College of Engineering
UNIVERSITY OF WISCONSIN–MADISON

SPRING 2025 NEWSLETTER

DEPARTMENT OF

BIOMEDICAL ENGINEERING

Greetings from Madison!

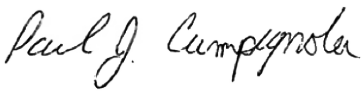
As we near the end of this academic year, I would like to reflect on department's successesover the last 12 months and highlight where we are going.

Once again, we had a near-record number of entering freshmen into our BME program this year (around 250). We are now the third-largest undergraduate program in the College of Engineering, and our BME program is now among the largest in the Big Ten. We are proud of our students, who are conscientious, community-minded young people who break the typical engineering mold by pairing technical knowledge with communications skills. They are curious, well-rounded and dedicated to making a difference in peoples' lives.

To accompany this increase in students and to also increase our research profile, the department is in a large hiring phase for new faculty members. In addition to four hires over the last two years, we are actively recruiting five new faculty members this year. Several of these positions are in traditional areas of tissue engineering. We are making additional hires through the Wisconsin Research, Innovation and Scholarly Excellence (RISE) campuswide initiatives on artificial intelligence/machine learning, focused on cellular engineering; and Transforming Healthspan through Research, InnoVation and Education, with an emphasis on the microbiome-immune system.

We continue to expand our efforts to train the next generation of biomedical engineers for careers in academia. Our faculty continue to participate in our college-sponsored WiscProf, which brings graduate students and postdoctoral researchers to our campus for an in-depth exploration of academic careers in engineering at a top research institution. I hope you and your loved ones are well, and I thank you for your support of our department.

On, Wisconsin!



Paul J. Campagnola
Professor and Peter Tong Department Chair
Kellett Faculty Fellow
pcampagnola@wisc.edu

engineering.wisc.edu/bme

linkedin.com/company/uwbiomedicalengr

instagram.com/UWMadison_BME

Meet the college's next dean

Devesh Ranjan, a mechanical engineer and a leader at one of the country's largest and highest-ranked engineering programs, will be the college's 10th dean. He will begin on June 16.

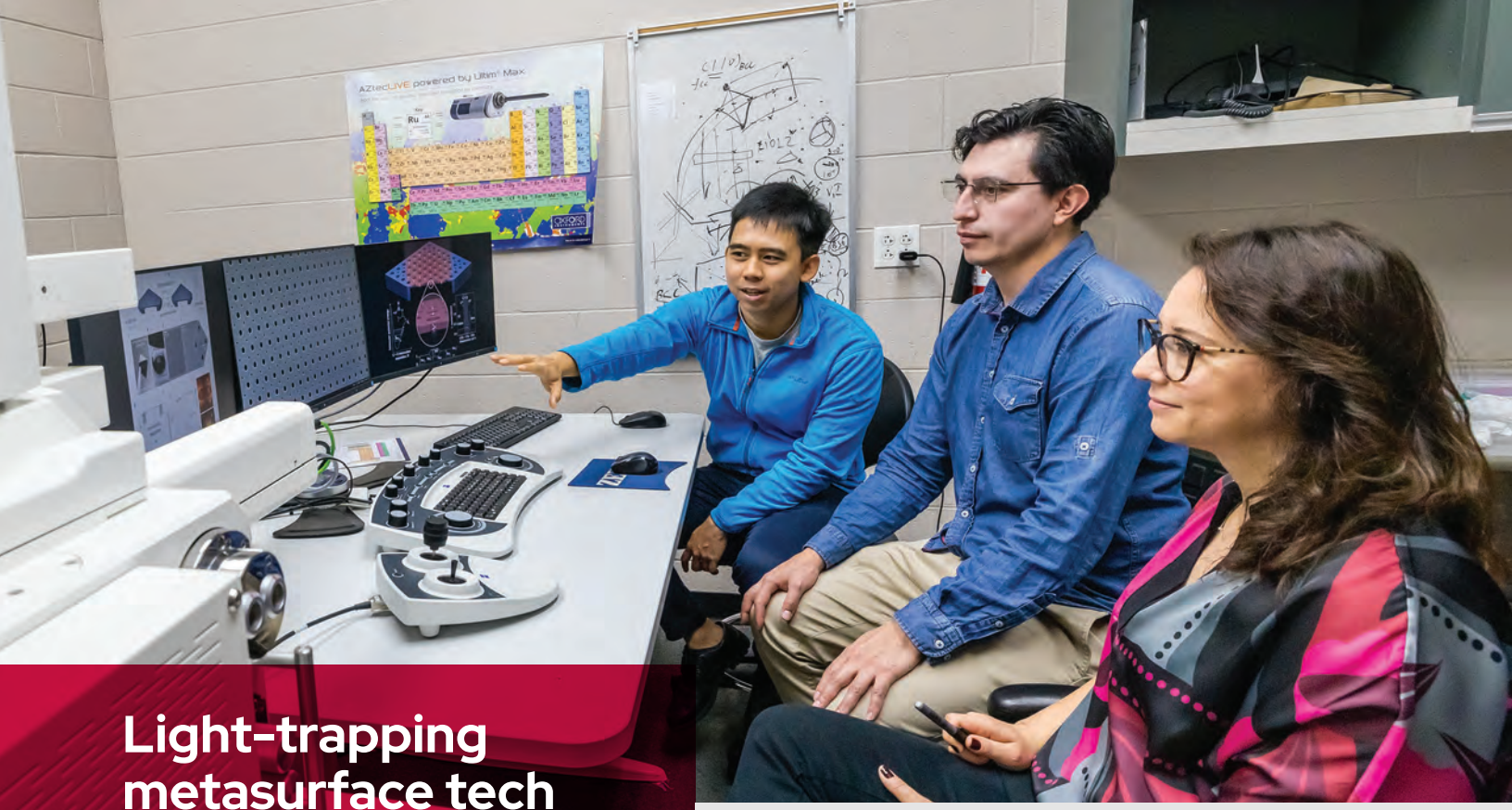
Ranjan, the Eugene C. Gwaltney Jr. School Chair and Professor of Mechanical Engineering at the Georgia Institute of Technology, remembers the promise he felt when he first arrived at UW-Madison in 2003 to begin graduate school in the college he will now lead.

"I've been blessed from that day onward," Ranjan says. "The thing I say about UW-Madison is if you dream about doing something here, it will happen. It will happen because of the opportunity and the support here for you at UW–Madison."

After earning a doctorate at UW-Madison in 2007 in the lab of Professor Riccardo Bonazza, Ranjan was a Director's Postdoctoral Fellow at Los Alamos National Laboratory before joining the faculty at Texas A&M University in 2009. He moved to Georgia Tech in 2014, where his own work has focused on the dynamics of fluids at very high speeds—air across the surface of supersonic jets, the plume of a volcanic eruption, shock waves that fragment kidney stones—and designing next-generation power cycles optimized for solar energy sources or incorporating the efficiency of supercritical carbon dioxide as in heat pumps.

Read more about incoming Dean Ranjan.

On the cover: Each semester, our undergraduate design program culminates with a poster session and award ceremony. Students present projects submitted by industry partners, community members and biomedical researchers. Photo: Renee Meiller.



Light-trapping metasurface tech boosts biosensors

PhD students Wihan Adi and Samir Rosas and Assistant Professor Filiz Yesilkoy, shown using a scanning electron microscope, hope to use their metasurface to uncover new biomarkers of diseases such as ovarian cancer. Photo: Tom Ziemer

A team led by Assistant Professor Filiz Yesilkoy developed a thin, patterned, silicon-based component that excels at trapping non-visible light and could open up low-cost manufacturing possibilities for biochemical sensors and more.

The group detailed its "substrate-less metasurface" in a paper in the journal *Nature Communications*. In particular, PhD students and co-lead authors Wihan Adi and Samir Rosas and their collaborators highlight the metasurface's ability to induce light and matter to couple into a hybrid state called polaritons. These quasi-particles are especially of interest in chemistry, where they could alter chemical reactivity.

Metasurfaces are tiny, engineered, nanoscale materials that can manipulate electromagnetic waves, much like how so-called "wave breakers" physically disrupt water waves, says Adi.

"We use our metasurface to trap light. And because the light is trapped, it can interact longer with the molecule," says Adi.

In this case, the waves are in the mid-infrared range of the electromagnetic spectrum. Infrared light, which has longer wavelengths than visible light, can be useful in applications ranging from astronomy to healthcare. Yesilkoy's lab is interested in the latter; mid-infrared light could reveal the various molecules in biological samples without requiring any sort of invasive labeling.

"It's a little bit of a challenging part of the electromagnetic spectrum, because you cannot use conventional materials that are used in traditional optics, where we're mostly interested in the visible—the wavelengths that we see," says Yesilkoy, whose research bridges optics (the study of light's behaviors and properties) and micro- and nanofabrication to develop and improve biosensors, imaging technology and other medical diagnostic tools.

The materials conventionally used in mid-infrared optics also tend to be either brittle or expensive, meaning any devices relying upon them would be difficult to cheaply mass manufacture. And for biosensors to be useful in collecting data from hundreds to thousands of patients to inform medical research, bulk production is essential.

"We really need these sensor chips to be manufactured in bulk so that we have a lot, so that we can decrease their cost and apply them for different applications," says Yesilkoy.

Instead, Yesilkoy and her students patterned an extremely thin silicon membrane—just one micron thick—that traps light in cavities. When they tested it in the mid-infrared spectral range, they found it trapped light so efficiently that polaritons formed when the light interacted with a polymer sample.

While that capability of the group's technology is of interest to researchers in the nascent field of polaritonic chemistry, the Yesilkoy lab's focus remains biosensors. In particular, the group hopes to use the interactions of light and biomolecules to uncover new biomarkers of diseases such as ovarian cancer.

Yesilkoy, Adi and Rosas continue to tweak the patterns on their metasurface to improve its performance.

"This was our first exploration, but now we have a different design that can actually have better control over light, more suited for biosensing applications," says Yesilkoy. "So that's where we are pushing."

mRNA-activated blood clots could cushion the blow of osteoarthritis

William Murphy

Professor William Murphy and collaborators have developed a promising technique for treating osteoarthritis using therapeutic blood clots activated by messenger RNA.

Osteoarthritis is the most common form of arthritis, affecting roughly 33 million adults in the United States, according to the Centers for Disease Control and Prevention. It occurs when cartilage in key joints like the knees and hips deteriorates, causing pain and stiffness and impeding mobility.

The research team detailed its new approach in a paper in the journal *Bioactive Materials*. With further development, it could one day offer a more effective option than treatments such as steroid injections, hyaluronic acid injections or even joint replacement surgeries.

"The best-case scenario is that this could be an injectable or implantable treatment for patients who have advanced osteoarthritis," says Murphy, the Harvey D. Spangler Professor, H.I. Romnes Faculty Fellow and director of the Forward BIO Institute. "This would be an alternative to the existing methods for treatment, which generally don't show a high level of long-term success."

Following the lead of his lab's previous work on mRNA-based vaccines, therapies for spinal cord injuries and more, the method relies upon mineral-coated microparticles to deliver mRNA that encodes for production of a protein that supports cartilage formation.

First, the team takes bone marrow aspirate (liquid bone marrow) and peripheral blood samples from a patient, mixes in the microparticles, and then forms the mixture into a blood clot. Then the mRNA-activated clot gets delivered to the site of the damage.

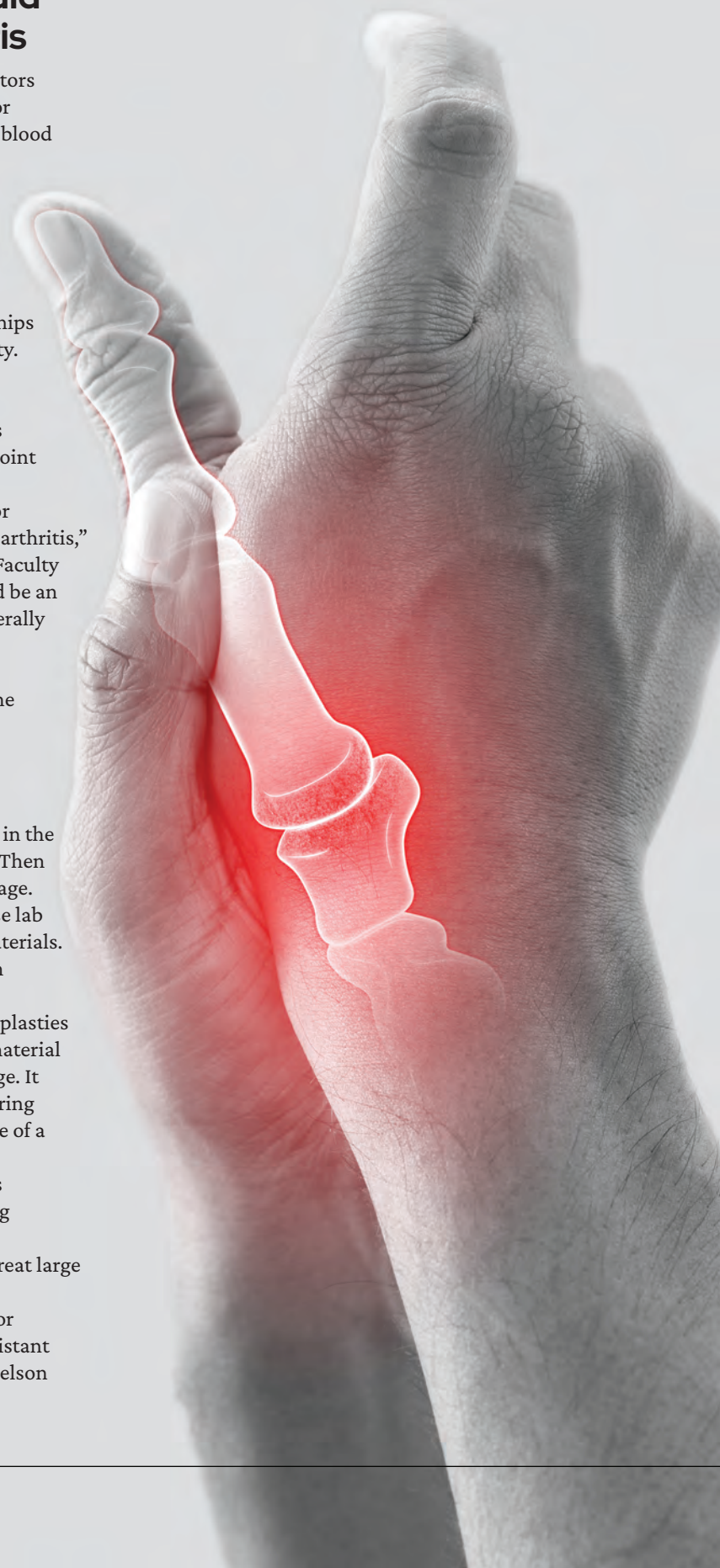
"This all happens in the same surgery," says Murphy, whose lab specializes in therapies that leverage biologically inspired materials. "This is all intra-operative, and it uses materials derived from the patient."

Whereas existing treatments such as arthroscopic chondroplasties can lead to the formation of fresh fibrocartilage tissue, that material doesn't boast the same mechanical properties of joint cartilage. It also degrades more quickly. Unlike traditional tissue engineering approaches, however, the new method doesn't require the use of a synthetic scaffold material upon which to grow cells.

After seeing success in rabbit models, the group will test its treatment strategy in a larger animal model before proceeding toward human clinical trials.

Murphy says his group is exploring the same approach to treat large skeletal muscle and bone defects as well.

Other BME authors on the paper include Associate Professor Wan-Ju Li; MD-PhD student Joshua Choe; Hongli Jiao, an assistant scientist in Wan-Ju Li's lab; and graduate students Michael Nelson and Margot Amitrano.

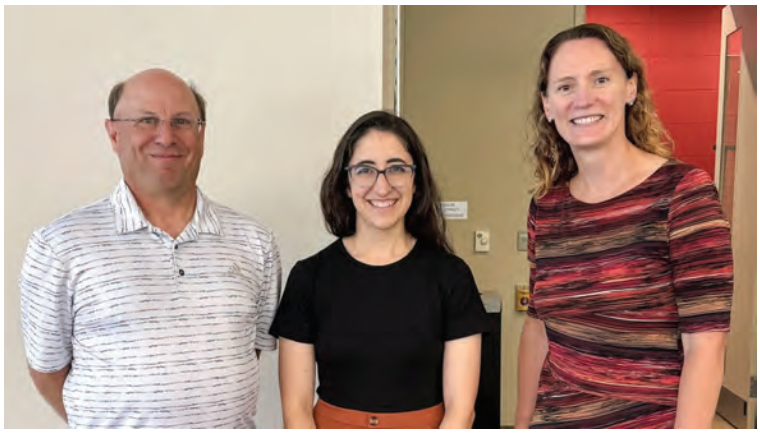


Collagen highway signs could show how to stop pancreatic cancer spread

Collagen is the most prevalent protein in the human body, keeping our joints healthy, our bones strong and our skin stretchy.

However, studies increasingly show that collagen in the extracellular matrix, the gelatinous material that surrounds our cells, also plays a key role in the spread of cancer (known as metastasis). And by better understanding the mechanics of how cancer cells move from the main tumor, researchers could pinpoint potential targets for cancer therapies to thwart the disease's progression.

In a paper in the journal *Acta Biomaterialia*, a BME team showed how the alignment of collagen fibers accelerates the movement of clusters of pancreatic cancer cells.



From left: Professor Paul Campagnola, recent PhD graduate Sophie Mancha and Professor Melissa Skala. Submitted photo.

"We all know that the extracellular matrix is a really critical component of pancreatic cancer, and that's why it's challenging to treat and it's very aggressive," says Professor Melissa Skala, who is also an investigator at the Morgridge Institute for Research on the UW-Madison campus.

By using a unique combination of microscopy imaging of real patient samples and fabrication techniques, researchers from the labs of Skala and Professor and Peter Tong Department Chair Paul Campagnola found that parallel-aligned collagen fibers acted as a highway for cancer cells. Beyond that, study lead author Sophie Mancha (PhD '24) and collaborators discovered that the cells moved especially aggressively in clustered groups. Previous research has focused predominantly on single-cell movement, as opposed to collective cell migration.

"It adds credence that this collective cell migration is really important in pancreatic cancer," says Campagnola.

Campagnola's lab has pioneered the combination of using an imaging technique called second harmonic generation microscopy to view patient biopsies and then fabricating them to create realistic scaffolds for cell cultures.

"Our technology is really the only way to make true mimics of the collagen structure," says Campagnola.

While analyzing cancer cell behavior across a range of patient-derived scaffolds, the group consulted Jacob Notbohm, an associate professor of mechanical engineering who studies collective cell movement. Grown on scaffolds that mimicked aligned collagen fibers, clustered cells displayed higher levels of traits associated with metastatic behavior than did single cells. The researchers also found that clusters grown on aligned scaffolds moved much more rapidly than groups grown on unpatterned surfaces, adding more evidence that collagen fibers provide a conduit for cancer cell spread.

The team already has another paper in the works examining the metabolic activity of multiple cancerous cell lines on the scaffolds. Moving forward, Skala and Campagnola are interested in using genetic sequencing to uncover which genes are at work in the cancer cells and in assessing chemotherapy agents on cell clusters to inform personalized medicine strategies.

Mancha, whose grandfather died from pancreatic cancer when she was in high school, got an immediate graduation present when the paper was accepted eight minutes after she finished her dissertation defense.

"This just continues to highlight that collagen is very important, and the reorganization of collagen is doing something," says Mancha, who's now in the scientific leadership development program at Tolmar, a pharmaceutical company based in Fort Collins, Colorado. "It's important that we continue to study that and see if collagen could be a future therapeutic target for pancreatic cancer patients."

Other BME authors on the paper include: Professor Kevin Elicieri, who holds the Retina Research Foundation Walter H. Helmerich Research Chair at the McPherson Eye Research Institute at UW-Madison; undergraduate researchers Meghan Horan (BS '24) and Ojaswi Pasachhe; and Adib Keikhosravi (PhD '20).

With CAREER Award, Witzenburg examines the mechanics behind a change of heart

A cell in a crucial heart valve leaflet feels a disruptive stretch, so it produces more of the structural protein collagen—and in extreme cases even produces calcium—to ease its physical stress.

It's a little remodeling job with broader consequences: If enough cells join in, the overall structure of the aortic valve leaflet thickens and hardens, impairing its ability to open and close as blood pumps. As the valve narrows due to this disease-induced feedback loop, it can have dire consequences for the heart, including congestive heart failure and sudden cardiac death. However, calcific valve disease has no viable treatment options—apart from surgically replacing the valve with a prosthetic.

"The problem in this pathologic situation is that what's good for the cell is not good for the organ," says Colleen Witzenburg, the Jane R. and John G. Mandula Assistant Professor.

Witzenburg is using a National Science Foundation CAREER Award to illuminate the unknown but important mechanisms behind the structural changes that accompany and drive calcific aortic valve disease.

By employing complex mechanical testing in combination with advanced imaging of lab-cultured aortic valve leaflets, the five-year, roughly $650,000 project will lay the groundwork to identify potential therapeutic targets to disrupt this feedback and slow, or even halt, disease progression.

Calcific aortic valve disease, the most common heart valve ailment, involves progressive thickening and stiffening—with fat, collagen and, eventually, calcium deposits—of the three leaflets that make up the aortic valve. These one-to-two-millimeter-thick leaflets open and close to pump blood from the heart out to the rest of the body, doing so billions of times over an average lifespan. That combination of fine physical structure and robust mechanical function is difficult to replicate in synthetic prosthetics, which require invasive surgeries and generally only last 10-15 years.

"We're able to diagnose and treat end-stage disease, but there are no options for early-stage disease except wait and watch," says Witzenburg. "Furthermore, drugs and less invasive solutions for other heart problems have not been successful in calcific aortic valve disease."

When calcification occurs, it does so in a patchwork manner, rather than uniformly across the tissue. The mechanical forces at play influence that spatial variability—making it difficult to study. Enter Witzenburg's lab, which uses a mechanical system to test leaflet cells in multiple directions and then culture them under mechanical loads with components typically featured in surgical robots. In this latest work, she and her students will also use an imaging technique called quantitative polarized light imaging to examine the alignment of collagen fibers in which the cells live. That work will help the researchers narrow down tissue sections to look at in greater detail; on that, they'll collaborate with Peter Tong Department Chair and Professor Paul Campagnola, whose second harmonic generation imaging offers unparalleled resolution.

"A lot of studies have shown that if you put these cells in different mechanical conditions, they behave in very different ways," says Witzenburg. "So mechanics plays a critical role in modulating their behavior. Therefore, our culture system will involve cyclic stretching in physiologic ranges."

In the outreach component of the project, Witzenburg's research group will develop heart-and mechanics-related science activities for kids to share with Camp Odayin, a Minnesota-based organization that offers programming for kids with heart disease and their families in Minnesota and Wisconsin.

"Science outreach rarely goes to kids," she says. "We usually ask them to come to us."

Faculty news

Assistant Professor **Aarushi Bhargava** was one of three UW-Madison researchers receiving Cardiology Challenge Grant funding from the Wisconsin Alumni Research Foundation and Route 66 Ventures. Bhargava, who studies novel uses of ultrasound technology, will lead a project exploring a noninvasive strategy for treating blood clots.

Professor **Krishanu Saha** was among 10 researchers touted by the science and healthcare media company STAT as leading the way in developing CRISPR-based therapies. Saha's work with CRISPR, a gene-editing toolkit, includes more safely producing CAR T cells to fight solid cancer tumors and developing new therapies for previously untreatable eye diseases.

Jane R. and John G. Mandula Assistant Professor **Colleen Witzenburg** received a five-year, $1.86 million grant through a Maximizing Investigators' Research Award from the National Institute of General Medical Sciences. Witzenburg will use the funding to improve multiscale imaging and mechanical testing of soft tissues.

Student news

PhD student **Samir Rosas** received a prestigious Grainger Fellowship for graduate researchers. Rosas' research is driven by his curiosity about light and its interactions with small molecules. By harnessing the unique properties of mid-infrared light coupled with nanophotonic optical chips, Rosas aims to rapidly and accurately find biomarkers, which can help with early disease diagnosis and other scientific studies.

BME spinoffs earn SEED funding

Two companies with BME ties were among the 2024 funding recipients of the annual State Economic Engagement and Development (SEED) program.

The first is Atrility Medical, a medical device company co-founded by alumni Phil Terrien (BS '17) and Matt Knoespel (BS '17) (pictured above) along with UW-Madison School of Medicine and Public Health Professors Nick Von Bergen and Vikas Singh. The company is working to further develop its AtriAmp device, which started as an undergraduate BME design project, for detecting postoperative cardiac arrhythmias in pediatric patients.

Professor Walter Block is part of a team that's created a disposable liner for MRI and CT scanners to help prevent hospital-acquired infections. Block's frequent collaborators Andrew Alexander, a professor of medical physics and psychiatry, and Azam Ahmed, an associate professor of neurosurgery and radiology, are also part of the team.

The SEED program is coordinated by UW-Madison's Discovery to Product office in partnership with the Wisconsin Economic Development Corporation. Seven companies founded by UW-Madison researchers received funding in total.

Department of
Biomedical Engineering
UNIVERSITY OF WISCONSIN–MADISON

1550 Engineering Dr., Room 2130
Madison, WI 53706
engineering.wisc.edu/bme

Top: from left, Molly Paras, Zach Spears and Lauren Fitzsimmons. Photo courtesy National Inventors Hall of Fame. Lower: The all-in-one device includes a forceps and scalpel. Submitted photo.

Best of the best

Senior Lauren Fitzsimmons and recent graduates Molly Paras (BS ’24) and Zach Spears (BS ’24) won first place in the 2024 Collegiate Inventors Competition in Alexandria, Virginia.

The group’s “Nerve Ninja” tool earned the $10,000 top prize in the undergraduate division of the annual competition, which is put on by the National Inventors Hall of Fame.

The surgical tool, which includes a forceps and scalpel to improve efficiency and reduce nerve injuries during carpal tunnel release surgeries, began as a BME undergraduate design project. John Puccinelli, associate chair of the undergraduate program and an associate teaching professor, was the group’s advisor. The team has also formed a company called Badger Surgical Solutions.

In addition to their cash prize, the group will receive a patent acceleration certificate from the United States Patent and Trademark Office.