

APRIL 25, 2011

C&EN

CHEMICAL & ENGINEERING NEWS

CYSTIC FIBROSIS

Transformative drugs get close to market **P.24**

REWIRED BACTERIA

Harnessing microbes' electrons for energy **P.34**



TOP INSTRUMENT FIRMS

Acquisitions shift lead positions in 2010 **P.13**



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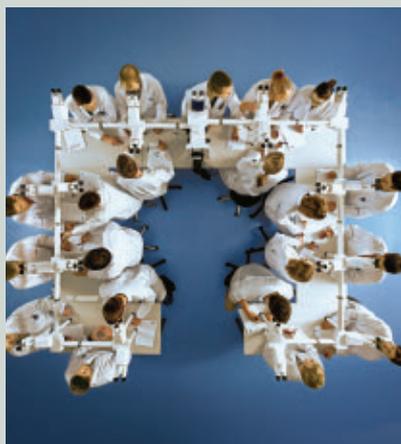




COVER STORY

TOP INSTRUMENT MAKERS

Mergers and acquisitions shuffled the top players in C&EN's ranking of analytical and life sciences instrumentation firms. PAGE 13



QUOTE OF THE WEEK

"You can't do research without knowing what's happening in your field."

MOUHOSSINE
NACRO, CHEMISTRY
PROFESSOR,
OUAGADOUGOU
UNIVERSITY, BURKINA
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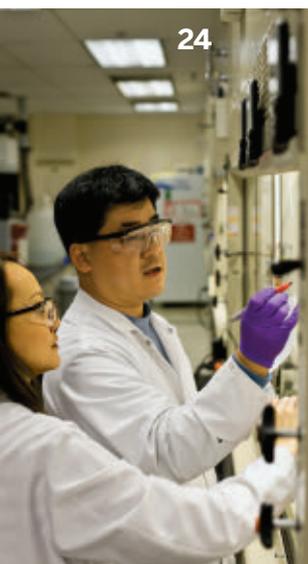
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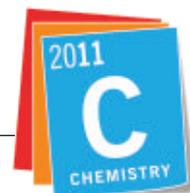
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Volume 89, Number 17

LETTERS

WHITHER NUCLEAR POWER?

LONG AGO, steam was found to be a fascinating, easily produced form of the universally available resource, water. “Boilers” safely producing steam heat and hot water for baths and myriad cleansing processes are now appreciated worldwide. But it took many decades to develop safe boiler pressure control. I estimate that there might have been several tens of thousands of individuals killed and injured over the past couple of centuries in boiler explosions. It took that much time to research, develop, engineer, produce, and regulate the materials, structural designs, and instrumentation to make the use of boilers both reasonably safe and common.

Now I watch with great concern the consequences of tsunami and earthquake damage to nuclear power plants and then to the people of Japan. We won't know for a while the human casualties caused by released radiation there. We just know for sure that massive research and engineering must be applied to the design, instrumentation, materials, siting, construction, start-up, operation, and controlled shutdown of nuclear power plants there and everywhere else.

My experience is in rocket science, industrial gases production, and operations with hazardous materials. Therein we proclaim safe operations as our first priority. That's the way we have to go forward with nuclear power in the U.S. In the quarter or half century ahead we should also solve the long-term storage, or more desirably, the detoxification, of waste products. In that same time span, we might be able to solve the knotty problems involved in switching to safe nuclear fusion power production.

E. Ellsworth Hackman III
Hockessin, Del.

THE SCIENTIST'S ENGLISH

IN HIS LETTER to the editor, Joseph Jablonski complains of English-language problems in manuscripts submitted to ACS journals by ESL (English as a Second Language) authors (C&EN, Feb. 21, page 4). He suggests that ACS could offer an editing/screening service and charge “a small fee” for revising such manuscripts so that the English is acceptable.

As a professional scientific editor with a master's degree in chemistry and more

than 15 years' ESL editing experience, I object to the notion that such services are worth only a “small” fee. The ability to efficiently transform mangled syntax into idiomatic English without introducing scientific inaccuracies is a valuable skill that can take years to acquire, and many ESL authors pay relatively large fees for skillful editing. A recent article in *Nature* (DOI: 10.1038/nj7324-721a) discussed the growth, and value, of manuscript-editing services.

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Mercury Measured In Soil Of U.S. Forests

The carbon-rich soils in northern U.S. forests contain up to 16 times as much mercury as do soils in southern forests,



SHUTTERSTOCK

according to a new study. Scientists want to understand mercury's fate because the toxic metal can wash from forest floors to water bodies, where it can accumulate in the aquatic food chain.

cenm.ag/env27

A LEGO-Like Microarray

Although high-throughput screening provides a powerful means to evaluate drug candidates, the expense of sophisticated facilities and robots limits access to its techniques. Now researchers demonstrate a simple, cheap polymer-based benchtop microarray that doesn't need a robot to deliver compounds.

cenm.ag/anl21

Braskem Mulls U.S. Cracker

Brazilian petrochemical company Braskem is considering building an ethylene cracker and polyethylene plant in the U.S., according to CEO Carlos Fadigas. C&EN Senior Editor Alex Tullo blogs about the likelihood of the project.

cenm.ag/blg8

IYC Profile: Burkina Faso

A Web-only slide show accompanies the

profile of chemist Mouhousseine Nacro of Burkina Faso (see page 41). Nacro conducts research on natural dyes and nutrition, and he travels the country to promote sweet potatoes as a source of vitamin A and other antioxidants.

cenm.ag/iycl



COURTESY OF MOUHOUSSINE NACRO

authors with a list of professional editing services, as well as a list of questions to ask before contracting for such services.

**Carlotta Shearson
Cornwall, N.Y.**

GRADUATE EDUCATION'S BRIGHT FUTURE

I MUST EXPRESSLY disagree with Hilton Weiss's letter describing the current state of chemical education as "sorry" (C&EN, March 7, page 4). In recent years, hundreds of chemistry departments in the U.S. have had to grapple with the realities of difficult financial situations. At these universities, increasing emphasis on research has tracked with the increasing need for highly sought grant-based funding.

However, a strong research program (and strong channels of research funding) still depends on a deep, insightful understanding of chemical theory. Graduate chemical education has become less about sheer memorization of facts and more about the creative application of general principles. America's best graduate students and researching undergraduates are gripped by the creative spirit and ultimately must take the bull by the horns—in the process they become critical thinkers and independent learners.

The true frontiers of chemical education remain, in my mind, at the undergraduate level. Justifying the relevance of chemistry is very difficult in an age when many students are looking ahead to extreme specialization in their careers. For example, what use does a future radiologist have for organic chemistry? To many ACS members the answer may seem obvious, but today's preprofessional undergraduates are (understandably) less convinced. Keeping chemistry relevant and general for preprofessional undergraduates remains an ongoing challenge for chemical educators.

Larger class sizes aren't necessarily the unilateral evil that Weiss purports them to be. Although larger class sizes may dilute the effectiveness of traditional lectures, they also challenge educators to develop meaningful, individualized learning experiences that place students in the driver's seat of their own education.

In chemistry, we are blessed with several extraordinary semantic formats for the expression of chemical structures by computers: SMILES, CML, MRV, MOL,

and XYZ come to mind. All kinds of existing software use these formats to create meaningful computer-based individualized learning and problem-solving experiences. At the same time, Web-based video brings the experience of lecture to students at any place and time. Meanwhile, teachers' roles shift from boring preachers of lecture material to active, dynamic coaches of students.

Modern chemical education will arm students for battle outside of class using independent learning experiences and with effective problem-solving skills in class (and it will do so in a largely scale-independent way). The future is bright.

**Michael Evans, graduate student
University of Illinois, Urbana-Champaign**

MUSK XYLENE BAN

C&EN'S COVERAGE of the recent European Union ban of musk xylene, formerly used in fragrances, missed an important point (C&EN Online Latest News, Feb. 17). The EU ban came two years after the International Fragrance Association banned the use of musk xylene in perfumery through IFRA Standards. IFRA Standards form the basis for a globally accepted and recognized risk management system for the safe use of fragrance materials and are a part of the fragrance industry's global self-regulatory safety system contained in the IFRA Code of Practice.

IFRA members produce more than 90% of all fragrances worldwide and standards are obligatory for all IFRA members. These standards cover areas of human health, occupational safety, and environmental safety and are established on the basis of comprehensive scientific review of materials in perfumery. They follow recommendations of the Research Institute for Fragrance Materials and an independent panel consisting of world-renowned experts from the fields of dermatology, toxicology, pathology, respiratory health, and environmental sciences.

IFRA's action on musk xylene years before a government ban clearly demonstrates that self-regulation and safety programs of the fragrance industry are viable, ensure safety of fragrance materials and products, and are far more stringent than many regulatory environments.

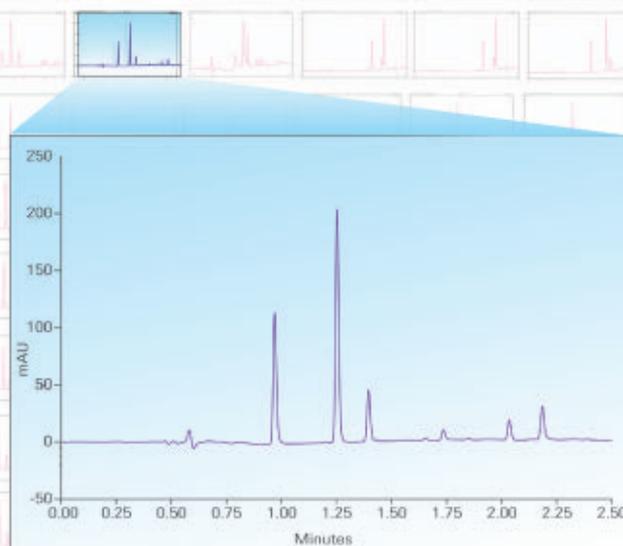
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JAPAN'S NUCLEAR CRISIS CONTINUES

NATURAL DISASTER: Plant operator says it will take six to nine months to contain radioactive leaks

IT WILL TAKE UP TO nine months before the crippled Fukushima Daiichi Nuclear Power Station in Japan is stabilized, facility owner Tokyo Electric Power Co. (TEPCO) said last week. Radiation has been leaking from the complex since a massive earthquake-triggered tsunami inundated Japan's Pacific coast and knocked out cooling systems at the plant's six reactors just over a month ago.

At an April 17 news conference, TEPCO officials unveiled a phased "road map" to bring the crisis under control. In the first three months of the plan, the company hopes to cool the reactors and gradually reduce the level of leaking radiation.

Three to six months after that, the utility expects all of the reactors to achieve "cold shutdowns," a stable condition in which temperatures drop and radiation leaks substantially decline.

"It is a sign of the extraordinary seriousness of the Fukushima nuclear disaster that TEPCO anticipates it may take nine more months before cold shutdown can be achieved," Daniel O. Hirsch, lecturer on nuclear policy at the University of California, Santa Cruz, tells C&EN. "Radioactive releases could continue for a long time."

TEPCO said the plan involves installing a concrete cover over the three badly damaged reactor buildings to contain the radiation. Hydrogen explosions in the buildings in days immediately after the quake blew off their roofs and scattered radioactive debris. The company has been pumping nitrogen gas into plant reactors to help prevent additional hydrogen blasts.

"We will do our utmost to curb the release of radioactive materials by achieving a stable cooling state at the reactors and spent-fuel pools," TEPCO Chairman Tsunehisa Katsumata told reporters at the briefing. "The company has been doing its utmost to prevent a worsening of the situation. We have put together a road map and will put all our efforts into achieving these goals."

Robots that are being used to measure the levels of radiation in the nuclear complex have reported radioactivity readings of up to 57 millisieverts per hour. Workers cannot enter these areas because the upper limit for nuclear workers in Japan is 250 millisieverts per year.

Meanwhile, very low levels of radioactive material linked to the damaged nuclear plant in Japan have reached the U.S. West Coast. But analyses of air and water samples for radiation contamination show that the U.S. remains safe, EPA Administrator Lisa P. Jackson told the Senate Environment & Public Works Committee earlier this month (*C&EN Online* Latest News, April 14).

"Let me be clear. EPA has not seen and does not expect to see radiation in our air or water reaching harmful levels in the U.S.," Jackson said. "All of the data that we have seen, which we continue to make public and

Debris is still piled outside Japan's Fukushima Daiichi Nuclear Power Station.



TEPCO

available on our website, indicates that while radiation levels are slightly elevated in some places, they are significantly below problematic levels."

EPA has 164 monitoring stations spread throughout the 50 states, and the agency measures radioactive substances in air, precipitation, drinking water, and milk.

Recent air samples have contained very small amounts of iodine, cesium, and tellurium, which are consistent with possible releases from the damaged Japanese reactors, Jackson testified. The largest amounts were found in samples from Alaska, she said, but all of the radiation levels detected "are hundreds of times below levels of concern."—GLENN HESS

COMPANIES ADVANCE BIOBASED CHEMICALS

CLEANTECH: Start-ups are poised to harness cellulosic feedstocks

Cobalt Technologies has developed a bacterium that ferments a variety of biomass-derived sugars.



BIOBASED CHEMICAL production is taking a step forward with the announcement of two new projects—both involving venture-capital-backed start-ups—to make chemicals out of nonfood cellulosic biomass.

Cobalt Technologies is joining with the process development firm American Process to build a demonstration-scale *n*-butyl alcohol plant in Alpena, Mich. Genomatica, meanwhile, has formed a partnership with the Italian plastics maker Mossi & Ghisolfi to make 1,4-butanediol in Italy.

High-volume industrial chemicals including lactic acid, propanediol, and citric acid are already manufactured by fermenting sugars derived from sugarcane or corn, and several companies are pursuing a new generation of sugar-based chemicals such as isobutyl alcohol,

succinic acid, and acrylic acid. To date, though, development of chemicals from cellulosic feedstocks has lagged.

Cobalt plans to jump-start the process by piggy-backing on a cellulosic ethanol project that American Process has already begun. Using \$22 million in grants from the Department of Energy and the State of Michigan, American Process intends to open an ethanol plant early next year that's based on a hemicellulosic waste stream from a neighboring wood-paneling firm.

The plant will switch to making *n*-butyl alcohol in mid-2012, the partners say, producing more than 3 million lb annually. Key to the process, says Cobalt Chief Financial Officer Steven Shevick, is a *Clostridium* bacterium that ferments five-carbon sugars more efficiently than do conventional yeast and *Escherichia coli*.

Similarly, Genomatica is taking advantage of a cellulosic ethanol project that is already under way at Mossi & Ghisolfi's Crescentino site. M&G expects to be producing 88 million lb per year of ethanol by the first half of 2012. Some of the biomass feedstock will be diverted to 1,4-butanediol production later that year.

Both deals are evidence that attention among developers of cellulosic biomass is shifting from ethanol to higher-value industrial chemicals, notes Erik Hoover, an analyst with Cleantech Data. The deals demonstrate momentum, but Hoover still sees many unknowns. "The opportunity for cellulosic biomass is enormous—if a hundred 'ifs' are satisfied," he says.—MICHAEL MCCOY

MENDING WITH LIGHT

MATERIALS CHEMISTRY: Light prompts metallosupramolecular polymers to repair themselves

The self-healing metallosupramolecular polymers are made from repeating units of a small polymer with ligands that bind to metals.

SCRATCHES, CUTS, and cracks, although they may seem small, can add up to big bucks when they're in polymer coatings. Just ask anyone who's found a scratch to their car's paint job. Thanks to a family of metallosupramolecular polymers, spot-repairing damage to paints, coatings, and polymer thin films could one day be as simple as shining an ultraviolet light on them (*Nature*, DOI: 10.1038/nature09963).

The self-healing material, which comes from a group led by Stuart J.

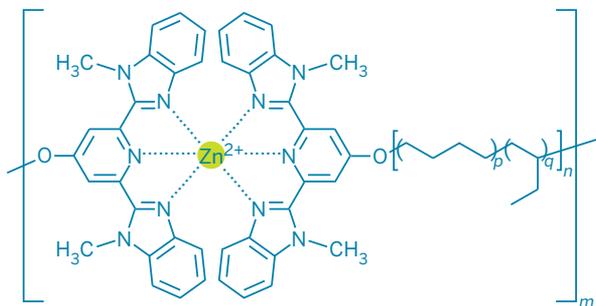
Rowan of Case Western Reserve University and Christoph Weder of the University of Fribourg, in Switzerland, is based on short polymer chains that terminate in a ligand that can

coordinate to a metal ion. "When we put in a metal ion—in this case either zinc or lanthanum—the components bind to the metal and essentially form a high-molecular-weight polymer," Rowan explains.

When light shines on the polymer, the metal-binding ligands absorb the light's energy and convert it into heat, which, in turn, makes the metal ion break ties with the ligands. "What you're doing is depolymerizing the system using this photothermal process," Rowan says. The depolymerized material is liquid and can flow into and heal cracks or scratches. "When you remove the light, the ligands rebind to the metal, polymerizing again and reestablishing the mechanical strength of the material," he adds. All of which takes place in under a minute.

There are other light-activated self-healing materials, but they rely on embedded particles or agents, which can be exhausted, or they use irreversible chemical reactions for healing. "We've used a reversible reaction," Rowan says, "so you can scratch and heal and scratch and heal."

The work "represents a major step forward in the nascent field of self-healing polymers," comments Michael R. Kessler, a materials science and engineering professor at Iowa State University. "What makes this approach potentially so useful is that the light can be directed locally at the damaged region, so that bonds are only re-formed where the damage occurs, allowing the undamaged material to continue to carry load during the healing process."—BETHANY HALFORD



BERG, NEUREITER RECEIVE ACS HONOR

AWARDS: Society bestows 2011 Public Service Award on two chemists

THE AMERICAN Chemical Society presented its 2011 Public Service Award to Jeremy M. Berg, a chemist who runs a \$2 billion-per-year research institute at the National Institutes of Health, and Norman P. Neureiter, the first science and technology adviser at the State Department, at an April 13 ceremony on Capitol Hill.

The award honors the scientists for their vision and leadership in science and engineering policy. "I am very pleased that ACS is recognizing two scientists who have dedicated their talents to public service," ACS President Nancy B. Jackson said in a statement.

Berg, director of NIH's National Institute of General Medical Sciences, "is an effective advocate for basic research who has worked to increase the visibility of chemistry at NIH," Jackson said. He has also focused his efforts on training and motivating the next generation of scientists and increasing the diversity of the biomedical workforce. Berg plans to leave NIH at the end of June to take a position at the University of Pittsburgh (C&EN, Dec. 13, 2010, page 8).

One of Berg's achievements at NIH was finding middle ground with ACS in 2004 when NIH wanted to launch PubChem, a publicly available chemical structure database. ACS officials were concerned that the free service would compete with ACS's private database, the Chemical Abstracts Service (CAS) Registry. "This turned into a very complex issue with lots of negotiation," Berg recalls. Today, both PubChem and CAS are thriving, he says.

Prior to joining NIH in 2003, Berg directed the In-

stitute for Basic Biomedical Sciences at the Johns Hopkins University School of Medicine, where he was also a professor and head of the department of biophysics and biophysical chemistry. He holds a Ph.D. in chemistry from Harvard University.

Neureiter, senior adviser to the Center for Science Diplomacy at the American Association for the Advancement of Science (AAAS), served as science and technology adviser to the secretary of state under Secretaries Madeleine Albright during the Clinton Administration and Colin Powell during the George W. Bush Administration. He is credited with increasing the number of Ph.D. scientists working at the State Department.

In 2004, Neureiter became the first director of the newly established Center for Science, Technology & Security Policy at AAAS. A former oil industry research chemist, Neureiter also has a 23-year career in international business with the semiconductor industry. He served as a scientific attaché in Germany and Poland, and spent four years in the White House Office of Science & Technology, from 1969 to 1973. "He has left a profound mark on both science and foreign policy, and ACS is particularly proud to be recognizing him in 2011 during this International Year of Chemistry," Jackson said.—BRITT ERICKSON

SEAN PARSONS/ACS



Berg (left) and Neureiter receive the 2011 ACS Public Service Award during a Capitol Hill reception.

PHARMACEUTICALS Merck and J&J settle arthritis franchise dispute

Merck & Co. and Johnson & Johnson have resolved their two-year-long legal wrangle over rights to market the J&J arthritis drugs Remicade and Simponi outside the U.S. Merck will make a one-time payment to J&J of \$500 million and give up rights to sell the drug in certain territories, among other concessions.

The dispute over the arthritis franchise originated in March 2009 after Merck announced its merger with Schering-Plough, which was then J&J's marketing partner for the two drugs. The carefully crafted deal left Schering-Plough as

the surviving company, operating under the Merck name. Merck calculated that the structure would avoid triggering a clause in the drug-marketing agreement between J&J and Schering-Plough that would return rights to J&J if Schering-Plough were to be acquired.

J&J didn't buy Merck's strategy. It filed a lawsuit in May 2009 claiming the merger triggered the change-of-control provision for the drug franchise.

Under the settlement, J&J gains exclusive rights to the drugs in Canada, Central and South America, the Middle East,

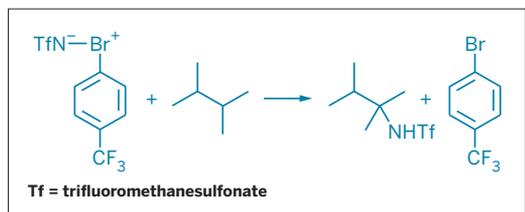
Africa, and Asia-Pacific. Merck retains rights in Europe, Russia, and Turkey—territories it says represent about 70% of the \$2.8 billion the drugs contribute to its revenues annually. In addition, the profit split on sales, which now favors Merck 58:42, will be equal in the future.

The deal "lifts a critical overhang" for Merck, says Seamus Fernandez, a stock analyst for Leerink Swann. Still, the loss of about a third of the company's stake in the Remicade/Simponi franchise could lower its earnings per share by 15 to 20 cents per year, he adds.—LISA JARVIS

NABBING NITROGEN

ORGANIC SYNTHESIS: Metal-free method adds amines to alkanes

WITHOUT a functional group to grab onto, chemists can't do much with alkanes other than burn them. Now, researchers in Japan have developed a metal-free method to outfit these hydrocarbons with amines (*Science*, DOI: 10.1126/



science.1201686), thus making them available for further reactions.

The room-temperature reaction is regioselective and offers a more environmentally friendly route than similar transformations

that use hypervalent iodine reagents with metal catalysts. The reaction makes use of an *N*-triflylimino- λ^3 -bromane compound, which inserts nitrogen functionality into C–H bonds to give triflyl-substituted amines. The hypervalent bromine reagent has a marked selectivity for tertiary C–H bonds over secondary ones but leaves primary C–H bonds alone.

The research team, led by Masahito Ochiai of the

University of Tokushima and Waro Nakanishi of Wakayama University, previously developed the hypervalent bromine reagent to transform alkenes into aziridines—a reaction that had already been done with hypervalent iodine and a metal catalyst. If the hypervalent bromine could replace the hypervalent iodine and metal catalyst in that reaction, the researchers reasoned, it could also replace those reagents for aminating aliphatic C–H bonds.

Ochiai says the hypervalent bromine reagent is fairly stable in the solid state, lasting up to a month in the refrigerator without decomposition. Its preparation is simple, he says, but because it uses bromine trifluoride and liberates HF gas, it demands certain safety precautions. “Care should be taken in handling bromine trifluoride because it will react violently with most organic compounds,” Ochiai warns.

Philippe Dauban, a chemist at France’s Institut de Chimie des Substances Naturelles, who has worked on aminations using hypervalent iodine reagents and transition metals, notes the hypervalent bromine reagents “might provide new opportunities” for aminations. But he points out that they are not without their limitations. For example, he says, using alkanes as solvents could be problematic.

“The problem of efficient selective amination of alkanes has not been solved by this study,” Dauban says, “but it clearly shows us new avenues to explore.”—

BETHANY HALFORD

WILLIAM LIPSCOMB DIES AT 91

OBITUARY: Harvard Nobel Laureate worked with boranes, enzymes

WILLIAM N. LIPSCOMB JR., 91, an emeritus professor of chemistry at Harvard University who won the 1976 Nobel Prize in Chemistry, died in Cambridge, Mass., on April 14 of pneumonia and other complications from a fall.

Born in Cleveland in 1919, Lipscomb earned a B.S. in chemistry at the University of Kentucky in 1941 and a Ph.D. in chemistry under Linus C. Pauling at California Institute of Technology in 1946.

Lipscomb then joined the faculty at the University of Minnesota; he moved to Harvard as a professor of chemistry in 1959. He was appointed Abbott & James Lawrence Professor of Chemistry in 1971 and retired in 1990.

Lipscomb’s Nobel Prize was awarded for his studies on the structure of boranes and the insight that that work provided into chemical bonding. His work on boranes and on carbon

compounds formed the experimental basis for the extended Hückel theory, the first widely applicable use of molecular orbital theory to study chemical bonding. Lipscomb also worked extensively on determining the structure and function of enzymes with the help of X-ray crystallography. His varied interests in biochemistry, as well as physical, inorganic, and organic chemistry, were linked by a common theme of structure and function.

His lab was a fruitful training ground for other future Nobel Laureates, including Thomas A. Steitz of Yale University, Ada E. Yonath of Weizmann Institute of Science, and Roald Hoffmann of Cornell University.

“I learned from Lipscomb’s sly wit that one should not take oneself too seriously,” Hoffmann says, “and that chemistry should be fun.”

Indeed, Lipscomb delighted in the lighter side of chemistry, frequently participating in the tongue-in-cheek Ig Nobel Prize ceremonies, which are held at Harvard each year shortly before the Nobel Prizes are announced. In 2008, he agreed to be the prize in the event’s Win-a-Date-with-a-Nobel Laureate-Contest.

Lipscomb’s varied interests extended beyond science. Colleagues noted that it wasn’t unusual to find Lipscomb practicing his clarinet in the lab while waiting for the latest experimental data.

He is survived by his wife, Jean; three children; three grandchildren; and four great-grandchildren.—SOPHIE ROVNER



Lipscomb

CHOPPING UP LIGNIN

ORGANIC CHEMISTRY: Catalyst selectively cleaves key bond in models of complex plant polymer

USING A nickel catalyst, chemists have found a way to break an aromatic ether bond while leaving the aromatic ring itself unscathed (*Science*, DOI: 10.1126/science.1200437). The work provides proof of concept that metal catalysts could be used to convert lignin—a biopolymer that is replete with aromatic ether linkages and that lends stiffness to plants—into fuels or commercial chemicals.

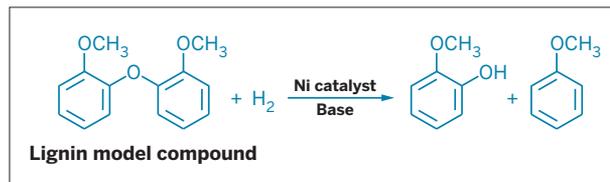
Lignin gums up some chemical processes for obtaining energy from other plant components such as cellulose. And although it can be burned to provide heat and energy, it's a solid that is tough to transport, says organometallic chemist John F. Hartwig of the University of Illinois, Urbana-Champaign. "It would be nice to be able to chop it up into small enough pieces to make it a liquid" suitable for processing into transportation fuels or aromatic chemical feedstocks, he says.

But enzymes have trouble breaking down lignin, and chemically cleaving aromatic ether bonds such as those in lignin is messy, requiring harsh conditions and lead-

ing to mixtures of products, some with reduced aromatic rings. Using hydrogen and a new nickel catalyst, Hartwig and postdoctoral researcher Alexey G. Sergeev selectively cleaved aromatic C–O bonds in lignin model compounds. So far, the method requires relatively high amounts of the catalyst and a strong base, but Hartwig says his team, which is among several

Illinois research groups in the BP-supported Energy Biosciences Institute, is working to eliminate those drawbacks. He has filed a provisional patent application on the process.

"There's a saying that you can make anything you want to from lignin except for money," says George W. Huber, an expert in biomass conversion at the University of Massachusetts, Amherst. Researchers have been trying to break down lignin for a long time, but selectivity has always been an issue, he says. The catalyst must be improved to work cost-effectively on lignin itself, but "this route shows that selective lignin depolymerization chemistry is possible," he says. "It shows the power of modern chemistry for solving energy problems."—CARMEN DRAHL



PATENT REFORM ON THE MOVE

INTELLECTUAL PROPERTY: House panel advances bill to reform patent process

LEGISLATION that would overhaul the nation's patent system took another step toward enactment on April 14 when the House of Representatives Judiciary Committee gave strong bipartisan approval to a reform measure that has the backing of big chemical and pharmaceutical companies.

The bill, H.R. 1249, was approved by a vote of 32-3 and would align the U.S. with other industrialized nations that use a "first to file" system, which awards patents to the inventor who filed an application first, rather than allowing a fight over who actually invented something first.

It would also allow the Patent & Trademark Office (PTO) to set its own fees and prevent Congress from diverting the revenue raised by those fees to other unrelated government programs.

Supporters say the bill will help ensure that the patent office has the resources it needs to hire more examiners and upgrade

its technology. PTO has been struggling to deal with a huge backlog of more than 700,000 applications.

"This important legislation is long overdue. The last major patent reform was nearly 60 years ago," said Rep. Lamar S. Smith (R-Texas), committee chairman and the bill's chief sponsor. "Since then, American inventors have helped put a man on the moon, developed cell phones, and launched the Internet. But we cannot protect the technologies of today with the tools of the past."

The measure, which will likely be considered by the full House later this year, is similar to a bill that easily passed the Senate on March 8 and has the backing of President Barack Obama (*C&EN*, March 14, page 30).

The bill also sets rules for patents to be challenged after they are granted through a PTO administrative procedure. Advocates say the new postgrant review process will allow disputes involving patent quality and scope to be settled without expensive litigation.

The legislation is supported by a diverse array of stakeholders, including the Coalition for 21st Century Patent Reform, whose members include Dow Chemical, DuPont, Pfizer, Eli Lilly & Co., and Novartis.

"Our coalition believes the legislation reported, with overwhelmingly broad bipartisan support, will improve the operations of PTO and procedures for obtaining and enforcing patents," says Gary Griswold, the group's director.—GLENN HESS

"We cannot protect the technologies of today with the tools of the past."

LAMAR S. SMITH
(R-TEXAS)



Smith

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TOP INSTRUMENT FIRMS

Mergers and acquisitions alter the landscape in **C&EN'S RANKING** of leading analytical and life sciences instrumentation companies

ANN M. THAYER, C&EN HOUSTON

WELCOME RELIEF came in 2010 to the analytical and life sciences instrumentation industry. Broad market recovery coupled with strong growth in emerging regions helped boost sales. In this more stable economic environment, customers were again willing to spend money on new and replacement instruments.

In 2009, instrument makers struggled, and most watched sales fall. C&EN's new survey of the top 25 firms reveals the rebound that 2010 brought. At \$24.5 billion, combined 2010 instrument sales for the top 25 companies were up a healthy 14% compared with 2009. About half of the group saw double-digit gains, and all but two firms posted higher sales.

The \$40 billion global instrumentation market grew 7% in 2010, a sharp contrast to its 3% decline in 2009, according to Strategic Directions International, a Los Angeles-based research firm. Sectors such as life sciences and food testing grew at a faster than average rate, while industrial markets grew more slowly. The academic and government funding environment was stable, and some pharma sectors recovered.

"There was an increased interest in applied markets, such as clinical research



and environmental and food safety," says Kevin Chance, president of Thermo Fisher Scientific's scientific instruments division. "Growth last year could be largely attributed to government stimulus funding, most notably in Japan and the U.S. This had a major effect, particularly in the academic end-use markets."

Europe lagged somewhat in growth, according to instrument makers. "Growth was more apparent in emerging markets

such as China, India, and Brazil," Chance continues. "The recent events in Japan will impact some areas of the market, but it is still too early to tell."

In 2010, the general trend was one of increased spending, industry participants say. "In light of the economic issues that we had in 2009, there was a lot of activity that was pent up," says Dusty Tenney, president of analytical sciences and laboratory services at PerkinElmer. Because purchases had been on hold or deferred, "2010 was somewhat of an anomaly because of the soft comparison to 2009," he adds.

Owing to the rebound in 2010, life sciences tools firms will find it hard to post robust gains in

2011, Morgan Stanley stock analyst Marshall Urist suggested in a report to clients earlier this year. "Revenue is still generally flat to below pre-recession 2008 revenue levels for most tools companies, favoring sustainable growth in 2011," he wrote.

Urist anticipates that stimulus funding will have a minor effect on business this year. He considers the overall stimulus impact to have been lower than expected and, for the majority of companies, "not a material contributor to top-line growth." Of more concern in coming months is flat research spending by governments worldwide.

The industry's sales growth this year will be in the mid-single digits, executives from many of the top 10 firms tell C&EN. New product introductions and expanding markets will contribute organically to

DIGITAL DEVICE
A semiconductor chip is the core of Life Technologies' Ion Personal Genome Machine sequencer.

"The midsized players get squeezed out as you get to a critical mass and scale."

TOP 25 INSTRUMENTATION FIRMS

Acquisitions caused shifts among industry leaders in 2010

RANK		COMPANY	INSTRUMENT SALES	CHANGE	INSTRUMENT SALES AS	HEADQUARTERS COUNTRY	INSTRUMENT OPERATING PROFITS	CHANGE	PROFITS AS % OF TOTAL OPERATING PROFITS	OPERATING PROFIT MARGIN ^a
2010	2009		2010 (\$ MILLIONS)	FROM 2009	% OF TOTAL SALES		(\$ MILLIONS)	FROM 2009		
1	3	Agilent Technologies ^b	\$2,679	29.9%	49.2%	U.S.	\$500	28.2%	88.3%	18.7%
2	1	Life Technologies ^c	2,672	7.3	74.5	U.S.	na	na	na	na
3	2	Thermo Fisher Scientific	2,300	9.5	21.3	U.S.	na	na	na	na
4	9	Danaher	2,298	54.7	17.4	U.S.	228	26.7	10.5	9.9
5	5	Shimadzu	1,715	7.0	55.8	Japan	184	2.7	110.1	10.7
6	4	Waters	1,643	9.7	100.0	U.S.	450	14.0	100.0	27.4
7	7	Bruker	1,225	15.3	93.9	U.S.	161	13.3	103.1	13.1
8	6	PerkinElmer	1,193	10.0	70.0	U.S.	na	na	na	na
9	10	Roche Diagnostics ^d	931	3.9	8.3	Switzerland	na	na	na	na
10	11	Mettler-Toledo	901	17.5	45.8	U.S.	na	na	na	na
11	12	Hitachi High-Technologies	701	-6.8	8.6	Japan	na	na	na	na
12	17	Nikon ^e	695	26.4	6.6	Japan	-67	nm	nm	def
13	18	Beckman Coulter	694	12.8	18.9	U.S.	75	-21.5	18.7	10.8
14	15	Bio-Rad Laboratories	662	2.8	34.4	U.S.	53	32.9	23.4	7.9
15	14	Olympus ^e	550	-7.3	5.2	Japan	na	na	na	na
16	16	Carl Zeiss ^f	541	8.8	13.3	Germany	na	na	na	na
17	21	JEOL ^g	500	14.4	48.3	Japan	na	na	na	na
18	—	FEI	480	9.1	75.7	U.S.	na	na	na	na
19	19	Spectris	464	11.3	33.0	U.K.	55	217.9	24.7	11.8
20	20	Dionex	447	15.0	100.0	U.S.	93	17.8	100.0	20.9
21	24	Horiba	398	0.3	27.5	Japan	62	236.8	41.5	15.7
22	25	Illumina	325	43.8	59.8	U.S.	na	na	na	na
23	23	Tecan	251	4.7	70.5	Switzerland	40	-13.5	75.1	16.1
24	—	Qiagen	152	7.6	14.0	Germany	na	na	na	na
25	—	Analytik Jena ^f	65	2.5	59.7	Germany	4	-33.9	90.7	6.0

NOTE: Results are for the calendar year unless otherwise stated. Some figures were converted at relevant exchange rates as of Dec. 31, 2010. **a** Instrumentation operating profits as a percentage of instrumentation sales. **b** Fiscal year ended Oct. 31, 2010. **c** Includes significant amount of noninstrumentation products. **d** Results for instrumentation sales within this division alone. **e** Company estimates for fiscal year ending March 31, 2011. **f** Fiscal year ended Sept. 30, 2010. **g** Fiscal year ended March 31, 2010. **def** = deficit. **na** = not available. **nm** = not meaningful.

company growth, they say, complementing the boost to revenues that many will see from acquisitions.

Consolidation was a hallmark of 2010 and is still under way. "There were actually two levels of consolidation," Tenney points out. One was within the instrumentation industry, where several major firms acquired businesses. Consolidation also took place among customers, most notably some major pharmaceutical and chemical firms.

ACQUISITIONS SHIFTED C&EN's ranking of instrument providers, starting at the top. With its \$1.5 billion purchase of Varian, which ranked 13th in last year's survey, Agilent Technologies moved up from third place to first. Life Technologies, formed in late 2008 from the merger of Applied Biosystems and Invitrogen, slipped to second. Thermo, meanwhile, moved from second

to third, just a hair's breadth above quickly rising Danaher.

With only a 0.3% difference in instrument sales, the top two companies are also neck and neck. Life Technologies' revenues, which include a significant amount of consumables, grew 7%, while Agilent reported a 30% increase in chemical and life sciences equipment sales for its fiscal year, which ended on Oct. 31. Even without the Varian purchase, Agilent's instrument sales would have grown at two to three times the industry average.

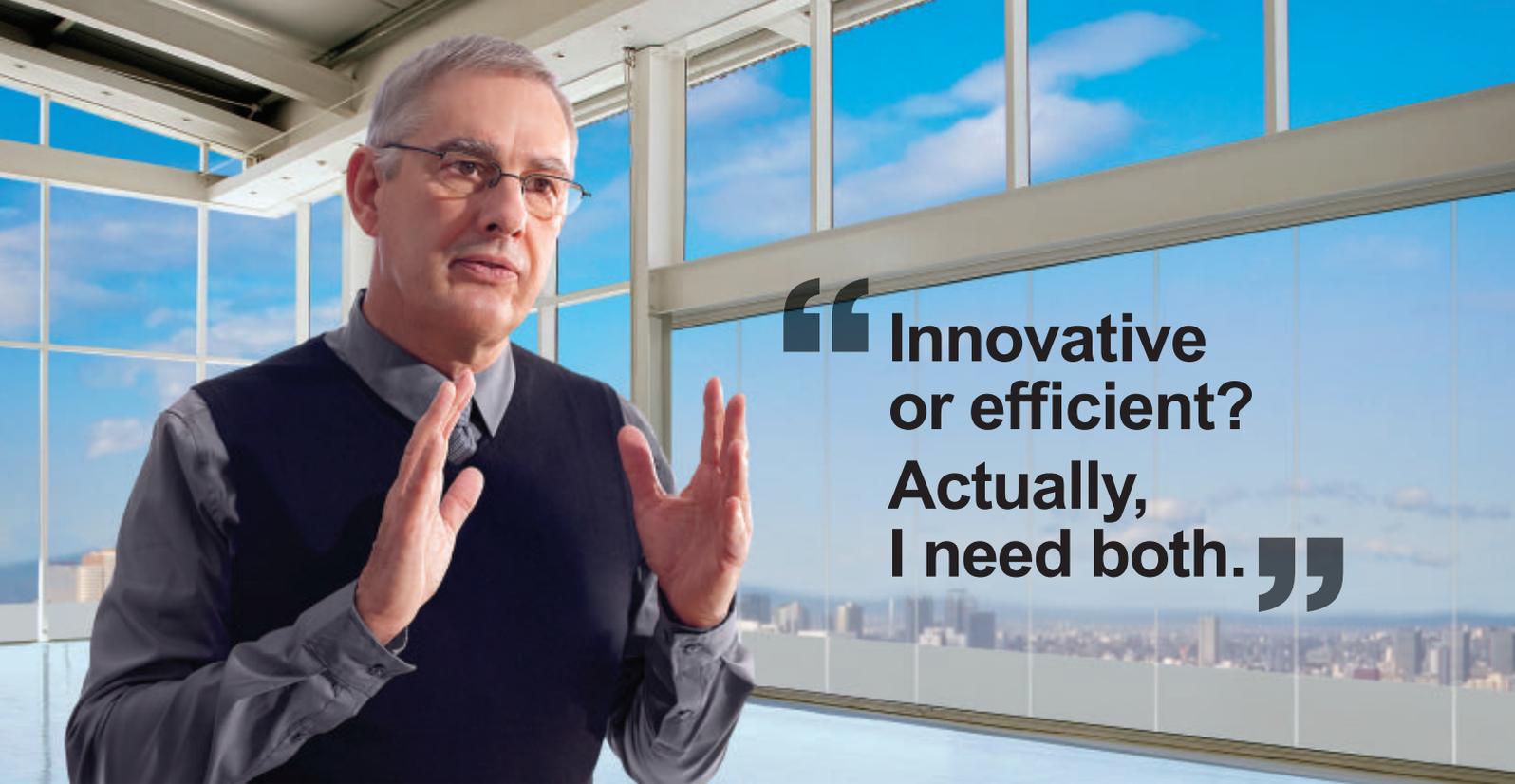
Agilent's outsized growth rate comes from having been an early entrant in applications such as food testing and in emerging markets, explains Chris Toney, vice president of Agilent's chemical analysis group.

In 2010, the company expanded its Life Sciences & Chemical Analysis Center of Excellence in Bangalore, India. It has been

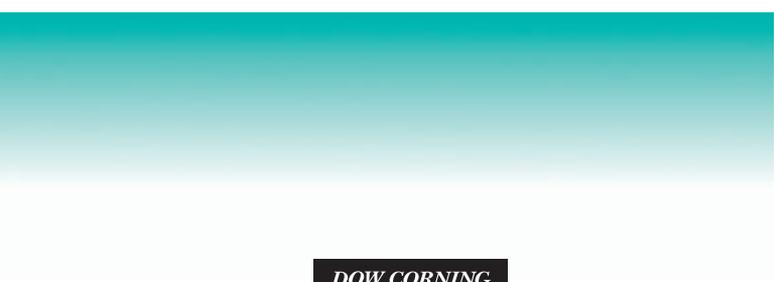
gradually shifting some manufacturing to the Asia-Pacific region, taking advantage of its wide footprint there. "We want to make sure that we are where we can get the most optimized supply chain possible, and that is not always just China," Toney points out.

For example, Agilent is moving production of its liquid chromatography/mass spectrometry (LC/MS) product lines from the U.S. East Coast to Singapore. And the manufacturing of consoles for nuclear magnetic resonance spectrometers will move from a Varian site in California to an Agilent facility in Penang, Malaysia.

As Agilent's largest-ever acquisition, the Varian purchase strengthened its chemical and bioanalytical groups. "We will continue to look at acquisitions that fit well with our strategy as a way of rounding out the portfolio," Toney says. "Our growth strategy is to expand the portfolio and make sure we are going after the fastest-



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growing application and geographic segments.”

Already in 2011, the company has added Fourier transform infrared instruments for lab and field use to its spectroscopy business by buying A2 Technologies. In the life sciences arena, it acquired electrophoresis product firm Lab901 and Biocius Life Sciences, a developer of high-throughput MS technology for drug screening.

Meanwhile, Life Technologies completed the sale of its half of AB Sciex, an MS business, to Danaher in 2010 and also acquired Ion Torrent. Within three months of the acquisition, Life Technologies launched Ion Torrent’s first semiconductor-based sequencing system, called the Ion Personal Genome Machine. It is already offering a faster version of the semiconductor chip that is the replaceable core of the Ion PGM.

“What we really liked about the Ion Torrent technology is that it marries biology and chemistry with years of development and billions in investment in the semiconductor industry,” explains Life Technologies President Mark P. Stevenson. “We see continued demand in both basic research and in molecular medicine and diagnostics for simpler and lower-cost sequencing.”

THE MARKET for affordable DNA sequencers—the Ion PGM costs about \$50,000—is growing about 35% per year, Stevenson says. “The price of sequencing a genome is approaching \$1,000, and by next year I expect we will break that mark. That then opens up a wide range of applications in molecular medicine, human health and safety, and forensic DNA analysis.”

Operating as an entrepreneurial entity within Life Technologies, Ion Torrent added to its new parent’s instrument business. Most of Life Technologies’ instrument-related business is consumables, which

sell well even during down times and contributed to the company’s strong growth in 2009.

“We like business models where we have consumables associated with the instruments,” Stevenson says. Although the MS business was a successful joint venture for many years, it didn’t fit with this model. “It

made sense to divest it to Danaher, which has put the two halves of the joint venture together and added high-performance liquid chromatography, which was the right thing to do,” he explains.

ACQUISITIONS have enabled Danaher to move up quickly through the instrumentation ranks. In addition to buying both halves of AB Sciex, last year it acquired MDS Analytical Technologies, which had been number 22 in C&EN’s ranking, and Eksigent Technologies’ chromatography business. Number nine in 2009, Danaher jumped to fourth place in 2010 with \$2.3 billion in lab instrument sales. It also bought the electronics equipment firm Keithley Instruments and Genetix, a maker of tools for cell analysis.

Despite more than doubling its instrumentation sales in just one year, Danaher isn’t finished. In February, the company announced that it would buy number 13 Beckman Coulter for \$6.8 billion. Beckman sells in vitro diagnostics, lab automation systems, and consumables. Adding that company’s nearly \$700 million in equipment sales will move Danaher up further in next year’s ranking.

Danaher has a chance to reach the top spot, although the competition is getting tight. Among those putting on the pressure, Thermo announced plans in late 2010 to purchase Dionex for \$2.1 billion. The addition will make Thermo a big player in the chromatography area, where it will compete with Shimadzu and Waters at numbers

five and six, respectively. It will also expand Thermo’s reach in the Asia-Pacific region and in environmental and food-testing markets.

Ranked 20th, with 2010 sales of \$447 million, Dionex will increase Thermo’s instrument sales by about 20%. At the same time, however, Thermo is selling its Athena

CONSOLIDATION

Recent instrumentation acquisitions will reshape competitors

ACQUIRER	TARGET	DEAL VALUE (\$ MILLIONS)
2011		
Agilent Technologies	A2 Technologies	na
Agilent Technologies	Biocius Life Sciences	na
Agilent Technologies	Lab901	na
Bruker	Michrom Bioresources	na
Bruker	Protect-US	na
Bruker	Sigma ElectroOptics	na
Danaher	Beckman Coulter	\$6,800
PerkinElmer	Chemagen Biopolymer-Technologie	na
Thermo Fisher	Dionex	2,100
2010		
Agilent Technologies	Varian	1,500
Bruker	Veeco’s AFM and optical industrial metrology	229
Bruker	Three Varian product lines	38
Danaher	MDS Analytical Technologies	650
Danaher	Life Technologies’ half of AB Sciex	450
Danaher	Keithley Instruments	300
Danaher	Genetix	82
Danaher	Eksigent Technologies’ chromatography unit	na
Illumina	Helixis	105
ITT	Nova Analytics	390
ITT	O.I. Corp.	29
Life Technologies	Ion Torrent	725
PerkinElmer	Danaher’s half of MS joint venture	na
PerkinElmer	VisEn Medical	na
Qiagen	ESE GmbH	19
Thermo Fisher	Ahura Scientific	145
Thermo Fisher	Finnzymes	na
Thermo Fisher	Lomb Scientific	na
Thermo Fisher	NovaWave Technologies	na

na = not available.

“Growth last year could be largely attributed to government stimulus funding, most notably in Japan and the U.S. This had a major effect, particularly in the academic end-use markets.”

Diagnostics and Lancaster Laboratories businesses. In 2010, the contract lab services businesses had about \$225 million in combined sales.

PerkinElmer and Bruker also made acquisitions during 2010 and are at it again this year. Bruker took advantage of an antitrust requirement that Agilent sell some overlapping businesses to pick up three Varian product lines. The company has long focused on academic markets and high-end research instruments used in the life sciences; the acquisition increased Bruker's exposure to applied and industrial markets.

Bruker then bought Veeco's atomic force microscopy (AFM) and optical industrial metrology instruments business. The addition further increased the company's exposure to industrial customers and to Asia-Pacific markets. After declining during the recession, sales and profits at the Veeco businesses have rebounded, and they are forecast to post \$130 million in sales this year, or about one-third more than in 2009.

"ORGANIC GROWTH is an absolutely key element that is not going to be replaced by growing through acquisitions," says Thorsten Thiel, Bruker's director of marketing communications. "Bruker keeps a very focused strategy on acquiring only technologies and products that really fit our existing portfolio." For example, it acquired the IR gas technology firm Sigma ElectroOptics to expand its detection business and is buying Michrom Bioresources to gain LC instruments to interface with its mass spectrometers.

Bruker's diversification strategy seems to be paying off. With its foray into new markets, the company's total sales rose 18% to \$1.3 billion last year, and its instrument sales moved it into seventh position, just ahead of PerkinElmer. Even without the acquisitions, sales would have been up about 12%. Bruker predicts that it will reach total sales of about \$1.6 billion in 2011, and the firm is targeting sales of more than \$2 billion by 2014.

PerkinElmer has also been active, buying out Danaher's interest in an inductively coupled plasma MS joint venture and acquiring VisEn Medical, which makes molecular imaging systems and reagents used in preclinical drug research. Moreover, it is buying two software firms and Chemagen Biopolymer-Technologie, a maker of systems for automated nucleic acid isolation.

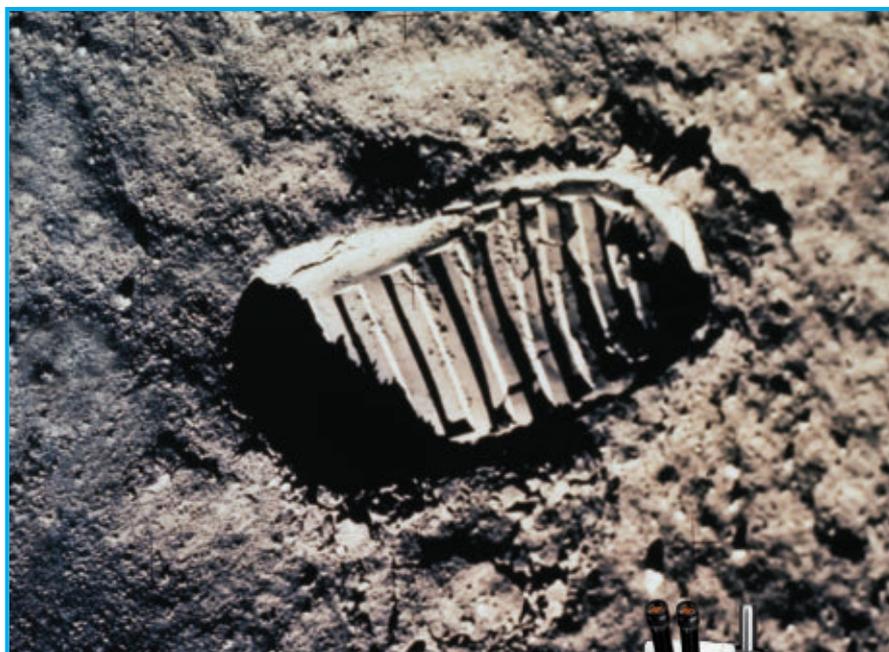
At the same time, PerkinElmer has sold its illumination and detection solutions

business to further focus on human and environmental health. The divested business was expected to generate revenues of about \$300 million in 2010. The company has forecast organic revenue growth in the mid-single-digit range for 2011.

"The majority of growth will manifest itself out of the emerging regions of the world," Tenney says about the industry

overall. In addition to experiencing greater financial capabilities, higher levels of investment, and population growth, "these regions are becoming much more buoyant in terms of adopting regulations that ultimately drive that level of demand," Tenney adds.

PerkinElmer's strategy for growth includes internal product development, regional expansion, and broader software



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and services offerings, Tenney explains. “Acquisitions can play a part in enabling us to move faster and are a way to fulfill the strategy in a shorter time frame.”

In 2010, the top five companies accounted for nearly 48% of revenues among the 25 firms in C&EN’s survey, up from about 45% in 2009. Still, the median company size leaves significant room for

continued consolidation, Morgan Stanley’s Urist has told clients. In addition, he believes that “concentrated end markets and a shared customer base make for a ripe M&A environment.”

Agilent’s Toney agrees that the competitive landscape is changing in analytical instrumentation. “What will emerge are a smaller number of much stronger players



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END MARKET	MARKET SIZE ^a (\$ BILLIONS)	ANNUAL GROWTH RATE
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Pharmaceuticals & biotechnology	9	5
Environmental & forensics	6	5
Industrial (computing & semiconductors)	5	4
Communications	4	5
Aerospace & defense	3	4
Chemicals & energy	2	5
Food	2	8
TOTAL MARKET^a	\$41	6%

^a For the 12 months ending Jan. 31, 2011.
SOURCE: Agilent Technologies estimates

in what has been a highly fragmented market,” he says. “In my view, it may be tougher for some of the smaller, second-tier competitors to have the global presence that is going to be necessary to compete.”

Stevenson sees a similar trend. “The mid-sized players get squeezed out as you get to a critical mass and scale,” he says. Life Technologies, for example, has thousands of field sales, service, and customer support employees that give it a broad geographic presence. It also can invest heavily in R&D and in its technology infrastructure.

Even as the big companies get bigger, Stevenson sees opportunities for small, innovative companies and start-ups. These companies have a chance to thrive and succeed, he believes, by developing new technologies and by being acquired by the larger firms. The challenge for large firms is to keep this innovation alive, he suggests.

CONSOLIDATION can affect customers as well. “There is always the question, ‘Are there too many competitors and too many choices?’” PerkinElmer’s Tenney says about what drives consolidation. Acquisitions will trim the number of suppliers, he acknowledges, but customers benefit if companies can then offer broader ranges of solutions.

“By the same respect, what can happen as companies keep getting bigger and bigger is that ultimately their ability to become more intimate with customers ac-

tually goes down, and understanding their needs and translating those into strategy becomes a slower process,” Tenney points out. Although PerkinElmer may invest to round out its instrument portfolio, he considers the company “uniquely positioned because of our size and the speed at which we can operate.”

Bruker’s Thiel says he hasn’t seen consolidation create disadvantages for customers. “Consolidation has not yet reached a critical level of not any longer having choices in more or less all fields of technologies and applications,” he says. Instead, “the companies probably can become more efficient and leverage certain aspects in their operating business.”

BENEATH THE TOP TIER being created by consolidation are a number of companies with instrument sales under \$1 billion. Among them are several Japanese firms, many of which struggled in 2010. Although Shimadzu had a strong year and Nikon reported higher sales, others fared less well. Sales were flat at Horiba and actually declined at Olympus and Hitachi High-Technologies. According to Hitachi, 2010 was a year of strenuous effort to find its way out of the financial crisis, during which it went into the red for the first time in its 10-year history.

JEOL had a good year in 2010, increasing sales by 14%. Recently, however, the company decided to spin off its magnetic resonance instrumentation business into a joint venture, to be called JEOL Resonance, with the Innovation Network Corporation of Japan. JEOL’s remaining scientific instrument division will consist of electron microscopes and other surface analysis equipment.

Another instrumentation business appears to be in the making. ITT Analytics, owned by the industrial conglomerate ITT Corp., is a provider of field, portable, lab, and online analytical instrumentation. It was formed in 2010 after ITT acquired Nova Analytics and later added O.I. Corp. ITT says it sees “very compelling growth characteristics in the analytical instrumentation market” and views its new businesses as a “new growth platform for the corporation.”

Bullishness by smaller players likely means more shifts among the top 25 firms this year. With three of the traditional acquirers—Thermo, Agilent, and Life Technologies—having made large acquisitions in the past two years, “the prospects for nontraditional players will be important to driving M&A in 2011,” Urist predicts. ■



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JAPANESE RESTARTS PROCEED HALTINGLY

Japanese chemical producers report some progress in restarting their facilities in Kashima, a major chemical complex north-east of Tokyo that was damaged by the March 11 earthquake and tsunami. JSR says it restarted synthetic rubber production at the site after steam and other utilities came back on-line. But the company notes that it is working with inventoried raw materials and that the situation will not be normal until a major supplier also restarts in late May. Mitsui Chemicals is repairing its petrochemical facilities and hopes to restart in late June. Shin-Etsu Chemical is repairing its polyvinyl chloride plant but says it won't be able to resume normal production until other suppliers at the site also come back on-line. The difficulty of restarting at Kashima was illustrated when Shin-Etsu had to stop production at its partially restarted optical fiber preform plant after a violent aftershock on April 11.—JFT

RHÔNE CAPITAL BUYING EVONIK CARBON BLACK

Seven months after putting its carbon black business up for sale, Evonik Industries has agreed to sell it to the private equity firm Rhône Capital. The deal, for more than \$1.2 billion, is expected to be completed this summer, in advance of an initial public offering (IPO) of Evonik stock. Evonik's main shareholder, the RAG Foundation, recently stated that it plans to carry out the IPO in the next 15 months. With revenues of about \$1.7 billion in 2010, Evonik's carbon black business is the world's third-largest producer of the rubber additive.—MM

RELIANCE PLANS HUGE POLYESTER EXPANSION

Reliance Industries has embarked on a large-scale expansion of its polyester business in India. The company will build a 2.3 million-metric-ton-per-year purified terephthalic acid facility in Dahej, a special economic zone in Gujarat. Also in Dahej, it will build a 540,000-metric-ton polyethylene terephthalate plant and a 290,000-metric-ton polyester staple fiber plant. In nearby Silvassa, Reliance will build polyester filament yarn and textur-

DOW PLANS ETHYLENE BOOST

The chemical industry's rush to tap into U.S. shale resources continued last week as Dow Chemical announced a series of investments to expand olefins production, and Brazil's Braskem disclosed it is considering building ethylene and polyethylene plants in the U.S. Dow plans to build a new "world-scale" ethylene cracker on the U.S. Gulf Coast by the end of 2017. It will start up an "on-purpose" propylene plant at its Freeport, Texas, complex in 2015. In addition, the company says it is exploring construction of a propane dehydrogenation plant, using its own technology, by 2018. Dow is pursuing near-term investments as well. The company will restart a cracker that it idled in 2009 in Hahnville, La., by the end of next year. Improvement projects in Plaquemine, La., and Freeport will allow crackers at those sites to process more ethane by 2014 and 2016, respectively. Altogether, Dow expects to add 2.3 million metric tons of ethylene and 900,000 metric tons of propylene capacity. To secure feedstock supplies, Dow is considering building a gas fractionator with a joint-venture partner. It has signed a memorandum of understanding with gas supplier Range Resources for ethane from the Marcellus region in Pennsylvania. Additionally, it has inked ethane and propane supply agreements with gas suppliers from the Eagle Ford shale gas region in eastern Texas.—AHT

ized yarn plants. The company isn't providing cost figures or completion dates.—JFT

DOW, U.S. AGENCIES DEVELOP COOL ROOFS

In a project funded by the Department of Energy, Dow Chemical is working with Oak Ridge National Laboratory, which itself will team up with Lawrence Berkeley National Laboratory, to improve elastomeric roof coatings. In particular, the partners want the coatings to resist the pickup of dirt and the growth of microorganisms to improve the white roofs' ability to reflect solar rays. DOE estimates the improved coatings

could reduce air-conditioning costs for commercial buildings by up to 25%.—AHT

RHODIA ANALGESICS ARE SOLD TO NOVACAP

Rhodia is selling its business in the bulk analgesics aspirin and acetaminophen to Novacap, a French firm that was created in 2003 out of several former Rhodia businesses. The deal, which also includes the intermediates salicylic acid and methyl salicylate, involves plants in France, China, Thailand, and Brazil that collectively employ about 390 people. Rhodia is in the process of being acquired by Solvay in a \$4.8 billion deal.—MM

CRYSTALLICS FORMS VIA AVANTIUM BUYOUT

Avantium's solid-state research and drug preformulation business will become a new company, called Crystallics, following a management buyout. Operating as a contract research organization, Crystallics will specialize in identifying physical forms of compounds and in crystallization process development. Avantium will continue its efforts in high-throughput R&D. It also develops green chemical building blocks.—AMT



Dow already offers elastomeric roof coatings.

BAXTER TO BUY PRISM, GETTING HEART DRUG

Baxter International has agreed to acquire Prism Pharmaceuticals, a privately held drug firm that recently received FDA approval for the antiarrhythmic agent Nexterone. Baxter will pay \$170 million at closing and up to \$168 million in sales-based milestones. Sold as a ready-to-use premixed intravenous bag, Nexterone requires no admixing, Baxter says, thus eliminating the risk of medication errors as a result of compounding. Prism had previously selected Baxter as its contract manufacturer.—RM

BAYER TO MODERNIZE ITS U.S. HEADQUARTERS

Bayer will spend \$17 million to renovate the two main buildings at its U.S. headquarters complex in Pittsburgh by June 2013. The updated buildings will feature Bayer materials such as polyurethane gel in seating and polycarbonate in workstations and light fixtures. The

Bayer's redesigned building will feature company-made materials.

materials such as polyurethane gel in seating and polycarbonate in workstations and light fixtures. The



ARTIST RENDERING/BAYER

buildings will also sport a line of energy-efficient windows made with a unique Bayer polyurethane resin.—MM

MOMENTIVE TO SELL RESINS BUSINESSES

Momentive Specialty Chemicals has signed a definitive agreement to sell its North American composites and coatings resins business to Investindustrial, a European private equity firm. Included in the sale are plants in Carpentersville, Ill.; Ennis, Texas; Forest Park, Ga.; and Lynwood, Calif. The sites collectively employ 225 people and generated sales of \$230 million in 2010. Investindustrial, with \$3 billion in assets, also owns Polynt, an Italian chemical intermediates and resins maker that was once part of Lonza. Polynt had \$850 million in sales last year.—MSR

IPSEN LICENSES PROSTATE CANCER DRUG

Paris-based Ipsen will pay \$35 million up front for the right to codevelop Active Biotech's prostate cancer compound tasquinimod outside of the Americas and Japan. Active Biotech could score up to \$285 million in milestone payments as the drug candidate progresses toward the market. Tasquinimod is in a Phase III trial involving men with metastatic castrate-resistant prostate cancer. Ipsen says the compound will complement its oncology portfolio.—LJ

SANOFI AND STANFORD ENTER RESEARCH PACT

Sanofi-Aventis and Stanford University will collaborate through the university's Bio-X program, which supports interdisciplinary, early-phase research projects. Financial terms were not disclosed, but Bio-X traditionally provides seed funding in the form of two-year grants of \$150,000. Sanofi will fund up to five programs per year over the lifetime of the pact. The French drug firm may also host Stanford postdoctoral fellows, and Sanofi scientists might work in the university's labs. Since the beginning of the year, Sanofi has signed a diabetes research pact with Columbia University and sealed two R&D agreements with the University of California, San Francisco.—LJ

MERCK MAKES CHANGES AT RIVERSIDE PLANT

Merck & Co. has told employees at its facility in Riverside, Pa., that it will cut back operations by the end of 2013. After being sold to PWRT Services in 2008, the plant became known as Cherokee Pharmaceuticals. Then, last summer, it was sold back to Merck after PWRT found the contract manufacturing business too challenging. Merck plans for the site to focus on producing the antibiotic ingredients imipenem, cilastatin, and ertapenem. Other product manufacturing and a third-party fermentation business will be outsourced or sold. It is not yet known to what extent jobs will be cut.—AMT

BUSINESS ROUNDUP

DORF KETAL Chemicals has acquired intellectual property from Johnson Matthey to produce Vertec brand polyester catalysts and Snapcure polyurethane catalysts and cure promoters. The company plans to produce the catalysts at its Mundra plant in western India. In 2010, Dorf Ketal acquired DuPont's specialty catalysts business.

LANXESS is planning a 20,000-metric-ton-per-year expansion of neo-

dymium-polybutadiene (Nd-PBR) and solution styrene-butadiene rubber capacity at its site in Orange, Texas. The \$14 million project, slated for completion by third-quarter 2012, is in addition to a 15,000-metric-ton Nd-PBR expansion it recently completed at the site.

SOLUTIA has been awarded a contract to supply its Therminol VP-1 heat transfer fluid to the Solana solar power project. The \$2 billion project, under construction in Gila Bend, Ariz., is expected to be the world's largest par-

abolic trough solar plant when it opens in 2013.

LOENZA has licensed a probiotic *Lactobacillus* strain developed by Berlin-based Organobalance. The strain depletes the stomach of *Helicobacter pylori*, a common cause of ulcers. Lonza says the strain expands its nutrition portfolio, which includes amino acids such as carnitine and vitamins such as niacin.

WARNER CHILCOTT will eliminate 500 jobs in a restructuring of its European operations.

The move follows the loss of patent protection last year for its osteoporosis drug Actonel. The drug accounted for 70% of the company's Western European revenues.

CIRCASSIA has raised \$98 million in its latest round of financing. The cash influx, the second largest by a private European biotech firm this year, will be used to fund Phase III studies of Circassia's cat and ragweed allergy therapies, as well as Phase II trials of its dust mite and grass allergy T-cell vaccines.

ALNYLAM Pharmaceuticals and Precision Nano-Systems will jointly develop small lipid nanoparticles using microfluidics technology. At approximately 20 nm in size, the LNPs will be designed to improve biodistribution of RNAi drugs.

GENMAB and Seattle Genetics have signed a second antibody-drug conjugate research deal. The companies will collaborate on using Seattle Genetics' ADC technology with HuMax-CD74, an antibody that Genmab is developing as an anticancer agent.



PARTS ON DEMAND

Polymer makers are helping **ADDITIVE MANUFACTURING** scale up into full parts production

ALEXANDER H. TULLO, C&EN NORTHEAST NEWS BUREAU

IMAGINE A CONTAINERSHIP crossing the North Atlantic in the midst of a hurricane. The violent storm damages the mount assembly and housing of the ship's radar antenna.

But instead of limping into port for repairs, the ship's engineer downloads drawings of the radar components he needs and produces the parts on the three-dimensional printer in his workshop. In a couple of hours, he installs them for a flawless repair.

The scenario is futuristic, but the technology the engineer uses—additive manufacturing—has advanced enough to make it nearly plausible today.

Additive manufacturing is a recent term adopted by an industry eager to leap into the production of finished parts, says Terry Wohlers, president of Fort Collins, Colo.-based market research and consulting firm Wohlers Associates. The term encompasses various processes that share a basic concept: building an object, usually out of a polymer, layer by layer from a mechanical drawing stored on a computer. "Some still call it 'rapid prototyping' because prototyping is the biggest application," Wohlers says. Another term often used is 3-D printing. Practitioners also tend to refer to the names of manufacturing processes such as stereolithography and laser sintering.

The technology is making the leap from the designer's studio to the factory floor. In addition to traditional prototypes and

models, workshops are churning out prosthetic limbs, hearing aids, surgical implements, metal casting patterns, designer furniture, and Boeing 787 *Dreamliner* parts. And by offering a wider palette of raw materials, polymer suppliers aim to bring additive manufacturing to even more users.

"It grabs the imagination," says Bill Miller, technical group leader for stereolithography resins at Huntsman Advanced Materials. "It is only natural for people to think that if you can extend it to the manufacturing arena, then you've really got something."

Additive manufacturing, observers say, is a natural choice for small production runs of customized parts. It offers greater freedom of design than other processes. A part can feature a near limitless number of twists, turns, nooks, and crannies. For example, additive manufacturing can produce a plastic model of a house complete with rooms and furniture inside, which would be impossible through traditional injection molding.

And to make a part by injection molding, a fabricator needs to spend thousands of dollars tooling molds and then make thousands of parts to justify the expense. "That makes us very good for medical and dental applications, where every single person is

OFF THE BENCH
The Monarch stool, by Amsterdam-based Freedom of Creation, is made by laser sintering of glass-filled nylon.

different, or in the case of aerospace where the unit count is very small so the cost of tooling is quite expensive," says Stephen Hanna, director of rapid manufacturing materials sales

and marketing for 3D Systems, a leading additive-manufacturing-technology firm.

Additive manufacturing is catching on. Wohlers says the market has been expanding at an average annual rate of 26% for the past 22 years, reaching \$1.1 billion in 2009. About 70% of sales of parts from the machine are models and prototypes. However, direct part production is a growing segment, representing 15% of activity.

Although additive-manufacturing processes are all similar conceptually, they differ in the specifics. Originally developed in the 1980s, stereolithography is the oldest. In this process an ultraviolet laser traces the cross section of a part in a vat of a UV-light-curable resin. After a layer is drawn, the platform on which the part rests is lowered by a fraction of a millimeter, and the laser draws the next layer.

THE PROCESS can take hours or days, depending on how thick the layers are and how large the part is. When the part emerges from the vat, it goes through finishing steps such as removal of resin residue and additional curing.

Other additive-manufacturing technologies make parts from thermoplastics. In laser sintering, an infrared laser traces the shape in a fine powder of a polymer such as nylon 12. When a layer is completed, the platform drops down, a roller applies another layer of powder, and the laser makes its next sweep across the surface.

Each additive-manufacturing process presents its own challenge to polymer suppliers as the technology scales up to the manufacturing stage. Their main goal is to make resins compatible with the technology and durable enough for real-world applications.

Stereolithography is good for making precise prototypes, but suppliers recognize that additional development is needed to capture more manufacturing applications.

The technology is making the leap from the designer's studio to the factory floor.

The problem is familiar to Huntsman Advanced Polymers and DSM Somos, which helped pioneer the transition from early stereolithography resins based on acrylics to ones based on epoxy blends.

"The drawbacks there were very noticeable," Huntsman's Miller says. "The parts and the vats of liquid were very unstable and the accuracies were low." Huntsman's and DSM's predecessors in stereolithography resin, Ciba and DuPont, respectively introduced epoxies to help solve some of these problems, he says.

One area of emphasis today is making the resins behave more like conventional thermoplastics, which are the standard polymer materials used in engineered parts. "These resins are not going to be exactly like ABS [acrylonitrile-butadiene-styrene] or exactly like polyethylene or polypropylene," Miller admits. "So you are not going to completely mimic them for a final part. But we are coming closer to that."

Laser sintering is also moving past prototypes and into the manufacturing arena. Nylon 12 has become the dominant polymer used in sintering because of its high crystallinity and its proclivity to form round particles only tens of micrometers in diameter, says Sylvia Monsheimer, business director of global market development for additive manufacturing at Evonik Industries, which makes nylon 12 for laser sintering.

The resin's high crystallinity allows sintered parts to have sharp edges and contours. Round resin particles can pack densely and uniformly in the thin additive layers. But finding the right morphology—or polymer shape—is one of the challenges in developing materials for laser sintering.

"You can grind the material," Monsheimer says, "but the result will not be the same because you will achieve only sharp particles," which will stick out of the layers, leading to rough surfaces on the final part.

When the small particles are sintered together, tiny pockets of air get trapped in the finished part. As a result, a laser-sintered part has mechanical properties that are different from those of a part made via injection molding. According to data from Evonik, the laser-sintered parts aren't as dense as injection-molded parts. And the elongation at break, which measures how far a material stretches before it gives way, isn't as high. However, the tensile strength of the laser-sintered part is higher, and the part is somewhat more elastic.

Depending on the application, the advantages of additive manufacturing should more than make up for shortcomings in part properties, argues 3D Systems' Hanna. "We are a free-form technology," he says. "But the trade-off will always be that we have limitations in the ultimate durability of the plastic."

CHEMICAL COMPANIES are well on their way toward developing materials that are suitable for manufacturing. "For prototyping, one material is fine and beautiful for most applications," Monsheimer says. "But if you look into manufacturing applications, then immediately we get higher requirements for the materials."

Evonik is coming up with grades of nylon that are more flame retardant, are more heat resistant, and are glass filled for greater reinforcement. The company also introduced polyether ether ketone (PEEK) for laser sintering. As it does in other applications, PEEK lends high-temperature and chemical resistance as well as flame retardancy.

Rhodia recently launched nylon 6 plastics with melt viscosity tailored for laser sintering. And the company's emulsion process yields particle size and morphology suitable for sintering, says Pierre-Emmanuel Lucas, new business project director for engineering plastics at Rhodia.

Lucas maintains that nylon 12 dominates laser sintering only for historical reasons. When the technology was developed 15 years ago, nylon 12 was available in powder form because of its use in coatings. "The machinery makers tried with what was available at the time," he says.

But nylon 12's relative rarity in the world of engineering polymers puts it at a disadvantage to nylon 6, Lucas argues. "It is very necessary, for this technology to move up the ladder from the prototyping world and into the manufacturing world, to offer the people designing parts the polymer they are familiar with," he says.

Executives don't expect additive manufacturing to take over the world right away, but they do expect the technology to coexist with other processing techniques. "I don't think that the lid is going to blow off this and that everything you have in your household is going to be manufactured this way," Hanna says. "But the number of parts directly manufactured is going to be steadily and progressively increased to the point where it becomes very visible in the near future." ■

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HIGH HOPES FOR CYSTIC FIBROSIS

TWO COMPOUNDS to treat the underlying cause of the disease are nearing commercialization

LISA M. JARVIS, C&EN NORTHEAST NEWS BUREAU

MORE THAN 15 YEARS of research and development is coming to fruition for the cystic fibrosis community: Two drug candidates that treat the underlying genetic defect causing the disease are on the verge of commercialization.

Vertex Pharmaceuticals expects to ask the Food & Drug Administration to approve VX770 later this year, and PTC Therapeutics should have a readout on late-stage trials for its drug Ataluren in early 2012. Although the drugs address just a small portion of the CF population, their success would be important first steps toward treating the underlying disease rather than just its symptoms.

CF is caused by a mutation in the CF transmembrane conductance regulator (CFTR) gene, which carries the instructions for assembling a protein that moves chloride ions from one side of epithelial cell membranes to the other. Some 800 different mutations in the CFTR gene have been documented, each causing a different malfunction. Most commonly, mutations result in a lack of protein at the cell surface to move chloride in and out; in other cases, the protein is abundant but not working properly.

As a consequence of the faulty protein, people with CF can't maintain the right balance of hydration in their lungs, causing the organ to be dotted with dried pockets that become clogged with mucus. It's a breeding ground for bacteria, and people with CF are saddled with a complicated regimen of medications to manage the chronic infections that the microbes cause.

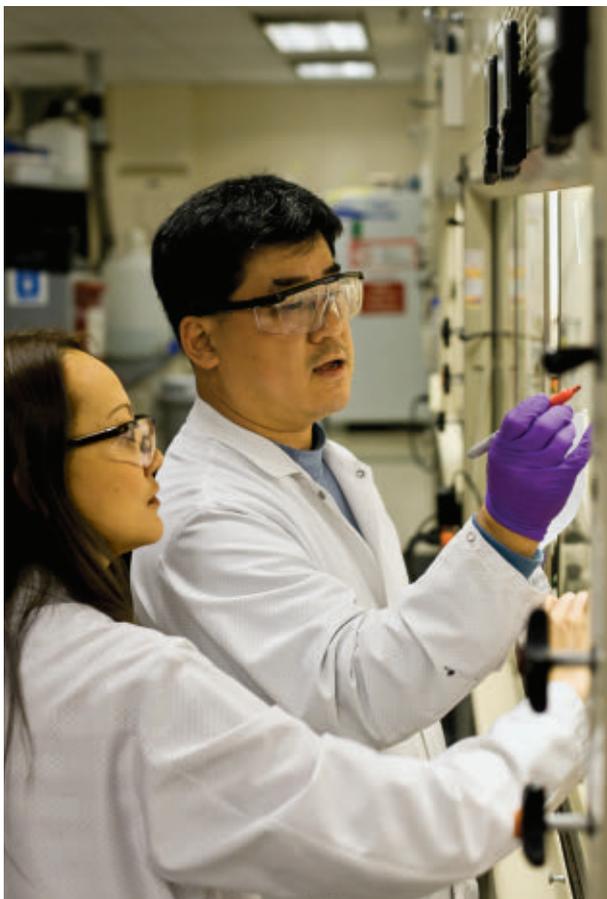
Vertex' VX770 addresses the 4-5% of people with CF whose disease is caused by the G551D mutation, which prevents the right flow of chloride ions in and out

of cells. In February, Vertex unveiled data from a Phase III clinical trial suggesting the compound does indeed correct the genetic defect. At the end of the 48-week trial of 161 people with the G551D mutation, lung function improved by 16.9% in people taking VX770 compared with a placebo.

Surprisingly, younger patients—6 to 11 years old—appeared to respond better to the drug. “We were thinking we might have more difficulty detecting an effect, because their lung function was closer to normal,” says Chris Wright, medical director for the CF program at

ELBOW GREASE
PTC developed Ataluren to correct a specific mutation in CF.

PTC THERAPEUTICS



Vertex. “We think there may be more reversible disease in the younger patients, and this tells us that we should focus on getting treatment to patients as early as we can.”

ALTHOUGH unambiguous improvement in lung function is a key finding, Vertex scientists are also excited about some of the other improvements seen in the trial. The rate of pulmonary exacerbations—flare-ups that occur when the disease worsens, forcing CF patients to take other medications and antibiotics—dropped by 55% compared with a placebo.

By improving lung function and cutting pulmonary exacerbations, the drug could permit people with CF to take fewer medications overall. Vertex is still analyzing the data, and Wright says longer-term studies will be needed to understand whether any of the other drugs in the CF regimen can be eliminated or used less frequently.

Howard Liang, who follows Vertex stock for the investment firm Leerink Swann, says the data for VX770 far exceed expectations from industry watchers and could be “game changing” for people with CF.

Vertex plans to file for approval of VX770 in the U.S. and Europe in the second half of this year.

Although the prospects for the first disease-modifying CF drug are encouraging, VX770 has only been effective in that small portion of the CF population with the G551D mutation.

Vertex has conducted in vitro studies that suggest the drug could also help people whose CF is caused by other mutations that, like G551D, hinder chloride ion flow. “We’re also doing some analyses of a variety of different mutations where we think we may have some positive effects,” Wright says. Vertex has yet to announce plans for clinical studies to test VX770 against those mutations.

Vertex did test VX770 in people whose CF is caused by the $\Delta F508$ mutation, which results in not enough protein sitting on the cell surface, but the compound failed to improve lung function. Thanks to financial support from the Cystic Fibrosis Foundation, the company is pursuing two other compounds, VX809 and VX661, that both work to move more CFTR protein to the cell's surface.

VX809 is already in Phase II trials. And earlier this month, the Cystic Fibrosis Foundation agreed to give Vertex up to \$75 million over the next five years to support the development of VX661, which is expected to start Phase II trials by the end of this year. The compounds act by similar mechanisms to increase CFTR on the cell surface, and Vertex “hopes to make a decision between them” as data become available, Wright says.

Ultimately, the idea is to use VX809 or VX661 in combination with VX770 to maximize effectiveness in people with the $\Delta F508$ mutation. Leerink’s Liang thinks the data validating the mechanism of action for VX770 mean a dual-therapy approach could work. He believes Vertex’ CF franchise could eventually be worth \$500 million in annual sales.

A SECOND FIRM’S DRUG to address a subset of the CF population is also nearing commercialization. PTC Therapeutics’ Ataluren is in a Phase III trial that is expected to be completed by the end of this year. Results should be unveiled in early 2012.

Ataluren addresses the roughly 10% of CF patients whose disease is caused by a “nonsense” mutation that prevents the full CFTR from being made. In normal cells, a ribosome attaches to the “start” site of messenger RNA and reads through the instructions for constructing the CFTR protein; with the mutation, the ribosome falls off early, rendering the protein inactive.

Ataluren enables the ribosome to continue reading through the protein recipe. In Phase II trials, PTC scraped cells from inside patients’ noses to test for the presence of the full protein and also to see whether it was actively moving chloride ions from one side of the cell to the other. The company showed that the full protein was being made, “which wasn’t seen in patients without the drug,” says Stuart W. Peltz, PTC’s chief executive officer.

The trials also demonstrated improvement in pulmonary function and a reduction in coughing in CF patients taking Ataluren. The Phase III study is testing the impact of the drug on people who have the nonsense mutation, who are six years of age or older, and who have some level of deterioration in lung function.

Peltz suspects few young patients are enrolled in the trial because of their better lung function. Yet in the long run, he says, children will ideally get the most benefit out of early intervention with the drug.

“What you ultimately want is to have a kid who may have CF by genotype, but because of being on Ataluren never suffers from the physical characteristics that occur as a consequence of having CF,” he says.

The success of the Vertex and PTC compounds shows that the genetic defect that causes the disease can be fixed. And although the drugs work only in a subset of

patients, researchers are encouraged by the progress in treating specific CF genotypes.

The field is on the cusp of “a new era where you have this genetics-based medicine that will go after the underlying cause of the disease,” Peltz says. “Now it’s a matter of finding other molecules for other mutations to help treat those patient populations.” ■



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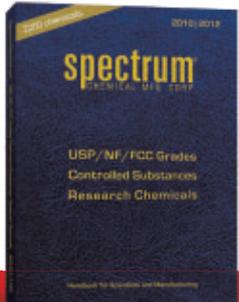
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PATRICK GRUBER

Gevo CEO shares lessons learned in the early days of making **RENEWABLE MATERIALS**

MELODY M. BOMGARDNER, C&EN NORTHEAST NEWS BUREAU

A 1970 DODGE CHALLENGER drove Patrick R. Gruber toward a career path that, back in those days, didn't even exist. As a high school student, Gruber was unable to afford fuel for the gas-guzzler, and he decided then it would be a good idea to replace petroleum with something better.

Since that time, Gruber, 50, has pursued the dream of replacing petroleum with unyielding intensity. Today, he is the chief executive officer of Gevo, a company that plans to ferment sugar into isobutyl alcohol for making renewable chemicals and fuels. The firm was backed in its early stages by venture capital wizard Vinod Khosla. Last month, it raised more than \$123 million in an initial public offering of stock.

Well before he became a CEO, Gruber realized he had the science chops needed to help high school auto enthusiasts. After earning degrees in chemistry and biology from the University of St. Thomas, he moved on to the University of Minnesota for a Ph.D. in biological chemistry. And for good measure, he got an M.B.A. from the same school.

"I wanted to work at the interface," Gruber tells C&EN, explaining his interest in both chemistry and biology. "That was when genetic engineering was really new science and a hot topic."

It turned out to be just the right time to pursue what Gruber had in mind, which he describes by asking, "Wouldn't it be cool if we could make chemicals from renewable resources and get rid of oil?" With a Ph.D. in hand, Gruber went on to work at agribusiness heavyweight Cargill.

He stayed there for 20 years. "At Cargill, I worked on half a dozen projects," Gruber says. "The biggest was plastics from corn—polylactic acid. I was very lucky that I spent my whole professional career working on what I wanted to do."

While at Cargill, Gruber gained a bit of notoriety by making the first batch of polylactic acid (PLA) on his kitchen stove with the help of his wife.

"I didn't have a lab at the time; our Cargill lab was being worked on," he recalls. "So we made some prototypes at home. We made paper coated with plastic, other plastic coatings, and films. We packaged candy with polymer made from corn." Gruber then showed his colleagues at Cargill. "It blew them away. Up until then I thought, 'These guys don't get it. I've got to show them.'"

The Cargill PLA project turned into a business called NatureWorks. In 2003, NatureWorks began producing PLA as a replacement for plastics such as polystyrene and polyethylene terephthalate (PET) in packaging and food service

applications. It was a tough sell, Gruber acknowledges. "To a consumer, a cup is a cup is a plastic cup." But to industrial customers, PLA represented additional costs. Tests had to be conducted. Supply chains had to be redirected. Molding machines had to be changed.

"Lesson learned: Don't do anything new," Gruber concluded.

He has taken this lesson with him to Gevo. The company plans to sell biobased isobutyl alcohol, a four-carbon alcohol, as a drop-in replacement for petrochemically derived isobutyl alcohol. And as a fuel component, isobutyl alcohol can be blended directly with gasoline with fewer complications than ethanol.

"Our game is really all about cleaner, greener, cost competitive or cheaper; to make the exact same molecules that the petrochemical industry knows how to use—and use reliably. From that we can make a business," Gruber says.

The other lesson he took away from his time at NatureWorks was about money. Building a facility to scale up PLA manufacturing cost \$300 million. For a young enterprise, that level of capital investment can be a handicap when it has to compete against established firms. "It was brutal, expensive, and hard," Gruber says. "I'm not doing that again."

INSTEAD, GEVO has told investors that it will retrofit existing ethanol plants to make isobutyl alcohol at a cost of as little as \$50 million per facility. In September 2010, the company acquired a 22 million-gal-per-year ethanol plant in Luverne, Minn. Gruber expects to have it producing isobutyl alcohol by early 2012.

Although developing PLA was arduous, Gruber makes the case that Gevo exists because of hard-won experience at Cargill. Gevo staffers such as David Glassner, executive vice president of technology, and Christopher Ryan, executive vice president of business development, are former NatureWorks scientists who are now developing renewable isobutyl alcohol with knowledge gained at the interface of chemistry, biology, and agriculture.

For example, Gruber says, his team developed proprietary technology to separate isobutyl alcohol from water after the fermentation step. It was a hurdle that experts in the petrochemical industry said would be too high.

But biologists can get it wrong, too, Gruber points out. "The products we have from chemistry are superb. Polypropylene and PET are superb. Synthetic rubber is very good. We should make them better by making them from renewables and at the same cost."

He adds, "With chemistry, the steps are already optimized; they've done it for 30 years. We believe in the best of both worlds." ■



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ARPA-E TO FUND NEW CLEAN ENERGY PROJECTS

The Advanced Research Projects Agency-Energy (ARPA-E) will spend up to \$130 million to develop five new program areas for clean energy technologies in the agency's fourth round of awards. "In addition to creating new jobs, breakthroughs in clean energy technologies can reduce our country's dependence on foreign oil, decrease the cost of clean electricity, and build a sustainable infrastructure for future generations of Americans," said Department of Energy Secretary Steven Chu in a statement. The first program, Plants Engineered To Replace Oil (PETRO), aims to optimize the biochemical processes of plants in capturing sunlight and converting it to energy so that biofuels will be more cost-effective than petroleum products. The High Energy Advanced Thermal Storage (HEATS) program will develop improved thermal energy storage technologies. The Rare Earth Alternatives in Critical Technologies (REACT) program will search for alternatives that reduce or eliminate the need for rare-earth materials in electric-vehicle motors and wind generators. The Green Electricity Network Integration (GENI) program will promote software and high-voltage hardware to reliably control the electrical grid. The fifth program, Solar Agile Delivery of Electrical Power Technology (Solar ADEPT), partners with DOE's SunShot Initiative, which aims to reduce the cost of solar technologies. ARPA-E's contribution to this program will be to invest in magnetics, semiconductor switches, and charge storage.—RRM

LLNL DIRECTOR TO RETIRE

George H. Miller has announced his retirement in October as the director of Lawrence Livermore National Laboratory (LLNL). He will also step down as president of Lawrence Livermore National Security (LLNS), which manages LLNL for the Department of Energy's National Nuclear Security Administration. Miller, a physicist who specialized in nuclear weapons, became LLNL's director in 2006 when the laboratory was under the management of the University of California. In 2007, he was appointed LLNS president when the laboratory's management



Miller

GERMAN TOXICOLOGISTS CONCLUDE BPA IS SAFE

Exposure to the estrogenic chemical bisphenol A (BPA), found in polycarbonate plastic containers and the linings of food and beverage cans, "represents no noteworthy risk to the health of the human population, including newborns and babies," an advisory committee of the German Society of Toxicology has concluded. The committee of independent toxicologists comprehensively reviewed the scientific research on BPA and found that the current tolerable daily intake value of 0.05 mg/kg body weight/day, set by the European Food Safety Authority (EFSA), "is adequately justified." The committee's findings, which are published in the journal *Critical Reviews in Toxicology* (DOI: 10.3109/10408444.2011.558487), add to the growing body of evidence that suggests current exposure to BPA from food and beverages is safe. According to the analysis, many positive results for health effects have not been confirmed in subsequent studies, rodent data are appropriate for evaluating human risk, and the half-life of BPA in human adults is less than two hours. In the U.S., FDA is currently studying the health impacts of BPA from food packaging and ways to reduce exposure to the chemical.—BEE

contract was awarded to LLNS. Except for serving as an adviser to former secretary of energy James D. Watkins in 1989–90, Miller spent his career at LLNL. As director, Miller guided LLNL through the new management transition, reduced operating costs, and explored ways to improve LLNL's security missions.—RRM

EPA TARGETS EMISSIONS FROM PVC FACILITIES

EPA is proposing new standards that would reduce the amount of toxic air pollution that can be released into the environment during the production of polyvinyl chloride and its copolymers. The standards would give facilities the flexibility to choose the most practical and cost-effective control technology or technique to reduce their emissions, the agency says in a statement. Facilities would also need to monitor emissions at certain points in the PVC production process to ensure that the standards are met. Currently, the U.S. has 17 PVC production facilities, with the majority located in Louisiana and Texas. All existing and any new PVC production facilities would be covered by the new rule. EPA estimates that the proposed standard would reduce emissions of hazardous air pollution from PVC production

facilities nationwide by 1,570 tons annually, including 135 tons of vinyl chloride and 33 tons of hydrogen chloride. EPA says the chemical industry will have to spend about \$16 million initially to comply with the new standards, and then \$20 million per year in operation costs. EPA will accept public comments on the proposed rule for 60 days after it is published in the *Federal Register* which is expected to happen soon.—GH

FDA'S STRATEGIC PLAN EMPHASIZES SCIENCE

In the wake of getting new responsibilities for food and drug safety, FDA has issued a "strategic priorities document" to guide the agency's actions through 2015. "It is clear that FDA's job is ... far more complex than it was even a few years ago," said FDA Commissioner Margaret A. Hamburg in a statement. "Science underlies everything we do. ... We must have the capacity to effectively oversee the translation of breakthrough discoveries in science into innovative, safe, and effective products." FDA lists five priorities in its plan: advance regulatory science and innovation, strengthen the safety and integrity of the global supply chain, strengthen compliance and enforcement activities to support public health, address unmet public health needs of special populations, and advance medical countermeasures and emergency preparedness.—DJH

CONGRESS MULLS FACILITY SECURITY

Committee turf wars complicate effort to renew chemical **ANTITERRORISM** program

GLENN HESS, C&EN WASHINGTON

CHEMICAL INDUSTRY officials are working to rally congressional support for antiterrorism legislation that would extend for several years the Department of Homeland Security's (DHS) authority to regulate security at thousands of chemical facilities across the nation, without imposing additional mandates and costs on U.S. manufacturers.

But before a bill is sent to the White House for the President's signature, supporters will have to coalesce around a single legislative vehicle and find a path forward through the political thickets on Capitol Hill.

Turf battles between committees have continually hindered efforts to pass homeland security legislation since the terrorist attacks in September 2001. Although Congress created homeland security committees in each chamber, it did not give them consolidated jurisdiction over homeland security issues, as recommended in 2004 by the bipartisan 9-11 Commission.

In both the House of Representatives and the Senate, multiple panels have overlapping jurisdiction over the Chemical Facility Anti-Terrorism Standards (CFATS), a temporary program created by DHS in 2007.

Under CFATS, the department requires high-risk chemical plants and other facilities that use or store threshold amounts of certain hazardous chemicals to complete vulnerability assessments, develop site security plans, and implement protective measures. DHS then conducts audits and inspections to ensure compliance.

Congress directed the department to establish a chemical plant security program in October 2006 under an amendment added to the Homeland Security appropriations bill for fiscal 2007. However, the legislation gave DHS only three years to get the program up and running.

Congress was expected to give DHS permanent authority to regulate security at chemical facilities before the temporary program expired in late 2009. But lawmakers have been unable to agree on how to structure the program long-term, and CFATS has been kept alive through the annual appropriations process.

This situation has led to the introduction of several bills in the House and Senate that would continue the security

plan largely as it now exists. The Obama Administration's budget proposal for fiscal 2012 requests that the authorization for the CFATS program be extended to Oct. 4, 2013, effectively a two-year extension. CFATS is currently authorized until Oct. 4, 2011.

"CFATS is by far the most robust, comprehensive, and demanding chemical security regulatory program to date," says Timothy J. Scott, the chief security officer and corporate director of emergency services and security at Dow Chemical, the nation's largest chemical maker.

The regulatory program offers flexibility and minimizes its economic impact "by not dictating the implementation of

specific measures, which allows facilities to take into account other important considerations, such as labor costs, managing energy consumption, and ensuring worker safety when securing their facility," Scott remarks.

The chemical industry has invested more than \$8 billion to enhance both physical and cybersecurity protections at its facilities since 2001, according to the American Chemistry Council, a trade group representing more than 140 major chemical manufacturers, including Dow.

Earlier this month, the House Homeland Security Subcommittee on Cybersecurity, Infrastructure Protection & Security Tech-

nologies advanced a bill (H.R. 901) that would extend DHS's current regulatory authority over chemical facilities through 2018, giving the department seven more years to fully implement the CFATS program.

"Although implementation has been slower than Congress wanted, CFATS is working," Rep. Daniel E. Lungren (R-Calif.), the bill's chief sponsor, remarked on April 14 shortly before the subcommittee voted to send the measure to the full Homeland Security Committee. "It is building a foundation of security in the chemical industry which will protect our citizens and our economy from future terror attacks," he remarked.

Significantly, the bill would codify the authority for the program within the Homeland Security Act—the law Congress passed in 2002 that created DHS. This would likely give the Homeland Security Committee primary oversight and funding responsibility for CFATS and jurisdictional advantage over the House Energy & Commerce Committee. The two panels now jointly oversee the program.

Reps. Tim Murphy (R-Pa.) and Gene Green (D-Texas), both members of the Energy & Commerce Committee, have proposed similar legislation (H.R. 908) that would simply

extend the existing CFATS program for six years through 2017.

Which bill will advance to the House

The Department of Homeland Security (DHS) has reviewed more than **39,000** security questionnaires submitted by potentially high-risk facilities.

More than **7,000** facilities were initially designated as high risk and were required to assess their vulnerabilities.

DHS has determined that **4,744** facilities are high risk and, therefore, covered under CFATS.

More than **4,100** of those facilities have submitted site security plans; DHS is reviewing those submissions.

DHS began inspecting the highest risk facilities in February 2010; approximately **175** inspections have been completed.



SHUTTERSTOCK

floor is ultimately up to party leaders, Lungen notes. But Murphy says the two bills will likely be reconciled. “We’ll work something out in the long run,” he says.

Democrats on the Energy & Commerce Committee have expressed strong support in the past for expanding the CFATS regulatory regime to also cover security at drinking water treatment plants, which use large amounts of chlorine and other toxic chemicals. The Murphy-Green bill would allow the Energy & Commerce Committee to maintain a role in congressional oversight of CFATS and could set the stage for amendments later in the legislative process that would alter security requirements at drinking water facilities.

Democrats have also expressed an interest in extending the CFATS regulations to wastewater treatment plants. That could add another procedural hurdle because the House Transportation & Infrastructure Committee has jurisdiction over those facilities.

Meanwhile, Sen. Susan M. Collins of Maine, ranking Republican on the Senate Homeland Security & Governmental Affairs Committee, has reintroduced a bipartisan bill (S. 473) that the panel unanimously approved last year. The measure would extend the current CFATS program by three years and direct DHS to provide more compliance assistance to the chemical industry. Sens. Mary L. Landrieu (D-La.), Rob Portman (R-Ohio), and Mark L. Pryor (D-Ark.) have signed on as sponsors.

“Simply put, the program works and should be extended,” Collins says. “Chemical facilities are tempting targets for terrorists. DHS has done a good job developing a comprehensive chemical security program.”

Landrieu says the legislation will improve CFATS by promoting collaboration with state and local authorities and providing facility operators with technical assistance, information about best practices, and enhanced opportunities for safety training and exercises. “Extending the program with those added improvements makes sense,” she remarks.

None of the legislative proposals would impose any additional requirements on chemical facilities, such as a mandate

CHEMICAL FACILITY SECURITY PROPOSALS

Current legislation under consideration in Congress would impact the Chemical Facility Anti-Terrorism Standards (CFATS). Here are the highlights of five different measures.

H.R. 901 would extend the CFATS program through 2018 and codify DHS’s authority to regulate security at high-risk chemical facilities within the Homeland Security Act of 2002.

H.R. 908 would reauthorize the current chemical plant security regulations through 2017.

S. 473 would extend CFATS for three years and create a voluntary technical assistance program that would allow DHS to help covered facilities comply with the requirements of the CFATS program.

S. 709 would require the highest risk plants to use safer chemical processes where feasible and cost-effective and would require the remaining high-risk plants to assess safer chemical processes.

S. 711 would expand CFATS’s coverage to 2,400 water treatment plants and 500 port facilities, including 125 petroleum refineries.

for so-called inherently safer technology (IST). A chemical security bill passed by the House in November 2009 (H.R. 2868) would have required high-risk facilities to consider whether they could reduce the consequences of a terrorist attack by using a less toxic chemical or a safer process.

IN ADDITION, facilities that DHS deems to pose the highest risk would have been required to adopt safer technology, provided implementation was feasible and would not merely shift the risk to another location.

The bill failed to become law in the last Congress, but the mandatory IST concept has been revived in legislation (S. 709) introduced by Sen. Frank R. Lautenberg (D-N.J.). The legislation would also eliminate

the current law’s exemption of 500 port facilities, including the majority of U.S. refineries. A separate proposal (S. 711) would give the Environmental Protection Agency authority under CFATS to regulate security at drinking water and wastewater facilities.

Lautenberg sits on the Senate Environment & Public Works Committee, which would have to approve expanding CFATS to cover the nation’s 2,400 water treatment plants because the panel oversees EPA’s regulatory activities under the Safe Drinking Water Act.

“A catastrophic accident or terrorist attack at one of America’s chemical plants or water treatment facilities would have devastating consequences for the surrounding communities,” Lautenberg says. “When companies use dangerous chemicals, it is essential that they also use the safest methods available. This commonsense legislation would ensure a thorough review of risk and help us move toward more secure plants and safer communities.”

Chemical industry officials are urging Congress to approve a long-term extension of CFATS, but they adamantly oppose an IST mandate.

“We’re encouraged by Congress’ swift attention to chemical security so early in the 112th Congress,” says William E. Allmond IV, vice president of government relations at the Society of Chemical Manufacturers & Affiliates (SOCMA), a trade group representing the batch, custom, and specialty chemical industry.

“SOCMA strongly supports extending the current standards without any significant programmatic changes to allow chemical facilities to fully comply,” Allmond says.

But the need for annual reauthorization of the program has created uncertainty for facilities regulated by CFATS, he notes.

“Without the assurance of a long-term authorization of these regulations, companies run a risk of investing in costly activities today that might not satisfy regulatory standards tomorrow,” Allmond asserts.

Andrew K. Skipp, chairman of the National Association of Chemical Distributors (NACD) and president and chief executive officer of chemical distributor Hubbard-Hall, says CFATS has been and will continue to be a major regulatory commitment for the industry.

“While we have been willing to invest the time and resources to comply with this important regulation, I know that Hubbard-Hall along with all of the other members of NACD who have CFATS-cov-

“Companies run a risk of investing in costly activities today that might not satisfy regulatory standards tomorrow.”

ered facilities would appreciate the certainty of a clean, long-term extension of the program,” Skipp says.

Lautenberg’s bills are strongly backed by environmental activists and labor groups, who argue that an IST mandate—along with bringing water treatment and port facilities under the CFATS umbrella—would close dangerous gaps in security.

The two House bills and Sen. Collins’ legislation “are an irresponsible distraction from a long overdue comprehensive security program,” says Rick Hind, legislative director for Greenpeace, an environmental organization. All three proposals “fail to require any disaster prevention at the highest risk chemical plants.”

Safer processes may not be feasible in some circumstances, but they should at least be considered in a security plan, says James S. Frederick, assistant director of health, safety, and environment at United Steelworkers (USW).

“Many safety measures may be possible without expensive redesign or new equipment. Safer fuels or process solvents can be substituted for more dangerous ones. The storage of highly hazardous chemicals can be reduced,” Frederick says.

MERELY EXTENDING the current CFATS regulations would jeopardize the hundreds of thousands of USW members employed at chemical-related facilities and residents who live in surrounding communities, adds USW International President Leo W. Gerard. “We support the more comprehensive bills introduced by Sen. Lautenberg to address the preventable hazards these plants pose,” he remarks.

The Obama Administration also supports expanding the CFATS program to include a requirement for safer technology. Rand Beers, under secretary of the National Protection & Programs Directorate at DHS, told the House Energy & Commerce Subcommittee on Environment & the Economy last month that all high-risk chemical facilities should conduct IST assessments.

In addition, Beers said, the federal government should have the authority to require plants posing the highest risk to adopt safer technology if the measures enhance overall security and are determined to be feasible.

SOCMA’s Allmond, however, says that IST is a process-related engineering concept, and there is no agreed-upon methodology to measure whether one process is inherently safer than another. “The world’s foremost experts in IST and chemical engineering have consistently recommended against regulating inherent safety for security purposes,” he remarks.

M. Sam Mannan, a Texas A&M University chemical engineering professor, testified in February that U.S. facilities could be “put at a competitive disadvantage if required to implement unproven technologies simply to meet a regulator’s position that such technology is more inherently safe.”

He told the House Homeland Security Committee that in some cases, a seemingly clear choice with regard to inherent safety may create some undesired and unintended consequences, such as reducing risk associated with transport of a chemical while increasing the risk of storing that chemical.

For most chemical distribution facilities, Hubbard-Hall’s Skipp contends, an IST assessment would likely produce limited options that would impede normal business operations.

“Particularly in these tough economic times, and in addition to the myriad regulations that already affect us, [an IST requirement] could be the final straw to put some companies out of business, which would result in further job losses,” he says. ■

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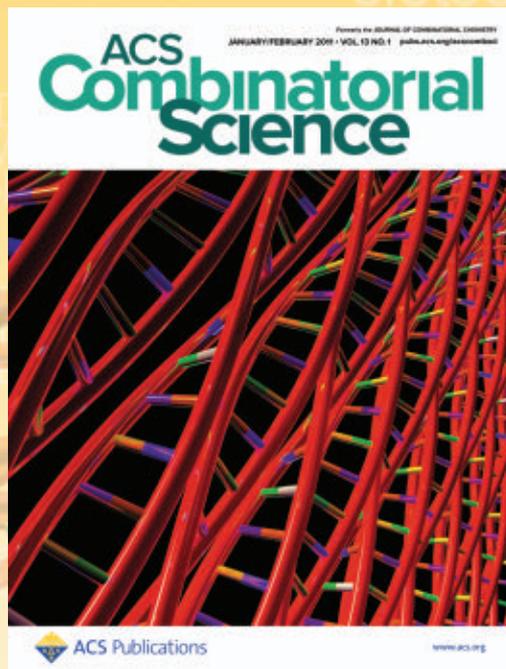
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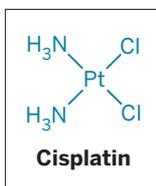


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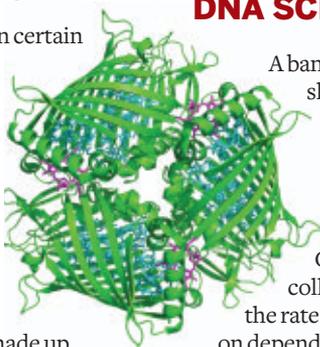
IMPEDING CISPLATIN'S POWER

New findings on cellular interactions of the chemotherapeutic agent cisplatin suggest ways the drug might be redesigned to have better potency and fewer side effects. Cisplatin is an important chemotherapy for severe connective tissue, lung, ovarian, and lymphatic solid tumors. But it has serious adverse side effects, and its tendency to bind cytoplasmic proteins diverts it from its main job—binding and damaging genomic DNA in cancer cell nuclei, killing the cells. Now, researchers led by Pernilla Wittung-Stafshede and Magnus Wolf-Watz of Umeå University, in Sweden, report that cisplatin binds in solution to Atox1, a chaperone protein that helps provide copper to newly biosynthesized metalloproteins, and causes Atox1 to slowly unfold and degrade (*Proc. Natl. Acad. Sci. USA*, DOI: 10.1073/pnas.1012899108). They also show that cancer cells that express higher levels of Atox1 are more resistant to cisplatin. Spending its precious time messing around with Atox1 may keep some administered cisplatin from reaching DNA, suggesting that inhibiting the interaction might be a good way to make the drug safer and more effective.—SB



EXTRA CHLOROPHYLL HELPS BACTERIA PHOTOSYNTHESIZE

A key photosynthesis protein in certain bacteria contains eight bacteriochlorophyll molecules—one more than previously realized (*Biochemistry*, DOI: 10.1021/bi200239k). The additional compound is critical to understanding and modeling exactly how the bacteria turn sunlight into chemical energy. In green sulfur bacteria, the photosynthetic machinery is made up of an antenna complex that acts like a satellite dish to gather energy from sunlight, a reaction center that does electron-transfer chemistry, and the FMO protein (trimer shown) that acts like a wire to connect the two. Energy flows through seven bacteriochlorophyll compounds in FMO through a delocalized, quantum coherence mecha-



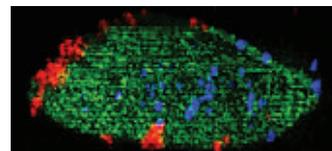
BIOCHEMISTRY

DNA SCRIBES SEEN LIVE

A bank heist is only as fast as the slowest thief, and according to single-molecule studies, genes have a similar limitation. With a fluorescence tracking method, Robert H. Singer at Albert Einstein College of Medicine and colleagues have learned that the rate at which genes are turned on depends on the time it takes for a protein called a transcription factor to hunt down its proper spot on DNA (*Science*, DOI: 10.1126/science.1202142). Molecular biologists want to learn more about the workings of transcription factor proteins, which bind to DNA to regulate gene expression. Singer's team engineered nascent RNAs to bind to a molecule of green fluorescent

IMAGING PLANT IMPRINTS

Indirect desorption electrospray ionization (DESI) mass spectrometry can be used to image the distribution of secondary metabolites in soft plant tissues, such as leaves and petals, Danish scientists report (*Anal. Chem.*, DOI: 10.1021/ac2004967). These small molecules are difficult to image because the waxy outer layer of plants hinders conventional mass spectrometric imaging. Instead of trying to obtain images directly from plant tissue, Christian Janfelt and coworkers at the University of Copenhagen collected mass spectrometric images of various metabolites in plant material imprinted on a porous Teflon surface. In *St. John's wort*, for example, they imaged the distribution of hyperforin and hypericin in the plant's leaves and petals. "The experiment preserves the simplicity of DESI imaging, and the sample preparation is a simple transfer step," says R. Graham Cooks, a chemistry professor at Purdue University and one of the inventors of DESI. "The fact that leaf material is difficult to image because of the waxy overlayer makes this simple method very attractive."—CHA



ANAL. CHEM.

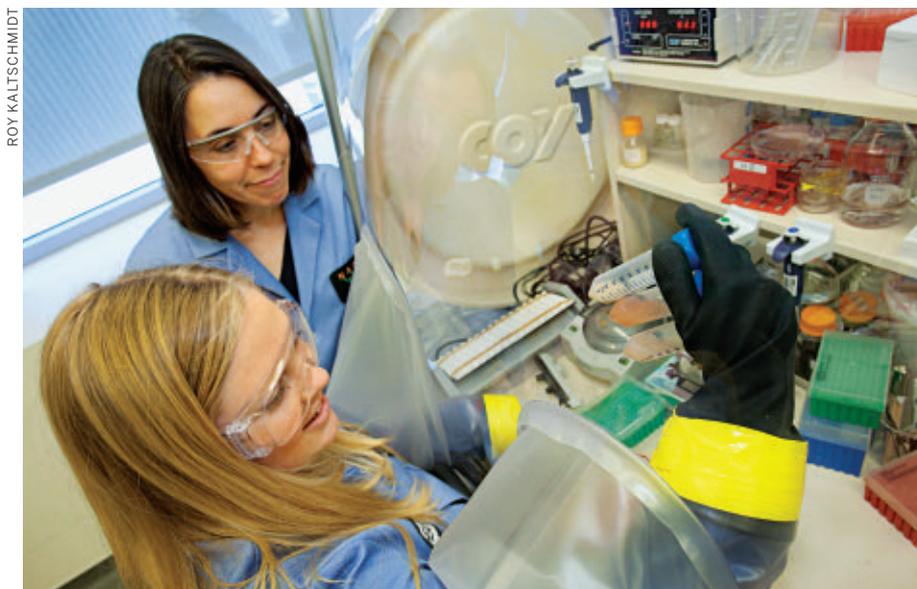
An indirect DESI image from a petal of *St. John's wort* shows hypericin (red), hyperforin (blue), and an unidentified ion (green) that reveals the shape of the petal.

nism, but researchers didn't understand how energy got from the antenna complex into FMO. In new work, Robert E. Blankenship, Michael L. Gross, and colleagues at Washington University in St. Louis used mass spectrometry to demonstrate that a previously unidentified bacteriochlorophyll (shown in pink) likely provides the missing link. The compound probably resides on the FMO surface in an area that would interface with the antenna complex.—JK

protein, which let them follow transcription in single, live yeast cells with a fluorescence microscope. They learned that the time it took a transcription factor called Mbpbp to find its binding site on DNA dictated gene turn-on rate. The authors say their live-cell technique could unravel the roles of many more players in transcription.—CD

PLATINUM-FREE FUEL-CELL CATALYST

The need to use the expensive and rare metal platinum as a catalyst remains a bottleneck for developers of hydrogen fuel cells. But a new group of catalysts composed of cheap and plentiful nonprecious metals may edge the field closer to a reality of inexpensive fuel cells that convert H₂ into electricity with H₂O as a by-product. Piotr Zelenay and Gang Wu at Los Alamos National Laboratory and their colleagues designed a polymer electrolyte fuel cell, the most common variety used in the development of cars, preparing the cell's cathode—which typically requires more platinum than the anode—from syntheses involving polyaniline, iron, and cobalt (*Science*, DOI: 10.1126/science.1200832). The authors say the resulting catalysts performed on par with platinum and also avoided a common problem of producing unwanted hydrogen peroxide.—EKW



ROY KALTSCHMIDT

BUILDING BETTER BACTERIA

Synthetic biologists turn to a **MICROBE NAMED SHEWIE** to ‘wire’ microorganisms for fuel production, energy storage

LAUREN K. WOLF, C&EN WASHINGTON

BIOLOGISTS PLAY with rats and mice, and microbiologists tinker with *Escherichia coli*. Researchers rely on the well-known genetic codes and physiologies of these model organisms to advance scientific knowledge and even make new products.

But there’s a new lab rat on the block. *Shewanella oneidensis*, a gram-negative bacterium capable of “breathing” metals in a way similar to how humans respire oxygen, has become a species popular with environmental microbiologists in recent years, says Kenneth H. Nealson, who discovered the organism in New York’s Oneida Lake, near Syracuse, in 1987.

Shewie, as it is affectionately called by some of the scientists who study it, contains a chain of heme-bearing proteins that allow the microorganism to shuttle electrons from its inside to its outside during anaerobic respiration. In other words, feed it and *S. oneidensis* can directly transfer charge to and reduce external aqueous metals or solid metal oxides.

This inherent capability makes Shewie attractive to scientists developing microbial fuel cells, with biofilms of electrode-reducing bacteria consuming components of wastewater and generating electric-

ity. Others want to use Shewie for soil remediation at sites contaminated with heavy metals or radioactive materials. For instance, researchers have shown that the microorganism can convert soluble uranium (VI) ions into insoluble, isolatable uranium dioxide nanoparticles (C&EN, Aug. 21, 2006, page 44).

But what really makes Shewie a model organism, explains Nealson, a University of Southern California geobiologist who has been studying metal-reducing bacteria for decades, is that it is harmless and has a fully sequenced genome. And although it thrives in an anaerobic environment, it also likes oxygen, making it easy to grow and use in the lab. These qualities have scientists—particularly synthetic biologists—working hard to understand the bacterium’s electron-transfer pathway and taking advantage of its metal-breathing capability to construct microorganisms that are even more useful.

Caroline M. Ajo-Franklin, for one, has her

REWIRING CELLS UC Berkeley graduate student Heather Jensen (bottom) and Ajo-Franklin examine *E. coli* cultures that they engineered to express electron-transfer proteins and reduce metals.

eye on Shewie’s respiratory pathway as a way to “wire” other types of microbes and cells for electronic communication. By enabling intracellular electrons to cross what in most cells are insulating outer membranes, says Ajo-Franklin, a synthetic biologist at Lawrence Berkeley National

Laboratory, scientists could create living biosensors that give an electrical readout when exposed to small molecules. Similarly, researchers could transform light-sensitive organisms into photocatalysts, rigging them to route the electrons they generate into batteries for storage.

AS A FIRST STEP toward making these cell-electrode systems a reality, Ajo-Franklin and her team took a portion of Shewie’s electron-transfer pathway and, via genetic engineering, inserted it into *E. coli* (*Proc. Natl. Acad. Sci. USA*, DOI: 10.1073/pnas.1009645107). This synthetically “tricky” feat, the LBNL scientist says, involved adding three *S. oneidensis* proteins—MtrA, MtrB, and MtrC—to the outer membrane region of *E. coli*.

MtrA is a decaheme protein that accepts electrons from the inner workings of *S. oneidensis* cells. It resides in the space between the two cell membranes characteristic of gram-negative bacteria such as *E. coli* and Shewie. This protein passes along its charged cargo through the pore of MtrB, an integral protein embedded in the outermost of Shewie’s two membranes. MtrB facilitates the transport of the electrons to MtrC, another decaheme protein that sits outside the cell and can move the charge to electrodes or other aqueous species.

After some trials and tribulations, and with help from chemical biologists Yuri Y. Londer and Peter Weigle of New England Biolabs, in Ipswich, Mass., Ajo-Franklin’s team eventually inserted the Mtr pathway into *E. coli*. As a result, the *E. coli* was able to reduce iron oxide nanoparticles in solution. Although the engineered bacterium reduces the particles an order of magnitude more slowly than does native *S. onei-*

Shewie could “open up the landscape for new types of industrial bioreactions.”

denis, “we’ve made *E. coli* that can breathe rust,” Ajo-Franklin emphasizes. The accomplishment provides a “blueprint” for adding the electron-transfer functionality to other cells, she says, and leaves room for optimization.

The next step for Ajo-Franklin is to send the electrons from the engineered *E. coli* to an electrode. Her team is now exploring both physisorption—letting the bacteria attach themselves to the surface—and controlled immobilization to achieve that goal.

For the latter scheme, Ajo-Franklin is collaborating with chemists Matthew B. Francis, Carolyn R. Bertozzi, and Richard A. Mathies of the University of California, Berkeley.

The researchers recently developed a way to bring the cells close to an electrode surface by chemically attaching single-stranded DNA to the outside of mammalian cells via naturally occurring amine groups on their membranes (*Lab Chip*, DOI: 10.1039/b82169oh). Complementary single strands of DNA anchored to an electrode hybridize with the

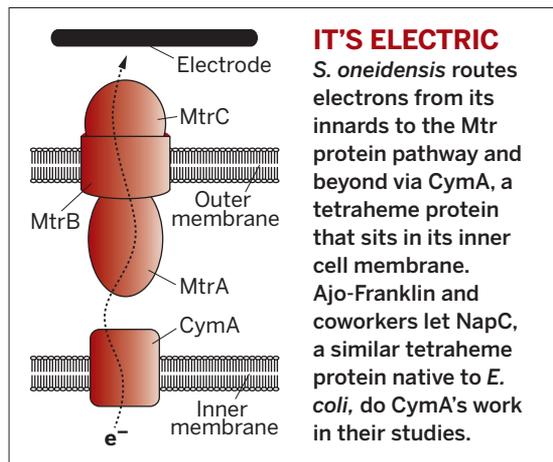
cell-bound strands, bringing the cells close to the surface for electron transfer.

But the amine linker needed for mammalian-cell attachment won’t work for

that this method will more efficiently route electrons to the surface because the DNA linkers should coax the engineered cells to bind to the electrode more tightly and densely than they would otherwise.

Rather than engineer bacteria to be a bit more like Shewie, Jeffrey A. Gralnick is trying to give Shewie some of the beneficial capabilities of other bacteria. “Using a native organism that already does something unique” has advantages, says Gralnick, a microbiologist at the University of Minnesota, Twin Cities, because “you don’t have to teach it the trick that you are really interested in”—in this case, Shewie’s ability to move electrons around.

Gralnick has been studying *S. oneidensis* with the ultimate goal of improving the efficiency of industrial reactions. Current bioconversion processes, in which microbes catalytically convert feedstocks into chemical products or fuels, often create unwanted side products because the cells don’t achieve redox balance, Gralnick says. But with bacteria like Shewie that can transfer electrons from the



gram-negative bacteria because of their double cell membranes, Francis says. So the Berkeley researchers are concocting a new type of chemistry to link the DNA to their engineered *E. coli*. Ajo-Franklin hopes

convert feedstocks into chemical products or fuels, often create unwanted side products because the cells don’t achieve redox balance, Gralnick says. But with bacteria like Shewie that can transfer electrons from the

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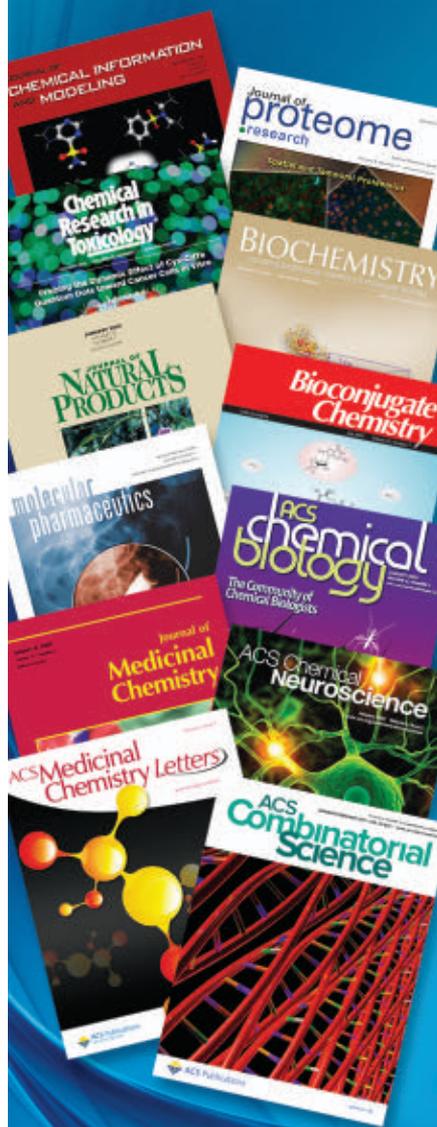
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inside out, excess charge could be removed with an external electrode acting as a sink. “That way, you could stoichiometrically convert your substrate into your product,” he says.

Along with Daniel R. Bond, another microbiologist and a collaborator at Minnesota, Gralnick has recently demonstrated the concept, using electrode-adsorbed *S. oneidensis* to transform glycerol into ethanol (*mBio*, DOI: 10.1128/mBio.00190-10). Through genetic engineering, the researchers added to Shewie proteins and enzymes from other bacteria that would allow *S. oneidensis* to ingest glycerol, shuttle leftover electrons to its native electron-transfer pathway, and eject ethanol.

When the electrode that held the engineered *S. oneidensis* was poised at a voltage to accept electrons, the new-and-improved Shewie sucked in almost 33-mM glycerol and pumped out about 28-mM ethanol—an 85% carbon conversion. The engineered microorganism generated only a small amount of acetate by-product (15%), rather than the multiple by-products *E. coli* might yield from a similar bioconversion.

REACTIONS OF THIS sort with Shewie could “in principle open up the landscape for new types of industrial bioreactions that maybe weren’t considered before because of redox imbalance,” Gralnick says, additionally citing glycerol-to-dihydroxyacetone conversion as an example. And although it’s not yet clear how to scale up this type of reaction for industrial-size fermenters, he says that the team he leads with Bond is working with engineers to figure out how to make it happen.

Despite his interest in applied work, Gralnick advises that researchers not forget the true beauty of engineering Shewie’s pathways and proteins into nonnative organisms: That tinkering can “help find out about how the bacterium actually works,” he says. Many things are still not known about Shewie, Gralnick adds. For instance, “there have been rumblings in the past year or so of X-ray crystal structures” of the Mtr

proteins, he says, but nothing has been published yet. So researchers aren’t sure how the hemes in the electron-transfer pathway are oriented.

In addition, researchers are trying to understand how Shewie routes electrons from MtrC to metal species or electrodes over large distances (greater than 10 nm). Transfer still occurs when direct MtrC-metal contact is obstructed. Some scientists, including Gralnick, think that flavins,

COURTESY OF CAROLINE AJO-FRANKLIN



PROTEIN EXPRESSION When added to *E. coli* (left), the Mtr protein pathway native to *S. oneidensis* causes the bacterial culture to turn pink, indicating the incorporation of heme groups.

which *S. oneidensis* secretes, are an electron shuttle between bacterium and metal in solution (*Proc. Natl. Acad. Sci. USA*, DOI: 10.1073/pnas.0710525105). Others, including Nealson and physicist Mohamed El-Naggar, also at USC, have observed conductive nanowires growing from the outside of Shewie that could function like extendable

arms, reaching out to transfer charge to other materials (*Proc. Natl. Acad. Sci. USA*, DOI: 10.1073/pnas.1004880107).

Ajo-Franklin might be able to answer some of these questions with her work, Gralnick says, because *E. coli* doesn’t inherently secrete flavins and presumably doesn’t grow nanowires. In optimizing electron-transfer efficiency in *E. coli*, she might also discover further details about the Mtr pathway, he adds with excitement. “Being able to show that the components that you’re looking at are not only necessary for a process but are also sufficient to reconstruct it is an important scientific achievement,” Gralnick contends.

Nealson is also confident that some of these unknowns will become clear in the next generation of studies with Shewie, the “bug” he discovered. “It is absolute fun to watch all the research activity,” he says. Young scientists such as Ajo-Franklin and Gralnick “are so good at what they are doing,” he adds, “I may have to look for another field.” ■

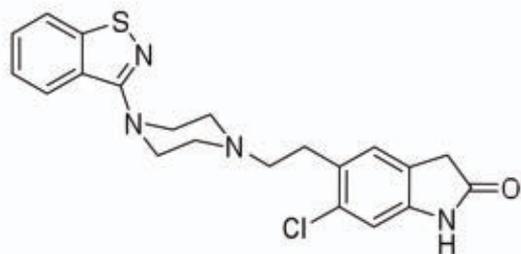
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CHALLENGES TO WATER REUSE

ACS MEETING NEWS: Projects to recycle wastewater face not only scientific but also economic and social hurdles

MICHAEL TORRICE, C&EN WEST COAST NEWS BUREAU

A FADING, decades-old photo illustrates California's ongoing water woes. It shows a man standing next to a telephone pole in the San Joaquin Valley, the agricultural backbone of the state. He's marked the pole with signs at different heights, each sign indicating where ground level sat in a particular year. The one at the very bottom reads "1977," and one about 30 feet up the pole reads "1925."

What made the ground drop almost 30 feet in five decades? The culprit is groundwater overdraft, when communities pump more water from a groundwater basin than rainfall and other sources can replenish. Farming communities in the San Joaquin Valley pumped so much groundwater that the region's aquifers began to compress and the soil above them collapsed, lowering the ground level.

Although the valley has reined in its groundwater pumping, overdraft is still a problem across the state. The California Department of Water Resources estimates this yearly deficit at as much as 650 billion gal of water. "It's like drawing down your savings account," says Richard G. Luthy, an environmental engineer at Stanford University. "Eventually you're going to get to zero."

But groundwater isn't the only water source at risk. Scientists expect climate

change to bring longer droughts to Southern California and to shrink snowpack in the Sierra Nevada Mountains, a major water source for the state.

To stabilize the state's water supplies, environmental engineers point to recycling wastewater as one possible solution. By purifying wastewater to irrigate crops or replenish groundwater basins, local communities can decrease their dependence on importing water from across the state or depleting local aquifers.

Currently, California recycles about 200 billion gal of water per year, according to the State Water Resources Control Board, and the state plans to reach 325 billion gal by 2020. At last month's American Chemical Society meeting, in sessions within the Division of Environmental Chemistry, Luthy and other environmental engineers discussed the economic and social barriers that stand in the way of local water reuse projects, as well as some possible solutions.

ALTHOUGH Luthy acknowledges the need for more scientific research on water reuse, such as developing methods to detect and remove new classes of contaminants from wastewater, he thinks that large engineering projects also face economic and social policy issues that need to be studied. So he stepped outside his lab and decided to look into the successes and failures of local

RECYCLING WASTE In Orange County, Calif., the Groundwater Replenishment System treats 70 million gal of wastewater every day and injects it into the region's groundwater basin.

water agencies to understand what drives or stalls water reuse projects.

Luthy and his graduate student Heather Bischel worked with social scientists to develop an online survey for managers at 134 water agencies

in northern California. The survey included questions about when the agency started its reuse project, what it used the treated water for, and what challenges the agency faced during the planning and development.

Of the 71 water agency managers who responded, about 90% listed a money-related issue as a challenge they faced. These hurdles included capital costs for the treatment facility, the cost of constructing pipelines to and from the facility, and determining who would pay for the treated water.

The fact that costs were a major challenge isn't surprising, according to Y. Jeffrey Yang, a scientist at the U.S. Environmental Protection Agency and coorganizer of the water reuse symposium. Recycling water is an energy-intensive process, which pushes costs up, he said. To lower water reuse's ticket price, engineers must develop new technologies to make the process more energy neutral, he added.

But Luthy was interested in how some agencies overcame the cost problem, especially the issue of who pays for the water. When the community directly receiving the recycled water is too small, water prices can become prohibitively expensive, Luthy said. So agencies look for ways to spread out the costs.

For example, the Pajaro Valley Water Management Agency in Watsonville, Calif., opened a water recycling plant for crop irrigation in 2009. Because the water district sits along the coast, years of overdraft had depleted the groundwater basin to the point that salt water from the ocean had seeped in and made parts of the basin too salty for use. To reduce groundwater pumping near the coast and supply farmers with nonsaline water, the agency now transports a mix of recycled water and water from other sources to coastal customers affected by the saltwater intrusion.

But instead of asking only these customers to bear the full cost of the new facility, the agency charges customers two different rates: a higher one for those directly receiving the treated water and a lower

one for anyone drawing from the basin. Because everyone using the basin's water is part of the problem, everyone pays something to the solution, Luthy said.

After costs, the next major hurdle facing water agencies is handling the public's perception of recycled water. About 25% of the managers surveyed by Luthy and Bischel identified this issue as a major challenge. "If you can't address public perception, then it doesn't matter if you can afford the project, because it isn't going to happen," Luthy said.

No one knows the perception problem better than Eleanor Torres, the director of public affairs for the Orange County Water District, which recycles 70 million gal of water every day. People worry about the water's safety when they learn that its source is sewage, she told C&EN in an interview. "It's essentially the yuck factor."

Luthy thinks that water agencies can overcome this issue if they help their communities understand how the system works and provide transparent data on the water's quality and safety. Torres agrees and said that gaining the public's trust was key in the lead-up to the Orange County project.

THE ORANGE COUNTY project brings treated wastewater closer to people's homes than the Pajaro Valley system does. In Orange County, the agency allows treated wastewater to filter into the county's groundwater basin to replenish the water supply. This process is called indirect potable water reuse, because the treated water mixes in with the groundwater and eventually makes its way to household taps.

To bolster its customers' trust, the agency set out to educate people on the wastewater treatment system. Agency representatives made about 1,200 presentations to community groups between 2003 and 2007. "We'd speak to anyone who would listen to us," Torres told C&EN. Agency management enlisted people outside the agency to talk about the treatment technology and the water's safety, including international water reuse experts and local doctors. Also, the district now offers tours, so visitors can watch how the plant works.

Luthy also stressed that agencies should explain the community's need for water recycling. From responses to his survey, he thinks that projects succeed more often when agencies engage their entire community and explain these issues openly. "When the whole community understands the need and shares in the outcome," he said, "the project seems to move forward." ■



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American Chemical Society

BURKINA FASO

In this landlocked West African country, chemist **MOUHOSSINE NACRO** hopes to preserve centuries-old traditions

KENNETH J. MOORE, C&EN WASHINGTON

IN A VILLAGE in Burkina Faso, Mouhossine Nacro watched nervously as a textile artisan slipped some of the dye that he was mixing into his mouth. To Nacro, a natural products chemist, the observation was a bit unsettling. But to the artisan, it made perfect sense. And then it dawned on Nacro: “When I thought about the chemical aspect of what he was doing, I realized that he was checking the pH,” which is important for dye adhesion and color.

Nacro, a professor of chemistry at Ouagadougou University and one of only two American Chemical Society members in Burkina Faso, travels this landlocked country in West Africa to document the craft of local artisans. “A lot of traditional know-how is disappearing,” Nacro says. Traditional products, such as home-dyed clothing, are being replaced by synthetic goods. So, after documenting artisans’ crafts, Nacro goes to the lab to better understand dye extraction, production, and application. He then looks at ways to innovate or improve these age-old traditions through chemistry—adjusting the pH, temperature, or extraction technique, for example.

Having grown up in Burkina Faso, Nacro is intimately familiar with the region and its people. But when he was studying in the 1960s, there were no universities in the country, so Nacro pursued a bachelor’s in biology from the University of Dakar, in Senegal. He went on to earn a Ph.D. in physical sciences from the University of Nancy, in France. In 1977, he returned to Burkina Faso as a professor at Ouagadougou. From 1982 to 1984, Nacro was a visiting biochemist at the University of Georgia, Athens.

When he returned to Ouagadougou, Nacro was “without contacts and without scientific information,” he says. “You can’t

do research without knowing what’s happening in your field.” He joined ACS to stay connected to his U.S. colleagues. At the time, one year’s membership cost him a month’s salary.

Nacro also subscribed to the *Journal of Agricultural & Food Chemistry* and the *Journal of Chemical Education* to keep abreast of advances in his field. These days, some students at Ouagadougou refer to his



TRANSFORMING LIVES Nacro (center) and postdocs Adama Héma (left) and Constantin Dabiré discuss data related to their research in natural dyes and nutrition.

journals for their own research. Upon graduation, many chemistry students find employment as teachers or in mining companies in the region, and a few go into the health field to

research plant-based drugs, Nacro says.

Conducting research in Burkina Faso is challenging. Reagents can take three to four weeks to arrive after ordering, and equipment may take several months. Accessing information online can also be difficult. “It takes hours to send a document over e-mail,” Nacro says. Lack of funding is another major constraint, he adds. Most research is funded by grants from philanthropic and international develop-

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TOP SUBJECTS in chemistry publications: Pharmacology; fertilizers, soils, and plant nutrition; plant biochemistry; food and feed chemistry; agrochemical bioregulators

SOURCES: CIA World Factbook, Chemical Abstracts Service

ment organizations; the Burkina Faso government provides little money for research.

Disease adds to the strain on resources.

When a coworker is out sick for a few days, it’s not a cold or the flu keeping the researcher at home—it’s usually malaria, Nacro says. “It’s a common reason to be out,” and it’s very incapacitating, he adds. “Your colleagues must take care of whatever research you were doing.”

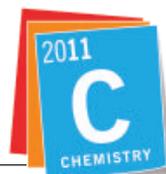
These difficulties don’t stop Nacro from conducting research and maintaining an active role in scientific communities. This year, he is on the scientific committee for the International Symposium & Exhibition on Natural Dyes, a biennial conference that brings together industry and academic researchers from around the world. The meeting is being held this week in La Rochelle, France.

Nacro has also been involved in Burkina Faso’s government: He has served as the country’s ambassador to Canada, as a member of Parliament, and as the minister of secondary and higher education and scientific research.

Even with the impressive array of research duties and offices held, Nacro has also raised a family with his wife, Rosette. He didn’t try to sway their four children to follow in his chemistry footsteps, he says, “because it’s so difficult to do chemistry here; it’s not always rewarding.” But for Nacro, chemistry is the way to solve problems, help people, and improve lives in Burkina Faso.

& PHOTOS ONLINE

View a slide show about Nacro’s research in Burkina Faso by clicking on *C&EN Online*, cenm.ag/iy1.



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NMR AND MRI SHARE LANDMARK STATUS

ACS HONORS magnetic resonance advances now considered indispensable in the lab and clinic

THE RELATED developments of commercial nuclear magnetic resonance spectrometry (NMR) and magnetic resonance imaging (MRI)—which have revolutionized the practice of chemistry and medicine—were recently honored by the American Chemical Society as its 68th National Historic Chemical Landmark.

The landmark designation was marked with two ceremonies. MRI was honored with a celebration on March 11 at the State University of New York, Stony Brook. And on April 8, celebrants gathered at Agilent Technologies, a measurement company in Santa Clara, Calif., to recognize NMR advances.

Varian—whose scientific instrument company is now part of Agilent—introduced the A-60, the first commercially successful NMR spectrometer, in 1960.

LAUTERBUR'S LEGACY Marburger (from left), Jackson, and Dawson examine the Varian A-60 that Lauterbur used at Stony Brook.

NMR was originally developed by physicists, but the affordability, reliability, and compact construction of the

A-60 allowed chemists to use the technique to perform nondestructive analyses to elucidate molecular structures. What had previously taken chemists a month to determine could be done in hours, leading to NMR's widespread use.

Stony Brook chemistry professor Paul C. Lauterbur used a Varian A-60 to take the science even further, demonstrating that NMR could generate multidimensional images. The discovery eventually led to the development of MRI, an important medical diagnostic tool for the noninvasive examination of body tissues such as the brain, heart, and other muscles. MRI scanning allows for early detection of cancer and other diseases. Lauterbur shared the 2003 Nobel Prize in Physiology or Medicine for his role in the development of MRI.

At the Stony Brook ceremony, ACS President Nancy B. Jackson presented the landmark plaque to John H. Marburger III, the university's vice president for research. And Lauterbur's widow, Joan Dawson, noted that the development of MRI originated in a "eureka" moment while Lauterbur was eating a hamburger at a local restaurant in 1971.

During the Agilent celebration, Abby Kennedy, chair of the ACS Santa Clara Valley Section, presented the landmark plaque to Nick Roelofs, president of Agilent Life Sciences Group.

ACS grants landmark status to seminal achievements in the history of chemical science and technology, including individual discoveries, bodies of work, resources, advances, or artifacts. Prospective



AGILENT TECHNOLOGIES

CELEBRANTS Kennedy (left) presents Roelofs with the plaque designating the Varian A-60 at Agilent as a landmark.

landmarks can be nominated by ACS local sections, divisions, or committees. The landmarks committee reviews nominees, and the ACS Board of Directors approves them.

By recognizing landmark achievements of chemists, chemical engineers, and the chemical enterprise, the program is intended to enhance the public's appreciation of the contributions of the chemical sciences and chemical engineering and to increase the sense of pride in their practitioners.—SOPHIE ROVNER

FLORIDA SECTIONS HOST ANNUAL MEETING

ACS'S FLORIDA SECTION and other local sections in the state will hold the 2011 Florida Annual Meeting & Exposition on May 12–14 at Innisbrook, a golf and spa resort in Innisbrook, Fla.

The meeting will feature symposia on analytical, computational, forensic, inorganic, materials, organic, and physical chemistry, as well as biochemistry, bioinspired peptidases, catalysis, chemical education, and metal organic/hybrid frameworks. The meeting will also include a Cope Scholar Symposium, the Florida Award Symposium and associated ceremony, and a Gulf of Mexico Geochemistry Summit that will examine science perspectives one year after the Deepwater Horizon accident and oil spill.

For further information, see chem.fsu.edu/chemlab/fame2011/fame2011.html or contact program organizer Stephanie Dillon at sdillon@chem.fsu.edu.—SLR



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Watering a plant is usually a simple task: Fill a container with water, hold it over the thirsty specimen, and pour. The process doesn't typically involve pulleys, toy train tracks, and waterwheels ... unless it's part of the annual **RUBE GOLDBERG MACHINE CONTEST**.

This year, the competition—named for the Pulitzer Prize-winning cartoonist who drew elaborate contraptions for completing simple tasks in complicated ways—required competitors to build a machine that takes at least 20 steps to water a plant in less than two minutes. The winning team, from the University of Wisconsin, Stout, entered a themed device in the March 26 national contest that did it in 135 steps. This is the second year in a row that the UW Stout team took first place.



Watering machine: Behnke presents UW Stout's device during the national Rube Goldberg contest.

The secret to the group's success, says UW Stout team captain Andrew Behnke, is a well-thought-out theme and layout. The machine needs "to maximize viewing angles for the audience but also be complicated enough to compete," he explains to NewscripTS. His team's winning contraption this year told the story of a haunted estate in the swamps of Louisiana where the dead spring to life when a gate is cranked open. For its grand finale, the device watered a faux venus flytrap.

What surprises people most about UW Stout's winning streak, Behnke says, is that "we actually don't have any engineers on our team." Behnke is a senior business education major, and other teammates study retail merchandising and applied science. Competitors just have to have a "natural love" for the contest to enter, Behnke contends, pointing out that UW Stout's machine this year took nine months and 2,000 hours to build.

Next year's contest will require teams to build devices that pop a balloon. Because Behnke is graduating soon, he's now recruiting students to the UW Stout team to carry on the tradition in 2012.

To see video of the winning device in action, visit the NewscripTS blog (cenblog.org/newscripTS).

Another seemingly nonsensical, but fun, activity that requires an inherent passion for the subject matter is calculating the 15 wealthiest characters in the fictional universe. Forbes.com ranks its favorite **FAKE BILLIONAIRES** from literature and screen annually, but this year, Executive News Editor Michael Noer took

some time to prove to readers that the list is based on serious, nerdy thought.

In an April 6 blog post entitled "How Much is a Dragon Worth?" Noer gives fans "some idea of just how deep the rabbit hole goes" by revealing his scientific formulas for ranking dragon in J. R. R. Tolkien's novel "The Hobbit," seventh on this year's list. Just behind sixth-place Tony Stark (aka Iron Man), Smaug has a net worth of \$8.6 billion, Noer says, owing primarily to the mound of gold and silver

that the dragon sleeps on, the diamonds stuck to his belly, and the dragon's coveted Arkenstone of Thráin—a gem Noer describes as "the Hope Diamond on steroids."

Noer estimates the dragon's size and the volume of his treasure mound by using details from the book and even consulting a guide from the fantasy role-playing game Dungeons & Dragons. He also explicitly calculates how many 5.99-carat diamonds would be encrusted on the protective scales of Smaug's belly to eventually arrive at the final ranking.

Despite the fact that Tolkien describes Smaug as "unassessably wealthy" and his gold as being "beyond price and count," Noer assessed and counted away. "Make up the numbers?" he scoffs. "Ha."

LAUREN K. WOLF wrote this column. Please send comments and suggestions to newscripTS@acs.org.

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