ChemiCAL Science and Engineering

College of Chemistry, University of California, Berkeley
Spring 2005, Volume 13, No. 1

Unique partneships to tackle malaria, AIDS

Jay Keasling dreams big. The chemical engineering professor has recently formed two unique partnerships to bring help and hope to the world's malaria and AIDS patients.

Conquering malaria is a tall order. The disease kills over a million people each year and is becoming more and more resistant to front-line medications, including the formerly invincible chloroquine. Treatment with drugs containing artemisinin can cure nearly 100 percent of patients in only three days. But the wormwood plant from which artemisinin is made is in short supply, and producing the drug is labor-intensive and expensive—at $2.40 per treatment, it's beyond the reach of many in need.

However, there is help on the way. Keasling and his colleagues have developed a breakthrough technology to make artemisinin much cheaper and more accessible. A recent grant of $42.6 million from the Bill & Melinda Gates Foundation to the Institute for OneWorld Health, a nonprofit pharmaceutical company, which will work in an unprecedented partnership with the Keasling group and with Amyris Biotechnologies, will facilitate the synthetic development of the life-saving drug and its migration from the lab in Berkeley to doctors' offices in afflicted countries.

Using synthetic biology, Keasling and his group have constructed an entirely new metabolic pathway inside bacteria using genes from three separate organisms. This novel pathway can produce a broad family of isoprenoids—compounds that are precursors to many plant-derived molecules used in industry, including anti-cancer drugs in addition to artemisinin.

Under the agreement with the Gates Foundation, Keasling will do further research, perfecting the bacterial factory that bypasses a long and difficult synthesis for the isoprenoid intermediates. Amyris, a new company founded by Keasling and Berkeley colleagues **Kinkead Reiling**, **Neil Renninger**, **Jack Newman** and **Vincent Martin**, will develop processes to produce large quantities of artemisinic acid from the bacterial factories and chemically convert it to artemisinin and other medicines. OneWorld Health will focus on drug development and regulatory requirements.

Jay Keasling

The scientists' goal is to reduce the cost of each treatment for malaria to less than 25 cents. These new processes can be easily scaled to meet the enormous demand for low-cost drugs in developing countries.

"This project will use some of the latest advances in molecular biology to engineer a microbial chemical factory and reduce the cost of a much-needed drug tenfold," Keasling notes. "In many ways, this project is a dream project: interesting science, high technology, rapid transition from the bench to the bedside, and most important, critical need."

Another area of critical need is that of AIDS therapy. The Keasling group is approaching this challenge by partnering with the Pacific Ocean island nation

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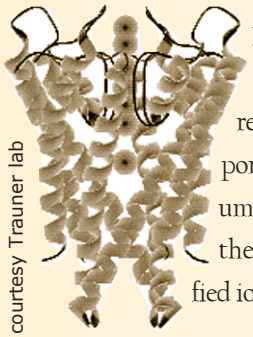
Research Highlights

Light sensitive channels

Ion channels are found in cell membranes and control the flow of ions in and out of the cell. They are especially important in the nervous system. By creating ion channels that change their configuration in response to light, scientists in the college have developed a valuable new method that may help neuroscientists tease apart how individual neurons are woven into complex neural networks.



courtesy Trauner lab

▲ A potassium ion channel

Chemistry professor **Dirk Trauner** and his colleagues introduced a reactive "handle" near the pore of a common potassium channel. The researchers then expressed this modified ion channel in rat neurons, tagged the handle with a compound that changes configuration upon exposure to light and added a tether tipped with a compound known to plug the ion-conducting pores of potassium channels.

When illuminated with long-wavelength light, the tag adopts a stretched out *trans* configuration that allows the plug to seal the pore. Short-wavelength light reversed the processes, condensing the molecule and removing the plug, thus allowing potassium to rush out of the now-inactive neuron.

A more efficient catalyst

An epoxide group may be small—a three-member ring with two carbon atoms and one oxygen atom—but its addition to existing molecules is a key step in numerous important chemical syntheses. Looking for ways to speed up epoxidation, chemical engineering professors **Alexander Katz** and **Enrique Iglesia** and graduate student **Justin M. Notestein** have found that attaching titanium-calixarene complexes onto silica produces more efficient epoxidation catalysts than the solution-phase version.

Their findings show that the immobilized form of the catalyst is over 20 times more active and far more selective than the solution-phase catalyst in specific reactions known as olefin epoxidations, in which organic hydroperoxides serve as oxidizing agents. The scientists propose that the bulky structure of the calixarene ligand keeps the metal centers far away from each other during reaction with alkenes, which prevents oligomerization to unreactive structures.

Finding negatively charged water clusters

Recent experiments by chemistry professor **Daniel Neumark** and his colleagues have shed new light on the fundamentally important interaction between electrons and water. By applying time-resolved techniques to gas phase processes that take place on a femtosecond time scale, the researchers were able to resolve two distinct forms of negatively charged water clusters—groups of water molecules that feature unique properties, somewhere between that of liquid water and steam.

The clusters are too large to be thought of as a molecule but too small to be classified as a bulk-phase liquid or a solid.

"We have confirmed the presence of two isomers of water cluster anions: internally solvated structures, in which a hydrated electron is localized within the cluster; and surface state structures, in which the hydrated electron is bound to the surface of the cluster," Neumark told *LBNL Research News*.

Sugar sulfation on demand

Carolyn Bertozzi and her coworkers have developed a small-molecule approach for controlling carbohydrate sulfation, a common type of sugar modification that occurs in the Golgi complex.

Sulfation of cell surface proteins and oligosaccharides has gained recent attention as a key regulatory mechanism for biological function. Sugars are often modified with sulfate groups in the Golgi complex before being routed to their final cellular destinations. Bertozzi's group is focused on the role of sugar sulfation in the initiation of an inflammatory response.

The scientists divided a sulfotrans-

ferase into two parts—a localization domain that directs the enzyme to the Golgi membrane, and the enzyme's catalytic center. By combining the two domains with others responsive to antibiotics, they were able to induce and control sulfation in cells whose innate sulfation ability had been removed.

Tracking peroxide in cells

Oh, the conundrum of peroxide. On the one hand, the significance of oxidative stress by molecules such as H_2O_2 is now recognized as contributing to numerous diseases. On the other hand, H_2O_2 plays a vital role in cell signaling. Now a new selective, cell-permeable optical probe for hydrogen peroxide, developed by assistant chemistry professor **Chris Chang**, promises to shed light on the dual nature of this reactive oxygen species. Of the many biological reactive oxygen species, only H_2O_2 removes the boronate protecting groups on the water-soluble, colorless sensor, converting it into visible-light-emitting fluorescein. The H_2O_2-specific sensor can detect extremely small amounts in the cell.

Is it toxic? Ask the MetaChip

courtesy Clark lab

A new biotech chip that mimics the metabolic reactions in the human liver will allow the rapid screening of potential drugs to identify those activated by the liver and to weed out those that are toxic.

"The MetaChip would allow testing a backlog of compounds for toxicity earlier in the drug discovery process—faster and more efficiently— and help remove a current bottleneck in the drug discovery process," says **Douglas Clark**, professor of chemical engineering. The liver is the body's detox station, degrading chemicals and often, in the case of drugs, activating them to become active elsewhere in the body.

Clark and his colleague J. P. Dordick, a professor at RPI, took several of the liver's major detoxification enzymes, called cytochrome P450 enzymes, and put them on a chip in order to create liver metabolites of drug candidates and rapidly test them for toxicity against specific cells.

The MetaChip [metabolizing enzyme toxicology assay chip] contains recombinant P450 enzymes encapsulated in a sol-gel that immobilizes them on a glass slide, so that many drug candidates can be tested simultaneously. The team plans to merge the current MetaChip with a complementary chip on which live cells are growing to enable seamless testing of the drug metabolites against an array of different cell types from the body. This will identify organ-specific drug toxicity and possible adverse drug interactions.

>>excerpted from Robert Sanders, UC Berkeley

Illuminating photosynthesis

Another important piece to the photosynthesis puzzle is now in place. Chemistry professor **Graham Fleming** and his colleagues have identified one of the key molecules that help protect plants from oxidation damage as the result of absorbing too much light.

The researchers determined that when chlorophyll molecules in green plants take in more solar energy than they are able to immediately use, molecules of zeaxanthin, a member of the carotenoid family of pigment molecules, carry away the excess energy.

Through photosynthesis, green plants are able to harvest energy from sunlight and convert it to chemical energy at an energy transfer efficiency rate of approximately 97 percent.

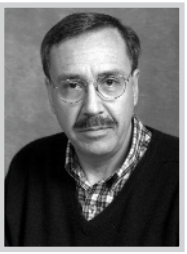
A potential pitfall for any sunlight-harvesting system is that if the system becomes overloaded with absorbed energy, it will likely suffer some form of damage. Plants solve this problem on a daily basis with a photo-protective mechanism called feedback de-excitation quenching.

The Berkeley researchers used femtosecond spectroscopic techniques to follow the movement of absorbed excitation energy in the thylakoid membranes of spinach leaves, which are large and proficient at quenching excess solar energy. They found that intense exposure to light triggers the formation of zeaxanthin molecules which are able to interact with the excited chlorophyll molecules. During this interaction, energy is dissipated via a charge exchange mechanism in which the zeaxanthin gives up an electron to the chlorophyll.

Additionally, by studying the interactions in plants lacking key genes, the scientists were able to verify that the zeanthin molecule was indeed the key player in the energy quenching.

>> excerpted from Lynn Yarris, LBNL

FACULTY *News*


courtesy LBNL

The American Association of Physics Teachers recently honored **Carlos Bustamante** with the Richtmyer Award for his work in conveying physics to public audiences. Bustamante, who has appointments in chemistry, physics and molecular and cell biology, uses optical tweezers to move objects as small as a single atom. A former Fulbright scholar from his native Peru, he is now working on the mechanical power of twisted DNA.

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Chemistry professor **Robert Bergman** received the 2004 LBNL award for Excellence in Technology Transfer, which recognizes inventors whose technologies bring significant benefit to society and Berkeley Lab. Bergman was recognized for a novel catalyst used to exchange deuterium or tritium into organic and organometallic compounds. The technology has found use in the pharmaceutical and chemical industries.

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Chemistry professor **David Chandler** was recently honored at the 2005 Berkeley Mini Statistical Mechanics Meeting. He was presented with a special issue of the *Journal of Physical Chemistry* that was dedicated to him to mark his 60th birthday.

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Assistant Professor of Chemistry **Christopher Chang** received a Camille and Henry Dreyfus New Faculty Award.

Jay Groves, an assistant professor of chemistry, received a Beckman Young Investigator Award in 2004. Groves studies the physical chemistry of cell membranes

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Chemical engineering professor **Enrique Iglesia** has been awarded the 2005 Robert Burwell Lectureship in Catalysis from the North American Catalysis Society. The lectureship provides an honorarium and a travel stipend that will allow him to visit many of the local clubs of the NACS.

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Peg Skorpinski photo

Chemistry professor **Richard Mathies** has been elected a Fellow of the Optical Society of America. He was recognized for his "innovative contributions to experimental and interpretative methods in resonance Raman spectroscopy, and the application of these methods to elucidate ultrafast dynamical processes in photochemistry and photobiology."

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Chemistry professor **Heino Nitsche** is the 2005 Vice Chair-elect of the American Chemical Society, Division of Nuclear Chemistry and Technology. Nitsche does research into heavy element nuclear and radiochemistry.

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Roy Kaltschmidt photo

Richard Saykally received the 2004 Ernest O. Lawrence Award in Chemistry from the U.S. Department of Energy "for the invention of velocity modulation spectroscopy of molecular ions; for the development of far-infrared vibration-rotation spectroscopy of radicals, clusters and carbon chains; for the elucidation of the structure and potential energy surfaces for water clusters; and for the development and application of cavity ring down spectroscopy techniques." Saykally, a professor of chemistry, is also the 2005 Reilly Distinguished Lecturer in Physical Chemistry at Notre Dame University.

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Chemical engineering professor **David Schaffer** has been appointed the first holder of the **Charles R. Wilke Endowed Chair** in Chemical Engineering. Schaffer applies engineering principles to enhance stem cell and gene therapy approaches for neuroregeneration.

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Chemistry professor **T. Don Tilley** is the new North American associate editor for the journal *Chemical Communications*.

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Peter Vollhardt, a professor of chemistry, received an honorary doctoral degree from the University of Rome in December 2004.

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STUDENT *News*

National Chemistry week tribute to Seaborg

Students from the professional chemical society, **Alpha Chi Sigma**, saluted the late professor Glenn Seaborg at the half-time show of the Cal-Arizona State football game in October as part of National Chemistry Week. **Colin Hughes**, chemistry professor **Sam Markowitz**, **David Seaborg** and **Sarah Nelson** helped hold a banner showing seaborgium, element 106, which has a half-life of less than one second and is the only element ever named for a living person.

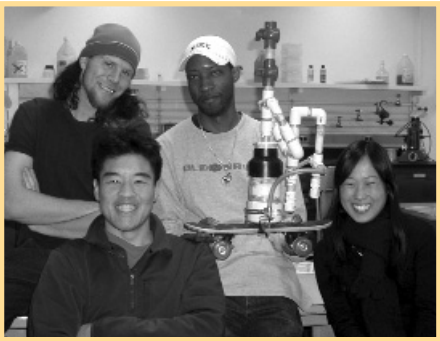
Also, as part of National Chemistry Week, members of Alpha Chi Sigma showed visitors how to read glucometers and urine test strips at the Family Science Night event at a local elementary school. http://www.calacs.org/NCW2004.html

Joseph Hickey photo

AIChE convention to feature chemical car

On March 12 the student AIChE group will host the western regional conference. The event will feature a poster session, talks from industry and academic leaders, and, the big draw, a "Chem-E-Car" race. "Everyone is looking forward to this year's event, especially since last year our car was accidentally destroyed en route to the national meeting," says **Catherine Mukai**, president of the Berkeley group.

The size of a skateboard—in fact, it is a skateboard—the Chem-E-Car must be powered solely by a chemical reaction. This year the Berkeley entry uses the copper Fenton reaction, in which hydrogen peroxide decomposes to water and oxygen gas when copper is added, explains team leader **Ernest Bradley**. "The oxygen gas then flows through the pipes and out the nozzles, sending the car forward. We've done many practice runs at night and are always amazed at how vigorous the reaction is."


The AIChE Chem-E-Car team. Top: Thom Maslowski, Ernest Bradley. Bottom: Matthew Jeung, Cecilia Lee.

The purpose of the competition is to control the chemical reaction and propel the car a certain distance and direction within a specific amount of time, according to fellow team leader **Thom Maslowski**. And in keeping with the rules, all cars are restricted from having any open flames or emitting smoke, so it should be safe as well as fun to watch. http://www.cchem.berkeley.edu/aiche/

Student Awards

Annalise Van Wyngarden, a graduate student with chemistry professor Kristie Boering, was awarded the American Chemical Society's Physical Chemistry Division Student Poster Award at the 2004 ACS National Meeting.

Congratulations to chemical engineering graduate students **Joseph Vegh** and **Brian Bush**. Vegh won the Dow Prize for Excellence in Teaching and is in Professor DavidGraves's group. Bush, who works with Professor Roya Maboudian, is the recipient of the Merck & Co. Outstanding Teaching Assistant Award.

Get to Know


Inger Coble

Inger Coble

Take a trip to the dungeon of Latimer, (yes, that's what the D-button in the elevator indicates), walk down the snaking hallway, all the way to the back and veer left. There you'll run into the friendly presence of **Inger Coble**, one of the hard-working administrative assistants who keep the labs of our illustrious faculty members running like clockwork. Coble, who works with Professor Gabor Somorjai, is essential to keeping his research budgets on track and guiding students and visitors through a maze of paperwork that the campus and college might need.

A native of Denmark, Coble moved with her American husband to California in the 1980s. Armed with a degree in languages—English and French with a business emphasis—she spent four years, from 1987-1991, in the chemistry department office. She then served as the administrative assistant to Ken Raymond for seven years, followed by three years in the nuclear science division of LBNL. "But I missed the chemistry department, so it was not hard to convince me to come back when Vijaya Narasimhan called me four years ago to say that Somorjai was looking for an assistant. And it has been a good experience . I like to stay busy, and Gabor certainly knows how to keep me busy."

Coble is also an avid reader and world traveler who recently spent three weeks in China and is already planning her next trip.

Aileen Harris

It's the busiest time of year—admissions and recruiting time—but **Aileen Harris**, the person to whom all paperwork for the more than 300 applicants to the chemical engineering department funnels, found a few minutes to talk about her dogs. She has four female dogs, with whom she spends most of her free time. "They are all mutts from the Oakland SPCA who walk us regularly around the numerous trails near our home."

Away from the dog trails, she can be found in Gilman Hall, where she has spent eight years as the student affairs officer. She has worked in various capacities within the chemical engineering department, spending a year as the chair's assistant, followed by two years in academic payroll. "I worked closely with Ferne Kasarda at that time, and when Ferne decided to retire, she thought I would be a good choice to take over. I really enjoy the diversity of the job, from helping students through the administrative maze to coordinating social events."


Aileen Harris

Harris grew up in Portland, Oregon, and received a degree in biology from Willamette University in Salem. After a year in a research lab, she worked in a sales organization for many years before deciding to come to Cal "because it's a great environment."

Away from her desk and dogs, Harris is an enthusiastic Cal men's basketball fan. "My husband and I go to all of their home games," she said. "It's how we survive the winters."

Winning for Inventing

Congratulations to Dr. **Jwa-Min Nam**, a postdoctoral researcher in Jay Groves's lab. Nam is the co-winner of the 2004 Collegiate Inventors Competition's Graduate Prize. He was recognized for his development of the "bio-barcode amplified detection system," a new method to detect and identify trace amounts of biological molecules in complex solutions. The technique was noted by *Scientific American* as "doing one better that PCR: not only does it recognize DNA from a few molecules in a sample, but it works the same trick with proteins." Nam did his award-winning research as a graduate student at Northwestern University.

Nano-opportunities in the New Year

The Berkeley Nanotechnology Club (BNC) is hosting the Nano Opportunity Challenge to encourage students across disciplines to mine the nanofields for business gold. The two-round competition, which culminates in February, includes a panel of prominent venture capitalists and entrepreneurs to judge the final presentations.

The BNC is also hosting the Berkeley Nanotechnology Forum 2005, to be held on Saturday, April 30, The BNF offers the opportunity to learn about the current realities of nanotechnology at Berkeley and in the Bay Area. Come listen to top scientists, entrepreneurs and venture capitalists speak, and meet fellow Berkeley community members who are interested in nanotechnology. More information can be found at the nanoclub website:

http://www.ocf.berkeley.edu/~nano/

In addition, the college alumni association co-sponsors nanotechnology forums throughout the year. The next few events are scheduled for March 17 and April 21 at Arrillaga Alumni Center at Stanford. Check the website for more information closer to the date.

http://mitstanfordberkeleynano.org

Changes in Postdoctoral Policies and Benefits

Postdoctoral fellows rang in the New Year with new insurance options. As of January 1, a number of benefits became available to postdocs through the University, all at competitive rates given the relatively young age of most postdocs.

"This is evidence of the University's recognition of post-doctoral scholar contributions to the UC Berkeley academic community," noted Beth Burnside, Vice Chancellor for Research. Postdocs should check with Auben Winters to learn more about their new choices.

Unique partnerships to tackle AIDS, malaria, continued from page 1

of Samoa. Keasling will use the bark of an indigenous Samoan tree to try to clone the gene for a promising anti-AIDS drug in hopes of both protecting rain forests and making the drug widely available. The agreement promises the country half of any royalties the university might ultimately derive from the genes.

The agreement also supports Samoa's assertion that it has national sovereignty over the gene sequence of prostratin, the drug extracted from the bark of the mamala tree. The medicinal properties of the bark have long been known to the traditional Samoan healers, who first taught American ethnobotanists how to use the plant.

"I think that UC Berkeley could set a precedent both for biodiversity conservation and genetic research by including indigenous peoples as full partners in royalties for new gene discoveries that result from their ancient medicines," Keasling said.

As Keasling's hopes for his research expand, his laboratory space is expanding as well. The campus and Lawrence Berkeley National Laboratory are cooperating to lease a large amount of lab space in West Berkeley for Keasling and other synthetic biology-minded faculty members on campus, with the move occurring this spring. Noted Dean Clayton Heathcock, "It is a big expansion of a relatively new program, and an interim solution to allow new exciting programs to develop while big building projects continue on campus."

Keasling is the director of the synthetic biology department at LBNL and a faculty affiliate of the California Institute for Quantitative Biomedical Research (QB3).

>> Yvette Subramanian and Robert Sanders

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ChemiCAL Science and Engineering

is published several times each year to support the college's mission of providing excellent teaching, research and public service in the fields of chemistry and chemical engineering.

Questions or comments should be directed to
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CALENDAR

Upcoming events for College of Chemistry alumni and friends:

check chemistry.berkeley.edu/alumni for the latest information

March 3
Cupola Era alumni luncheon

Gather with fellow classmates from the graduating years 1946 - 63 and hear about what is going on in the college and around campus, as well as a talk titled "What Makes Water Wet" from chemistry professor Richard Saykally (see page 4).

chemistry.berkeley.edu/alumni

April 15 & 16
Inauguration of the Chancellor & Cal Day

The inauguration of Berkeley's ninth chancellor, Robert Birgeneau, will take place on Friday at 2:00 p.m. in Zellerbach Auditorium. The festivities continue with Cal Day on Saturday. This campus-wide open house will include college tours and events.

http://inauguration.berkeley.edu/

http://www.berkeley.edu/calday/

April 11 & 13
Berkeley Lectures in Chemical Engineering

Professor Frances Arnold (Ph.D. '85) from Caltech will deliver two lectures: "Design by Directed Evolution: Towards a Cytochrome P450 Monooxygenase," and "Protein Evolution by Structure-Guided Recombination."

chemistry.berkeley.edu/seminars

May 21
Commencement

This year's College of Chemistry Commencement Ceremony will take place at 7:00 p.m. in Zellerbach Auditorium, and chemistry professor Charles Shank will be the speaker. A reception at the Alumni House will immediately follow the ceremony. Come join us in recognizing our students.

chemistry.berkeley.edu/commencement