



College of Engineering
UNIVERSITY OF WISCONSIN-MADISON

FALL 2024 NEWSLETTER

DEPARTMENT OF

BIOMEDICAL ENGINEERING





Greetings from Madison!

As we begin a new academic year, I would like to reflect on our successes, while also looking to the future. In September 2024,

we celebrated the 25th anniversary of the BME department with an all-day gala held at the Memorial Union, where we invited alumni to speak about their career paths and provide speed mentoring for our current students. Current and emeritus faculty also provided historical overviews of the department.

Our faculty continue to obtain prestigious research grants. Our undergraduate major is the second-largest in our college. The PhD and MS programs have strong and growing enrollments, while we have increased our hands-on lab courses for senior undergraduate and graduate students. Collectively, these courses will provide real-life experiences and better prepare our students for the range of careers that biomedical engineers are equipped to pursue.

This is also an exciting time of growth in new faculty positions. Assistant Professor Aarushi Bhargava arrived in summer 2024 and specializes in therapeutic uses of ultrasound technology. Randy Bartels, hired through a collaboration with the Morgridge Institute for Research, is now on campus as a full professor after spending last year as a visiting professor. Duc-Huy Nguyen, who specializes in using microdevices to study liver diseases, will join us in summer 2025. We will be searching for four new faculty members this year, two of which will be part of the Wisconsin Research, Innovation, and Scholarly Excellence (RISE) Initiative on artificial intelligence.

We continue to expand upon our efforts to ensure a welcoming environment for all. Notably, several of our BME faculty participated in the third annual WiscProf workshop to help prepare graduate students and postdoctoral fellows for careers in academia. BME also co-sponsored the third Rising BME Scholar workshop hosted at the University of Illinois-Chicago, which covered a broader range of careers for BME PhDs. Our department will host this event in June 2025.

I hope you and your loved ones are well, and I thank you for your support of our department.

On, Wisconsin!

Paul J. Campagnola

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On the cover: Mitchell Josvai, a PhD student, uses stem cells to study biomechanical properties of a variety of cell types. Photo: Tom Ziemer.



New model will help researchers connect dots at the intersection of our joints

The myotendinous junction is a key connective point in the human body, where skeletal muscle meets tendon. When muscles contract, the junction transmits the force to tendons, facilitating movement.

As the intersection of two different types of tissues, though, it's also vulnerable to injuries—think strains or even tears in the rotator cuff or the Achilles tendon—making it especially relevant to study to explore potential therapies.

But the myotendinous junction has proven difficult to replicate in cell cultures because of its complex architecture, which features interlocking structures between myocytes (muscle cells) and tenocytes (cells that make up tendons).

Using human induced pluripotent stem cells and a micropatterned platform, UW-Madison researchers created a more representative model-in-a-dish of the junction, which will better allow researchers to study its fundamental properties, learn how it heals after injury, and explore patient- and disease-specific models.

Led by BME PhD student Mitchell Josvai, researchers from the College of Engineering and the School of Veterinary

Medicine published their work in the journal *Acta Biomaterialia*. Professors Wendy Crone and Masatoshi Suzuki oversaw the project.

“If you just put the two cell types together in a dish, you’re not going to get an accurate representation of what you’d find in the body,” says Josvai (BS ’22), a Madison native and member of Crone’s lab.

To produce a more accurate model, the researchers micropatterned proteins from the extracellular matrix, the support material that exists between cells in the body, in neighboring lanes on a substrate. Then, they cultured myocytes on one side and tenocytes on the other.

“We allow them to stick to this patterned protein matrix and then they expand, they proliferate, they make new cells, and they grow toward each other,” says Josvai. “It’s pretty similar to what happens in development in the body.”

Within a week, the myocytes and tenocytes had formed interlocking structures called interdigitations. When the researchers electrically stimulated the myocytes after three-and-a-half weeks, under a microscope they could see the muscle cells contract and pull on the tenocytes, demonstrating functional behavior.

“The strength of the micropatterned culture is it’s quite useful to study the individual cell behaviors and then also interactions,” says Suzuki, a professor of comparative biosciences. He’s also an affiliate faculty member in BME who’s working with engineering faculty Randolph Ashton, Padma Gopalan, Wan-Ju Li and William Murphy on other projects.

Suzuki believes the group’s two-dimensional myotendinous junction model is the first in the field to use myocytes derived from human stem cells. Moving forward, he and Crone are interested in using patient-derived stem cells to create models of muscular and connective tissue disorders like muscular dystrophy, Ehlers-Danlos syndrome and Marfan syndrome. He and Li are also working on creating a three-dimensional version of the model, which would allow them to study the cells over a longer timeframe.

More broadly, though, Josvai says their method could inform how researchers model other tissue connections.

“There are all kinds of interfaces over the body where you have two cell types meet,” he says. “The general idea of the platform could be applied to a number of different use cases.”

Serendipity reveals new method to fight cancer with T cells

A promising therapy that treats blood cancers by harnessing the power of the immune system to target and destroy cancer cells could now treat solid tumors more efficiently.

Thanks to a study published in *Molecular Therapy – Methods & Clinical Development* by PhD student Dan Cappabianca and Associate Professor

cancer cells, specifically those in tumors. T cells can “remember” a pathogen after first exposure, allowing a quicker and stronger response if encountered again, like how vaccines train the immune system to recognize and fight off specific pathogens.

But for the cells to be used as a robust cancer treatment, they must be made in specific conditions in the lab.

“We were comparing two distinct T-cell media formulations with varying nutrient levels,” explains Cappabianca. “Interestingly, our breakthrough came

stresses the cells and triggers specific processes that can enhance their ability to target tumors, promote the formation of T memory cells, and select the more resilient cells that can survive with such low levels of energy. The second step supports rapid growth and T cell multiplication.

The result of this “metabolic priming” was that treated cells retained their stem cell-like qualities, thus enhancing their ability to kill cancer cells, transform into durable memory cells, and survive longer in the body.

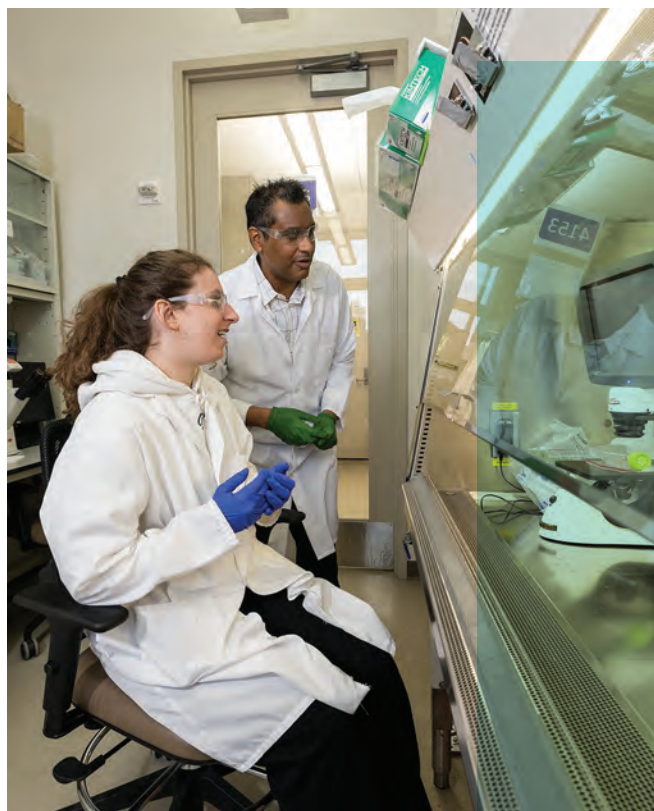
“We discovered that by briefly restricting sugar exposure, akin to a three-day ‘keto diet,’ our T cells showed reduced maturity at the end of the manufacturing process. The less mature they are when reinfused into a patient, the longer they live fighting cancer,” says Cappabianca.

The two-step process also appeared to help with cell memory. In CAR T-cell therapy, boosting these memory properties helps T cells better recognize and combat cancer over time.

In recent studies using T cells grown with the lab’s new approach, 63% of patients experienced a partial or complete reduction in tumors for a time. That’s an improvement from clinical trials using CAR T cells that were not grown with the lab’s two-step process, where just 15% of patients experienced a partial or complete reduction in tumors after treatment.

More research is needed to understand the key factors that help these CAR T cells live longer and become effective against solid tumors. Looking ahead, researchers hope that this process of “metabolically priming” these specific kinds of CAR T cells can be adapted for large-scale manufacturing with the ultimate goal of treating patients within the next few years.

“A famous aphorism by French chemist Louis Pasteur is that ‘chance favors only the prepared mind,’” says Saha. “Our unplanned media switch—really by chance—led us on a new path of discovery.”



Associate Professor Krishanu Saha reviews cells in his laboratory with a student. Saha researches CRISPR, which can be used to modify pieces of genetic code within our cells. Photo: Joel Hallberg.

Krishanu Saha, chimeric antigen receptor (CAR) T-cell therapy can be improved by altering the conditions in which the T cells are grown. And it was all discovered by chance.

T cells are white blood cells crucial for the immune system’s response to infections and cancer. They can be modified with CRISPR/Cas9 genome editing technology to express a specific receptor that redirects their natural “killing instincts” toward targeting

entirely by chance. I inadvertently placed the cells in the wrong medium, which unexpectedly became the focal point of my entire thesis!”

In the body, T cells develop from stem cells in the bone marrow. In the lab, researchers activate the T cells in a nutrient-deficient medium with low concentrations of glucose and glutamine, which the cells need for energy. Then they move them to a high-nutrient medium. The first step

PhD student Zack Harmer, right, and Associate Professor Megan McClean have developed a technique for greatly accelerating the design and optimization of optogenetic systems. Photo: Tom Ziemer.

Machine learning illuminates experimental design for synthetic biology



When Zack Harmer's advisor and lab leader, Associate Professor Megan McClean, suggested he explore a potential collaboration with Chemical Engineering Professor Victor Zavala's computational group, the PhD student didn't need to look far.

David Cole, Harmer's roommate for three years, was a PhD student in Zavala's lab, which has a litany of experience applying computational techniques to engineering challenges.

The initial conversations between the students eventually led to a project that brought together the McClean lab's platform for high-throughput testing of optogenetic systems with the Zavala group's machine learning toolkit. Together, the team created a framework for designing advanced synthetic biology systems that could be useful for generating biotherapeutics or other bioproducts.

The researchers detailed their approach in a paper in the journal *ACS Synthetic Biology*.

In optogenetic systems, scientists manipulate biological processes through light-responsive proteins. Many of those proteins respond to blue light, which presents a challenge when trying to design more complex systems that allow for independent control over multiple processes. One potential solution is to take advantage of different dynamics of blue light; for example, pulsed light might activate one such function, while sustained light turns on another.

"How can we just use one wavelength of light to independently control multiple different biological outcomes?" says Harmer (PhD cellular and molecular biology '23), who's now a synthetic biology scientist at a California-based biotechnology company.

"Finding those sweet spots is hard," adds McClean.

Harmer and McClean had previously developed a system named Lustro for high-throughput testing to accelerate the design and optimization of optogenetic systems, technology

for which they're pursuing a patent through the Wisconsin Alumni Research Foundation. By teaming with Zavala, they harvested the trove of data generated by Lustro.

"All of a sudden you have access to all of this data, to test all of these different conditions, and we were able to apply more sophisticated techniques than what I originally envisioned," says Zavala, whose research group develops computational techniques for optimization and control. "We were able to use machine learning approaches to construct this model directly from data, trying to find optimal conditions and trying to recommend experiments in a closed-loop manner. That was transformational."

Zavala's group developed neural networks that, given a range of experimental conditions (proteins involved, light inputs), could predict outcomes while also quantifying the level of uncertainty in those predictions. Jaron Thompson, a PhD student co-advised by Zavala and Ophelia Venturelli, associate professor in the Department of Biochemistry, primarily developed the machine learning tools.

"Experiments are not free, in either reagent cost or time," says McClean. "I think what's particularly nice about the model is, in addition to making predictions about specific behaviors of the system, it can tell you where to do experiments and where it's most informative to do experiments. That's really powerful."

McClean and Zavala are already exploring additional opportunities to apply similar approaches to more complex biological systems, as well as developing and leveraging more sophisticated modeling techniques.

"Wisconsin has a pretty unique environment for fostering these types of collaborations," says Zavala. "I think the College of Engineering is very cohesive. It's easy to start these types of collaborations, and people are very friendly. It's just really a pleasure to collaborate with people around here across different departments."

FOCUS ON NEW FACULTY

Aarushi Bhargava expands ultrasound's impact



When you hear the term ultrasound, you likely think of pregnancy and fuzzy images of developing babies. And the technology, which relies upon reflected soundwaves to generate images, is indeed frequently used to monitor fetal growth or to examine other parts of the body to inform diagnoses.

But high-intensity ultrasound can also destroy unwanted tissue, such as tumor cells or uterine fibroids—and researchers like Aarushi Bhargava are exploring its other possibilities.

Bhargava joined BME as an assistant professor in summer 2024, bringing her interdisciplinary research on the mechanics of soft materials and acoustics for developing biomedical technologies.

“A major obstacle to successfully bringing a technology to market is poor communication between the different experts involved in its development. For instance, researchers with expertise in mechanics investigate how materials react to mechanical stimuli like sound. On the other hand, clinicians focus on the induced bioeffects of ultrasound in materials like tissues,” says Bhargava, who studied mechanical engineering and biology at the Birla Institute of Technology and Science in India. “As new ultrasound-based technologies move to the clinical evaluation phase, a disconnect often occurs between these two domain experts. This disconnect prevents the optimization of the technology’s performance. The goal is, therefore, to bridge this gap across different disciplines—in this case, material experts and clinicians—throughout an ultrasound technology’s development.”

While earning her PhD at Virginia Tech and completing postdoctoral research stints at the University of Chicago and the Max Planck Institute for Intelligent Systems in Stuttgart, Germany, Bhargava has used ultrasound for drug delivery, to break up blood clots, and to activate medical microrobots. And she says those are just a few examples of how ultrasound can augment or replace existing treatment strategies.

“It’s a huge range,” says Bhargava, who’s originally from Jaipur in western India. “Ultrasound traditionally has been used to heat cells and tissues. And now we are using it to mechanically manipulate a material, opening up a wide variety of applications. You can induce drug delivery, perform neuromodulation, disintegrate a tissue—all through the mechanical force of sound, and it just depends on few ultrasound parameters such as its intensity and frequency, and then, obviously, on the material.”

Bhargava sees herself as a natural fit in BME, where nearly all research spans departmental and college boundaries and requires collaborative expertise in biology, materials and technology.

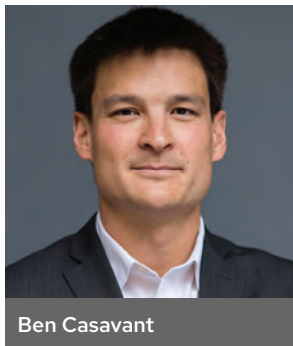
“Many faculty members in BME are working in complementary fields,” she says. “For instance, researchers like Melissa Skala and Kevin Eliceiri focus on immune cells and extracellular matrix behaviors, while I specialize in how ultrasound interacts with various soft materials. This synergy brings exciting opportunities to develop new treatment technologies. Additionally, researchers like Chris Brace are using other noninvasive methods, especially microwaves, to interact with tissues in ways similar to ultrasound. These aligned interests create a vibrant and collaborative environment for innovating hybrid therapeutic strategies.”

In the classroom, Bhargava will teach biomechanics courses, which will allow her to share her research with undergraduate students.

“One thing about teaching I like the most is that it’s a two-way transfer of knowledge,” she says. “A classroom makes you examine a concept you are teaching from different perspectives, not just your own, and that in my opinion is a very comprehensive way to increase your knowledge about that topic. You see students getting excited about things that you’re also excited about. It’s a very nice and satisfying feeling.”



Erwin Berthier



Ben Casavant

BME honors alumni duo for medical device success

In the earliest days of Tasso, before any regulatory approvals, rounds of financing or major contracts, Erwin Berthier (PhD '11), Ben Casavant (PhD '13) and another friend huddled to decide whether to put their own money behind their fledgling idea.

They each chipped in \$300, a tiny sum in retrospect, but enough to 3D-print prototypes to show funding agencies.

"It got us the traction that we needed to get to the next level," says Berthier. "For me, it's a reminder of no matter how much money you have, look at what you can do with what you have. There might be a way."

More than a decade later, Tasso is now a thriving medical device company specializing in tools for at-home blood draws. The company, co-founded by Berthier and Casavant in 2012 based on their work in the lab of Professor David Beebe, has raised more than \$100 million in private financing while shipping out more than 1 million devices.

Berthier and Casavant are BME's 2024 Early Career Award honors as part of the college's annual Engineers' Day celebration.

Tasso, which is Italian for badger, has created a platform that allows for painless at-home blood draws. The Seattle-based company's technology is currently used to gather data in support of clinical trials for new drugs, in research studies, and in drug testing for Major League Baseball and the Olympics.

Casavant says the company's roadmap includes at-home testing for chronic disease management in the near future.

"What I would love to see is that you go to your doctor and they say, 'You can do the blood draw or we can just send you a Tasso,'" says Casavant, Tasso's CEO. "I think that's the future. I think we're looking to become a standard way that people can get critical health and diagnostic information. And I think one step further than that is stitching together that patient information and looking at it over time. I think you can start using that data to make better predictions, to help make better interventions a little bit earlier."

Berthier, the company's CTO, credits Tasso's success, in part, to the two partners' experience in Beebe's lab.

"It's a lot of the values that we took out of Dave's lab," he says. "It's this idea of listen to the data. A lot of people get into startups with the mindset of build it and they will come. And that is tempting. We're taking the right risks at the right time based on the right kind of learnings from the data."

Faculty News



In research published in the journal *Optica*, Professor **Randy Bartels** and collaborators describe a new optical imaging approach that

looks into biological samples to uncover hidden information within cells and tissues. The researchers demonstrated for the first time the use of third harmonic generation holographic microscopy—where the frequency of laser light is tripled when it interacts with materials—to collect measurements of light intensity as well as phase information.



Professor **Paul Campagnola**, the Peter Tong Department Chair, will bring his unique combination of fabrication and imaging techniques to a new \$11 million project funded by the U.S. Department of Defense to better understand the scarring lung disease idiopathic pulmonary fibrosis.



Vilas Early Career Assistant Professor **Aviad Hai** has received an early-concept grant for exploratory research from the National Science

Foundation to support his research developing new types of minimally invasive sensors for brain imaging.



Professor **Kevin Eliceiri**, the Retina Research Foundation Walter H. Helmerich Chair, received the college's Byron Bird Award for Excellence in a

Research Publication in recognition of five papers that have become seminal articles and shaped the field of image informatics.



Student follows late brother's path at Medtronic

Colin Peck, a senior studying computer engineering and computer science, found inspiration from the loss of his brother to help others. When Brian Peck, a BME major, tragically passed away in 2019 from cardiac arrest at the age of 20, he was planning to begin an internship at Medtronic, a healthcare technology company.

In summer 2024, Colin carried forward his brother's legacy as an intern with the same company—a story that was featured by *People* magazine in July 2024.

"At the start, losing my brother invoked a loss of identity. It forced me to grow up very fast, as I was 16 at the time. It was

just before the outbreak of COVID-19, so the isolation was inconveniently timed with my grief. However, I was able to take a lot of time to reflect and work on myself, to determine what I could be, and rediscover my purpose," Peck says.

While still in high school, the Orland Park, Illinois, native organized EKG drives to perform screenings used to detect potentially harmful cardiac conditions in his classmates.

"Brian's passing gave me a new perspective of mortality and how fragile life can be," he says. "It motivated me to advocate for the prevention of sudden cardiac death."

Colin fell in love with the UW–Madison campus during visits to see his brother and was drawn to technology much the same way Brian had been. As an undergraduate student, Colin has sought to apply his classroom knowledge to enhance the quality of life for others.

"During Brian's interviewing process, I heard great things about Medtronic. They were very kind and supportive after hearing about Brian," says Colin, who worked in the same operating unit (cardiac rhythm management) that his brother was planning to.

"Connecting with others here has put into perspective how much of a difference each individual role and person makes at Medtronic. Even little impressions made as an intern go a long way. It is an honor to be able to contribute to such an important cause."

Submitted photo