SCHLINGER LAB DEDICATED

Caltech's third new building in as many issues of *E&S* opened its doors on a blustery March 9. Almost a decade in the planning, the Warren and Katharine Schlinger Laboratory for Chemistry and Chemical Engineering is Caltech's first new facility specifically and exclusively designed around the research needs of chemists and chemical engineers since the construction of the adjacent Noyes Laboratory of Chemical Physics in 1967. At the dedication, Warren Schlinger noted that there had been some growth in the years since he arrived on campus as a freshman in 1941, when chemical engineering "had a department made up of two professors and a secretary"—Katharine Stewart, whom he married the year he got his master's degree. (Schlinger contributed to the faculty's growth by staying on as an instructor until 1953.)

Like the recently opened Cahill and Annenberg buildings, the Schlinger Lab is on track to earn a gold certification under the LEED (Leadership in Energy and Environmental Design) Green Building Rating System. Besides using locally derived or recycled building materials, the Schlinger Lab uses 28 percent less energy and 30 percent less water than typical build-

From left: Will Webster (BS '49); Katharine Schlinger; Warren Schlinger (BS '44, MS '46, PhD '49); Chemistry and Chemical Engineering Division Chair Jacqueline Barton, the Hanisch Memorial Professor and professor of chemistry; and President Chameau cut the ribbon.

Above: Even while you're standing at a fume hood, the outdoors beckons. Below: The Grand Promenade. To see more pictures, check out the slideshow at http://images.caltech.edu/slideshows/Schlinger-architecture/.

ings designed for chemical research. Meeting the stringent energy savings required for a gold rating was particularly challenging, as the fume hoods gulp electricity 24/7.

Fume hoods, for the chemically declined, are the enclosed cabinets in which experiments are done. The front side of the hood is a shatterproof windowpane that can be raised for access or lowered until it is almost, but not quite, shut. Powerful fans up on the roof suck a steady draft of room air in under the sash and through the hood in order to keep noxious vapors away from the lab's occupants. The higher the sash is raised, the more air whooshes through the hood and the harder the fans have to work.

Above each of the Schlinger's hoods is an electric eye that constantly scans its vicinity. If nobody is around, the sash automatically lowers to the fully closed position, minimizing the volume of air being pulled in. (A second eye on the sash's underside keeps a lookout for protruding glassware or other objects, stopping the descent if the beam is broken.) This high-tech hood design was pioneered in Europe but is new to the States.

Another European innovation new here can be found in Schlinger's rotary evaporators, which are vacuum-assisted stills. Banks of rotovaps, as they are affectionately known, are essential to any synthetic-chemistry lab—whenever you dissolve something to make it react, you eventually have to get rid of the solvent in order to retrieve your product. A rotovap needs a strong vacuum to get the solvent out as fast as possible, which means either a centralized system with heavy-duty piping, or lots and lots of individual vacuum pumps—noisy, sewing-machine-sized beasts that like to leak their oil all over the lab floor. Instead, each of Schlinger's rotovaps gets its suction from a pump the size of a large paperback book, efficiently and quietly powered by the campus's compressed-air system.

Energy-efficient double-glazed floor-to-ceiling windows flood the labs with natural light, a feat that was made possible by relocating all the plumbing and ducting—normally carried from floor to floor by a "wet" wall—to within a set of elliptical pillars out in the central hallway. By contrast, the entire west facade of Noyes Lab is windowless, hiding the giant utility core that serves the labs. Schlinger's pillars, inlaid with green glass tiles, complement the rich maple accent panels and similarly hued flooring to give an effect reminiscent of the grand corridors of the *Queen Mary*.

Other eco-friendly features include a "bio-swale" on the north side that

collects the runoff from the adjoining planters, sidewalks, and parking stalls, filtering it naturally before returning it to the groundwater. There's also a dedicated room in the basement for collecting and sorting recyclables.

Weather permitting, you can even get in touch with nature without ever leaving the building. One entire wall of the first-floor classroom/conference room folds up into the ceiling like a set of glass garage doors, opening onto a courtyard.

As Division Chair Jacqueline Barton remarked at the dedication, "When you bring chemists and chemical engineers together in one laboratory, the results will be far greater than the sum of the parts." Schlinger's reconfigurable lab spaces will house the research groups of three chemists and three chemical engineers, working in fields ranging from drug design to pollution control. The Center for Catalysis and Chemical Synthesis will also move in, and there's enough room remaining for two new hires.

The building's architects, Bohlin Cywinski Jackson, are known for sustainable design and have done labs and other academic buildings across the nation. Rudolph and Sletten was the general contractor.

Besides the Schlingers, support for the building and its research was provided by the Gordon and Betty Moore Foundation, Will and Helen Webster, Victor and Elizabeth Atkins, the John Stauffer Charitable Trust, Barbara Dickinson, the Ralph M. Parsons Foundation, John Willard Jones (BS '41), Patricia Beckman, and Gregory P. Stone (BS '74, MS '74). — *DS* E&S

OF FLIES AND MEN

The poet and mystic William Blake saw a world in a grain of sand. A fly's brain is scarcely larger, yet Caltech scientists see in it a window for exploring the biological roots of our own behavior and emotions. The brain of *Drosophila melanogaster*, the common fruit fly, contains barely 20,000 neurons—yet two recent papers from the lab of David Anderson, Benzer Professor of Biology and an investigator with the Howard Hughes Medical Institute, offer glimpses into its genetic hardwiring that may throw light on what makes us tick.

For example, both inconsiderate boors and unthinking flies will elbow their way to the front of the press at a crowded lunch counter, causing the less assertive to go elsewhere. Now grad student Liming Wang and Anderson, writing in the January 10 edition of *Nature*, have identified an aggression-promoting pheromone that appears to help drive competitors away from a crowded piece of, say, overripe banana, and pinpointed the neurons in the fly's antennae that detect it.

Pheromones are chemicals used by particular species to communicate with their own kind, but proving that a pheromone released by the insects themselves—rather than being provided in a synthetic form by inquisitive scientists—normally controls aggressive behavior "required the ability to experimentally interfere with the insects' capacity to sense the pheromone," Anderson notes. "And that, in turn, meant identifying the receptor molecules that detect aggression pheromones, and finding the olfactory sensory neurons that express these receptors." According to Wang, the paper's first author, the only insect meeting these requirements was *Drosophila melanogaster*. "The genetic and molecular architecture of *Drosophila*'s olfactory system is well understood," he explains. "One can easily test whether a specific receptor or neuron is involved in a given behavior."

Wang discovered that 11-*cis*-Vaccenyl Acetate (cVA), a pheromone present in the male fly's cuticle, or exoskeleton, promotes aggression in pairs of male flies. An aggressive fly will "lunge," rearing up on its hind legs and snapping its forelegs down on its opponent. When Wang and Anderson added synthetic cVA to the "arena" in which combatant flies were tested, the frequency of lunges dramatically increased. Building on earlier work elsewhere that had identified cVA's receptors, Wang next showed that silencing the cVA-sensitive neurons in the antennae mellowed the flies out.

To find out whether natural cVA from other flies had the same effect, Wang and Anderson then trapped between 20 and 100 "donor" male flies—so called because they donate their pheromones into the surrounding environment—in a tiny cage surrounded by a fine mesh screen. The screen allowed the pheromones to escape, but not the flies. A pair of "tester" males would be placed on top of the cage, where they could sense the pheromone but not interact with the donors. "Remarkably," says

On March 9, Mylar dirigibles battled for the skies—or at least for the airspace within Brown Gymnasium—in "Revenge of the Hindenberg," this year's installment of the ME 72 (Engineering Design Laboratory) contest. For full coverage, see http://weblab.caltech.edu/features/16.

Anderson, "the presence of the caged donor flies strongly increased aggression between the tester flies, and this aggression-promoting effect increased with the number of donors." And again, the testers' testiness was assuaged by inactivating their cVA-sensing neurons.

Which brings us back to the lunch counter—or more aptly, the free food at happy hour. Male flies are attracted to food not only to eat, but also to mate with feeding females. And, of course, the more guys there are, the harder it gets to score. Since feisty flies tend to chase away their competitors, an aggression-promoting pheromone might keep the number of males down to an equitable level.

Wang tested this hypothesis by allowing a small number of flies to compete for a limited food supply, after genetically manipulating their cVA-receptor neurons to make them more excitable. The flies quickly dispersed. "They fought one another until a dominant fly became 'king of the hill' and drove the others away," Anderson explains.

According to Wang and Anderson, this suggests that when the population of male flies reaches a certain density, the concentration of cVA rises to a level that promotes aggression, forcing some of the flies off the food. Their departure decreases the ambient concentration of the pheromone, decreasing aggression. "The population becomes stabilized at an optimal density until more flies become attracted to the food, and the cycle repeats itself," says Wang.

Because pheromones evolved as "private" communications channels within a given species, it's unlikely the fly pheromone would work on us. However, that doesn't necessarily mean that humans lack aggression pheromones, Anderson notes. They've been discovered in mice, which are evolutionarily closer to us than flies, so it's possible we might have our own as well. But whether such pheromones can keep lines short at the buffet, Anderson remarks, "only time will tell."

Anderson's lab has also seen signs of a primitive emotion-like behavior, specifically a state of agitation, that might illuminate the relationship between the neurotransmitter dopamine and attention deficit hyperactivity disorder (ADHD). Most of *Drosophila*'s genes are also found in humans—including those for the neurons that produce dopamine and serotonin, both of which have been implicated in psychiatric disorders.

A team led by then-postdoc Tim Lebestky found that a rapid succession of brief, brisk puffs of air caused flies to run around their test chamber in what Anderson calls a "frantic manner" for several minutes after the last puff. "Even after the flies had calmed down," he adds, "they remained hypersensitive to a single air puff." These "hyperactive" flies were picked out from the crowd via an automated machine-vision-based system developed in the lab of Anderson's colleague Pietro Perona, the Puckett Profes-

sor of Electrical Engineering. These flies proved to have a mutation called *DopR* that inactivated a dopamine receptor known as D1—a result that was published in the November 25, 2009, issue of *Neuron*.

This discovery dovetails with what is known about ADHD, which is characterized by impulsivity, hyperactivity, and a short attention span, and is often treated with drugs such as Ritalin that increase dopamine levels in the brain. The way the mutant flies responded to the air puffs is, moreover, "reminiscent of how individuals with ADHD display hypersensitivity to environmental stimuli and are more easily aroused by such influences," says Anderson. Furthermore, ADHD often goes hand in hand with learning disabilities, and Anderson's collaborators at Penn State have shown that flies with the *DopR* mutation can't learn to associate a particular odor with an electric shock. They don't avoid the odor afterward, while flies without the mutation quickly catch on.

It's often assumed that ADHD kids have difficulty learning precisely because they are hyperactive and easily distracted. But this work shows that hyperactivity and learning disabilities are unconnected—in flies, at least. "We could separately 'rescue' the hyperactivity and learning deficits in a completely independent manner," says Anderson, "by genetically restoring the dopamine receptor to different regions of the fly's brain." If it turns out that ADHD works in a similar way, Anderson believes that it may be better to develop drugs to treat the two issues separately. The broad-spectrum pharmaceuticals now used to attack both at once tend to have undesirable side effects.

Besides Lebestky, Anderson, and Perona, the other people involved in the work are Caltech biology research technician Jung-Sook Chang, then-postdocs Heiko Dankert and Lihi Zelnik; Young-Cho Kim and Kyung-An Han from Penn State; and Fred Wolf from UC San Francisco.

That flies exhibit emotion-like behaviors controlled by some of the same brain chemicals as in humans "opens up the possibility of applying the powerful genetics of this model organism to understanding how these chemicals influence behavior through their actions on specific brain circuits," says Anderson. "While the specific details of where and how this occurs are likely to be different in flies and in humans, the basic principles are likely to be evolutionarily conserved, and may aid in our understanding of what goes wrong in disorders such as ADHD."

The research described in both papers was supported by grants from the National Science Foundation and the Howard Hughes Medical Institute.
—LO e&s

ANOTHER ALUM GOES TO WASHINGTON

The brain drain from Pasadena to Foggy Bottom continues. Karina Edmonds, MS '93, PhD '98, director of JPL technology transfer, joined the Department of Energy as its first technology transfer coordinator on April 12. She will work with the DOE's national laboratories to help accelerate the process of moving discoveries from the laboratory to the private sector.

Edmonds, an engineer by training, has held key technology-transfer positions at Caltech and JPL for over a decade. As director of JPL technology transfer, she was responsible for technology licensing, managing the JPL patent portfolio, and assisting Caltech/JPL start-up companies.

This is the first time the DOE has appointed a full-time person to fill the role, which was created by the Energy Policy Act of 2005. "I am pleased to have Karina join our team," says Energy Secretary Steven Chu, who was also Caltech's commencement speaker last year. "Having Karina oversee a coordinated, strategic effort on behalf of the department will help increase the rate of successful technology transfers, creating clean-energy jobs and providing more solutions to our energy challenges." *—AB* e&s

The six figures on Calder's arches represent (from left) Nature, Art, Energy, Science, Imagination, and Law.

CALTECH TURNS 100—AGAIN

Although founded in 1891, Caltech can once again celebrate its 100th anniversary. On June 8, 1910, the first building on the present-day campus was dedicated before local dignitaries and a large public audience. Dubbed Pasadena Hall (and renamed Throop Hall in 1920), it was hailed as a monument to civic pride. The first students to be educated in it arrived the following September—30 in total, all male, and all enrolled in a college-level engineering curriculum. Tuition was $150 annually.

Throop Polytechnic Institute, as it was then known, had just split apart at the seams. The old Throop had evolved into an agglomeration of six schools, teaching at levels from elementary to collegiate, with a heavy emphasis in the upper division on such practical skills as stenography, typing, and operating machine tools.

The leap from vo-tech to high-tech was the work of noted solar astronomer George Ellery Hale, who had come west in 1903 to be the founding director of the Mount Wilson Observatory. Hale was soon deeply in the flow of Pasadena's civic, cultural, and educational schemes, becoming a tireless booster of Southern California in general and Pasadena in particular. He soon became bent on establishing a local technical school to train engineers (construed at that time to mean men only) to meet the needs of a booming region—in particular, to bring water and electricity over the mountains to a sun-drenched but utility-starved Los Angeles basin. By 1907 he had begun a campaign for the creation of a "high-grade institute of technology" in Pasadena and was elected to the Throop board of trustees. In that same year, an anonymous benefactor secured a site for a new, expanded campus—some 22 acres of orange groves dotted with stately oak trees in the southeast part of the city.

Throop's original campus—acquired after a start-up year in the old Wooster Block, still a presence on the corner of Fair Oaks Avenue and Green Street in the heart of Old Pasadena—crammed all six schools into three buildings at Lincoln Avenue and Fair Oaks, a site that is today under the 210 freeway. Hale envisioned the new campus two miles east as an opportunity for an idealized building scheme in harmony with a new civic center, a campus whose laboratories would be fitted out with the latest and best equipment. Such an institute would redound to the glory of Pasadena and would surely inspire the generosity of Pasadena's well-to-do residents.

Hale was right. The mission-style structure by architects Myron Hunt and Elmer Grey was paid for entirely by local subscriptions, to the tune of approximately $165,000. The arcaded entrance was adorned by a set of reliefs created by Pasadena's Alexander Stirling Calder, whose son would invent the mobile. Touted at the time as the most significant artwork

Throop Hall (with Dabney Hall to the left) in April 1965. The president, the provost, the treasurer, and the deans had offices on the first floor. Various business offices—payroll, personnel, accounting, central files, and so on—occupied the second floor. Ed Hutchings, editor of *E&S*, lived in the basement with the news bureau, the alumni office, and most of development.

Throop Hall was demolished after the San Fernando earthquake, and the Calder Arches now adorn the facade of the Arnold and Mabel Beckman Laboratory of Chemical Synthesis. The Throop site is now a vest-pocket park in the middle of campus—a perfect place for a photo op. Here Lemelson winner Heather Agnew (right) and finalist Yvonne Chen enjoy their accolades.

in the city, the elaborate, allegorical figures were, in Calder's words, "to give plastic utterance to the aims and scope of the school."

The new building's 62 rooms housed what the 1910 catalog boasted as being "the only college devoted primarily to Technology west of the Mississippi River." Meanwhile, the other five schools were closed down or divested. The elementary school moved to a new location a block west of the new campus and became the Polytechnic School. Throop Academy remained at the old campus and eventually merged with a new public high school. And, after almost becoming UC Pasadena in 1911 and completing the Gates Laboratory of Chemistry in 1917, Throop College of Technology rebranded itself as the California Institute of Technology in 1920—so we have another 10 years to wait for that party.

An online exhibit about the 1910 campus may be found at the Caltech Archives website: http://archives.caltech.edu/ . —*SE* E&S

LEMELSON WINNERS ANNOUNCED

Deep in the Amazon, a woman is keeling over with stomach pains and vomiting. Does she just have the flu, or is she one of two billion people worldwide who has been afflicted with Hepatitis B, a potentially deadly liver disease? Today's diagnostic tools are too delicate for health workers to use in the steamy environment of a remote jungle. But in the future, a drop of blood from a prick of the finger and a cheap, simple device that works in nearly all conditions may change that. Heather Agnew (PhD '10) and Jim Heath, the Gilloon Professor and professor of chemistry, are working to make such devices a reality. For her role in this effort, Agnew has won the $30,000 2010 Lemelson-MIT Caltech Student Prize.

A diagnostic test, or assay, can measure the amount of a protein specific to some disease by allowing it to bind to another molecule, called an antibody, that is tailor-made to recognize it. Assays can be packaged into easy-to-use kits for diagnosis outside the lab, and they're not restricted to blood. For example, the home pregnancy test assays a hormone called human chorionic gonadotropin in urine.

The problem with such assays, though, is that the antibodies themselves are proteins, sensitive to heat, humidity, and other factors. For instance, HIV assays have to be performed within hours of opening the package or the antibodies degrade, Agnew says. But the developing world, which needs such simple diagnostic tools the most, isn't always air-conditioned. Furthermore, antibodies are expensive to produce. Today, many tests look for just one or two proteins, Agnew says. But diseases like cancer are complex, so an accurate diagnosis might require the measurement of more than a dozen proteins, each by its own antibody.

Agnew and her colleagues are building cheap, durable antibody replacements called protein-capture agents out of synthetic peptides, which are relatively short chains of amino acids—the building blocks of proteins. Peptides are cheap to make, and can be designed to have all sorts of nice properties, including heat resistance and biological or chemical stability. But since they're small molecules, they don't stick to their target proteins as well as antibodies do.

Reasoning that two peptides of middling stickiness might do the trick if they worked together, Agnew and her coworkers tested millions of them. And here the project got help from the target protein itself—when appropriately primed versions of the peptides recognized the protein and bound to it, it held them in just the right orientations that they could "click" together to create a new molecule that is 10 to 100 times better at binding to the target protein than

either peptide alone. Repeating the process to add a third peptide further enhances the binding.

As for durability, Heath's benchmark is what he calls the Pasadena Test: will it work even after a year spent baking in the trunk of his car? Agnew says her protein-capture agents have withstood airplane travel and years of sitting on a shelf in her office.

A second award of $10,000 went to Yvonne Chen (MS '07), a grad student working with Christina Smolke, a former assistant professor of chemical engineering at Caltech who's now at Stanford. Chen developed a way to help T cells fight cancer. T cells are a part of the body's protective army, and other researchers have been able to engineer them to attack cancerous tumors. "We can keep putting them in the blood supply until they home in on the tumor," Chen explains. "The problem is that they die really quickly." Because T cells are a part of the body's natural immune response, they die by default if they aren't instructed to attack. "Our challenge then is to figure out how to engineer this T-cell population to be sustainable so they can finish killing the tumor cells."

T cells are kept alive by molecules called cytokines. But you can't just inject cytokines into someone to keep the T cells going—you'd need a lot, and too much would put the patient into shock. One solution is to engineer the T cell to produce its own cytokines. But you also have to regulate cytokine production carefully, because an excess will cause the T cells to reproduce nonstop, resulting in leukemia.

With Smolke, Michael Jensen from City of Hope medical center, and other researchers, Chen made a molecule of RNA—which is similar to DNA—that acts like a switch, turning cytokine production on when exposed to theophylline, a caffeine-like molecule (see *E&S* 2005, No. 4). When the theophylline infusion stops, so does cytokine production, and the T cell dies. This is just a demo, as large doses of theophylline can cause an irregular heartbeat and even death. Fortunately, the RNA switch can easily be designed so that it responds to a harmless molecule, such as a vitamin. Chen is now working to make it more versatile and easier to control.

The Lemelson-MIT Caltech Prize is funded by the Lemelson-MIT Program, founded in 1994 by Jerome H. Lemelson to inspire young innovators. Chen's prize as a finalist was donated by Michael Hunkapiller (PhD '74). Lemelson-MIT student prizes are also at MIT, Rensselaer Polytechnic Institute, and the University of Illinois at Urbana Champaign. The Caltech prize was first awarded last year.
—*MW* E&S

VOYAGER NEARS THE LOCAL FLUFF

Our solar system is plunging through a vast cloud of wispy gas called the local interstellar cloud, also known as the "Local Fluff." About 30 light-years wide, the Fluff is made of 6,000°C hydrogen and helium. The Fluff is about twice as dense as the interstellar meduim surrounding it, and what holds it together has been a mystery—until now, thanks to a discovery by JPL's twin Voyager spacecraft.

By rights, the Fluff shouldn't exist. A group of nearby stars exploded about 10 million years ago, and the resulting blast of million-degree gas is now blowing past us. The Fluff is neither hot enough nor dense enough to withstand the onslaught, says Merav Opher, a former JPL postdoc now on the faculty at George Mason University. But in the December 24, 2009, issue of *Nature*, Opher and her colleagues reported that the latest data from Voyager 2 reveal a magnetic field strong enough to enable the Fluff to push back. "Voyager data show that the Fluff is much more strongly magnetized than anyone had previously suspected—between four and five microgauss," Opher told Science@NASA. "This magnetic field can provide the extra pressure required to resist destruction."

Previous estimates of the Fluff's field had been in the 1.8 to 2.5 microgauss range. By comparison, Earth's magnetic field is about half a gauss, or roughly a million times stronger.

Inside the Fluff—and encompassing us—is a 10-billion-kilometer-wide bubble called the heliosphere, which helps shield us from constant bombardment by high-energy cosmic rays from the depths of space. The heliosphere is kept inflated by the solar wind, a stream of charged particles emitted by the sun, so its size is determined by the balance of forces between the solar wind pushing out and the local interstellar cloud pressing back. In 2004 and

2007, respectively, Voyagers 1 and 2 crossed into the heliosphere's outer layers, a region called the heliosheath. (See *E&S* 2008, No. 3.) Once there, they could measure the size of the heliosphere, allowing scientists to calculate how much pressure the Fluff is exerting on it. This pressure, in turn, partly depends on the strength of the Fluff's magnetic field.

This discovery raises the possibility that other clouds in our galactic neighborhood are also strongly magnetized, and when the solar system collides with them, they will push back even harder. If the heliosphere is further compressed, more cosmic rays might reach Earth. "There could be interesting times ahead," Opher says. But there's no need to get out the tinfoil hats quite yet—we won't run into the next cloud for hundreds of thousands of years. —*MW* E&S

TUNE IN TO "TODAY"

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MONEY ON YOUR MIND

It's perhaps not surprising that aversion to losing money is hardwired into our brains, but a sense of fairness seems to be as well. These are just two results from recent work at Caltech's Brain Imaging Center, where a multidisciplinary team of biologists and social scientists are using functional Magnetic Resonance Imaging (fMRI) to map behavior onto brain structure with millimetric precision.

An fMRI scanner tracks blood flow in the brain as a proxy for brain activity. The test subject lies in the scanner and is then asked a series of questions or told to perform some other sort of mental activity, such as memorizing a list of names, while the experimenters literally watch him or her think. Many experiments use pairs of volunteers, each in their own scanner, trying to outwit each other in various strategy games where cash is on the line.

It turns out that the fear of losing money lives in the amygdalae, two almond-shaped clusters of tissue located in the medial temporal lobes. (The amygdala registers rapid emotional reactions and appears to play a role in depression, anxiety, and autism.) Benedetto de Martino, a visiting researcher from University College London; Colin Camerer, the Kirby Professor of Behavioral Economics; and Ralph Adolphs (PhD '92), the Bren Professor of Psychology and Neuroscience and professor of biology, found the seat of this fear by studying two patients whose amygdalae had been destroyed by a very rare genetic disease.

These two people, as well as other volunteers, were each given $50 in cash and then offered a series of bets on the outcome of a computer-generated coin toss. Each potential wager had the same odds, 50/50, but a different ratio of payout to loss. For example, you might get the chance to win $20 or lose $5 (a risk most people will accept), or you might stand to lose $20 for the same $20 return (a bet most people will decline). In general, people shied away from the prospect of large losses, so even the proposition of winning $20 versus losing $15 got few takers, "even though the net expected outcome is positive," Adolphs says.

Neither of the amygdala-damaged patients were fazed by the prospect of losing money, taking risky gambles much more often than control subjects. "We think this shows that the amygdala is critical for triggering a sense of caution," explains Camerer. This function, he says, may be similar to the amygdala's role in fear and anxiety. "Loss aversion has been observed in many economics studies, from monkeys trading tokens for food to people on high-stakes game shows," he adds, "but this is the first clear evidence of a special brain structure that is responsible for fear of such losses."

A paper on this research appeared in the February 23 issue of the *Proceedings of the National Academy of Sciences*. The work was supported by the Gordon and Betty Moore Foundation, the Human Frontier Science Program, the Wellcome Trust,

the National Institutes of Health, the Simons Foundation, and a Global Center of Excellence grant from the Japanese government.

Another study, by Professor of Psychology John O'Doherty, Camerer, then-postdoc Elizabeth Tricomi, and Associate Professor of Economics Antonio Rangel (BS '93), looked at the brain's reward centers. It's long been known that we don't like inequality, especially when it comes to money. Tell two people working the same job that their salaries are different, and there's going to be trouble, notes O'Doherty. "It's not just the application of a social rule or convention; there's really something about the basic processing of rewards in the brain that reflects these considerations."

The experimenters watched how the ventromedial prefrontal cortex (VMPFC) and the ventral striatum—two well-known reward centers in the brain—reacted to the prospect of being offered various amounts of money. But there was a twist—the 40 volunteers were paired off beforehand, and one person in each pair was given an extra $50 before the experiments even began. Then, in each trial, the pair would be told how much more money they could potentially get—from zero dollars up to another $50—in a payout scheme selected at random at the end of the run.

As it turned out, the way the volunteers—or, to be more precise, the reward centers in their brains—reacted depended strongly upon whether the volunteer was the "poor" or the "rich" member of the pair. "People who started out poor had a strong reaction to getting money, and essentially no reaction to money going to another person," Camerer says. "By itself, that wasn't too surprising." What was surprising was the other side of the coin—"people who started out rich had a stronger reaction to other people getting money than to themselves getting money. In other words, their brains liked it better when their poorer partner got the money."

"We now know that these areas are not just self-interested," adds O'Doherty. "They don't exclusively respond to the rewards that one gets as an individual." Instead, contrary to the prevailing wisdom about human nature, the brain evaluates the overall equity of the situation. "It shows that the basic reward structures in the human brain are sensitive to even subtle differences in social context."

Camerer, too, found the results thought provoking. "We economists have a widespread view that most people are basically self-interested, and won't try to help other people," he says. "But if that were true, you wouldn't see these sort of reactions to other people getting money." Still, he says, the rich may have been at least partly motivated by self-interest—or a reduction of their own discomfort. "We think that, for the people who start out rich, seeing another person get money reduces their guilt over having more than the others."

O'Doherty says that the next step is to attempt to figure out how these reactions translate into changes in behavior. "For example, the person who finds out they're being paid less than someone else for doing the same job might end up working less hard. It will be interesting to try to understand the brain mechanisms that underlie such changes."

These findings were published in the February 25 issue of *Nature*. The project was funded by grants from the National Science Foundation, the Human Frontier Science Program, the Gordon and Betty Moore Foundation, and the Caltech Brain Imaging Center. —*KS/LO* e&s

"People who started out rich had a stronger reaction . . . . Their brains liked it better when their poorer partner got the money."

GETTING INSIDE A FLY'S HEAD

What goes on in the tiny brain of a fruit fly? We're beginning to find out, now that Michael Dickinson, the Zarem Professor of Bioengineering, and postdocs Gaby Maimon and Andrew Straw have succeeded in recording the activity of individual brain cells as the fly flies. This is no mean feat, considering that each fly is only about 2.5 millimeters long.

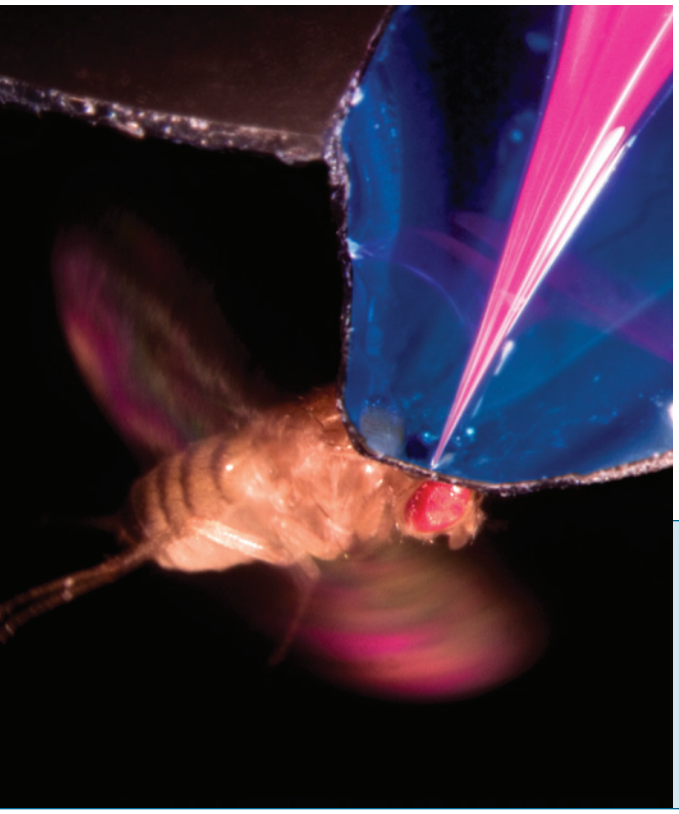
"Researchers have recorded the neural-cell activity of fruit flies before, but only in animals that had been stuck or glued down," Dickinson explains. "Gaby was able to develop a preparation where the animal is tethered"—its head clamped into place—"but free to flap its wings." By slicing off a patch of the hard cuticle covering the brain, "we were able to target our electrodes onto genetically marked neurons," he says. As the electrodes took data, high-speed digital cameras simultaneously recorded the flies' behavior.

The study focused on a set of visual-system neurons that "basically help the fly detect when its body posture changes" in order to maintain stable flight, Dickinson says. When the wings started flapping, these cells immediately ramped up their activity. "The neurons' responses to visual motion roughly double when the flies begin to fly, which suggests that the system is more sensitive during flight," Dickinson says. "The increase is very abrupt. It's not at all a subtle change, and so we suspect that there is a neurochemical quickly released during flight that sets the animal's brain in this different state."

Previous studies in locusts—which are far bigger and thus far easier to study—had suggested the existence of this effect. However, the genetics of locusts are not nearly as well understood as those of *Drosophila*. Now, says Dickinson, it should be possible to "figure out specifically what causes the change in sensitivity. Is the system turned off when the fly is on the ground? What neurochemicals are involved? We can use all the genetic tricks that are available in fruit flies to get a better idea of what is going on." Adds Maimon, "Sensory neurons in many species—including birds, rodents, and primates—change their response strength depending on the behavioral state of the animal, but why these changes take place is not entirely clear."

The researchers also plan to spy on olfactory and motor cells to see if they display similar behavior. "The question is, 'Is the entire brain completely different in flight?'" Dickinson says. "We suspect that this phenomenon is not unique to the visual cells we have studied. Most cells care whether the animal is flying or not."

A paper describing the research was published in the March issue of *Nature Neuroscience*; the work was funded by the National Science Foundation and a Caltech Della Martin Fellowship. —*KS* E&S



This fruit fly has a dye-filled glass electrode (pink) inserted into its brain. The fly's head is clamped to the underside of a reservoir filled with a sterile saline solution (colored blue here) that bathes the electrode and the brain. At rest, the fly clings to the reservoir; a gentle puff of air starts it flapping its wings in tethered flight.

OLD MAGAZINES NEVER DIE . . .

The Intel Science Talent Search, formerly the Westinghouse Science Talent Search, is to high-school science fairs what the World Series is to sandlot baseball. The grand prize is $100,000, and recent winners of this nationwide competition have done such things as creating a 50-gene model for predicting the probability of a specific colon cancer recurring, building a Littrow-type spectrograph, and designing a nanosensor for neurotoxins.

This year's top honor went to Erika DeBenedictis of Albuquerque, New Mexico, for "a software navigation system that would allow spacecraft to exploit low-energy orbits . . . for more efficient transit routes through the solar system."

DeBenedictis built on research by JPL's Martin Lo (BS '75 and a Science Talent Search winner himself), in collaboration with control and dynamical systems professor Jerrold Marsden's research group, on what Lo calls the "Interplanetary Superhighway"—a set of low-energy routes connecting every massive body in the solar system through the intersections of rotating Poincaré manifolds. In fact, Lo, a colleague of Erika's father, Sandia National Lab's Erik DeBenedicits (BS '78, PhD '83), helped her get started on a precursor project in 2007–8.

If the Interplanetary Superhighway sounds vaguely familiar, it's because an article on it appeared in *E&S* in 2002, when DeBenedicits would have been a fifth-grader. In a presentation she gave at JPL on April 15, she cited *E&S* as her inspiration.

Contacted by email, she elaborated, "I think what happened (as with most interesting science articles) was that I saw something I liked and asked my dad to explain it to me. That's why when I thought of it a few years later he remembered it too and was able to find it again.

"You would probably be surprised how much difference the articles you write make—*E&S* is one of my favorite magazines to flip through and look at the cool stuff."

DeBenedictis will be matriculating at Caltech in the fall, and hopes to work at JPL when she graduates.
—*DS*

MAKING BOOK ON THE LHC

As you no doubt know by now, the Large Hadron Collider, or LHC, is back up and running again at a stable, record-setting collision energy of seven trillion electron volts. The LHC was switched on with great fanfare in September 2008 (see "Beam On!," *E&S* 2008, No. 3) and shut down again nine days later due to a faulty electrical connection that led to a massive coolant leak and ultimately damaged 53 of the more than 1,600 superconducting magnets. It took over a year to repair everything, and the LHC was restarted again in November 2009, just in time for the regularly scheduled winter shutdown.

Caltech physics faculty, staff, and students pulled an all-nighter to watch the restart on a live video feed from Geneva, where the European Organization for Nuclear Research (CERN) and the LHC are located. And it was a long night—after two false starts, the countercirculating proton beams were finally brought into collision just after lunch in Switzerland, which unfortunately translated into 3:58 a.m. our time.

Meanwhile, according to a press release received by this office, a publicly traded Irish online betting firm named Paddy Power is laying odds on what the LHC will discover first. "The mysterious and previously undetectable form of matter known as Dark Matter is the red-hot 11/10 favourite, followed by Black Holes at 8/1 and Dark Energy at 12/1. God remains the 100/1 outsider."
—*DS*