Northwestern | McCORMICK SCHOOL OF ENGINEERING

FALL 2018

CHEMICAL AND BIOLOGICAL ENGINEERING

UNCOVERING TIME-DELAYED INTERACTIONS IN GENE REGULATORY SYSTEMS

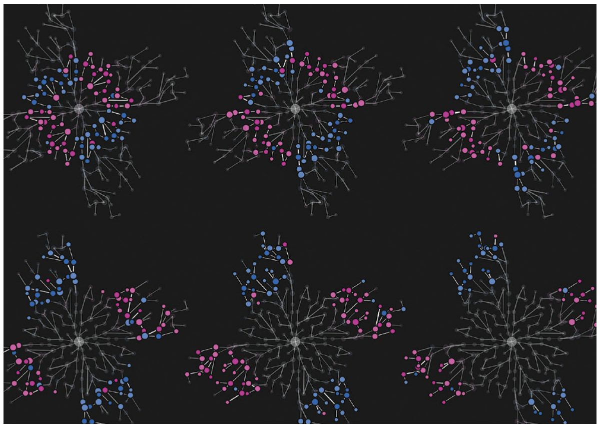
Machine learning algorithm uses time-series data to uncover biological networks

Biologists have long understood the various parts within the cell. But how these parts interact with and respond to each other is largely unknown.

“We want to understand how cells make decisions, so we can control the decisions they make,” said Northwestern Engineering’s **Neda Bagheri**. “A cell might decide to divide uncontrollably, which is the case with cancer. If we understand how cells make that decision, then we can design strategies to intervene.”

To better understand these mysterious interactions, Bagheri and her team have designed a new machine learning algorithm that can help connect the dots among the genes’ interactions inside cellular networks. Called “Sliding Window Inference for Network Generation,” or SWING, the algorithm uses time-series data to reveal the underlying structure of cellular networks.

Supported by the National Science Foundation and National Institutes of Health, SWING puts together a more complete picture of the cause-and-effect interactions happening among genes by incorporating time delays and sliding windows. Rather than only looking at the individual perturbations and responses, SWING uses time-resolved, high-throughput data to integrate the time it takes for those responses to occur.



Neda Bagheri’s SWING puts together a more complete picture of cause-and-effect interactions among genes.

“The dynamics are really important because it’s not just if the cell responds to a certain input, but how,” Bagheri added. “If I introduced a drug, for example, would the cell have an immediate response and then recover or become resistant to the drug? Understanding these dynamics can guide the design of new drugs.”

After designing the algorithm, Bagheri’s team validated it in the laboratory in both computer simulations and in vitro in E. coli and S. cerevisiae models. The algorithm is open source and now available online. And although it was initially designed to probe the interior, mysterious life of cells, the algorithm can be applied to many subjects that display activity over time.

“The framework is not specific to cell signaling or even to biological contexts,” Bagheri said. “It can be used in very broad contexts, such as in economics or finance. We expect that it could have a great impact.”

LEONARD HONORED WITH 2018 UNIVERSITY TEACHING AWARD

Award celebrates excellence, innovation, and influence in undergraduate teaching

By Kayla Stoner

Northwestern Engineering's **Joshua Leonard** was among five Northwestern faculty members who received the 2018 University Teaching Awards in May.

Leonard received a Charles Deering McCormick Professor of Teaching Excellence award, which honors outstanding performance and dedication to undergraduate education at Northwestern.

> "PROFESSOR LEONARD EXEMPLIFIES TEACHING BOTH IN THE CLASSROOM AND AS A MENTOR."
>
> ChBE STUDENT

The Charles Deering McCormick Professorship Award has a three-year term and for each year of the award term, the recipients receive $7,000 as a salary supplement and $3,000 for professional development. A one-time $3,000 award also is given to the recipient's home department to support activities that enhance undergraduate education.

Leonard is an associate professor in the Department of Chemical and Biological Engineering. He is a leader in teaching innovation that promotes students' independent thinking and problem-solving skills. Passionate about student-directed learning, Leonard has redesigned longstanding courses and created new courses to build hands-on learning opportunities that immerse students in real science and engineering.

A current student explained that Leonard challenges students to understand the material so they can apply what they've learned in a novel way, which although difficult, encourages them to take ownership of their understanding of the material.

Leonard has directly mentored nearly 40 students in his lab, many of whom go on to earn competitive awards and author publications, and he is a long-serving member of the Office of Undergraduate Research's team that provides feedback on student-led projects. Leonard co-founded and is lead adviser for Northwestern's international Genetically Engineered Machines (iGEM) team, which prepares students for careers in the emerging engineering discipline of synthetic biology, and he serves as a mentor in the Murphy Institute, which enables McCormick School of Engineering undergraduates to pursue an extended, self-directed project.

A student wrote, "Professor Leonard exemplifies teaching both in the classroom and as a mentor."

The award highlights a busy and successful year for Leonard. In July, he and Professor **Neda Bagheri** received the first-ever research project grant (R01) dedicated to synthetic biology from the National Institutes of Health. He also presented a TEDx talk on synthetic biology at the American School Foundation of Monterrey, Mexico, to inspire high school students to pursue STEM careers.

Josh Leonard presents a TEDx talk on synthetic biology at the American School Foundation of Monterrey, Mexico.

MILLER JOINS THE NATURE CONSERVANCY'S BOARD OF TRUSTEES

Appointment highlights growing partnership between Northwestern and conservation organization

By Mike M. McMahon, ISEN

The Nature Conservancy (TNC), a global science-based organization whose driving mission revolves around conservation efforts for people and nature, has appointed Professor **William Miller** to their Illinois Board of Trustees, a move that highlights the growing partnership between Northwestern and the conservation organization.

Professor William Miller (middle) worked with The Nature Conservancy to study how Indian Boundary Prairies can help manage Chicago's stormwater runoff and alleviate flooding for nearby residents.

"THERE'S TREMENDOUS POTENTIAL WHEN IT COMES TO SHARING KNOWLEDGE AND RESOURCES BETWEEN OUR TWO INSTITUTIONS"

WILLIAM MILLER

"Current and emeritus members of The Nature Conservancy Board of Trustees are really devoted to the work, and I'm proud to now count myself among them," said Miller, who has been a member of the organization's Science Advisory Committee since 2016. "I've worked closely with many Nature Conservancy scientists over the years and am always highly impressed with their work, knowledge base, and commitment."

Miller recently worked with TNC on studying the Indian Boundary Prairies, a 500-acre undeveloped area about 20 miles south of Chicago. The study, part of a partnership between TNC, Argonne National Laboratory, and the Institute for Sustainability and Energy at Northwestern (ISEN), utilizes technology to monitor how the preserve's prairies can help manage Chicago's stormwater runoff and alleviate flooding for nearby residents. Miller and **Aaron Packman**, professor of civil and environmental engineering and director of Northwestern's Center for Water Research, are using sensor nodes to measure everything from soil moisture to rain to water levels.

"In joining our Board of Trustees, Professor Miller is bringing his passion for nature and subject-area expertise to the table, but he also brings complex, system thinking about how we can advance," said Michelle Carr, director of the Illinois chapter of TNC. "That's a big asset and will allow us to look beyond our current collaborative projects."

As the governing body of TNC's Illinois Chapter, the Board of Trustees is charged with helping find creative ways to align the regional work with the organization's stated global priorities: protecting water, acting on climate change, saving oceans, conserving land, and transforming cities.

"As a new trustee, I love the idea of looking for innovative ways that Northwestern faculty and students can provide support for TNC projects," Miller said. "There's tremendous potential when it comes to sharing knowledge and resources between our two institutions — it's really mutually beneficial."

New Biotech Technique Accelerates Protein Therapy Research

Dubbed GlycoSCORES, the technique rapidly screens sequences for making glycoproteins

A Northwestern-led synthetic biology research team has developed a new biotech technique that promises to accelerate research into protein therapies that could become the next defense against antibiotic-resistant supergerms or the next new drug.

Michael Jewett, the Charles Deering McCormick Professor of Teaching Excellence and professor of chemical and biological engineering, and Milan Mrksich, the Henry Wade Rogers Professor of Biomedical Engineering, chemistry, and cell and molecular biology, joined forces to lead the research, which combined the Mrksich lab's mass spectrometry technology with the Jewett lab's expertise in glycosylation and rapidly making proteins.

Glycosylation, which is the attachment of sugars to proteins, plays a critical role in how proteins form and work in cells and how cells interact with other cells. It is also important in the study of disease and biotechnologies.

Working with Cornell University Professor Matt DeLisa, they developed a new platform for characterizing and optimizing sequences for making glycoproteins using cell-free protein synthesis and mass spectrometry.

The new technique promises to vastly speed up the time needed to test compounds for potential new drugs. As recent as a few decades ago, drugs were based on natural products that were tediously isolated and characterized from plants and other natural sources.

"We have radically accelerated the process," Mrksich said. "Where researchers today can evaluate a couple of hundred potential glycosylation tags in a given period, we've brought together two high-throughput technologies that allow us to evaluate several thousand in that same time frame."

A new technique, dubbed GlycoSCORES, rapidly screens sequences for making glycoproteins. Credit: Justin Muir

"Our method allows us to not just pick the winners, which we commonly look for in scientific experiments, but the failures too," Jewett said.

DNA Drives Design Principles for Lighter, Thinner Optical Displays

Lighter gold nanoparticles could replace polymers used in displays' back-reflectors

By Amanda Morris

A Northwestern University team led by Professor **Chad Mirkin** and Weinberg College of Arts and Sciences Professor George Schatz has developed a new set of design principles for making photonic crystals akin to the ones that are typically used in computer, television, and smartphone displays. By using synthetic DNA to assemble particles into crystalline lattices, the researchers have opened the door for much lighter and thinner displays compared to what is currently available.

"Most people look at a laptop display every day, but few people understand what they are made of and why," Schatz said. "One component of the display is the back-reflector, a mirror-like device that directs the light emitted by the LCD to the viewer. These reflectors are made using layered polymers that are much thicker and heavier than our crystals."

Northwestern's approach not only replaces these polymers with gold nanocrystals but also spaces them apart to leave air among them. The result is a lighter, more compact, precisely designed, and reconfigurable structure that is still highly reflective.

In 1996, Mirkin, a courtesy professor in the Department of Chemical and Biological Engineering, invented ways to link synthetic DNA to gold nanoparticles to produce new materials not found in nature. Then, in 2008, Mirkin and Schatz collaborated to make crystals from particles linked by DNA. By attaching strands of synthetic DNA to tiny gold spheres, the duo found they could build three-dimensional crystalline structures.

Despite these advances, Mirkin and Schatz did not initially realize that the crystal lattices they made in the laboratory had optical properties similar to the polymer layers found in device displays.

"Through computer modeling, we realized by accident that the crystalline materials with gold nanoparticles had properties that we missed earlier in the work," Schatz said. "We then optimized the optical properties using computations, and these demonstrated that the non-touching metal spheres could, in some cases, be better than the touching polymer spheres."

Methodology Helps Study of Promising Targeted Drug Delivery Scaffold

Northwestern-UC Berkeley collaboration develops technique for studying self-assembling virus shell with potential for medical applications

Northwestern Engineering researchers have developed a new way to manipulate a virus shell that self-assembles from proteins and holds promise as a carrier for disease detection, drug delivery, and vaccinations.

Viruses have shells that are built to survive in harsh conditions, protecting their cargo until they find a cell to infect. The shell can be used for good, however, because that stability makes it suitable for protecting more useful cargo, such as medications, that can be delivered to specifically-targeted cells.

The research focused on a protein used by a bacterial virus called the MS2 bacteriophage. This protein can self-assemble, creating a harmless scaffolding out of the viral shell, said **Danielle Tullman-Ercek**, associate professor of chemical and biological engineering.

"In biology, everything has its place. Biology is great like that — except we don't know the rules," Tullman-Ercek said. "Our discovery was the method for determining those design rules."

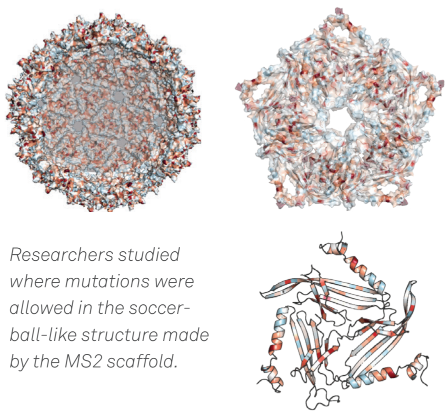
The study, done in collaboration with chemistry professor Matthew Francis and his colleagues at the University of California at Berkeley, took more than two years.

The work allowed the researchers to examine which specific protein mutations broke the virus scaffold or changed the properties of the structure. To do that, the team developed a new technique called SyMAPS (Systematic Mutation and Assembled Particle Selection), which separated out the mutated scaffold proteins that remained intact from those that broke apart during mutation.

The team believes that understanding how mutations change the scaffolding provides important insight into how these repurposed virus proteins could be used in medicine.

For instance, a structure that falls apart in a specific environment could help targeted drug delivery, such as chemotherapy.

In addition, the study offers insight into what might naturally arise in a mutating virus, such as influenza. "This could give us an idea of which places in the virus could have a higher rate of mutation. That information could be used by scientists to develop new vaccines," Tullman-Ercek said.



Researchers studied where mutations were allowed in the soccer-ball-like structure made by the MS2 scaffold.

Researchers Find Way to Keep Proteins Functioning Outside of the Cell

Discovery led to the development of a protein 'mat' that soaks up pollution

Professor **Monica Olvera de la Cruz** and collaborators at the University of California at UC-Berkeley have discovered a way to keep proteins active outside of a cell. The discovery could lead to a new class of materials with functions found only in living systems.

Ting Xu, professor of materials science and engineering and chemistry at UC-Berkeley, created random heteropolymers (RHPs), which comprise four types of monomer subunits, each with chemical properties designed to interact with chemical patches on the surface of proteins of interest. When connected, the monomers mimic a natural protein to maximize the flexibility of their interactions with protein surfaces. The RHPs act as unstructured proteins, commonly seen inside cells.

Monica Olvera de la Cruz

Led by Olvera de la Cruz, Northwestern's team ran extensive molecular simulations to show that RHPs would interact favorably with protein surfaces, wrap around protein surfaces in organic solvents and adhere weakly in water, leading to correct protein folding and stability in a non-native environment.

The researchers then tested whether they could use RHPs to create protein-based materials for bioremediation of toxic chemicals. They mixed RHPs with a protein called organophosphorous hydrolase (OPH), which degrades the chemicals used in insecticides and chemical warfare agents. They then used the RHP/OPH combination to make fiber mats.

After submersing the mats in an insecticide, the researchers found that the mats degraded the chemical in just a few minutes. This could open the door for the creation of larger mats that could soak up and trap toxic chemicals in places such as war zones.

MASTER OF BIOTECHNOLOGY PROGRAM CAPS OFF BUSY YEAR

The program hosted annual Biotechnology Day and summer synthetic biology workshop

The Master of Biotechnology Program (MBP) recently concluded a busy year of outreach and engagement.

In March, the program hosted Biotechnology Day, a life sciences festival organized every year that inspires and informs students and scientists interested in learning more about the field. The day's events included outreach activities, tours of facilities, career panels, and an open networking session.

MBP's summer synthetic biology workshop brought together area teachers to learn how to bring biological engineering to their classrooms.

MBP Leadership

Professor **William Miller**, who has directed MBP since 2007, will serve as joint-director in 2018-19 with Associate Professor **Danielle Tullman-Ercek**, who will take over as sole program director in September 2019.

Organized in partnership with the pre-doctoral Biotechnology Training Program and Northwestern's Office of STEM Education Partnerships, Biotechnology Day 2018 included a keynote lecture from Northwestern alumnus Jeff Baker, deputy director of the FDA's Office of Biotechnology Products in the Center for Drug Evaluation and Research. Baker presented an overview of the regulation of biopharmaceuticals in the United States in the face of new technologies and manufacturing strategies.

This summer, MBP teamed up with the Baxter Center for Science Education to host a synthetic biology workshop for area teachers. Teachers from 14 different schools spent three days in MBP labs learning how to bring biological engineering to their classrooms.

Co-taught by PhD student **Jessica Stark** and Glenbard East High School science teacher Thomas Martinez, with assistance from MBP alumna and current PhD student **Jazzy Hershewe**, the workshop introduced participants to the BioBuilder curricula developed by MIT. Teachers learned to transform color-generating plasmids, make bacteria smell like bananas, design a genetic device, and model genetic circuits.

Since enrolling its first class in 2004, MBP has nearly 350 graduates, many of whom interned with or were hired by large and small biotechnology companies. Contact Natalie Champagne, assistant director of external relations and career management, at natalie.champagne@northwestern.edu if you would like to consider MBP students for an internship or job at your company or to invite a group of students for a company visit.

MBP aims to develop graduates with:

- A strong foundation in bioprocess engineering theory and practice
- Ownership and an ability to overcome challenges during a 1000-hour independent research project
- Learning and innovation skills and strategic biotechnology business competencies

Julio Ottino and Linda Broadbelt Receive AIChE Awards

Ottino will be honored with the 2018 Founders Award and Broadbelt will receive the R. H. Wilhelm Award

Julio Ottino

Linda Broadbelt

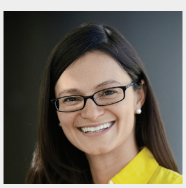
Northwestern Engineering Dean **Julio M. Ottino** and Associate Dean for Research **Linda Broadbelt** have both been honored with awards from the American Institute of Chemical Engineers (AIChE).

Ottino, Walter P. Murphy Professor of Chemical and Biological Engineering and Distinguished Robert R. McCormick Institute Professor at the McCormick School of Engineering, received AIChE's 2018 Founders Award for Outstanding Contributions to the Field of Chemical Engineering. The award recognizes one individual each year for their impact in the chemical engineering field and whose achievements have advanced the profession.

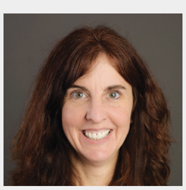
Broadbelt, Sarah Rebecca Roland Professor in the Department of Chemical and Biological Engineering, was awarded the R. H. Wilhelm Award in Chemical Reaction Engineering, one of AIChE's prestigious Institute Awards. The honor recognizes an individual's significant contributions to the field of chemical reaction engineering.

Ottino and Broadbelt will formally accept their awards at AIChE's Honors Ceremony in October during the AIChE 2018 Annual Meeting in Pittsburgh, Pennsylvania.

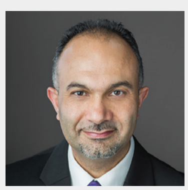
FACULTY NEWS



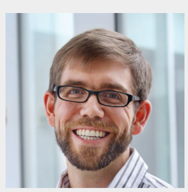
Neda Bagheri was invited to serve on the scientific advisory board for the Allen Institute for Cell Science. She was also invited to be a distinguished speaker at the Accelerated Discovery Lab at IBM Research - Almaden.



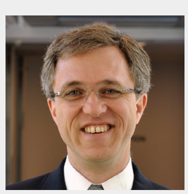
Linda Broadbelt published a cover article in *Energy & Environmental Science* unveiling the first mechanistic model of the pyrolysis of hemicellulose, with implications for the design of processes for biomass conversion.



Omar Farha published a paper in *Nature Catalysis* on chemoselective functionalization of methane in a metal-organic framework material.



Michael Jewett was named the conference chair for the 8th International Conference on Biomolecular Engineering.



Randall Snurr and Omar Farha's groups published a paper in *Nature Communications* on computer-aided discovery of a nanoporous material with superior oxygen storage properties.

"Cells can heal, cells can produce therapeutics on demand, and cells can hunt and kill harmful invaders. While this seems like something out of science fiction, this idea is very much already part of our real world."

— PROFESSOR JOSHUA LEONARD, who presented a TEDx talk on synthetic biology at the American School Foundation of Monterrey, Mexico in June.

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Using Big Data to Analyze Soccer

Professor **Luís Amaral** has investigated complex social and structural networks in areas ranging from healthcare and biology to gender discrimination and gun violence. His diverse research interests and innate curiosity eventually led him to study soccer — his favorite sport.

Amaral used his knowledge of network complexity to create an algorithm that objectively ranks professional soccer players. Using sophisticated coding techniques and analytical tools, Amaral created an "Average Footballer Rating" (AFR) for each player, based on how influential they are in soccer matches. Taken together, the AFR values of all players on a given team indicate that team's strength — its success at making passes that result in goals.

"A player with an AFR greater than 70 is pretty much superhuman," Amaral said.

Amaral and his collaborator Jordi Duch used this algorithm to build the "World Cup Dream Team": a May 2018 snapshot of the 10 best outfield players at their respective positions.