FALL 2019

BIOMEDICAL ENGINEERING

UNIVERSITY OF WISCONSIN-MADISON

RESEARCH AND DEVELOPMENT:

SHAPING TALENT AND CREATING TECH FOR TOMORROW'S WORLD

CHAIR'S MESSAGE

Twenty years ago, the biomedical engineering program at UW-Madison had little more than an email address and a phone number. We started as an interdisciplinary master's degree in the 1970s. Because of student demand and the work of visionary faculty, staff and administrators, the bachelor's and doctorate degree programs arrived in 1998. And in July 1999, BME became the newest department in the College of Engineering.

Over the past 20 years, the landscape of engineering education has changed faster than ever before. As fundamental shifts occur in technology and society, we must consider how to best prepare our students to lead and succeed, and I am enthusiastic about what lies ahead.

Our two new master's programs focus on combining the fundamentals of the biomedical sciences with advanced engineering methods of analysis and design, all while preparing students to become industry-leading innovators. We are also expanding the tools available to our undergraduates, who will soon have access to cutting-edge technology in biomechanics, optics and tissue engineering in a newly renovated lab space.

I am excited to welcome Kevin Eliceiri, director of the Laboratory for Optical and Computational Instrumentation and a longtime BME affiliate, to our faculty this fall, as well as Filiz Yesilkoy, who will join us for the spring 2020 semester.

I want to extend an invitation to any of you who are attending the BMES annual meeting in Philadelphia. Join us at our reception on Friday night to celebrate all that we have accomplished together and share your BME stories, or stop by booth 211. We are on a strong trajectory!

ON, WISCONSIN!

Justin Williams
Peter Tong Chair of Biomedical Engineering and Vilas Distinguished Professor
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Read the latest BME news on our website (**engr.wisc.edu/bme**), and be sure to connect with us on Facebook (**@UWBME**) and Twitter (**@UWMadison_BME**).

Invested in BME's success

Longtime BME supporters Peter (MSEE '65) and Janet Tong returned to campus in June to formally award their endowed chair to Vilas Distinguished Professor Justin Williams. College of Engineering Dean Ian Robertson, right, joined the three for the celebration.

The Peter Tong Chair of Biomedical Engineering, supported by the largest gift in BME department history, is among a simultaneous trio of the first endowed department chair positions in the college. To read more about the Tong Chair and how it will enhance the BME student experience, visit **go.wisc.edu/engrnews-022619**.

Come visit us at BMES

Are you headed to the Biomedical Engineering Society's 2019 annual meeting Oct. 16-19 in Philadelphia? Stop by booth 211 to learn about how our faculty and students are driving the field forward, and join us for a reception on Friday, Oct. 18.

BMES
BIOMEDICAL ENGINEERING SOCIETY

BREAKING BONES AND BARRIERS:

Program introduces young women to engineering, orthopedics

On a Saturday in late April 2019, on the northeastern edge of Madison, Wisconsin, a group of high school girls worked in pairs to perform spinal fusions. Across the room, others sutured pig feet, while another group took turns drilling into femur bones.

After all, what better way to learn about orthopedics and biomedical engineering than by actually trying out some procedures? That idea is at the heart of The Perry Initiative, which aims to inspire young women to pursue careers in orthopedic surgery and related engineering fields.

BME PhD student Christa Wille (BS '12) helped lead efforts to bring the initiative's outreach programs for high school and medical students to Madison for the first time. Wille worked with Ana Ebrahimi, a postdoctoral fellow in mechanical engineering, to make it happen.

Biomedical engineering PhD student Christa Wille (left) assists Perry Outreach Program students in Madison. *Photo courtesy of The Perry Initiative.*

> **"Young girls in general are not encouraged to tinker or play or problem-solve as much. This is a program that really tries to give them confidence by having them actually learn how to use the power tools."**
>
> — Ana Ebrahimi

The program drew 11 medical school students and 25 high school students from across southern Wisconsin and beyond. They heard from practicing orthopedic surgeons and engineers and got to try their hands at a few techniques on artificial bones.

"Young girls in general are not encouraged to tinker or play or problem-solve as much," says Ebrahimi, who got involved in The Perry Initiative as a graduate student at the University of Delaware. "This is a program that really tries to give them confidence by having them actually learn how to use the power tools: how to use the oscillating saw, breaking things, figuring out ways to put things back together—just basically problem-solving and being hands-on with people who have gone through the whole process themselves."

When Ebrahimi came to Madison in 2018 to work in the lab of Mechanical Engineering Professor and BME affiliate Darryl Thelen, it was only natural the initiative would soon follow. Wille, who is also a physical therapist in sports medicine at UW Health, got involved after Thelen mentioned the idea during a meeting.

"I thought, 'Well that sounds cool. I want to be a part of that,'" says Wille, who also works in the UW Neuromuscular Biomechanics Lab, directed by Thelen and Bryan Heiderscheit, a professor of orthopedics and rehabilitation in the School of Medicine and Public Health.

Wille leveraged her connections to UW Health's orthopedic surgeons, found sponsors and began organizing the event more than a year in advance.

According to a 2015-16 report from the Association of American Medical Colleges, just 6-8% of practicing orthopedic surgeons were women. The numbers in BME are substantially better, with 44% of bachelor's degrees going to women, per 2017 data from the American Society for Engineering Education (ASEE). But ASEE also reported the proportion of women among tenured or tenure-track faculty in BME was just 22.7%.

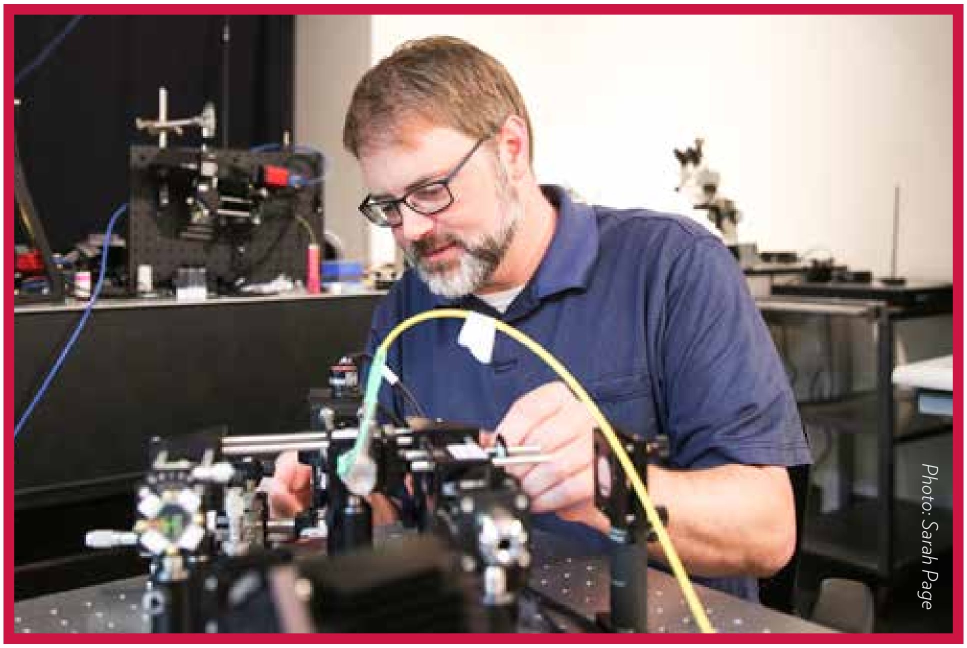
Wille and Ebrahimi point to a dearth of role models, limited opportunities to develop technical skills, and perceptions about work-life balance as barriers young women face in pursuing careers in science, technology, engineering and math fields. They're hoping The Perry Initiative can be part of the solution—85% of its high school program participants have gone on to pursue STEM majors—as an annual event in Madison.

"It takes other people believing in you, and that's what really The Perry Initiative is about: getting a group of people to say, 'Hey, you can do this,'" says Ebrahimi.

NSF CAREER AWARD

Rogers eyes imaging improvements for studying cells

Inside the eye's retina, retinal pigment epithelial cells dutifully tend to the photoreceptors, delivering them nutrients and clearing away their waste.



These essential transportation tasks are two of the many jobs retinal pigment epithelial (RPE) cells perform that are crucial to maintaining vision. The scale of movement is too small to register on standard medical imaging instruments, but detecting material transportation is one way to confirm the RPE cells are healthy and properly functioning.

Since they are often early casualties in vision diseases that result in blindness—such as age-related macular degeneration (with the photoreceptors usually the next to go)—monitoring RPE cell function could allow clinicians to diagnose conditions sooner and more precisely, informing personalized treatments.

Assistant Professor Jeremy Rogers will use a National Science Foundation CAREER Award to develop an optical instrument that's tailored to spying RPE cell function on a minute scale by tracking the changes in how light scatters as the cells move around particles. He hopes that by using the five-year, $500,000 grant to build a customized tool called an optical coherence microscope, he also will create a blueprint that could lead to monitoring cellular function in other parts of the eye.

"As we develop expertise in customizing these optical instruments to be able to see dynamics in RPE cells, I think then we can start to look at dynamics in other cell types," says Rogers, who has previously focused much of his work on using optical techniques to improve cancer screening. "And that really has the potential to be an essential tool for a wider range of vision-related diseases."

Clinicians can readily image a patient's retina and diagnose diseases with existing technology like optical coherence tomography that shows regions of different cell types, stacked like a layer cake. But that's as fine as the resolution gets.

"You can't see the fine-grain cellular structure and you can't assess function," says Rogers. "If we can actually see activity at a cellular scale, there's opportunity for earlier diagnosis or more accurate, personalized diagnosis, so the treatment options can be more customized to an individual."

That cellular view could also allow doctors to thoroughly study the effects of treatment—whether through traditional drugs or emerging options like gene therapy or cell replacement using stem cell technology—on an ongoing basis and adjust tactics as needed.

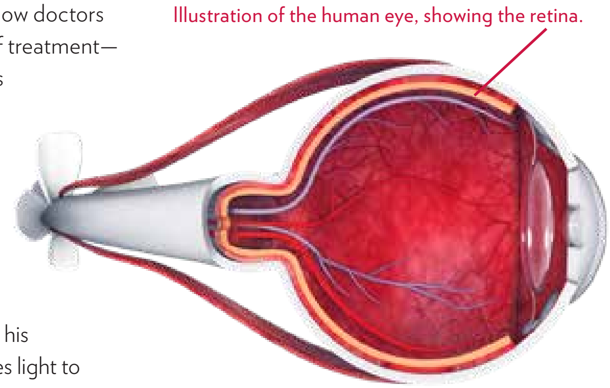
Of course, those scenarios all depend on imaging an actual patient. Rogers will begin by using his customized microscope, which uses light to create images in a manner similar to how an ultrasound machine employs sound waves, to image cultured RPE cells in a dish.

If the technique proves successful, it would offer an alternative to a current labeling method of genetically altering cells to express fluorescent proteins to enable imaging. Instead, the cells would remain in a completely natural state.

As part of the project's educational activities, Rogers plans to work with staff in the Discovery Building on the UW-Madison campus to create interactive optical demonstrations, both for school field trips to campus and for teachers to replicate in their classrooms. He sees optics and imaging as lending themselves particularly well to community outreach.

"We're very visual beings," he says. "We tend to interpret everything through vision, and that's part of the reason I think losing our sight can be so devastating. It is exciting to be working on technology that may help to restore that vision."

Illustration of the human eye, showing the retina.



IN FOCUS: MASTER'S PROGRAMS OPEN OPTIONS


Beth Meyerand

Undergraduate students and young professionals looking for either a deeper dive into biomedical engineering or an entrepreneurial approach to the discipline are in luck. BME has launched two one-year master's programs in the fall 2019 semester.

Students can choose an accelerated version of the department's traditional master's program, minus the research requirements, or opt for a master's in biomedical innovation, design and entrepreneurship through a partnership with the Wisconsin School of Business.

"I think it's going to give them more specific, focused, advanced training in an area that matches their career goals, be it entrepreneurship or biomedical engineering," says Beth Meyerand, professor and associate chair of graduate advising for BME.

The department created the offerings based on feedback from students, alumni and companies that recruit BME students, such as Medtronic, General Electric and Siemens.

The inherent interdisciplinary nature of the field means undergraduate students must juggle coursework in BME, chemical and biological engineering, electrical and computer engineering, mechanical engineering and more, depending on their chosen area of focus. But gaining that broad experience can make it challenging to take many advanced BME courses. The accelerated master's program allows students to study topics such as tissue engineering, medical imaging or instrumentation in greater depth.

"This allows them to get that specific training," says Meyerand, who also sees the accelerated program as an effective forerunner to medical school.

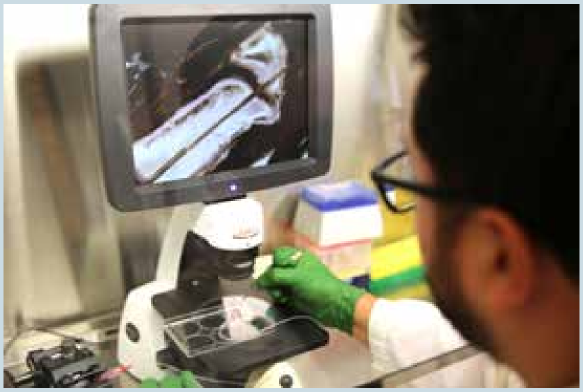
The innovation, design and entrepreneurship option pairs advanced biomedical and other engineering courses with business offerings on topics like intellectual property rights, strategic management and venture creation.

"They already have these fantastic courses in the business school that are related to technology and innovation," Meyerand says. "This is going to serve our students well who want to go into industry or start their own companies."

NEW TECHNIQUE ENABLES VERSATILE 3D CONTROL OVER ORGANOIDS

To bake a cake in a certain shape, you need the right mold. The same logic applies to creating organoids—collections of pluripotent stem cells that have formed tissues complex enough to mimic human organs.

But shape isn't simply a cosmetic concern for organoids. It can have a direct effect on cellular diversity and organization, huge considerations when the whole point of the endeavor is to create tissues that replicate the ones in our bodies.


PhD student Carlos Marti-Figueroa works on injecting stem cells into alginate hydrogels. *Photo: Renee Meiller.*

Assistant Professor Randolph Ashton has partnered with Lih-Sheng "Tom" Turng, a professor of mechanical engineering, to create hydrogel molds that will allow researchers to more precisely control the three-dimensional structures of organoids. They detailed their work in a paper in the journal *Acta Biomaterialia*.

"At the scale of human development, which is micron to millimeters, there are not a lot of great technologies to control how tissues form at that level and in three dimensions," says Ashton.

Enter Turng, who in recent years has applied his expertise in injection molding and polymer processing to the microscale, allowing him to work with Ashton to create a water-soluble plastic template.

Ashton's lab then encapsulates the template in a hydrogel and the plastic dissolves, leaving a cavity that's specifically shaped to drive anatomical tissue formation as the stem cells fill the gap and differentiate down a specific organ pathway.

They're increasing the level of control in a process generally governed by stem cell self-assembly into three-dimensional spheroids, which do not possess the natural geometrical constraints found in an embryo. Ashton says that method leads to an uncontrolled, spontaneous process of differentiation, yielding organoids with unnatural anatomies.

"We're trying to harness the ability of the stem cells to self-form a lot of these structures that we as scientists cannot form ourselves," says Carlos Marti-Figueroa, a PhD student in Ashton's lab and one of the paper's first authors. "A lot of the cellular diversity that occurs has to do with the self-organization capabilities of the cells."

LEADING CHANGE:

Chesler pens how-to on promoting diversity, inclusion in BME

On more occasions than Naomi Chesler would prefer, she's heard academic colleagues respond to discussions about diversity and inclusion with a familiar refrain.

"I'll have to ask our [insert underrepresented minority label] faculty member about that."

Chesler, a Vilas Distinguished Achievement Professor, would like to help change the default response about matters of racial, ethnic, gender, gender identity and sexual orientation inequality to: "I'll have to do some learning about that on my own."

With that in mind, Chesler published "A how-to guide for promoting diversity and inclusion in biomedical engineering" in the *Annals of Biomedical Engineering*. It's part of her efforts to create a more inclusive environment in the field.

Among engineering disciplines, biomedical rates highly in measures of gender diversity; only environmental engineering boasts larger percentages of bachelor's and doctoral degrees awarded to women, as well as tenured and tenure-track women faculty. But when it comes to racial diversity, the biomedical specialty lags behind general engineering averages in those same measures, with the exception of Asian-Americans.

For that to change, Chesler says, those in positions of power—senior faculty members, department chairs, college deans, industry leaders and other roles overwhelmingly occupied by white individuals—must take responsibility.

"Just like men have to stop expecting women to lead efforts for gender equity, white people have to stop expecting people of color to lead efforts for racial equity," she says. "You must go to the power structures to make change. It is generally ineffective for those without power to make change. So if we want to be a more diverse and inclusive discipline, then the people in power need to start learning how to do that and, in fact, doing it."

Chesler's how-to guide builds off a 2010 status report on gender diversity in BME, which she wrote for the same journal. She also consulted work by White Men as Full Diversity Partners, a group that helps organizations build more inclusive cultures, and then distilled her research into six broadly applicable recommendations for a largely academic audience:

- Accept complexity in understanding diversity and working across difference.
- Seek to understand your own privilege in society and academia.
- Speak out about diversity issues; use your privilege to advocate for change.
- Accept that you will make mistakes; when you "know better, do better."
- Learn the difference between intent and impact.
- LARA: Listen, affirm, respond, add.

"I hope this will speak to the people who want their institutions and departments to be more inclusive and provide some guidance as to how to do that," she says.

Chesler is a longtime advocate of fostering greater diversity and inclusivity in engineering. She directs UW-Madison's Women Faculty Mentoring Program and is a founding member of the Biomedical Engineering Society's Diversity Committee. She earned the 2014 Biomedical Engineering Society Diversity Award for her work on gender inequality and received the College of Engineering's Equity and Diversity Award in 2017.

"As a relatively senior person in my field with established research and teaching expertise, I feel it's my responsibility to give back," she says. "And one way I enjoy giving back is by promoting a more inclusive environment in the field of biomedical engineering."

Always an inventor: Webster lands patent for sleep apnea therapy device

Even into his mid-80s, John Webster is still inventing.

The professor emeritus, one of the pioneers of the biomedical engineering field, received a U.S. patent for a new kind of device to treat sleep apnea.

The disorder, in which a person repeatedly stops and starts breathing while sleeping, may affect as many as 1 billion people worldwide, according to a 2018 study led by the medical device company ResMed.

The most widely used type of therapy device, a continuous positive airway pressure machine, blows air down a person's throat to keep the airway open. But patients often complain about nasal and mouth dryness, swallowing too much air, the noise of the machine and other drawbacks.

Webster's device takes an alternative approach. It collects expired air, then uses a sensor and control system to feed the user back an appropriate amount of carbon dioxide—just enough to trigger the body's automatic impulse to breathe.

The device emerged from BME's design curriculum, when a project connected Webster with Jerome Dempsey, a professor emeritus in the Department of Population Health Sciences in the School of Medicine and Public Health.

Webster has turned over rights to the patent to the Wisconsin Alumni Research Foundation (WARF), the independent, on-campus technology transfer organization that partners with UW-Madison researchers. WARF will seek to license the design to medical device or technology companies.

READING THE ROADMAP OF STEM CELL DIFFERENTIATION

The path a stem cell takes toward its identity as a fully defined cell, the analogy goes, is like a ball rolling down a hill. Along the way, it encounters bumps, obstacles and varied terrain that influence its final destination.

Unfortunately for stem-cell researchers, seeing each transition in a cell's state—and understanding what drives that change—isn't yet possible in real time.

Assistant Professor Melissa Kinney is working to uncover new details of dynamic biological processes, such as stem cell differentiation, with the hopes of better guiding cells down that path toward a desired identity.

In a paper in *Nature Biotechnology*, Kinney and collaborators outline a method they developed to glimpse transitional phases in the differentiation of hematopoietic stem cells toward red blood cells and describe how it pinpointed a key regulator of blood cell development.

She sees it as a proof of concept for a versatile computational approach that researchers could use with different types of cells and processes beyond stem cell differentiation, including CAR-T cell activation.

"The data that we collect tend to give us snapshots. What we're trying to answer is: Can we use those static snapshots to figure out the 'why'—why cells transition from one state to the other?" she says. "We can't actually see everything that is happening in the cell in real time, so we use computational methods to infer what's happening from one stage to the next during these dynamic processes."

MORE: **go.wisc.edu/engrnews-071019**

Quick study

Chris Klundt (BS '05) has helped millions of high school and college students learn. Klundt, the CEO and co-founder of StudyBlue, is representing BME as an Early Career Achievement Award recipient at the College of Engineering's annual Engineers' Day celebration.

StudyBlue, an app that allows students to use crowdsourced electronic flashcards and take quizzes, was acquired by Chegg in 2018.

DEPARTMENT NEWS

Vilas Distinguished Achievement Professor **Naomi Chesler** was elected to the board of directors of the American Institute for Medical and Biological Engineering.

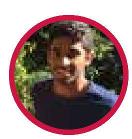
Associate Professor **Melissa Skala** earned recognition as a fellow of both the American Institute for Medical and Biological Engineering and SPIE, an international society for optics and photonics.

Assistant Professor **Megan McClean** received a $426,679 grant from the National Institutes of Health to develop optogenetic tools that could help researchers better target fungal infections with drugs. *Cellular and Molecular Bioengineering* also named McClean a 2019 Young Innovator. McClean will present her work during a special session at the BMES annual meeting.

Turba, a startup led by John D. MacArthur Professor and Claude Bernard Professor **David Beebe**, gained funding from the UW-Madison's Discovery to Product unit as part of the state of Wisconsin's State Economic Engagement and Development Research Program. Turba is creating a new test to help doctors select the most effective antibiotics to treat infections where multiple bacterial organisms are present.

Assistant Professor **Colleen Witzenburg**, PhD student **Christa Wille** and Vilas Distinguished Achievement Professor **Naomi Chesler** received an educational innovation grant from the college to implement an educational motion capture laboratory to enhance biomechanics learning.

Alumna **Bailey Flanigan** (BS '17) was one of 11 recipients nationwide of the prestigious Hertz Fellowship, which gives promising young researchers the support and flexibility to pursue ambitious and novel projects with societal benefits. Flanigan plans to work at the interface of theoretical and applied problems in algorithms, machine learning and game theory while working toward a doctorate at Carnegie Mellon University.



Undergraduate **Akshith Mandepally** landed a Wisconsin Idea Fellowship to refine an affordable solar-powered air filtration prototype to reduce household air pollution from combustible fuel in Uganda.

PhD student **Joseph Burns** received an NSF Graduate Research Fellowship to support his graduate studies. Alumni **Isabella Reichardt** (BS '19), **Jason Wan** (BS '17), **Karam Khateeb** (BS '18) and **Samantha Bremner** (BS '17) also earned fellowships.

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LOOKING AT MELANIN IN A NEW WAY

A Madison-Milwaukee scientific partnership is powering an effort to better understand the complicated mechanics of human vision.

Associate Professor Melissa Skala develops applications in photonics-based imaging that offer many research benefits, most notably that they do not damage living tissue. That has made her technology an ideal candidate for sensitive imaging related to treating a variety of cancers, immunotherapy, stem cells, eye disease and predicting pre-term birth, to name a few.

Skala has connected with Joseph Carroll, an ophthalmologist at Medical College of Wisconsin and a pioneer in eye imaging research, to tease out the role that melanin plays in healthy vision and disease. Melanin, of course, is best known as the compound that determines skin pigmentation, but it's also essential to vision.

"Melanin is responsible for absorbing excess light that comes into our eyes, so it serves a protective role," Skala says. "But we're actually uncertain of all the roles it plays."

Together, Skala and Carroll developed an imaging technique that offers 3D, color images of melanin in the eye. It was the first time a technique called photo-thermal optical coherence tomography had been applied to eye research.

The work has led to three published papers and a patent disclosure, and both scientists are actively pursuing next steps for potential human clinical applications.

"This is a nice, specific technique to measure not only whether the melanin is there, but how much of it is there, and that's what Joe really needed to answer his questions about how melanin affects the visual system," Skala says.

Wisconsin leaders have long encouraged more active research partnerships between the state's two largest urban centers. For Skala, this partnership was less about proximity than it was about seeking out the best science.

"I think it's all about talent," she says. "Joe's really interested in new technology and how it can tell us how the visual system works. So we tried very hard to work with him and we succeeded."