

FEARLESS SCIENCE



THE GALAXY WITHIN
New imaging technologies enable
scientists to explore unseen frontiers

FEARLESS SCIENCE MAGAZINE

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Morgridge is an independent
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is structured to help scientists push
into new frontiers of biology to
advance human health. Learn more
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ABOUT THE COVER

The vast uncharted reaches of
space mirror the understudied
corners of human biology
waiting to be explored by curious
scientists. Here a starry night sky
and aurora are depicted as facets
of biological research, including
DNA, fluorescent molecules, and
microscopy data. This issue features
the Morgridge imaging pioneers
who develop powerful new tools
so that we can see the unseen.
Illustration by Matt Stefely.

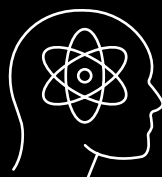


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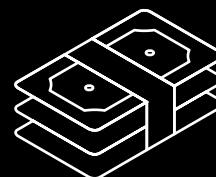
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FEARLESS FUN PUZZLE ANSWER:
TRAVELING LIGHT

 **MORGRIDGE**
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Discovery needs transformational tools

Imagine a new satellite mapping technology that is so powerful and precise it could capture you sitting in your favorite living room chair, at this very moment, while you sip coffee and thumb through this magazine.

OK, that might be a little unsettling. But think about that same capability and how it could be applied to biological research. A microscope, for example, that could provide rich images of real biology, in real time, in dynamic states of movement and change, all while leaving that biology completely undisturbed — a proverbial “fly on the wall.”

Scientists have done more than imagine this. We have many active inquiries into the new world of dynamic imaging, with nicknames like “the virtual cell project” and “Google Maps for the body,” that help us serve as eyewitnesses to internal biological processes over time, rather than just capturing single, static snapshots.

These are incredibly exciting times in the world of biomedical imaging. And at the Morgridge Institute for Research, we have a front-row seat. Imaging was among the first defining research themes when Morgridge was founded 20 years ago, and today it has blossomed in many new directions. This issue of Fearless Science explores some of those new directions and the research partnerships they help inspire.

Collaboration is really at the heart of imaging, since the ultimate proving ground for any imaging advance is when it helps solve an intractable biology challenge. Our lead story on Morgridge PI **Melissa Skala** follows her fluorescence imaging research odyssey through the lens of many collaborators, who are working on everything from neural stem cells to the innate immune system.

“Discovery is empty without tools,” Melissa observes.

Another master architect of collaboration networks, Morgridge PI **Kevin Eliceiri** opens this issue with reflections on how Wisconsin has become a special bioimaging powerhouse. A case in point is BioImaging North America’s 2026 Community Congress returning to Madison this fall.

You’ll also read about how a corresponding revolution in science — that of big data, AI and research computing

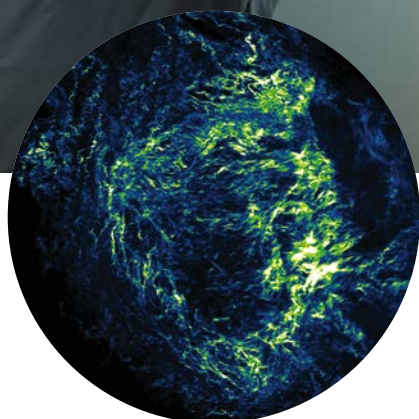


— is helping fuel fundamental advances in imaging. Morgridge PI **Juan Caicedo** is embarking on a project called CHAMMI-75, which brings together millions of cellular images, from a range of modalities, into a single queryable database. Morgridge’s own Center for High Throughput Computing is helping make this massive data challenge a reality.

And you will also be introduced to some fundamentally new approaches to observing biology. Morgridge PI **Randy Bartels**, a physicist by training, is applying the rules of quantum physics to a new generation of microscopes that exploit properties of light that are invisible to classical measurements. And PI **Tim Grant**, an expert in cryo-EM technology, is helping a genetics researcher image the mysterious process of how bacteria repair their DNA — a discovery that could open the door to a new class of antibiotics.

As the cover of this magazine alludes to, imaging tools that help us explore beyond the inherent limits of human sight are fundamental to understanding the world. Whether your scientific query is cosmic or molecular in scope, seeing is believing.

Brad Schwartz



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Kevin Eliceiri explains why imaging is the ultimate pursuit for science omnivores

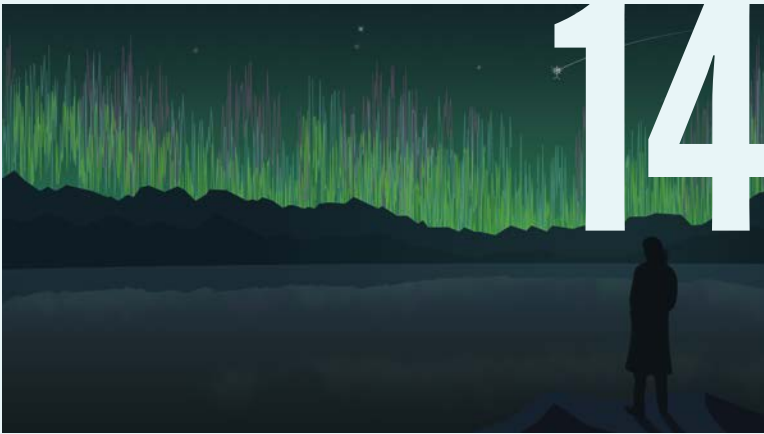
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When ideas **COLLIDE**

The Melissa Skala Lab sits at the center of an expanding universe of collaboration

QUANTUM IMAGING

Can we harness the power of quantum to open new windows into the nanoscale universe?



CHAMMI-75

A new feat in computational biology finds common ground across millions of biology images



SOLVING STRUCTURES

Collaboration between Morgridge and UW reveals “high-wire act” of bacterial replication





IMAGING

The ultimate pursuit for science omnivores

It's easy for visitors to lose their bearings in the Laboratory for Optical and Computational Instrumentation (LOCI), a nondescript wing of the 54-year-old Animal Sciences Building at UW–Madison.

Thin hallways snake through more than a dozen small, interconnected labs, each one overstuffed with gleaming stainless-steel hardware, computer screens and black, wall-sized nylon partitions. Adding to the claustrophobic feel of the rooms is the near-complete absence of outside light.

The space certainly doesn't give off the vibe of a high-tech wonderland. Yet for scientific imaging pioneers in Wisconsin, make no mistake: This is where the magic happens.

For **Kevin Eliceiri**, a professor of medical physics and biomedical engineering and inaugural biomedical imaging investigator at Morgridge, this space holds special meaning. He worked here as an undergraduate imaging assistant in the mid-1990s under the tutelage of two giants in modern cell biology, imaging pioneers

Hans Ris and John White. Ris created the annex, now home to LOCI, to house a purpose-built three story million-volt High Voltage electron microscope to study cellular architecture. White built a prototype of a laser-scanning confocal microscope that became instrumental to modern biology.

Eliceiri continues this legacy of developing biological imaging instrumentation through his own work, yearly lectures named in honor of White and Ris, and a small microscopy museum documenting some of the history of microscopy at UW–Madison.

Six blocks from Discovery Building where Morgridge sits, LOCI serves as a “second campus” for instrument innovators at Morgridge who can stretch out and do their thing. As part of the Office of the Vice Chancellor for Research Center for Quantitative Cell Imaging (CQCI), directed by Eliceiri, it is the umbrella entity for the Eliceiri group and its sister biological optics lab run by Cell and Regenerative Biology Assistant Professor Abhishek Kumar. CQCI is a collaborative hub for

biophotonics, the study of biology with light, at UW–Madison.

“One of the things that makes bioimaging so strong here is the breadth and depth across the board, because we’re a campus that has bought into the idea of strong arts and humanities, space sciences, physical sciences and biosciences, all working together,” Eliceiri says. “It allows imaging to thrive, because imaging fundamentally dips into all disciplines.”

That campus history helped fuel the biomedical imaging research theme at Morgridge, and the same interdisciplinary spirit served as the guiding force in hiring new investigators. Eliceiri describes ideal candidates as “the omnivores of the research world.”

Recruits have included biomedical engineer **Melissa Skala**, a leader in creating optical imaging technologies for use in cancer research and immunology; **Randy Bartels**, a physicist by training who is taking microscopy to new levels of depth and resolution; and data scientist **Juan Caicedo**, who is developing a digital atlas of cell behavior based upon billions of biological images.

“One thing I like about Morgridge is that we understand the power of imaging technology development for biology, which not everybody has traditionally invested in,” he says. “Some biologically focused centers would have been more conservative and said, ‘just hire a great cell biologist who uses imaging.’

But at Morgridge we also hired people that will take the imaging itself to new heights, and we’ve surrounded them with world-class biological faculty. We’ve been fairly unique in our goals to have co-localized experimental biologicals and imaging technologists.”

Eliceiri says this is a golden age for imaging. It began in the last 30-plus years with the digital revolution making staggering amounts of visual data available to science and now has the capabilities of deep learning and AI to extract greater biology insights from the images in ways that would be impossible for the human eye.

Morgridge serves as an amplifier of research potential and a hub for a lot of the expertise that exists in dozens of campus fields. Much like the Morgridge Metabolism Initiative, it is building community among like-minded scientists and seeding new directions.

“Imaging might be the most unifying element of all of Morgridge,” he says, noting that most of the 20-plus investigators at Morgridge have utilized or collaborated on improved imaging. “We have focused on hiring brilliant synthesizers between fields.



KEVIN ELICEIRI

It’s an interesting question: ‘Are the biologists driving us or are we driving them?’ The relationship is cyclical: biological needs inspire new imaging breakthroughs, and those breakthroughs open the door to unprecedented biological insights.”

One of the hallmarks of that collaboration is the Morgridge Fab Lab, which Eliceiri oversees. Located in the basement of Morgridge, it serves as a research-driven makerspace for all sorts of new ideas in biomedical imaging. That includes innovations in 3D printing; better visual diagnostics for cancer; improved transient lighting for surgery; and new instrumentation for multiscale imaging.

Another hallmark is Bioluminescence Imaging North America (BINA), an organization housed at Morgridge and supported by the Chan Zuckerberg Initiative (CZI). BINA is dedicated to helping biomedical imaging scientists better understand one another and the technologies they develop and utilize. It began in 2018 and has grown to more than 1,200 members from across the globe, including 200 core imaging facilities in the U.S., Mexico, and Canada.

Eliceiri has also been instrumental in improving and expanding an open-source imaging analysis software known as ImageJ. It’s an essential tool used by thousands of imaging scientists every day, valued for its ability to be customized for different fields and seamlessly plug in new capabilities like deep learning.

As a reflection of Morgridge’s innovative spirit, it is home to four distinct projects supported by CZI, which has a goal of supporting the science and technology that will make it possible to cure, manage or prevent all diseases by the end of the 21st century.

The future of imaging science in Madison is equally bright. Eliceiri organized a retreat this summer of two dozen UW–Madison scientists interested in building novel instruments for multiscale imaging. These developments could lead to novel imaging platforms for cell-informed medical imaging.

“We are at the cusp of fully appreciating the amazing phenomenon where everything good or bad in your life is happening within cells,” he says. “If you want to understand cells, you need novel technology to get to the dynamic fingerprints of the cell. We are well set up to do that.”

**“IT’S AN INTERESTING QUESTION:
ARE THE BIOLOGISTS DRIVING
US OR ARE WE DRIVING THEM?”**

Microscopes across time

Among the high-tech work stations in the Laboratory for Optical and Computational Instrumentation (LOCI), visitors will come across glass cabinets of curiosities that hold vintage microscopes spanning three centuries of science.

The collection has been a labor of love for Kevin Eliceiri, who has assembled more than 100 historically important pieces of bioimaging history. The collection is named after famed microbiologist Harlyn O. Halvorson, former director of the Marine Biological Laboratory in Woods Hole, Mass. and long-time UW–Madison faculty.

Eliceiri recently pulled together a few of his favorites (right) and offered more details on their significance to biology.



Harlyn O. Halvorson (1925-2008) Memorial Microscopy Collection at LOCI

REPRODUCTION OF 17TH-CENTURY ANTONIE VAN LEEUWENHOEK MICROSCOPE



R & J Beck, London, circa 1870–1880s

A reproduction of a 1673-era microscope of Antonie van Leeuwenhoek, known as the “Father of Microbiology.” This microscope was donated to LOCI in 2008 by Harlyn O. Halvorson, a founding chair of the UW Laboratory of Molecular Biology, and was made in his father’s machine shop. Eliceiri’s collection is named in Halvorson’s honor.

THE “SIMPLE” BOTANICAL MICROSCOPE



Bausch & Lomb, Model W, circa 1893

Unlike “compound” microscopes with multiple lenses, this dissecting microscope uses a single lens system — a design often called a “botanical” microscope. This specific Model W features a rack-and-pinion focus for the delicate control required in anatomical studies and was formerly used in the Botany laboratories at UW–Madison.

AMERICAN PRECISION MICROSCOPE



Ernst Gundlach, North America, circa 1885–1890

A fine example of late 19th-century American craftsmanship. Ernst Gundlach, a prolific designer who worked with both Bausch & Lomb and his own firms, was instrumental in bringing European optical standards to the United States.

VICTORIAN SCHOLAR’S MICROSCOPE



R & J Beck, London, circa 1870–1880s

This antique brass instrument reflects the precision of the late Victorian era. Its design is characteristic of the renowned London firm R & J Beck, featuring the signature articulating sub-stage mirror and an arm-mounted focus mechanism.

THE MOGINIE-STYLE TRAVELING MICROSCOPE



Charles Baker, London, circa 1870

Designed for the naturalist on the move, this “Moginie-style” instrument prioritizes portability without sacrificing Victorian precision. Its folding tripod legs allowed it to be packed away for field use. Defining features include a striking mix of polished brass and a black-enameled main tube, a rack-and-pinion focusing system, and a monocular eyepiece and a single objective lens.

THE “JUG-HANDLE” COMPOUND MICROSCOPE



Bausch & Lomb, Rochester, N.Y., circa 1913

By the early 20th century, microscope design moved toward the iconic “jug-handle” frame, which provided a secure grip for transporting the instrument. This transition piece features a polished brass body paired with a durable black-finished limb and a dual-objective nosepiece for quick magnification shifts and a sub-stage mirror for light reflection. It was historically used in the anatomy laboratories at UW–Madison.

BIG IDEAS

EARLY CAREER SCIENTIFIC JOURNEYS AT MORGRIDGE



PIERRE GILLOTAY

SECRETS OF SPINAL CORD REGENERATION

As a highly regenerative vertebrate and versatile model system, zebrafish are star players in the study of regeneration. Among the many tissues zebrafish can regrow are injured spinal cords, holding potentially crucial clues to one day curing spinal cord injury in humans.

But some injured zebrafish — a small but persistently present proportion — remain paralyzed. Pierre Gillotay, a postdoc in the Poss Lab, studies this phenomenon. **“If we know what’s failing in those cases and can rescue it,”** Gillotay says, “maybe we could trigger a non-regenerative animal to get to the point of regeneration.” Few scientists in the field are conducting research along the same lines, and Gillotay is seizing the freedom to take a higher risk, higher reward approach.



RAISON DSOUZA

SOLVING CRYO-EM’S ‘WHERE’S WALDO’ PROBLEM

Thanks to the shortwave radiation of the electron beam, cryogenic electron microscopy (cryo-EM) can provide exquisite detail about the structure of small biological molecules. But the need to limit inevitably damaging irradiation leads to “noisy” raw cryo-EM images, and considerable computational effort is needed to arrive at final 3D reconstructions.

In the Grant Lab, Raison Dsouza is developing new computational methods to analyze these images. “It’s like playing ‘Where’s Waldo,’ because you have all of these proteins interacting with each other and we need to locate a protein of interest inside of cells,” Dsouza says. He also develops software that leverages virtual reality to visualize molecular data. **“Science is not just to solve a problem, but to understand what the problem is,”** Dsouza says. “And then once you find the solution, how does that work?”



BETH MOORE

THE BIOINFORMATICS OF THE FUTURE

Computational biology has become a pillar of biomedical research because of its power to sort through enormous amounts of data. Beth Moore, a scientist in the Stewart Computational Biology Group, creates the bioinformatics tools that can sort through and analyze this data, often at the single-cell level.

“The really special and fun thing about bioinformatics is that you are helping people with data. You get to learn as the projects go on, and you get as excited as the researchers,” Moore says. And it’s not just mile-high experimental data that require these tools, but the enormous corpus of scientific literature. Using text-mining algorithms and artificial intelligence models, Moore offers scientists a targeted compendium on specific topics to reveal potentially important relationships across key terms and new, testable hypotheses.



CORINNE MOSS

WHAT URINE METABOLOMICS CAN UNLOCK

For decades analytical chemists have used mass spectrometry to determine the mass of biomolecules and break them into pieces to determine their components. Corinne Moss, a recent graduate of the Coon Lab, uses the latest generation of instrumentation to study human biofluids like plasma and urine.

“I can remember going into the Coon Lab and sending a picture to a friend, saying ‘Can you believe this exists? These people have so many mass spectrometers, and they look at so many biological systems. This is fantastic.’”

Moss’s work with mass spectrometry-based urine metabolomics lays the foundation for preventative and precision medicine — a future where diagnostic testing isn’t just a response to symptom onset but can be integrated into a real-time and longitudinal view of health and disease.



SABINA FARHADOVA

VISUALIZING THE BIRTH OF NERVE CELLS

A fundamental question in neuroscience is how neural stem cells leave their inactive, “quiescent” state, a necessary step before new neurons can be generated in the brain. Current technologies have not been sensitive enough to detect these dormant neural stem cells.

Sabina Farhadova, a postdoctoral fellow, works with the labs of Melissa Skala at Morgridge and Darcie Moore at UW–Madison to apply cutting-edge imaging technologies to close this gap. **“Never be afraid to ask bold questions,”** Farhadova says. “That’s where the true innovation happens.” In this case, innovations in imaging neurogenesis will be critical to better understanding cognitive decline, as neural stem cells go into a deeper state of quiescence, or newly born neurons do not mature and die off, during aging or disease.



NICK ARP

CHASING BIG QUESTIONS IN MACROPHAGE METABOLISM

When immune cells respond to an attack from a pathogen, their metabolism gets reprogrammed in ways that orchestrate immune function and inflammatory state. Nick Arp, a recent graduate of the Fan Lab, has focused his research on the metabolism of macrophages, the first responders in innate immunity. His work has shed light on the role of signaling molecules in the immune response and sought to reveal as-yet unannotated parts of the metabolome.

An MD-PhD student, Arp says that **“it’s important to chase questions that are going to be close to patient care.”** The knowledge you gain in medical school has given me a toolbox to contribute to a conversation or point out alternatives that someone who’s very deep in a scientific area might not think about.”



HELENA JARAMILLO MESA

UNRAVELING MYSTERIES OF VIRAL REPLICATION

Positive-strand RNA viruses comprise a large and diverse roster, ranging from deadly pathogens like Zika to the rhinoviruses that cause the common cold. In the Ahlquist Lab, Helena Jaramillo Mesa studies how these viruses replicate by assembling specialized structures inside host cells.

“Each virus has its own way to do it,” she says. **“The major limitation we face in controlling viruses is that we’re developing one antiviral against one virus, and that is a losing game.”** That virus is going to mutate and overcome the specific antiviral. What we need is broad-spectrum antivirals and identify mechanisms that these viruses have in common.” A key first step is understanding the most conserved and essential features of viral replication like the structures Jaramillo Mesa studies.



ALEX DUCKWORTH

WHAT THE ELECTRON MICROSCOPE CAN REVEAL

Cryogenic electron microscopy has revolutionized our ability to visualize the structure of molecular machinery in near-atomic detail. The biological questions that it can be used to illuminate are potentially endless. Alex Duckworth, a postdoc in the Grant Lab, turns the microscope on applications ranging from rare diseases to genome replication in bacteria.

“I like cross-disciplinary science,” says Duckworth. **“Cryo-EM takes a lot of physics and puts it together with biology.”** The structural insight it offers lays the foundation for a deeper understanding of how proteins and other molecules work. And it can be used to design new drugs to target these molecules and ultimately provide therapeutic treatment for disease.

When ideas

COLLI

AN EXPANDING UNIVERSE OF COLLABORATION

By Mariel Mohns

Melissa Skala quickly responds to an email from a collaborator before digging into a grant proposal with another. She's stationed at a raised standing desk set up in her office — only she isn't just standing, she's walking on a portable treadmill tucked underneath.

"I'm very high energy, and I kind of have to use that energy to be able to focus," she says enthusiastically.

Perhaps this energy is her secret to being a great scientific collaborator. It's what drives her love for problem-solving. It powers her enthusiasm for championing others. And it's infectious.

Over the past decade, the Skala Lab has become a powerhouse in the world of biomedical imaging. Skala has established collaborative relationships nationwide, working with researchers studying cancer, eye disease, maternal-fetal medicine, and more.

Underlying all these applications is a universe of cell biology that is always in motion. By pushing her lab's signature imaging technologies to unveil its inner workings — without disrupting the system — the Skala Lab offers a transformative set of tools to biologists and clinicians alike. And with endless curiosity, she is fully charged to keep going.

DE



BROADENING THE SCOPE

Skala knew that she wanted to be a scientist in the first grade, when she developed a fascination with telescopes and their ability to reveal the secrets of the universe.

“I originally studied physics to be an astronomer,” she recalls from her early years of undergraduate studies at Washington State University. “I enjoyed working with my hands and building things.”

She eventually refocused her studies. Rather than using telescopic tools to observe the galaxies in the sky, she tinkered with lasers and light to build microscopy instruments that look at the galaxy within.

“There’s so much connection between astronomy and microscopy because of the technology, but we’re looking at cells and molecules in our bodies to see what we are made of, instead of looking at and beyond the universe,” she says.

Skala went on to complete her MS in Biomedical Engineering at UW–Madison and her PhD and postdoctoral training in Biomedical Engineering at Duke University. She then started her own lab at Vanderbilt University centered around her tool of choice: photons.

Pushing the boundaries of what is possible with photonics-based technologies, Skala’s research developed new ways to manipulate light and optics to better understand cancer and develop more effective therapies.

With a passion for big, fundamental research, Skala caught the attention of the Morgridge Institute for Research, a private biomedical research institute affiliated with UW–Madison. In 2016, she began her dual appointment as a Morgridge investigator and UW professor.

“We’re not metrics-driven at Morgridge. I have the privilege to be evaluated on if I’m doing good science,” Skala says. “I can take risks, think more deeply and hold on to a project until I think it’s ready to be published, which I think makes for better science and helps the scientific community more.”

Skala says that the partnership between the institute and the university helps advance science through building powerful research collaborations. It was this relationship that made the institute a particularly attractive place to establish her lab.

“It puts me in this great position to make connections between not only my lab, but other labs at Morgridge and UW. It just expands your network,” she adds. “Science is not done in isolation. You can do so much more if you partner with other people with expertise that is different than yours, but you have a similar goal. You ask more questions, get to learn more, and you just do better science.”

When approaching a project, Skala and her collaborators ask different questions. They want to know how to understand the biology of a system and she wants to know how to develop tools that can make things easier and better for them.

“I think it’s a good example of how to do science the right way — a way that benefits everyone and produces great results,” Skala says.

OF TOOLS AND TRAINEES

The Skala Lab works with a technique called fluorescence lifetime imaging microscopy (FLIM), specifically autofluorescence lifetime imaging. Instead of introducing fluorescent chemical tags to “label” biology of interest, the method uses naturally occurring fluorescence produced by cells when they are metabolically active.

The lab is best known for an innovative label-free technique called optical metabolic imaging (OMI). OMI uses two-photon microscopy to probe the fluorescence intensities and lifetimes of two metabolic co-enzymes, NAD(P)H and FAD. The intensity signals are used together to calculate the optical redox ratio — a way to quantify the metabolic changes and shifts in energy production and consumption within a cell. Calculating the fluorescence lifetimes of NAD(P)H and FAD gives additional insight into cell metabolism and functional states.

Since the method is non-invasive and non-toxic, it doesn’t damage living cells or tissues. This is a key benefit for biomedical research, where the ability to visualize living systems provides a critical advantage.

“It’s really exciting, because with her platform, we don’t have to perturb the cells,” says **Dr. Christian Capitini**, professor





of pediatric hematology and oncology at UW–Madison School of Medicine and Public Health and a frequent collaborator with the Skala Lab. “We decrease the risk of contamination, and we also don’t waste any product for our assays.”

Early applications of OMI focused on methods to better understand cancer metabolism, particularly in breast cancer and pancreatic cancer. But over the years, Skala’s work became an attractive solution for biomedical researchers in various fields of expertise — neuroscience, eye disease, pre-term birth, and more.

“We’re making tools that can be used in very creative ways across disciplines and on many different problems, and I think that’s what makes them impactful,” says Skala. “And when you make them easier for others to use, the applications multiply and you don’t know where it’s going to go. That’s the fun part!”

As excited as she is when talking about technology and problem solving, she lights up even more when talking about being both a collaborator and mentor to those who come through her lab.

“The real impact is in the people I train and what they go on to do; I think that

has 10 times more impact than any of the actual science that I’m doing in my lab,” she says. **“I’m most excited seeing them succeed and learn and contribute in their own way.”**

Skala cites the Morgridge Postdoctoral Fellowship program as a great boon to the collaborative nature of her work. Trainees are co-mentored by two principal investigators — one established at Morgridge and the other at UW–Madison. Less constrained by grant funding, these fellows have the flexibility to explore different disciplines that benefit from bridging research areas.

“I’ve learned the most about other areas of research through them,” she says. “It’s a great way to formalize a collaboration that you otherwise wouldn’t have initiated, because you need that person to introduce the idea.”

A case in point is Sabina Farhadova, the Carl E. Gulbrandsen Morgridge Postdoctoral Fellow. With Skala and **Darcie Moore**, associate professor of neuroscience at UW–Madison, Farhadova is applying optical metabolic imaging techniques to answer fundamental questions about stem cell biology and

neurogenesis — the process by which new neurons are generated in the brain.

“The emphasis on collaboration, innovation and risk-taking creates an environment in which scientists can explore groundbreaking ideas without the constraints often found in traditional research settings,” Farhadova says.

One of the largest groups at the Morgridge Institute, the Skala Lab includes nearly 20 regular staff — including assistant scientists, technicians, postdoctoral researchers, and graduate students — plus a rotation of undergraduates and a few high schoolers throughout the school year.

Whether encouraging someone to follow their own career path into academia, industry, or somewhere in between, Skala offers the same advice: always keep your minds open to curiosity and collaboration.

THINKING LIKE AN ENGINEER

Communication is vital in a good collaboration — and that can take time as engineers and biologists or clinicians learn each other’s language. **Sean Palecek**, a professor in chemical and biological



CHRISTIAN CAPITINI

engineering at UW–Madison, says he and Melissa found their shared language rather quickly.

“As engineers, we’re very process focused and not so much product focused,” he says. “And she has this great unique ability to match the technology with a problem and get excited by the applications as well as the technology.”

“I had a postdoc in my lab who came from Sean’s lab who started making me work on stem cells against my will. And now I’m like, ‘oh, I guess they’re okay,’” Skala says cheekily.

The Palecek Lab uses engineered microenvironments to study human pluripotent stem cells, which can differentiate into any cell type. Gaining a fundamental understanding of how these cells differentiate, develop, and mature will advance progress toward cell-based therapeutics and other clinical applications.

There are multiple factors that influence the fate of a cell, whether it is chemical, physical, or environmental. Thinking like an engineer, Palecek uses a systematic approach armed with a toolbox of multiple research strategies, including gene editing, tissue engineering, predictive modeling, multiomic data analysis, and now advanced imaging.

“I was really excited by Melissa’s skill set to be able to monitor metabolism, which is an important aspect of development — especially the heart, which is very metabolically active,” says Palecek. “And we really needed new technologies to help us track and characterize everything.”

The Palecek Lab developed several different protocols to differentiate stem cells into specialized heart cells, including cardiomyocytes, epicardial cells, smooth muscle cells and fibroblasts.

To completely characterize each of these cell types at every stage of differentiation would require nearly limitless resources. Standard methods of gathering those data require assays that are often time consuming, limited in scale, and use chemical reagents that often kill the cells.

“Right now, these stem cell differentiation processes are like following a recipe in a cookbook. You have your ingredients, you

have your instructions, but you don’t do much characterization in the middle,” he says.

OMI offers a way to gather information collected over the cells’ lifetime, all without disrupting or damaging the cells. Palecek says this gives them a quick glance at the metabolic state of the cells, so if a batch is deviating from what they expect, they have a better fundamental understanding of why and how they might correct it to lead to different outcomes.

Skala says the approach is almost like working backwards — they know the final product should look like a batch of healthy and mature cells, so they need to figure out how to best monitor and control the process to achieve those results.

“The majority of people in science are hypothesis driven, but those of us who are engineers think about things in a fundamentally different way,” she says. “We’re asking ‘what are the tools you wish you had that you don’t know you need?’”

Palecek also serves as the deputy director for the NSF Engineering Research Center for Cell Manufacturing Technologies (CMA^T), a national consortium that brings together collaborators from academia and industry working toward improving cell therapies. Their north star is to be able to design manufacturing methods that are simple, efficient, robust, reproducible and scalable.

“Almost all biomanufacturing these days uses this sort of monitoring and control, but cells aren’t there yet. And that’s where we’re trying to get the field,” he says.

ACTIVATING NEW SCIENCE

When roaming the open common areas at Morgridge, it’s easy to find members of different labs congregating together for a casual lunch or briefly sharing their latest research finding. This interdisciplinary environment is by design.

Morgridge Investigator **Jing Fan** describes the workplace with an analogy fitting for a biochemist — it’s a giant catalyst for collaboration.



JING FAN



DARCIE MOORE



SEAN PALECEK



KRIS SAHA

“You need to reach a point of activation energy for a reaction to occur. Being at an institute like this is basically catalyzing and bringing down that activation energy enough to spark a collaboration,” Fan says. “We’re exposed to different scientific questions and can learn, understand, and appreciate what others are doing and what technologies they are using.”

Fan came to the Morgridge Institute in 2017 with an office next door to Skala. She says right away, they were excited to chat each day and start building toward that activation energy.

A chemist and an engineer found their shared language in metabolism.

Like Skala, Fan’s early research initially focused on cancer metabolism, but her work expanded into the field of immunometabolism. The adaptive immune system uses T cells, which help establish immunological memory over the course of time. But the innate immune system requires cells like neutrophils or macrophages to act as first responders, rapidly warning the body of infection or disease.

“Innate immune cells are fascinating to me because they are very dynamic and heterogenous, even within their population they are metabolically different,” Fan says.

Techniques like mass spectrometry and isotope tracing provide detailed information about the biochemical mechanics of the molecules involved in cell function, but the cells are effectively destroyed after they are extracted and processed. Fan says learning more about OMI from the Skala Lab offered a way to better observe dynamic changes over time.

“The techniques they use and the approaches we use complement each other really well,” says Fan. “The imaging is really strong in that it uses live cells, it’s not destructive, and it has good resolution for bulk or single cells in different activated states.”

A short drive across campus, the Moore Lab is using OMI to study the inactive state of cells — neural stem cells, the precursor to “newborn” neurons that eventually mature and establish themselves in the circuitry of the brain.

With aging or disease, neural stem cells go into a deeper state of quiescence, or newly born neurons do not mature and die off, leading to cognitive decline. Moore says the regenerative process of stem cells in the brain is poorly understood due to limited tools that are sensitive enough to detect them in their dormant state.

“You can’t make newborn neurons if you can’t get the stem cells out of quiescence. If we can’t isolate these cells or identify them better, then we are not going to be able to understand how we can harness their power to start to make newborn neurons again,” she says.

In addition to reestablishing neuron pathways in the brain, neural stem cell regeneration could serve as a model for developing therapies for spinal cord injuries.

While the Moore Lab already had experience with several different imaging techniques, the collaboration with the Skala Lab pushed their technology, and the science, toward new applications.

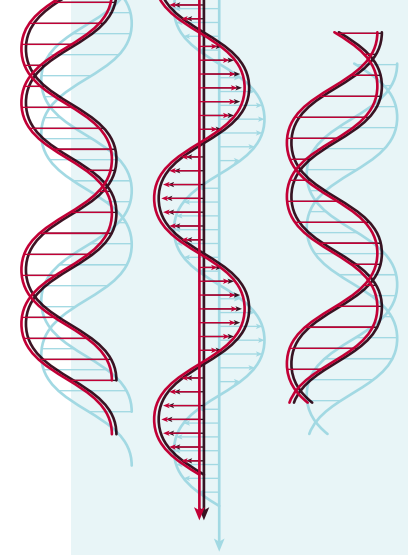
“Darcie wanted to use our technology with a cell sorter so she could do single-cell RNA sequencing and relate it to what the cell will do later, if it has self-renewal capacity or not,” says Skala. “I never would have thought of that!”

Not unlike metabolism, great collaborations are dynamic as well, Moore says. The brainstorming phase is important, but you need that “spark” to turn ideas into action.

“When both people put the same energy into it, it’s very intoxicating to have really good chemistry with someone addressing different problems and for the science to move forward,” she says. “It feeds my scientific soul to have such a productive and exciting relationship where we can both say, ‘let’s try this crazy thing!’ and just do it.”

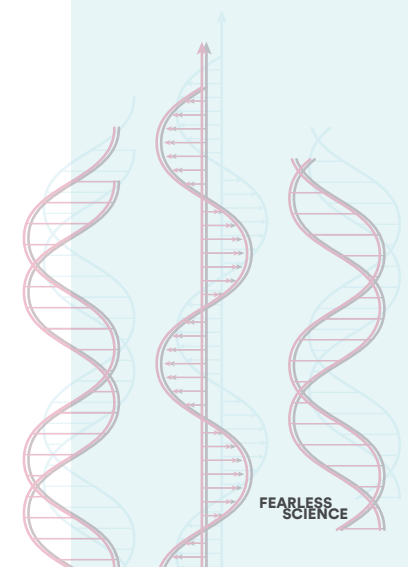
A BRIDGE TO BETTER CELL THERAPIES

Traditional cancer therapies like radiation or chemotherapy are powerful options to combat cancer cells, but they also damage healthy cells



A CHEMIST AND AN ENGINEER FOUND THEIR SHARED LANGUAGE IN METABOLISM.

METABOLISM
LANGUAGE IN
SHARED
FOUND THEIR
ENGINEER
AND AN
A CHEMIST



in the body, resulting in undesired side effects.

There is great potential in chimeric antigen receptor therapy, or CAR T cell therapy, which uses a patient's own immune cells — reprogramming the T cells to fight cancer cells. On the one hand, it is better tolerated by patients. But on the other hand, it takes time and resources to develop a personalized therapeutic.

“We work with **Kris Saha**, a CAR T cell expert, and **Christian Capitini** who is actually delivering cell therapies to cancer patients,” says Skala. “I’m never going to have the depth of expertise in those areas. I just know what a laser is and what it can do.”

Saha, a professor of biomedical engineering at UW–Madison and the Wisconsin Institute for Discovery, uses genomic editing tools like CRISPR-Cas9 to create CAR T cells that will specifically target cancer cells in a patient, leaving healthy cells alone.

Capitini, who recently became the director of the UW Carbone Cancer Center, treated patients with acute lymphoblastic leukemia at the UW Health American Family Children’s Hospital as part of the multi-site clinical trial that led to the first FDA-approved CAR T cell therapy in 2017. Since then, the FDA has approved only six other CAR T cell therapies for adults — all of them for blood cancers.

“Most cancer patients in the United States die from metastatic solid cancers, so that’s an area with a lot of potential for CAR T cell trials,” he says. “We’re looking at ways to weaponize the immune system to better recognize and fight targets on solid tumors.”

CAR T cell manufacturing technologies can take a small sample of cells to modify and expand to produce the millions of cells required for cell therapeutics. However, this rapid expansion makes the cells prone to exhaustion, says Capitini. The result is a mixture of some CAR T

cells that highly effective at targeting and killing cancer cells, but others in the batch will be less potent.

Saha and Capitini found that the CRISPR-based approach gives more precise control of modifying the cells, making them less prone to exhaustion and more efficient at recognizing cancers, including in solid tumors. “That gives them a higher chance of forming memory once it’s infused into people,” Capitini says.

Supported by CMaT, like the collaboration with Palecek, Skala is adapting OMI technology to help Saha and Capitini monitor and control CAR T cell production by measuring and comparing the metabolic state of the cells in real time.

“We want to know how we can identify more effective CAR T cells and promote their growth so they end up in the patient product and generate a better response,” she says.

Capitini also sees potential to take the technology from the pre-clinical side and make it a standard in the clinical practice. With personalized medicine like CAR T cell therapy, there is a benefit to real-time technologies that can help clinicians make a “go or no-go” decision on how to treat their patients.

Pre-clinical testing to fully characterize the CAR T cells includes methods like next-generation sequencing to gather data on genetic signatures that could help make predictions on treatment outcomes in the patient. But in a clinical setting, time is not often on their side.

“You have a patient waiting to receive therapy — you don’t want to wait two weeks until you have interpretable results — you want something that could be done the same day or next day and then make a decision,” he says. **“We’re trying to figure out with this technology, can we get real-time information that is easily interpretable, and does it actually influence the outcome?”**

For now, expertise in performing OMI techniques and data analysis is limited to the Skala Lab. But they are working to make their technologies more accessible and easier to use. Amani Gillette, an assistant scientist in the Skala Lab, recently founded SeLight, LLC, a startup company developing a portable imaging device to screen a patient’s cells before manufacturing.

“Our microscopes take up half a lab room, so we are engineering considerably smaller prototypes to get them out to clinics where doctors can use them,” Gillette says. “The more patients you can measure, the better understanding you have of what’s going on with a particular disease.”

With real-time imaging that is label-free, customizable, and low cost, Skala and Gillette hope their devices will prove to be a successful example of how academic research can translate into innovations that will advance healthcare.

Capitini shares that sentiment. While they are still in early stages of exploring the potential of live imaging for CAR T cell manufacturing, he hopes that through this collaboration, UW–Madison will eventually start using their own homegrown CAR T cell therapies.

“Melissa represents one of many investigators that are invested in improving these types of technologies,” he says. “It would be a new and exciting opportunity to really do this at scale and develop our own in-house workflows that incorporate her and others’ technologies and apply them to make cell therapy work better.”

THE NEXT FRONTIER

Does scientific discovery necessitate new tools, or must tools be developed for scientific discovery to occur? For Skala, the answer is clear.



**“IT’S IMPORTANT
TO INNOVATE.
I THINK THAT’S
WHAT HUMANS
ARE GOOD AT,
INNOVATING
AND IMPROVING
OUR LIVES.”**

“I think discovery is empty without tools,” she says. “Discoveries can’t happen without new tools — it’s not possible.”

Tools are often seen as means to an end, says Skala, but it’s the tools that are opening doors and driving progress. Throughout history, major leaps of scientific discovery happened because of the tools that people used to explore the world around (and inside) them.

The first microscope was created in the late 16th century. Eighty years later, Antonie van Leeuwenhoek used a single-lens microscope to observe “tiny animals,” or single-celled microorganisms, in pond water. The first telescope was designed by

a Dutch eyeglass maker as a magnification tool before Galileo Galilei pointed it to the sky to make astronomical observations. And NASA built the Voyager space probe to set out for the distant reaches of space, providing unexpected new information about the outer planets of our solar system along the way.

To Skala, science is a journey of discovery, and she sees imaging technology as the next frontier. What’s on the horizon? Higher resolution, greater specificity, faster speeds, computational models, and more.

“We’re just pushing the boundaries of what’s possible. There are a lot of opportunities for imaging, but it’s enormously complex,”

she says. “If we can see smaller things, see faster things, see deeper things, we’re going to understand them better. We just don’t know how to do all that yet.”

With cutting-edge tools comes a higher level of expertise, which means fewer people who initially have the knowledge to use them. But for Skala, that’s what makes collaborative work so exciting.

“We ask, how are these tools useful? Then, how can we develop something that others can use? That’s our expertise,” she says. “It’s important to innovate. I think that’s what humans are good at, innovating and improving our lives. We enjoy it, and that’s why we do it. Bottom line.”

QUANTUM IMAGING

**could open new window
to nanoscale universe**

As spectacular as modern imaging can be in illuminating the tiniest aspects of life, some avenues of biology are still cloaked in darkness.

Biological processes that happen over long periods of time — for example, exchanges of materials between cells — are hard to capture with conventional microscopy. Likewise for processes that occur quickly, such as interactions between organelles.

A team of physicists-by-training has a novel strategy for breaking through this roadblock: Merge modern light microscopy with the rules of quantum physics to usher in a new era of super-resolution imaging that can aid in diagnosing and treating disease.

Scientists at Morgridge, Colorado State University and the Colorado School of Mines have teamed together on a multi-year project to build a new generation of microscopes that marry both classical and quantum measurements. The project is supported by the Gordon and Betty Moore Foundation, an organization that works to advance knowledge through pioneering technological advances.

“Quantum” is having a major moment in the world of computing, where scientists are actively pursuing ways to harness rules of quantum mechanics to make computers many times faster than today’s technology. But how would quantum physics relate to how we view the biological world?

Randy Bartels, a Morgridge biomedical engineer and lead investigator, says current approaches to super-resolution imaging rely on fluorescent labeling, where biomolecules of interest are “tagged” by fluorescent molecules that can be detected by microscopes. But these elements only produce light for very short periods before vanishing, limiting their ability to capture dynamic features. The fluorescence process can also disrupt or alter the biology taking place.

Quantum optics allows researchers to exploit properties of light that are not seen by normal cameras, making greater use of natural rules that already exist. Bartels says quantum approaches will be based on more universal properties of light and photon statistics that are invisible to classical measurements. In this way the new microscope will capture more information than current microscopy technology, unveiling the secrets of cells scientists have not yet been able to disclose.

“We believe that the ability to measure the quantum behavior of light, beyond the conventional strategies open to classical imaging, will create a critical path to advancing super-resolution imaging and open a new window into the nanoscale universe,” says Bartels.

Co-investigators on the project include Jeff Squier, physics professor at the Colorado School of Mines, and Olivier Pinaud, professor of mathematics at Colorado State University. Squier has worked extensively on establishing single-element detection imaging technologies with applications from advanced manufacturing to the biological sciences. He pioneered third harmonic generation (THG) microscopy with application to biological imaging, a key component of this new research program. Pinaud is an expert in the mathematics of quantum mechanics and quantum optics. His contributions include the theoretical analysis of partial differential equations in the context of wave propagation and quantum physics.

In the first phase of the project, the team will continue basic research on the nature of quantum optics and photon statistics to determine how these principles can be incorporated into microscopy. This includes understanding the physics of how photons are distributed through coherent nonlinear scattering — a process where strong light passes through a material and generates greater light frequency. They will exploit quantum correlations and improve the spatial resolution and speed of microscopy over classic coherent nonlinear imaging approaches.

Once the microscope is built, the researchers will conduct imaging experiments to understand intricate biological dynamics of nanoscopic structures that stand to gain the most from this new quantum approach. This includes research on tiny structures inside our cells, known as organelles, to understand how their movements and interactions directly influence our overall health.

Other possible imaging targets include investigating tiny bridges called nanotubes that cells use to swap materials, especially since cancer cells can cleverly use these bridges to disable the immune system’s T cells. “To fight back, we need to improve immune therapies, which requires using advanced microscopes to watch T cells change shape and move in real time without damaging them,” Bartels says.

These improved imaging tools will also be deployed to help improve understanding of structures called biomolecular condensates, which act like liquid droplets to organize vital tasks such as how the cell responds to stress.

“Our goal is to apply this new microscope to study aspects of biology and biomedical research that cannot be observed with current imaging technology. Our aim is to open a new world of observations into intercellular and subcellular dynamics,” says Bartels. “Understanding these dynamics is the foundation to analyzing the mechanisms at play in health and disease as well as designing and manufacturing treatments.”



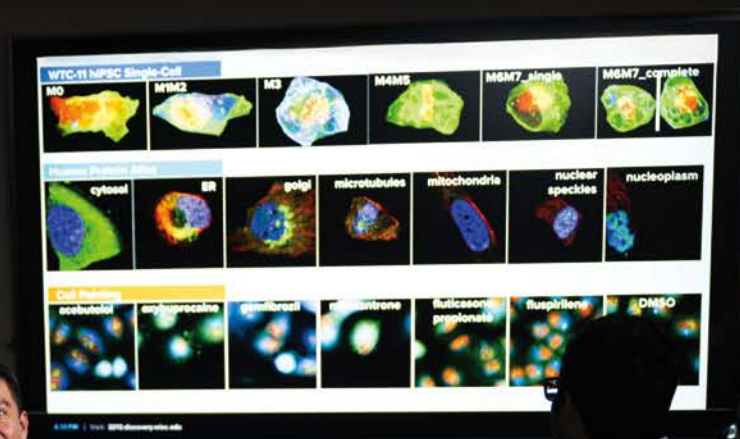
RANDY BARTELS

CHAMMI-75

Finding common ground across millions of biology images

Scientists at the Morgridge Institute for Research are raising the ante on the common phrase, “Every picture tells a story.”

The research team has developed a database that combines 2.8 million cellular images — captured across a wide range of imaging modalities — which can be used to train machine learning models to help answer questions about basic biology, functional genomics, and treatment design.



Morgridge investigator **Juan Caicedo** says the ultimate goal is to provide researchers with a more universal tool to examine cellular morphology for biological studies. Cell morphology involves analyzing the size, shape, structure and patterns of cells to better define the differences between healthy and diseased states. Using machine learning, these tools have proven to be a very powerful way to study how cells respond to treatments, among other biological applications.

“If you look at how artificial intelligence is applied to microscopy today, most of these models are trained on one specific type of microscopy image,” says Caicedo, also an assistant professor of biostatistics at UW–Madison. “So we started to realize that if we really wanted to make progress, we need to create models that can be more broadly applicable for scientists.”

The database, made publicly available to researchers in early 2026, is called CHAMMI-75, which stands for “channel-adaptive models for microscopic imaging.” The number 75 represents the different data sources of cellular images that are included in the database.

All told, the model collects images of more than 1.8 billion cells, which have been standardized through common formatting and metadata, essentially getting them to “speak the same language” even as they are derived from vastly different sources. The dataset includes images from 14 different imaging modalities, such as fluorescence, confocal, cryo-electron, or other “flavors” of microscopy. And it incorporates images across 16 different organisms and 15 different magnification levels.

The concept of “universal morphology” actually takes a cue from early successes in large language models (LLMs), Caicedo says. About a decade ago, AI researchers began to develop LLMs that are trained across many different languages. Rather than having to create new AI platforms in each language, AI proved capable enough

to analyze and find similarities across virtually all languages.

“I remember reading a paper where they made experiments with 100 languages at the same time for the first time, and the results were amazing,” Caicedo says. “The more languages you put in, the more fluent the model becomes, even when the language doesn’t produce a lot of data — imagine a very rare language.”

“It turns out that languages that have very few resources benefited the most from that joint modeling, because there are some commonalities in all human languages,” he adds. “If you specialize a model for this rare language, you are constrained to only the few documents that you have for that language.”

Caicedo says he hopes CHAMMI-75 can provide the same kind of effect, where AI can apply some of those commonalities across all cells to shed light on rare or poorly understood diseases. After all, there are more than 200 cell types in the human body, and all have common elements such as DNA, nuclei, membranes, and organelles. There is bound to be evidence from well-studied disease states that can inform lesser-understood conditions, he says.

One of the immediate applications will be in drug development and repurposing, as a confirmation and prediction tool to help scientists choose the best direction when hundreds of different compounds are tested. It may also inform smarter forms of microscopy, that can be programmed to identify different phenotypes in real time, while experiments are being conducted.

Examples of some of the imaging data used in CHAMMI-75 include not just human-derived cells, but cells from other mammals, bacteria and even plants. It includes data from genetic screens, drug screens, 3D imaging and specialized cell biology. Much of the data comes from

some of the world’s largest existing cell atlases, such as the Image Data Resource, the Human Protein Atlas, and the Cell Painting Consortium.

Several biology research labs have been using methodologies from the Caicedo Lab on their own image collections. Morgridge investigator Ken Poss, for example, studies regeneration in zebrafish hearts, and their data helps show how heart activity evolves under certain genetic conditions. A team at Johns Hopkins University is using it for a database of human-derived cell lines from schizophrenia patients, and a Copenhagen University team is using it to quantify micronuclei formation.

“We’re trying to find as many examples of image-based experiments as possible to enrich the quality of the measurements that we provide to real-world biological studies,” Caicedo says. “Every microscopy lab needs this type of capability, there is a real need, and we believe that our approach can help them.”



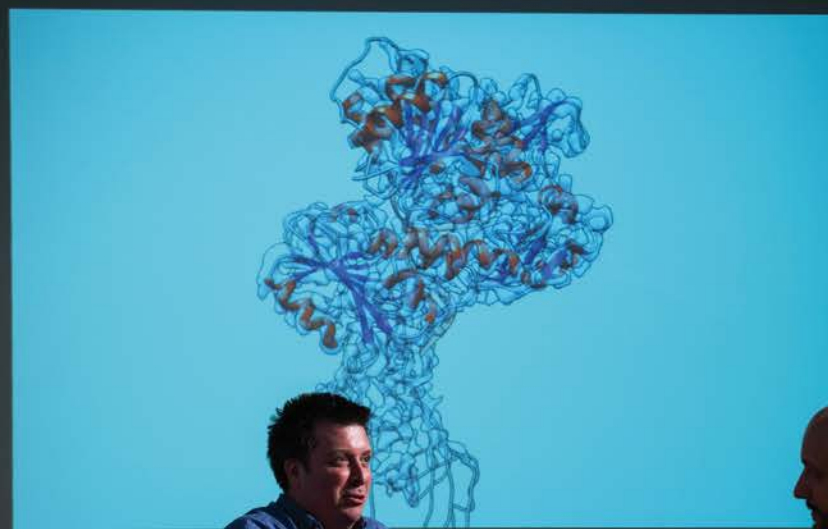
JUAN CAICEDO

SOLVING STRUCTURES

reveal the ‘high-wire act’
of bacterial replication

Bacteria have a replication problem. In nearly every attempt to copy their genome, some kind of glitch — exposure to UV light, or an obstruction within the cell — occurs that throws the process off.

Normally this would be a lethal error, but bacteria have finely tuned proteins that race to the site of the break and repair it on the fly. This “replication restart” process is a little-understood but essential activity for bacteria — and thus, a very intriguing future target for antibiotic development.



James Keck, a professor of biomolecular chemistry at UW–Madison, has been studying the replication restart process for years, and has used crystallography techniques to determine the structures of key proteins that guide the DNA repair. But the replication restart process is so dynamic, Keck says, these structures rarely “sit tight” long enough to get detailed images through crystallography. Keck has taken a huge leap forward in recent years through a partnership with Morgridge Investigator **Tim Grant**, a pioneer in cryo-electron microscopy (cryo-EM). In a 2023 project, the team used cryo-EM to reveal a switch-like mechanism that initiates the restart process and a major restructuring of proteins that allows DNA repair to take hold.

This process is essential to the survival of bacteria. This initial look at replication restart in *E. coli*, led by **Alex Duckworth**, revealed the early protein and DNA interactions that kickstart assembly. Now, Duckworth and colleague **Peter Ducos** have uncovered more of the replication restart domain.

The latest chapter in the partnership between the Grant and Keck Labs is a more complete look at the DNA replication machinery in *E. coli*, out this spring in *Nature Communications*. Cryo-EM uses cryogenic temperatures and electron microscopes to see tiny molecules in their near-native states. This technique is key to uncovering “structure–function” relationships — here, the way *E. coli* assembles a “preprimosome” complex to restart replication at abandoned or damaged replication forks. One of the most striking discoveries is the apparent parallel between the master initiator of DNA replication, DnaA, and DnaT, whose role in replication restart completes the picture the teams started sketching out years ago. That parallel suggests a conserved mechanism for initiating and restarting replication.

“The new structure showed, for the first time, an unexpectedly similar arrangement

for proteins involved in DNA replication restart between our structure and those that drive normal replication initiation at chromosomal origins of replication,” says Keck. “This parallel hints at a universal mechanism used both for starting and restarting DNA replication in bacteria.”

Adds Keck: **“Since the process driven by the proteins in our complex occurs in all bacteria via similar mechanisms, and is not found in human cells, the structures are excellent potential targets for antibacterial therapeutic development.”**

Grant notes that these are fascinating structures from a cryo-EM perspective, given that they are both heterogenous and dynamic — and could never be captured by X-ray crystallography.

“Deriving the models required combining relatively complex image processing with AlphaFold3 predictions,” Grant says. “The final model really demonstrates how complex the arrangement of all the components is and highlights the power of cryo-EM in solving the structures of dynamic samples.”

Grant used a software package he developed called cisTEM to process the cryo-EM data, which was drawn from thousands of movies. The software provides a more user-friendly interface for biologists and is adept at analyzing and predicting motion in biological processes. Data was collected at the UW–Madison Cryo-EM Research Center.

“Cryo-EM showed us that a large motion in one protein is key to controlling the process,” Grant says of the 2023 findings. “It achieves a number of cool things, opening up a pore that encircles one part of the DNA and opening up interfaces for other proteins. The process cannot continue until this movement occurs.”

Chromosomes in bacteria are circles of DNA that duplicate starting at a single origin point, with two replication

processes running around the circle bidirectionally until they meet at the bottom — basically, two events starting at 12 o’clock and meeting together at 6 o’clock. This differs from the linear replication of DNA in human cells. For bacteria, replication mistakes can happen anywhere along that clock face, a big reason why the replication restart process is so critical to survival.

“That makes replication a little bit of a high-wire act for bacteria,” Keck says.

Despite the differences between bacteria and eukaryotic cells, having a basic understanding of the bacterial replication restart machinery will have benefits for biomedical pursuits beyond possible antibiotic development, Keck says. Human DNA repair systems are studied extensively because they’re so important to oncology. The widely used chemotherapy drug Cisplatin, for example, works by actively knocking down the capacity of tumors to replicate and repair DNA.

“Our findings give us more clues about what kind of features we might expect in a protein that does this kind of thing in humans,” Keck says. “And that helps you narrow the list of potential candidates in the human proteome to perhaps a handful that warrant further study.”



JAMES KECK



TIM GRANT

Life

AGLOW

Scientists harness a phenomenon called fluorescence to reveal the cellular secrets underlying health and disease otherwise destined to remain hidden from view. Last year, we created a beginner's guide on fluorescence imaging to celebrate the power of this technique in the hands of Wisconsin scientists. Take a peak at some of the highlights below.

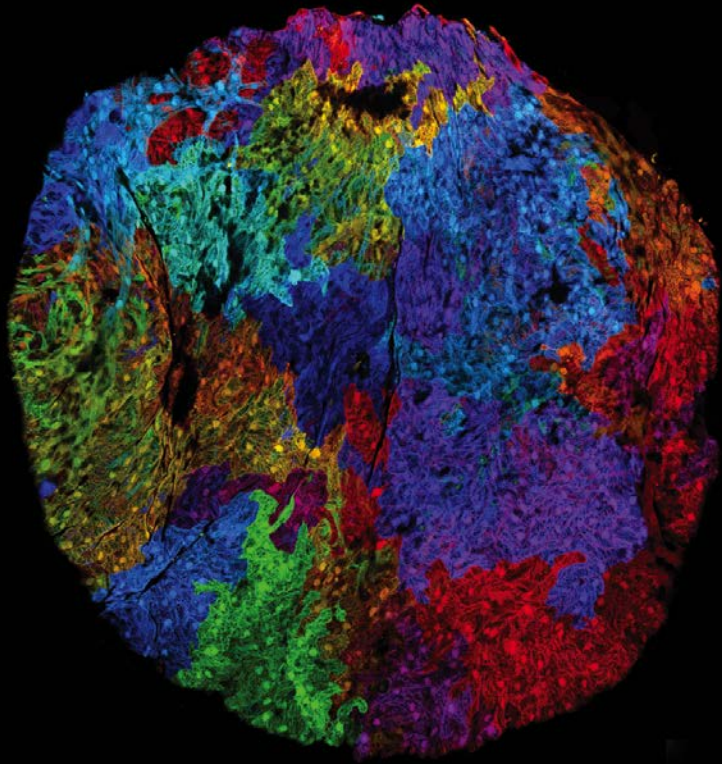
Light is made up of massless particles called photons, the tiniest possible packets of electromagnetic radiation. When photons hit special molecules responsible for fluorescence — called fluorophores — they excite electrons that had been buzzing around at their most stable “ground state.” The excited, higher energy state does not last long.

During relaxation, the fluorophores re-emit the light they had absorbed. This time, the light has a longer wavelength and thus a different color.

This is fluorescence, and it all happens in billionths of a second — about 200 million times faster than the blink of an eye. Fluorescence works like a visual microphone, amplifying otherwise invisible details and interactions happening inside cells.

The ability to ask and answer questions with fluorescence is a system in constant motion, fueled by scientific curiosity. Every time biologists unlock a new discovery, we find out where tools like fluorescence microscopy need to evolve. And with untold biological questions remaining to be answered, it's safe to say the future of is bright.



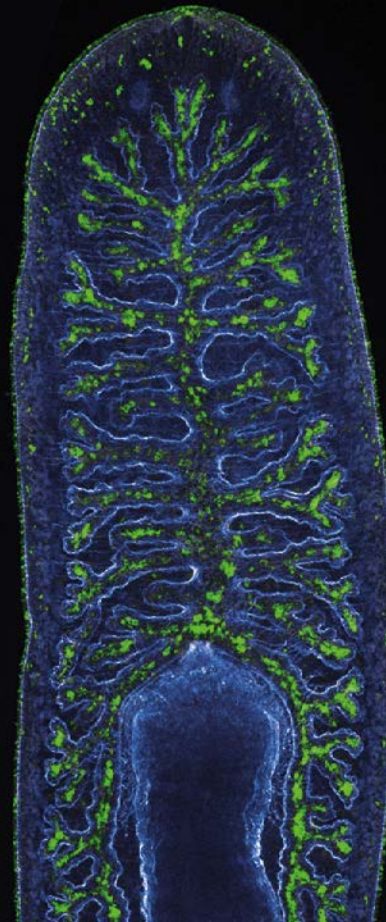


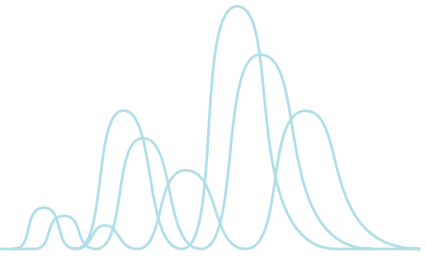
1 Here, the lab of developmental biologist **Ken Poss**, director of regenerative biology at Morgridge, integrated a variety of fluorescent hues into zebrafish — effectively color-coding the different muscle cells that form into the adult zebrafish heart. With this multicolor analysis, the group revealed for the first time two previously unknown layers of the wall surrounding the heart's ventricle. The discovery, made over a decade ago, opened a path for the group to explore how molecular factors control movement and division of heart muscle cells during regeneration.

Credit: Ken Poss.

2 In the planarian *Schmidtea mediterranea*, a model organism capable of regenerating its organ, the intestine (green) is labeled with an antibody that recognizes the digestive cells. The muscles (blue) surrounding each intestinal branch are labeled with a different antibody. The **Newmark/Issigonis Lab** uses planarians to understand how stem cells are regulated to produce missing tissues and organs in the context of a whole organism.

Credit: David Forsthoefel and Phil Newmark.





TODAY, IMAGING SCIENTISTS AT WISCONSIN ARE PUSHING A WIDE ARRAY OF FLUORESCENCE IMAGING APPROACHES TO VISUALIZE BIOLOGY WITH EVER **HIGHER PRECISION, AT GREATER DEPTHS, AND IN MORE DYNAMIC LIVE IMAGING CONTEXTS.**

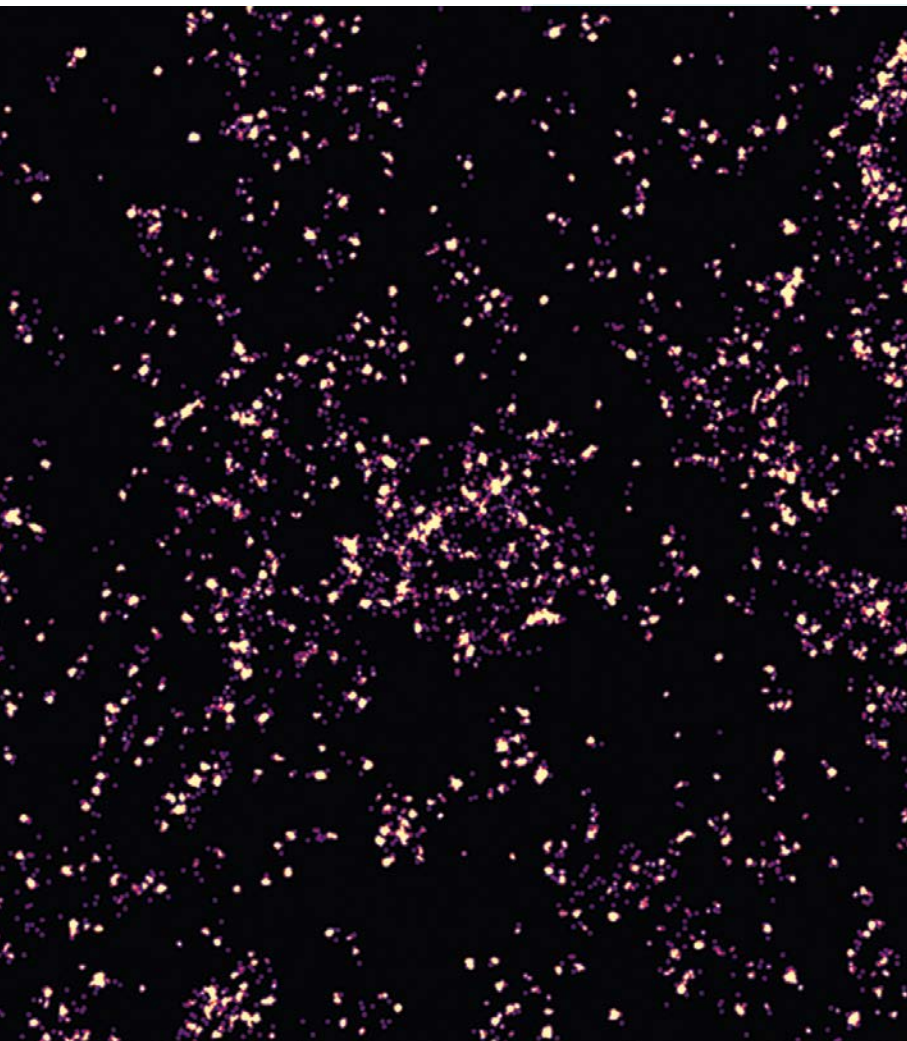
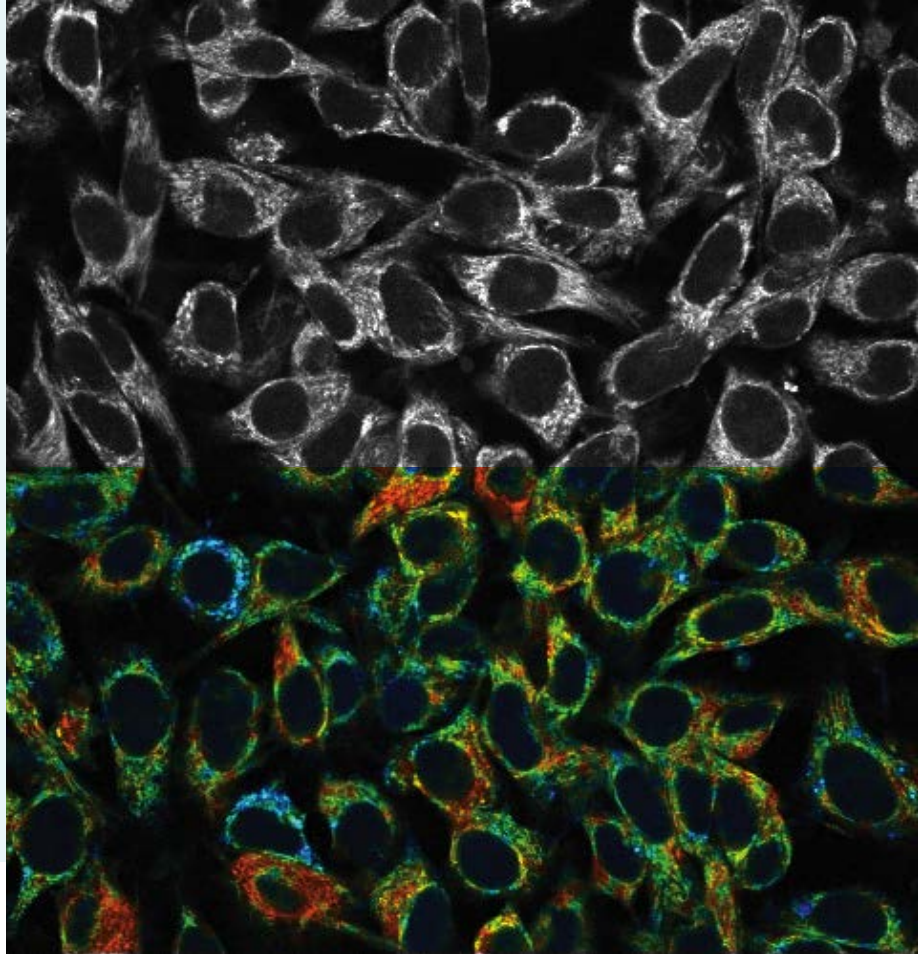


3 Super-resolution fluorescence imaging encompasses a suite of approaches that surpass the *diffraction limit of light* — allowing light microscopes to resolve objects smaller than 200 nanometers, including viruses, ribosomes, and proteins. Here, scientists in the lab of **Daniela Drummond-Barbosa** use a super-resolution approach to show how much antioxidant protein (green) the cell is producing in developing fruit fly egg chambers; nuclei are stained white.

Credit: Ana Paiva Gandara.

4 Scientists in the **Skala Lab** at Morgridge capture autofluorescence intensity (top) and mean lifetime (bottom) of NAD(P)H in mouse melanoma cells. The lifetime image is more comprehensive and shows the heterogeneity that exists even within a monolayer of cells in culture. Warmer colors (reds, yellows) indicate where NAD(P)H is active in the mitochondria and cooler colors (blues, greens) indicate where NAD(P)H is active in the cytoplasm.

Credit: Alexa Heaton.



5 The **Joshua Brockman Lab** at UW–Madison designs molecular-tension probes that attach to cellular receptors — such as the T cell receptor, which regulates if and when T cells kill virally infected or cancerous cells — and open like bobby pins when force is exerted, emitting fluorescence. Those forces are incredibly tiny, at the piconewton scale, or roughly one-trillionth the force required to lift an apple.

Credit: Joshua Brockman.



6 A line confocal microscope custom-built in the **Abhishek Kumar Lab** at UW–Madison captured a mouse embryo that had been rendered transparent in a process called “clearing” and immunostained so that part of its nervous system appears blue — revealing a clearly resolved cluster of neurons in the dorsal root of the spinal cord.

*Sample provided by Ivan Candido-Ferreira;
imaging by Matthew Parent.
Credit: Abhishek Kumar.*

Credit: Abhishek Kumar

EXPLORE THE FULL EXPLAINER HERE





NEXT GEN

MORGRIDGE ALUMNI PUSH THE FRONTIERS OF SCIENTIFIC CAREERS.

Profiles by Dennis Chaptman





AMRITAVA DAS, BIOETHICS

National security work grows out of scientific expertise

There comes a time for many postdoctoral scholars when they have to make a life-changing decision: Do I go into private-sector work? Do I become a professor? Do I stay at the lab bench, immersed in science?

Former Morgridge postdoc Amritava Das found himself at that juncture, weighing his options back in 2021. He considered an offer to work for a biotech startup and sent out a half-dozen applications for faculty positions.

“There are intellectual parts of being a faculty member that are very appealing. And then there is the daily grind of the job itself, writing grant applications,” Das says. “I found applying for faculty jobs to be tiring. Some people send out 40 or 50. I thought the fatigue setting in at six was problematic.”

Das, whose interdisciplinary work at Morgridge straddled

biomedical engineering and bioethics as it relates to patient care, had been developing a need to take his career beyond the theoretical realms of science.

“I wanted to get off the bleachers and get onto the field,” he says. “I wanted to be on the pragmatic end of it. Intellectually, I’ve always been interested in the empirical.”

That’s when he applied for, and won, an AAAS Science and Technology Policy Fellowship — the first ever at the U.S. Department of the Treasury. During a year at the agency, he worked with the Committee on Foreign Investment in the United States, reviewing financial transactions involving foreign investments in the U.S.

“They were very interested in some of the training I had that helped me articulate risk in a very organized way,” Das says, adding that the job demands a

high degree of technical and strategic knowledge.

That experience led Das to a Washington, D.C.-area career in defense contracting.

Das, who was born in Rochester, N.Y. but moved with his parents to India at age two, had a family that prioritized education. After two years at a college in India, he transferred to the University of Manchester in England where he obtained a master’s in chemical engineering.

During his undergraduate years, Das recalls a close family friend’s reaction when he mentioned that he might not pursue a PhD. “She said, ‘But if you don’t do a PhD, people will think you’re illiterate.’ It’s just a thing you’re supposed to do.”

At UW–Madison, Das earned a doctorate in chemical and biological engineering and became a Morgridge postdoc working with Kris Saha, Christian Capitini, and Pilar Ossorio.

His experience was diverse. In bioethics, he worked to understand how clinical trial investigators navigate dual roles as physicians and scientists. At the same time, in biomedical engineering he was developing mathematical models for understanding outcomes from gene therapy and studying production of new CAR T cells for treating cancer.

“The term I’ve used to describe my experience at Morgridge is ‘intellectual whiplash,’” he says. “I was switching between doing gene editing experiments, immunology experiments and working in bioethics. But it

ended up being a fascinating 4½-year intellectual journey.”

After his Treasury fellowship ended, Das took a job as a senior consultant with 11th Hour Service, a Department of Defense contractor. In that role, Das analyzed military supply chains — notably minerals and textiles.

“A lot more than weapons are sourced by the military. The job gave me a great idea of the workings of the U.S. government, understanding how the Department of Defense works, and the critical role it plays in the U.S. economy,” Das says.

In late 2024, Das took a job as senior expert control analyst at American Systems, another defense contractor. In that role, he investigates foreign direct investments in the U.S. to determine if adversarial nations are making investments in firms and technologies that could affect U.S. national security.

Das says his work at Morgridge, while it seems far afield from his work today, built relevant, valuable competencies.

“It was a postdoc experience that was designed for wide-ranging interdisciplinary intellectual curiosity. There was a high degree of intellectual fulfillment that carries over,” Das says. “The Morgridge fellowship allowed me to see a vast, scientific world outside of biology and engineering, which I don’t think I would have seen otherwise.”



PETER FAVREAU

Soft skills, technical know-how build a career in microscopy

One of the lessons that Peter Favreau learned as a postdoctoral scholar at Morgridge was that developing interpersonal skills is an indispensable attribute.

“The biggest skills I lean on now are soft skills,” says Favreau, now business development manager for cancer research at Zeiss Microscopy, a leading manufacturer of microscopes worldwide. **“At some point, my technical expertise stopped mattering as much and what mattered more was that I could talk to people, and they would not come away thinking, ‘This guy’s a loon.’”**

Favreau cares about communication and considers himself to be good with people, but as a postdoc in Melissa Skala’s lab for three years beginning in 2016, those

skills grew within Morgridge’s collaborative culture.

“It’s to Morgridge’s credit, because that kind of collaboration is so easygoing,” Favreau says. “If you’re getting coffee, it’s hard not to talk to people about the science you’re doing.”

Favreau, whose scientific curiosity was piqued as a child exploring the tropical rainforest in Puerto Rico where his father was stationed in the Navy, earned his PhD in basic medical sciences and biophotonics at the University of South Alabama.

Although his undergraduate degree at South Alabama was in physics, he wanted to apply his skills to an area that could more directly help people.

“They were just starting a biomedical engineering

program, and I was one of the first graduate students,” he says. “My mentor’s background was in optics, so I figured, ‘I can learn new things.’”

As a doctoral student, Favreau worked on technology to help detect cancerous cells by shining a light on tissue, causing the cells to glow a different color. As part of the work, he also built a microscope.

After earning his doctorate, Favreau was undecided on a career and took up Skala’s offer to join her lab at Morgridge, figuring it might provide a softer career landing. “She gave me the freedom to pursue my career,” Favreau says of Skala. “She never tried to push me one way or another. She offered me opportunities that another mentor would close doors on.”

The lab investigates drug reactions on lab-grown organoids to determine which drugs are most effective on cancerous tumors. Favreau used a technique called fluorescence lifetime imaging to view how the tumor cells react.

As his postdoc came to an end, Favreau mulled teaching and a continued career in lab research.

“I never felt confident as a scientist,” he says. “I don’t think my brain is quite wired to do the detail-oriented work of a bench scientist. I’ve always enjoyed teaching and working collaboratively, which can be elements of a great scientist, but are generally not the focus.”

Instead, he took a job as director of UW–Madison’s Biochemistry Optical Core, a

central hub for sophisticated optical gear such as confocal and epifluorescence microscopes on campus. He also briefly worked for a local startup, Stem Pharm, as a scientist. While he enjoyed the new opportunities Stem Pharm offered, he still found himself looking for a position that combined his soft skills and technical knowledge of the microscopy field.

Then one night, while searching LinkedIn for jobs, he entered the word “confocal.” Up popped a listing at Zeiss Microscopy. And there he found a fit for his soft skills and technical knowledge, first as product marketing manager for Zeiss’s Lattice line of microscopes and, beginning in late 2024, as the North American business development manager for cancer research.

In his role, Favreau — based in Minneapolis — is in charge of positioning the entire Zeiss portfolio of microscopy products for potential clients primarily in the cancer research field across North America.

“I draw a lot of satisfaction in collaborating with everyone,” he says. “Product launches are very satisfying because they require a lot of input from many people and finding new ways of marketing and positioning things.”

Asked what advice he would give to graduate students, Favreau again leaned into interpersonal skills and developing the ability to network with colleagues.



ALEX WALSH, BIOMEDICAL IMAGING

Family ties spark lasting passion for science

Growing up in Austin, Texas, Alex Walsh was surrounded by scientific rigor and enthusiasm.

Her grandfather, a professor at the University of Texas, founded its biomedical engineering department and was active in the biphotonics field. Her parents, who left graduate school at Stanford to co-found a software development company, also lit a pathway for Walsh's development as a scientist.

"I've always had an aptitude for science and math, and an innate curiosity. They encouraged me to think about careers in medicine and science, and biomedical engineering seemed like a good direction," says Walsh, now an associate professor in the Department of

Biomedical Engineering at Texas A&M University.

Her academic journey led her to Vanderbilt University, where she earned bachelor's, master's and doctoral degrees in biomedical engineering. That's where, while earning her PhD, she worked alongside Melissa Skala, now a Morgridge investigator.

In Skala's lab, Walsh focused on developing optical microscopes that could predict drug response for cancer patients using lab-grown tissues called organoids.

"She's a fantastic mentor. She's been super supportive of letting me explore ideas, helping to train me to be a good scientist, and teaching me to write grants," Walsh says. "She was a great example

of how to be a scientist but also have a family and collaborate with a large number of diverse people."

Armed with a PhD, Walsh did postdoctoral work at the U.S. Air Force Research Laboratory at Fort Sam Houston in San Antonio, investigating the effects of infrared light on neurons and cells and developing a fast fluorescence lifetime imaging system.

But Walsh soon found herself missing academia, contact with students, and multidisciplinary work. When Skala left Vanderbilt for Morgridge, there was a chance in 2017 for Walsh to come to Wisconsin and continue her postdoctoral work with her mentor.

"Melissa offered me a job at a really critical time in my career when I had applied for faculty positions and hadn't found any," Walsh says. "I couldn't stay with the Air Force, because federal cuts made that job evaporate. I may not have stayed in science if there hadn't been a position at Morgridge."

As an assistant scientist in the lab, Walsh led a project to use non-invasive fluorescence imaging to identify and sort T cells — promising weapons for fighting cancer — for use in immunotherapy treatments.

The technology, which has since been patented, won the 2018 Innovation Award from the Wisconsin Alumni Research Foundation (WARF). The award certificate is displayed prominently on her office wall in College Station.

The Morgridge experience, she says, was foundational in developing her career.

"It was a unique and collaborative place," she adds. "The Wisconsin ecosystem trained Melissa and me in how to communicate our ideas in a way that WARF patent attorneys could understand. That's helped me here. We've had two disclosures go through and the patents submitted, so it was really valuable."

After two years in Skala's lab at Morgridge, Walsh landed a faculty position at Texas A&M.

There, she teaches and leads the Quantitative Optical Imaging Laboratory. The lab uses a variety of imaging technologies — including light sheet microscopy, fluorescence imaging, infrared stimulation, and others — to study cell metabolism, drug response, and immune cells.

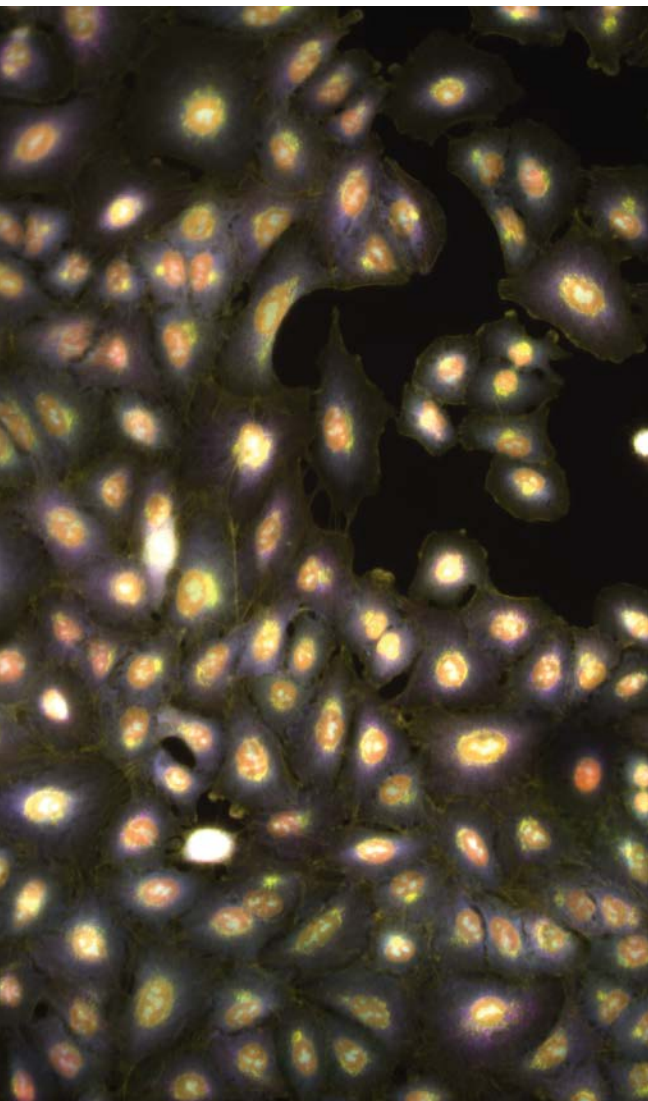
Her lab staff numbers more than 20 graduate students and undergraduates. "I learned a lot from Melissa about how to recruit people who are honest, hard workers. I try really hard to make time for them. I help guide them along the way, but I don't want to do the work for them. It's guiding and mentoring without dictating."

Walsh adds: **"My favorite part is working with students, watching them develop their skills. It's fun to see them become more confident in themselves, and confident in their work."**

These researchers are making image analysis

EASY

By Cassandra Willyard



▲ A microscopy image showing Cell Painting

Anne Carpenter’s most significant research project was born out of frustration. In the late 1990s, Carpenter began a doctoral program in cell biology and started studying the structure of chromatin. The work required poring over microscopy images and painstakingly measuring the diameter of thousands of dots.

“This is terrible,” she remembers thinking. “There’s got to be a better way.”

Eventually she found image processing software called NIH Image (now known as ImageJ/Fiji, developed by Morgridge investigator Kevin Eliceiri) that allowed her to measure the slides in a quantitative and automated way. “I fell in absolute love,” she says. She had to tweak the program a bit to get it to do what she wanted, but once she got it working, “It was so much more satisfying,” she says.

Carpenter never dreamed she would go into computer sciences, but after her experience with NIH Image, she was hooked. She began writing her own software, an open-source program geared to the high-throughput experiments that she knew were coming. By 2005, she had drafted a program called CellProfiler that could easily locate the cellular features in a microscope image and measure various properties about them — shape, size, color, and pattern. In 2007, she established her lab at the Broad Institute of MIT and Harvard.

“The whole purpose is to — in a user-friendly and systematic way — help researchers extract the most information they can out of images.” CellProfiler can count a neuron’s synapses, measure the fat content of a worm, track cells as they move through time lapse images, count tumors in a mouse lung, and much, much more.

In academic science, success is often measured by the size of an individual’s lab. As the popularity of CellProfiler grew, so did Carpenter’s lab and, with it, her workload. In 2020, however, joint pain forced Carpenter to reevaluate the trajectory of her career. “I think scientists are often on autopilot. You just assume you should keep growing and getting as many grants and building your lab as large as possible,” she says. A doctor’s suggestion to reduce stress



“THERE’S GOT TO BE A **BETTER** WAY.”

forced her to pause and think. “Where am I heading if I just keep going in this direction?”

Carpenter realized she wanted to stay closer to the science, not just oversee it as the head of a large lab. So she made an unconventional decision. She named Shantanu Singh, a computer scientist, as co-leader of her lab and transferred the future development of CellProfiler to staff scientist Beth Cimini, who was just launching her own group.

Cimini, who joined Carpenter’s lab as a postdoc in 2016, had been working on CellProfiler for years. She started using the software in graduate school and quickly became an evangelist. But there’s always room for improvement, and today Cimini spends much of her time trying to make image analysis even easier. “I spent a lot of years in graduate school doing things that felt like they were too hard,” she says. **“I want to give people the knowledge to figure out how to make things work.”**

For example, computers often struggle to define the boundaries of objects. “They rely basically on things either being dim at the edge or being round, and that’s not always how we see the boundaries of things.” But there are workarounds. Cimini recently helped Morgridge’s Melissa Skala, a biomedical engineer who works with images of cancer cells, find one. By incorporating a deep learning segmentation program called CellPose into CellProfiler, they figured out a better way to find the borders of these cells. “Now they don’t have to have all of these undergrads chained to desks for 10 hours a week circling cells,” she says.

With CellProfiler in good hands, Carpenter has been focused on a strategy she developed in 2013 called Cell Painting. In many microscopy

experiments, biologists stain cells to highlight one feature that they expect to change in response to some perturbation. To Carpenter, that seemed like a missed opportunity. “You’re just cherry-picking this one thing that you happen to be researching,” she says. But “you have the potential to read out so many different things from every image.”

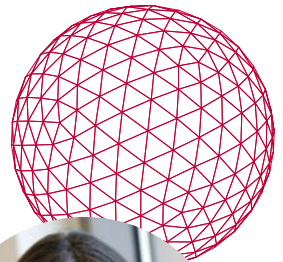
So Carpenter developed an assay to do just that. With Cell Painting, scientists douse the sample with six different dyes to highlight the cell’s most prominent organelles. This suite of simple stains can yield a surprising amount of information about the cells’ state and how different diseases, drugs, and genes affect them.

This is especially useful in drug discovery. If researchers expose cells to thousands of chemicals, for example, they can group them according to their effects. One group might be toxic to the liver. Another might be particularly effective for treating a disease. Pharmaceutical companies are already leveraging Carpenter’s tools to develop new therapies.

And Carpenter has her own drug discovery ambitions. In 2023, she co-founded SyzOnc, a startup that leverages Cell Painting and AI to develop therapies for hard-to-treat solid tumors.

Carpenter spent the first half of her career developing tools and methods. “I really hope to spend the next decades pushing forward different applications,” she says. “It feels to me like the time is right to really apply image analysis at large scale to accomplish great things for medicine.”

Editor’s note: Dr. Carpenter will be moving back to her Midwestern roots this summer, as her lab transitions to her undergraduate alma mater, Purdue University.



ANNE CARPENTER

BETH CIMINI



Unraveling the mysterious beauty of

BUTTERFLY WINGS



By Cassandra Willyard

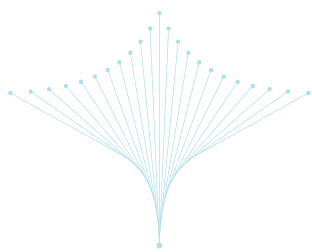


NIPAM PATEL

When Nipam Patel was eight years old, he found a tiger swallowtail butterfly in his yard. The insect had died, but its yellow and black wings were perfectly preserved. Patel set about learning how to mount the insect. Patel's butterfly collection now contains thousands of specimens, including that swallowtail. But these days Patel, a developmental biologist and director of the Marine Biological Laboratory, is more interested in studying these insects than collecting them. Specifically, he wants to know how butterflies create the vibrant, shimmery hues that make their wings so mesmerizing.

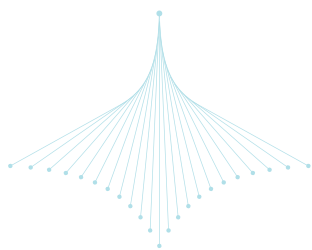
Most materials appear a certain color because they contain pigments or dyes, molecules that absorb certain wavelengths of light and reflect others. Some butterflies get their color from pigments. But the brilliant blues and greens on their wings are often the result of an entirely different process. Their wings have minuscule structures that refract light waves rather than absorbing them. When the light waves hit these structures, some colors are canceled out and others are amplified. The phenomenon is called structural coloration. It's the reason soap bubbles floating in the sun seem to shimmer with many colors. Structural coloration isn't unique to butterflies, but "they happen to do it especially well, and they make really, really brilliantly bright colors."

Physicists have long understood the math behind structural coloration. They have worked out how different geometries and materials give rise to different colors. But for the past decade Patel has been trying to understand how butterflies create these structures with such remarkable precision. "If they're 10 nanometers the wrong thickness, they're the wrong color," Patel says. "How does a living cell make something like that?"



The surface of a butterfly's wing is covered in hundreds of thousands of tiny ridged scales that overlap like shingles on a roof. Within each lie nano-sized, light-scattering structures — everything from simple reflective surfaces to complex honeycomb formations. The brilliant metallic hue of blue Morpho butterflies, for example, is the result of structures that contain overlapping ridges. **“If you cut through the scale, it looks like this giant Christmas tree,”** Patel says. When white light hits this structure, the blue light waves collide and combine, amplifying the color.

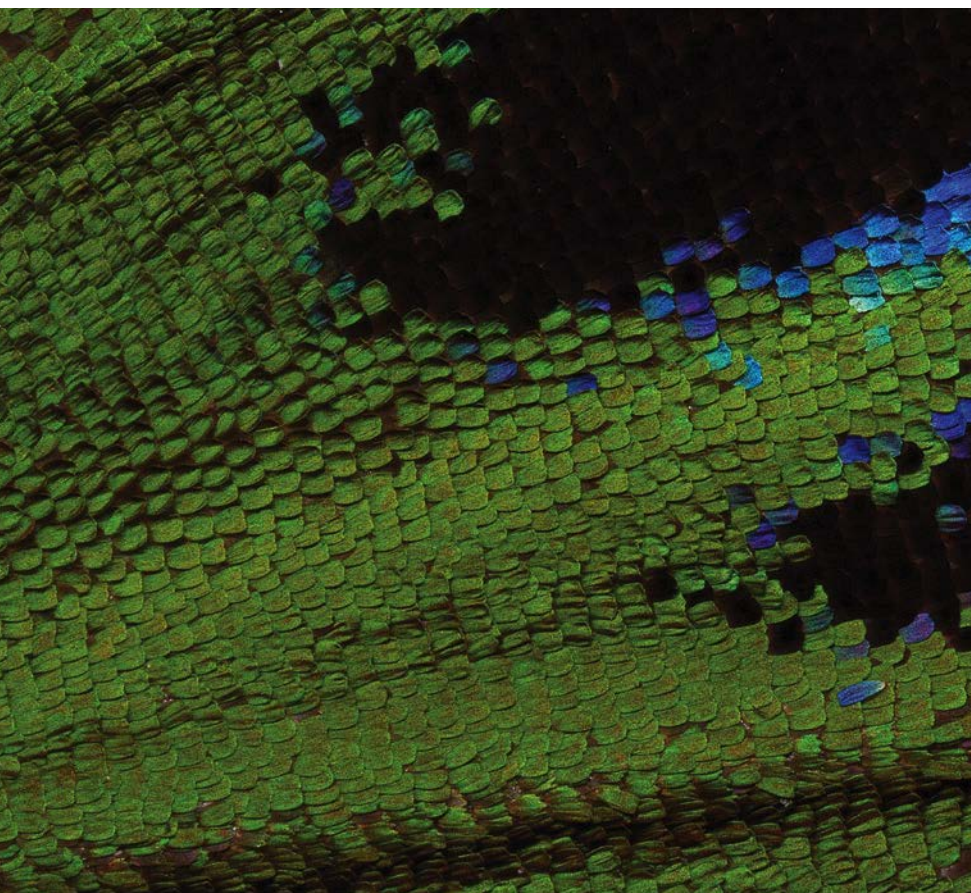
How butterflies create these structures is still mostly a mystery, but Patel and his team are beginning to uncover some of their secrets. A few years ago, the researchers connected with Edith Smith, a butterfly breeder in Florida who raises common buckeye butterflies, which have drab brown wings. These butterflies have close relatives that are brilliantly colored, but “for whatever sad reason, the North American one isn't a pretty butterfly,” Patel says. Smith noticed, however, that some of the butterflies had a few blue scales on their wings. After a year of selectively breeding these blue-tinged butterflies, “she made them shockingly blue,” he says.



▲ A *Juniper hairstreak* on a red rose



▲ A closeup of brown and blue *Buckeye* scales



▲ A closeup of *Eterusia repleta* scales

“THE **TECHNOLOGIES** THAT HAVE BEEN DEVELOPED OVER THE LAST FEW DECADES HAVE MADE MANY, MANY ORGANISMS MUCH MORE **ACCESSIBLE**”

Back in the lab, Patel and his team worked to understand how this change occurred. When they sectioned buckeye scales and put them under a helium ion microscope, with sub-nanometer resolution, they discovered that the blue scales had undergone a structural change. The bottom reflective layer of the scale was about 75% thicker. That small shift was enough to turn brown scales blue.

Next, Patel’s team began breeding generations of these butterflies to find the genes responsible for this trait. Their hunt led them to a previously identified gene called *optix*, which controls coloration in another species of butterfly. When they knocked out the *optix* gene in buckeye butterflies, their wings turned from brown to blue.

Visualizing the development of these tiny structures is a challenge because butterflies grow inside a chrysalis. But Patel and his team have found a way to create a clear window into the chrysalis to watch the wings develop, and they can now see the wings shift from gold to green to blue as that reflective portion of the scale thickens.

Not all color-producing structures are so simple. In emerald swallowtails, the top of each scale is covered in tiny dimples that appear yellow in the middle and blue around the edges. Because the structures are so tiny, our eyes perceive the butterfly as green, which provides camouflage in the rainforest where they live. However, the blue light reflecting off these dimples becomes polarized. Predators can’t see polarized light, but butterflies can. That allows the butterflies to find each other while remaining hidden to predators.



▲ *American painted lady*

Butterflies aren't a typical model organism. But that has never deterred Patel. He has spent most of his career working with animals that aren't commonly found in labs. Before he started investigating structural coloration in butterflies, he spent years developing tools to study how body segments develop in tiny crustaceans known as sand fleas.

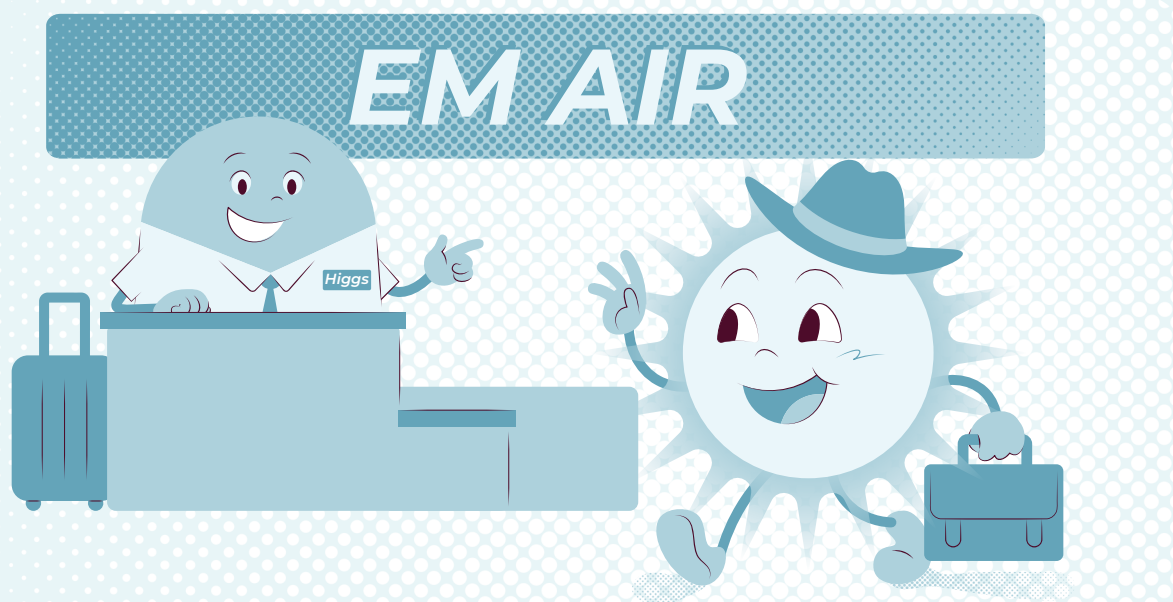
"The technologies that have been developed over the last few decades have made many, many organisms much more accessible," Patel says. CRISPR/Cas9 has revolutionized gene editing, and advances in microscopy have made even the tiniest things visible. **"We can do all these things that ten or twenty years ago were unimaginable,"** he says.

Patel's work has myriad real-world applications. But that's not what drives him. "There's intrinsic value in just knowing how the world works," he says. Understanding butterfly coloration could take some time, but he's in no hurry. "It's the usual kind of problem," he says. "The more answers we get, the more questions we have."

FEARLESS FRIENDS PROFILES LEADING SCIENTISTS IN THEIR FIELDS WHO HAVE BUILT STRONG TIES WITH MORGRIDGE INVESTIGATORS ACROSS COLLABORATIONS IN RESEARCH, TEACHING, AND PROFESSIONAL DEVELOPMENT.

Unscramble these four words themed around Morgridge imaging science.

HOW THE PHOTON ANSWERED AT THE AIRPORT:



“Checking any bags today?”

Now use the circled letters to form the answer to the cartoon’s prompt.

GLEWTHAVEN

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SREFASLE

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INLEOTUORS

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NEEGREIN

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A: NO, I’M

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(Answer on page 2)



Search for these science terms and discover your inner investigator!

S	M	C	A	O	I	O	C	N	T	U	L	R	H
T	N	I	Y	T	I	S	O	I	R	U	C	C	Y
N	O	I	T	A	V	O	N	N	I	L	R	S	E
O	E	C	D	A	T	A	C	T	Y	A	L	O	C
D	E	F	A	C	C	B	P	O	E	C	S	D	M
M	E	E	C	O	D	I	D	S	Y	I	C	I	S
Y	G	O	L	O	I	B	E	A	O	T	I	S	I
L	S	D	E	O	E	R	C	R	N	P	E	C	L
S	Y	P	C	P	O	O	O	O	T	O	N	O	O
S	S	E	O	L	E	C	D	O	V	C	C	V	B
U	O	C	Y	N	D	O	E	E	L	S	E	E	A
N	S	C	O	M	P	L	E	X	I	T	Y	R	T
C	O	M	S	I	M	A	G	I	N	G	C	Y	E
E	C	N	E	C	S	E	R	O	U	L	F	A	M

BIOLOGY
COMPLEXITY
CURIOSITY
DATA
DECODE
DISCOVERY
FLUORESCENCE
IMAGING
INNOVATION
METABOLISM
OPTICAL
RESEARCH
SCIENCE
SCOPE

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WHAT HAS BEEN DONE;
ONE CAN ONLY SEE WHAT
REMAINS TO BE DONE.”**

— MARIE CURIE

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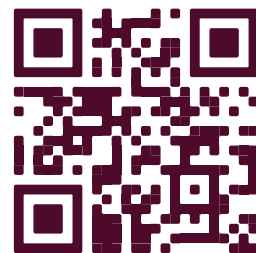
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