an excerpt from the book proposal for *The Body Electric, the Shared Truths of Art and Science*

# the taste of protein

**What is it about denatured protein, the taste of life past, that we find so inexplicably appealing?**

**by Jonah Lehrer**

*...After all, Wordsworth and Coleridge wrote verse about chemistry experiments, the magic tricks of their day. Darwin was influenced in his idea of a continual creation by Milton. As recently as the 19th century, our two cultures dared to share their knowledge and assimilate their reflections. This dialogue of art and science is essential. All systems of truth should be interrogated by their antonym. To be meaningful, to be more than a mere physiological detail, the scientific molecule must be juxtaposed against the feeling, returned to its source. Despite the disparity of their languages, our separate cultures exist congruently, each requiring the other for completion...*

## the taste of protein

Sight is the newest of our senses. In the vast terms of evolutionary time, it is a rather recent invention. Smell, that most primitive of impressions, is our oldest sense. Even unicellular creatures have a way of breathing in their environment and "tasting it". Perhaps because olfaction seems so crude an input, cooking, that mirror to our tongue and nose, has rarely (at least outside France) been considered an art.

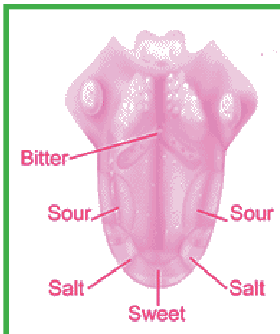
Nevertheless, the kitchen is a testament to our cravings. Behind the most elaborate of recipes lies the basic human need for salt, glucose and fat. The chef translates these basic needs into the artifice of deliciousness, creating an aesthetic space out of bodily requirements.

The history of that aesthetic space, the moment when people began paying large sums of money for a meal cooked by a stranger, begins in early 19th century France, with a one-time dishwasher. His name was Escoffier and he invented veal stock. Others had boiled bones before, but no one had codified the recipe. Before Escoffier, the best way to make veal stock lay cloaked in mystery; cooking was like alchemy, a semi-mystical endeavor. But Escoffier came of age during the zenith of positivism, a time when knowledge, some of it true, some of it false, was being made public at a dizzying rate. Encyclopedia's were the book of the day. And Escoffier wanted to do for fancy food what Lavosier had done for chemistry. And so a man who began his cooking career as an 8 year old dishwasher ended up forever changing the way we eat.

At the heart of Escoffier's insight (and the source of more than a few heart failures) was his use of stock. He put it in everything. He reduced to a gelatinous jello, made it the base of pureed soups, boiled meats in it and enriched it with butter and booze for sauces. But most importantly, Escoffier deglazed with his stocks. More than anything else, French food is defined by this very simple process. Essentially, deglazing is when a cook burns meat in a pan (to produce a nice seared Maillard Crust, a crosslinking and "carmelizing" of amino acids) and then adds a liquid. The *fronde,* the burned bits of protein that rise up from the pan (deglazing also makes life easier for the dishwasher) gives sauces their divine depth; its what makes beef *bourguignon*, *bourguignon*. Deglazing is why expensive menus the world over always are in French.

But what is it about stocks and deglazing that the tongue finds so delicious? They seem to appeal to no distinct part of our tongue, being neither sweet or sour or especially salty. So why does it taste so good? What does our tongue taste when we eat a spoonful of a viscous and profound beef daube, its deglazed bits simmered in wine and stock until the sinewy meat is appropriate for a spoon ? Or for that matter, what do we taste when we eat a smelly cheese? What is it about denatured protein, the taste of life past, that we find so inexplicably appealing?

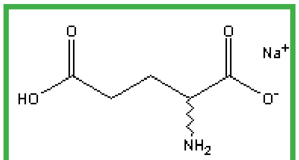
The answer is umami. The Japanese word for delicious, umami is an unlikely answer to Escoffier's insights. But, according to science, umami is what you taste when you bite into decay. To be precise, umami is actually the taste of L-glutamate, the dominant amino acid in the composition of life. L-glutamate is released from life forms by proteolysis (a shy scientific word for death, rot and the cooking process). It's only in its free form that you can taste it.



The taste map myth

The story of umami begins at about the same time that Escoffier invented Filet ala Rosselini, a filet mignon sauced with a reduced veal stock and a scattering of black truffles. The year was 1907 and Japanese chemist Kikunae Ikeda asked himself a simple question: what does dashi taste like? Dashi is a classic Japanese broth made from kombo, a dried form of kelp. It's used in Japanese cooking like the French use meat stock, as a universal solvent, a base for every sauce. But to Ikeda, dashi didn't taste like any of the four classic tastes or even like some unique combination of them. It was all of them at once, only more so. It was delicious. Or as the Japanese would say, it was *umami*.

And so Kikeda began his quixotic quest for this unknown taste. He distilled fields of kelp, searching for the essence that might trigger the same mysterious feeling on the tongue as a steaming bowl of soup. After patient years of lonely chemistry, Kikeda emerged with an odorless, white powder. It's name was monosodium glutamate. It was salty, but not like salt. Nor was it sweet, sour or bitter. But it was delicious. He named this sensation umami.



Monosodium glutamate.

Kikeda's research, while representing a potentially seminal finding in the physiology of taste, languished. His discovery was completely ignored; science thought it had the tongue solved. Umami these rational people said, was an idle theory unique to Japanese food, a silly idea concerned with something called "deliciousness", whatever that was. And so while cooks the world over continued to base entire cuisines on the use of dashi, parmesan cheese, tomato sauce, chicken stock and soy sauce (all potent sources of glutamate), science persisted in its naive belief in four, and only four, tastes.

Even more erroneously, science believed each taste was relegated to a specific section of tongue (ie, bitterness at the back, sweetness at the peninsular tip). No one seems to know why science perpetuated this myth, but it is completely wrong. Beyond a mild concentration of bitter receptors at the back of our tongue (poisons tend to be bitter so it should be the last thing we taste) our taste cells are equally distributed.

Despite the willful ignorance of science at the time, Kikeda's idea gained a certain cult following. His salty white substance, MSG, a powder that science said couldn't work because we had no means to taste it, nevertheless became an overused staple of cheap Chinese food (MSG was sold in America under the label "Super Seasoning"). With time, other pioneers began investigating their local cuisines and found their own densities of L-glutamate. Everything from aged cheeses to ketchup was rich in this magic little amino acid. Furthermore, its chemical discovery began to answer some of the culinary world's deepest questions: Why do so many cultures, beginning with ancient Rome, have a fish sauce? (salted, slightly rotting anchovies are like glutamate speedballs) Why does ketchup taste so good on French fries? (the L-glutamate in ketchup somehow heightens our sensitivity to all other tastes. Add ketchup and the fry becomes more French.) And of course, umami theory also explains Escoffier's genius. The burned bits of meat in the bottom of a pan are unraveled protein, dense in glutamate. Dissolved in the sauce, they fill your mouth with a now quantifiable deliciousness. Umami also explains why meat tastes so good. It's former animal, and is thus all amino acid. The Atkins diet should be officially renamed the "pure Umami diet".

So the culture of the kitchen had articulated a biological truth of the tongue long before science did solely because it was forced to feed us. It lived and died by the capricious whims of the tongue. But what every cook knew for sure, science was still denying. The taste of the delicious, said these lab coats, was all in our imagination.

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# Does Quantum Physics Set Us Free?

**By Kristen Fountain**

Prominent physicists Werner Heisenberg, Erwin Shroedinger, Albert Einstein, and Niels Bohr famously disputed the certainty of a particle's position.

You are rushing down College Walk, late for giving a class presentation when out of the corner of your eye you see a friend sitting bent over on the steps, her shoulders shaking, head in her hands. She didn't see you and would never know if you don't double-back. What do you do? We face this kind of mundane ethical dilemma every day. They are tough calls and most of the time, the decision could go either way. Or so it seems, until you start thinking like a scientist.

The mechanics of human thought are still incredibly murky. But inevitably choosing must happen in the brain. It has to involve the chemical signals flowing between our billions of neurons, prompting the in and outflow of positively charged atoms that is increasingly well described. A decision is a lightening-fast chain of events leading back to the initial stimulation of our senses and so is fundamentally predictable. With a large enough computer and perfect knowledge of your brain structure, I could theoretically know what your decision will be before you even make it. In the same circumstance, you will make the same decision over and over again. It actually couldn't have happened otherwise. Freedom of choice, or free will, is an illusion; our daily experience of choosing is just a trick of the brain.

That's one way of tying up a stubborn philosophical knot. The scientific worldview is phenomenally successful at helping us to understand and control the world around us. One of its pillars is that events are causally determined by past events. Under that paradigm, how can a person (a soul, a self) possibly be the sole cause of his or her own actions? Thinkers have been picking and pulling at the problem for centuries with the same arguments until the early twentieth century when the pillar started to crack.

A small group of European physicists found that causal relationships on incredibly small scales are not so straightforward. Paul Dirac and Pascual Jordan showed that only the mathematics of probability could describe the strange properties of photons and electrons. Then Werner Heisenberg argued convincingly that this statistical uncertainty is no sly mathematical tool: it is engrained in the dual nature of the quanta as both particle and wave. From that, his Danish mentor Niels Bohr concluded that it is impossible to pinpoint the location and momentum of a particle without abandoning the classical concept of deterministic causality.

Almost immediately, colleagues who indulged in metaphysics suggested that there is room for free will alongside the wiggle inherent to matter's basic components. Early famous converts to this idea were physicist Arthur Compton, the mathematician John von Neumann, and astronomer Arthur Eddington. Although the possibility has continued to enthrall philosophical physicists, few academic philosophers and neuroscientists are persuaded.

First, despite its experimental success, the ruling way of thinking about quantum mechanics, the so-called Copenhagen Interpretation, remains controversial. Albert Einstein was never happy with the notion that chance is an essential part of the fabric of the universe. God does not play dice, he said, and spent much of the rest of his life looking for the theory's missing components, the hidden variables that would return deterministic order to the quantum level. Then there is Schroedinger's bothersome cat.

Even Bohr agreed that classical Newtonian physics still is a workable theory for things larger than electrons According to the view out of Copenhagen, that's because footballs and pendulums contain gazillions of interacting quanta and uncertainty gets lost in the mathematical noise. However, quanta and everyday objects sometimes interact, particularly in the laboratory. What happens then? Irwin Schroedinger forced the issue by envisioning a cat inside a steel cage attached to a "diabolical device" with radioactive material inside that will release poisonous gas when an atom decays and an electron shoots off. Quantum orthodoxy says that at any given moment the atom both decays and doesn't decay and, implausibly, the cat is both alive and dead, fluctuating from one state to the other like an eerie flickering flame.

To give us free will, the indeterminate behavior of particles must affect similar large-scale items like proteins and cells. In the 1990's, two scientists suggested how in their best-selling books of popular science. The end of the line for a neuron is the axons, stubby splayed cul-de-sacs where neurochemicals jump to the branch-like dendrite receivers of a nearby cell. Axons are lined with a membrane just a few molecules thick involved in choreographing the leap. John Eccles, an Australian neuroscientist who won the Nobel Prize in Medicine, proposed that quantum-scale activity could be important in such a small space. For prominent Oxford physicist Roger Penrose, it all happens in the microtubules, long tubular molecules filled with water that are part of the supporting skeleton of the neuron. He suggests that particles in tubules throughout entire sections of the brain could achieve some form of the superconductivity seen in Bose-Einstein condensates, materials and liquids that have quantum characteristics. Eccles and Penrose are world-class scientists, but so far neurologists seem to think their hypotheses are as wacky as they sound.

By far the deepest problem with the idea that you can sneak free will through the backdoor of quantum physics is that its foundation is uncertainty and chance. The possibility that your decision is not fundamentally predictable still doesn't mean that you have any control over it. If quantum indeterminacy rules the brain, then in some versions of your run down College Walk you'll double back, in others, you won't. But so what? Randomness is not the same as freedom to choose. There is only one way to get freedom from quantum uncertainty. A mind or a self, some being that is more than molecules, has to be what ultimately collapses the wave and determines where the particle is going to be. Anyone satisfied with that result might as well look to Rene Descartes. His brand of dualism is much more straightforward and requires a lot less math. ■

*Kristen Fountain is in the science journalism program at the Journalism School. She earned a Master's degree in philosphy at Oxford, where she was a Rhodes Scholar.*

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## the taste of protein

What Kikeda needed before science would believe him was molecular evidence that the tongue could actually taste glutamate. Anecdotal evidence from cookbooks and all those who added ketchup to their fries wasn't enough. Finally, 95 years after Kikeda first distilled MSG from seaweed, molecular biology discovered a distinct receptor on everyone's tongue that only senses glutamate and L-amino acids. It is rightly named the Umami receptor in honor of Kikeda. The data, published in *Nature* by Greg Nelson et. al at UCSD, demonstrated once and for all that umami is not a figment of a hedonist's imagination. We actually have a sense that not only responds to shattered protein, but conveys a certain sense of the sublime. It brings the other disparate tastes into a coherent union, the memory of which makes us drool. It's probably responsible for why we like to eat.

This, of course, is all perfectly logical. Why wouldn't we have a specific taste for protein? We love the taste of decay, the flavor of denatured protein, because, being protein and water ourselves, we need it. (Species which are naturally vegetarian find the taste of umami repellent. Unfortunately for vegans, humans are omnivores.) The body, always practical, has a way of learning to love what it needs. And if, while feeding our bodies, we satisfy some other needs, like those for pleasure, our invisible umami receptors will be none the wiser. ■

*Jonah Lehrer graduated from Columba College in 2003 and is studying at Oxford University as a Rhodes Scholar*

# the colder sound of music

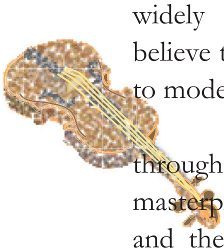
## How Europe's Little Ice Age may have caused Violin's Golden Age

**by Nan Ma**

*Research on the climate of seventeenth and eighteenth century Europe offers new explanations on why Italian violins made in this period are unsurpassed in quality.*

In 1802, Niccolo Paganini, barely twenty years old, was forced to pawn his violin after suffering heavy losses at gambling. With a concert to perform that night, the virtuoso violinist and composer borrowed a 1735 Guarneri violin, the now legendary instrument dubbed *the Canon*. The wealthy French merchant who lent Paganini the violin was enthralled by Paganini's talent and refused to take it back after the concert. *The Cannon* became Paganini's most prized possession. After his death, Paganini's violin was bequeathed to the city of Genoa, his hometown, where it has been preserved in a bulletproof vault in the town hall. In the rare event that the violin leaves the vault (as only one musician a year is chosen to play it), Paganini's famous violin travels with armed police, flashing lights, and numerous caretakers.

Similar protection and esteem is afforded to other fine Italian violins of the 17th and 18th centuries, instruments that now easily sell for millions of dollars and are among investments which have appreciated the most in the last thirty years. The art of violin making reached its unsurpassed peak in the city of Cremona, Italy during this period in the workshops of Nicolò Amati, Giuseppe Guarneri, and the more widely known Antonio Stradivari. Most experts believe that these violins are superior in tonal quality to modern ones.



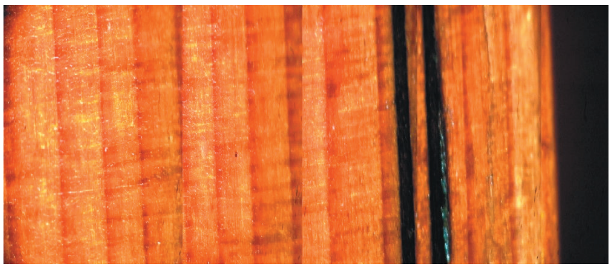
A great deal of work has been done throughout the years to emulate the sound of the old masterpieces; experts have painstakingly measured and then reproduced every dimension of the old violins. They have conducted various analyses of the varnishes to determine their content. They have made sound plates to match exactly the vibrational patterns of the Stradivari. However, despite centuries of persistent effort, no one has quite been able to figure out the mystique behind the Cremonese violins, and why exactly modern instruments just don't sound as good.

Explanations have ranged from the meticulous craftsmanship (Stradivari was known to spend over six months in creating a single violin) to the special treatments applied to the wood (as claimed by Joseph Nagyvary in 1977, who believed that the chemical properties of the violin were at least as important as the craftsmanship, an idea that incited the musical world). Instruments makers have laid claim to much of centuries old timber lost off ships and still sitting at the bottom of lakes for salvage divers to bring up for a hefty price. They believe that treating this old growth timber in water for over a hundred years allows the resin and starchy matter in the wood to seep out, creating better sounding instruments.

Recently, researchers at the Lamont-Doherty Earth Observatory (LDEO) at Columbia University and the Laboratory of Tree Ring Science at the University of Tennessee have come up with a novel alternate theory. These scientists also believe that the secret is in the wood, but instead of looking towards mysterious treatments and varnishes, they have focused instead on the wood itself and the trees that it came from. They propose that the wood used to make the famed violins were denser and of better quality than what we would find today due to a cold spell that gripped Europe during that time.

Lloyd Burckle, a geologist and senior research scientist at the LDEO studies past global climate change. He, when doing what he calls "idle time research," was first to make the connection between a period of very cold weather in Western Europe and the prime days of violin making. Beginning around the 15th century and lasting until the late 19th century, glaciers advanced in Europe, Asia, and North America in what is known as the Little Ice Age. Average air temperature dropped one to two degrees around the world.

The coldest of this period, known as the Maunder Minimum spanned from about 1645 to 1715. Physicists estimate that during this period, the sun was about a quarter of a percent dimmer than usual. The leading explanation for this reduced solar activity is the dramatic scarcity of sunspots during the Maunder Minimum. Scientists have found that periods of increased sunspot activity usually correspond to warmer temperatures here on Earth.



Rings on Stradivari's *Messiah*. Photo courtesy of Henri Grissino-Mayer.

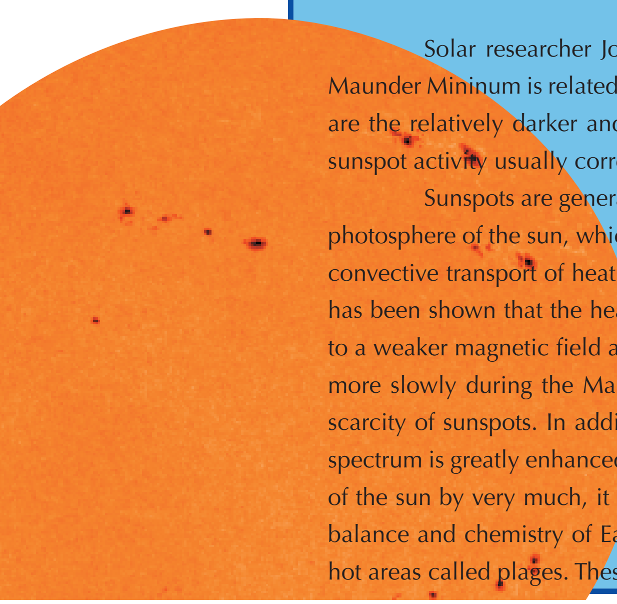
Though it is the leading theory, scientists have debated whether the absence of sunspots was principally responsible for the climate change. Some have instead looked towards more terrestrial causes such as increased volcanic activity or changes in ocean circulation for an explanation. Whatever the cause was, the bitterly cold and long winters of the Maunder Minimum distinctly affected tree growth in Western Europe.

Burckle figured that Stradivari, who interestingly was born in 1644, a year before the Maunder Minimum began, must have used spruce from the nearby Italian Alps. He wondered if the unusually cold climate affected the spruce, the universally preferred wood of instrument builders for constructing the soundboards of not only violins, but pianos, harpsichords, guitars, mandolins, cellos, violas, lutes, basses.

For more help in developing this theory, Burckle contacted Henri D. Grissino-Mayer at the Laboratory of Tree Ring Science, a dendrochronology expert who had a few years ago authenticated the most renowned violin in the world, Stradivari's *The Messiah*.

In tree rings are written perfectly preserved history lessons; a journal of sorts, in which is recorded the lengths of the seasons, the amount of rain, the frequency of fires. One tree ring is produced by a tree per year, and it consists of two layers. The inner layer, the *earlywood,* is made of larger thin-walled cells earlier in the spring. The outer and more dense layer, the *latewood,* is made of smaller thicker-walled cells and produced later in the summer. Together, these two layers represent the annual growth of the tree.

Experts by observing these tree rings can



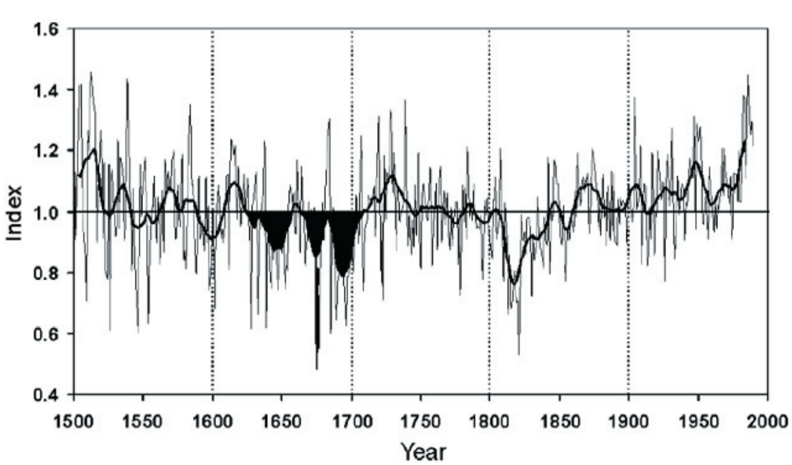
## Less Sunspots, Colder Temperatures?

Solar researcher John Eddy speculated in 1976 that the cause of the reduced solar activity during the Maunder Mininum is related to the drastically reduced number of sunspots during that period. Even though sunspots are the relatively darker and cooler regions on the surface of the sun, scientists have found that periods of high sunspot activity usually correspond to a slight increase in the energy output of the sun.

Sunspots are generated by toroidal magnetic fields (with field lines parallel to the sun's equator) below the photosphere of the sun, which are brought to the surface by buoyancy. The strong magnetic field interferes with the convective transport of heat to the surface, causing the sunspots themselves to be darker and cooler. However, it has been shown that the heating of the sun's atmosphere is magnetic. Thus, reduced sunspot activity corresponds to a weaker magnetic field and lower temperatures. Evidence has been found suggesting that the sun was spinning more slowly during the Maunder Minimum, and as a result had a lesser toroidal magnetic field, explaining the scarcity of sunspots. In addition, during periods of heightened sunspot activity, the ultraviolet region of the solar spectrum is greatly enhanced. While increased ultraviolet radiation from the sun does not change the energy output of the sun by very much, it may have a significant effect on the atmosphere of the Earth, especially in the energy balance and chemistry of Earth's outer atmosphere. Also, darker sunspots are surrounded by bright and intensely hot areas called plages. These may also contribute to the increased luminosity of the sun study and reconstruct past climate. Grissino-Mayer was able to develop a 500 year standard tree-ring index chronology, from 1500 to the present day by combining chronologies of 16 individual high elevation alpine forests ranging from Western France to Southern Germany. This composite chronology incorporates information from hundreds of trees of three different species- European larch, Norway spruce, and Swiss stone pine. Grissino-Mayer discovered from this chronology a period of unprecedented slow growth that coincided with the Maunder Minimum.

Trees under warmer conditions grow faster, producing softer and more porous wood. Violin soundboards, which enable the instrument to project amplified vibrations of musical notes, constructed from these less dense woods produce a dull, muffled sound. These softer woods also tend to be self-dampening, limiting the resonance of the instrument.

During the longer winters and cooler and wetter summers of the Maunder Minimum, trees underwent slower and more even growth. The tree rings were markedly narrower and more compact,




Standard tree-ring chronology composed from 16 high elevation pine forests in central Europe. The bold line represents an 11yr moving average that accentuates the low frequency trends. The Maunder Minimum is shaded. Burckle L, Grissino-Mayer, HD, 2003. *Stradivari, violins, tree rings, and the Maunder Minimum: a hypothesis*. Dendrochronologia, 21/1: 41-45

but the climate change also offset the normal ratio of earlywood to latewood, leaning more towards the latter. The wood was thus stronger and denser.

Burckle and Grissino-Mayer propose that the climate of the Maunder Minimum provided the ideal wood for the superior tonal quality and resonance found in Stradivari and other Italian violins.

So far though, this theory has received a lot of attention, both from the scientific community and the violin making community. The latter, just as they had reacted after Nagyvary's proposal, are according to Grissino-Mayer "harsh and vocal," in their criticism of the theory," insisting that "no way could the Maunder Minimum have caused the superior tone in violins."

This proposal at present is still just a hypothesis. "We're hoping other scientists and acoustical engineers will test this hypothesis," Grissino-Mayer says. Regardless of whether the proposal will test true or not, Grissino-Mayer will be satisfied with his work. "This is the whole point of being a scientist," he says, "-to generate new science."

Many other proposals suggesting that factors external to the craftsmanship of these violins are responsible for their exquisite quality have proven false in the past. Burckle believes however, that even if his hypothesis does not hold after experiment, there still must be some other explanation. "...Violin makers of this day are every bit as careful and artistic,

In tree rings are written perfectly preserved history lessons; a journal of sorts, in which is recorded the lengths of the seasons, the amount of rain, the frequency of fires....

so if Stradivarius are better, there must be some other explanation," Burckle explains.

If however the hypothesis is proven true, that climate indeed had a profound effect on the quality of the wood, such a revelation would suggest that much of the allure of the Cremonese violins could be attributed to happenstance. The master violin makers, under this scenario, used the only wood available to them, and they lucked out because the wood was a perfect product of the unusual climate. This, however, still should not discount the mastery of Stradivari, Guarneri, and others. Surely, the nature of these prized instruments, bordering on the mystical, will never completely be reduced to science. Nineteenth century British novelist George Eliot writes:

*'Tis God gives skill,*
*But not without men's hands: He could not make*
*Antonio Stradivari's violins*
*Without Antonio.* ■

*Nan Ma is a third-year in the College, double majoring in Biology and Economics.*

**Fridolin Kummer** finishes off a piece of glassware. After nearly three decades at Havermeyer as Columbia's inhouse glassblower, Kummer retired last year.

# SCIENCE Under Glass

**By Ken Kostel**

Fridolin Kummer's name is still attached to a door at the end of a dim hallway in the basement of Havermayer Hall. But aside from a collection of fragile glass instruments scattered throughout Columbia University's chemistry department, the nameplate is all that remains of a carefully crafted legacy supporting research at the university.

A scientific glassblower, Kummer spent the last 50 years shaping hot glass into tools that permitted chemists and physicists to probe the building blocks of life and matter. Some of his creations are as ordinary looking as test tubes. Others are intricate assemblages of that sprout like flowering plants. Many border on the artistic or whimsical, but all were carefully designed and painstakingly constructed to serve specific purposes in the laboratory.

Last year, Kummer, 73, locked his basement shop and went home for good, taking with him decades of experience and countless more years of knowledge handed down from masters that had supported generations of scientists and students. The university, like many across the country that are scaling back their glass, metal, and machine shops, has no plan to replace him.

Bruce Berne, chair of the chemistry department at Columbia, said he instead plans to convert the basement glass shop to space for the research group headed by George Flynn, who specializes in capturing high-magnification, high-resolution images of individual atoms using lasers and scanning tunneling microscopes. "Flynn's a good chemist, but he doesn't need glass much," said Kummer from his home in Connecticut recently. "The theoretical chemists need it even less. All they need is a computer."

In order to attract the best candidates for faculty positions in a department that has produced six Nobel Prize laureates in chemistry, Berne said he needs to upgrade the department's facilities in order to meet the needs of modern research. "The space we have now," he explained, "is sub-standard for new chemistry."

To many, however, the choice of new faculty over more people who support their research is not so clear-cut, despite the fierce competition for space at many universities. "I would never think of moving to a university without the services of a glassblower," said Will Happer, dean of the physics department at Princeton. "The steady loss of craftsmen from universities is a very bad sign. Some experiments simply can't be done. Without real experiments backed up by the services of such craftsmen, we are at the mercy of the commercial sector. I would rather do with a few less professors or administrators."

A third-generation glassblower, Kummer grew up in Thuringia, a state in the former East Germany with a history of glass making that dates back more than 400 years. After he finished his public school education at 14, Kummer joined one of the many glassblowing shops in his hometown as an apprentice and began learning the basics of his craft from men who learned from previous masters.

He spent three years studying and working six days per week just to earn the right to take the journeyman's test, which he passed. With his country's post-war economy in ruins and many of his town's glass manufacturers moving to West Germany, Kummer left. In 1951 at age 20, he emigrated to join an uncle already in the United States who was also a glassblower. Over the half century that followed, Kummer worked with scientists and students at Brookhaven National Laboratory on Long Island and, since 1974, at Columbia.

During his time in the basement shop in Havermayer, where the windows looked out at street level to the feet of pedestrians walking along Broadway, Kummer worked mainly alone. With no one to pass his knowledge along to, the shop became a dead end in more ways than simply its placement at the end of a maze-like hallway.

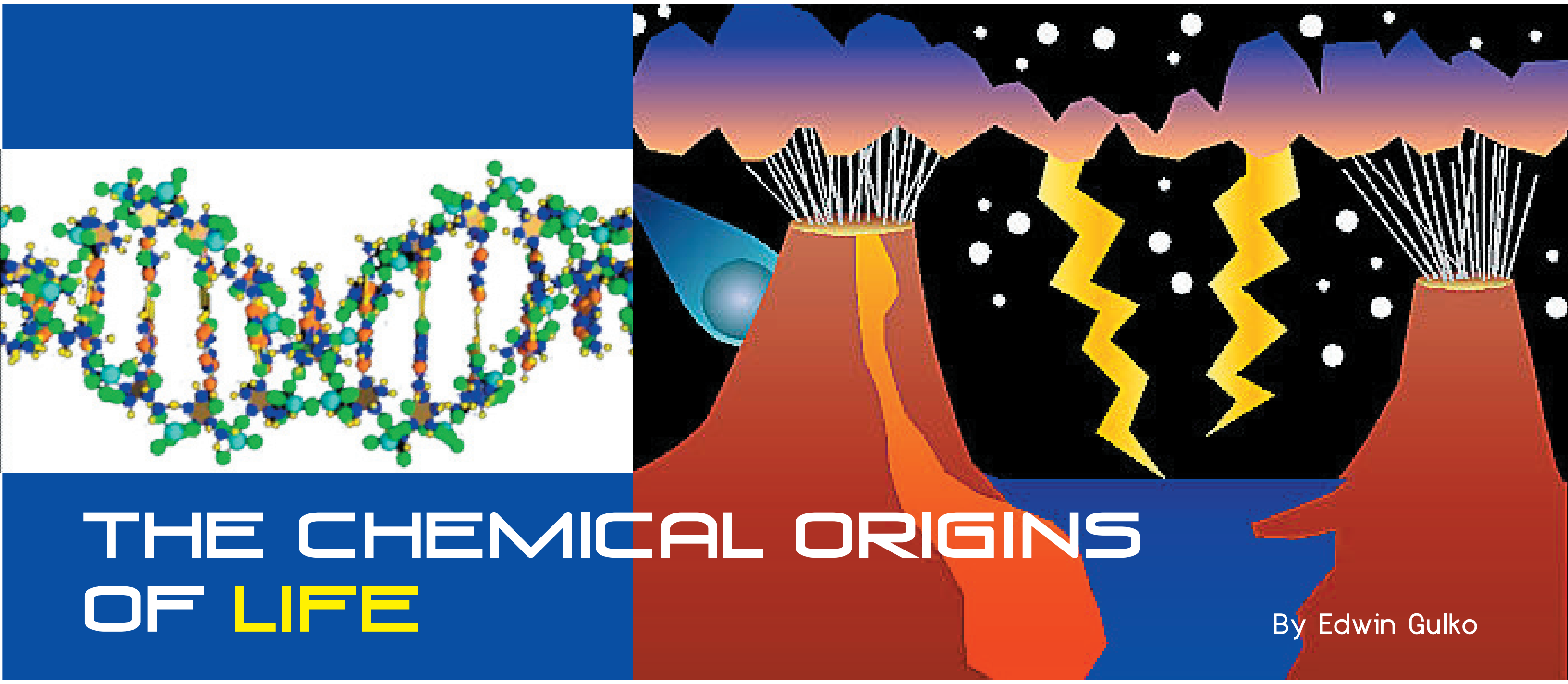
Mike Wheeler, a glassblower at Arizona State University who is in the process of writing the first comprehensive book on scientific glassblowing techniques in more than 40 years, said the impending retirement of experienced craftsmen such as Kummer who have no apprentices has created a crisis in the field. "A lot of glassblowers employed at universities are between 50 and 65 years old," said Wheeler, 52. "Because of a lack of training, there are fewer young glassblowers to replace them."

Currently, Salem Community College in New Jersey has the only program in the United States designed specifically to train scientific glassblowers. But many believe that the two-year curriculum is too short to prepare graduates to work with researchers. What is needed, Wheeler believes, is an apprenticeship system similar to the one that helped train Kummer and many of the other aging masters to ensure that the intricacies of their knowledge is not lost forever.

"A lot of what university glassblowers do is not just getting a drawing," Wheeler said. "We get an idea and it's up to us to turn that idea into a piece of glass. There's a real interaction with the researcher. We're not just making glass, but interpreting what researchers' needs are."

Six floors above Kummer's now quiet glass shop, Tracy Morkin reached beneath a cluttered lab bench and pulled open a large wooden drawer. The contents tinkled faintly as the drawer banged against its stops. "Everything in here Fred made," she explained, holding up small, branching test tube that she and her colleagues use to prepare samples for analysis in a spectrophotometer.

Morkin is a post-doctoral fellow at Columbia who studies photochemical reactions involving zeolites, a type of catalyst that may have broad applications to removing toxic wastes from soil. In another room, she pointed to a collection of glass bulbs and a maze of clear tubing bolted to one wall. The custom-designed vacuum pump, another of Kummer's creations, is a mainstay of her lab's daily operation. Without it, she said, her work and the work of 11 other graduate students and post-docs would come to a standstill. "No researcher wants to be limited by glassware that's commercially available," she explained. "You only want to be limited by your imagination."



# THE CHEMICAL ORIGINS OF LIFE

By Edwin Gulko

One of the most perplexing questions to plague man is the origin of his existence. Philosophies, religions, sciences each have attempted to answer this question, yet since the age of man's birth the question continues to remain a source of curiosity and bewilderment. Possibly, the question of existence was a source of motivation for Darwin when he first began his famous studies of evolution. Yet where Darwin's work culminated into a scientific theorem describing how life evolved into complex forms from simpler ones, it still remains unknown what were the first initial events that sparked life. What now exists in science currently is a gap in understanding the events between the Big Bang and Darwinian evolution.

A quiet area of biological inquiry seeks to close this gap by probing the possible chemical mechanisms that may have initially created the basic building blocks of life: amino acids, carbohydrates, nucleotides. The challenge facing scientists is to find the hypothetical prebiotic reactions that synthesized these building blocks, taking into consideration earth's environmental conditions and the prevalent simple compounds present during the primordial time period (young earth). Despite the ambiguity involved in understanding events that happened so many millions of years ago, studies within the past century have proposed interesting scenarios to confront these questions, allowing modern science presently to inch closer and closer to understanding the origins of life.

## The First Experiment

Acting as a precedent for future studies, the benchmark for research concerning the origins of life was set by Stanley Miller in 1953. In a simple experiment he subjected a gaseous sample of $CH_4$, $H_2$, $H_2O$, $NH_3$, supposedly similar to earth's early atmosphere, to continuous electric charges for one week. The electric charges, meant to mimic lightning strikes, provided the energy to produce an array of amino acids, the structural unit of proteins. Even further, some of the amino acids created are of biological importance to many organisms. Of significance, these results indicated that from simple molecules, important biological compounds can be made in a non-biological fashion. In 1955 Miller proposed a mechanism for the synthesis of the amino acids, which he adapted from a modern method of amino acid production entitled Strecker synthesis.

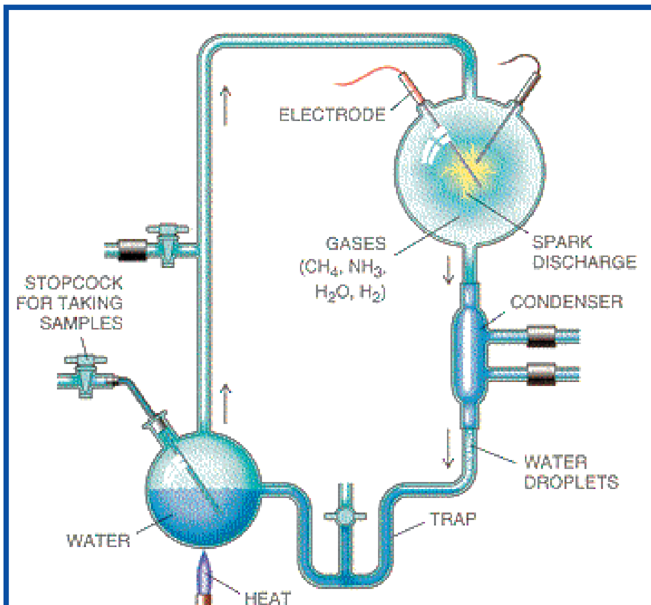
A complication, however, arose in Miller's hypothesis, in that a Strecker synthesis of an amino acid would require ammonium ($NH_4^+$). On the young earth, $NH_4^+$ would decompose quickly from UV degradation in a reducing atmosphere that lacked an ozone layer ($O_3$). A reducing atmosphere would contain compounds capable of giving off electrons during a particular reaction, for instance $CH_4$. On other hand, an oxidizing atmosphere would contain molecules like $CO_2$ or CO that would not give off electrons. The mixture of gases Miller used resembled a reduced atmosphere. There lies controversy between prebiotic chemists and atmospheric scientists as to whether the young earth's atmosphere was in a reducing state or an oxidizing state.

An argument for a mildly reducing atmosphere was made, when Miller redid his original experiment using other carbon sources instead of $CH_4$, like $CO_2$ or CO. Results showed that with $CO_2$ or CO, only glycine (the simplest amino acid) was made. Only with $CH_4$ as the carbon source, were other amino acids produced. This indicated that $CH_4$ is the best carbon source for amino acid synthesis, implying that the atmosphere of young earth should have been reducing in order to make diverse products. Miller and Antonio Lazcano proposed a solution to this dilemma by stating that it may have been possible to maintain a mildly reducing atmosphere with $CH_4$, $N_2$, $H_2O$, and $H_2$ with traces of $NH_3$ as opposed to Miller's original suggestion of $CH_4$, $NH_3$, $H_2O$, $H_2$. This new mixture of gases was shown by Miller in 1998 to be equally effective in producing a diverse array of amino acids.

## Nucleic Base Synthesis

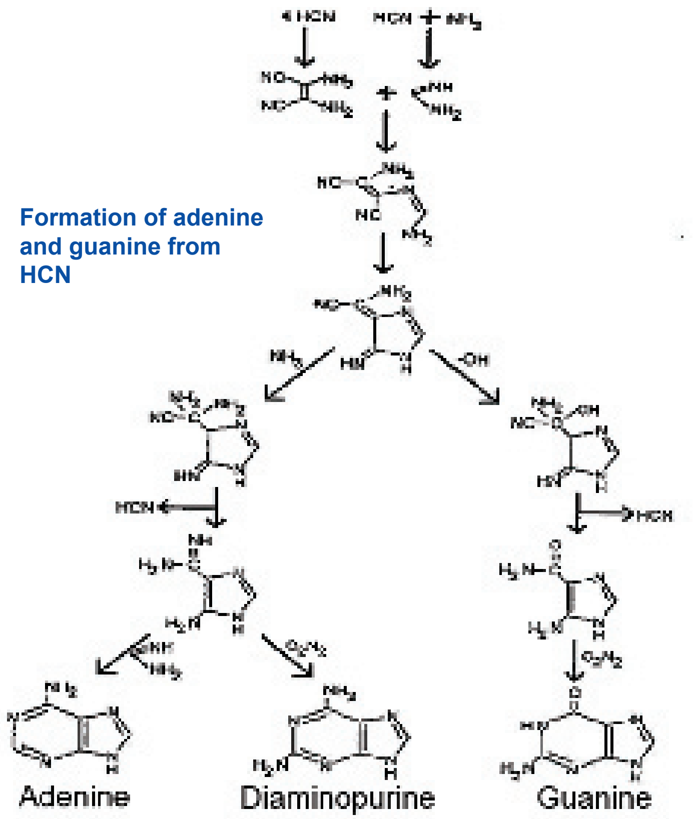
Midway through the twentieth century, significant evidence showed that DNA was the hereditary material of the cell. As DNA provides the necessary information for an organism to function and sustain life, possibly the key to discovering life's origin lay in understanding how the first nucleotides (the monomers of DNA and RNA) were originally synthesized in prebiotic conditions. John Oró in 1960 created a protocol under prebiotic conditions for the synthesis of adenine, one of the four nucleic acid bases found in DNA. Oró's study showed that concentrated solutions of hydrogen cyanide (HCN) formed small amounts of adenine when refluxed. Oró's proposal for the prebiotic formation of adenine is quite similar to Miller's original mechanism for amino acid synthesis, in that hydrogen cyanide is the principle reactant. Due to its electron configuration and subsequent high free energy, HCN is an attractive candidate for such reactions that require a molecule to build upon itself.

Simple variations of this reaction can lead to different products, as reported by Sanchez, Ferris, and Orgel in 1968. As originally proposed by Oró, the fourth step in the synthesis of adenine produces aminoimidazole carbonitrile. Depending on the conditions and the reactants present, this molecule can form different purines, most notably guanine. It follows then, that a comprehensive mechanism could have existed to form both adenine and guanine from HCN, with aminoimidazole carbonitrile as an intermediate. Consequently in analyzing the origins of life, it is apparent that there existed a gradual process of chemical evolution, allowing for the creation of compounds based upon the prevalent conditions on the young earth. For instance assuming that enough HCN was present in the lower atmosphere, imagine that by a random event HCN started to react with itself to form aminoimidazole carbonitrile. As aminoimidazole carbonitrile was stably furnished over a period of time, another chance event occurred that either introduced a new reactant or changed an environmental condition, resulting in




**Miller's Amino Acid Synthesis Setup**

The gaseous mixture, representing early Earth's primordial atmosphere is subjected to a continuous electric current, which simulates lightning. The flask of water represent's the primitive ocean. The mixture is kept circulating by boiling and then condensing. At the end of the week, Miller verfied by paper chromatography that several amino acids had been synthesized, including glycine, alanine, aspartic and glutamic acid.




Formation of adenine and guanine from HCN

the chemical reaction of aminoimidazole carbonitrile to several purines. It is through this continuation of random events over long periods of time, that simple molecules evolved into more complex ones. Imagine, had the earth's environment been different to accommodate other molecules, life as we know it could have been structured on other basic biological building blocks. Instead of proteins and nucleic acids, life could have been built upon any other conceivable structural unit, given that the environment allowed for the propagation of those molecules!

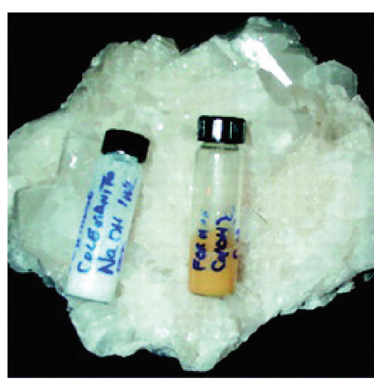
Geoffrey Zubay, professor at Columbia University since 1963, has spent the last 12 years studying the origins of life. Up until the early 1990's, Zubay had been an accomplished researcher in microbiology, having won the Selman A. Waksman Award for Outstanding Contributions to Microbiology. He left his stable world of microbiology in order to begin research on the Origins of Life, a move he claims has made him happier, "I got out of biology, in which a lot was known and we were just filling in the details. I had to be on the edge in order to be happy."

Zubay's research is an extension of Oró's, concerning himself with the production of the first nucleotides. His lab has developed efficient conditions for the production of the nucleic bases adenine and hypoxanthine, hypoxanthine being a precursor to guanine. Zubay has developed a hypothesis that adenine and hypoxanthine, both purines, were the first nucleic acids. Considering the ease in making purines relative to pyrimidines, the probability of making both classes of nucleic acids during young earth was just too unlikely. As Zubay believes, in order to make all the nucleic acids simultaneously too many events had to go right at the exact same time. This hypothesis is made more attractive when considering that adenine and hypoxanthine can form double strand helices, possibly the origins of double stranded nucleic acids.

## Sugar Synthesis for Nucleotides

As Oró's and Zubay's work help to draw an initial picture of how nucleic bases might have been created during prebiotic times, uncertainty still lay in understanding how nucleic acid bases could form. Briefly, nucleotides are the monomers of DNA and RNA that are of comprised of a nucleic acid base and a ribose sugar. Consequently, to understand the formation of nucleotides during prebiotic times, one must analyze the possible mechanisms of ribose formation. This question turned out to be rather difficult for researchers. Studies attempting to synthesize ribose under prebiotic conditions failed miserably, as the sugar was unstable under prebiotic conditions, often turning into tar. Miller, himself, tried relentlessly to find a way to make ribose, quitting his efforts in 1995 claiming, "The first genetic material could not have contained ribose or other sugars because of their instability."

Using lead as a catalyst, Zubay's lab has demonstrated with 30% yields, the production of aldopentoses. Aldopentoses are the linear form of



Colemite, white substance in the background, contains borate which stabilizes ribose formed from simple organic molecules found in prebiotic interstellar dust. The vial on the left contains borate stabilized ribose. The vial on the right contains tar, decomposed from ribose that was not stabilized by borate.

ribose sugars. In addition at University of Florida, a team led by Steven Benner reported in the January 2004 issue of Science to have synthesized ribose sugar with the aid of borate minerals. Starting with glycoaldehyde ($C_2H_4O_2$) and formaldehyde ($CH_2O$), ribose formation was stabilized by borate minerals that prevented the sugar from decomposing into a brown tar. Benner proposes that modest amounts of borate minerals existed during early earth, and possibly could have stabilized any formations of ribose.

### Connecting One to Another

The above studies provide possible mechanisms of how nucleotides and amino acids may have been created under prebiotic conditions. Yet, those structural units that are so vital to the cell's function do not exist as individual units, but in long, enormous polymers. A human cell contains many DNA strands, each hundreds-of-millions base pairs long. One is compelled to ask how this exact sequence of nucleotides is maintained through successive cell divisions, the answering being: the cell has a well-established system of enzymes that replicate and proofread the present genome. Yet during earth's prebiotic era, there were no proteins present to orchestrate this colossal task of arranging nucleic acids. While it is thermodynamically feasible to consider that conditions on the young earth could have allowed the creation of an amide bond between two amino acids, or a phosphate ester bond between two nucleotides, it is highly improbable that a long polymer of either would form. Experiments that attempted to create RNA strands in the absence of a catalyst succeeded in only creating polymers of 10 or less units.

Professor Geoffrey Zubay

Scientists always considered, and what mostly likely inspired Steven Benner in his studies, the possibility of clay minerals as catalysts for the origins of life. James Ferris and colleagues in 1992 showed that with montmorillonite clay, they were able to form RNA strands roughly 55 bases long. Interestingly enough, and of crucial importance is that montmorillonite clay, which acts as a solid support for the RNA monomers to polymerize on, promoted 3'-5' linkages between purines, the same linkage found in biological organisms. The clay also promoted distinct dimers of the nucleic acids, showing that polymerization of nucleic acids on montmorillonite favors certain sequences over others. Currently, little is understood regarding the polymerization of amino acids under prebiotic conditions. Zubay provides a strong argument in his text, Origins of Life on the Earth and in the Cosmos, that the polymerization of *useful* peptides had to wait the emergence of a system that could catalyze there *specific* assemble, in order to promote their amplificaiton:

> *"In a large pool of peptides or polypeptides with random sequences, it is highly likely that occasionally one is produced that is quite useful for structural or catalytic purposes. However, in a dilute sea of other useless peptides, its function can never have a meaningful impact. Without the amplification and selection provided by the Darwinian process there is no apparent way in which such a system could be useful."*

### Ribozymes

Science has learned the purposes and utilities of RNA and proteins. Yet, at what point in time did RNA and/or proteins begin to function and catalyze reactions that resemble life processes? As Zubay describes, in traveling backwards to dissect the origins of life, we can take the simplest organism, a bacterial cell, and strip away all its nonessential parts. What is left is a pool of RNA and proteins, swimming around catalyzing life reactions. The idea is easy to imagine on the young earth, yet we are left with the chicken and egg paradox of what came first, RNA or proteins?

A revolution in understanding the origins of life was made in the early 1980's, when Sidney Altman and Thomas Cech discovered RNA strands capable of performing enzymatic functions, later to be called ribozymes. Since the Nobel-prize winning discovery, ribozymes with other catalytic properties have been found: synthesis of nucleotides, nucleotide phosphorylation, and even replication of certain RNA strands. These findings provide scientists with an attractive model, The RNA World. Possibly on young earth, with conditions permitting, these RNA strands acted to create the first life-resembling reactions. Ribozymes would be capable of synthesizing important polypeptides and replicating themselves. In an aqueous environment, RNA is highly susceptible to being degraded, which was most likely the case during prebiotic times. There must have existed a mode for RNA to replicate itself, otherwise it would have been eradicated easily. Possibly there existed RNA strands

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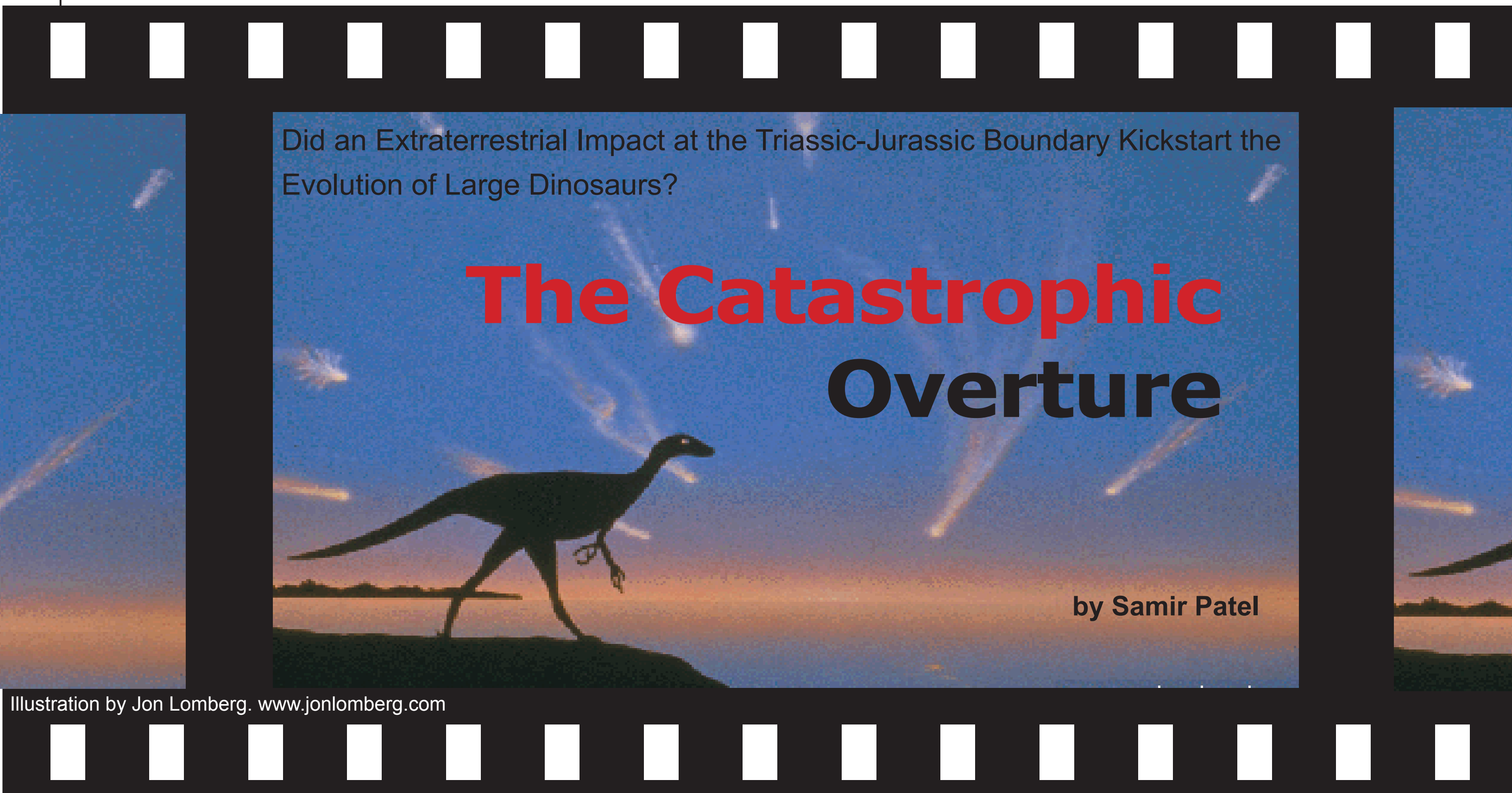


Did an Extraterrestrial Impact at the Triassic-Jurassic Boundary Kickstart the Evolution of Large Dinosaurs?

# The Catastrophic Overture

**by Samir Patel**

Illustration by Jon Lomberg. www.jonlomberg.com

Sixty-five million years ago we were freed by a rock from space. That is to say, the common ancestor that we share with all mammals was freed from the 135-million-year reign of dinosaurs by the impact of an asteroid 10 km across traveling 30 km/s. The celebrated cataclysm between the Cretaceous and Tertiary Periods—known in the rock record as the K/T boundary—was the end of one regime and the beginning of another. The survivors of the mass extinction, including small mammals scurrying through the underbrush, experienced "ecological release," an opening of niche space that probably allowed the evolution of the tremendous diversity of mammalian forms that inhabit the world today. Now there is evidence that the dinosaurs may actually have been victims of a karmic boomerang—they may have been liberated in a similar way 135 million years prior.

Paul Olsen of Columbia's Lamont Doherty Earth Observatory theorizes that an extraterrestrial impact occurred 202 million years ago between the Triassic and Jurassic Periods (the Tr/J boundary), freeing small carnivorous dinosaurs from large reptilian competitors and allowing them to evolve the massive size that has inspired Hollywood special effects technicians for decades. It makes for a grand tale, the rise and fall of a dynasty. The theory could give structure, a narrative arc, to one chapter in the long and complicated story of evolution. This framing device certainly is tantalizing, but for now it resides in the realm of theory. The patterns are there, but many more data will be needed before the theory can reach the level of acceptance enjoyed by its K/T cousin.

"When you look at specific sections at the Triassic-Jurassic boundary," Olsen says, "where the fossil record is good, [it] shows for the fossils that are present an abrupt transition." But even that seemingly simple statement, like almost every other part of Olsen's theory, has its critics. "Two hundred years of fossil collecting across the Tr/J boundary do not document a mass extinction. That's all there is to it," says Spencer Lucas of the New Mexico Museum of Natural History & Science. Olsen, whose easygoing enthusiasm sometimes betrays frustration with such criticism, bases his impact theory on a suite of observations that echo the K/T boundary. The evidence is compelling, but piecing together events—even global catastrophes—that took place 200 million years ago is tricky business.

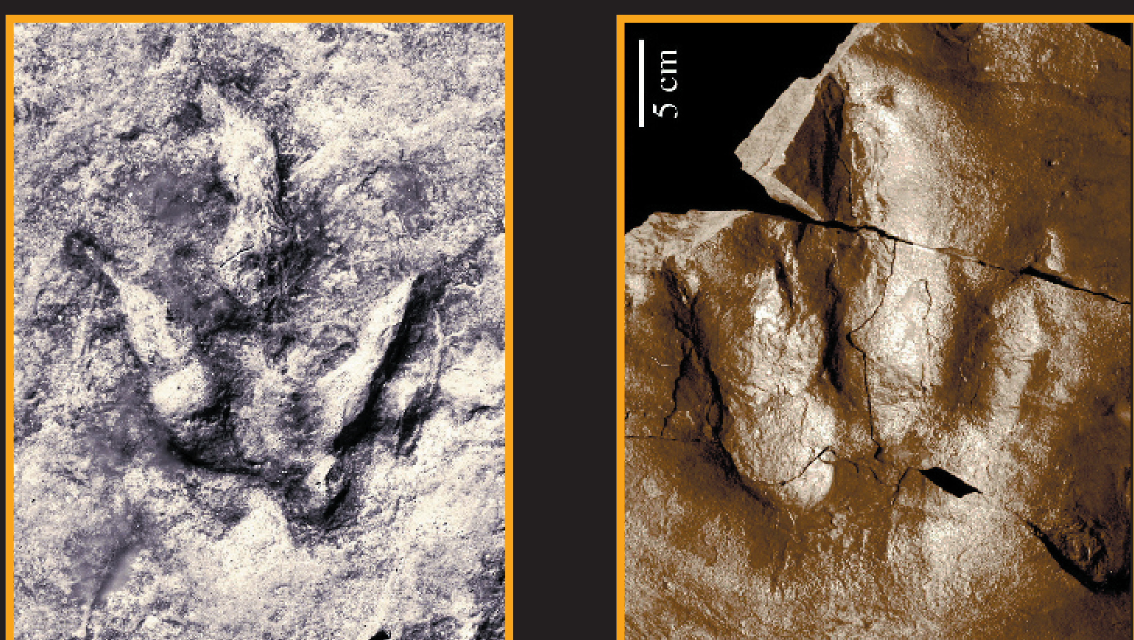
Olsen does much of his work on the boundary in the Newark Supergroup, thick successions of sedimentary rock in Eastern North America that were once rift lakes much like those in East Africa today. These rock sections record changes in global climate, contain ancient mudflats that preserved the footprints of the locals and provide several intriguing pieces of evidence for an impact at the Tr/J boundary. Most significantly, Olsen recently reported in *Science* a hint of the characteristic signature left by the K/T impactor—an iridium anomaly. The metal iridium is rare on the surface of the earth but exists in higher concentrations in the earth's interior and in extraterrestrial objects. At the K/T boundary there is a narrow, almost global layer of clay with a concentration of iridium much higher than normal—one of the strongest pieces of evidence for a disaster from the sky. Olsen's anomaly is far smaller than the one at the K/T, leading some to theorize it might actually be volcanic in origin.

The rocks also record a change in fossilized pollen. It is known that fossils of all kinds change across the geologic boundary—in fact that is how such boundaries are defined—but right at the boundary Olsen and his colleagues found a sudden jump in the presence of fern pollen. This so-called fern spike, which also is observed at the K/T boundary, is associated with the initial recovery from an ecological disaster. Even today opportunistic ferns often are the first to move in after a disturbance. There also are carbon isotope changes associated with the boundary, which indicate some kind of global change in how carbon cycles through the atmosphere, ocean and organisms. An impact that killed off the tiny but influential aquatic organisms that form the basis of marine food chains could cause this, and the same pattern of isotope changes are observed at the K/T boundary. But there are other potential explanations, including some—again—tied to volcanism.

All these observations coincide with a change in fossilized footprints, which tell an interesting story. They appear to track a sudden large extinction followed by an evolutionary lurch in which carnivorous dinosaurs quickly grew in size. Prior to the boundary there was a diverse assemblage of terrestrial species. The large carnivores at this time were reptiles—squat and sometimes sail-backed rauisuchians and crocodile-like phytosaurs—and the largest dinosaurs were modest-sized herbivores called prosauropods. There was global diversity as well; fossil beds in other parts of the world contain different groups of species.

After the boundary, however, diversity appears to plummet. Terrestrial communities are dominated by a much smaller group of lizards, crocodilians and carnivorous dinosaurs called theropods. Interestingly, Olsen says this phenomenon is global—all over the world the very Early Jurassic is dominated by similar species-poor communities. Notable in this section is

Larger theropod footprints began to appear in the Jurassic period, supporting Olsen's impact theory. The image on the left is the largest Late Triassic theropod track, while the image on the right is an example of the earliest Jurassic theropod track *Eubrontes giganteus*. The increase in track size of twenty percent indicates a doubling of body mass.




Courtesy of Paul Olsen

the first appearance of *Eubrontes giganteus*, a carnivorous dinosaur whose tracks are 20 percent larger, which correlates with a doubling of body mass, than any theropod track before the boundary. This observation is consistent with ecological release; the large reptilian predators were swept off the earth and large dinosaurs rose up in their place. Of this Olsen is confident, but doubts about his evidence are common. For example, some claim that large carnivorous dinosaurs could have existed before the boundary. "What [the critics] have to do if they disagree with the observations around the Triassic-Jurassic boundary of eastern America, they have to come up with some observations that show that's incorrect," says Olsen. There is one problem: such evidence may exist. A footprint found in Australia in the 1960s is larger than *Eubrontes* and was dated to 20 million years before the boundary. According to Lucas, the Australian footprint was a glaring oversight on Olsen's part and falsifies his ecological release theory. "It was an embarrassingly bad mistake," he says. Olsen counters that the cast of the footprint is incomplete and may not be from a dinosaur at all. But it is not out of the realm of possibility, he concedes, that an impact could have cleared the way for a large species, a superpredator, from another part of the world to migrate into the Newark Basin.

Olsen admits that the evidence for an impact is "still rather paltry," but most of his observations are constrained within 50,000 years of sediments around the boundary—a blink of the eye in geologic time. More evidence needs to be found, particularly in other locations, to establish the global scale of the event. "I would argue that the iridium anomaly that I describe has to be shown to be present in other sections, and that's just an incredibly labor-intensive operation," admits Olsen. "Work on that is underway, but it's going to take a long time."

"It is viable," says Lawrence Tanner of Bloomsburg University in Pennsylvania of Olsen's impact theory, "but it still falls far short of the evidence we have of an impact at the Cretaceous-Tertiary boundary."

"IT IS VIABLE," SAYS LAWRENCE TANNER OF BLOOMSBURG UNIVERSITY IN PENNSYLVANIA OF OLSEN'S IMPACT THEORY, "BUT IT STILL FALLS FAR SHORT OF THE EVIDENCE WE HAVE OF AN IMPACT AT THE CRETACEOUS-TERTIARY BOUNDARY."

In fact, many more data will be necessary to convince some. "[Olsen]'s made a monumental contribution and he'll continue to. That doesn't mean he's always going to be right. And I'm more than happy to point out where I think he's wrong," says Lucas. Lucas and others, including Tanner and Peter Ward of the University of Washington, argue that the Tr/J extinction was a puny afterthought to a series of two to four earlier step-wise extinctions. This alternative theory paints the world of the Late Triassic as a very unpleasant place, a seething greenhouse wracked by repeated paroxysms of extinction. Proponents of this theory argue that the belief in a mass extinction is the result of using poor temporal resolution, which leads to the artificial lumping of separate events. Olsen disagrees. "It's legalese. It's arguing science like a lawyer," he says, positing that because fossils are discrete data points, looking at small portion of the rock record will always give the illusion of a step-wise pattern due to a sampling artifact called the Signor-Lipps effect. "In reality, it's extremely difficult to demonstrate a step-wise extinction because all extinctions will look step-wise in the fossil record at some level of sampling around a boundary that was catastrophic," he adds.

Poor resolution is a real problem in the rock record. It can be difficult to determine when a species went extinct or the rate at which a mass extinction occurred. Some groups of marine fossils, for example, which are used to define geologic boundaries because of their relative abundance, appear to wink out before the boundary, but others go out with a bang right at it. Another problem lies in correlating terrestrial and marine sections. The fossil record is capricious in this way, so it can be hard to come down in favor of one theory or the other. "Did this event cause the instantaneous extinction of all these creatures or is it just simply correlated with the extinction of all these creatures or is the record so crappy worldwide that we can't even really tell that these things all went extinct all at the same time anyway?" asks Mark Norrell of the American Museum of Natural History. "I'm sort of thinking of the latter."

Whether the extinction occurred all at once or in a series of steps may have an effect on theories about its cause. A sudden mass extinction may be better explained by an impact, a sudden global event, Photo by NASA

**MANICOUAGAN PENNINSULA**, Quebec, a candidate crater site for Olsen's proposed Triassic-Jurassic boundary.

while a series of extinctions might be more likely to be caused by an ongoing earth-based process. It may come down to a question of parsimony—which mechanism provides the simplest explanation for the observations?

Olsen argues that the impact makes the most sense because the observations match a well understood pattern—that observed at the K/T boundary. "I prefer the parsimonious explanation, that both events were due to the came causes," he says via e-mail. In fact, he places the burden of proof on those who believe the extinction was step-wise because they will need many more data to make their case. The other side of this argument asserts that it makes more sense to look for a known earth-based mechanism that can explain all of the observations, rather than to rely on the *deus ex machina* of an extraterrestrial visitor. A few potential culprits for this mechanism have been proposed. It is known that around the Late Triassic and Early Jurassic the Central Atlantic Magmatic Province (CAMP), one of the largest volcanic releases ever, was active. While most of this volcanic activity, which covered 10 million of $km^2$ with basalt over the course of 1 to 2 million years, is believed to have taken place after the Tr/J boundary, related activity might be able to explain the iridium anomaly. Also, outgassing associated with the volcanism and the release of methane from ocean floor sediments could begin to explain the carbon isotope changes. Step-wise extinctions and a fern spike might result and the earth belches its way through a series of environmental changes. However, Olsen is quick to point out that if volcanic activity was the cause of the observations, it would be the first of its kind; there is no precedent for an iridium anomaly caused by volcanism. Two of the proposed mechanisms—impact and volcanism with methane release—are not necessarily mutually exclusive. An impact could have been the coup de grace that polished off taxa that had staggered through the first few extinctions. "This issue really comes down to what percentage of the extinction event does that impact explain," says Neil Shubin of the University of Chicago.

One discovery that would strengthen Olsen's position would be a big hole in the ground. The K/T crater was found on the coast of Mexico, but if a Tr/J impactor hit the ocean, its crater almost surely would have been subducted below another crustal plate by now. But if it landed on a continent there would be a scar, and there is a potential candidate—the Manicouagan Crater in northern Quebec. The current date of the Manicouagan places it several million years before the boundary, but "there's reason to believe that the age that's commonly reported and accepted in the literature might be a little too old," according to Andy Winslow, a graduate student at SUNY Stony Brook who is redating the crater. Older grains taken as part of samples may have skewed the dating, making the crater appear older than it is.

Even if the Manicouagan redating comes back right at the Tr/J boundary, the issue still may not be settled because of lingering questions about the nature of the extinctions. And if the crater does not correlate with the boundary, scientists will be left to determine what, if any, effect that impact actually had. Theoretical capacity is up to the task, but the data are lacking, so scientific consensus on the Tr/J boundary will remain elusive.

"This one ain't over," says Lucas. "The fat lady isn't going to sing on this one for a long time."

*Samir Patel is a graduate student in the Deparment of Earth and Environmental Science.*

# A BRIEF HISTORY OF BEN

by Gisela Telis

## a profile of planet hunter Ben Oppenheimer

The man in the black turtleneck chain-smokes. He loves electronic music. As he runs his fingers through spiky hair that has been neon-yellow, purple, copper and white, he reflects, "I like changing it, just for the hell of it. It throws people for a loop." After a whopping six months in his natural dark brown, he's already considering his next color. But Ben Oppenheimer is not the average post-punk hipster or struggling skater-artiste. He is principal investigator of the Lyot Project, an undertaking that may forever change the way we study our cosmic neighborhood.

On a December afternoon, Ben Oppenheimer sweeps through the lobby of the Museum of Natural History with snow on his shoulders and the smell of smoke about him. His energy and enthusiasm crackle. He stalks briskly down the corridors of the museum and into the steel elevator just as it closes. Mike Shara, the museum's Curator-in-Charge of Astrophysics, asks him what's going on. "We've got it," says Oppenheimer. "It worked in the lab. Less than an hour ago."

After further discussion with Shara, Oppenheimer marches down another hallway, past the loft-like space where the astrophysics department once planned to build its offices – "prime Manhattan real estate", he likes to call it – and into the Lyot lab. Inside, his eyes adjust to the darkness and focus on a table encased in a glass cleanroom that occupies half the lab. The table supports a maze of glass, metal, and gold-plated mirrors that bounce a light beam back and forth, over and over again, before finally feeding it to a camera. He looks now to the screen where the camera's image glows. It shows a central light source and its halo, separated by a clear, perfectly dark ring. This innocuous-looking ring may produce the first snapshots of other solar systems that the world has ever seen.

You may wonder, at this point, who Oppenheimer is and how he came to devise the first working method for imaging worlds around other suns. The problem is that he won't tell you. "Oh, I dunno," says Oppenheimer, 31, if you ask him about his achievements. "I don't do much."

The truth, however, is that the man who claims he doesn't "do much" is humanity's best bet for seeing other planets and other life in the near future. And as a discoverer of a new class of substellar object (while a mere Ph.D. student), a hub of the dark matter controversy, and a fixture on the edge of astrophysics research, he is exceptionally well-suited for leading astronomy into a new age – even perfect, some would say. David Helfand, chairman of Columbia's astronomy department and Oppenheimer's mentor for many years, sums him up with: "His only fault is that he still smokes."

But Oppenheimer's perfection in the eyes of the rest of the astronomy community is far from assured. His track record of major discoveries and great promise now hangs on that little ring, the picture it may yield, and the answers it may provide in our age-old quest for another Earth.

Oppenheimer, in bright blonde hair, with other members of the Lyot Project Team

## The (Renaissance) Man behind the Machine

Born in New York City in 1972, Ben Oppenheimer grew up fifteen blocks south of Columbia University. His father teaches English and Medieval Literature at City College; his mother is a secretary. Although middle-class by most standards, the Oppenheimers were never carefree about money. It was this fact that brought young Ben from Horace Mann High School to Columbia.

"Yeah, I thought I should get out of the City for a while, but Columbia gave me a much better financial aid package. That made a big difference to me, because my family was not very wealthy."

Financial aid arrived in the form of the I. I. Rabi scholarship, a Columbia fellowship designed to expose scientifically gifted incoming students to undergraduate research experiences. Ben Oppenheimer belonged to the first class of Rabi Scholars, and has since been called the "poster child" of the program.

"Poster child? Oh my God!" he erupts, laughing loudly. "Jesus! I'm honored!"

Oppenheimer laughs often, especially when nervous, and praise makes him very nervous. Unassuming and ambitious, bold and bashful, his personality merges disparate elements into a charismatic, contradictory whole. Perhaps it is this kaleidoscope-like character that so enamors those who cross paths with him. But diversity brought with it some disadvantages when an 18-year-old Oppenheimer began to think about focusing his talents.

"I've always had this passion for writing," he says. "I mean, my dad was an English professor, I guess that might be where that comes from…There's that, and I've always loved art as well, and how do you combine that stuff, in addition to astronomy, which has always been a very strong passion? The thing is, you *can* carve out your own career. You just can't be too afraid of these tracks that everyone follows. I think that people automatically do that stuff without thinking about it too much. It's the more imaginative people who question everything. "

Oppenheimer first thought of carving out his own career by choosing particle physics and working from there, but his early research experience in the astronomy department placed him on a different path. "Maybe it's just a function of the people I met, I don't know," he explains, "but when I met David Helfand and Jacqueline van Gorkom, I knew that this was what I wanted to do. I mean, they treat you so well, and welcome you into the field so quickly."

Helfand, who refers to Oppenheimer as "the Anti-nerd", noted immediately the breadth of his personal and intellectual curiosity, and suggests that his "broader range of interests than most scientists and science students I know" is one of his greatest assets as a researcher. His research assistant, Laura Newburgh, is just as effusive: "Every little thing about research, he just loves it. I think that's the main thing that comes across – I mean, he's just such a kid in some ways…he's always really excited about almost anything."

The fact that "almost anything" includes drafting, physics, photography, public outreach and writing gives Oppenheimer's innovation, and his thinking, a uniquely interdisciplinary bent. His love of engineering and architectural drawing, for example, has led him to design and build his own instruments, which in turn allows him to control every step of his research projects – a rarity in the instrumentation-phobic astrophysics community. You may find quotes from Kant and Alexander Pope's poetry in his technical papers, physics in his often poetic nonfiction, and a philosophical perspective in his discussions of quantitatively exacting problems.

"There are so many cool things that people do," he shrugs. "Why lock yourself into one thing?"

## Brown Dwarfs, White Dwarfs and Dark Matter

While visiting Caltech in his senior year, Oppenheimer met Shri Kulkarni, who had a reputation for doing unconventional and groundbreaking research. At the time, Kulkarni was interested in applying coronagraphy (a starlight-blocking technique) and adaptive optics (self-adjusting mirrors) to the problem of finding brown dwarfs. "I got really excited about this whole business of adaptive optics and high-resolution imaging. So I thought, ok, I'll go out there and do this stuff, and if we don't get any science out of it, at least I'll have learned this crazy technique, and someone must have a need for people who know that stuff. And it worked out really well."

Brown dwarfs are objects that form as stars do – in the gravitational collapse of a cloud of hydrogen gas – but aren't quite massive enough to ignite the hydrogen burning process that makes stars shine, making them very hard to see.

Shortly after starting graduate study at Caltech, Oppenheimer began hunting brown dwarfs with Kulkarni at the Mt. Palomar 60-inch telescope. "We found this very faint, red object orbiting the star Gliese 229, and it looked very exciting to me – I remember calling up Shri and saying, 'Look, man, there's something really interesting here, can we get some data on it?' Then we waited a year for Gliese 229 to move across the sky…and saw that this faint red object moved in the same direction and distance, so we knew it had to be physically [gravitationally] associated with the star. Its luminosity was a few million times less than the sun's luminosity, way below the lowest mass stars, and then we knew, we really knew, that we were on to something quite amazing."

They were on to Gliese 229b, the brown dwarf companion to Gliese 229. Oppenheimer, Kulkarni, and the rest of the Caltech-Johns Hopkins team analyzed the spectrum of the dwarf and found methane in its atmosphere, which is commonly seen on Jupiter-like planets, but never in stars. It was the first so-called "methane dwarf" ever detected.

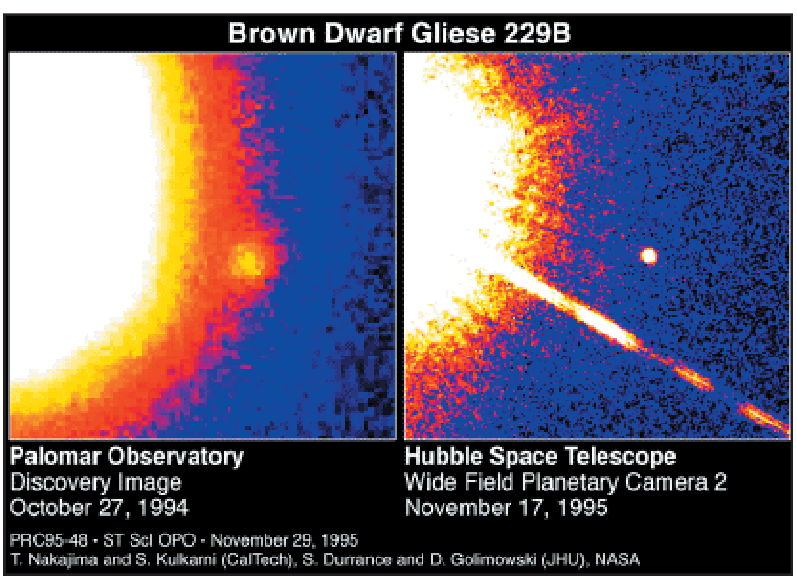
The discovery landed Oppenheimer's name on astronomers' tongues, and his work on the instrumentation and combined use of coronagraphy and adaptive optics for brown dwarf detection later informed his development of the Lyot Project, which pushes this same technique to its physical limit. "It seems a little weird – I've gone back to my thesis work, although it's very different from what I was doing then."

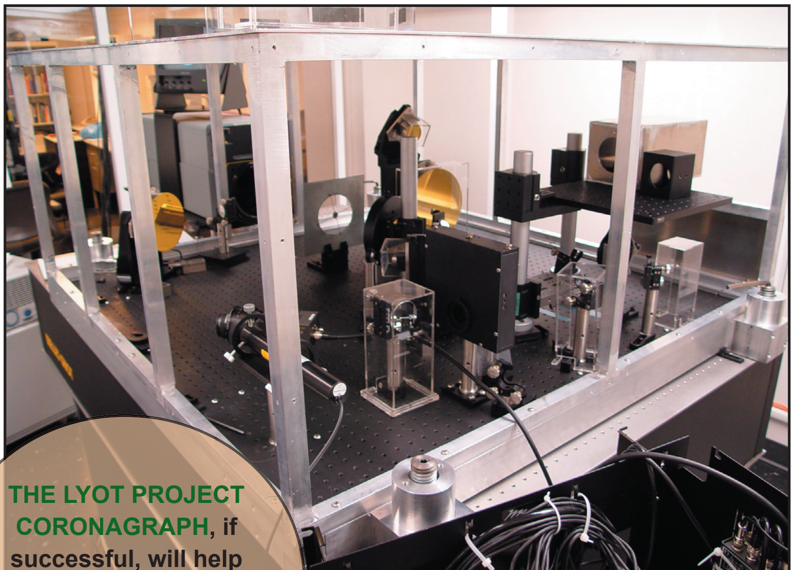
In 1999, Oppenheimer completed his doctorate. He won a Hubble Fellowship for post-doctoral research and opted to take his fellowship to UC Berkeley.

"I enjoyed LA a lot…there're just so many people doing weird things," laughs Oppenheimer. "The art was fantastic, there was so much new music, crazy things going on…in that way, LA is more interesting than San Francisco, but harder to live in. But I think after a while I wanted to get back to the New York lifestyle. So I moved to San Francisco."

At Berkeley, Oppenheimer and three collaborators completed a survey of white dwarfs in our galaxy's halo. White dwarfs are dim remnants of stars that were once similar to our sun, but belonged to an earlier generation of stars. Oppenheimer used a sample of 38 of these remnants, many of them never seen before, to estimate that cool white dwarfs make up 2% of the dark matter – the unseen stuff that actually makes up as much as three-fourths of our universe – surrounding the Milky Way. In other words, he claimed that a dark stellar junkyard takes up as much mass as our whole galaxy. Although this controversial result confirmed the estimates of theoretical projects like MACHO and EROS, it troubled many more traditional researchers and brought about a flurry of debate and media attention that has not yet disappeared. But after less than two years, the excitement of his time at Berkeley failed to quiet the call of New York.

"Well, I guess I got homesick. New York was calling somehow, and I started thinking about how I could get back here. I heard about what Neil Tyson and Mike Shara were doing over here and thought, well, to





**THE LYOT PROJECT CORONAGRAPH**, if successful, will help researchers detect planets usually drowned out by the bright light of nearby stars.

work in the Museum would be amazing. So I sort of strong-armed my way into a job here."

### The Next Big Thing

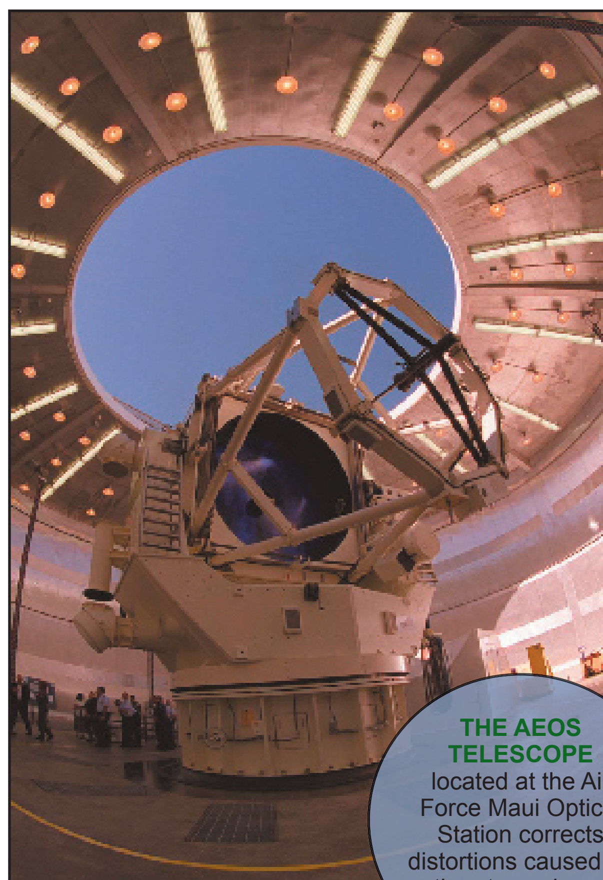
Every time the media report the discovery of a planet in another solar system, what they are actually reporting is the *indirect* detection of such a planet. Astronomers don't actually "see" or "find" planets around other suns; they "see" quantifiable evidence that the planet is there. Because stars are so much larger and shine so much more brightly than planets, they drown out their planets with their light and make visual detection of the planets all but impossible. Planet hunters must turn to gravity and try to find a planet's very small, but more easily detectable gravitational effect on its sun.

Starlight-blocking devices do exist, however, as mentioned before. They are called "coronagraphs", because they have been used to study our sun's corona for decades. The Lyot Project enhances and optimizes the traditional coronagraph to more effectively block out the light of distant suns, thus finally revealing their faint planetary companions.

"The point of a coronagraph is to block out most of the light of the star by putting what's essentially an opaque disk over the image of the star," explains Oppenheimer. "Now, when you do that, the starlight is going to diffract around the edges of this disk, so if you then bring the light completely out of focus again, and look at a picture of the telescope's pupil or entrance aperture, you see that the light that has diffracted around your spot is actually all located in a ring around the edge of this defocused image. So the Lyot stop blocks *that* stuff out. That's where Lyot [French physicist, inventor of the Lyot stop] got so clever. I mean, say you see a plane flying by the sun – you hold your hand up and you can see the plane much closer. It's a similar idea, but by having the second stop, the Lyot stop, you end up increasing the contrast further in the final image. You end up removing far more of the starlight than you do if you're only putting one little spot up."

The Lyot Project combines these "stops" with the Air Force's Advanced Electro Optics System (AEOS), the highest-order adaptive optics system in the world. An adaptive optics (AO) system is essentially a mirror that can be deformed, via hundreds of miniscule motors or actuators, to correct any distortions that our atmosphere may effect in the signal received by the telescope. The 3.6-meter AEOS telescope operates on the Air Force Maui Optical Station, 10,000 feet above sea level, to lessen the atmosphere's distortion, and has 941 deforming actuators, or one for every 10cm of mirror.

"On most AO systems today – the Palomar AO system, for example – the spacing is something more like one every 20-30cm," says Oppenheimer. "So,



**THE AEOS TELESCOPE** located at the Air Force Maui Optical Station corrects distortions caused by the atmosphere.

by virtue of the fact that this enormously controllable, deformable mirror is on a relatively small telescope, we're able to control very fine features in the wave front when it comes through the telescope."

This pairing – the unparalleled distortion control of the AEOS telescope, and the unprecedented sensitivity of Oppenheimer's Lyot coronagraph – will make possible the mapping of solar system-sized regions around nearby stars, and will revolutionize research on all kinds of hard-to-detect objects. As Helfand puts it, "We won't be seeing continents and giraffes, or anything like that, but the Lyot Project is an important step for humankind."

Oppenheimer phrases his hopes for the project with typical understatement. "One of the great things about this new project is that we're going to be looking in a parameter space that people have never explored before. And so, even if we find nothing, I will find that interesting. I mean, it would be really weird if we found nothing!"

The Lyot Project, due to begin observing later this month, will first target circumstellar disks, or dusty areas around stars where planets are thought to form. After the coronagraph's December success in the lab, things bode well for Oppenheimer and his Lyot dream. But what if it doesn't work in Hawaii, where it counts?

"It *has* to work. I will sit in that lab and tweak it until it does."

## On the Horizon

"In the long run, I think that a lot of this work that I'm doing…is leading up to searching for signs of biological activity on extrasolar planets. It's not clear to me at all how such work will take place, but as far as I can tell, the best way we have to find signs of biological activity is through spectroscopy, looking for chemical disequilibrium that could only be caused by biological activity. That, I think, would be a tremendous discovery. In a way, it's the Holy Grail for a lot of science. I think that within our lifetimes, there'll be pretty damn good evidence for life out there, outside our solar system. *That* will be amazing. I mean, I want to know what kinds of drinks they have." ■

*Gisela Telis is a Research Staff Assistant in the Department of Astrophysics and a 2003 graduate of Columbia College.*

continued from **page 14** *Chemical Origins of Life*

that were capable of catalyzing RNA replication.

## Implications

A theme constantly reiterated in studying the origins of life, is whether the prebiotic environmental conditions were adequate to stabilize a particular molecule. This parallels Darwin's theory of evolution in which a species' existence is solely dependent on its capability to survive and pass genetic information to future generations. In similar fashion for prebiotic molecules, those stable on young earth were selected for, later to participate in other reactions. Had the first nucleotides been formed in unfavorable conditions, there existence would not have lasted long. Consequently, the random event that produced them in the first place, would be nothing more than that, forever lost in time as a past attempt in creating life. And yet, this was not the case for biological molecules that constitute today's organisms on earth. These simple molecules were stable, and later reacted with each other to form other complex molecules, until eventually they evolved to interact on a greater scale in a system.

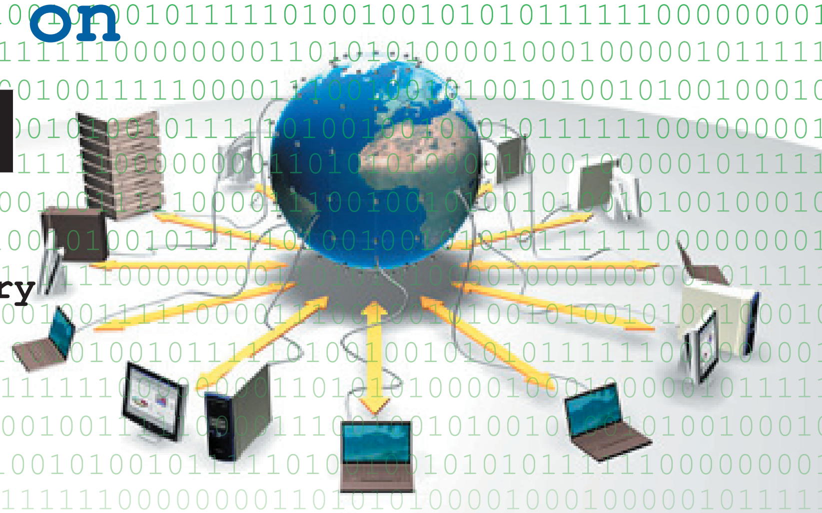
The brilliance in understanding the origins of life is not dependent on the notion that life spawned from chemical reactions between simple molecules. On the other hand, it is absolutely spectacular to think that these reactions eventually led to the intricacies of human life. The mayhem of love, the thirst for knowledge, the wonders of music, the treasures of friendships: to contemplate that these aspects of human life are lineaged to the first chemical reactions that occurred on earth is for one, truly inspiring. ■

*Edwin Gulko is a Columbia College senior studying Biology*

# Getting a Grip on THE GRID

## Computing in the 21$^{st}$ Century

**By Christine Aidala**



In 2007, a few short years from now, the Large Hadron Collider (LHC) at CERN, the European Organisation for Nuclear Research, in Geneva, Switzerland will turn on, marking the beginning of its quest for phenomena beyond the Standard Model of particle physics and its search for the long-sought Higgs boson, hypothesized to give every elementary particle its mass. Approximately 6,000 physicists from dozens of countries around the world will find themselves in a scientist's fantasyland, with petabytes of new data rolling in each year. But data is only valuable as long as it can be feasibly stored, accessed, and processed. Just a few years ago, giving thousands of researchers scattered around the globe the ability to access and analyze such large quantities of data would have been unthinkable. But now scientists working on experiments at the LHC are looking to Grid computing to provide the solution.

The fundamental, long-term idea behind Grid computing is to make computing resources a public utility or commodity, similar to water or electricity. In some ways, it can be viewed as the logical extension of the connectivity offered by the Internet, making wide-area distributed resources available to individuals. Each end-user would have some kind of interface such as a PC with which to tap into a publicly available network, or "grid", of resource providers whenever he wished, paying only for the CPU cycles, memory, data storage, etc. consumed. All of these resources would be available on demand. Just as the Web is a means of sharing information between computers, the Grid can be thought of as a means of sharing computer resources between computers. Through the Grid, users share computational power, data storage capabilities, and scientific instruments as if they were part of one large computer.

The possibilities are endless. A meteorologist could easily locate, aggregate, and analyze data about weather patterns; a small-business owner could do his own analysis of local, regional, and global market trends relevant to his products or services; a high school physics student could access enough data from a particle physics laboratory to calculate the mass of the top quark – all from a school computer. Just as we are not concerned with where the electricity we consume has been generated or how it has been transported, the Grid end-user would have no need to think about where the CPUs and data storage disks are physically located or how communication between the interface and remote facilities is accomplished.

Computing performed in this way would offer a wealth of advantages and possibilities across the realms of research, business, and leisure. Pooling assets into large, virtual systems would allow them to be utilized much more efficiently, since these broad resources would be allocated dynamically at runtime according to availability, capacity, performance, cost, and the quality of services required by the user. The geographically distributed nature of Grids would permit loads to be redistributed among facilities in different time zones to accommodate local peak usage times. Perhaps most importantly, individuals

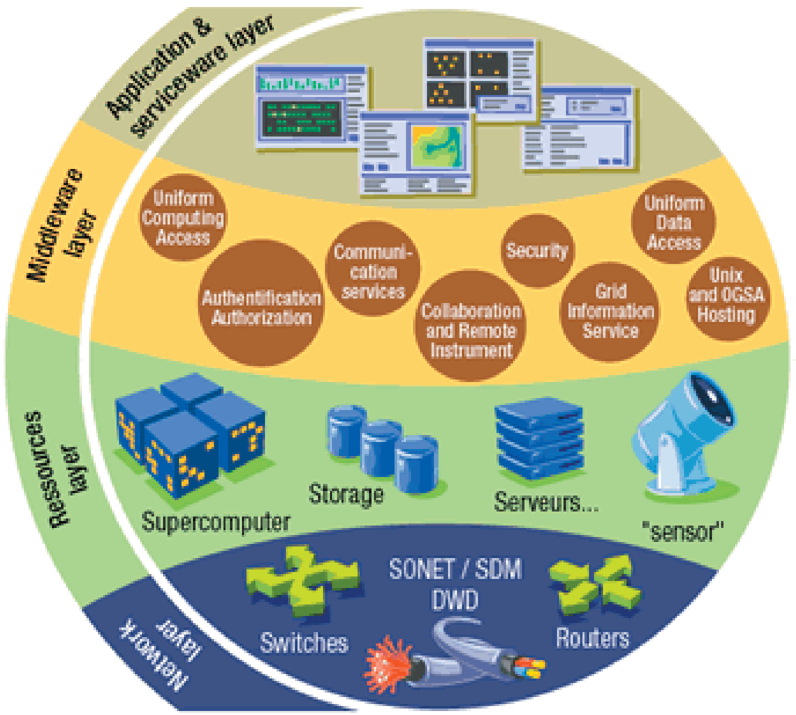


Image courtesy of CERN. CERN copyrights.

## GRID ARCHITECTURE

A Grid is a system that pools computer power and data storage from different locations, and makes these resources accessible from a local computer. So how exactly does the Grid work? Grid technology has several components, often referred to as layers.

*Network layer* Includes the hardware and networks that connect the globally distributed resources, allowing for communication between processors.

*Resources layer* This layer consists of all the physical resources to be shared, such as computers, data storage, media, networks, and perhaps sensor instruments such as video cameras, radio telescopes.

*Middleware layer* Grid middleware refers to the many software programs that integrates the disparate servers, networks, storage resources to make communication and transactions smooth. A crucial part of Grid middleware is the information about how, when, and by whom data was collected. It also records where it is located, to make data readily availible.

*Application and Serviceware layer* Includes all of the user applications that, for example, locate and request data, obtain credentials to acquire the data, and use computational resources to analyze and aggregate data for the user.

and small businesses would have reliable, consistent, inexpensive, and transparent access to computational capabilities for large-scale projects that would have previously been infeasible.

This long-term potential of Grid computing has generated considerable hype in recent years, but a large-scale Grid intended for use by the general public, similar to the electric power grid, remains a rather distant goal.

However, certain communities, such as the scientific research community, already utilize Grid computing for particular applications. At the Large Hadron Collider at CERN, the Computing Grid Project (LCG) is being developed to simulate, process, and analyze LHC data (see Table 1 for more information). The LHC, which in 2007 will become the world's largest and most powerful particle accelerator, will be used by thousands of scientists – including several from the Department of Physics at Columbia – who will use it to learn more about the structure of matter and to test what might have happened in the instants that followed the Big Bang. Once operations begin, the LHC expects to generate 12-14 petabytes (12-14 million gigabytes) of data per year. It will have high requirements for computational power, data storage, data access, and support manpower, at a scale not practical for a single site. The Grid will integrate the assets of participating scientific computing centers in Europe, North America, and Asia. With thousands of scientists from different parts of the globe working together to answer the same questions, seamless, single-authentication access to large volumes of data and to powerful processors from anywhere in the world will be critical. A simple first step would be having some kind of catalog that keeps track of where among the various sites each individual data file is kept and providing transparent access to it. The researcher is not interested in where the files are, and he certainly does not want to spend his time hunting around for each one he needs and then copying the final set to a single location for processing. Grid tools will enable him to access files without knowing where they are located by using a higher-level description, e.g. run number, run conditions, date of data collection, etc. Submitting analysis jobs to run on files located at different geographical sites would also become transparent. Beyond LCG, other projects contributing to the development of Grid technologies for the LHC include the International Virtual Data Grid Laboratory and the Grid Physics Network.

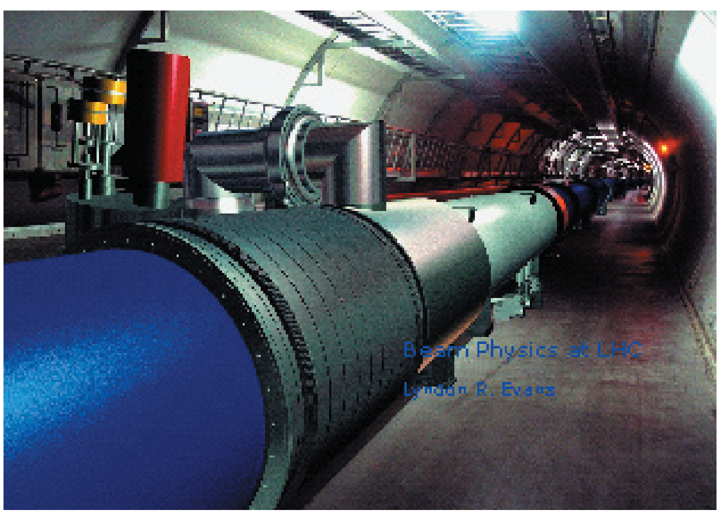
The astronomy community has also benefited significantly from the advent of Grid technology. Some of the most spectacular events in the universe, such as supernova explosions, occur rapidly and unexpectedly. To observe such events, astronomers on the eScience Telescopes for Astronomical Research

| Project | Scope | Website |
|---|---|---|
| Earth System Grid | Climate Research | www.earthsystemgrid.org |
| eSTAR | Astronomy | www.estar.org.uk |
| European DataGrid | Particle physics, medical image processing, Earth observations | www.eu-datagrid.org |
| Globus Alliance | Grid technology development | www.globus.org |
| LHC Computing Grid Project | Particle physics | lhcgrid.web.cer.ch/LHCgrid |
| Particle Physics Data Grid | Particle physics | www.ppdg.net |
| Biomedical Informatics Research Network | Integration of biomedical data | www.nbirn.net |
| National Fusion Grid | Fusion | www.fusiongrid.org |

**Table 1**

(eSTAR) project have recently created "Intelligent Agents." These Agents use Grid technology to communicate with telescopes and each other – after receiving observations and data from the telescopes, they can quickly analyze the data and, if the data is remarkable enough, they can get more observations. This technology allows for research follow-ups without any human intervention, offering a much more efficient and promising method of observing events in the universe.

The development of existing Grid technologies was initially inspired by the computing needs of research communities. Technological innovations originally intended for use within the




scientific community frequently find widespread applications in other sectors. For instance the World Wide Web was first developed at CERN for high-energy physicists to communicate and share information. Only subsequently did it explode into a means of information exchange for millions of private individuals. Now, the proliferation of the Internet and the Web as well as the availability of low-cost, high-performance computers is what has enabled these limited-scale computational Grid applications to become a reality.

Although Grid computing has potential applications throughout society, the computing needs of just a few, specific communities have primarily driven the development of Grid tools thus far. Grid computing is currently being developed largely for research applications, and the groups that make use of Grid technologies right now are also the same ones that design them

Currently computing resources for individual use are generally private. Consider for a moment what our lives would be like if every individual had private, personal access to basic resources such as water and electricity. Each individual would have his own well, available to him alone, from which to draw water in relatively small units whenever personal need arose. In the case of electricity, everyone would have his own household generator or backyard power plant, to be turned on and off as his demand for electricity required. Individual ownership and maintenance of these resources would be impractical if not impossible as well as extremely inefficient.

Today when most of us wish to access computing resources, we sit down in front of a personal computer and work—or play, as the case may be—locally, using mainly the capacities of the machine directly in front of us. This approach of distributed ownership is more convenient for users than, for example, the older computing model of having to request and wait for time on a large, shared mainframe. In addition, these mainframes were not typically available to private individuals, but rather only to members of specific groups such as workers at a particular company. However, while the proliferation of personal computers has offered convenience and widespread availability of computer power, at the same time it has created a much less efficient usage of existing resources, as PCs, now relatively powerful machines themselves, spend a great deal of time with idle CPUs.

Individual ownership and usage is not the only computing model currently in use. Departments in universities and in many workplaces offer access to local clusters of computers, in which a group of processors is networked together and shared by a particular community. Users, via individual accounts, can tap into the pooled resources of these machines, but usage of the cluster remains limited only to members of the community.

How exactly is a computational Grid defined? For one thing, it must involve geographically distributed, separately administered sites, often with diverse, mixed resources, e.g. machines at different sites running different operating systems. This is the fundamental difference between a Grid and a cluster. While a cluster also pools computing resources for shared use, it is local to a single site, administered centrally as a single unit, and frequently has uniform components. A Grid must also provide a single point of access to this conglomerate of distributed resources. An additional key feature of computational Grids is scalability. Grids consist of Internet-based networks of geographically distributed computing assets that can be selected and aggregated as needed in order to solve small- or large-scale problems. For example, businesses that have large seasonal fluctuations could rent more or fewer computing resources depending on the time of year, exactly enough to meet their needs at any given point.

If the power of the Grid comes from transparently interconnecting numerous geographically distributed, heterogeneous resources, clearly standards are needed in order to link all relevant components in a stable, interchangeable way. After the original Grid projects began in the mid-1990s, in 1999 an initial attempt to discuss and create standards was made, and a North American-based group called the Grid Forum was established for this purpose. In 2001 the Grid Forum merged with its European and Asian counterparts to form the Global Grid Forum. The Global Grid Forum holds meetings three times a year and maintains more than forty working-group and research-group mailing lists, to which more than 2,500 people from around the world are subscribed.

A significant development with regard to standards was made recently, paving the way for enhanced collaboration between research Grid efforts and commercial enterprises. Along with the Globus Alliance, which has been leading the implementation for Grid middleware since the inception of Grid endeavors, several corporations, including HP and IBM, proposed in January a new set of Web services specifications that will integrate Grid and Web services standards. While various members of the commercial sector have already initiated a number of Grid projects, this strong expression of interest in and support for Grid technologies by major companies holds promise for enhanced collaboration between the scientific and commercial communities in continued development of Grid tools. The speed with which Grid technologies become more widely available will depend greatly on the role the computing industries choose to take in upcoming years.

As the scientific and commercial communities join forces in continuing to design and create Grid tools, we look forward to an accelerated development of Grid technologies. In the long term, Grid computing could offer greatly enhanced computational capabilities on an on-demand basis to basically all members of society. As other computing-related technologies advance in the meantime, what even a private individual may eventually be able to accomplish with inexpensive access to such powerful resources seems limited only by imagination. But keeping our eyes set on a closer horizon, limited-scale Grid computing has already arrived and is beginning to make contributions in particular to scientific research in a variety of fields. As collaboration among institutions on the local to the international level becomes more and more common and increasing numbers of virtual organizations involving multiple institutions are formed, Grid technology promises to be a powerful and effective tool enabling and enhancing this collaboration. ■

*Christine Aidala is a Ph.D. candidate in Physics at Columbia and this year's winner of the Luise Meyer-Schutzmeister Memorial Award, for women in physics.*

**Want to Know More about the Grid?**

www.gridforum.org
www.gridcomputing.com
www.gridtoday.com

# poking at ATOMS

## The Scanning Tunneling Microscope

**By Hayn Park**

In 1981, G. Binning and H. Rohrer at IBM Zurich Research Laboratory unveiled an instrument that has had a tremendous impact in fields as diverse as physics, chemistry, biology, and now the budding field of nanotechnology. The *scanning tunneling microscope* (STM) allowed scientists for the first time to "see" the individual atoms that make up molecules, crystals, and larger nanostructures – and nowhere is "seeing is believing" truer than in the natural sciences.

Since then, tunneling microscopy has evolved into a variety of different techniques that fall under the general group of scanning probe microscopy (SPM). The core idea is the same: an atomically sharp probe, positioned with angstrom-level precision using piezoelectric materials, is scanned over a surface. In STM, a *tunneling current* between the probe tip and the sample is recorded and collected together to form a topographic image.

### mode of operation

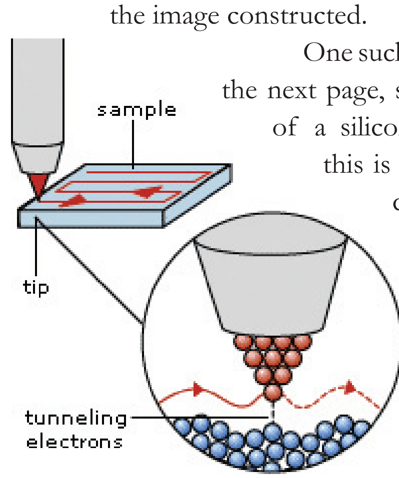
The STM operates by detecting "electron tunneling" between the probe tip and the sample under investigation. Tunneling is a uniquely quantum-mechanical phenomenon where a particle (in this case, an electron) can go from one place to another, even though the intervening space is classically inaccessible. This is because the electron, being a quantum mechanical object, is not localized at a precise point in space; instead, its position is a hazy smear, determined by physical laws that are probabilistic rather than deterministic. Parts of the "smear" can be found on the other side of the barrier, "leaking" through it, and resulting in a small but nonzero probability of being found on the other side. The electron can get to the other side in this way, even if it does not have enough energy to go over the barrier.

When an STM tip is brought within a few nanometers of the substrate, electrons from the atoms that comprise the tip can tunnel across the vacuum gap to the sample, and vice-versa. (In fact, it is this tunneling leakage that hinders the unlimited miniaturization of computer circuits.) Normally this tunneling happens in both directions – however, when a bias voltage is applied across the junction, there is net current flow in one direction which can be detected by a sensitive amplifier.

The STM can operate in two modes: constant height, and constant current. In *constant-height mode*, the tip is kept at a fixed vertical position while it is scanned laterally across the substrate. The tunneling current is exponentially dependent on the separation between the tip and the sample; variations of this tunneling current during the scan are assembled into a topographic image. In fact, it is this exponential dependence that makes the STM so sensitive; a 1-angstrom change in separation leads to an order of magnitude difference in tunneling current. (For a sense of scale: covalently bonded atoms in molecules are separated from each other by 2-3 angstroms.)

The danger of operating in constant-height mode consists mainly of the possibility of crashing into a tall structure during the scan. Thus, constant-height mode is only practical when one is absolutely certain of atomically-flat conditions at all points. Since one is never sure of this beforehand, and many interesting structures can have high peaks and deep trenches, the STM is most commonly operated in *constant-current mode*. Here the STM operates in a feedback loop: a bias voltage is applied, and a set-point current fixed – the control electronics adjust the tip-sample separation (by controlling the piezo) during the scan to keep the tunneling current constant. The variations of the piezo displacement are recorded, and the image constructed.

One such image is *Figure 1* on the next page, showing the surface of a silicon crystal. Because this is a map of tunneling current, the bright-dark corrugation corresponds to electron density as a function of




From www.nobel.se

The conducting probe scans the surface of the sample. Electrons tunnel between the surface and the tip of the probe, and the signal produced is formed into a topographical image.

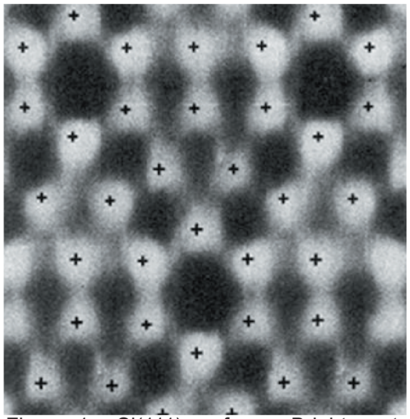


Figure 1: Si(111) surface. Bright spots (crosses) correspond to individual silicon atoms. G. Binning et al., “7x7 reconstruction on Si(111) resolved in real space," Phys Rev Lett 50 (1983) 120

position. For nonmetals, since the electrons of each atom stay fairly close to their own nuclei, we can interpret the bright spots in the image as “atoms”.

*Figure 2* below shows the surface of a metal – gold. The delocalized electrons of the metal are not resolved individually; however, interesting ridges are visible. These ridges arise from buckling of two different packing arrangements of the gold atoms: *face-centered cubic* and *hexagonal close-packed*. There is a buckling mismatch where the distinct packing arrangements meet, giving rise to the ridges known as the “herringbone reconstruction” in Au(111). This structure was inferred by helium atom scattering experiments, but directly observed for the first time by STM.

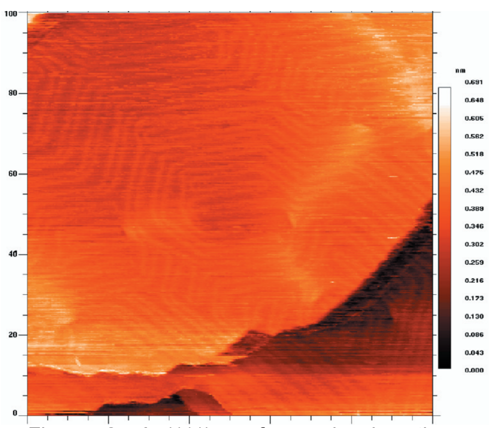


Figure 2: Au(111) surface, showing the “herringbone” reconstruction. Unpublished image from the T. F. Heinz lab, Columbia University.

## impact of STM in the physical sciences

STM has had a tremendous impact in physics. For the first time, it has permitted the direct observation of atomic and molecular wavefunctions, reinforcing our belief that stuff is indeed made of atoms, and that their electrons are best described by probabilistic clouds whose shapes are predicted by the Schrodinger equation. It is physics’ first and most precise local probe; before the STM, scattering and diffraction experiments only gave information on samples that possessed long-range crystalline order. STM has revealed a wealth of information on the irregular and disorderly phenomena that occur at surfaces – an important area of investigation, since it is through surfaces that we interact with our surroundings.

Since the STM is an electrical probe, it has also revealed a wealth of information on superconductivity. Unlike conventional superconductivity, which is based on phonon-mediated reactions, *high-Tc superconductors*

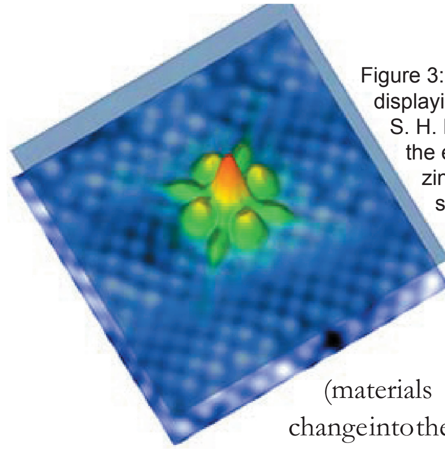


Figure 3: Zinc impurity atom, displaying d-wave symmetry. S. H. Pan et al., “Imaging the effects of individual zinc impurity atoms on superconductivity in BiSrCaCuO," Nature 403 (2000) 746

(materials that make the change into the superconducting state at a relatively high temperature) are thought to owe their electrical properties to “d-wave symmetry” (*Figure 3*, above). Direct images of a zinc impurity[3] validated this model.

In chemistry, STM has opened up the new field of *single-molecule chemistry*. The STM tip has been used to create and make individual bonds, manipulate individual constituents and bring them together to form molecules – a single molecule at a time. By operating at cryogenic temperatures to reduce thermal jitter, researchers are able to synthesize molecules that is more like assembling lego blocks than the traditional methods of synthetic chemistry: *Figure 4* (below) shows how the tunneling current from the STM tip was used to break the bond in an oxygen molecule.

Though STM has been used in biology down to the scales of individual nucleotides in DNA, efforts are often hindered by the requirement that the sample must be at least semiconducting, because a current must flow. In biology, a related probe technique, *atomic force microscopy* (AFM) is often used. In AFM, instead of the tunneling current being used to construct a topographic

continued on **page 42**

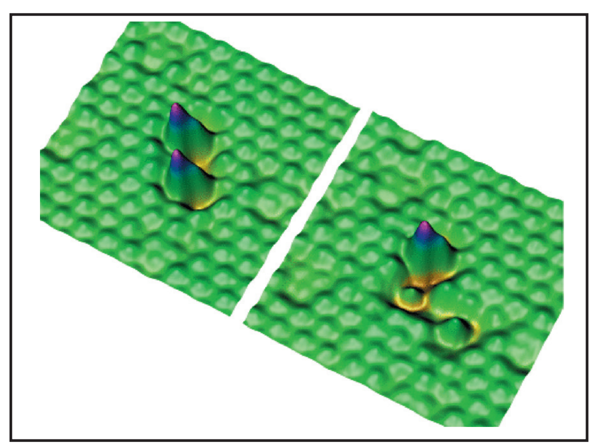


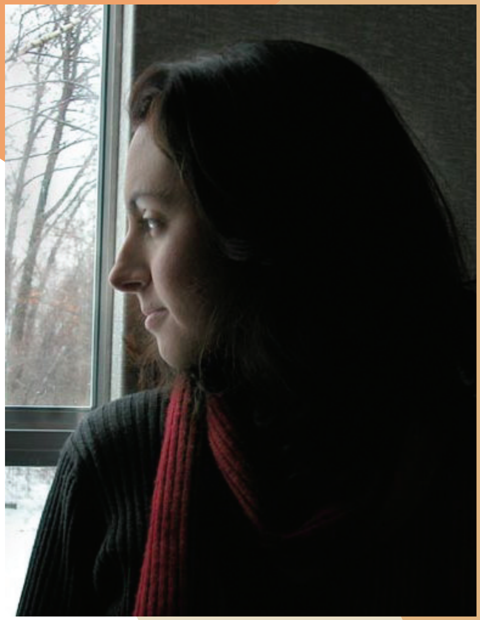
Figure 4: Left: 2 oxygen molecules adsorbed on a platinum surface. A voltage pulse is applied to the bottom molecule. Right: Subsequent scanning shows the top molecule intact, and the bottom molecule dissociated into two oxygen atoms. B. C. Stipe et al., “Single-molecule dissociation by tunneling electrons," Phys Rev Lett 78 (1997) 4410

WITH

# Science and Faith

## A Young Chemist Finds Her Place in the World

**by Miranda Weiss**



Alison Keimowitz

On a Friday evening in a rural town in southern Maine, half a dozen Columbia University scientists studying groundwater pollution from a nearby landfill gathered for dinner at the local Mexican restaurant. For one of the researchers present, a Ph.D. student in environmental geochemistry, it wasn't just the end of a long day of field work, it was the beginning of Shabbat, the Jewish observance of the Sabbath. And so, though 400 miles away from her Jewish community and her husband, a rabbinical student with whom she traditionally shared this ritual, Alison Keimowitz made the blessing over the wine.

Looking back on that evening, Keimowitz laughs, "One of my colleagues asked me 'Is there anything we can do to help?'" For this 28 year-old woman, whose life is rooted deeply in both her religious and scientific pursuits, that evening was one of many instances in which she's had to make accommodations to fully realize these seemingly disparate parts of her life. Although she straddles these two worlds—which often conflict and rarely collaborate—it is the synthesis of science and faith that brings meaning to Keimowitz in her work.

### Reconciling Ethics and Atoms

At the beginning of her career as a chemist, while working towards a Masters degree in physical chemistry at Yale, Keimowitz realized that science could articulate her deeply-held religious views. She was steeped in theoretical chemistry and quantum mechanics and studying Schrodinger's wave equation. "I felt like I could understand better how the universe was put together," Keimowitz says. For many people, the explanation of the workings of the world lies not just within the jurisdiction of science, but in more personal beliefs, religious or otherwise. For this young chemist, it is one and the same. "It was really exciting to see what I look at as God's handiwork written out in these equations," she says. "The idea that God works in math, while ridiculous to say, makes perfectly good sense to me."

Keimowitz describes her physical chemistry studies as "beautiful" but says that she was frustrated by the research because it lacked real world applications. It was the search for an opportunity to use the principles she had learned in her studies to improve people's lives that led Keimowitz away from the theoretical to a more applied discipline. "The work I'm doing now addresses a different part of my religious life, the ethical component," she says. "I feel a really strong compulsion to do science that I think is ethically relevant and useful to someone, and not just cool but fundamentally unhelpful."

Keimowitz belongs to a Jewish congregation started by a group of young people—many of them students—interested in being part of a community that maintains many of the traditional Jewish practices while taking a liberal approach to gender equality and social action. Keimowitz's husband organizes the congregation's social justice activities, which include working with Habitat for Humanity and a homeless shelter and tutoring local middle school students. Helping to make the world a better place is a call to action raised by her faith that Keimowitz pursues through her work as a chemist.

*"The idea that God works in math, while ridiculous to say, makes perfectly good sense to me."*

At Columbia, Keimowitz is studying a rural site only eight miles west of Maine's capital, Augusta, where arsenic has contaminated wells and the waters of a picturesque lake rimmed by about sixty homes. The source of the pollution is a landfill excavated before the adoption of regulations requiring clay or plastic liners. Leachate from wastes—including industrial solvents and resins—dumped at the site since the 1930s has moved directly into the ground below. Chemicals in the leachate created reducing conditions in the sediment, which contains a significant amount of naturally-occurring arsenic. The reducing conditions make this inorganic arsenic—classified by the Environmental Protection Agency as a human carcinogen—water-soluble, so it moves readily into groundwater and down gradient into nearby Lake Annabessacook, known locally as one of the best spots to fish for bass. Because arsenic behaves in the human body similarly to the essential nutrient phosphorous, it is easily picked up by tissues where it causes oxidative damage to cells and is linked to numerous types of cancers including bladder and lung, and to disruption of cardiovascular, pulmonary, immunological, neurological, and endocrine processes.

According to Keimowitz, however, the health threat caused by the landfill is minimal because no nearby residents drink groundwater anymore and the area isn't heavily populated. But Keimowitz sees a profound humanitarian element to her work because it relates to the lives of roughly 50 million people in Bangladesh, where arsenic has contaminated thousands—perhaps millions—of wells through a process similar to what she's seeing in Maine and in a number of New Jersey landfills. Keimowitz's project is part of a larger collaboration between Columbia, the Environmental Protection Agency, Bangladesh's Dhaka University and others and she hopes that what she learns by researching the Maine landfill can be used to improve the lives of millions of Bangladeshis.

### Commitment to Science, Faith

With Keimowitz's deep, personal investment in her work as a chemist, she often finds society's profound lack of respect for scientific knowledge to be a personal affront. "When people ask me what I do for a living and I tell them I'm a chemist, sometimes they'll say something like 'I hated chemistry in high school.' I think 'Who told you that was a socially acceptable response?'"

Keimowitz views her expertise in science as an integral part of her role as an informed citizen, ethical person, and observant Jew. There is a surprising similarity between her scientific and religious pursuits: both require a close attention to the daily details and a sense of the big picture. While working to assess the mobilization of arsenic, Keimowitz must focus on the small actions every day, on repetitive investigations in the field and laboratory, to help answer the big questions she's asking. In her faith, it's the day-to-day continuation of traditional rituals of prayer and celebration that bring Keimowitz closer to the essence of her religious life.

But while scientific research requires an obsession with surging ahead, faith requires holding onto the past, onto rituals revered for thousands of years, onto being slow, deliberate and quiet. "I feel myself to be in tension between the modern aspects of my life and the more traditional aspects." Keimowitz says. "Part of what that means is not just doing only traditional things." In order to fully pursue her work at Columbia, Keimowitz sometimes breaks her Shabbat practice of not traveling or working on Saturdays, or finds herself blessing wine over enchiladas far from her home and her Jewish community.

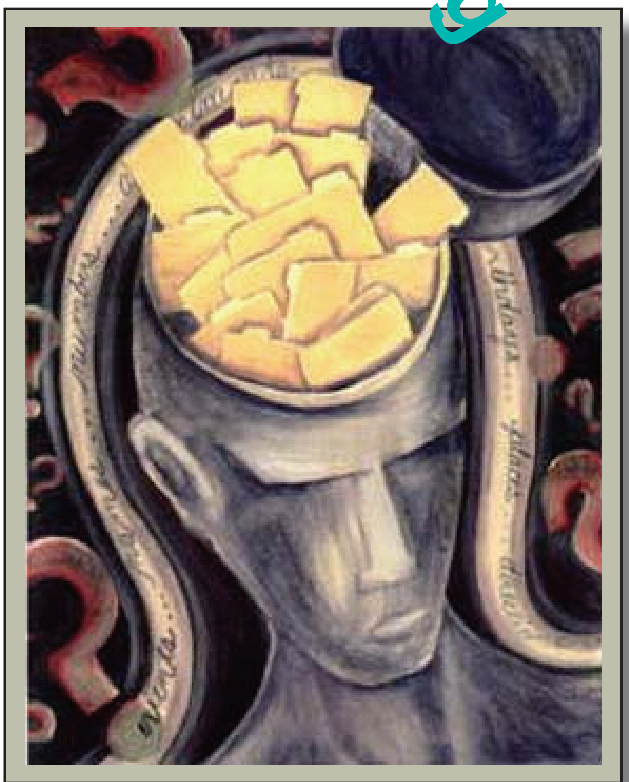
But these small sacrifices haven't quelled Keimowitz's passion for her work. When asked how she ended up being drawn so strongly towards her work in sciences, she says, "You can say God gave us brains and tools to understand this world," but in the end, she explains, that's not really it. "It's just who I am. I want to know how this stuff works."

In the process of trying to figure out how it all works, Keimowitz has learned that typical methods to mitigate arsenic pollution won't work under the conditions she's studying. With the health of millions of Bangladeshis in her mind, Keimowitz is charting new territory in her work at Columbia. "I don't know if there's a best solution and I don't think that everything can be solved," she says. But Keimowitz hopes that the incremental gains in understanding she makes in the field and laboratory will, at some point down the road, bring positive changes to people's lives. This hope, however, requires a little faith.

# the science of forgetting

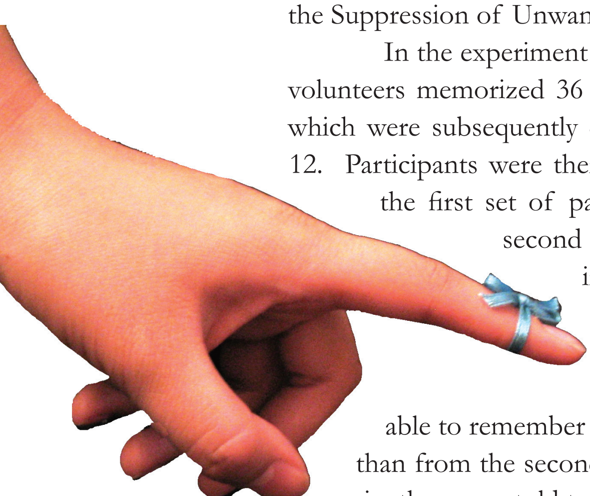
by Patricia Peter

Undoubtedly, there are many times in your academic career (most notably around midterm/finals week) that you wished there was some switch in your brain that would enable you to remember every fact and figure staring at you from that unforgiving textbook. However, instead of criticizing its apparent shortcomings, maybe it's about time you thanked your brain for helping you to forget. After all, who wants to be constantly reminded of that gruesome Orgo midterm, your baggy pant-bedecked MC Hammer phase, or the 125 minutes of your life that was *Gigli*? A recent study conducted by researchers at Stanford University and the University of Oregon unveils the truth about our positively wonderful ability to forget those not-so fond memories.



"Memory" Illustration courtesy of Patti Kern

"The big news is that we've shown how the human brain blocks an unwanted memory, that there is such a mechanism and it has a biological basis," said Stanford psychology Professor John Gabrieli, a co-author of the paper published in the Jan 9 issue of Science magazine entitled "Neural Systems Underlying the Suppression of Unwanted Memories."



In the experiment conducted at Stanford, 24 volunteers memorized 36 pairs of unrelated words, which were subsequently divided into three sets of 12. Participants were then instructed to remember the first set of paired words, to forget the second set, and were given no instructions on the third or baseline set. Results of the study found that volunteers were better able to remember pairs from the baseline set than from the second set containing the word-pairs they were told to forget.

Brain scans using functional magnetic resonance imaging (fMRI) taken of the subjects during the experiment enabled researchers to pinpoint specific areas of the brain connected with memory repression. Increased activation of the dorsolateral prefrontal cortex accompanied a simultaneous decrease in hippocampus activity, suggesting that the overactive prefrontal cortex, linked to advanced thinking and planning skills, inhibits the normal memory-encoding function of the hippocampus. In fact, the results correlated so well with the experimental observations that researchers could predict how well a subject would repress a memory based on the degree of prefrontal cortex activation shown on his/her brain scan.

Now that this study has made great progress in identifying a visible cognitive process connected to the phenomenon of suppression, future implications for the study include examining the harmful effects of repression, not merely from a psychological point of view but from a biological perspective as well. It could also prove to be the basis of further and more fruitful investigations into the mechanisms of coping with psychologically disabling memories and eventually, into the reasons for the inactivity of these mechanisms in victims of post-traumatic stress disorder.

"To me what's most important is achieving a better understanding of how we learn to adapt mental function in response to traumatic life experience," Michael Anderson, the lead author of the study from the University of Oregon, explained. "Survivors of natural disasters, crime, acts of terror such as 9/11 and the loss of someone close all undergo a process that may continue for a very long time--a process of learning to adjust both physically and mentally to those events."

A mechanism of physically inducing repression could allow trauma victims who are unable to block out painful memories to lessen their emotional distress by helping them forget, a mode of treatment whose benefits are debatable. While some psychological schools of thought would perhaps champion the easing away of painful memories in patients, others are in favor of an open confrontation with the traumatic experience. Although Sigmund Freud investigated the effects of unconscious memory suppression and not the voluntary action investigated in this experiment, extrapolation from his theories could suggest that the voluntary repression of memories, like the involuntary act, might fester into full-blown neuroses, harming the patient more than helping him.

More remotely, the study has the potential to utilize the principles of neurobiology to treat other complex psychological ailments. For example, a derivation of the concept of memory suppression is the repression of thoughts related to cravings, which could be used as a means of combating addiction.

Of course, all of these potential applications are at this point speculative. Like any initial laboratory findings, it is difficult to extrapolate from the innocuous memorization of word-pairs in a controlled laboratory environment to the traumatic memories of an incident such as 9/11. However, this study retains its importance through its identification of an intriguing neurological mechanism, providing us a small glimpse of the innumerable secret workings of our fascinating brains.

So, the next time you feel the lyrics of "Cant't Touch This" surreptitiously emerging from that cobweb-laden corner of your brain, in the words of many a New Yorker, fuhgeddaboutit!

*Patricia Peter is a first-year in the College.*

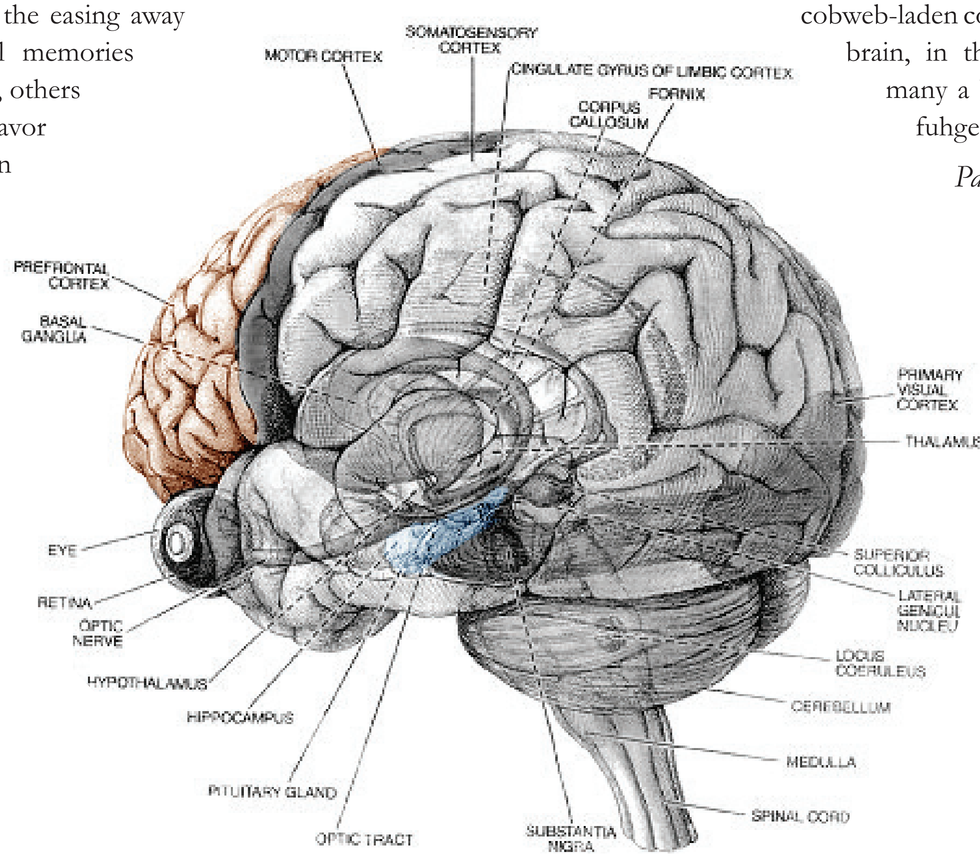
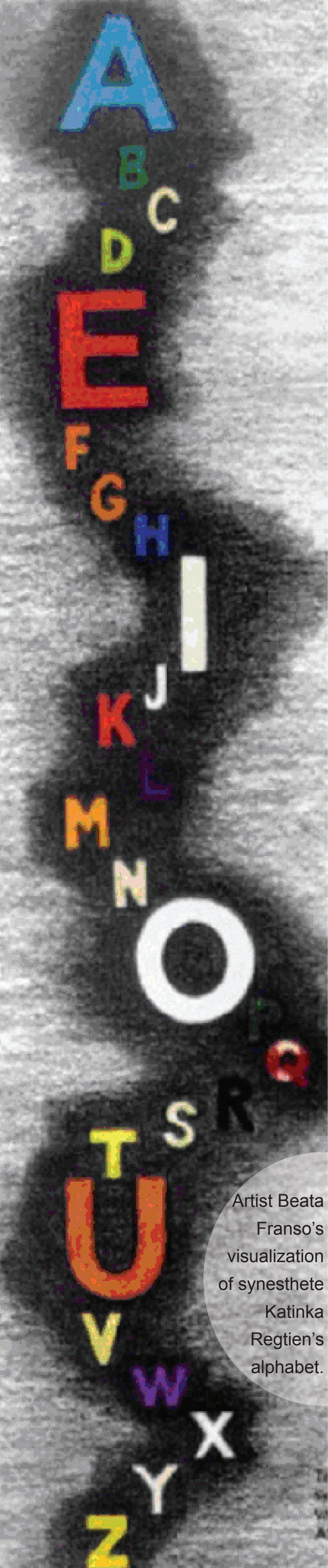



Illustration courtesy of Carol Donner



Artist Beata Franso's visualization of synesthete Katinka Regtien's alphabet.

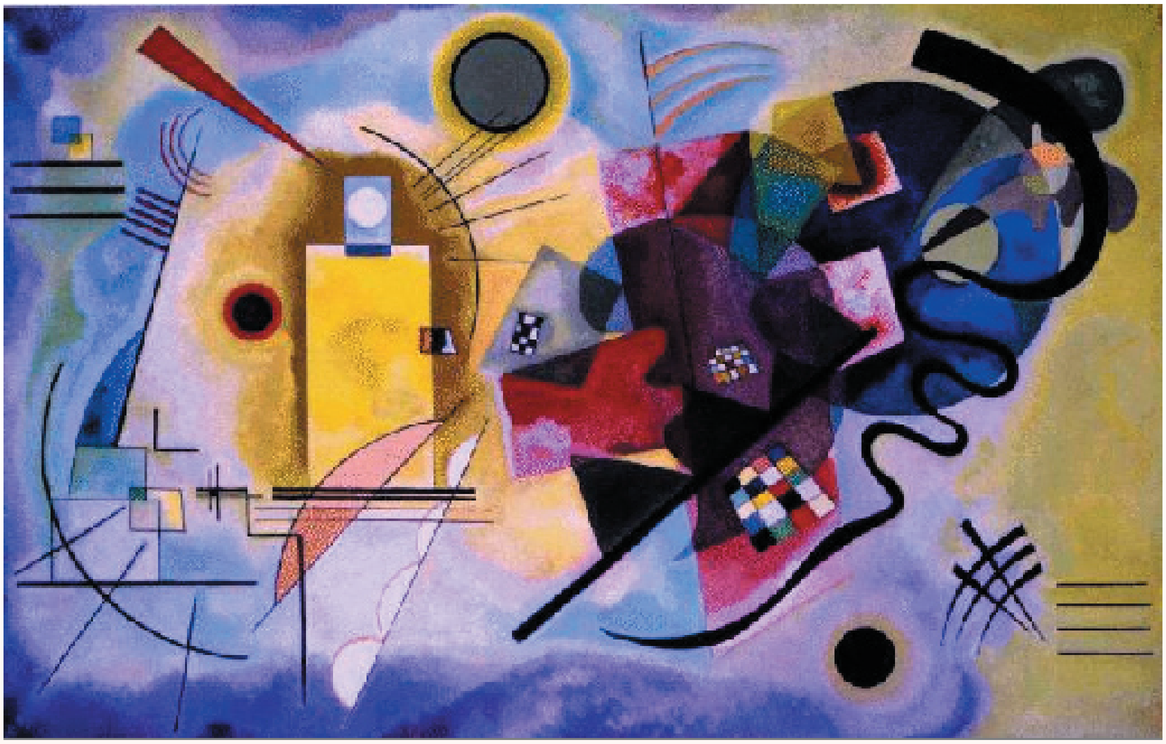
# Blue MONDAYS

By Hila Esther Katz

Rachel*, who in all respects leads a normal life, has a condition that adds a little more color to her days. For instance, when she hears a word beginning with an 's' sound, a specific shade of green appears before her eyes. Mentioning the month of May evokes pink in her vision, while June elicits a shade of blue. For as long as she can remember, Rachel has been seeing colors in response to hearing certain words or sounds. Until a point in her life when she learned otherwise, she had thought that everyone experiences joined perceptions of sound and color – that December, when spoken aloud, makes all people see green, whereas Sunday is yellow in the world's shared vision. Rachel has her own personal kind of synesthesia, a phenomenon that for many decades was documented as firsthand, subjective accounts, but only in recent years has begun to elicit a flurry of experiments and tests from the scientific community. Here in Columbia University's psychology department, Dr. Michele Miozzo and his language laboratory have been working with Rachel to explore her unique manifestation of synesthesia. Not only was this an opportunity to investigate the various claims that Rachel has made about her condition, but also to answer questions about what exactly triggers the colors that she perceives – is it only the sounds of the word that evoke blue or green, or do other aspects of a word also elicit color? As it turns out, Rachel has a rare form of synesthesia, more complex than the joining of basic speech sounds and colors.

Synesthesia, or "joined sensations", assumes many forms and can conceivably occur between any two senses. One individual, described in Richard Cytowic's *The Man Who Tasted Shapes*, reported that certain flavors elicit tactile sensations of basic shapes; after preparing roasted chicken, he remarked that, because it did not taste pointy enough, it must not have come out right. Even within a more commonly reported form of synesthesia, where sounds and colors are paired, there is wide variation. Sometimes the auditory synesthesia involves musical tones and colors; in other cases, the colors are joined to different speech sounds, or phonemes. And if two people share the same kind of synesthesia, such as tone-color, there will be individual differences in the colors and intensities that are linked to each sound; playing the note C on the piano will elicit murky brown in one person, and a molten orange in another.

Wassily Kandinsky, who was deeply interested in synesthesia, painted “Yellow, Red, Blue” (1925), seen at right.



Regardless of the specific kind of synesthesia, the phenomenon seems to have common characteristics. Synesthetic perceptions are involuntary and automatic. When Rachel hears the word Sunday, she does not have to consciously think of the color yellow; it arises unbidden, without any active effort on her part.

Another characteristic of synesthesia is stability over time – in Rachel, the same color is always elicited by the same auditory stimulus; the synesthetic associations do not change over months or years. After Rachel first reported her synesthesia to Miozzo, he presented her with a vast chromatic spectrum on Microsoft Word and asked her to point out the particular shade of each color elicited by its corresponding stimulus; for instance, when she mentioned that December evokes green, she had to select, from the mind-bogglingly numerous shades of green, the tint that most closely matched what she saw. A few months later, when she was asked to point out the colors again, there was virtually no variation from the highly specific choices she had previously made; a sneaky non-synesthete, attempting to trick the scientific establishment, would not have been able to replicate the original choices with any credible degree of accuracy.

As in other reported cases of synesthesia, Rachel’s perceptions seem to arise in the external world. When exposed to a word, Rachel sees the corresponding color as a translucent film, appearing briefly at a few centimeters before her eyes; to her, the colors are very real and do not seem to exist in her head, the way a sensation conjured up the imagination would.

Rachel’s synesthesia lies entirely within the auditory realm. Though she also sees colors after hearing the names of numbers, the experiments conducted by Miozzo and his lab focus on the facets of her synesthesia involving words and speech sounds, or phonemes. The first phoneme of every word that she hears elicits a color. Giraffe and gunslinger, for instance, evoke different colors because they begin with different sounds; giraffe and geranium, on the other hand, share the same color. However, Rachel’s synesthesia is not limited to phoneme colors. The names of months and days of the week also elicit a color that is independent of the word’s individual sounds, and instead seems to correspond to the word as a whole. For example, Saturday and Sunday have the same phoneme color, because they both begin with ‘s’ sounds. However, Saturday also elicits a red word color, and Sunday elicits yellow.

It is difficult to imagine how Rachel experiences both a word color and a phoneme color when she hears the name of a month or day of the week. The way she describes it, the two seem to appear simultaneously in her vision. Initially, however, the word color is much more intense than the phoneme color and so predominates in her visual field; but, intense as it is, the word color fades very quickly, while the phoneme color lingers in her vision a little bit longer.

Because all of this happens very rapidly, one of Miozzo's goals was to capture, in a quantifiable way, the timings and intensities that Rachel reports in regards to the two classes of colors; a more objective measure could separate out when each color appears in her vision and for how long. In studying the differences between the two colors, Miozzo was also investigating whether they arise from two different levels of language processing in the brain. Does Rachel's synesthesia reflect certain aspects of how all of us process language input?

Rachel was given a series of auditory priming tasks. For one experiment, she heard an auditory stimulus such as "Saturday". 200 milliseconds later, she was presented visually with one of two color patches: either green, which is the phoneme color for Saturday, or an unrelated color like brown; her task was to name the color. In another variation of the task, she was presented, after 200 milliseconds, with either the stimulus's word color or an unrelated color; for Saturday, the patch corresponding to the word color would have been red. The logic is that if Rachel were indeed seeing green/and or red within 200 milliseconds after hearing "Saturday" she would be faster at naming those colors than she would an unrelated color.

Rachel was significantly quicker at naming both the word color and the phoneme color. However, though both word and phoneme colors showed a significant priming effect, the word color was named more quickly than the phoneme color and exhibited a stronger priming effect. The results correspond with Rachel's subjective account, in which she reported that although both colors appear simultaneously after she hears a month or day of the week, the word color is a much more intense hue and overshadows the phoneme color.

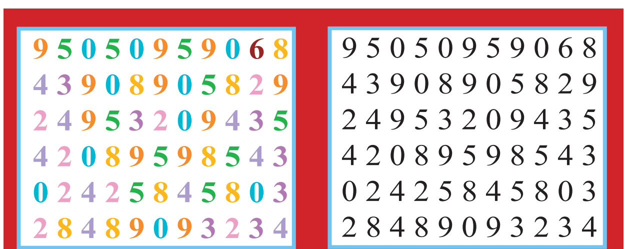



*Fig 1.* A sample pop-out test. An assortment of numbers is printed in black and white. A synesthete with a visual association between numbers might see this assortment like the figure on the left.

What if the interval between the presentation of the auditory stimulus and the display of the color patch were lengthened? When Miozzo extended the interval to 400 milliseconds, the results also changed in one key respect. Though the phoneme color still showed a significant priming effect of the same strength it had shown at 200 milliseconds, the word color's effect was now weak and no longer significantly stronger than that of the unrelated color patch.

Again, the results support Rachel's account. She had reported that the word color makes an intense initial appearance in her vision, but fades very quickly; in the 200 millisecond priming task, the color patch that she named most quickly was the one that corresponded to the word color, but when the interval was lengthened to 400 milliseconds, she could no longer name the word color significantly faster than the unrelated color. On both the 200 millisecond and 400 millisecond versions of the task, the speed with which she named the phoneme color remained virtually unchanged; unlike the word color, its effect had not weakened at all with the extension of the interval. Just as Rachel had earlier stated, the phoneme color never reaches the same intensity as the word color in her vision and does not fade as quickly.

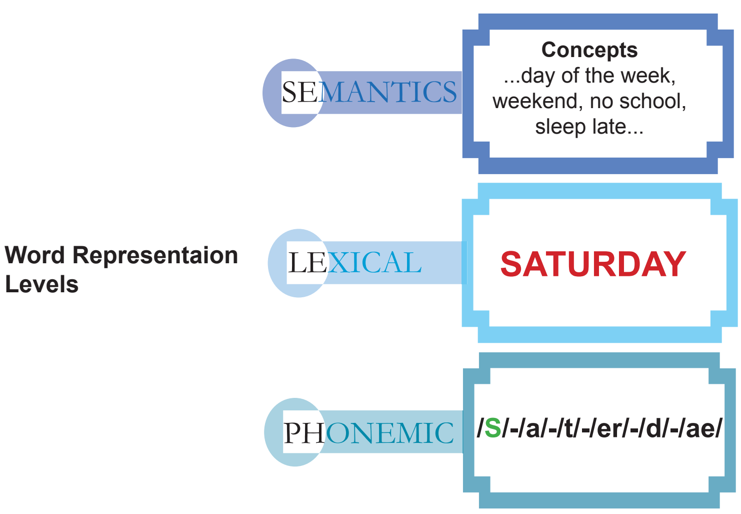
"The auditory priming tasks," Miozzo says, "have been a unique approach to seeing the synesthetic process unfold dynamically, over real time." And by revealing that the word colors and phoneme colors are independent of one another – in the kind of color, in their time courses, and in their intensities – the auditory priming paradigm provides evidence that they are elicited by two different kinds of language-related information in the brain.

It is generally believed that, in the brain, there are different levels of information for each word that we know. There is a level of semantics, which contains the meaning of the word and all of the word's relevant associations; at the semantics level, "Saturday" might be tied in to concepts of "weekend" and "no school" and "sleeping in late". Another kind of information lies at the phonemic level, where a word is broken down into its sound components – s-a-t-er-d-ae. It is the phonemic level of representation that Miozzo believes elicits the phoneme color; whenever Rachel processes the word "Saturday" and accesses the 's' phoneme, green appears in her vision.

What kind of linguistic information elicits the word color? The word color is independent of the phoneme color and hence the individual sounds that make up a word. Miozzo also does not believe it stems from the conceptual level. The word color is evoked only when Rachel hears the word, not when she sees it; however, if the color did indeed arise from the level of meanings and associations, it should be elicited regardless of how the word is accessed. Meaning does not change depending on whether one scans a word's letters on the page or listens to it spoken aloud.

The word color most likely stems from a representation intermediate between where the word's meanings are stored, and where it's individual sounds can be accessed. These intermediate representations are known as lexical; between the level in the brain that tells you that you are thinking of a school-free weekend day, and the level in the brain that gives you its different sounds – s-a-t-er-d-ae – there is this lexical representation, which gives you the word as a whole, in an abstract form: SATURDAY.

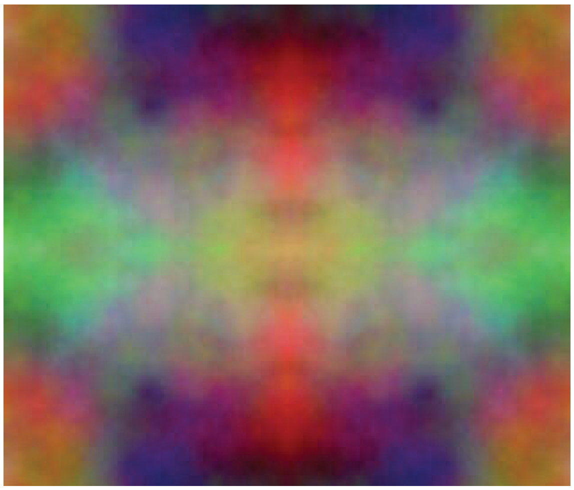
The lexical representations that elicit Rachel's word color are accessed only when Rachel hears the word spoken aloud. The phoneme color, on the other hand, is not elicited only when a word is heard aloud. If Rachel is presented visually with a word and given a chance to read it at leisure, after 400 milliseconds she will see the phoneme color. The reason, Miozzo explains, is that viewing the word for this amount of time has given her a chance to "hear it in her head"; the letters on the page link up to the corresponding phonemes, which trigger the appropriate color. The word color, on the other hand, is not evoked.




Rachel's synesthesia, however, is not visual; individual letters, for example, will not appear in color. When given a visual priming task – similar in all respects to the auditory priming task, except that the word is flashed on a screen rather than spoken aloud – Rachel showed no priming effects. Miozzo also gave her a visual search task, a test employed by researchers to investigate whether a synesthete really does see color when exposed to certain visual forms or features. A synesthete with an association between number form and color is presented with an array of numbers such as sixes, nines and zeroes. To the synesthete, one of the numbers has a color distinct from all the others; for instance, a six might induce bright red, while other numbers on the display elicit yellow, green, or light blue. When presented with an array where a six is embedded among many other numbers, the synesthete sees the six "pop out"; because it is different from all the other numbers by one feature – its color – the synesthete is able to point to it immediately, regardless of how many distractors there are. A non-synesthete, on the other hand, would see all the numbers in black print, as presented. The six would not stand out, requiring a search for the number that would increase in time as more distractors are added to the array. Rachel, who sees colors when hearing the names of numbers, does not experience a visual "pop-out" effect.

The experiments conducted by Miozzo's lab have explored the complexities of Rachel's unique kind of synesthesia; corroborating and complementing her personal account with experimental results have shown that she has a form of the phenomenon that has been hardly documented. She does not associate only the basic sounds of speech with color, but – when it comes to days and months of the week – her color perceptions are connected to a more abstract level of linguistic representation. Studying her synesthesia has further illuminated specific facets of language processing – the levels of representation that we tap into when hearing speech, how fast we may hear, in our heads, the sounds of a word after reading it; what is seen in her condition corresponds to much evidence from other studies, unrelated to synesthesia, that have been gathered in the field.

Researchers are interested in synesthesia not only because it is a fascinating condition in and of itself, but because it might give us insights about the brain in general. A generally held belief is that in the normal human brain there is some degree of separation, or modularity, between different sensory systems. Because synesthesia appears to be a breach in modularity – mixing, for instance, basic sensations of tone and color, or in Rachel's case, joining color to a word's lexical representation – scientists hope that by studying it, they might better understand how different systems of the brain interact and the degree to which they share information. Another issue researchers are interested in is what is known as the "binding problem" – when we look at an object, such as a tree, how do we combine all our separate perceptions of it? The details of its color, its texture, the lines of its form, the shape of its trunk and branches are all bound together by our brain, so that we know that we are seeing a single object. Can the study of synesthetes, with their inextricably joined perceptions, reveal to us something of how the brain binds percepts together? There is much that remains to be investigated.



**Courtesy of Dr. Elizabeth Pector**

Miozzo has demonstrated that synesthesia itself has some flexibility and can be extended across sensory modalities. In a classical conditioning paradigm, Rachel was trained over the course of a few days to associate the months and days of the week with arrows of different orientations; for instance, every time she heard "Saturday", she was shown an arrow pointing up, whereas Sunday was paired with an arrow pointing down. Within a short time, the arrow alone was able to automatically elicit both word and phoneme colors, and when given a priming task where an arrow was followed by a color patch, Rachel showed significant priming effects in naming synesthetically relevant colors. The colors that were ordinarily linked to phonemes and lexical representations were now joined in an involuntary, automatic relationship with arrows; the synesthesia's modalities had been manipulated.

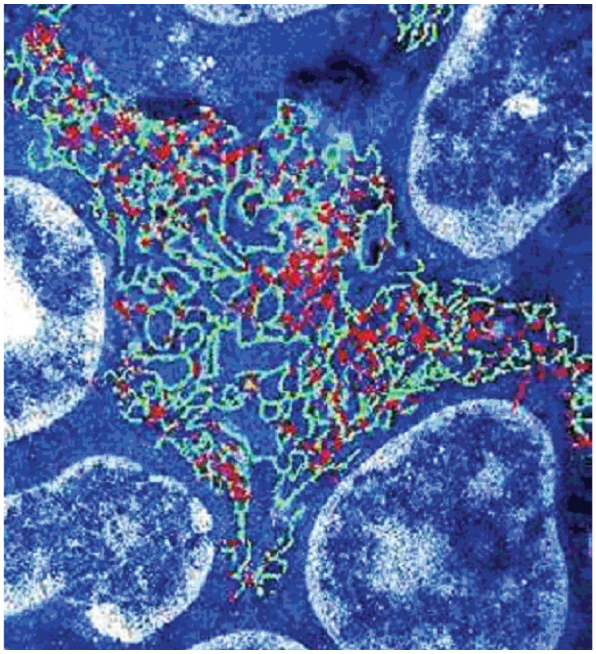
The effect of the conditioning, however, faded after a week of no further training, contrasting with Rachel's long-lasting, constant form of auditory synesthesia – what she has always remembered having.

How synesthesia originates is still a mystery; though it is thought to have a strong genetic component, running in families and appearing more commonly in females than in males, scientists are still unsure of how it arises in the brain. One popular theory posits that all infants are born with a lot of cross-wiring between different senses, but that a non-synesthete's brain will eventually prune its neural connections in a way that establishes greater modularity between the senses; in a synesthete, some of those intersensory connections would remain. The specific form of the synesthesia might also be influenced by experiences the synesthete has during early development, when the brain is most malleable.

That much remains to be researched about synesthesia and what it can tell us about both the adult and infant brain, and that much of what is known of the condition so far comes from subjective accounts of those synesthete's willing to describe their experiences, contributes to the skepticism often felt towards synesthesia. The main charge leveled against synesthetes is that the relationships between their eliciting stimuli and corresponding perceptions are associations that they consciously taught themselves over years and years, driven by whatever motive. Often the association is likened to a metaphor that has been taken to the extreme, a particularly catching idea given that several synesthetes achieved their prominence as artists – Vladimir Nabokov associated letters with colors, while composer Michael Torke writes works such as *Ecstatic Orange* – a composition with a central tonality of orange G-sharp.

The evidence collected by Miozzo and a growing number of other researchers help take synesthesia away from the realm of purely subjective accounts and establish it as a real phenomenon deserving of scientific inquiry. The various tests and tasks conducted on Rachel have served as a new lens through which to view synesthesia, lending greater credence to Rachel's specific account and to the more common characteristics of the condition. Rachel's unique form of synesthesia has also given us further glimpses into facets of language processing. Synesthesia is a fascinating phenomenon, worthy of being investigated not only its own right, but also for the insights it can provide about the brain in general.

*Hila Esther Katz is a third-year in the College, studying psychology and creative writing.*



Dendrites of a follicular dendritic cell (green) in spleen, covered with prion proteins (red). Image courtesy of Martin Jeffrey.

# Mad Cow Disease

## can we stop the madness?

By Donghun Lee

Mad cow disease does not immediately eat holes into the brain. For several years an infected cow might seem perfectly healthy; the disease has a long incubation period in which the animal displays no symptoms. Farmers can be fooled by the cow's apparent well-being, and it's only when the strange behaviors kick in that they know that something is wrong. The animal seems sluggish and depressed; it becomes hypersensitive to its environment and shies away from narrow gates and pens. Soon after, the signs of illness are more pronounced. The creature may involuntarily grind its teeth and salivate in excess; it experiences a loss of muscle control, and may not be able to stand up or walk. All of these symptoms arise from irreversible destruction to the brain; BSE, more commonly known as mad cow disease, blots out nerve cells and forms pores in the neural tissue, resulting in death some weeks or months after the initial appearance of the symptoms.

The first BSE-infected cow was found in Great Britain in 1986. The meat-and-bone meal (MBM) that was fed to the cows contained bones and intestines from scrapie-ridden sheep. Scrapie, which affects sheep and goats, belongs to a larger category of neurological disorders called Transmissible Spongiform Encephalopathy (TSE); TSE also includes chronic wasting disease, which afflicts deer and elk, and kuru, or laughing disease, which arose among New Guineans as an unfortunate byproduct of cannibalism. Diseases grouped under TSE exhibit similar symptoms of spongiform lesions in the brain, making it as porous as Swiss cheese. Until 1986, when BSE broke out in cows, and 1996, when it was first documented in humans, the various disorders in the TSE category were considered unable to spread outside the host species.

In 1988, when the British government banned feeding MBM to cattle, scientists still did not know of the disease's lengthy incubation period, which averages ten years. It was not until 1996 that they discovered that eating fully cooked food containing a small amount of an infected cow's nervous system could cause the same disease in humans. Because of its symptoms, which are similar to Creutzfeldt-Jakob disease (CJD), the human BSE-like disease is called variant CJD (vCJD). The same pathogen that engenders BSE afflicts human victims of vCJD, who undergo BSE-like symptoms such as depression, loss of coordinated muscle movement and eventual pre-senile dementia. And like BSE, vCJD is degenerative and incurable. Follow-up experiments conducted on mice and monkeys proved the disease's adaptability; the BSE agent caused diseases similar to BSE and the human form of BSE in both animals.

In 1982, S.B. Prusiner postulated the nature of the pathogen causing scrapie, BSE, and the human form of BSE. Prior to then, scientists believed that pathogens must contain nucleic material, so as to be able to replicate themselves. However, after exposing the BSE pathogen to ultraviolet rays and radiation, which destroy DNA and RNA, the infectivity of the pathogen was not affected. Thus, DNA and RNA were ruled out as the pathogen's core. Surprisingly, it was determined

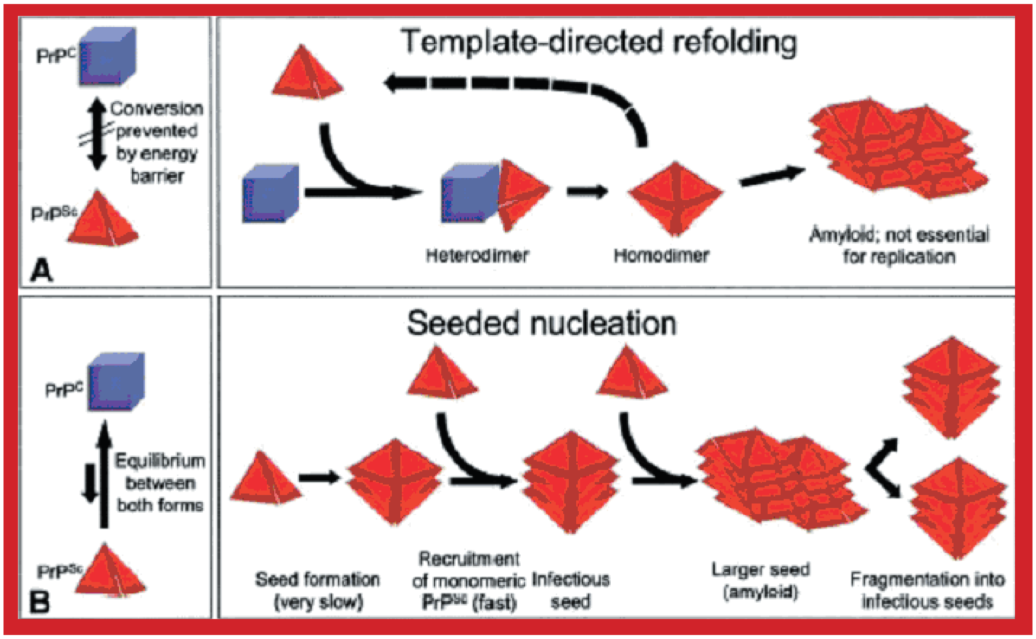



**Figure 1:** Suggested mechanisms of prion particle accumulation and amyloid formation.

that protein is behind the infectivity of the pathogen, and that it was able to reproduce itself without RNA or DNA. Moreover, scientists were stunned to note that these proteins survive most types of heat denaturation and enzymatic digestion – including exposure to proteinase K, an enzyme that digests many proteins. Never having before encountered proteins that alone could transmit infectious diseases, Prusiner coined the word prion, short for "proteinaceous infections particle."

The first prion protein was purified from scrapie and called PrPsc (sc for scrapie). Though the exact mechanism is still vague, PrPsc seems to reproduce itself neither like cells nor like viruses. PrPsc catalyzes the conversion of PrPc (PrP-cellular), which exists on the cellular membrane of neurons, into PrPsc. Because the two are the same proteins folded in different ways, the conformation change is the only step to create PrPsc from PrPc, not involving any alteration on the DNA or RNA level (Fig 1).

The accumulation of PrPsc is the inevitable step toward destroying brain cells. Though the mechanism of PrPsc dealing damage to neurons is not yet clear, hypothetical models suggest they work by forming fatal holes in the cell membrane or by aggregating inside the cell and disrupting certain pathways. PrPsc molecules assemble into filaments in brain tissue, and these filaments accumulate in space between neural cells to form amyloid plaques, the protein-polysaccharide substance found in the brains of dementia victims (Fig2).

Experiments have shown that it is possible to induce infection by feeding animals with prion-contaminated tissue, as well by directly injecting the tissue into the brain or blood stream. Human beings are vulnerable in these three respects, as well: by eating contaminated food, by getting transfusion of contaminated blood, and by contacting contaminated surgical instruments, lab supplies, medicine, or cosmetics.

If the infected food is eaten, how might prion particles travel to the brain? There are a number of different pathways. As seen in experiments involving mice, prions can travel along the digestive tract and accumulate at Peyer's patches, lymphoid tissues lining the small intestine. From there, prions migrate to the spleen along the nerves called thoracic sympathetic fibers up to the spinal cord, and eventually to the brain. More recently, scientists spotted another probable route involving the vagus nerve – the tenth cranial nerve responsible for controlling digestive responses. The nerve is distributed along the most of the digestive tract, so prions can infiltrate the tongue and hitchhike on the vagus nerve, which is connected directly with the brain, bypassing the spinal cord. By means of axonal transport, prions seem to travel the long journey along nerves. If there is a tongue infection, the cranial nerves can be invaded directly. On the whole, the body contains numerous points of vulnerability to the pathogen; lymphoid organs, such as the lymph nodes, spleen, and nerves comprising the peripheral nervous system (PNS) all appear to be crucial gates through

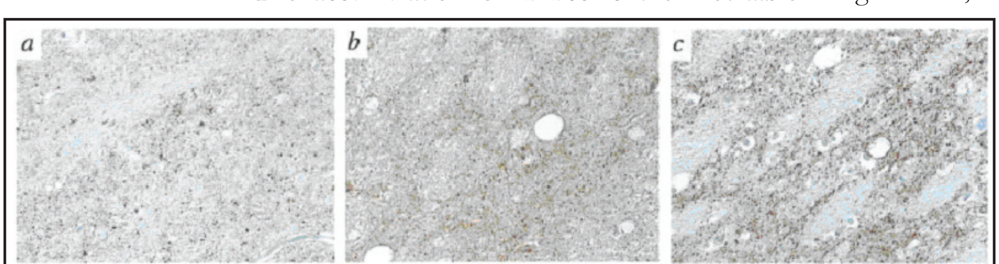



Figure 2: TSE-infected thalamus tissue in monkey (Cynomolgus macaques). Agents are (a) kuru, (b) BSE, (c) vCJD prions. *Corinne Ida Lasmezas, et al. "Adaptation of the bovine spongiform encephalopathy agent to primates and comparison with Creutzfeldt-Jakob disease: Implications for human health." PNAS March 27, 2001 vol.98 no.7: 4146. Fig. 4 Copyright 2001 National Academy of Sciences, U.S.A.*

which prions enter the central nervous system.

Humans and animals can also be infected if prion-contaminated blood enters the blood stream. Because prions can survive UV radiation and 131-degree-Celsius pressurized heating, basic sterilization methods in hospitals and research institutes are unable to disarm the prions' infectivity. Although research has yet to map out the exact migratory route from lymphoid organs to the PNS, prions will invade the brain so long as a lympathic network exists in the vicinity regardless of the initial injection point, and the blood vessel is no exception. Contaminated blood transmits vCJD, a contention supported by experiments on animals and the case of the first suspected victim of vCJD, who contracted the disease after exposure to red blood concentrate in 1996. As a result, many countries have prohibited people who received a blood transfusion in England from donating their blood.

An endoscopy, the operation in which the interior of a bodily canal or hollow organ is examined, also bears a potential risk because an instrument travels through a digestive tract such as the stomach or colon, where PrPsc is also distributed. Unless a special sterilization method against PrPsc is taken, the device may transmit prions lingering on it to other patients receiving an endoscopy.

**WHEN RESEARCHERS erased the PrPc gene in mice, the mutant mice developed normally but they were resistant to prion infection.**

Another risk is that various portions of a cow such as the sera, tallow, and gelatin are either included or involved in producing vaccines, cosmetics, and laboratory supplies. Although the infectivity of such tissues is not fully investigated because of its low relevance to prion's infection route, those tissues may turn out to be Trojan horses.

In addition to prions' fatal prognosis and versatile invasion route, their adaptability aggravates the problem. A strain of prion, such as scrapie prion, cannot infect animals except its original host when a small amount is infected. However, a horde of prions can override the species barrier, because mutant particles may exist in the pathogens in higher probability. Moreover, a few generations in a new host is enough for prions to adapt and show symptoms within much shorter incubation period, according to experiments on mice. This adaptability poses a new threat: the advent of human-adapted prions, a trace amount of which can infect human beings more quickly.

Scientists have found various compounds delaying the onset of BSE or scrapie, ranging from organic dyes and antibiotics to anti-psychotic drugs. However, most of them work only in the laboratory, and many obstacles still exist such as minimizing cellular toxicity and appropriate drug delivery. At this point, preventing further spread of BSE or vCJD is still the most effective action.

Unfortunately, current immunohistochemistry detections are not sensitive enough to spot a hamster scrapie prion population, large enough to infect other hamsters, lurking in a mouse brain. BSE prions lying low in the contaminated tissue can even escape the current screening method. To make matters worse, this method cannot be performed without damaging the suspected tissue, and it will not even detect prions until a few months before the manifestation of vCJD. Given its long incubation period, the lack of reliable early detecting methods may have led to an underestimation of the disease's capabilities and scope. The recorded 145 vCJD cases in Europe, one case in Florida in 2002, and one case in Saudi Arabia in 2004, may be a part of larger population of asymptomatic carriers. Therefore, developing a highly sensitive biopsy detection method against prion particles is crucial to investigate vCJD epidemiologically.

To prevent further infection in cattle and sheep populations, most countries have banned using meat-bone-meal (MBM) as fodder for ruminant animals. Although prions seem incapable of infecting pigs and chickens by oral route, intra-cranial infection performed on pigs caused vCJD-like disease in pigs. Considering the potential for prions to infect these animals, not only cattle and sheep but also non-ruminant livestock should be incorporated into the current MBM ban. Moreover, since BSE prions are not only localized in high-risk tissues such as brain, spinal cord, or lymphoid tissues, further studies on the possible infectivity of industrially consumed parts in cows are needed. Most of all, the false belief that cooking prions removes its infectivity must be purged. Scientists who treated infected tissue at 360 degrees for one hour still found lingering infectivity; cooking the infected tissue cannot prevent contracting vCJD. Thus far, the best way to prevent contraction is to avoid eating prion-contaminated food.

Considering possible human-to-human transmission by carriers, who appear normal during the incubation period of the disease, systematic tracing of surgical implements used on people with vCJD-like disorders is necessary. Introducing special sterilization procedures that will completely inactivate prions is also an urgent issue to curtail human-to-human transmission. Furthermore, the infectivity of contaminated blood components calls for new screening criteria in blood transfusion.

Although the UK government's national project to build a BSE- and scrapie-resistant sheep stock by selective breeding seems to be unsuccessful, scientists have sought for fundamental treatments. They have focused on the fact that prions cannot proliferate without PrPc, a normal form of prion in animals. When researchers erased the PrPc gene in mice, the mutant mice developed normally but they were resistant to prion infection. Moreover, these Prnp knockout mice produce PrPsc antibodies when exposed to prions, whereas the immune systems of normal mice consider PrPsc a friendly molecule because they have PrPc in their own cells and do not produce an antibody against PrPsc. If this can be directly applied to cattle, the resulting genetically engineered cow may be resistant to BSE.

Despite this promising research, the PrPc-gene deprived mice turned out to suffer mental abnormalities such as late-onset ataxia and minor learning impairment. Also, a recent study in Columbia's Kandel lab suggests that long-term memory storage may be related to prion-like functioning of a neuronal protein. Before scientists can apply the knowledge of prions to human beings, they must have a deeper understanding of PrPc—the infective prions' normal counterpart.

Pathogenic prion proteins have opened a new field of research and became another cornerstone to understand how the brain functions. However, a pharmaceutical or genetic approach to vCJD is still far from realization, due to our insufficient understanding about prions and their normal role in humans. The epidemiological approach still has many blind spots without a high-sensitivity detection method that can identify carriers of BSE and vCJD in advance to prevent inadvertent transmission within and across species. Therefore, minimizing additional contract is the most realistic and effective action currently available.

*Donghun Lee is a first year Rabi scholar at Columbia College studying biology.*

continued from **p. 29** STM

map, the electrostatic repulsion between the electrons of the tip and sample are recorded during the scan. The AFM can also operated in a liquid environment, allowing the probing of cells and the workings of biomolecules.

## nanotechnology

In no other field has the STM received as much attention as nanotechnology. The STM has proven itself as not only the premier method for the imaging of nanoscale structures, but also as a promising tool for manipulation and assembly. Pioneering work in 1989 by D. M. Eigler and coworkers is perhaps the most famous, where his group at IBM assembled 35 Xenon atoms on a Nickel surface to spell out their corporate logo. Though impractical at present, researchers at UW-Madison and University of Basel, Switzerland, have made a storage device where the binary bits are individual silicon atoms on a silicon surface. (The present impracticalness arises from the near-impossibility of finding the same spot on a silicon platter after the tip is retracted.) The demonstrated device sports a storage density of 250 terabytes per square inch, versus the 30 gigabytes per square inch today.

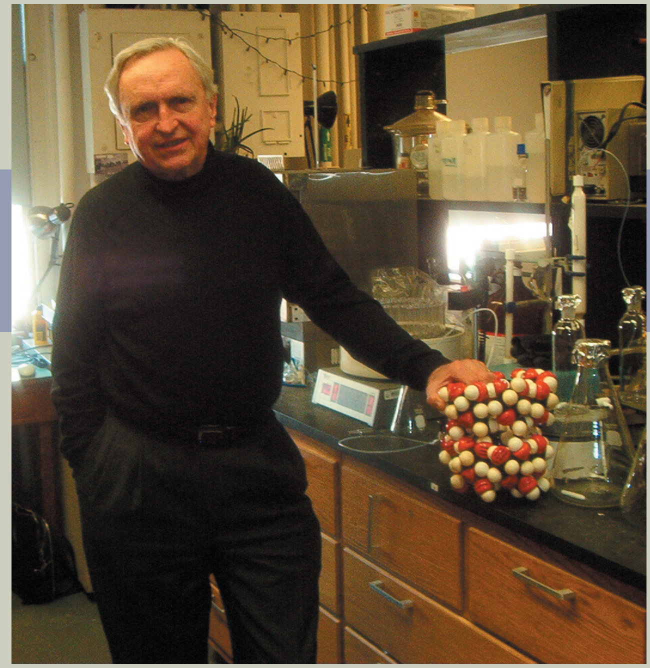
In another vein, researchers are looking into the possibility of using individual molecules as possible transistor devices for the next generation of computing devices. Transistor-like switching would occur from the shape changes induced in the molecule by external means. This opens up a whole new realm of possibilities of electronics based on tunneling transport, and not on dissipative electron flow.

## outlook

In the short 20-odd years so far, STM has invigorated existing areas of research, and created entirely new ones. As developments in nanotechnology grow beyond the "heroic experiments" stage, STM and related scanning probe techniques will usher in a new era of scientific investigation and nanoscale technologies. STM is at the heart of "atom engineering"; D. M. Eigler provides a peek into this future: "I imagine the day when some 15-year-old realizes that atoms are not just the things that we're made of, but that he can put them wherever he wants, whenever he wants, just like that."

*Hayn Park is a Ph.D. candidate in Physicss. He is involved in research on STM of organic molecules, in the Columbia Nanotechnology Science and Engineering Center program.*

# Ronald Breslow:
## a profile



**by Adam Kaufman**

When Professor Ronald Breslow was in high school, he was not your typical science student. Taking his fascination of chemistry home with him from school, the zealous young scientist attempted to synthesize new aromatic compounds in the basement of his house. Little did he know, what began as a teenage curiosity about aromatic compounds would turn into one of his most renowned scientific achievements, made within the first year of his arrival at Columbia as an instructor in 1956. Ronald Breslow redefined aromaticity with his work with cyclopropenes, and his findings are incorporated into chemistry texts and studied universally by college chemistry students. That same year, the young researcher also discovered how vitamin B1 functions.

Now, after nearly fifty years of research at Columbia University in what must be one of the school's most luminous careers, Ronald Breslow is not your typical professor. His passion and enthusiasm for his work remain as palpable and undimmed as that first year. His contributions to the field of chemistry have not gone unnoticed either, with four hundred publications to his name and numerous awards and honors including the ACS Award in Pure Chemistry, the Norris Award in Physical Organic Chemistry, the National Medal of Science presented to him by the first President Bush, the Priestly Award, and the Welch Award given to him just this year.

With so much experience under his belt, Professor Breslow has a simple approach to thinking about research: "It's all about formulating a project that can be done and makes a difference," he says as he sits in office in Havermeyer Hall, "anyone can formulate a project that will work but not make any difference. And anyone can formulate a project that if it would work would be fantastic, like inventing an anti-gravity machine, but no one knows how to do it. Research has to be somewhere in between." Understanding that fine line has been, in part, the key to Professor Breslow's successful research endeavors.

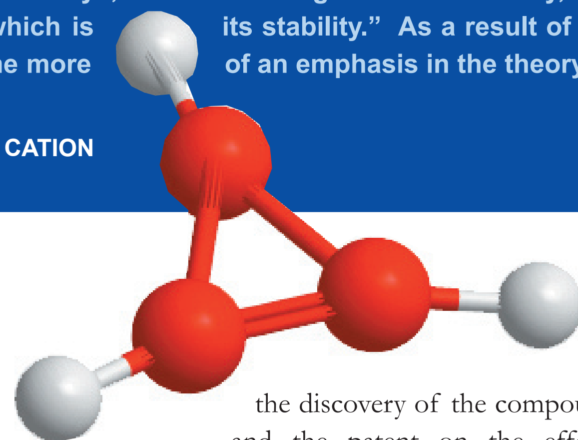
Besides his work with cyclopropenes, Breslow's other great research interest has been in biomimetics, a term he originated to describe the making of artificial enzymes that imitate natural chemistry in the body. The fundamental concept underlying biomimetics is to look at nature and learn from it. Breslow has made great progress making artificial enzymes that work like enzymes without copying every detail. Presently, his lab is working on the relationship between water solvents and organic chemistry reactions. "What is interesting about natural chemistry is that it generally goes on in water, but most organic chemistry was not done in water," Breslow explains, "We showed that certain organic reactions, like the Diels-Alder reaction, went much faster in water than in other solvents, and we showed why. We were then able to turn that into something quantitative where we could calculate exactly what the geometry looked like when things came together. It is a way to find what the shape is of the highest energy point—the transition state of chemical reactions."

But what may ultimately prove to be Professor Breslow's most recognizable contribution to the lay person is his work on a compound known as SAHA. He was approached by the head of Memorial Sloan Kettering Institute's Cancer Research with a rudimentary discovery by a researcher at Albert Einstein School of Medicine of an ordinary organic solvent that when placed with cancer type cells turned them into normal cells. Breslow was asked what he could do with this potentially exciting lead.

# Cyclopropenes and the Magic Number

**Professor Breslow is responsible for opening up the field of cyclopropenes for further study by chemists. With his discovery of the cyclopropenyl cation, Breslow redefined aromaticity which is a key concept in chemistry that explains why certain compounds are more stable than chemistry suggests they should be. Prior to Breslow's finding concerning aromaticity, chemists only had a 6 pi electron aromatic compound. By uncovering a 2 pi electron aromatic compound, Breslow proved that there were compounds smaller than Benzene that were aromatic.**

**Of equal significance was Breslow's ability to generate the cyclopropenyl anion which had four electrons in the same cyclopropenyl ring. Breslow labeled these compounds anti-aromatic, a term he personally coined to describe the highly unstable nature of these compounds. In explaining about anti-aromaticity he says, "Some molecules have the wrong number of electrons (four electrons is not good number) and are, therefore, unstable and are anti-aromatic. We were able to generate this compound in various ways, and using electrochemistry, we were able get measurements on its energy which is its stability." As a result of his work, the "magic number" of electrons became more of an emphasis in the theory of chemistry.**



**THE CYCLOPROPENYL CATION**

Acknowledging the help of his team of post docs and grad students, Breslow says, "We went to work on it, and we developed SAHA, a compound that is probably ten million times more powerful than that original solvent, and therefore, feasible to be used as a drug. With ten million fold increase in potency it's a compound that patients swallow once a day. The results are fantastic."

The Food and Drug Administration has looked at Professor Breslow's human data and have given him approval for Phase III trials. "Based on what we already have, the drug companies are convinced that this vitamin size pill works. Astonishingly, we don't see toxicity, whereas with most cancer compounds there is high toxicity." Breslow acknowledges at this juncture that they do not know how general the application of this drug is. The lead compound in this drug appears to have many applications in non cancer areas. He clarifies, "With cancer cells, SAHA is fantastically general, but we have had only a certain number of clinical trials with people. For that reason, we are interested in becoming part of a bigger organization so that they can fund more trials."

Breslow concedes that money issues can be a "nightmare" when doing research, but prospects for funding continued SAHA research look extremely promising. In fact, Columbia University and Sloan Kettering Institute, respectively, own the patent on the discovery of the compound and the patent on the effects of the compound on the cancer, and both institutions stand to make substantial money when a major pharmaceutical company comes on board, which is anticipated to happen within the coming weeks. Breslow is pleased that there will be financial support for this research as he is confident that "there are a lot of sick people for whom this drug can make a big difference."

Not only has Professor Breslow made tremendous contributions in chemistry, his impact at Columbia University is felt beyond the laboratory and the world of science. Over the years, Breslow has received many enticing offers for professorship from other prestigious institutions, but he has always maintained a steadfast commitment to Columbia and to improving Columbia's community. The coed campus is a testament to this commitment. Appointed chairman of the committee to make Columbia University a co-educational institution, he surveyed various other men's colleges in the nation that had become co-ed but that had still maintained a viable women's college. The committee produced a document which convincingly

## SAHA

**SAHA (suberoylanilide hydroxamic acid) is a cytodifferentiation agent that has the potential to treat many cancers. SAHA functions by inhibiting the activity of histone deacetylase, HDAC (shown as the open mesh in the diagram). HDACs remove acetyl groups from histones (the globular proteins around which DNA is wound), which keeps the DNA tightly wound and inhibits transcription of genes. Scientists suspect that HDACs are overactive in many cancers. As a result, crucial tumor suppressor genes are not expressed. Researchers have found that SAHA induces the expression of cell cycle inhibitors, which can stop cancer cells from proliferating.**

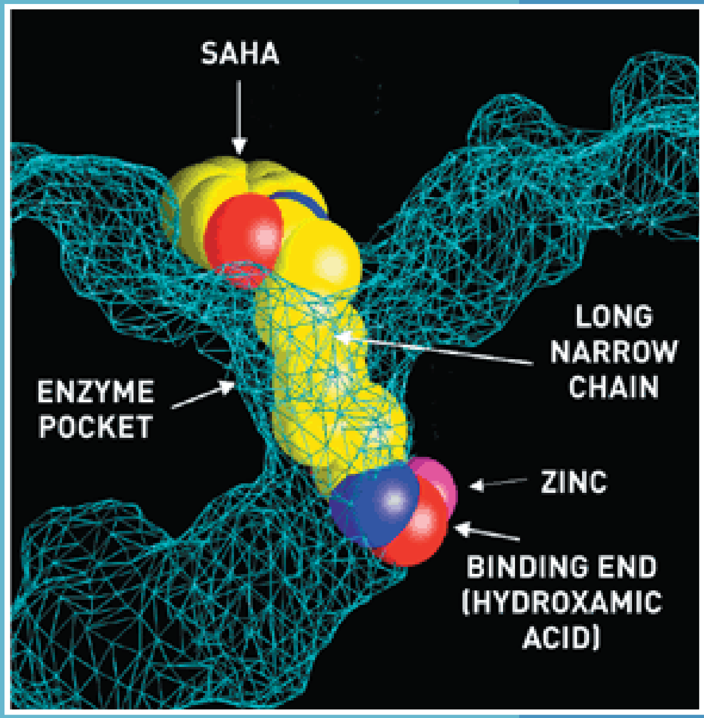



Figure courtesy of Nikola Pavletich and Nature Publishing Group.

demonstrated that Barnard would survive the change if Columbia became a co-ed university. The incoming class that first year in 1983 was 45% female and Barnard's allure as a small liberal arts college remained undiminished.

Looking back upon his career at Columbia University where he is the Samuel Latham Mitchill Professor of Chemistry and a University Professor, one of only twelve at Columbia, he states that "a good academic career is unbeatable." He points to two reasons, "Research at a university allows a researcher to pick his own topic as opposed to working for a pharmaceutical company where their needs are dominant." Additionally, he says, "I am in constant contact with excited, young students at an upbeat and nice time in their lives. I like teaching, and I find it interesting to expose students to different things that they hadn't thought about before. It is extremely satisfying." Over the years, Professor Breslow has had students that have gone on to work in private industry and others that have gone on to teach and become heads of chemistry departments at some of the finest universities in the country.

What about the future? Not one to rest on his laurels, Breslow notes, "There are so many interesting things to do in this world, and I anticipate another thirty to forty years in this business." He adds, "The nice thing about the research business is that feeling of elation you get when you successfully figure out a way to get around a problem." More than anything, however, Breslow is excited about his current research and the discoveries that are on the horizon.

*Adam Kaufman is a first-year and Rabi scholar in the College*

# Hot Town, Farming in the City

**by Alisa Opar**

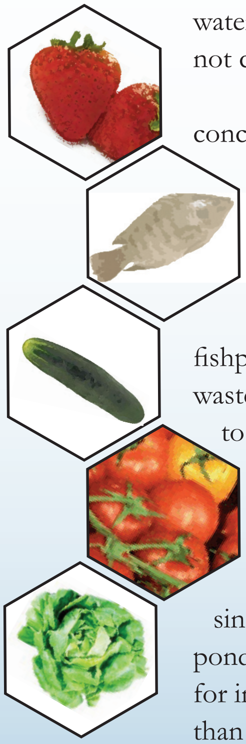
Imagine a tall building, externally similar to surrounding buildings, drastically different inside. A fishpond covers the ground floor, and near the ceiling of every other floor, strawberries and lettuce grow in suspended tanks of water. Although this vision sounds farfetched, buildings working along this principle exist in Virginia and are being built in Holland, and researchers at Columbia University are hoping they can bring one to New York City soon.

The concept appeals to Columbia's Dickson Despommier, a professor of environmental health sciences and leader of the vertical farm project, and a team of urban architects because it could have global implications. As Despommier and his colleagues see it, food grown locally in farms that produce no waste could safely ease food shortages that might arise as the human population grows beyond 10 billion over the next 50 years. Despommier intends to present the plan—dubbed the New York City Vertical Farm Project—to Columbia's president, Lee Bollinger, in the spring. If Bollinger is taken with the idea, the team hopes that a vacant building will be found and converted. In both Holland and Virginia, the goal has been to create a sustainable system that recycles waste and thus creates little pollution.

Although the vertical farm is still in the design stage, huge obstacles to its construction are already evident. "New York City is not an easy place to get a project like this off the ground because land is so expensive," said Leslie Hoffman of Earth Pledge, a local foundation that works to increase environmental sustainability in New York City. Not only is the entire project contingent on Bollinger's approval and on locating an empty building in New York City but the track record for vertical farms is too young to be instructive. According to Hoffman "The City has a long history of experimental projects," and if funding can be found, the vertical farm could be one of the successful projects.

The initial idea for vertical farming arose in the late 1990's in Holland. In response to flooding of farmland, growing agricultural pollution from pesticide runoff and the rise of livestock diseases, such as swine fever, that affect people, the Dutch government provided seed money for a pilot vertical farm called

Deltapark. The farm is in blueprint form, and the long-term financing is still being worked out. At about the same time, the Department of Energy gave the community of Eastville, Virginia, a grant to develop a so-called eco-park. The park is publicly owned and operated and managed by the Northampton Country Department of Sustainable Economic Development/ Joint Industrial Development Authority. The park began operating in 1999, and links several industries including a sawmill, wastewater treatment facility, and a chlorine plant. The waste from one company is used by another. Initially, it was hoped that water from the treatment plant and sawmill would be treated and piped to a building where fish were grown in tanks and vegetables and fruit were raised in nutrient-rich water, a process called hydroponics. However, it is not currently active.



Hoffman does not see any problems with the concept itself. “The idea is not new, and I know the idea works. Fish farming and hydroponics have been around for years,” said Hoffman.

If realized, the New York City vertical farm will work in a similar manner. Tilapia, a hearty, subtropical finfish, would live in the fishpond until they were large enough to eat. The wastewater from their tank would be transported to the basement where it would be processed with wastewater piped in from the city. Water containing human waste would pass through a methane reactor to create energy for the system. Regular drain water from showers and sinks would be treated and then used to fill the fish pond and the hydroponic tanks that could produce, for instance, enough sweet potatoes per day for more than 12,000 people and enough tomatoes for nearly 2,500 people, according to Despommier. Other crops would include lettuce, cucumbers and strawberries. Compost from produce refuse, and perhaps local restaurants, would produce worms to feed the fish.

Despommier sees what he calls "political lull" as the largest obstacle. “People have to understand the sense of urgency,” he said. Another setback is that the price of the project is still unknown and investors have not been identified. “Until the project is safe, cheap, and productive, it won’t be ready,” says

**Hydroponic Lettuce**

Despommier.

One problem he may not have is selling the food. Alan Zimmerman, produce buyer at the Park Slope Food Coop, said that the Coop, which currently has over 10,000 members, would provide strong support for the vertical farm, as it is local and most New Yorkers already eat hydroponic produce. “You know those tomatoes on the vine? They’re imported from Holland,” he said, “If we can buy local, instead of imports from Holland, we’ll do it.”

Steve Frillman, executive director of the Green Guerillas, a local community garden group, echoed Zimmerman. “People in New York City have generally been supportive and enthusiastic about growing food in the city. Community gardeners are growing food in low-income neighborhoods where supermarkets and grocery stores are few and far between. Any effort that would increase the supply of fresh, healthy food in these communities would be embraced.”

Currently in the Port Charles Eco-park “nothing is going on because there’s nobody here to do it,” said manager Ray Otton. He explained that the population of Eastville is too low to provide a viable workforce to run the system. “That’s a definite advantage you’ve got in New York – enough people to do the work.”

# A Receptor for the SARS Virus

## How does the virus affect physiology on a molecular basis?

**By Jennifer Fung**

Severe Acute Respiratory Syndrome (SARS) and its accompanying coronavirus SARS-CoV emerged last year as an international public threat. But how exactly does the virus work? Viruses usually take advantage of host cells by using proteins protruding from cell surfaces as their receptors. Li et al. has recently found that the virus binds to angiotensin-converting enzyme 2 (ACE2). This may be the receptor that the virus uses to gain access to the interior of the host cell, in order to make many copies of the virus. ACE2 exists in the bronchus, lung parenchyma, heart, kidney, and gastrointestinal tract. The physiological role of ACE2 in most of these organs, however, is unknown. Scientists believe ACE2 to be an important regulator of cardiac function, perhaps regulating permeability of the blood vessels, but they have not ascertained if SARS-CoV interferes with ACE2 enzyme activity as part of the pathogenesis of SARS.

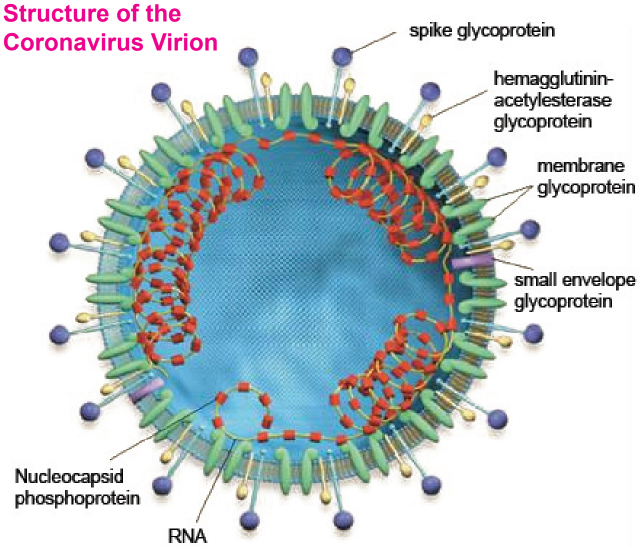
In general, coronaviruses express glycoproteins, which fuse with the human host cell through the aid of a receptor. SARS Co-V expresses glycoprotein S, which is then linked to ACE2, an enzyme located on the host cell's surface. "S" stands for spike proteins, which is the distinguishing characteristic of coronaviruses.

The glycoprotein S is usually cleaved into a S1 and S2 subunits by a cellular protease in virus-producing cells. Although the S protein of SARS-CoV is not cleaved, the S1 and S2 domains can be identified through their homology with the S1 and S2 subunits of normal S proteins. In fact, the S1 domain of all characterized coronaviruses seems to mediate a high-affinity association with their respective receptors. In other words, they bind to their receptors so tightly that the receptors cause a possible change in 3D conformation of the viral protein. However, this property of the SARS-CoV glycoprotein on the SARS virus remains to be proven.

ACE2 binds well with the S1 domain of the SARS-CoV S protein. Li et al. used 293T cells, which come from a human renal epithelial cell line and which are ideal for research purposes. 293T cells expressing the SARS-CoV S protein fused with human kidney 293T cells expressing ACE2 because of the proteins' high affinity for each other. In the researchers' study, a codon-optimized gene synthesized glycoproteins S and S1. Codon optimization enhances the effectiveness of DNA expression by increasing protein expression. 293T cells expressing ACE2 formed syncytia (ie. masses of cytoplasm with multiple nuclei but without normal cellular boundaries) with cells that expressed S protein, an indication SARS-CoV was replicating inside its host cell.

To establish that ACE2 mediates viral replication, 293T cells transfected with ACE2 were compared to uninfected 293T cells (which underwent the same procedures to serve as negative control samples). After 2 days of incubation in culture, many detached, round, and floating cells were observed in the ACE2-transfected cell culture, which is consistent with viral replication. Reverse transcriptase polymerase chain reaction (RT-PCR, a mechanical process that converts single stranded RNA to double stranded DNA) then quantified viral RNA; the scientists found that within those 48 hours, the viral genomic copies of RNA in ACE2-transfected cells increased by more than 100,000 fold. In comparison, the uninfected cells had only a tenfold increase in viral genome copies, resulting from baseline replication of 293T cells.

**Structure of the Coronavirus Virion**




New Eng J Med 348; 20: 1948-1951 May 16 2003

When an anti-ACE2 antibody was added, Li et al. also found that syncytia formation was blocked by more than 95%. A control antibody was used to show that syncytia formation would not be blocked until anti-ACE2 antibody was used. This cessation of viral replication in the host cells provides more evidence that ACE2 is likely the functional receptor for SARS-CoV.

The discovery that the ACE2 receptor binds to SARS-CoV glycoproteins may possibly help in the development of therapeutics and vaccines. While current ACE2 inhibitors are unlikely to be useful, perhaps antibodies, other proteins that bind to ACE2, or even other small molecules will be discovered to interrupt the ACE2-S protein interaction. Finally, studies of the interaction between the SARS-CoV S protein and ACE2 in other animals can provide knowledge on the origins of the virus.

# Breaking Down Bone to Make 'em Strong

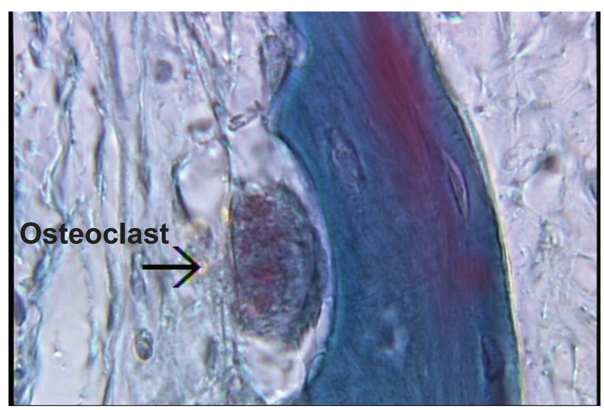
## Strong bone development requires almost as much break-down activity as build-up activity.

**By: Vivian Ng**

"Drink your milk so you can build strong bones" are words that most people have heard repeatedly throughout their lives. However, strong bone development requires almost as much break-down activity as build-up activity. In order for bones to grow, bone-building cells called osteoblasts lay down a soft protein matrix that attracts free calcium from the bloodstream. Calcium hardens the bone structure, which is why everyone needs to have an appropriate dietary calcium intake. Without the calcium, a person's bones would be composed primarily of the soft protein matrix. However, if this were to occur continuously, the build-up of bone structure would weigh down a person's body, making mobility difficult. As a result, the body must compensate for the increase in bone length by using cells called osteoclasts to degrade the centers of bone. Osteoclasts clamp tightly to the calcified matrix, forming a small space between themselves and bone. Into this isolated space, osteoclasts release acids and enzymes that corrode the bone, eliminating the exposed bone beneath the osteoclast. As numerous osteoclasts eat away on the inner portion of the bone, the bone loses the solid cylindrical shape formed by the osteoblasts and becomes a pipe-like structure.

As expected, these two processes of building and destroying bone must be highly regulated in the body. The body must be aware of when to build bone and when to break down some of that same bone in order to maintain the integrity of its skeletal system. Furthermore, the control center for bone growth must be able to signal both osteoblasts and osteoclasts to turn on and off during appropriate times. Deviations in either direction can have detrimental effects on the body. For example, if there is too much osteoblast activity or too little osteoclast activity, the bones become massive and render the individual handicapped. On the other hand, if there is too much osteoclast activity and too little osteoblast activity, the bones become soft and brittle, resulting in osteoporosis in the elderly or rickets in the young. Determining how these cells are activated to perform their jobs is thus a heavily researched topic.

Recently, Chiusaroli et. al. have elucidated the function of an enzyme, tyrosine phosphatase epsilon (PTPε), found within osteoclasts. PTPε adds chemical groups – phosphates, which are made up of phosphorous and four attached oxygens – to specific tyrosine residues of proteins. This enzyme is present in many different cell types; however, its effects vary depending on what proteins PTPε acts on. Chiusaroli investigated how a lack of PTPε could affect osteoclast function in mice. These mice were genetically altered such that their cells lacked the ability to make PTPε. The investigators observed both male and female mouse bone development for abnormalities. In addition to looking at cross sections of bones, the scientists measured levels of degraded collagen in the blood stream. Collagen is a protein found in bones that is degraded as osteoclasts disintegrate sections of bones. If there is a large amount of bone degradation, there would higher levels of degraded collagen in the blood. Interestingly, they found that only young female mice experienced an increase in bone mass. This was evident from the histological bone cross-sections and from the decreased amounts of degraded collagen in the blood. This increase in bone mass is evidence of malfunctioning osteoclasts.




The scientists suspected that the specificity of bone characteristics to young female mice was in part due to the effects of sex hormones. Their data suggest that osteoclasts lacking PTPε were unable to properly respond to sex hormones, since all the mice had normal sex hormone levels.

In addition to the changes in the overall bone structure, PTPε-deficient mice contained abnormal osteoclast structures. In order for osteoclasts to clamp onto the bone surface, they must form nubs on their cell membrane that are equivalent to the suction cups on octopus tentacles. These nubs, called podosomes, are found in various forms, depending on the state of the osteoclast. In PTPε-lacking mice, osteoclasts with podosome structures similar to non-binding osteoclasts were present. This suggests that PTPε is necessary for the osteoclasts to form the necessary podosome structures to bind osteoclasts to the bone. Furthermore, these abnormal podosomes were only found in the young female mice and not in the adult female mice. The researchers suggest that as the female mice began to produce larger quantities of sex hormones, the hormones compensate for the lack of PTPε.

As more information is uncovered about the cellular mechanisms of bone growth, scientists will apply this knowledge to treatments for different bone diseases. For example, osteoporosis, the weakening of the bone structure, has become a major health concern in the US as the average life span increases. One suspected cause of osteoporosis is the increased activity of osteoclasts and decreased activity of osteoblasts. Researchers hope that medicines subduing osteoclasts will maintain the integrity of the bone structure at the same time. Chiusaroli and associates' research provide new insight as to the specific cellular mechanisms that are crucial to osteoclast function; the information may prove helpful in future therapies alleviating osteoporosis.

*Vivian Ng is a biology major in Columbia College.*

# Nutlin: a small molecule with big potential

**by Tian Zhang**

Cancer is a word that most of us would rather not hear on our next visit to the family doctor. We readily observe the outward deterioration of the cancer patient, but what exactly happens on a cellular basis and how might we target these malfunctioning cells to re-activate normal cellular processes?

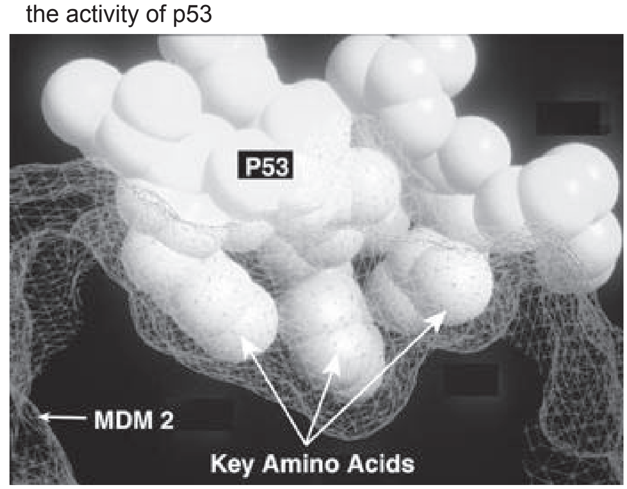
In normal cells, the cell cycle includes protein production for cell function during the first growth (G1) phase, DNA replication during the synthesis (S) phase, more protein production during another growth (G2) phase, and cell division during the mitotic (M) phase. DNA damage in these cells stabilizes a protein called p53, which then acts as a transcription factor and activates gene expression of proteins that stop the cell cycle and activate repair pathways before the cell goes ahead and replicates damaged DNA. When the cell finishes repair of the DNA damage, it can then proceed into the S phase of the cell cycle. In this case, another protein, named MDM2, represses p53 activity to allow the continuation of the cell cycle. If, on the other hand, the DNA is too damaged to repair correctly, p53 allows programmed cell death, apoptosis.

Something goes wrong in a cancerous cell, however, and normal cellular repair of DNA damage does not occur. Instead, mutations accumulate while the cells replicate without limit, leading to an increasingly malignant cell. Scientists have found that many tumors produce too much MDM2; even in cases where the p53 protein functions normally, MDM2 represses the p53 pathway and does not allow either repair or apoptosis to occur.

In the February 2004 issue of *Science*, Vassilev et al published their findings of a family of small molecules, named Nutlins, which inhibit MDM2-p53 binding by preferentially binding MDM2 on the same spot where p53 binds. Even at low concentrations, these Nutlins are optimized to bind MDM2. Indeed, the scientists visualized the Nutlin-MDM2 interaction using crystal structures; treatment of cancerous cells with these small molecules activates the p53 pathway (in presence of wild type p53) and begins the cellular arrest process.

Vassilev et al continue by describing a phenomenon that characterizes many drugs: the handedness, or chirality, of Nutlin-1. Similar to the way the right and left hand are mirror images of each other and can never be superimposed on each other, these molecules are enantiomers of each other – i.e.

MDM2 binds p53 through key amino acids, suppressing the activity of p53



they exist as mirror images. In particular, enantiomer-a of Nutlin-1 activates the normal p53 pathway in and stops proliferation of cells with wild type p53, while enantiomer-b has extremely small effects on these same cells. Indeed, untreated negative control cells behaved similarly to cells treated with the wrong enantiomer. This phenomenon shows the preciseness and specificity of the binding site on MDM2; even a mirror image of the correct molecule does not bind.

Strikingly, Vassilev and colleagues were able to regulate growth of tumors in living nude mice. Given orally twice a day, Nutlin-3 inhibited tumor-cell division in 90% of all established tumor xenografts (that is, grafts of tumor from other species) after only 20 days of treatment. Nutlin-3, when bound to MDM2, displaces the p53, freeing up the much-needed p53 for its customary role as instigator of cellular arrest, repair, and apoptosis in cases of excess DNA damage. This powerful intervention of a small molecule, if proven effective in further research, can very well revolutionize treatment of both tumors that express too much MDM2 and those with wild-type p53.

Disadvantages of an orally delivered drug include the possibility that the drug would not be absorbed by the body. Nude mice lack mature T-cells, leading to a severely impaired immune system; indeed, even foreign xenografts are tolerated. Will the Nutlin drug survive in a normal human body with a fully functioning immune system?

Molecular biology and the chemistry of small molecules have made possible the investigation and design of these powerful small molecules. Furthermore, visualization of these molecules using techniques such as X-ray crystallography have also shown our skeptical human minds that indeed, the activation of the p53 pathway comes from the Nutlins' replacement of the p53 molecule on the MDM2 binding site. With further research, Nutlins may prove to be one effective, valuable method of treating certain human cancers.

*Tian Zhang is a third-year biology major in the College, and a 2004 recipient of the Barry M. Goldwater scholarship.*

# a Healthy level of Disgust

**by Patricia Peter**

Though it is commonly thought that the causes of disgust are determined by societal and cultural influences, a recent study suggests that there is an evolutionary component to disgust that transcends cultural bounds. According to a team of researchers led by Dr. Valerie Curtis from the United Kingdom's London School of Hygiene and Tropical Medicine, disgust is an evolved mechanism that teaches us to avoid indications of harm and infection-causing substances such as feces, wounds, rotting substances, and bodily fluids.

In one of the largest Web-based experiments ever performed, 40,000 subjects rated pictures according to the degree of disgust educed by each image. Some pairs of images resembled each other but differed in that one was associated with disease and the other was not. Subjects consistently rated the pictures associated with disease as more disgusting than their more innocuous counterparts. For example, a filled subway car made people queasier than an empty one and a towel with a yellow, mucous-like stain was more repulsive than a towel with a bright blue stain. Women experienced higher levels of disgust than men; an observation that Dr. Curtis explains is related to woman's evolutionary role as a mother who has "to protect [her] own genes and those of [her] offspring." Age also mattered in the study, which noted that children were less disgusted than their parents and that while levels of repulsion increased over the reproductive years, as subjects became too old to reproduce any more, the levels of disgust decreased. Evolutionarily speaking, people are most careful to avoid disease-causing agents when they have offspring to protect, an instinct that guides them to care for the survival of the species. To test out your evolutionary disgust mechanism, try the survey yourself at www.bbc.co.uk/science/humanbody/mind/surveys/disgust.

Not shown consecutively in the survey, the two towels above exemplify the survey's use of paired objects, one associated with disease, the other not.

# As the World Turns... Faster

**by Patricia Peter**

Does time seem to be flying by lately? Well, for once, you're right! The Earth has been rotating faster for the past five years, or to be more precise it has finally stopped slowing down. Since the very beginnings of our humble planet, the Earth's rotation has been decelerating by 1.5 milliseconds per century, which might not seem like much but in the long run, could lead to inconsistencies in the timing of astronomical events such as the sunrise or sunset. To compensate for the Earth's slow rotation, global timekeepers initially utilized a "rubber second." Its length was adjusted each year so that every year would be comprised of exactly 31,536,000 seconds, but understandably, this got a bit complicated. A leap second thus seemed a more attractive if less precise option and has been added to 22 years since 1972, keeping our time here on Earth in accord with actual astronomical time.

Now, however, a speedier Earth means that for the fifth year in a row no leap second will be added to Coordinated Universal Time, the official global time determined by highly accurate atomic clocks dispersed around the globe. This five-year stretch without the addition of a leap second is the longest in recent history.

So, what's the rush? Some blame global warming. The Earth routinely speeds up during summer months and periods of increased global temperature, as increased evaporation leads to higher levels of precipitation over the landmasses, the bulk of which are located in the Northern Hemisphere. Then, "It is as though Earth is an ice skater holding her hands up as she completes a spin, which can increase the rate of rotation," explains Tom O'Brian, a physicist and chief of the National Institute of Standards and Technology's Time and Frequency Division. Other environmental factors like the melting of glaciers, the movement of other planets, tidal changes, and magma movements can also affect the rate of rotation.

## Wrong Turn

Do toilets in the northern hemisphere always flush counterclockwise?

A popular episode of The Simpsons begins with a friendly competition between Bart and Lisa. Bart, armed with a tube of toothpaste, and Lisa with a bottle of shampoo, both dump their products into the sink of their bathroom in a race to see which will reach the drain first. The toothpaste and shampoo swirl around the drain in counterclockwise fashion, until the shampoo passes into the drain and Lisa declares herself the winner. Bart protests the outcome of the contest, asserting that had the products rotated in the clockwise direction, he would have won. Lisa, in terrifically didactic form, proclaims that in the northern hemisphere the rotation of a liquid in a basin will never follow a clockwise path – a result of the Coriolis effect. That is, she claims, liquids in a toilet or sink will always rotate counterclockwise north of the equator and clockwise south of it.

Lisa's belief that the Coriolis effect dictates the rotation of a liquid is often echoed by high school teachers and trumpeted by trivia buffs. Nevertheless, this belief is incorrect.

The Coriolis effect is the result of what physicists call a fictitious force; it is created when a body in a rotating – and thus, accelerating – reference frame undergoes motion. It is popularly known by physicists as the "merry-go-round force," because if you attempt to walk on a rotating merry-go-round along a radius, either toward or away from the center, the Coriolis force will pull you in a direction exactly perpendicular to your direction of motion. Conceptually, the force arises because an object close to the center of a rotating disc has a slower velocity than an object farther from its center. As you walk outward on a disc the speed of the surface beneath you is increasing – as you take a step the surface rotates a slight distance underneath you, displacing you a certain distance perpendicular to your direction of motion. Thus, the Coriolis force does not affect an object that is not moving – in that case the speed of the surface underneath the object is not changing. Similarly, an object moving parallel to the disc's axis (for example, a person jumping in place on a merry-go-round) is not affected by the Coriolis force.

Just as on a merry-go-round, objects at the earth's equator travel at different speeds than objects north or south of it. As a result, the Coriolis force does affect the movement of objects on the earth's surface; it has great implications for the movement of objects over large distances and long periods of time. For example, it affects the movement and circulation of air around low and high pressure centers, and is responsible for hurricanes. And although the Coriolis force reaches the movement of a liquid in a sink, its effect on the liquid is so small because it acts over such a small distance and time period. Indeed, Lisa was wrong. The rotation of liquids in a sink does not depend on the Coriolis effect. So what does affect the swirling direction of your sink or toilet? It's just what you would expect - in a sink the direction of rotation depends largely on the angle of the surface and the position of the faucet; in a toilet the water's rotation is determined by direction of the water spout.

At the US Embassy in Australia:
Bart: *"Do the toilets go backwards here?"*
U.S Embassy ward: *"No. To combat home sickness, we've installed a device that makes them swirl the correct American way."*
*Flushes toilet. Machine kicks in and water swirls counterclockwise*
Homer (weeping, singing): *"Sweet land of liberty..."*

## Dead Men Grow No Nails

Do hair and nails grow after death?

Did you ever wonder why zombies have freakishly long nails and hair? Or did you, like most people, believe that hair and nails continue to grow after death? For ages, authors and intellectuals have propagated this unfounded myth, including Nobel prize winner Gabriel Garcia Marquez. In one book, Of Love and Other Demons, he describes a girl whose hair continues to grow two hundred years after her body is interred. More recently, the remake of George A. Romaro's cult classic, "Dawn of the Dead," depicts the deceased as grotesquely ungroomed.

Putting aside folklore and shock entertainment, it may seem from immediate observation that these body parts indeed do grow after death. Often people have noted that the length from the tip to the base of the hair or nail increases slightly after a person dies. However, in death all human body cells, deprived of essential nutrients and oxygen, cease their functions sooner rather than later. Naturally, follicle cells and those that produce fingernails are no exception. So, why do they appear to grow?

There is a rather simple explanation. Even after cells die and no longer create new hair and nails, the preexisting portions remain. Both auxiliaries are made of keratin, the most stubborn protein in humans. Very few microorganisms can digest this protein, so hairs and nails outlive any other portion of a dead body second only to bones and teeth. Meanwhile, the scalp or flesh surrounding their roots of hair and nails become degraded as the skin and flesh of corpses dehydrate and gradually decay. Unveiled roots add to the total length, so hairs and nails seem to grow even after death. The residents of graveyards do not grow claws and mops when they move-in; they simply lose their softer sides instead.

## Infinity

Did you know that Galileo published groundbreaking research on the mathematical concept of infinity? With lots of time on his hands during his house arrest in Siena, Galileo wrote the Discourses Concerning Two New Sciences, continuing to flaunt his "heretical" and madcap ways. Though primarily concerned with church-friendly physics concepts such as free-fall acceleration and projectile motion, one digression in his Discourses delves into the more troubling matter of what became later known as "Galileo's Paradox." Galileo reasoned that there are more elements in the set of all whole numbers (which includes both squares and non-squares) than there are in the set of squares alone. For example, from 1 to 100 there are only 10 squares but 100 whole numbers. So far so good. However, when whole numbers are listed with their corresponding squares the paradox rears its ugly head.

$$\begin{array}{l} 1\ 2\ 3\ \ 4\ \ 5\ \ \ 6...\ \ n \\ 1\ 4\ 9\ 16\ 25\ 36...\ n^2 \end{array}$$

The two sets of numbers seem to contain an equal number of elements! Each additional whole number has a corresponding whole number square, both sets of numbers extending to infinity with the two infinities appearing to be equal. Galileo concluded that "This is one of the difficulties which arises when we attempt, with our finite minds, to discuss the infinite, assigning to it those properties which we give to the finite and limited...for we cannot speak of infinite quantities as being the one greater or less than or equal to another." His paradox served as the basis for Georg Cantor's later development and enhancement of the theory of infinity (and subsequent insanity).

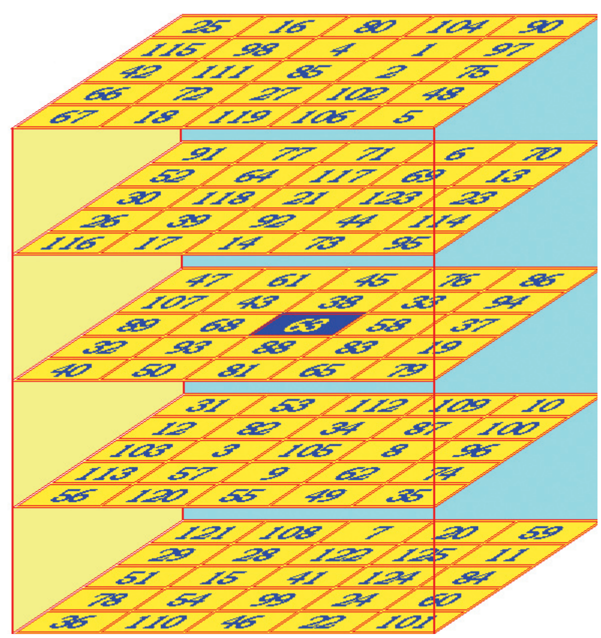
## Perfect Magic Cube

Here is an interesting problem for you math buffs. You want to build a 5x5x5 cube, thus requiring 125 unit blocks. You label each block 1 through 125. Next, arrange the blocks in such a fashion that the numbers in every column, row, pillar, space diagonal, and orthogonal diagonal of the cube add to the exact same number. Solutions to such problems are entitled perfect magic cubes.

Since the 19th century mathematicians have sought solutions to perfect magic cubes of various orders, as if searching for a mystical artifact. In 1866, the first perfect magic cube was solved having the order of 7, meaning a perfect 7x7x7 cube. Following in 1875, a perfect cube of order 8 was found. For quite some time, mathematicians remained perplexed as to whether perfect cubes of the order of 5 and 6 existed.

A startling breakthrough came in November 2003. Requiring many computers to run for several weeks, German Walter Trump and Frenchman Christian Boyer together solved a perfect cube of the fifth order. Only months beforehand, Trump alone discovered a sixth order perfect cube.

In their solution of the fifth order perfect cube, all 109 possible ways to add the numbers in a row, column, pillar, diagonal, or orthogonal diagonal lead to the same value of 315, the magic sum. As to what may motivate mathematicians to attempt such problems, that may be best addressed by Gustavus Frankenstein, the founder of the first perfect cube of order 8, "This discovery gives me greater satisfaction that if I had found a gold mine under my door-sill; and it is delight like this that makes poverty sweeter that the wealth of Craesus."



Trump and Boyer's Perfect Magic Cube of Order 5