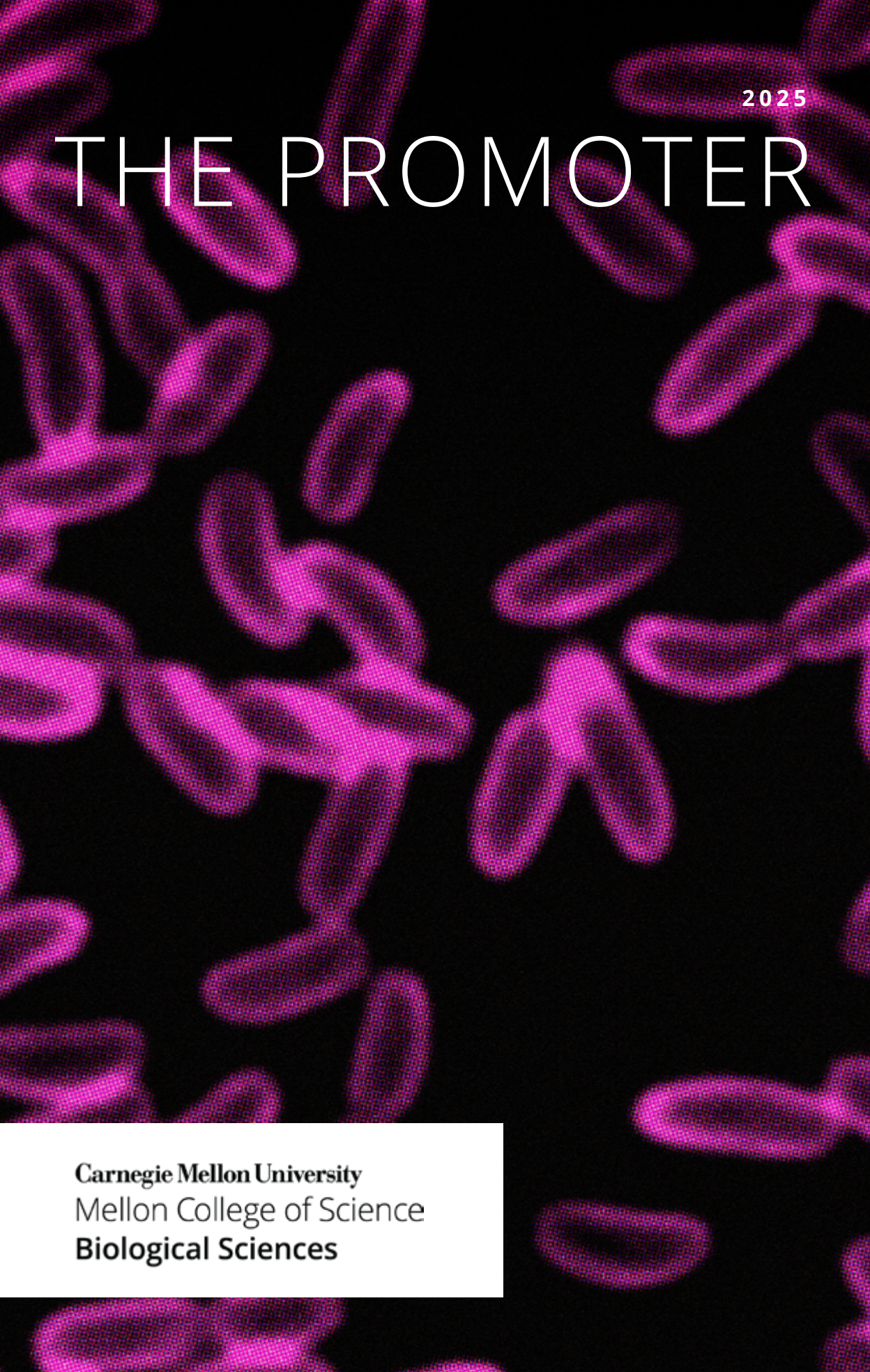

2025

THE PROMOTER

Carnegie Mellon University
Mellon College of Science
Biological Sciences

THE PROMOTER

The Department of Biological Sciences

The Promoter is published yearly by the Department of Biological Sciences at Carnegie Mellon University for its students, alumni and friends to inform them about the department and serve as a channel of communication for our community. Readers with comments or questions are urged to send them to rule@andrew.cmu.edu. The department is headed by Gordon Rule.

Editor-in-Chief
Gordon Rule, Interim Department Head

Editor
Heidi Opdyke, Associate Dean for Marketing & Communication

Design & Layout
Samantha Zemanek, Graphic Designer

Contributing Writers
Angela Ford, Kirsten Heuring, Amy Pavlak Laird, Shane Landis, Heidi Opdyke, Ann Lyon Ritchie, Gordon Rule, Elizabeth Speed

Photography & Images
Jonah Bayer, Digital Producer
Courtesy of Carnegie Mellon University, unless otherwise noted

Online Magazine
Gigi Wiltanger, Web Manager
Iulia Dumitriu, Web Content Administrator

The Department of Biological Sciences
Carnegie Mellon University
5000 Forbes Avenue
Pittsburgh, PA 15213
www.cmu.edu/bio

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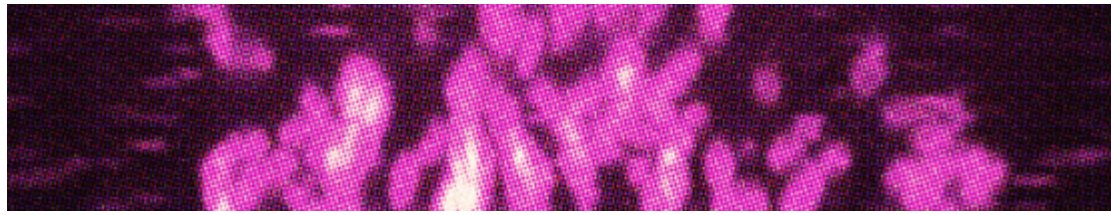


Letter from the Department Head

Greetings! I am thrilled to share some of the exciting advancements and achievements happening in the Department of Biological Sciences. Research in this area is playing an increasingly important role in understanding fundamental biological processes, leading to the treatment of human diseases. Please take the time to read about current scientific advancements in the department as well as our efforts in scientific education.

Our department continues to be at the forefront of interdisciplinary groundbreaking research. In 2024, Joel McManus received a grant to work with University of Pittsburgh researchers to study a key gene deleted in patients with Prader-Willi syndrome. Aryn Gittis won a neurobiology of brain disorders award for studying Parkinson's disease, and Leon Zhao is conducting pioneering work that supports research aimed at making vision-restoring whole eye transplants a reality.

One of the most fascinating areas of our research involves the study of biofilm communities and their communication mechanisms. Understanding how these microbial communities interact is crucial for developing new strategies to combat infections and improve health outcomes. Furthermore, our investigations into the importance of microbiomes are shedding light on the complex relationships between microorganisms and their hosts, with implications for everything from gut health to disease resistance.

I'd also like to highlight our colleagues based on the Carnegie Mellon University in Qatar campus. I have spent more than a decade at Doha and know first-hand how important fostering a culture of collaboration and shared purpose is. This collective spirit has led to a number of joint projects that enhance our ability to impart essential biological knowledge to non-majors as well as to teach complex biological topics, ensuring that all biological sciences majors receive the best from their education.

I am proud to celebrate the achievements of our students, who continue to excel and gain recognition for their work. Their dedication and innovation are truly inspiring, and their accomplishments reflect the high standards of our department.

Moreover, I am delighted to highlight the pioneering work of one former student in the field of pediatric immunology, David Hill. David completed his bachelor's degree in biological sciences in 2005 and his M.D./Ph.D. from University of Pennsylvania in 2013. David specializes in diagnosing and treating children with food allergies and asthma. As a physician-scientist he works to give his patients a healthier life.

If you find yourself in Pittsburgh, let me know. I'd love to chat with you about the department and our people.

Gordon Rule, Ph.D.

Professor and Interim Head, Department of Biological Sciences

Faculty Notes

Three CMU Biologists Receive Kaufman Foundation Grants

Assistant Professors Jonathan Henninger and Catherine Armbruster and Associate Professor Luisa Hiller were awarded funding from the Charles E. Kaufman Foundation in late 2024. The grants are designated for faculty at Pennsylvania institutions conducting innovative, fundamental scientific research.

A grant of $150,000 over two years was awarded to Armbruster for research that investigates the potential advantage of biofilm genetic diversity to survive transitions from one environment to another — such as moving from a water pipe into a human host. Recent work has shown that biofilms harbor elevated levels of genetic diversity, even among biofilms populated by a single species of bacteria. This proposal aims to better understand the evolutionary consequences of this diversity.

A New Investigator grant of $150,000 over two years was awarded to Henninger for research on an overlooked gene expression regulation mechanism that Henninger discovered in which RNAs regulate their own production. Henninger seeks to explore this mechanism by understanding how widely it is used in cells as well as the molecular basis for its function. If successful in whole or in part, it could cause a paradigm shift in how biologists think about gene expression regulation.

A New Initiative grant of $300,000 over two years was awarded to Hiller; Phil Campbell, co-investigator and research professor in the Department of Biomedical Engineering; and Xi Ren, co-investigator and associate professor in the Department of Biomedical Engineering. Their research seeks to understand the immune consequences of the uptake of extracellular vesicles from the bacterium *Streptococcus pneumoniae* by mammalian cells. This proposal originated from an observation by Hiller's lab, and the proposal aims to investigate whether this is a closed loop in which only mammalian cells uptake the bacterium's extracellular vesicles or whether bacteria also uptake mammalian vesicles and alter their behavior or physiology in response.

Catherine Armbruster, Jonathan Henninger and Luisa Hiller (left to right)

Zhao Joins Project To Make Whole Eye Transplants a Reality

Carnegie Mellon University is part of a major undertaking that brings together more than 40 scientists, doctors and industry experts hand-picked from around the country to make vision-restoring whole eye transplants a reality.

The team received an award of up to $56 million from the Transplantation of Human Eye Allografts program at The Advanced Research Projects Agency for Health within the U.S. Department of Health and Human Services. The project is led by Stanford University.

Leon Zhao, Eberly Family Associate Professor of Biological Sciences and a member of Carnegie Mellon's Neuroscience Institute, is part of the team. The Zhao Biophotonics Lab will apply its Magnify Expansion Microscopy technology to address a critical challenge in whole eye transplantation: the precise mapping and reconstruction of optic nerve fascicles (arrangements of fibers) to corresponding layers in the lateral geniculate nucleus (LGN), located in the thalamus deep within the brain.

"This is a pivotal step toward enabling functional vision restoration in animal models and, eventually, human patients," Zhao said.

Zhao's team will provide nanoscale tissue structure resolution through physical expansion up to 11 times, retaining proteins, lipids and nucleic acids within the expanded gels. Through the process, samples are embedded in a swellable hydrogel that homogenously expands to increase the distance between molecules allowing them to be observed in greater resolution.

The innovative technique allows visualization of the intricate architecture of the optic nerve and LGN at resolutions approaching 25 nanometers using conventional microscopes and as fine as 15 nanometers when paired with advanced imaging modalities.

"Our team will produce a detailed, high-resolution map of the optic nerve's 200+ fascicles, which collectively house over a million axons," he said. "This mapping will guide the reconnection of donor and recipient optic nerves with unprecedented precision, a critical milestone in making functional whole-eye transplantation a reality."

■ *Heidi Opdyke*

McManus Awarded Grant To Advance Prader-Willi Syndrome Research

Prader-Willi syndrome (PWS), a genetic condition that affects 350,000 people worldwide, causes chronic hunger, growth hormone deficiency and behavior challenges. In most cases, PWS is caused by a random genetic error — a section of the paternal copy of chromosome 15 is deleted. Several genes are in the missing section, and it's not yet known how their loss contributes to the complex combination of symptoms experienced by patients.

Carnegie Mellon's Joel McManus, associate professor in the Department of Biological Sciences, and Pitt's Robert Nicholls, professor in the Department of Pediatrics, received a $162,000 grant from the Foundation for Prader-Willi Research to study the regulation and function of a key gene, *SNURF-SNRPN*, that is usually deleted in patients with the disorder.

"*SNURF-SNRPN* is a very complex gene — and a unique one — because it makes two proteins from the same gene," McManus said. "So, the same messenger RNA makes two proteins. And that's pretty unusual."

In one focus of the grant, the team will work to understand how the two proteins are translated from the same mRNA. They are also looking into what *SNURF-SNRPN*'s normal function is in the cell to help pinpoint what might go wrong when it is missing.

McManus's lab focuses on understanding the mechanisms that regulate mRNA translation and how variation in RNA sequences and structures affects protein production. Even though he has largely worked with yeast in the past, McManus said he is excited to turn his focus toward human genes, and Nicholls said he is thrilled to be partnering with McManus.

"A lot of important biomedical and clinical breakthroughs come from the basic sciences, so you need people like Joel with the foundational science work from yeast who can bring insight into complex human disease issues," said Nicholls, who received a lifetime achievement award in 2013 from the Prader-Willi Syndrome Association USA.

■ *Amy Pavlak Laird*

Gittis Receives Neurobiology of Brain Disorders Award for Studying Parkinson's Disease

Biological Sciences Professor Aryn Gittis received a 2024 Neurobiology of Brain Disorders (NBD) Award by the McKnight Endowment Fund for Neuroscience. The NBD Awards support innovative research by U.S. scientists studying neurological and psychiatric diseases. Gittis' work is one of four projects selected for the honor. Each project will receive $100,000 annually for three years.

Gittis, who is also a member of the Carnegie Mellon Neuroscience Institute, investigates how neural circuits control movement in humans and how to retrain those circuits after injury or damage. Her new research explores ways to tap into the brain's plasticity to help ameliorate the effects of dopamine depletion — a key characteristic of Parkinson's disease — and improve movement function for longer periods of time using electrical impulses.

Deep brain stimulation, in which wires implanted in the brain deliver a constant, nonspecific electrical charge, has been approved and used to help relieve symptoms of Parkinson's disease for some time. However, it only addresses the symptoms, which reappear immediately when the charge is turned off. Gittis' lab aims to find exactly what neuronal pathways are required for locomotor recovery, how electrical pulses can be "tuned" to affect just these subpopulations and how these subpopulations can be stimulated to essentially repair themselves, offering longer-lasting relief from symptoms without ongoing stimulation.

Preliminary work shows promise: Working with a dopamine-depleted mouse model, Gittis and her team have identified specific subpopulations of neurons in the brain stem necessary for the relief of symptoms. Excitingly, when stimulated with a pulse of carefully tuned electricity (rather than a constant flow) the cells' activity is changed in a way that results in hours of improved mobility with no further stimulation. Her research aims to determine whether these activity changes can be made more permanent to start healing and rewiring neural circuits.

■ *Heidi Opdyke*

New Faculty

CATHERINE ARMBRUSTER

Assistant Professor

Catherine Armbruster's lab investigates the ecology and evolution of opportunistic pathogens in biofilms, especially *Pseudomonas aeruginosa*, as they transition from the environment to the host and vice versa. Armbruster earned her Ph.D. in microbiology from the University of Washington and her master's degree in public health at Emory University. Prior to joining Carnegie Mellon, she completed her postdoctoral training in the laboratory of Jennifer Bomberger at the University of Pittsburgh and Dartmouth College, where she studied how bacteria evolve in cystic fibrosis biofilm infections.

JONATHAN HENNINGER

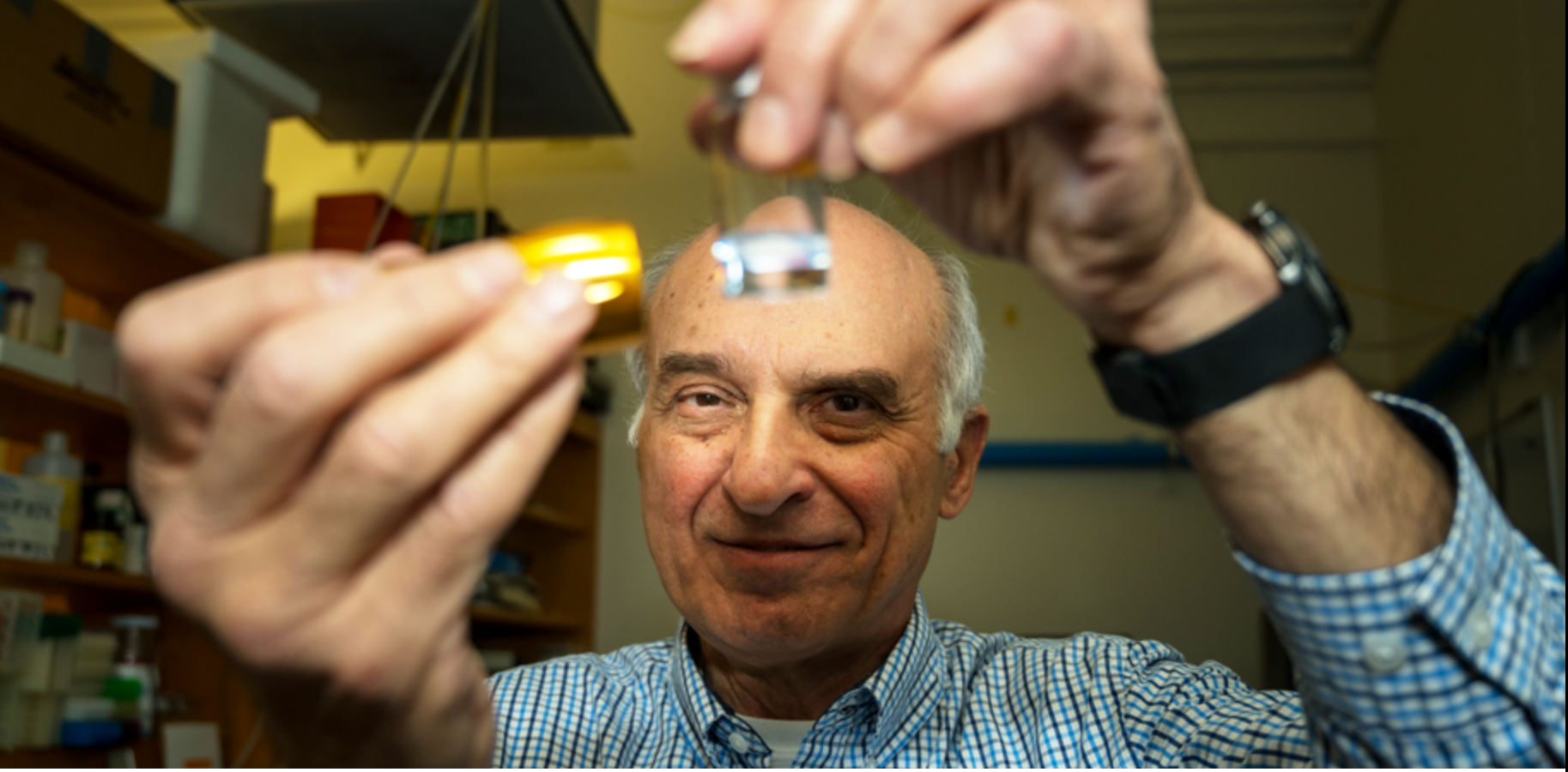
Assistant Professor

Jonathan Henninger investigates how cells control gene expression, what happens when things go awry as cells take shape and how the cells lose their identity during early stages of disease. Henninger earned his Ph.D. at Harvard University in developmental and regenerative biology. Prior to Carnegie Mellon, he joined the Whitehead Institute for Biomedical Research at MIT as a postdoctoral fellow. There, he and his team discovered that RNA molecules born during the early stages of gene expression are intimately involved in their own production.

IRENE KAPLOW

Assistant Professor

Irene Kaplow earned her Ph.D. in computer science from Stanford University. After graduation, she joined Carnegie Mellon as a Lane Postdoctoral Fellow in Andreas Pfenning's lab in the Computational Biology Department, where she developed methods to identify regulatory elements whose regulatory activity differences between species are associated with the evolution of neurological phenotypes. Her research investigates how gene expression has evolved and applies techniques she used at Duke, where she worked as a research scientist, to see the roles of different regions of the genome in evolution.



After 42 Years, Fred Lanni Changes Focus

Examining cells in a microscope has always been a big deal for Carnegie Mellon University Associate Professor of Biological Sciences Frederick Lanni, proving that sometimes the smallest things can have the greatest impact.

Lanni arrived at Carnegie Mellon as a postdoctoral researcher in August of 1982 to work with Professor D. Lansing Taylor. Taylor, along with the late Professor Alan Waggoner and Emeritus Professor Robert F. Murphy, had created the Center for Fluorescence Research in Biomedical Sciences, and Lanni wanted to be part of it.

"The original goal was to bring modern methods of imaging, fluorescence technology, and computer analysis into cell biology where problems in that field could really be addressed," Lanni said.

One of the steps to enhance cellular imaging was to improve the tools to examine cells. When the Fluorescence Center was founded, fluorescence microscopy involved using night vision camcorders to take video of the cells. Then, researchers would photograph the videotape playback and develop and print the film based on what they were attempting to examine.

Lanni and his colleagues wanted a better way to see the structures within a cell, so they developed what they called standing wave fluorescence microscopy (SWFM), an early version of what is now better known as structured illumination microscopy (SIM). This technique allowed researchers to see the 3D structure of cells by fluorescence at a higher resolution than they could before.

"It was a way to use the interference of light to improve the three-dimensional resolution of the fluorescence microscope," Lanni said. "It was the first working instrument to use this principle."

Lanni has taught generations of Carnegie Mellon students, mostly in Modern Biology, the introductory course for students in the Department of Biological Sciences, and a popular science elective for others. He also developed and taught Biological Imaging and Fluorescence Spectroscopy, a course for graduate students and upper-level undergraduates. There, he shared his passion for microscopy with students who needed a research-level understanding of the instrument.

Lanni retired at the end of the fall 2024 semester. He plans to conduct research as an emeritus professor, and he hopes to spend more time with his adult children, who live across the U.S. He said he is proud of the discoveries he has made as a researcher.

"The greatest thing about science is, every once in a while, you realize that you're looking at a result that no one else has ever seen before or gotten before," Lanni said. "I'm so glad I've had those moments."

■ *Kirsten Heuring*

RESEARCH REVEALS UNDERLYING MECHANISM THAT RENDERS CERTAIN HIGH-RISK CANCERS IMMORTAL

Researchers at Carnegie Mellon University have uncovered a key mechanism that promotes telomere elongation, a discovery that has implications for understanding and potentially treating some of the world's deadliest cancers.

Telomeres are the protective caps at the end of chromosomes, like the plastic piece at the end of a shoelace. Telomeres shorten with every cell division, until they disappear and the cell dies.

Most cancer cells use telomerase to continuously lengthen their telomeres, keeping the cell alive. But some cancer cells use a process called alternative lengthening of telomeres (ALT). Because the ALT process protects telomeres in tumor cells, it is an attractive target for cancer treatments.

The researchers, led by Huaiying Zhang, Eberly Family Assistant Professor of Biological Sciences, focused on a specific ALT component called SUMO.

SUMOs (small ubiquitin-like modifiers) attach to other proteins to modify their function, from adjusting how they fold to directing where they move around the cell. They mediate numerous processes in healthy cells. In ALT cancer cells, SUMO tags DNA repair proteins, steering them to the telomeres that need to be lengthened.

Rongwei Zhao, a graduate student in Zhang's group, used a novel approach to study how SUMO-tagged proteins behave once they are gathered at a telomere. Along with collaborators, Zhang and Zhao developed a chemical dimerization system that allows researchers to target specific proteins to specific places on a chromosome.

Their findings suggest that SUMO is the key driver for phase separation and recruitment of DNA repair factors on telomeres. It is a step toward putting the pieces together to understand how SUMOylation functions in ALT cancer cells and in other cellular processes.

■ *Amy Pavlak Laird*

Maya Kemaldean, Emily Drill and Nesrine Affara (left to right)

Faculty Exchange Encourages a Unified Learning Experience

Faculty in Carnegie Mellon University's Department of Biological Sciences cross borders to inspire a world of learning. The department bridges two continents and two campuses — the flagship campus in Pittsburgh, Pennsylvania, and the undergraduate campus in Doha, Qatar.

Yasser Majeed, assistant teaching professor of biological sciences at CMU-Q, is the first faculty member from biological sciences to participate in a faculty exchange. Majeed, who joined Carnegie Mellon in 2024, spent seven weeks in Pittsburgh during the fall of 2024. The experience helped him understand the teaching philosophy and methods at Carnegie Mellon.

"CMU follows a Socratic approach, which encourages students to arrive at answers through guided questioning," Majeed said. "It teaches students how to think through problems."

Majeed teaches a genetics laboratory course and works closely with Carrie Doonan, teaching professor and director of undergraduate laboratories for biological sciences. Doonan guided Majeed in key aspects of teaching laboratory courses and introduced him to the department's culture and philosophy.

"Carnegie Mellon emphasizes the educational experience, and in lab courses this is particularly important," Majeed said. "I really value how connected our faculty in Qatar is with our colleagues in Pittsburgh. We collaborate and we align our teaching practices so students in both places receive the same experience."

CMU-Q offers programs in biological sciences, business administration, computer science and information systems. Students who attend CMU-Q have identical graduation requirements as those on the main campus. CMU-Q graduates have CMU degrees, conferred from the Pittsburgh campus.

While Majeed was in Pittsburgh, Emily Drill, associate teaching professor of biological sciences on the Pittsburgh campus, traveled to CMU-Q to teach lab courses and learn about the campus.

"We work hard to make sure that course structure and the learning objectives are very much the same between the Pittsburgh campus and the Qatar campus, and these lab courses are really critical to the student experience," Drill said. "This was a chance to see firsthand how courses run there and see what we could do to make sure that we're aligning our teaching objectives."

Drill taught Experimental Techniques in Molecular Biology lab and Neurobiology of Disease, an elective class that typically is not offered on the Qatar campus.

"The latter was a really fun class to teach," Drill said. "Since it's an introductory course, you get a big mix of students, so I had first years, second years and fourth years. They all really enjoyed it."

Doonan, who spent two weeks at the Qatar campus in January 2025, is a strong supporter of faculty exchange: "Students learn better when they hear different perspectives. Faculty exchange fosters collaboration and teamwork, and I think that makes us all better teachers."

Majeed strongly recommends faculty exchange, especially for professors new to Carnegie Mellon.

"This was such an enriching experience, and an excellent way to begin teaching at CMU-Q," Majeed said. "I strongly recommend other new faculty members to make the most of this opportunity."

Drill said that the experience is just as valuable for faculty who have been at Carnegie Mellon for years.

"Getting to spend time in that environment was really impactful," Drill said. "It helps to connect the department and give the students across both campuses a richer experience."

■ *Angela Ford and Kirsten Heuring*

BIOLOGICAL SCIENCES MICRO-COURSES BRIDGE CAMPUSES

During the spring 2025 semester, Ken Hovis, teaching professor of biological sciences and MCS Assistant Dean for Educational Initiatives, taught Biology for Life Special Topics Micro: Understanding the Demented and Delusional Brain. In micro courses, professors based in Pittsburgh travel to Doha for a week to teach then spend the next two weeks instructing students virtually. This micro course supplemented Drill's mini course, and students who took both qualified for the same credits as a full neuroscience course.

■ *Kirsten Heuring*

Research Roundup

Tuft Cell Expression Changes with Sleeping, Eating Cycles

A team of researchers from Carnegie Mellon University's Department of Biological Sciences and the University of Texas Southwestern Medical Center have uncovered how a subset of cells in the intestines change throughout the day.

"We found abundance of the sentinel tuft cells is higher at dusk, the beginning of the active phase, and low at dawn, the beginning of the resting phase," said Jianglin Zhang, a postdoctoral fellow in biological sciences at Carnegie Mellon and first author on a paper published in Science Immunology. "However, if feeding times were reversed, the abundance of tuft cells was also reversed."

Tuft cells are found in the lining of the intestines and are implicated in monitoring the immune system. They survey the gut's luminal environment and signal other cells if they detect potential immune threats.

To study these cells, the researchers altered mice's feeding schedules, disrupted mice's gut microbiota or infected mice with gut parasites or viruses. They then measured changes in tuft cells and various signals.

"We were the first to study tuft cell biology across day-night cycles," said Zheng Kuang, assistant professor of biological sciences at Carnegie Mellon. "It was extremely labor intensive and required extra caution to study this process in both the daytime and nighttime."

The researchers found that HDAC3, a histone modifying enzyme, promotes the creation of tuft cells and the changes in abundance throughout the day. They also found changes to a developmental pathway that HDAC3 targets reduces the amount of tuft cells and reduces the body's ability to fight infections.

"Tuft cells play key roles in immunity and are also implicated in diseases including obesity, inflammatory bowel disease and colorectal cancer," Kuang said. "Our findings suggest new avenues for fighting against these diseases by targeting these tuft cells."

The researchers plan to further study the implications of tuft cell rhythms in healthy and diseased mice.

Zhang and Kuang were joined by Junjie Ma, Yiran Duan, Samskrathi Sharma, Sarah Oladejo, Xianda Ma and Giselle Arellano from Carnegie Mellon and Guoxun Wang, Robert Orchard and Tiffany Reese from the University of Texas on "HDAC3 Integrates TGF-β and Microbial Cues to Program Tuft Cell Biogenesis and Diurnal Rhythms in Mucosal Immune Surveillance." Their work was funded by the National Institutes of Health, the Charles E. Kaufman Foundation and the Shurl and Kay Curci Foundation.

■ *Kirsten Heuring*

RUST BELT MICROBIOME CONFERENCE BRINGS RESEARCHERS TOGETHER

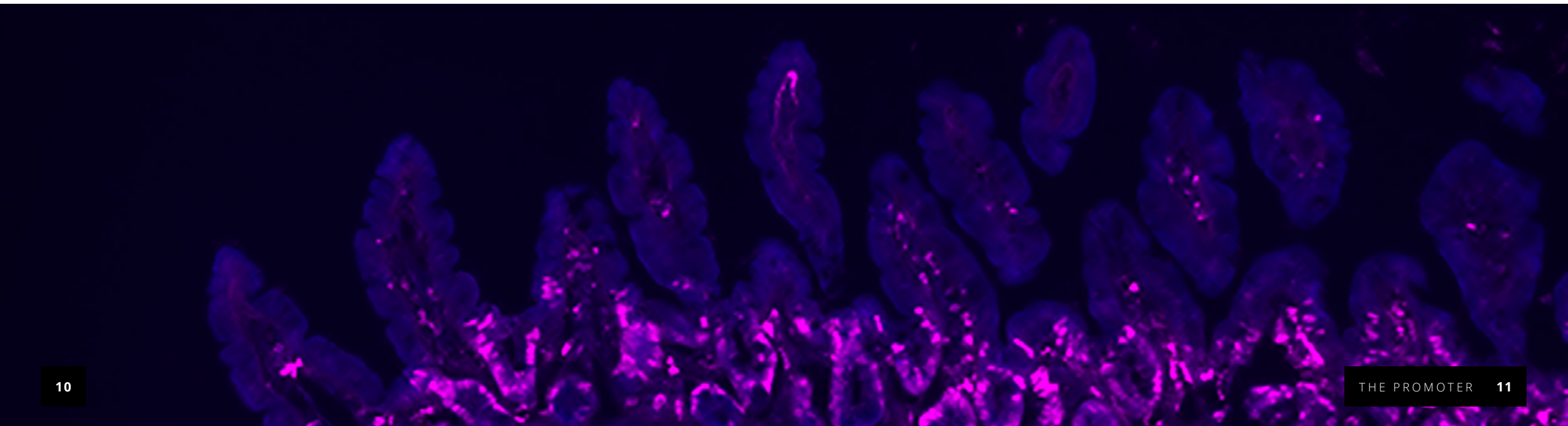
The Rust Belt Microbiome Conference (RBM), a joint effort by Carnegie Mellon University's Mellon College of Science, the Center for Medicine and the Microbiome and the University of Pittsburgh, allowed researchers from across the country to learn more about the field.

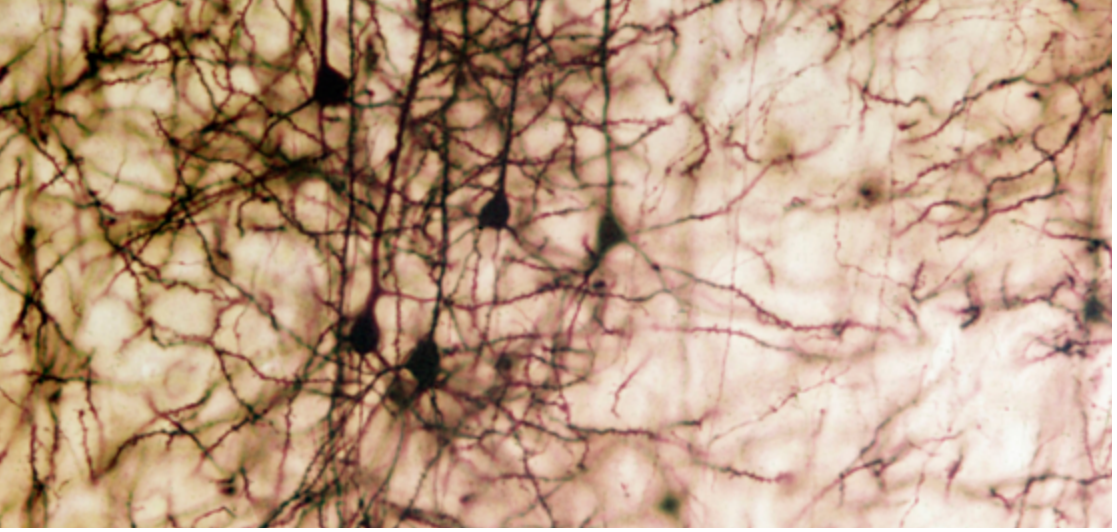
The conference, held in November 2024, covered microbial ecology and the role of the microbiome in human health. Luisa Hiller, Eberly Family Career Development Associate Professor of Biological Sciences at Carnegie Mellon, is a co-host and co-founder of the event.

"The RBM was designed to integrate concepts from microbial pathogenesis, ecology, evolution and genomics with microbiome studies to foster collaborations and discussion among scientists and physicians at all levels of their careers," Hiller said. "After our third iteration, it is such a great pleasure to see the group develop."

In addition to keynote speeches, the conference provided undergraduate students, graduate students and postdoctoral trainees with the opportunity to present their research. The event concluded with abstract awards to recognize extraordinary originality in research.

■ *Shane Landis*





Brain Activity Changes During, After Learning, Researchers Find

Carnegie Mellon University researchers have found that activity in pyramidal neurons, a type of cell commonly found in the brain's cerebral cortex, change in activation when the brain is learning.

"Learning happens every day," said Mo Zhu, a neuroscience graduate student and first author on the paper. "We found learning shapes the stimulus-evoked responses of neurons, but this neuroplasticity might be transient."

Researchers placed mice in an automated home-cage system, so the mice could learn how to receive a reward by themselves without set training times. While the mice were training, the researchers used calcium imaging, which allowed them to consistently measure the populations of pyramidal neurons in the sensory cortex, a part of the cerebral cortex dedicated to processing senses, over time.

Scientists have long believed that sensory processing would be enhanced during learning, increasing brain activity for behaviorally-important cues. However, Zhu and colleagues discovered that this was not the case. Although sensory responses were modestly strengthened at the very onset of training, once mice learned the task this effect disappeared.

"It looked like there was maybe a little burst of enhanced sensory response, and then responses actually decrease compared to their pretraining levels," said Alison Barth, Maxwell H. and Gloria C. Connan Professor in the Life Sciences. "We think that once animals figure out the task, neural circuits reorganize. It looks like neural activity becomes more sparse, which may more efficiently encode the stimulus."

Sandra Kuhlman, associate professor of biological sciences at the University of Buffalo and a former Carnegie Mellon faculty member, assisted with data analysis.

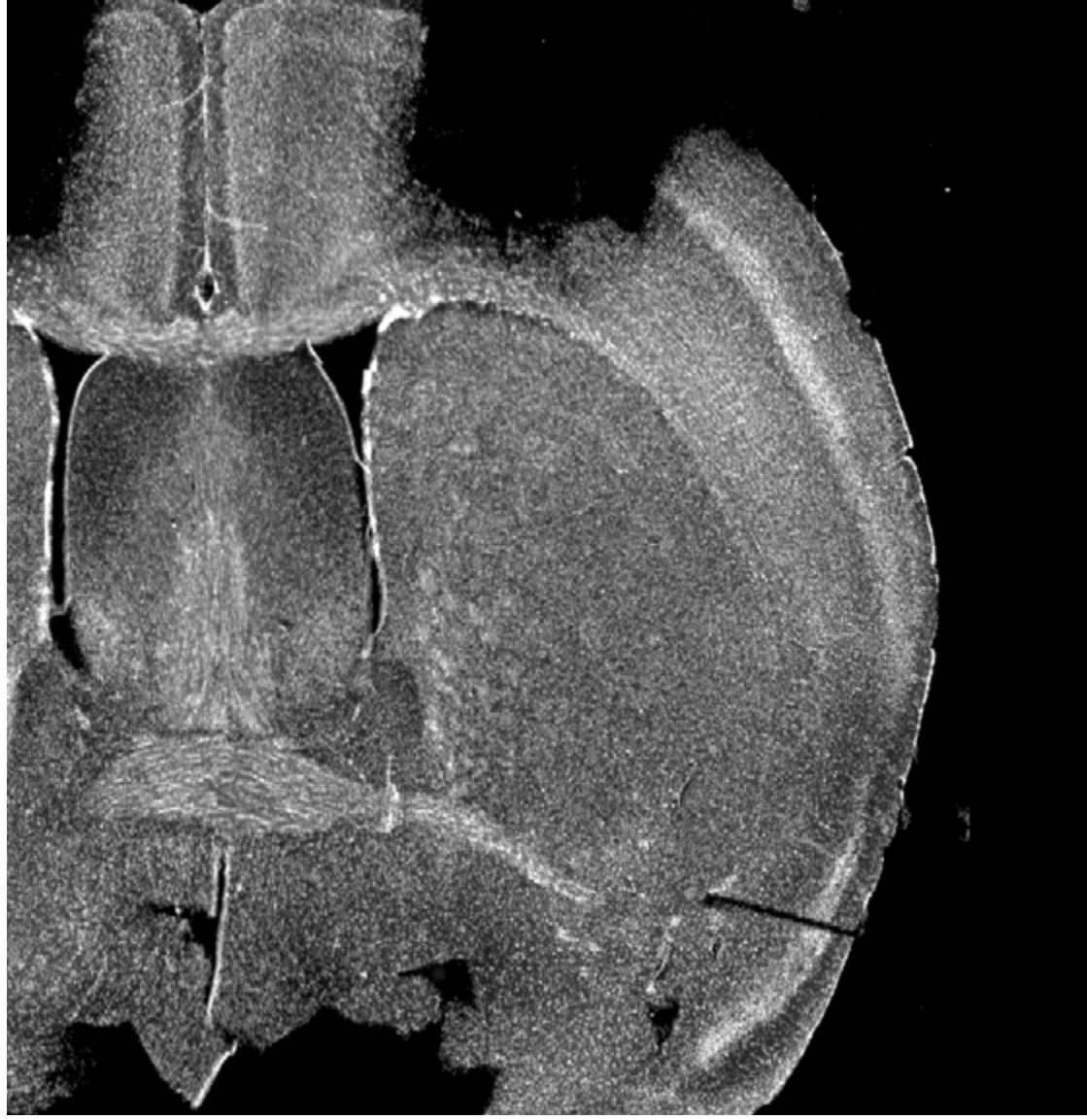
"The data sets collected during this project were large and complex," Kuhlman said. "My lab was able to share and adapt some of our analytical approaches to be used for this project."

The researchers plan to further investigate neuroplasticity in the sensory cortex. They want to investigate where the inhibition occurs in the learning process. They believe that inhibition is caused by a different neuron in the same area of the brain. They also theorized that once an action is learned, it is encoded in a different area of the brain.

"We're going to work on monitoring that activity, and we believe they can help interpret all the sensory input and modify the activity in the cortex," Zhu said.

The paper "Transient Enhancement of Stimulus-Evoked Activity in Neocortex during Sensory Learning" was published in Learning & Memory. The research was funded by the National Institutes of Health.

■ *Kirsten Heuring*



New Moves in Neuroscience

According to Carnegie Mellon neuroscientists, there is a clear leader and sidekick when it comes to generating movements.

During purposeful movement, like reaching for a cookie, two parts of the brain are vital, the motor cortex and the striatum. These brain areas are a dynamic duo for controlling movement, yet despite their importance for movement, their relationship with each other is not well understood.

To understand their connection, researchers damaged the motor cortex in mice and observed its impact on behavior and striatal activity. They found that the striatum relies heavily on cues from the motor cortex to control movement. Mice with damaged motor cortexes exhibited reduced striatal activity and struggled with tasks requiring fine motor skills. Though activity improved somewhat over 10 days, the mice continued to display altered activity such as clinical freezing of gait (FOG), which occurs during conditions such as Parkinson's disease.

"This series of experiments gave us some key insights, but it still only gives us a fairly broad perspective," said Eric Yttri, Eberly Family Associate Professor of Biological Sciences. "We will be following up with more in-depth studies of the freezing of gait effects and the communication between these areas. The goal is to get down in the finer details, to better establish the connections of elements of the circuit."

■ *Kirsten Heuring*

Study Suggests Bacteria's Internal Dialog Controls External Messaging

Bacteria may have been following the old adage "think before you speak" for millions of years.

Bacteria communicate in an incredibly complex chemical language, making and sending chemical messages to neighboring bacteria. Those conversations can be about deciding whether there's enough of them to launch an attack against the host or if it's time to lay low and keep eating, dividing and growing the community.

Research from CMU scientists reveals that individual bacterial cells coordinate their messaging internally before sending it out to neighbors.

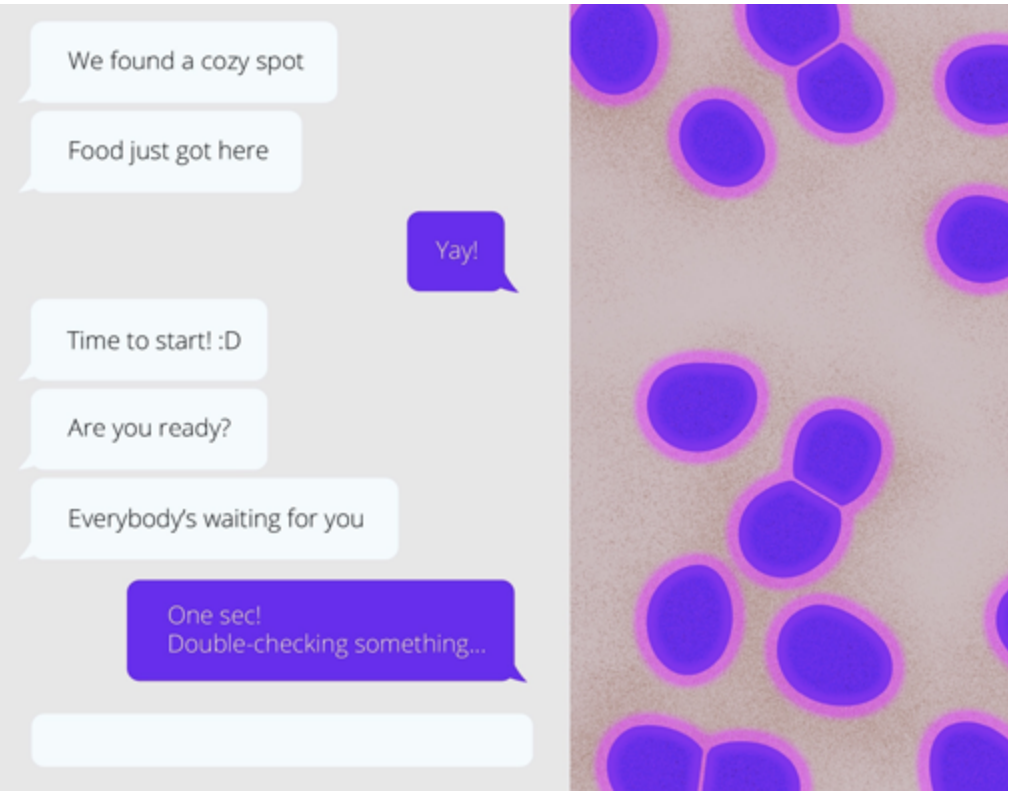
And, as an individual bacterial cell is orchestrating how it is 'talking,' it is still 'hearing' what the rest of the nearby bacterial community is saying.

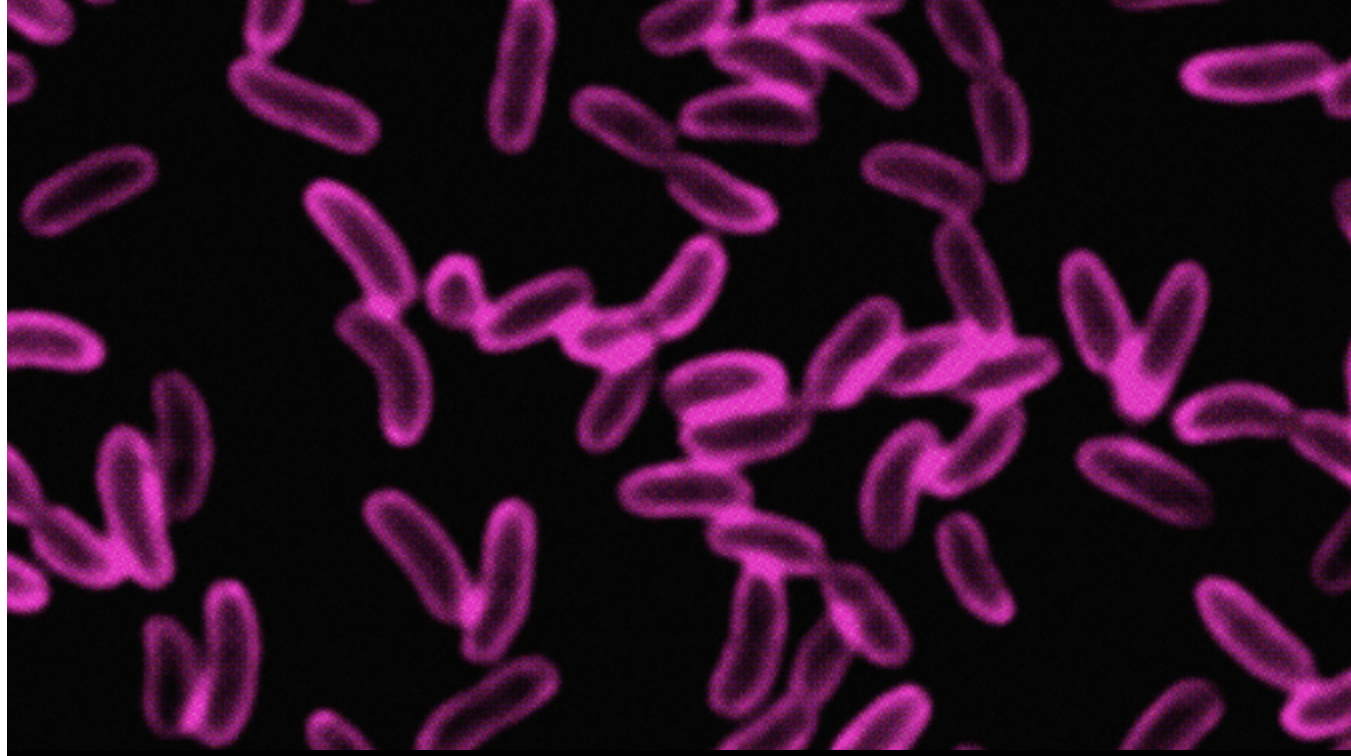
"It can still respond to signals from other cells, but it's controlling how it's transferring information to the world. It's very elegant, very intricate," said N. Luisa Hiller, associate professor of biological sciences.

Karina Mueller Brown, a Carnegie Mellon alumna and a postdoctoral research scholar at the University of Pittsburgh School of Medicine, studied multiple signaling pathways in parallel. In doing so, she identified a common thread that connects two key signaling pathways, both of which contribute to Streptococcus pneumoniae's ability to set up shop in a host and cause disease.

The findings, published in Cell Reports, may have important implications for strategies to develop antibacterial drugs and vaccines.

■ *Amy Pavlak Laird*





RESEARCH FEATURE

We're Outta Here

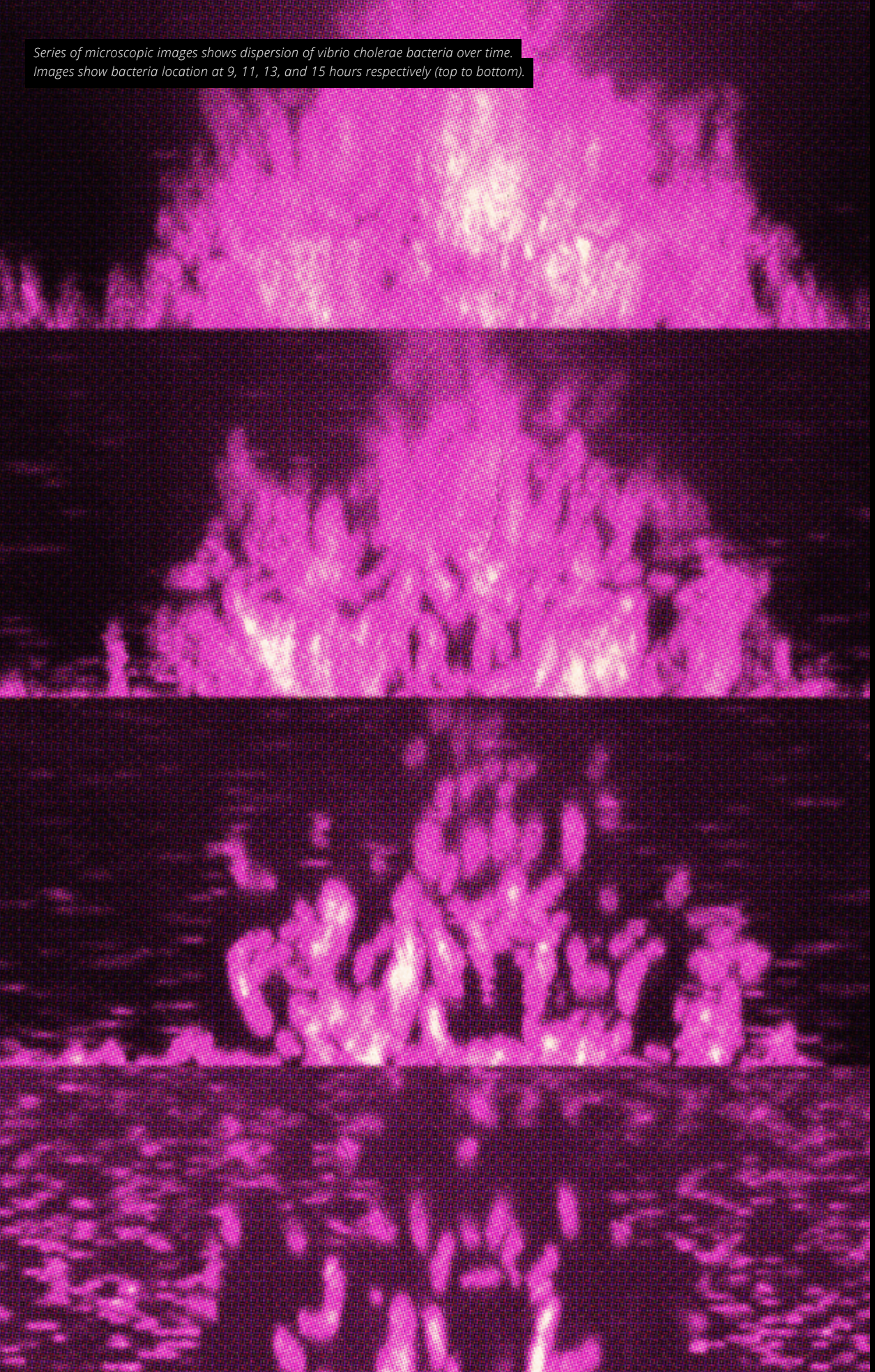
Novel imaging technique tracks individual bacterial cells as they leave their biofilm community

by Amy Pavlak Laird

An innovative imaging technique developed at Carnegie Mellon University reveals, for the first time, single bacterial cells leaving their biofilm community. Watching the bacteria in real-time at high resolution affords unprecedented views that advance the understanding of how single cells in biofilms move and how biofilms disperse. The findings, published in PLOS Biology, provide fundamental insights into the mechanisms underlying how pathogens in biofilms spread.

Most bacteria spend much of their lives in multicellular communities called biofilms. Living in the biofilm allows bacteria to collectively acquire nutrients and resist threats, including antibiotics and chlorination. By some estimates, up to 70 percent of human bacterial infections are caused by biofilm-forming bacteria.

Although attached to surfaces, biofilms are not static. Many types, like those formed by *Vibrio cholerae*, undergo repeated rounds of



Series of microscopic images shows dispersion of vibrio cholerae bacteria over time. Images show bacteria location at 9, 11, 13, and 15 hours respectively (top to bottom).

biofilm formation and disassembly, allowing the newly free bacteria to roam.

"Being able to transition in and out of the biofilms is critical for bacteria to be able to spread between niches. It could be between some environmental locations or, more relevantly, it could be between hosts or infection sites," said Drew Bridges, assistant professor in the Department of Biological Sciences.

Biofilm disassembly and dispersal play a key role in disease spread, but studying these processes with microscopy and related imaging techniques has been impossible. Until now.

"No one had been able to image biofilm dispersal with the sort of resolution that we were able to achieve," Bridges said. "And it is because of FAP labeling technology."

FAPs, short for fluorogen activating proteins, emit fluorescent light only when bound to a fluorogen, an otherwise non-fluorescent dye. They emit light in a region of the visible spectrum that is not commonly utilized — the far-red region. Far-red light is typically less toxic to living organisms and better for imaging through tissues.

FAPs are an ideal workaround for a common problem scientists face when trying to image biofilms. Traditional fluorescent proteins require oxygen to emit light. But in biofilms, the bacteria are so densely packed that oxygen becomes scarce, preventing the dyes from lighting up. Bridges said it was a challenge to do good microscopy without having probes that worked in biofilms.

"It was a problem that I figured we would just have to work around. And then, when I got to Carnegie Mellon, I learned about FAPs. And they're the perfect alternative because their mechanism is very different from how other fluorescent proteins work. They're not sensitive to oxygen limitation," Bridges said.

FAPs were developed at Carnegie Mellon in 2008. Since then, CMU researchers and collaborators have published more than 150 papers developing FAP technology for diverse biological applications. This study marks the first time FAPs have been used to image biofilms.

Working closely with project scientist and FAP expert Robert van de Weerd, the Bridges lab incorporated FAPs into the genome of the *Vibrio cholerae* bacteria. The scientists added malachite green-derived fluorogens to the growing bacterial colony, which bound to the FAPs and emitted far-red fluorescence. Using spinning-disc confocal microscopy, the team followed cells in *V. cholerae* biofilms as they moved, disassembled and dispersed.

"No one had been able to image biofilm dispersal with the sort of resolution that we were able to achieve."

The real-time, single-cell imaging revealed that the bacteria start dispersing from the edges, which wasn't necessarily surprising. What did interest Bridges was seeing that a sub-population of cells, about 20-25%, stays behind and never leave. He's investigating further to determine whether their staying is based on simply being trapped or if there's something else going on.

The imaging also revealed the development of localized dynamic regions, or dispersal "hot spots," where cells exhibited large outward displacements. They also observed that some cells in the biofilm's periphery didn't leave but instead compressed toward the biofilm core. Bridges' hypothesis is that cells themselves are a major mechanical component in the biofilm, and, as they start to leave, the overall structure collapses.

Overall, Bridges said the findings suggest a model in which certain areas of biofilms become more fluid-like, enabling localized outward motion of cells even from the interior. At the same time, the more rigid cell groups undergo compression to fill newly unoccupied space. The Bridges lab is investigating how these localized differences in mechanical properties are established during biofilm development and dispersal. They also plan to apply the FAP labeling technology to other notorious biofilm formers.

This work was supported by NIH grant R00AI158939, a Shurl and Kay Curci Foundation grant, a Kaufman Foundation New Investigator Research Grant, a Damon Runyon Cancer Research Foundation Dale F. Frey Award for Breakthrough Scientists and startup funds from Carnegie Mellon.

Student & Postdoc Stories

Camphire Receives Glen de Vries Fellowship

Trillions of bacteria live in and on the human body. While these bacterial roommates are often harmless or even beneficial, they can sometimes cause disease. Carnegie Mellon's Shaw Camphire is working to understand what makes good bacteria turn bad.

Camphire, a fourth-year Ph.D. student in the Department of Biological Sciences, studies *Streptococcus pneumoniae* (often termed pneumococcus), bacteria commonly found in the upper respiratory tract of healthy people. But if the bacteria disseminate to other tissues, like the ears or lungs or blood, they can cause a problem.

"It's really fascinating to me that these bacteria — which most frequently cause no symptoms or damage when colonizing us — can be misregulated and cause really severe harm," said Camphire, who is a member of Associate Professor of Biological Sciences N. Luisa Hiller's lab.

Pneumococcus exists in complex bacterial communities, where each individual bacterium produces and receives signals to sense the environment and communicate with neighbors. Camphire is studying one of these communication systems, which involves the Rgg144 gene and the signaling molecule SHP144. Turning off the RGG144/SHP144 system makes a big impact on the bacteria's ability to make a mouse sick, so Camphire is investigating when and why a pneumococcal cell activates the system, including how and under what circumstances the Rgg144 gene turns on or off.

Interestingly, nearly all strains of pneumococcus and several closely related species use RGG144/SHP144. Camphire is also looking into whether these different strains and species talk to each other. He's using computational tools to analyze genomes from more than 7,500 different pneumococcus strains and from a close relative, *Streptoccocus mitis*.

Camphire's efforts have been recognized with the Glen de Vries Fellowship, which celebrates outstanding research achievement and potential among Ph.D. students in biological sciences. The fellowship is made possible by the generosity of the late MCS alumnus Glen de Vries.

■ *Amy Pavlak Laird*

Chou Named 2024 Paul and James Wang - Sercomm Graduate

By focusing on the smallest aspects of cell biology, biological sciences graduate student Shannon Chou will make a big impact on the life sciences one day.

Chou researches the cytoskeleton, a filamentous network in all animal cells and other eukaryotes, with a focus on two specific components: actin filaments and microtubules. Her work seeks to understand how these cytoskeletal components are being regulated during oogenesis.

Chou conducts her research in Associate Professor Brooke McCartney's lab, which uses a drosophila model to study the cytoskeletal processes in vivo.

"A significant gap in our understanding of the cytoskeleton is how different cytoskeletal networks interact and coregulate," McCartney said, "and that's exactly where Shannon is focusing her attention."

Results from her work could have broad impacts. Drug design and discovery, for example, often rely on the knowledge cell biologists like Chou provide.

Chou presented a poster titled "Microtubules and Microtubule-associated Proteins Regulate Actin Cable Assembly, Cortical Association, and Stability" at Cell Bio, a joint meeting of the American Society of Cell Biology and European Molecular Biology Organization in December 2023. She presented two posters and delivered an invited short talk titled "Actin-Microtubule Interplay Regulates Actin Cable Assembly during Oogenesis" at Cell Bio 2024.

"Opportunities to present work have been some of my greatest moments in graduate school because people just come up and talk to you about a project that you're really passionate about, and some of these people are great figures in the world of cell biology," Chou said. "I always come back with so many ideas."

Through her commitment to research, Chou was named this year's Paul and James Wang - Sercomm Graduate. Carnegie Mellon bestows this honor on a graduate student who shows dedication and a commitment to excellence.

■ *Ann Lyon Ritchie*

Processing New Sounds

Sophomore Eric Parker II's brain is wired for music. Since his early teens, he has helped his father produce music, from mixing tracks to playing tenor saxophone for recordings. Over the summer, the family business expanded to Vietnam.

"The music production isn't as big in Vietnam, so my dad and I got pulled in to help," said Parker, who is studying neuroscience. "We wanted to blend American sound production with Vietnamese vocals."

When producing for international artists, Parker developed a strategy of understanding each artist's musical influences. Before he starts music production, he listens to the music each artist likes to get a feel for their tastes.

"Tones are a huge thing in Vietnamese culture, so a lot of stuff involves being able to sing with these tones," Parker said. "Vocals are a bigger thing, so their music is less production-heavy and more vocal heavy."

Recognizing the talent and potential in Vietnam's music scene, Parker and his father helped to establish LAMERIC Entertainment Group in Ho Chí Minh City, which he hopes will provide Vietnamese artists with more opportunities for music production and global distribution. Parker plans to return to Vietnam to continue his work in 2025.

Until then, he said he is excited to learn more about neuroscience. To Parker, understanding neuroscience helps him learn more about music.

"Music is a really subjective thing between people, and neuroscience makes it clearer," Parker said. "You can learn how you elicit this kind of reaction, and it can help you realize what to add to make a song more complete."

Parker is a sponsored musician and producer partnered with Universal Music Group while in the midst of his undergraduate studies. In the future, he said he hopes he can pursue both his passion for neuroscience and his love of music.

■ *Kirsten Heuring*

Cappella Wins Niccolai-Fustanio Award

Anna Cappella's interests vary as much as the cells in the human body.

"I've worked a lot on prioritizing what's important to me," said Cappella, a senior double majoring in biological sciences and professional writing. "I like to get involved with a lot of different activities."

From a mock trial attorney to an editor-in-chief of The Tartan, Cappella has a diverse array of interests. She earned the Niccolai-Fustanio Families Scholarship Award, which is given to a senior who has achieved academic success while pursuing other experiences outside of the classroom. The scholarship was established in 2016 by Mellon College of Science alumni Nilo A. and Phylis F. Niccolai.

After doing mock trial, Cappella said she became interested in using her biology background to do pharmaceutical patents or something like that in the scientific world. But a summer spent interning at Thermo Fisher Scientific, a biotechnology company, changed her course.

"I thought I'd start in the lab and see if I could meet some people who worked on the law side. But I absolutely fell in love with the lab," Cappella said.

She interned at Thermo Fisher again the summer after her junior year, working with a team that would develop a uniform media that labs could use to investigate tumor cells.

During the school year, Cappella is a key part of The Tartan, Carnegie Mellon's student-run newspaper. She started off as a writer her first year, and by her junior year, she became editor-in-chief. She also serves as a community advisor for Carnegie Mellon housing, is highly involved in first-year orientation, and has been a part of numerous other clubs and organizations, including the dance team and Scotch N' Soda.

"I really enjoy getting to see how other people approach life at CMU," Cappella said.

■ *Kirsten Heuring*

Creating Community

When students are well, they excel, which is why faculty in the Department of Biological Sciences nurture and engage with undergraduate students outside of the classroom.

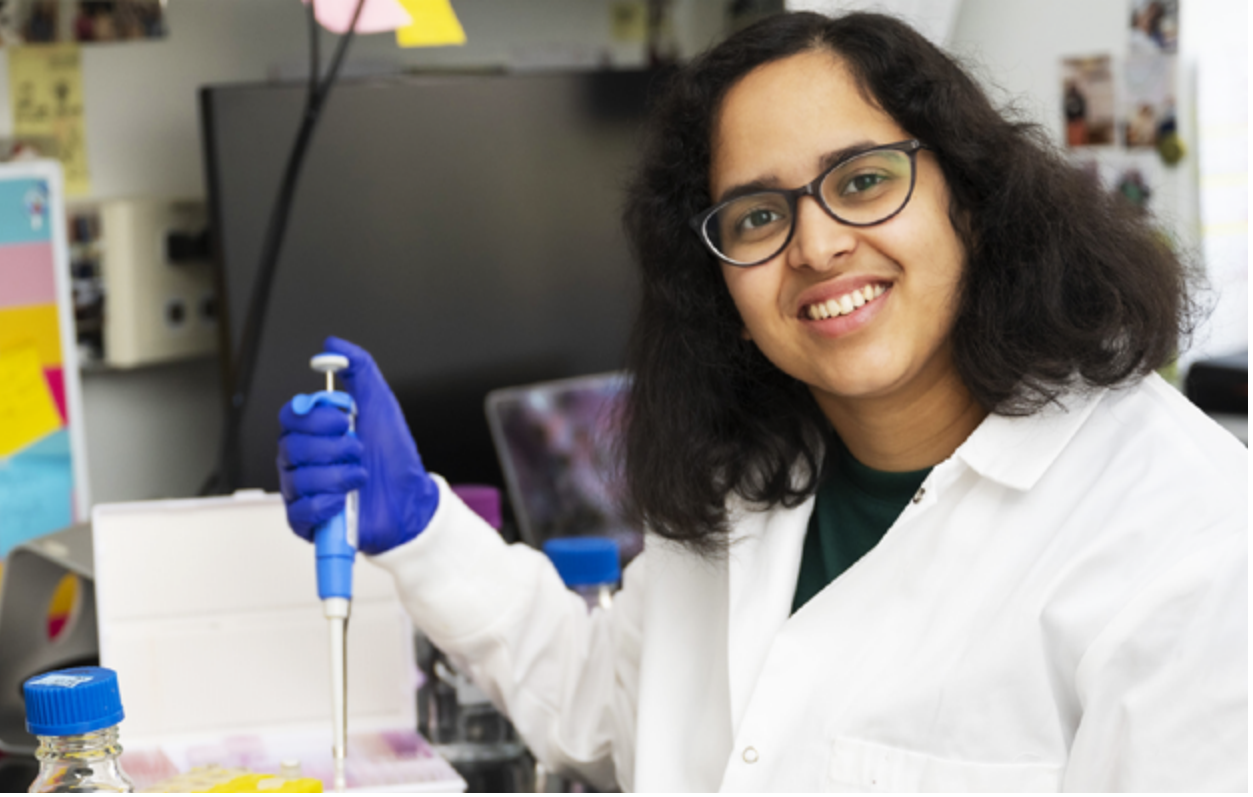
"When students can identify and see that faculty take an interest in them, they feel support," said Carrie Doonan, director of undergraduate laboratories. "They tend to do better in the classroom, and that association really makes a difference in their academics."

Doonan and others organize a variety of events through the university, labs and courses to allow members of the department to connect for professional development and fun.

"Our focus is always on community," said Amanda Willard, assistant teaching professor and undergraduate adviser. Both Doonan and Willard were among the faculty serving omelets at the university's midnight breakfast before winter finals.

Events like Bio Brownie Bingo allow students and faculty (or alumni at Carnival) to mingle and introduce themselves as participants fill out bingo cards by learning about and interacting with each other. At Halloween, trick or treating masks a study session as students visit spooky stations and trade quiz answers for sweet treats. And milestones like graduation, major declaration and others are extra opportunities to celebrate and engage.

"Engagement often means a student will go to a faculty member's office and have a conversation. And that sharing of ideas between a faculty member and an undergraduate who feels validated through this sharing, I can't put a price on it," Doonan said. "One of my greatest pleasures of my job is to see a senior leave here confident in knowing they can go out into the world."



Through 3MT, Doctoral Students Share Accessible Research

Doctoral students Shaw Camphire, Sandhya Kasivisweswaran and Samskrathi Sharma represented the Department of Biological Sciences in this year's finals of the Three Minute Thesis (3MT) competition. Each won their preliminary rounds. The competition challenges doctoral students to explain complex research and captivate their audience in just three minutes.

This is Sharma's second year competing in 3MT, and science communication is a subject she has long been passionate about. She was recently awarded the 2024 Quad Fellowship after emphasizing the responsibility scientists have to make STEM research more accessible to the public — a goal she wants to further elevate through participating in 3MT.

"When we scientists are involved in experimental pursuits, we can get caught up in the nitty-gritty details specific to our fields," she said. "However, I think we owe it to society to explain the implications of the scientific discoveries we make. I believe that even if we are doing the most interesting science, if we cannot communicate the relevance of these findings to a general audience, it can never truly benefit society."

Sharma's research explores the role of the circadian clock in metabolism, examining how circadian rhythms contribute to the way humans absorb nutrients from food. This work could ultimately provide therapeutic solutions for people with irregular sleep-wake cycles, like those who work a night shift, who might be prone to metabolic disorders like obesity as a result.

To reach a general audience unfamiliar with her discipline, Sharma has experimented with a variety of creative forms to communicate the implications of her research.

"Often, creative art forms and science are considered distinct," she said. "But as a scientist and artist, I think science can be communicated more effectively when used with art, as it is visually appealing and relatable. I have been trying to communicate my scientific findings to diverse audiences using presentations, hands-on activities, outreach and paintings."

■ *Sarah Bender*

Program Prepares New Researchers

As an undergraduate student at Arizona State University, Joseph Peterman did not get the research experience he thought he needed to enter a Ph.D. program. Then, he heard about Carnegie Mellon University's Postbac Research Fellowship in Quantitative Biology.

Created in 2022, the postbac fellowship in Carnegie Mellon's Department of Biological Sciences provides students with one to two years of research training, mentorship and professional development within departmental research labs. These experiences prepare them for the next steps in their academic careers.

Stephanie Wong-Noonan, associate teaching professor of biological sciences, serves as head of the postbac fellowship program and advisor to the fellows. She says the program is an excellent chance for the fellows to delve into academic research in preparation for Ph.D. programs.

The initial cohort included two students. This year's cohort has five students, including Peterman and Yeritmary Rodriguez Delgado.

Rodriguez Delgado graduated from the University of Puerto Rico-Cayey and wanted to gain more research experience in biological sciences before starting graduate school. While participating in Carnegie Mellon's Data Analytics Summer Immersion Experience (DASIE), she learned about the postbac program and saw it as an opportunity to advance her scientific career.

Peterman and Rodriguez Delgado work with Liz Ransey, assistant professor of biological sciences, to advance their research training and professional development.

"The postbac program enriches our community with diverse trainees who are eager to learn and to contribute to our cutting-edge research programs," Ransey said.

Besides developing their research skills with Ransey, Peterman and Rodriguez Delgado work with Wong-Noonan to prepare for their future graduate school applications. Both hope to earn graduate degrees from Carnegie Mellon.

"It's really exciting to see the students grow as researchers and watch them gain confidence about research," Wong-Noonan said. "Seeing them get set up for their future paths and have success is really rewarding."

■ *Kirsten Heuring*

Alumni News

David Hill Pioneers Allergy Research for Healthier Childhoods

As he navigated the long path toward his M.D./Ph.D., David Hill felt like he was swinging on a pendulum. First, it was two years of medical school coursework. Swing. Then, a few years of graduate school and research in the lab. Swing. Next, clinical rotations, a residency in pediatrics and a clinical fellowship in allergy and immunology. Swing. Finally, a postdoctoral fellowship.

Hill, who graduated from Carnegie Mellon University with an undergraduate degree in biological sciences in 2005, said it was challenging to navigate those big transitions between two very different worlds. These days the amplitude of the swing is much smaller.

"Now, I literally think about science and medicine every day," he said.

Hill is an assistant professor of pediatrics at the University of Pennsylvania Perelman School of Medicine and a pediatric allergist, immunologist and attending physician at Children's Hospital of Philadelphia. He specializes in diagnosing and treating children with food allergies and asthma, and he is actively researching new diagnostic tools and cutting-edge treatments for children with these conditions.

He spends most of his time in his lab, except for Thursday afternoons, when he sees patients.

"I love seeing new patients and thinking about the diagnostic conundrum that a new patient, an undifferentiated patient, provides," he said. "I'll never give that up."

When he arrived at Carnegie Mellon, Hill knew he wanted to be a pediatrician. During his very first biology seminar, Professor Elizabeth Jones gave a lecture on genetics — and that interaction shaped the trajectory of his career.

"I was so impressed by her, I went up to her after class and said: Hi, my name is David. I just got here from Seattle. I'm interested in research. Could I come by the lab?"

Jones not only invited him to come by her yeast genetics lab, but she also gave him a job. He started with autoclaving, washing glassware and pouring plates. He was carrying out his own experiments in no time.

"I had the opportunity to practice the practical aspects of science in an incredibly intense way. I felt like a graduate student in Dr. Jones's lab," said Hill, who aims to give students in his lab that same type of early exposure to rigorous research.

Hill's lab tackles research questions related to how diet and metabolism influence the immune system. He's especially interested in the immune system's role in pediatric allergy and obesity, including associated conditions like diabetes and asthma. Hill's research ranges from the very small, like identifying how the immune system recognizes food antigens, to the very large, including epidemiological studies of hundreds of thousands of pediatric allergy patients.

A big research focus is food allergy, including eosinophilic esophagitis (EoE), a chronic allergic inflammatory disease that can be triggered by specific foods. The Hill lab was the first to discover EoE as a manifestation of the allergic march, the natural progression of allergic conditions as they develop during childhood. Recently, Hill led a multi-institutional study that identified one of the allergens responsible for EoE. The study was the first to describe the molecular machinery that mediates food allergen recognition by the immune system in this condition.

"If we understand what's happening at a molecular level, it will allow us to develop better, more accurate diagnostic tests to find out which foods trigger this disease and ultimately reduce the morbidity associated with EoE," Hill said.

Hill said he chose allergy as a clinical and research specialty because he saw a tremendous opportunity to positively impact the health of children. And he loves his work — even the arduous path that got him here.

"The M.D./Ph.D. path is a long one, and you live a lot of life during the journey," Hill said. "I met my wife when I was a graduate student, we bought a house together in Philadelphia and we had two kids. Now I volunteer with the school gardening club. I've been very lucky."

■ *Amy Pavlak Laird*

NO 'NO'S' AT CMU

Among the three degrees Tartan on the Rise Shaun Ranadé earned from Carnegie Mellon was a bachelor's degree in biological sciences in 2015. He also earned a bachelor's degree in Japanese Studies and a master's degree in biomedical engineering. He is among this year's Tartans on the Rise awardees. The honor celebrates recent alumni who are making an impact in their organizations and in their communities, across the nation and around the world through leadership, innovation and career achievements.

"I credit CMU with fostering my multidisciplinary mindset and approach to medicine. No one there ever told me no," Ranadé said. "It was always, 'Yes, you can. We can make it work.' Whether it was studying humanities, science, engineering or the arts, CMU nurtured my diverse interests and encouraged me to take on challenges that might have seemed unconventional elsewhere. The culture of interdisciplinary learning prepared me to approach global health problems with a unique and holistic perspective."

■ *Elizabeth Speed*

From Bench to Bioinformatics

When the Richard King Mellon Hall of Sciences opens in 2027, faculty from the Department of Biological Sciences will be among the new residents, including Catherine Armbruster.

Armbruster, assistant professor of biological sciences, studies how bacteria and other pathogens evolve to survive in host environments. She said that through the collaborative spaces of the new Hall of Sciences, researchers will have the potential to revolutionize scientific discovery.

"I like to describe my lab as a damp lab. Traditional wet labs analyze biological matter at a lab bench. Dry labs focus on computational methods for analysis. We do both," she said.

Armbruster employs next-generation sequencing techniques to unravel the genetic diversity of pathogens within a single infection. This generates vast data sets, which are meticulously analyzed by bioinformatics experts.

"This approach develops a loop where we generate data sets from experiments at the bench and then go to our computers to analyze them, which then drives our next set of experiments and so on," she said.

In the new building, the department's microbiologists will all share a common space.

"You can imagine the new angles to our work that will arise through organic, serendipitous collaboration," she said.

While infrastructure for the new building is still being put into place, Armbruster and the other microbiologists aren't waiting.

"Ideas are already forming for how to leverage our new location, new resources and new collaborations to advance my lab's research. I can't wait to get started!" she said.

For more information on the Richard King Mellon Hall of Sciences, please visit: cmu.edu/hall-of-sciences

To make your gift, please contact:

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jbelardi@andrew.cmu.edu · 412-268-8810

Threads of Inquiry

Faculty in the Department of Biological Sciences are transforming foundational science and changing the world. A new webinar series, "Threads of Inquiry," weaves together stories about groundbreaking research from experts who cross boundaries and forge new fields of exploration.

NEXT UP:

Decoding Bacterial Communities: Implicatons for Therapy and Biotechnological Advances

Drew Bridges, assistant professor of biological sciences
Luisa Hiller, associate professor of biological sciences

Bacteria are the most ancient inhabitants of our planet. Though bacteria were originally considered to be simplistic life-forms, we now know that they partake in complex behaviors that allow them to survive and persist across planet Earth. For example, it is now appreciated that bacteria are social entities: they communicate with one another, they form multicellular communities called biofilms and they work together to carry out tasks. The Bridges and Hiller laboratories in the Department of Biological Sciences at Carnegie Mellon University study biofilm communities in major human pathogens that cause respiratory and intestinal infections. The Hiller lab studies bacterial languages: they conceptualize these molecular signals as words and study the consequences of using these signals (a dictionary), the means by which they are coordinated over time (grammar) and how they vary across diverse bacterial strains and species (dialects). The Bridges lab studies bacterial decision making: they develop cutting-edge microscopy and automation tools to understand how bacteria interpret environmental cues to signal the formation, development and dispersal from bacterial communities. The labs also collaborate; recently they have adopted concepts and tools developed in the Bridges lab to understand the genetic underpinning of biofilms studied in the Hiller lab. Because these communities are integral to the lifecycle of pathogens, understanding bacterial decision-making processes and languages can guide the development of novel anti-infective therapies that overcome the antibiotic resistance crisis.

June 3, 2025
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Carnegie Mellon University
Mellon College of Science
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5000 Forbes Avenue
Pittsburgh, PA 15213

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