have to do as often as several times a day. "Optical approaches have been getting tantalizingly close to being able to detect glucose noninvasively," Yang says. Many researchers have been trying to pick out the few unscattered photons lucky enough to have penetrated the tissue and returned, but this method is limited-you can't go much deeper than a millimeter before the number of unscattered photons dwindles

altogether. Hundreds of ricochets may seem hopelessly complex and random. But it turns out that scattering is what physicists call deterministic. Every bounce can be described by the laws of physics, so if you know some basic information—the initial velocity of the photon and the characteristics of the tissue, for example—you can, in principle, recreate the photon's path. Returning to the analogy

to zero. Yang wants to eliminate scattering



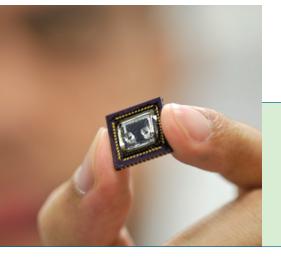
The diagonal arrangement of the holes allows the CCD to take a picture of different parts of the specimen at different times as it flows by. The diagonal arrangement keeps a one-to-one correspondence between each pixel and hole. Computer software puts the image slices together to create a complete picture.



of the inebriated wanderer, this means you can deduce a map of the lost drunkard's route. And by retracing his steps, he can find his way back out of the forest. If another photon could follow the same, exact path back out of the tissue, then it could enter your eyes, allowing you to see into the tissue. Of course, sitting around and calculating every photon's path would be impossible in practice. Instead, you can reproduce light paths with a hologram.

A hologram is a two-dimensional record of how light has traveled from an object. Analogous to a sound recording, a hologram allows you to "play back" a three-dimensional image. To make a hologram, you combine laser light passing through the object with another beam called the reference beam. The two light waves combine, making an alternating pattern of light and dark called an interference pattern. The pattern is recorded on a holographic plate, which then undergoes chemical processing to make the recording permanent-similar to developing a photo. Embedded in the interference pattern is information detailing the path of every photon. When a new laser light shines on the plate, the photons retrace the paths of their predecessors, recreating the threedimensional image of the object.

More than 40 years ago, Emmett Leith,



An up-close representation of the optofluidic microscope. The green specimen flows across the gray metal sheet. The detector underneath captures images of the specimen through the holes.

one of the pioneers of holography, used holograms to map the paths of photons scattered by a piece of ground glass. He then sent other photons backward from behind the glass to retrace those paths. Normally, a light beam shone through the glass would appear blurry. But those photons retraced the scattering path and made it through the glass, resulting in a sharp light beam. Leith had successfully cancelled out the scattering. Yang had wanted to try this with tissue since he was a graduate student at MIT, he says, and when he came to Caltech, he got his chance.

Changhuei Yang's skin and flesh scatters light, rendering him opaque. The jellyfish behind him does not, so it appears transparent.

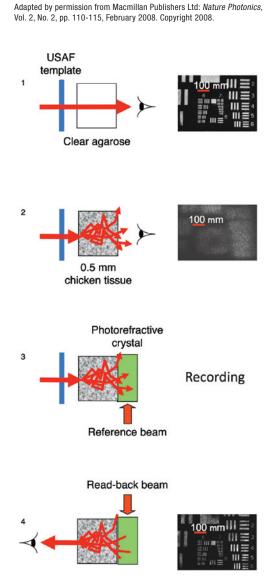


"If we can remove the scattering component," Yang says, "I should appear more or less like a jellyfish."

Traditional holographic plates must be removed from the apparatus for processing. But in order to ensure that the photons retrace the route taken by scattered light, you would have to put the plate back exactly where it had been so that all the light paths would line up—not an easy task. Yang's group uses a material called a photorefractive crystal, which doesn't need to be processed. The crystal takes a temporary snapshot of the interference pattern, which lasts for a few days. Then the team shines a laser through the crystal to retrace the scattered light paths, and a CCD captures the resulting image.

Graduate student Guoan Zheng (MS '08) holds up a microchip that contains the optofluidic microscope. In their initial experiments, the researchers, who include former postdoc Zahid Yaqoob; Demetri Psaltis, the former Myers Professor of Electrical Engineering and now at the Ecole Polytechnique Fédérale de Lausanne in Switzerland; and Michael Feld of MIT, tried their technique with a piece of chicken breast. To test how well they could retrace scattered light, they placed a special glass template in front of the chicken slice, which was less than a millimeter thick. The template—first devised by the U.S. Air Force and used to test the resolution of microscopes and cameras—lets in light through a

If you could send light deeply into tissue, then you might be able to stimulate the brain without wires—and without having to drill a hole in the patient's head.



simple pattern of rectangular windows. The team shone light through the template and into the piece of chicken. The light scattered, and a photorefractive crystal placed on the opposite side recorded the interference between the scattered light and a reference beam, which was hitting the side of the crystal. (See figure on the left). After removing the template, the researchers fired a different laser beam into the crystal, sending photons back through the chicken, retracing the scattered-light paths. In doing so, the photons recreated a clear image of the template pattern, which was recorded with a CCD. A proof-of-principle experiment, this was the first time anyone had lifted the blurring effect of scattering from biological tissue.

"When we started this, my expectations were fairly low," Yang recalls. Recording the complex process of scattering is a precise task, and he worried that if you couldn't capture every nuance and detail of the light waves, it wouldn't work. But they found the process to be much less sensitive than they had thought-it turns out that you only need to recover a fraction of a percent of the scattered light. The researchers also thought that when the light retraced the paths of the scattered photons, it would lose information along the way. But the team found that the quality of the reconstructed light was just as good as the original. Both results were pleasant surprises, giving Yang confidence that their technique would work well in realworld applications.

The researchers are moving beyond the simple setup of their first experiments, de-

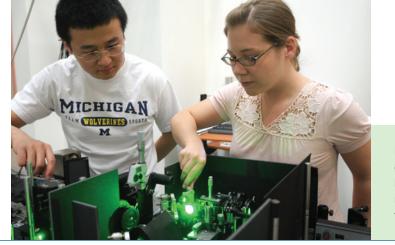
veloping a way to see through tissue without having to place a photorefractive crystal on its far side. If you want to look through skin to count glucose levels, for instance, you can't put the crystal underneath your skin and shine a laser from the inside of your body. The new method will involve shining weak light into the front of the tissue. Some of the photons will scatter and come back out—a process called backscattering—and the photorefractive crystal will record their paths. With a map to guide the way, the team can then shoot additional photons to light the way through the tissue.

Light with longer wavelengths goes farther before scattering. To see this, just cup your hand over a flashlight. Only the long-wavelength light makes it through your skin, so any part of your hand that's illuminated appears red—the color that corresponds to the longest wavelength in the visible spectrum. Using light at a wavelength of 500 nanometers—a blue-green hue—the researchers can deliver photons about one centimeter deep into tissue. They can go deeper if they use red or infrared light, but there aren't many photorefractive crystals that work at those wavelengths. One of the lab's goals, then, is finding better materials.

The team is also working on ways to reconstruct scattered light in real time, taking videos rather than snapshots. With this approach, doctors can examine moving specimens behind tissue, like blood flowing through veins.

You could put photons to work in other ways, too, such as fighting cancer with a

1. Light from the template that goes through a clear piece of agarose gel and straight to the eye is clearly visible. 2. When a piece of chicken is put in front of the template, the light scatters and the pattern is blurred. 3. A photorefractive crystal is inserted to record the scattered light. 4. Light sent through the plate retraces the scattered-light paths back into the eye, recreating the image of the templates.



Meng Cui and graduate student Emily McDowell reconstruct scattered light.

technique called photodynamic therapy, which is used for cancers like skin cancer and certain kinds of lung cancer. A doctor injects a patient with a dye that's absorbed by the body's cells. The dye sticks to cancer cells longer, and when only they still have the dye, the doctor shines a laser onto the cancerous area. With esophageal cancer, for example, doctors insert a fiber-optic cable into the esophagus to deliver the photons. When exposed to the light, the dye produces cell-killing singlet oxygen, a highly reactive substance. The problem, though, is that the light can only penetrate about a centimeter of tissue, making photodynamic therapy only effective for tumors near the surface. "If we have a technique that allows us to deliver light more deeply into tissue, then photodynamic therapy will have a broader range of applications," Yang says.

Another application is in treating Parkinson's disease. Helped into the public consciousness by the likes of Muhammad Ali and Michael J. Fox, this degenerative disorder makes movements slow and rigid. and causes the hands to tremble uncontrollably. Eventually, sufferers can no longer speak or walk. The disorder is caused by the lack of brain cells that make dopamine, an important chemical that relays signals in the nervous system. When drugs don't seem to work, an alternative form of treatment is to directly stimulate the brain with implanted electrodes. But if you could send light deeply into tissue, then you might be able to stimulate the brain without wires-and without having to drill a hole in the patient's head.

Sending photons into the body can also be a way to deliver power to implanted devices, Yang says. A pacemaker, for instance, could be outfitted with photovoltaic cells, and could be recharged by shining light through the chest. The technology isn't quite a solar-powered heart, but without the need for a large battery, smaller pacemakers would be less intrusive and easier to implant.

The lab is still laying the groundwork, and is years away from turning these ideas into marketable devices for doctors, according to Yang, but the work shows a lot of promise. "The problem of scattering is a big one, and there are tricks people can do" to get around it, he says. "But to tackle it head on, there aren't too many tricks. This one works quite well."

A WIDER FIELD

Postdoc Jigang Wu (MS '05, PhD '09) is spearheading yet another project, this one with more short-term goals. Conventional microscopes have a limited field of view, so Wu, who worked on the optofluidic microscope as a graduate student, is developing a new design that could have, in principle, as wide a field as you want without loss of resolution and magnification power. Like the optofluidic microscope, the wide-field design also does not use lenses.

The microscope consists of a holographic plate and a CCD, with the specimen sandwiched in between the two. The holographic plate is made so that when it's hit by a laser beam, it generates a grid of tiny light spots. The network of light spots scans the specimen, casting a shadow that's recorded by the CCD. The size of the holes determines the resolution, and you can enlarge the field of view by expanding the grid.

Yang foresees an immediate application for patients with advanced cancers. When cancer metastasizes, tumor cells leak into the bloodstream, spreading throughout the body. But finding them among a sea of blood cells isn't exactly easy-for every circulating tumor cell, there are 10 billion blood cells, Yang says. A wider field of view would improve the chances of a bad cell being included inside the frame. Yang is collaborating with Richard Cote, a pathologist and professor at USC, and Yu-Chong Tai, professor of electrical engineering and mechanical engineering, whose lab is building a tiny sieve to filter out most of the blood cells. This way, Yang says, the problem is more akin to finding one cell among 10,000. Even though Wu just started on the widefield microscope at the end of 2008, he should be able to have a working prototype within a year, he says.

From a gadget based on a video game to tiny microscopes and looking through chicken meat, Yang's research may seem playful. Indeed, he says he wants to develop gamechanging tools and techniques to improve the way people do biology and medicine. He got into the field because he wanted to make an impact, he says. "I wanted to do something useful, interesting, and tough" and that's hardly child's play.



The wide-field microscope. A laser is reflected down through the holographic plate, which is the square of glass seen in the middle. The specimen would go between the plate and the CCD, which is hidden below. Postdoc Jigang Wu looks from behind.

Spitzer in the infrared heavens, looking at a star-forming region called Rho Ophiuchi. The band of light is dust in the Milky Way glowing at a wavelength of 100 microns.

Spitzer Warms to the Task



Things are getting a little balmy for NASA's Spitzer Space Telescope. After almost six years, the infrared observatory's liquid mojo, its coolant, will run dry any moment now. But don't reach for the Kleenex—it will continue to peruse the cosmos in a "warm" mode for at least two years, with one of its three instruments still usable. (Incidentally, the so-called warm mode is still quite chilly. For most of the mission's life, it has been a frosty 1.5 kelvins—nearly absolute zero, or the temperature at which all atomic motion ceases. The warm mode is 25–30 kelvinsstill far more glacial than an ice cube, which freezes at a toasty 273 K.)

Spitzer's frigid life has warmed the hearts of astronomers around the globe. "Spitzer has been enormously productive and gratifying," says JPL's Michael Werner, Spitzer's project scientist. JPL manages the mission, and the Spitzer Science Center, which schedules observations and processes and disseminates the data, is on the Caltech campus. "For those of us who work on it, as Bobby Rydell sings, 'Every day's a holiday, and every night is Saturday night." The Spitzer Space Telescope ends its primary mission when the last of the liquid helium used to cool its infrared detectors runs out. Here's a look at just a few of the observatory's accomplishments, and a quick preview of what lies ahead as Spitzer moves into the extended "warm" mission.

Spitzer's launch, in August 2003, ended a nearly 30-year journey to get the telescope off the ground-a circuitous trek around budget cuts and other roadblocks that involved four top-to-bottom redesigns into successively smaller, less-costly spacecraft. [See E&S 2003, No. 4.] All that rethinking has proved to be good thing. The spacecraft has operated incredibly efficiently, filling the plates of astronomers from an all-you-can-eat buffet of data guaranteed to give overindulging grad students heartburn for years to come. The mission's sweetest treats include making the first direct measurements of light from planets circling other stars, finding signs of planets in very strange places, creating a new map of our Milky Way, and unmasking hundreds of "missing" black holes.

The carving knife, serving fork, and slotted

By Whitney Clavin

spoon that serve our astronomical gastronomes are a short-wavelength infrared array camera, a long-wavelength multiband imaging photometer, and an infrared spectrograph. These three instruments together span wavelengths from 3.6 to 160 microns (millionths of a meter) in the infrared region, which we humans can't see-infrared light lies just beyond red in the rainbow, starting at about 0.78 microns. Humans perceive infrared radiation as heat, and that's what it is: objects that are too cold to glow visibly shine in the infrared. Equally importantly, unlike visible light, infrared wavelengths are just right to sneak through much of the dust that chokes our galaxy and blocks our view. Thus Spitzer can have its cake and eat it, too. Depending on the wavelength being observed, the telescope can both see the dust that envelopes newborn stars and cloaks the farthest galaxies, or see through the dust to the stellar nurseries and other objects hidden within. Spitzer pries open the cold and dusty places where the universe's "dirtiest" secrets hide.

WEATHER ON EXOWORLDS

Millennia from now, when orbiting observatories litter the sky like space junk, Spitzer will ultimately be remembered for its pioneering research on exoplanets, planets circling stars beyond our sun. Spitzer is the first telescope to ever see the actual light from an exoplanet—an accomplishment that took everyone by surprise. "I was astonished that Spitzer could do this," says Werner. "We had no idea that this would be possible when we were designing and building it."

The first exoplanets were discovered in the early 1990s, well before Spitzer's launch, and now more than 350 are known. Astronomers typically learn of these alien worlds indirectly; for example, the most common planet-hunting tool is the radialvelocity technique, in which a planet is detected via the friendly tug it exerts on its parent star. The wobble is seen as a subtle shimmy in the position of the star's spectral lines. Most of these planets are "hot Jupiters"—portly balls of gas so close to their suns that their temperatures can be as

> high as 2,300 K. The tighter the orbit, the faster they go, so these hopped-up heavyweights whip feverishly around their stars in just days. Their masses make them easier to detect, but their speed helps too—since they complete each lap in a short time, you don't

have to watch very long for them to betray their presence.

When it comes to telescopes, bigger is usually better. Bigger mirrors catch more light. How then did Spitzer, with its relatively small, 85-centimeter primary mirror, see the shine of planets that bigger telescopes had not? The trick is to watch an exoplanet pass in front of, then disappear behind, its star. Currently, astronomers know of several dozen planets whose orbital planes just happen to be oriented edge-on to our point of view.

When a planet passes in front of its star, an event called a transit, some of the star's light travels through the planet's atmosphere en route to us. By comparing the starlight when the planet is in the way-like a rude moviegoer walking in front of the screenwith the starlight when the planet has taken its seat, as it were, astronomers can identify atoms in the planet's atmosphere. This is possible because every chemical has a unique spectral "fingerprint," absorbing a specific pattern of wavelengths of lightin this case, the light of the star shining through from behind. (NASA's Hubble Space Telescope first used this technique to identify sodium, carbon, and oxygen in a hot Jupiter called HD 209458b.)

Spitzer, on the other hand, can also watch planets slip around behind their stars. First, the total light from the star and planet is measured, followed by the light of just the star as the planet disappears from view. By subtracting the star's light from the system's combined light, astronomers are left with the

This false-color Mardi Gras mask is two galaxies, NGC 2207 and IC 2163, caught in the act of merging. The blue eyes are the galaxies' cores. Spitzer discovered the mask's strings of pearls, glowing red—dusty clusters of newborn stars that formed when the galaxies began their embrace 40 million years ago.



planet's contribution. The method works because planets, particularly hot Jupiters, are relatively bright in the infrared, where they yell, "Hey, look at me!" This lets us identify chemicals in a planet's atmosphere directly, and even take its temperature. Every body, including human ones, radiates over a range of wavelengths, and the colder the body, the longer the wavelength at which it emits the most energy. These ranges of wavelengths—so-called black-body curves—let astronomers act like exoplanet weathermen.

Not surprisingly, the weather varies widely from planet to planet. Some have split personalities—for example, a team led by Joseph Harrington of the University of Central Florida, and including Brad Hansen (PhD '96) of UCLA and six colleagues, measured a whopping 1,400-K temperature difference on the two faces of Upsilon Andromedae b. This planet, like all hot Jupiters, is thought to be tidally locked. Like our moon, it always presents the same face to the body around which it orbits. In this case, one side perpetually boils in its star's heat, while the other side never sees the light of day.

Other hot Jupiters are more even-keeled. Take HD 189733b, which has fairly uniform temperatures globally, though it too is locked in place. The team that made this discovery, led by Heather Knutson of the Harvard-Smithsonian Center for Astrophysics, included her Harvard colleague David Charbonneau, a former Caltech postdoc; Adam Showman (MS, PhD '99) of the University of Arizona at Tucson; Tom Megeath (BS '86) of the University of Toledo; and five other collaborators. They concluded that atmospheric circulation must carry the heat from the planet's sunlit side to its dark side, and forecast steady, supersonic winds of some 36,000 kilometers per hour. Chicago seems becalmed by comparison.

Spitzer also witnessed the fiercest storm ever seen. HD 80606b—a wildly eccentric planet whose orbit shuttles it nearly as far out from its star as Earth is from our sun, then back in to a distance much closer than from the sun to Mercury—was found to have a temperature swing of more than 700 K over the six hours when it passed closest to the furnace. Computer models predict this extreme heating triggers winds on the order of 18,000 kilometers per hour. The planet's rotation—HD 80606b is not tidally locked, rotating some 65 times per orbit—would curl these winds into megahurricanes that could toss all of Florida into Louisiana.

PALE BLUE DOTS

Just as biologists began by collecting trays of insects on pins and then moved on to classifying and studying individual species, astronomers are now sorting and cataloging populations of exoplanets. "This is brand-new science," says Werner. "At this early stage, the differences between our specimens loom larger than any underlying similarities." In a few years, NASA's James Webb Space Telescope will saunter onto the scene, and we'll get an even better look at many more specimens. The Webb should be able to pick out cooler gas planets farther from their stars, and possibly even analyze the atmospheres of planets only a few times larger than Earth.

But finding pale blue dots like our own will require different sets of eyes. Kepler, whose development was managed by JPL, was launched on March 6. [See Random Walk, page 6.] Kepler will look for Earthsized planets in the habitable zone-that perfect-day-at-the-beach part of a solar system where water is liquid-by watching 100,000 nearby sunlike stars for the periodic dimming due to transiting planets. After clocking the intervals between several transits, a process that will take a few years, Kepler scientists will be able to calculate each planet's orbital period and determine whether it is basking in the warm glow of the habitable zone.

Kepler won't do spectroscopy on the planets' light, however-that job will fall to NASA's Terrestrial Planet Finder (TPF), now in the very early stages of development at JPL. TPF's mission is to photograph small, rocky, Earth-like worlds and look for chemical signs of life in their atmospheres. The giveaway will be finding oxygen, water, and methane coexisting: water and oxygen for obvious reasons, and methane because it can be a metabolic byproduct. (See the SETI article on page 12 for more about this.) "The exoplanets we've been able to study in detail so far certainly don't have any beachfront property to buy up," says Charles Beichman, the executive director of



Caltech's NASA Exoplanet Science Institute and a Spitzer scientist. "But we will build on these studies to search for life in the universe."

PLANETS HERE, THERE, AND EVERYWHERE

For those of you who gaze up at the stars and hope with all your hearts that friendly little green aliens do exist, Spitzer has good news. It didn't discover life, or habitable planets, but it has revealed that building planets is as easy as growing weeds; and if planets are ubiquitous, chances are pretty good that life is too. Planets, like dandelions, crop up in the darnedest places—the infrared glow of planetary dust gives them away. Dust is a lot easier to see than a planet, because dust has more total surface area. Imagine that you're standing in the end zone at the Rose Bowl, and a pal under the

Top: This dusty star-forming region, called W5, covers four full moons' worth of sky in the constellation Cassiopeia. The two caves were hollowed out by the radiation pressure and stellar winds from the bright blue stars in their centers; this compression triggered a second burst of star formation—the pink dots on the tips of the dust pillars. A third wave of star formation is now happening in the white knotted regions. Right: A simulation of the swirling winds on the night side of HD 80606b after its closest approach to its star, based on Spitzer temperature data. The frames are spaced six hours apart.

Planets, particularly hot Jupiters, are relatively bright in the infrared, where they yell, "Hey, look at me!"

opposite goal posts is holding up a stick of chalk. You'd really have to squint to see it ... if you could make it out at all. But if your friend used that chalk to color in an entire chalk board, the white rectangle would be as plain as day.

Luckily for astronomers, planetary systems are dustier than the floor underneath your bed. As stars form, swirls of gas and dust begin to take shape in the so-called protoplanetary disks surrounding them. Denser regions—dust bunnies—become the seeds of planets. These seeds collide, sometimes sticking together to form larger bodies called planetoids. The planetoids, in turn, keep running into each other. Gentle fender benders result in mergers, eventually leading to full-grown planets. More violent encounters shatter the planetoids, forming debris disks of fresh dust.

Planets and debris disks can coexist, and the disks may be handy signposts for future planet hunters. Spitzer surveyed 26 nearby sunlike stars known from radial-velocity studies to have one or more planets, and found faint debris disks around six of them. These disks were 10 to 100 times thinner than protoplanetary disks-what Beichman, the study leader, calls "leftover piles of rubble." His 12 coauthors include JPLers Geoffrey Bryden, Karl Stapelfeldt (PhD '91), Christine Chen (BS '96), and Werner. More evidence for the link between disks and planets came from images from the W. M. Keck Observatory atop Mauna Kea and from the Hubble, when a nine-person team led by UC Berkeley's Paul Kalas and including

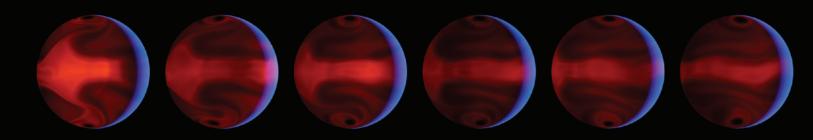
Eugene Chiang (PhD '00), Stapelfeldt, and fellow JPLer John Krist spotted a Jupitermass planet orbiting the star Fomalhaut just inside a dust ring detected by Spitzer.

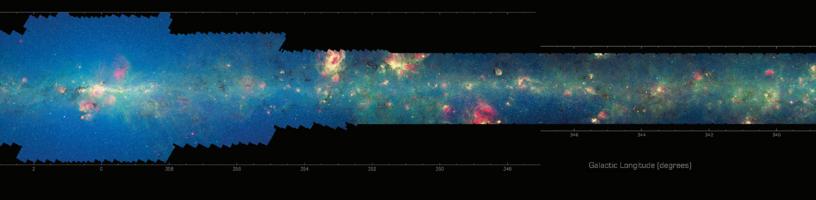
Another group, led by Michael Meyer of the University of Arizona at Tucson and including Caltech senior research associate in astronomy John Carpenter, associate professor of astronomy Lynne Hillenbrand, and member of the professional staff John Stauffer (plus 10 other people), looked at 309 stars of all ages but about the same mass as our sun, and found that at least 20 percent of them were swimming in dusty debris disks. The real number could be far higher-up to 60 percent, in some interpretations-and there are undoubtedly some stars whose dust is too faint for Spitzer to see. Other large studies have shown similar results. The inevitable conclusion: most stars are likely to have planets.

This includes binary, or twin, stars. Another Spitzer survey found that twins are at least as likely to host planets as are loners like our sun. There are more twins than singletons in the Milky Way, and therefore presumably in other galaxies, which means more prime real estate for planets. The universe may well be teeming with Tatooines, where a Luke Skywalker would see a stunning double sunset.

It turns out that the distance between the stars determines the likelihood of planet formation. Snug binaries like Luke's home system, separated by distances of under three astronomical units, and binaries that prefer a lot of personal space, with 50 or more astronomical units between them, are the most likely to parent planetary disks. (An astronomical unit is the distance between Earth and the sun.) Binaries at intermediate distances are nowhere near as planetfriendly, with very few of them having disks. This makes sense, as a planet could orbit a tight pair as if it were a single star, while a companion star 50 astronomical units away would be comfortably beyond Pluto's orbit, allowing planets to form undisturbed. "Binary stars may have to be very close, or very far apart, for planets to arise," says coauthor Stapelfeldt. "Location is everything." This seven-person effort, led by David Trilling at the University of Arizona at Tucson, also included Bryden; Andrew Boden, a member of the Caltech professional staff; and Beichman.

Spitzer even found disks swirling around brown dwarfs. Starting at about 10 times the mass of Jupiter, these lukewarm balls of gas could intimidate even the mightiest of planets. But compared to stars, they're downright puny, having only a few percent of the sun's mass. Brown dwarfs start out like stars, but never quite ignite. Yet the telescope not only found dust disks around brown dwarfs, it also detected signs that the planet-formation process is under way. And in one oddball discovery, Spitzer found a potentially planet-forming disk around a brown dwarf that itself could pass for a planet. At eight times the mass of Jupiter, the clumsily named Cha 110913-77344 is smaller than some known exoplanets. Could this little dude eventually become a





parent? And if so, what would you call the offspring—moons or planets? This team, led by Penn State astronomer Kevin Luhman, also included Tom Megeath.

"These brown-dwarf discoveries demonstrate the ubiquity of the planet-forming process and further blur the distinction between stars and planets," says Werner. "Brown dwarfs are about as common in our neighborhood as are all other types of stars put together, so it's entirely possible that the nearest exoplanets orbit brown dwarfs, not sunlike stars." Given that brown dwarfs may

Trying to map the Milky Way from here is a bit like trying to draw a blueprint of a house when you can only see the insides of a few rooms.

have entourages, could they be so gracious as to host life? A planet would have to snuggle up awfully close to be in the cozy habitable zone. "Our knowledge about planets and life is so rudimentary that anything is possible," says Beichman.

REIMAGINING THE MILKY WAY

At this point, you might be forgiven for thinking Spitzer is an exoplanet monomaniac. Not so—the telescope has also spent a lot of time on the rest of the cosmos, starting with our own Milky Way galaxy. For decades, astronomers have used radio telescopes to map out its structure—a difficult task, considering that we can't step outside it to see it whole. Worse, the galactic center is clogged with dust that blocks our view, not only of the middle but of what lies beyond. Trying to map the Milky Way from here is a bit like trying to draw a blueprint of a house when you can only see the insides of a few rooms.

Nevertheless, a picture eventually emerged of an elegant spiral galaxy with four long arms—named Norma, Scutum-Centaurus, Sagittarius, and Perseus after prominent constellations within them—wrapped around a slightly elongated core. Our sun sits in a relatively empty region between the Perseus and Sagittarius arms, in a small nub of an arm called Orion-Cygnus. Some astronomers suspected that the core was elongated enough to make the Milky Way a barred spiral, a hunch that was confirmed in the early 1990s when the first generation of infrared telescopes revealed the starlight from this bar.

Spitzer's observations confirmed and extended this elongation-and then came the bombshell. In a survey stretching almost halfway across the sky, Spitzer was able to get the best picture vet of three of the four arms. (Perseus was outside the field of view.) As expected, Scutum-Centaurus was jam-packed with stars old and young. However, Norma and Sagittarius proved to be mostly gas, with scattered clusters of young stars. Just like that, two big arms became vestigial, leaving Scutum-Centaurus attached to one end of the central bar, and Perseus attached to the other. But before you drop a bunch of money at your local observatory's gift shop on a shiny Milky Way map, keep in mind that it's still subject to change. Team leader Robert Benjamin of the University of Wisconsin-Whitewater, says, "We will keep revising our picture in the same way that early explorers sailing around the globe had to keep revising their maps."

ECHOES FROM THE BEYOND

Dying stars can go out with a bang. Literally. The details vary, but in general when a star more than about eight times the mass of our sun starts to run out of hydrogen fuel, it begins to implode until it gets hot and dense enough to start fusing pairs of helium atoms into carbon. When the helium runs low, the cycle begins again, turning carbon and helium into oxygen. The star works its way through the periodic table all the way up to iron, which won't burn. (Caltech physics professor Willy Fowler, PhD '36, shared the Nobel Prize in 1983 for working out the sequence of fusion reactions involved in this process.) The star implodes for the last time, crushing its interior into a neutron star or a black hole, while the outer layers rebound in a supernova explosion that can be seen across the galaxy.

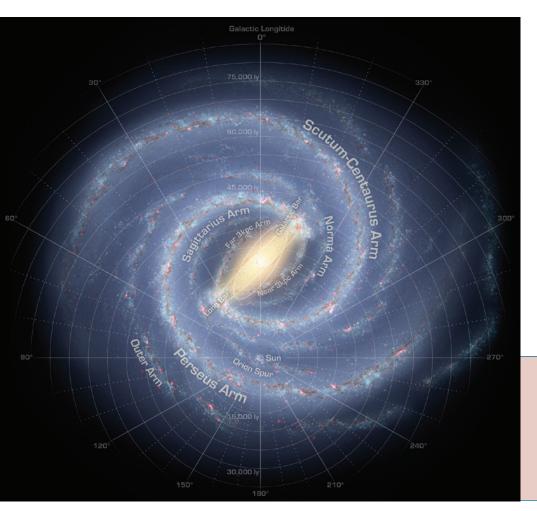
But some of the explosion's light can reverberate around the neighborhood, revealing secrets the star would otherwise have taken to its grave. We are intimately familiar with Cas A. as one supernova remnant is affectionately known, because at a mere 11,000 light-years away it is close enough for us to make out its fine details. Even so, we don't know what type of supernova it was, and thus what class of star Cas A was in life. The tangled, spherical structure we see today is a tombstone bearing a date of about 9300 BCE, when the star blasted itself into smithereens. And while this funerary monument has been carefully examined, the coroner's report was written in the light from the explosion that swept past Earth around 300 years ago. But Spitzer found that the blast had heated up adjacent dust clouds, causing them to reradiate infrared light that is just now reaching Earth.

By following the trail of the infrared echoes, astronomers were able to find similar visible-light echoes that solved the mystery of how Cas A died. The visible spectrum toe-tagged Cas A as a rare Type

Ilb supernova. This means that in life, Cas A was a bloated red supergiant star—ironic for a denizen of a constellation, Cassiopeia, named for a notoriously vain queen in Greek mythology. Fortunately, perhaps, for her self-image, Cas A shed several dress sizes before dying, shucking off her hydrogen envelope before her core collapsed in her final blaze of glory. Astronomers have since listened to similar ghostly whisperings from the remnants of other supernovas, describing the eerie details of their deaths.

WE ARE SUPERNOVA DUST

Joni Mitchell was right when she sang, "We are stardust, billion-year-old carbon," at Woodstock. The carbon, and essentially any other atom in our bodies that's not hydrogen, was smelted in the nuclear furnaces deep within stars—foundries that take about a billion years to work their alchemy. This stardust is then seeded through the universe in the explosions of dying stars that themselves formed out of gas clouds seeded with the dust from other dying stars. We can trace the dust all the way back almost to the very beginning of time . . . but here we have a problem. The primordial universe was hydrogen and helium. Nothing else. Stars



are born out of swirls of gas and dust when the force of gravity pulling in overwhelms the pressure of the gas pushing out. As the gas cools, the cloud collapses, and when it gets dense enough, nuclear fusion ignites. A thick blanket of dust speeds up the cooling by reflecting the ambient heat from other stars in the neighborhood that have already lit up, meaning that gravity triumphs more quickly and today's stars can begin to shine with relatively little mass. Bereft of dust, the earliest pioneers, called Population III stars, would have needed inordinate amounts of gas in order to collapse. They would have been behemoths that, when they did finally ignite, would have burned fast and furiously before their fiery demise.

Which brings us to the second part of the problem. When a star blows up, most of the heavy elements it has made remain in its former core. Proving that those first explosions would kick out enough dust to grow future generations of stars has been trickyuntil now. In another study of Cas A, Spitzer detected 10.000 Earths' worth of fresh dust in the clouds around her—3 percent of the sun's mass, and enough dust, in proportion, to have been an enormous help in the early universe. Since Cas A is so close, the team, led by Jeonghee Rho at Caltech's Spitzer Science Center, was able to map the dust onto the gaseous ejecta known to have come from the explosion, proving the two have a common origin. Member of the Professional Staff William Reach participated in the work, as did seven people from other institutions.

Top: A swath of the Milky Way from the galactic center (zero longitude) through the Norma and Scutum-Centaurus arms. The blue specks are stars, the green swirls are clouds of organic molecules, and the red and yellow knots are dust-rich star-forming regions. Left: The new, improved map to the stars' homes.



AS FAR AS SPACE TELESCOPES CAN SEE

Spitzer has also uncovered hundreds of millions of hidden, ravenous black holes. You can't see a black hole directly because it's, well, black, but when feeding, it betrays itself by belching. If a bright beam of visible light or X-rays makes it to Earth, we call the unruly diner a quasar. Other black holes are more discreet, concealing their gluttony behind blankets of dust, like Lewis Carroll's Walrus "holding his pocket handkerchief before his streaming eyes" so that the Carpenter couldn't count how many oysters he had eaten. These "missing" quasars have been at the top of astronomers' "most wanted" list for almost two decades.

Spitzer fingered many of the fugitives by picking up the glow of dust warmed by the X-rays, allowing NASA's Chandra X-ray Observatory to go back and find the faint, telltale signatures of the quasars lurking within. They turned up in droves-hundreds of them were found between 9 and 11 billion light-years away in one relatively small patch of sky. "Active, supermassive black holes are everywhere in the early universe," says Mark Dickinson of the National Optical Astronomy Observatory in Tucson, Arizona. "We had seen the tip of the iceberg before. Now, we can see the iceberg itself." Other team members included Spitzer Science Center staff scientist Ranga-Ram Chary, then-postdoc Minh Huynh, Member of the Professional Staff David Frayer, Niel Brandt (BS '92) of Penn State, and 14 others.

Once upon a time, before the age of black holes, the universe itself was black.

The Cas A supernova remnant, as seen by Spitzer (red), Hubble (yellow), and the Chandra X-ray Observatory (green and blue). The three telescopes are mapping temperatures ranging from a few hundred kelvins (Spitzer) to about 10 million K (Chandra).

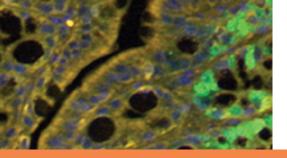
Almost completely black-no stars and no galaxies, just the remnant glow of the Big Bang, the colossal explosion that brought the universe into being. These "dark ages" arrived some 400,000 years after the Big Bang, when things had cooled enough that free-roaming electrons and protons could combine to form hydrogen atoms. As the cosmos continued to expand and cool, the young universe got socked in with a fog of cold hydrogen gas. And so things stood until the universe was about a billion years old, when the collective light of the very first star-making galaxies burned through, heating the mist like a warm spring sun. Spitzer, working with the Hubble Space Telescope and the W. M. Keck Observatory atop Mauna Kea, Hawaii, has spied some of these dark-age denizens-small galaxies compared to our Milky Way, yet teeming with stars. The infrared signatures show that many of these stars were already over 100 million years old when seen by Spitzer, meaning that star formation had kicked in surprisingly early.

Richard Ellis, the Steele Family Professor of Astronomy, has led several of these hunts, which have also variously included Daniel Stark (PhD '08), Member of the Professional Staff Mark Lacy, then-postdoc Johan Richard, visiting associate Jean-Paul Kneib, Michael Santos (PhD '04), and assorted people from other institutions. The galaxies lie so far back in time that the light they originally emitted at ultraviolet and visible wavelengths has been stretched into infrared by the expansion of space itself—in fact, they can't be seen at all with visible light. You find them by comparing an image from the Hubble or Keck, where they don't appear, with one from Spitzer, where they do. Because these galaxies are so far off, and thus so faint, Ellis and his colleagues often exploit a phenomenon Einstein predicted called gravitational lensing. If the ancient galaxy happens to lie behind a massive cluster of galaxies, the cluster's gravity will bend the light on its way to us, acting like a giant magnifying glass.

Studies like these will be a big part of Spitzer's "warm mission." The two shortest wavelength channels (3.6 and 4.5 microns) on the infrared array camera will remain fully functional, and in these wavebands Spitzer will still have the most sensitive infrared eyes around. The telescope will finally have the leisure to kick back and survey larger patches of sky for longer periods of time. In the process, Spitzer will continue to attack such questions as the fate of our expanding universe, whether Earth-like planets are common, and even how often we can expect big asteroids to bruise Earth. "We like to think of Spitzer as being reborn," says Werner. "The warm mission is very exciting because much of the science will be totally different from anything that we've done before-it's a brand new observatory." ess

Whitney Clavin is a science writer who shares her time between the Public Affairs Office at JPL and the Spitzer Science Center at Caltech.

This article was edited by Douglas L. Smith.



Say Hello to Your Little Friends

By Marcus Y. Woo

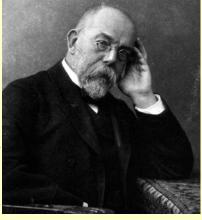
Bacteria are mostly known for making you sick. But not all microbes are malicious, and in fact, trillions of them live in your gut. It turns out that these bugs aren't just harmless, they may be crucial for your health.

Your bowels bustle with about a hundred trillion bacteria. That's 10 times more microorganisms than you have cells in your body. Put another way, if you had a buck for every bug, you could lift the U.S. federal government out of debt not once, but 10 times over. These intestinal bacteria consist of thousands of species, perhaps as many as 35,000. You may squirm at the thought of trillions of bugs crawling inside youafter all, bacteria don't exactly have a good reputation. These microscopic critters are known for causing deadly diseases, such as pneumonia, syphilis, cholera, tuberculosis, and meningitis. To counter these invisible scourges, people have developed antibiotics and an arsenal of disinfectant-laced household cleaners.

But those wayward pathogens in your bloodstream account for just a tiny fraction of bacteria. "I think we've done these organisms an injustice," says Sarkis Mazmanian, assistant professor of biology. "We group all of them as being bad, but it's really a small subset that are out to get you." The ones in your intestines are mainly harmless or even helpful. Some species assist in digestion while others monopolize the resources in

A cross section through a mouse colon. The tissue is stained so that immune cells that are influenced by beneficial bacteria glow green. your intestinal ecosystem and prevent bad bugs from colonizing. "To put things in perspective," Mazmanian says, "there are over 60,000 different species of bacteria that are known. Only 170 of them cause diseases in mammals. Only about 90 cause disease in humans." Some microbes, namely, those dubbed probiotics, help metabolism or provide nutrients—for example, people have long turned to yogurt, which has digestionaiding bacteria like *Bifidobacterium* and *Lactobacillus*, to settle the stomach.

But can these microbes act as more than just Maalox and multivitamins? "These are organisms that we've harbored for millions and millions of years," Mazmanian says. Because they have evolved with us, it's not hard to believe they've become an integral part of our biology. For at least two decades, scientists have been batting around the hypothesis that bacteria could keep people healthy, but the idea hasn't gained much traction for lack of evidence. "Even as recently as five years ago, it was not mainstream to talk about microbes as having benefits," Mazmanian says. But now, he and his colleagues have found that a common gut microorganism called Bacteroides



BAD BUGS

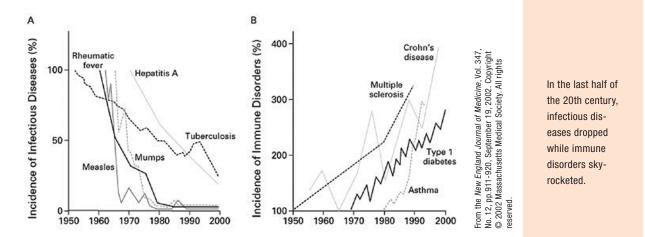
One of the founders of microbiology and the germ theory of disease was Robert Koch, a German physician born in 1843. In 1872, he became the district medical officer in Wollstein. a small town in present-day Poland. There, cut off from the medical community and armed with only some modest equipment in a small laboratory that doubled as his home, he experimented with anthrax, a widespread disease that was killing farm animals at the time. He confirmed earlier work by other scientists that a bacterium called Bacillus anthracis caused the disease. He also showed that the microbe alone-without having had prior contact with animals-was enough to trigger anthrax. Later in his career, Koch would also isolate Vibrio cholerae and Mycobacterium tuberculosis, the bacteria that lead to cholera and tuberculosis, respectively. For his work with tuberculosis, he would win the Nobel Prize in 1905.

Koch, along with others like Louis Pasteur-who developed pasteurization, the process that slows the growth of bacteria in milk and other foodsrevolutionized health and hygiene. As a result, new sanitation methods and antibiotics have saved countless lives. In 1900, Americans lived, on average, around 50 years. Global life expectancy was only 30. Now, life expectancy around the world is pushing 70, and is above 80 in some countries. And the fighting continues today-the 2005 Nobel Prize in Physiology or Medicine was given to Barry Marshall and J. Robin Warren for finding that many ulcers are caused by Helicobacter pylori. e&s *fragilis* prevents inflammatory bowel disease in mice—a seminal piece of evidence that shows bacteria boosting the immune system. These findings are spurring other researchers to study beneficial bacteria, revamping our perception of the microbial world. In recognition of his work, Mazmanian has been named as one of *Discover* magazine's "20 Best Brains under 40," a list of innovative scientists around the country who are changing their fields.

Inflammatory bowel disease, also called IBD, is a group of disorders whose symptoms include abdominal cramps, diarrhea, intestinal bleeding, and weight loss. Affecting about one million Americans, according to the Crohn's and Colitis Foundation of America, IBD is one of a handful of immunological disorders-chronic ailments that arise when the immune system goes awryincluding asthma, type-1 diabetes, and multiple sclerosis. If B. fragilis inhibits IBD, could it-or some other bug-mitigate those other diseases? No one knows yet how tiny bugs in the gut could so profoundly affect the rest of the body, and there's no evidence that bacteria cause any of these diseases. On the other hand, recent data have pointed to a puzzling pattern that suggests gut bacteria may be more important than scientists have realized.

Despite our improved overall health over the last century, immunological diseases have increased in recent decades, particularly in developed countries—places with superior health and sanitation systems. In a 2004 report, the Global Initiative for Asthma estimated that 300 million suffer from asthma around the world and 100 million more could become asthmatic by 2025. The report also noted that asthma increases as countries become more westernized and urbanized. Of course, the exact cause of asthma is a complex issue in itself (see E&S 2008, No. 3), and much of the increase might be attributable to rising air pollution. But studies show that other immunological diseases have also been skyrocketing. Multiple sclerosis increased by more than 300 percent from 1950 to 1990. Crohn's disease, one of the main forms of IBD, has gone up 400 percent in the last 50 years. Type 1 diabetes has risen by almost 300 percent since 1970. Meanwhile, infectious diseases caused by pathogenic bacteria are falling.

In 1989, an epidemiologist named David P. Strachan published a paper in the British Medical Journal proposing the so-called hygiene hypothesis. From studying hay-fever and eczema incidences in British children, he found that those from big families were less likely to develop the diseases-both of which are immunological. With more kids running around, bacteria get swapped like baseball cards. The immune system gets lots of exercise, and people harbor a more diverse population of bacteria. Was our overall improved hygiene as a society contributing to the proliferation of allergic diseases? In the past few years researchers have begun to find supporting evidence for Strachan's hypothesis, showing that a drop in gut bacteria accompanies the rise in



immunological disorders. Although no one has yet been able to show that one causes the other, scientists like Mazmanian think it's more than just a coincidence.

THE "FORGOTTEN ORGAN"

Autoimmune diseases strike when the immune system gets out of balance. The body is quite adept at ridding itself of nasty invaders, but our defensive system has its flaws. Instead of killing pathogens with precise, laser-guided missiles, the immune system might attack an entire area—or even the whole body. "The system realizes there's

Instead of killing pathogens with precise, laser-guided missiles, the immune system might attack an entire area or even the whole body. "The system realizes there's something to kill, and it just throws every weapon at it," Mazmanian says. something to kill, and it just throws every weapon at it," Mazmanian says, and healthy cells often become casualties of war. Running a temperature helps roast pathogens to death, but your entire body suffers as a result, and a prolonged fever can become life-threatening. Alternatively, the immune system may respond locally to an invader, but continue to attack even after the enemy has been eradicated. Sepsis is a menace in intensive care units—the immune system carpet bombs the entire body and everything becomes inflamed. The mortality rate ranges from 30 to 50 percent, and in cases of septic shock, the rate can be even higher.

In a healthy immune system, what Mazmanian calls the anti-inflammatory arm stops the system from damaging too many healthy cells. He and his colleagues discovered that *B. fragilis*, which he says lives in roughly 70 to 80 percent of us, helps regulate this. It turns out that if the microbe is missing, the gut becomes susceptible to IBD.

Mazmanian and colleagues first began research by raising mice from birth with no gut bacteria at all. Without their bacterial fauna—called the microbiota—the mice had deficient immune systems. Their lymph nodes and spleen follicles, which filter blood, were underdeveloped, and they had an imbalance of the immune cells called Th1 and Th2 helper cells. But when *B. fragilis* was introduced, these problems disappeared; the immune system healed itself. A sugar molecule—a polysaccharide called PSA, produced by the bacteria—turned out to be responsible. When given *B. fragilis* engineered to lack PSA, the mice didn't recover. The researchers also saw that PSA pumped up the production of an important family of immune cells called CD4 T cells, but nobody knew what this meant until later.

Published in 2005, these results were only general observations. Still, they allowed Mazmanian to ask the next question: can B. fragilis and PSA actually prevent or cure IBD? As Mazmanian points out, just because a roof looks like it has holes in it, you don't know for sure if it'll leak until it rains. So the researchers decided to seed the clouds. A microbe called Helicobacter hepaticus triggers an illness in mice that's reminiscent of Crohn's disease. The researchers used the bug to give mice IBD, and those colonized with B. fragilis and those injected with just PSA remained disease free. But mice that were colonized with the strains of B. fragilis that lacked PSA did get sick, showing that PSA was the crucial ingredient in preventing IBD. PSA molecules are captured by dendritic cells, scouts that scour the body for pathogens. The dendritic cells then tell the CD4 T cells mentioned above to become a more specialized cell subtype called the regulatory T cell. These cells produce anti-inflammatory IL-10 molecules. These molecules, small proteins called cytokines, are one of the ways the immune system stops inflammation. Without PSA, CD4 T cells can also become inflammationinducing helper cells called Th1, Th2, and Th17. In particular, Th17 makes an important pro-inflammatory cytokine called IL-17. Thus PSA restores the balance between

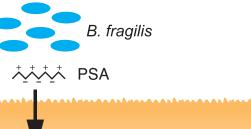
B. fragilis in the gut alleviates inflammation in mice by restoring a balance of immune cells. The microbe produces a sugar molecule called PSA. A scout-like cell called a dendritic cell (green) captures PSA and tells a T cell (orange) to become a specialized subtype called a regulatory T cell (yellow). Regulatory T cells produce a molecule called IL-10 that stops inflammation.

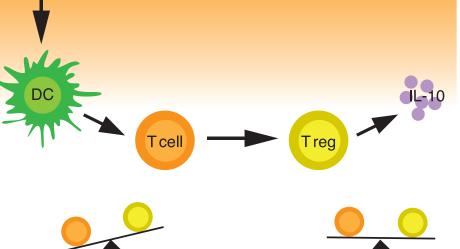
the pro- and anti-inflammatory arms of the immune system.

"Most people believe-and it's probably or partially true-that the absence of regulation comes from genetics," Mazmanian says. "We and a handful of other laboratories believe that certain bacteria are actually inducing those regulatory cells." If those bacteria are missing, the immune system becomes unbalanced, leading to the chronic inflammation behind IBD and other immunological disorders. The researchers call the gut's bacteria the "forgotten organ"-not just a mass of microbes that have tagged along for the ride, but an important part of our bodies. "I don't view any beneficial functions from these organisms as functions that we've turned over to them with time. I think they've been supplying these functions throughout our evolution."

The next step is to see if *B. fragilis* actually helps maintain a healthy immune system. "Is this the default?" Mazmanian says. "Is good health a result of the bacteria constantly sending these signals?" Experiments involving germfree mice are hardly realistic. The next set of experiments will involve regular mice with a complete set of microbiota, and the lab has already started the effort. But with thousands of species of bugs in the bowel, it won't be easy to isolate the effects of individual ones.

Says Mazmanian, "*B. fragilis* has had millions of years to figure out which molecules work and which don't, and how it's going to deliver them and in what doses—things that we think about now in terms of medicine, of





giving the right compound in the right way at the right time and at the right dose. But the bug has already figured this out, so we're trying to understand what the bug already knows, and to use that, to harness that, to exploit that as a therapy." In other words, the researchers want to reverse-engineer evolution's experiment.

LET'S GET DIRTY?

The first two years of a baby's life could be crucial. A fetus is germfree, but once it enters the world, bacteria begin to colonize the newborn's intestinal tract. After a couple of years, an infant's microbiota is the same as an adult's. "My leading theory is that everything happens in the first two or three years of life," Mazmanian says. "It puts you on a trajectory toward a balanced immune system or an inflamed immune system."

Which brings us back to the hygiene hypothesis. Our cleaner world has undoubtedly reduced infectious diseases, but at the same time, it's possible that our intestinal tract is not being colonized with the same bacteria we've had for millions of years. "What we've done as a society, over a short period of time, is completely change our association with the microbial world," Mazmanian says. "Our intention—the impetus—was to reduce pathogens, but antibacterial soaps, antibiotics, hygiene, and sanitation don't discriminate between bad bacteria and good ones. These organisms are just as sensitive to antibiotics as the *Strep* that gets in your throat."

Breeding germfree humans to replicate Mazmanian's mouse experiments has obvious drawbacks, but researchers have started to look for correlations between immunological diseases, such as IBD and asthma, and the patients' microbiota. Many years of measuring bacteria in infants, children, and adults may point to some immunological predictors—say, excesses of various inflammatory molecules—for these disorders. Recent studies have shown that people suffering from IBD harbor fewer microorganisms in their guts, according to Mazmanian. But because these studies are only snapshots in time, you can't distinguish cause from effect—either species of *Bacteroides* were somehow lost and then IBD ensued, or IBD created an environment in the immune system that's hostile to the bugs.

So far, the scientific community is still hesitant to fully accept that tiny organisms in your intestines could affect far-removed parts of the body like the lungs or the nervous system, according to Mazmanian. These ideas are highly speculative, but given recent progress in demonstrating just how helpful bacteria can be, they're not necessarily that wild. Consider B. fragilis's possible far-reaching influence-the dendritic cells could carry the PSA molecules elsewhere in the body to stop inflammation, while the microbe itself remains in the gut. "It's going against dogma to think that bacteria would help our immune system develop," he says. "Maybe it's because as humans, we're narcissists-we think we have everything we need."

In 2008, the National Institutes of Health started the Human Microbiome Project. The five-year endeavor seeks to compile the entire human microbiota in order to assess its role in health and disease. As part of the program, researchers will sequence 600 genomes of bacteria, and, in conjunction with other efforts, will put together a database of 1,000 genomes.

TRILLIONS OF LITTLE FRIENDS

The Th17 helper cell that makes the proinflammatory IL-17 molecule and gives rise to IBD also happens to drive asthma, type-1 diabetes, and multiple sclerosis. What effect might *B. fragilis* have on them? No one knows if the bug can lead to treatments for these diseases, but it's a question that begs to be answered. Meanwhile, Mazmanian is embarking on another direction that could point toward a potential treatment for colon cancer.

IBD increases cancer risk by as much as five times, and although 90 percent of IBD sufferers do not get colon cancer, the two diseases are closely related. In fact, H. hepaticus, the bacteria that induces IBD in mice, also gives them colon cancer. IBD constantly inflames and kills cells, prompting the body to regenerate them. Continual cell division means more mutations, heightening the chance of cancerous defects. "Constant inflammation actually feeds the cancer," Mazmanian explains. "What people have begun to realize in many types of cancer is that inflammation, though it may not be the cause, is critical for the progression." Could PSA, a natural anti-inflammatory molecule, prevent the disease from progressing?

Last year, the Damon Runyon Cancer Research Foundation awarded Mazmanian with a grant to try to find out. The private organization aims to support young researchers pursuing riskier lines of research—and linking colon cancer with bacteria certainly fits the bill. "There's no evidence at all, one way or another, that bacteria are involved in colon cancer in humans," Mazmanian says. "But just because people haven't looked doesn't mean it's not there." Mazmanian's group will remain focused on the immune system for the foreseeable future, but his basic goal is to understand the relationship between gut bacteria and health. As biologists are learning, that relationship appears to be quite intimate. So the next time you make a toast to good health, maybe you should also give thanks to your trillions of little friends within.

"It's going against dogma to think that bacteria would help our immune system develop," Mazmanian says. "Maybe it's because as humans, we're narcissists—we think we have everything we need."



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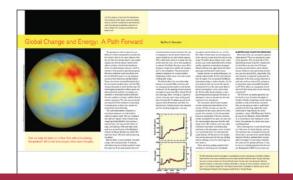
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LETTERS

Last issue's "Global Change and Energy: A Path Forward" by Paul Dimotakis (BS '68, MS '69, PhD '73) drew quite a number of comments, including at least one in the blogosphere ("Critical Section" by Ole Eichhorn, BS '79), http://www.w-uh. com/posts/090115a.html:

"Want to learn about global warming? Really? Then check out *Global Change and Energy: A Path Forward* (PDF) by Paul Dimotakis in Caltech's *Engineering & Science* magazine. He sets politics and sensationalism aside and honestly examines global warming from a scientific standpoint. This is the best analysis I've read, by someone who really understands the underlying science. (The punch line: global warming is real, it is exacerbated by human activity, and it isn't as bad as Al Gore thinks.)"

Not everyone applauded. Peter Metcalf (BS '62) called it "junk science at its worst," saying:

"We know the British climate was warmer in Roman times, and in the times of the Norman Conquest than it is today. Although the CO_2 concentration in the atmosphere has increased a bit in recent times, and the temperature is currently going up a bit, there is little evidence that increasing CO_2 concentrations has a significant effect on the earth's temperature compared with, say changes in solar radiation. . . . Specific errors in the Dimotakis article include, but are not limited to, the following:

"• The phrase 'the CO₂ increase [is] traceable to fossil-fuel burning' is followed immediately by the counter example of thrusting tectonic plates.

"• The main greenhouse gas—water vapor—is not mentioned at all.

". The article included a material

balance showing that $[CO_2]$ generation from fossil fuels—6.3 gigatons (gt)—is absolutely trivial compared with total CO_2 generation (209 gt). And the material balance cited does not include 'thrusting tectonic plates' or volcanoes which are probably the biggest sources of CO_2 . As a chemical engineer with many years of experience in carrying out material balances, I cannot image attributing changes in the CO_2 concentration to such a small source of CO_2 as the burning of fossil fuel."

Many readers proffered their own paths forward, usually by endorsing solar or nuclear power.

Some were more visionary: Roy Britten, an emeritus senior research associate in biology, proposed fleets of millions of floating wind turbines to be distributed over hundreds of thousands of square kilometers and anchored to mid-ocean seamounts to harvest the steady energy of the trade winds.

Olivier Roy (MS '80) went even farther: "If a fraction (1% or maybe even less?) of the solar energy reaching the earth could be reflected on top of what the earth already reflects, the global energy balance between Earth and space would be slightly modified so that more energy leaves the earth than is captured. Say a satellite is sent to space and when in orbit, it expels particles . . . made of a light, highly reflective material like Kevlar.... The confetti would not be too much of a disturbance for people looking up in the sky if the cloud [was] loose enough, [and] the potential interference with geostationary satellites could be avoided if the orbit is at a higher altitude."

"This is the best analysis I've read, by someone who really understands the underlying science. (The punch line: global warming is real, it is exacerbated by human activity, and it isn't as bad as Al Gore thinks.)"

Professor Dimotakis replies:

Dear Editor,

Thank you to all the readers of E&S for their gracious notes and thoughtful discussion. I would like to reply to a few specifically here.

Roy Britten suggests that midocean wind turbines be used to electrolyze water to produce hydrogen that is then compressed and shipped to shore. From a thermodynamic standpoint, it would be preferable to produce work directly from the electricity, which can be done with high conversion efficiency. Hydrogen must be burned to produce work, with a much lower conversion efficiency. One can do better with fuel cells, but there's still an overall loss.

Olivier Roy proposes space-borne reflectors to help cool the planet. Other similar proposals have been put forth. Their main difficulty is the great expense of lofting the requisite mass, even to low-Earth orbit. However, if we fail to trim our carbon emissions, such ideas, generically referred to as geoengineering, may prove necessary.

Peter Metcalf noted that man-made carbon sources are a small contributor to the carbon cycle. He and others also noted that water vapor was not mentioned at all. Water vapor is, indeed, the most important greenhouse gas. However, its concentration is dictated by temperature; the atmosphere has access to plenty of water. Increase the temperature and water vapor content increases, and conversely. As a result, water vapor *amplifies* the greenhouse effect, but does not cause it.

Earth is a dynamic, chaotic system capable of large excursions-both ice ages and warming periods-without help from humans. The climate record indicates, however, that we are presently already experiencing warming outside that of human experience, with more anticipated even without adding to the human-emitted carbon that has already led to extraordinary atmospheric concentrations of CO_o. (See the figure at right.) Predicted temperature increases from this buildup-ranging from analyses done a century ago to those based on present-day computer modelscorrelate well with the rising concentrations of greenhouse gases from fossil-fuel burning. Such increases are above and beyond whatever nature doles out.

I would also like to acknowledge some more of the many people who contributed supporting material to the

* * *

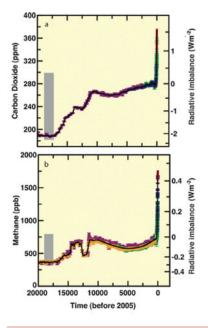
article, and correct or amplify a couple of points:

The Orbiting Carbon Observatory (OCO)'s principal investigator is David Crisp of JPL. OCO would have significantly reduced uncertainties in carbon sources and sinks on Earth's surface, providing important data on the carbon cycle. Unfortunately, OCO's launch on February 24, 2009, was unsuccessful. Indications are that the fairing on the Taurus XL launch vehicle failed to separate. A reflight is under consideration at this writing.

The Microwave Limb Sounder (MLS)'s principal investigator is Nathaniel Livesey, also of JPL. MLS measures the amount of atmospheric water vapor from about 9 kilometers up to about 80 kilometers. The Atmospheric Infra-Red Sounder (AIRS) measures water vapor from the surface up to about 11 kilometers. In combination, they measure water vapor from Earth's surface to the edge of space. When correlated with sea-surface temperatures estimated by other means (MLS does not measure sea-surface temperature), MLS and AIRS observations show an increase of cirrus clouds and water vapor over warm oceans, indicating that cloud and water-vapor feedbacks amplify global warming. Sources of sea-surface temperature data include the National Weather Service and AMSR-E instrument measurements on NASA's Aqua satellite. My thanks to Jonathan Jiang and Hui Su of JPL's Microwave Atmospheric Science Team for this.

CloudSat is operated by NASA/ JPL and Colorado State University. The principal investigator is Graeme Stephens of Colorado State. And finally, the results derived from the JPL-UCLA collaboration on water and the snow pack on the Sierras were based on model runs executed for the IPCC 2007 report. This analysis was performed by Duane Waliser of JPL.

Thank you again, Paul Dimotakis

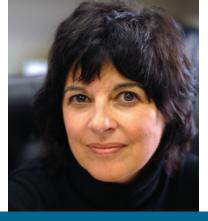


The left-hand scale shows the atmospheric concentrations of carbon dioxide (top) and methane (bottom) frozen into the ice and snow of Antarctica and Greenland over the last 20,000 years. The gray bars span the range of values recorded over the last 650,000 years. The right-hand scale shows the estimated radiative imbalance, or atmospheric heating, attributable to that gas at that concentration. Adapted from figure TS.2 of *Climate Change 2007: The Physical Science Basis. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change.*





FACULTY FILE



OBITUARY

THOMAS C. MCGILL

1942-2009

Thomas C. McGill, professor of applied physics, emeritus, passed away on March 19. He was born on March 20, 1942, in Port Arthur, Texas. He received his BS from Lamar State College of Technology in 1964, and his MS and PhD from Caltech in 1965 and 1969, respectively. In 1971, he was the first faculty member hired in the new discipline of applied physics. He was Fletcher Jones Professor of applied physics from 1985 to 1999 and became emeritus in 2008.

A pioneering researcher in semiconductors, he exploited such solid-state phenomena as Schottky barriers, heterojunctions, and superlattices, as well as his vast knowledge of the properties of amorphous materials, to develop devices for applications ranging from infrared detectors and high-speed memory chips to solid-state lighting.

McGill authored or coauthored hundreds of publications, and directed the theses of over 50 PhD students in electrical engineering, physics, and applied physics. He served for nearly 30 years as a consultant to the Defense Science Research Council of the Defense Advanced Research Project Agency, was a member of the congressionally mandated Semiconductor Technology Council, and served as chief of the Naval Operations Executive Panel.

He is survived by his wife, Toby Cone McGill, and two daughters, Angela McGill Avogaro and Sarah McGill.

TWO DIVISION CHAIRS NAMED

Ares Rosakis, the von Kármán Professor of Aeronautics and Mechanical Engineering, has been named chair of the Division of Engineering and Applied Science, effective May 1. Rosakis, an expert in the ultrafast fracture mechanics in materials ranging from airplane wings to the continental crust, joined the Caltech faculty in 1982. Since 2004, he has served as director of the Graduate Aeronautical Laboratories (GALCIT), where he spearheaded the creation of a new master's degree option in aerospace engineering and oversaw the remodeling of the Guggenheim Aeronautical Laboratory building to house it.

And Jacqueline Barton, the Hanisch Memorial Professor and professor of chemistry, has been named chair of the Division of Chemistry and Chemical Engineering, effective July 1. Barton's research focuses on molecular properties of DNA, such as how electrons can travel along the "rungs" of the DNA ladder, which may have implications for how cells find and repair damage to their DNA; and how small molecules containing metal atoms can recognize and bind to specific sites on DNA, particularly to mismatches that may promote cancer. She has been a Caltech faculty member since 1989.

HUANG ELECTED AAAS PRESIDENT



Senior Faculty Associate in Biology Alice Huang has been elected president of the American Association for the Advancement of Science for the year 2010–2011. A distinguished virologist, Huang has been a strong advocate for women in science throughout her career. She has also consulted on science policy for various governmental agencies in Singapore, Taiwan, and China. The AAAS is the world's largest general scientific society, with nearly 120,000 individual and institutional members.

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