the chemists club

Spring 2014

THE UNIVERSITY OF CHICAGO

Bio-based chemistry

Catherine Poor makes microbes do the work

Consider acrylic. Its physical properties—gloss, hardness, adhesion, and flexibility—make it highly useful. In different forms it makes paint coat, diapers absorb, adhesives stick. It is found in detergents, shaving cream, and pet shampoo. The global market for acrylics is worth $10 billion a year. All of it is made from petroleum.

Catherine Poor, PhD'11, is trying to make acrylic another way, using bacteria and sugar. She is a scientist in protein engineering at OPX Biotechnologies, a company in Boulder, Colo., that is developing new ways of making chemicals on a commercial scale using biological chemistry, not traditional synthetic chemistry. OPXBIO engineers microbes, like bacteria or yeast, to produce chemicals out of simple and renewable feedstocks, like sugar or carbon dioxide and hydrogen.

Continued from cover:

Bio-based chemistry

"In terms of bio-based stuff, we're on the cutting edge of bringing this to market," Poor says. "We're making the same products, we're just making them in a more environmentally friendly and sustainable way."

Poor did not become a chemist right away. An all-American midfielder at Amherst College, she first spent four years playing professional soccer in England. She supported herself by working in a nanomedicine lab at Imperial College London. But she always intended to study chemistry. She returned to the United States to enroll in UChicago's PhD program, where she studied protein crystallography as an NSF Graduate Research Fellow under Chuan He. She stayed after graduating to work as a postdoctoral fellow under Jared Lewis.

As a PhD student, Poor studied transcriptional regulators in *Staphylococcus aureus* — MRSA — and baker's yeast. For her postdoc she shifted from trying to understand the structure of proteins to figuring out how to make enzymes work better. She became interested in directed evolution and protein engineering. "I had a lot of knowledge of protein structure," she says. "You can look at a protein and figure out rational ways to make it better."

Her academic research was immediately applicable to her work at OPXBIO. The privately held company, funded by venture capitalists, started up in the foothills of the Rocky Mountains in 2007. Biologically produced acrylic was its first big project. The company has other projects underway, including one that uses microbes to turn CO_2 into fatty acids. These can then be used in cleaning products, lubricants and plastics, and can be turned into diesel and jet fuel.

Poor focuses on what she calls the "bottlenecks" in the cellular process. She and her colleagues introduce massive numbers of genetic mutations into microbes like *E. coli* or yeast. They then run experiments and analyze the data to determine which changes produce the enzymes they want. In the case of acrylic, they search for the enzymes that will turn sugar into 3-hydroxypropionic acid, a precursor to acrylic. Poor says they analyze a wide variety of different enzymes — "from a plant, a mouse, or whatever, if we think we can do it. We then engineer the microbe by mixing and matching the key genetic changes to produce the products we are interested in."

OPXBIO is not the only company trying to do this. Its chief innovation is a proprietary method, which it calls Efficiently Directed Genome Engineering. This allows its scientists to introduce genetic changes in millions of microbes at once and then track the changes to figure out which have the characteristics they are looking for. The company has developed a partnership with Dow Chemical to bring its product, BioAcrylic, to market by 2017, at a price comparable to petroleum-based acrylic and with what it says is a significant reduction in greenhouse gas emissions. Meanwhile, the company has received a $6 million grant from the Department of Energy for its efforts to make biologically based fatty acids.

It's not easy work. The stakes are high, the deadlines tight. "It's a very high pressure environment," Poor says. But it is part of a growing effort among scientists to make the industrial production of chemicals more efficient, less wasteful and less energy intensive, and to do it out of renewable materials. Poor loves being part of it.

"It's absolutely my dream job," she says. "It combines my graduate work and postdoctoral work into an environmental cause. It's a combination of my intellectual and emotional passions."

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Toward a greener chemistry

Mitch Smith and the challenge of molecular carpentry

Milton "Mitch" Smith, PhD'90, grew up on a small farm in West Virginia. He fed the chickens in the morning and at night, sheared sheep in the spring, and helped make things around the farm, including a barn, a woodworking shop, and furniture for the house. It was only a short step from that to becoming a chemist.

"I was used to building things with my hands," he says. "Chemistry was kind of molecular carpentry."

Smith is a professor of chemistry at Michigan State University. He leads a research group that is creating new syntheses using organometallic complexes, especially ones involving the transition metal chemistry of boron. In 2008, he and his colleague at Michigan State, Robert Maleczka, Jr., received a Presidential Green Chemistry Challenge Award from the US Environmental Protection Agency for this work. They were honored for developing a new catalytic method that allowed the manufacture of complex molecules, such as those used in pharmaceuticals and agriculture, under mild conditions with minimal waste and toxicity.

"This technology allows for rapid, low-impact preparations of new chemical building blocks that currently are commercially unavailable or only accessible by protracted, costly, and environmentally unattractive routes," the EPA said in making the award.

Smith and Maleczka have in the meantime started BoroPharm, Inc., a company based in Ann Arbor, Mich., that supplies chemical intermediates to the manufacturers of medicines and agricultural chemicals, as well as to companies making the thin flexible organic displays that go into energy-efficient organic LEDs. A 55" television that uses OLEDs costs $7,000 at Best Buy, but Smith expects the price to fall. "They're trying to improve the process, to make it more efficient, to drive costs down," he says. "They want everyone to be able to buy one."

BoroPharm also sells its expertise. "Customers come to us and say, 'We really want to make these things, but we don't know how to do it, can you help us?'" Smith says.

Smith's group is pursuing two other research projects. One involves the development of polylactic acids, a family of polymers for applications ranging from the manufacture of renewable plastics to the delivery of drugs. The group has developed degradable polymers that can be used in medical applications like resorbable sutures. It also has developed polymers that can be tailored to highly specialized requirements. One example is a polymer that has both water soluble and insoluble groups attached along its backbone. An amphiphilic polymer like this becomes a unimolecular micelle with a soluble exterior and an insoluble interior. "The thing coils up into a little ball, nanometer size," Smith says. One possible use is to deliver insoluble drugs into cells. The micelle can carry the drug through the cell membrane. If it is degradable, it can release the drug there.

"It's very far away," Smith acknowledges. But he says this kind of chemistry offers potential solutions to a widespread problem in medicine. Sometimes promising drugs are given up on simply because they are not soluble enough to deliver to where they are needed. Other drugs, including some used to fight cancer, are difficult to get directly to the targeted cells. "You take a drug and the stuff goes everywhere," he says. "Almost every drug has a delivery problem."

The Smith group's most recent project is figuring out how to chemically store wind and solar energy. One popular idea is to use wind and solar power to convert carbon dioxide to methanol. But the concentration of carbon dioxide in the atmosphere is small. "CO_2 is not efficient," Smith says. His group is focusing on ammonia. Ammonia is energy dense when liquefied—about the same as methanol. But in contrast to methanol, ammonia can be made from the most abundant gas in the atmosphere—nitrogen. Ammonia has already been used as a fuel. It ran cars in Belgium during World War II, and it powered the X-15 that set altitude and speed records in the early 1960s. Smith's group wants to make a fuel cell that runs on ammonia. One advantage to ammonia is that it is already used widely in agriculture to make fertilizer. A network of pipelines is in place to transport it.

Smith studied chemistry at Caltech, working with Terrence Collins. He earned his PhD under UChicago's Gregory Hillhouse, studying the synthesis and reactivity of metal diazene complexes. He spent the next two years at the University of California, Berkeley, where he worked with Richard Anderson, synthesizing and exploring the reactivity of early transition metal oxo and imido complexes.

Smith's molecule building has immense potential for use in industry and medicine. But he says his first commitment is to basic research and the training of new generations of scientists. "That is what I learned from my teacher, mentor, and friend, Greg Hillhouse," Smith says. "My days at U of C were some of the fondest of my life, and Greg was the biggest part of it. I would not be where I am today without him."

Renovating the labs has not been her biggest contribution to improving the lab experience of UChicago's undergraduates. Keller is also responsible for the manual that guides them through organic chemisry lab each week.

O-Chem's impresario

Lab director Valerie Keller is the energy behind the reactions

Fifteen minutes before Thursday afternoon O-Chem lab, a clutch of four teaching assistants gathers in Valerie Keller's office. Keller is Lab Director for Undergraduate Organic Chemistry, Senior Lecturer, and Assistant Director of Undergraduate Studies. She is the manager behind the scenes, working to make sure the labs run smoothly. If they do not, it is up to her to make them better.

This happened recently when it became clear that the organic chemistry labs needed renovation. The laboratories are in Kent Hall, otherwise known as the Sidney A. Kent Chemical Laboratory. Kent was built in 1894 and is one of the university's oldest buildings. The Regenstein Library has photos of the interior as far back as 1900. The labs then look much as they do today, with light streaming in from tall windows and falling across rows of benches with wooden cabinets. The years have brought significant changes, of course, including florescent lighting and modern hoods. The students no longer work at the benches. They also have shed their ties. And many more of them are women.

By the time Keller took her job in 2006, the labs were quite old. They had last been renovated in 1985. The vacuum lines, used mainly for filtration, had deteriorated and needed frequent repair. Perhaps the biggest flaw was in the wiring of the hoods. Several hoods were connected to the same electrical circuit. It often happened, then, that at the end of an afternoon, when students were hurrying to finish and go eat dinner, they would turn their heating plates on high, all at once. The circuits would overload, the power would shut off, and the building would plunge into darkness. "Nobody could believe how they were wired," Keller says.

Last year, money was found to renovate the organic labs and Keller was instrumental in overseeing the renovation. The hoods were replaced — and rewired so that each had its own circuit. More efficient water spigots and air handling equipment were installed. The floors were covered with a new layer of clean white linoleum. The old wooden cabinetry remained, but it received a new coat of varnish. In the future, the department hopes to also do the general chemistry labs on the second floor.

Keller is one of the teaching staff indispensible to making the Department of Chemistry run smoothly. As lab manager, she designs the lab curriculum, and she and a staff of two order chemicals, set up the experiments, and make sure the glassware and reagents are ready. Each quarter she oversees a cadre of 20 teaching assistants. Through them she communicates to the students policies like academic honesty and instructions on how to set up the hoods, keep notes, and successfully do the experiments. "I have a lot of 'Please clean up after yourself,'" she says.

Renovating the labs has not been her biggest contribution to improving the lab experience of UChicago's undergraduates. Keller is also responsible for the manual that guides them through organic chemistry lab each week. She has worked constantly to upgrade it, usually replacing one experiment each year with one that works better or introduces students to a technique not previously covered.

"One lab was fine, but students got a 20 percent yield," she says. "That was frustrating." The lab was titled "Synthesis and Purification of Tetraphenylporphyrin," but people called it "The Purple Lab" because it stained everything purple. It was an old experiment that O-Chem students had done for many years. Keller replaced it with "Multistep Synthesis of Hexaphenylbenzene." The yields were better—"better than 20 percent," she says—and the product was a white solid. "Which is sad because organic chemistry is basically colorless liquids and white solids," she says. "I wanted to introduce some color, but it stains everything."

Of the 17 experiments in this year's manual, she has introduced seven. She is working on a new one for next year.

"You have to develop something that's foolproof," she says. "Even if I can do an experiment, it doesn't mean that 300 students can do it in the same amount of time, on a small budget, and not using horribly toxic chemicals."

Keller grew up near Kalamazoo, Mich. She went to DePaul University and then earned a PhD in organic chemistry at the University of Wisconsin. She came to UChicago as a postdoc in 2004-5 to work in Sergey Kozmin's lab. And stayed.

She does more than direct the labs. She has also managing the organic chemistry classes, which means doing tasks like training teaching assistants, and supervising the administration and grading of exams. In the summer, she teaches organic chemistry. But the labs are the heart of organic chemistry, and that is where you will usually find her.

On Thursday afternoon, Keller goes over issues that have cropped up during the week. The experiment is "Bleach Oxidation of 9-Hydroxyfluorene." She is good humored, but direct. "When some kids add the hexane they don't see the separation," she tells the TAs. "Probably they added too much hexane." And: "Did you hear about the chunks coming out of the nitrogen line? I think they're all blown out." (She had the line purged.) There are housekeeping issues. "The instrument rooms get really messy," she warns.

Undergraduates are streaming into the building. Two poke their heads into the office, then shyly withdraw. It's time. "You ready?" she says. "This is a long one."

Creating stronger bonds

PhD student Landon Durak makes new chemicals while fostering community in the Department of Chemistry

Landon Durak raises a round-bottom flask a little smaller than a tennis ball. A teaspoon's worth of orange crystals lies at the bottom. It is the result of a day's work mixing and heating a stew of chemicals, including iridium. "Right now it's in an early state of synthesis," he says.

Durak is a fourth-year graduate student in the research group led by Jared Lewis and devoted to finding new and better ways to synthesize organic chemicals. Chemical synthesis has produced an astonishing variety of chemicals for use in industry and in biological and materials research. But it has been limited by the complexity and wastefulness of the synthetic processes, with extended sequences and the need to isolate intermediate compounds. Researchers in the Lewis group are using enzymes and metal catalysts to functionalize C-H bonds quickly and more efficiently. The goal is to make it easier to turn cheap and abundant hydrocarbons into the kinds of complex organic compounds used widely in industry and medicine.

"If you directly converted C-H bonds into desired functional groups, you eliminate the need for intermediate steps," Durak says. "It dramatically increases the efficiency of synthesis."

Durak works with transition metals, mostly iridium, platinum, and palladium. He's trying to find ways to use these metals to selectively break the carbon-hydrogen bonds in hydrocarbons, and install new carbon-carbon bonds. "It has very practical applications," Durak says, "especially in something like the pharmaceutical industry." The trick, he says, is to make the substitution selective.

Durak grew up in Buffalo, N.Y., where his high school physics and chemistry teachers turned him on to science. "We did a lot of demos," he says. "Blew a lot of things up in class." At Boston College he took the honors chemistry track and did research under James Morken. "I learned a lot about synthetic chemistry. It helped me a lot in graduate school."

Indeed, Lewis says Durak arrived at UChicago unusually well prepared to do research. "He was very strong," Lewis says. "All the basics were still there. I needed to do very little to get him going with experimental techniques…He was able to get into research that required a sophistication in the lab that's not present with most students." In recognition of this talent, the Department of Chemistry this year awarded Durak the Everett E. Gilbert Memorial Prize for the Best Third Year Experimentalist in Organic Chemistry.

Durak says the challenge of synthesizing useful compounds in a more efficient way "really resonated" with him when he came to UChicago. "This whole matter of making useful molecules with abundant and inexpensive materials, under mild conditions, and energy efficiently—it's fundamentally important," he says.

But he's not just interested in practical chemistry. His first paper, published last year with Jared Lewis, was a detailed mechanistic analysis of a reaction he discovered. "The focus of our group is function," he says. "But we definitely want to understand how our enzymes work, how our catalysts work. We want to understand better how our reactions work." His second paper described a synthetic reaction using metal catalysts: "Ir-Promoted, Pd-Catalyzed Direct Arylation of Unactivated Arenes."

Durak has also contributed to the Department of Chemistry in important ways outside the lab. Two years ago, feeling a need to hear from researchers in other groups working on organometallics, he organized a monthly colloquium for postdocs and graduate students to present their work to each other. The colloquium has met on a regular basis ever since, drawing not only graduate students and postdocs, but also some faculty.

"I think it's really important to develop this sense of community," he says. "I think we need to have healthy conversations between students and faculty."

Once Durak finishes his degree, he plans to take his interest in applied chemistry to the field of materials and engineering. "Having this fundamental knowledge of chemistry is really important, but ultimately I'd like to do practical things," he says. One problem that interests him is the "enormous amount of waste" in the batch processing of pharmaceuticals and other chemicals. "When I think about problems in chemical systems, the matter of scale comes to mind," he says. "We need to make large amounts of a lot of things." He wants to help do it better.

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the chemists club

Spring 2014

Dear friends,

It is with great sadness that I begin this letter with the news that our colleague, Professor Gregory Hillhouse, passed away earlier this year. Greg was a pillar of excellence in our department and the University. As a word class researcher, dedicated mentor and role model for his students, and engaged citizen of the University community, he epitomized what the University is all about. His research will inspire new lines of inquiry in inorganic chemistry for decades and his influence on his students will reverberate for generations. He was a great friend and superb colleague who will be sorely missed by many. The next issue of the Chemists Club will be devoted to Greg's work and legacy.

In honor of Greg's dedication to student mentorship, I wish to remind all of us how important our students are. We are fortunate to have recruited some of the best graduate students in the country and have a record number this year: 192. In this issue, you will meet one of our outstanding students, Landon Durak. Landon has excelled in and out of the lab. Two years ago, he started a monthly colloquium on organometallic chemistry for students, postdocs, and faculty. His contributions highlight the important role that our students play in creating a sense of community within the department.

We are also attracting a growing number of excellent undergraduates. Well over 50 chemistry and biological chemistry majors graduate from the College each year, and most go on to top graduate or professional programs or challenging positions in the private sector. I congratulate Samuel Greene, a chemistry major who won a Rhodes Scholarship to study at Oxford. We have long recognized the importance of independent research in the undergraduate curriculum and, and over 90 percent of our undergraduates conduct research. This experience helps them learn how to analyze and solve problems in creative ways and gives them an advantage in their post-Chicago careers.

The department is a very active operation, with 22 faculty, 3 joint faculty whose primary appointments are with other departments, more than 50 postdoctoral fellows, and many technicians, all working with the graduate and undergraduate students to purse our educational and research goals. We rely heavily on our staff to keep things running smoothly. In this issue you will meet a member of the staff who has done an exceptional job in modernizing the undergraduate organic chemistry labs. Valerie Keller not only oversaw the renovation of these labs last summer, but has also been instrumental in putting together a challenging and modern lab experience for our undergraduates.

Two alumni figure prominently in this issue, both leaders in the development of green approaches to synthesizing chemicals for medicine and industry. Mitch Smith, PhD'90 with Greg Hillhouse, is a professor at Michigan State University and co-founder of BoroPharm, Inc. Smith received the US EPA's Presidential Green Chemistry Challenge Award in 2008 for his work on a new method that minimizes waste and reduces the hazard of making pesticides and pharmaceuticals. Catherine Poor, PhD'11 with Chuan He, is a scientist at a start-up company in Boulder, Colo., where she uses genetic engineering approaches to develop microbes that make industrially important chemicals from renewable feedstocks. We are proud of their achievements.

Best Regards,

Richard F. Jordan

Richard F. Jordan
Professor and Chair

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