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RESEARCH

LINKING LABORATORIES TO LIVES

NJIT

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From the Senior Vice Provost for Research

For too long, academic research languished on the bench, relegated to journals consumed by insular, elite audiences. But the world has changed. The need for real-time fixes to global problems, from health care to the environment, requires our ingenuity and intellectual discipline. We embrace that challenge, and what's more, we're ready to adopt new ways to meet it. Primary among them is collaborating on ideas, early on in their development, with the outside experts who will help us translate them into beneficial technologies.

Point-of-care technologies are a case in point. They have the potential to improve health outcomes for millions of people in resource-poor regions across the globe, including impoverished pockets in wealthy nations. Operated by non-experts, including patients themselves, at-home diagnostic devices can help untold others stay on top of chronic disorders and out of emergency rooms.

As chair of the NIH Point-of-Care Technologies Research Network's (POCTRN) Independent Expert Board, and from my own three decades of experience in translational research, I strongly believe the pathway to a healthier global society will depend on precise and affordable point-of-care technologies to ensure more early diagnoses and effective therapeutic interventions.

There is no better model to follow than the highly coordinated effort to speed the development, manufacture and deployment of COVID-19 test kits during the pandemic. Launched by POCTRN in April 2020, the *Shark Tank*-style initiative known as RADx, (Rapid Acceleration of Diagnostics) resulted in 52 FDA authorizations and the distribution of more than seven million tests, some of them by the end of that summer.

But how do we replicate and expand upon that extraordinary success to address other problems, from the spread of new pathogens, to fetal health monitoring, to cancer detection? RADx developers, after all, received feedback all along the way from distinguished subject matter experts and seasoned entrepreneurs. They had an unusually interactive relationship with government regulators.

As the Chief Research Officer of NJIT, I have made

collaborative research and innovation partnerships a priority. This helps inventors determine early on whom their technology will help, how people will use it and even how to produce it. Two years ago, we launched the Technology Innovation Translation Acceleration (TITA) program, which drills down on the potential commercial benefits of university research at the earlier stages of the translation and market validation process. TITA provides seed grants of up to $75,000 per project over three phases of development, as well as guidance and feedback from an industrial advisory board. Inventors must have external partners.

The NSF's Directorate for Technology, Innovation and Partnerships recently awarded us $6 million to expand that program, which brings vital additional funding to move research past the initial proof of concept to determine interest and acceptance by potential users and identify purchasers of the technology, such as clinicians, municipalities or businesses. The award will also strengthen the university's entrepreneurial culture by funding training workshops in technology translation for undergraduates, Ph.D. students, postdoctoral researchers and faculty, through the newly created Center for Translational Research at NJIT.

Our job is to turn this center into a hub for commercialization training and development on campus, but also into a meeting place to receive feedback on our ideas and to generate new ones. Through workshops, forums and demonstration events, we will draw external collaborators, advisors and investors, as well as people in the community with their own thoughts about what's needed. We intend to listen.

Atam P. Dhawan
Senior Vice Provost for Research

Expanding Health Care's Reach: From Development to Delivery

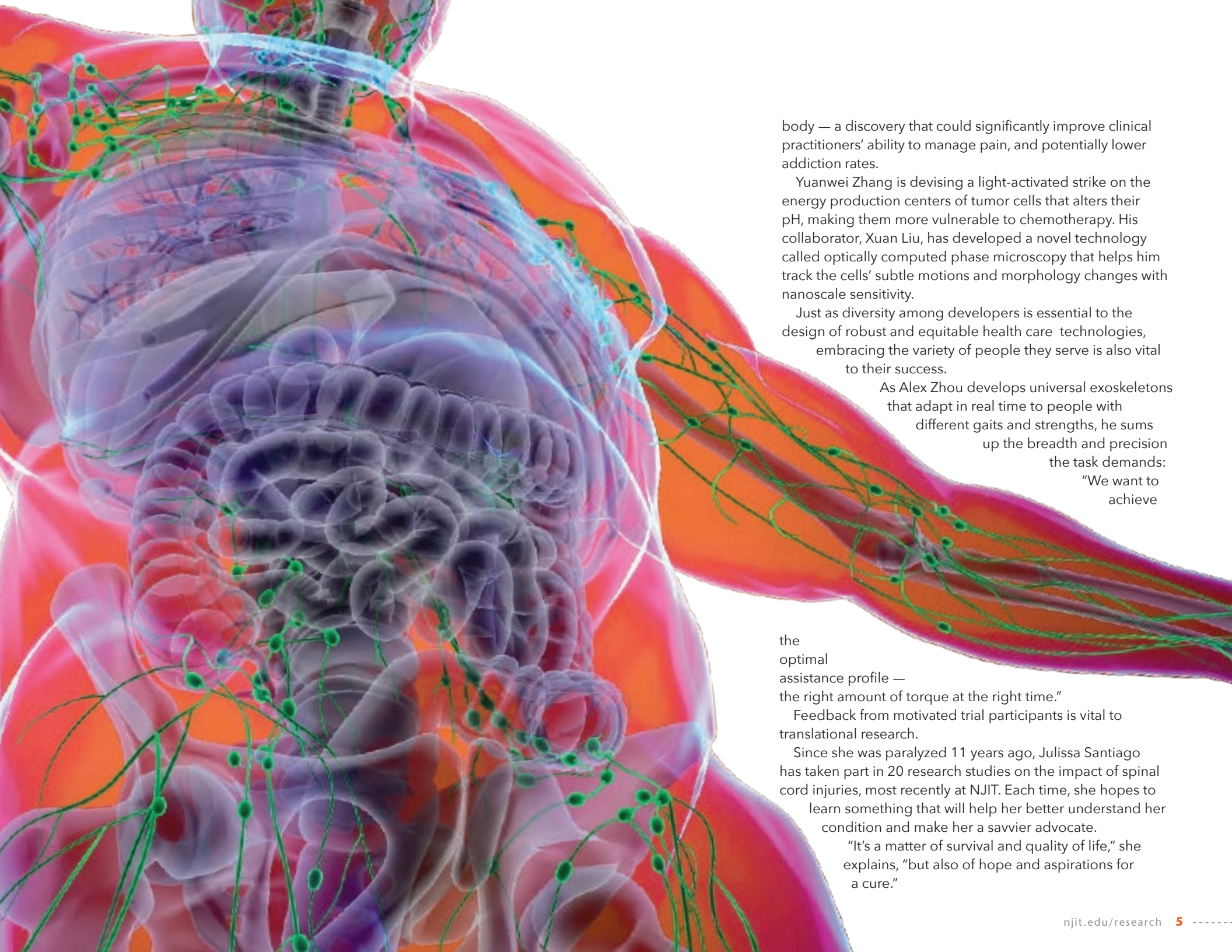
Computer scientist Sanmi Koyejo '05 co-founded the organization Black in AI to tackle the shortage of Black people building tools that shape experiences and outcomes in areas ranging from health care to criminal justice. Informatics Assistant Professor Alisha Pradhan includes older adults in her research on the development and testing of computer programs that routinely exclude their voices. Krystal Hunter, the lead statistician for a research hospital, focuses on disparities in women's reproductive health in her own scholarship.

Widening the pool of people who build influential technologies and have access to them are just two ways that researchers on the frontiers of health care are determining who benefits from scientific advances and at what cost. Expanding that scope, while also improving results for individuals through new knowledge about biological processes, novel therapies and refinements to existing treatments, is core to their mission.

Engineers Eon Soo Lee and Sagnik Basuray work at the nanoscale to develop inexpensive, portable tools that enable non-technical people outside of clinical settings to detect diseases in humans and animals in their earliest stages. In Lee's device, a nanoelectrode is electrochemically programmed to detect the distinct electrical signal emitted when antibody meets antigen. Basuray's biochip focuses on dual technologies that enhance both selectivity and sensitivity. Typically, if one is emphasized, the other is compromised.

Using diverse technologies, neuroscientists at NJIT seek out undiscovered connections between the brain and a range of disorders to hasten diagnoses and better evaluate treatments. Bharat Biswal and Farzan Nadim investigate how diseases such as Alzheimer's and Parkinson's, for example, compromise neural networks. Donna Chen studies the cognitive impacts of spinal cord injuries with an eye to improving rehabilitation, while Elisa Kallioniemi uses transcranial stimulation to directly retrain disrupted motor neuron circuits following strokes. Bryan Pfister and his team at the Center for Injury Biomechanics, Materials and Medicine are probing the mechanisms by which mild, repetitive injuries harm the brain over time in order to develop new protections.

On a different front, engineers and chemists are researching ways to boost the efficacy of treatments and minimize harmful side effects by optimizing their delivery and dosage. Kathleen McEnnis works on improving the targeting prowess of cancer-killing drugs packed into tiny, biodegradable nanoparticles. Ecevit Bilgili develops new modeling and manufacturing techniques to help deliver the growing arsenal of large molecule drugs that dissolve poorly in the bloodstream. Wunmi Sadik is leading new research into nano-sized analytical sensors for measuring pain biomarkers in the human



body — a discovery that could significantly improve clinical practitioners' ability to manage pain, and potentially lower addiction rates.

Yuanwei Zhang is devising a light-activated strike on the energy production centers of tumor cells that alters their pH, making them more vulnerable to chemotherapy. His collaborator, Xuan Liu, has developed a novel technology called optically computed phase microscopy that helps him track the cells' subtle motions and morphology changes with nanoscale sensitivity.

Just as diversity among developers is essential to the design of robust and equitable health care technologies, embracing the variety of people they serve is also vital to their success.

As Alex Zhou develops universal exoskeletons that adapt in real time to people with different gaits and strengths, he sums up the breadth and precision the task demands: "We want to achieve the optimal assistance profile — the right amount of torque at the right time."

Feedback from motivated trial participants is vital to translational research.

Since she was paralyzed 11 years ago, Julissa Santiago has taken part in 20 research studies on the impact of spinal cord injuries, most recently at NJIT. Each time, she hopes to learn something that will help her better understand her condition and make her a savvier advocate.

"It's a matter of survival and quality of life," she explains, "but also of hope and aspirations for a cure."

Tricking the Body into Replacing Lost Muscle

The human body can heal itself, but only up to a point. If an injury removes 20% or more of a muscle — as can happen in car accidents, certain surgeries or explosions in combat zones — natural processes can't, on their own, replace it. Instead, the wound seals up, covered by scar tissue.

"The body sees this extensive loss of tissue as an insurmountable void," says **Jonathan Grasman**, an assistant professor of biomedical engineering.

His lab is developing implants to boost muscles' regenerative power and provide a more effective option than the surgeries currently used to treat these injuries. The material he and his colleagues are developing mimics the internal scaffolding that organizes muscle, serving as a template for healing.

"I like to describe it as tricking the body into thinking that it has a smaller injury," Grasman says.

After more minor damage, including that caused by a strenuous workout, muscle fiber-forming cells known as myoblasts arrive to heal damaged muscle fibers and produce new ones. But this repair mechanism falls short in more traumatic injuries, such as those involving volumetric muscle loss.

To treat these bigger wounds, doctors remove muscle from elsewhere in the body, typically from within large muscles such as the quadriceps of the thigh, or the back's broad latissimus dorsi. They then graft this muscle into the wound. This surgery has some significant drawbacks: Grafting creates a second injury with all the accompanying risks, is prone to complications, and, even when successful, leaves patients with reduced control over fine movement. Scar tissue, for example, is composed of aligned collagen fibers that don't contract like myofibers, thus limiting functionality within muscle.

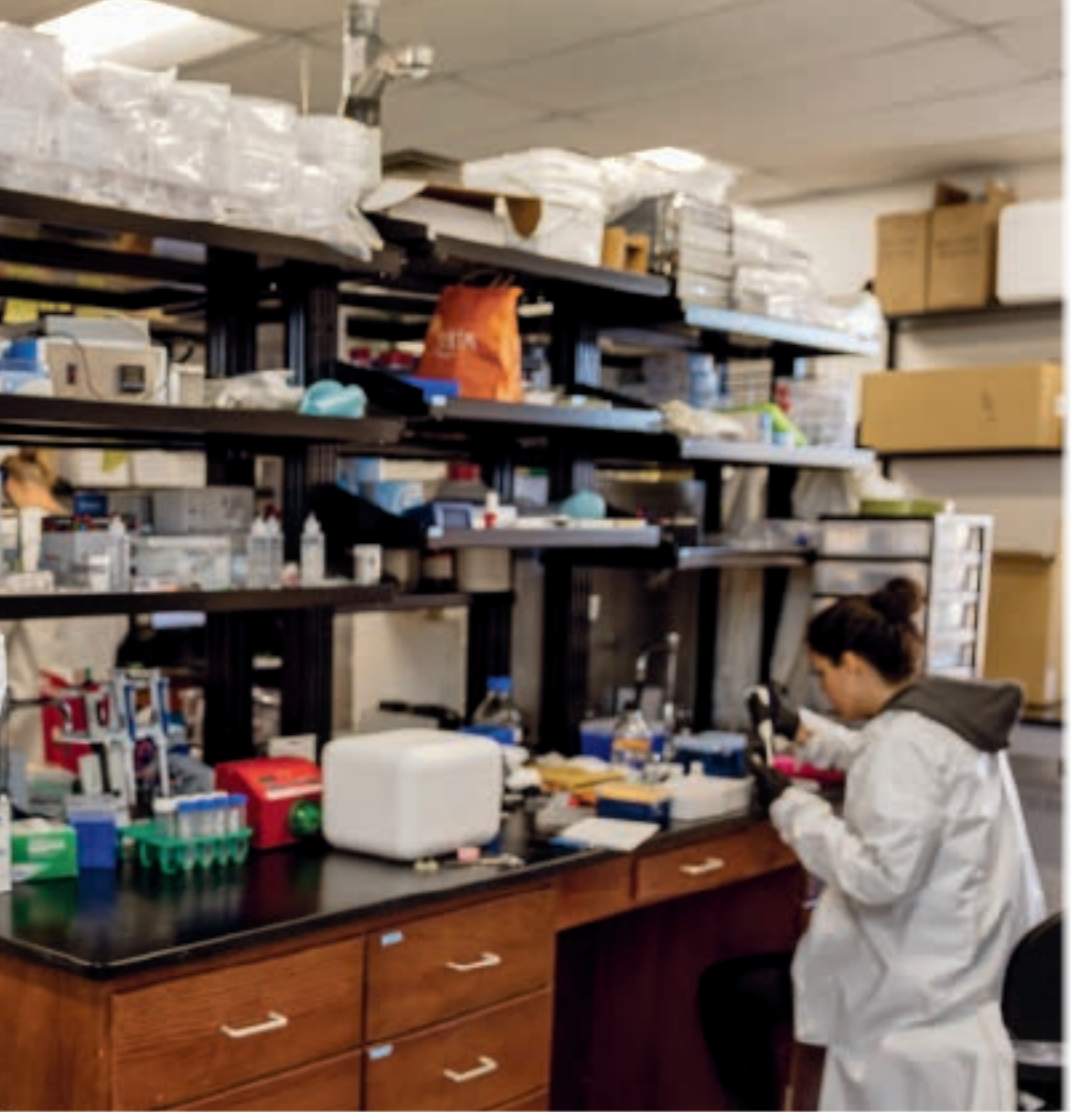
Grasman and others are exploring alternative ways to augment healing. One strategy would fill the wound with muscle grown in a lab, possibly from patients' own cells. Another approach — and the focus of his recent work — provides a structure to guide cells already present at the wound site as they form new muscle.

Within muscle, cable-like muscle fibers run parallel to each other, generating force by contracting. A framework made of collagen, a protein that provides structure throughout the body, organizes these fibers, which must align for muscles to work as they should. Following nature's lead, Grasman and his colleagues are experimenting with sponges made of collagen, containing pores that mimic this architecture.

In recent experiments described in the *Journal of Functional Biomaterials*, his team focused on determining the best size for the pores. Because they create these openings by freezing the collagen, researchers can manipulate their size by adjusting the temperature. These dimensions matter because if the pores are too small, the myoblasts can't enter to form fibers. If the pores are too large, they can't guide fiber growth. In this study, they determined they could best balance these competing needs by making the sponges at -20 degrees Celsius.


Jonathan Grasman

Recovering from an injury requires more than just making new muscle fibers, however. New blood vessels must infiltrate the muscle to feed it oxygen, and new nerves must carry information to and from the brain. With help from a collaborator, Grasman's lab is experimenting with making collagen sponges containing molecules that promote the growth of new blood vessels. His group is also exploring a variety of ways to encourage the growth of neurons and examining the potentially beneficial interactions between these cells and those that line blood vessels.



In the end, Grasman hopes to create a material that requires minimal preparation.

"Hypothetically, it could be two components that you mix together, wait two hours, then give to the surgeon," he says. "Implanting it would then allow native muscle to regrow and restore the patient's ability to function normally."

Although other groups are working on this problem, no alternatives — involving cells or scaffolding — have received approval from the FDA for use in injuries.

While the need is very real, Grasman traces his inspiration back to a long-standing interest in science fiction and fantasy stories in which bodies are created from mere DNA or wounds healed with a spell. Regeneration also occurs in nature, he notes. Starfish and salamanders can regenerate limbs; cut in half, each side of a worm can turn into another worm.

The prospect of accomplishing something similar for humans remains far off on the horizon, however. "My dream is to team up with somebody who understands bone and derive a strategy for potentially recapitulating an entire limb," Grasman says.

Testing New Drugs on Lab-Fabricated Diseases


Amir K. Miri

Using two kinds of 3D bioprinters, AMIR K. MIRI synthesizes a solid breast cancer tumor, stacking 100-micron-thick layers of hydrogels that serve as its structural tissue before injecting it with malignant cells. At its center is a microchannel that circulates a biological fluid containing nutrients and oxygen to fuel its growth and migration.

"By modeling disease tissues, we're coming up with a more efficient way to conduct preliminary tests of new drugs and therapeutics," says Miri, director of NJIT's Advanced Biofabrication Lab. "The goal is to quickly screen drug candidates and to optimize them without using animals in the early stages."

Among other collaborators, he's working with a cancer biologist at Rutgers University who studies the role of an insulin-like growth factor receptor in breast cancer metastasis and develops novel therapies against invasion behavior to counteract it. The team also studies the role of biophysical factors, such as microstructures and extracellular matrix gradients, on cancer growth and metastasis. With backing from the National Science Foundation, they initiated a project using focused ultrasound waves to create pressure on tumor cells. For both projects, they are fabricating the cell-laden models with a light-assisted bioprinter made by Miri's team in 2020.

In a separate project funded by the National Institutes of Health, his team is modeling the potential treatment of a more common disorder, vocal cord fibrosis, in conjunction with a researcher at NYU who is developing a therapy. "The big challenge is to induce growth and migration of multiple cell types as the cells have a different growth rate, including the epithelial cells that build the mucosa," Miri notes.

To conduct the tests, the researchers mix the therapeutic molecules with the cultured tissue media in the microfluidic chamber. They then measure cell metabolic activities, such as the expression of certain genes that induce fibrosis in the scar tissue.

In the future, he says, they will print biosensors that will monitor real-time cell growth, differentiation and death as cancer-associated and stem cells develop into distinct tissues.

Equity in Research

Q&A

Photo: Ananya Navale

Bias, Diversity and Truth in AI

Sanmi Koyejo '05

Assistant Professor of Computer Science, Stanford University

Founder and President, Black in AI

Q: SHOULD WE BE ALARMED ABOUT THE RISE OF AI?

A: AI has been around for a long time and its deployment is ubiquitous. Almost every online platform has some automated decision making: Google web searches; fraud detection; and hiring decisions based on automated systems. What has changed recently, in the public consciousness at least, is that ChatGPT and OpenAI got released and people saw that these tools seemed to work well, but also in a way they could engage with easily. I'm trying to make sure that the impact on society is more beneficial than not.

Q: HOW CAN YOU COUNTER BIAS?

A: The way these tools are built depends strongly on the data that exists, so behavior in the past is used to make predictions about behavior in the future. This can be problematic, as in decisions that are correlated with past histories of discrimination. It shows up in a benign way in how different video cameras work for people with different skin tones, but it also shows up in police applications that make more mistakes on people with darker skin tones and can result in people being in prison incorrectly. Having people in the room that have different lived experiences, not just diversity of thought, has a direct impact on building tools that work for everyone.

Q: HOW CAN AI IMPROVE OUR HEALTH?

A: You often get a diagnosis for a disease because there are symptoms. But we built tools that take existing information from people, including a tool that looks at X-ray images and can diagnose things that are not necessarily tied to a medical visit. This means there are now possibilities to find diseases early, before there are different symptoms and before it's too late to have significant interventions. We started with diabetes, but I'm quite excited about this kind of technology for lots of diseases that are pressing in the U.S. and across the world.

Q: WHAT CAN AI TEACH US ABOUT THE BRAIN?

A: My lab is building tools that help better estimate, from observing signals, how different regions of the brain are connected to each other, how those connections are related to brain function, behavior and brain disorders and how we can use this as a diagnostic tool.

Q: CAN AI HELP US DETECT BIASES IN HEALTH CARE THAT AFFECT OUTCOMES?

A: Unfortunately, a lot of the history of medical care has systemic biases of different care being administered to different groups, sometimes by demographics and sometimes by wealth status. It's sometimes hard to tell which differences are biological and which are due to the biases of the decision makers. We were looking at care around COVID and found systematic differences in care and outcomes that were tied to demographics. An interesting finding was that language seemed to be a really good predictor of who got better or worse care. If people came in and they didn't speak English sufficiently well, their care was systematically worse, their outcomes were systematically worse.

Q: WHAT PROMPTED YOU TO BE A FOUNDING MEMBER (AND CURRENT PRESIDENT) OF BLACK IN AI?

A: Circa 2016, a few of us came together with the shared experience of being the only Black person we knew working in the field. At the time, some impacts of technology could be explained by the fact that there was no one in the room with the lived experience to speak to a tool being built that would have a worse outcome for certain demographics. We're about 5,000 people now and international. It's rewarding to hear stories from people who tell us they would not be in the field if they had not engaged in the group early on, and they've gone on to have incredible careers.

A Statistician Delves into Health Disparities

Krystal Hunter '21, Ph.D.

Biostatistician, Cooper Research Institute

Associate Professor, Cooper Medical School of Rowan University

Q: WHAT IS YOUR ROLE AS THE LEAD BIOSTATISTICIAN FOR A RESEARCH HOSPITAL?

A: If a physician notices a phenomenon in a segment of the patient population, he or she may initiate a research study to examine the characteristics of those affected by it. A surgeon may notice, for example, a high rate of surgical site infections with a type of suture. As a biostatistician, I help set up the statistical plan for the study, including the statistical tests that will be run to test the hypothesis. I also provide a sample size to ensure that there is enough data within the study to avoid a false negative result due to a lack of sample. At the end, I analyze the numbers using the methodology I outlined. I also help administer survey studies where I quality-check the data (looking out for double-barreled or confusing questions) in research and process improvement surveys of patients and staff.

Q: WHAT'S AT STAKE?

A: Making sure that we collect the correct data that will enable the team to answer their research question. What if we spend years collecting data and can't use it? Not only does that waste resources, it also can present an ethical issue as we either exposed study participants to risk without reporting a result or we risked confidentiality when doing a review study of health records. It's also important that we look at the collected data and are aware of confounders. Let's say we're looking at the relationship between the outcome of chronic pain and age and find a statistically significant relationship between the two. But we also have another explanatory variable of arthritis. People with arthritis tend to be older. This bears the question: Is it truly age that is affecting chronic pain or is it the age-effect of arthritis?

Q: WHAT IS YOUR FOCUS AS A RESEARCHER?

A: I'm focused on health disparities, and birth outcomes in particular. With pre-term births, for example, there's always been a disparity between white women and Black women, who are at higher risk. This includes Black women with high economic status. The gap between high and low economic status white women is large, but it's much tighter with Black women. Foreign-born Black women from sub-Saharan Africa have comparable rates of low-birth-weight babies with white women. Unfortunately, a study of low birth weight showed that foreign Black women were the only group where with each succeeding generation, their risk increases. The goal is to bridge those gaps.

Q: DID YOU UNEARTH ANY DATA IN YOUR RESEARCH THAT SURPRISED YOU?

A: I found that with women of lower economic status, their optimal weight during pregnancy is slightly obese, indicating an obesity paradox. Being underweight or even a normal weight increases the risk of a pre-term birth with this group of women. The answer is not, however, to gain weight! These outcomes could be connected to malnourishment, substance abuse or other conditions contributing to weight loss. The obesity paradox has also been cited in cardiac patients. Another finding is that the disparity between low-risk Black and white women declined at freestanding clinics manned by midwives. This could be that midwives take a more holistic approach to health and spend more time with their patients. They're also more cost effective, although insurance won't always pay for them.

Q: ARE THERE POSSIBLE FACTORS WE'VE YET TO EXPLORE?

A: We need to look at health issues more holistically. While physical health is important, it's also important to examine social determinants of health, nutrition, mental health and lifestyle factors. As a researcher, I would love to examine the effect of systematic disadvantage over generations on birth outcomes in the United States and in other countries. Social disadvantage affects most aspects of life and affects access to opportunities. I believe that may account for disparities in maternal health, and health in general.

Researchers Close in on New Technology for Objectively Measuring Pain

On a scale of one to 10, how much pain do you feel? It's a question patients are rountinely asked by their doctors, often accompanied by the Visual Analogue Scale from 1-10 that was first introduced in clinics in 1921. A century later, the simple assessment is perhaps the most widely used technique for measuring pain — a chronic symptom for 21% of U.S. adults estimated to cost up to $635 billion annually.

However, while relying on patient self-reporting is the current standard for assessing pain, it's not always a valid and reliable tool, says **Wunmi Sadik**, chair of NJIT's Department of Chemistry and Environmental Science.

"Pain triggers both cognitive analysis and emotions, making its objective measurement challenging," says Sadik. "Determining its intensity, and the underlying cause it signals, is critical not only for effective pain management, but for diagnosis and treatment as well. People addicted to opioids may exaggerate their pain. Children, the unconscious and people with disabilities may not be able to describe their symptoms at all."

Wunmi Sadik, left, performs a pain experiment.

As director of NJIT's BioSensor Materials for Advanced Research and Technology Center, Sadik has led new research into nano-sized analytical sensors for measuring pain biomarkers in the human body — a development that could significantly improve clinical practitioners' ability to manage pain, and potentially reduce cases of addiction in patients.

"The most significant aspect of this work is that it holds the potential for a point-of-care technology that will not require highly trained staff to operate and will enable cheap and minimally intrusive measures of biomarkers related to pain," says Sadik, whose research has been supported by the SUNY Health Network of Excellence Program.

Sadik says her lab's biosensors measure two biochemical compounds that appear in the bloodstream when pain is present — cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) — requiring only a patient's finger-prick blood samples for analysis.

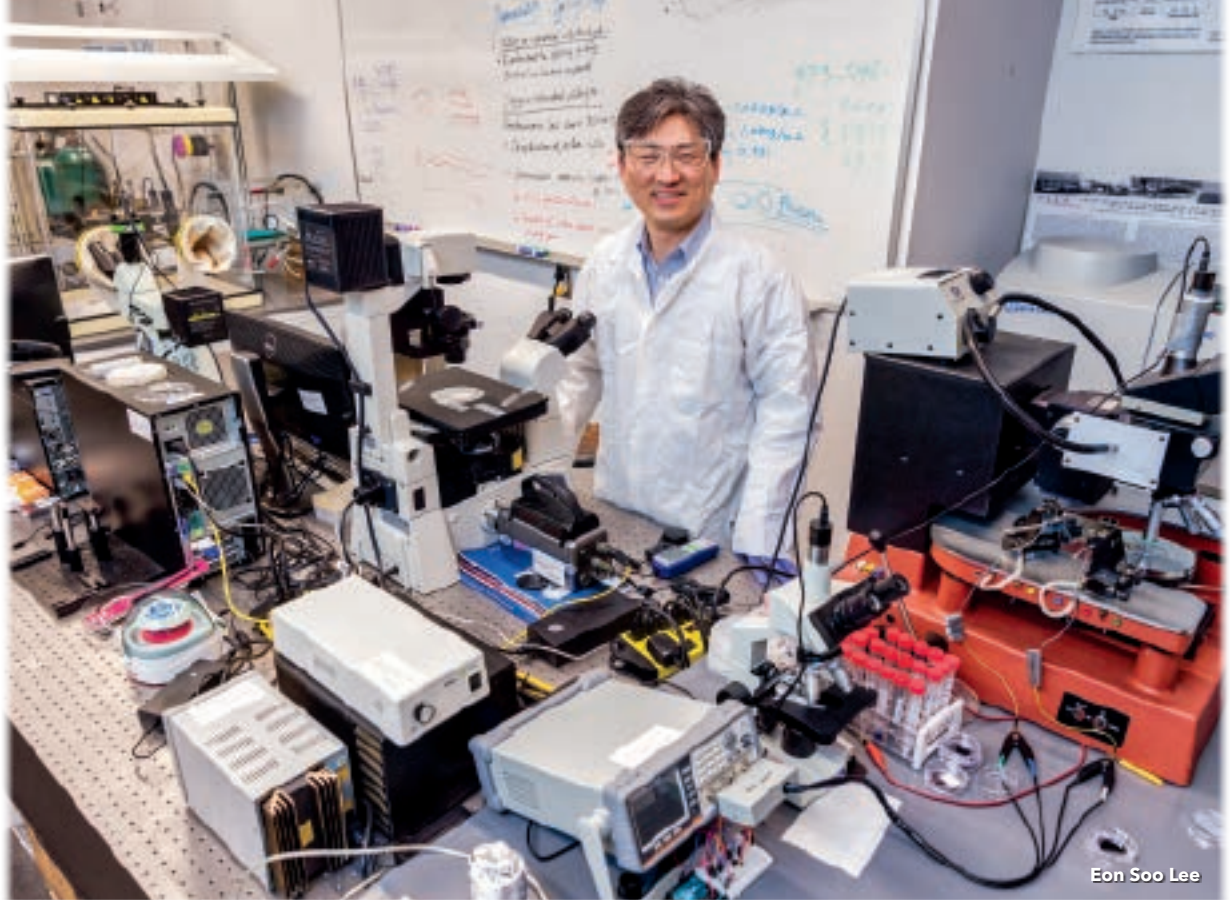
The team has also implemented artificial intelligence to offer clinicians an easy-to-grasp summary of the results, which can be processed within minutes.

"Our approach combines calibratable measures of pain-related biomarkers with patient self-assessments of perceived pain using AI methods, which can provide a view of how consistent the inflammatory markers are with the reported pain to corroborate," explains Sadik.

The technique has demonstrated promising accuracy. In the journal *JMIR Biomedical Engineering*, the team published results of the first clinical trials testing the approach with patients experiencing various levels of pain from Manisa Merkez Efendi State Hospital in Manisa, Turkey.

"Our preliminary data from trials with 379 patients showed close to 80% consistency between the biomarker data and the patient's self-reported pain," says Sadik. "It's encouraging. … Similar to the Food and Drug Administration's accuracy requirements for continuous glucose monitoring systems, we expect the pain biosensor accuracy to be greater than or equal to 87% within ±20%."

Sadik's lab has now begun testing their biosensors with healthy volunteering athletes at NJIT, comparing levels of pain biomarkers with patients' self-assessment in response to increasing applied temperature using Medoc thermal simulation technology. "This stage is important to create baseline levels of the biomarkers in healthy volunteers," says Sadik. "After establishing this, our next step is to work with our partners to fabricate these sensors for real-world application. Ultimately, we anticipate a hand-held, field-deployable device that can offer health care professionals valuable insights into patient pain."


Eon Soo Lee

Detecting Disease While It's Still a Whisper

In its earliest days, ovarian cancer discharges telltale proteins into the bloodstream, if only we could detect them. The problem is they're specks in an ocean, swimming with comparative giants: red blood cells that at just eight microns wide are more than 1,000 times their size. To identify them before they proliferate, **Eon Soo Lee** is developing a nanoscale instrument with outsized sleuthing powers.

"Around 600,000 lives are lost to cancers each year in the U.S. alone. Many of these people could have been saved if they had been diagnosed at an early stage," notes Lee, an associate professor of mechanical engineering.

His goal is to give health care providers and patients the ability to detect deadly diseases early in their progression. The device is designed for use by specialists and primary care doctors and, Lee hopes, health care workers in remote clinics who lack sophisticated equipment, and even individuals at home. They would administer the tests with a simple finger prick and wait about two minutes for a result.

His biochip includes a microfluidic channel through which a tiny amount of drawn blood flows past a sensing platform coated with biological agents that bind with antigens — biomarkers of disease that elicit an immune response by the body. The chip's biosensors are highly sensitive to very small amounts of these specific molecules. A nanoelectrode in the channel is electrochemically programmed to detect the distinct electrical signal emitted when antibody meets antigen.

To reduce the chance of sample contamination, he eliminated the need for external flow control devices and connecting tubes. One of the device's core innovations, for example, is a spiral mechanism in the channel that, powered by surface tension alone, separates blood plasma from whole blood. It then winnows out large particles, such as blood cells and platelets, before the proteins reach the sensor. This self-separation process also dims the background noise in the microenvironment, enhancing its sensitivity. He has obtained four patents on the technology so far.

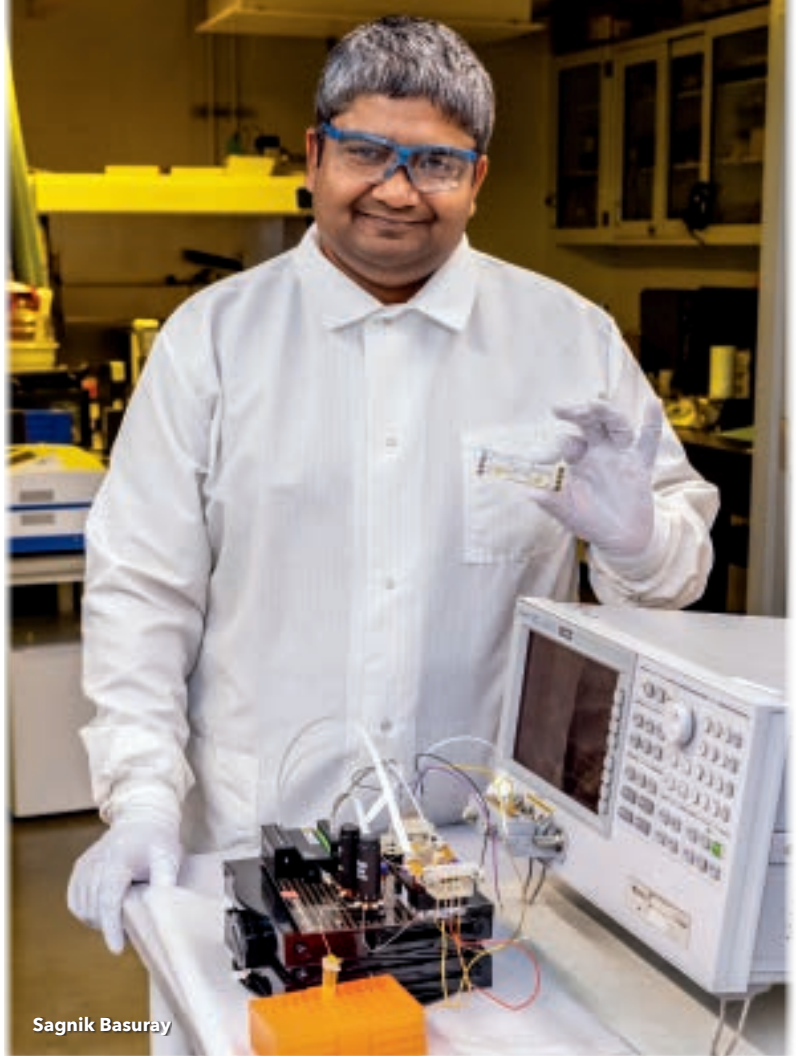
If successful, the device would expedite the diagnosis of diseases including viral infections such as HIV, sexually transmitted diseases and toxoplasmosis; malignancies such as ovarian, prostate, liver and thyroid cancer; and infectious bacterial diseases such as tuberculosis.

"TB, a scourge in the developing world, is very difficult to detect. It's symptomless at first," he notes. "With the ability to check for it at home, more people will get treated and avoid infection."

In its first iteration, he used gold nanoparticles and graphene to immobilize the antibodies and serve as the signal enhancing layer. He has since replaced this coating with a polyethylene glycol polymer that is cheaper to make and more sensitive as it provides a smoother and better-aligned coating surface for the antibodies. He works with collaborators at Weill Cornell Medicine to identify and test the reactions of the biomarkers.

Lee says he'd ultimately like to combine antibodies for up to 20 diseases on the chip's biocoating, although it would increase the device's complexity considerably — ratcheting up the background noise with multiple antibody-antigen interactions. He's currently refining the self-separation mechanism and enhancing the device's ability to detect distinct signals simultaneously.

Protecting Humans from Animal-Borne Disease


Sagnik Basuray

Triggered by infected bats, the COVID pandemic amplified worries about animal-borne diseases humans struggle to fend off. An avian flu that has killed millions of wild and domesticated birds in recent months is prompting renewed jitters across the globe.

"Animal disease is a threat to economic, health and food security," notes **Sagnik Basuray**, director of NJIT's Opto and Microfluidics Laboratory. "Containment depends on rapid diagnosis. Ideally, if we can detect these pathogens before they jump to humans, then we can break the chain."

Funded by the U.S. Department of Homeland Security (DHS), Basuray and TDA Research, an engineering research and development firm, are developing diagnostic technology to detect early outbreaks of diseases in livestock. They include influenza, vector-borne viruses such as Zika and the prion-based bovine spongiform encephalopathy, known as mad cow disease. Their device is programmed to identify multiple diseases simultaneously.

Housed in a portable machine the size of a backpack, a microfluidic bio-detection system Basuray developed analyzes tiny samples of 5-10 microliters of blood on disposable single-use chips. Its electrochemical sensors use nanoporous electrode technology to enhance precision.

By packing nanostructures between electrodes, he can generate high shear forces capable of dislodging one object or material from another. Finely tuned, these forces ensure that the so-called capture molecules deployed in the test bind with the targeted disease molecules, and that others, which represent test noise, are washed away.

Potential users are individual livestock farmers, border control and customs agents, U.S. Department of Agriculture inspectors and DHS personnel, who have pointed out the urgency of securing rapid, point-of-care testing for animals.

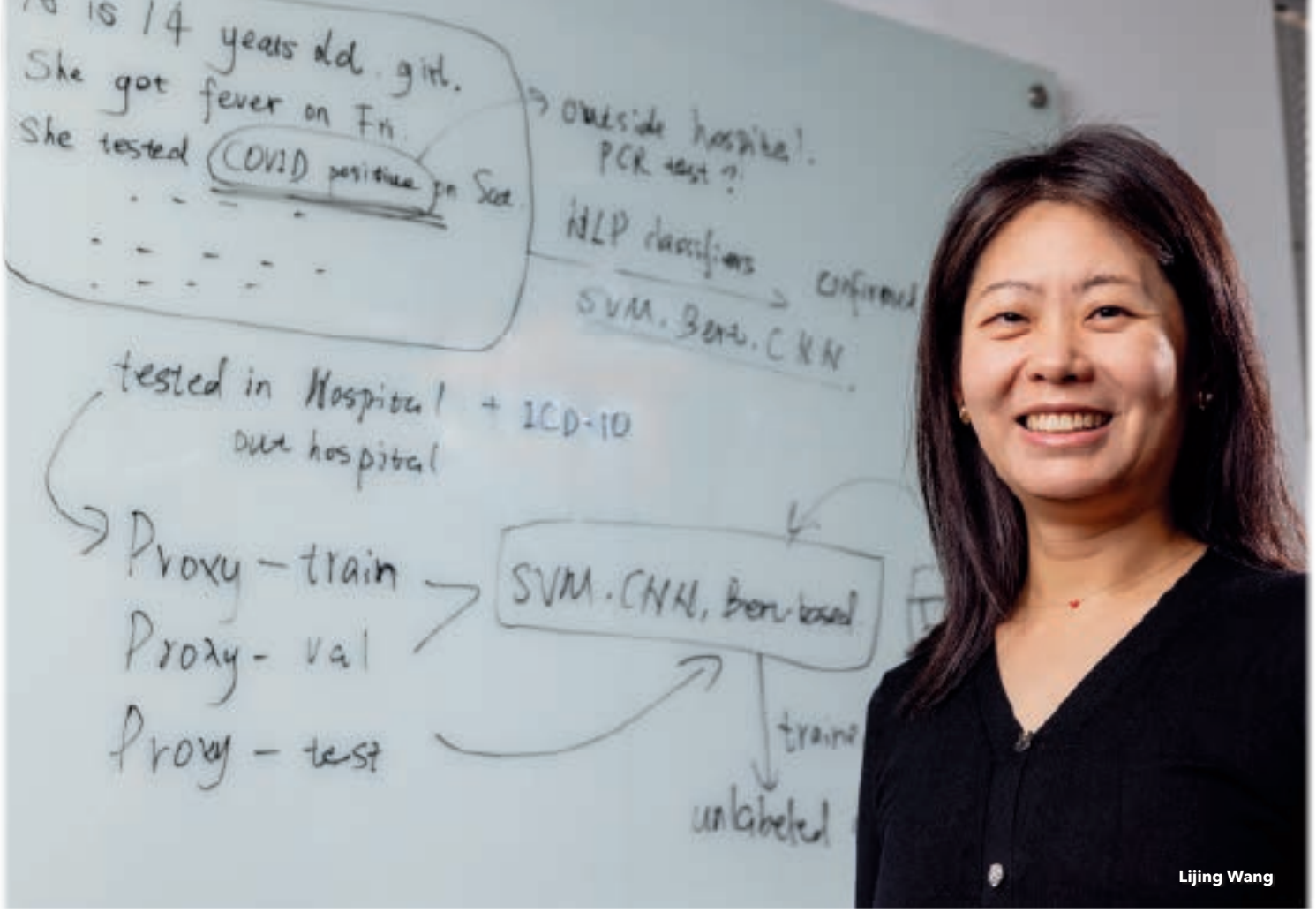
"There are currently no rapid diagnostic tools specifically for zoonotic diseases that can be used in the field," Basuray says. "Samples must now be taken to the lab for analysis and sometimes repeated."

Basuray's technology seeks to improve upon biosensors currently used in point-of-care devices such as dipsticks, for example, which often suffer from either limited specificity — the ability to identify a particular disease, or sensitivity — the ability to detect it at low expression levels. Typically, if one is emphasized, the other is often compromised, resulting in false negatives and false positives, respectively.

He balances the two by decoupling them, "like a radio with two knobs that we can tune accordingly." This allows the device to distinguish among diseases with very similar features, such as healthy proteins and prions, which cause proteins to fold abnormally, and to detect slight mutations in DNA, such as single base mismatches. The latter could be predictors of disease, including cancers and so-called lifestyle ailments, such as Type 2 diabetes and nonalcoholic fatty liver disease.

In the lab, the team has successfully detected mad cow disease at low levels. With added funding from an NJIT commercialization grant, they are now building a prototype to test in the field.

"Our goal is to seamlessly integrate sample collection, testing and analysis," Basuray says. "What we envision is a farmer drawing blood with a syringe and injecting it into the device, which would then take over. He might then get a notification on his phone."



Lijing Wang

Correcting the Growing Undercount in COVID Reporting

When the Centers for Disease Control and Prevention ended the COVID public health emergency last year, centralized reporting on confirmed cases plummeted. Locally, the rise in home testing has made it hard for emergency care centers to accurately tally infections among their outpatients. Together, gauging the number of infected people in any given area is now a challenge.

"With hospitals underestimating the number of positive cases, it's difficult for them to optimize resources, to decide how to apportion limited equipment, such as oxygen tanks, to support different types of patients with serious diseases," notes **Lijing Wang**, an assistant professor of data science who develops natural language processing (NLP) models to identify cases from sources outside of official records.

As a research fellow at Boston Children's Hospital and Harvard Medical School during the pandemic, Wang took part in one of the first studies testing NLP's ability to extract indicators of COVID from clinicians' notes.

"With the prevalence of home tests, and especially after the government distributed free kits, we saw the numbers go down," Wang recalls, noting that after the initial phase of the pandemic, when some hospitals tested all patients with COVID symptoms, they later may have skipped it if the patient self-reported a positive test. Those cases don't make it into the hospital's electronic health records.

"We hypothesized that we could detect these patients by teaching a machine learning model to read clinicians' electronic notes for mentions of positive tests," Wang recalls, noting that losing this data risks introducing bias into research down the road if it turns out that specific cohorts tend to test at home.

She is now working on the next step: applying NLP models to multiple hospitals. But data scientists must first figure out how to gather this information and share it among facilities, while ensuring it's kept private and secure.

"And that," she notes, "is a challenging problem."

Essay

Survival of the Good Enough

Allison Edgar

Assistant Professor of Biology

In Florida, Allison Edgar collects *Mnemiopsis leidyi*, a species of marine invertebrate in the Ctenophora phylum that has lost the ability to regenerate body parts. Edgar, who researches developmental and evolutionary biology, is trying to understand what brought about the loss of this useful trait.

As a biologist equally interested in development and evolution, I study the evolution of animal life histories, the major events of a life cycle: patterns of development, growth, maturation, maintenance and reproduction. I focus in particular on features that are retained and lost across species, such as the ability to regenerate. It's easy to make sense of obviously adaptive gains and losses of apparently neutral traits, but loss intrigues me wherever it seems paradoxical to give up something beneficial.

My recent focus is *Mnemiopsis leidyi*, a species of marine invertebrate in the Ctenophora phylum. Named from Greek words for "comb-bearer," each individual moves by beating eight rows of comb-like plates running down its transparent body. *Mnemiopsis* is known for its ability to regenerate: if you cut it into eight pieces, each can pattern a whole; major wounds close within an hour. However, some groups of ctenophores have lost this impressive ability and one of my recent research projects focused on identifying changes in the genome underlying this loss.

There are some simple explanations for losing a complex trait such as regeneration. The simplest is that not all changes are adaptive. Sub-optimal traits don't lead directly to extinction. Trade-offs are another, such as the sea urchin species I studied previously that entirely lost the feeding larval life stage, perhaps in favor of shortening the period in which it is especially vulnerable to predation. It's possible we don't know what's advantageous, while we're good at making up narratives to explain what we observe, as in Kipling's "Just So Stories."

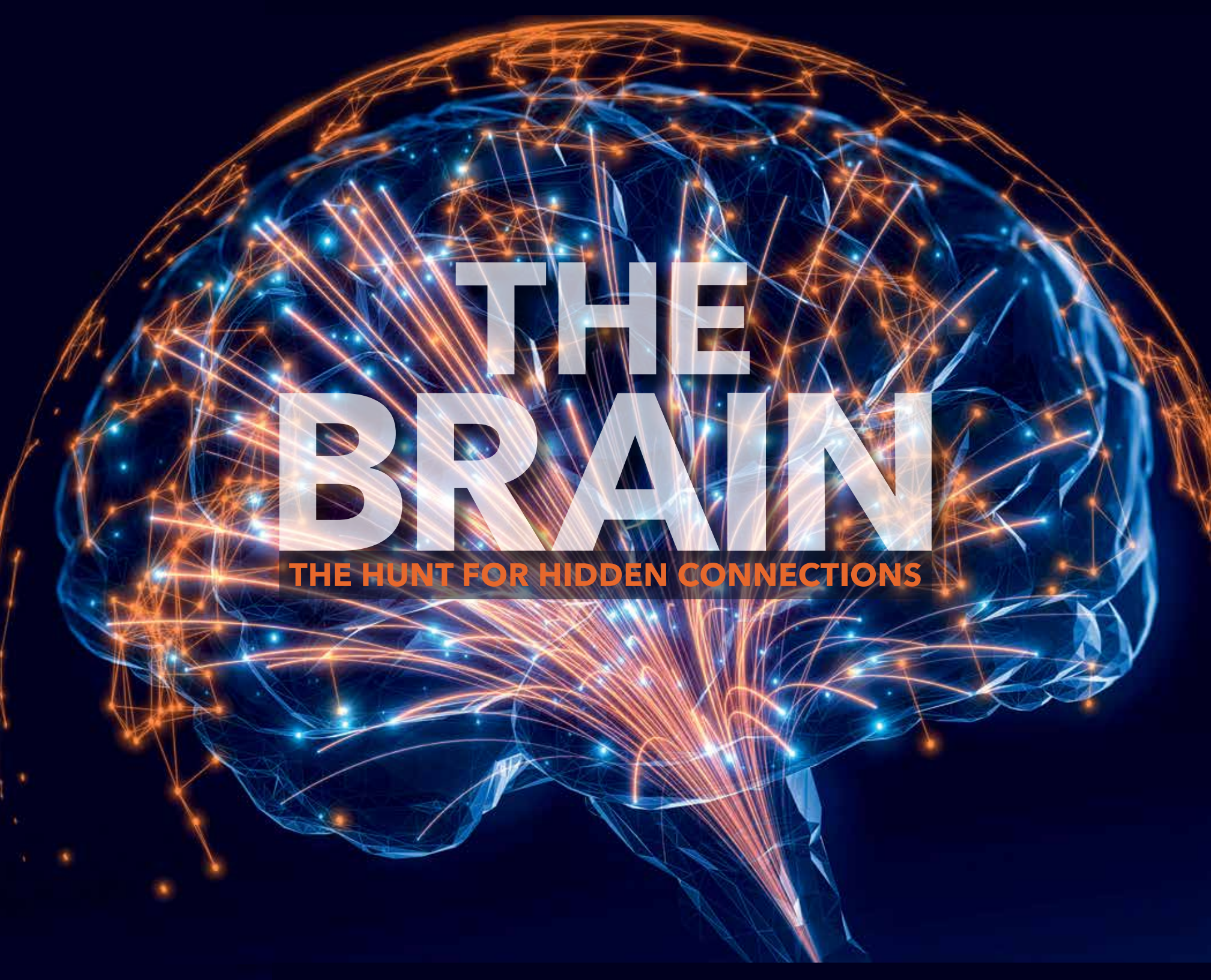
A conditional release from natural selection is another explanation. Humans, along with a few other animals, possess a notable disadvantageous loss. We have a dietary requirement for vitamin C, thanks to a genetic mutation that prevents our bodies from making it. If we don't consume enough in fresh foods, we develop scurvy and eventually die. In each of the species that lost the ability to make vitamin C, an ancestor got enough from its diet that nothing happened when that gene mutated. For humans, it wasn't until the age of long sea voyages that we encountered major problems. We often fall into the trap of thinking about "survival of the fittest," but evolution is clearly about survival of the "good enough."

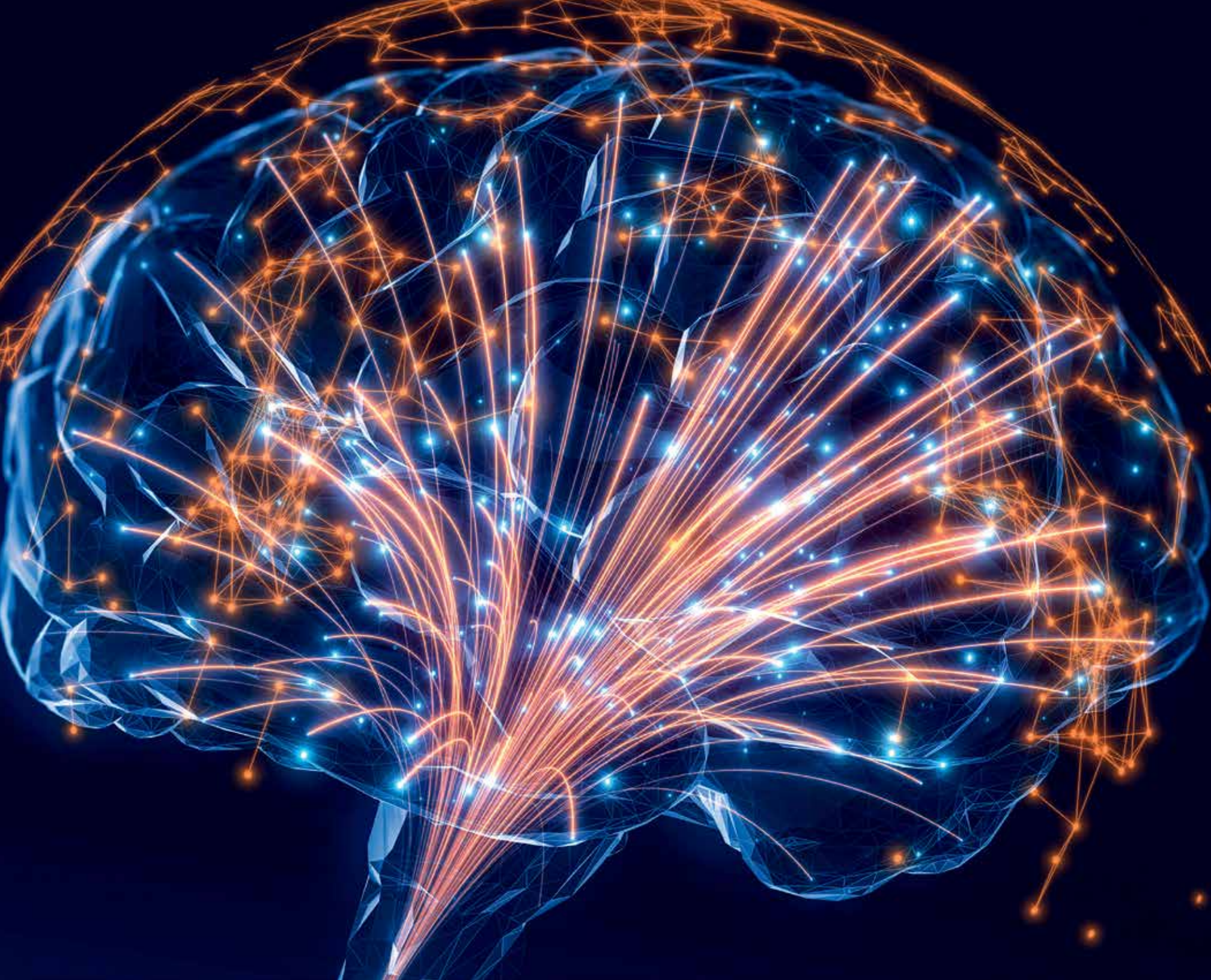
Many biological processes are deeply conserved across animals, lost rarely or never in the course of evolution. For example, nearly every animal on earth develops from an embryo. This appears to be an innovation that works too well to part with in most circumstances. Biologists understand regeneration to be related to reproduction in important ways: both are tightly regulated processes in which cells divide, change their identities and organize together to pattern the shapes of various body parts. Humans would dearly love to regenerate damaged or missing body parts, and it seems obvious to us that it would increase the fitness of any animal with this fortunate ability. How can we explain its repeated loss in the evolutionary history of animals?

One of the things we don't know is if regeneration is the same in all animals, if the underlying process is conserved across species. As we consider biomedical engineering problems in regeneration, it may be crucial to know what's universal rather than particular if we wish to restore a long-lost ability.

This brings me back to the ctenophore, *Mnemiopsis*. Why study this species so distant from humans? Well, some of my recent work showed that *Mnemiopsis* requires a diet containing a specific fatty acid previously known to affect fertility in vertebrates. Thus, a requirement to synthesize this nutrient or obtain it from food might be common to all animals, just as with vitamin C. Since prior work has shown that ctenophores' regeneration is also nutritionally regulated, I have become interested in understanding how the life history processes of growth, reproduction and regeneration are related and possibly co-regulated by their environment. Our current best understanding is that ctenophores are the sister group to all other living animals, meaning that phylum branched off the animal tree of life before any other. What if, instead of selecting animals as close to humans as reasonably practical, we focused on animals that could tell us something that might be true about the last common ancestor of all animals? I hope my work will ultimately allow us to understand such shared underlying processes across animals, identify how they may have broken by chance in evolution, and how we might harness the ability to turn them on and off in the cell.

Photos: Roman Testroet


THE
BRAIN
THE HUNT FOR HIDDEN CONNECTIONS



At any moment, the brain's 86 billion neurons are chatting away, firing off trillions of messages to regions near and far. With a growing cache of technologies, scientists are exploring new ways to eavesdrop on these conversations and spot errant dispatches that signal disease and disorder.

Bharat Biswal, an electrical engineer, made a foundational discovery that shed new light on these exchanges: imaging the entire brain at rest, he learned that neural networks maintain meaningful functional activity through wide-ranging connections even while the brain is not actively making computations. Breakdowns in these systemic communications, it turns out, are key biomarkers of neurological diseases.

With advances in mapping techniques, the hunt for hidden connections is accelerating. By revealing correspondences between white and gray matter, for example, and the basal ganglia and the cerebellum, researchers are delivering insights into disorders such as multiple sclerosis, Parkinson's and addiction. For applied scientists, the goal is to translate this new knowledge into precise diagnoses, improved treatments and novel interventions.

By scanning the brain with functional MRI (fMRI) and functional near-infrared spectroscopy (fNIRS), which both map the flow of oxygenated blood to the brain's command centers, technologists can evaluate how well a therapy is working and guide its development. They are also harnessing their understanding of the connections to devise their own therapies. By restoring disrupted neural circuits with non-invasive transmagnetic or direct-current stimulation, for example, they hope to identify a low-impact alternative to drugs.

Probing a Still Mysterious Region of the Brain for Clues to Alzheimer's

In the early 1990s, as scientists began mapping the brain with functional MRI (fMRI), **Bharat Biswal** proposed a radical new approach to imaging: observing all of the regional networks at once while the patient focused on nothing in particular.

"At the time, it was perceived as a crazy idea in neuroscience, which was focused on task and response," recalls Biswal, then a graduate student at Wisconsin Medical Center. "As an engineer, I wanted to understand the entire system of neural networks at baseline conditions. With one scan, we could observe activity in the motor, visual and speech regions, for example."

Biswal, now a distinguished professor of biomedical engineering, says he was particularly interested in what the scans would reveal about brain-related diseases, such as where and how those brain's regions connect and where the conversations falter. With those maladies, the brain may be compromised in several regions, so

he thought that performing a particular task, such as solving a puzzle, wouldn't be that useful.

Thirty years later, what is known as resting-state brain connectivity is the primary vehicle for examining brain connections in infants, very young, elderly and neurologically impaired people who can't perform tasks on command. Biswal is now using it to compare neural signaling in people with Alzheimer's disease with those aging normally. He is zeroing in on the connections between the gray matter of the brain and the white matter.

"Alzheimer's is particularly challenging because people can't perform tasks and may forget right away they have been asked to perform," he notes. "We want to see which regions, such as memory or emotion, have been compromised — where connections are weak — and try to correlate that with clinical measures, including cognitive tests."

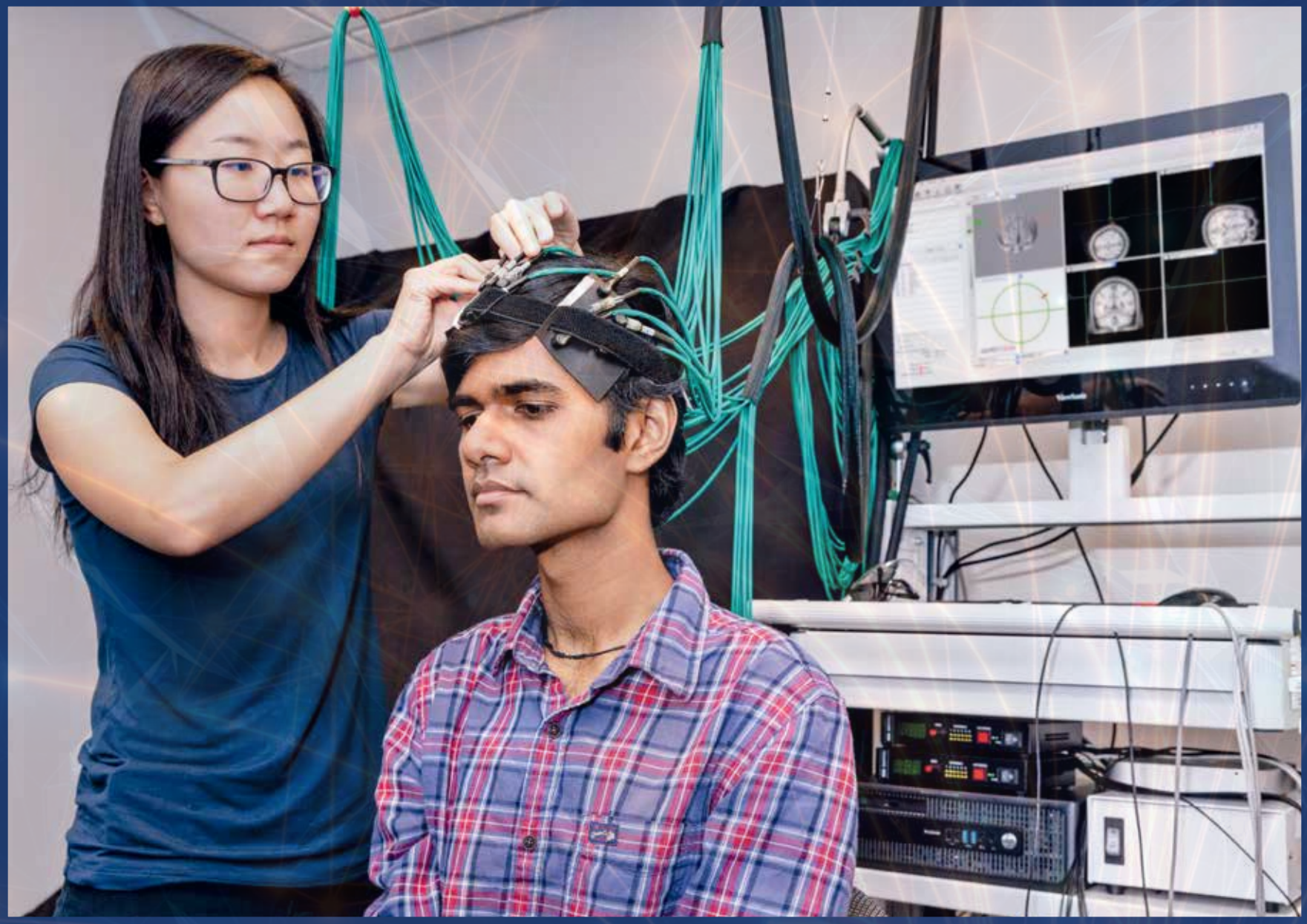
A primary goal of the study is to apply fMRI for a more reliable diagnosis, prognosis and treatment of Alzheimer's. It is one of the first to perform a comprehensive analysis of white matter function using fMRI and its effects on cognition in the two groups. His team is applying advanced analytic and machine learning approaches to identify white matter functional networks and to test the reliability of their findings using data gathered on the test subjects over time.

"We're realizing that these networks in the two tissues complement and interact with each other," he says.

As part of his study, he's collaborating with groups around the world to gather a vast and diverse data set of more than 104,000 subjects who've undergone fMRI scans. He's observing the tests to ensure that testing methodologies and practices are as similar as possible. Small differences matter, such as whether people are instructed to close their eyes at one site and to keep them open at another.

His team is working on a set of toolkits to track and explain the progression of Alzheimer's to give clinicians a window into who might be at risk, for example, and to assess what therapies might be effective at different stages of the disease.

"We don't just want to be able to diagnose it, but to help in assessing treatments," he notes. "We can see what happens when we try different therapies: How do the networks change? Do they look more like healthy ones?"



Mending the Mind After a Spinal Cord Injury


Julissa Santiago

A quadriplegic for the past 11 years, **Julissa Santiago** is the master of her own comfort. With the precision of a polite drill sergeant, she delivers instructions at bedtime for a series of minute body shifts and covers placed just so. And yet she still struggles to sleep.

"If I sleep for five hours, I'm lucky. My brain is constantly going, and it drains me," she says. In her wheelchair during the day, she occasionally experiences a sudden drop in blood pressure that is mentally discombobulating in its own way. These disruptions are deeply frustrating for the observant 35-year-old who soaks up information about her condition, types with her pinkie knuckle and hopes to one day tell her story.

Santiago's struggles are the focus of an ongoing study led by **Donna Chen**, a Ph.D. student in biomedical engineering, who is interested in the cognitive impacts of spinal cord injuries (SCI).

"People with spinal cord injuries commonly report shortened attention span and short-term memory difficulties," says Chen, who asks her study participants to perform simple recall and verbal dexterity tests and to respond to figures as they pop up on a computer screen.

While the causes are murky, key contributors may include problems with sleeping, lack of exercise, depression and anxiety, chronic pain and cardiovascular dysfunction. Chen adds, "Another theory posits that inflammatory signals travel to the brain as a secondary response to the trauma and these changes are associated with impairment."

While they're performing cognitive tasks, Chen scans their brains with functional near-infrared spectroscopy (fNIRS), which uses near-infrared light to measure the amount of oxygenated blood in regions of the brain associated with particular functions. Preliminary data revealed decreased functional brain connectivity in the sensorimotor networks, but also the prefrontal cortex, which controls executive functions, such as planning and organizing, and working memory.

Compared to able-bodied individuals, the differences in connectivity suggest reorganization of the brain's connections after injury, she notes. Similarly, seeing lower levels of oxygenated blood in a brain region may explain lower levels of cognitive performance in some people with SCI.

Chen's study of about 50 people is funded by the New Jersey Commission on Spinal Cord Research. Little is known about cognitive impairment in SCI patients, as most studies focus on motor disabilities below the site of the injury.

"There are a few studies that showed attention span and memory decline more rapidly with age in people with spinal cord injuries than people who are able-bodied. But those were mostly pencil and paper tests, which may be subjective. We want to give more quantitative answers."

She has noticed that people who had lots of physical therapy experienced smaller declines than less active people, and recommends that follow-up studies test the effects of exercise and other forms of rehabilitation on cognitive status.

"People active in rehabilitation seem to improve, but the data is not conclusive, as we don't currently monitor their brains as they exercise," she said. "But rehabilitation facilities and exercise programs are out of reach for many who can't get to them or afford them. The specialized equipment they use at them is expensive."

Her long-term goal, Chen says, is to facilitate the development of rehabilitation treatments for people with SCI, where they could accurately monitor their recovery by studying the effects of therapy over time.

Restoring Muscles by Stimulating the Brain

Elisa Kallioniemi slides a circular disk over her head, stops above her right ear and clicks. Her left hand jumps. She moves it a couple of inches back, clicks again, and is suddenly speechless, mid-sentence. With a single pulse of electromagnetic energy, her device can activate or inhibit the brain's major command centers.

What she is now trying to determine is whether multiple pulses in the motor cortex can produce longer-term therapeutic results by retraining neural circuits. Her first focus is people who have lost some control of their limbs following a stroke.

"We know from psychiatry that by activating neurons with transcranial magnetic stimulation (TMS) we can change the way the brain functions," says Kallioniemi, an assistant professor of biomedical engineering. The therapy has FDA approval for clinical treatment of depression, obsessive-compulsive disorder, smoking cessation and migraines with auras.

"But there are no FDA-approved TMS therapies at this point for motor rehabilitation," she adds. "People need to relearn motor skills such as grasping after a stroke, for example, which changes brain structure and function."

Funded by the New Jersey Alliance for Clinical and Translational Science, she will first test healthy people to get a better understanding of the neurophysiological effects of TMS. She'll measure their speed and accuracy in typing a series of numbers and record changes in the peripheral muscles with electromyography to see how effectively TMS activates the motor system.

For some maladies, researchers in the field hope to develop a non-invasive, more precise alternative to drugs, for example, which target neurotransmitters throughout the brain and cause side effects. By contrast, the only sensation electromagnetic waves cause is a slight contraction in the muscles of the scalp.

One goal is to reduce opioid use for chronic pain. Another is to enable surgeons to map the brain before operating on a tumor to determine which muscles they could potentially affect with its removal.

"But we don't fully understand how TMS works, so we're developing different protocols to measure impacts on the motor cortex. Mine is to administer pulses in pairs with particular timing," she says. As in psychotherapy, the aim is to figure out the correct parameters needed to restore some movement and function and how often the procedure needs to be repeated for maintenance.

To advance fundamental research, Kallioniemi's lab is part of a global consortium studying the two neurophysiological systems in the brain: one that excites neurons into action and another that inhibits it.

"There is an interplay between these two systems at all times," she notes. "With brain disorders, there is an imbalance by which the systems may be moving too quickly or too slowly. The impacts are not only visible, such as the inability to move a hand properly, but also operate at a deeper level affecting cognition and memory, for example."

Together, they're creating a large dataset to determine the reliability of biomarkers in both systems. Down the road, it could be used to identify neurophysiological features for brain disorders and other conditions and to see how people respond to treatment over their lifespan. Beginning with the motor cortex, the researchers plan to make all of their data, data analysis and testing protocols open to the public.

As Kallioniemi explains, "We want to know if we're getting the same results."


CagVenture

Making Zebrafish Move Like Icelandic Horses to Explore Motor Control

The transparent larval zebrafish (*Danio rerio*) is only 4mm long, but for biologist **Kristen Severi**, the vertebrate offers an expansive window for exploration into how the brain and nervous system control behavior.

"Like putting a big puzzle together, we're trying to understand all the circuits in the brain that control locomotion," says Severi. "If the spinal cord is damaged, it can result in paralysis, but we still don't understand all the pieces we'd need to restore full function.

"The same types of neurons that form the circuits for locomotion in humans can be found in zebrafish, and because they only have about 80,000 neurons at the larval stage, it's a much smaller puzzle to study," Severi adds. "Zebrafish are see-through, so we can image their brains fully under a microscope to see the neuronal activity involved in controlling the animal's movement while they perform behaviors in real time."

Sharing more than 70% of genetic material with humans, zebrafish have been a well-studied model organism since the 1960s. However, Severi's team has put an unusual twist on the fish in her lab and has adopted a novel combination of techniques to study them.

Her lab is using a genetically encoded Botulinum toxin, a form of Botox, to inhibit the synaptic output of certain neurons in zebrafish. Severi says the non-destructive, gene-silencing technique is being used to create a line of transgenic zebrafish that possess a gait-altering genetic mutation found in Icelandic horses.

"We're basically making Icelandic horses out of zebrafish," says Severi. "We want to learn more about the function of neurons comprising circuits for gait and speed control, and this gene was implicated in exactly that."

Unlike most horses with four gait patterns (walk, trot, canter and gallop), Icelandic horses have two others ("tölt" and "flying pace") due to a mutation in a gene called DMRT3. The mutation enables lateral gaits, ambling and pace, but inhibits the ability to transition from trotting to galloping.

"Typically, mouse models are used to study how tetrapods transition from walking to running, but fish also use limb-like pectoral fins to change speeds," Severi explains. "They have equivalents to our deltoid and adductors, and those muscles have motor neurons that sit in the spinal cord. The timing of the activation of those motor neurons is controlled by interneurons, like DMRT3, making it a great candidate for study."

The lab employs high-speed cameras capable of capturing up to 1,000 frames per second, as they use an artificial neural network to capture micromovements of the animals' tails and fins, and study behavioral changes that occur in the experimental group.

"We can analyze the difference between fish that are 'control' group and fish that have Botox in this group of neurons in the spinal cord to better understand the mechanisms under which this circuit is behaving inappropriately," says Severi. "We are trying to approach one cell type at a time with the zebrafish, where we have amazing genetic and optical tools to dissect these different neuronal classes that humans share.

"Ultimately, we hope our studies will help us understand the role of the different players in the spinal cord that control locomotion."

Revealing the Heavy Impacts of Repeated Low-Level Head Traumas

Soldiers training on heavy artillery and athletes in contact sports are routinely exposed to repetitive mild shockwaves and injuries. Unlike someone who has just dodged a missile explosion or been smacked by a linebacker, they may feel little immediate impact.

The cumulative effects of these low-level blasts can, however, cause neurological problems such as sleep disorders and attention deficits, notes **Bryan Pfister**, director of NJIT's Center for Injury Biomechanics, Materials and Medicine.

He explains, "If you have a mild hit, the first hit, does that exposure put your brain in a vulnerable state, even if there is no detectable injury? Research on animals shows us that a mild shock wave doesn't do much, but if the subject is hit again, then yes, we see neuroinflammation and measurable behavioral changes. With repetitive injuries, deficits develop over time."

Center researchers began studying these injuries five years ago to explore their impact on service members. Their goal is to understand the precise mechanisms driving persistent and chronic changes, which can then become targets for treatment.

In one approach, they're focusing on damage to the blood-brain barrier, a tightly packed layer of capillaries around the brain that are the central nervous system's first line of defense. Under normal conditions, they admit only the tiniest molecules, repelling pathogens and most foreign substances.

Earlier studies by NJIT researchers showed how cascading chemical effects from traumatic blasts can disrupt and destroy integral brain vasculature in the blood-brain barrier, promoting chronic inflammation.

Recent research reveals related effects from repeated low-level impacts. The brain becomes more permeable, admitting foreign molecules such as white blood cells from the peripheral system known as monocytes, which release cytokines to fight inflammation. The brain's own immune cells, microglia, also mount an anti-inflammatory response.

"If this process is sustained, it can become pro-inflammatory and turn toxic, killing neurons," says **Tulika Das**, a Ph.D. student in biomedical engineering who studies these responses in transgenic mice. "We saw this cause not only neurodegeneration, but behavioral deficits such as anxiety and memory impairments."

Her team is now trying to determine whether the invading immune cells or the brain's own are driving the harmful cytokine cascades. They recently tested a polymer called Poloxamer 188 as a membrane resealing reagent to block the former.

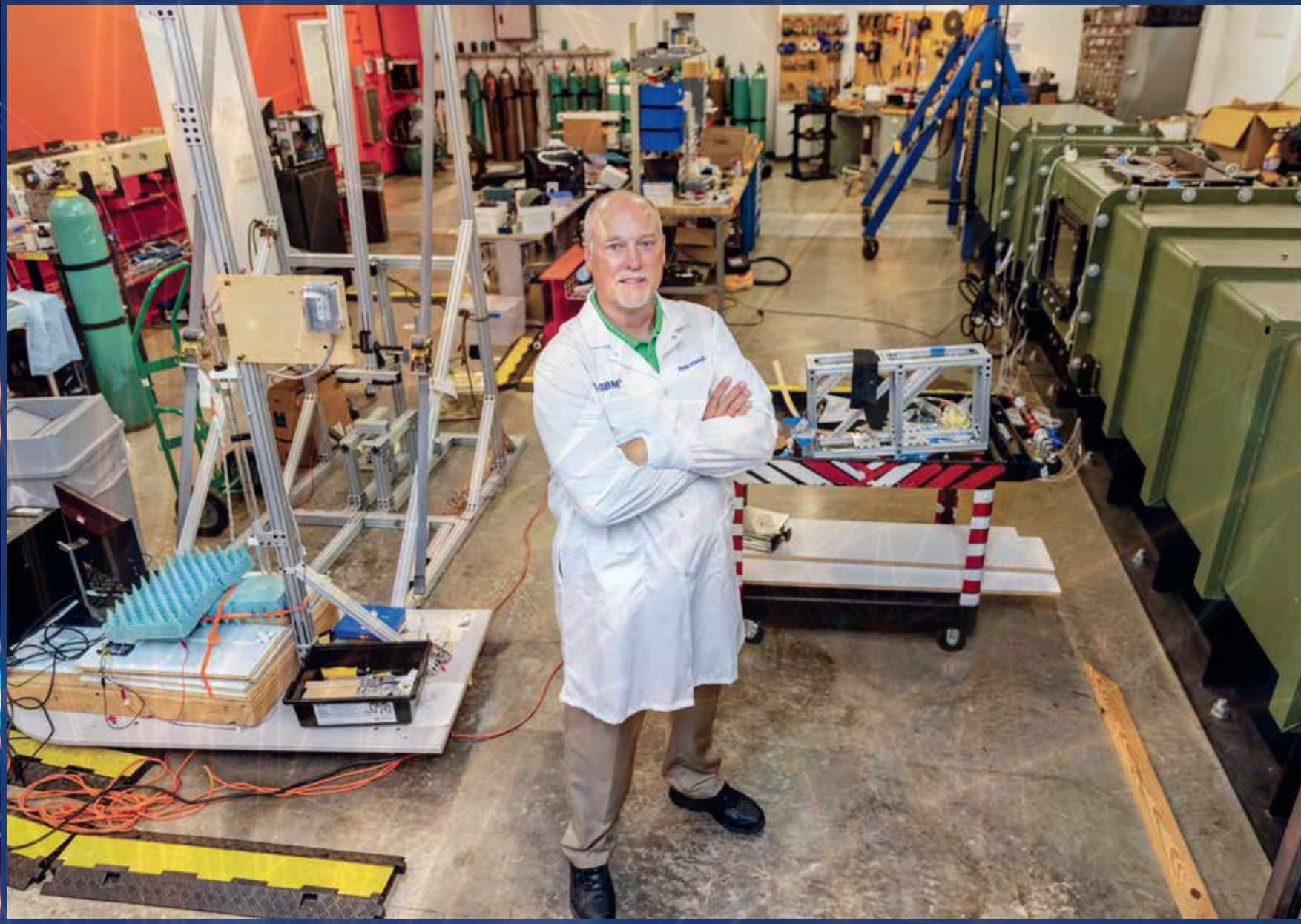
"The mice seemed less anxious and memory-impaired," she notes, "but we're still trying to pin down the chemical pathways."

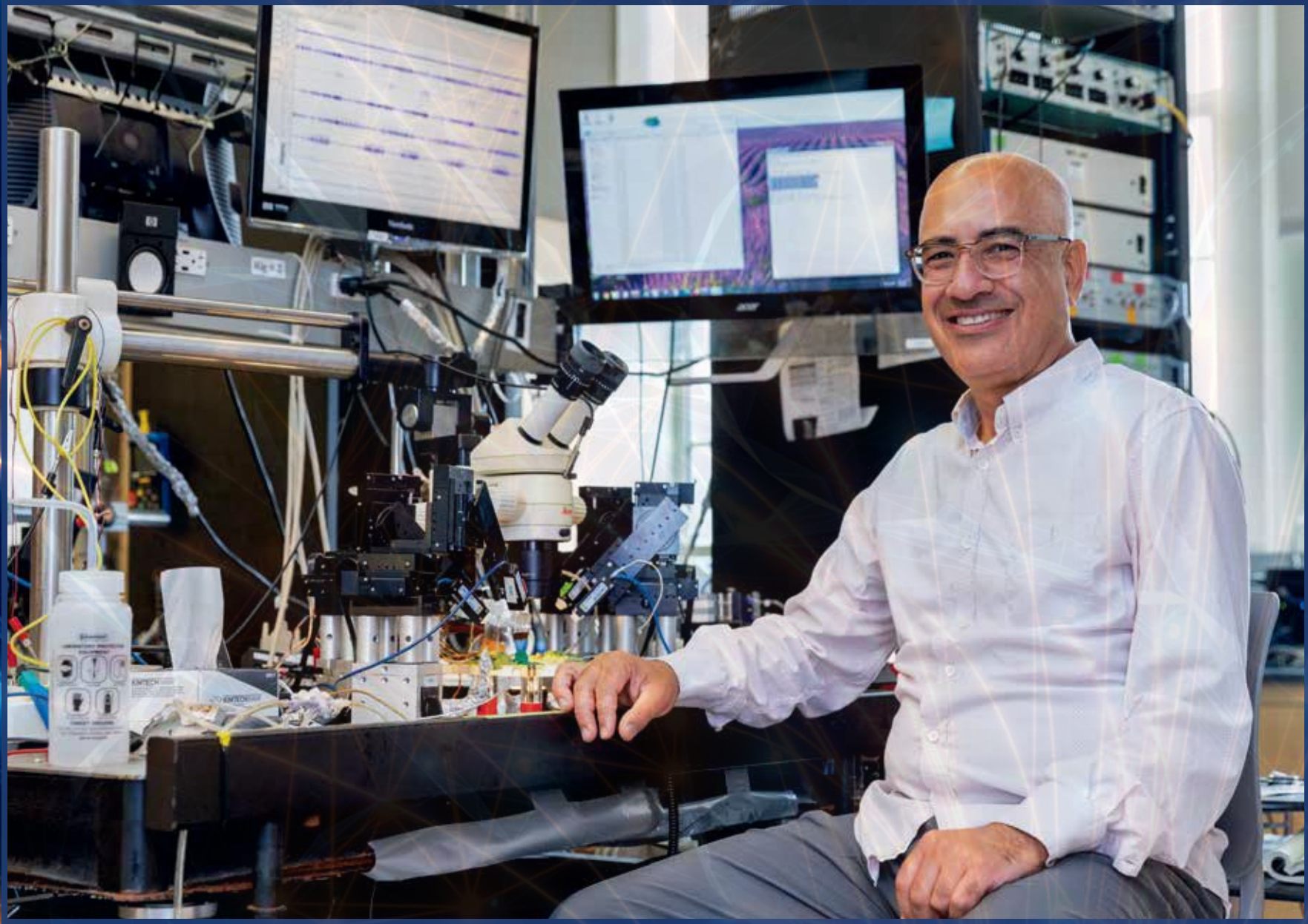
Researchers at the center also seek to pinpoint the exposure levels that put the brain into a vulnerable state to help decide when someone returns to duty or a game, for example.

"Is it the number of times someone is hit, how hard, or the intervals between the hits that matter? There are many biomechanical parameters involved in head injury. How each parameter leads to injury remains to be determined," Pfister says. "This is essential to setting exposure standards and to provide a threshold above which immediate treatments should be made."

Das notes that brain researchers are concerned about the growing number of people around the world subject to these repetitive injuries.

"Blast-induced neurotrauma is a signature injury of soldiers exposed to explosive devices, but it may also be experienced by civilians in wartime," says Das, citing just one little-studied group. "With increases in the use of weapons such as improvised explosives, they are at high risk."





Researchers Establish a Brain Pathway Linking Motivation, Addiction and Disease

Over 86 billion neurons are in the human brain, roughly 450,000 of which generate dopamine — a powerful neurotransmitter that drives motivated behavior, learning and habit formation. Now, researchers say one brain region may hold more influence over these dopamine neurons than realized.

Neuroscientist **Farzan Nadim** is shedding light on a mysterious pathway between the reward center of the brain that is key to how we form habits, known as the basal ganglia, and another anatomically distinct region where nearly three-quarters of the brain's neurons reside and assist in motor learning — the cerebellum.

The connection between the two, he's discovering, changes our fundamental view of how the brain processes voluntary movements and conditioned learning, and may lend fresh insight into the neural mechanisms underlying addiction and neurodegenerative diseases.

"We are exploring a direct communication between two major components of our brain's movement system, which is absent from neuroscience textbooks. These systems are traditionally thought to function independently," says Nadim, chair of NJIT's Department of Biological Sciences whose research with collaborators at Albert Einstein College of Medicine is being funded by the National Institutes of Health. "This pathway is physiologically functional and potentially affects our behaviors every day."

While both subcortical structures have long been known for their separate roles in coordinating movement through the cerebral cortex, they are also critical to both conditioned and error-correction learning. The basal ganglia, a group of midbrain nuclei which Nadim describes as the "brain's go-no-go system" for determining whether we initiate or suppress movement, is also involved in reward-based learning of behavior triggered by the release of dopamine.

"It's the learning system that promotes motivated behavior, like studying for a good grade. It's also hijacked in cases of addiction," says Nadim. "On the other hand, every behavior that we learn — whether it's to hit a baseball or play violin — this motor learning is happening in your cerebellum at the back of the brain. It's your brain's optimization machine."

However, Nadim suggests the cerebellum could be involved in both.

In a study that recently appeared in the journal *Nature Neuroscience*, Nadim's team offered the first direct evidence that the two systems are intertwined — showing the cerebellum modulates basal ganglia dopamine levels that influence movement initiation, vigor of movement and reward processing.

"This connection starts at the cerebellum and goes to neurons in the midbrain that provide dopamine to the basal ganglia, called the substantia nigra pars compacta. ... We have brain recordings showing this signal is strong enough to activate the release of dopamine within the basal ganglia," explains Nadim. "This circuit may be playing a role in linking the cerebellum to motor and nonmotor dysfunctions."

Nadim's group is seeking to identify exactly where cerebellar projections to the dopamine system originate at the nuclei level, a key step in learning whether the function of this pathway can be manipulated, he says. But the team's findings so far could have research implications for neurodegenerative diseases such as Parkinson's, which is associated with the death of dopamine-producing neurons in the substantia nigra.

"This pathway seems very important to our vigor of movement and speed of cognitive processes. Parkinson's patients not only suffer from suppression of movement, but apathy in some cases," says Nadim. "The cerebellum's location at the back of the brain makes it a much easier target for novel therapeutic techniques, such as non-invasive transmagnetic or direct-current stimulation.

"Since we've shown the cerebellum is directly exciting dopamine neurons in the substantia nigra, we might now use mouse models for Parkinson's to explore such techniques to see if that jump-starts activity of these neurons and relieves symptoms of the disease."

Training Exoskeletons to Adapt to the Uncertainties and Variability of Human Locomotion

Alex Zhou

In **Alex Zhou**'s BioDynamics Lab, there are wearable robots for a range of needs: an ankle device to give flagging walkers a boost; experimental gear to lighten the burden for firefighters; and a lightweight hip and knee exoskeleton for people who are in rehabilitation or simply aging. An upper-limb device to help industrial workers with daily lifting is poised to make the leap from simulation to hardware.

Broadly, their purpose is to enhance mobility by reducing the load on weakened joints and muscles. The engineering finesse lies in finding "the optimal assistance profile — the right amount of torque at the right time," as Zhou, associate professor of biomedical engineering, puts it. And the challenge is to accommodate individuals whose gait, strength and weight distribution vary substantially.

Using deep reinforcement learning, Zhou is designing a controller for a lower-limb rehabilitation exoskeleton developed by colleagues at NJIT and Kessler Institute that would dynamically adapt to peoples' diverse musculoskeletal properties and impairments as they navigate daily life. Currently, most devices maintain a preprogrammed trajectory, meaning the robot determines parameters such as step frequency and stride, while wearers can adjust their speed only.

"Traditional exoskeletons used in rehabilitation essentially carry you," Zhou notes. "What we're designing would adjust these variables for different body and mobility conditions and respond robustly to unpredictable forces as the person moves, such as trips, slips and sudden upper body movements that cause instability."

His controller is driven by a neural network that acts on a stream of signals, including joint velocity and acceleration, and subsequently computes in real time how much force the robot should apply for the next step. In the modeling phase, two other neural networks predict the human-exoskeleton interaction forces to ensure coordinated movement.

He first trains his model in a simulation environment, placing it on a virtual person to evaluate the impact on muscles and kinematics, while also teaching it to respond to unforeseen motion disturbances by pushing randomly on different parts of the body. To test the device's ability to respond to changing conditions, he also randomizes body types, motion dynamics and muscle strengths throughout the training.

Photo: Zihang You

Ph.D. student Neethan Ratnakumar tests a lower-limb exoskeleton for people with mild muscle weakness that was developed in the BioDynamics Lab.

Once transferred to physical hardware, the trained neural network controller would adapt the robot's movements to data from embedded sensors that compute joint angles, velocity and acceleration at the hip, knee and ankle. There are also four sensors in a shoe insert that assess stability and others that measure body position and velocity. The device responds by adjusting motor torques, which modifies the force exerted by straps around the waist, femur and other body parts.

In the lab, his team tests a device's efficacy by measuring how much a person's muscles contract — less is better if they're reducing load — and the amount of energy they burn by seeing how much oxygen they consume and carbon dioxide they produce. Using motion capture cameras, the researchers build patient-specific musculoskeletal models to determine how much of a boost a given person needs.

"The goal is to enable healthy people to walk faster and longer, while also helping people with rehabilitation needs with daily assistance that they would gradually become less reliant on," Zhou explains. "Ideally, people could use these robots at home to work at their own pace and to save medical costs."


Peter Balogh

Modeling the Body's Tiniest Operations in Vivid 3D

Threaded throughout the body are networks of capillaries so miniscule that red blood cells must contort to squeeze through them one at a time. It is this world that **Peter Balogh** brings to dynamic, 3D life on computer screens.

"The most important biological processes associated with blood flow occur in the tiniest vessels. This is where oxygen is exchanged between red blood cells and tissues, where new arteries sprout and where cancer cells enter tissues and metastasize," says Balogh, a mechanical engineer who specializes in computational fluid dynamics.

He has written new code that runs on supercomputers which allows him to model biological cells as they move through complex geometries, simulating the physics of bodily operations that experimental biologists can't see. The capillaries he studies range in size from 5 to 50 microns in diameter. Blood cells, by comparison, are about 8 microns wide.

One of the forces Balogh studies is the shear stress that blood flow exerts on the walls of these vessels, which directly influences the growth of new vessels. In tissues that lack oxygen, the vessel wall senses the force and coordinates with chemical growth factors, causing new vessels to form. In the case of an artery blockage, the body may revascularize to improve blood flow around the blocked region. Diseases such as diabetes, however, inhibit this new growth, impairing the delivery of oxygen and nutrients that feed the retina, for example, which can lead to blindness.

"Our high-resolution images, coupled with the simulations, give a better idea about what promotes their formation and what prevents it. The accuracy in modeling these forces goes up in 3D," he notes. "We try to determine why there is growth in one region and not in another."

Red blood cells are remarkable in that they've evolved to not break. When they become stiff, as in sickle cell anemia, they are no longer able to flex in order to flow through capillaries and the narrow openings in the spleen. Backed up, the spleen becomes swollen and painful.

"We can model the flow of any blood cells, including those trying to squeeze through and failing," he says.

Balogh is currently collaborating with biologists at the University of Florida who send him high-resolution images of capillary networks in laboratory rats with particular disorders. He then reconstructs them digitally and models their blood cell flow to understand at a root level what the forces on the wall look like.

With patient-specific images of retinal capillaries in people with diabetes, he would be able to identify key differences in how blood flows through them compared to healthy networks. A further goal is to simulate the transport of drug particles with blood cells to see how they're distributed through the retina, or in the case of sickle cell anemia, whether they can get through at all.

"These networks vary from one patient to another and so simulations would allow us to model the effects of a drug before we try it," he notes. This could be a key tool in devising therapies for solid tumors, which he describes as "nasty and chaotic," and thus even more patient-specific.

Photo: Theta Pavis

Modernizing Health Records for the Most Vulnerable

Over a decade ago, an NJIT health care startup took up a daunting challenge: to train 5,000 primary care providers in the state to adopt electronic health record systems that would allow them to better track their patients, improve their quality of care and securely share information.

The federal government, which funded the $50 million effort, had identified cumbersome and sometimes illegible paper records as one of the health care system's principal vulnerabilities. The group, NJ-HITEC, ultimately trained 6,500 providers.

Years later, at the request of the state, a successor organization at NJIT is plugging a gap in that initiative: modernizing record-keeping systems for one of the most complex and vulnerable segments of the patient population — people with substance use disorders.

"This is a severely siloed system. The aim is to integrate it and enable interoperability so that facilities can share information," notes **Renu Tadepalli**, who runs the program for the health care division of the university's New Jersey Innovation Institute (NJII). A primary goal is to reduce opioid abuse, but treatment centers say their new systems also allow them to keep better track of patients' overall health and to respond quickly to crises.

By connecting with the New Jersey Health Information Network, an electronic exchange of patient health information run by NJII, treatment centers receive alerts, for example, when a patient checks into a facility or a doctor orders a new prescription.

"We're able to see when a patient is in and out of the hospital and what they were admitted for," says **Katy Linton**, CEO and facility administrator of Greater Essex Counseling Services in downtown Newark. "Some of our clients have a number of problems, such as schizophrenic disorder, hypertension and diabetes, and we can find out if they're in touch with a family member or whether they need us to act on their behalf. Finding out where they are and what they need will help with more accurate diagnoses."

She adds, "In general, we want to focus on helping patients maintain a happy, healthy and whole lifestyle. You can't work hard on substance use issues if you're not feeling good."

Patricia Ackermann-Blanco, the center's clinical director, recalls the time a patient was losing weight, seemed disoriented and then dropped off the radar. Then she got an alert from a hospital apprising her of a dementia diagnosis for that patient. "We're able to follow up with clients that would otherwise get lost in a very cumbersome health system," she says.

Left to right: Renu Tadepalli, Katy Linton, Chris Vadas and Patricia Ackermann-Blanco

Managing 250 clients with substance use and other problems is complicated, and the new system can help in multiple ways. In just one small part of the operation, the center processes between 170-200 urine tests a week. Tracking that is now easier.

Critically, they also receive alerts when a doctor orders a prescription, so staffers can monitor what's called "pharmacy shopping," helping them to "prevent overdose or death and to see when a patient is struggling with sobriety," Ackermann-Blanco says.

Greater Essex first talked about adopting electronic records a decade ago.

"But the cost, at $50,000 to $70,000, was prohibitive," recounts **Chris Vadas**, the facility's co-owner and COO.

With funding from the New Jersey Department of Health and the New Jersey Department of Human Services for both the systems and the training, NJII has so far enrolled 110 facilities in the program.

Mapping Wounds in Three Dimensions

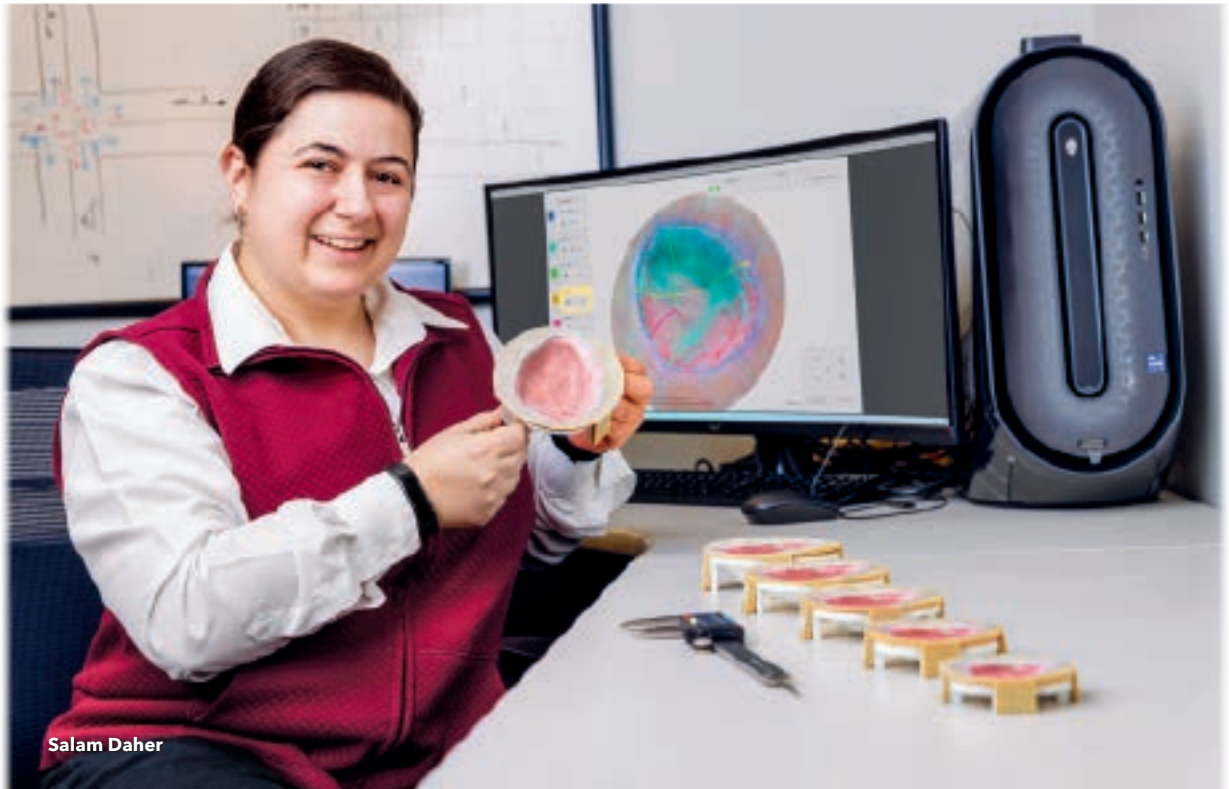
When assessing a skin injury, nurses and physicians often determine its dimensions with tools as basic as a ruler for length and width and a Q-tip for depth. While simple, this approach has drawbacks.

"With these tools, it's hard to capture contours with precision," says **Salam Daher**, an assistant professor of informatics at NJIT. Moreover, over the course of several shifts, measurements vary depending on the people taking them, the methods they use and their perception, for example, of features such as the widest part of the wound.

Partnering with Frank Guido-Sanz and Mindi Anderson and other professors at the University of Central Florida's College of Nursing, Daher is developing a more reliable alternative: software that can generate three-dimensional models of wounds. Using images captured by an off-the-shelf scanner or cell phone, this technology could capture the extent of an injury more accurately than the ruler-and-Q-tip method. What's more, it could align scans taken over time, allowing nurses or other health care providers to quickly tell if an injury is improving or not.

"We need health technology that is precise and objective so we're not giving treatments based on data that is not accurate," Guido-Sanz says.

Known for now as ViMeT (for Visualize, Measure and Track skin abnormalities), the system received an NJIT Technology Innovation Translation and Acceleration Program seed grant, which supports efforts to commercialize new technology. So far, Daher and her colleagues have focused on one potential application, pressure ulcers, also known as bedsores, which develop when patients stay in the same position for too long, among other factors. To effectively treat these injuries, caregivers must monitor their size to evaluate their progress, adjusting treatments, such as dressings and medications, if needed.


Salam Daher

However, the conventional means for doing so leaves plenty of room for error. In one published study, another team compared a ruler-based method for calculating the two-dimensional area of a wound with measurements derived from a digital camera equipped with lasers to detect the body's natural curvature. The ruler method, they found, overestimated the wound's area by about 40%.

As for the third dimension, depth, the device provides essential insight. Wound healing begins at the bottom and moves upward, so by assessing the topography of a wound's floor, it becomes possible to readily track its progress, Daher says, noting that ViMeT would give nurses unprecedented ability to make such measurements across wounds.

"The earlier you know that a treatment is not working, the earlier you can address it, potentially shortening hospital stays, reducing costs and improving quality of life," Anderson notes.

To use ViMeT, a caregiver would first take a series of overlapping photos of a wound. With an approach called photogrammetry, the hand-held scanner triangulates the images to construct a three-dimensional mesh representation of the wound. Software generates measurements and aligns subsequent scans to show if it is shrinking or growing.

Further down the line, Daher sees potential to expand ViMeT's utility. The system could, for example, employ a thermal camera to capture temperature across a wound. Meanwhile, the software could incorporate patient data, such as health conditions that impede healing, into assessments of a wound's trajectory. Ultimately, it could be used for burns and other injuries, she says. "Anything that you see on the skin's surface could be measured, stored and tracked."

Helping Cancer-Fighting Nanoparticles Hit Their Targets

Cancer care is moving away from the scorched-earth approach of chemotherapy and radiation to more targeted treatments with fewer side effects. One option: packaging cancer-killing drugs into tiny, biodegradable nanoparticles and injecting them directly into the blood. The nanoparticles are programmed to circulate through the body until they locate the tumor, penetrate its tissue and release their poison.

The problem? These specially designed nanoparticles don't always reach their intended destination. In fact, within minutes of being injected, many end up in the spleen or liver, where they're filtered out of the body's general circulation and earmarked for disposal.

"We don't really know what's happening to the nanoparticles," says **Kathleen McEnnis**, an assistant professor of chemical and materials engineering. "There's a big disconnect between this concept of targeted nanoparticle cancer treatment and actually developing a feasible process."

But recently, McEnnis took a crucial step toward closing that gap. By adapting a commercially available method for measuring nanoparticle size, she developed a novel technique to examine what's really happening to these nanoparticles in blood.

Her first hypothesis was that, once injected into the blood, the nanoparticles became covered with a layer of proteins, much in the way that ships amass an accumulation of algae after some time at sea. This layer, known as a protein corona,

Kathleen McEnnis

was likely the reason that the nanoparticles were quickly identified as foreign invaders and disposed of by the body, McEnnis says.

While previous researchers would extract the nanoparticles from the blood and rinse them to determine the size of a protein corona, McEnnis' new method allows them to be measured while still in the blood. With her technique, the instrument not only measures size, but also uses fluorescent labeling to follow the nanoparticles as they move through the blood in real time.

Using this method, McEnnis found that nanoparticles incubated into blood grew by up to 100 nanometers as they were covered in protein coronas, versus nanoparticles that were incubated into saline. In an effort to prevent the protein coronas from forming, McEnnis coated the nanoparticles with polyethylene glycol (PEG), a hydrophilic polymer found in shampoos and other products. But while the PEG created a water layer around the nanoparticles, it didn't prevent proteins from sticking to the nanoparticles — or protein coronas from forming.

"That was unexpected," says McEnnis, a polymer scientist. She says she had hoped adding PEG to the nanoparticles would solve the protein corona problem. Instead, McEnnis learned that she was likely trying to solve the wrong problem.

As she watched the nanoparticles move through the blood over time, she noticed something surprising at about 12 hours post-incubation. Along with single nanoparticles drifting through the blood, she also spotted a large clump of the particles stuck together with other matter. "You can imagine that giant aggregate is not going to be good in the body," McEnnis says. "That might be why the nanoparticles are all ending up in the liver."

When McEnnis examined which nanoparticles were collecting in the aggregate, she found that, unlike with the protein coronas, a PEG coating made a difference. Nanoparticles without PEG had much more aggregation, McEnnis says, than nanoparticles that were coated in it. "The size of the protein corona probably doesn't matter. What matters is how it's aggregating."

While many questions remain unanswered — such as how much PEG needs to be on the surface of the nanoparticle for ideal results — McEnnis has already begun to use her novel technique in other projects. In separate work on using platinum nanoparticles for breast cancer treatment, she found these nanoparticles had about 11 hours to find their cancer target before becoming aggregated and sent to the spleen for disposal. "This will start letting us know what kind of timeframe we have to work with," she says, "until this significant aggregation occurs."

McEnnis has published several papers on her novel technique and findings, in publications including the journal *Particle & Particle Systems Characterization*. The next step: verifying the technique by testing it in mouse models. "It lets us peer into the black box," she says. "We can finally start to deduce what's happening to these particles when they're in blood."

Pharmaceutical Nanotechnology for Better Drug Delivery


Ecevit Bilgili

With computer modeling and nanoengineering, ECEVIT BILGILI tackles a growing obstacle in modern pharmacology: The hunt for powerful precision therapies has yielded drug molecules so large they have difficulty dissolving in the bloodstream. Manufacturing has not kept up.

Bilgili, director of NJIT's Particle Engineering and Pharmaceutical Nanotechnology Laboratory, mills drug compounds into particles as tiny as 100 nanometers in diameter to increase their dissolution and dispersion rate before repackaging them with other materials that will enhance their delivery.

He has, for example, interspersed drug nanoparticles with polymeric colloids, which soak up water like sponges, then expand and burst, breaking up the packets of nanoparticles and spreading them quickly. He recently reengineered a cholesterol medication as a nanoparticle suspension with these agents to improve its release rate.

In another approach, he coats drug nanoparticles with polymers that readily mix with water, thus causing them to dissolve faster. By manipulating the coating thickness and selecting the polymer judiciously, they ensure a drug's immediate release.

"If you have acute symptoms, such as a migraine, the last thing you want is a slowly dissolving drug. Some drugs will never achieve therapeutically effective levels if they disintegrate slowly," says Bilgili, who works with companies to improve medications that are already on the market.

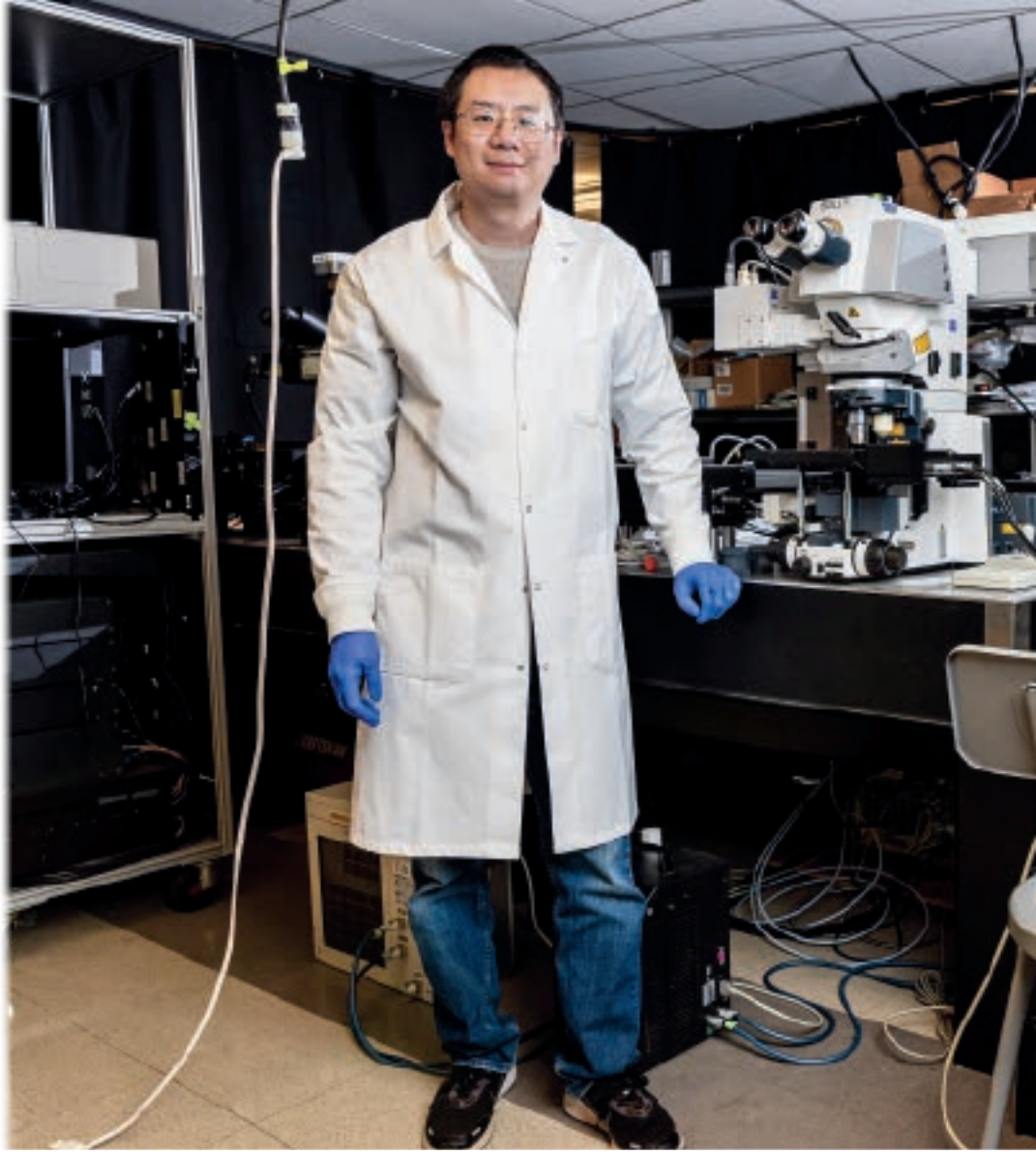
He grinds drug compounds with beads made of polymers, ceramics and steel, as well as their mixture — a novel process he was the first to use — and uses computer modeling to optimize the particle size for different applications.

The temperature in the milling equipment is also critical. If it rises unpredictably, it may degrade a drug or even render it toxic or carcinogenic. Bilgili is currently working with the pharmaceutical company GSK to simulate the milling process and develop approaches to reduce temperature.

Experimental methods in the industry are slow, costly and energy intensive.

"We use mathematical modeling to predict parameters such as temperature and particle size in the mill, as well as a drug's development time more generally," he says. "The goal for a client is to come up with a solution in five experiments, rather than 50."

Triggering Light-Activated pH Bombs to Destroy Cancer Cells



In the hunt for precision cancer therapies, **Yuanwei Zhang** is developing a "pH bomb," a light-activated strike on the energy production centers inside malignant cells.

Compared to chemotherapy drugs, phototherapy can target cancer tissues with precision from the outside, steering clear of healthy tissue by delivering light and activating the pH-altering compounds only in the tumor.

Zhang's technology is a new twist on photodynamic therapy, which uses compounds that absorb light to attack cell operations. To date, most of these treatments work by transferring light energy to oxygen molecules in cancer tissue. The process converts the molecules into a toxic form of reactive oxygen species that breaks down the living structures around them.

"One of the limitations of this approach, however, is that tumors have low levels of oxygen. They grow so fast, they're burning up oxygen like crazy," he notes. "We can bypass the need to target oxygen by altering their pH instead."

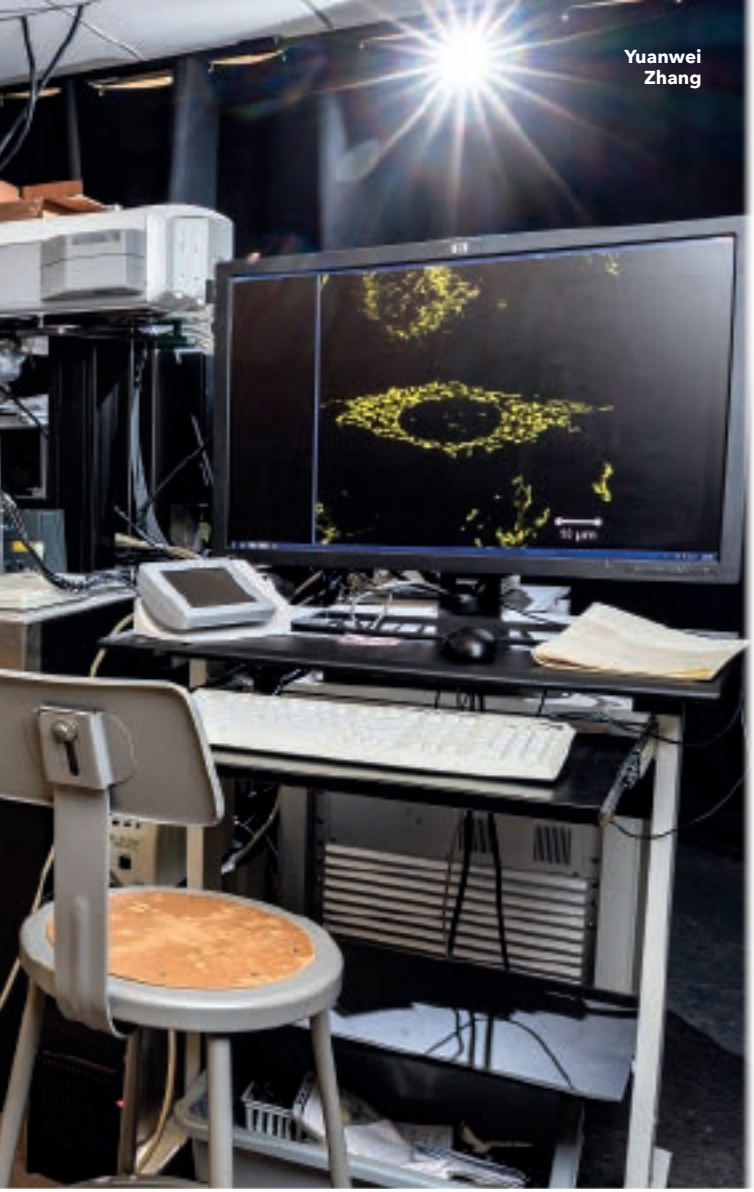
By shining a beam of LED light on breast cancer cells that have been immersed in a photosensitive compound, Zhang triggers changes inside the mitochondria that modify their pH in destructive ways, causing them to morph from tubes into more permeable spheres. This allows cancer drugs to enter more easily.

"Like a switch, we can turn the pH modulators on and off," he says.

Zhang notes that diseases themselves use pH, which regulates cellular production of enzymes and proteins, among other cell functions, for their own advantage. Coronaviruses, for example, target the pH of lysosomes in healthy cells, disrupting their uptake of vital resources, while also weakening them so the virus can escape and invade more cells.

Tumors are drug resistant in part because their pH is different from normal tissues: They're acidic on the outside and basic on the inside. "We want to reverse that balance with our therapies," he says.

His technology includes three essential engineering elements he is now refining. He can program his pH bombs to


Yuanwei Zhang

target different organelles, either mitochondria or lysosomes. He can also trigger different pH changes that break different chemical bonds to release acids or bases.

"Acids and bases are very important to the maintenance of biosystems and we can make them go in either direction," he says. "If the mitochondria in a cancer cell is more basic, for example, we'll make it acidic."

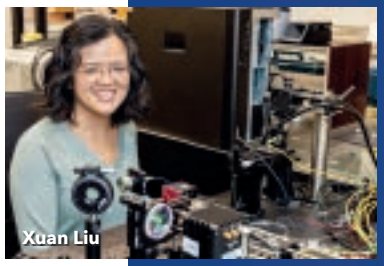
Lastly, he can adjust the wavelength of the light he uses to penetrate different cancers. Green light waves are relatively short and thus suited to skin cancers, while red light, which has longer waves, can reach deeper tissues, such as breast cancer.

Working with chemist **Kevin Belfield** at NJIT and collaborators at Sanford-Burnham Prebys Medical Discovery Institute, he's currently studying how safe his light therapies are on surrounding normal cells, such as the photosensitive compounds that are injected before the light is applied. "Are they safe in the dark, for example, and only activated when we turn on the light?"

The progress of these cells is difficult to monitor, however, as the fluorescent labeling typically dims after just a few hours. He's addressing that hurdle with an NJIT electrical engineer, **Xuan Liu**, who is developing new methods to study the cells that don't require fluorescence. To date, they've extended the viewing period to three days.

"Over this longer period," he says, "we're able to better track cell morphology changes and to study the tumor's response to drugs, which take hours to take effect."

Observing a Cancer Cell's Migration at Nanoscale


Xuan Liu

Under her microscope, XUAN LIU observes the nanoscale movements of a cancer cell as it interacts with its environment and other cells. Her precise observations reveal an unusual dynamic: the unhealthy cell appears to adhere with less strength to the substrate than the others, potentially facilitating its continued migration.

"How these cells migrate is very important to how the cancer develops," notes Liu, director of NJIT's Biophotonics Imaging and Sensing Lab. "If there is a local tumor, we can cut it out, but if it travels everywhere, it becomes more difficult. Our goal is to understand the correlation between molecular and mechanical behavior."

What allows her to track subtle motions with nanoscale sensitivity is a novel technology called optically computed phase microscopy (OCPM). It can not only see the structure of the tiniest particles in visible light, but also infer their position, hence movement, in relation to the phase of an electromagnetic wave as it interacts. Liu developed an exceptionally precise method for computing these movements in high resolution.

"We're creating a movie frame by frame," she says, "at a very tiny scale."

The technology offers another key advantage to disease researchers: the ability to observe cells without tagging them with fluorescence, which dims quickly and can disrupt their behavior.

To date, Liu's collaborator, YUANWEI ZHANG, has used OCPM to watch tag-free cancer cell movements and morphology changes over the course of three days, as compared to a few hours with fluorescence, giving him a clearer picture of its evolution.

They are both eager to apply the technology to drug delivery research as it can image both cells, which are transparent, and particles, which are not, with continuous observation.

"We can see, for example, whether a small particle enters a cell more easily than a large one, among other variables," Liu explains. "We can also understand the timescale of the delivery — how quickly it enters the cell and takes effect."

Left to right: Marieli Jimenez, Sara Elsayed, Kennedy Cash, Rana Balah, Carla Blandura

Preventing Miscarriages with a Simple Device

For women with a cervical condition that puts them at risk of miscarriage, there are no easy fixes. The primary method to prevent early labor when the cervix dilates prematurely is cerclage — closing it with sutures. That's a costly surgical procedure with potential complications. Two longtime remedies, bed rest and hormonal therapy, are no longer recommended.

With the goal of designing a simpler, less risky alternative, an undergraduate team of women biomedical engineers took up a senior capstone challenge presented to them by **Emre Kayaalp**, M.D., Ph.D., an obstetrician, gynecologist and engineering enthusiast.

"There is a gap in the market," explains Kayaalp, chair of the Department of Obstetrics, Gynecology and Women's Health at Overlook Medical Center, calling the condition, known as cervical insufficiency, both unpredictable and understudied.

As the five-member team contemplated structures and materials at the outset, they toggled among three ideas: zip ties, snaps and rubber bands. Ultimately, they settled on a circular ring that wraps around the cervix, bolstering it against contractions and other uterine forces. They tapped into wide-ranging knowledge of mechanical devices for inspiration.

"We wanted to create something that would expand to fit around the cervix, but then contract to secure it. There was really nothing out there to compare it to," recounts **Carla Blandura**. "We settled on the circular ring design so that it would be easier for insertion and removal for general OBGYNs even in the office."

To develop a prototype, the biomaterials engineers chose polydimethylsiloxane (PDMS), a silicone-based polymer that is strong, highly flexible and conforms easily to the body's shape. Research into other medical uses, such as dental devices, reassured them that it would not react chemically inside the vaginal canal. They 3D-printed molds that could be adjusted according to each patient's individual requirements "to personalize the product," as **Sara Elsayed** puts it.

"We then simulated intrauterine forces in an engineering software program called ANSYS that allowed us to see, for example, how much the head of a baby would cause it to stretch sideways," recounts **Marieli Jimenez**.

To test how easily they could insert and remove the device in a medical office — a key design requirement — they constructed a model of a cervix using Styrofoam and a tennis ball placed 3-6 inches deep into a box to simulate the vaginal canal. In their report, they called the first part of the procedure a work in progress, noting that "it took two sets of hands to complete the task."

Cost is a hurdle, physicians note. Cerclages must be done in the operating room with another doctor assisting. In some cases, people must have experienced the loss of a fetus before they qualify for it.

Kayaalp says he appreciates the "fresh perspective" that students bring to a problem that "we as clinicians may not consider. They don't have pre-existing notions of how a problem is solved."

Blandura says she found the project professionally illuminating — and liberating.

"In school, there is often one right answer, while in the outside world there are so many different mechanisms and viewpoints that go into creating a device. If you try something and it doesn't work, that's okay," Blandura says. "Understanding this changed the team's mindset. We saw the broader picture in terms of designing the project rather than nitpicking and losing team motivation whenever certain designs would not work."

NJIT Scholar Asks: How Safe Is Your Mobile Health Data?

Ricky Hernandez

Information technology major **Ricky Hernandez** '24 says that while Apple has implemented privacy protection in iOS for user health data, Google has yet to fully integrate the same protection for its Android users.

With funding from NJIT's McNair Scholarship Program, Hernandez launched a research project last year, titled *Privacy Aspects of Smart Medical Apps*, to understand whether health app developers are being transparent about the data they collect.

It's a privacy issue that Hernandez says has been relatively unaddressed as the harvesting of user metadata has exploded into a billion-dollar industry.

"We asked a simple question. When a mobile user downloads an application, can they know all the permissions that will be used by the app from reading the app description alone? … We believe app descriptions supplied by developers should encompass all of what a user should expect from using their app," says Hernandez. "The point of this research has been to shine a light on a glaring issue in mobile ecosystems."

Under the advisement of NJIT Computer Science Assistant Professor **Shantanu Sharma** and Colorado State University graduate student Ethan Myers, Hernandez applied trained language models to search Android app stores to explore potential discrepancies between health app descriptions and the permissions for users' legally protected personally identifiable information.

"We wanted to explore the description-to-permission fidelity on a large dataset of mobile apps provided on the Google Play store … a poor fidelity would prove a need for stricter publishing guidelines for app developers," explains Hernandez.

While the Google Play store hosts more than 50,000 medical health apps (mHealth), the team used the World Health Organization's definition of the popular app category to manually vet app descriptions for appropriate consumer health-related content. They then narrowed down a pool of 400 mHealth applications for analysis.

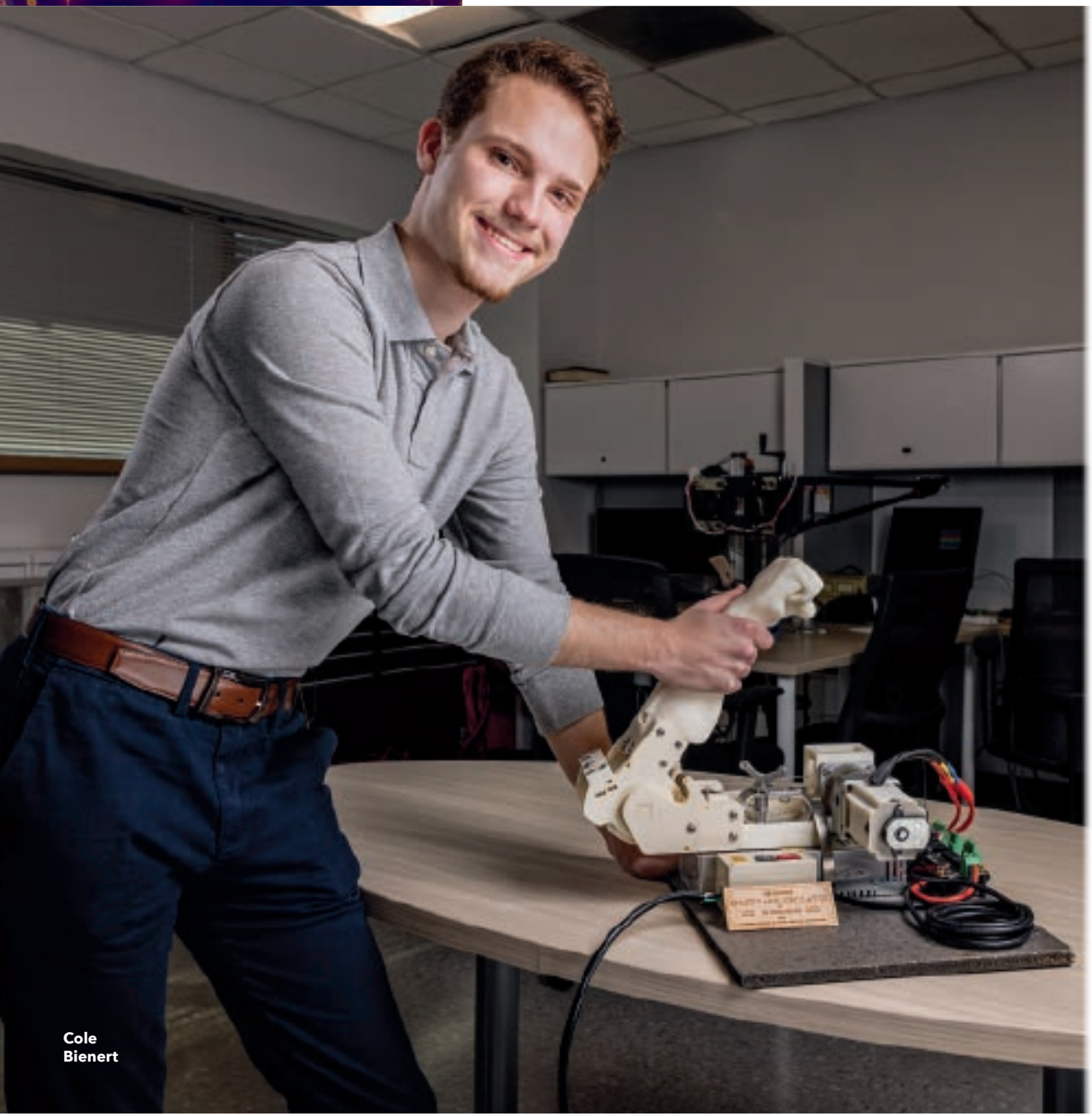
Over the course of three months, the team trained a natural language processing model with more than 7,000 additional key sentences for accurately identifying permissions each app was requesting, comparing the data to app descriptions they collected using a Google Play store data scraper.

In all, they found nearly 650 permission requests from the 400 apps — such as requests for control over a phone's microphone and camera, storage and phone app — absent from descriptions that users typically review when deciding to download.

"The results were shocking," says Hernandez. "These large numbers of unlisted permission requests would be in violation of laws in the European Union, but the U.S. doesn't have such legislation to protect citizens' personal information in the virtual realm. Instead, Google needs to do a better job of policing app developers."

Hernandez says future work could similarly examine privacy policies and terms of service to provide insights into how user data is managed by the app in accordance with legal disclosures.

"This could give us a more comprehensive evaluation of app behaviors and their alignment with user expectations," he says. "User trust is essential for the growth and development of health apps. If the public cannot trust app developers to tell them why or how they are using their data, they will stop using them."



Cole Bienert

Device Simulating Human Spasticity Can Help Train Clinicians

Teaching physical therapists to treat patients with neuromuscular conditions such as spasticity presents several challenges. Individual clinicians may classify the same patient with different levels of severity and getting real-life training experience can be difficult in an educational setting.

"The crux of the problem is consistency," explains **Cole Bienert** '23. "A lot of the training now is subjective or experience based. But if you can give multiple schools a single device, they'll all get the exact same experience."

Working with fellow biomedical engineering majors **Hayder Khan**, **Ashwin Kurian**, **Roark McFadden** and **William Kroeger**, Bienert and his classmates built a device that realistically recreates a spastic human arm — one that is stiff or rigid from disability or another cause. During their research they found that some professors resort to demonstrating spasticity on their own limbs when training physical therapists; the student trainees, in turn, end up practicing on each other.

The spastic arm simulator the students built is a software-controlled mechanical arm model consisting of a forearm, elbow and bicep that utilizes cable systems to simulate upper extremity spasticity. Spasticity is characterized by an abnormal increase in muscle tone or stiffness, which can interfere with movement and reflexes and cause discomfort or pain.

The SpasTECH Spastic Arm Simulator can be used to train future physical therapists and other health professionals to identify and treat spasticity with clinical accuracy. It allows

students to learn first-hand how a patient's arm will react during a spasticity evaluation.

The device won the 2023 VentureWell Design Excellence Prize for undergraduate teams from the National Institute of Biomedical Imaging and Bioengineering. The students were part of a capstone class advised by **Jongsang Son**, an NJIT assistant professor of biomedical engineering whose research focuses on the neuromuscular mechanisms of motor impairments.

The mechanical arm is connected to a motor that is connected to a computer, running code to mimic a patient's spasticity. It gives haptic feedback as the motor resists the tester and varies torque levels to represent each level of severity.

Early in their work, the team was also accepted into the National Science Foundation's Innovation Corps (I-Corps), a seven-week program for inventors whose projects have commercialization possibilities.

The team's initial design task was to create a mechanical arm model that would recreate spasticity based on a 6-point clinical scale. The more severe the spasticity in the arm, the more difficult it is to straighten from a bent position. A flexible arm is less resistant to movement.

Researching mechanical systems, they conceptualized their model — from the bicep and elbow to the forearm and hand — with computer-aided design software. The arm model was produced with a 3D printer.

To give the model movement, the team inserted two steel cable systems into the arm, one for flexion (bending) and one for extension (straightening), controlled by an attached motor. The motor connects to a controller that directs the arm's movement based on code programmed into a computer.

The prototype was working well — until the team began modeling the higher severities of spasticity. "The forces started getting really big," Bienert says. "An arm at severity 4 is nearly locking up. It takes a lot of force to recreate that. The cables were breaking and the motors were burning out."

After some mechanical problem solving, the group found a remedy by doubling the diameter of the cables in the model arm, Bienert says. They also added a gearbox between the motor and the model arm to create more torque. The device had become so realistic that its motor could be programmed to lock up or back drive at a particular arm angle to create resistance that mimics a flare up of spasticity.

Could the next step be commercialization? The device is fully customizable, Bienert says, so it can be programmed to function with different spasticity scales and be updated as spasticity research advances.

"The only thing that has to change is the code," Bienert says. "The device has so much room for improvement and customizability. It's not a product that's going to become dated. It can keep up with the times and be relevant."

Designing New Tech for Older Voices


Alisha Pradhan

Seeking information on the internet, older adults say their voice queries are too often met with the frustrating refrain, "Sorry, I'm having trouble understanding you." AI assistants may also act on a command before they've finished it or time out if they pause briefly. After a couple of tries, some give up.

"Speech recognition systems have a high error rate for this group, because they don't take their speech patterns into account," explains ALISHA PRADHAN, assistant professor of informatics. "They are significantly underrepresented in the speech data that trains the machine, which is largely composed of young, Western voices."

Older Black adults, more than others, receive unrelated answers, notes Pradhan, who has conducted several studies in which she invited elderly participants to discuss their challenges, as well as the features they would like to see in AI and smart devices.

Her main takeaway: "It's important we don't assume what they want or treat them as a homogeneous group. Technologies shouldn't, for example, perpetuate the stigma that all older people are in decline. Such assumptions lead to designing technologies they don't find meaningful or useful, and they may not adopt them."

"There is a real need for technologies to support health and well-being in older adults, but we need to build and test them with older adults," she adds.

Pradhan argues for more customization. Medication prompts are a good example in which functionality, privacy and social embarrassment are all concerns to be managed. Some reminders could be spoken, while smart watches could beep or lockets vibrate. "The social context is important," she notes.

She's currently working on a project on customizable reminders for people in the early stages of dementia that connects their digital calendars with home objects like a door mat that would remind them as they leave what they need for specific appointments.

"Current reminders are predominantly digital, but as dementia progresses, people may be less likely to want to navigate them."

New Faculty

COLLEGE OF SCIENCE AND LIBERAL ARTS

Trevor Del Castillo, assistant professor of chemistry and environmental science, synthesizes polymers for use in drug and gene delivery and the manufacture of easily recyclable commodity plastics. A technology he helped develop, in which self-assembled polymer nanoparticles convey mRNA cargo to combat viruses and cancers, has been licensed by a major drug maker.

Allison Edgar, assistant professor of biology, studies how animals' life histories — strategies for reproduction, survival and growth — originate and evolve, and seeks to identify features that are likely shared by all animals, versus those molded by evolutionary pressures. She examines, for example, gene regulatory differences between species that can and cannot regenerate.

Jonathan Jaquette, assistant professor of mathematics, explores change over time in complex systems with many interacting components. These dynamical systems include the climate, neuronal activity and traveling waves. He develops computer-assisted proofs to bridge the gap between what can be proven mathematically and what can be computed numerically.

Eugene Cho Snyder, assistant professor of humanities and social sciences, studies the psychological effects of emerging media technologies, such as AI-supported virtual agents and recommendation systems. She investigates privacy issues stemming from covertly applied automated suggestions from machines and examines ways to empower users against them with customizable information filters.

NEWARK COLLEGE OF ENGINEERING

Adeel Akhtar, assistant professor of mechanical and industrial engineering, works on nonlinear control systems and robotics, including multiagent drone systems. He develops global geometric controllers for robotic devices, for example, that enable them to analyze ground, aerial and underwater systems and navigate cluttered environments without colliding.

Rajarshi Chattaraj, assistant professor of biomedical engineering, develops colloids and nanostructures to diagnose and treat diverse illnesses. Using ultrasound, he activates droplets to detect disease biomarkers and directs bubbles to release therapeutic gases that inhibit molecular cascades that exacerbate brain injury. He also designs self-assembling recombinant proteins to inactivate viral and bacterial pathogens and toxins.

Yanxiao Feng, assistant professor of applied engineering and technology, studies the interface between humans and buildings' physical environments to improve sustainability, resilience, environmental health and comfort, including thermal resilience and energy efficiency under extreme weather conditions. She measures building data and human feedback with wearable sensors, data mining techniques and user-centered experiments.

Arnob Ghosh, assistant professor of electrical and computer engineering, researches learning-based decision-making in complex systems, such as smart grids, transportation and wireless networks. His algorithms seek to optimize the performance of systems while providing safety guarantees. For example, he developed an algorithm to minimize autonomous vehicle trip-times while avoiding collisions.

Maryam Hajfathalian, assistant professor of biomedical engineering, develops theranostic nanomaterials that target delivery of organic and inorganic nanoagents to specific cells or tissues to detect and treat cancer and infectious diseases. She has used complex metal nanoparticles, for example, to treat infections caused by biofilms that grow on teeth and wounds.

Josh Taylor, associate professor of electrical and computer engineering, works on problems in energy and water infrastructure, drawing on mathematical tools from control theory and optimization. He invented financial storage rights, a mechanism for enabling electricity storage devices, such as batteries and flywheels, to be integrated into the power grid in a financially viable way.

Arjun Venkatesan, associate professor of civil and environmental engineering, focuses on the occurrence, fate and treatment of toxic chemicals in the environment. Additionally, he develops novel analytical and monitoring approaches to assess human and environmental health risks associated with toxic exposures and drug use.

HILLIER COLLEGE OF ARCHITECTURE AND DESIGN

Addison Godel, assistant professor of architecture, studies how design aesthetics, technology and politics shaped little-studied infrastructure in the mid-20th century, such as wholesale produce markets, telephone exchanges and sewage treatment plants. His topics include AT&T's "good neighbor" approach: windowless skyscrapers with sculpted façades in dense downtowns and faux ranch houses in the suburbs.

Aleksandr Mergold, AIA, associate professor of architecture and a practicing architect, reimagines existing structures, materials and systems. His Oculi project, developed collaboratively as a proof of concept for the reuse and repurpose of old metal grain bins, now resides at Art Omi, an art, sculpture and architecture park.

Etien Santiago, assistant professor of architecture, studies the evolution of building technologies during the 20th century. He demonstrated, for example, how political debates constrained architects' use of steel and reinforced concrete in rebuilding following WWI, as some critics associated these materials with modernizations adopted by the authoritarian governments that flourished during the war.

Richard Thompson, associate professor of design, devises technologies to bring virtual characters to life and to improve visual storytelling through animation, environmental narratives and immersive game world design. In his career in entertainment and advertising, he has worked on the History Channel's *Engineering an Empire* and *Word World*, an EMMY Award-winning TV series.

YING WU COLLEGE OF COMPUTING

Kasthuri Jayarajah, assistant professor of computer science, designs systems that support sensing, processing and communication across platforms with limited battery power, computer capacity and memory, such as smartphones, personal wearable devices and AR/VR systems. She develops systems that efficiently team humans and robots by monitoring human performance and adapting robotic systems accordingly.

Nathan Malkin, assistant professor of informatics, researches how human factors contribute to cybersecurity and privacy failures. He then designs and empirically validates systems that overcome these challenges through more usable interfaces, for example, by automating systems and eliminating confusing choices in smart home settings.

Alisha Pradhan, assistant professor of informatics, explores the design of emerging smart technologies, such as AI assistants and smart homes, to support the health and well-being of older adults and people with disabilities. She examines the accessibility benefits and barriers and the socially responsible design of these technologies to facilitate equitable use by underrepresented groups.

Akshay Rangamani, assistant professor of computer science, studies how large deep neural networks solve complex learning tasks, such as identifying objects from noisy and incomplete radar measurements and predicting brain waves for brain stimulation. He models learning and memory in the brain, with a focus on mechanisms that underpin working memory in the pre-frontal cortex.

Zhihao "Zephyr" Yao, assistant professor of computer science, focuses on improving system security and trustworthiness in mobile computing and operating systems, minimizing the need to trust hardware and system software, for example, in security-critical applications. Yao co-invented a solution called "bowknots" that prevents unpatched vulnerabilities in the Linux kernel from being exploited by hackers.

Shuai Zhang, assistant professor of data science, researches efficient and trustworthy AI and develops theoretical foundations to address transparency concerns. He creates learning algorithms to reduce model complexity and the required number of training samples, improving reliability and efficiency in applications such as cyber-physical systems, computer vision and spatial-temporal data analysis.

MARTIN TUCHMAN SCHOOL OF MANAGEMENT

Shubham Gupta, assistant professor of decision sciences, applies optimization, game theory and machine learning in collaborative environments, e-commerce and social media platforms, and health care. His models, for example, seek to untangle emerging contractual issues and identify crucial trade-offs that arise from strategic interactions among parties involved in the value creation process.

Yanguang "Alice" Liu, assistant professor of financial technology, studies the role of machine learning and other Fintech in the delivery of information to investors and firms' fundamental operations, in sectors ranging from financial markets, to labor and finance, to mergers and acquisitions. She has measured the use of robots in reducing operations risk, for example.

Jae-Hyuck Park, assistant professor of decision sciences, focuses on sustainable grocery store operations, food supply chains, food waste and revenue management. He examines problems such as how long to keep food on shelves, whether to time-stamp packages and the optimal ordering of fresh and older items in food case displays.

Faculty Accomplishments

AMERICAN ASTRONOMICAL SOCIETY, KAREN HARVEY PRIZE

Bin Chen, associate professor of physics and a researcher at NJIT's Center for Solar-Terrestrial Research, develops new observational techniques using radio waves to detect and measure magnetic reconnection, termination shocks and energetic particles — the central processes that power solar flares. He has been instrumental in developing the next generation of solar radio telescopes.

AMERICAN INSTITUTE OF CHEMICAL ENGINEERING, FELLOW

Ecevit Bilgili, professor of chemical and materials engineering, boosts the therapeutic efficacy of pharmaceutical drugs through nanoengineering. He develops nanoparticle formulations, for example, that enable the immediate release and dispersion of poorly water-soluble drugs and processes that enhance the performance of long-acting injectable drugs.

NATIONAL ACADEMY OF INVENTORS, FELLOW
AMERICAN CHEMICAL SOCIETY, FELLOW

Wunmi Sadik, distinguished professor of chemistry, develops innovative biosensing technologies used in applications ranging from bomb detection, to environmental monitoring, to cancer and COVID-19 detection. She is currently developing a biosensor to accurately measure pain biomarkers in the human body to better manage pain and drug addiction.

AMERICAN PHYSICAL SOCIETY, FELLOW

Linda Cummings, professor of mathematics, focuses on mathematical modeling of real-world phenomena that arise in industrial, environmental and biological processes, including metallic nanoparticle manufacture, membrane filtration and tissue engineering. Her work aims to identify key features that can be exploited to optimize processes, leading to predictions for improved product yield or better design.

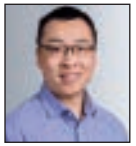
NATIONAL SCIENCE FOUNDATION CAREER AWARD

Dibakar Datta, associate professor of mechanical and industrial engineering, studies the electro-chemo-mechanical phenomena of nanomaterials, including crystalline solids and two-dimensional materials. He seeks to optimize the performance of these materials through alterations in their structure and the creation of mixed-dimensional composites, with applications in energy storage, electronics and medical devices.

Fatemeh Ahmadpoor, assistant professor of mechanical and industrial engineering, studies the mechanics of flexible nanostructures and biological systems. Her goal is to understand how these materials' imperfections and thermal fluctuations impact the mechanical behavior of nanodevices. Her study will enable the mechanics-guided design of nanodevices for applications in nano- and biotechnologies.

Junjie Yang, assistant professor of physics, explores the unusual properties of quantum materials that hold the potential to propel the next generation of smaller, more energy-efficient electronic devices. He is investigating atomic vibrations within hafnia-based crystals, ferroelectric materials that exhibit a spontaneous electric dipole that can be manipulated by an external voltage source.

NATIONAL ACADEMY OF INVENTORS, SENIOR MEMBER



Wen Zhang, professor of civil and environmental engineering, develops novel nanotechnology-based materials and membrane filtration systems for a host of applications: sustainable irrigation, food disinfection, pollution mitigation and resource recovery. He exploits, for example, the colloidal and chemical interactions between pollution targets, such as microplastics and microbes, and engineered micro- and nanobubbles.

RESEARCH AT NJIT: By the Numbers

R1
Carnegie Classification®
Research University

150
patents and intellectual property assets held by NJIT faculty

160
research institutes, centers and specialized labs

13
fellows of the National Academy of Inventors

42
entrepreneurial teams, startups and companies advised in 2023 by NJIT's Martin Tuchman School of Management and NJII

1
medical-grade ophthalmic diagnostic headset, the world's first, with automated refraction and visual field examination technology to expand access to care

$10 MILLION
awarded to NJIT by the U.S. Environmental Protection Agency to help communities clean up brownfields

104,000
fMRI brain scans gathered from researchers globally for an NJIT study on brain messaging changes in Alzheimer's patients

$6 MILLION
from the National Science Foundation to expand NJIT's Technology Innovation Translation Acceleration program

Since 2014:

120%
increase in external research funding

25
winners of National Science Foundation CAREER awards

$8 MILLION
spent on undergraduate student research stipends

On the Path to a Cure, Research Trials and Self-Expression

Julissa Santiago recalls the night she woke up in a hospital bed, breathing through a tracheotomy tube. No one told her that she was paralyzed, but she could feel it.

"I could only express myself with my eyes. I was still me, but I was trapped," she recounts. "I wondered: How am I going to break through this? How am I going to move forward? This is not what my life is going to be. What's the next step?"

Since her fall 11 years ago, Santiago has devoured information about her condition. She's taken part in 20 research studies on the physical and cognitive impacts of spinal cord injuries. Most recently, NJIT's **Donna Chen** scanned her brain with functional near-infrared spectroscopy (fNIRS) as she recounted number sequences. Chen tracked the amount of oxygenated blood, a measure of performance, flowing to the region associated with that task.

"I'm very much my own advocate. It's up to me to understand what's wrong with me and to help myself," Santiago explains. "It's a matter of survival and quality of life, but also of hope and aspirations for a cure."

She is also powerfully self-expressive. A cosmetologist before her accident, Santiago converted her living room into a salon, where she does clients' make-up and hair for fashion shows and photo shoots.

"My work is a form of art expression. Art is the way I survive. My art reflects my progress," she says, noting that she began painting right after her accident, before she could even lift her arms.

"The art therapist attached a string to my finger and dangled my arm over a piece of paper with drops of paint on it. I dragged the string over them, making my own design," she describes. The walls of her apartment now explode with her own artwork, including an entire flower wall.

"Right now I'm healing my inner child. I'm creating things that are pink and glamorous and that feature a lot of my favorite cartoons, like *Pinky and the Brain* and *The Powerpuff Girls*," she says.

She also posts about the challenges of navigating the world in a wheelchair, makes ASMR (autonomous sensory meridian response) videos and dances on TikTok.

"I'd love to be in a music video," she says, "just to prove I can."

- *See related story in* The Brain *insert*

Julissa Santiago's artwork hangs in her Newark, N.J. home.

"I'm very much my own advocate. It's up to me to understand what's wrong with me and to help myself. It's a matter of survival and quality of life, but also of hope and aspirations for a cure."

- Julissa Santiago

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