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Chemical and Biological Engineering

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Researchers Gain Fuller Picture of Cell Protein Reactions

UNIQUE PEPTIDE ARRAY TECHNOLOGY PROVIDES FAST, LOW-COST, LABEL-FREE METHOD FOR UNDERSTANDING PROCESSES THAT MODULATE PLATELET PRODUCTION

William Miller

Milan Mrksich

Northwestern University researchers have developed a new technique for profiling enzyme activities in cell lysate, a fluid containing the internal contents of cells. The process uses surfaces that present an array of peptides that each interact with enzymes in a lysate. The changes the enzymes make to the peptides can be directly read using a laser to determine the changes in mass of those peptides.

William Miller, professor of chemical and biological engineering, initiated the project to find new methods for growing blood platelets in cultures. Transfusions of platelets—tiny cells in the blood that promote clotting—can prevent complications from bleeding, but maintaining supplies of the cells is challenging because several donors are often required to collect one transfusion and samples must be used within days.

Researchers can grow platelets by differentiating blood stem cells into megakaryocytes, the cells in bone marrow that produce platelets, but the process falls far short of nature. In humans, megakaryocytes undergo DNA replication without cell division to form giant cells that extend processes called proplatelets and produce thousands of platelets, but in culture they produce fewer than 10 because the cells do not get as large and many die before they release platelets.

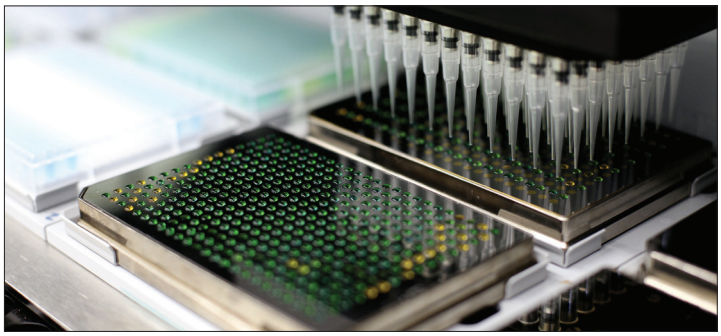
Miller's colleague, Milan Mrksich, the Henry Wade Rogers Professor of Biomedical Engineering, Chemistry, and Cell and Molecular Biology at McCormick, had been developing bioanalytical techniques for just this type of problem. The two partnered with graduate students Teresa DeLuca (chemical and biological engineering) and Hsin-Yu Kuo (chemistry) to profile a cell line model of the bone marrow cells that produce platelets.

> "With SAMDI mass spectrometry, we obtain a global picture of how complex cell functions are regulated."
> *Milan Mrksich*

"If we understand the enzyme activities that occur during megakaryocyte differentiation, it may be possible to prevent or promote differentiation for platelet production and other purposes," Miller said.

Using Mrksich's unique process of self-assembled monolayers desorption ionization (SAMDI) mass spectrometry, a super-fast, low-cost, and "label-free" method of measuring biochemical activities on a surface, the researchers were able to identify patterns of enzyme activities in cell lysates. The technique allowed them to separately tether hundreds of different acetylated peptides to a gold-plated surface, then introduced lysate to see if a reaction would occur. When the reaction was complete, the plate was struck with a laser that released the peptides from the gold base. The contents of each site were weighed, allowing researchers to make an educated assumption about what occurred in each reaction.

"Until now, measuring the activity of enzymes in cell lysate has been a tremendous challenge because lysates contain tens of thousands of different molecules," Mrksich said. "With SAMDI mass spectrometry, we can use arrays having thousands of peptides to identify those many activities, and through sophisticated analysis we obtain a global picture of how complex cell functions are regulated."



A paper about the research was published as an Editor's Highlight in the journal *Analytical Chemistry*.

Building ‘Smart’ Cell-Based Therapies

LIVING DEVICES MAY SELECTIVELY KILL CANCER CELLS WITHOUT DISRUPTING HEALTHY CELLS

A Northwestern synthetic biology team has created a new technology for modifying human cells to create programmable therapeutics that could travel the body and selectively target cancer and other sites of disease.

Engineering cell-based, biological devices that monitor and modify human physiology is a promising frontier in clinical synthetic biology. However, no existing technology enabled bioengineers to build such devices that sense a patient’s physiological state and respond in a customized fashion.

“The project addressed a key gap in the synthetic biology toolbox,” said Joshua Leonard, assistant professor of chemical and biological engineering. “There was no way to engineer cells in a manner that allowed them to sense key pieces of information about their environment, which could indicate whether the engineered cell is in healthy tissue or sitting next to a tumor.”

Leonard’s team worked for nearly four years to close this gap. The end result is a protein biosensor that sits on the surface of a cell and can be programmed to sense specific external factors. For example, the engineered cell could detect big, soluble protein molecules that indicate that it’s next to a tumor. When the biosensor detects such a factor, it sends a signal into the engineered cell’s nucleus to activate a gene expression program, such as the production of tumor-killing proteins or chemicals. Since this toxic program would be activated only near tumor cells, such an approach could minimize side effects as well as improve therapeutic benefits.

Called a Modular Extracellular Sensor Architecture (MESA), the biosensor platform is completely self-contained so that several different biosensors can be present in a single cell without interfering with one another, allowing bioengineers to build increasingly sophisticated functional programs. The platform is also highly modular, enabling the biosensors to be customized to recognize factors of relevance to various patients’ needs.

“By linking the output of these biosensors to genetic programs, one can build in a certain logical command, such as ‘turn the output gene on when you sense this factor but not that factor,’” Leonard explained. “In that way, you could program a cell-based therapy to specify which cells it should kill.”

Leonard said doctors could potentially collect immune cells from a patient’s body, engineer the cells using MESA, and put them back into the patient. From there, the cells would do the work of detecting cancer or the disease they are designed to identify.

This is the first completely ground-up engineering of a receptor, and now that the core technology has been established, Leonard’s team is moving forward to program cells to recognize specific tumor-associated factors. They are also looking toward applications beyond advanced cell-based therapies.

“This seems to be what always happens in synthetic biology,” he said. “When you start building something, you first learn a lot about the system that you are trying to modify. In the end, you come up with not only useful applications but tools that facilitate basic science.”

Joshua Leonard

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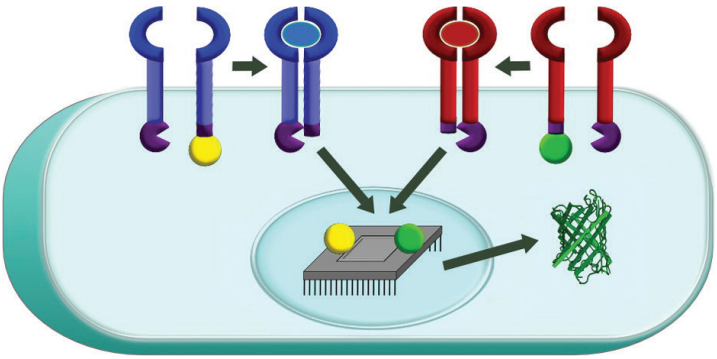


A new technology for engineering human cell-based devices can monitor and modify human physiology.

McCormick Professors Evaluate Energy Efficiency and Sustainabilty

MASANET RECENTLY ANALYZED MOVIE WATCHING AND INTERNET STORAGE; YOU EXAMINED SOLAR PANELS

What's greener: streaming a movie or renting a DVD? McCormick professors Eric Masanet and Fengqi You are answering questions like this by using life-cycle analysis of products and processes to quantify the effects of current and future technologies.

Masanet, associate professor of mechanical engineering and chemical and biological engineering, recently led two projects: one examining the most efficient way to watch a movie and another to evaluate different types of Internet storage.

Moving streaming vs. DVDs

In the first project, Masanet found that watching a live stream of a movie can be more energy-efficient than watching the movie on DVD, especially if the latter involves driving to a rental or retail store to rent or buy the DVD. Masanet and his collaborators studied five different ways of viewing movies and, using a systematic method called life-cycle analysis, estimated the energy used and carbon dioxide emissions produced for each. They determined that video streaming can be more energy efficient and emit less carbon dioxide than the use of DVDs, depending on the DVD viewing method.

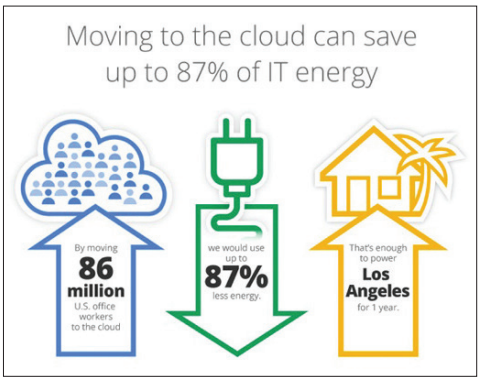
"End-user devices are responsible for the majority of energy use with both video streaming and DVD viewing," Masanet said. "Much of the energy savings estimated in shifting to video streaming comes from shifting end-user devices to more energy-efficient alternatives—in other words, away from old DVD players."

The researchers compared five basic movie-viewing cases: watching a movie live-streaming over the Internet, renting a DVD through a mail-based service, renting a DVD at a local store, buying a DVD from an Internet source and receiving it in the mail, and buying a DVD at a local store.

Estimating the life-cycle energy use of the various cases required accounting for the energy used to manufacture DVDs; to transport DVDs by mail truck; to drive to and from local stores and rental locations; to stream movies over the Internet; and to manufacture and operate the in-house devices ultimately used to watch the movies.

The study estimates that the total video viewing in the United States in 2011 required about 192 petajoules of primary energy and emitted about 10.5 billion kilograms of carbon dioxide. Shifting all DVD viewing in 2011 to video streaming would have reduced the total primary energy use to about 162 petajoules and the carbon dioxide emissions to about 8.6 billion kilograms. This figure represents a savings equivalent to the primary energy used to meet the electricity demand of nearly 200,000 US households each year.

The study also shows that data transmission energy and consumer travel account for significant portions of the total streaming video and DVD viewing energy use. Streaming data at a higher rate to support complex video increases the energy use of streaming beyond that of DVD viewing. Reducing the consumer energy use of travel to and from store locations makes the DVD viewing of movies more energy-efficient than streaming.



Eric Masanet; a schematic shows the breakdown of how moving Internet storage to the cloud can save energy.

"We can't fly by the seat of our pants when it comes to assessing sustainability. Well-thought-out analysis is especially important with new technology, which can have unforeseen effects." *Eric Masanet*

Moving Software to the Cloud

In Masanet's second study, his team found that moving common software applications used by 86 million US workers to the cloud could save enough electricity annually to power Los Angeles for a year.

Researchers looked at three common business applications—email, customer relationship management software, and bundled productivity software (spreadsheets, file sharing, word processing, etc.). Moving these software applications from local computer systems to centralized cloud services could cut information technology energy consumption by up to 87 percent—about 23 billion kilowatt-hours. This is roughly the amount of electricity used each year by all the homes, businesses, and industry in Los Angeles.

A primary goal of the project was to develop a state-of-the-art model that both researchers and the general public could use to analyze the energy and carbon impacts of cloud computing. This is the first time such a model is available to the public in open-access form.

"We can't fly by the seat of our pants when it comes to assessing sustainability," Masanet said. "We need numbers—hard data—to properly analyze how cloud computing compares to how computing is done now. Well-thought-out analysis is especially important with new technology, which can have unforeseen effects. Our public model allows us to look forward and make informed decisions. What we found overall is that by hosting services on the cloud as opposed to locally, the savings are pretty robust."

Fengqi You

Environmental Costs of Solar Panels

You, assistant professor of chemical and biological engineering, led new research comparing the environmental costs of solar panels manufactured in China and Europe. His team found that solar panels made in China have a higher overall carbon footprint and are likely to use substantially more energy during manufacturing than those made in Europe.

"We estimated that a solar panel's carbon footprint is about twice as high when made in China and used in Europe, compared to those locally made and used in Europe," said You. "While it might be an economically attractive option to move solar panel manufacturing from Europe to China, it is actually less sustainable from the life-cycle energy and environmental perspective— especially under the motivation of using solar panels for a more sustainable future."

The team performed life-cycle analysis to come up with these hard data. Life-cycle analysis tallies up all the energy used to make a product—energy to mine raw materials, fuel to transport the materials and products, electricity to power the processing factory, and so forth. This provides a more accurate picture of the overall energy consumed and produced and the environmental impact of making and using a solar panel.

Assuming that a solar panel is made of silicon—by far the most common solar panel material—and is installed in sunny southern Europe, a solar panel made in China would take about 20 to 30 percent longer to produce enough energy to cancel out the energy used to make it. The carbon footprint is about twice as high.

"While it might be an economically attractive option to move solar panel manufacturing from Europe to China, it is actually less sustainable from a life-cycle energy and environmental perspective." *Fengqi You*

According to You, the biggest reason is that China has fewer environmental and efficiency standards for its factories and plants and generates more electricity from coal and other non-renewable sources.

To encourage more sustainable production of solar cells, You suggests a break-even carbon tariff. "The break-even carbon tariff we calculated, which is at the range of 105 to 129 euros per ton of carbon dioxide, depending on the possible carbon tax to be imposed by these two regions in the near term, is close to the reported carbon dioxide capture and sequestration cost."

Published in the journal *Solar Energy*, the paper has received significant media attention, appearing in *Nature News*, *National Geographic*, *The New York Times*, and *BusinessWeek*.

Department News

FACULTY NEWS

Luis Amaral was selected as a fellow of the American Physical Society.

Linda Broadbelt was appointed as an associate editor of *Industrial Engineering and Chemistry Research*, was elected to the electorate nominating committee of the engineering section of the American Association for the Advancement of Science, and was elected as the second vice chair of the catalysis and reaction engineering division of the American Institute of Chemical Engineers. She will succeed to first vice chair and then chair in subsequent years.

Wes Burghardt was elected vice chair of the polymer physics division of the American Physical Society and will help lead the division for the next four years through succession.

Michael Jewett received the 2014 Cole-Higgins Award for Excellence in Teaching from McCormick and was appointed as an associate editor of the *ACS Synthetic Biology*, editing a special issue of the journal, where his art was featured on the cover. He was also invited to speak at the first-ever SEED SynBio Conference and at the National Academy of Sciences Industrialization of Biology workshop.

Michael Jewett

Harold Kung was selected as a fellow of the American Institute of Chemical Engineers and elected as a member-at-large of the industrial science and technology section of the American Association for the Advancement of Science.

Eric Masanet was selected to participate in the National Academy of Engineering's 2014 US Frontiers of Engineering Symposium and was featured on WBEZ's Worldview program to discuss food waste.

Randall Snurr was named as one of Thomson Reuters Highly Cited Researchers for 2014.

Papers published by ***Fengqi You***'s group in the *AIChE Journal* were the number one and four most highly cited papers in 2012 and the number one and three most highly cited papers in 2013. You's work on solar panel manufacturing has received significant attention from the press.

STUDENT NEWS

Yamil Colon (Snurr group) earned the AIChE Computational Molecular Science and Engineering Graduate Student Award.

Jim Griffin was named a 2014 ISEN (Institute for Sustainability and Energy at Northwestern) Fellow.

Krishnan Iyer (Torkelson group) received the inaugural Biomaterials Graduate Student Award at the National AIChE meeting.

James Jeffryes was selected for the University's Fellowship in Leadership.

Ashty Karim was selected as a Brady Fellow in ethics and civic life.

Jennifer Kay received the "Breakthrough Technology" poster award given by *Biotechnology Journal* at the Metabolic Engineering X conference.

Michelle Marcus received an Excellence in Research Award from the American Society of Cell and Gene Therapy.

Heather Mayes (Broadbelt group) earned the AIChE Computational Molecular Science and Engineering Graduate Student Award.

Alumnus ***Henry Pennline***'s book, *Mercury Control for Coal-Driven Gas Streams*, was published by Wiley-VCH.

Jessica Stark received the Henry Luce Foundation's Clare Boothe Luce Graduate Fellowship from the Society of Women Engineers.

Julianne Wagoner was named McCormick's 2014 Walter P. Murphy Cooperative Engineering Education Student of the Year.

Mary Wang received a Ryan Fellowship for continuing students.

Ying Yu received the top poster prize at the 2014 Midwest Theoretical Chemistry Conference.

Dajun Yue, a graduate student in Fengqi You's group, received a student paper award by the Sustainable Engineering Forum of the American Institute of Chemical Engineers.

Several students in the department received NSF Graduate Fellowships. We congratulate the following students:

Fellowship awardees:
Michael Ashley, ***Ben Des Soye***, ***Alexandra de Paz***, ***Scott Nauert***, and ***Rachel Scholes***.

Honorable Mention:
Daniel Garcia, ***Justin Finkle***, ***James Hedrick***, ***Robert Kuo***, ***Lindsay Oakley***, ***Kelly Schwarz***, ***Jessica Stark***, and ***Albert Xue***.

MBP Celebrates 10th Anniversary

The Master of Biotechnology Program (MBP) recently celebrated its 10-year anniversary. Over the past decade, the MBP has steadily grown in size and impact, consistently attracting bright and motivated domestic and international students. The 2014 class is the second largest in the program's history with 40 students, and it is the most selective regarding matriculates.

Under the leadership of Professor William Miller, director, and Igor Kourkine, associate director, the MBP curriculum has grown to include industry-focused skills alongside traditional technical components. The addition of Zoe Hoeppner, industrial liaison and assistant director for external relations, has reinvigorated program interactions with the biotech industry and has expanded the resources available for student professional development. MBP's success is partly due to the dedicated efforts of Arthur Felse, lecturer and assistant director of research, to manage research fellowships and facilitate research projects.

Due to its focus on communication, collaboration, and critical thinking in addition to having a solid understanding of the technical and business components of the industry, MBP interns and graduates work at the top biopharmaceutical and biotech companies, including Genentech and General Electric, where they discover and develop innovative therapies and devices.

MBP continues to offer students opportunities to learn from outstanding faculty and industry professionals so that they can develop a skill-set well suited to fulfilling careers in the 21st century. The program will offer more than a dozen scholarships (up to $10,000 each) annually to US citizens and residents beginning in the fall of 2015.

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Graduate Recruitment: A Record Year

The Department of Chemical and Biological Engineering has experienced a banner year for graduate recruitment.

The graduate program has its best-ever selectivity (13 percent) and yield (57 percent), while nearly matching the record for highest number of applications. More significantly, it achieved high numbers for the recruitment of under-represented minorities, who represent 20 percent of newly enrolled students, and females, who represent 45 percent of the new class.

Bruce Lindvall, assistant dean for graduate education, and Iman Nasser, graduate program assistant, have played critical roles in the process, maintaining a commitment to keep in touch with prospective students. Rachel Watson, Teresa Deluca, and Quentin Dudley led this past year's recruitment committee, which also added to the success. "The recruitment weekend is run by amazing graduate students," Nasser said. "I couldn't have asked for a better group to organize the events and connect with recruits."

Nasser said the recruits were able to pick up on the obvious enthusiasm of current graduate students in the department. "They've really become a family, and with that kind of environment, it's easy to see how well-rounded they are," Nasser said.

Graduate students (left to right) Quentin Dudley, Teresa Deluca, and Rachel Watson led this year's recruitment committee.