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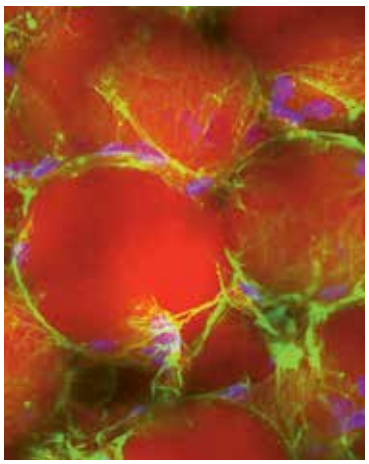
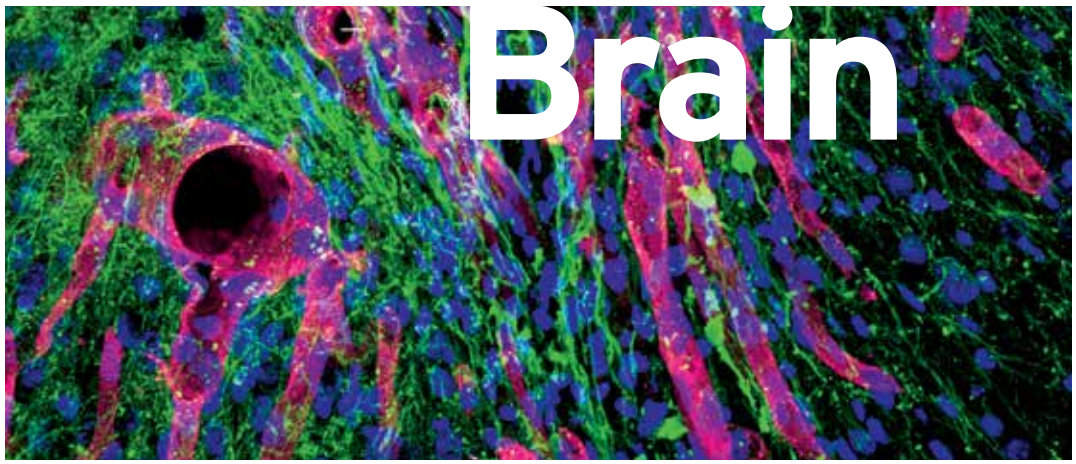
Engineering light to change the world

FACULTY HIGHLIGHTS:
Segura, p. 8

Imaging Biomaterials *in the* Brain





2019 VOLUME 12 ISSUE 1

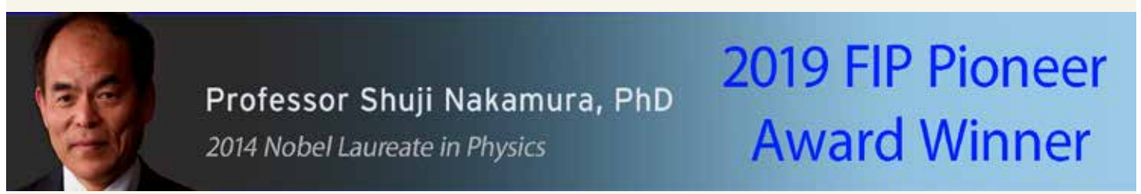
DIRECTOR'S MESSAGE

Tuan Vo-Dinh

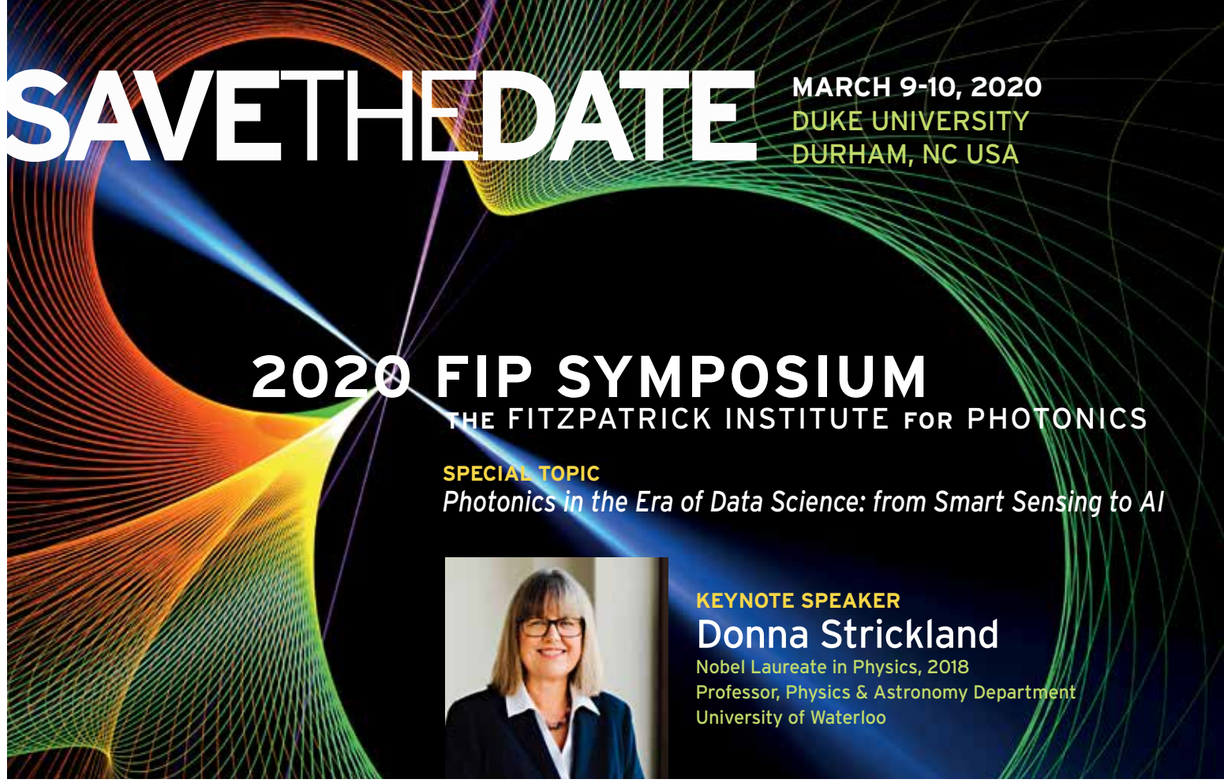
Welcome to the 2019 issue of BROADBAND, the newsletter of the Fitzpatrick Institute for Photonics (FIP). One of the main goals of the Institute is to promote the interdisciplinary and collaborative spirit between engineers, scientists, medical researchers and clinicians across the Duke campus. The FIP continues to experience outstanding growth, now including over 150 faculty members with participation from 39 departments and institutions ranging from Biomedical Engineering, Electrical and Computer Engineering, Mechanical Engineering & Material Science, Chemistry, Physics, Computer Science, and Mathematics to Anesthesiology, Cell Biology, Chemical Biology, Neurosurgery, Oncology, Orthopedic Engineering, Ophthalmology, Pathology, Pediatrics, Radiology and Surgery as well as Art, Art History & Visual Studies, and Philosophy.

We successfully organized the 2019 FIP Annual Symposium with the Keynote Lecture presented by Shuji Nakamura, 2014 Nobel Laureate in Physics. The Plenary Lecture was presented by Ulrich B. Wiesner, Spencer T. Olin Professor of Engineering, Department of Materials Science of Engineering, Cornell University and the special topic was Materials & Photonics: Advancing the World. On the morning of the second day of the symposium, we organized a Special Session on Advancing the World Through Global Health Students, which was organized in collaboration with Duke Engineering World Health and the Global Public Service Academies. The symposium also included special topic sessions on Materials & Photonics: Advancing the World and lectures from distinguished speakers, contributed papers, and posters by investigators from academic institutions covering various topics ranging from biophotonics, nanophotonics, medical diagnostics, nano & microsystems, to molecular biomaterials, and advanced photovoltaic systems.

Professor Tuan Vo-Dinh
Director, Fitzpatrick Institute for Photonics
R. Eugene and Susie E. Goodson Professor of Biomedical Engineering
Professor of Chemistry



ON THE COVER: Top, a Zeiss Axio Scan large fluorescent image of a precast porogen mold Hyaluronic Acid hydrogel (orange) seeded with mouse mesenchymal stem cells (MSCs) (green=actin, blue=nuclei). Bottom left, microporous annealed particle (MAP) scaffold geometry influences 3D cell spreading (red: MAP, green: F-actin, blue: DAPI). Bottom right, a stained slide showing regrowth in neural cavity caused by stroke. The red segments are the new blood vessels while the green depicts new nerve fibers.



PARTICIPATING DEPARTMENTS AND INSTITUTIONS

150 Faculty Members | 42 Participating Departments, Centers, and Institutions at Duke University

The Fitzpatrick Institute for Photonics is an extremely interdisciplinary Duke effort to advance photonics and optical sciences. The institute leverages Duke's faculty from the Pratt School of Engineering, Trinity College of Arts and Sciences, and the Duke School of Medicine to explore problems at the boundary nexus of nano-bio-info-opto convergence.

DEPARTMENTS

Anesthesiology
Art, Art History & Visual Studies
Biochemistry
Biology
Biomedical Engineering (BME)
Cell Biology
Chemistry
Civil & Environmental Engineering (CEE)
Computer Science
Dermatology
Electrical and Computer Engineering (ECE)
Environmental Toxicology
Gastroenterology
Geriatrics
History
Literature
Mathematics
Mechanical Engineering and Materials Science (MEMS)
Molecular Genetics and Microbiology
Neurobiology
Neurosurgery
Obstetrics and Gynecology
Oncology
Ophthalmology
Orthopaedic Surgery
Pathology
Pediatrics
Pharmacology and Cancer Biology
Philosophy
Physics
Radiation Oncology
Radiology
Surgery
Urology
Center for Applied Genomics and Precision Medicine
Center for Genomic and Computational Biology (GCB)
Center for Metamaterials & Integrated Plasmonics (CMIP)
Duke Cancer Institute
Global Health
Nicholas School of the Environment
School of Medicine
School of Nursing

FIP RESEARCH PROGRAMS AND DIRECTORS, LEFT TO RIGHT: **Biophotonics:** Joseph Izatt **Nano & Micro Systems:** Nan Jokerst **Quantum Optics and Information Photonics:** Jungsang Kim **Systems Modeling, Theory & Data Treatment:** Weitao Yang **Novel spectroscopes:** Warren Warren **Photonic Materials & Advanced Photonics Systems:** Steven Cummer & Charles Gersbach **Nanophotonics:** Fan Yuan

HIGHLIGHTS | 2019 FIP Symposium

Duke University, Durham, NC, USA

We successfully organized the 2019 FIP Annual Symposium with the Keynote Lecture presented by Dr. Shuji Nakamura, 2014 Nobel Laureate in Physics, CREE Distinguished Professor, Materials Department, University of California, Santa Barbara. Dr. Nakamura was awarded the Nobel Prize from his invention of efficient blue light-emitting diodes which has enabled bright and energy-saving white light sources. Dr. Nakamura was also the recipient of the 2019 FIP Pioneer Award (photo of award presentation below). The meeting's special topic session "Materials & Photonics: Advancing The World" presented lectures from distinguished speakers, contributed papers, and posters by investigators from academic institutions covering various topics such as biophotonics, nanophotonics, medical robotics, nano & microsystems, global health, and renewable energy photonics. Additional highlights of the meeting included: Plenary Speaker, Dr. Ulrich Wiesner, Spencer T. Olin Professor of Engineering, Department of Materials Science of Engineering, Cornell University; and Invited Speakers, Dr. Gerald Meyer, Professor, Department of Chemistry, University of North Carolina at Chapel Hill, Dr. Carlos Silva, Professor, School of Chemistry, Biochemistry & Physics, Georgia Institute of Technology, Dr. Andre Taylor, Associate Professor, Department of Chemical and Biomolecular Engineering, New York University, Dr. Yaroslava Yingling, Professor and University Faculty Scholar, Department of Materials Science & Engineering, North Carolina State University delivered lectures for the FIP symposium. Link to the videos: http://fitzpatrick.duke.edu/fip-annual-symposia

LEFT TO RIGHT: *Gerald Myer, Harold Baranger, Ulrich Wiesner, Tuan Vo-Dinh, Shuji Nakamura, Jie Liu, David Beratan*

engineeringworldhealth

Symposium Chair: Tuan Vo-Dinh, Director, Fitzpatrick Institute for Photonics
Symposium Manager: August Burns, Department Business Manager, Fitzpatrick Institute for Photonics
Scientific Program Committee: Steve Cummer, Charles Gersbach, Nan Jokerst, Jungsang Kim, Warren Warren, Weitao Yang, Fan Yuan
Symposium Workshop Program Chair: Robert Malkin
Symposium Workshop Program Committee: Brittany Ploss, Leslie J. Calman, Tamara Fitzgerald

PANELISTS LEFT TO RIGHT: *Tamera Fitzgerald, Leslie Calman, Robert Malkin*

Engineering World Health (EWH), Global Public Service Academies (GPSA) and The Office of the Vice-Provost, Duke University co-hosted with the Fitzpatrick Institute for Photonics to provide a special morning session and panel on Global Health STEM Outreach during the second day of the symposium. In addition the GPSA & EWH invited their students to present a special poster session after the panel. ■

The Corporate Partnership Program (CPP) is established to strengthen interactions between FIP faculty and industrial developers, and to enhance the translational aspects of our educational and research programs. Our current CPP members are Hamamatsu Photonics, BD Technologies, Cisco and Optimax. With the improving economy and the emergence of strong partners in photonics, the Institute will continue to strengthen its industrial relations programs in the coming years.

Partners have access to a website containing an overview summary of key topics and areas of active research activities at the FIP which also displays their corporate logo as a member of our CPP. During the FIP Annual Meeting, the Corporate Partners are provided with an industry booth, a program listing all FIP faculties and also displaying the partners' corporate logo as a CPP member. The Corporate Partners also receive information about our FIP professors, research topics, and graduate students. Throughout the year we provide our Corporate Partners with recruiting assistance via exclusive access to resumes of students who are approaching graduation. Representatives of all Corporate Partners are invited to attend our special Seminar Series, guest lectures, presentations and special events. Corporate Partners may also join our faculty members and students in accessing our collection of student theses and dissertations.

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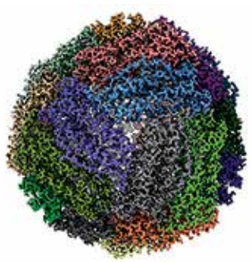
Pulling the Signal from the Noise

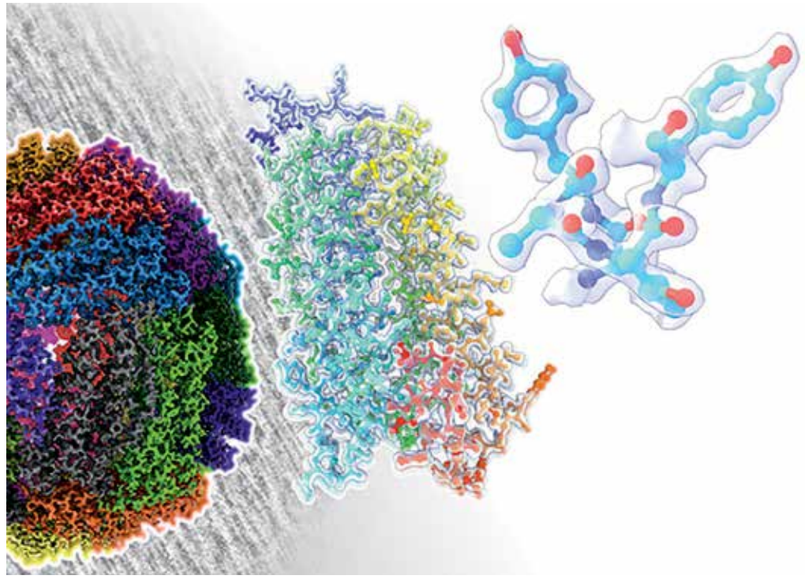
Alberto Bartesaghi is using his background in image processing to develop new techniques to elucidate the structure of proteins using Duke's newest cryogenic electron microscope

Sitting by itself in a back room in the farthest corner of the Shared Materials Instrumentation Facility in the Fitzpatrick Center is an unassuming 15-foot-tall monolith that is allowing Duke researchers to peer at the microscopic shapes of proteins like never before. Known as a cryogenic electron microscope—or cryo-EM for short—the machine blasts proteins with a 300,000-volt beam of electrons so that highly-sensitive detectors underneath can tease out their shapes based on the interaction that occurs. Being able to "see" proteins—life's crucial building materials—can help determine how they work. And recognizing protein structure and function is essential for scientists trying to design better drugs to tackle some of the world's most devastating diseases, including HIV, cancer and Alzheimer's disease.

A 300,000-volt electron beam is, however, extremely damaging to the proteins it is trying to image. To help protect the samples in the machine, researchers cryogenically freeze them to help maintain their integrity over thousands of electron blasts. This freezing process allows researchers to obtain images of intact proteins and other biomolecular structures that were previously inaccessible to other technologies.



This image of a human protein was built from 1,000 scans of more than 315,000 individual molecules, and then assembled in a computer.



Proteins, such as this human apo-ferritin molecule, are the stuff of life. We need to see them in great detail, in this case, down to 1.6-Angstrom-resolution.

Although cryo-EM has been around since the 1970s, Duke just got its machine two years ago to the tune of nearly $10 million. It wasn't until recently that advances in detector technology, software algorithms, and computing revolutionized the field to the point that commercializing the technology became feasible.

At the National Institutes of Health, **Alberto Bartesaghi**, associate professor of computer science, biochemistry, and electrical and computer engineering at Duke, worked in one of the laboratories leading this revolution. With a background in image processing, Bartesaghi develops techniques for getting detailed images of proteins using this technology, which is not nearly as easy as developing a roll of film.

"These images are extremely noisy," said Bartesaghi, who came to Duke in 2018 to work with the university's new cryo-EM machine. "If you look at these images with your naked eye, you would just see noise. But by using sophisticated data analysis technologies that combine several hundred thousand of those images, we can bring out that signal."

Other researchers have been taking advantage of Bartesaghi's expertise, imaging HIV spikes on the surface of HIV viruses in the search for a vaccine, obtaining molecular snapshots of G-protein coupled receptors as they bind to various proteins, and much more. Structural biologists using X-ray crystallography—a time-honored technique that involves crystallizing a molecule and then measuring how X-rays diffract when the crystal is hit—may find that cryo-EM is an effective alternative to study hard-to-crystallize proteins, according to Bartesaghi.

"Until recently, there were many important biomolecules where the biochemistry was well understood but researchers couldn't determine their structures because they had a hard time crystallizing them," said Bartesaghi. "Thanks to the recent technological advances in the field, all of a sudden these targets became tractable by cryo-EM and that has created a tsunami of new structures."

Now that he's settling into his position at Duke, Bartesaghi is also beginning to explore opportunities to collaborate with researchers working on other imaging modalities as well, including light-based techniques. After all, the techniques he uses to improve cryo-EM could be applied to pretty much any system that captures noise-corrupted signals.

"The methods we develop use basic principles that are applicable to other kinds of noisy images," said Bartesaghi. "If you take an image with your cell phone under very low light conditions, you could apply these same techniques to bring out the features in the scene you're looking at. In general, there are many parallels to be found with other biological or medical imaging modalities, including MRI, ultrasound or even light-based microscopy. I'm looking forward to exploring the common ground between the different techniques that could form the base of new collaborations with FIP." ■

"Thanks to the recent technological advances in the field, all of a sudden these targets became tractable by cryo-EM and that has created a tsunami of new structures."

COVER STORY

Imaging Biomaterials in the Brain

Tatiana Segura is leveraging the photonics expertise of her new colleagues to investigate how well her biomaterials promote healing in the brain

Absent some sort of genetic defect, everybody in the world has amazing abilities to heal themselves. The regeneration process, however, can be hindered by a wide variety of obstacles. Diseases can suppress the biological signals or disrupt the physical support systems needed for a speedy recovery. The body's own immune system can overreact to damage, causing obstructive inflammation. Even aging slows down the healing process.

Tatiana Segura, professor of biomedical engineering at Duke University, engineers hydrogel biomaterials that support and promote cell growth in an effort to unlock the body's innate ability to repair damaged or diseased tissue. This artificial material creates an environment that helps native stem cells do their best work to promote healing—providing the physical structure as well as the biological cues that encourage cells to grow. Because the material is made of natural substances, it breaks down and is removed by the body as the tissue heals around it.

Tatiana Segura

"Everyone has seen children who get hurt and then are jumping around again the next day," said Segura, who works primarily on the healing of brain and skin tissues. "But when adults get hurt, it takes a while before we're up and about again. One of the things that changes with age is the matrix that surrounds and supports all of the cellular functions of our organs and tissues. This material gets old and degrades. But we think we can engineer an artificial material to make the body act young again."

For much of her career, Segura has relied mostly on confocal microscopes and tissue staining to investigate how well her hydrogels are working. But having joined Duke's faculty in the summer of 2018 and the Fitzpatrick Institute for Photonics soon after, Segura is using the photonics expertise of her new colleagues to try new methods of monitoring healing progress.

For starters, Segura is teaming up with **Yiyang Gong**, assistant professor of biomedical engineering, to capture videos of neurons in action via calcium signaling.

"We work with damage caused by strokes, but right now we have no way of knowing if the neurons we see regenerating are firing or not," said Segura. "Being able to watch the neurons in action as they repair over time would be terrific."

In another new collaboration, Segura is working with **Junjie Yao**, assistant professor of biomedical engineering, to visualize how well blood is flowing through new blood vessels in the brain and how much oxygen they are transporting with the help of photoacoustic tomography. This emerging imaging technology converts light beamed through tissue into ultrasound waves that can then be analyzed to create high-resolution images.

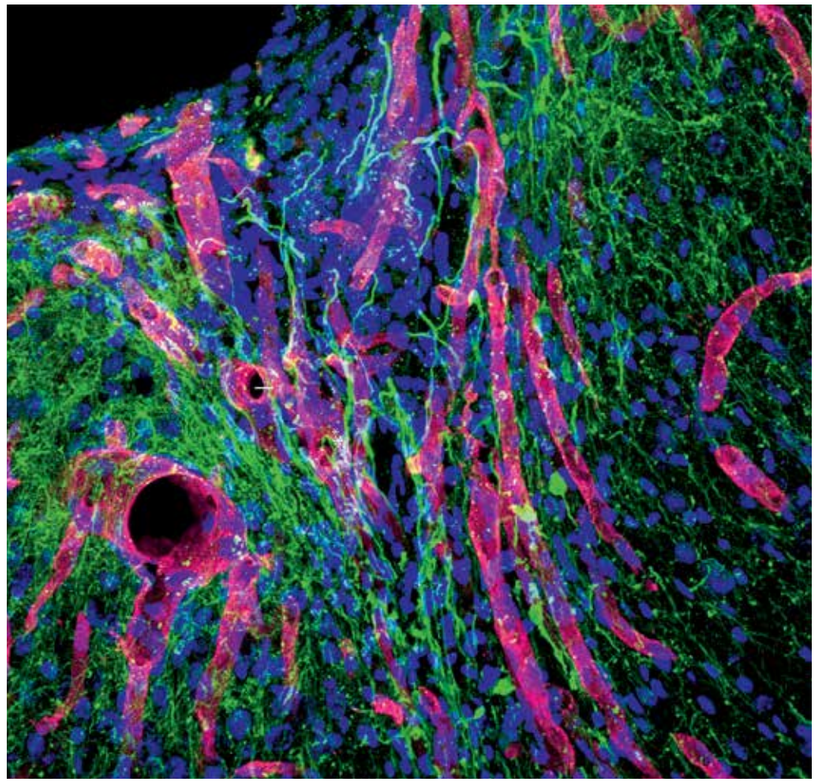
"We work with damage caused by strokes, but right now we have no way of knowing if the neurons we see regenerating are firing or not. Being able to watch the neurons in action as they repair over time would be terrific."

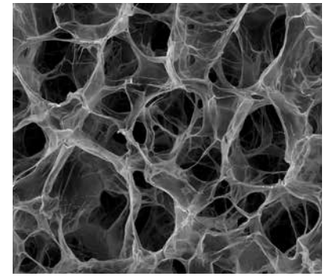
Segura's lab is also leaning on Duke collaborations to move its research into the realm of machine learning. One of the biomaterials the team is developing creates a network of bead-like spheres that form a scaffold for cells to grow into. Because different cells respond to tight confines in different ways, knowing the exact sizes and shapes of the spaces between the beads is vital to understanding how the scaffold promotes growth.

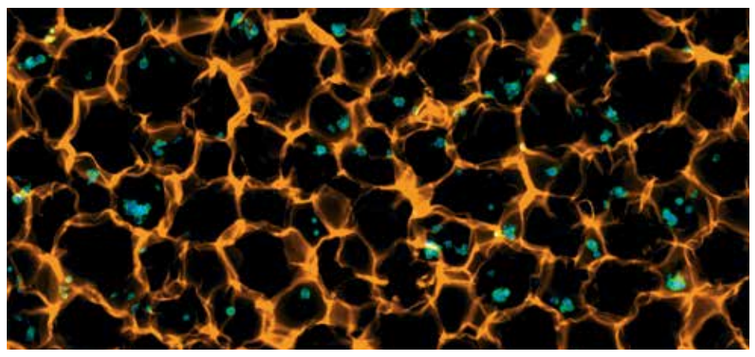
"If a macrophage is put into a space too small for it to expand, it can't activate in the same way and becomes more pro-repair instead of inflammatory," explained Segura. "The size of these spaces also dictates how blood vessels and neurons might grow in them. If a crevice is really thin, for example, a neural axon might be able to get through but not much else."

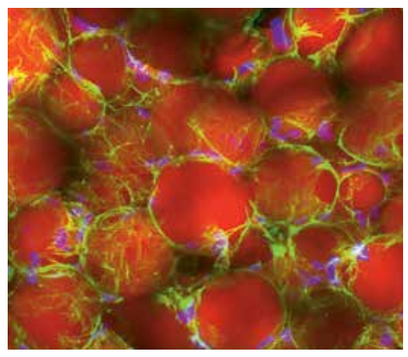
The difficulty comes in determining just what these 3D spaces look like from 2D photos. To solve this challenge, Segura's students begin with simulated photos mimicking a known 3D configuration and introduce "noise" or "fuzziness" to blur the beads' boundaries. A machine learning algorithm designed in collaboration with **Roarke Horstmeyer**, assistant professor of biomedical engineering, is then fed these photos along with the correct answers as to what is bead and what is open space and finds its own methods for distinguishing between the two.

"We're trying to understand what it is about these shapes that is so important to the different biological responses you see," said Segura. "But that's really hard to do without knowing exactly what those shapes are to begin with." ■









LEFT: *A stained slide showing regrowth in a neural cavity caused by stroke. The red segments are new blood vessels while the green depicts new nerve fibers.* TOP RIGHT: *ESEM of a pre-cast porous scaffold* BOTTOM LEFT: *Zeiss Axio Scan large fluorescent image of a precast porogen mold Hyaluronic Acid hydrogel (orange) seeded with mouse mesenchymal stem cells (MSCs) (green=actin, blue=nuclei).* BOTTOM RIGHT: *Microporous annealed particle (MAP) scaffold geometry influences 3D cell spreading (red: MAP, green: F-actin, blue: DAPI).*

Sina Farsiu

Pioneering Photonics-Based Machine Learning

For over a decade, Sina Farsiu has worked to find novel uses for machine learning in photonics-based ophthalmological technology

With appointments in biomedical engineering, ophthalmology, electrical and computer engineering, and computer science, **Sina Farsiu** has a wide range of past and present projects pertaining to photonics-based applications of machine learning. And having been at Duke for more than a decade, his mark can be seen through many interdisciplinary collaborations across campus.

"My laboratory develops machine learning algorithms for a variety of photonic imaging systems to enhance the quality of the images and reduce the amount of time needed to take them," said Farsiu, the Paul Ruffin Scarborough Associate Professor of Biomedical Engineering. "These efforts create an avalanche of data, so we also develop artificial intelligence algorithms to quantify biomarkers of ophthalmological and neurodegenerative diseases from them."

One of the imaging technologies that Farsiu has a long history with is optical coherence tomography (OCT)—essentially a 3D microscope for retinal imaging. Working with **Joseph Izatt**, the Michael J. Fitzpatrick Professor of Engineering at Duke, Farsiu has helped produce smaller and more portable devices with many advantages. His lab was also the first to develop an artificial intelligence system to detect multiple diseases of the eye from OCT images of the retina.

Another technology Farsiu works with, adaptive optics scanning laser ophthalmoscopy, can show researchers the neurons in the eye in vivo. For years, researchers have spent weeks counting photoreceptors by hand while trying to avoid being tripped up by imaging artifacts. Farsiu's PhD student **David Cunefare** found a way around both issues by combining data from two imaging settings and using a deep learning algorithm to spot photoreceptors automatically.

"It's very hard for a human to combine information from two different imaging modalities, but with an AI system, the computer can do it easily," said Farsiu. "Our technology can analyze these images in just a few seconds with an accuracy equal to or even greater than humans."

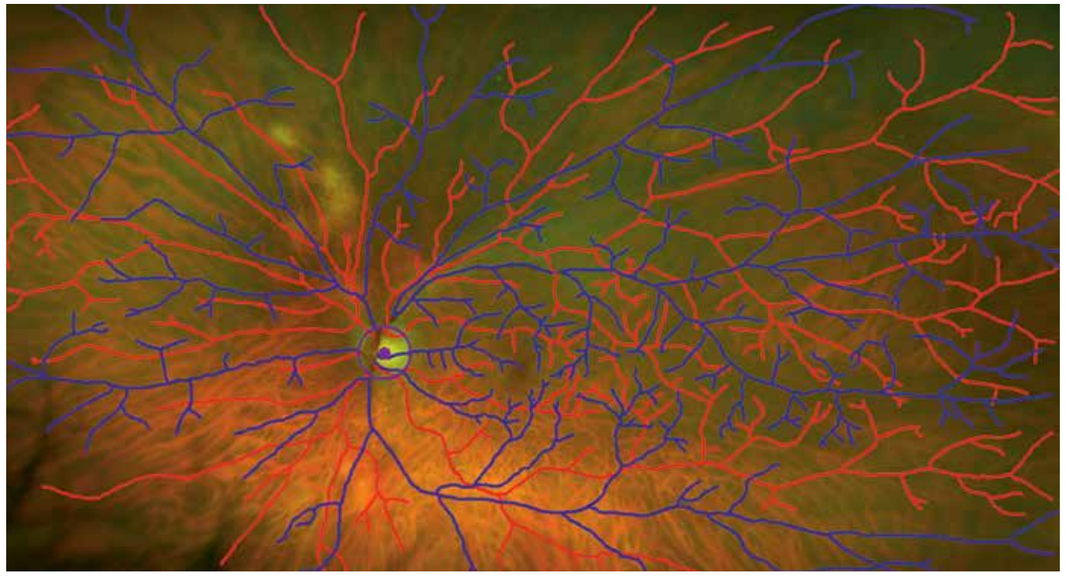
Algorithms such as this are proving a boon to researchers conducting clinical trials. A recent study showed that software built by Farsiu's PhD student **Jessica Loo**, John T. Chambers Scholar could accurately inspect tens of thousands of images from a phase II clinical study in a matter of minutes and essentially for free. When compared to paying people for weeks to complete the same task, the benefits are obvious.

Farsiu's team led by postdoctoral researcher Reza Rasti Borujeniare now working toward tailoring treatments to specific patients afflicted by diabetic macular edema—a leading cause of blindness in working-age Americans.

The first treatment most patients receive for this disease is called anti-VEGF. Besides being expensive and requiring an injection into the eye, the drug doesn't work for everyone. If the patient doesn't respond after months of invasive, inconvenient treatments, the doctor will try a different approach. And it will continue like that until a treatment succeeds or the patient goes blind.

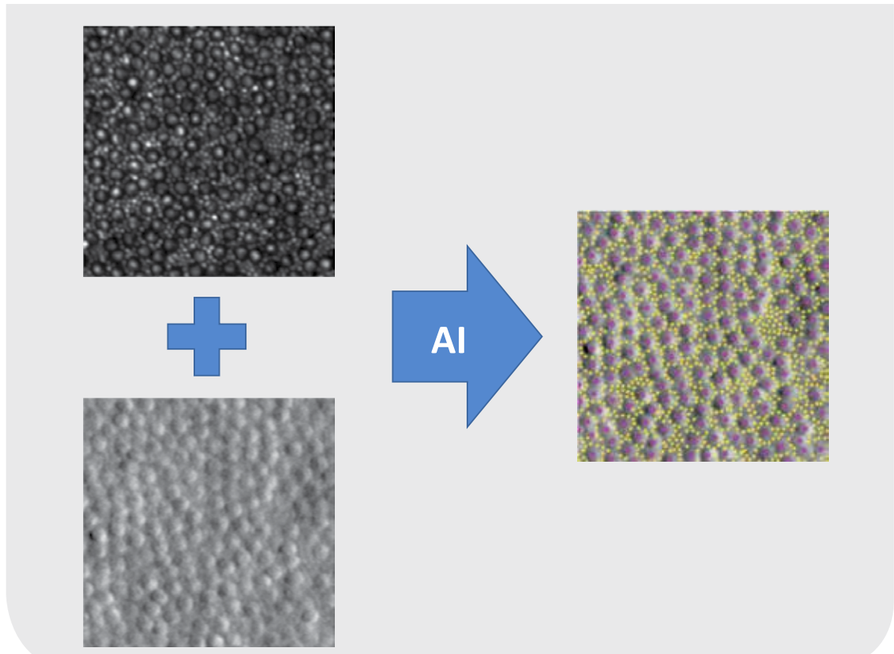
"It's very hard for a human to combine information from two different imaging modalities, but with an AI system, the computer can do it easily."

"But we have developed an artificial intelligence system that can predict which patients will respond to anti-VEGF treatment," said Farsiu. "This would greatly reduce the cost and save many eyes from going blind. For the next few years, we plan on taking this technology that has proven successful in retrospective studies and applying it to large-scale clinical trials to see if we can get the same effect from its use." ■



Retinal arteries and veins overlap each other throughout a wide field-of-view color image. Each edge in the graph is either an artery (in red) or a vein (in blue).

R. Estrada, M.J. Allingham, P.S.. Mettu, S.W. Cousins, C. Tomasi, and S. Farsiu, "Retinal Artery-Vein Classification via Topology Estimation", IEEE Transactions on Medical Imaging, 34(12):2518-34 Dec. 2015



Multi-modal adaptive optics scanning light ophthalmoscope images of human retina are combined using AI to detect rod and cone photoreceptors with accuracy on par with human performance.

D. Cunefare, A.L. Huckenpahler, E.J. Patterson, A. Dubra, J. Carroll, and S. Farsiu, " RAC-CNN: multimodal deep learning based automatic detection and classification of rod and cone photoreceptors in adaptive optics scanning light ophthalmoscope images", Biomedical Optics Express, 10(8), pp. 3815-3832, August 2019

Blocking the Virus Torpedo

Kevin Welsher uses "smart" microscopy techniques to make never-before-seen 3D videos of viruses like flu and HIV just before they invade human cells

When Duke assistant professor **Kevin Welsher** describes the earliest stages of a viral infection, it sounds like a cross between the invasion of Normandy and a moon landing.

Using advanced microscopy techniques to make never-before-seen 3D movies of viruses just before they break into cells, Welsher produces videos with titles such as "approach and landing," "search and invade" and "a closer look at the landing site."

Kevin Welsher

If we can understand what happens to viruses such as flu or HIV before they latch on to the cell surface, he says, we might eventually be able to prevent viral infections altogether.

"It's like blocking oncoming torpedoes before they reach their target, rather than trying to fix the damage after they've hit," said Welsher, who joined the chemistry department in 2015.

Viruses are hard to capture on video. They're tiny, for one.

A typical virus is thousands of times smaller than the period at the end of this sentence—a size once thought impossible to see through traditional light microscopes.

The second challenge is that viruses are free-floating. With most microscopes, Welsher says, capturing a virus as it moves through the body is like watching a high-speed car chase through a traffic cam—it's hard to make out the details of specific cars as they zoom in and out of the camera's field of view.

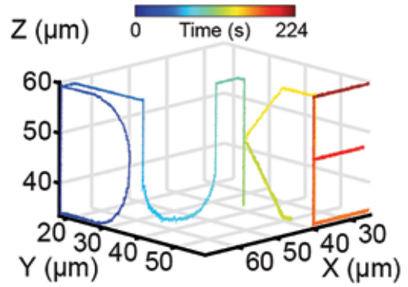
To get around these problems, Welsher has developed a hybrid microscope that combines two imaging techniques. One locks onto fluorescent molecules embedded into the virus and tracks it as it drifts around. The other simultaneously gives a bird's-eye view of nearby cells, many of which are a hundred times the virus's size.

"Really what we are trying to investigate is the very first contacts of the virus with the cell surface—how it calls receptors, and how it sheds its envelope," said Welsher. "We want to watch that process in real time, and to do that, we need to be able to lock on to the virus right from the first moment."

As a postdoctoral researcher at Princeton, Welsher built a prototype model that could track a bright fluorescent bead as it gets stuck in the membrane of a cell. But working with Duke postdoc **Shangguo Hou**, the pair have managed to take the work to another level.

Their new virus cam can track particles that are faster-moving and dimmer compared to the earlier models. "We were trying to overcome a speed limit, and we were trying to do so with the fewest number of photons collected possible," Welsher said.

The ability to spot dimmer particles is particularly important when tracking viruses, Welsher said. These small bundles of proteins and DNA don't naturally give off any light, so to see them under a microscope, researchers first have to stick something fluorescent on them. But many bright fluorescent particles, such as quantum dots, are pretty big compared to the size of most viruses. Attaching one is kind of like sticking a baseball onto a basketball—there is a good chance it might affect how the virus moves and interacts with cells.

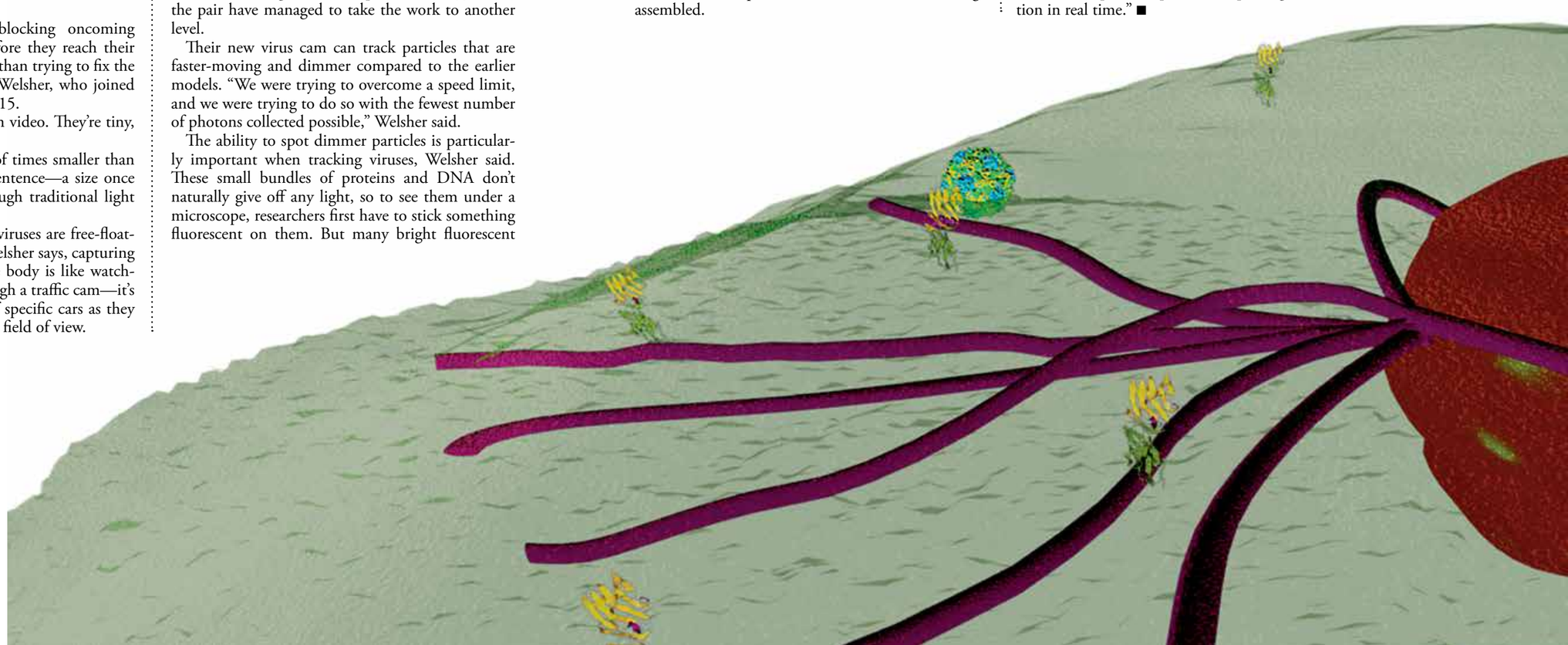


To test out the microscope, the team attached a fluorescent bead to a motion controller and tracked its movements as it spelled out a familiar name.

The new microscope can detect the fainter light given off by much smaller fluorescent proteins—which, if the virus is a basketball, are approximately the size of a pea. Fluorescent proteins can also be inserted into the viral genome, which allows them to be incorporated into the virus as it is being assembled.

"That was the big move for us," Welsher said. "We didn't need to use a quantum dot, we didn't need to use an artificial fluorescent bead. As long as the fluorescent protein was somewhere in the virus, we could spot it."

Now that the virus-tracking microscope is up-and-running, the team is busy building a laser scanning microscope that will also be able to map cell surfaces nearby. "So if we know where the particle is, we can also image around it and reconstruct where the particle is going," Welsher said. "We hope to adapt this to capturing viral infection in real time." ■



A rendering of a virus landing on the surface of a cell membrane

Spotting Trends from Tiny Organs and Tracking Stem Cells

***Shyni Varghese** is exploring how photonics and machine learning can help track implanted stem cells and find cohort-level trends in organ-on-a-chip experiments*

With an appointment spanning three departments and two schools, **Shyni Varghese** is no stranger to building interdisciplinary research enterprises. And as a new member of the Fitzpatrick Institute for Photonics (FIP), she's planning to continue this trend in the coming years.

A leader in the field of biomaterials and stem cells, Varghese is working to shed light on two of her major areas of research—organ-on-a-chip technology and musculoskeletal tissue repair. Besides using standard staining and imaging techniques, she is exploring ways of integrating new photonics and machine learning technologies into her research enterprise.

One of the major hurdles to developing new pharmaceuticals and understanding diseases is the wide variety of responses they provoke in different tissues in the body. Using animal models is imperfect, and drug effects and disease symptoms can vary greatly from person to person.

To develop better models, Varghese is simulating human tissues in lab-on-a-chip technologies and combining them into an integrated system that mimics the complex functions of the human body. Once these systems are up and running, she plans to use optical imaging and machine learning to find patterns in how different cohorts of patients respond to different therapies.

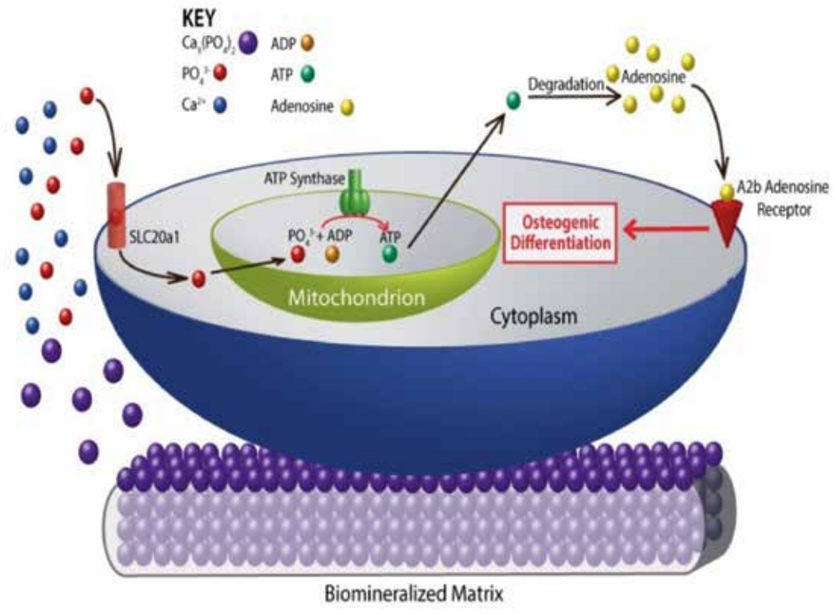
Shyni Varghese

"We can make hundreds of thousands of tissues to test therapies on, but it would take graduate students forever to sit down and analyze them," said Varghese, who has joint appointments in the Departments of Biomedical Engineering, Mechanical Engineering and Materials Science, and Orthopaedic Surgery. "But if we can just run antibodies, stain them and scan them, machine learning algorithms can figure out the patterns and we can start to figure out why different populations have different responses to different drugs."

In the realm of musculoskeletal tissue repair, Varghese's laboratory uses stem cells both to integrate into the existing tissue and to excrete factors that recruit and activate a patient's own cells to promote tissue repair and regeneration.

Varghese is looking into potential collaborations within FIP to use photonics tools to track and monitor the behavior of the transplanted stem cells as a function of time. Not only will this allow the researchers to see where the stem cells go, if they survive long-term and if they begin differentiating into the damaged tissue.

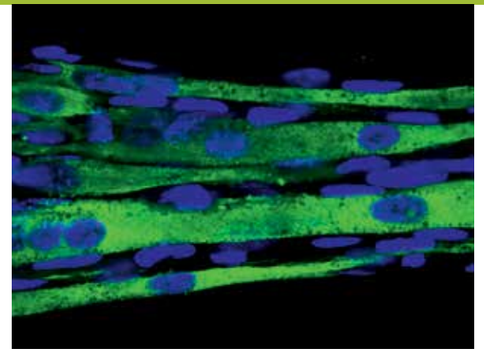
"Not enough is known about what is happening to these stem cells once we transplant them," said Varghese. "If we can track them them, we can analyze the stem cells to characterize exactly how they've changed and how they are behaving throughout the therapy." ■



Schematic showing the molecular mechanism by which the mineral environment in bone tissues promotes osteogenic differentiation of human mesenchymal stem cells

"if we can just run antibodies, stain them and scan them, machine learning algorithms can figure out the patterns and we can start to figure out why different populations have different responses to different drugs."

ABOVE: *Smart biomimetic hydrogels with self-healing abilities.*



Bioengineered skeletal muscle tissues (skeletal muscle-on-a-chip)

Teaching Smart Phones to Screen for Autism

Guillermo Sapiro is using machine learning algorithms to connect children's facial expressions to potential signs of autism spectrum disorder

When it comes to detecting and treating autism spectrum disorder (ASD) in children, the earlier the better. Starting treatment for ASD before 24 months can increase a child's IQ by up to 17 points, significantly improve their quality of life and save the family more than $1 million in lifetime medical costs.

Screening for ASD in young children, however, is easier said than done. The current process relies on a questionnaire given to parents about their child's behavior. This method is inaccurate, adding to the already overburdened licensed ASD clinicians that can have wait times extending past a year, delaying treatment past the ideal time window.

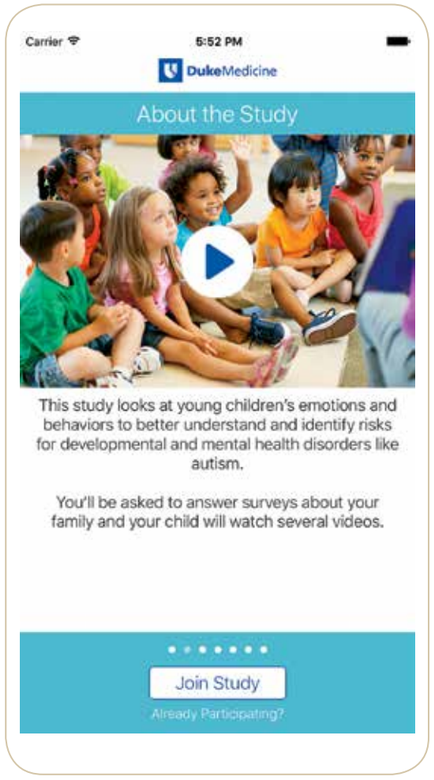
ABOVE: *Guillermo Sapiro accepting the Stansell Family Distinguished Research Award*

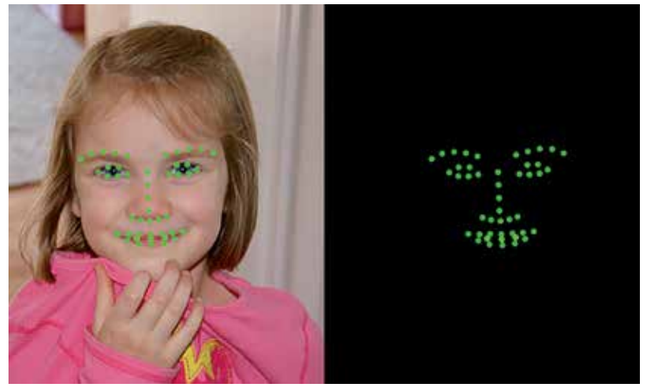
Guillermo Sapiro, the James B. Duke Professor of Electrical and Computer Engineering, in collaboration with Geraldine Dawson, director of the Duke Center for Autism and Brain Development, is developing an app for smartphones and tablets for caregivers and clinicians to use instead. While there are obvious social hurdles to getting caregivers to actually use and trust an app, the primary technical challenge is to convert facial movements data into meaningful information.

Sapiro is building machine learning algorithms that connect facial expressions and eye movements to the human emotions and attention patterns being displayed. He's also using machine learning to develop privacy filters for the images and videos collected by the app.

"We're trying to tackle the challenge of extracting the information we need from a person's face while simultaneously implementing filters to block information users might not want to share," said Sapiro. "We're also working to make our algorithms become better over time with each user and make them scalable and more user-friendly."

In its first year of beta testing, there were more than 10,000 downloads of the app, and 1,756 families with children aged one to six years participated in a study. Parents completed 5,618 surveys and uploaded 4,441 videos. Usable data were collected on 88 percent of the uploaded videos, demonstrating for the first time the feasibility of this type of tool for observing and coding behavior in natural environments.





A screenshot from the beta test version of an "autism app" (left) that helps screen young children for signs of autism by creating landmarks on a child's face (above) to help software analyze facial expressions.

"This demonstrates the feasibility of this approach," said Geraldine Dawson, director of the Duke Center for Autism and Brain Development. "Many caregivers were willing to participate, the data were high quality and the video analysis algorithms produced results consistent with the scoring we produce in our autism program here at Duke."

"We're trying to tackle the challenge of extracting the information we need from a person's face while simultaneously implementing filters to block information users might not want to share."

The researchers also tested the app results against evaluations conducted by ASD specialists. They found that the app was almost 90 percent accurate in some subset of behaviors—a promising first step. Moving forward, the researchers hope the app will become a useful complementary tool for these specialists, providing a more detailed look at a child's actions and reactions than possible by the human eye.

The researchers are also looking to see if this approach could be applied to other behavioral disorders, such as eating disorders, dementia or Alzheimer's. They also hope this work will eventually make its way into the developing world, where screening for ASD is expensive and time consuming, and specialists are often unavailable. If the app is ultimately successful, however, Sapiro estimates that it would only cost $1 and 10 minutes to process data collected by a parent anywhere in the world.

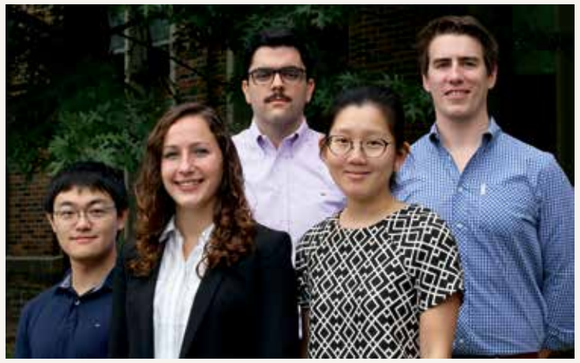
"This technology has the potential to transform how we screen and monitor children's development," said Sapiro. ■

FIP Fellows & Scholars

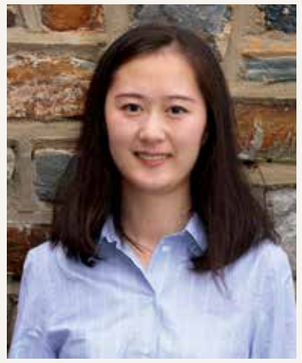
THE SCHOLARS PROGRAM provides existing Duke graduate students within the FIP approximately $50,000 each toward their stipend, tuition remission, grad school fees and health insurance for two years. This program is designed to reward the most outstanding individuals within FIP for their accomplishments and potential. Each candidate, nominated by a FIP professor, was judged on the criteria of demonstrated excellence in their academic studies, research and projects that involved inter-group or interdisciplinary research stimulating new collaborations among FIP faculty.

THE FELLOWS PROGRAM, used as recruiting tool for the top candidates, provides incoming graduate students a one year fellowship program, which awards $10,000 top-up on their stipend and $1000 towards educational travel. Each candidate is nominated by a FIP professor and judged on the criteria of research accomplishments, research potential, personal qualities and collaborative potential.

2018 FIP Fellows & Scholars



LEFT TO RIGHT: *2018-2019 John Chambers Fellows & Scholars Junfei Li (Scholar), Erika Chelales (Fellow), E. Tomas Barraza (Scholar), Jessica Loo (Scholar), Evan Jelly (Fellow)*



2018 Fitzpatrick Foundation Scholar Mucong Li

2019 FIP Fellows & Scholars

LEFT TO RIGHT: 2019-2020 John Chambers Fellows & Scholars Adriana Stohn (Fellow), Betul Teymur (Scholar), Enakshi Sunassee (Fellow), Jessica Loo (Scholar), Shan Yang (Scholar)

THE FITZPATRICK INSTITUTE FOR PHOTONICS (FIP) was able to award several graduate student fellowships through the continued support and generosity of **John T. Chambers** and the **Fitzpatrick Foundation**. Each candidate was nominated by a FIP Professor and judged on the criteria of research accomplishments, research potential, personal qualities and collaborative potential.

Why Duke **MEng?** Meet two of our Photonics Master's Students:

Perry Wang

After earning a bachelor's degree in optical engineering with a minor in business from the University of Rochester, Perry Wang knew that Duke's Master of Engineering in Photonics and Optical Sciences program was the best place for him to continue his studies. He felt the program offered opportunities to learn about the different applications of photonics in the cross-disciplinary context of industry in research. And paired with the business courses included in the degree, the program looked to be excellent preparation for improving himself in a more well-rounded way. The program led to an opportunity to intern at Lumedica, a startup company in Durham building affordable optical coherence tomography (OCT) imaging systems to aid in medical diagnostics. Besides working on the technical details of a dual-axis system for improved imaging depth, the small size of the company has also allowed Perry to conduct market research and become heavily involved in the details of both the design process and the business side of the company.

"I knew that I would be getting strong guidance from world-class professionals."

Xiaowei Gong

With limited exposure to optics through her undergraduate degree in physics from the Ohio State University, Xiaowei Gong decided Duke's Master of Engineering in Photonics and Optical Sciences program was the perfect fit. The program's advanced optics course gave her the basic knowledge she needed, while its business classes taught her how to communicate with people more effectively. It also provided the opportunity to conduct summer research with Professor Warren Warren studying the temporal characterization of mid-infrared femtosecond laser pulses. The research experience helped her realize what kind of job she wanted to pursue, helping her to land a job in China with a LiDAR company as an optical engineer.

"The Master of Engineering program offered specialized technical classes plus business leadership and management courses, which perfectly met my need."

Matriculated in 2018: Xiaowei Gong, Ohio State University, Perry Wang, University of Rochester, Kai Wang, Shanghai University, Liangze Cui, Beijing Univ of posts and telecommunications (BUPT)

Matriculated in 2019: Daiwei Li, Delaware State University, Ye Tian, Beijing Univ of posts and telecommunications (BUPT) Zhanghao Yang, Beijing Institute of Technology, Dingzhe Zheng, University of Rochester

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Heather E. Whitson, MD, Assoc. Prof.
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Aimee K. Zaas, MD, Assoc. Prof.

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Georgia M. Beasley, MD, Assist. Prof.
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