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Professor, alum, earn nation's top engineering honor

chemical and biological engineering professor known for his work in chemical process monitoring and control and a chemical engineering alumnus who is a leader in the pharmaceutical industry were among 80 U.S. and 22 foreign members elected to the National Academy of Engineering in 2016.

Election to the academy is an honor reserved for those who have

made outstanding contributions to engineering research, practice or education. The **NAE** cited James B. Rawlings, the Paul A. Elfers and W. Harmon Ray professor. for contributions to control engineering theory, practice and education. Brian Kelley

TOUNDED 1962

Brian Kelley

(BSChE '86) has led efforts to develop bioprocess technology and cost-effective manufacturing processes for recombinant protein therapeutics.

Jim Rawlings

Jim's research has had worldwide impact on fundamental understanding and industrial practice in the field of process monitoring and control. His research results on linear and nonlinear model-based process monitoring and control strategies in the presence of process constraints—such as limited controller power or temperature, pressure and composition limits—have led to deeper theoretical understanding of the problem, as well as new widely available plant control schemes and many process applications.

In addition to pioneering research, Jim also has been a leader in chemical engineering education, through his use of technology and experiential learning in the classroom and through development of textbooks for both undergraduate and graduate student audiences. In recent years, he has co-authored *Chemical Reactor Analysis and Design Fundamentals*, second edition (2015), *Modeling and Analysis Principles for Chemical and Biological Engineers* (2013), and *Model Predictive Control: Theory and Design* (2009).

Jim earned his BS in chemical engineering from the University of Texas at Austin, his PhD in chemical engineering from the University of Wisconsin-Madison, and was a postdoctoral fellow at the Institute for System Dynamics and Process Control at the University of Stuttgart, Germany. His research and teaching have garnered myriad honors; among them, a "Doctor technices honoris causa" from the Technical

University of Denmark, the inaugural High-Impact Paper Award from the International Federation of Automatic Control, and the Ragazzini **Education Award** from the American Automatic Control Council, all in 2011. He also received the **UW-Madison**

Chancellor's Distinguished Teaching Award (2013) and the Byron Bird Award for Excellence in a Research Publication from the UW-Madison College of Engineering. He is a fellow of the Institute of Electrical & Electronics Engineers and of the American Institute of Chemical Engineers.

Vice president for bioprocess development with the U.S. Biologics Pharma Technical Development arm of Genentech, Brian also holds a PhD from the Massachusetts Institute of Technology. Active in the American Chemical Society biotechnology division, he is a fellow of the American Institute of Medical and Biological Engineering. At Genentech, he oversees the unit responsible for development and tech transfer for fermentation, cell culture, chromatography and filtration operations for producing recombinant therapeutic proteins.

Also elected to the academy were engineering alumni **David Sedlak** (PhDWaterChem '92), who has made an impact in environmental aqueous chemistry in water reuse, contaminants and urban water infrastructure; while **Adam Diedrich Steltzner**'s (PhDEM '99) major accomplishment was developing the Mars *Curiosity* 2011 entry, descent and landing system and for contributions to control of parachute dynamics.



Manos Mavrikakis

his spring, we were thrilled with the news of the election of **Jim Rawlings** and **Brian Kelley** (BS '86) to the National Academy of Engineering and we celebrated Professor Emeritus **Ed Lightfoot**'s 90th birthday with a symposium and banquet in his honor. For me, the event drove home everything that is special about this department: a proud history, a deep and continuing commitment to excellence in

all academic endeavors, and a familial sense of camaraderie.

And like the strongest of families, we pull together when faced with challenges. As you may know, we are in the midst of a UW-wide comprehensive fund-raising campaign. Over the past year, we have nearly doubled the number of alumni who made gifts to our department; we are both humbled by and grateful for this surge in support for our department. Additionally, a \$125-million matching gift from UW-Madison alumni John and Tashia Morgridge enabled us to add five new

professorships to CBE (and many others campus-wide). With these new professorships, we now have the opportunity to both recruit new world-class faculty and to recognize and retain exceptionally performing CBE faculty.

Graduate student fellowships and funding for facilities—
renovations of existing labs, as well as a new CBE building—
are currently at the very top of our department's fund-raising priorities. These are critical in our ability to remain competitive relative to our peers. As we seek to recruit additional faculty for our core areas of excellence, we also must be prepared to provide space for their labs and students—and, much like our competitors, a new building will allow us to construct

modern, flexible teaching and lab space that the configuration and age of Engineering Hall simply can't accommodate. State-of-the-art facilities will strengthen our ability to recruit and retain exceptional faculty, postdocs, graduate and undergraduate students. In addition, these facilities will enhance our ability to support team-based learning.

If you're interested in making a leadership gift to help us launch our planning efforts for a new building, I invite you to reach out to me or Ann Leahy, our director of development at ann.leahy@supportuw.org.

Currently, we are recruiting a senior faculty member for the Distinguished Ernie Micek Professorship, which the Wisconsin Alumni Research Foundation established in honor of our alumnus **Ernie Micek** (BS '53), who retired as CEO of Cargill Corp. and who has made significant contributions to the department and the university through his service on key boards and committees. In parallel, CBE

is heavily involved in recruiting faculty through the Grainger Institute for Engineering, generously supported by a \$25M commitment made by The Grainger Foundation to the College of Engineering. Further, we recently



welcomed **Reid van Lehn** to the CBE faculty. Reid is an expert in statistical mechanics and will further enable impactful research and teaching in the CBE.

We are fortunate to have **Bill Banholzer** among our ranks. Bill joined the department in fall 2013 after he retired as executive vice president and chief technology officer of The Dow Chemical Company. Not only has his business acumen been invaluable to our

faculty as they seek funding to establish new multidisciplinary research centers, but Bill also has developed a business-centric course, Aspects of Industrial Chemistry and Business Fundamentals (CBE 505), that augments our students' technical education with practical knowledge about how to move a discovery from research to a commercial product.

Bill's wisdom is welcome at a time when demand for our major is high and we are enrolling more students than ever. This summer, more than 110 students will participate in summer lab sessions here on campus and at locations around the world, including the new session we are thrilled to offer at **Hong Kong**

University of Science and Technology.

As a department, we are increasing efforts to keep in touch with our extended family of alumni, and we are thrilled to do that in a variety of ways. One of those is through events we (and the college as a whole) host annually around the country. In January, for example, we visited Houston, and our event there had a large and lively turnout of CBE alumni who work in the oil and gas and chemical industries. Look for information about similar events in your area in the upcoming months. In between, I encourage you to keep sending us the latest of your news by email to che@che.wisc.edu.

ON, WISCONSIN!

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Class teaches students the business behind the science



f you're going to make a profit in business, you need to be able to answer three crucial questions: What do people want, what can they afford, and what are they willing to pay for?

Chemistry and chemical engineering students at UW-Madison acquire outstanding technical skills; however, Chemistry 505/Chemical and Biological Engineering 505: Aspects of Industrial Chemistry and Business Fundamentals also teaches them how to apply that technical knowledge to decision-making on the business side of industry. "We had this fundamental mismatch in that we're not preparing students beyond their technical knowledge for their future in government or industry," says Research Professor Bill Banholzer, who retired from his position as an executive vice president and the chief technology officer of Dow Chemical in 2014. "This course helps our students and our departments remain relevant to industry."

In spring 2015 and 2016, Banholzer and Ive Hermans, an associate professor of chemistry who also has a master of business administration degree, have co-taught the course, which is designed for seniors and graduate-level students. Banholzer says there is a pressing need to introduce business fundamentals into the engineering curriculum. "Producing students—and faculty—who have a stronger appreciation of industrial realities and technical evaluation skills will provide a more competent workforce, as well as more knowledgeable government employees," he says.

In addition to a healthy dose of "real-world" chemistry—for example, C1, C2, C3, C4, and C6 chemistry; organic feedstocks, aromatics, and plastics, among other topics—students in the class learn how a discovery moves from research to commercial product through case studies, which challenge them to form their own responses to real-life scenarios.

The business-for-non-business-students-style course also covers business "jargon" and fundamentals such as net present value, cash flow, pricing mechanisms, industrial value chains, competitive dynamics, risk, ethics, venture capital and others, as well as how to communicate and to dress for a presentation. By thinking about how these concepts factor into engineering, students more fully understand the broad implications of chemical processes.

The students' final project is a business simulation in which students work in teams to revive a failing business. Pranav Karanjkar, a chemical engineering PhD student in the course, found this simulation to be particularly intriguing. "Students became technical managers of a company, and were made responsible for the financial losses of the last two years," Karanjkar explains. "Their job was to figure out how to spend that year's budget in order to start making money. It was a really open-ended problem that involved marketing, research and development, and sourcing, as well as different perspectives that diverge from just the chemistry of the process."

Expanding students' knowledge to include business concepts is critical to an education in chemical engineering, says Banholzer. Having spent 30 years working in industry, he fully understands the value of developing business acumen. "My hope is that students understand the context in which technology and engineering are functioning," Banholzer says. "Just because something is

possible, doesn't mean it's practical. Engineers impact society when they develop processes and products which are financially grounded, generating sufficient return for investors. A lot of things are possible—like using photons to drive a reaction—but to determining if they are practical requires both engineering judgment and business fundamentals."

Very few chemical engineering departments around the country offer courses like Aspects of Industrial Chemistry and Business Fundamentals, says Banholzer. He and Hermans currently are developing a series of simulations covering topics such as sizing a plant expansion within the context of expected market growth and competitive dynamics, and the importance of closing energy and mass balances to find losses. The simulations will be available publicly online starting in summer 2016—and that allows faculty members anywhere the opportunity to incorporate similar methods in their own classrooms.

Courses such as this one help keep engineering departments grounded, Banholzer says. Students are not only able to develop some of the "soft" skills that are crucial to their future careers, but acquire knowledge that is—in most cases—directly tied to situations they will face in their jobs.

Brett DuCharme, who graduated in 2016 with his bachelor's degree in chemical engineering and certificates in business and math, will be working for LyondellBasel Industries. For him, the class provided yet another opportunity to supplement his engineering knowledge. "I wanted to learn about the chemical market at large," he says. "This class really bridges the gap between what you're doing, and why you're doing it."

ontemporary computer simulations can apply basic laws of motion at the molecular level to replicate the behavior of synthetic nanoparticles, and build understanding of how these complex structures interact with the body. Reid Van Lehn, who joined the department in spring 2016 as an assistant professor, uses computer-based experiments to answer questions about how—for instance—a nanoparticle can help drugs reach a cell via targeted drug delivery.

Assessing design criteria for nanoparticles via computational approaches provides a huge benefit to those who study their interactions with cells. "Anything you do experimentally in this type of research requires both nanoparticle synthesis and incubation with cells," Van Lehn says. "These are messy experiments that are expensive and time-consuming—and ultimately you don't gain extensive information about what is physically happening when the nanoparticles and cells interact."

REID VAN LEHN:
Simulating the behavior of biologically active nanoparticles

By modeling parts of such experiments with a simulation, Van Lehn can isolate what is occurring during specific stages of the nanoparticle-cell interaction. He can also observe specific and minute characteristics of nanoparticles, such as how strongly they bind to the cell surface, or what causes them to bypass the protective cell membrane. These types of information are crucial when it comes to targeted drug delivery.

One of Van Lehn's primary areas of expertise is developing vehicles that can carry small molecules, such as gene-modulating siRNA (small interfering RNA), through a cell membrane, to the interior of a cell. "If a therapeutic small molecule can't bypass the membrane by itself, by putting it on the surface of a nanoparticle that does have the ability to bypass the membrane, we have an essential two-component therapy that can increase efficacy," he says.

Van Lehn, who was selected to the *Forbes* 2016 "30 Under 30" list in the science category, also applies his research to biosensing and bioimaging.

Biosensing involves designing certain materials that detect different toxins or alterations in the body, such as increases in acidity, or the aggregation of bacteria. With a material that can light up, or release some sort of alert when it senses—for example—a tumor's microenvironment, doctors could more effectively detect and treat diseases like cancer. Through computer simulations, Van Lehn and his research group can identify the physical and chemical composition unique to these environments.

Because his simulations preserve chemical structures at an atomistic length scale—incorporating distinct molecular details—Van Lehn can make concrete recommendations and design guidelines that also incorporate data from physical experiments.

"We're never going to be perfect; the complexity of biological systems is something that evades complete modeling by computers at the molecular level, and will continue to do so for the foreseeable future," he says. "But we can take bits and pieces of the system by studying interactions with specific biological molecules, and in combination with experimental as-

says— because everything we do has to be tied to experiments to make sure we're grounded in reality—the computer simulations become very valuable when designing new materials."

Van Lehn is a graduate of the Massachusetts Institute of Technology, where he received both his bachelor's degree and PhD in materials science and engineering. Before arriving in Madison, he studied as a National Institutes of Health Ruth-Kirschtein postdoctoral fellow at the California Institute of Technology. Growing up in a family of educators, he looks forward to developing his own teaching style, and trying to enhance the classroom experience for engineering students.

"I'll first be teaching statistical mechanics, and several major findings of this field happen to be useful in computer simulations, so it all nicely ties together in terms of how we can use what we teach in the classroom to inform real-world knowledge, and make sure people see the downstream consequences of what we're learning," he says. "I also think it's important to take students out of the typical collegiate lecture environment, whether through project-based learning techniques, or active participation within a classroom setting."

In terms of developing his lab, he has secured a space, and is hoping that his enthusiasm will encourage students—both graduates and undergraduates—to find a place in his lab. A gift to the department from Mike and Sherri Miske also is helping to fund Van Lehn as he sets up the lab and begins his faculty career here.

Since his early interactions with UW-Madison faculty, Van Lehn has embraced the synergy offered by the college's collaborative environment. Not only was he able to find his research niche, but he foresees immense possibility in terms of future interactions, both outside of his department and even outside of the college.

"The campus is stunning, and the sheer enthusiasm the faculty has for one another is really great," he says. "On my first visit, I got the vibe that everyone here wanted to work with each other, both with faculty in the department and with students and postdocs. There are tons of opportunities for collaboration."



Lightfoot, seated at center right, surrounded by some of his academic progeny.

dwin Lightfoot's academic family tree branches far beyond his Wisconsin roots.

The Hilldale professor emeritus, who in 2015 celebrated his 90th birthday, mentored 49 PhD students during his time on campus, 11 of whom went on to establish their own research programs at top institutions.

Recently, multiple generations of academics and CBE alumni reunited during the Ed Lightfoot symposium, held April 7 and 8, 2016, in the Discovery Building on campus. During the two days of talks and an afternoon poster session, three of Lightfoot's distinguished former students—Bernhard Palsson, Abraham Lenhoff and James Liao—were among the key researchers who presented on topics ranging from brain diseases to biofuels—unified by the quantitative principles that Lightfoot, along with colleagues Warren E. Stewart and R. Byron Bird, set forth more than 50 years ago in the seminal text *Transport Phenomena*.

Transport phenomena—the principles that diverse physical, chemical and biological processes in the universe follow the same fundamental laws governing mass, energy and momentum exchange—underlie the flourishing fields of quantitative and systems biology, which use tools from the physical sciences to untangle seemingly impossibly complex biological systems and processes.

Quantitative biology, by definition, takes a cross-disciplinary approach to resolving problems in biology. Palsson (PhD '84) is the Galletti professor of bioengineering, professor of pediatrics, and the principal investigator of the systems biology research group in the Department of Bioengineering at the University of California, San Diego. One of his first forays into systems biology started as a final project

ED LIGHTFOOT SYMPOSIUM 2016 MULTIPLE GENERATIONS OF RESEARCH EXCELLENCE

for Lightfoot's class. The young student's undertaking, which used econometric models to analyze how bacteria allocate resources during growth, went on to become a paradigm-shifting publication. "Ed got his hands on my term paper and rewrote it in such a clear and elegant way that it got into *Science*," says Palsson.

Symposium speaker Lenhoff (PhD '84), the Allan P. Colburn professor and department chair in chemical engineering at the University of Delaware, uses information from atomic-level protein structures to predict the sometimes counter-intuitive behaviors in solutions.

Increasingly, researchers recognize that quantitating life's processes is a powerful first step to harness them for humanity's benefit. Mathematical models can help design living photovoltaic cells based on bacteria that store energy from the sun in the form of biological hydrocarbons, as discussed by speaker Liao (PhD '87), the Parsons Foundation professor and department chair in chemical and biomolecular engineering at the University of California, Los Angeles. Or, they can help predict the best interventions to promote wound healing, as described by Biomedical Engineering Associate Professor Pamela Kreeger.

Liao credits Lightfoot's mentorship for defining his career. "One afternoon with Ed Lightfoot changed my life," said Liao. "I knew nothing about biology; I was interested in polymer chemistry. He convinced me to apply control theory to the biology of metabolism."

Rather than effusively praise Lightfoot for his contributions to the field, speakers at the

"One afternoon with Ed Lightfoot changed my life."

—James Liao

symposium instead shared lessons they learned from their former advisor. "We learn to mentor from our mentors," says Associate Professor and Harvey D. Spangler Faculty Scholar Jennifer Reed, who received her PhD training in bioengineering under Palsson's advisorship, making her Lightfoot's "academic granddaughter."

Lightfoot's legacy resonates in Reed's research, which predicts complex synthetic networks based on simple information about the relative amounts of inputs and outputs in a cell. The resulting models can inform strategies for

engineering bacteria to produce useful chemicals.

Cross-disciplinary connections also emerged throughout the symposium. After a presentation by Genetics Associate Professor Audrey Gasch, describing genetic regulation in yeast, Richard H. Soit Assistant Professor Victor Zavala noted that he uses the same language and similar concepts in his own work, which develops and optimizes algorithms for energy infrastructure.

The symposium to honor Ed's birthday was organized by the Vilas Distinguished Achievement Professor John Yin, the systems biology theme leader in the Wisconsin Institute for Discovery.

Lightfoot's influence also shaped Yin's career. A chance encounter with a college roommate's textbook motivated his decision to study chemical engineering. "*Transport Phenomena* opened my eyes to realize I could apply what I learned in physics and math to chemistry and biology," says Yin.

The spirit of creative, open-minded, multi-disciplinary scientific inquiry also shone through during poster presentations and rapid-fire lightning talks from graduate students and post-doctoral scholars—the newest budding branches on an extensive academic family tree.

"Ed Lightfoot set some of the standards that all of the current faculty are striving for," says Vilas Distinguished Achievement Professor, Paul A. Elfers Professor, and department chair Manos Mavrikakis. "It's a heavy tradition, but one that we're eager to uphold."

hen a drug enters the human body, it's no surprise that the resulting changes can have wide-ranging effects on cells and their interactions with each other. However, the challenge lies in defining how these interactions happen.

In a paper published Feb. 23, 2016, in the Proceedings of the National Academy of Sciences (PNAS), chemical and biological engineers at the UW-Madison and biomedical engineers at the Georgia Institute of Technology and Emory University (through a joint program) described what happens to white blood cells under the effects of certain classes of commonly prescribed medications. **Cell processes**

Mike Graham, the Vilas Distinguished Achievement Professor and Harvey D. Spangler Professor, typically uses theory and computational tools in his fluid mechanics research.

However, after Wilbur Lam, an assistant professor of biomedical engineering at Georgia Tech and Emory, approached him at the 2012 International Congress on Theoretical and Applied Mechanics conference in Beijing, his focus turned toward how drugs affect these phenomena.

Their joint research now provides both a theoretical and experimental model for how particles in blood vessels move differently when they are affected by the widely used drugs epinephrine and dexamethasone, producing a phenomenon called demargination.

Margination is the process by which white blood cells—cells that protect the body against disease—accumulate along

This process can significantly increase the number of white blood cells found in a blood sample, which is a well-known effect of antiinflammatory drugs. However, what researchers did not know is that cell stiffness plays a crucial role in this process.

While Lam mimicked cell changes in a microfluidic environment (essentially, a tiny blood vessel on a chip), Graham and his students developed computational and mathematical models to help explain

can increase

white blood cell count

in patients who

take certain

anti-inflammatory

drugs

how cells migrate and interact in a blood vessel. They used these two very different approaches in tandem to

> provide an overarching picture of why and how demargination happens. "It's something that helps physicians understand why they see these changes (in white blood cell count) when they give people drugs, and that's important when considering certain drug interactions," Graham says.

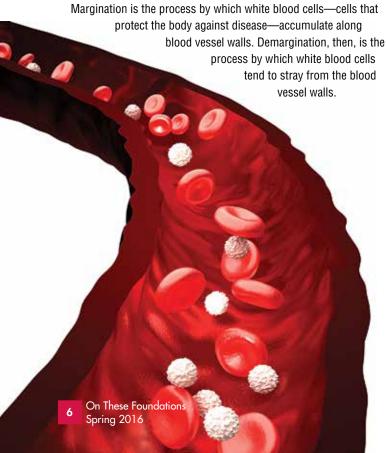
Through simulations, Graham's group discovered a variable—the margination parameter—which determines a white blood cell's propensity to demarginate. The higher the parameter, the higher the likelihood the cell will demarginate—so as white blood cells become softer due to the presence of the steroid drugs, the velocity of the cells increases, and they are far more likely to find a

new equilibrium position further away from blood vessel walls. Lam's experiments corroborated the theory: When white blood cells are exposed to glucocorticoids, for instance, their cytoskeletonwhich gives the cell structure, among other functions—tends to loosen, and the cytoskeleton's internal network of filaments decreases in density. Lam measured white blood cells' stiffness using atomic force microscopy—and the reduction in stiffness corresponded to

the degrees of margination Graham observed computationally.

Graham, who refers to crossing paths with Lam as a matter of serendipity, foresees many potential avenues of future research based on their findings. For people who have sickle cell disease, stiff cells can cause irritation along the wall of the blood vessel; Graham and Lam are now working to understand that phenomenon. Future applications also could include detecting cancer cells that escape from a tumor and cause cancer to metastasize. "There are people who are making microfluidic devices to conduct certain separation processes," Graham says. "If you segregate certain cells, you can remove them—and now we have a theory that underlies that."

Other authors on the paper include Amit Kumar of UW-Madison. and Wilbur A. Lam, Meredith E. Fay, David R. Myers, Cory T. Turbyfield, Rebecca Byler, Kaci Crawford, Robert G. Mannino, Alvin Laohapant, Erika A. Tyburski, Yumiko Sakurai, Michael J. Rosenbluth, Neil A. Switz, and Todd A. Sulchek of Georgia Tech. Funding for the research came from the National Institutes of Health. National Science Foundation and American Heart Association as well as the Harvey D. Spangler Professorship.



UW-Madison engineers create custom tuning knobs to turn off any gene

Factory managers can improve productivity by telling workers to speed up, slow down, or stop doing tangential tasks while assembling widgets. Unfortunately for synthetic biologists attempting to produce pharmaceuticals, microbes don't respond to simple spoken directions like human personnel. Now, however, an advance allows scientists fine-tune biological functions in their bacterial employees.

Synthetic biology has progressed by leaps and bounds since researchers first induced *E. coli* to make human insulin in the 1970s. Today, biological engineers coax microorganisms to perform numerous complex chemistries, such as breaking down plant material for biofuels. However, scientists still rely on a limited complement of components to control their synthetic circuits.

"We were frustrated because synthetic biology is littered with examples of artificial factors that can turn on and turn off gene expression under different conditions, but they only work for

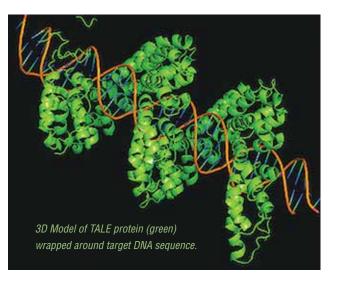
certain genes," says Brian Pfleger, the Walter J. and Cecile Hunt-Hougen Faculty Scholar and an associate professor.

Pfleger's group developed a way to turn off almost any gene in *E. coli*. Their approach, published Feb. 8, 2016, in the advance online edition of the journal *Nature Chemical Biology*, borrowed a trick from nature to achieve human goals. The team modified proteins called TALEs to make tools that seek and silence diverse arrays of genes. TALE proteins come from bacteria that normally infect plants—the bugs typically inject TALEs into plant cells to make them more susceptible to infection. "These pathogens piggyback on the molecular biology of higher organisms to manipulate them," says PhD student Mark Politz, the lead author on the paper. "It's kind of an ingenious little trick they're playing on their host."

Politz and Pfleger took advantage of the same sneaky strategy. Natural TALEs attach to specific sections of plant genomes. The protein reads the DNA sequence and wraps itself around specific regions of the double helix like a boa constrictor. Once a TALE finds its target, it recruits the plant's own machinery to activate nearby genes. Previous research established which parts of the TALE recognize specific letters in the DNA alphabet, giving the Pfleger group a way to program these proteins to target any sequence they desired. Additionally they tweaked the TALEs so that the proteins repressed rather than promoted gene expression.

The engineered TALEs allowed them to temporarily turn off specific genes, without drastically altering the original organism.

"The great possibility for using TALEs is adding another layer of gene regulation that we can apply over top of what's already present in the natural bacteria," says Politz.



Scientists can easily erase genes by removing sections of DNA from some bacterial genomes. However, large deletions lack subtlety and often carry unforeseen consequences.

"Instead of going in and messing up all of the things nature has created in the cell, I just want to make less of a protein. And I want to do it in an inducible manner. I want to make less only when I want to make less," Politz says.

Counterintuitively, the most significant obstacle to creating the tool was finding a way to turn off the off-switch. Once TALEs wrap themselves around their target, they typically remain in position, exerting

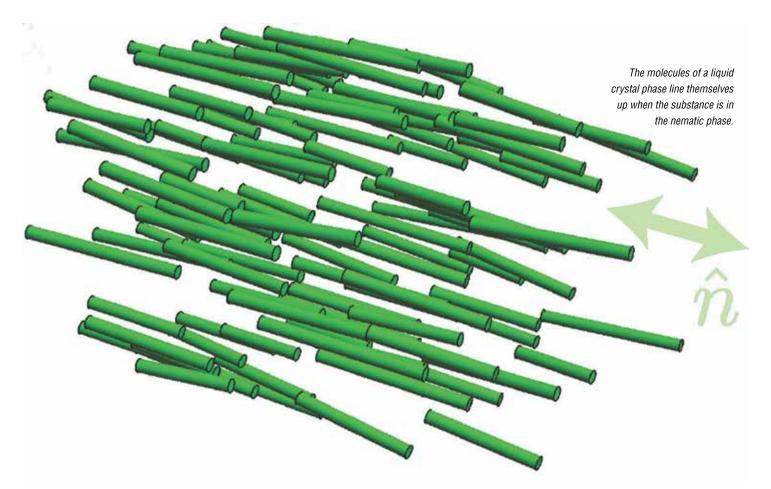
their effects indefinitely. In order to engineer a truly inducible system, the team introduced a deactivation mechanism.

The results established proof of principle in *E. coli*, one of the most commonly used organisms in modern biology. However, the researchers see applications for their approach across the tree of life.

"The tools that Mark's been developing are an example of what's taking place in biotechnology right now," says Pfleger. "We're generalizing what we could do with organisms that have better inherent properties, like metabolisms that would be useful for biofuels."

Several members of the Pfleger group contributed to the effort. Former postdoctoral scholar Matt Copeland, now employed at Proctor & Gamble, designed several experiments and worked with Politz to write the manuscript. Andrew Markley, a postdoctoral fellow, ideated an important control. Charles Johnson, an undergraduate researcher who is now pursuing a PhD at Washington University in St. Louis, was instrumental in designing the TALEs.

The research was funded by grants from the National Science Foundation, the National Human Genome Research Institute, and the National Institutes of Health.



Squished cells could shape design of synthetic materials

ife is flexible. All living cells are basically squishy balloons full of water, proteins and DNA, surrounded by oily membranes.

Those membranes stand up to significant amounts of stretching and bending, but only recently have scientists started to fully appreciate the useful organization and functions that result from all that stress.

Inspired by this emerging understanding, a multidisciplinary group working within the Materials Research Science and Engineering Center (MRSEC) at UW-Madison is trying to recreate aspects of those broad design principles in synthetic systems comprised of simple membranes and complex fluids.

The researchers' results, published May 2, 2016, in the journal *Proceedings of the National Academy of Sciences*, reveal that previously unappreciated parameters can shape soft materials like biological membranes.

"What we're trying to do is take design principles in bacteria and see if we can translate them to synthetic systems," says Nick Abbott, MRSEC director and John T. and Magdalen L. Sobota and Hilldale Professor. "This is a model, trying to recreate some of the properties of bacteria to understand, in a simpler system, what's going on."

One of the key ideas in the paper is that strain in complex fluids and membranes can be shared in unanticipated ways to control the shape and properties of soft materials.

Scientists previously hypothesized that membrane strain plays a role in how living organisms control the compositions of different areas on their cells' surfaces. For example, paper co-author Douglas Weibel, a professor of biochemistry at UW-Madison, investigates how elastic energies in the membrane may shift cellular components to the curved ends of bacterial cells.

For their model, the researchers made tiny synthetic shells, called vesicles, composed of materials similar to the membranes that surround living cells. The miniature spheres approximated biological membranes, without any of life's complicated internal machinery or external decorations to confound the results.

To squeeze, stress and strain the membrane orbs, the researchers suspended the vesicles inside a complex fluid called a liquid crystal.

Liquid crystals, such as those widely used in digital watch displays, can exist in different states. Like most liquids, their components move around freely in all directions. At specific temperatures or electromagnetic conditions, however, the molecules making up liquid crystals adopt similar orientations, leading to so-called nematic phases in which they are all pointed in the same direction.

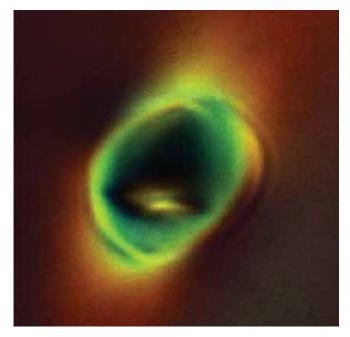
Previous research established that objects floating in liquid crystals can influence the molecular alignments of a nematic phase. But liquid crystals don't just passively accommodate disruptions. These complex fluids push back on rigid objects.

Nobody knew what would happen, however, if something soft and squishy like a synthetic vesicle got into the mix.

The researchers observed that switching on the nematic phase caused distortions in the floating orbs. But not every vesicle reacted in the same manner. While the larger spheres remained round overall, smaller spheres became highly pinched and flattened, squeezed into elongated shapes akin to American footballs.

To untangle the energetic mechanisms at play, the team enlisted the expertise of UW-Madison mathematics professor Saverio Spagnolie. Using an entirely new numerical technique, Spagnolie calculated the forces that could be responsible for the distinct patterns of deformation they observed.

The physics responsible for those shapes took everybody by surprise. "Usually when people think about membranes, the primary



Microscopic image shows dramatic deformation of soft vesicles floating inside liquid crystals in the nematic phase.

forces they consider are associated with elasticity," says Spagnolie. "But it turns out that the bending stiffness has absolutely nothing to do with the shapes that we see in this work."

Counterintuitively, a competition between surface tension and elasticity of the liquid crystal drove the distortion in the vesicles, completely independent of stiffness or flexibility in cell membranes. "Going into the problem, there was no obvious reason to think that surface tension would be a relevant piece of the puzzle," says Spagnolie.

Moving forward, the researchers hope to further clarify the source of the surface tension in the system. They also intend to investigate whether similar forces could mold the local compositions of membranes made from mixed components akin to the surfaces on living cells.

Support from the National Science Foundation-funded MRSEC, which brings together scholars from multiple disciplines to tackle complex problems in materials science, made the research possible.

Peter S. Mushenheim, a former graduate student in Abbott's laboratory, was lead author on the paper.





Several CBE students recognized for outstanding research and service

ur undergraduate students are highly intelligent, motivated and creative. They are using their skills and passion to conduct impressive research in fields as diverse as the inside of the human mind to a galaxy far, far away—and they've earned Hilldale Undergraduate/Faculty Research Fellowship funding from UW-Madison to support their efforts. Those students include:

- **Cyrus Colah**—"Development of nanoparticle-based artificial antibodies for the detection of cardiac troponin-I" (with advisor Ying Ge)
- Madeline Faubion—"Analyzing the mechanism of tight junction proteins in human stem cell blood brain barrier model" (with advisor Eric Shusta)
- Michael Khor—"Dissecting the physiological response of microbial assemblages performing phosphorus removal" (with advisor Katherine McMahon)
- Zachary Konz—"Building a novel electrochemical reactor for green industrial alcohol oxidation: Pharmaceuticals and fine chemicals" (with advisor Shannon Stahl)
- Zachary Matusinec—"Synthesis of atomically thin transition metal dichalcogenides heterostructures: Exploring the fundamentals of next-generation solar devices" (with advisor Song Jin)

- **Daniel Vigil**—"Connecting thermodynamics to kinetics: A DFT study of Bronsted-Evans-Polanyi correlations at high coverage on transition metal catalysts" (with advisor Manos Mavrikakis)
- **Bo Zhang**—"Influence of defect cores on the process of defect annihilation" (with advisor Nick Abbott)
- **Jingyi Zhao**—"User-friendly synthesis of amides under ambient air using copper/nitroxyl-catalyst" (with advisor Shannon Stahl)

Additionally, one of our students earned the University Book Store award for academic excellence:

 Thejas Wesley—"Probing interfacial water-gas shift surface chemistry on platinum-molybdenum and platinum-ceria catalysts" (with advisor Jim Dumesic)

ALUMNI NEWS—Send us your news: che@che.wisc.edu



Mahriah Alf (BS '06) was promoted to project manager at Mars & Co., at the management consulting firm's San Francisco office. She began her career with the company as a senior associate consultant in its New York City-area office in 2011, after earning her PhD in chemical engineering from MIT. Her responsibilities have included high-profile engagements for some of the firm's major consumer packaged goods, consumer durable goods, and retailing clients in both the United States and in Latin America. In addition, she also is involved in the firm's recruiting efforts and is a standout performer on its triathlon teams.

Joseph Martinelli (BS '02), a senior research scientist in small molecule design and development with Eli Lilly & Co., was among the recipients of the American Chemical Society Award for Affordable Green Chemistry. Joseph shares the award with colleague Martin Johnson and Shannon Stahl, the John & Dorothy Vozza Professor of Chemistry at UW-Madison. The organization cited the trio for chemistry and engineering advances that enable commercial application of scalable aerobic oxidation reactions in the development and manufacture of pharmaceuticals.

Momentum builds behind **Dumesic's new biomass process**

or a world hooked on fossil carbons, the vials of amber syrup in Jim Dumesic's lab are full of sweet potential. Dumesic's group caused a stir in research circles and the media in 2014 by publishing a paper in the journal Science describing a new scheme for breaking down biomass and unlocking its polysaccharides. Those sugars—candy for microbes—can be fermented to ethanol or upgraded into a host of high value chemicals currently made from petroleum.

At the crux of their fast, inexpensive method is a solvent derived from biomass itself, called gamma valerolactone (GVL). It's an elegant process. The GVL created in the reaction is recycled and used to drive it again. "Our process can work in a matter of hours and on any biomass we have ever used, such as corn stover, wood, leftovers



Dumesic and graduate student Ali Hussain Motagamwala are optimizing an exciting new biomass process.

from sugar cane and residues from paper mills," says Dumesic, the Vilas Research Professor and Michel Boudart Professor.

Now, Dumesic and colleagues have proved their method can scale up. He reports that the team has bumped up production by 80-fold, with sugar yields topping 75 and 65 percent for xylose and glucose, respectively. Along the way they've learned to streamline steps and optimize factors like reaction temperature and acid concentration.

In addition to the sugars, they're also producing strong streams of "native" lignin that can be used for a variety of products from construction materials to paint. ("Native" means the lignin is not chemically altered by the process and therefore prized by researchers normally restricted to the byproducts of paper mills.)

Achieving these milestones took an unexpected collaboration. Colleagues in engineering and at the Forest Products Laboratory helped Dumesic augment a reactor already in use, saving significant time and resources.

He credits the WARF Accelerator program for bringing the two camps together. "The funding enabled us to work with the Forest Products Laboratory to modify their apparatus. Without that we never could have scaled up to the two-liter level. No way," he says.

Now, those same colleagues are interested in taking things to the next level by designing an extruder system that operates in a continuous flow mode, like a real refinery. "That means we need a system that takes biomass, feeds it to a reactor and sends it through in a continuous process," says Dumesic. "No one has been able to do that yet."

More: www.engr.wisc.edu/momentum-builds-behind-jim-dumesics-new-biomass-process/





The GVL reaction progressively dissolves biomass into product streams rich in (left to right) lignin, hemicellulose and cellulose-derived sugars.

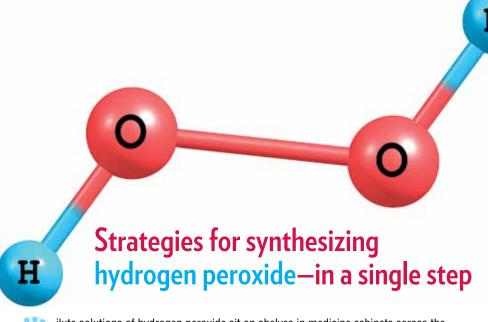
BIOMASS BLUES Breaking up not so hard to do

Using a chemical crowbar—actually, a solvent—made from the very organic matter it deconstructs, a CBE spinoff business is advancing an audacious effort to convert plant waste, or biomass, into three profitable streams of industrial chemicals.

Vilas Research Professor and Michel Boudart Professor Jim Dumesic's discovery of a new way to tear apart biomass is the basis for GlucanBio, a St. Louis company licensed by the Wisconsin Alumni Research Foundation (WARF) to use patents from Dumesic's lab.

Biomass contains three groups of compounds: cellulose, hemicellulose and lignin. All three can be useful, if they can be produced at the right price. The process that Dumesic pioneered in research supported by the Great Lakes Bioenergy Research Center can split biomass into three separate streams. Glucan's hurdle is to prove that this process is both workable and profitable on the industrial scale. And, the company's future rests on its ability to profit from all three streams, says CEO Larry Clarke. "Several companies can take biomass and make one stream and either destroy the other two, or create low-value products from them. A few now use two streams, but if you can only do one or two, in real-world economics, it tends not to work. We are working on the trifecta, using three of the three revenue streams."

More: www.engr.wisc.edu/biomass-bluesbreaking-not-hard/



ilute solutions of hydrogen peroxide sit on shelves in medicine cabinets across the world. Yet synthesizing the chemical on large scales requires a surprisingly complicated process that is economically unfeasible for all but a few industrial facilities. One significant challenge can be stabilizing hydrogen peroxide once it forms because of its propensity to break down during synthesis.

Now, chemical and biological engineers have uncovered new insight into how the compound decomposes. This advance, published March 21, 2016, in the *Proceedings of the National Academies of Sciences*, could inform efficient and cost-effective single-step strategies for producing hydrogen peroxide. "A single-pot reaction would permit on-site production and make hydrogen peroxide an economically feasible oxidant for a number of chemical processes, in particular to replace more environmentally harmful oxidants such as chlorine," says PhD student Tony Plauck, first author on the paper.

Scientists first proposed a single-step procedure to synthesize hydrogen peroxide in 1914 by combining pure hydrogen and oxygen gases over a catalyst.

Unfortunately, as more and more of the final hydrogen peroxide product accumulates in the vessel containing the mixture, the catalyst can also facilitate a subsequent undesirable chemical reaction wherein hydrogen peroxide breaks down into oxygen gas and water in a process called decomposition.

"One of the biggest catalytic challenges is finding a material that can actively produce hydrogen peroxide, but also something inactive toward decomposing hydrogen peroxide, which is a very thermodynamically favorable reaction," says Plauck.

Some of the most widely studied materials for direct hydrogen peroxide synthesis are palladium-based catalysts—yet, palladium can also catalyze the decomposition reaction.

"Typical palladium catalysts exist as tiny highly dispersed palladium nanoparticles, which contain a variety of surface features that may vary in their ability to decompose hydrogen peroxide. If we understand where and how does hydrogen peroxide primarily decompose, we can propose some design criteria for future iterations of palladium catalysts," says Plauck.

Plauck and his advisors, Vilas Distinguished Achievement Professor and Paul A. Elfers Professor Manos Mavrikakis and Vilas Research Professor and Michel Boudart Professor Jim Dumesic, used both theoretical and experimental approaches to describe the decomposition reaction. Their results suggested that multiple surface features of palladium nanoparticles can significantly contribute to the overall hydrogen peroxide decomposition activity of these catalysts. And, the theoretical models provided detailed insight into how the decomposition

The work was supported as part of a Dow Chemical Company university partner initiative with UW-Madison. Eric E. Stangland of Dow also contributed to the research.

reaction might be suppressed on palladium.

Two generations
of faculty and graduate students,
connected by the generosity of CBE alum R. Fenton-May
(standing, right). Fenton-May sponsored a graduate fellowship
that supported student Tony Plauck (standing, left), the first author
on the paper. Plauck's advisor, Professor Manos Mavrikakis (left), is
seated next to Fenton-May's former advisor, Professor Charlie Hill (right).



Digging into a biological tool patent

Patent secured by the Yin group enhances single-cell research

John Yir

ncremental changes can reap big rewards. And, recently,
Professor John Yin, who also is the systems biology theme
leader in the Wisconsin Institute for Discovery, and his former
students Jay Warrick and Stephen Lindsay, received U.S. Patent
No. 8,945,486 B2 for improvements to a microwell device.

Microwell devices are fairly common tools in biological lab settings; however, the group's modifications were significant.

Yin and his students study the Vesicular stomatitis virus, which contains only five genes and makes it ideal for modeling how it produces more virus. Warrick's background includes physics and mechanical engineering, and his biomedical engineering thesis work under John D. MacArthur Professor and Claude Bernard Professor of Biomedical Engineering David Beebe, an expert in microscale tools, involved surface tension and passive pumping.

Passive pumping is the principle that small droplets, which have a small radius and therefore high internal pressure, could pump their contents to larger droplets, which in turn have a larger radius and therefore lower internal pressure. This study of water droplets and surface tension turned out to be an ideal fit for improving the types of experiments Yin and his students were performing.

Lindsay had been working on quantifying single cell fluorescence experienced challenges putting the cells on a traditional culture. When infections occurred, it became very hard to keep track of a single cell, as the cells were dying and crawling over one another. There was so much prep work and handling that although the method was accurate, it yielded very few data points. The challenge was how to increase the throughput.

Warrick and Lindsay felt that using microwells would be a good option. "You would literally pour fluid over all the wells so stuff falls in. Your cells fall in there, your viruses diffuse in there and then you seal it with a lid; that separates each well. By doing this we can shrink everything down to the scale of a cell and we can do thousands of these experiments in under a few drops," says Warrick.

However, working with a standard microwell can be messy. Armed with his background in passive pumps, Warrick decided to leverage

surface tension: A droplet beads up and defines a region on the microwell array. That's the source of the invention.

To help define the region of that droplet, Warrick built a "moat" of air into the microwell so the droplet expands until it reaches the end of the moat but goes no further because of surface tension. Essentially, adding that moat now enables researchers to address the enhanced microwells using

a hand pipette or liquid handling automation and high throughput screening applications where

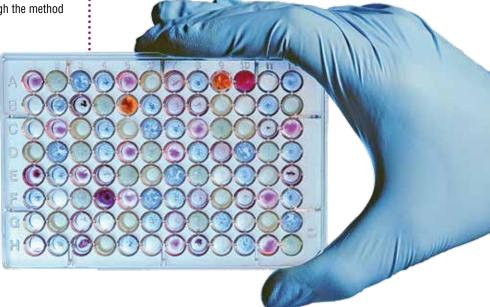
robots move pipettes.

Initial screening approval, back and forth with the Wisconsin Alumni Research Foundation patent attorneys, and the patenting process itself took more than 18 months.

In the interim, Lindsay earned his PhD and now works as a research scientist at Kimberly-Clark. Warrick now is a postdoctoral researcher in Beebe's group and still works with

the microwells, this time studying prostate cancer and multiple myeloma. He foresees future uses of this technology for single cell polymerase chain reaction and single cell secretion assays.

Eventually he thinks it could be used as a unique assay that would provide a clinical readout on patient samples to determine responses to a therapy.



Two join ranks of biomedical elite

In 2016, the American Institute for Medical and Biological Engineering (AIMBE) named four UW-Madison engineering faculty members—among them, two from our department—fellows of the institute.

Their election places them in the top-2 percent of biomedical scientists working in the United States; to be part of this elite group of only 1,500 members of the AIMBE College of Fellows, researchers must demonstrate a commitment to embracing innovation in the service of improving the healthcare and safety of society.



Nicholas Abbott, the John T. and Magdalen L. Sobota Professor and Hilldale Professor, researches the materials that make up

and surround living cells. In a recent *PNAS* publication, Nick and colleagues in the Department of Biochemistry and the Department of Mathematics developed a synthetic system to understand the interplays of forces that shape biological membranes in complex fluids.



Associate Professor and Spangler Faculty Fellow **Jennifer Reed**'s research defies classification into a single silo. As a quantitative

and systems biologist, she uses massive mathematical models to uncover new strategies for making useful chemicals with bacteria. Her work recently revealed that *Escherichia coli* bacteria potentially could be coaxed into synthesizing more than 50 commercially important compounds from the common sugar pyruvate in fewer than five chemical steps.

In addition to Jennie and Nick, AIMBE also named Lynn H. Matthias Professor and Vilas Distinguished Achievement Professor of Electrical and Computer Engineering Hongrui Jiang and Vilas Distinguished Achievement Professor of Biomedical Engineering Justin C. Williams fellows of the institute. The four new elections bring the total number of UW-Madison faculty in the AIMBE College of Fellows to 26.

FACULTY/STAFF NEWS



Dumesic



Huber

Jim Dumesic, the Vilas Research Professor and Michel Boudart Professor, and **George Huber**, the Harvey D. Spangler Professor, were both named to the 2015 Thomson-Reuters highly cited researchers list, which recognizes some of the most influential voices in science. The 3,000 researchers on the list were chosen based on having written the greatest number of reports designated by essential science indicators as highly cited. Their research papers ranked among the top 1-percent most cited for their field and year of publication.

George also has made the *Biofuels Digest* list of the top 100 people in the advanced bioeconomy for 2016. George was ranked No. 58 on the list. The readers of *Biofuels Digest* and the trade publication's editorial board nominated and voted on the top 100 people to be included on the list. George studies a class of catalysts that are used to make fuels, chemicals and fertilizers. He is currently investigating how similar catalysts can be used to make renewable gasoline, diesel and jet fuel, all of which have a low carbon footprint and are made from domestically available biomass resources. Researchers

have used expensive precious metal catalysts such as platinum for biomass conversion. George's research group, however, has been working to develop new catalytic materials that are orders of magnitude cheaper than precious metal catalysts.



Graham

Mike Graham, the Vilas Distinguished Achievement Professor and Harvey D. Spangler Professor, has delivered several invited lectures this past academic year. In February 2016, he gave the talk, "Stokes flow, Green's functions and advanced Brownian dynamics," at the CECAM workshop on Hydrodynamic Fluctuations in Soft-Matter Simulations, Prato, Italy. In November 2015, he delivered a plenary lecture at the Chemical Engineers in Medicine topical conference during the AIChE annual meeting; in October 2015, he spoke to attendees at the UW-Madison Engineers' Day event, and

in July 2015, he gave a plenary lecture at the Brazilian Conference on Rheology, Curitiba,

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Seven faculty honored with UW-Madison Vilas awards

Extraordinary members of the UW-Madison faculty were honored in May with awards supported by the estate of Professor, Senator and Regent William F. Vilas (1840-1908).

Jim Rawlings and **John Yin** were among faculty recipients of Vilas Distinguished Achievement Professorships, an award recognizing distinguished scholarship as well as standout efforts in teaching and service. The professorship provides flexible funding over five years—two-thirds of which is provided by the Office of the Provost through the generosity of the Vilas trustees, and one-third provided by the school or college whose dean nominated the winner.

Additionally, **George Huber**, **Dan Klingenberg**, **Regina Murphy** and **Eric Shusta** received Vilas Faculty Mid-Career Investigator Awards, recognizing research and teaching excellence. The award provides flexible research funding for one year.

Brian Pfleger received a Vilas Faculty Early Career Investigator Award, recognizing research and teaching excellence in faculty who are relatively early in their careers. The award provides flexible research funding for one year.



UW-Madison Chancellor Rebecca Blank, John Yin, and Provost Sarah Mangelsdorf.



Codner earns college achievement award

On Feb. 11, 2016, College of Engineering Dean Ian Robertson honored eight individuals whose service to the college and to their profession goes above and beyond. Each of these people was nominated by—and chosen by a committee of—their peers.

Recipient of the Bollinger academic staff award, Eric Codner is known within the department as a selfless leader, an enthusiastic teacher and an experienced, go-to lab expert. As the undergraduate laboratory manager for the department, he maintains and updates lab equipment, using his skills as an analytical chemist to make informed improvements and develop new experiments for students. Says department chair Manos Mavrikakis: "He greets every problem as an opportunity and avoids nothing."

Eric's expertise extends far beyond the laboratory. He also teaches a number of courses, including *Instrumental Techniques* and *Chemical Engineering Materials*, an important senior-level course—and he receives high praise from his students, who laud the interest, expertise

and the passion he brings to a classroom. In fact, Eric once designed a game of *Jeopardy!* to help students in the *Transport Phenomena* laboratory course study. Eric's creative, innovative approaches in both the lab and the classroom show his dedication to the department, and his deep passion for the skills and principles underlying an education in engineering.



CBE undergrad receives prestigious Goldwater scholarship

our UW-Madison students—including two from the College of Engineering—have received the Barry M. Goldwater Scholarship for undergraduate excellence in the sciences. CBE undergraduate Thejas Wesley is among the recipients. Out of the 1,150 nominations received in 2016, 252 scholars were named nationwide. All four of UW-Madison's nominees received the award.

Thejas is a junior from Madison. He hopes to earn his doctorate in chemical engineering, conduct research in heterogeneous catalysis.



Thejas Wesley

and ultimately teach at the university level.

Congress established the Barry M. Goldwater Scholarship and Excellence in Education Program in 1986. The program aims to develop highly qualified scientists, engineers and mathematicians through its undergraduate scholarship award.



Department of Chemical & Biological Engineering 1415 Engineering Dr. Madison, WI 53706



Kuech, Robertson elected Materials Research Society fellows



Tom Kuech, the Milton J. and A. Maude Shoemaker Professor in chemical and biological engineering, and Ian M. Robertson, the dean of the College of Engineering, were elected as Materials Research Society fellows.

Kuech was recognized for his use of chemical vapor deposition of compound semiconductors for forming optical and electronic devices. His research focuses on methods of forming compound semiconductors, which drive high-power devices such as those used for wireless and optical telecommunications. He has made significant developments in the realm of chemical vapor deposition, a method for developing semiconductors with controlled electronic and optical properties.

Robertson was honored for his contributions to the understanding of processes associated with the degradation of materials exposed to extreme conditions, as well as

his leadership in the materials community. Formerly the Donald B. Willett professor of engineering at the University of Illinois and director of the National Science Foundation Division of Materials Research, Robertson focuses his research on how microstructure evolves in materials in extreme conditions, encouraging greater knowledge of macro-scale material changes.

The MRS fellowship, which is highly selective, recognizes members for their significant contributions to materials research. MRS Fellows will be honored at the MRS 2016 spring meeting in Phoenix, Arizona.

