SPRING 2022 | BIOMEDICAL ENGINEERING

DEVELOPMENT OF THE BIONIC ARM

Cleveland Clinic Researchers Restore Natural Behaviors in Patients with Upper Limb Amputations

FULL STORY, p. 4

Photo by Cleveland Clinic

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Biomedical Engineering Alliance

Cleveland Clinic

IN THIS ISSUE

The Biomedical Engineering Alliance
at Case Western Reserve University and Cleveland Clinic

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Cover image: Researchers in Cleveland Clinic Lerner Research Institute's Laboratory for Bionic Integration look at the inside of the touch robot system. Each small black box provides individual finger sensation to the user through a neural-machine interface. Photo by Cleveland Clinic.

FROM THE CHAIRS

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Although the spring semester is winding down and many students are looking forward to heading home for the summer, faculty and researchers in the Biomedical Engineering Alliance remain as busy as ever. This issue of the newsletter highlights many of their accomplishments, including research funding, publications and awards. We'd like to call out one achievement in particular: Zheng-Rong (ZR) Lu, the M. Frank Rudy and Margaret Domiter Rudy Professor of Biomedical Engineering, was elected as a fellow to the National Academy of Inventors. Congratulations to ZR on this well-served recognition of his groundbreaking research in cancer detection and gene therapy delivery.

ZR is just one of many people in the Alliance making an impact on the field of biomedical engineering. As we put together this newsletter, we were reminded that the culture of excellence and commitment to innovation within the Biomedical Engineering Alliance was fostered by our forefathers and continues to be embraced by our faculty and passed on to the next generation. The three feature stories are a testament to this – a profile of a legend in neuromodulation, a look into ongoing development of a bionic arm and an article on a new workshop training young neurotechnology professionals.

Professor Emeritus Thomas Mortimer, creator of the first spinal cord stimulator, has devoted 60 years to the field of neuromodulation. His influence is profound, not only because of the devices he helped invent, but also the people he brought on board at Case Western Reserve University who are leaders in neurostimulation. Tom's work undoubtedly informed future research, such as that currently conducted by the team in the Laboratory for Bionic Integration in the Cleveland Clinic BME department.

A group of researchers in the Cleveland Clinic BME Laboratory for Bionic Integration, led by Paul Marasco, has developed a bionic arm that incorporates a neural-machine interface that connects with the wearer's limb nerves, enabling them to send nerve impulses from their brain to the prosthetic when they want to use it. The arm gives the person "agency" over the limb and allows the wearer to function more like a person without an amputation.

The study, published in the September 2021 issue of *Science Robotics*, has garnered a lot of attention in mainstream media, too, in venues as varied as *People* magazine and MSN and from all major media outlets in the United Kingdom.

Who knows the impact these news items may have in attracting budding researchers and professionals? The Cleveland NeuroDesign Entrepreneurs Workshop, held for the first time last fall, is doing its part to turn passion for neurotechnology into tangible products.

More than 30 early-stage professionals attended the inaugural workshop, which focused on identifying clinical needs and brainstorming solutions that could lead to commercialization. The second NeuroDesign Entrepreneurs Workshop is slated for Sept. 22 – 26, 2022, at Case Western Reserve University.

Along with these articles, there are other gems within our spring newsletter, including announcements about stand-out students and alumni. We hope you take time to read this issue and are as inspired as we are by the success stories. It's an exciting time to be part of the biomedical engineering community, and we're already working on our next batch of news and in-depth articles for the fall issue. Until then, enjoy your summer.

STUDENT SPOTLIGHT

Send updates to bme-news@case.edu to be considered for the newsletter, website highlights, and social media

NSF Graduate Research Fellowship

Justin Kim was awarded an NSF Graduate Research Fellowship for the PhD study he began as an undergraduate. He will be working on AI as applied to cardiovascular imaging with David Wilson, Robert J. Herbold Professor of Biomedical Engineering at Case Western Reserve University.

Paper Presentations at MICCAI Conference

Amir Reza Sadri, a research engineer in the Case School of Engineering's INVent Lab, and Amogh Hiremath, a PhD candidate in biomedical engineering, received travel awards to MICCAI 2021, the 24th International Conference on Medical Image Computing and Computer Assisted Intervention. Sadri presented a paper entitled "SPARTA: An Integrated Stability, Discriminability and Sparsity based Radiomic Feature Selection Approach." Hiremath presented a paper entitled "Integrated Lung Deformation Atlas and 3D-CNN Characterization of Infiltrates LuMiRa for COVID-19 Prognosis." Hiremath is mentored by Anant Madabhushi, the Donnell Institute Professor of Biomedical Engineering and director of the Center for Computational Imaging and Personalized Diagnostics at Case Western Reserve University.

Presidential Poster Award

CCIPD co-authors Avani Muchhala, Prathyush Chirra and Katelin Amann received the Presidential Poster Award at the 2021 American College of Gastroenterology Annual Scientific Meeting & Postgraduate Course for their abstract, "Radiomic Features on Baseline Magnetic Resonance Enterography are Prognostic of Disease Severity in Pediatric Crohn's Disease."

Notice of Award for F31

PhD Candidate Prathyush Chirra received a notice of award for an F31 Predoctoral Individual National Research Service Award from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The award supports his research on radiomics-based risk prediction for therapy selection in Crohn's disease via MRI. Chirra is mentored by Satish Viswanath, assistant professor of biomedical engineering at Case Western Reserve University.

INSOFE Student is Exemplar of Success

Vinay Sudha Ethiraj is a student in the INSOFE program, which offers a MS degree in biomedical engineering with a dual specialization in digital health analytics. He also works as a data scientist at Capitalogix, a Dallas startup that leverages artificial intelligence (A.I.) to create financial solutions. "Ethiraj is an exemplar of success," says Colin Drummond, professor and assistant chair of the Department of Biomedical Engineering.

While at Case Western Reserve University, Ethiraj has become involved in analytics with Paul Bryson, director of the Cleveland Clinic Voice Center and head of the health system's Section of Laryngology. Ethiraj presented his research at the 2021 BRAIN Initiative meeting and two papers at VOICE 2021, an event focused on conversational A.I. "He did a fantastic job and his career moved in a totally new direction as a result," says Drummond.

FACULTY & STAFF HIGHLIGHTS

Suneel Apte

Suneel Apte, staff, Lerner Research Institute Department of Biomedical Engineering, received a three-year, $300,000 award from the Arthritis Foundation titled "Synovial fluid degradomics for advancing clinical research for post-traumatic knee osteoarthritis (PTOA) management."

Jillian Beveridge

Jillian Beveridge, assistant staff, Lerner Research Institute Department of Biomedical Engineering, was appointed to a 2-year term as Orthopaedic Research Society (ORS) Knee Topic Co-Chair. She will oversee abstract submissions for one of the largest topic portfolios at the ORS Annual Meeting.

Margot Damaser

Margot Damaser, staff, Lerner Research Institute Biomedical Engineering Department, was awarded a sponsored research agreement from SRS Medical. In addition, a paper from Damaser and her colleagues received the Best Paper Award at the Engineering and Urology Society annual meeting.

Chaitali Ghosh

Chaitali Ghosh, Staff Scientist, Cleveland Clinic BME Department, was appointed to the Neurological Sciences and Disorders A Study Section, National Institute of Neurological Disorders and Stroke. Ghosh was also chosen as a speaker/discussion leader for the "Barriers of the CNS Gordon Research Conference," June 12-17, 2022 at Colby-Sawyer College in New London, New Hampshire.

Colin Drummond

Colin Drummond, professor of biomedical engineering at Case Western Reserve University, received a two-year National Institute of Standards and Technology (NIST) Award in October 2021 for "Standards Modules for Engineering Curriculum: A Case Study Approach." This is a collaboration between the Kelvin Smith Library, Case Western Reserve Department of Biomedical Engineering, and University of Mount Union. The goal is to develop standards education modules centered on case studies that can be integrated into an Introduction to Engineering Course, Senior Design Capstone courses and graduate BioDesign curriculum and build on students' enduring understandings of ethical approach in engineering design and practice.

Umut Gurkan

Umut Gurkan, the Warren E. Rupp Associate Professor in the Department of Mechanical and Aerospace Engineering and Associate Professor (secondary appointment) in the Department of Biomedical Engineering at Case Western Reserve University, has been elected to the American Institute for Medical and Biological Engineering (AIMBE) College of Fellows. Gurkan's research has led to new biomedical microtechnologies that improve patients' access to timely diagnosis and personalized monitoring of emerging therapies.

Linda Graham, Ela Plow

Linda Graham, staff, and Ela Plow, assistant staff, Lerner Research Institute Department of Biomedical Engineering, received Lerner Research Institute (LRI) Awards for Excellence. Graham was given the Excellence in Service Award for chairing the Committee on Appointments and Promotions for six years, and Plow received the Rising Star Award, which is given to an early to mid-career scientist in the first 10 years of independence who has shown a rising trajectory in publications and funding as well as a strong commitment to making the LRI a better place.

Vinod Labhasetwar

Vinod Labhasetwar, staff, Lerner Research Institute Department of Biomedical Engineering, received a Caregiver Catalyst Grant from the Cleveland Clinic Philanthropy Institute for his idea demonstrating that increasing anti-cancer drugs in lymph nodes is more effective in treating advanced-stage cancer than IV injection and minimizes side effects through lower, more targeted doses.


Xiaojuan Li, Carl Saab

Xiaojuan Li, staff, and Carl Saab, staff, Lerner Research Institute Department of Biomedical Engineering, were among the recipients of the first Artificial Intelligence in Medicine internal funding program, a new rapid response RFP that supports new, ambitious and speculative AI projects with the objective of bringing cross-cutting ideas to implementation and developing impactful initial outcomes that can lead toward establishing a collaborative research program and institutional know-how.

Anant Madabhushi

Anant Madabhushi, the Donnell Institute Professor of Biomedical Engineering and director of the Center for Computational Imaging and Personalized Diagnostics at Case Western Reserve University, has been elected as a Crain's Notable Entrepreneur, was recently named to the Pathologist's Power List for a third consecutive year and was named distinguished research faculty.

Paul Marasco

Paul Marasco, associate staff, Lerner Research Institute Department of Biomedical Engineering, received a 2022 Top Ten Clinical Research Achievement Award from the Clinical Research Forum, which recognizes groundbreaking achievements in clinical research from across the nation that demonstrate a vital impact on patient care. Marasco was honored for his work "Bionic Arm Restores Natural Behaviors." (See story in this issue.)

Ela Plow

Ela Plow, assistant staff, Lerner Research Institute Department of Biomedical Engineering, was appointed to Regular Study Section Membership on the NIH Motor Function, Speech and Rehabilitation Study Section.

Geoge Muschler

George Muschler, staff, Lerner Research Institute Department of Biomedical Engineering, co-edited *Orthobiologics* (published by Springer), exploring non-surgical injectable therapies for musculoskeletal applications. He has also received a $250,000 gift that will help his lab team develop an iPS cell fabrication resource in the Lerner Research Institute.

Anirban Sen Gupta

Anirban Sen Gupta, professor of biomedical engineering at Case Western Reserve University, has been inducted into the American Institute for Medical and Biological Engineering (AIMBE). Sen Gupta was also appointed to the editorial board of Biomaterials and Journal of Haemostasis and Thrombosis.

His research is garnering global attention. One paper on next-generation artificial platelets was published in Science Translational Medicine. Another, "Haemostatic functions of novel synthetic platelets," was featured in Nature Review Cardiology.

Satish Viswanath

Satish Viswanath, assistant professor of biomedical engineering at Case Western Reserve University, has been elected as a senior member to the National Academy of Inventors. Also, his submission as senior author won Best Paper in the Computer Aided Diagnosis Track at the 2022 SPIE Medical Imaging conference with co-authors and PhD candidates Amir Reza Sadri, Thomas DeSilvio and Prathyush Chirra.

David Wilson

The Case Western Reserve University Department of Biomedical Engineering, Cardiology and BioInVision, Inc. received a SBIR Phase II research grant to develop computed tomography (CT) cardiac perfusion and clinically evaluate it in a prospective study at the University Hospitals of Cleveland Cardiovascular Imaging Center. With the addition of perfusion to CT, one can measure functional blood flow in addition to coronary anatomy with CT angiography. This promises a one-stop shop for evaluation of coronary artery disease that can uniquely diagnose microvessel disease. Leading the grant are Wilson (professor of BME), Sanjay Rajagopalan (director of the Cardiovascular Research Institute and professor of Internal Medicine at the Case School of Medicine), and Debashish Roy (president, BioInVision, Inc. and PhD alumnus of CWRU BME).

Maciej Zborowski

Maciej Zborowski, staff, Lerner Research Institute Department of Biomedical Engineering, received the 2021 Lumley Interdisciplinary Research Award from the Ohio State University 's College of Engineering.

Zheng-Rong Lu Elected Fellow of National Academy of Inventors

Zheng-Rong Lu, the M. Frank Rudy and Margaret Domiter Rudy Professor of Biomedical Engineering at Case Western Reserve University, has been elected as a fellow to the National Academy of Inventors (NAI). The fellows program highlights academic inventors who have demonstrated a prolific spirit of innovation in creating or facilitating outstanding inventions that have made a tangible impact on quality of life, economic development and the welfare of society.

Lu's research has focused on two areas: early cancer detection with tumor-detecting contrast agents and the novel delivery of gene therapy into the body. The latter has been used to combat Stargardt disease, a rare but debilitating genetic eye disease.

Lu's cancer detection research accelerated in 2021 when the U.S. Food and Drug Administration approved human clinical trials to test the safety of a molecular-targeted imaging agent for prostate cancer developed by Lu and licensed to the company he founded, Molecular Theranostics. (An article on the technology and clinical trials appeared in the fall issue of the Biomedical Engineering Department newsletter.)

Lu is honored to be elected as a fellow to the NAI.

"It means our work in this lab is appreciated and that we are making a difference," he says. "I get emails every week, most often from people who are desperately looking for some hope, some news about what we are finding and when there will be clinical trials. This reminds me that our work has real meaning, not just to write papers and do more research, but to really help people."

Best of Luck on Retirement!

Carol Adrine

Carol Adrine retired in February after working at Case Western Reserve University for 25 years. She joined the Department of Biomedical Engineering 17 years ago as the student affairs coordinator during a huge surge in undergraduate student interest in biomedical engineering.

Adrine was the first person in the office every morning and managed the entire office. She had an amazing network and was a resource to help find information on just about anything at the university or in Cleveland.

As part of a crafter's community group, Adrine crocheted and donated items to those in need. Through the years, she crocheted many hats and mittens for BME students. She was dubbed the official department baker. Her most memorable creation was the three cakes she baked for the department's 40th anniversary celebration in the shape of a giant B, M and E.

Adrine was truly a team player, pitching in wherever needed. She will be greatly missed.

BIONIC ARM USHERS IN A NEW AGE OF PROSTHETICS

Cleveland Clinic researchers develop bionic arm that restores natural behaviors in patients with upper limb amputations.

Photo by Cleveland Clinic

Researchers in Cleveland Clinic Lerner Research Institute's Laboratory for Bionic Integration look at the inside of the touch robot system. Each small black box provides individual finger sensation to the user through a neural-machine interface.

Paul Marasco, associate staff, Cleveland Clinic Department of Biomedical Engineering

For someone who has lost an arm, either through trauma or disease, a prosthetic can add immeasurably to their adjustment and a return to the life they knew before. Over the years, advances in prosthetic design and sophistication have made this transition easier. Still, there are limitations to current iterations of a prosthetic arm. Perhaps the biggest hurdle is the inability to fully use the arm in the manner the person was used to-namely, to initiate an action simply by thinking about it.

Paul Marasco, associate staff, Cleveland Clinic Department of Biomedical Engineering, thought there was a better way. To help enable people with upper limb amputations regain a sense of ownership over their body and arm, Marasco and his lab, along with collaborators from the University of Alberta and University of New Brunswick, have engineered a more intuitive "bionic arm," which allows the wearer to function more like a person without an amputation.

The idea behind this first-of-its-kind bionic arm is that it gives the person with an amputation agency over the limb. "The person can control the limb essentially by thinking about it," says Marasco. "Then the limb itself provides feedback via the movement of the hand and of the touch that it feels. This allows the person to feel more like the limb is their own."

The Bionic Arm Neuromechanics

Photo by Cleveland Clinic

Marasco's team modified a standard prosthetic with a complex bionic system that combines motor control, touch and grip kinesthesia (the person's awareness of the hand opening and closing). The neural-machine interface connects with the wearer's limb nerves and enables patients to send nerve impulses from their brains to the prosthetic when they want to use or move it and to receive physical information from the environment and relay it back to their brain through their nerves.

The new arm builds on research that Marasco and his team performed in the past, in which they aimed to restore natural movement sensations in patients who had prosthetic arms. With the new bionic arm, when the patient undergoes the surgical amputation the surgeon redirects the severed nerves to the patient's remaining muscle and skin. The nerves then regrow out into the muscle and skin, enabling them to serve as neurorobotic gateways to communicate back-and-forth with the bionic arm.

"This new regrowth allows the person to sense complex grip movements and feel a touch on the arm as if it were their natural arm," says Marasco. "And when they think about moving, the muscles contract and they can move the arm."

It is the first system to test all three sensory and motor functions in a neural-machine interface at once in a prosthetic arm. "The more channels of communication you have, the more natural and human-like the function of the limb," says Marasco.

"We built the system using an off-the-shelf prosthetic as our basis, but then we put in high-level computing, and touch and movement sensation, so it looks like any other limb," he says. "But you can't tell that there's a highly sophisticated, computerized communication and feedback system running inside of it."

Using a prosthetic system with standard-of-care capabilities instead of advanced mechatronics allowed the team to show that the increased function was attributed to more functional communication between the user and their limb. "When we did the study, we wanted to show that it's the communication that's the important piece of this," Marasco says. "It's not the fanciness of the arm, not the robotics or all of the mechanical pieces, but simply the ability to communicate with it in a natural way that provides the specific and exciting advantages and improvements."

Study Participants Feel Hand Movements

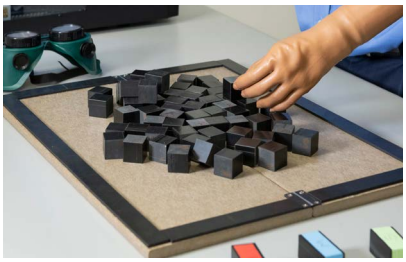


Photo by Cleveland Clinic

In their study, published in the journal *Science Robotics*, Marasco and his collaborators tested the bionic arm on two participants who had earlier had the nerves in their amputated arms relocated and were then fitted with the arm. The participants then performed certain tasks, including finding blocks of different stiffness among distractors. The participants were able to feel the movement of the hand closing around objects to sense stiffness via activation of the kinesthetic sensory receptors in the muscles. They were also able to perform other basic tasks such as grasping a paper cup with the correct amount of pressure and moving it to another location without crushing or dropping it.

Another notable enhancement of the new arm is that the person does not need to look at their arm while completing a task. "We take for granted that when we reach for something, we quickly look at the thing, pick it up and then turn our attention elsewhere," says Marasco.

"Without this system, the person with an amputation has to compensate for all of the lost sensation and movement by using their eyes to make sure they don't drop things. Our system releases the person from that. It enables them to multi-task – they can look for something, pick it up, know that they have it, and then look away and move it and do other things."

Measuring the Bionic Arm's Performance

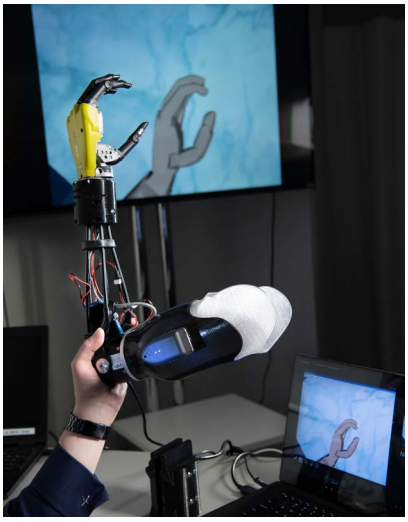


Photo by Cleveland Clinic

The other important innovation that Marasco and his team developed was a suite of metrics, a concrete way to quantify how well the arm was performing. These metrics comprised distinct tasks that mirrored everyday behaviors that require the intent and sensation of a fully operational hand and arm. In particular, the metrics looked at certain functions, such as visual attention, intrinsic error correction and strategic decision making.

"Our metrics were every bit as sophisticated as the limb we were testing," says Marasco. "The metrics dealt with the decisions and errors that people make and how they correct for those errors. This provided a window into how participants' brains were operating with these systems."

With these advanced evaluation tools, the researchers were able to assess how the performance of the bionic limb compared with that of able-bodied people, as well as people with amputations who have traditional

prosthetic devices. The results demonstrated that people with upper-limb amputations who use this bionic arm are now able to again think like an able-bodied person – to make judgments and decisions and calculate for their mistakes like a person with a natural limb.

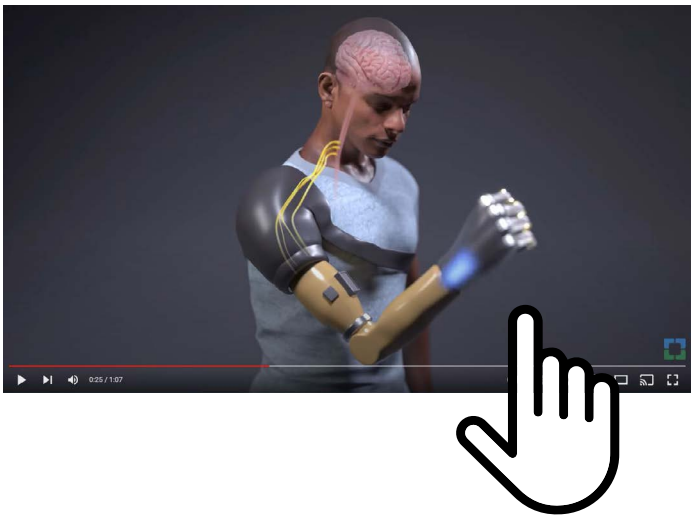
This type of evaluation is vital, Marasco notes. "Revealing the benefits of advanced bionics in comparison to standard-of-care prosthetic options is a key requirement for effectively translating emerging technologies to clinical care," he says.

Reintegration into Daily Life

According to Marasco, another major benefit of the bionic arm is an increase in the person's autonomy and self-reliance.

"Over the last decade or two, advancements in prosthetics have helped wearers to achieve better functionality and manage daily living on their own," says Marasco. "Our findings are an important step toward providing people with amputation with complete restoration of natural arm function, which can help enable seamless reintegration back into daily life."

Watch the Video of the Bionic Arm



Bionic Arm Receives Recognition from Around the World

The Science Robotics story on the bionic arm attracted attention in the popular press and from fellow researchers, not just in the United States, but around the world.

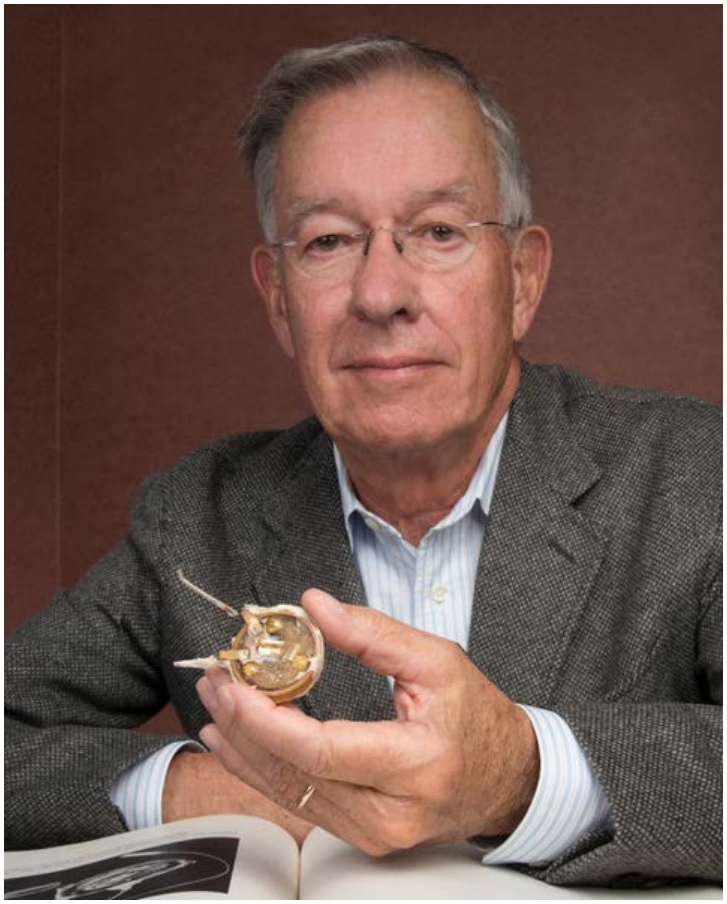
The story was picked up by WOIO-TV/ Channel 19, in Northeast Ohio as well as in national news outlets, including *U.S. News*, People Magazine and MSN. In addition, Reuters and the *Daily Mail* created videos that were posted on their YouTube channels and picked up by other outlets.

Marasco also received a 2022 Top Ten Clinical Research Achievement Award from the Clinical Research Forum (CR Forum), a non-profit association of clinical research experts and thought leaders dedicated to providing leadership to the national clinical and translational research enterprise and promoting understanding and support for clinical research and its impact on health and healthcare. The awards honor groundbreaking achievements in clinical research from across the nation that demonstrate a vital impact on patient care.

Marasco was nominated for the CR Forum award by Serpil Erzurum, chief research & academic officer and chair, Cleveland Clinic Lerner Research Institute. As Erzurum stated in her nomination, "Marasco's study has great implications for improving outcomes and quality of life in wounded soldiers and veterans."

"I am honored to receive the CR Forum 2022 Top 10 Clinical Research Achievement Award," says Marasco. "It is my privilege to work under Dr. Erzurum's leadership and to be recognized for our work. We are grateful to the CR Forum for recognizing the importance of clinical research for positively impacting patient outcomes."

A FOUNDING FATHER OF NEUROMODULATION



Creator of the first spinal cord stimulator, Thomas Mortimer influenced the field's top innovators and the trajectory of neuroengineering.

In January 1964, Thomas Mortimer packed up his 1948 Ford and drove from the panhandle of Texas to the shores of Lake Erie to begin graduate school at the Case Institute of Technology. It marked the start of 58 years of research, teaching and learning in the field of neurostimulation.

Mortimer, professor emeritus of biomedical engineering at Case Western Reserve University (CWRU), earned a Lifetime Achievement Award in January from the North American Neuromodulation Society (NANS) in recognition of his significant and lasting contributions to the field.

"It is an understatement to say how deserving Tom is for this award," says P. Hunter Peckham, professor emeritus of biomedical engineering at CWRU and the first graduate student to work in Mortimer's lab. "He has been the lifeblood of the inception of the field of biomedical engineering, neurostimulation and neural engineering from the very start."

"Tom has been the lifeblood of the inception of the field of biomedical engineering, neurostimulation and neural engineering from the very start."

- **P. Hunter Peckham**
Professor Emeritus of Biomedical Engineering
Case Western Reserve University

Humble Beginnings

Mortimer and his two siblings were raised by their mother in Amarillo, Texas. As an 11-year-old boy, he got a summer job 27 miles south in Palo Duro Canyon State Park with his friend Joe. They worked at the park for two summers, earning $1 a day and $3 on Sunday, plus room and board.

Mortimer as a young man in Palo Duro Canyon State Park.

"It was a remarkable experience," recalls Mortimer. "Then, between the 10th and 11th grade, Joe was in an automobile accident and rendered quadriplegic. I think that was a big factor in my career trajectory."

After earning a bachelor's degree in electrical engineering from Texas Technological College, he applied to Case for a master's degree, alluding to his interest in the budding field of biomedical engineering spawned by his friend's spinal cord injury. Mortimer was accepted and joined the Engineering Design Center led by Jim Reswick, who began work in the early 1960s on a pneumatically powered upper extremity assist device with closed-loop control to restore function to people with high-level spinal cord injuries (SCI).

During his first semester, Mortimer took a course taught by professors Robert Plonsey and David Fleming, who later founded the Department of Biomedical Engineering at Case Western Reserve University in 1968 alongside Reswick. He learned about the role of muscle spindles and Golgi tendon organs in the nervous system.

"These are transducers that play a role in muscle length, velocity and force – parameters that a closed-loop control system would use," says Mortimer. "I thought, 'How cool would it be to use these signals in a neurostimulation device?'" He shared his idea with Reswick, who encouraged Mortimer, funded his research and introduced him to people who were instrumental in turning the idea into reality.

"The environment created by Jim Reswick – who I consider an engineer's engineer – was so special," says Mortimer. "He didn't tell students what to do. We were free to pursue our interests, no matter how crazy they seemed."

Connections Kick-Start Career

One of the key connections Reswick made for Mortimer was to the chief of neurology at Western Reserve Medical School (now the Case School of Medicine), who then connected him with neurosurgeon C. Norman Shealy. Having read about the Gate Theory of Pain in a 1965 Science publication, Shealy envisioned using dorsal column stimulation to suppress pain. Mortimer, pushed by Reswick, set out to design and construct implantable devices to test Shealy's idea.

Just two years later, Shealy implanted devices in two patients with cancer.

"The end result of the 1967 Shealy, Mortimer and Reswick experiments qualify as the birthing of the field of neuromodulation," says Mortimer. "I could not have done it without them. Reswick believed in me and funded the work, Shealy had the idea for a pain suppression device, and I liked to build things."

While Mortimer was working on the pain suppression device, Lojze Vodovnik, who also came to Case in January 1964, was reimagining Reswick's arm-hand device by employing electrically stimulated muscles to power the paralyzed upper extremity. Vodovnik's concept hit an obstacle that many believe doomed it: electrically stimulated muscles fatigue quickly.

After earning his PhD, Mortimer did a year of post-doctoral study in Sweden, collaborating with a team interested in changes in the electrical activity of a fatiguing muscle. While there, he discovered why Vodovnik and his colleagues had a problem with rapid fatigue in electrically stimulated muscles. In 1969, Mortimer returned to Case Western Reserve University as a faculty member in the Department of Biomedical Engineering.

"I brought with me a fix for the rapid fatigue problem – electrically induced muscle exercise to build back strength and endurance into the muscles that had atrophied from disuse," says Mortimer. That idea breathed new life into the work Vodovnik and Reswick had begun five years earlier.

"Tom worked with Karl Frank, director of the Neural Control Laboratory at NIH and a very powerful figure at NIH, to support the first contracts for electrical stimulation of neural tissue," says Peckham. "This was multidisciplinary activity discovering the fundamental basis of electrical stimulation, exploring the safety issues and developing novel electrodes." In 1972, Mortimer named his laboratory the Applied Neural Control Laboratory, a tip of the hat to Frank.

Influence on Students

Through the years, Mortimer had a hand in developing six neuroprosthetic devices, including a visual prosthesis, diaphragm pacing system, bowel and bladder activation system, and muscle activation system for scoliosis correction. Just like with his doctoral work, Mortimer credits others with his successes.

"While I built the first dorsal column stimulation device, all the others were built on the work of the 36 students who trained in the Applied Neural Control Laboratory," he says. "Those students were my teachers."

One of those students was Peckham, whose dissertation showed that muscle strength and endurance could be rebuilt by electrically induced therapy.

"This experience set the course of my career," says Peckham. "Tom is my academic father." During his career, Peckham developed the first commercially available neuroprosthesis for people with SCI, founded the Cleveland FES Center and received 11 patents for functional neural stimulation systems and neural prostheses.

Dave Peterson (BS '81, MS '84, PhD '89) was another stand-out student and member of the Applied Neural Control Laboratory (ANCL).

"My education on the engineering interface with physiology has been the cornerstone of my career," says Peterson, head of product development at Galvani Bioelectronics. "It has enabled me to repeatedly help translate concepts from the laboratory to commercial applications in cardiac rhythm management and neural modulation." He is named on more than 90 patents.

Peterson adds that the open, student-friendly culture nurtured by Mortimer was equally important to the work conducted at the ANCL. He fondly recalls Friday morning lab meetings, led by members on a rotating basis.

"There were only two rules for the presenters: Prepare a presentation on any topic of your choice and bring the donuts, including Mortimer's favorite – chocolate sprinkles, if I recall correctly," says Peterson. "The topics we heard at meetings included ongoing research projects, as one might expect. But there were also presentations on everything from contemporary social justice to sky diving and mountaineering."

A Lasting Legacy

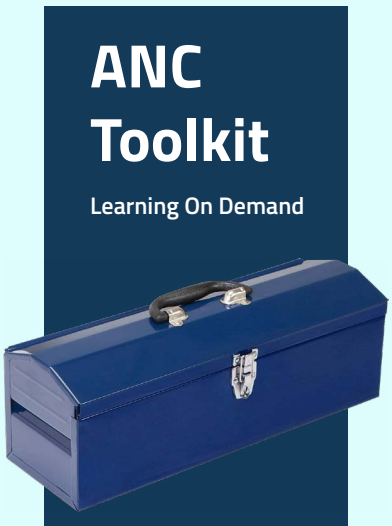
Reflecting on his body of work, Mortimer is most proud of the people that followed him, whether they landed in industry like Peterson or in academia like Peckham.

"That was my real contribution," says Mortimer. The contribution is particularly evident in the halls of the Wickenden Building, home to Case's Department of Biomedical Engineering (BME).

In the early 1980s, Mortimer convinced Dean Eric Bear of the potential for a BME branch focused on engineering solutions for neurological problems. That led to the creation of two new faculty positions filled by Patrick Crago, former chair of the Department of Biomedical Engineering and associate dean of the Case School of Engineering, and Dominique Durand, Elmer Lincoln Lindseth Professor in Biomedical Engineering and director of the Neural Engineering Center. Crago, in turn, brought in Robert Kirsch, current chair of the Department of Biomedical Engineering and director of the Cleveland FES Center.

"When one considers how much Tom's work has been multiplied by the hundreds of students he has trained and who have gone on to make additional contributions," says Peterson, "well, you could say that he has had a hand in virtually every neural engineering advancement for over half a century."

Applied Neural Control Lab '96
From Left to Right:
Back: Mark Lybukin, Jim Warren, James Cavanaugh, Albert Guzman, Frank Cuoco, Dan Leventhal, Matthew Tarler, Michael Miller
Middle: Jack Lin, Phil Hahn, Dominique Durand, Kai Hsu, Nancy Caris, Warren Grill, Mesut Sahin, Narendra Bhadra.
Front: Anila Jahangiri, Hani Kayyali, Jennifer Crossen, Zhenxing Jin , Elaine Socarras, J.T. Mortimer, Raphael Carbanaru, Dan Merrill.
Not Shown: Patrick Crago, Graham Creasey, Dustin Tyler, Harish Aiyar, Boris Makovos, Don Atzberger, Bethany Allen, Cameron McIntyre.



Online Toolkit Guides Next-Generation of Innovators

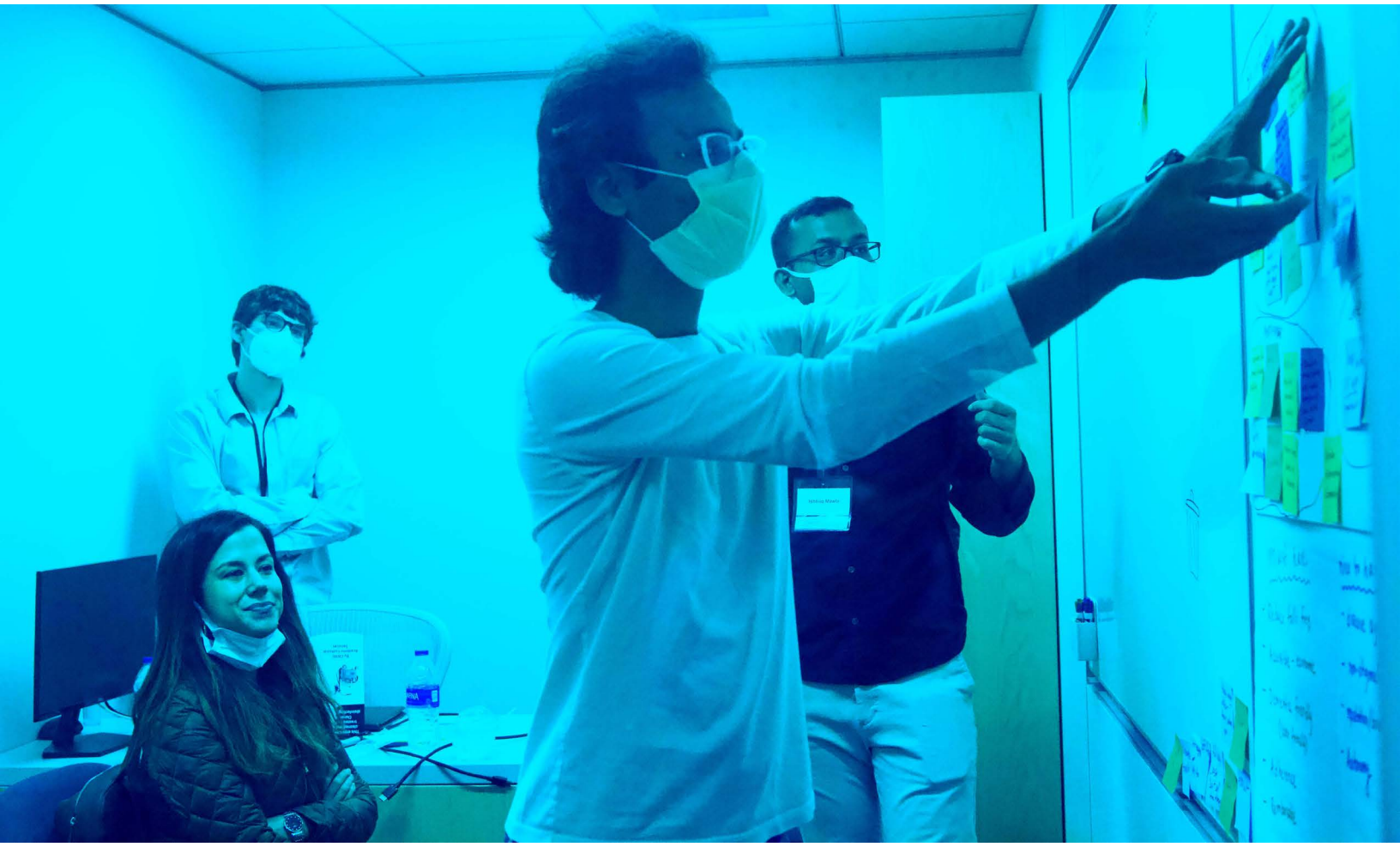
Tom Mortimer retired from Case Western Reserve University in 2002, but he continues to share his knowledge about neuromodulation. For several years, Mortimer presented seminars at companies such as Medtronic and Boston Scientific using content generated from the graduate course on applied neural control he taught at CWRU. With the rise of the internet, he realized he could reach even more people.

Mortimer created the Applied Neural Control Toolkit, a free online repository of information for engineers who want to develop neural prostheses. The toolkit features a compilation of material from Mortimer's work and that of his former students presented through videos. Modules delve into the basic aspects of electrically activating the nervous system, with emphasis on non-linear properties of voltage gated sodium ion channels – the gateway to innovating new devices.

"I continue to this day adding material to that repository and expect that adding material will keep me out of trouble for a few more years," quips Mortimer.

A DISCIPLINED APPROACH TO INNOVATION

NeuroDesign workshop provides entrepreneurs tools to solve real-world clinical problems.



Cleveland NeuroDesign Entrepreneurs Workshop

Case Western Reserve University EST. 1826

Cleveland Clinic

Laura Szklarski has worked in the field of electroencephalography (EEG) and epilepsy for 11 years on both the clinical and commercial side. "In that time, I have witnessed the impact of epilepsy and the lengthy procedures that patients and their families undergo in order to have a better understanding of their condition," says Szklarski, a senior clinical applications specialist at Persyst Development Corporation, an EEG software company based in Solana Beach, Calif.

Her experience and compassion for patients were instrumental during the 2021 Cleveland NeuroDesign Entrepreneurs Workshop, a weekend event at Case Western Reserve University (CWRU) aimed at training the next generation of neurotechnology professionals. At the workshop, Szklarski and three other group members designed a discreet EEG monitoring solution for patients with epilepsy to use at home and provide physicians with real-time data.

Szklarski was one of 32 attendees at the event hosted by Cleveland NeuroDesign with support from CWRU and Cleveland Clinic. The workshop is based on the well-known BioDesign six-step methodology focused on identifying clinical needs, inventing solutions and implementing ideas.

"Case Western Reserve University and other biomedical engineering programs do an outstanding job preparing students with the technical expertise they need," says JoJo Platt, co-director of the NeuroDesign Entrepreneurs Workshop. "The workshop gives them a taste of the business acumen needed to accompany that expertise and the tools necessary to evaluate their research and the technologies they develop."

Flipping the Model

The curriculum, which is geared toward early-stage professionals with graduate degrees, includes didactic instruction, mentoring sessions and one-on-one advising. Participants work in teams to design a solution to a clinical need, build a business plan and pitch their ideas to a panel of judges.

"Most academic researchers work really hard on a technology for a long time, then start looking around for commercial applications," says Andrew Cornwell, workshop co-director. He also serves as director of industrial and strategic collaborations at the Cleveland FES Center, associate director of the Case Coulter Translational Research Partnership and director of the VA Translational Education and Mentoring Center. "This program is focused primarily on identifying a clinical need first, then designing a viable solution. It flips the traditional model of translational research."

Prior to the workshop, attendees are divided into teams and identify a clinical need, working from a list of real-world observations. Then, during the workshop, the teams learn how to invent a solution and develop a business plan to address the need. In 2021, these issues ranged from the challenge of stroke rehabilitation for patients with paralysis to the difficulty of predicting patients' postoperative pain requirements.

"Most academic researchers work really hard on a technology for a long time, then start looking around for commercial applications. This program is focused primarily on identifying a clinical need first, then designing a viable solution. It flips the traditional model of translational research."

- **Andrew Cornwell**
Co-director, NeuroDesign Entrepreneurs Workshop
Director of Industrial and Strategic Collaborations, Cleveland FES Center
Associate Director, Case Coulter Translational Research Partnership
Director, VA Translational Education and Mentoring Center

During the workshop, experts from industry and academia deliver lectures, covering topics such as intellectual property, regulatory issues, reimbursement, prototyping, healthcare business models and more. Following each didactic session, attendees meet with their groups to develop strategies around that topic in relation to their intended solution.

The weekend ends with the pitch competition, which Szklarski's team won in 2021.

"It was very meaningful to work with a team that could grow a simple observation into a clinical product with the potential to help thousands of people," says Szklarski. "I now know what is possible."

Focus on the Process

Although some of the solutions generated may one day come to fruition, that's not the primary goal of the NeuroDesign Workshop.

"The idea is to teach participants a set of skills they can apply to their research and entrepreneurial careers," says

Cornwell. "Innovation isn't this eureka moment. It's a discipline that can be learned."

The BioDesign process, originally created at Stanford University, offers a systematic approach to innovation. Such an approach is paramount to tackling the monumental challenges faced by the healthcare industry.

"We can't afford failures. We need to focus on helping the next generation of entrepreneurs be more effective in delivering solutions that have an impact," says Platt. "If we can shortcut those failures by teaching proven skills, then hopefully we can accelerate successes, minimize dead ends and make an impact on an aging and failing healthcare system."

The importance of that mission is echoed by corporate sponsors of the NeuroDesign Workshop, which included Medtronic Neuromodulation, Abbott Neuromodulation, Meta, the Cleveland FES Center, the IEEE Brain Initiative, Blackrock and Ripple in 2021.

"The spirit of the workshop attracts tops trainees from all over the world who are passionate about making a difference for people's lives with the help of technology. They are driven to use their skillsets to address unmet human needs in unique ways," says Erika Ross, director of R&D for Abbott Neuromodulation. "We share this ethos within Abbott's Neuromodulation business."

Endless Possibilities

The 2021 NeuroDesign Entrepreneurship Workshop was so successful that organizers have added another day to this year's event, scheduled for Sept. 22 – 26. Cleveland NeuroDesign also offers a 10-month, full-time Innovation Fellowship at Case Western Reserve University and Cleveland Clinic for early career professionals to dig deeper into the BioDesign process.

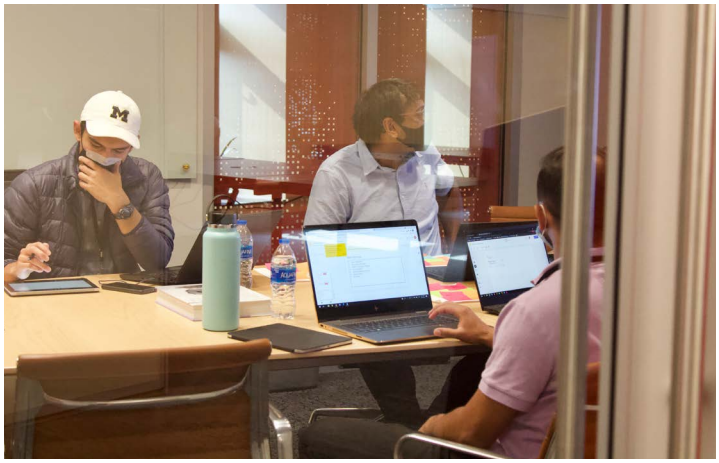
"Cleveland is one of the world's top neurotechnology centers, with clinical access at Cleveland Clinic, research access at Case and the entrepreneurship programs at NeuroDesign," says Cornwell. "It's the only place that's tops in all three areas."

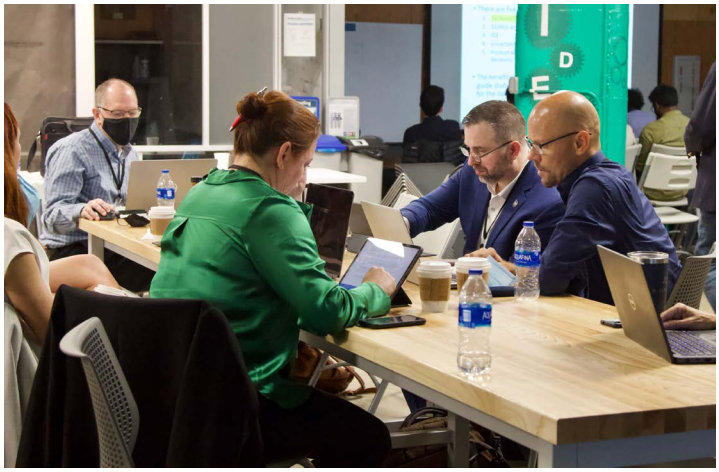
Szklarski is confident she will use the BioDesign process she learned during her weekend in Cleveland throughout her career designing medical devices. Just as important are the connections she made.

"The workshop introduced me to a supportive community of talented individuals who are equally passionate about innovation in neurotechnology," she says. "I have no doubts that our shared interests and diverse backgrounds will one day unfold into viable products that will make a real impact. The possibilities feel endless."

Erika Ross, director of applied research at Abbott, spoke to the workshop students about patient-centric innovative design for commercial deployment.

Spencer Matonis, doctoral candidate at Carnegie Mellon University, brainstorms with his team to identify opportunities for transdermal device implantation.





More than 30 early-stage neurotechnology professionals attended the NeuroDesign Entrepreneurs Workshop last fall, where they gained valuable insight from industry experts and worked in teams to develop solutions to real-world clinical issues.

IN THE NEWS

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CHECKING IN WITH ALUMNI

Nate Braman (GRS '20), started a position with Tempus after graduating in 2020. Braman was mentored by Anant Madabhushi, the Donnell Institute Professor of Biomedical Engineering at Case Western Reserve University. Tempus is a technology company that has built the world's largest library of clinical and molecular data and an operating system to make that information accessible and useful for patients, physicians and researchers.

Send updates to bme-news@case.edu to be featured in the newsletter

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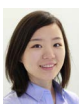

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Welcome New Faculty

Shuo Li

The Departments of Biomedical Engineering and Computer & Data Science at Case Western Reserve University welcome Shuo Li as an associate professor. Li is an academic artificial intelligence (A.I.) scientist with a background in machine learning, medical data analytics, imaging, computer science and software engineering. His current research focuses on the development of image centered A.I. systems to solve the most challenging clinical and fundamental data analytics problems in radiology, urology, surgery, rehabilitation and cancer, emphasizing innovations of multiple learning schemes (deep learning, regression learning, reinforcement learning, adversarial learning, sparse learning, spectral learning, manifold learning, etc.).

David Escobar

The Lerner Research Institute Department of Biomedical Engineering welcomes David Escobar as assistant staff. Escobar comes to Cleveland Clinic from the Department of Neurology at the University of Minnesota, where he led pre-clinical and clinical research focused on advancing closed-loop deep brain stimulation (DBS) therapies for Parkinson's disease. He brings a multidisciplinary background in feedback (closed-loop) control systems, signal processing, data-driven mathematical modeling, neurophysiology and neuromodulation. Within Cleveland Clinic BME, Escobar and his team are dedicated to advancing neuromodulation therapies for Parkinson's disease and epilepsy, translating research into medical technology, training students and mentees in neuroengineering, and partnering with clinicians, scientists and engineers to improve therapies for distinct brain conditions.

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Case Western Reserve University
WORLD RANKINGS

21st for U.S. utility patents

Based on data from the U.S. Patent and Trademark Office (USPTO), CWRU secured 105 patents in 2020 – more than double the number it earned in 2016.

The Top 100 list is compiled and released by the National Academy of Inventors (NAI) and the Intellectual Property Owners Association (IPO).

#10 on list of Best Universities for Biomedical Engineering

EduRank based their rankings on research performance in Biomedical Engineering. A graph of 5.46M citations received by 195K academic papers made by 992 universities in the world was used to calculate publications' ratings, which then were adjusted for release dates and added to final scores.

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