Boston University Neurophotonics Center

Annual Report | 2023

BOSTON UNIVERSITY

Table of Contents

Letter from the Director

During 2022, the Boston University Neurophotonics Center (NPC) went through the process of renewing its charter to operate as a University Center. The charter was approved, and I very much look forward to continuing to work with the internal and external neurophotonics community. As our resources were stretched with preparing the renewal last year, we did not produce an annual report and as such this annual report is covering the last two years, academic years 2022 and 2023.

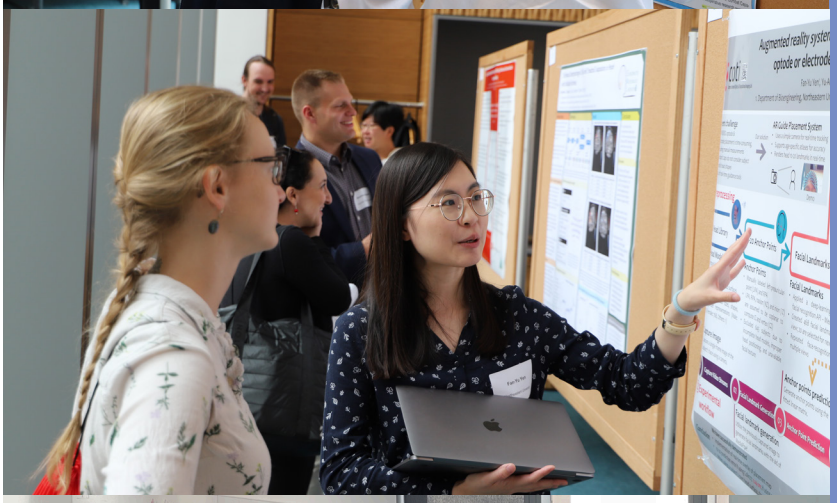
The biggest change in the NPC over these last two years, other than renewing its charter, was the addition of two new Associate Directors – Jerry Chen and Chris Gabel – joining Associate Director Anna Devor. I am grateful to being working with these three to maximize the impact that the NPC can have on the neurophotonics community. Each of them has their own particular focus for enhancing NPC's impact. Anna continues to foster new collaborative efforts amongst the NPC faculty and their trainees. Chris joins Anna in this endeavor but with a focus on enhancing the impact of NPC on the Medical Campus (MED). And Jerry is focusing on improving the Neurophotonics Research Training (NRT) program. Over the coming year you will see more connections being made between the MED and Charles River Campus (CRC) as will be facilitated by an annual NPC MED Symposium and targeted brainstorming sessions for launching new cross campus collaborative activities. In addition, to help improve the NRT, we have submitted an NIH T32 graduate fellowship training grant and optimistically await its review.

The NRT trainees have been busy the last two years promoting and solidifying their activities. Our monthly social is a great opportunity to catch up with peers and meet new ones from whom you might just learn something new to help your own research. The trainees are now preceding the monthly social with a Neuro-Technology Tutorial, lead by one of the trainees who takes the opportunity to teach their peers about a tool they are utilizing to advance their neuroscientific research. Another group of trainees decided we needed regular discussions on neuroethics and are now arranging a few gatherings a year, including seminars and discussions led by outside neuroethics experts. And the trainees are continuing their roles in organizing the NPC Faculty Spotlight to introduce new students to the breadth of neurophotonics research opportunities at BU, in organizing the poster session for the annual NPC Symposium, and in hosting external speakers during their visits to BU to give seminars. I am very grateful to these various trainee committees for strengthening our community through their continued efforts.

Continuing its role in promoting faculty research programs and new collaborative initiatives, the NPC has supported over 25 projects over the last two years. Many of these projects are summarized in the pages that follow. Several research groups are taking advantage of the advanced microscopy tools available through the NPC imaging core for diverse projects studying the brains of rodents, songbirds, and flies! And more and more faculty from outside of the neurosciences are being drawn to the available imaging tools to enhance their research in other organs, for example in tumor biology and wound healing. These faculty continue to push for more advanced and versatile microscopy tools. For instance, the three-photon microscope is being utilized more and more, and another collaborative effort is developing a wearable two photon microscope. The study of human brain function with functional Near Infrared Spectroscopy (fNIRS) is another area with tremendous collaborative activity at BU as it presently engages 10 faculty and their teams. Applications span autism, post-stroke gait and language rehabilitation, impact of Parkinson's Disease and arthritis on gait, audio perception in the cocktail party problem, neurodegeneration, and the study of perception, attention, and memory in everyday world settings. A major focus of these groups is leveraging fNIRS and other wearable technologies to do Neuroscience in the Everyday World. This group is gaining traction in launching this NEW field that will draw upon multidisciplinary expertise from across campus beyond the core NPC faculty.

The NPC Associate Directors and I are always on the look-out for new projects and collaborative initiatives that the NPC can support. We have two funding mechanisms to help faculty: a seed award to support faculty in the utilization of core imaging equipment, and a Collaborative Award for Neurophotonics Devel-Opment (CAN DO). Details can be found on our web-page and we encourage faculty to reach out to us to discuss their ideas. I am excited to see what new activities will develop this coming year.

David Boas
Director, Neurophotonics Center



At a Glance

46
Faculty Members

68
Students in NRT

28
Projects Supported

52
Publications from NPC Faculty Collabrations

44
Collaborative Grants Funded

Who We Are

Leadership

David Boas, Ph.D.
Director

Anna Devor, Ph.D.
Associate Director

Jerry Chen, Ph.D.
Associate Director

Christopher Gabel, Ph.D.
Associate Director

Technical Directors

Zahid Yaqoob, Ph.D.
Technical Director

Meryem Yücel, Ph.D.
Technical Director

The mission of the BU Neurophotonics Center (NPC) is to build and support an interdisciplinary community that can develop and broadly deploy impactful photonics technologies in the neurosciences to advance our understanding of how the brain works in health and in disease.

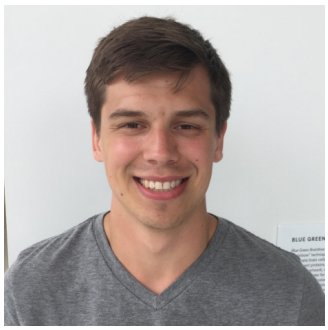
We are excited to welcome new and returning personnel to the NPC. Kivilcim Kilic is returning to the NPC after a brief excursion to the West Coast. She was instrumental in launching the NPC and we are excited to have her back with us on the East Coast. We also welcome Martin Thunemann to the NPC. He joined the department of Biomedical Engineering in 2020. He received his PhD in Biochemistry from Eberhard Karls Universität Tübingen, Germany. During his graduate studies, Dr. Thunemann gained extensive knowledge in molecular biology, cell culture, cardiovascular physiology, mouse transgenesis and the Cre/lox system. He joined Dr. Devor laboratory at UCSD in 2015, first as a postdoctoral fellow, later – as a Project Scientist. He has been leading a number of bioengineering efforts including those based on multiphoton imaging and multiplexed electrophysiological recordings in awake behaving mice, and will be assisting the NPC community in the adoption of these methods.

Who We Are

Scientists

Kıvılcım Kılıç, Ph.D.

Martin Thunemann, Ph.D.



John Giblin, Ph.D.

Staff

Parya Farzam, fNIRS Specialist and Administrative Director

Danny Giancioppo, Communications Manager

John Jiang, Lab Manager

Faculty

Lou Awad
Associate Professor (Health & Rehabilitation)

Works to develop, test, and translate rehabilitation technologies and interventions for people living with impaired neuromotor control.

Thomas Bifano
Professor (ME, MSE, BME)

Deformable mirrors; Microelectromechanical systems (MEMS); Adaptive optics; Biphotonic microscopy; Astronomical telescope instrumentation; Laser wavefront control

Irving Bigio
Professor (BME, ECE)

Medical application of optics, lasers and spectroscopy; Biophotonics; Nonlinear optics; Applied spectroscopy; Laser physics

David Boas
Professor (BME, ECE)
Director of Neurophotonics Center

Neurophotonics; Biomedical Optics; Oxygen delivery and consumption; Neuro-vascular coupling; Physiological Modeling

Jerry Chen
Professor (Biology)

Large-scale neuronal networks; Sensorimotor integration; Decision making; Neurodevelopment; Non-linear microscopy

Ji-Xin Cheng
Professor (ECE, BME, MSE)

Molecular spectroscopic imaging technologies; Label-free microscopy; Medical photonics; Neurophotonics; Cancer metabolism; Photonics for infectious diseases

David Chung
Assistant Professor (Medicine)

Cerebral aneurysms, stroke, traumatic brain injury, neuromonitoring

Alice Cronin-Golomb
Professor (Psychological & Brain Sciences)

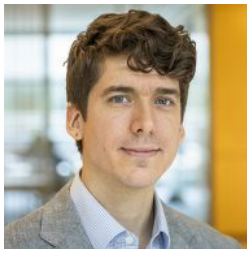
Neural correlates of perception and cognition in aging and age-related neurodegenerative disease

Alberto Cruz-Martin
Assistant Professor (Biology)

Neural circuits; Sensory processing; Visual pathways

Ian Davison
Associate Professor (Biology)

Pheromones and innate social behaviors; Cortical computations and plasticity



Jeffery Demas
Research Assistant Professor (ECE)

Advanced optical imaging; Multiphoton Microscopy; Neurophotonics; Structured light; Nonlinear optics

Brian DePasquale
Assistant Professor (BME)

Machine learning; Computational Neuroscience; Theoretical Neuroscience

Faculty

Anna Devor
Professor (BME)

Cellular and systems-level neuroscience, microscopy, physiological underpinning of noninvasive imaging

Michael Economo
Assistant Professor (BME)

Neural circuits, Cognitive function, Neurodevelopmental disorders

Terry Ellis
Associate Professor (Physical Therapy)

Neurorehabilitation; Parkinson disease; Clinical Practice Guidelines; Physical Therapy Models of Care; Mobile health technologies; Digital Therapeutics

Claudio Ferre
Assistant Professor (Health & Rehabilitation)

Development of manual skills in typically developing children and children with disabilities (e.g., cerebral palsy)

Chris Gabel
Associate Professor (Physiology & Biophysics)

Femtosecond laser surgery and optical neurophysiology for the study of the nervous system of the nematode worm C. elegans

Jefferey Gavornik
Assistant Professor (Biology, BME)

Cortical circuits; Synaptic plasticity as the basis of learning and memory; The neural representation and processing of time; The biophysical basis of visual perception

Simone Gill
Associate Professor (Medicine)

We are interested in how people's bodies and environmental demands influence walking and motor functioning across the lifespan.

David Greer
Professor (BMC)
Chair and Chief of Neurology

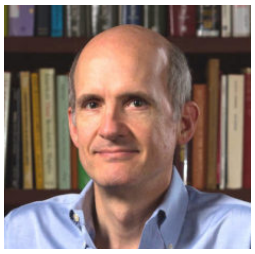
Predicting recovery from coma after cardiac arrest, brain death, and multiple stroke-related topics, including acute stroke treatment and stroke prevention.

Lee Goldstein
Associate Professor (Neurology, BME, ECE)

The role of abnormal protein aggregation in chronic degenerative disorders of aging

Xue Han
Professor (BME)

Neurotechnology; Optical neural modulation; Optogenetics;
Neural prosthetics; Neural network dynamics; Brain rhythms; Neurological and psychiatric diseases; Cognition



Michael Hasselmo
Professor (Neuroscience)

The role of oscillatory dynamics and neuromodulatory regulation in cortical mechanisms for memory-guided behavior

Mark Howe
Assistant Professor (Psychological & Brain Sciences)

Basal ganglia circuit mechanisms for learning and action

Faculty

Swathi Kiran
Professor (Speech, Language, and Hearing Sciences)

Bilingual aphasia; Aphasia rehabilitation; Functional neuroimaging; Language recovery; Impairments in naming, reading, writing

Deepak Kumar
Asisstant Professor (Health & Rehabilitation)

Development of more effective and personalized treatment interventions that reduce disability and directly impact patient care.

Sam Ling
Associate Professor (Psychological & Brain Scientists)

Imaging human behavior to explore how the brain mediates between the "buzzing confusion" of the visual world and our limited processing power

Jerome Mertz
Professor (BME, ECE, Physics)

Development and applications of novel optical microscopy techniques for biological imaging

Hadi Nia
Assistant Professor (BME, MSE)

Interface of physical sciences and molecular biology with a focus on links between mechanical forces and cell biology in health and disease.

Timothy O'Shea
Assistant Professor (BME)

Developing new treatments for brain and spinal cord disorders by engineering glia to perform specific reparative functions.

Siddharth Ramachandran
Professor (ECE, MSE, Physics)

Optical physics of guided waves; Micro- and nano-structured optical fibers; High-power fiber lasers and fiber sensors; Biomedical imaging and microscopy with optical fibers

Steve Ramirez
Assistant Professor (Psychological & Brain Sciences)

Revealing the neural circuit mechanisms of memory storage and retrieval, and artificially modulating memories to combat maladaptive states

Darren Roblyer
Associate Professor (BME, ECE)

Optical functional imaging; Diffuse optics and spectroscopy; Monitoring of therapies in oncology; Non-invasive monitoring of tumor metabolism

Shelley J. Russek
Professor (Biology, Pharmacology & Experimental Therapeutics)

Deciphering the complex networks of gene regulation that control the function of inhibitory neurotransmission in the brain

Michelle Sander
Associate Professor (ECE, BME, MSE)

Femtosecond lasers; Ultrafast photonics and nonlinear processes; Fiber and integrated optics; Frequency combs; Infrared spectroscopy and biomedical applications

Benjamin Scott
Assistant Professor (Psychological & Brain Sciences)

Develop and apply new technologies to study the neural basis of cognition and complex learned behavior

Faculty

Kamal Sen
Associate Professor (BME)

Neural coding of natural sounds; Neural discrimination; Population coding of natural sounds

David Somers
Professor & Chair (Psychological & Brain Sciences)

Functional MRI, psychophysics, and computational modeling to investigate the mechanisms underlying visual perception and cognition

Chantal Stern
Professor (Psychological & Brain Sciences)
Using fMRI to study how the normal brain encodes, stores and subsequently recognizes visual, spatial and verbal information

Robert Stern
Professor (Neurology)
Director of CTE

Long-term effects of repetitive brain trauma in athletes, including the neurodegenerative disease, CTE

Helen B. Tager-Flusberg
Director of Center for Autism Research

The phenotypic characteristics of the language, communication and associated social-cognitive deficits in autism (ASD) and other neurodevelopmental disorders

Martin Thunemann
Assistant Professor (BME)
Neuroimaging; Electrophysiology; Neurovascular coupling; Neurometabolic coupling; Cerebral blood flow regulation; Neurological and psychiatric diseases; Cognition

Lei Tian
Assistant Professor (ECE, BME)
Computational imaging and sensing; Gigapixel, 3D microscopy; Compressive imaging; Phase retrieval; Imaging through complex media; X-ray phase imaging

Michael Wallace
Assistant Professor (Anatomy & Neurobiology)

Circuit and basal gangalia guidance of motivated behaviors; electrophysiology; molecular biology; genetics;

Tianyu Wang
Assistant Professor (ECE)

Applied engineering and physics

John A. White
Professor & Chairman (BME)

Mechanisms of episodic memory; Pathophysiology of epilepsy; Computational neuroscience; Design of real-time instrumentation

Benjamin Wolozin
Professor (MED)

Neurodegenerative diseases; RNA binding proteins; Translational regulation in disease processes

Chen Yang
Associate Professor (ECE, Chem, MSE)

Nanomaterial-based photonics and electronics for neuromodulation and live cell sensing

Faculty

Meg Younger
Assistant Professor (Biology)

Neurobiology; Olfaction; Odorant Receptors; Chemosensation; Mosquitoes; Synaptic Transmission; Calcium Imaging; Neurophysiology; Behavior

Meryem Yücel
Associate Professor (BME)

Functional neuroimaging (fNIRS, fMRI, EEG); fNIRS signal processing; cognitive neuroscience

New Faculty

Jeffery Demas
Research Assistant Professor (ECE)

Advanced optical imaging; Multiphoton Microscopy; Neurophotonics; Structured light; Nonlinear optics

Brian DePasquale
Assistant Professor (BME)

Machine learning; Computational Neuroscience; Theoretical Neuroscience

Jefferey Gavornik
Assistant Professor (Biology, BME)

Cortical circuits; Synaptic plasticity as the basis of learning and memory; The neural representation and processing of time; The biophysical basis of visual perception

Hadi Nia
Assistant Professor (BME, MSE)

Interface of physical sciences and molecular biology with a focus on links between mechanical forces and cell biology in health and disease.

Shelley J. Russek
Professor (Biology, Pharmacology & Experimental Therapeutics)

Deciphering the complex networks of gene regulation that control the function of inhibitory neurotransmission in the brain

Michael Wallace
Assistant Professor (Anatomy & Neurobiology)

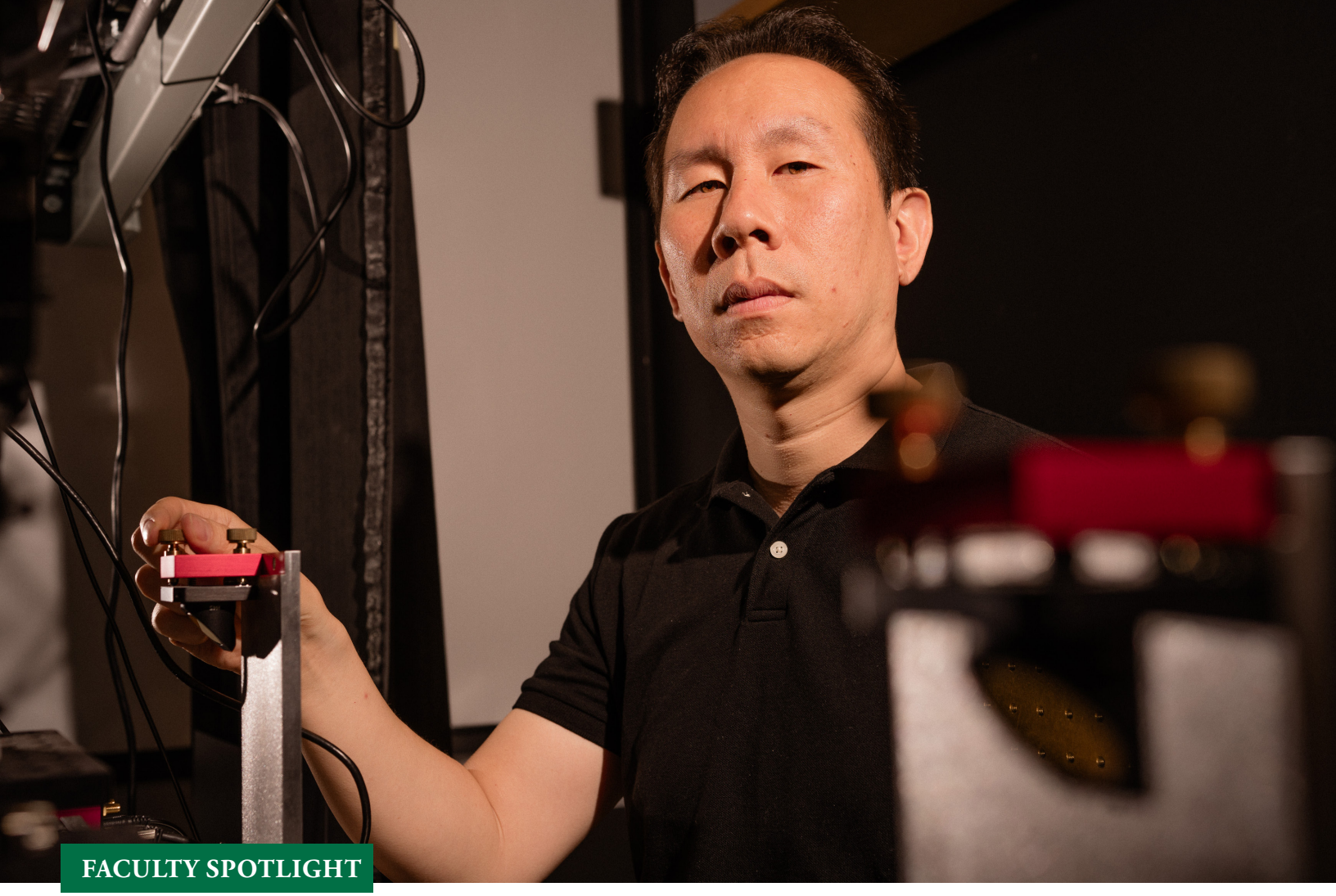
Circuit and basal gangalia guidance of motivated behaviors; electrophysiology; molecular biology; genetics;

Tianyu Wang
Assistant Professor (ECE)

Applied engineering and physics

Meg Younger
Assistant Professor (Biology)

Neurobiology; Olfaction; Odorant Receptors; Chemosensation; Mosquitoes; Synaptic Transmission; Calcium Imaging; Neurophysiology; Behavior



FACULTY SPOTLIGHT

HOW DO DECISIONS MADE IN THE BRAIN INFLUENCE BEHAVIOR? – JERRY CHEN'S LAB IS ENGINEERING NEW TOOLS TO VISUALIZE THE BRAIN'S PROCESSES

by Tess Joosse, Photos by Christopher McIntosh

At the crux of Jerry Chen's research are some of the most elemental questions about the cognitive experience. "How do we perceive the world? How do we use that information to make decisions? We're interested in understanding the basic functions of how we behave," he says.

For each event perceived and decision made, there is a complex web of neural circuitry involved. Understanding how the central nervous system's many layered parts work to create knowledge from past experiences is an overarching goal in Chen's lab, which has published papers in Science, Nature Communications, Nature Methods, and Neuron, just to name a few.

"We're interested in studying this question at different scales. In the brain, we're interested in how genes give rise to molecules that define how neurons function, how the neurons themselves come together to form circuits, and how those circuits then carry out computations," says Chen, a faculty member in both the Photonics Center and the Neurophotonics Center, College of Arts and Sciences assistant professor of biology, and affiliated College of Engineering assistant professor of biomedical

engineering.

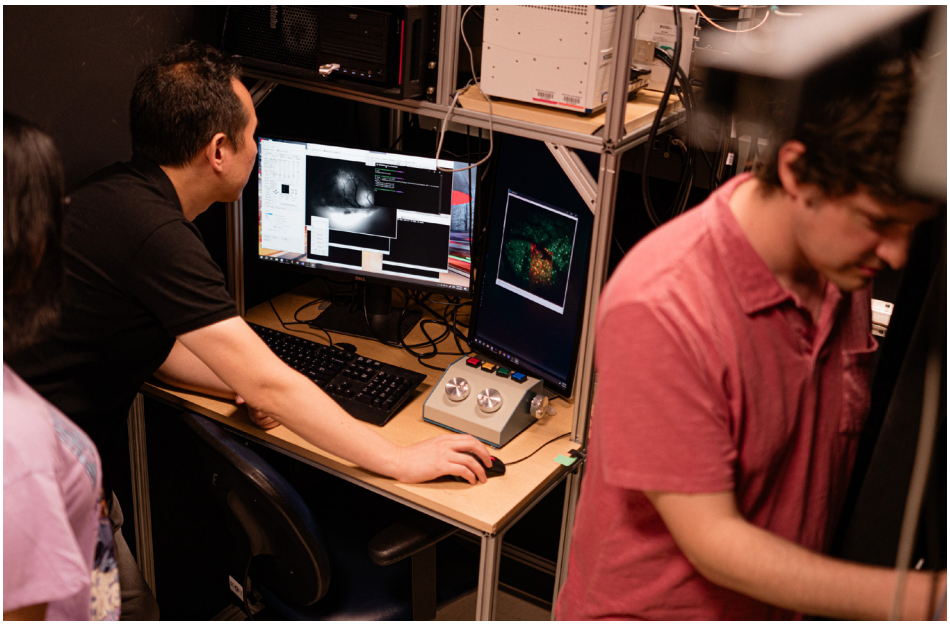
Across these many scales, Chen and members of his lab use an array of imaging techniques to get a front row seat to what's happening within the brain. "As researchers, we like to actually be able to look at things we're measuring and observe these processes," he says. They use these tools to zoom in on individual molecules within a neuron, and "zoom out to look at how all these neurons are talking to each other."

The team's approaches aren't just focused on spatial scales but also on temporal ones, investigating what's happening in sections of the brain across time. Neurons communicate with one another within milliseconds, Chen explains, while processes like learning and memory occur over longer ranges of time.

And even two brain cells sitting next to each other can have vast differences. "All the neurons in our brain are not all the same. They're very diverse, and they're potentially carrying out a lot of distinct roles. And their roles are largely defined by the genes that are being expressed," Chen says.

To study the relationships between gene expression, neuronal activity, and behavior, Chen's lab created a workflow called "comprehensive readout of activity and cell type markers", or "CRACK" for short. The experiments involve first training mice to lick a sensor when they detect a matching pair of stimuli, a task similar to the card game known as "memory", Chen explains, in which a player flips over cards (arrayed face down on a table) one by one with the goal of matching pairs.

In the lab's mouse version, the researchers use a rotor to brush the whiskers of a mouse either towards or away from its face. Whiskers are highly sensitive and convey important information to the animal, Chen says. "They have very fine tactile acuity with their whiskers, similar to what we have



with our fingertips," he says. The mouse is rewarded with a sip of water for not licking in response to two brushes that don't match. "The animal has to generalize and make a rule to say, 'These two bits of whisker stimuli were the same, or they were different,'" Chen says.

As mice perform this memory task, Chen and the members of his lab—including David Lee, a sixth-year PhD student—capture their behavior on high-speed video and use 2-photon calcium imaging to peer deep into their brains. Calcium rushes into a neuron as it fires, and 2-photon imaging allows the team to track these changes at single-cell resolution to determine where and when neurons are active.

"Then at the end of our experiments, we take the tissue out, and we find the neurons that we imaged previously in the living brain," Chen explains, using a technique called fluorescent in situ hybridization to stain these samples for mRNA of multiple genes. Combined, the techniques paint a picture of what genes and circuits are involved in different scenarios of learning and decision making.

These detailed visualizations first piqued Lee's interest as a new graduate student, when Chen showed them in a first-year seminar research presentation. "When I first saw videos of neurons actually lighting up while an animal was awake and behaving and thinking, I was like, 'That's exactly what I want to do,'" Lee says. "We're able to see what happens as animals learn and think."

Since then, in Chen's lab Lee has used these techniques to study the perirhinal cortex, an area of the brain that receives information from the whisker system in mice and is linked to regions implicated in learning and memory. As the animals figure out the whisker-brush memory "game", Lee images the same set of cells twice a day, in the end looking at how those cells changed in the process.

He's found that as a mouse learns how to accomplish the task over time, a "reward" signal in the mouse's brain starts to show up earlier and earlier during the whisker-brush trials. Initially, the reward signal can only be detected at the end of the memory task. But then, "as the animals begin to have enough information to know they're going to be rewarded," Lee says, "it begins to occur not just at the end of the trial but during the stimuli, when the animal is actually thinking about it and saying, 'Oh, I have enough information. I can get water here.'"

Members of the Chen lab are also developing new microscopic tools to assist in their investigations of neural circuits. Xin Ye, a seventh-year PhD student in the lab, has created a microscope for viewing changes in voltage between cells. While 2-photon calcium imaging is a powerful tool for visualizing neuronal activity, calcium is still just a proxy for the change in voltage that actually indicates a neuron is firing. A tool that can image voltage directly is highly desirable, Ye says. "It's something that scientists want."

To design the microscope, Ye and her colleagues employed a phenomenon called temporal multiplexing, in which multiple paralleled laser beams are pulsed at delayed time intervals. "We have this [concept], but nobody has actually applied it to ultrafast imaging," she says. To build it, they combined, modeled, and tested many different components in a long process of troubleshooting and trial-and-error. They created a bespoke setup that placed multiple laser beams in the same field of view, enabling them to scan a small area of the brain for changes in voltage.

"The concept is set at the very beginning, but the middle is more like an engineering project to put this concept into an actual microscope," Ye explains. "It's extremely exciting … to start building something totally new, from scratch," she says of the project.

Chen notes that this type of voltage imaging is now more practical and feasible to do and will likely be more widely adopted across neuroscience research in the coming years. "What everybody wants to measure is voltage," he says.

Meanwhile, Lee is developing automated methods of whisker training the mice, hoping not just to teach them the memory task but also employing new techniques to measure if and how the mice learn it. While manually training the mice, the team has observed a remarkable range of idiosyncrasies in how different mice try to chip away at the task. "Some are running around in circles, some mice are just impulsively engaging with the system, some animals appear to be more deliberately trying to pay attention to the stimulus and respond accordingly," Chen says. "Behaviorally, you see a lot of differences that we're trying to characterize."

Automating the training frees up the group to study this behavioral diversity in depth, he says. "It allows us to look more broadly at the variations in individuals, and then start to hone in on what are the neuronal differences that could be causing these behavioral differences."

These questions about variations in gene expression and circuitry are linked to why Chen chose to study the brain in the first place: "Introspection — just understanding who I am as a person," he says. "We're all individuals, right? Being

able to look at [and compare] individual brains across scales allows us to answer questions about how we are different, and how we think differently."

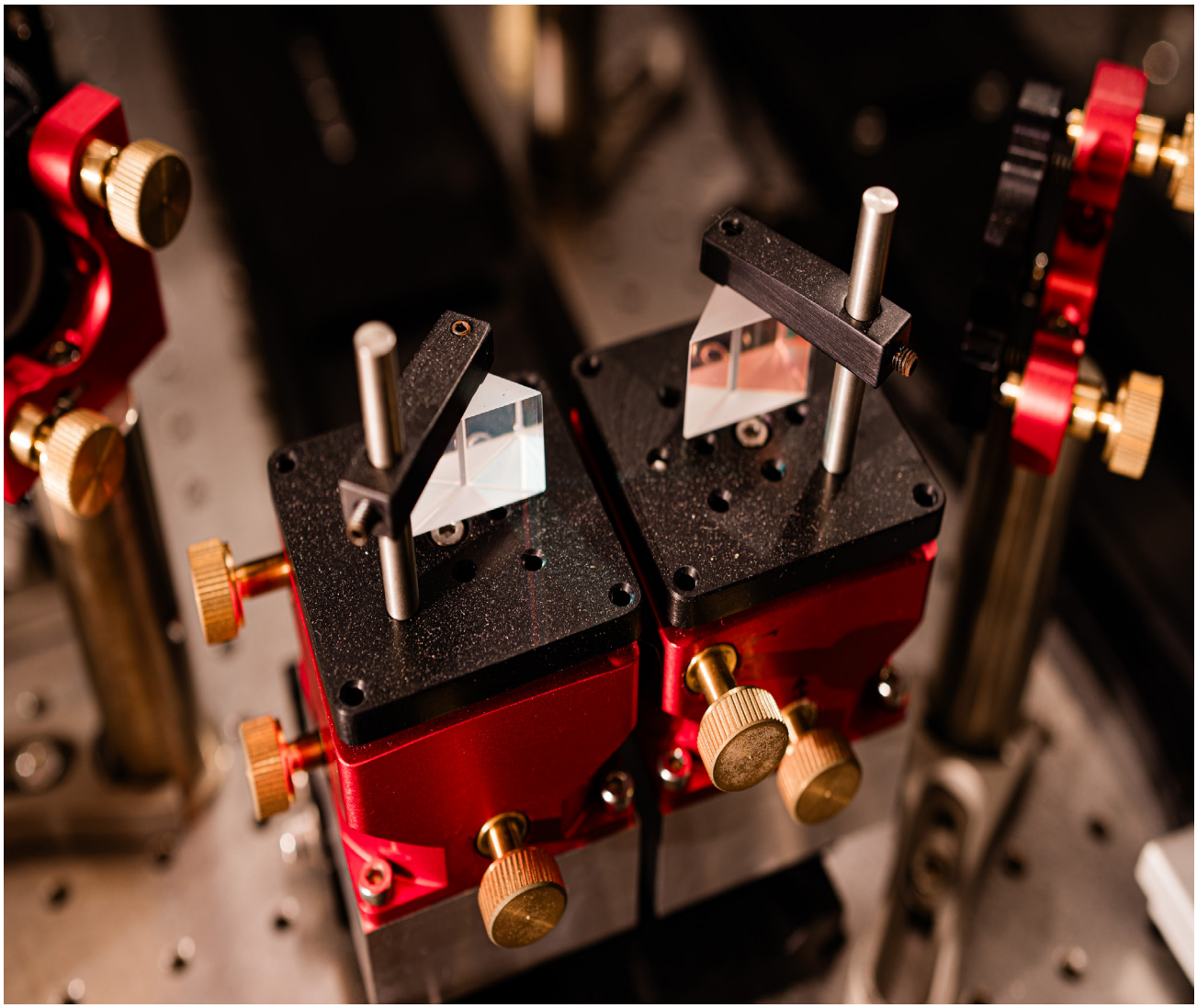


Photo taken in Jerry Chen's lab. Credit: Christopher McIntosh

FACULTY SPOTLIGHT

HOW ULTRAFAST LASERS DEVELOPED IN MICHELLE SANDER'S LAB ARE SPEEDING UP BIOLOGICAL RESEARCH

by Kat J. McAlpine, Photos by Christopher McIntosh

Michelle Sander and her lab group at Boston University are seeking out new ways to build ultrafast lasers – lasers that emit such short-lasting pulses of light that their duration is difficult to fathom.

"I'm particularly interested in developing lasers on the femtosecond scale – a fraction of a second so small that its ratio is the same as one second to 32 million years," Sander says.

At these incredibly ultra-short timescales, Sander and her team are interested in the way light and matter interact. "When you shine light onto a material, you can characterize that material or change its properties," she says. "Light pulses can travel up to 300 nanometers within one femtosecond – a distance that's just a fraction of the width of a human hair – and create new phenomena that we don't see with longer-lasting or continuous laser light. We're working to design novel lasers that can emit these femtosecond pulses and to better understand the formation of these pulses and their effect on materials."

Sander, who at BU is a faculty member at the Photonics and Neurophotonics Centers and a College of Engineering associate professor of electrical and computer engineering, launched her lab more than 10 years ago after earning a PhD from Massachusetts Institute of Technology. But her career in engineering began at an early age. When she was a young student growing up in Germany, she remembers being fascinated by physics and technology during high school.

"There was a program aimed at recruiting more women in STEM fields, offering hands-on experiences in different types of labs," she says. "At that time, less than 5 percent of electrical engineering students were women." Sander jumped at the opportunity to intern in an electrical engineering lab at a local university, which helped cement her interest in the field. After high school, she started taking university-level engineering courses in Germany, and then earned a Fulbright fellowship that brought her to the Georgia Institute of Technology in Atlanta for graduate studies.

Today, at BU, Sander's team is looking beyond fundamental research to develop practical, real-world applications based on various lasers and further elucidate what these lasers can reveal about different materials. She considers her team to be a "research family," made up of many deep connections within the group that have developed through intense discussions about science and common goals.

"I think it's really important to have an atmosphere where people can get direct feedback and also communicate directly with others," says Sander, who is also affiliated with BU's biomedical engineering and materials science and engineering departments. "Every paper a lab member publishes, every presentation a student gives at a conference, these are really exciting and meaningful moments for our team."

She invites innovation and creativity into the lab and says it's hard to predict which direction the team's research will go in – she and her team are always open to new ideas and external partnerships.

When optics, physics, and biology collide

Right now, the team is excited about several multi-institutional collaborations that apply their expertise towards biological applications.

For example, the Sander group has been designing photothermal microscopes that use mid-infrared light to detect chemical signatures. As mid-infrared light is absorbed by a sample, the material is excited and heated up. Different materials feature unique characteristic responses, absorbing or losing heat more quickly or slowly depending on their chemical makeup and properties, which allows for complex structures to be analyzed and visualized. One such use for photothermal microscopy is the imaging of cells and biological structures.

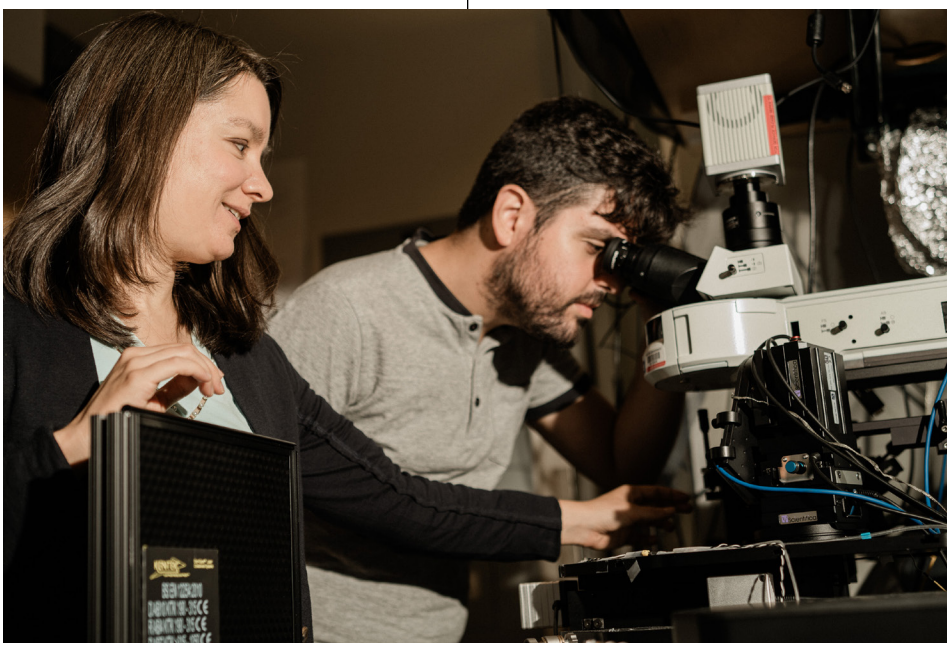
But many conventional microscopes struggle to image cells and tissues inside water or other media without labeling cells with stains or fluorescent dyes. "If you have a lot of similar materials under the microscope, how do you differentiate between biological structures and the medium they're in?" Sander says. "Water has strong background absorption at mid-infrared wavelengths, which can easily mask the signal from interesting biological features."

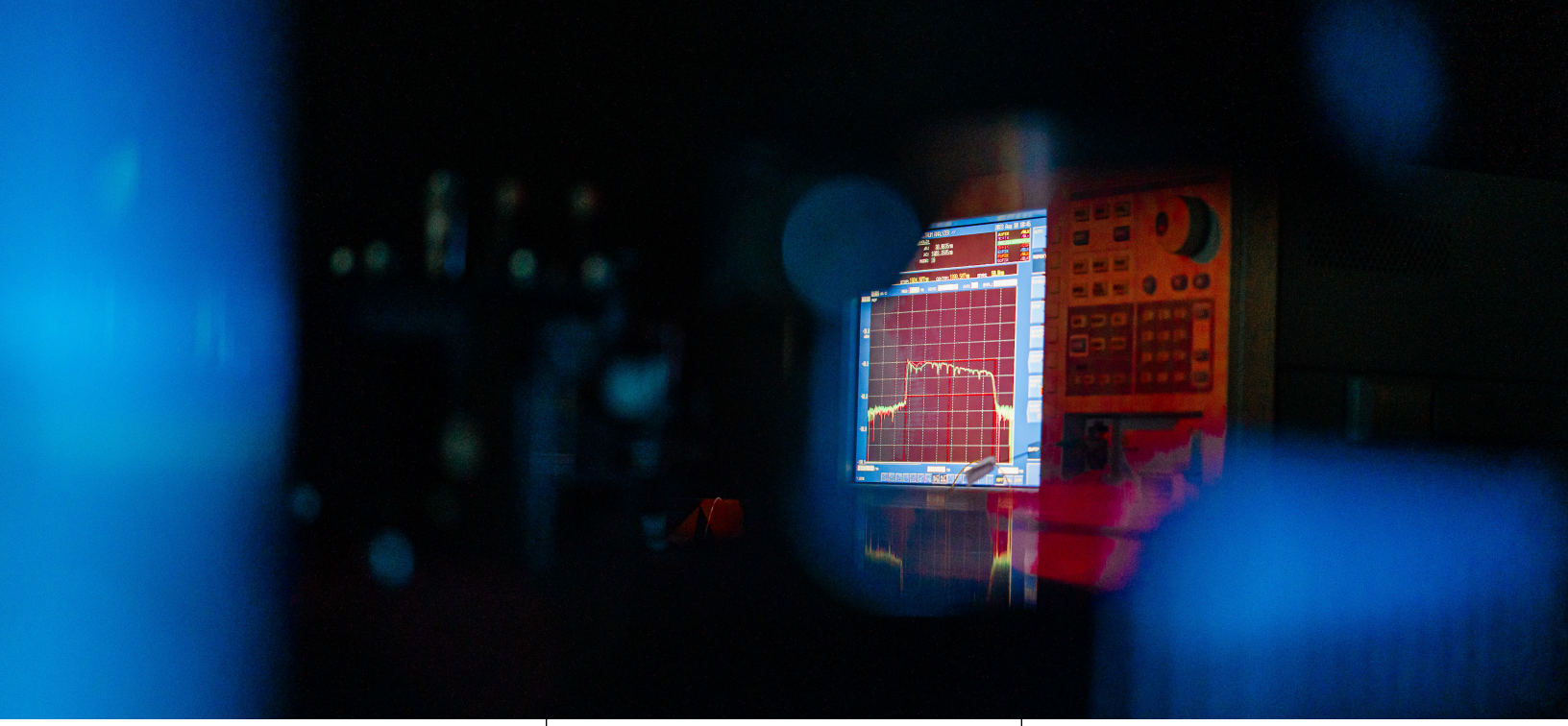
By adding a shorter-wavelength laser pulse to this imaging system, Sander and her team have enhanced the spatial resolution of mid-infrared microscopy in a label-free manner.

"This technology has allowed us to investigate chemical content in a variety of samples for biological and material science applications, as well as visualize heat transfer dynamics across a variety of interfaces," says Panagis Samolis, a postdoctoral associate who first came to Sander's lab as an undergraduate researcher in 2016 before staying on with the team to earn his PhD. "It's been a very dynamic imaging technique with a lot of room to explore both optics as well as the fundamental physics of heat transfer."

They recently used their approach to provide a closer look at axons – long, tendril-shaped parts of neurons that transmit signals to neighboring cells – in their natural watery environment. Their findings are forthcoming in Analytical Chemistry and will be highlighted on the front cover. Given that cells throughout the human body are about 70 percent water, these new capabilities could have exciting implications for biological research.

For another project, her team is working with collaborators at the Swinburne University of Technology in Australia. "We're looking at





fibroblast cells, which are these cells that form connective tissues," Sander says.

In humans and animals, fibroblast cells make up the matrix of collagen that connects various tissues. "Using our photothermal system, we were able to image fibroblasts in their natural medium of collagen, revealing the cell and nucleus membranes on the scale of nanometers," she says. "In our imaging technique, the fibroblasts' cell membranes act like a thermal barrier, allowing us to better differentiate the structure of the cells and achieve heightened detail based on their heat diffusion dynamics."

New frontiers for fiber-based laser imaging

Another major focus of the lab, originally supported by an Air Force Young Investigator Award from the Air Force Biophysics program, has been developing new fiber laser techniques to probe and control the activity of neurons. Fiber lasers are extremely fine strands of silica that can transmit light from one end to the other without losing much energy and power. They are the backbone of modern-day fiber-optic telecommunications and are also an important tool used by biologists to image precise areas of biological tissues and cells.

"We are collaborating with groups in Italy from their National Research Council in Bologna (Consiglio Nazionale delle Ricerche) and the University of Bari. They are the experts in neuronal biology, and we are the experts in imaging and probing. Together, we are working to understand how brain cells develop and communicate with each other," Sander says.

To enable a detailed view into electrical activity between neuronal cells, and to ensure robust control while modulating brain cell activity, Sander's team has developed fiber lasers that produce longer wavelengths (two microns) than more conventional fiber lasers.

In crayfish and other animal models, "we are using our two-micron fiber lasers to trigger neuronal activity through tiny changes in temperature caused by light," Sander says. "Most researchers to date have focused their attention on stimulating axons, but we have instead focused on synapses," or the junctions between neurons that send and receive electrical and chemical signals between cells. "We found that by modulating the synapse using our laser, rather than the axons, we can use less energy to induce neuronal activity."

Ultrafast, high-energy lasers at the two-micron wavelength can also be converted to shorter wavelengths, enabling a fiber-based light source for two-photon microscopy, an imaging technique with enhanced excitation localization, improved

"EVERY PAPER A LAB MEMBER PUBLISHES, EVERY PRESENTATION A STUDENT GIVES AT A CONFERENCE, THESE ARE REALLY EXCITING AND MEANINGFUL MOMENTS FOR OUR TEAM."

– Michelle Sander

depth, and spatial resolution than more traditional microscopy. Sander's lab is currently working with a broader BU team to apply their amplified two-micron fiber laser system to enable two-photon voltage imaging of neuronal activity in mice.

"Ultrafast fiber lasers can be described by a single, universal math equation, but in experiments, rich, complex, and sometimes extreme or even mysterious light dynamics can be generated from these lasers," says Shutao Xu, a fifth-year PhD student in Sander's group. "I enjoy designing and optimizing these fiber laser systems, trying to understand each unique system's operation in detail, and the overall process of organizing random and chaotic light into stable, coherent, ultrashort pulses. I'm very excited about seeing our lasers applied to two-photon imaging setups so that scientists can look deeper into biological tissues at a faster speed."

Ideas, ambitions, and genuine care

In the lab and in the classroom, Sander says she is fueled by everyday moments of learning and inspiration, and by mentoring up-and-coming engineers. To date, her lab has brought more than 30 undergraduate researchers onto their team. "When you see a lab member or student struggling to make a breakthrough, and then all of a sudden they get it, and you see the light in their eyes, it's extremely rewarding."

She's also recruited students from other countries, including Australia, Germany, and France, to visit and join her lab. "Creating a working environment where there is perspective from other cultures and from external institutions is very enriching for our team" she says. "I think BU has been a great place for my team to be – with all BU's interdisciplinary centers, there are so many opportunities locally and abroad to network with colleagues from other fields. It feels unique to be in an institution that creates so many different points of contact for researchers to explore."

Members of her team say they have developed genuine care and appreciation for their teammates in the lab and beyond work on a personal level. "In this environment, I've found myself able to openly share ideas and ambitions, as well as find and keep the self-motivation needed throughout my [eight-plus] years in Dr. Sander's lab," Samolis says. "She always leaves room for her students to find their pathways as future scientists while providing support and accommodating our individual characters, strengths, and weaknesses."

Supporting new research directions between faculty is an important component of the *Center's mission: to build and support an interdisciplinary community that can develop and broadly deploy impactful photonics technologies in the neurosciences to advance our understanding of how the brain works in health and in disease.* Neuroscientists are dependent on new technologies that enable them to measure previously inaccessible aspects of brain function and structure. Scientists advancing photonics methods are on the lookout for impactful applications to motivate and direct their technological developments. The Center aims to connect the technology developers with the users to accelerate the advancement and early adoption of novel photonic methods. The following pages describe seven such innovative efforts that the Center is supporting.

Neurophotonics Center-Supported Research Projects

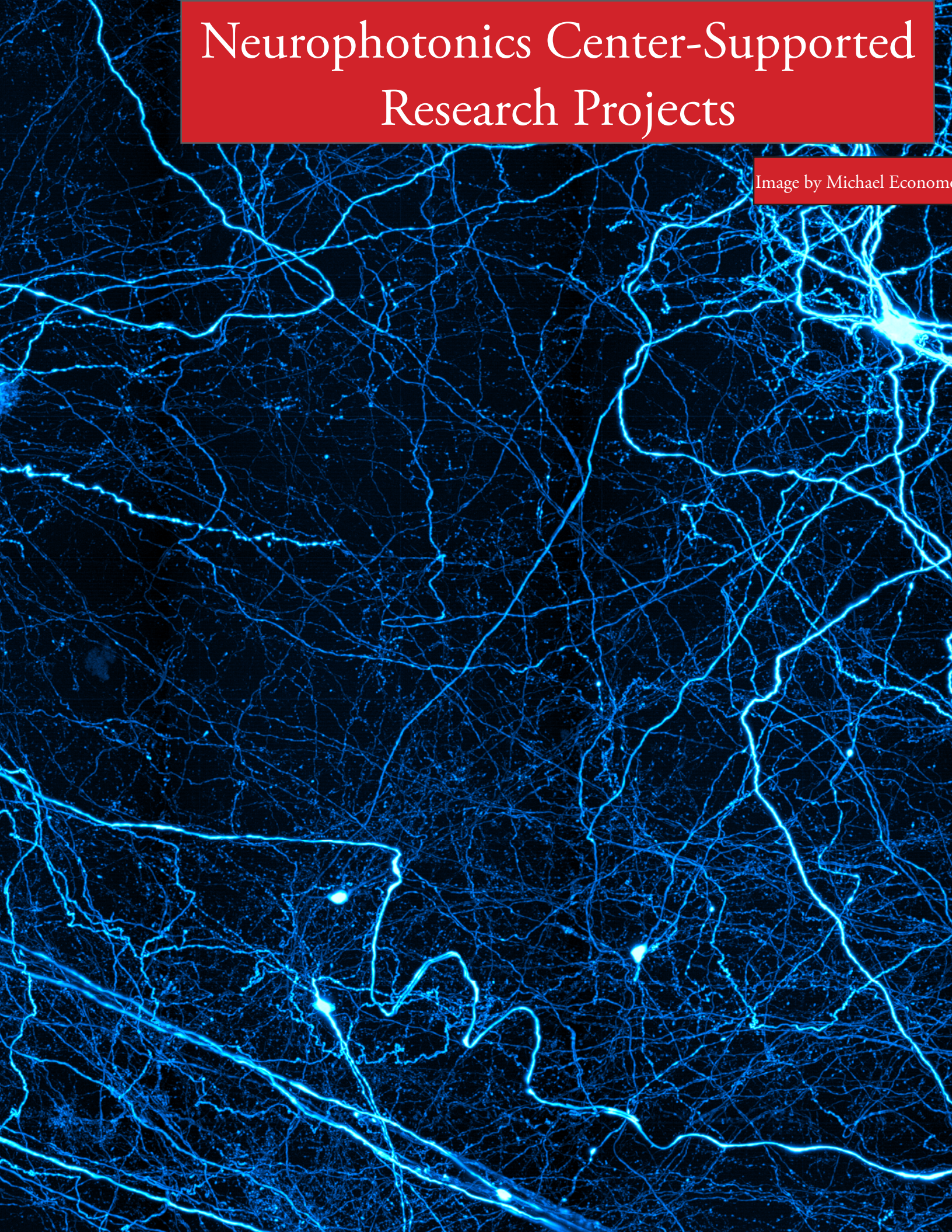
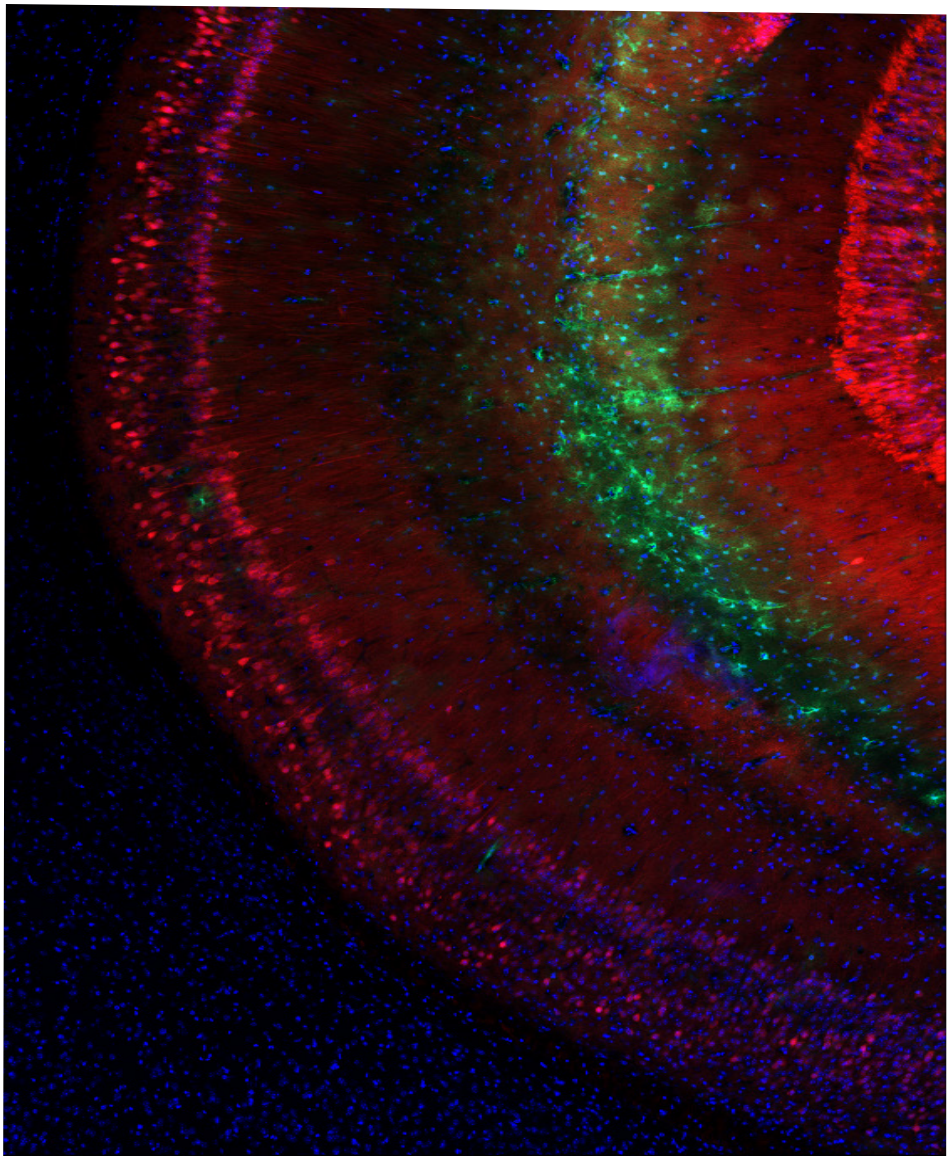


Image by Michael Economo

Visualizing Memories in the Rodent Brain

Memories thread and unify our sense of being. In recent years, the labs of **Steve Ramirez** and **Benjamin Scott** have pioneered novel genetic and imaging tools to manipulate and visualize memories in the rodent brain. The lab focuses on areas known to be involved in learning and memory, including the hippocampus, and uses activity-dependent strategies coupled with calcium sensors to enable the study of memory with cellular resolution. In one line of work, the lab has used multiphoton imaging to study which cells in the brain will become memory-bearing cells, how their activity is modified over time and experience, and whether or not memories leave a physiological signature in the brain. This multiphoton approach will provide novel insight into how patterns of activity in cells drive the formation and retrieval memories, as well as to causally link their activity to cognition and behavior. The overarching goals of the lab include studying defined sets of memory-bearing cells and restoring health to the brain, while also providing novel avenues for molecular, circuit, and systems-wide interrogation of learning and memory.

Using the NPC's 2P system, the team has first successfully imaged hippocampus cells processing discrete memories and tracked their activity over days-long timespans. Moreover, they recently have identified physiological signatures that predict which brain cells will become memory-bearing cells (unpublished).



They are currently delineating the in vivo dynamics of memory-bearing cells to study what makes their properties different from non-memory-bearing cells, as well as relating their activity to behavior.

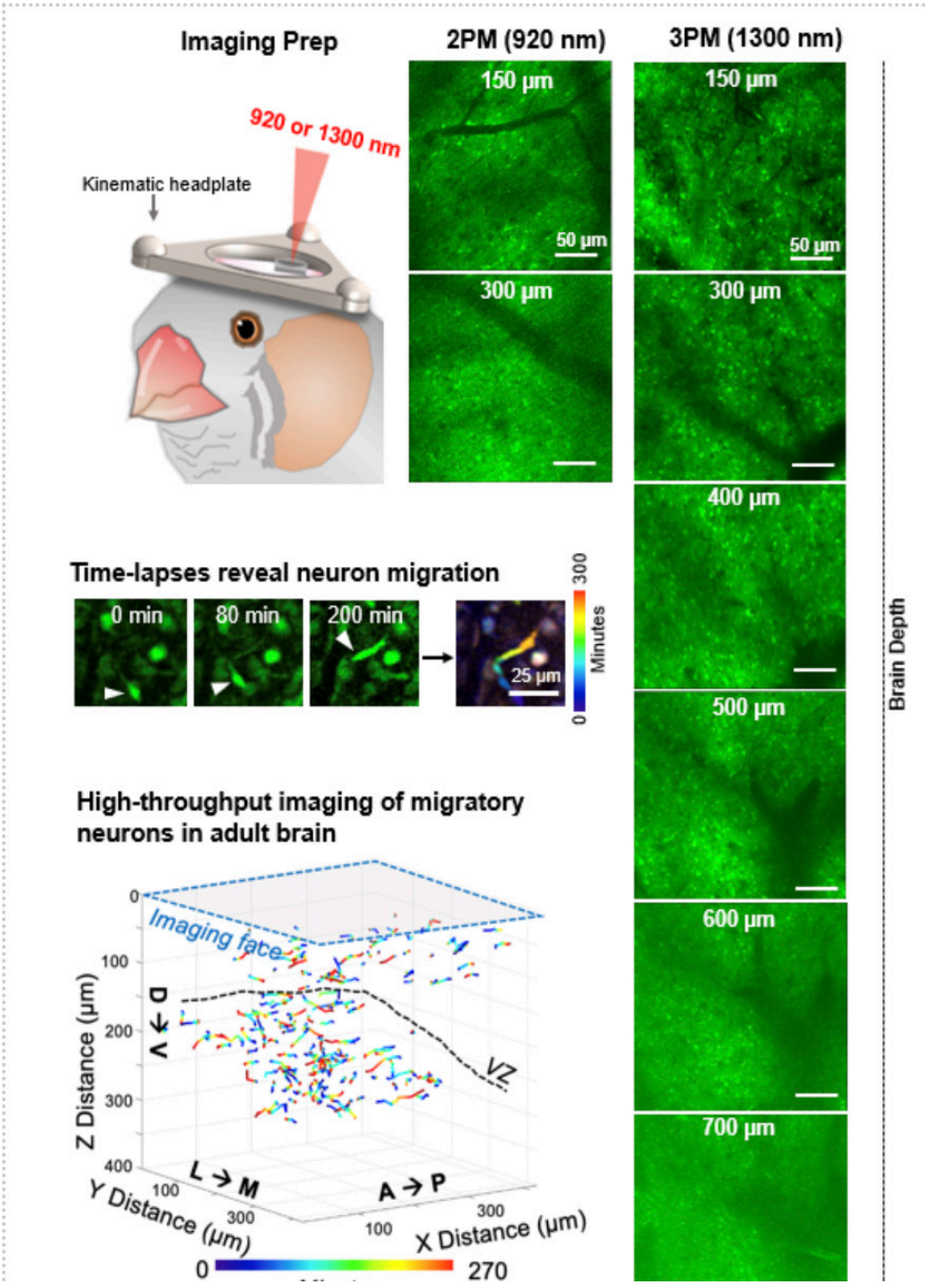
In vivo imaging of neuron migration in the adult brain

Adult neurogenesis, the addition of new neurons to the mature brain, involves three main stages: cell birth, migration, and integration. Migration is a critical component of adult neurogenesis, involving the navigation of new neurons from their birthplace to the functioning circuits where they will integrate into. Little is known about the migratory mechanisms that allow for the dispersion of new neurons throughout the adult forebrain due to the technical challenges of observing this phenom-

enon in vivo.

The Scott lab aims to learn more about adult neurogenesis by applying advanced imaging tools to characterize neuron migration in the brains of transgenic songbirds. In songbirds, new neurons are added throughout the brain, including to circuits involved in learning and memory. By using the NPC's Bruker Investigator two-photon microscope (2PM) in transgenic songbirds that express GFP in migrating neurons, Ben Scott and his team discovered a form of diffusion-like migration that underlies the formation and maintenance neural circuits in the adult brain (Shvedov et al. 2023, bioRxiv).

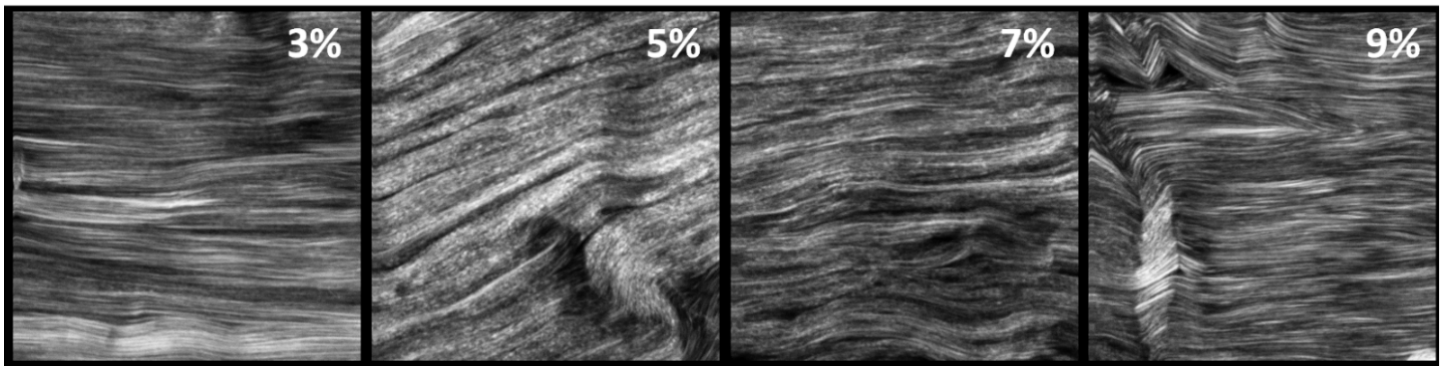
More recently, Scott, with collaborator **Jerome Mertz**, has been exploring the potential of three-photon microscopy (3PM) to study adult neurogenesis deep within the brain. Whereas 2PM is limited to the first several hundred micrometers below the brain surface, 3PM enables optical access to brain depths beyond a millimeter. In collaboration with Jerome Mertz's group, which has recently developed a novel, custom-built 3PM in the NPC facility, Ben Scott's team demonstrated deep brain cellular resolution imaging in transgenic songbirds. They were able to image large populations of putative migratory neurons at depths exceeding 700 microns below the brain's surface. In ongoing experiments, this team will use 3PM to study how new neurons integrate into deep brain structures in the adult. This work demonstrates the exciting potential of multiphoton microscopy to yield fundamental knowledge of circuit development and plasticity in the adult brain. In the future, these insights may lead to potential new therapies for neurodegenerative disorders.



Extra-Cellular Matrix Remodeling with Tissue Explant Models

Tendons and ligaments are essential to efficient movement of the musculoskeletal system, allowing us to perform activities of daily living as well as exercise and sport. This function is entirely dependent on the tissue's extracellular matrix, which consists primarily of intricately organized collagen. Collagen fibers mitigate stress directly on cells through their dynamic mechanical behavior but can also exhibit microstructural damage due to excessive use. Due to its importance, the structure of the tissue is maintained through a delicate balance of protein synthesis and breakdown. **Brianne Connizzo** and her team study the process of extracellular matrix remodeling through the use of tissue explant models, which enable real-time application of exercise to live tissues and examination of changes to tissue structure over time. Using these models, they have been exploring the types and intensities of mechanical stress that lead to tissue microdamage.

Using second harmonic generation (SHG) imaging, members of the lab can quantify the organization of the collagen structure in tendon explants that have been subjected to mechanical loading in culture and assess remodeling of the tissue over time. When subjected to cyclic tensile loading over one week in culture, the presence of tissue 'kinks' can be visualized with increasing strain level, indicating increased tendon microdamage that has not been repaired (Fig. 1, bottom). This technique has also been used to verify the lack of microstructural damage after tissues are subjected to acute compression injury (Fig. 2, right) in both young and aged samples. The young tissues did exhibit significant matrix turnover (production of new matrix components and matrix-degrading

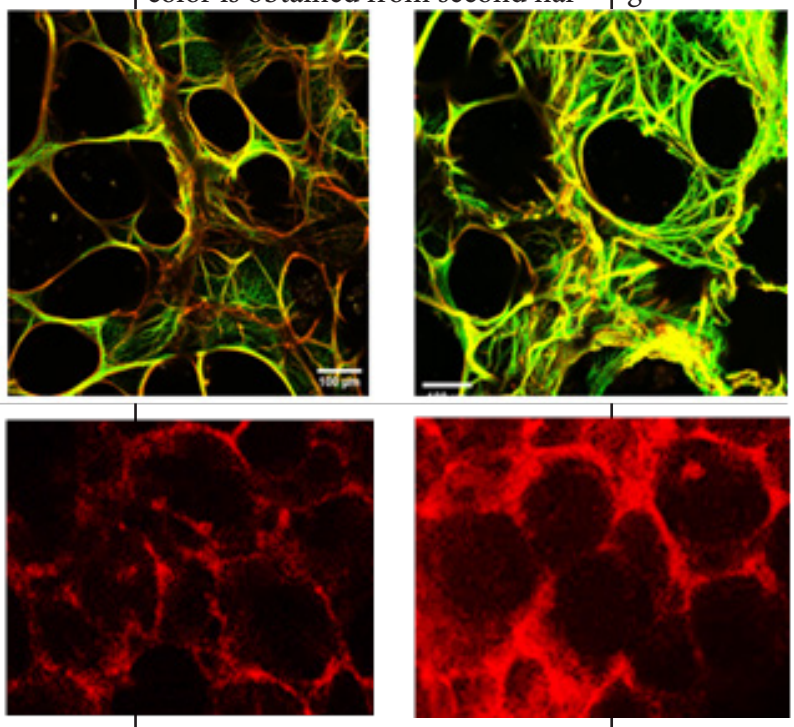


enzymes), and adaptations that suggest matrix remodeling through gene expression. However, this did not result in macroscale changes to collagen structure, suggesting insufficient time to remodel or lack of stimulus to make significant structural changes. Together, these data help the lab to identify which types of loading are beneficial to tendon health and which could lead to injury or disease.

Ultimately, the lab wants to use this information to develop strategies to better maintain tissue function over lifespan, keeping us active and healthy for longer.

Imaging to Enhance Lung Tissue Mechanobiology

The lung is a complex mechanical organ designed to provide gas exchange for the body. With every breath, the soft and delicate tissue components and cells of the lung experience stretching. While stretching the extracellular matrix provides the elasticity needed for gas exchange, cells in the lung respond to cyclic inflation and deflation by mechanotransduction. The **Suki lab** focuses on understanding how mechanical forces affect the lung extracellular and cellular components. The lab has built various tissue and cell stretcher devices that can be placed under the microscope for imaging normal and diseased tissue before, after and during stretch. The images in the top row of the figure show human lung parenchymal tissue slices from a healthy donor (top left) and a donor with idiopathic pulmonary fibrosis (top right). The red color is tissue autofluorescence corresponding mostly to elastin whereas the green color is obtained from second harmonic generation that exclusively visualize type I collagen. There is a noticeable difference in collagen content and organization between the healthy and the fibrotic lung tissues. In another study, the lab examined the effects of simulated coughing by stretching mouse lung slices using a stretcher device. Epithelial cells were labeled to visualize mitochondrial reactive oxygen species (ROS). Images in the bottom row demonstrate that while there is little ROS following normal stretching mimicking calm breathing (bottom left), coughing that induces significantly larger mechanical stresses, substantially upregulated mitochondrial ROS (bottom right).



Studying the lung at cellular resolution in real-time is essential in understanding the dynamic pathogenesis and treatment response in pulmonary diseases. While there has been recent progress in intravital imaging, optical imaging of the lung during active respiration and circulation has remained an unmet need. In this study, **Hadi T. Nia** introduces the crystal ribcage: a transparent ribcage that (i) allows truly multiscale optical imaging of the lung in health and disease from whole-organ to single cell, (ii) preserves the 3-D architecture, air-liquid interface, cellular diversity, and respiratory-circulatory functions of the lung, and (iii) enables the modulation of lung biophysics and immunity through intravascular, intrapulmonary, intraparenchymal, and optogenetic interventions. Utilizing these unprecedented capabilities on murine models of primary and metastatic lung tumors, respira-

tory infection, pulmonary fibrosis, emphysema, and acute lung injury, Nia's team probed how disease progression remodels the respiratory-circulatory functions at the single alveolus and capillary levels. In cancer, the team identified the earliest stage of tumorigenesis that compromises alveolar and capillary functions, a key state with consequences on tumor progression and treatment response. In pneumonia, they mapped mutual links between the recruited immune cells and the alveolar-capillary functions. They found that neutrophil migration is strongly and reversibly responsive to vascular pressure with implications for understanding of how lung physiology, altered by disease and anatomical location, affects immune cell activities. The crystal ribcage and its broad applications will facilitate further studies of real-time remodeling of the alveoli and capillaries during pathogenesis of nearly any pulmonary disease, leading to the identification of new targets for treatment strategies.

Rohin Banerji#, Gabrielle N. Grifno#, Linzheng Shi#, Dylan Smolen#, Rob LeBourdais#, Johnathan Muhvich#, Cate Eberman#, Bradley Hiller, Jisu Lee, Kathryn Regan#, Siyi Zheng#, Sue S. Zhang#, John Jiang, Riley Phil, Katrina Traber, Giovanni Ligresti, Joseph P. Mizgerd, Bela Suki, Hadi T. Nia, "Probing lung function at high spatiotemporal resolution using a novel crystal ribcage," Accepted in Nature Methods, 2023

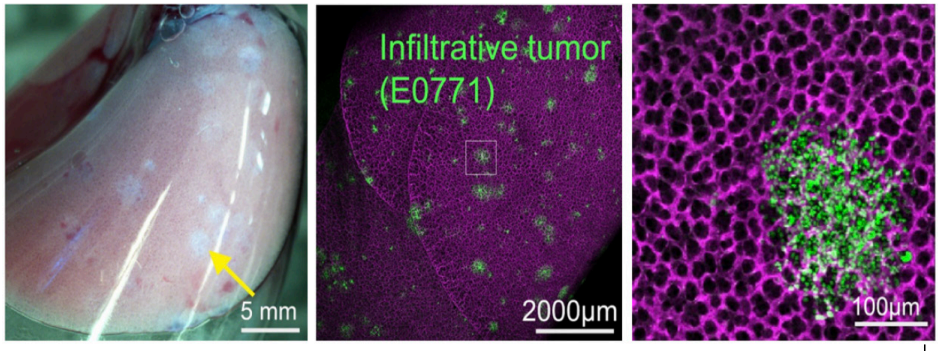


Figure 1. Left: whole-organ view of the lung with metastatic tumors inside crystal ribcage. Middle: whole-lobe view of multiple metastatic tumors in the lung. Right: the microscale view of a metastatic tumors occupying several air sacs.

A recently identified physical abnormality in fibrotic tumors is an elevated level of tensile and compressive solid stresses, defined as the mechanical stresses generated and transmitted by the solid components of the tumor within itself and surrounding tissues. These stresses are found to promote tumor progression and impede drug delivery by compressing blood vessels, promoting invasiveness of cancer cells, stimulating tumorigenic pathways, and inducing neuronal damage. However, the origins and consequences of solid stresses are still poorly understood due to a lack of appropriate measurement tools. Despite the recent progress in measuring solid stress ex vivo and in vitro, the in vivo measurement of solid stress in tumors is an unmet need. In this project, Nia's team used intravital multi-photon microscopy and optical coherence tomography at NPC to quantify the

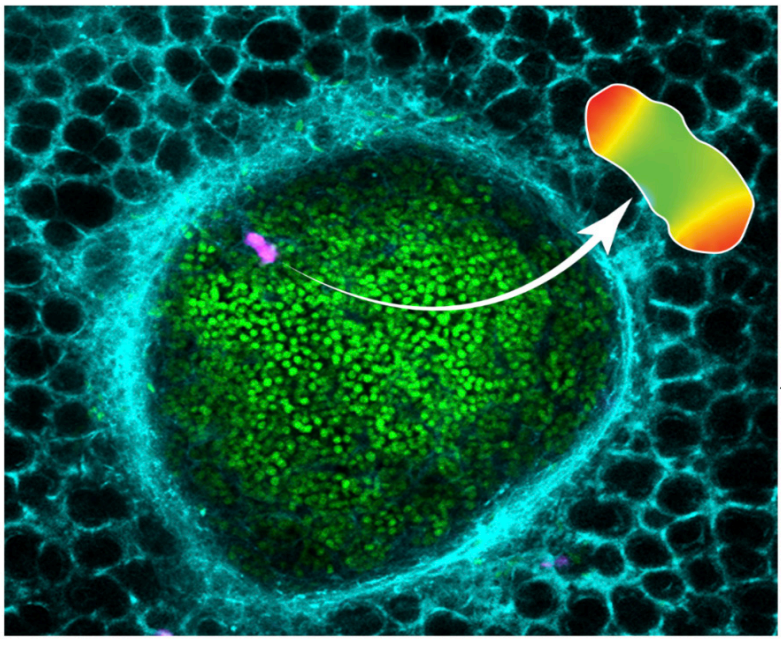
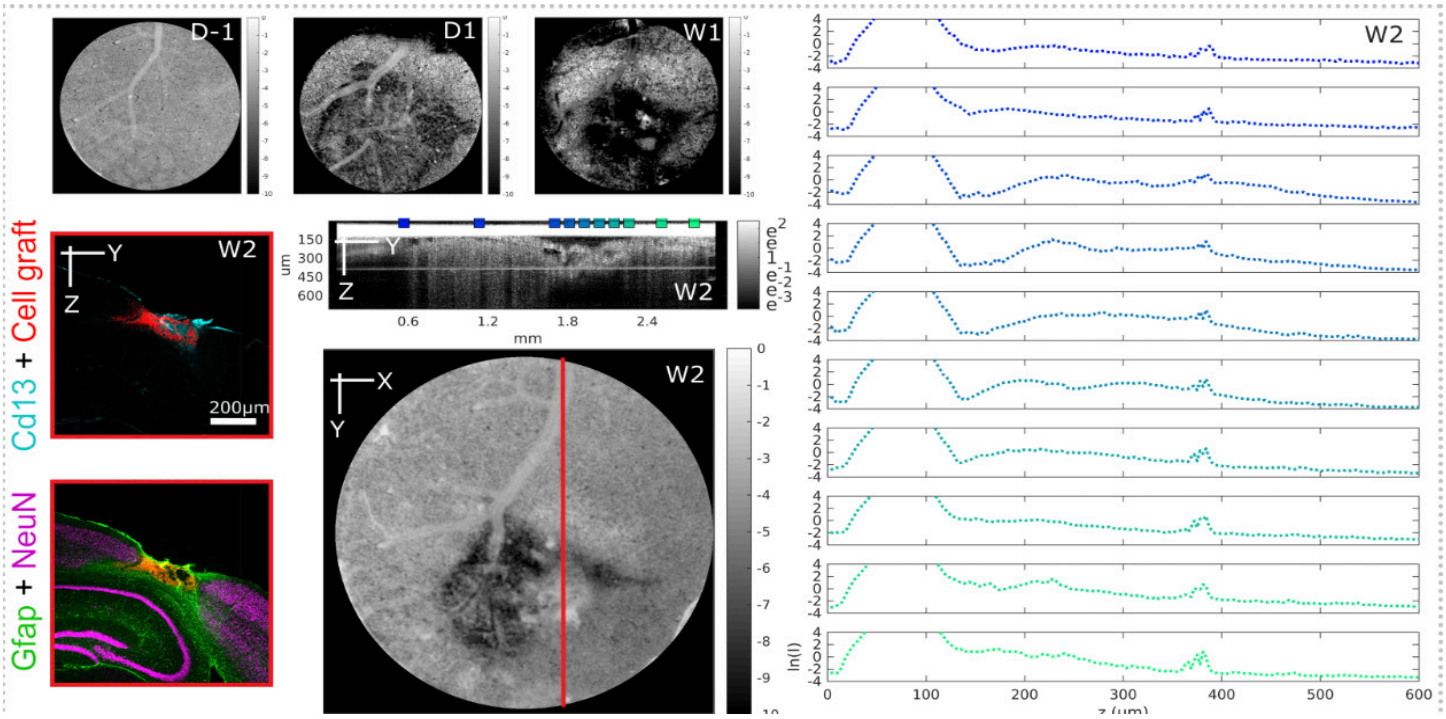


Figure 2: Our methodology enables measurement of solid stress in a metastatic lung tumor (individual cancer cells in green, lung capillaries in cyan) via deformable hydrogels (magenta). Mathematical modeling is used to quantify the solid stresses in the local region of the tumor.

intratumoral mechanical stresses in vivo. This will lead to better understanding of the origins and consequences of mechanical stresses and how they evolve in different stages of tumorigenesis.

Traumatic injury to the adult central nervous system

Such injuries as following stroke can cause damage to neural tissue which does not spontaneously regenerate. Thrombolytic therapies have proven to be effective as an acute intervention in ischemic stroke to prevent neural tissue damage, but many patients cannot receive these treatments for various reasons. Consequently, there is an important unmet need for new stroke treatments that can be applied beyond the narrow acute phase of injury. **Tim O'Shea** and his team are investigating new cell grafting strategies to direct glia-based repair to provide important cell support for neural circuit regeneration at stroke lesion cores. Understanding the functions of cell grafts and the mechanisms of glia repair requires the ability to monitor lesion phenotypes longitudinally but most pre-clinical cell grafting studies in stroke rely on immunohistochemistry taken at discrete timepoints to characterize outcomes. Seldom are the phenotypes of grafted cells, or the changes to lesion phenotype induced, tracked longitudinally *in vivo*. In this project Dr. O'Shea's team is collaborating with **David Boas** and his team to innovate the use of intravital imaging methods to track grafted cells and their effects on stroke lesions. As a first step the group has been refining the use of Optical coherence tomography (OCT) as a quick, label free, and noninvasive method for evaluating stroke lesion changes and vascular remodeling induced by cell grafts applied to a photothrombosis stroke model in vivo. Detailed multicellular immunohistochemistry is being used to correlate the unique signals detected by OCT with specific lesion compartments as well as the cell and molecular features of graft-derived glia repair. Next steps in this project will involve using two photon microscopy (2PM) to track numbers and phenotypes of reporter labeled cell grafts and tracer labeled vasculature. The new protocols developed by this team will enable powerful techniques for non-invasively tracking cell graft morphology and functions *in vivo* as well as characterizing the dynamic changes in cortical stroke



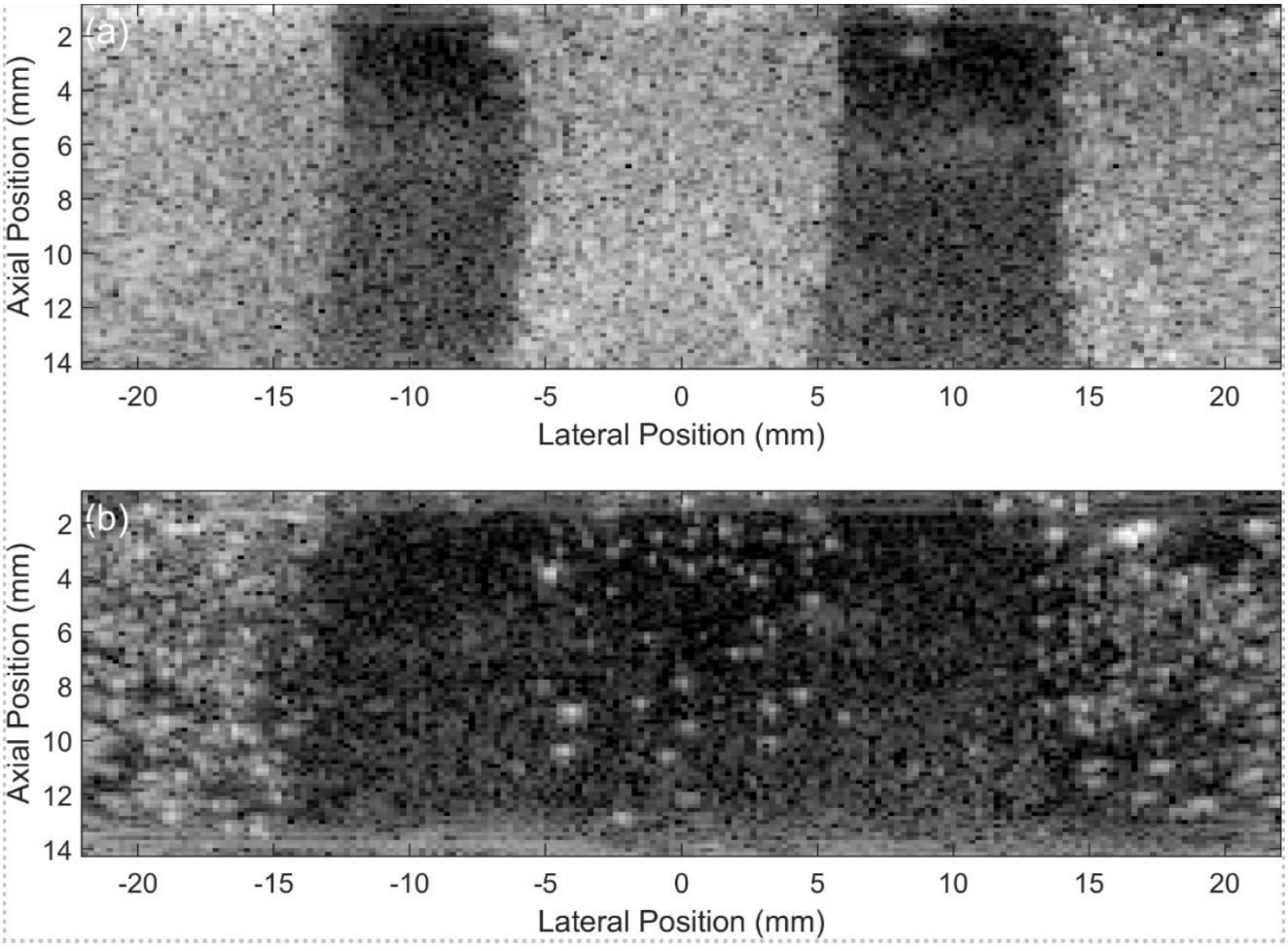
lesions associated with glia repair.

Imaging Abdominal Surgical Adhesions

Joyce Wong and her team have been developing molecularly targeted ultrasound contrast agents (microbubbles) for the early detection of abdominal surgical adhesions. Adhesions are deposits of fibrous scar tissue that form in the peritoneal cavity after almost all abdominal surgeries and are linked to a number of long-term complications that include small bowel obstructions, female infertility (e.g. after C-section), and chronic abdominal and pelvic pain. The total annual cost of surgical adhesion-related complications was estimated to be as high as $5 billion in the US alone in 2008. Detecting and diagnosing abdominal surgical adhesions is a major clinical unmet, and traditional methods require surgery to detect adhesions, which ironically can create more adhesions, thereby setting off a vicious cycle of adhesion formation and pain.

The figure above shows images of the acoustic signal from microbubbles in an agarose phantom and is the result of a new collaboration between **Joyce Wong** and **Jerome Mertz**.

Ultrasound B-Mode Images of Bubbles in Agarose Phantom: (a). Ultrasound image of three agarose wells containing microbubbles. High contrast is likely due to multiple scattering. (b). Ultrasound image of three agarose wells containing bubbles at half the concentration as in (a). The multiple scattering has notably reduced in this image.



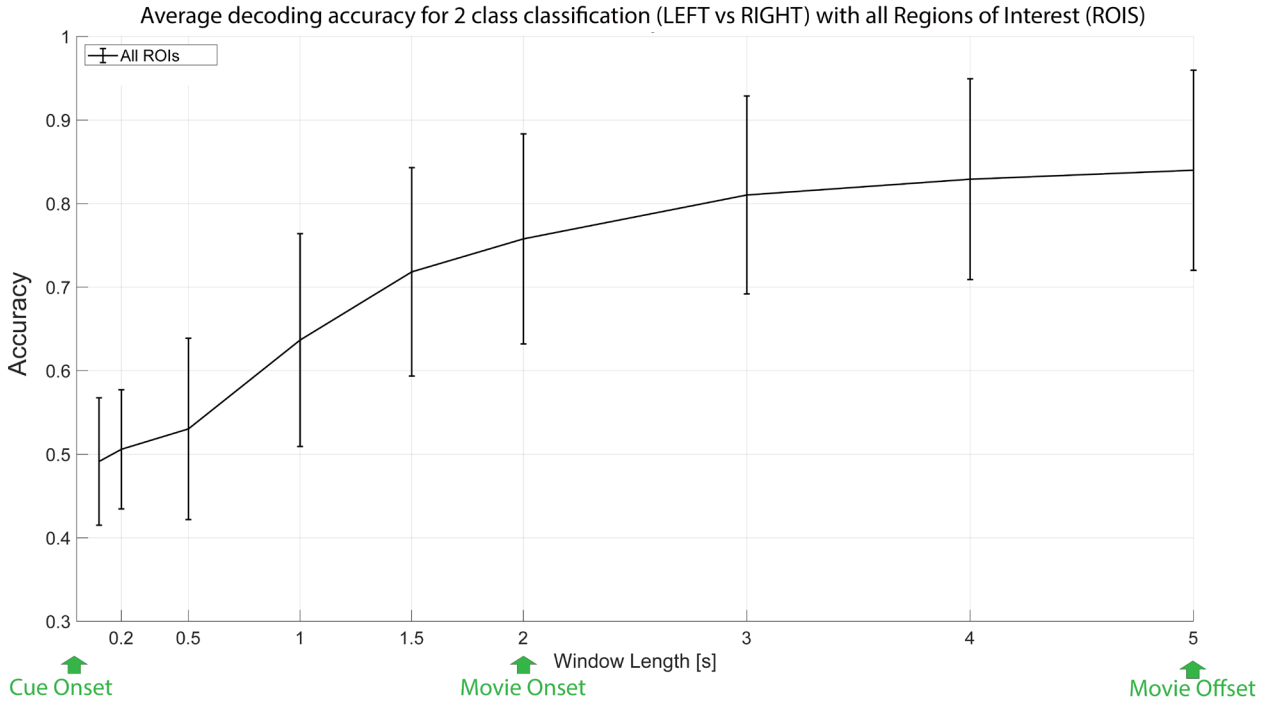
Supported fNIRS Projects

Decoding spatial location of attended audio-visual stimulus with fNIRS.
Matthew Ning , Sudan Duwadi, Meryem A. Yücel, Alexander Von Lühmann, David A. Boas and Kamal Sen.

Complex Scene Analysis (CSA), i.e., selectively processing important objects in a scene using audio-visual information, is essential for humans in everyday world. Although some humans perform this seamlessly, others, e.g., those with hearing impairments, ADHD and autism, are severely challenged by this task. Algorithms and devices for helping humans with CSA are currently under development. Knowing where the subject is attending in a scene can be used to inform assistive algorithms. The goal of this project is to decode where a subject is attending in a scene using fNIRS. In our experiments, we present 3 videos of individual talkers simultaneously at 3 locations (in front and 45 degrees to the left and right) and cue subjects to attend to one of the 3 locations. After each trial the subject is asked to identify the face and the words in the video at the attended location. Simultaneously, we measure fNIRS signals, and then use machine learning to classify the response into left and right (2-class) or left, center and right (3-class). In subjects who performed well in the task, we found robust decoding of attended location. Moreover, we found that the frontal eye field (FEF) region of the brain makes a high contribution to the decoding performance. Our results suggest that fNIRS can provide a powerful extension in brain machine interfaces to decode attended location in a scene.

High-density, Multi-distance fNIRS Improves Detection of Frontotemporal Activation
Jessie Anderson, David Boas, Mohammad Zaman

Use of functional Near-Infrared Spectroscopy (fNIRS) to detect frontotemporal activation demonstrates great potential as a tool to probe psychiatric disorders [1] and with greater accessibility for low-and-middle-income countries than the neuroimaging gold standard [2]. The fNIRS systems most commonly used have sparse grid-pattern optode arrays across the frontal region with 30mm source-detector channel length; this relatively low spatial resolution has the risk the miss the brain activation area [3]. Enabled by fNIRS' technology advancements, we have designed a novel multi-distance (33mm and 19mm), high-density (HD) hexagonal optode array and directly compared its detection of frontotemporal activation to that of a standard single-distance (30mm), sparse grid array to quantify expected improvements afforded by our HD array. Both arrays include eight 10mm short-separation channels for regression of superficial tissue signal. Monte Carlo photon migration simulations [4] demonstrate improved sensitivity, localization error, and resolution of the HD design over sparse array. Systems for each array were built via 3D ninjaCaps [5] populated with NIRx NIRSport 2 systems and both worn by each of 15 healthy adult subjects performing a Word-Color Stroop task modeled after Levels 1 and 3 of an existing paradigm [6]. Signal processing follows standard NIRS procedure: prune channels with low SNR, convert intensity to optical density, apply motion artifact correction [7],



apply low-pass filter, derive oxy-deoxy- and total hemoglobin via Beer-Lampert Law [8], and perform generalized linear model regression to produce hemodynamic response function [9]. To compare each array's ability to detect functional activation, t-testing was performed for each channel at the subject level using HbO mean and standard deviation across task blocks. Our regions of interest (ROIs) on both the left and right extend from the dorsolateral prefrontal cortex to the temporal region [10]. Maximum t-values per subject per ROI were averaged to produce group-level results for each optode array, and arrays compared via paired t-test across subjects. We have successfully demonstrated via group-level t-test analysis of empirical data that our HD fNIRS array detects greater frontotemporal functional brain activity during Incongruent Word-Color Stroop compared to a traditional sparse array. A surprising result is that this improvement in HD seems to be provided by the measurements at 19 mm separations providing greater statistically significant measures of the brain activation. We are presently extending the analysis to see if further improvements are obtained with image reconstruction. This work helps lay the groundwork for improving future studies probing psychiatric disorders with fNIRS.

[1] Ehlis, Ann-Christine, et al. "Application of functional near-infrared spectroscopy in psychiatry." Neuroimage 85 (2014): 478-488.

[2] Blasi, Anna, et al. "fNIRS for tracking brain development in the context of global health projects." Photonics. Vol. 6. No. 3. MDPI, 2019.

[3] Novi, Sergio Luiz, et al. "Integration of spatial information increases reproducibility in functional near-infrared spectroscopy." Frontiers in Neuroscience 14 (2020): 746.

[4] Aasted, Christopher M., et al. "Anatomical guidance for functional near-infrared spectroscopy: AtlasViewer tutorial." Neurophotonics 2.2 (2015): 020801-020801.

[5] von Lühmann, Alexander, et al. "Towards Neuroscience in the Everyday World: Progress in wearable fNIRS instrumentation and applications." Optics and the Brain. Optica Publishing Group, 2020.

[6] Jahani, Sahar, et al. "Attention level quantification during a modified stroop color word experiment: an fNIRS based study." 2015 22nd Iranian conference on biomedical engineering (ICBME). IEEE, 2015.

[7] Jahani, Sahar, et al. "Motion artifact detection and correction in functional near-infrared spectroscopy: a new hybrid method based on spline interpolation method and Savitzky–Golay filtering." Neurophotonics 5.1 (2018): 015003-015003.

[8] Swinehart, Donald F. "The beer-lambert law." Journal of chemical education 39.7 (1962): 333.

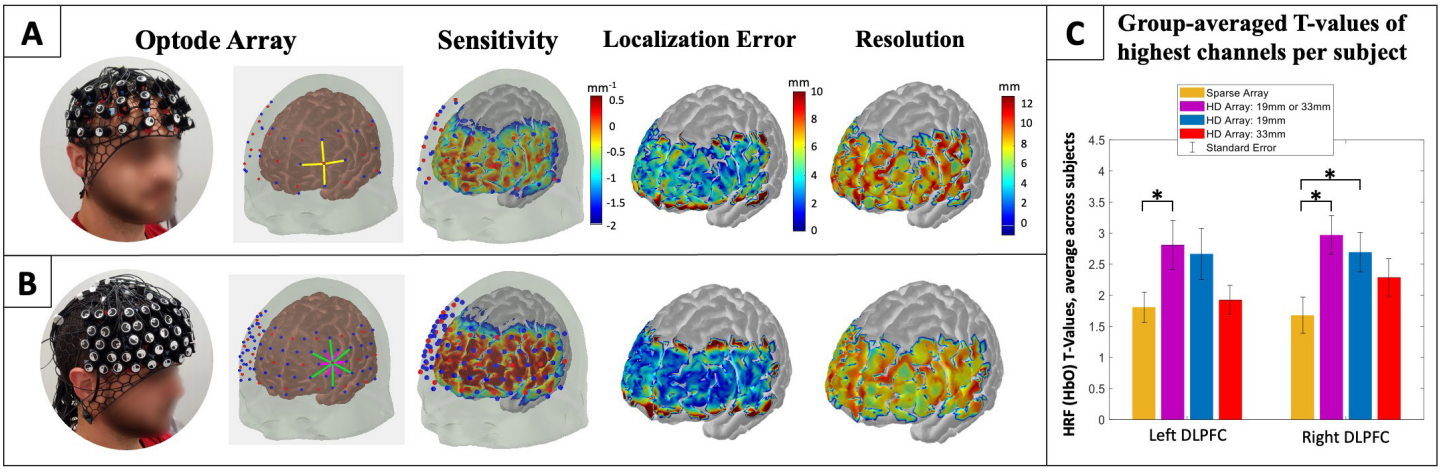
[9] Ye, Jong Chul, et al. "NIRS-SPM: statistical parametric mapping for near-infrared spectroscopy." Neuroimage 44.2 (2009): 428-447.

[10] Yennu, Amarnath, et al. "Prefrontal responses to Stroop tasks in subjects with post-traumatic stress disorder assessed by functional near infrared spectroscopy." Scientific reports 6.1 (2016): 30157.

fNIRS Investigation of Prefrontal Regions Associated with Single-task and Dual-task Walking in Healthy Adults and Parkinson's Disease

Rini Kaplan, Alice Cronin-Golomb

Significance/rationale: In Parkinson's disease (PD) there is reduced automaticity of movement. To com-



pensate, persons with PD (PwPD) allocate increased attention resources to the task of walking, which leads to difficulty engaging in secondary tasks (e.g., walking while talking).

Aim: While most studies using fNIRS for walking in PD have been restricted to lab-based experimental conditions, our work with fNIRS has focused on: 1) systematically working towards more ecologically valid experimental designs, and expanding on prior research by 2) capturing behavioral as well as walking data, and probing prefrontal cortex activity across a wider range of regions of interest.

Approach: We have developed a "varying baseline" protocol, which we believe is better at mimicking everyday conditions than are standard designs. In this protocol, there are 4 conditions: quiet standing, standing serial-3 subtraction (cognition), single-task walking, and dual-task walking (walking+serial-3 subtraction). The order of the conditions is randomized so that any of the other conditions can precede the condition of interest (e.g., quiet standing, standing serial-3 subtraction, or dual-task walking can precede single-task walking), resulting in 4 trials for each condition of interest for each baseline. Participants are assessed on both an oval overground track and on a treadmill. The fNIRS probe consists of 16 sources, 15 detectors, and 8 short-separation detectors covering 8 bilateral prefrontal regions of interest (ROIs).

Results: Preliminary results for the overground single-task walking condition of interest in people with PD (PwPD) revealed that from quiet standing baseline (i.e., rest) there is not activation in any prefrontal ROIs. By contrast, when starting from either the standing serial-3 subtraction or dual-task walking baselines, there is activation in all prefrontal ROIs.

Summary/conclusion: These findings suggest that baseline condition matters for fNIRS data. Specifically, switching from an active task (e.g., standing serial-3 subtraction, dual-task walking) to another active task (e.g., single-task walking) is effortful for PwPD, which is consistent with impaired set-shifting ability observed on cognitive tasks in PwPD.

fNIRS Measuring Changes in Oxygenated Hemoglobin Concentration in Prefrontal Cortex (PFC)
Regina Slutsky, Lou Awad

Background: Stroke-induced brain lesions result in deficits in the neuromotor control of walking. A compensatory shift from automatic to attention-demanding locomotor control is thought to underlie the markedly slow, asymmetric, and energetically effortful walking that is common after stroke. Our

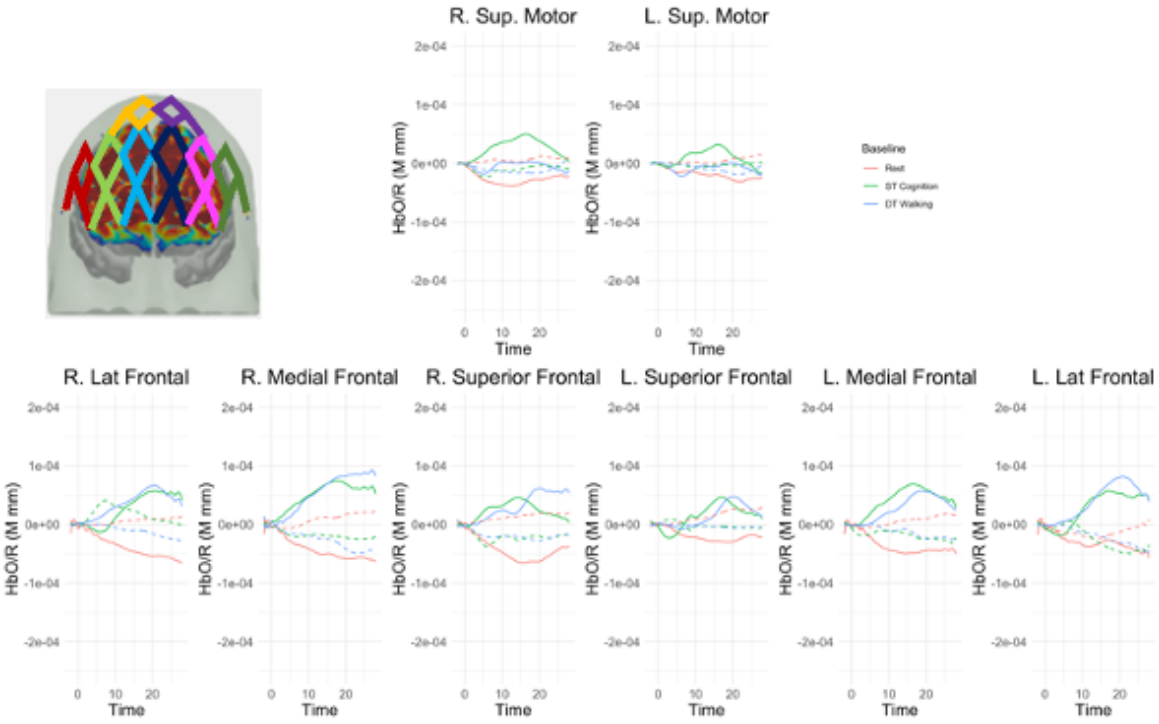


Figure 1. Results for the single-task walking condition in PwPD in each ROI. Solid lines=HbO; dashed lines=HbR. Red=quiet standing (rest) baseline; green=standing serial-3 subtraction (ST cognition) baseline; blue= dual-task walking baseline.

team is studying and developing the application of soft wearable robotic exosuits to overcome these neuromotor deficits. Exosuits use mechanical assistance to augment the residual force-generating ability by the paretic limb. Our previous work shows that compared to walking without an exosuit, exosuit-augmented walking is associated with faster, more symmetric, and more efficient walking. We believe that exosuit-assisted walking may influence selection of neural pathways involved in locomotor control. To test this hypothesis, we are using functional near-infrared spectroscopy (fNIRS) to evaluate the effects of the soft robotic exosuit on the neural control of walking, predicting an exosuit-induced shift toward more automatic walking. Moreover, to facilitate the clinical translation of this work, we are also studying the effects of two different exosuit tuning approaches: automaticity-tuning that aims to maximize the reduction in

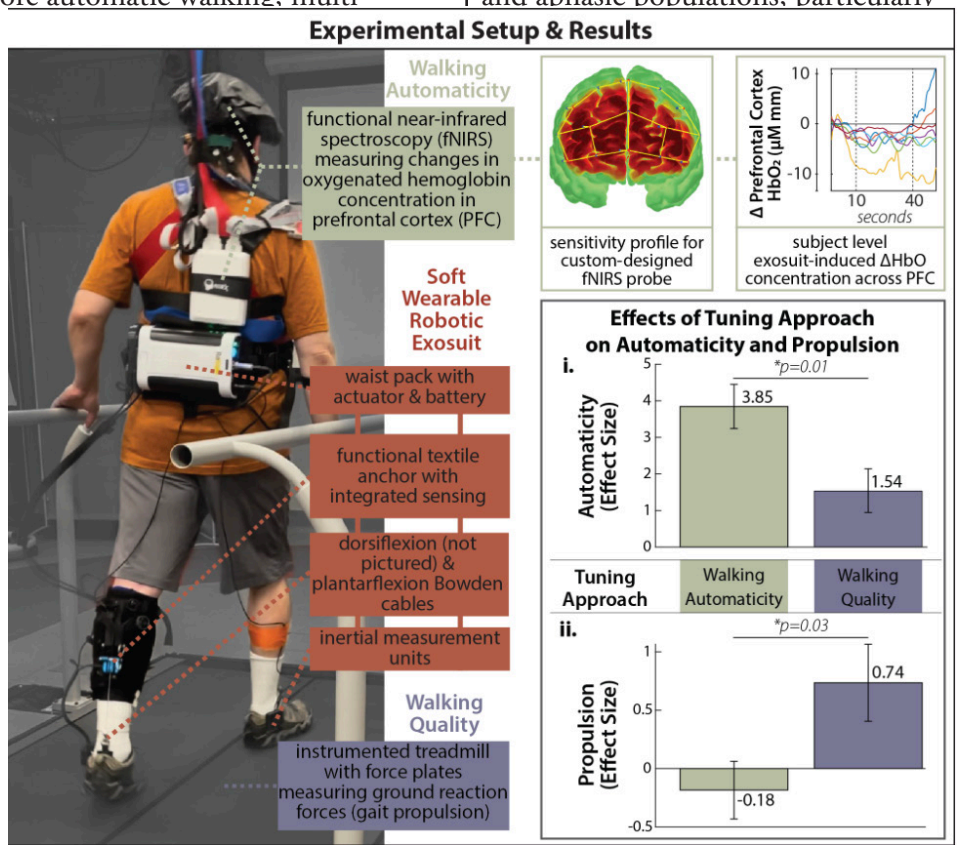
fNIRS-measured prefrontal cortex activity and gait-tuning that aims to maximize the improvement in walking quality.

Methods: Prior to deployment of the technology and experiment to the everyday world, we have completed an in-lab, treadmill study. In this study, seven individuals with chronic post-stroke hemiparesis walked on a speed-fixed, instrumented treadmill with and without exosuit assistance. Changes in walking automaticity were measured as changes in oxygenated hemoglobin concentration in prefrontal cortex, and changes in walking quality were measured as changes in gait propulsion, (i.e., the peak of the paretic limb's anteriorly directed ground reaction forces), with a reduction in prefrontal cortex activity and an increase in gait propulsion indicative of an improvement in each respective outcome.

Results: A large reduction in prefrontal cortex activity was observed when the exosuit was individualized to maximize walking automaticity (Cohen's d effect size: 3.85±0.61). An attenuated, but still large effect (Cohen's d effect size: 1.54±0.60), was observed when the exosuit maximized walking quality (p=0.01). However, directionally different effects were observed for walking quality; whereas maximizing walking quality resulted in a moderate-to-large increase in gait propulsion (Cohen's d: 0.74±0.33), maximizing automaticity resulted in a modest propulsion deficit (Cohen's d: -0.18±0.25) (p=0.03).
Conclusions: Soft robotic exosuits tuned to maximize walking quality concurrently improve post-stroke walking automaticity; however, and in contrast, when tuned to maximize walking automaticity, exosuits can impair walking quality. Though exosuit tuning to maximize walking quality appears sufficient to induce a shift in post-stroke locomotor control towards more automatic walking, multi-objective control approaches may be needed to balance these potentially competing objectives.

** Regina's platform presentation based on this work received the Marilyn Gossman Graduate Student Seminar award and will be part of a special session at the APTA's annual meeting in February.*

A central objective of aphasia research is understanding the neural correlates of language processing in aphasia and how this may diverge from language processing healthy individuals. Historically, fMRI has been the main method used to investigate this topic, however there are several limitations to this technique including large amounts of ambient noise, which can interfere with performance on language tasks, and being limited to very constrained tasks, as motion artifact can significantly impact signal quality during fMRI acquisition. Therefore, fNIRS, is a suitable alternative to examine the cortical activity in healthy and aphasic populations, particularly



NPC Faculty Collaborative Publications

Abdelfattah, A. S., Ahuja, S., Akkin, T., Allu, S. R., Brake, J., **Boas, D. A.**, Buckley, E. M., Campbell, R. E., **Chen, A. I.**, **Cheng, X.,** Čižmár, T., Costantini, I., De Vittorio, M., **Devor, A.**, Doran, P. R., El Khatib, M., Emiliani, V., Fomin-Thunemann, N., Fainman, Y., Fernandez-Alfonso, T., … Zhao, Y. Neurophotonic tools for microscopic measurements and manipulation: status report**.** *Neurophotonics* (2022).

Ayaz, H., Baker, W. B., Blaney, G., **Boas, D. A.,** Bortfeld, H., Brady, K., Brake, J., Brigadoi, S., Buckley, E. M., Carp, S. A., Cooper, R. J., Cowdrick, K. R., Culver, J. P., Dan, I., Dehghani, H., **Devor, A.**, Durduran, T., Eggebrecht, A. T., Emberson, L. L., Fang, Q., … Zhou, W. Optical imaging and spectroscopy for the study of the human brain: status report. *Neurophotonics* **(2022).**

Aykan, S. A., Xie, H., Lai, J. H., Zheng, Y., **Chung, D. Y.**, Kura, S., Anzabi, M., Sugimoto, K., McAllister, L. M., Yaseen, M. A., **Boas, D. A.**, Whalen, M. J., Sakadzic, S., & Ayata, C. Focal Subcortical White Matter Lesions Disrupt Resting State Cortical Interhemispheric Functional Connectivity in Mice. *Cerebral cortex* (2021).

Aykan, S. A., Xie, H., Zheng, Y., **Chung, D. Y.**, Kura, S., Han Lai, J., Erdogan, T. D., Morais, A., Tamim, I., Yagmur, D., Ishikawa, H., Arai, K., Abbas Yaseen, M., **Boas, D. A.**, Sakadzic, S., & Ayata, C. Rho-Kinase Inhibition Improves the Outcome of Focal Subcortical White Matter Lesions. *Stroke* (2022).

Ayoub, M. J., Keegan, L., **Tager-Flusberg, H.**, & **Gill, S. V.** Neuroimaging Techniques as Descriptive and Diagnostic Tools for Infants at Risk for Autism Spectrum Disorder: A Systematic Review**.** *Brain sciences* (2022).

Chang, S., Varadarajan, D., Yang, J., **Chen, I. A.**, Kura, S., Magnain, C., Augustinack, J. C., Fischl, B., Greve, D. N., **Boas, D. A.** & Wang, H. Scalable mapping of myelin and neuron density in the human brain with micrometer resolution. *Sci Rep-uk 12, 363* (2022).

Chen, G., Shi, L., Lan, L., Wang, R., Li, Y., Du, Z., Hyman, M., **Cheng, J. X.**, & **Yang, C.** High-precision neural stimulation by a highly efficient candle soot fiber optoacoustic emitter. *Frontiers in neuroscience* (2022).

Cheng, X., Sie, E. J., **Boas, D. A.**, & Marsili, F. Choosing an optimal wavelength to detect brain activity in functional near-infrared spectroscopy. *Optics letters* (2021).

Cheng, X., Sie, E. J., Naufel, S., **Boas, D. A.**, & Marsili, F. Measuring neuronal activity with diffuse correlation spectroscopy: a theoretical investigation**.** *Neurophotonics* (2021).

Clough, M., **Chen, I. A.**, Park, S. W., Ahrens, A. M., Stirman, J. N., Smith, S. L., & **Chen, J. L.** Flexible simultaneous mesoscale two-photon imaging of neural activity at high speeds**.** *Nature communications* (2021).

Giblin, J. T., Park, S. W., Jiang, J., Kılıç, K., Kura, S., Tang, J., **Boas, D. A.**, & **Chen, I. A**. Measuring capillary flow dynamics using interlaced two-photon volumetric scanning. *Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism* (2023).

Gilmore, N., **Yücel, M. A.,** Li, X., **Boas, D. A.**, & **Kiran, S.** Investigating Language and Domain-General Processing in Neurotypicals and Individuals With Aphasia - A Functional Near-Infrared Spectroscopy Pilot Study. *Frontiers in human neuroscience* (2021).

Hartung, G., Badr, S., Mihelic, S., Dunn, A., **Cheng, X.**, Kura, S., **Boas, D. A.**, Kleinfeld, D., Alaraj, A., & Linninger, A. A. Mathematical synthesis of the cortical circulation for the whole mouse brain-part II: Microcirculatory closure. *Microcirculation* (2021).

Jiang, L., Lin, W., Zhang, C., Ash, P. E. A., Verma, M., Kwan, J., van Vliet, E., Yang, Z., Cruz, A. L., Boudeau, S., Maziuk, B. F., Lei, S., Song, J., Alvarez, V. E., Hovde, S., Abisambra, J. F., Kuo, M. H., Kanaan, N., Murray, M. E., Crary, J. F., … **Wolozin, B.** Interaction of tau with HNRNPA2B1 and N6-methyladenosine RNA mediates the progression of tauopathy. *Molecular cell* (2021).

Kılıç, K., Desjardins, M., Tang, J., **Thunemann, M.**, Sunil, S., Erdener, Ş.E., Postnov, D.D., **Boas, D.A.** and **Devor, A.**, Chronic cranial windows for long term multimodal neurovascular imaging in mice. *Frontiers in physiology* (2021).

Leman, D.P., **Chen, I.A.**, Bolding, K.A., Tai, J., Wilmerding, L.K., Gritton, H.J., Cohen, Y., Yen, W.W., Perkins, L.N., Liberti III, W.A. and **Kilic, K.**, 2021. Large-scale cellular-resolution imaging of neural activity in freely behaving mice. *BioRxiv* (2021).

NPC Faculty Collaborative Publications

Li, Y., Jiang, Y., Lan, L., Ge, X., Cheng, R., Zhan, Y., Chen, G., Shi, L., Wang, R., Zheng, N., **Yang, C.**, & **Cheng, J. X.** Optically-generated focused ultrasound for noninvasive brain stimulation with ultrahigh precision. *Light, science & applications* (2022).

Lin, H., Lee, H. J., Tague, N., Lugagne, J. B., Zong, C., Deng, F., Shin, J., **Tian, L.**, Wong, W., Dunlop, M. J., & **Cheng, J. X.** Microsecond fingerprint stimulated Raman spectroscopic imaging by ultrafast tuning and spatial-spectral learning. *Nature communications* (2021).

Liu, C., **Kılıç, K.**, Erdener, S. E., **Boas, D. A.**, & Postnov, D. D. Choosing a model for laser speckle contrast imaging. *Biomedical optics express* (2021).

Liu, C., Platisa, J., Ye, X., Ahrens, A.M., **Chen, I.A.**, **Davison, I.G.**, Pieribone, V.A., **Chen, J.L**. and **Tian, L**. DeepVID: A Self-supervised Deep Learning Framework for Two-photon Voltage Imaging Denoising. *In Optics and the Brain* (2022). Optica Publishing Group.

Lowet, E., Sheehan, D. J., Mount, R. A., Xiao, S., Zhou, S. L., Tseng, H. A., Gritton, H., Shroff, S., Kondabolu, K.,Cheung, C., **Mertz, J.**, **Hasselmo, M.**, & **Han, X.** Single and complex spikes relay distinct frequency-dependent circuit information in the hippocampus. *bioRxiv* (2022).

Mächler, P., Broggini, T., Mateo, C., **Thunemann, M.**, Fomin-Thunemann, N., Doran, P. R., Sencan, I., **Kilic, K.**, Desjardins, M., Uhlirova, H., Yaseen, M. A., **Boas, D. A.**, Linninger, A. A., Vergassola, M., Yu, X., Lewis, L. D., Polimeni, J. R., Rosen, B. R., Sakadžić, S., Buxton, R. B., … **Devor, A.** A Suite of Neurophotonic Tools to Underpin the Contribution of Internal Brain States in fMRI. *Current opinion in biomedical engineering* (2021).

Mächler, P., Fomin-Thunemann, N., **Thunemann, M.**, Sætra, M. J., Desjardins, M., **Kılıç, K.**, Amra, L. N., Martin, E. A., Chen, I. A., Şencan-Eğilmez, I., Li, B., Saisan, P., Jiang, J. X., Cheng, Q., Weldy, K. L., **Boas, D. A.**, Buxton, R. B., Einevoll, G. T., Dale, A. M., Sakadžić, S., … **Devor, A.** Baseline oxygen consumption decreases with cortical depth. *PLoS biology* (2022).

Marar, C., Jiang, Y., Li, Y., Lan, L., Zheng, N., **Yang, C.**, & **Cheng, J. X.** Wireless Neuromodulation at Submillimeter Precision via a Microwave Split-Ring Resonator. *bioRxiv* (2022).

Ortega-Martinez, A., Rogers, D., Anderson, J., Farzam, P., Gao, Y., Zimmermann, B., **Yücel, M. A.**, & **Boas, D. A.** How much do time-domain functional near-infrared spectroscopy (fNIRS) moments improve estimation of brain activity over traditional fNIRS? *Neurophotonics* (2023).

Rodríguez, C., Chen, A., Rivera, J. A., Mohr, M. A., Liang, Y., Natan, R. G., Sun, W., Milkie, D. E., **Bifano, T. G.**, Chen, X., & Ji, N. An adaptive optics module for deep tissue multiphoton imaging in vivo. *Nature methods* (2021).

Shi, L., Jiang, Y., Fernandez, F. R., Chen, G., Lan, L., Man, H. Y., **White, J. A.**, **Cheng, J. X.**, & **Yang, C.** Non-genetic photoacoustic stimulation of single neurons by a tapered fiber optoacoustic emitter. *Light, science & applications* (2021).

Shi, L., Jiang, Y., Zheng, N., **Cheng, J. X.**, & **Yang, C.** High-precision neural stimulation through optoacoustic emitters. *Neurophotonics* (2022).

Shpokayte, M., McKissick, O., Guan, X., Yuan, B., Rahsepar, B., Fernandez, F. R., Ruesch, E., Grella, S. L., **White, J. A.**, Liu, X. S., & **Ramirez, S.** Hippocampal cells segregate positive and negative engrams. *Communications biology* (2022).

Sloutsky, R., **Yücel, M.A.**, Collimore, A.N., Ottman, E., **Ellis, T.D.**, Walsh, C.J., **Boas, D.A.** and **Awad, L.N.**, 2021, May. Targeting post-stroke walking automaticity with a propulsion-augmenting soft robotic exosuit: toward a biomechanical and neurophysiological approach to assistance prescription. In *2021 10th International IEEE/EMBS Conference on Neural Engineering, IEEE*. (2021).

Shpokayte, M., McKissick, O., Guan, X., Yuan, B., Rahsepar, B., Fernandez, F. R., Ruesch, E., Grella, S. L., **White, J. A.**, Liu, X. S., & **Ramirez, S.** Hippocampal cells segregate positive and negative engrams. *Communications biology* (2022).

Sloutsky, R., **Yücel, M.A.**, Collimore, A.N., Ottman, E., **Ellis, T.D.**, Walsh, C.J., **Boas, D.A.** and **Awad, L.N.**, 2021, May. Targeting post-

stroke walking automaticity with a propulsion-augmenting soft robotic exosuit: toward a biomechanical and neurophysiological approach to assistance prescription. In *2021 10th International IEEE/EMBS Conference on Neural Engineering, IEEE*. (2021).

Stern, C. E., & **Hasselmo, M. E.** Mechanisms for maintaining information in working memory. *Cognitive neuroscience* (2022).

Sunil, S., Evren Erdener, S., **Cheng, X.**, Kura, S., Tang, J., Jiang, J., Karrobi, K., **Kılıç, K.**, **Roblyer, D.**, & **Boas, D. A.** Stroke core revealed by tissue scattering using spatial frequency domain imaging. *NeuroImage. Clinical* (2021).

Tabassum, S., Tank, A., Wang, F., Karrobi, K., Vergato, C., Bigio, I. J., Waxman, D. J., & **Roblyer, D.** Optical scattering as an early marker of apoptosis during chemotherapy and antiangiogenic therapy in murine models of prostate and breast cancer. *Neoplasia* (2021).

Tang, J., **Cheng, X.**, **Kilic, K.**, **Devor, A.**, Lee, J., & **Boas, D. A.** Imaging localized fast optical signals of neural activation with optical coherence tomography in awake mice. *Optics letters*, (2021).

Thunemann, M., Hossain, L., Ness, T.V., Rogers, N., Lee, K., Lee, S.H., **Kılıç, K.**, Oh, H., **Economo, M.N.**, Gilja, V. and Einevoll, G.T., Imaging through Wind and see electrode arrays reveals a small fraction of local neurons following surface MUA. *bioRxiv* (2022).

Tsang, J. M., Gritton, H. J., Das, S. L., Weber, T. D., Chen, C. S., **Han, X.**, & **Mertz, J.** Fast, multiplane line-scan confocal microscopy using axially distributed slits. *Biomedical optics express* (2021).

Von Lühmann, A., Zheng, Y., Ortega-Martinez, A., Kiran, S., Somers, D. C., **Cronin-Golomb, A.**, **Awad, L. N.**, **Ellis, T. D.**, **Boas, D. A.**, & **Yücel, M. A.** Towards Neuroscience of the Everyday World (NEW) using functional Near-Infrared Spectroscopy. *Current opinion in biomedical engineering* (2021).

Weber, T. D., Moya, M. V., **Economo, M. N.**, & **Mertz, J.** Multi-plane 3D optical voltage imaging using high-speed multi-Z confocal microscopy. *In Neural Imaging and Sensing* (2022).

Xiao, S., **Davison, I.**, & **Mertz, J.** Scan multiplier unit for ultrafast laser scanning beyond the inertia limit. *Optica* (2021).

Xiao, S., Lowet, E., Gritton, H. J., Fabris, P., Wang, Y., Sherman, J., Mount, R. A., Tseng, H. A., Man, H. Y., Straub, C., Piatkevich, K. D., Boyden, E. S., **Mertz, J.**, & **Han, X.** Large-scale voltage imaging in behaving mice using targeted illumination. *iScience* (2021).

Xiao, S., Lowet, E., Gritton, H., Fabris, P., **Mertz, J.**, & **Han, X.** Large-scale optical voltage imaging in behaving animals. *Neural Imaging and Sensing* (2022).

Xue, Y., **Davison, I. G.**, **Boas, D. A.**, & **Tian, L.** (2021, March). Large-scale high-resolution 3D fluorescence imaging with a computational miniature mesoscope. In Three-Dimensional and Multidimensional Microscopy: Image Acquisition and Processing XXVIII. *SPIE* (2021).

Yang, J., Chang, S., Chen, I. A., Kura, S., Rosen, G. A., Saltiel, N. A., Huber, B. R., Varadarajan, D., Balbastre, Y., Magnain, C., Chen, S. C., Fischl, B., McKee, A. C., **Boas, D. A.**, & Wang, H. Volumetric Characterization of Microvasculature in Ex Vivo Human Brain Samples By Serial Sectioning Optical Coherence Tomography. *IEEE transactions on bio-medical engineering* (2022).

Yücel, M. A., Lühmann, A. V., Scholkmann, F., Gervain, J., Dan, I., Ayaz, H., **Boas, D.**, Cooper, R. J., Culver, J., Elwell, C. E., Eggebrecht, A., Franceschini, M. A., Grova, C., Homae, F., Lesage, F., Obrig, H., Tachtsidis, I., Tak, S., Tong, Y., Torricelli, A., … Wolf, M. (2021). Errata: Best practices for fNIRS publications. *Neurophotonics* (2021).

Yücel, M.A., Lühmann, A.V., Scholkmann, F., Gervain, J., Dan, I., Ayaz, H., **Boas, D.**, Cooper, R.J., Culver, J., Elwell, C.E. and Eggebrecht, A., Best practices for fNIRS publications. *Neurophotonics* (2021).

NPC Faculty Collaborative Publications

Zhang, Y., Jia, D., Yang, Q., Xue, Y., Tan, Y., Guo, Z., Zhang,M., **Tian, L.**, **Cheng, J. X.** Single-shot Volumetric Chemical Imaging by Mid-Infrared Photothermal Fourier Light Field Microscopy. *bioRxiv* (2022).

Zhao, J., Matlock, A., Zhu, H., Song, Z., Zhu, J., Wang, B., Chen, F., Zhan, Y., Chen, Z., Xu, Y., Lin, X., **Tian, L.**, & **Cheng, J. X.** Bond-selective intensity diffraction tomography. *Nature communications* (2022).

Zheng, N., Jiang, Y., Jiang, S., Li, Y., Jia, X., **Yang, C.**, & **Cheng, J. X.** (2022, April). Deep Brain Optoacoustic Stimulation Enabled by a Multifunctional Fiber-based Optoacoustic Emitter. *Optics and the Brain* (2022). Optica Publishing Group.

Zheng, S., Xiao, S., Kretsge, L., **Cruz-Martín, A.**, & **Mertz, J.** Depth resolution in multifocus laser speckle contrast imaging. *Optics letters* (2021).

Zilpelwar, S., Sie, E. J., Postnov, D., Chen, A. I., Zimmermann, B., Marsili, F., **Boas, D. A.**, & **Cheng, X.** Model of dynamic speckle evolution for evaluating laser speckle contrast measurements of tissue dynamics. *Biomedical optics express* (2022).

Zong, C., Cheng, R., Chen, F., Lin, P., Zhang, M., Chen, Z.,Li, C., **Yang, C.**, **Cheng, J. X.** Wide-field surface-enhanced coherent anti-Stokes Raman scattering microscopy. *ACS Photonics* (2022).

NPC Faculty Collaborative Grants

The table below summarizes the NPC Center, New Collaborative, and Ongoing Collaborative grants. Additional grants to NPC Director Boas are included as well as they contribute to the resources of the Center that are made available to NPC members through the 2021 and 2023 academic years.

PI	AWARD TITLE	SPONSOR	FUNDS FY 22 & 23
BIGIO J IRVING	VALIDATION OF LIGHT SCATTERING SPECTROSCOPY FOR INTRA-OPERATIVE MARGIN GUIDANCE DURING ORAL CANCER RESECTION	NIH	$180,322
BIFANO G THOMAS	MRI: ACQUISITION OF A SPINNING DISK CONFOCAL SUPER-RESOLUTION MICROSCOPE FOR TRANSCRIPTOMICS RESEARCH AT BOSTON UNIVERSITY	NSF	$615,508
BOAS DAVID	TIME-GATED DIFFUSE CORRELATION SPECTROSCOPY FOR FUNCTIONAL IMAGING OF THE HUMAN BRAIN	NIH	$253,579
BOAS DAVID	THE NEUROSCIENCE OF EVERYDAY WORLD- A NOVEL WEARABLE SYSTEM FOR CONTINUOUS MEASUREMENT OF BRAIN FUNCTION	NIH	$2,731,494
BOAS DAVID	NEUROPHOTONIC ADVANCES FOR MECHANISTIC INVESTIGATION OF THE ROLE OF CAPILLARY DYSFUNCTION IN STROKE RECOVERY	NIH	$693,711
CHENG JI-XIN	UNVEILING THE MECHANISMS OF ULTRASOUND NEUROMODULATION VIA SPATIALLY CONFINED STIMULATION AND TEMPORALLY RESOLVED RECORDING	NIH	$1,612,761
CHENG JI-XIN	SUB-MILLIMETER PRECISION WIRELESS NEUROMODULATION USING A MICROWAVE SPLIT RING RESONATOR	NIH	$247,500
DEVOR ANNA	LOCAL NEURONAL DRIVE AND NEUROMODULATORY CONTROL OF ACTIVITY IN THE PIAL NEUROVASCULAR CIRCUIT	NIH	$8,276,515
DEVOR ANNA	UNDERSTANDING THE RELATIONSHIPS BETWEEN FUS-BBB OPENING, NEUROINFLAMMATION, AND THE NEUROVASCULAR RESPONSE	NIH	$137,092
DEVOR ANNA	MICROSCOPIC FOUNDATION OF MULTIMODAL HUMAN IMAGING	NIH	$134,300
DEVOR ANNA	INTEGRATION OF HIGH DEFINITION DISPLAY TECHNOLOGIES WITH PLATINUM NANOROD MICROELECTRODES FOR LARGE SCALE IN-VIVO RECORDING AND STIMULATION	NIH	$636,423
DEVOR ANNA	EFFECTS OF INTRINSIC AND DRUG-INDUCED NEUROMODULATION ON FUNCTIONAL BRAIN IMAGING	NIH	$759,747

NPC Faculty Collaborative Grants

ECONOMO/CHAND	LINKING MOTOR CORTEX ACTIVITY AND MOVEMENT IN THE MOUSE OROFACIAL SYSTEM.	NIH	$902,250
ECONOMO	REVERSE ENGINEERING THE BRAIN STEM CIRCUITS THAT GOVERN EXPLORATORY BEHAVIOR	NIH	$195,124
ECONOMO/MERTZ	HIGH-THROUGHPUT MAPPING OF SYNAPTIC CONNECTIVITY BETWEEN TRANSCRIPTOMICALLY DEFINED CELL TYPES	NIH	$1,423,833
ECONOMO	CAREER: HIGH-LEVEL CONTROL OF LOW-LEVEL CIRCUITS IN THE MAMMALIAN MOTOR SYSTEM	NIH	$700,000
GABEL	COMPREHENSIVE MULTI-NEURON IMAGING OF NEURODEGENERATION IN C. ELEGANS	ON / ASSOCIATION	$200,000
HOWE	STRIATUM WIDE DYNAMICS AND NEUROMODULATION OF CELL-TYPE SPECIFIC STRIATUM POPULATIONS DURING LEARNING	NIH	$1,062,600
HOWE	MAPPING THE MODULATORY LANDSCAPE GOVERNING STRIATAL DOPAMINE SIGNALING AND ITS DYSREGULATION IN PARKINSON'S DISEASE	Science Across Pa	$580,190
MERTZ/NIA/CRUZ-MARTIN	FAST, LARGE-SCALE NEURONAL IMAGING WITH MULTI-Z CONFOCAL MICROSCOPY	NIH	$599,124
MERTZ	MULTI-LAYER NEURONAL IMAGING WITH REVERBERATION MULTIPHOTON MICROSCOPY	NIH	$801,032
MERTZ	ULTRAFAST HIGH-CONTRAST VOLTAGE IMAGING IN FREELY MOVING ANIMALS	NIH	$655,123
NIA/SUKI	CLASSIFYING MALIGNANT PULMONARY NODULES USING BIOPHYSICS-ENHANCED ARTIFICIAL INTELLIGENCE	NIH	$660,000
NIA/SUKI	CELLULAR RESOLUTION IMAGING OF DRUG DELIVERY INTO TUMORS IN FUNCTIONING EX VIVO LUNG	Industry	$250,000
NIA/SUKI	CAREER: LUNGEX FOR PROBING MULTISCALE MECHANOBIOLOGY OF PULMONARY RESPIRATION-CIRCULATION COUPLING IN REAL-TIME	NSF	$566,473
NIA/SUKI	PROBING THE PHYSICAL AND IMMUNE MICROENVIRONMENT IN LUNG TUMORS AT HIGH SPATIOTEMPORAL RESOLUTION	Industry	$250,000
RAMIREZ	ARTIFICIALLY MODULATING MEMORIES TO ALLEVIATE PSYCHIATRIC DISEASE-LIKE STRESS	NIH	$412,500
RAMIREZ	SINGLE-CELL AND TARGET SPECIFIC RESOLUTION OF MULTIPLE MEMORIES ACROSS THE BRAIN	NIH	$770,988
RAMIREZ	THE EFFECT OF ADOLESCENT DRUG-INDUCED NEUROIMMUNE SIGNALING IN SEX-SPECIFIC SOCIAL DEVELOPMENT AND REWARD LEARNING	NIH	$28,416
RAMIREZ	RESTORING THE BRAIN WITH ACTIVATED MEMORIES	NIH	$300,000
ROBLYER	FREQUENCY DOMAIN DIFFUSE OPTICAL SPECTROSCOPY AND DIFFUSE CORRELATION SPECTROSCOPY FOR ASSESSING INSPIRATORY MUSCLE METABOLISM IN MECHANICALLY VENTILATED PATIENTS	NIH	669,944.00
ROBLYER	EFRI CEE: OPTICALLY CONTROLLED LOCALIZED EPIGENETIC CHROMATIN REMODELING WITH PHOTOACTIVATABLE CRISPR-DCAS9	NSF	122,343.00
ROBLYER	LABEL-FREE MEASUREMENT OF BLOOD LIPIDS WITH HYPERSPECTRAL SHORT-WAVE INFRARED SPATIAL FREQUENCY DOMAIN IMAGING TO IMPROVE CARDIOVASCULAR DISEASE RISK PREDICTION AND TREATMENT MONITORING	NIH	$20,923
ROBLYER	ESTIMATING BLOOD PRESSURE CHANGES USING LASER SPECKLE CONTRAST MEASUREMENTS ON THE WRIST AND HAND	Industry	$269,561
TAGER-FLUSBERG/GILL	PREDICTING AND OPTIMIZING LANGUAGE OUTCOMES IN MINIMALLY VERBAL CHILDREN WITH AUTISM SPECTRUM DISORDER	NIH	$2,586,804
TIAN	COMPUTATIONAL MINIATURE MESOSCOPE FOR CORTEX-WIDE, CELLULAR RESOLUTION CA2+ IMAGING IN FREELY BEHAVING MICE	NIH	$825,000
TIAN	COMPUTATIONAL MESOSCOPE FOR ULTRAFAST MULTISCALE 3D IMAGING	NIH	$1,310,540
RUSSEK	THE STAT3 RESPONSE OF EXCITATORY NEURONS TO EPILEPTOGENIC BRAIN INJURY	NIH	$671,398
WALLACE/DAVISON	HABENULA	NIH	$620,402
WHITE	TRAINING PROGRAM IN QUANTITATIVE BIOLOGY & PHYSIOLOGY (QBP)	NIH	$530,535
YANG	UNDERSTANDING THE MECHANISM OF MICROWAVE NEURON INHIBITION	DOD	$299,117
YANG	FABRICATION OF FLAT PHOTOACOUSTIC FILM FOR RETINAL STIMULATION	Industry	$9,999
YANG	NEURO-MODULATION	ON / ASSOCIATIOI	$80,000
YANG	STIMULATION	Industry	$29,999

Boston University Neurophotonics Center

24 Cummington Mall, Boston,
MA 02215

WWW.BU.EDU/NEURO-PHOTONICS

Visit our LinkedIn Page: **LINKEDIN.COM/SHOWCASE/BOSTON-UNIVERSITY-NEURPHOTONICS-CENTER**