SPRING 2018 | BIOMEDICAL ENGINEERING

ON A MISSION TO SAVE LIVES

Full story, p. 8

ALSO INSIDE:

A joint department between the Case School of Engineering
and Case Western Reserve University School of Medicine

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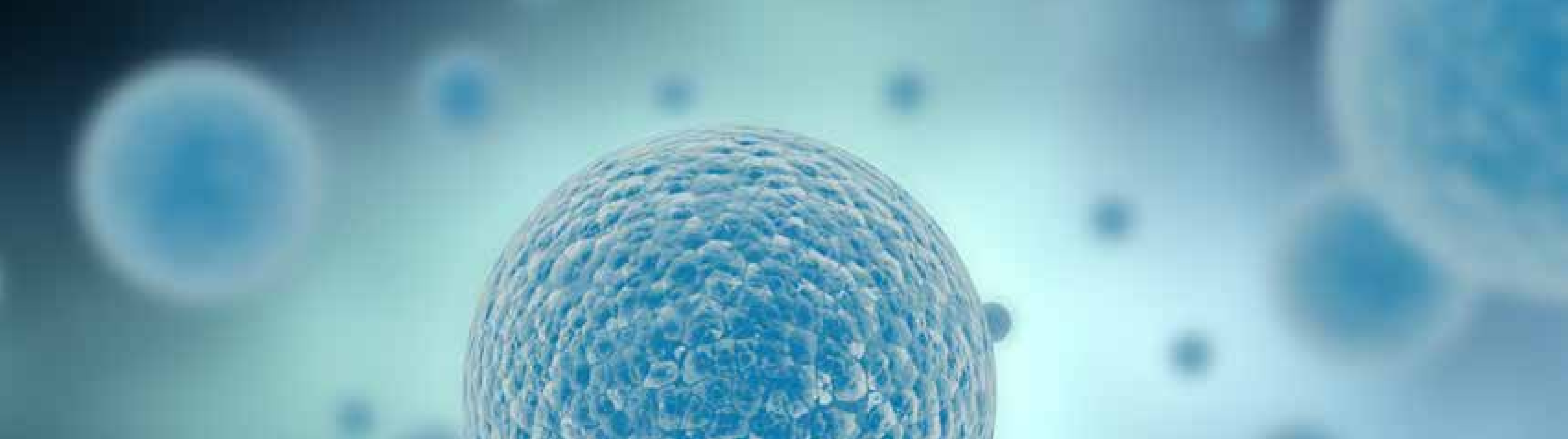


A LOOK INSIDE

Biomedical Engineering
at Case Western Reserve University

Spring 2018 Newsletter

bme.case.edu

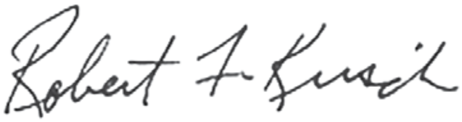
FROM THE CHAIR

Welcome to our spring 2018 newsletter. As you will see, our students, faculty and alumni continue to make discoveries and create technologies that provide new tools and techniques for enhancing medical care. This impact is nothing new to our department – in fact we are turning 50 years old this year!

Our department was born in 1968 during a period of major change and experimentation, and we continue to reflect the creativity and curiosity of that time to address the needs of society. Biomedical engineering has come a long way since the creation of the department, and our anniversary provides a perfect opportunity to recognize the many faculty and students who blazed the path for those working in the field today. Our graduates are leaders, innovators and entrepreneurs. They are medical doctors who lead technical innovation in clinical care. They are cutting-edge researchers whose ideas address the unmet needs of medical diagnosis and treatment. We are proud of the collective accomplishments of the Case Western Reserve University Biomedical Engineering Department, and we take inspiration from our faculty and students – current and past – to continue to be a leader in the field.

We will hold a series of events over the next year or so to celebrate our first 50 years and, as we have always done, to look forward to the future. We will provide information on these events during the next couple of months, and we hope that you will be able to join us for some or all of them.

Best wishes for a relaxing and productive summer – and at least another 50 years of biomedical engineering at Case!



Robert F. Kirsch
Allen H. and Constance T. Ford Professor
Chair of Biomedical Engineering
Case Western Reserve University

BY THE NUMBERS: BIOMEDICAL ENGINEERING FUNDING

funding from
>50 institutions including **12** NIH Institutes

half of primary faculty
>$500,000 NIH funding

Statistics provided by NIH Reporter

FACULTY HIGHLIGHTS

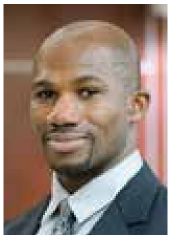
Steve Fening

Director of the Case-Coulter Translational Research Partnership, Steve Fening, has been recognized as one of *Crain's Cleveland Business*' "Forty Under 40."

For Fening, the power of biomedical engineering research was evident early in his career. As a researcher, he was surrounded by potentially life-altering innovations. But he wanted to bring that research from bench to bedside even faster. As director of the Case-Coulter Translational Research Partnership, Fening has the opportunity to help researchers fulfill their commercialization potential.

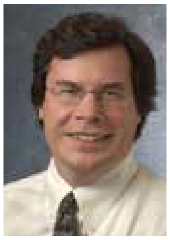
"I have figured out over time that my career aspirations are to move as many technologies to help people as possible," Fening says. "This really helped to fulfill that, rather than me working in the lab and hoping that maybe two or three things over the course of my life might make their way to helping people."

Fening is honored to be recognized as one of *Crain's Cleveland Business*' "Forty Under 40." "After I got the award, I looked back at some of the classes from 10 to 15 years ago," says Fening. "A lot of [the honorees] are the people leading a lot of the business aspects of Cleveland, so it was humbling."



Bolu Ajiboye and Jeffrey Capadona

Bolu Ajiboye, assistant professor of biomedical engineering, and Jeffrey Capadona, associate professor of biomedical engineering, were featured in an article in *Nature Magazine*, "The Mind-Reading Devices That Can Free Paralyzed Muscles," about technologies that restore movement and the sense of touch and are helping people to overcome the physical effects of stroke and spinal-cord injury. "It's a big deal scientifically, but it's also a big deal clinically," says Ajiboye. To read the full article, visit www.nature.com.



Colin Drummond

Colin Drummond, professor of biomedical engineering and assistant department chair, authored *Financial Decision-Making for Engineers* from Yale University Press. The textbook is a much-needed practical guide, particularly suited for readers with engineering or science backgrounds, that provides the financial decision-making skills necessary for a management career.

Based on materials used by students in a Master of Engineering and Management program at Case Western Reserve University and informed by both classroom and industry experience, this essential guide can be used in courses or independent study. The chapters introduce and integrate key concepts relevant to basic management, accounting, and finance that will enhance the critical thinking and confidence necessary for success as a chief technology officer or in any business career.

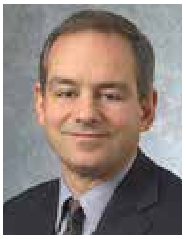
Efstathios Karathanasis

Efstathios Karathanasis, an associate professor of biomedical engineering and Susann Brady-Kalnay, a professor of molecular biology and microbiology, have been awarded a 2-year, $250,000 Innovation Grant from Alex's Lemonade Stand Foundation, which is a nonprofit dedicated to finding cures for children with cancer. The title of the project is "Targeting Pediatric Brain Tumors Using PTPmu Nanochains with Radiofrequency-Releasable Therapeutics."

Karathanasis also gave a TEDx Talk recently entitled, "Downsizing the Fight with Cancer." The full video may be found on the "CWRU BME Recommended Videos" playlist on YouTube.

Xin Yu

Professor of biomedical engineering, Xin Yu, was awarded a $1.8 million R01 grant from the NIH National Institute of Biomedical Imaging and Bioengineering (NIBIB) entitled, "Phosphorus-31 MR Spectroscopic Imaging and Fingerprinting." The four-year project aims to develop fast magnetic resonance spectroscopy and imaging methods for sensitive detection of changes in tissue metabolism. In this project, these methods will be applied to the understanding of the role of mitochondrial dysfunction in insulin resistance and diabetes. The methods developed in this project are highly translatable to clinical assessment of a range of metabolic diseases, such as diabetes and obesity.



James P Basilion

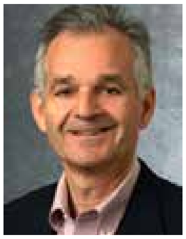
James P Basilion, professor of radiology, biomedical engineering, and pathology, has received several awards and honors in the recent months. In the fall of 2017, Basilion was elected president of the World Molecular Imaging Society, an international society dedicated to the betterment of molecular imaging and translational tools. In 2018, he has been inducted as a Fellow to the National Foundation for Cancer Research.

Also for a number of years, Basilion has been a standing member on several study sections including the Cancer Prevention and Research Institute of Texas (ITI), and the Center for Scientific Review, NIH, Clinical Molecular Imaging and Probe (CMIP).

Nicole Seiberlich

Elmer Lincoln Lindseth Associate Professor of Biomedical Engineering Nicole Seiberlich, was a keynote speaker and award winner at the 2017 Annual Meeting of the International Society for Magnetic Resonance in Medicine (ISMRM) in Honolulu. Seiberlich received the Outstanding Teacher Award for the Sunrise Session, “MR Fingerprinting." Seiberlich also gave the National Institute of Biomedical Imaging and Bioengineering (NIBIB) New Horizons Keynote Lecture, “Strength in Numbers: Unleashing the Power of Quantitative MRI," which features a rising star from ISMRM's junior faculty membership.

The ISMRM also holds workshops between the annual meetings. Vikas Gulani, associate professor of radiology, was chair of the October 2017 Workshop on Magnetic Resonance Fingerprinting, held at the Cleveland Museum of Art. Other Case Western Reserve University faculty on the organizing committee included Nicole Seiberlich and Mark Griswold, a professor in the Department of Radiology at the Case Western Reserve University School of Medicine. The focus of this meeting was to address the technology and refinements, its strengths and weaknesses, clinical implications, and future directions.



Dominique Durand

Elmer Lincoln Lindseth Professor of Biomedical Engineering, Dominique Durand, was featured on the National Institutes of Health (NIH) National Institute of Biomedical Imaging and Bioengineering website for his article, "Carbon Yarn Taps Nerves for Electroceutical Treatments and Diagnostics." The article discusses how yarn weaved from carbon nanotubes monitors brain control of organ functions, and paves way for the disease diagnosis and treatment at the single nerve level.

FUNDING ROLLS IN FOR COMPUTATIONAL IMAGING RESEARCH

"The funding is truly a validation of the need and utility of this kind of technology."

— Anant Madabhushi

NEARLY **$9** MILLION in 2018

9 PROJECTS

6 FUNDING AGENCIES

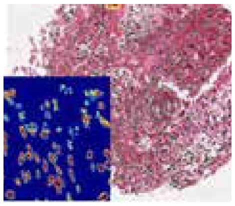
Last fall's issue of the Biomedical Engineering Department's newsletter included a profile of the Center for Computational Imaging and Personalized Diagnostics (CCIPD) directed by Anant Madabhushi, the F. Alex Nason Professor II of Biomedical Engineering at Case Western Reserve University. The overarching goal of the CCIPD is to extract as much value as possible from medical imaging scans to predict disease presence, prognosis and treatment response in order to facilitate patient management and appropriate therapy.

Between 2015 and 2017, the CCIPD received more than $13 million in total funding. That figure has since grown almost 70 percent, with the center receiving nearly $9 million in funding so far in 2018. "What is so exciting about this funding is that it's a recognition that you need decision support tools to complement and augment human decision-making. These tools are meant to empower pathologists, radiologists and oncologists, not obviate them," says Madabhushi. "The funding is truly a validation of the need and utility of this kind of technology."

The CCIPD focuses on four broad subject areas: image guided interventions, digital pathology, machine learning and personalized medicine, and computational diagnostics. The center's most recent awards touch upon all these areas.

Lung Cancer Risk Stratification

National Cancer Institute

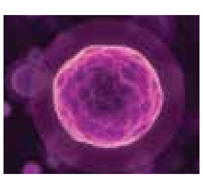


The National Cancer Institute (NCI) awarded the CCIPD a five-year, $3.15 million R01 grant to more accurately determine which early-stage lung cancer patients would most benefit from chemotherapy following surgery and which would not. Using computer analysis of digitized tissue biopsy images, researchers are attempting to identify patients who could get additional therapeutic help from chemotherapy, while avoiding the adverse side effects of the therapy for other patients who don't require such an intervention.

"The goal of this computerized tissue analysis is to generate a risk score to then inform oncologists about the need for chemotherapy," says Madabhushi, who is the principal investigator of the project. Vamsidhar Velcheti, a thoracic oncologist at Cleveland Clinic, serves as the co-principal investigator. Also involved in the project is Florida-based cancer diagnostics company Inspirata Inc. They hope the NCI grant will result in the first validated predictive tool for identifying which early-stage lung cancer patients will benefit from chemotherapy after surgery.

Risk Stratification of Head and Neck Cancers

National Cancer Institute

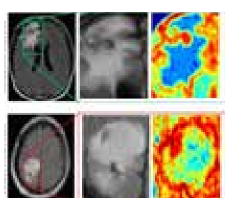


The CCIPD also received a $3.15 million R01 grant from the NCI for a head and neck cancer project in collaboration with Cleveland Clinic, Vanderbilt University and Inspirata Inc. The goal of the research is utilize images of tissue specimens to predict and stratify risk for oropharyngeal cancers.

"There are a lot of head and neck tumors that end up being treated fairly aggressively," says Madabhushi. "The question is how can we identify patients that could benefit from de-escalation of therapy?" Clinical trials to demonstrate that a reduction in therapy is appropriate in some patients have not yet been conducted, in part, because there's a lack of prognostic biomarkers for risk stratification. Funding from the NCI will help the CCIPD establish a validated prognostic test, which in turn could set the stage for development of clinical trials to demonstrate that de-escalation is warranted in some of these less aggressive tumors.

Predicting Treatment Response for Brain Tumors

Congressionally Directed Medical Research Program (CDMRP)



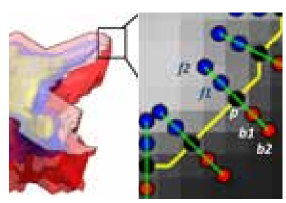
In 2017, brain cancer was added to the list of disorders eligible for study by the Department of Defense's (DoD) Peer Reviewed Cancer Research Program (PRCRP). In February, Pallavi Tiwari, an assistant professor of biomedical engineering, landed a $577,280 grant from the DoD for her work developing neuroinformatics techniques for evaluating the presence of brain tumors and response to treatment of the disease.

The three-year grant, which begins in July, will allow Tiwari's team in the CCIPD to develop artificial intelligence and computational imaging tool to identify from MRI scans which brain tumor patients are most likely to respond to therapy. "We are interested in identifying which patients will respond to chemo radiation and which ones will not," says Tiwari. "If we are successful, clinicians can use our noninvasive model to help guide their patients' treatment decisions. They will be able to figure out what treatments should be given if chemo radiation is not going to work out."

Tiwari's team, in collaboration with Jennifer Yu, from Cleveland Clinic's Brain Tumor and Neuro-Oncology Center, also was awarded a three-year, $200,000 grant from the Dana Foundation to develop neuroimaging tools for predicting treatment response to metastatic brain tumors following chemo-radiation. The Dana Foundation is a private philanthropic organization that supports brain research through grants, publications and educational programs.

Lung Cancer Screening

Congressionally Directed Medical Research Program (CDMRP)



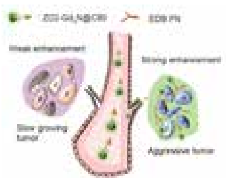
The DoD awarded $608,000 to researchers at the CCIPD to conduct a lung tumor screening project. "We know that CT scan screening saves lives," says Madabhushi. "However, if something shows up on a CT scan, the challenge is figuring out if what you are looking at is malignant or benign."

There is a high false-positive rate associated with lung nodules on CT scans, so patients often undergo unnecessary biopsies, bronchoscopies and even wedge resections. "With the DoD project, we are developing decision support tools and algorithms that include risk characterization of these nodules from CT scans," says Madabhushi. "This could allow us to distinguish between what are truly benign and truly malignant nodules."

The work is also supported via a $125,000 grant from the Case-Coulter Translational Research Partnership and a $75,000 grant from the Ohio Third Frontier Technology Validation Fund.

Breast Cancer Project

United States – India Science and Technology Endowment Fund

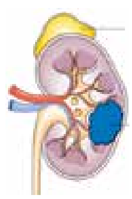


For more than two years, the CCIPD has collaborated with the Tata Memorial Centre, a national cancer center in Mumbai, India, focused on cancer prevention, treatment and research. Earlier this year, the U.S. - India Science and Technology Endowment Fund awarded the partners and Inspirata Inc. a two-year, $356,000 grant. "We are partnering with Tata to develop and validate a low-cost tissue image-based predictor for identifying women with early stage breast cancer to figure out who will benefit from chemotherapy and who may not need it," says Madabhushi.

It would be advantageous for patients to avoid costly chemotherapy, if possible, especially in a country like India. "It's a lower-middle income country, so economics play a much greater role in deciding treatment options," says Madabhushi. The CCIPD and Tata Memorial Centre hope to begin prospective testing during the course of the grant.

Digital Pathology Analysis of Kidney Biopsies

NephCure Kidney International

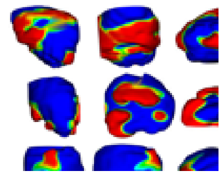


The CCIPD received the 2017 Neptune Ancillary Study Award from NephCure Kidney International, an organization committed exclusively to supporting research related to focal segmental glomerulosclerosis (FSGS) and the diseases that cause Nephrotic Syndrome. FSGS is a rare disease that attacks the kidney's filtering units, causing serious scarring that leads to permanent kidney disease and, in some cases, kidney failure.

The $150,000 award will fund a one-year pilot study led by Madabhushi to develop and apply novel machine learning tools for notation of structures within kidney pathology images. This will allow for construction of annotated kidney atlases, which could lead to the discovery of prognostic morphologic outcome signatures for FSGS. More information on the project can be found at nephcure.org under the "Recent News" tab.

Prostate Cancer Stratification

Congressionally Directed Medical Research Program (CDMRP)



The DoD awarded a three-year, $542,000 grant to researchers to study noninvasive risk stratification of prostate cancer patients using radiomic features derived from magnetic resonance fingerprinting (MRF) and MRI. The tools can be used to capture subtle sub-visual differences between benign and cancerous tumors, as well as ascertain the different grades of cancer.

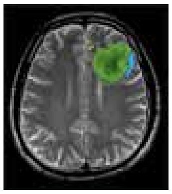
"This funding will enable development of computational imaging-based methods to determine the risk or aggressiveness of disease of a prostate cancer patient," says Rakesh Shiradkar, principal investigator and a senior research associate in CCIPD. "The current standard of care uses core needle biopsies and blood tests, which are both painful and inaccurate. Leveraging radiomics and machine learning methods using MRF and MRI can definitely advance management and care of prostate cancer patients."

INNOVATIONS RECEIVE FUNDING BOOST FROM CASE-COULTER TRANSLATIONAL RESEARCH PARTNERSHIP

Translational Research Partnership

The Case-Coulter Translational Research Partnership, which helps to commercialize projects by clinicians and biomedical engineering faculty that improve human health and well-being, has awarded more than $1.1 million in financial backing and other support for the most recent round of funding.

Novel molecular imaging agent for surgical resection of invasive brain tumors



Research leads: Susann Brady-Kalnay, professor of molecular biology and microbiology; James Basilion, professor of radiology and biomedical engineering; and Andrew Sloan, professor of neurosurgery.

The team's novel technology is a highly selective fluorescent imaging agent, called SBK2, which could be delivered pre-surgically to cancerous tissue to make it more visible during surgery.

Minimally invasive direct current nerve block

Research leads: Tina Vrabec, research assistant professor; Elias Veizi, assistant professor of anesthesiology and perioperative medicine; Niloy Bhadra, research assistant professor of biomedical engineering; Jesse Wainright, research professor of chemical engineering.

The team's novel technology uses minimally invasive direct current to block a nerve electrically. As compared to pharmaceuticals, this nerve block provides a focused block — without side effects — that can be applied and removed instantly and can be personalized for each patient.

Oropharynx appliance to maintain airway patency

Research leads: Dominique Durand, the Elmer Lincoln Lindseth Professor in Biomedical Engineering; and Kingman Strohl, professor of physiology and biophysics.

The team's novel technology is a device to treatoObstructive sleep apnea (OSA) in a form expected to deliver much higher patient compliance. The project aims to test the new design for the treatment of OSA.

Point-of-care device for monitoring and diagnosis of oral cancer

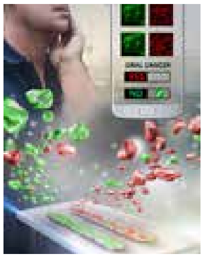
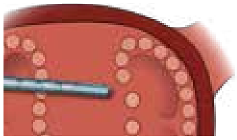


Image Credit: Grace Gongaware

Research leads: Aaron Weinberg, associate dean for research, chair of the Department of Biological Sciences and professor; Umut Gurkan, assistant professor of mechanical and aerospace engineering; and Santosh Ghosh, senior research associate.

The team's novel technology builds on a recent discovery that the two proteins produced in early stages of oral cancer change their ratios in cancerous cells, and that the ratio could be used as a non-invasive diagnostic tool. The researchers have developed a point-of-care microfluidic device which, when connected to a smartphone, obtains ratio results within 15 minutes.

noodle1Polarization-sensitive OCT (PSOCT) image guidance for RFA therapy of atrial fibrillation



Research leads: Andrew Rollins, professor of biomedical engineering and medicine; and Mauricio Arruda, associate professor of medicine.

The team's novel technology incorporates optical coherence tomography (OCT) imaging at the catheter tip, which could improve the acute success rate; reduce recurrences, procedure time and complications; and improve safety.

Point-of-care device for diagnosis of cystic fibrosis in newborns

Research leads: Miklos Gratzl, associate professor of biomedical engineering; and James Chmiel, associate professor of pediatrics.

The team's novel technology promises to detect the presence of the disease in newborns at twoweeks old, which would allow early treatment and more promising clinical outcomes.

Image Credit: Erika Woodrum unless otherwise noted

For more information, please visit bme.case.edu/cctrp.

ON A MISSION TO SAVE LIVES

Researchers are fighting to save patients with the creation of synthetic blood platelets that promote hemostasis and healing.

Photo by Russell Lee

Too often, trauma events lead the daily newscast, whether it is a car accident or a mass shooting event like the ones in Las Vegas or Parkland, Fla., that left dozens dead and many injured. Any loss of life is tragic. And trauma-associated severe bleeding remains the most common cause of death in people 1 to 46 years old. One researcher at Case Western Reserve University is trying to mitigate the losses.

"Deaths in trauma are often preventable," says Anirban Sen Gupta, associate professor of biomedical engineering. "They happen because first responders don't have access to blood components like platelets at the point of injury." Platelets are blood cells that promote hemostasis, helping clots form at the site of an injury and stop bleeding. Trauma patients often require transfusion of platelets to rapidly reduce blood loss and save their lives. But platelet transfusions are unavailable through emergency medical services or at small hospitals, so many patients may die before they can be brought to a large trauma center that has platelets.

Sen Gupta is the founder and director of the Bioinspired Engineering for Advanced Therapies (BEAT) Laboratory,

> "Deaths in trauma are often preventable. They happen because first responders don't have access to blood components like platelets at the point of injury."
>
> — Anirban Sen Gupta

which has developed synthetic platelets. “Imagine if you could put synthetic platelets in ambulances so emergency medical technicians can treat civilian patients at the roadside or military patients in the field, stabilize the patients and buy time to take them to a trauma center?” says Sen Gupta.

The artificial platelets created in the BEAT Lab — called SynthoPlate™ — have wider applications than hemostasis in trauma patients. They could also be potentially utilized in blood transfusions for patients with cancer, congenital blood disorders, gastrointestinal bleeds or undergoing major surgery. “Our hypothesis was that we could make artificial platelets from modular design components and customize these components to tailor their purpose and function, depending on the target disease or injury,” says Sen Gupta.

Taking Inspiration from Nature

In 2007, Sen Gupta started his lab, simply called the Sen Gupta Lab at the time. It began with a grant from the American Heart Association to study functionally integrated liposomes as synthetic platelet substitutes. Since then, the lab has expanded its scope and received approximately $6 million in funding from a variety of sources, most notably the National Institutes of Health (NIH) and the U.S. Department of Defense (DoD). The lab seeks mechanistic understanding of biological and pathological phenomena at the cellular, sub-cellular and biomolecular levels, then uses that knowledge to create bioinspired therapeutic and diagnostic technologies to interrogate, support or treat various phenomena.

"All the research we do is based in determining how things work in nature and what we can leverage from nature," says Sen Gupta. “The focus of my interest isn’t just the biology part only or the materials part only, but the interface between the two.” That interest in bioinspired research led him and a team

of student researchers to rename the lab the Bioinspired Engineering for Advanced Therapies Lab several years ago.

Today, the main focus of the BEAT Lab is in the field of platelet-inspired technologies for hemostasis and drug delivery. Sen Gupta works alongside a dozen or so researchers, ranging from postdoctoral researchers to high school students. "We are trying to make synthetic platelets that work like real platelets, going to the area of bleeding and acting like sandbags to stack upon each other and stop the bleeding," he says. "We have mimicked the functional aspect of how platelets form clots, using a combination of synthetic peptides on nanoparticles."

Collaborating on a Larger Goal

Each year in the United States, approximately 2 million platelet transfusions are given to treat bleeding complications in the management of trauma, surgery, myelosuppression and congenital blood disorders. However, such platelet products suffer from supply shortages, the need for blood typing, a high risk of bacterial contamination, limited portability and shelf life, and biologic side effects. This has prompted research in synthetic platelet products that can offer high availability, portability, extended storage life and point-of-injury applications.

While the work done by the BEAT Lab focuses on synthetic platelets for enabling hemostasis, other researchers in the broader field of blood substitution are taking a different approach. For instance, some labs are creating synthetic or semi-synthetic red blood cell substitutes for facilitating oxygen transport. Others are developing white blood cell substitutes for enabling cell-specific immune response.

"We all collaborate with the vision that someday we can put together one lab's artificial red blood cells, another lab's artificial platelets and still another lab's artificial plasma and essentially come up with a surrogate formulation for blood," says Sen Gupta. "The goal is not to replace blood, but to make something that works like blood when blood is not readily available."

That has significant implications. Consider the military. According to the DoD, the U.S. has 1.3 million men and women on active duty, many deployed in conflict zones like Afghanistan, Iraq and Syria. When troops are injured in the field, medics have very limited access to blood components. Synthetic blood products could be given to wounded soldiers, stabilizing them while they are transported to a major trauma center, which could save lives

The BEAT Lab works with many collaborators, including researchers and clinicians from the Cleveland Clinic, Harvard University, University Hospitals Cleveland Medical Center, the University of Pittsburgh, the University of Cincinnati, Marshall University and the U.S. Army Institute of Surgical Research.

Testing the Synthetic Platelets

The BEAT Lab has conducted in vitro lab scale studies on its synthetic platelets, as well as several in vivo biologic studies. The goal of the first in vivo study was to see if the synthetic particles would go to the point of bleeding and work with existing platelets to form blood clots. When that succeeded, the researchers substituted real platelets with synthetic particles. "The first job was to prove our particles work like platelets," says Sen Gupta. "The second job was to prove that if there aren't any platelets, the particle can still do its job. And it did."

The next study examined the viability of SynthoPlate in a test subject with acute injuries. "If somebody gets shot in Mansfield, Ohio, 80 miles southwest of Cleveland, by the time the person can be transported to a major trauma center, like at MetroHealth, they may die," says Sen Gupta. "That's the problem we try to solve, and our study signified we can keep the subject alive for the average time period it takes to reach a trauma center and receive a blood transfusion."

The studies were supported by the NIH Center for Accelerated Innovations at Cleveland Clinic (NCAI-CC), Case-Coulter Translational Research Partnership (CCTRP) and Ohio Technology Validation and Start-up Fund (TVSF) Phase I programs. The findings were recently published in *Nature Scientific Reports.*

With these promising findings, Sen Gupta has established a collaboration with the University of Pittsburgh to study a biologic model that mimics diffused injuries sustained in traumatic car accidents or when a soldier steps on an improvised explosive device. The model will combine extremity and truncal injuries, and the study will compare treatment with synthetic platelets to a control group that receives saline administration (the current point-of-injury standard of care). These findings and collaborations have also contributed to the BEAT Lab receiving a $1 million grant from the DoD last fall to evaluate the treatment efficacy of SynthoPlate in the biologic polytrauma model, as well as its influence in healing burn wounds.

Creating a Spin-off Technology Company

Lab studies can be limited for clinical translation. So in 2016, Sen Gupta founded a company with Christa Pawlowski, one of his former students who is currently working in the lab as a postdoctoral researcher, for translation and commercialization of SynthoPlate. Taking its name from the Greek word for blood, Haima Therapeutics has received funding from various sources, including a Phase 1 Small Business Innovation Research (SBIR) grant totaling $225,000 from the National Science Foundation to pursue chemistry, manufacturing and controls (CMC) characterization of the SynthoPlate technology.

Pawlowski began working in Sen Gupta's lab as an undergraduate at Case Western Reserve and continued there through graduate school. "I was enthralled with the research topic," says Pawlowski, chief scientific officer of Haima Therapeutics. "The idea of using nanoparticles to provide a therapeutic effect or deliver payload in a site-selective manner, thereby reducing harmful side effects and enhancing drug response, was exciting to me. I got to use an engineering approach to solve real-world human health problems."

She continues to use her engineering background and

How SynthoPlate™ Works

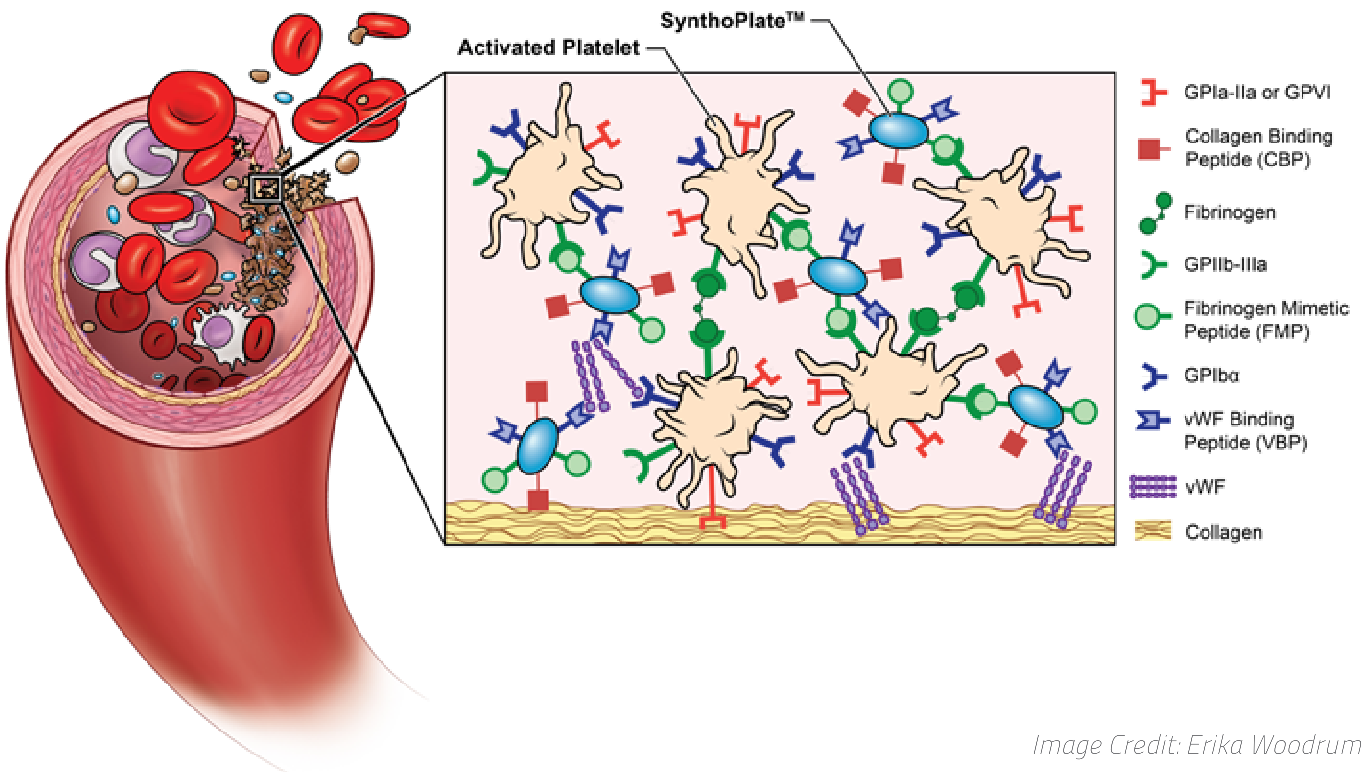


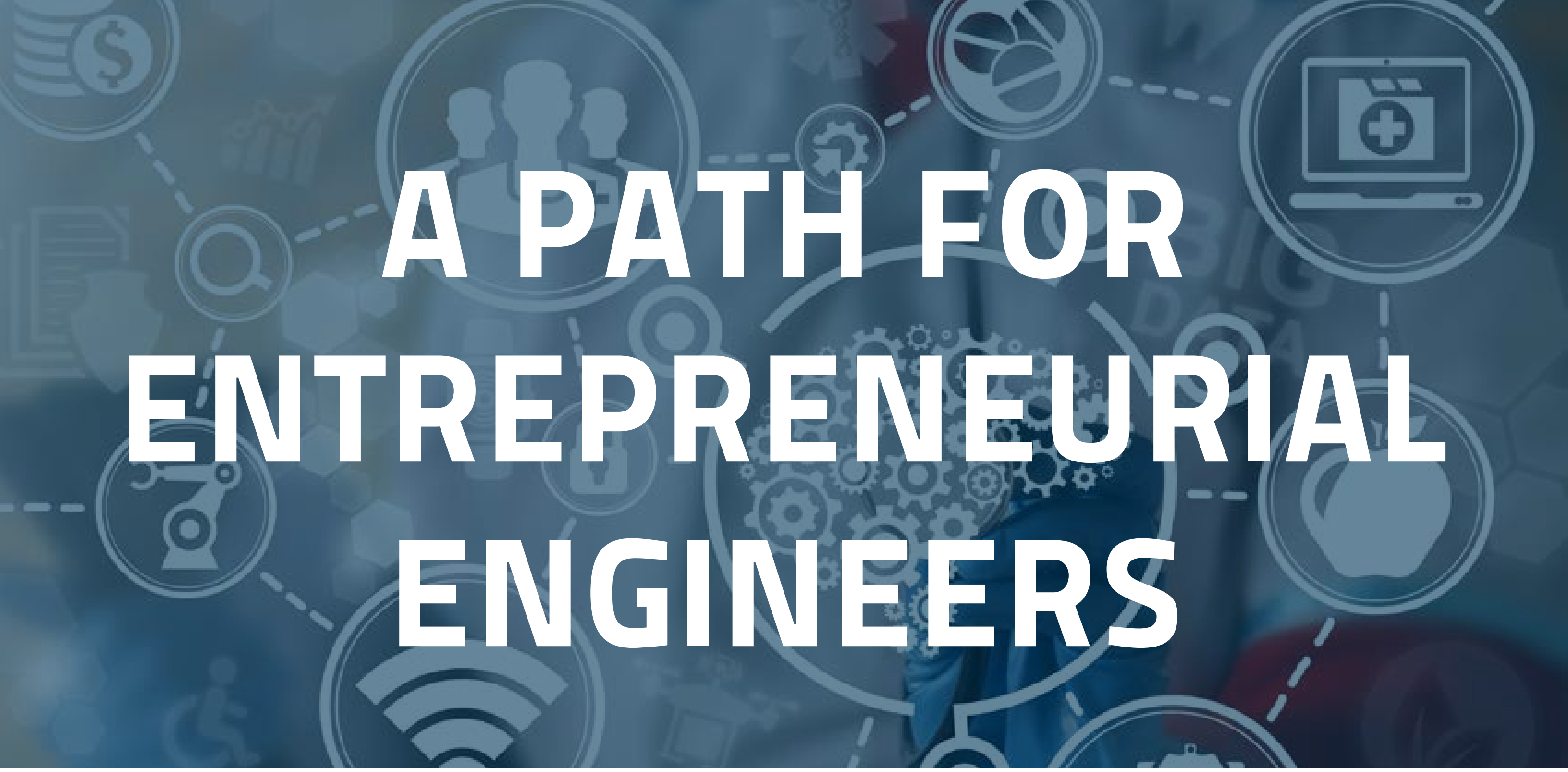
Image Credit: Erika Woodrum

experience from the BEAT Lab at Haima Technologies. "The BEAT Lab has done a fantastic job at characterizing the SynthoPlate technology and evaluating proof of concept in vitro, as well as in several small and large animal models," says Pawlowski. "Haima's work includes further vetting of the technology from a drug development standpoint."

This year, the BEAT Lab is collecting data on batch-to-batch reproducibility of the product, conducting a shelf-life analysis and performing pharmacology/toxicology studies to determine maximum tolerated dose and half-life. These studies are being supported with the assistance of an NIH-sponsored program called Science Moving Towards Research Translation and Therapy (SMARTT), as well as an award from the Council to Advance Human Health (CAHH) program at Case Western Reserve School of Medicine. This data will be combined with CMC data from Haima for a pre-investigational new drug meeting with the U.S. Food and Drug Administration.

The work that Sen Gupta began more than a decade ago may be coming closer to clinical reality. That's good news for him, his lab and millions of people worldwide. "SynthoPlate has the potential to address the unmet clinical need for a widely available agent that can act rapidly to staunch internal, non-compressible hemorrhage," says Pawlowski. "Ultimately, SynthoPlate has the potential to save many lives."

> "I got to use an engineering approach to solve real-world human health problems."
>
> — Christa Pawlowski



A PATH FOR ENTREPRENEURIAL ENGINEERS

The master's track in translational health technology helps students convert research ideas into commercial success.

Graduate students Sriram Boppana and Connor Swingle are working on a project to improve medication adherence for patients with chronic debilitating conditions and help them manage drug interactions. The work is being done as part of their project-based Master of Science degree in biomedical engineering with a concentration in translational health technology. Case Western Reserve University began offering the educational track several years ago to help students become leaders at transforming research breakthroughs to clinical implementation.

"What really sold me on this program was how it lets students lead their own research projects, which can pave the way for entrepreneurial endeavors," says Boppana, who earned his bachelor's degree in biomedical engineering from Purdue University last spring. While there, he started a student organization called Purdue M.I.N.D. (Medical Innovation, Networking and Design), which enables students to pursue an independent year-long biomedical research project. When Boppana began considering graduate schools, he looked for programs that would nurture his interest in engineering, medicine and entrepreneurship. Case Western Reserve's master's degree track in translational health technology was the perfect fit.

The program, which can be completed in one year by studying full time or two years by studying part time, comprises nine courses and a final project. Students take classes in entrepreneurship, clinical ethics, biodesign, bio-regulatory affairs, health care system models and other related topics. The coursework helps students formulate and hone their final project ideas.

"Graduate students in biomedical engineering have a choice as to whether they want to focus on mastering the application of knowledge or begin the first phases of creating new knowledge," says Colin Drummond, professor and assistant chair of the Department of Biomedical Engineering. "The master's in translational health technology is designed for those students who are not going to pursue research careers, but are interested in taking technology and seeing it go to market."

Drummond created the translational health technology master's degree track with two colleagues: Dominique Durand, the Elmer Lincoln Lindseth Professor in Biomedical Engineering and director of the Neural Engineering Center, and Alia Hdeib, a neurosurgeon with University Hospitals Cleveland Medical Center.

The program has attracted between two and five students a year. "We spent the first few years really understanding what creates value for the students and fine-tuning the program," says Drummond. "Now we can scale up and serve more students." He anticipates enrolling 12 to 15 students each year, which will allow the track to remain highly personalized.

The translational health technology track is small, in part, because it includes hands-on work in clinical settings. Case Western Reserve is located in northeast Ohio's health technology corridor, allowing students to partner with leading clinicians from Cleveland Clinic, University Hospitals, the MetroHealth System and other local healthcare organizations. Drummond says students have worked alongside clinicians on "pragmatic and patient-facing" final projects that range from development of an early detection system for strabismus to creation of a wireless system to assess an infant's health and prevent sudden unexpected postnatal collapse.

"The program offers an incredible opportunity for individuals who are really self-motivated and have a deep interest in health care technology," says Boppana, who plans to attend medical school after receiving his master's degree. "My hope is that the knowledge and experience gained through clinical training, combined with the experience of the translational health technology program, will enable me to become an inventor within the medical industry."

Several of Boppana's predecessors have already reaped the rewards of the program, filing patents, landing funding and creating startup companies to commercialize their inventions. "The program offers a quality alternative for students who want to pursue a master's degree in biomedical engineering, but are very serious about a startup," says Drummond. "For certain students with a translational objective or specific career plans, this works for them."

"The program offers a quality alternative for students who want to pursue a master's degree in biomedical engineering, but are very serious about a startup."

— Colin Drummond

STUDENT SPOTLIGHT

Kelsey Bower

PhD candidate, Kelsey Bower, was awarded a National Institute of Health F31 entitled, "Computational Models of Deep Brain Stimulation of the Cerebellothalamic and Subthalamopallidal Pathways." Bower is creating computational models of the brains of numerous patients with Parkinson's disease, who are being treated with deep brain stimulation (DBS). These models can be used to identify which areas of the brain, or neural pathways, are being stimulated by different DBS settings. They can then identify how stimulation of different areas or pathways improves their symptoms and use that knowledge to better inform targeting and application of DBS therapy. These models will be used to identify the effects associated with stimulation of two specific pathways in the brain.

Utilizing her education and research experience, Bower recently completed a six-month internship at Boston Scientific, a medical device company with multiple products in the neuromodulation field. She was in the R&D department at their neuromodulation site in Valencia, Calif., focusing on DBS modeling. Bower participated in several computational projects aimed at advancing software capabilities and improving user experience.

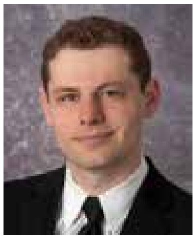
Michaela Cooley

Senior undergraduate student and current Medical Scientist Training Program (MSTP) candidate, Michaela Cooley, won the Student Research Award from the Society for Biomaterials Drug Delivery Special Interest Group.

Cooley has conducted research in the Bio-inspired Engineering for Advanced Therapies Laboratory for two-and-a-half years under the guidance of Anirban Sen Gupta, associate professor of biomedical engineering.

Her research focuses on the role of particle geometry and stiffness in enhancing the performance of particulate drug-delivery systems in the vascular compartment. The research is part of a collaboration between the labs of Sen Gupta at Case Western Reserve University and Samir Mitragotri at University of California, Santa Barbara.

Cooley gave a podium presentation entitled, "Effect of Particle Shape and Size on Margination and Wall-localization in Vascular Drug Delivery" on her research findings in the Drug Delivery session at the Society for Biomaterials annual conference in Minneapolis in April.



Nate Braman

PhD candidate, Nate Braman, received a travel award to participate in the Rally for Medical Research Hill Day Sept. 13-14, 2017, in Washington, DC, as a member of the Coalition for the Life Sciences.

Held every September, this Capitol Hill Day event continues the momentum established in 2013, and includes nearly 300 national organizations. The purpose of the Rally is to call on our nation's policymakers to make funding for the National Institutes of Health (NIH) a national priority and raise awareness about the importance of continued investment in medical research that leads to more progress, more hope, and more lives saved.

MAKING AN IMPACT

ALUMNI HIGHLIGHTS

Luis Solorio

Luis Solorio (GRS '12) helped create a lifelike cancer environment out of polymer to better predict how drugs might stop its course.

Past studies have used 3-D printers to recreate a controlled cancer environment, but these replicas do not have the fine resolution needed for drug screening.

Solorio and a team of researchers have proposed 3-D writing. The device that they developed, a 3-D jet writer, acts like a 3-D printer by producing polymer microtissues as they are shaped in the body, but on a smaller, more authentic scale with pore sizes large enough for cells to enter the polymer structure just as they would a system in the body.

"Ideally, we could use our system as an unbiased drug screening platform where we could screen thousands of compounds, hopefully get data within a week, and get it back to a clinician so that it's all within a relevant time frame," Solorio says.

Initial findings were published on Feb. 27 in *Advanced Materials* based on Solorio's work as part of a team at the University of Michigan Biointerfaces Institute. Continuation of the work is being performed at Purdue University and is funded by the National Cancer Institute.

Solorio worked in Agata Exner's Lab in the Department of Radiology of the School of Medicine.

Amr Salahieh

President and CEO at Shifamed LLC, Amr Salahieh (CWR '89, '90) is a seasoned entrepreneur with over 25 years of experience in the medical device industry. Salahieh is the founder of Shifamed LLC, a Silicon Valley-based medical device incubator founded in 2009, from which Legacy Portfolio Companies Maya Medical, Kalila Medical, and Apama Medical have successfully exited and through which three additional companies are currently under incubation.

Prior to founding Shifamed, Salahieh founded Sadra Medical, a percutaneous aortic valve replacement company, which was sold to Boston Scientific in 2011, and co-founded Embolic Protection, Inc. (EPI), which was sold to Boston Scientific in 2001.

Salahieh has extensive R&D management experience stemming from his engineering consulting firm, Sobek Medical LLC, which he sold to EPI, and from his work at CardioThoracic Systems and Guidant. Salahieh is the inventor or co-inventor on more than 100 granted and over 140 published U.S. patent applications.

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