

grow

Wisconsin's Magazine for the Life Sciences SPRING 2021

food systems • health • bioenergy • environment • climate • communities

COLD, BOLD

CLARITY

Cryo-EM reveals
the intricate
architecture of
cells, viruses,
and proteins

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College of
Agricultural & Life Sciences
UNIVERSITY OF WISCONSIN-MADISON

A double rainbow glows over the Kemp Natural Resources Station boathouse and classroom on Tomahawk Lake in Woodruff, Wis., on April 2, 2019.

PHOTO BY SCOTT BOWE





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Wisconsin's Magazine for the Life Sciences

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ON THE COVER: A 3.2 Å resolution single particle cryo-EM reconstruction of the HexaPro variant of the SARS-CoV-2 spike. Data were collected on a Thermo Scientific Titan Krios G3i cryo-transmission electron microscope using a Gatan K3 direct electron detection camera. Learn more on page 18.

IMAGE BY MATTHEW LARSON. DATA COLLECTION AND PROCESSING BY ELIZABETH WRIGHT, ERIC MONTEMAYOR, AND BRYAN SIBERT. HEXAPRO SARS-CoV-2 SPIKE COURTESY OF JASON McLELLAN.

Dean Kate VandenBosch

A Synchrony of Investments



Last spring, I happily announced that our faculty ranks welcomed a tremendous influx of new talent, with 19 new hires in 2019. Now I'm pleased to report that the trend continued in 2020.

During the last calendar year, we had another 19 new faculty begin their appointments in eight different academic departments. These talented folks bring expertise in areas ranging from animal welfare and fruit pathology to quantitative genomics and science communication. Collectively, they will increase our research capacity, foster new collaborations on and off campus, and position CALS to serve more students while offering a wider variety of course subject matter.

There's always variation in hiring from year to year, but the last two years were especially good. And the timing was fortunate. It was vital that we fill these positions, especially as we anticipate leaner years to come while budgets recover from the effects of the pandemic. But whether times are lean or prosperous, it's also critical that we align our investments — in people, in equipment, and in facilities — as best we can. That's precisely what we did with many of our recent hires, who have come to CALS to run some of our new, cutting-edge facilities.

In fall 2020, the new Meat Science and Animal Biologics Discovery (MASBD) building opened with a virtual celebration. And the new UW–Madison Cryo-EM Research Center will be up and running in spring 2021, followed by the Midwest Center for Cryo Electron Tomography in early 2022. These highly advanced facilities represent significant investments in time and capital. The MSABD building stands on the foundation of more than 90 years of

meat-related research at UW, and it was made possible through a commitment of \$57.1 million from the State of Wisconsin, the UW campus, and scores of individual and corporate donors. Likewise, our cryo-EM hub owes its existence to decades of prior campus work in structural biology; the accumulation of significant extramural funding, including a \$22.7 million grant from the National Institutes of Health; and \$15 million in contributions from campus partners.

These facilities began with grand visions, and they moved forward through substantial commitments of time and planning from on-campus experts and off-campus stakeholders. Finally, through major investments of funds, they became real. Now, it's an absolute pleasure to see our newest

faculty and staff arriving on campus and working their magic. It's the perfect combination of assets: highly trained experts — among the best in their respective fields — leading and utilizing our state-of-the-art buildings and hardware, on their way to accomplishing incredible things.

And it doesn't stop there — one investment begets another. Our cryo-EM centers will draw researchers from other institutions, scientists who want to learn and apply cryo-EM technologies, use our unique facilities, and collaborate with our experts. And the advanced BSL2 (biosecurity level 2) lab in the MSABD building will offer a place for food industry researchers to investigate and address some of the biggest challenges they face.

I hope you're as excited about these new facilities and faculty as I am. You can learn more about our cryo-EM centers, and the amazing people involved, in our cover story, "A Cold, Hard Look at Macromolecules," on p. 18. For more about the MSABD building and its experts, see "Meat' Our New Building" on p. 11, and look for a *Grow* feature in summer 2021.

"It's critical that we align our investments in people, in equipment, and in facilities."

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Volume 14, Issue 2 · SPRING 2021

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Seven Things Everyone Should Know about . . . **Tardigrades**

By Thea Whitman

1. Tardigrades are tiny, water-loving animals. They prefer wet environments, and as long as the conditions are right, they can be found all over the world in soils, oceans, and lakes. With body lengths usually less than 1 mm, they are difficult to see unless viewed under a microscope, where their charming appearance becomes quite apparent.

2. Their forms and behaviors have earned tardigrades many different names.

Biologist **Lazzaro Spallanzani** named the animal “il tardigrado,” or “slow stepper,” which refers to its ponderous way of moving. When zoologist **Johannes Goeze** described one in 1773, he called it a “little water bear,” a nod to its resemblance to a plump, lumbering, ursine mammal (albeit one with four pairs of legs). A third name for tardigrades, because they often reside in the water attached to damp moss, is “moss piglets.”

3. There are more than 1,000 different species of tardigrades, and they have many surprising attributes.

They represent their own phylum and are related to arthropods (insects, spiders, and crustaceans) and nematodes (very small worms). They have many other notable features, including beautiful, ornate eggs, and they come in unexpected colors, such as red, green, and yellow. In the soil, they eat all sorts of other organisms that are smaller than themselves, such as fungi, algae, and microscopic animals called rotifers.

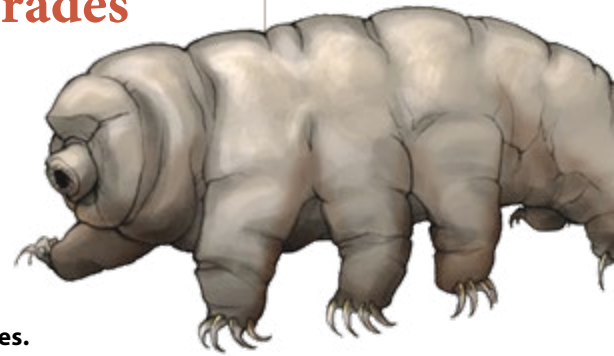
4. Tardigrades have been around a long time. Fossils date their existence on Earth to more than 500 million years ago. This means tardigrades have survived the planet’s last five mass extinction events. They owe their longevity to some special characteristics.

5. They are perhaps best known for their ability to enter into a state called “cryptobiosis,” or “the act of hidden life.” To achieve

cryptobiosis, tardigrades slowly lose almost all of their water and shrivel down to small, dehydrated forms. This seemingly lifeless little ball is called a “tun.” Given the right conditions, tardigrades can rehydrate and resume active living.

6. Tardigrades are extremely resilient. In their tun state, they can survive extreme conditions, ranging from -130°C (-200°F) to temperatures above the boiling point of water! Tardigrades have also survived exposure to outer space, extreme pressure, near-total desiccation, and high levels of radiation. They can emerge from cryptobiosis after enduring immensely challenging conditions, even after years of remaining in that state.

7. Their extraordinary abilities offer us ways to better understand how life thrives in extreme conditions. Often, in such situations, DNA can easily be damaged. Scientists are exploring how tardigrades prevent and repair damage to their DNA. For example, in one species, researchers recently discovered a specific protein that helps protect DNA, and they are investigating whether this ability could be applicable to other organisms.



Thea Whitman is an assistant professor in the Department of Soil Science, where her areas of expertise include soil ecology and microbiology, terrestrial carbon biogeochemistry, and climate change. She is always on the lookout for tardigrades plodding around under the microscope.

A Moveable Feast for Predators

Wild carnivores living near people are relying more on human food, and ecosystems may suffer as a result



PHOTO BY JEFF MILLER

A young adult fox is pictured before being released from a cable restraint on campus near UW–Madison’s Lakeshore Nature Preserve in January 2015. A new study of carnivores nationwide shows that many living near human development are eating human food sources — with potentially harmful ecological consequences.

This work was supported in part by the National Science Foundation (grant DGE-1144752), the National Institute of Food and Agriculture (Hatch Projects 1006604 and 1003605), and the National Park Service.

Ecologists at CALS have found that carnivores living near people can get more than half of their diets from human food sources, a major lifestyle disruption that could endanger North America’s carnivore-dominated ecosystems.

The researchers studied the diets of seven different predator species — gray wolves, coyotes, bobcats, fishers, American martens, and red foxes and gray foxes — across the Great Lakes region of the U.S. They gathered bone and fur samples for chemical analysis from areas as remote as national parks to major metropolitan regions such as Albany, New York. They found that the closer carnivores lived to cities and farms, the more human food they ate — and the greater risks they faced.

Professor of forest and wildlife ecology **Jon Pauli** and his former graduate student, **Phil Manlick** MS’15 PhD’19, published their findings recently in the *Proceedings of the National Academy of Sciences*. The study is the most comprehensive look yet at how most of the region’s major carnivores have changed their diets in response to people.

How much human food they ate varied consider-

ably by location and species, the study found. On average, in the most human-altered habitats, more than 25% of the carnivores’ diets came from human sources. And committed carnivores like bobcats ate a relatively small amount of human food.

“But what you see is that the sort of generalist species that you might expect — coyotes, foxes, fishers, martens — in human-dominated landscapes, they’re getting upwards of 50% of their diet from human foods,” says Manlick, the lead author of the study who is now a postdoctoral researcher at the University of New Mexico. “That’s a relatively shocking number.”

Pauli and Manlick found that relying on human food sources increased how much carnivores overlapped one another in their competition for food. Compared to when these predators vie for distinct prey, this increased competition could lead to more conflicts between animals. Their reliance on human food could also make the carnivores vulnerable to human attacks near towns or even change how and when they hunt traditional prey, with potentially harmful ecological consequences.

The researchers gathered bone and fur samples from nearly 700 carnivores in Minnesota, Wisconsin, New York, and Michigan's Upper Peninsula with the help of state and federal researchers and citizen-science trappers. They compared the carnivores' diets to the extent of human development in the region, which varied from essentially pristine wilderness to urban sprawl.

Thanks to quirks in how plants incorporate carbon as they grow, a sample of bone or fur is enough to get a snapshot of an animal's diet. Varying weights, or isotopes, of carbon are common in different plants — and in the animals who ultimately eat them.

“When you change the landscape so dramatically in terms of one of the most important attributes of a species — their food — that has unknown consequences for the overall community structure.”

—JON PAULI

“Isotopes are relatively intuitive: You are what you eat,” says Manlick. “If you look at humans, we look like corn.”

Human foods, heavy in corn and sugar, lend them distinctive carbon signatures. In contrast, the diets of prey species in the wild confer their own carbon signatures. The ratio of these two isotope fingerprints in a predator's bone can tell scientists what proportion of their diet came from human sources, either directly or by consuming prey that ate human food first.

The geographic extent of the study and the large number of species the ecologists examined demonstrate that the trend of human food subsidies in carnivore diets is not limited to a single location or species. The ultimate outcome of such widespread disruptions remains unclear.

“When you change the landscape so dramatically in terms of one of the most important attributes of a species — their food — that has unknown consequences for the overall community structure,” says Pauli. “The onus is now on us, as ecologists and conservation biologists, to begin to understand these novel ecosystems and begin to predict who are the winners and who are the losers.”

—ERIC HAMILTON

Awards and Honors

IN THE UPPER ECHELON OF AG ENGINEERING

The Department of Biological Systems Engineering (BSE) earned high marks in the most recent college rankings from *U.S. News & World Report*. UW–Madison's biological/agricultural engineering specialty (which includes BSE) was rated 13th overall and 12th among public institutions. The rankings included 389 national doctoral universities.

MODELS FOR MICROSCOPIC ROBOTS

In October, assistant professor of biochemistry **Scott Coyle** was named a 2020 Packard Foundation Fellow in Science and Engineering. The fellowship provides \$875,000 over five years. Coyle will use the funds to develop models for how tiny components encode and program the structure and behavior of single cells, which he likens to microscopic robots.



Number Crunching

There's a lot more to soil than just dirt. It's estimated that 20,000 pounds of organic matter can be found in the top six inches of an acre of soil, says **Zac Freedman**, an assistant professor of soil science who studies microbial communities. And it's a crowded living space: One tablespoon of soil harbors more organisms than there are people on Earth. These microbes help keep our ecosystems healthy.

GRAPHIC BY JANELLE JORDAN NAAB. IMAGES BY ISTOCK.COM/SORBETTO, CHRISTIAN DAHLHAUS, TTSZ

Correction

In “Seven Things Everyone Should Know about the Economic Impacts of COVID-19” (Fall 2020), we included an incorrect dollar figure for the Coronavirus Aid, Relief, and Economic Security Act. It should have been listed as \$2.2 trillion.

Kit Chow

Entrepreneurial Spirit ‘Boosts’ Undergrad’s Career Prospects

When **Kit Chow** BSx’21 decided to study biological systems engineering at CALS, he knew he would get to do one of his favorite things — devising creative solutions for real-world problems. But he had no idea that his passion for problem-solving, even outside of his degree program, would lead to a full-time job.

ago,” Chow says. “A lot of my friends were involved with Transcend UW, so I decided to join in the fall. I hadn’t really thought about entrepreneurship as my path before.”

Like many college students, Chow and Parihar had developed an affection for caffeinated beverages, which led to their problem-solving moment. “We’re engineers,” they speculated, “so what if we just made our own drinks?”

As is often the case in entrepreneurship, the duo’s first idea turned out to be a false start. While their “boosted juice” was tasty, its high sugar and caloric content didn’t match consumer trends and preferences for healthy products. After meeting with staff from the Center for Dairy Research to get advice, they pivoted to chocolate as their base. They quickly gained traction after that, testing out various iterations with fellow students in dorms and lecture halls.

“You can develop a chew with a lot of different formulations, and the texture can be pretty finicky,” Chow says. “There were a ton of early forms of Boosted Chews that are nothing like what we have right now.”

The original chew was something akin to a Tootsie Roll. Another iteration sandwiched caramel between two layers of chocolate, but it turned out to be too complicated for their manufacturing process.

The team also sought guidance from UW’s Discovery to Product, a program that assists campus innovators as they take their ideas and inventions to market. Mentor **Cecily Brose** helped them expand their marketing and sales strategy and connected them with key players in the Madison startup ecosystem.

“I have been so inspired by Kit’s and Adi’s innovative thinking and determination to see Boosted Chews succeed in the marketplace,” Brose says. “It has been amazing to see what they have accomplished in such a short time — and in the midst of the COVID pandemic.”

“Boosted Chews doesn’t feel so much like work, necessarily,” Chow says. “It is work a lot of the time, but it’s also just kind of fun. I love the constant opportunity to be learning new things. I’ve always been interested in hopping onto something that I don’t know how to do and then figuring out how to do it. And with entrepreneurship, you get to wear many hats.”

—JEN KOBYLECKY



Kit Chow, a biological systems engineering major and co-founder of Boosted Chews, poses near Library Mall and State Street where several establishments carry the product.

(Inset) Chow holds an assortment of the product.

PHOTOS BY MICHAEL P. KING

Along with chemical engineering major **Aditya Singh Parihar**, Chow is the co-founder of Boosted Chews, a startup company that makes bite-sized caffeinated chocolates in four flavors: regular, mocha, hazelnut, and mint. The company has sold more than 1,000 bags since launching in early 2020, despite operating almost entirely during a global pandemic.

Chow and Parihar met through Transcend UW, a student organization that runs a university-wide startup competition focused on encouraging student innovation.

“We both lived in Chadbourne [Residence Hall] our freshman year, across the hall from each other, but we didn’t really actually talk until about a year

A Cheese Treatment for Hypertension?

CALS scientists look to develop cheeses that can lower high blood pressure

High blood pressure contributes to almost half a million deaths in the United States each year. To help manage the condition, called hypertension, health care professionals recommend exercise and a healthy diet. For many patients, changing these habits is a difficult task. But how easy would it be if cheese — yes, cheese — could help reduce hypertension?

It sounds far-fetched, but researchers at the Center for Dairy Research (CDR) have good reason to think it's possible to make cheese with measurable, positive impacts on hypertension. "Functional foods," such as probiotic-rich yogurt and kefir, provide specific health benefits. And while interest in these specialty products continues to grow, most people wouldn't look to cheese as a potentially anti-hypertensive food. But special compounds generated during the cheesemaking process might lend the product this quality.

As cheese is crafted and aged, rennet and other enzymes break down proteins into smaller fractions called peptides. In some cases, dairy-derived peptides serve regulatory functions in the human body that help reduce hypertension, boost immunity, and promote anti-inflammatory and antioxidant activity.

Because they initiate a physiological response, these peptides are called "bioactive peptides," and they're the focus of study for **Rodrigo Ibáñez**. An associate scientist at CDR, Ibáñez will be using traditional and non-traditional cheesemaking techniques to try to produce cheeses with higher amounts of bioactive peptides.

"We have two research questions," Ibáñez says. "Can we make cheeses that have increased levels of bioactive peptides that confer antihypertensive properties, and, if so, what happens after we consume the cheese?"

It's not yet known whether bioactive peptides survive the digestion process so they can be absorbed by the body and confer their health benefits. To find the answer, Ibáñez will collaborate with **Brad Bolling** BS'02 PhD'07, a professor in the Department of Food Science. Bolling and his team will put the new cheeses into a simulated gastrointestinal digestion model to see what happens.

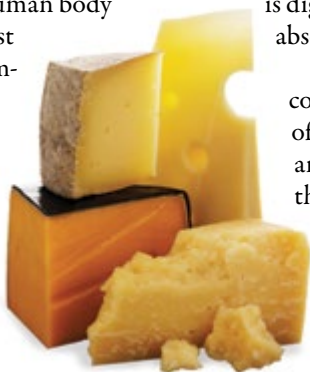


PHOTO COURTESY OF WISCONSIN MILK MARKETING BOARD



"With any food, we need to consider the metabolism and bioavailability of functional ingredients, which means taking a closer look at how the food is digested and how these compounds are absorbed," Bolling says.

Cheese is a traditional food that has been consumed for thousands of years, but studies of its potential antihypertensive properties are very new, with the CDR contributing to this body of work. In 2016, CDR scientists, including director **John Lucey**, published a paper describing how commercially produced cheddar cheese contains significant levels of bioactive peptides. But more questions remain.

"We don't know how much cheese you would need to consume to get an antihypertensive effect," Ibáñez says. "But maybe it would be possible one day to make a single-serving portion of cheese you could eat to help control hypertension."

For Lucey, it's this potential to help create healthier new products — or put new twists on current dairy products — that makes the research worth pursuing.

"Most people think of cheese as tasty but don't really think of the nutritional side of cheese, even though it contains lots of important nutrients like proteins, vitamins, and minerals," Lucey says. "This work has the potential to help enhance cheese's image as a healthy food."

—SHELBY ANDERSON

Associate scientist
Rodrigo Ibáñez works in his lab at the Center for Dairy Research. Ibáñez is looking for ways to make cheeses with higher amounts of bioactive peptides, which could help reduce high blood pressure.

PHOTO BY TIM HOGENSEN

The Dairy Innovation Hub, a state-funded, cooperative research effort between UW–Madison, UW–Platteville, and UW–River Falls, is supporting this project with a grant.

How a Renaissance Molecule Is Made

Furan fatty acids have many talents — they safeguard cells, they house the building blocks of biofuels, and more — and now scientists know the details of their production

Fatty acids, the compounds that provide antioxidant and anti-inflammatory benefits through diets rich in leafy greens and fish, are now also heralded for their versatility as raw materials in bioenergy production.

Scientists at the Great Lakes Bioenergy Research Center (GLBRC) are enamored with one particular kind of long-chain fatty acid, called furan fatty acid, because it could substitute for petroleum-based products, including fuel, engine lubricant, medicines, and food additives. Now, a team of GLBRC collaborators at UW–Madison, including two with CALS connections, have identified a pathway for furan fatty acid production in bacteria and other cells.

Similar to other fatty acids, furan fatty acids, or FuFAs, are found in the membrane that forms a cell's border. These fatty acids act like an oily filter to protect the interior of the cell against changes in the external environment. They can also serve as chemical messengers that alert the cell to a toxin or stressor.

FuFAs are a special class of fatty acids with broad appeal to biofuel scientists because an oxygen atom is attached in the middle of the hydrocarbon chain.

“The chemistry of FuFAs helps the bacterial cell fight off damage in the membrane; the oxygen atom in FuFAs is also what makes it interesting to the biofuel and other industries,” says **Rachelle Lemke** BS’00, MS’10, a GLBRC senior research specialist. She led a study of FuFA production published recently in the *Journal of Biological Chemistry*. “Think of oxygen as the lighter that helps ignite all the other molecules in a fuel to burn. The [hydrocarbon] chain length of FuFAs also makes it a potential lubricant for engines and other devices.”

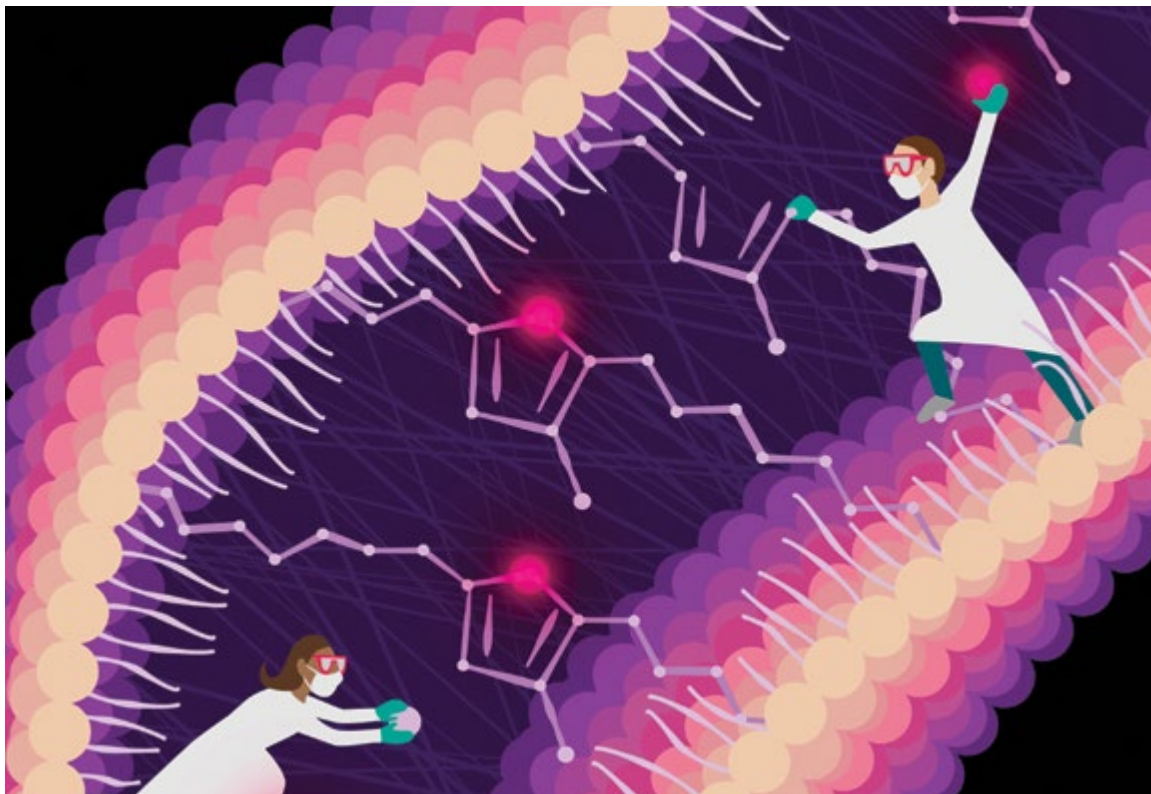
Lemke previously identified FuFAs while exploring why a bacterium, *Rhodobacter sphaeroides*, dies when exposed to a hyperreactive oxygen molecule called singlet oxygen. As a graduate student studying with bacteriology professor and GLBRC director **Tim Donohue**, Lemke originally found that singlet oxygen kills *R. sphaeroides* unless FuFAs are present. Still, they lacked information on how this important class of fatty acids is made.

In their new study, Lemke and a team of GLBRC researchers identified the steps this and other bacteria use to produce FuFAs. The team's findings reveal

Great Lakes Bioenergy Research Center scientists with connections to CALS identified the step-by-step creation of furan fatty acids in the cellular membrane of the bacterium *Rhodobacter sphaeroides*, which could have implications for biofuel production.

GRAPHIC BY CHELSEA MAMOTT

This work was supported in part by a grant from the Department of Energy (DE-SC0018409).



previously unidentified intermediate molecules that ultimately get converted into FuFA. They also found enzymes that add oxygen to the FuFA chain while decorating the ring with methyl groups that serve as the chemical makeup for the genesis of fuels.

Lemke and the Donohue lab partnered with GLBRC chemists at UW–Madison to collect the biochemical signatures of the intermediate molecules using high-resolution mass spectrometry and nuclear magnetic resonance imaging. Those biochemical signatures, like fingerprints, can be compared to fragments of known molecules to provide the ultimate proof of identity.

“If they look the same, we know it’s a match,” says Lemke.

The team also used genome sequences and genetics to identify enzymes that perform chemical reactions that have never been observed until now. With these genetic GPS signals, the team was able to identify proteins that catalyze the same reactions in one other bacterium and predict the presence of this newly described pathway for FuFA production in both microbes and plants.

The next steps for GLBRC scientists are to understand the molecular basis of these newly discovered enzymes and to train cells to make more FuFAs so researchers can test the fatty acids in a variety of applications.

“With more tests, it’s possible we will understand how the new classes of enzymes work and design cells to crank up FuFA production in bacteria and other cells,” Lemke says.

What began more than a decade ago with a simple question — Why do some bacteria die when there’s oxygen around? — has added another layer to the production line of fuels and bio-products from plants, now patented and available for licensing through the Wisconsin Alumni Research Foundation.

“This discovery is another great example about how interdisciplinary GLBRC teams can mine genomes to reveal previously unknown biochemical pathways,” says Donohue. “In addition, we have received interest in evaluating furan fatty acids as lubricants, as compounds with antimicrobial activity, and as food additives from groups around the globe.”

— MARK E. GRIFFIN



PHOTO BY MICHAEL P. KING

‘Meat’ Our New Building

On Nov. 6, CALS celebrated the opening of the new Meat Science and Animal Biologics Discovery (MSABD) building.

Part of the Department of Animal and Dairy Sciences, the state-of-the-art facility is home to the MSABD program, which develops meat industry leaders, discovers new uses for animal components that enhance animal and human health, provides expertise and education about foods derived from animals, and improves the safety and nutritional quality of animal-based proteins.

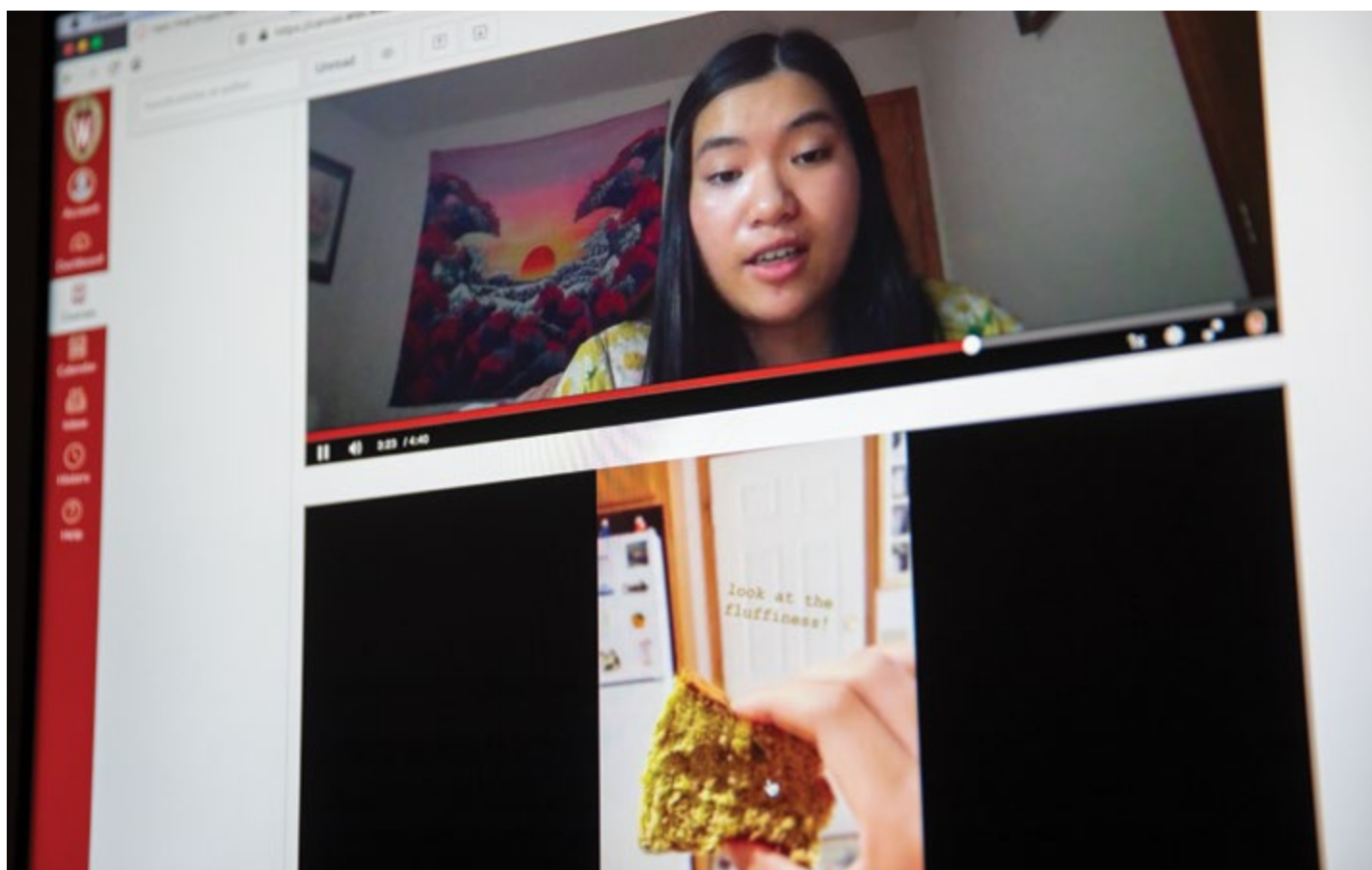
The event was conducted remotely to comply with pandemic restrictions. A series of recorded videos at msabd.cals.wisc.edu feature comments from Dean **Kate VandenBosch**, Gov. **Tony Evers**, Chancellor **Rebecca Blank**, Wisconsin Department of Agriculture, Trade and Consumer Protection Secretary-designee **Randy Romanski**, state Sen. **Howard Marklein**, and MSABD Program Director **Steven Ricke** PhD’89.

The MSABD website also showcases photos of the facility, profiles of program faculty and staff, messages from alumni and other friends of the program, and a special playlist of songs called “Meaty Beats.”

Look for a feature story about the MSABD building in the summer 2021 issue of *Grow*.

A Taste of Many Cultures

Nutritional sciences course counters the negative consequences of American food hegemony by showcasing how diverse palates and perspectives meet the definition of healthy



Kelly Luu, a junior nutritional sciences and Asian languages and cultures major, gives a presentation about matcha, a fine powder made from special green tea leaves, as part of a class project for Nutri Sci 377: Cultural Aspects of Food and Nutrition, an online course, in summer 2020. For the assignment, Luu made a honey matcha castella cake.

IMAGE PREPARED BY MICHAEL P. KING

How does the American ideal of healthy eating exclude other cultures? That was the question posed to students by instructor **Erika Anna** BS'13 in a creative writing exercise called "six-word stories."

"Eurocentric diets promoted over others' cultures," one student wrote.

"Only American foods represented as healthy," wrote another.

A third put it more bluntly: "Others feel their food is bad."

It gets to the heart of what students explore in Nutri Sci 377: Cultural Aspects of Food and Nutrition. It began as an online summer term course in 2019 and was a fall semester offering for the first time in 2020.

"We have a workforce of food and nutrition professionals that is mostly white and identifying as female," says Anna, a registered dietitian

and assistant faculty associate in the Department of Nutritional Sciences. "As a result, curriculum for students, nutrition education for patients and communities, and health care practice are largely developed through a singular lens, and lacking broad cultural relevance. I knew going into course development that my role would largely be as a conduit for diverse voices, research, media, and resources."

A host of collaborators from across the nation lend their expertise to the course throughout the semester, thanks to a grant from the UW Division of Continuing Studies. This gives students an opportunity to see many different dietitians and food and nutrition professionals as the leaders and innovators they are within the field, Anna says.

At the start of the semester, students examine how implicit bias, microaggressions, and the ideology of racial colorblindness influence human interactions. This portion is led by **Teresa Turner**,

“It’s been really wonderful to see their worldview expand into more of a systems-level thinking.”

—ERIKA ANNA

a nutritionist with Army Child and Youth Services at Fort Meade and a past chair of the Diversity and Inclusion Committee of the Academy of Nutrition and Dietetics.

The course doesn’t stop there. Anna and co-instructor **Amber Haroldson** BS’08 help students explore the food preferences and cultures of Indigenous people, Latin Americans, Black and African Americans, and the religiously observant. **YaQutullah Ibraheem Muhammad**, a clinical dietician with the Veterans Administration and chair of the nutrition academy’s Religion Member Interest Group, talks to students about halal and haram foods, nutritional considerations for fasting during Ramadan, and the Five Pillars of Islam.

The class also dives deeper into federal food assistance programs (SNAP, WIC, and FDIPIR) and how well they work — or don’t work — for those they serve. The programs have added culturally relevant items to lists of approved foods, but the extent of that can vary regionally, and requesting added traditional foods can be a lengthy process.

“WIC, SNAP-Ed, and FDIPIR include nutrition education along with food packages,” notes Anna. “But if the education delivered isn’t culturally relevant or ignores or violates cultural beliefs, practices, or customs, it could lead to a complete rejection of essential health care information.”

The course satisfies UW–Madison’s ethnic studies general education requirement and is the lead course in *We Are What We Eat: Food and Identity*, a CALS-based First-Year Interest Group. It is available to all students regardless of major or college.

Ayda Mohd Ayob is a senior dietetics major from Perak, Malaysia, and is also pursuing a certificate in business management through CALS. She hopes to earn the registered dietician credential and become a clinical dietician in the United States. For Ayda, the biggest takeaway from the course was embracing a mindset of “cultural humility.”

“There’s always something we don’t know about other people or cultures,” she explains. “It’s definitely okay to not know all of it. But try to ask, become more open-minded in approaching people and understanding things of importance.”



Senior dietetics major Ayda Mohd Ayob prepares a meal using the tropical cassava plant as part of her final project for Nutri Sci 377: Cultural Aspects of Food and Nutrition.

PHOTO COURTESY OF
AYDA MOHD AYOB

For the course’s final project, students choose a food, dish, or ingredient; research its cultural and nutritional significance; cook with it; and consider how easily ingredients could be procured under a food assistance program.

Ayda selected cassava, a tropical tuberous root that can be baked or fried and is often processed into a flour and tapioca. Although she became familiar with it while growing up in Asia, her research taught her how widespread cassava is globally, including in parts of Africa and its native Latin America. She notes how the cultural history of the Makushi people in Guyana is intimately linked to the crop.

Marie Shoemaker, a senior from Milwaukee majoring in food science, chose the “three sisters” — a combination of corn, beans, and squash grown and sometimes eaten together by numerous Indigenous groups of North America. The trio’s synergy goes beyond their time in the soil, Shoemaker notes. Nutritionally, the individual foods compensate for the others’ essential amino acid deficiencies to form a complete protein profile — perfect for vegetarians or when animal protein is scarce.

“Together they work like a family,” she says. “They’re stronger together.”

Anna relishes the students’ transformation over the course of the semester. “Students who, early on, report that health status is largely determined by an individual later identify that there are many social, political, and environmental influencers determining an individual’s health,” she says. “It’s been really wonderful to see their worldview expand into more of a systems-level thinking.”

—MICHAEL P. KING



ZAMBIA

Six-Legged Livestock Could Solve Food Shortages — Sustainably

The two-spotted cricket is the focus of a UW research project on the viability of insect farming as a sustainable source of protein.

PAUL VENTER, CC BY-SA 3.0 VIA WIKIMEDIA COMMONS



In the Midwest, we're used to seeing big fields dotted with cattle and steel barns bustling with broiler chickens. Beef, poultry, and pork are common in our daily meals, whether mixed in pasta or placed on a bun.

But in many countries, where food shortages are common, such protein abundance is a luxury. To help alleviate this global food security problem, a group of UW–Madison researchers, led by entomology professor **Susan Paskewitz**, is turning to an overlooked solution: insect farming.

"[Insects] are an understudied and underutilized food resource," says **Valerie Stull**, a postdoc with the UW Global Health Institute (GHI) and co-investigator for the project. "But that doesn't mean that people aren't already eating them."

For many cultures, insects are a traditional and revered food source. To date, however, the vast majority are harvested from the wild, which means their availability varies with the seasons. Proper storage of foraged insects can also be tricky, and food safety concerns can arise. Plus, gathering insects in bulk is labor intensive.

Insect farming may be a way around these issues. An added bonus: Insects need less water, feed, and land than conventional livestock, and they emit fewer greenhouse gases, so they can be a more sustainable and environmentally friendly alternative. This is one of the many reasons insect farms keep popping up in the U.S., Europe, and elsewhere.

But is insect agriculture actually viable? Is there

enough potential demand? Are the financials and logistics feasible for farmers in low-resource areas? Can it be beneficial for both human and environmental health? These are some of the main questions driving the UW research team.

In their search for answers, they've partnered with some like-minded organizations, including GHI, the Mission to Improve Global Health Through Insects (MIGHTi), and an Italian non-profit called NutriPeople. Together, these groups are assessing small-scale cricket farming in the Southern African nation of Zambia.

"Our project is really evaluating the impact of these small farms on the health and wellbeing of people in terms of their perceptions of farmed insects, their livelihoods, their food security, and then — really critically — their access to dietary iron," Stull says.

Low-iron diets can cause anemia, a lack of healthy red blood cells. Many Zambians are especially vulnerable to this condition because of their corn-based diet, which can be deficient in numerous nutrients. Stull and the team are collaborating with researchers from Colorado State University to assess the bioavailability of iron in crickets relative to iron in other plant and animal food sources. In other words, they're trying to determine through lab tests how much iron crickets can absorb from their feed and then pass on to the people who in turn eat them.

The researchers have also been surveying two new cricket farms in Zambia over the past year. Their



Cricket-rearing containers inside a farm in Monze, Zambia.

PHOTO BY COLLEEN HENEGAN

corn, such as lignin, that humans and crickets can't. Lignin is a complex, organic molecule that gives plants their sturdy nature, and a lot of it is found in corn stover, the material left in a cornfield after harvest.

In Zambia, stover is traditionally fed to livestock, removed from fields, or burned. While burning frees up space, the process releases harmful particulates and greenhouse gases into the air. But what if stover could instead be used to grow mushrooms that serve as cricket feed?

Ventura's looking for a way. He keeps a large barrel in his backyard for pasteurizing stover. It "cooks" the stover at 80 °C (176 °F) for about two hours to kill competing organisms and make it easier for mushrooms to digest. Next, the stover is dried and mixed with mushroom spawn in small plastic bags. About a week later, the first vegetative growth, or mycelium, emerges.

"The mushrooms that we're using — oyster mushrooms — will go into that maize stover and secrete enzymes to bust apart lignin, which increases available polysaccharides and actually allows the fungus to concentrate amino acids," Ventura says. "We're hoping we can turn straw into gold."

Ventura's DIY pasteurizer, constructed with help from Russell Labs Hub instrument maker **Tim Lorenz**, was one way to continue the project while the pandemic limited lab access. This continuity is vital because Ventura and the team need to collect and analyze quite a bit of data before they can determine if the mushroom method is viable for farmers in Zambia. And the crickets did get their first taste of fungi in December, a major step in the process.

"We're growing mushrooms to feed insects to feed people, all with the idea of improving human health and environmental sustainability," Stull says. "And we're really excited about it."

—JORI SKALITZKY BSx'22

Oyster mushrooms grow on a corn stover substrate inside of a large incubator.

This DIY pasteurizer allowed graduate student Martin Ventura to continue work in his backyard when lab access was limited during the COVID-19 pandemic.

PHOTOS BY MARTIN VENTURA



focus: farm productivity, farmer perceptions, and cricket quality in terms of nutrition. Stull and other members of the team were not able to travel this past summer because of the COVID-19 pandemic. But another collaborator, environmental studies graduate student **Colleen Henegan**, was in Zambia in January 2020 — before widespread travel bans — to collect data from the farmers and keep the project moving.

"Eventually, [our] goal is to actually support the cricket farmers so they can consume crickets on a regular basis, and we can measure health outcomes directly," says Stull.

The farmers have been successful in raising crickets, but not at quantities high enough to make a widespread impact on the health of Zambians. This is one of the reasons why another part of the team, back in Madison, is studying ways to improve cricket farming and boost production without ramping up cost.

Martin Ventura is an entomology graduate student and a member of Paskewitz's lab. He's known as the "cricket wrangler" — he cares for the crickets housed in UW's Russell Laboratories, along with the help of junior entomology major **Michael B. Smith**. The cricket in question is *Gryllus bimaculatus*, more commonly known as the two-spotted cricket, which is native to Zambia.

Ventura is developing "low-cost, low-tech" cricket feed options — essential for minimizing farmers' start-up and maintenance costs — that are also healthier for the insects. In Zambia, farmers mainly raise crickets on corn and other grain. But there's a more nutritious option, Ventura says, with potential environmental benefits.

In the wild, two-spotted crickets will eat fungi when more preferred food sources are unavailable. Mushrooms can also break down compounds in

Agriculture as Resilience, Resistance, and Liberation

In her latest book, Monica White upends the narrative about African Americans and farming

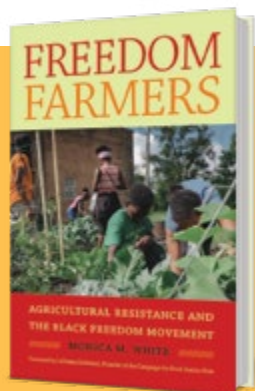
Interview by **Nicole Miller MS'06**

When Monica White joined the UW faculty in 2012, she was already hard at work on the project that would become *Freedom Farmers*, a book that tells a different story about the relationship between African Americans and agriculture. Early on, as a new assistant professor in Department of Community and Environmental Sociology at CALS and the Nelson Institute for Environmental Studies, she traveled regularly to gather more information for the book. It was time well spent.

Freedom Farmers, published in 2018, was an immediate hit, selling out before its official release date. White later received the 2019 Eduardo Bonilla-Silva Outstanding Book Award from the Society for the Study of Social Problems and the 2020 First Book Award from the Association for the Study of Food and Society.

Now an associate professor, White says there was a big resurgence in book talk requests in 2020. “A lot of people are asking questions like, ‘What stories don’t I know?’” she says. “And the story of Black agriculture is one of those stories that people don’t know.”

BOOK COVER IMAGE COURTESY OF THE UNIVERSITY OF NORTH CAROLINA PRESS



WHAT MOTIVATED YOU TO WRITE THIS BOOK?

I was applying for a position in Detroit that would allow me to move back home and take care of my parents. I needed a research question, and I’d heard about the urban agriculture movement in Detroit, and some of my family members grew food there. But the press didn’t include many African Americans in their coverage, so the stories that were being held as examples were missing folks like my family — as well as groups like the Detroit Black Community Food Security Network (DBCFSN).

Some of the people who founded the DBCFSN, their parents had grown food in the South and then moved

to Detroit [during the Great Migration] to work in the automobile industry. And almost everybody had a backyard garden. They kept growing food. That was just what we did. I really wanted to understand why DBCFSN members choose to grow food. And when you create these community-based food systems, how does that change the community itself?

The relationship between African Americans and agriculture has often been told through the lens of tenant farming, sharecropping, and slavery. Working with the African Americans in Detroit, who were reconnecting to their agricultural roots as a way to provide nutrient-rich food to their community, I heard a different reason. For them, agriculture was a strategy of resistance and resilience and a way to build healthy, whole communities.

My book offers a counter-narrative about the relationship between African Americans and agriculture, moving from one of tenant farming, sharecropping, and slavery to one that emphasizes a positive relationship between land, food, and freedom.

HOW DID YOU GET STARTED?

I didn’t want to ask any questions at first. I just went to all the meetings, every event, all the Harvest Festival dinners and related functions. I did a whole immersion for two years. And I fell in love.

I offered to help with an organizational history and organize their papers. I ended up serving as the co-director of the education and outreach committee. They trusted me because of my willingness to do whatever they asked me to do.

WHAT DID YOU LEARN BY PARTICIPATING?

I found that many DBCFSN members have backyard gardens for themselves, but they also contribute to the collective. Many of them said things like, “My kids are grown and gone, but I want to make sure the children in the neighborhood have nutrient-rich food for breakfast instead of pop and chips.” They also prefer a co-op [over a chain grocery store] because it’s a regenerative model. When they buy produce, they want to know the farmer and the farming practices. And using a co-op model, they know that the money regenerates within the community.

It made me question, have there been other times when African Americans have turned to agriculture to provide for their families but also as a mechanism to transform their neighborhoods, their communities?

I recognized that, at every economic downturn, African Americans would turn to agricultural roots. And if that’s what we did in hard times, the only frame to understand it could not have been using a deficit model of slavery, tenant farming, and sharecropping. There had to be another lens. It

couldn't have just been oppressive. It had to also be liberatory.

I decided, before I could write a case study of Detroit's urban agricultural history, I had to set a theoretical framework. That, then, meant it couldn't just be about Detroit; I had to follow where that led.

WHERE DID THAT LEAD YOU?

How do you get to Detroit? You've got to go to the South.

Many Black people left the South because they were tired of being exploited by doing agricultural work with the deck stacked against them. They weren't able to benefit from the fruits of their labor, literally and figuratively, because of deeply entrenched exploitive relationships. That's why they left — not because it was hard work.

But some people stayed. And they started the Southern Cooperative Movement. There's not a lot of scholarship on it, so I was reading, reading, reading [old Black agricultural co-op records]. And I found that these co-ops had economic, political, and social agreements, or strategies.

That's where the book's central concept — my theoretical framework — of collective agency and community resilience comes from. This was the new foundation on which to build my case. The book starts out talking about the Black intellectual traditions of agriculture. Then it really digs into three co-ops that implemented this concept.

WHAT DO YOUR STUDIES SAY ABOUT DBCFSN?

In the midst an economic downturn, you're seeing a community where folks choose to stay and create their own food system, which we know is not easy. So you're seeing collective agency and community resilience.

Something that was an eyesore, such as a vacant lot overgrown with grass and

weeds, has been transformed into a purveyor of social services. At DBCFSN's D-Town Farm, during the Harvest Festival, you can get your diabetes checked, your blood pressure measured, learn how to cook organic veggies from a culturally appropriate perspective. There's music, there's art, there are all kinds of celebrations.

This book helps people understand the historical precedent for today's urban agriculture. It shows how communities respond to catastrophic events by engaging in food production as a way to have a greater voice, to feel partly in control of the decisions that impact our lives. The ability to feed oneself creates all kinds of political, social, and economic options that people wouldn't have if they were beholden to somebody else.

Feeding ourselves is the beginning of a conversation of transformation. Because if we can create some form of alternative food system, then can we also talk about community education? Can we talk about community policing? [It can be a step toward] having a greater voice in what happens to the community.

HOW DO YOU HOPE THIS BOOK IMPACTS PEOPLE?

People think they understand the relationship between Black people and agriculture. Nobody says, "Let's ask the question again." That's the danger of the single story. I think that's a part of the reason that the book appeals to people: It answers questions they thought they knew answers to.

I also hope that *Freedom Farmers* allows us to think differently about farmers. We don't often think about the laborers, all the hands that touch our food from the seed to the grocery store. And so it is my hope that we can appreciate the centuries of Black farmers who have been central to our food ways.

ONLINE EXTRA

Learn about Monica White's next projects, and the little-known connection between southern farm co-ops and Madison, Wisconsin, at grow.cals.wisc.edu.



PHOTO BY JOHN FICENEC



Talos Arctica



A COLD HARD LOOK

AT MACROMOLECULES

Cryo-EM, an advanced microscopy technique that utilizes extremely cold temperatures and electron beams to illuminate the structures of some of the tiniest building blocks of life, has come to UW after years of investment — and it could help CALS scientists reach new frontiers in the biosciences



BY NATASHA KASSULKE
PHOTOS BY MICHAEL P. KING

Eric Montemayor, facility manager for the Cryo-EM Research Center, pours liquid nitrogen while demonstrating the process for loading samples into the Thermo Scientific Talos Arctica cryo-transmission electron microscope (cryo-TEM) at the center's secondary facility in the DeLuca Biochemistry Building.

AT its most basic level, it takes pictures. For biochemistry professor **Elizabeth Wright**, that's the scaled-down explanation of cryogenic electron microscopy, or cryo-EM. But it's so much more than that. Through rapid freezing, controlled beams, and advanced lenses, this game-changing research tool reveals the intricate architecture of cells, viruses, and proteins, all at molecular resolution — or better. Cryo-EM makes the truly complex much easier to understand.

"It's satisfying to think, both creatively and technically, about how to take images that reveal information at a structural level about a particular object," says Wright, who is also an affiliate with UW's Morgridge Institute for Research and a leader of cryo-EM efforts on campus. "One thing that makes life fun in my line of work is being among the first people to see something and to be able to provide scientists and others an understanding and appreciation for what we are seeing."

Cryo-EM is revolutionizing the biosciences by enabling imaging of macromolecules, viruses, and cellular substructures at near-atomic to atomic resolutions. Advances in detectors, computation, and electron microscopy design now produce high-resolution images of rapidly frozen samples that rival current methods, such as X-ray crystallography, because these new techniques require far less material, capture natural states, do not require crystallization, and allow the advantages of high-contrast, time-resolved imaging.

With cryo-EM, scientists can peer into the surfaces where drugs and proteins interact, where diseases occur, and where viruses orchestrate their attacks. It has the potential to impact every corner of medicine, from Alzheimer's research to vaccine development to protein and cellular engineering. And its reach extends to many other research areas, including biofuels, engineering, and computer sciences.

Scientists from CALS and throughout UW have already been using cryo-EM to make advancements in these fields, but they've had to rely on facilities outside of the university. Now they'll have a place right on campus where they can conduct their groundbreaking work. The UW–Madison Cryo-EM Research Center (CEMRC) is set to open in spring 2021, and the Midwest Center for Cryo Electron Tomography (MCCET) will soon follow with an opening in early 2022.

Both centers, to be housed in the Hector F. DeLuca Biochemical Sciences Complex, will be directed by Wright. And they both represent a continuation of the university's long history of contributions to structural and cell biology, virology, and medicine, as well as a major return on long-term campus investment in the technology (see sidebar, "Cryo-EM: A Whetstone for UW's Competitive Edge.") The centers will be pivotal in many ways: for building on the important work



Elizabeth Wright, biochemistry professor and director of the Cryo-EM Research Center, with the Thermo Scientific Titan Krios G3i cryo-TEM in the DeLuca Biochemical Sciences Building.

of talented researchers of the past and present, for honing UW's competitive edge in a rapidly evolving field, and for making vital discoveries that have the potential to transform lives.

CENTRAL TO BIOSCIENCE SUCCESS

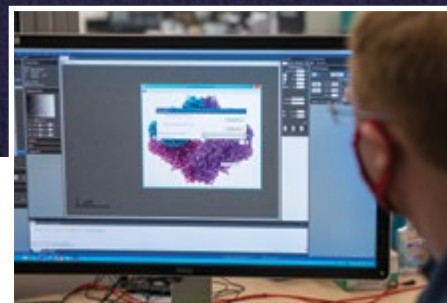
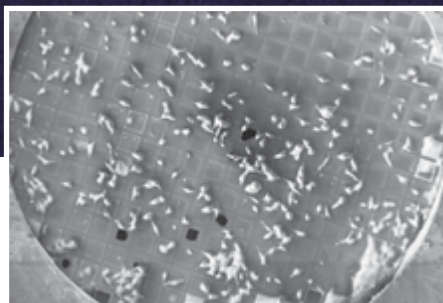
The goal of the CEMRC is to provide instrumentation, technical assistance, training, and access to cryo-EM for the UW–Madison research community.

The facility houses four Thermo Scientific microscopes in three buildings, including the powerful Titan Krios G3i cryo-transmission electron microscope (TEM), located on the first floor

HOW DOES CRYO-EM WORK?

During the cryo-EM process, aqueous samples are frozen, or vitrified, at approximately -183°C (about -297°F). The rapid freezing process supports the formation of a non-crystalline phase of ice that is amorphous and vitreous (glass-like). No dyes or other alterations are needed to view the structures.

Next, electron beams are shot at the frozen molecules in the microscope to capture an image of their structure. When electrons hit the biological sample in the microscope, they scatter and then pass through a series of lenses to generate an image. In single particle cryo-EM, which is often used on protein complexes, hundreds of thousands of such images in random orientations are combined digitally to reconstruct the molecular structure.



of the Biochemical Sciences Building. A smaller Talos TEM, which is the first step in the cryo-EM research pipeline, is located in the Biophysical Instrumentation Facility and Biochemistry Optical Core. The Deluca Biochemistry Building houses two more state-of-the-art microscopes — a Talos Arctica cryo-TEM and an Aquilos cryo-FIB-SEM — as well as specimen prep equipment and lab space for UW investigators, external collaborators, and industry partners.

Construction and installation have been complex because the rooms need tight temperature and humidity control and sophisticated shielding to make sure the microscopes are acoustically, electronically, and vibrationally isolated. All of this advanced technology requires highly trained personnel. Staff have been busy preparing to support the center's users. In 2019, **Eric Montemayor**, CEMRC facility manager, served for three months as an embedded trainee at the National Center for Cryo-EM Access and Training (NCCAT), which is housed in the New York Structural Biology Center at The City College of New York and is funded by the National Institutes of Health (NIH). CEMRC systems administrator **Matt Larson**, a computer scientist with a doctoral degree in physiology and biophysics, has also been essential to the launch, and he will continue to be so as he develops new computational systems for the center.

UW researchers are planning to use the center in diverse and innovative ways that will help keep the campus at the bioscience frontier. Word is spreading about the CEMRC, laying the groundwork for collaborations.

"Some of our researchers understand how to do the computational aspects of the pipeline, and we may just support them with sample optimization and cryo-preservation and data acquisition and then hand off images where they handle the computations on their own," Wright says. "For other investigators, we support them through the entire process and provide them with their structure and its interpretation on the back end."

A recent masked and physically distanced tour of the CEMRC was a simultaneous walk down memory lane and glimpse into the future for **Kate VandenBosch**, dean of CALS, and **Bill Barker**, associate dean for research. Both used electron microscopy earlier in their research careers. For VandenBosch, it was a treat to get up close and personal with technological advances she says she could only have dreamed of in her postdoc days, and it enhanced her appreciation of the privilege that comes with peering into the inner workings of life.

"With EM, I always felt that I had a window into the beauty of biological structure that most people didn't get to see," she says.

Barker couldn't help but imagine what cryo-EM

From left to right, at the Cryo-EM Research Center:

A liquid nitrogen tank off-gasses while connected to a Thermo Scientific Aquilos cryo-focused ion beam scanning electron microscope (cryo-FIB-SEM).

A low magnification cryo-scanning electron microscope (SEM) image of frozen-hydrated HeLa cells cultured on an electron microscope grid. The grid was imaged with a Thermo Scientific Aquilos FIB-SEM.

IMAGE BY JAE YANG

Computer scientist and systems administrator Matt Larson demonstrates the use of a microscopy program he developed.

“WE can be a nucleating point to do a lot of good for the state and bring people together.”

— ELIZABETH WRIGHT

capabilities will bring to CALS. “Now it will be possible to explore the nature of soil organic matter and microbial communities in a hydrated state, or the structure of the rhizosphere, or the spike protein of the novel coronavirus,” he says. “And just imagine what this technology could add to our understanding of frozen dairy desserts!”

As wowed as they were by the array of brand new, state-of-the-art equipment, VandenBosch and Barker were more impressed by the vision and hard work of the people.

“It was equally exciting for me to meet today’s postdocs and staff who are putting the ‘scopes through their paces, making sure things are running as they should, and perfecting specimen preparation,” VandenBosch says. “The machines are impressive, but it’s the human element that

will really make this facility soar. Their expertise will enable other users to ask and answer important biological questions.”

But the CEMRC is only one of two cryo-EM facilities set to open at UW. Construction of a national hub on campus is also underway, in partnership with the UW Division of Facilities Planning & Management.

In 2019, NIH announced it was investing in cryo-electron tomography (cryo-ET) to get ahead of the game in understanding how cells work and respond to viral and bacterial infection, neurodegeneration, and more. In September 2020, the NIH announced that it will provide \$22.7 million over six years to create a national research and training hub at UW–Madison — the MCCET. The center will support investigators by providing access to well-trained

staff and state-of-the-art equipment for routine and advanced cryo-ET specimen preparation, data collection, and computation. The MCCET will also provide hands-on, remote, and virtual training in cryo-ET specimen preparation, data collection, and data processing and validation.

MCCET staff will collaborate with centers at the University of Colorado Boulder, the New York Structural Biology Center, and the SLAC National Accelerator Laboratory to offer the research community cryo-ET training and access. The NIH is supporting the large investments needed to pay for the equipment, personnel, and service contracts necessary to operate these cutting-edge research facilities.

Members of Wright’s team will have roles at both the national hub and the UW center. It will take a year to renovate the space for the national hub, order the equipment, and complete its installation, so it is scheduled to be fully operational by early 2022.

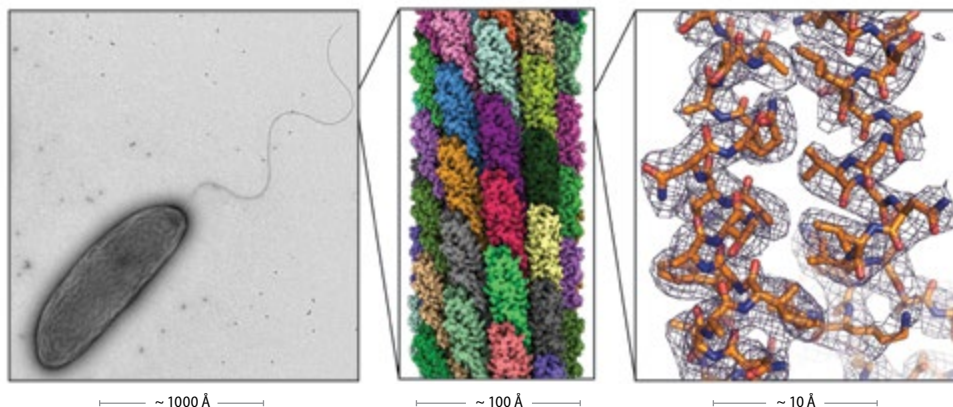
“Often, in structural biology, we work as separate units, and having this network of centers is special because we are building a community,” Wright says. “This allows us to work as a larger team of cryo-EM pioneers to support the greater research community. Each one of the new cryo-ET centers has its own strengths and specialization in how staff consider processing samples and data collection.”

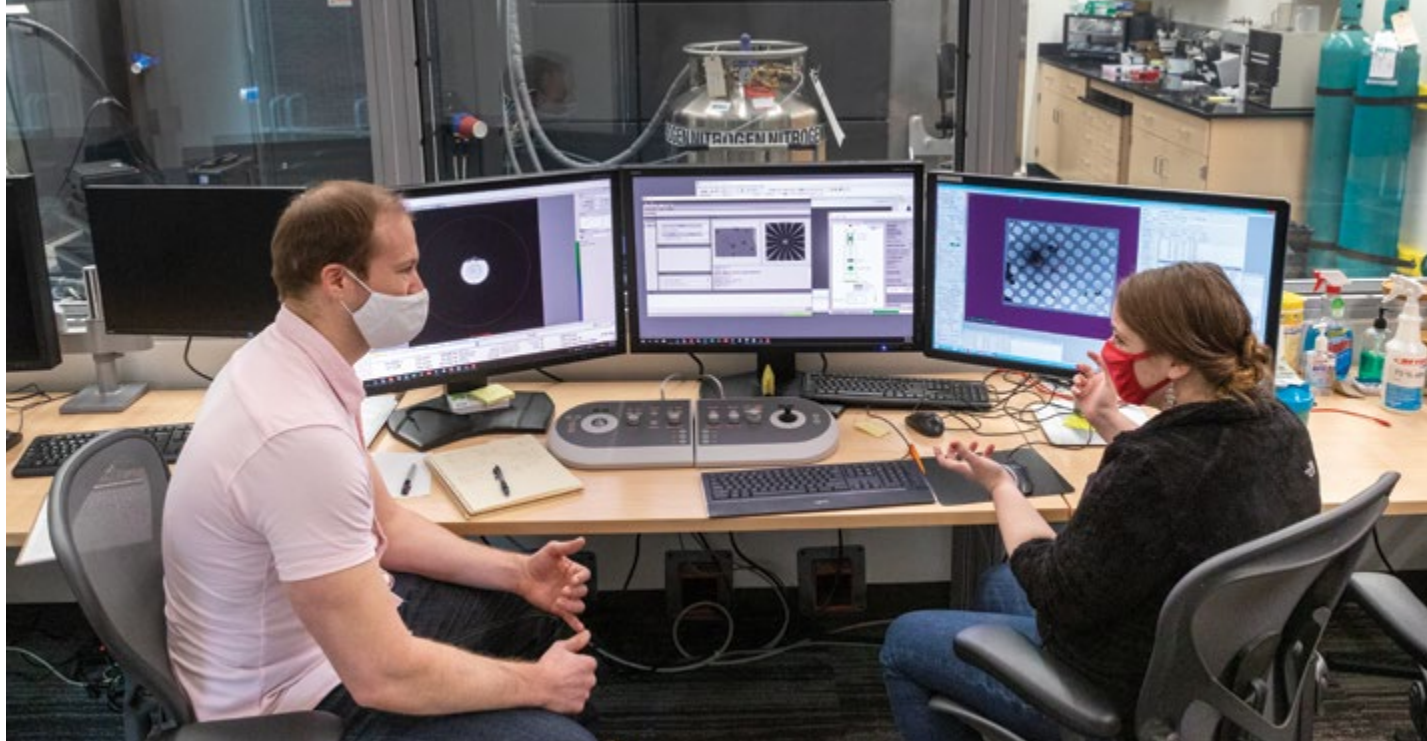
The UW centers also create jobs and are leading to engagements with surrounding tech and biotech companies. The CEMRC and UW–Madison are pursuing non-disclosure and confidential disclosure agreements with companies that are developing new drugs and therapeutics.

“We look forward to long-term partnerships with these companies,” Wright says. “We are also

A 3.2 Å resolution cryo-EM helical reconstruction of the “FljK” flagellum of the bacterium *Caulobacter crescentus*. Data were collected on a Thermo Scientific Titan Krios cryo-TEM using a Gatan K3 direct electron detection camera. Å, or angstrom, is a unit of length equal to one ten-billionth of a meter.

IMAGE BY ERIC MONTEMAYOR. DATA COLLECTION AND PROCESSING BY NICOLETA PLOSCARIU AND ERIC MONTEMAYOR.





using training grants to provide internships for our students to bring their advanced training to industry. We can be a nucleating point to do a lot of good for the state and bring people together.”

A LURE FOR THE A-LIST

UW–Madison is also making major investments in the people who rely on cryo-EM and cryo-ET for their research. Wright’s experience with both technologies was critical to securing the NIH hub.

Wright completed her undergraduate education in biology and chemistry at Columbus State University and her Ph.D. in chemistry at Emory University, followed by postdoctoral work at the University of Southern California and the California Institute of Technology. She was an associate professor in the Department of Pediatrics at the Emory University School of Medicine and the director of the Robert P. Apkarian Integrated Electron Microscopy Core at Emory University before joining UW–Madison in 2018.

Wright studies pathogenic bacteria and how cells regulate interactions with the environment. She also investigates the structures of viruses such as HIV-1, measles virus, and respiratory syncytial virus, and she explores neurodegenerative diseases, such as Alzheimer’s, caused by defective proteins. Understanding at the molecular level how these proteins impact neuronal cell structure and function can help in the development of new therapeutic and curative approaches.

The large neuroscience group and Alzheimer’s Disease Research Center on campus were important factors in Wright’s decision to call UW–Madison home. The same is true of several other recent additions to the faculty.

The Department of Biochemistry and CALS

have also hired assistant professors **Robert Kirchdoerfer** BS’06, an expert in cryo-EM applications in virology, and **Ci Ji Lim**, an authority in cryo-EM applications in DNA biology. The Morgridge Institute for Research hired investigator and assistant professor of biochemistry **Tim Grant**, who develops computer programs to improve cryo-EM and cryo-ET data collection and analysis, and investigator **Brian Bockelman**, who specializes in research computation.

When Kirchdoerfer was offered a faculty position in the Department of Biochemistry and Institute for Molecular Virology in 2019, it was a homecoming. The Oregon, Wisconsin native was hired as part of the Metastructures of Viral Infection cluster hire initiative. (UW–Madison’s Cluster Hiring Initiative was launched in 1998 as an innovative partnership between the university, state, and the Wisconsin Alumni Research Foundation.) The cluster created three positions to leverage and improve UW–Madison’s strengths in RNA virology, DNA virus epigenetics, and atomic-level imaging. Another goal of the cluster is to expand the institute’s research portfolio into the evolving field of metastructural virology, which studies how viruses infect and modify living cells.

Following his UW bachelor’s degree with majors in biochemistry and genetics, Kirchdoerfer earned his Ph.D. in biophysics at The Scripps Research Institute in Southern California and continued there as a postdoctoral scholar before coming back to UW–Madison.

“I was thrilled to take up this position at UW–Madison to look at the structures of macromolecular virus complexes and, particularly, look at virus spikes and viral replication complexes,” Kirchdoerfer says.

Robert Kirchdoerfer, assistant professor of biochemistry, talks with **Juleen Dickson**, a postdoctoral research associate, at the Cryo-EM Research Center in the DeLuca Biochemical Sciences Building.

CRYO-EM

A WHETSTONE FOR UW'S COMPETITIVE EDGE

UW–Madison has a strong record of contributions to structural biology, cell biology, virology, and medicine, and it hosts a vibrant community of structural biologists. But to remain competitive in their respective fields, many researchers with expertise in molecular biology, cell biology, microbiology, and biomedicine need to use cryo-EM. Until recently, they have had to seek out those resources at better-equipped and better-staffed cryo-EM facilities located primarily on the U.S. coasts.

To meet the growing on-campus need for cryo-EM equipment and expertise, several years ago, a core of researchers across campus began working to assemble the full power of cryo-EM at UW.

UW–Madison and the Department of Biochemistry have been at the forefront of structural biology research for decades, says **Brian Fox**, chair and professor of biochemistry and associate vice chancellor for research policy and integrity. This includes 35 years of operation of the National Magnetic Resonance Facility at Madison, which was established by biochemistry professor emeritus **John Markley**, and 15 years of contributions to the NIH-funded Protein Structure Initiative, which was led by Fox, Markley, biochemistry professor emeritus **George Phillips**, and former biochemistry professor **David Pagliarini**.

“Knowledge of the structure of biological molecules is profoundly transformative and enabling, leading to better questions and answers to the key challenges of our research endeavor,” Fox says. “These efforts have positioned us well to embrace cryo-EM as a newly emerging, transformative technology.”

Paul Ahlquist, lead investigator for the John W. and Jeanne M. Rowe Center for Research in Virology at the Morgridge Institute for Research and professor of oncology, molecular virology, and plant pathology, teamed up with Fox and Morgridge Institute director **Brad Schwartz** to initiate a campus-wide push for a major investment in cryo-EM.

A project led by biochemistry and bacteriology professor **Robert Landick**, with funding from the UW2020: WARF Discovery Initiative, set the stage for creating the CEMRC. Landick was joined on the project by **Desirée Benefield**, a scientist and expert in cryo-EM. Benefield played an integral role in the facility's success by providing early guidance to future users, including training them in sample preparation, imaging, and analysis.

Funding was needed to equip the center. Groups contributing funding to the \$15 million-plus initiative included the Department of Biochemistry and College of Agricultural and Life Sciences, Morgridge Institute for Research, Office of the Vice Chancellor for Research and Graduate Education, School of Medicine and Public Health, and Departments of Biomolecular Chemistry and Neuroscience.



Tim Grant, assistant professor of biochemistry, demonstrates part of the process of loading samples into cassettes for the Thermo Scientific Talos Arctica cryo-TEM in the DeLuca Biochemistry Building.

Kirchdoerfer studies coronavirus. Most of these viruses are not harmful, and some cause mild flu-like symptoms. However, some, such as SARS-CoV-2 (which causes the disease COVID-19) are more dangerous — they jump between animal species and find their way into humans. His research uses structural biology methods, such as cryo-EM and X-ray crystallography, combined with more traditional biochemistry approaches, to examine the protein machines of viruses in great detail. In viewing how these viral machines are put together and how they function, he's probing for vulnerable points in the virus where vaccines and antiviral drugs could intervene.

Kirchdoerfer, whose research has taken on increased urgency over the last year due to the COVID-19 pandemic, has been doing much of his cryo-EM data collection at the Simons Electron Microscopy Center at the New York Structural Biology Center.

“We send them samples, and it's helpful, but not as convenient as having a center here across the driveway,” he says. “We are really looking forward to the new facility at UW. Having greater access to microscope time means greater access to data.”

“I also think this is going to be a huge boon to people in my lab to be trained on how to collect EM data. This will accelerate our ability to do our research. The technology and computational advancements in recent years have put cryo-EM in a place to be a game-changer for structural biology. It's highly attractive to new faculty to have this cutting-edge resource and very attractive to students and postdocs.”

It was definitely attractive to Grant, formerly a research specialist at the Howard Hughes Medical Institute's Janelia Research Campus, who joined the ranks of UW–Madison faculty in early 2020.

“One of the main reasons that I came to Madison was the investment made in cryo-EM, in the equipment, but also in hiring professors with a specialty in cryo-EM,” Grant says.

Grant's first exposure to cryo-EM was in the early 2000s as an undergraduate at Imperial College in London. He was drawn to the technology's combination of biology and computing.

Grant contributes to cryo-EM and its broader use as primary developer of a software package called cisTEM, which is used to process cryo-EM images of macromolecular complexes and obtain

high-resolution 3D reconstructions from them. The software comprises a number of tools, including movies, micrographs, and stacks of single-particle images, and this creates a complete pipeline of processing steps for obtaining high-resolution, single-particle reconstructions.

“I spend half my time developing techniques and methods to improve the quality of images and results that you get from the electron microscopes and the other half collaborating with people to solve important structures,” he says. “A large part of cryo-EM is computation — the processing of images. For every day you spend on the microscope, you probably spend weeks or more on the data processing.”

Grant is excited about the growth of cryo-EM in Madison. “A lot of people are going to be drawn here because of the facility and national hub,” he says. “I’m excited about the opportunity to interact with them, something that I hope will lead to some interesting collaborations. It will be a focal point — a great place to meet people and share ideas.”

Access to a leading cryo-EM research facility also was a draw for Lim, who arrived in Madison in August 2020. Lim came to Madison from Colorado, where he pursued postdoctoral training in biochemistry and cryo-EM in the Cech lab at the University of Colorado Boulder. There, he was using cryo-EM technology to study how mammalian telomeres are regulated and achieve genome stability. Telomeres act as protective caps at the ends of chromosomes, holding genetic information in place. Without telomeres, some of the genetic information is lost every time a cell undergoes division. This loss of genetic information at the cellular level can lead to cancer and age-related diseases.

Lim developed an interest in telomere biology during his undergraduate research work in

Singapore, where he grew up. This work led him to a Ph.D. in single-molecule biophysics at the National University of Singapore and then his first trip to the United States for postdoctoral training in Colorado.


Lim, who helps teach a course at UW in single molecule biophysics, is eager to develop more courses on this topic so he can contribute to the university’s long-standing tradition of training and mentoring the next generation of scientists in his field.

“The field of telomere biology is very specialized,” he says. “But in the broader field of structural biology, cryo-EM, as a key methodology, is important, and students need to know about it. I’m excited to share the applications of cryo-EM in biology. It’s very visual — and seeing is believing.”

EXTENSION OF THE ARTIST’S EYE

Like Lim, Wright has a passion for teaching, especially elementary school children. Simple microscopy lessons, she says, can allow students to use their eyes, magnifying glasses, and microscopes to see the same object at different scales and resolution levels. With these snapshots, Wright instills a sense of wonder and curiosity about the complexity of living things.

It’s a wonder that Wright has felt much of her life. She studied chemistry and biology as an undergraduate in Georgia, and she made science her career, but she also took just about every art class that was offered on the way. Today, her hobbies include drawing, painting, and photography. She says imaging technologies like cryo-EM help her retain her artistic eye.

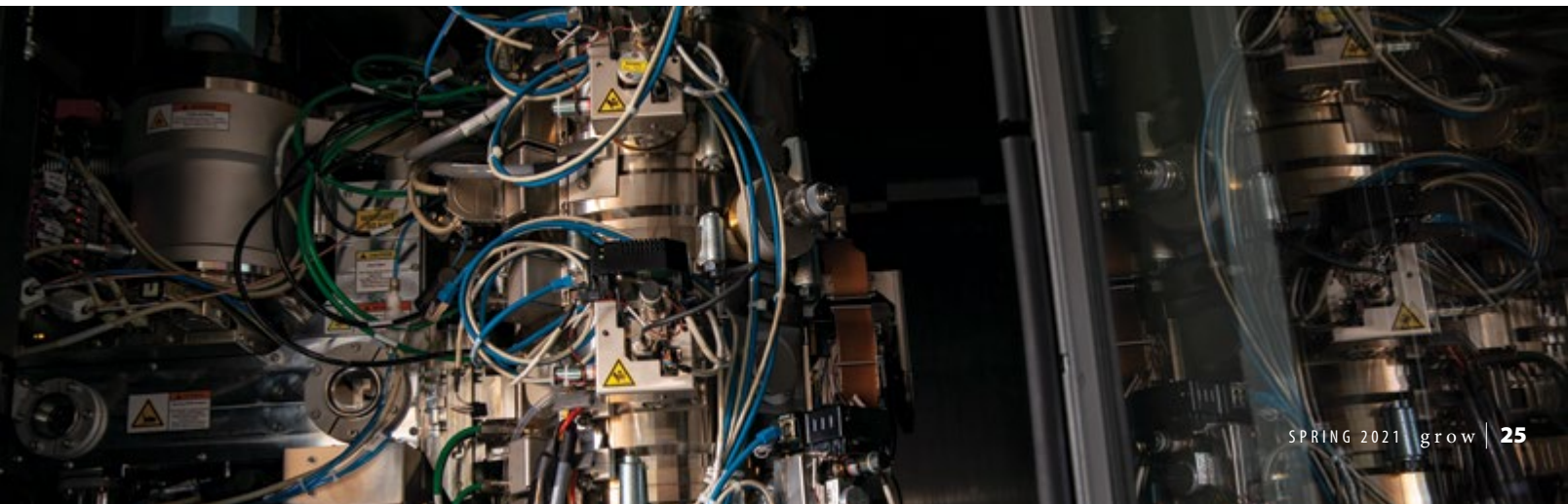
“Art, like the technology that we are using in the lab, helps us to see the world in a different way,” Wright says, “and sometimes that is beautiful and life changing.” 


EXPLORE ONLINE

Take a virtual tour of the Cryo-EM Research Center at cryoem.wisc.edu/cemrc-virtual-tour.



A look inside the Thermo Scientific Titan Krios G3i cryo-TEM at the Cryo-EM Research Center.





> ./New_Frontiers_of_Potato_Tech

By Nicole Miller MS'06 | Caroline Schneider MS'11 | Nik Hawkins

It's the number one vegetable crop in the United States. Wisconsin happens to be its third largest producer (after Idaho and Washington), with 3.1 billion pounds and 68,000 acres harvested in 2019. It comes in russet and red, yellow and purple, in fingerlings and petites. It can be frozen or fresh, dehydrated or refrigerated, roasted or grilled, scalloped or au gratin, mashed or smashed.

An unmanned aerial vehicle carrying a hyperspectral camera collects data from potato fields at the Hancock Agricultural Research Station. The goal is to develop computer-assisted models that help farmers better manage fertilizer applications.

PHOTO BY BECKETT HILLS

That's right — it's the nutritious and delicious, versatile and delectable, potato.

Despite its many virtues, this vegetable gets a bad rap as a junk food. That's because one of the most common cooking methods — frying — depletes nutrients while upping the calories. There's also the less-than-healthy fixings we often heap upon them. But on their own, prepared properly, potatoes boast high levels of fiber, antioxidants, and several vitamins. And they contain zero fat and cholesterol, little sodium, and less than 10% of the recommended daily intake for carbohydrates.

The potato is a near-complete source of nutrition, and many now tout it as a superfood, one that the developing world relies upon. Potatoes also have untapped potential for the U.S. and beyond. This is why CALS scientists are working hard to find better ways to grow and breed them. Here are two examples of horticulture experts breaking new ground on the sandy soils of potato research fields.

> Hyperspectral Imaging Shines New Light on Crop Growth

This is a potato farming fact of life: During critical stretches of the growing season, nitrogen levels in potato plants need to be closely monitored. By keeping careful track of nitrogen status in their crop, farmers can make sure they apply fertilizer in the most efficient and sustainable way possible.

The most common monitoring approach involves collecting large numbers of petioles — the part of the plant that connects leaflets to stems. The samples are mailed to a lab for a quick nitrate analysis; within a few days, results tell growers whether they need more nitrogen fertilizer to get a proper yield. The system works, but it has its downsides, says **Yi Wang**, assistant

These processed aerial images of potato research plots show the reflectance of certain spectral bands, which indicate the nitrogen sufficiency or deficiency of different varieties.

IMAGE BY BECKETT HILLS

professor in the Department of Horticulture.

“Collecting the petioles is time-consuming and labor-intensive,” she says. “And sometimes the results can be misleading because a lot of factors can affect petiole nitrate numbers, such as weather conditions or the time of day of sample collection. Plus, the results don’t catch spatial variation [of nitrogen needs] within the field.”

Wang, who focuses her research on sustainable vegetable production, is also an extension specialist, so she pays close attention to the needs of farmers. And she knows the status quo isn’t ideal for them. Insisting there must be an easier, faster, and more comprehensive way for potato growers to assess the true nitrogen needs of their crops, Wang and her team have set out to find one — and prove its effectiveness.

She’s leading a new project, funded by a \$475,000 grant from the U.S. Department of Agriculture (USDA) National Institute of Food and Agriculture, that involves collecting data with a hyperspectral camera mounted on a UAV (unmanned aerial vehicle) or low-flying airplane. The camera gathers images as the plane passes over research plots with potato plants grown at different nitrogen levels. Researchers then process and use the data to develop computer-assisted mod-

els that link the imagery with in-season plant nitrogen status and end-of-season yield, quality, and economic return.

“The ultimate goal of the project is to assist potato growers with their nitrogen management using a platform that blankets the entire field in a timely manner, unlike the traditional petiole nitrate testing,” Wang explains. “My collaborators and I hope to develop an online program that will translate the hyperspectral images into information about when to apply fertilizer, and how much to apply, so that maximum profitability can be achieved for the growers with minimum environmental impacts.”

Hyperspectral cameras are powerful pieces of equipment, able to capture images that detect hundreds or thousands of spectral bands of sunlight reflected from the crop canopy, explains **Trevor Crosby**, a graduate student in Wang’s laboratory.

“Factors that cause variation in canopy health — such as nutrient status, water status, or disease pressures — are all related to the spectral reflectance, so they can be visualized in the hyperspectral images,” he says. “We use image processing to extract the most useful information for our research project.”

And there’s certainly a sizeable pile of data to process. One flight over a 70-by-150-meter research field can

collect dozens of images, each with hundreds of spectral bands. It takes long hours to crunch the numbers, so the research team is looking to expedite the image processing.

The challenges of this complex project led Wang to bring in two key collaborators. **Phil Townsend**, professor in the Department of Forest and Wildlife Ecology, is a national leader in utilizing remote sensing technologies (see “Drones, Joysticks, and Data-Driven Farming” in the summer 2018 issue of *Grow*). And **Paul Mitchell**, professor and extension specialist in the Department of Agricultural and Applied Economics, is helping with the economic analysis that informs the computer model’s nitrogen application recommendations.

Crosby is taking the lead on collecting ground measurements for the project, gathering a wide array of data from the field research plots at different potato growth stages over the course of several growing seasons. He’s looking at leaf area index, leaf and vine total nitrogen content, and environmental factors, such as soil moisture and temperature, solar radiation, and wind speed. At harvest, he measures total tuber yield and

Yi Wang, assistant professor of horticulture, and graduate students Guolong Liang (left) and Trevor Crosby (right) are shown here in a potato research plot at the Hancock Agricultural Research Station in July 2019.

PHOTO BY MICHAEL P. KING



size profile. Using the measurements, Crosby will develop advanced models to link the hyperspectral imagery with the ground measurements.

Finding optimal fertilization levels through these models could lead to positive outcomes in the real world, and not just in terms of farm profitability. Excess fertilizer often finds its way into groundwater, leading to nitrate contamination. High nitrate levels are linked with numerous health problems in people and aquatic plant overgrowth that can cause ecological damage.

“With all the issues in the state around nitrates in groundwater, we need to find ways to make better use of our fertility inputs, and we are hopeful that Yi’s new project can help direct those efforts,” says **Andy Diercks** BS’93, a fourth-generation potato grower at Coloma Farms, LLC. “The potential is significant. Yi’s new project represents an opportunity to really leap forward [in nitrogen management].”

This is just one of Wang’s ongoing efforts to support potato and vegetable growers in Wisconsin. Her portfolio of research focuses on cutting-edge technologies that can improve irrigation, nitrogen, and storage management for common vegetables in the state. This includes potatoes, of course, but also green beans, dry beans, and sweet corn.

She shares her findings with farmers through the UW Vegetable Crop Update

e-newsletter, grower meetings, farm visits, field days, and her “Proud to be a spudbadger!” YouTube channel.

For the hyperspectral imaging project, Wang’s team plans to provide results online through a publicly available spreadsheet, at least in the near term. But with additional funding, they hope to develop a free app that growers can use on smart phones and tablets. Many, including Diercks, eagerly await these next steps.

“Hyperspectral imaging has the potential to show the plant’s response to deficiencies in inputs before the human eye can see that response,” says Diercks. “If we can gain a few days in responding to nutrient stress, the impact to the health of the plants would be quite significant, not to mention the possibility of using less inputs to remedy the situation — which would be a serious win-win.”

> ‘Potato 2.0’ Will Speed Up Breeding, Yield Better Varieties

Although potatoes may be a superfood to some, they’re far from perfect. For one, they present a big challenge for plant breeders who are trying to develop more savory, sustainable, storable, and growable varieties.

“Potato may be the world’s leading vegetable crop, but it hasn’t realized the genetic gains needed to keep pace with industry and consumer demands,” says **Jeff Endelman**, associate professor in the Department of Horticulture and



leader of the university’s potato breeding program.

One of the main hurdles when breeding potatoes is its tetraploid genome. Tetraploids inherit two sets of chromosomes from each parent, instead of just one set like humans and most animals. “Tetraploidy is common enough among flowering plants that scientists believe it has advantages on evolutionary time scales,” says Endelman. “But for plant breeders, it makes it difficult to understand the genetics of traits and get rid of unfavorable genes through selection.”

To circumvent the challenges of tetraploidy, potato breeders around the world — in an effort informally known as Potato 2.0 — are working to reinvent cultivated potato as a diploid crop.

“One reason to do this is the simplicity,” says **Shelley Jansky** MS’84, PhD’86, a USDA Agricultural Research Service scientist and professor emeritus of horticulture who has spent her career working with wild potatoes to identify



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Nutrition Facts

Serving size One 6 oz. (170g) russet baked potato with flesh & skin

Calories
per serving

168

	Amount/serving
Total Fat	10g
Sodium	24mg
Carbohydrate	37g
Fiber	4g

Rich in antioxidants, including flavonoids, carotenoids, and phenolic acids *Recommended daily intake, according to the federal “Dietary Guidelines for Americans 2015-2020.”

	% daily intake
Vitamin C	37%
Vitamin B6	31%
Potassium	27%
Manganese	20%



From left, Lin Song, a Ph.D. student with the Endelman lab, and, from Rhinelander Agricultural Research Station, research gardener Jaden Olski and superintendent Becky Eddy, prepare slices of diploid potatoes for frying in the kitchen at Hancock Agricultural Research Station as part of an assessment of different varieties.

PHOTOS BY MICHAEL P. KING (3)

genes for traits that potato breeders deem important. “Another reason is that most wild potatoes are diploid, so it’s just easier to make the crosses on the same level.”

Potato 2.0 builds on groundbreaking breeding work Jansky and others started at the Hancock Agricultural Research Station around eight years ago. Although all major potato varieties worldwide are tetraploid, the Jansky team created a diploid potato variety by crossing a cultivated potato with a wild one and discovered that it displayed desirable characteristics.

“At harvest, the potatoes looked just like what you’d see in a regular breeding program,” says Jansky. “They were the same size, had the same yield. So that really made me think, boy, why are we working so hard to go up to the tetraploid level when maybe we can just do this at the diploid level and still get the same quality?”

Given this prior work, it’s no surprise that UW–Madison is now serving as the lead institution for Potato 2.0,



Jeffrey Endelman, associate professor in the Department of Horticulture, stands in front of the Walnut Street Greenhouse, where he conducts potato research on the UW campus.

“Our goal is to create and sequence the genomes of 100 diploid potatoes, representing the russet, chip, and red market types that make up most of U.S. potato production,” explains Endelman.


The next step is to create lines that can be maintained as “true seed,” which is potato jargon for what everyone else simply calls seed. The “seeds” currently used in potato production are whole or pieces of tuber with at least one “eye,” from which sprouts develop to generate the next crop. But seed tubers are bulky and expensive to transport.

“It takes about 2,000 pounds of seed tubers to plant one acre, but the amount of true seed needed would fit in the palm of your hand,” says Endelman.

Seed tubers also act as vectors for diseases, such as Verticillium wilt, soft rot, silver scurf, common scab, and Potato Virus Y. It’s another problem the use of true seeds could address.

“Nearly every major disease the potato gets is carried in seed tubers,” Jansky says. “None of them are in true seeds.”

Another major focus of the project is to produce inbred, or self-pollinated, lines. Although it may sound trivial, this is actually a big challenge in diploid potatoes, which typically lack the ability self-pollinate. But self-pollination is key to creating hybrid lines with big boosts in yield. That crossbreeding process took decades in the early 20th century for corn breeders, but Endelman hopes to do it more quickly in potato now that researchers have the genomic tools needed.

Endelman is excited to see the future impacts of the project across the potato industry, in Wisconsin and beyond. “This project marks a turning point for Potato 2.0 in the U.S., and everyone is enthusiastic about the potential to more efficiently deliver genetic improvements for disease resistance, climate resilience, nutritional value, and more.” 



The color of crushed diploid potato chips is analyzed by a spectrometer.

which is funded through a \$3 million award from the USDA Specialty Crop Research Initiative and \$3 million in matching funds from PepsiCo (the parent company of potato chip and snack food producer Frito-Lay) and eight collaborating universities and research institutions.

The first step of the project is to produce diploid potatoes that still have the optimal genetics of their tetraploid relatives. This is done by pollinating tetraploid potato with existing special diploids that can act as “haploid inducers.” Haploid induction is a technique used in many crop species to reduce chromosome numbers. It results in an embryo without the chromosomes of the pollen donor.

LEARN MORE

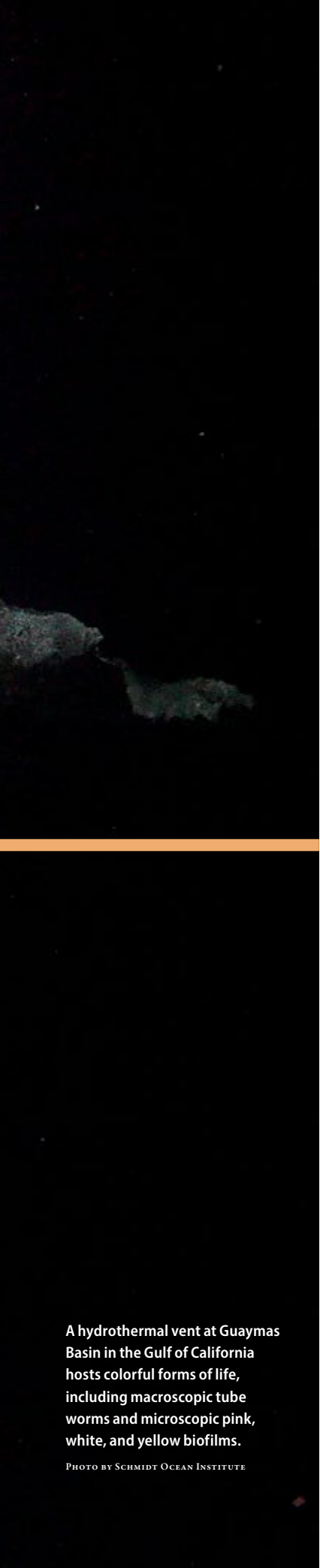
Visit the Potato 2.0 Project at go.wisc.edu/potato2.0.



THE ANSWERS AWAIT ON THE OCEAN FLOOR

So that's where you'll find Karthik Anantharaman — where the Earth feeds sulfur to strange creatures that live and die in the dark — as he deciphers the mysteries of a biological process with potent ecological and medical ramifications

BY CAROLINE SCHNEIDER MS'11



A hydrothermal vent at Guaymas Basin in the Gulf of California hosts colorful forms of life, including macroscopic tube worms and microscopic pink, white, and yellow biofilms.

PHOTO BY SCHMIDT OCEAN INSTITUTE

It's December 2018. **Karthik Anantharaman** awakens at 6 a.m., afloat in the middle of the Pacific Ocean. He's barely slept, adrenaline is flowing. There's little time, and he and Alvin need to get ready.

Anantharaman goes through a series of checks — a blood pressure measurement, a health status questionnaire — to make sure he's fit for what's ahead. He eats breakfast at precisely 7:15 while Alvin gets connected to several harnesses. Weather patterns are monitored. At 8:00, he and Alvin finally meet up. They dive from the deck of the R/V Atlantis and slip beneath the waves.

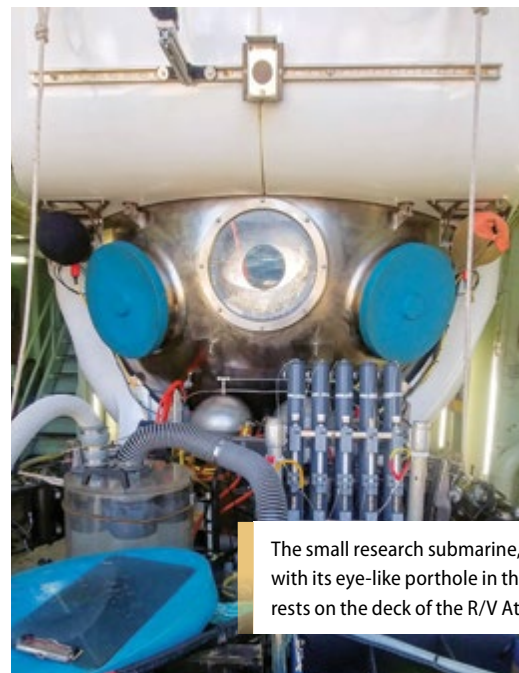
Alvin is a small submarine. Its job is to carry Anantharaman, along with another scientist and a pilot, down to the ocean floor.

The first few hundred meters of the slow descent are uneventful. Waves and currents rock the small vessel, but light still penetrates the water here. The craft has no downward propulsion, so weights are used to pull it into the depths. Around 300 meters down, darkness starts to close in, and the pilot turns off Alvin's lights. The passengers are immersed in black.

That's when the light show starts.

All around them, thousands of bioluminescent organisms appear as small, gleaming figures in the dark water. "It's unreal," says Anantharaman, an assistant professor of bacteriology. "It's just one shape after another glowing an incredibly brilliant blue. It's all the way through the water column, and it's one of the most brilliant sights you can imagine."

But the dazzling display is just a perk of the trip, not the destination. They're heading toward the East Pacific Rise hydrothermal system, where they will



The small research submarine, Alvin, with its eye-like porthole in the bow, rests on the deck of the R/V Atlantis.

PHOTO BY KARTHIK ANANTHARAMAN

navigate the ocean floor and collect samples near deep-sea fissures that discharge water heated by the earth's interior. The samples will be sent all the way back to Anantharaman's lab on the UW campus, where he and his team will try to unravel the mysteries of sulfur metabolism as it's carried out by the bacteria and viruses that live deep in the sea.

ANANTHARAMAN CALLS HIMSELF

and the members of his lab "microbial ecologists." They use DNA sequencing, data analysis, and even in-house bioinformatic tools — they developed their own software called VIBRANT and METABOLIC — to study bacteria and other microbes in both environmental systems and humans. Their goal is to better understand sulfur metabolism in multiple systems.

Metabolism is the formation and use of energy required for life. In humans, this involves compounds such as carbohydrates and oxygen. But bacteria are more versatile. They can use other elements, such as sulfur. In the absence of light at deep-sea vents, higher organisms rely on sulfur-transforming bacteria. Tube worms, clams, mussels, and other animals that have lost the ability to eat host these symbiotic bacteria, relying on them to consume sulfur and produce the energy they can't make themselves.



Karthik Anantharaman prepares a set of 24 containers that are used for collecting deep sea water samples. They are controlled by electrical pulses sent from the ship.

PHOTO BY THOM HOFFMAN

This arrangement can be found in ecosystems that thrive near deep-sea hydrothermal vents.

But the origins of Anantharaman's adventure into the depths lie nowhere near the ocean. It began when he was studying iron compounds and nanoparticles during a civil and environmental engineering master's program at the University of Michigan.

"We use engineered iron nanoparticles to treat pollutants, but when you think about it, it's microbes that produce [the nanoparticles] in the environment," explains Anantharaman. "I had this awakening moment where I thought, why am I thinking about synthesis and chemistry? I want to study the biology of how these bacteria are actually producing these nanoparticles in nature."

With that realization, Anantharaman decided to pursue a Ph.D. in microbiology. But as he started down his new academic path, the field began to change. DNA sequencing exploded. It was being used extensively to study microorganisms such as bacteria. The computational skills Anantharaman acquired during his engineering training became very useful when he started using DNA sequencing to find microorganisms that metabolized sulfur. That's what led him to hydrothermal vents on the bottom of the ocean.

Hydrothermal vents are an ideal place to study microorganisms and

ocean biology. The vents release trace elements, such as iron, manganese, zinc, and copper, which are often carried by currents for hundreds or thousands of miles. These elements are extremely limited in the ocean environment, and they are necessary in the surface ocean for photosynthesis by bacteria and algae. These algae, in turn, are the base of the food chain for nearly all ocean life. Hydrothermal vents, therefore, control ocean chemistry.

The vents are also perfect places to study sulfur metabolism. They serve as conduits for energy and chemicals that travel from deep within the earth into the oceans. Consequently, hydrothermal vents have some of the highest levels of naturally occurring sulfur compounds on the planet. Over billions of years, these high concentrations of sulfur have resulted in the evolution of microorganisms that can utilize the compound for generating energy.

"This is a unique ecosystem that does not depend on the energy source of light, unlike most other ecosystems on the planet," says **Zhichao Zhou**, a postdoctoral fellow in Anantharaman's lab. "It is a chemosynthetic ecosystem that is solely dependent on the chemicals brought out from the vents."

Although it's a useful energy source, sulfur can also cause a lot of problems in biological systems. The sulfur compound that's produced by hydrothermal vents is hydrogen sulfide, a toxic gas that smells like rotten eggs. It's poisonous to



aquatic organisms and humans alike. In the environment, microorganisms can metabolize hydrogen sulfide into non-toxic compounds such as sulfate, but it's an intricate process that science hasn't fully apprehended.

"A lot of microbes can use sulfur compounds, and it's a cycle we really need to understand," says Anantharaman. "If we want to study sulfur metabolism and look at the diversity of organisms associated with this process, the hydrothermal vents are a great environment to do that."

Anantharaman has taken two separate trips to hydrothermal systems. In addition to East Pacific Rise via the R/V Atlantis, which is owned by the U.S. Navy and operated by the Woods Hole Oceanographic Institution, he also journeyed to the Guaymas Basin aboard the Schmidt Ocean Institute's R/V Falkor in March 2019. Onboard, he collected samples with the assistance of a submersible robot named ROV SuBastian rather than a manned submarine. Both vessels sail from Manzanillo, Mexico.

As locations for study, the vent systems are ideal, but the research process is not. Collecting samples from hundreds of meters under the ocean is incredibly difficult, and processing everything collected at those sites is another enormous undertaking.

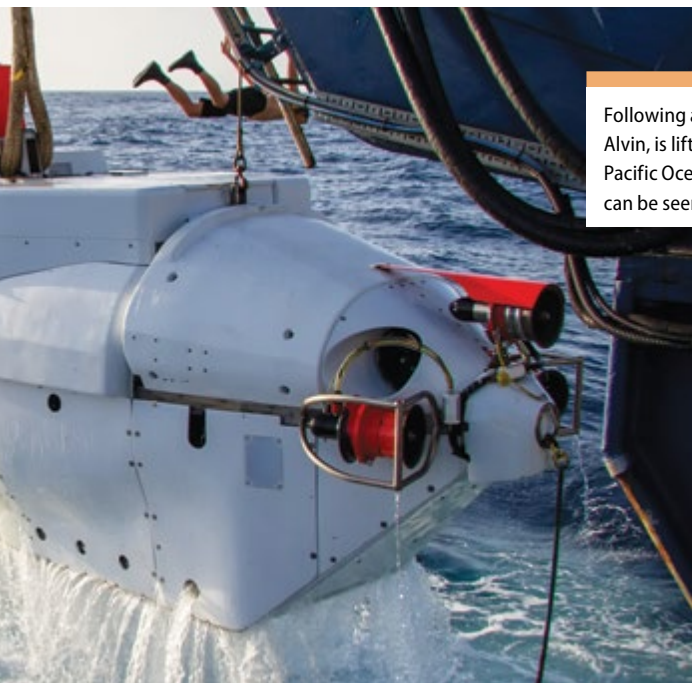


PHOTO BY KEN KOSTEL, WOODS HOLE OCEANOGRAPHIC INSTITUTION

Following a deep-sea dive, the small research submarine, Alvin, is lifted out of the water next to the R/V Atlantis at the Pacific Ocean's East Pacific Rise in December 2018. A diver can be seen leaping from the sub after completing checks.

BACK INSIDE ALVIN'S CLOSE

quarters, Anantharaman and his colleagues first gather animals such as snails, worms, clams, and mussels. Then the researchers collect mats of bacteria that are oxidizing sulfur compounds. And finally, they filter fluids.

Since this step takes the longest, it's left for last. Due to oxygen limitations, passengers can stay in Alvin's confines for only eight hours at a time; and even in that brief stay, carbon dioxide concentration can get up to 1% in the submarine (compared to atmospheric levels around 0.03%). So any time remaining on the bottom of the ocean is spent filtering fluid, looking for the bacteria and viruses in the water that are oxidizing sulfur. The dive day is long and intense. Researchers go directly from collecting one sample to the next while following a carefully designed plan.

"I had taken a sandwich and a couple of energy bars and water," Anantharaman says. "You don't get a break; there is no lunch break on the submarine. You just keep sampling and eat on the go. Usually one scientist is taking notes while the other has eyes outside."

Once sampling is complete, it's time to start shutting things down. Alvin and the researchers are to be on the surface

by 5 p.m., and the ascent takes a bit more time and control than the descent. Before heading to the surface, several safety checks must be conducted, and communication has to be established with the ship. A slow rise is important: The submarine contains sensitive scientific samples stored on the outside that could

become loose or be damaged.

During this particular dive, Anantharaman and his colleagues have a fun opportunity before they reach the surface. They speak, via satellite, to attendees at the American Geophysical Union conference about their work. Undergraduates and graduate students ask questions as they watch the dive team, with hydrothermal vents in the background. "It was one of the most memorable sites I can imagine, and that was a fantastic conversation," Anantharaman recalls.

Finally, at 3:30 p.m., the Alvin crew drops the weights that hold the sub on the ocean floor, and it begins to rise. After about an hour, they reach the surface. Typically, a boat attaches to the submarine, stabilizes it, and leads it back to the ship. But after the short delay from talking with students at the conference, the boat has drained its battery. Anantharaman and his colleagues are stuck inside Alvin.

"We had to wait, and the surface was very choppy," says Anantharaman. "We survived, thanks to Dramamine, but we were not in good shape when we got out of the submarine. We had waves really bashing us for about an hour."

With that ordeal behind them, there is still no time to rest. Once back onboard the R/V Atlantis, which is one of the most sophisticated research

vessels afloat, all the samples need to be processed and stored. Finally, autonomous vehicles take over during the night and map the sea floor. Bottles are also dropped over the side of the ship during sleeping hours to collect water for further filtration and measurements, such as oxygen and pH levels and temperature.

Even when using a robot, such as SuBastian, rather than sending scientists down in a submarine, the research is still exceptionally time-consuming. The robot begins its dive at 6 a.m., and scientists are awake well before that completing preparations. Once the submersible starts sampling, it's all hands on deck as researchers keep a constant eye on cameras and computer screens. While the manned submarine can only dive for about eight hours for the safety of the passengers, the robot is not constrained in any way. SuBastian can stay underwater for 24 hours or more.

"Fieldwork in the ocean is quite challenging," Anantharaman says. "What exacerbates that on a ship is that there's a limited number of scientists. Everyone's trying to do their own research, and you don't get too much help. You just have to suck it up and work your 16- or 18-hour days."

AT THE LAB IN MADISON,

Anantharaman (after a much-deserved rest) works with his team to further process the microorganisms and viruses he filtered from water at the hydrothermal vents. They extract DNA and RNA and sequence them. They apply bioinformatics — the use of computational technology to analyze large sets of biological data — to reconstruct the genomes of nearly every bacterium or virus in the sample. From there, they can start to decipher what sort of metabolism those organisms might be carrying out in the deep oceans.

"I am working to characterize the microbial community based on the



A deep-sea, high-temperature thermometer measures the temperature of extremely hot fluids (greater than 300 °C or 572 °F) from hydrothermal vents.

PHOTO BY SCHMIDT OCEAN INSTITUTE



This portable filtration system, called HIFIV, was used onboard research vessels to quickly process deep-sea samples of bacteria and viruses.

PHOTO BY KARTHIK ANANTHARAMAN



Graduate student Patricia Tran collects samples from Lake Mendota for a study of the role of sulfur in controlling phosphorous levels.

PHOTO BY PATRICIA TRAN

genomes of microbes and to investigate how these microbes transform energy and elements in the hydrothermal plume,” explains Zhou. “Based on the data, I can investigate the function and activity of these microbes at a very high resolution.”

The team also works to analyze the data collected from a custom filtration system that Anantharaman takes on the ships. The system allows them to load three different filter sizes. The largest filter collects algae and large bacteria, the middle filter catches most of the remaining bacteria, and the small filter snags viruses. This on-the-spot filtration is necessary because bacteria can change their activity in very little time, making it vital to process samples promptly.

“We used the filtration system, which we named HIFIV [pronounced “high five”], on both of the cruises, and it worked fantastically,” says Anantharaman. “We are now in the process of analyzing a lot of data, and we’re very excited to see what results we find.”

Anantharaman and his lab are discovering new bacteria and, along with them, the processes associated with sulfur metabolism. They hope that this knowledge will transform scientists’ understanding in a variety of areas, including low oxygen environments, which can be important contributors to climate change; the role of sulfur metabolism in human health; and, through discoveries of new microorganisms, the intricacies of the tree of life.

OF COURSE, SULFUR CAN BE

found in many locales beyond deep-sea hydrothermal events — anywhere life exists, really. So Anantharaman and his team are studying sulfur cycling in other environments, including freshwater lakes and even the human gut.

Anantharaman’s interest in the digestive tract stems from his postdoc position in the lab of **Jillian Banfield** at the University of California, Berkeley. There, he saw how concepts used in environmental microbiology can be applied to human health.

Specifically, Anantharaman is interested in gastrointestinal disorders such as colorectal cancer and Crohn’s disease. If hydrogen sulfide is formed in the gut, it can throw things out of sync and exacerbate both conditions. Using the deluge of publicly available data related to the human gut, his team has identified a number of sulfur pathways that could be contributing to human disease.

They are now expanding these studies through a collaboration with a group of University of Illinois scientists who study colorectal cancer. Using their cohort of patients, Anantharaman’s lab is uncovering how sulfur compounds are being produced and how they affect the progression of the cancers. They are also finding interesting viruses that may be associated with producing hydrogen sulfide or killing beneficial bacteria and therefore exacerbating cancer.

“I utilize data generated from DNA

sequencing to determine what these viruses are doing, which microbes they infect, and how this can affect the health of the planet and impact humans,” says **Kristopher Kieft**, a microbiology graduate student in Anantharaman’s lab. “I’m primarily interested in how viruses can manipulate how bacteria metabolize sulfur. When possible, I also cultivate viruses in the lab to measure any effects on sulfur metabolism.”

Another graduate student, **Patricia Tran**, is taking on the lab’s efforts on the freshwater front. A Ph.D. candidate



in freshwater and marine sciences, Tran is looking at both Lake Tanganyika in Africa and Lake Mendota, right on campus. The latter is often called the most studied lake in the world.

“[Bacteriology professor] **Trina McMahon** and her group have been studying the lakes for years. There is a lot of microbiology and chemistry data,” says Anantharaman. “But what was missing with Lake Mendota, and where we saw an opportunity, was an understanding of sulfur and viruses in the lake.”

Phosphorus is widely analyzed in lakes because of its role in eutrophication — the presence of excess nutrients in water bodies due to runoff — and the problematic algal blooms that stem from it. Sulfur plays a role in controlling phosphorus, and Anantharaman and Tran want to understand that process better. They are sequencing the genomes of both the bacteria and viruses from samples of Lake Mendota, and they aim

to tease out how those microorganisms might be associated with sulfur cycling. To filter those samples, they’re using the same HIFIV system that was used in the ocean.

Tran oversees much of the work in Lake Mendota, from study design to data interpretation. She also plays a major role in the study of Lake Tanganyika. There, she is leading the analysis of nearly 500 genomes of microorganisms.

“The analyses consist of characterizing the whole microbial community of the lake,” says Tran. “We study their distribution patterns and abundances and use their genomes to identify their roles in carbon, nitrogen, and sulfur cycling.”

ANANTHARAMAN’S WORK — from hydrothermal vents to the human gut — hit a speed bump when the coronavirus pandemic closed labs in early 2020. While about half of what


the lab does is computational and could continue remotely, the other half is experimental. There was little warning before labs were shuttered, and the bacteria and viruses Anantharaman’s team was growing slowly died off.

“There was a time where we completely shut down experiments, and that affected us very badly,” says Anantharaman. “It took us a good two months to get those experiments up and running again. Similarly, our collaborators were affected, and they had to prioritize their work.”

Even in late 2020, graduate students were only allowed to be in the lab for 20 hours per week, a less-than-ideal schedule for students trying to stay on top of coursework, conduct experiments, and calculate results.

What drives Anantharaman is knowing that full-scale and full-time research will return, as will trips to the bottom of the sea. He has National Science Foundation funding for another ride with Alvin in the spring of 2022. His team will conduct 18 submarine dives in collaboration with **Samantha Joye** of the University of Georgia and **Roland Hatzenpichler** from Montana State University.

“Unfortunately, on my previous trips, my graduate students could not go because they were taking classes,” Anantharaman says. “I’d definitely love to take my graduate students and postdocs on future trips.”

Such a trip would be a once-in-a-lifetime chance for those graduate students: a chance to see the source of the samples they work with for hours in the lab, to witness the depths of the ocean where sulfur is cycling, and, on the way down, to take in a stellar lightshow seen nowhere else on earth. 



Hot sulfur and metal-rich hydrothermal fluids gush out from a hydrothermal vent. The area that looks like black smoke (where some observers have seen a “face”) consists of precipitating minerals.

PHOTO BY SCHMIDT OCEAN INSTITUTE

in the Field

Vigilant Eyes on COVID-19

Animal science alum Chris Salm has co-founded a testing service for organizations looking to continue safe operations during the coronavirus pandemic

In late March 2020, COVID-19 struck Wisconsin's Brown County. The virus hit workers in the area's meat industry especially hard. But Salm Partners, a Denmark, Wisconsin-based meat-packing company that is focused on pre-cooked, ready-to-eat sausage and hot dog products, managed to avoid an outbreak among its team members.

Initially, Salm's suggestion was met with skepticism — the logistics seemed too overwhelming to some. Nevertheless, Salm forged ahead. Four days later, he oversaw the construction of a mobile sampling trailer. About two weeks after that, Salm Partners began testing all of its team members.

That was the beginning of CoVigilance, with Eric Salm as its new CEO.

Eric had a little help from his father, **Chris Salm BS'75**, who happens to be one of the founders of Salm Partners. Thanks to Chris's skills in forming partnerships as president of CoVigilance, the new company quickly gained traction.

"I'm just a facilitator of connections," says Chris. "Because people know Salm Partners and know our story, we've had calls from a lot of companies."

CoVigilance has completed multiple rounds of testing for Salm Partners' entire 600-person workforce and now administers testing for half a dozen other companies, each with multiple testing locations. They also work with eight Wisconsin college campuses and, beginning in the spring 2021 semester, helped facilitate a new testing approach at UW–Madison.

"It's grown rapidly," says CoVigilance COO **Jeff Grider**, adding that their reach extends beyond Wisconsin to Virginia, Minnesota, Iowa, Oklahoma, and California.

One of the objectives of CoVigilance is to make people feel as safe as possible at work. And after the third round of testing directed by CoVigilance, that feeling returned to Salm Partners, says Chris Salm. No one was calling in to say that they felt unsafe at work. "They look forward to it, they look forward to getting the results," he says, "and to knowing that they are safer at work than they might be in the community."

That's the end goal for every organization that partners with CoVigilance, says Grider — finding a way to support people who want to continue to work or attend class safely through the pandemic.

And the company is eyeing expansion in the future, if it's needed. Says Chris Salm, "Our goal is to serve the world."

—JORI SKALITZKY BS'22



CoVigilance president and CALS alum Chris Salm is pictured near one of his company's COVID-19 testing trailers, which is stationed next to UW–Madison's WARF Building.

PHOTO BY MICHAEL P. KING

Unfortunately, some news coverage of the county's outbreak lumped in Salm Partners with affected meat industry businesses. It left the company's leadership scrambling for a way to counteract negative media attention and reassure the public. For **Eric Salm**, a longtime associate of the company with a vested familial interest in its success, the solution was simple: regular testing of the company's entire workforce.



PHOTO BY KELLY BURGESS

How to Neutralize a Virus

Laura Walker creates antibody treatments for COVID-19 — and beyond

In the fight against COVID-19, public attention has largely focused on vaccines. But researchers around the world have been racing to find treatments, too. One treatment option is the use of monoclonal antibodies, laboratory-designed proteins that create an efficient and powerful virus combatant.

As the chief scientific officer at biotech company Adagio Therapeutics, **Laura Walker** BS'07 helped develop a monoclonal antibody for the new coronavirus. "The treatment works against the current version of the virus but also the other viruses in the family that are out there now — and could be in the future," she says.

Walker's interest in science is perhaps genetic. Her father was a professor of neuroscience at Brown University. But when she decided to major in biology or chemistry, he encouraged her to look at big state schools "with lots of funding for science," she says.

Eventually, she chose UW–Madison, where she pursued a biochemistry degree at CALS. She followed up with a Ph.D. from The Scripps Research Institute and a postdoc at the University of California, San Francisco.

Her post-baccalaureate work focused on antibody response to viral pathogens. That led her to an antibody discovery

company called Adimab, which she describes as doing "academic research in an industry setting." Adimab recently launched Adagio Therapeutics to manufacture monoclonal antibodies, and they put Walker in charge of its scientific operations.

"[Walker] has the ability to distill down large volumes of complex information and to know what important questions remain to be answered," says Adimab chief scientific officer **Eric Krauland**. "You'll oftentimes see scientists that are more 'thinker' and others that are more 'doer.' Laura is a rare combination of both."

To develop monoclonal antibodies for the new coronavirus, Walker and her team worked with a blood sample from a survivor of severe acute respiratory syndrome coronavirus (SARS-CoV), which was responsible for a global epidemic in 2002-04. It's a suitable place to start because 80% of the protein spike of the SARS-CoV virus is the same as that of the new coronavirus (SARS-CoV-2) that causes COVID-19.

Antibodies from the SARS-CoV survivor were "broadly neutralizing, but their potency was modest" against COVID-19, Walker says. They sampled every amino acid at every position across the antibody gene to see if they could

manipulate it to work better. Eventually, they devised a monoclonal antibody that is 100 times more effective at neutralizing COVID-19.

The practical use of the antibody will depend on how many people choose to be vaccinated for COVID-19 and how well the vaccines perform. If vaccines only provide protection for a year or don't work well for certain populations, such as the elderly or immunosuppressed, then the antibody could become a competitive option, Walker says. The antibody could also be used as a prophylactic if administered to someone who is not vaccinated but has a known exposure. And it may be needed if the virus mutates beyond the powers of the vaccines or a similar virus emerges from animals again in the future.

"We already know there are many different SARS-related viruses circulating in bat reservoirs; it's only a matter of time before we see the next one," Walker says. "Having a broad-spectrum antibody in our toolbox will be important to help mitigate the next coronavirus outbreak."

—JEN A. MILLER

Laura Walker, pictured above, is chief scientific officer at Adagio Therapeutics, where she led the development of a monoclonal antibody treatment for the coronavirus.



(CLOCKWISE FROM TOP) PHOTO BY MARTIN SANCHEZ ON UNSPLASH; COURTESY OF STUDENT RESEARCHERS; BY MICHAEL P. KING; COURTESY OF THE LAND PROJECT

New Major Improves Student Prep for Global Health Field

The past year has shone an intense spotlight on public health efforts all over the world. Their complexity, their interconnectedness, and their importance have never been more apparent as they have been during a global pandemic.

It's timely, then, that UW–Madison is launching a new global health major. It's an expansion of the existing global health certificate for students who want more depth and background to help them make a greater impact in the field.

"The value of any global health training lies in the way it forces us to think about the day-to-day experiences of other people and to face the extreme inequities that still exist in disease incidence and other threats to good health, regardless of whether it's looking at communities across the ocean or in our own backyard," says entomology professor **Susan Paskewitz**, who helped create the new major. "There's an emphasis on empathy, on cultural awareness and humility, and on collaborative efforts to improve health at the population level."

The new global health major is both a bioscience and public health major. Students study human health and well-being through population-level and world health perspectives. They explore how human health intersects with climate change, food systems, disease ecology, environmental health, economic development, health care access, and other interconnected systems.

"It's a really broad field, so the major is designed to help students find their passion area and go deeper into what they

care about most," says **Todd Courtenay**, lead advisor for the major.

Housed in CALS, the major will help prepare students for a wide variety of careers. Students can go on to become health care professionals with a deep appreciation for the large, complex systems that impact the health of their patients. They can become epidemiologists or research scientists in academia or with government agencies, such as the U.S. Centers for Disease Control and Prevention. Graduates with the major can also take on roles as community health professionals who work on policy, education, or communication with a wide variety of organizations locally, nationally, or internationally.

"Science is something I've always known my career would center around, but I didn't quite know how to combine it with my love for travel and languages," says **Zari Dehdashti**, a junior global health major. "Global health opens so many doors in realms that include these interests."

UW–Madison students have already shown a strong interest in global health. The 15-credit global health certificate, which has been available to all UW–Madison majors for more than a decade, is among the most popular on campus. Around 300 students earn one each year.

The major builds on this success and on student demand for deeper engagement. It requires 62 credits worth of fundamental courses, core courses, depth courses, foundational science courses, and a capstone. A new advising hub has been established to support students pursuing the new major and the certificate. And the curriculum has been designed to make it easy for students to switch from the certificate to the major, and vice versa.

After graduating, Dehdashti plans to spend a few years working in global health, return to school for a Ph.D. in epidemiology, and then seek an epidemiology position with a multinational organization.

"Something central to being a 'global citizen' is being willing to go out there and roll up your sleeves," says Dehdashti, "and that's exactly what I intend to do!"

—NICOLE MILLER MS'06

To make a gift in support of the global health major, visit supportuw.org/giveto/globalhealth or contact Henry Lagrimini at henry.lagrimini@supportuw.org or 608-308-5375.



DAY OF THE BADGER

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to support CALS students.

On April 6-7 2021, we will direct all gifts to the college to CALS QuickStart. This “early start” program helps incoming first-year students get a summer jump on their UW–Madison coursework, reduce their time to graduation, and join a supportive cohort of fellow scholars.

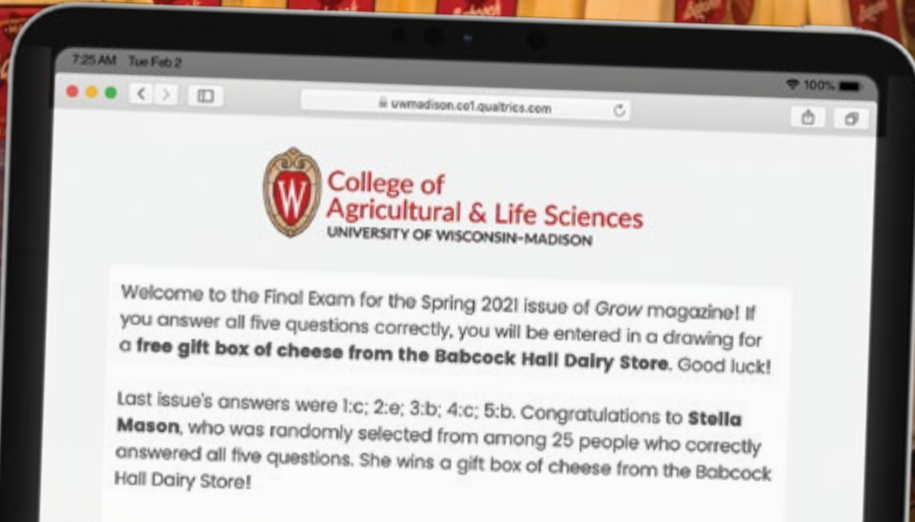
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A GROWING APPRECIATION

Undergraduates from F.H. King Students for Sustainable Agriculture pose after harvesting more than 300 pounds of fresh produce from their farm plot at Eagle Heights Community Garden in September 2020. The students later distributed the fresh bounty for free to nearly 100 people during a Harvest Handout outreach event.

PHOTO BY JEFF MILLER