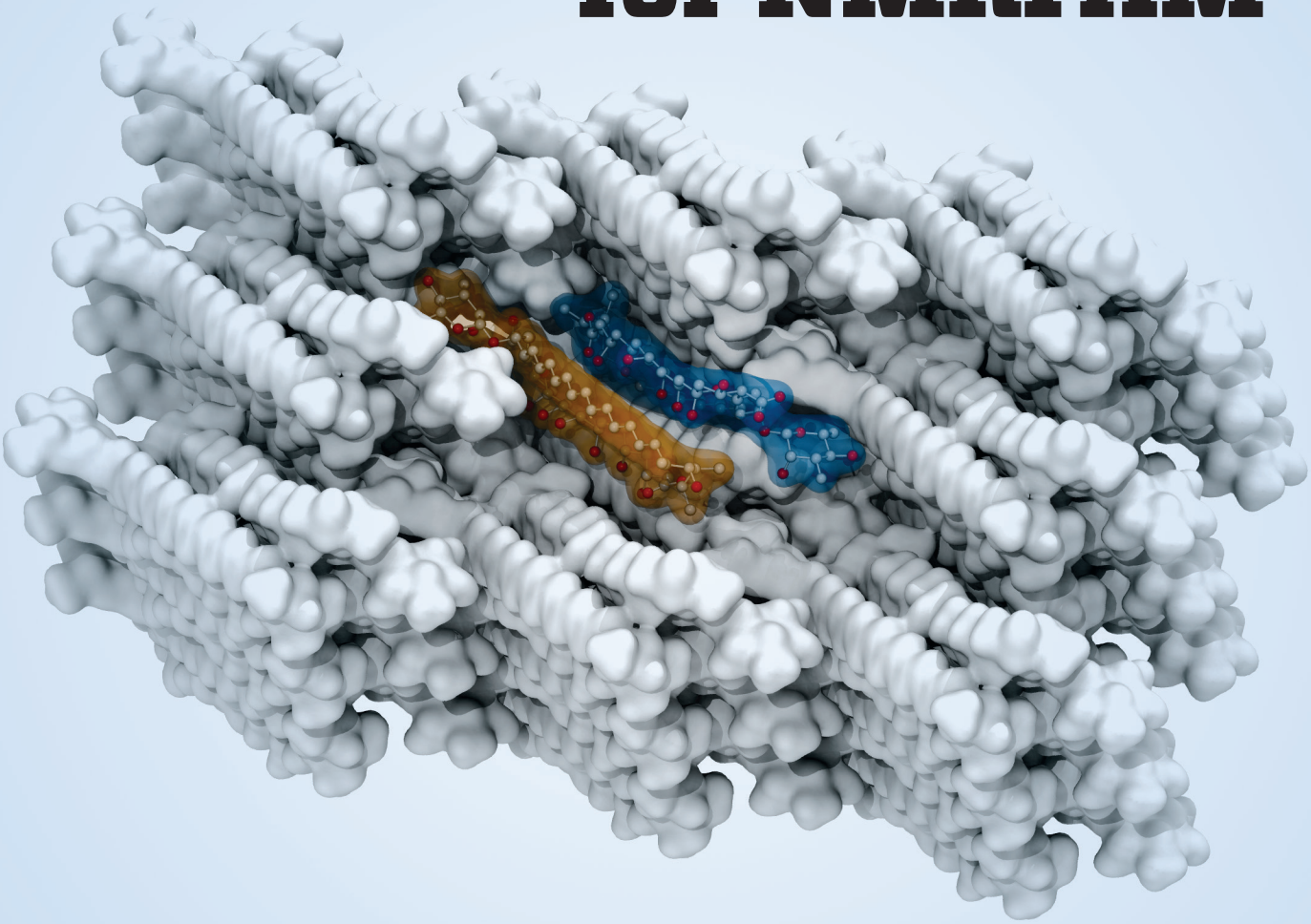
BIOCHEMISTRY *In Vivo*

Department of Biochemistry - College of Agricultural and Life Sciences - UW–Madison

2021 Education | Research | Innovation

For our alumni, supporters, and friends

A Banner Year for NMRFAM



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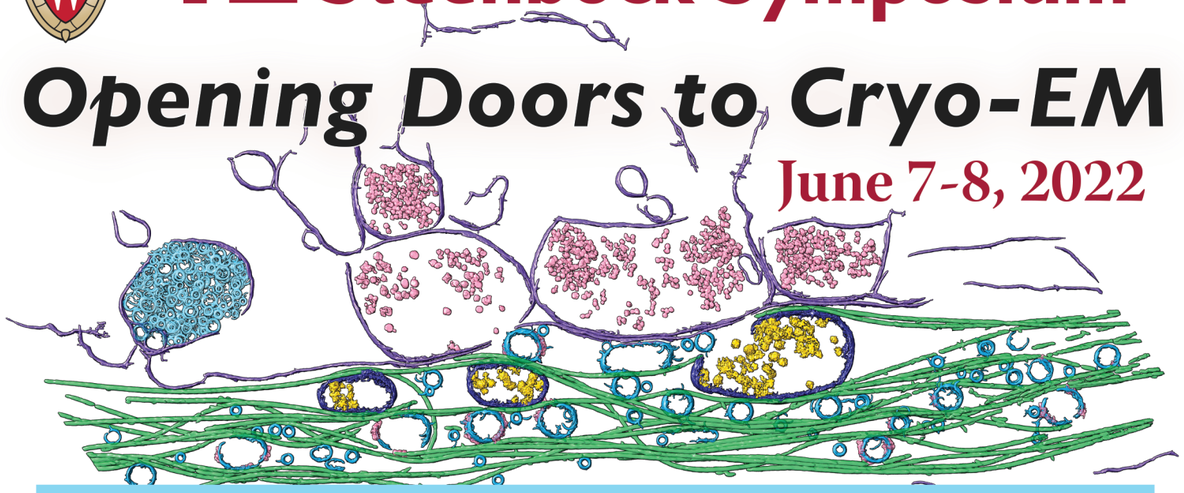
Special Feature on SARS-CoV-2
Faculty Profile Series
And more

42nd Steenbock Symposium

Opening Doors to Cryo-EM

June 7-8, 2022



Grand Opening of Two New Research Centers

biochem.wisc.edu/symposia/steenbock/42nd

Read more about the cryo-electron microscopy and cryo-electron tomography centers on pages 14-15.

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If you have questions or feedback for the department, please contact us!

Cover image:
Structure of Amphotericin B, an antifungal drug, as determined by nuclear magnetic resonance spectroscopy.
Story on p. 3.

Image courtesy of Chad Rienstra lab

From the Chair

Professor Brian G. Fox

The *Biochemistry In Vivo* newsletter keeps our community of researchers, students, alumni, supporters, and friends at UW–Madison and around the world up to date on happenings in the department. It is our sincere hope that you will find this newsletter engaging, enlightening, and inspiring. The 2021 edition is a presentation of achievements and continued success as we adapt to challenges and move forward on so many fronts.

This year's cover, titled *A Banner Year for NMRFAM*, celebrates the beginning of a new phase for NMR research in the department. Through the herculean efforts of Professors **Chad Rienstra** and **Katherine Henzler-Wildman**, NMRFAM was selected to be part of the NSF-funded Network for Advanced NMR (NAN), a Mid-Scale Research Infrastructure project and multi-institution effort to make advanced NMR instrumentation, analysis methods, and data sharing readily available to the broader scientific community. The NAN is led by Professor **Jeff Hoch** at the University of Connecticut, Professor **Arthur Edison** (Biophysics, PhD'93) from the University of Georgia, and Katherine and Chad here in Madison. Two additional NMR instruments have already been acquired for this national center in the past year, and the planning and renovations needed to bring a 1.1 GHz solid-state NMR instrument into NMRFAM are now well under way. On top of the effort needed to bring NAN to fruition, Chad and Katherine also secured highly competitive Program Project funds from the National Institute of General Medical Sciences to continue state-of-the-art research and development on the application of solid-state NMR to a breadth of biological problems. More information on these efforts is provided on p. 6-7. New NMR technology and methods are already being applied to research. The structure of antifungal Amphotericin B, featured on the cover, is just one example (story on p. 3).

Just three years ago, *Biochemistry In Vivo* introduced Professor **Elizabeth Wright**, who came to UW–Madison to lead our efforts in cryo-electron microscopy (cryo-EM). One year ago in October, remodeling of space in the DeLuca Biochemistry Building began. Work was completed on time by a remarkable collaboration between the department, **Megan McBride** from campus Facilities Planning & Management, and Project Engineer **Gabriel Neves** from C.G. Schmidt. This space will be home to the Midwest Center for Cryo-Electron Tomography (MCCET), an NIH-funded national center of research excellence. Two additional state-of-the-art cryo-EM systems are now being installed, and the grand opening of the center will be part of our Steenbock Symposium next year. Please read more information about the centers and the symposium on p. 14-15.

Also, signaling more to come, the Department of Biochemistry faculty generously elected to provide space to Professor **Josh Coon** from the School of Medicine and Public Health to house his NIH-funded national center on the application of mass spectrometry to biological research. With this move, the Department of Biochemistry will house three federally funded national centers of research excellence within 100 yards of one another. These are remarkable achievements accomplished in three short years for and by the department and its faculty, staff, and students. We hope to attract new worldwide talent to these outstanding programs and facilities.

We are pleased to provide

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From the Chair *Continued on next page*

a fascinating educational primer, coming from the research of Assistant Professor **Rob Kirchdoerfer**, Professor **Katherine Henzler-Wildman**, Professor **Chad Rienstra**, and Professor **Ann Palmenberg**, on the surface proteins of SARS-CoV-2, the virus that causes COVID-19 (p. 10-13). These are essential determinants of infectivity and immune system protection. At this point, an exceedingly high level of personnel in the department, including high school interns and undergraduate employees, are vaccinated against COVID-19.

In June, when the COVID-19 delta variant was mostly rumor and omicron had yet to evolve, Biochemistry and Biomolecular Chemistry sponsored an outdoor ice cream social where masks came off and people saw each other socially for perhaps the first time in over a year. Voices of greeting and elated conversation rang through the building courtyard where Elmer once stood. It was a beautiful sunny afternoon, and the Babcock Dairy Store ice cream went quickly.Although natural evolution has brought us new challenges (and will still), the people of the department have continued onward. We know that some have lost loved ones, and our sympathy for your losses pours through to you. Until the pandemic is over, please practice recommended personal hygiene, make safe choices in your daily activities, and continue to live and support those around you at work and at home.

This year, Assistant Professor **Amy Weeks** won the 2021 Packard Fellowship (p. 4). As chair, it was a great pleasure to conspire with the Packard Foundation to make a surprise announcement of this award to Amy, and to bring last year's award winner, Assistant Professor **Scott Coyle**, in on the congratulatory Zoom call. Yet another remarkable achievement, with a nod to Professor **Ann Palmenberg** for leading the department awards committee so effectively these past few years.

Assistant Professor **Tim Grant** won a Chan Zuckerberg Initiative award to continue his groundbreaking work in image analysis with emphasis on cryo-EM (p. 4), Associate Professor **Aaron Hoskins** was named a Vilas Associate (p. 16), and IPiB graduate student and Biotechnology Training Grant trainee Mr. **Edrees Rashan** was inducted into the Edward A. Bouchet Graduate Honor Society (p. 17). I am also most pleased to acknowledge the contributions of Professors **Michael Cox** and **James Ntambi** for their leadership in the American Society for Biochemistry and Molecular Biology (p. 16).

This newsletter contains other compelling stories highlighting the spirit of excellence that permeates the department. Assistant Professor **Judith Simcox** is discovering new biomarkers for metabolic disease with emphasis on underrepresented communities (p. 5). Assistant Professor **Jason Cantor** is showing at the molecular level how the adage "you are what you eat" may lend important new cellular insights for cancer research (p. 9). Assistant Professor **Ophelia Venturelli** has been modeling the microbial community found in a natural strain of maize from Central America that confers the property of nitrogen fixation (p. 8). And, code from a patent filed by Assistant Professor **Philip Romero** and coworkers **Bennett Bremer** and IPiB graduate student and Biotechnology Training Grant trainee **Jacob Rapp** graces the back cover. In distinct ways, these examples outline a bright, innovative, productive future for the department.

The department thrives on the diversity, skills and commitment of its members, alumni, supporters, and friends, and as outlined above, we are dedicated to excellence in all facets of our lives. If you can, please join us by becoming a donor to the Department of Biochemistry. Our need for your support in these challenging times is greater than ever, and so we request your consideration of generosity in three areas: named fellowships for support of students across all genders, ethnicities and need levels; named professorships to support the innovative work of the faculty; and, named opportunities to support our nationally recognized facilities. A highlight on biochemistry alum **Daniel Klessig**, BS'71, on p. 15 provides a great example of how generosity combined with insight can provide impact.

If you are so inclined, please contact us, or the University of Wisconsin Foundation, about your interests in supporting a bright future for the department. Contact details for the department can be found at the front of this newsletter, and details for the Foundation on p. 31. We encourage all of you to interact with us, and we look forward to receiving your comments, advice, and referrals as we continue to affirm our commitment to excellence. Also let us know if there is something you would like to see featured in future editions of the newsletter.

Mostly, we hope you are able to be safe in the year ahead and look forward to hearing from you.

Scientists Pinpoint Structure of Antifungal, Challenge Binding Mechanism

Nearly seventy years after the discovery of Amphotericin B, scientists are still learning from this enigmatic drug. UW–Madison scientists, in collaboration with scientists at the University of Illinois at Urbana-Champaign and the National Institutes of Health, applied innovative nuclear magnetic resonance techniques to reveal the structure of Amphotericin B as it's about to bind to ergosterol. Their results challenge a long-standing paradigm for the drug's mechanism of action and suggest new avenues for drug development.

Professor Chad Rienstra

Reliable yet potent

Amphotericin B, or AmB for short, is powerful and reliable. Used to treat many different types of infections, its broad-spectrum activity saves lives by obliterating serious fungal infections that can't be diagnosed quickly.

One of the reasons AmB is so effective is also, paradoxically, why it can be toxic. It can bind to ergosterol, a major component of fungal membranes, as well as cholesterol, a component of human cell membranes. When AmB binds to ergosterol, it stops fungal infections in their tracks. When it binds to cholesterol, though, AmB can target cholesterol-containing membranes, wreaking havoc on those cells. AmB is so potent that while doctors have adapted to minimize toxicities associated with the drug, up to 80% of patients receiving AmB will still experience side effects such as fevers or kidney failure.

This year, a team led by biochemistry professor and Morgridge Institute for Research investigator Chad Rienstra elucidated the structure of Amphotericin B as it prepares to bind to a sterol like ergosterol or cholesterol. This work comes out of a longstanding collaboration with Martin Burke and Taras Pogorelov, professors at the University of Illinois at Urbana-Champaign. The scientists' results, which were published in *Nature Structural & Molecular Biology*, call into question AmB's mechanism of action.

"Our findings show that Amphotericin doesn't exist as a single molecule that binds to a single spot in a fungal cell membrane [as previously thought] — it works in a collective manner, forming 'sponges' of many Amphotericin molecules that work together like a team to absorb sterol," Rienstra says.

The research team's results also provide evidence about why fungi find AmB so hard to evade. If a fungus wants to bypass Amphotericin B, it needs to evolve to work with a sterol other than ergosterol. And that requires time the fungus just doesn't have when AmB is around.

Innovations in NMR

AmB poses a challenge for standard nuclear magnetic resonance (NMR) spectroscopy. When an AmB sample is placed in a magnetic field and excited into nuclear magnetic resonance by radio waves, the signals emitted by the AmB nuclei are messier than scientists would like. The result is that spectra of AmB, in its sponge-like lattice, have multiple sets of overlapping peaks that are hard to tease apart.

Rienstra's team needed to make major modifications to their NMR methods if they were to build the structure of Amphotericin B.

The scientists altered their sample preparation techniques and NMR sequences to make it easier to identify each peak. They conducted additional NMR experiments at the National Magnetic Resonance Facility at Madison (NMRFAM) to figure out which sets of peaks were connected. And through their collaboration with the NIH, they also modified the computational models that calculate structures of molecules from spectroscopic data.

Says Rienstra, "We wanted to know how the AmB sponge fits together to accommodate ergosterol. Just like sponges that absorb water, if it's dried out and crusty, it doesn't move well and won't do a very good job of absorbing sterols. Once it's a little soft, it does a better job of absorbing because then it's flexible."

Ultimately, the Rienstra Lab discovered that their data were consistent with multiple forms of AmB sponges, suggesting that AmB has some sort of inherent flexibility that may be essential for binding sterols. For example, pockets in AmB sponges are irregular, but molecules appear to shift to make room for ergosterol.

With this new knowledge about AmB's binding structure and eager to develop less toxic versions of AmB, Rienstra's lab and NMRFAM are developing technologies to help them get there. Rienstra says that higher field magnets and new types of NMR probes that can look at samples that behave like AmB but which can only be procured in smaller amounts will be essential to this work. "This project is a really nice synergy between technology development and application, because as we develop higher field instruments that are more sensitive, we can use smaller quantities of samples," he says. "That will open up opportunities for studying many other categories, or the sort of 'extended family,' of Amphotericin."

Original story by Catherine Steffel, Ph.D., Biochemistry

Professor Amy Weeks

Assistant Professor Amy Weeks Named Packard Fellow

Amy Weeks, a biochemistry assistant professor, was selected as a Packard Fellow for Science and Engineering.

The fellowship is awarded annually to early-career scientists from across the United States and provides $875,000 of funding over five years. Since 1988, the fellowships have supported the scientists and engineers whose research over time has led to new discoveries that improve people's lives and enhance our understanding of the universe. Amy Weeks is one of 20 members chosen for the 2021 class and is UW–Madison's 17th Packard Fellowship winner.

"Packard Fellows are at the cutting edge of research into crucial issues and have gone on to receive the highest accolades," says Brian Fox, associate vice chancellor for research policy and integrity and the chair of the Department of Biochemistry. "Amy takes a creative approach to her research and thinks big."

Packard Fellows are indeed encouraged to think big and look at complex issues with a fresh perspective. For Weeks, this thinking means organizing her research around a grand challenge in biology: assigning functions to the hundreds of thousands of modifications that occur in human cells to the proteins the cells produce from mRNA. Her research group draws from diverse disciplines, including protein engineering, chemical biology, cell biology and proteomics, using a host of different tools and technologies.

"If we can do this, I think it will be really powerful in different areas of both fundamental biology and also medicine," Weeks says. "When graduate students come into my office and are interested in joining the lab, the main pieces of advice I give them are to be curious and to be willing to learn. You don't have to come in knowing everything, but you have to be willing to try to figure it out."

Weeks came to UW–Madison in 2019 and set up her lab just six months before the COVID-19 pandemic forced much of campus to go online. "The Packard Fellowship award is exciting and it is a real relief right now to have some extramural funding for my research that will support my lab going forward," she says.

Original story by Natasha Kassulke, OVCRGE
(Office of the Vice Chancellor for Research and Graduate Education)

Chan Zuckerberg Initiative Project to Enable High-Resolution Mapping of Molecules within Cells

New and emerging tools such as cryo-electron microscopy (cryo-EM) give scientists a way to define the structures of molecules at high resolution. But identifying exactly where these molecules reside within an ocean of structures inside a cell — and exactly how they interact with their neighbors — remains unknown.

Biochemistry assistant professor and Morgridge Institute for Research investigator Timothy "Tim" Grant is part of a new project supported by the Chan Zuckerberg Initiative that hopes to create a three-dimensional map that aligns these molecules in their proper neighborhoods within a cell.

Grant is partnering on the $1.3 million project with scientists Nikolaus Grigorieff, a professor of RNA therapeutics at the University of Massachusetts Medical School, and Bronwyn Ayla Lucas, a postdoctoral fellow in the Grigorieff Lab.

Professor Timothy Grant

The group is using an innovation called high-resolution template matching, a computational approach that takes existing known structures of molecules and finds their most likely matches within cryo-EM images of a cell.

"What's really useful is you can see things that are commonly located next to each other, and so likely interacting," Grant says. "They could be part of a pathway, for example. This should give us an idea of how systems actually function within living cells."

The grant is part of the Chan Zuckerberg Initiative's visual proteomics focus area. Being able to view protein molecules within cells opens a new frontier in medicine that can help determine the origins of cellular diseases and what treatments might be most effective.

Original story by Brian Mattmiller, Morgridge Institute for Research

Developing Equitable Biomarkers for Diagnosing Metabolic Syndrome

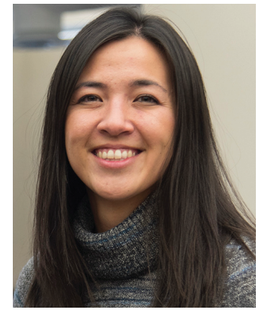
Diabetes disproportionately impacts underrepresented minorities, who have a higher prevalence of diagnosis and complication rates of diabetes compared to white individuals. Despite this, the prevalence of metabolic syndrome — the proportion of a population that at any given time has a group of five conditions that can lead to health problems like heart disease and diabetes — is similar across races. Why?

"Traditional health markers for metabolic syndrome — high blood glucose, low levels of HDL which is known as the "good" cholesterol, a high body mass index, high levels of LDL which is known as the "bad" cholesterol, and elevated triglycerides — were developed from studies including only men of Western European descent," says biochemistry assistant professor Judith "Judi" Simcox. "But what works for them doesn't work for others."

For example, a woman's body mass index (BMI) isn't indicative of whether she is likely to develop metabolic disease, and correlations between HDL, blood pressure and metabolic syndrome don't hold for African Americans. Scientists need to identify and develop more equitable biomarkers for metabolic syndrome, Simcox says. Then, new interventions to prevent and treat diabetes that work for more people can be developed.

Simcox's research will identify and classify previously unstudied lipids to determine whether these could be possible biomarkers for metabolic disease in women and underrepresented minorities. Lipids are a class of biomolecules with a diverse array of functions essential for life, and scientists have yet to characterize thousands of lipids that appear in biological samples obtained from humans.

In a recent study, Simcox and students in her lab took plasma samples from individuals participating in two longitudinal studies based at UW–Madison and processed the samples using mass spectrometry, a technique that measures the mass-to-charge ratio of ions to identify and quantify molecules in samples. The scientists identified 529 lipids in Caucasians and 137 in African Americans that might inform diagnoses of metabolic syndrome, and over 100 lipids that overlapped between the two groups of people. Further analysis identified 76 lipids that predict metabolic syndrome and that could help diagnose metabolic syndrome in Black women.



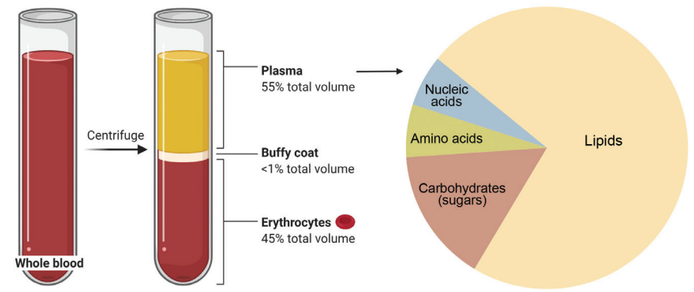
Professor Judith Simcox

These findings have opened new lines of investigation for Simcox and her team. Their next steps will be to learn more about the lipids they identified: can they be clinically measured? What cells or tissues are producing the lipids, and how are they circulating throughout the body? Are these lipids precursors to inflammation, and could an inflammatory panel be used as a biomarker for metabolic syndrome?

"One of the great things about UW–Madison is that it is the head of giant longitudinal population studies like the Midlife in the United States study and the Survey of the Health of Wisconsin, so we can perform studies like this one," Simcox says.

Simcox and her collaborators may soon be able to explore their questions on an even larger scale and with more collaborators. Last year, Simcox and Dudley Lamming, a professor in the Department of Medicine, received a UW2020: WARF Discovery Initiative Award. Since then, they have established and staffed research facilities and funded twelve pilot projects like Simcox's to bolster innovative research in diabetes, obesity and metabolism. These projects will help advance diabetes research and support a new Comprehensive Diabetes Center at UW–Madison.

Original story by Catherine Steffel, Ph.D., Biochemistry



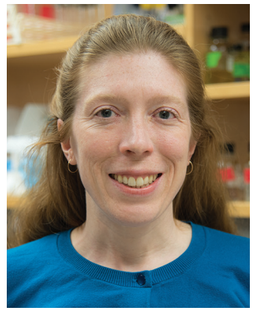
A large fraction of the plasma metabolite pool is lipids.
Image courtesy of Judith Simcox

Grants to NMRFAM Support User Access, Help Pioneer New Methods

Professors Katherine Henzler-Wildman and Chad Rienstra, co-directors of the National Magnetic Resonance Facility at Madison (NMRFAM), were awarded two pivotal grants from the National Institutes of Health.

The first grant, a P41, will provide the facility with $6.5 million over five years to pioneer new methods for solid-state nuclear magnetic resonance (NMR) spectroscopy, a tool that can be used to determine the chemical composition, local structure and dynamic properties of solids. With this grant, Henzler-Wildman, Rienstra and NMRFAM scientists will focus on NMR development in three areas: sample preparation, instrumentation, and algorithms and software. Advances in sample preparation will bridge gaps in structural biology research and improve our understanding of how essential membrane proteins function, while fundamental algorithms and software will be automated.

Substantial progress has already been made on advancing solid-state NMR instrumentation. NMRFAM installed a 750 MHz magnet that will contribute to the continuing development of NMR technology at NMRFAM for the next two to three decades. This wide-bore magnet operates at about 350,000 times the strength of Earth's magnetic field and will help scientists develop new technologies such as probes that can operate at four or five NMR frequencies simultaneously, and pulse sequences and receivers that provide improved resolution and sensitivity.



Professor Katherine Henzler-Wildman

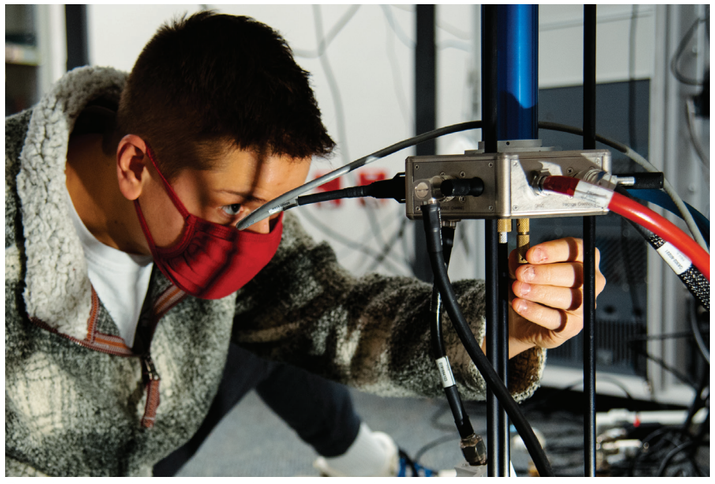
Professor Chad Rienstra

The magnet and custom probes have already enabled researchers to solve structures implicated in Parkinson's disease in a collaboration with biochemistry assistant professor Timothy Grant, who is developing computational tools to utilize NMR structural information alongside cryo-electron microscopy (cryo-EM) and cryo-electron tomography (cryo-ET). The new magnet was also used to study the antifungal drug Amphotericin B (see p. 3).

"This unique opportunity at the interface of cryo-EM and NMR is something that our department and campus are especially well-equipped to pursue," Rienstra says. "We have now one of the only — perhaps the only — sites in North America where such state-of-the-art capabilities in cryo-EM, cryo-ET, solution NMR and solid-state NMR are all in the same department."

The second grant is an R24 award that will help NMRFAM maintain and excel in the services it provides to scientists and other users, such as facilitating experiments that scientists may not be able to perform at their home institutions.

"This award will support continued implementation of state-of-the-art methods into our established solution NMR user program so that users have access to the latest technology," says Henzler-Wildman. "It will also enable us to expand our user program to include solid-state NMR methods that will be of interest to scientists studying membrane proteins, fibrils and other complex biological materials."



Ben Harding, a biophysics graduate student who works in Rienstra's lab, inserts a probe into the new 750 MHz magnet.

Story by
Catherine Steffel, Ph.D., Biochemistry

Original P41 story Original R24 Story

NSF Award Establishes Network for Advanced NMR

This year, the National Science Foundation announced a $40 million award to establish the Network for Advanced NMR (NAN) linking three institutions: UConn School of Medicine, the University of Georgia and UW–Madison's National Magnetic Resonance Facility at Madison (NMRFAM). Professors Katherine Henzler-Wildman and Chad Rienstra, co-directors of NMRFAM, will lead the installation at UW–Madison of the first of two new NMR spectrometers planned for NAN, the first of their advanced 1.1 GHz type in the United States available for shared used. The UW–Madison scientists and their colleagues throughout the network will organize NAN to help scientists tap the shared NMR technology and make results available to other researchers.

The diversity of applications and techniques in NMR is both a strength and a challenge. NMR can describe the structure and interaction of complex molecules by using magnetic fields to measure the orientation of the nuclei in the molecules' atoms. NMR technology can be applied to elucidate interactions between drugs and drug targets, aid in the search for new antibiotics and more. As such, NMR is generally limited to experts who can manipulate the technology and raw and processed data, but NAN intends to make NMR more accessible.

"We have a responsibility to be good stewards of the instruments as well as of the data that's obtained with the instruments," says Rienstra.

Instruments incorporated into NAN will automatically archive raw data, linking it to information about the sample, experiment and more to make it findable, interoperable and reusable. The project will also help develop a knowledge base to share fundamental information often absent from scientific literature.

"It's [this type of information] not written down because the experts already know it," says Henzler-Wildman. "Knowledge bases will help users figure out which experiment is most appropriate to get the data they need, how likely it is to work for their particular sample, what kind of information they can get out of an NMR experiment, and how that can help solve their problem. Knowledge bases provide translations so we can bring outside users in and make the whole field more accessible."

NAN will also further NMRFAM's role in pioneering techniques and commissioning state-of-the-art equipment to expand its broad user base.

NAN's three partner facilities have a combined 50 years of operational experience, space, infrastructure and strong institutional support. UConn will be responsible for managing data stewardship and developing new technologies for consolidating, organizing, annotating, sharing and archiving NMR data. Georgia will house a second 1.1 GHz NMR spectrometer as well as small molecules for metabolomics and drug screening. The NSF funding comes from the agency's Mid-scale RI-2 Program, part of NSF's set of "Big Ideas" unveiled in 2016: ten long-term research and process ideas that identify areas of investment at the frontiers of science and engineering.

Once instrument installation and network connection are complete, an open call for membership by shared NMR facilities will be issued, further expanding the reach of NMR projects and technology.

Original story by Sarah Lynn Traver Saunders, Biochemistry

Professors Chad Rienstra and Katherine Henzler-Wildman

Crop Harvests and Bacterial Blends

Drive down Wisconsin's county roads on a crisp fall day and you'll see farmers maneuvering combines across their fields, harvesting bushels upon bushels of corn. Farmers help ensure a bountiful harvest by applying fertilizers that provide crops with nutrients.

One such nutrient, nitrogen, makes individual plants stronger and improves crop yields. Until the mid-1900s, farmers turned to animal manure and legumes to provide crops with this essential nutrient, but the adoption of synthetic fertilizers by industrial agriculture in the 1950s changed the game. Though they've increased food production worldwide, these fertilizers are often applied in excess of what plants require, leading to surface and groundwater contamination and other environmental issues.

Meanwhile, UW–Madison scientists have been studying nitrogen fixation — the process by which atmospheric nitrogen is converted into a form useable by plants — and looking for alternatives that might help reduce applications of synthetic fertilizers from another angle. In 2018, bacteriology and agronomy professor Jean-Michel Ané and his collaborators identified another potential game-changer for industrial agriculture in the form of a variety of corn from Mexico. The corn uses a viscous and slime-like gel to host bacteria that fix nitrogen on aerial roots, clumps of roots that protrude from the plant's stalks. Indigenous Oaxacan communities, recognizing that this gel helped their plants thrive in poor soils, have actively grown and selected this corn in their fields for centuries. But for the academic community, it was the first time that they had observed a variety of corn that could acquire a significant amount of nitrogen from the air by partnering with bacteria.

Professor Ophelia Venturelli

Since then, Ané and his team have identified and performed experiments in other plants, like sorghum, that also fix nitrogen in this way. Their preliminary tests suggest that approximately 10% of bacteria in the gels help these varieties of corn and sorghum fix 30% to 80% of their nitrogen; the function of the remaining bacteria remains unknown.

Now UW–Madison scientists want to see if they can harness the bacteria to help cereal crops like corn and sorghum fix nitrogen longer and more efficiently.

For this project, Ané has teamed up with assistant professor of biochemistry Ophelia Venturelli. Venturelli models bacteria and other microbial communities on computers and then moves to the lab, where she creates communities in the lab to study how they interact and how those interactions lead to community-level behaviors, such as the production and degradation of compounds that influence plant phenotypes.

"These microbial communities are complex, highly dynamic networks that respond to their environment. They have a collective behavior that's more than the sum of their parts," says Venturelli.

So far, the team has isolated bacteria from the gels of corn and sorghum plants. Ané is studying the basic properties of each bacterium and identifying which ones to use in a representative synthetic community. A postdoctoral researcher in the Venturelli Lab, Claire Palmer, will create and study this representative community in the lab and improve its ability to fix nitrogen using computational modeling. The models help the team identify which microbes and microbe-microbe interactions play a critical role in nitrogen fixation.

"There's such a big space of how many random combinations you can put together, that the model is much more efficient at getting us there," Venturelli explains.

Using the results of their models, Palmer and Venturelli will introduce different diazotrophs — bacteria that fix atmospheric nitrogen gas into a more usable form — into the community. They'll observe how the microbes within the community affect the diazotrophs' growth and nitrogen-fixing behavior and then model these interactions. Then, microbial blends will be applied to cross-bred plants and to native varieties that rely on gels and aerial roots for nitrogen fixation. If all goes well, farmers may witness another shift in the field of fertilizers — one toward gel-based sources of nitrogen.

Gel exudes from the aerial roots of a special nitrogen-fixing corn variety growing at West Madison Agricultural Research Station.

Photo: Michael P. King

Original story by Catherine Steffel, Ph.D., Biochemistry

The (Cell) Medium is the Message: Studying Cell Biology in a Dish

When communications scholar Marshall McLuhan coined the famous phrase "the medium is the message" in the 1960s, he was saying that our understanding of an idea will be shaped by how we receive it — whether it's conveyed through a book, a lecture, a movie or a song.

Biochemistry assistant professor and Morgridge Institute for Research investigator Jason Cantor has an interesting equivalent for researchers: The medium used to grow cells in a lab has a similarly profound impact on the "message" cells receive on how to grow and respond. This is the concept behind Cantor's innovation of a new cell culture medium — a biological research tool that since the 1950s has been as ubiquitous in labs as microscopes and pipettes.

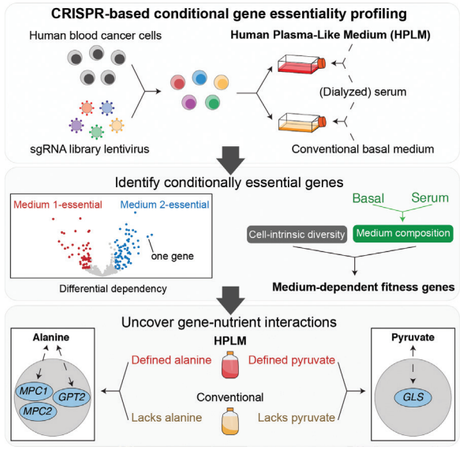
Not long into his postdoc, Cantor had posed a deceptively basic question: How closely do classic cell culture media reflect biochemical conditions in the human body? The answer: Not too well. This question ultimately led to the development of Human Plasma-Like Medium (HPLM), a physiologic medium that more closely reflects the metabolic composition of human blood. HPLM contains more than 60 components at concentrations that reflect average values reported in human blood. This innovation in cell culture media design was a long time coming, as the formulations for these reagents haven't changed much since Johns Hopkins physician Harry Eagle developed "Minimal Essential Medium" in 1955.

Professor Jason Cantor

Cantor reported the design and initial studies using HPLM in *Cell* in 2017 while a postdoc at the Whitehead Institute/MIT. Since that initial publication, HPLM has generated a great deal of interest from biologists across the scientific community.

Now Cantor's laboratory is taking HPLM to the next level. Thanks to a commercialization agreement with Thermo Fisher Scientific, Cantor and his laboratory at UW–Madison no longer need to continue their simultaneous role as "kitchen." In March 2021, Thermo Fisher announced the wide-scale availability of HPLM for the scientific community. "It's exciting to see this go from publication a few years back to now officially bringing a product to market," Cantor says. "And it should be pretty exciting to see what others discover with HPLM, as well."

In a paper published earlier this year in *Cell Metabolism*, the Cantor Lab, together with colleagues at Whitehead Institute, also used HPLM to show that medium composition can have a profound impact on gene essentiality — in other words, the extent to which a gene contributes to cell fitness, which is a characteristic critical to many human diseases.



Most forward genetic screens in human cells are performed *in vitro* using media with little relevance to human physiology. Rossiter et al. reveal the profound impact of medium composition on gene essentiality by performing CRISPR screens of human cancer cells in conventional versus human plasma-like medium (HPLM).

Image courtesy of Jason Cantor

"The really core essential genes," says Nicholas Rossiter, a former technician in the Cantor Lab and lead author on the paper, "are almost universally important for growth across all human cell lines tested in any condition. When you knock them out, cells aren't going to grow." But by performing CRISPR-based screens of cancer cells in different media, the researchers identified conditionally essential genes, and in specific cases highlighted in follow-up work, trace such effects to the availability of components uniquely defined in HPLM (versus traditional media).

"This shows that there are aspects of the environment that we can tinker with to make a gene become more or less critical for cell growth. Certainly, there are also implications here in terms of how to potentially increase the fidelity of what we see in the lab and what might happen in the body," Cantor adds.

Such implications could be far-reaching. Use of HPLM may allow researchers to conduct experiments that are more directly relevant to human disease. If, for instance, scientists can alter the importance of a specific gene for cancer cell growth, then its encoded protein could become a more promising target for treatment. And smarter therapeutic approaches can be developed as researchers understand more about the target's response to various perturbations.

Original stories by Sarah Lynn Traver Saunders, Biochemistry and Brian Mattmiller, Morgridge Institute for Research

Unpacking SARS-CoV-2

Less than a year after he joined the Department of Biochemistry, Robert Kirchdoerfer BS'06 and his nascent coronavirus research program were thrust into the spotlight. The new assistant professor was quickly becoming known around the UW–Madison campus as "the coronavirus guy," a linchpin of efforts at the university to understand the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19.

Kirchdoerfer is an expert in using cryo-electron microscopy and other advanced techniques to characterize viral proteins and complexes. As a graduate student and then as a postdoctoral researcher at The Scripps Research Institute in Southern California, he was a member of one of the first teams to stabilize spike proteins, notoriously tricky proteins that rapidly change configurations to adopt a shape that's not relevant for recognition by antibodies. By keeping spike proteins in a single configuration, scientists could use cryo-electron microscopy (cryo-EM), an imaging technique used to visualize molecules on sub-nanometer scales, to study the spike protein's structure, investigate the transitions the protein takes to recognize host protein receptors, and design vaccines with it as an active ingredient.

Today at UW–Madison, Kirchdoerfer and his colleagues are studying the structures and functions of proteins and RNA synthesis complexes from SARS-CoV-2. Their research, which synthesizes expertise and results from several disciplines and state-of-the-art technologies, demonstrates just how much of the "life cycle" of SARS-CoV-2 remains to be discovered — every research study, every experiment, informs another, and lives hang in the balance.

Professor Robert Kirchdoerfer, right, explains the inner workings of the Talos Arctica cryo-electron microscopy (cryo-EM) system to Thomas Anderson, left, a cellular and molecular biology graduate student who works in Kirchdoerfer's lab.

Complementary Data

In spring 2020, scientists at the National Magnetic Resonance Facility at Madison (NMRFAM), a campus-wide and national facility housed in the biochemistry department, were looking for ways to contribute to the fight against COVID-19. Nuclear magnetic resonance (NMR) spectroscopy could complement Kirchdoerfer's cryo-EM research, said biochemistry professor and NMRFAM co-director Katherine Henzler-Wildman, by providing new insights into parts of the virus that are too small to study individually with cryo-EM.

Henzler-Wildman and her NMRFAM co-director, biochemistry professor Chad Rienstra, decided to study the membrane protein and two nonstructural proteins, nsp7 and nsp8, as part of an international consortium called the COVID19-NMR Project. Improved knowledge of nonstructural proteins, parts of the RNA synthesis machinery responsible for replicating and transcribing the viral genome after a virus infects a host cell, can lead to antiviral drugs that halt a virus' replication process.

The scientists' NMR experiments, performed using protein produced by Kirchdoerfer's lab, confirmed that SARS-CoV-2 nsp7 is spectroscopically and structurally similar to the nsp7 in the original SARS virus, SARS-CoV. In an ideal world, their studies on nsp8 and the membrane protein would also be straightforward. But that isn't how research often progresses.

"We can't say much more right now, but our results for nsp8 aren't what we expected," remarks Henzler-Wildman. "We thought that nsp8, which joins with other nonstructural proteins like nsp7 to form the larger complexes necessary for replicating the virus' genetic material, would be dynamic with multiple conformations in solution. It actually has concentration-dependent oligomerization." Now, the scientists must consider a different set of potential dynamics, including what nsp8 does in solution and how it ends up in its various conformations.

The NMRFAM team faced a different challenge with the membrane protein: it had never been reliably produced in a laboratory. So, while scientists believe the protein plays an important role in viral "budding," a process viruses can use to exit host cells, the protein remains understudied — and, some experts say, underutilized — in the fight against COVID-19.

By fall 2021, the UW–Madison team was making significant progress at purifying the membrane protein and was pondering their next steps. Data they collect may be especially important: research being conducted nearby suggests that this protein may be an active ingredient in the next SARS-CoV-2 vaccine.

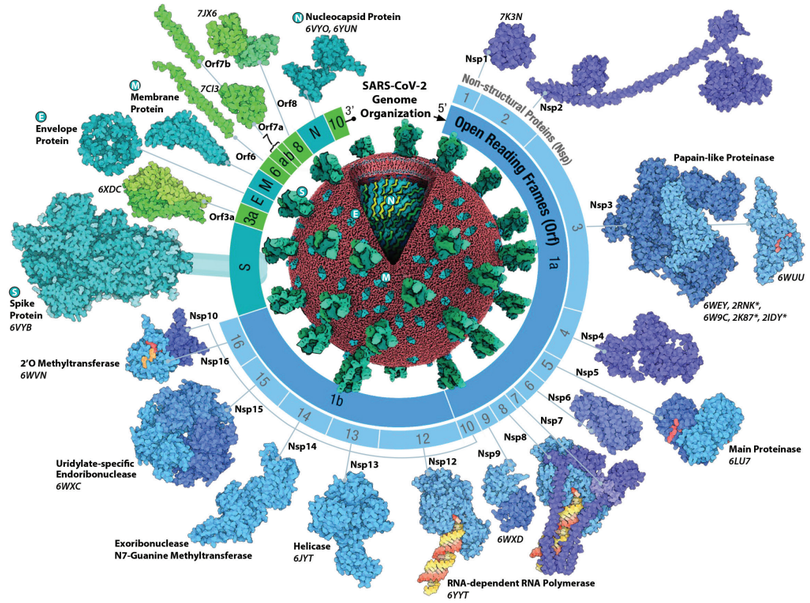


Illustration of the SARS-CoV-2 genome and proteins. Biochemistry department scientists have improved our knowledge of the spike protein, membrane protein, nsp7, nsp8, nsp12 and more.
Reprinted with permission from RCSB PDB-101

The Next Vaccine Candidate?

In a collaboration with researchers at UW–Madison's School of Medicine and Public Health, preeminent virologist Ann Palmenberg had been identifying molecular interactions between rhinovirus-C, a virus closely linked to wheezing and asthma, and its cellular receptor when the pandemic hit.

"Basically, we're dissecting components of the immune system down to the biochemical level of, what are the antibodies you want to induce, what are the antibodies you don't want to induce, and why does one work but not another," Palmenberg, a biochemistry professor and Institute for

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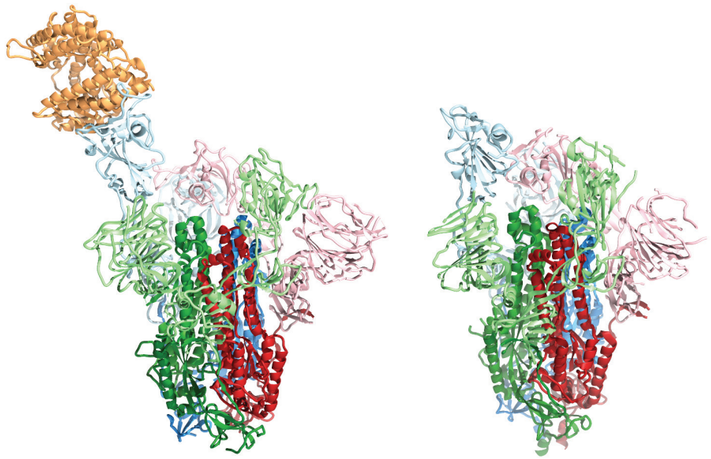


Spike glycoproteins from SARS-CoV, left, and SARS-CoV-2, right. Both are in the open, or standing, conformation and contain the same stabilizing mutations. Only the SARS-CoV spike is bound to ACE2, indicated in orange.

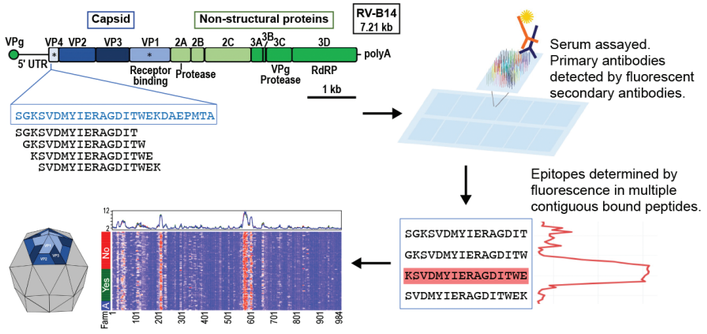
Images courtesy of Robert Kirchdoerfer

Molecular Virology affiliate, explains. "We were just about to make the next batch of chips and collect data [on rhinoviruses]...when COVID-19 came. We said, you know what, instead of designing the rhinovirus sequences on this chip, let's put coronavirus sequences on it."

The peptide array technology Palmenberg used was a brainchild from UW–Madison scientists including biochemistry professor and Biotechnology Center affiliate Michael Sussman (the technology was transferred to Roche, a Swiss multinational healthcare company). Each chip contains the entire genome of a virus in the form of peptides, or fragments of proteins. By identifying where antibodies stick on these fragments, and by comparing this information to viral structures from cryo-EM, scientists can pinpoint how to kill a virus.

Palmenberg and her collaborators decided to pivot their long-standing rhinovirus-C project to study how protein snippets from SARS-CoV-2 and the six other coronaviruses known to infect humans responded to plasma samples from two groups of people — patients with COVID-19 and individuals who hadn't been exposed to the virus. Nimble Therapeutics, a Madison-based company spun out of Roche Sequencing Solutions in 2019, built the chips at a substantial discount, and Kirchdoerfer, an Institute for Molecular Virology affiliate, helped the scientists match antibody-sequence pairs from the protein chips to structures from cryo-EM.

Their results demonstrate that humans mount strong, broad antibody responses to the spike, membrane, and nucleocapsid proteins. Because the immunogenicity of spike-based mRNA vaccines is variable, and because not all individuals who get COVID-19 produce detectable antibodies against the spike or nucleocapsid proteins, the scientists suggest that membrane proteins could be a promising target for future SARS-CoV-2 diagnostics, vaccines, and therapeutics.



Tiling peptides on peptide binding arrays.

Image from Irene Ong, an example of serum reactivity against an RV capsid peptide array

Signal from Noise

Though his role may not always be obvious, Kirchdoerfer has played a part in many projects that aim to understand SARS-CoV-2. He's had a hand, for example, in devising new strategies to characterize the activity of enzymes, substances that act as catalysts in biological processes. This project, led by Michael Sussman, is expected to be important for rapid, timely characterization of enzymatic activity in SARS-CoV-2.

Kirchdoerfer's own ongoing research using cryo-EM may also provide insights into the workings of the SARS-CoV-2 RNA synthesis complex and lead to new antiviral drugs that could help treat patients with COVID-19.

"Rob works on a number of fronts surrounding how coronaviruses function, from isolated components to intact viruses. To investigate how SARS-CoV-2 replicates, he has started by assembling and examining the structure and function of components of the virus' replication complex," says biochemistry professor and Morgridge Institute for Research affiliate Elizabeth Wright.

"He does the fundamental molecular biology, protein expression, and functional assays in his lab to determine if samples are of sufficient quality for cryo-EM imaging. We at the Cryo-Electron Microscopy Research Center then support him during the sample preparation, imaging, and initial data processing steps," Wright says. The center, which Wright directs, provides services to UW investigators who are working on SARS-CoV-2 and other projects.

Kirchdoerfer brings techniques from multiple disciplines — virology, structural biology, cell biology, and biochemistry, among them — together to explore the function of enigmatic SARS-CoV-2 proteins. But cryo-EM remains a mainstay of his work.

"A lot of the strengths for looking at SARS-CoV-2 with cryo-EM are the general strengths of the technique," he says. "You don't need a crystal. It's great for larger complexes. We also have different moving parts in this machine... With cryo-EM, so much of the data is handled computationally to address that movement that we can access even those moving regions."

But understanding SARS-CoV-2 isn't his end goal — it's just the beginning.

"During an outbreak, there's intense scientific interest, but as soon as that outbreak ends, interest also ebbs. What I would like to do with my lab is more pandemic preparedness — looking for the next virus that's going to cause a pandemic."

To that end, Kirchdoerfer is studying other coronaviruses and other virus families, and he's kicking off projects on viral entry — how viruses recognize cells, enter cells, and how virus evolution tunes the spike protein to undergo fusion with host cells — in collaboration with classical virologists, veterinary biologists, and epidemiologists at UW–Madison.

Beyond Science

Kirchdoerfer and his colleagues are just now getting back to research they were working on before the pandemic started. But their pandemic-related outreach, service and teaching activities continue.

Biochemistry professor Paul Friesen PhD'83 has taught biochemistry courses for majors and non-majors for nearly two decades. His teaching philosophy — getting students to understand not only the what but also the why of diseases and disease prevention — hasn't changed during the pandemic. Though he jokes that he didn't have gray hair before the week that courses went online, he's more certain than ever about the importance of the university's connection to students and the rest of the community.

"I like to talk about general principles so students can go back and advocate, to their parents, to their neighbors, to whomever, that science is important. Now, that has taken on a more dramatic role," reflects Friesen.

When he wasn't teaching, Friesen was thinking of ways to keep his students engaged and connected. Since most of his students were off campus, he brought campus to them by taking photos of familiar sights and sharing them during lectures. To re-create the in-classroom experience, he even recorded student lectures in a lecture hall, and he emphasized SARS-CoV-2 in all his classes.

Friesen, who's the director of the Institute for Molecular Virology, has also responded to public queries about the virus — whenever, wherever. He recalls a time early in the pandemic when he shared what he knew about viruses, and SARS-CoV-2 in particular, to commuters on a packed Madison Metro bus. Palmenberg, who has spent much of the pandemic reviewing grant applications so that scientists can acquire funding to study SARS-CoV-2, likewise fielded countless phone calls and emails. And since January 2020, Kirchdoerfer has participated in 24 interviews and panels (not including conversations for this story) and counting.

Whether they are studying a new virus, sharing knowledge with inquisitive minds or engaging communities throughout Wisconsin, scientists in the Department of Biochemistry manifest one exceptional quality: creativity.

"Often people think of scientists as being incredibly objective and precise and that's very true," says Kirchdoerfer. "But it really comes down to creativity, I think, in trying to bring together pieces of data that on the surface might not appear to talk to one another. It's a little bit of an art form — but then, an art form you go back to test."

Original story by Catherine Steffel, Ph.D., Biochemistry

Also in Biochemistry

Jean-Yves Sgro, senior scientist and director of the Biochemistry Computational Research Facility (BCRF), released a bioinformatics tutorial to assist researchers in understanding the SARS-CoV-2 spike glycoprotein sequence while performing multiple sequence alignments with closely-related coronavirus spike sequences. Sgro also released a coloring book of SARS-CoV-2 structures. You can find more information about the tutorial and coloring book on the BCRF website.

Cryo-EM and Cryo-ET Centers to Open

UW–Madison and the Department of Biochemistry have been at the forefront of structural biology research for decades, including 35 years of operation of the National Magnetic Resonance Facility at Madison and 15 years of contributions to the NIH-funded Protein Structure Initiative. Scientists throughout UW have been using cryo-electron microscopy (cryo-EM) to make advancements in molecular biology, cell biology, microbiology, virology, and biomedicine, but they've had to rely on facilities outside of the university. To meet the growing on-campus need for cryo-EM equipment and expertise, a core of researchers across campus began working to assemble the full power of cryo-EM at UW.

Several years later, scientists now have a place on campus where they can conduct their groundbreaking work.

The Cryo-Electron Microscopy Research Center (CEMRC) provides instrumentation, technical assistance, training, and access to cryo-EM for the UW–Madison research community. Groups contributing funding to the $15 million-plus initiative include 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. Though the pandemic delayed the grand opening of the CEMRC, UW researchers are already using the center in diverse and innovative ways that will help keep the campus at the bioscience frontier.

Professor Elizabeth Wright

The grand opening of the UW–Madison Cryo-EM Research Center will be held as part of the Department of Biochemistry's 42nd Steenbock Symposium on June 7-8, 2022.

"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," Brian Fox, chair and professor of biochemistry and associate vice chancellor for research policy and integrity says. "These efforts have positioned us well to embrace cryo-EM as a newly emerging, transformative technology."

The symposium will also be the grand opening of the Midwest Center for Cryo-Electron Tomography (MCCET), a national research and training hub at UW–Madison that is part of a cryo-electron tomography (cryo-ET) network supported by the National Institutes of Health. The MCCET, constructed in partnership with the UW Division of Facilities Planning & Management, C.G. Schmidt Construction, and architectural firm Aro Eberle, will support investigators across the United States by providing access to well-trained staff and support 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.

The CEMRC and the MCCET represent a continuation of UW'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. The centers will be pivotal in many ways: for building on the important work 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.

Jae Yang, a staff scientist in the Wright Lab, the Cryo-Electron Microscopy Research Center and the Midwest Center for Cryo-Electron Tomography, loads a sample.

Through rapid freezing, controlled beams, and advanced lenses, cryo-EM reveals the intricate architecture of cells, viruses, and proteins, all at molecular resolution — or better. 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 imaging. And its reach extends to many other research areas, including biofuels, engineering, and computer sciences.

Both centers are housed in the Hector F. DeLuca Biochemical Sciences Complex and are directed by biochemistry professor Elizabeth Wright.

"Some of our researchers understand how to do the computational aspects of the [cryo-EM] 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 about the CERMC. "For other investigators, we support them through the entire process and provide them with their structure and its interpretation on the back end."

The CEMRC is also creating jobs and leading to engagements with tech and biotech companies. CEMRC and UW 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 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."

Of the MCCET, Wright says, "Often, in structural biology, we work as separate units, and having this network of centers is special because we are building a community... Each one of the new cryo-ET centers has its own strengths and specialization in how staff consider processing samples and data collection."

Original story by Natasha Kassulke, OVCRGE

An Alum Gives Back

Financial support for faculty, staff, post-docs and graduate students who conduct research in the Cryo-electron Microscopy Research Center (CEMRC) is provided by biochemistry alum Daniel Klessig BS'71. Klessig's annual gifts are matched by the Department of Biochemistry.

Klessig, professor and former president and CEO of the Boyce Thompson Institute and an adjunct professor of plant pathology and plant-microbe biology at Cornell University, says that he has lived a life that has enabled him to support research and professorships at several institutions, and that he feels strongly about helping improve and further his field.

"One of the reasons I became so excited as an undergraduate at UW–Madison about molecular biology is that it gave one the ability to alter genes and thus figure out what the encoded proteins do. Cryo-EM gives one another level of molecular clarity by being able to actually see where and how those proteins fit in a large biological structure. You can now look at very large molecular complexes and see the working parts," he says.

Klessig grew up on a dairy farm near Chilton, Wisconsin. The combination of hard farm work and intensive studying to reach the top of his class, despite his dyslexia, meant that 18-hour days were the norm. Those long working days, six-seven days per week, were in part what drove him to get the "hell" off the farm and follow in his brother's footsteps to study biochemistry at UW–Madison. He did "too well" though, he says, and the excitement, enjoyment and satisfaction of accomplishments he realized through molecular biology research meant that his dream of having a 9-5 job never materialized. However, he wouldn't change a thing. He's still excited about the new discoveries in biology being made almost daily, and the potential of the CEMRC to advance so many different types of research for researchers across the country.

"I've had a lot of opportunities in my life. My undergraduate training at the University of Wisconsin and the Department of Biochemistry gave me a leg up, so they are pretty close to my heart," Klessig says. "It's time to give back."

"Dan's vision of supporting research in impactful ways stems from his insights and experience in research," biochemistry department chair Brian Fox says. "Through his creation of a generous and flexible endowment to support cryo-EM research, the department is able to support advanced training for students and staff and invest in the operation and enhancement of microscopes needed to keep us at the forefront of this important technology."

Hoskins Named 2021-2022 Vilas Associate

Professor Aaron Hoskins

Professor Aaron Hoskins was selected as a 2021-2022 Vilas Associate. The Vilas Associates Competition, administered by the Office of the Vice Chancellor for Research and Graduate Education, recognizes new and ongoing research of the highest quality and significance. Twenty-three winners were announced for the 2021-2022 award cycle.

Hoskins' research focuses on RNA splicing, a biological process requiring assembly of large RNA-protein complexes called spliceosomes from dozens of individual components. RNA splicing is fundamental and essential to gene expression in all eukaryotes. Hoskins brings to the UW–Madison campus new technologies that allow high-resolution studies of nucleic acid interactions to be carried out simultaneously across tens of thousands of sequence variants.

Outside of research, Hoskins has assumed a major role in the undergraduate biochemistry curriculum, and he's a new co-author on *Lehninger Principles of Biochemistry*, a definitive reference text for biochemistry students around the world.

Cox Named ASBMB Fellow

Professor Michael Cox

Professor Michael Cox was named a fellow of the American Society for Biochemistry and Molecular Biology (ASBMB). The 2021 fellows, the inaugural class, are a distinguished group of scientists who have contributed to multiple missions of ASBMB over a sustained period of time and enriched the world through their efforts and accomplishments.

Cox's lab studies the fundamental life processes and cellular mechanisms of DNA metabolism and is best known for contributions to understanding the RecA and FlP recombinases, which have become widely used tools for biotechnology and developing transgenic model organisms. He has a long-standing record of service as a member of the ASBMB Council and an associate editor of the *Journal of Biological Chemistry*. He was a member of the steering committee that developed concept-driven teaching strategies, and he advises UW–Madison's ASBMB Student Chapter. He is a co-author of the definitive reference textbook *Lehninger Principles of Biochemistry*. He also has served for many years as a judge in the undergraduate research poster competition at the ASBMB annual meeting.

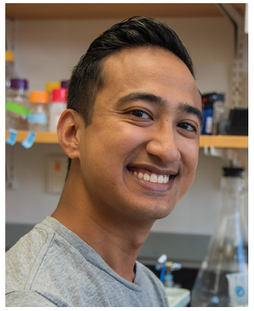
Ntambi Re-elected to ASBMB Council

Professor James Ntambi

Professor James Ntambi was re-elected to the American Society for Biochemistry and Molecular Biology (ASBMB) Council this year. Ntambi has served as a member of the council since 2018. The ASBMB Council serves as an advisory board to the president and executive director for setting priorities and strategic directions, overseeing resource allocations, and ensuring that all activities align with the society's mission.

Ntambi's lab studies the genetic regulation of metabolism in health and disease, including the physiological role of the stearoyl-CoA desaturase genes in lipid and carbohydrate metabolism in obesity, diabetes and fatty liver disease. Ntambi is also involved in building the African National Sciences Research Consortium, which brings together academic and research institutions across the East and Central African region with the goal of building a Ph.D. training program in basic laboratory research in biochemistry and nutritional sciences.

Graduate Student Rashan Inducted into Edward A. Bouchet Graduate Honor Society



Edrees Rashan

Edrees "Eddie" Rashan, an Integrated Program in Biochemistry (IPiB) doctoral candidate and research assistant in biochemistry, was selected for the 2021 cohort of the Edward A. Bouchet Graduate Honor Society. The Bouchet Society commemorates Edward Alexander Bouchet, the first self-identified African American to earn a doctoral degree from an American university. Bouchet scholars are chosen for five qualities that exemplify the spirit of Bouchet: scholarship, leadership, character, service and advocacy for historically under-represented students.

Rashan's commitment to empower excellence in students is driven by challenges he witnessed and experienced as a child of immigrant parents. His parents escaped violence, poverty and war in their home countries and met new challenges in the United States as they navigated barriers to education, employment and stability for themselves and their son.

"At a young age I helped my parents navigate the job application process, such as editing resumes and helping them practice for interviews," Rashan says. "As their only child, I realized the importance of using the privileges and skillsets I had to empower and manifest opportunities for those from disadvantaged backgrounds."

As a graduate student in IPiB, Rashan has helped organize departmental talks to better serve underrepresented trainees. He is a SciMed Graduate Research Scholars Peer Mentor, an IPiB representative at the Society for the Advancement of Chicanos and Native Americans in Science meeting, and an IPiB representative at the Annual Biomedical Research Conference for Minority Students meeting. Rashan also volunteered as a supply chain manager for the New York Biomedical Technician Rapid Response Team, where he coordinated the acquisition of essential personal protective equipment (PPE) and testing supplies during the height of the COVID-19 pandemic.

Rashan's research focuses on characterizing the enzymatic activities and functions of under-studied mitochondrial proteins, particularly those implicated in lipid metabolism. He and his collaborators are investigating whether these enzymes can protect cells from harmful lipids and determine how their degradation impacts human health.

"Eddie is a remarkable scientist and a model lab citizen," says David Pagliarini, Rashan's primary mentor and professor at Washington University School of Medicine in St. Louis. "Through his diligence and passion for science, he is constructing a beautiful thesis on atypical lipid metabolism; through his advocacy, he is helping establish a more diverse and equitable scientific community from which we will all benefit."

Original story by Sarah Lynn Traver Saunders, Biochemistry

Around the Department

Biochemistry 501 Summer Term Course Provides Popular Class in Online Format

When Hawra Aljawad made her 2020 summer plans, the idea was to take one class and conduct research. Then came coronavirus. With campus essentially shutting down in spring 2020 and undergraduates unable to work in labs, Aljawad, a senior studying chemical and biological engineering and biochemistry, pivoted.

"I had to be flexible with my plans," says Aljawad. "Activities and socializing became limited, and I couldn't gain lab experience. So, I chose to take more classes and focus on finishing some degree requirements."

One of the classes she decided to take was Biochemistry 501: Introduction to Biochemistry. The online summer course fulfilled the advanced biology elective needed for her degree, and a friend who had taken the class encouraged her to sign up.

Biochemistry 501 is a three-credit course that is offered every semester. The overarching goal of the course is to foster an understanding of how life works at a molecular level. Students explore how proteins, lipids, carbohydrates and nucleic acids are used in various cellular processes. A popular — and required — class for a variety of majors, attendance during the school year, when the class is typically offered in-person, can exceed 600 students many semesters. For the online course in the summer of 2020, more than 250 students enrolled.

Continued on next page

"Enrollment keeps going up. Last summer [summer 2019], the first time we offered it, enrollment was around 100. In 2020 it shot way up to around 260 students," says professor Richard Amasino, who is a Biochem 501 instructor along with professor Samuel Butcher and faculty associate Mario Pennella.

In the online version of the course, students had access to the entire course right away and could watch pre-recorded lectures at any time. Quizzes and exams were provided at intervals throughout the summer. Several resources and discussion platforms, including discussion boards, such as Piazza and PeerWise, where students could ask questions and instructors could respond, were also supported. The instructors also consider conversation and interaction an important part of online courses. They held a discussion section every day during the online summer session. Grad students and undergraduate peer mentors also provided additional discussion sessions, and many former undergraduate students came back to help.

Biochemistry 501 instructor Mario Pennella, helped move the course online.

Of her time in the course, Aljawad says, "I'm grateful that all the professors were understanding and flexible. It shows that they've tried their best to provide students with the best experience even with classes being online. I really enjoyed this course."

Original story by: Caroline Schneider, CALS

If I Weren't a Professor, I Would Be...

When we were growing up, many of us wondered what it would be like to encounter our teachers "in the wild." Outside the confines of school, what did they wear? Who were their friends? What would they be doing if they weren't a teacher?

Over the past year and a half, administrative staff embraced this inquisitiveness, asking biochemistry faculty about everything from their worst subject in school to how they got into science. They learned that assistant professor Judith Simcox enjoyed competing in barrel racing — a rodeo event involving quick turns and high speeds — when she was young. Professor Aaron Hoskins says that his friends would describe him as, "Socially awkward but occasionally funny." If professor Michael Cox weren't a professor, he would be a winemaker.

Megan Pierce, a program assistant who's also the face of the administrative staff to many faculty members, came up with the idea. "You spend so much of your day at work, and you realize that every person is unique," she says. "This gives everyone the opportunity to read about the people they work with, but on a different level."

When Pierce pitched her idea to team members Sarah Lynn Traver Saunders and Georgette Paxton, they jumped at the opportunity to make the series a reality. Paxton, a senior financial specialist, emailed faculty and came up with questions to ask, while Saunders, an administrative office manager, organized. The trio see the series, which ended last summer, as an uplifting part of the time when they saw faculty only over Zoom: They conducted most of the work for the series during the work-from-home portion of the pandemic. By showing students and staff that faculty have full lives outside of their careers, the series also strips away academic hierarchies and demonstrates that professors are people, too.

"For me, as a nonscientist, the profiles drew me in. I think they humanize our scientists in a way," says Saunders. "Through this series I hope that we are reminded that we're all people, that we all have varied backgrounds and paths and interests."

The staff interviewed 16 faculty. Visit each profile on the series' collection page: https://biochem.wisc.edu/facultyprofiles.

Top to bottom, Megan Pierce, Georgette Paxton, and Sarah Lynn Traver Saunders are pictured in 2020, when the idea for the faculty profile series was conceived and much of the series itself was written.

Original story by Catherine Steffel, Ph.D., Biochemistry

Degree	Name (Major Professor)	Thesis Title
Ph.D. Dec 2020	**Zachary Kemmerer** (Pagliarini)	Understanding atypical kinases as essential factors for the biosynthesis and cellular distribution of coenzyme Q
Ph.D. April 2021	**Kyle Robinson** (Pagliarini)	Defining steps in coenzyme Q cellular distribution and precursor biosynthesis
Ph.D. May 2021	**Justin McKetney** (Coon)	Advancing mass spectrometry-based proteomic analysis strategies for the investigation of human health and disease
Ph.D. May 2021	**Lucas O'Neill** (Ntambi)	Investigating the effects of stearoyl-CoA desaturase on diet-induced adiposity and regulation of insulin-like growth factor-binding protein-1
Ph.D. July 2021	**Elizabeth Duchow** (DeLuca & Butcher)	Serum vitamin D binding protein plays an essential role in utilizing naturally produced vitamin D
Ph.D. July 2021	**Megan Leander** (Raman)	Elucidating the molecular basis of allostery in bacterial transcriptional factors
Ph.D. July 2021	**Yang Liu** (Landick)	Regulatory circuits to program *Zymomonas mobilis* metabolism for cellulosic advanced biofuel production
Ph.D. July 2021	**Sébastien Ortiz** (Hull)	Exploiting pathogenic fungal spore germination as an untapped source of fungal specific targets
Ph.D. July 2021	**Harriet Saunders** (Wildonger)	Regulation of neuronal microtubule function by acetylation and acetyltransferases
Ph.D. July 2021	**Nathan Thomas** (Henzler-Wildman)	The proton/drug coupling mechanism of EmrE
Ph.D. Aug 2021	**Sophia Sdao** (Merrins)	Cyclin-dependent kinases 1 and 2 control beta-cell metabolism and insulin secretion
Ph.D. Oct 2021	**Jessica Cárdenas** (Bednarek)	Elucidate the role of PUX1 in GA signaling through its interaction with the GA receptor, GID1 to control cell growth
Ph.D. Nov 2021	**Tina Lynch** (Kimble)	From niche signaling to its transcriptional control over *C. elegans* stem cells: an *in vivo* view
Ph.D. Nov 2021	**Kanika Jain** (Cox)	Elucidating the role of the *E. coli* RarA protein in DNA recombination and repair processes

IPiB Graduates

Biochemistry Advisor Degrees 2021

Degree	Name (Major Professor)	Program	Thesis Title
Ph.D. Aug 2021	**Sonali Gupta** (Romero & Venturelli)	Biophysics	Investigating the dynamics of programmed microbial consortia in spatially structured environments
Ph.D. Sept 2021	**Xiangyang Liu** (Raman)	Biophysics	Design of synthetic transcription regulators in bacteria
Ph.D. Oct 2021	**Kevin Mayer** (Amasino)	Genetics	Investigating molecular mechanisms of flowering time across plant lineages
M.S. Jan 2021	**Jin Wen Tan** (Venturelli)	Bacteriology	

****Degrees Dec. 1, 2020 - Nov. 30, 2021****

Diversity, Equity and Inclusion Committee Update

In June 2020, the Department of Biochemistry made a commitment to invest in diversity, equity, and inclusion initiatives. Together we unequivocally stated that diversity adds tremendous richness to our intellectual landscape and that everyone deserves access to the wonder that scientific discovery potentiates.

As a community we came together to deliver on this investment. In 2020-2021 we:

- Established a Department of Biochemistry diversity, equity, and inclusion committee that consists of faculty members and graduate and undergraduate student representatives, and staff members.
- Established a travel scholarship for faculty, staff, and graduate and undergraduate students to attend conferences to promote diversity in STEM including the Society for Advancement of Chicanos/Hispanics and Native Americans in Science (SACNAS), American Indian Science and Engineering Society (AISES), and Annual Biomedical Research Conference for Minority Students (ABRCMS). We sent nine members of our community to these conferences in 2020, and we sent six to SACNAS and ABRCMS in 2021.
- Increased the training of our community through hosting several national experts in STEM diversity, equity, and inclusion to speak in our Biochemistry Colloquium including Drs. Tracy Johnson, Sean Whelan, and Manu Platt.
- Our support of the AISES Chapter through departmental resources led to a significant increase in student retention in STEM fields. In 2019 only 15% of AISES students had an undergraduate research experience (URE); by 2021, 87% are in URE programs with funding secured for 63%. In 2019 only 37% of AISES students obtained acceptance to their postgraduate applications; by 2021, 100% obtained acceptance, including NIH postbaccalaureate training programs and two admissions into graduate schools.
- We have added a land acknowledgement statement on our departmental website.
- Brian Fox was appointed to the Native Nations UW–Madison Phase 2 Working Group to advance research activities in partnership with 12 Native Nations of Wisconsin.

We are proud of our community and what we have accomplished as faculty, staff, and students, but we acknowledge that there is a tremendous way to go. In 2021-2022 we will:

- Continue these initiatives, including support through travel scholarships; hosting outstanding National Researchers for the Biochemistry Colloquium; and, support of the AISES Chapter.
- Expand the mission of diversity, equity, and inclusion on our departmental website by adding resources available to students, staff, and faculty.
- Continue working to develop relationships with Historically Black Colleges and Universities and with Minority Serving Institutions to open our graduate program to researchers from diverse backgrounds. This will begin through a grant, supported by the Office of the Vice Chancellor for Research and Graduate Education and the Nelson Institute, obtained by Drs. Grace Bulltail, Judith Simcox, Lucas Zoet, and Shaun Marcott to build an Indigenous Environmentalism Working Group that includes a collaboration with the College of Menominee Nations. This grant will also support an Indigenous research symposium to be held at UW–Madison.
- Culturally aware mentorship training for our faculty.
- Commission an art piece by a Ho Chunk artist to be built from the wood of 'Elmer', the elm tree that was the heart of the biochemistry complex and which served as a marker tree used by Native people as a waypoint to guide travelers on their journey.

Meaningful change takes the strength and commitment of the entire community. We are proud of how far we've come and excited to continue building a future that better serves the department, STEM fields, and the greater Wisconsin community.

Honors & Awards

Faculty

Samuel Butcher	Steenbock Professorship of Biomolecular Structure
Michael Cox	2021 ASBMB Fellow - one of the inaugural class of ASBMB fellows
Katie Henzler-Wildman	Jean V. Thomas Professorship in Biochemistry
Aaron Hoskins	Wasson Professorship in Biochemistry of Higher Animals 2021-2022 Vilas Associate
Ann Palmenberg	2020 National Academy of Inventors Fellow
John Ralph	2021 Clarivate Analytics Highly Cited Researcher
Amy Weeks	2021 Packard Foundation Fellow in Science and Engineering

Staff

Ben Minkoff	Sussman	2020 Boyer Award
Canan Sener	Ralph	First place in the Professional Category of the Sustainable Engineering Forum (SEF) poster competition at the 2020 AIChE Annual Meeting

Postdoctoral Staff Fellowships

Christopher Emfinger	Attie	American Diabetes Association Fellowship
Daniel Parrell	Wright	NIH Ruth L. Kirschstein Postdoctoral Fellowship
David White	Hoskins	NIH Ruth L. Kirschstein Postdoctoral Fellowship

Postdoctoral Staff Training Grants

Christopher Emfinger	Attie	Metabolism and Nutrition Training Program (MANTP)
Erin Ostrem Loss	Venturelli	Genomic Sciences Training Program (GSTP)
Tara Price	Attie	Training Program in Translational Cardiovascular Science (TPTCS)

Graduate Student Awards

Dana Dahhan	Bednarek	Denton Award for Graduate Student Excellence in Teaching & Mentoring
Dylan Plaskon	Record	Denton Award for Graduate Student Excellence in Teaching & Mentoring
Tina Lynch	Kimble	Sigrid Leirmo Memorial Award in Biochemistry
Raghav Jain	Simcox	2021 UW–Madison Diabetes Day Nest Graduate Student Speaker Award
Edrees Rashan	Pagliarini/Simcox	2021 Edward A. Bouchet Graduate Honor Society Inductee

Graduate Student Fellowships

Yu Bao	Landick	James Chieh-Hsia Mao Wisconsin Distinguished Graduate Fellowship
Matthew Blackburn	Sussman	Sam C. Smith Graduate Fellowship in Biochemistry
Joshua Choi	Senes	Denis R. A. and Martha Washburn Wharton Fellowship in Biochemistry
Kanika Jain	Cox	William H. Peterson Fellowships in Biochemistry
Josephine Mitchell	Wildonger	Biochemistry Teaching Fellowship
Jacob Rapp	Romero	Steenbock Predoctoral Fellowship in Biochemistry
Maxwell Rector	Record	William R.& Dorothy E. Sullivan WI Distinguished Graduate Fellowship in Biochemistry
Jonathan Tai	Pagliarini	NIH Ruth L. Kirschstein Predoctoral Fellowship
Abigail Bartlett	Pagliarini	NSF Graduate Research Fellowship Program
Nina Bonde	Cox/Keck	NSF Graduate Research Fellowship Program
Christine Hustmyer	Landick	NSF Graduate Research Fellowship Program
Dean Jarois	Gellman	NSF Graduate Research Fellowship Program
Nathan Murray	Pagliarini	NSF Graduate Research Fellowship Program
Katherine Senn	Hoskins	NSF Graduate Research Fellowship Program
Ross Soens	Cantor	NSF Graduate Research Fellowship Program
Helaina Von Bank	Simcox	NSF Graduate Research Fellowship Program
Kwame Frimpong	Rotator	Science and Medicine Graduate Research Scholars (SciMed GRS)
Gilbert Loiseau	Senes	Science and Medicine Graduate Research Scholars (SciMed GRS)
Sierra Love	Hoskins	Science and Medicine Graduate Research Scholars (SciMed GRS)
Robert Mejia	Rotator	Science and Medicine Graduate Research Scholars (SciMed GRS)
Anthony Meza	Buller	Science and Medicine Graduate Research Scholars (SciMed GRS)
Johnson Saba	Landick	Science and Medicine Graduate Research Scholars (SciMed GRS)

Graduate Student Training Grants

Jackie Chen	Raman	Biotechnology Training Program (BTP)
Clara Frazier	Weeks	Biotechnology Training Program (BTP)
Lauren Mazurkiewicz	Weeks	Biotechnology Training Program (BTP)
David Rivera-Kohr	Fox	Biotechnology Training Program (BTP)
Juan Sanchez	Wright	Biotechnology Training Program (BTP)
Andrea Wegrzynowicz	Henzler-Wildman	Biotechnology Training Program (BTP)
Anna Zmich	Buller	Biotechnology Training Program (BTP)
Aspasia Amiridis	Weeks	Chemistry-Biology Interface Training Program (CBI)
Merissa Brousseau	Henzler-Wildman	Chemistry-Biology Interface Training Program (CBI)
Rohith Rajasekaran	Coyle	Chemistry-Biology Interface Training Program (CBI)
Kimberly Huggler	Cantor	Genomic Sciences Training Program (GSTP)
Juan Diaz Rodriguez	Romero	Genomic Sciences Training Program (GSTP)
Benjamin Harding	Rienstra	Molecular Biophysics Training Program (MBTP)
Joshua Kraus	Lim	Molecular Biophysics Training Program (MBTP)

Postbaccalaureate Awards

Paula Gonzalez	Simcox	SACNAS Travel Award for 2021 National Conference

Undergraduate Awards

Hunter Coplien		Alpha Helix Scholarship Award
Qianyun (Lexi) Luo		Astronaut Scholarship
Xi Chen	Cavagnero	Biochemistry Mary Shine Peterson Award
Anna Christenson		Biochemistry Mary Shine Peterson Award
Leta Landucci	Fox/Ralph	Biochemistry Mary Shine Peterson Award
Renxi Li	Record	Biochemistry Mary Shine Peterson Award
Qianyun (Lexi) Luo		Biochemistry Mary Shine Peterson Award
Justin Myrah		Biochemistry Mary Shine Peterson Award
Xin Qing		Biochemistry Mary Shine Peterson Award

Undergraduate Awards *continued*

Tristan Argall	Hoskins	Biochemistry Undergraduate Summer Research Award
Pak Lun Kevin Cheung	Venturelli	Biochemistry Undergraduate Summer Research Award
Sarah Fahlberg	Romero	Biochemistry Undergraduate Summer Research Award
William Langholz	Record	Biochemistry Undergraduate Summer Research Award
Evelyn Okal	Romero	Biochemistry Undergraduate Summer Research Award
Qiuwen Quan		Biochemistry Undergraduate Summer Research Award
Ann Seliger	Kimble	Biochemistry Undergraduate Summer Research Award
Xindi Tang		Biochemistry Undergraduate Summer Research Award
Lukas Voigts	Hoskins	Biochemistry Undergraduate Summer Research Award
Qianyun (Lexi) Luo		Barry Goldwater Scholarship
Cade Harkner	Hoskins	Chemistry Regine Deutsch Undergraduate Summer Research Award
Mae Hurtado-Thiele	Simcox	Hispanic Scholarship Fund Recipient for 2021
Taka Ishikuri	Record	National ACS Undergraduate Award in Chemical Biology for 2021
Jiayin Tang	Record	National ACS Undergraduate Award in Chemical Biology for 2021
Armor Rupanya	Record	National ACS Undergraduate Award in Physical Chemistry for 2021
Qianyun (Lexi) Luo		Rhodes Scholarship (Finalist)
Hawra Aljawad		Rhodes Scholarship (Finalist)
Mae Hurtado-Thiele	Simcox	SACNAS Travel Award for 2021 National Conference
Fidelia Beatrice Alvina	Kimble	Singapore's Agency of Science, Technology and Research (A*STAR) Scholarship
Autumn Chevalier	Simcox	UW–Madison Indigenous Working Group Undergraduate Research Internship Award

Undergraduate Fellowships

Tristan Argall	Hoskins	Hilldale Undergraduate Research Fellowship
Cole Aschenbrener		Hilldale Undergraduate Research Fellowship
Pak Lun Kevin Cheung	Venturelli	Hilldale Undergraduate Research Fellowship
Anna Christenson		Hilldale Undergraduate Research Fellowship
Sarah Fahlberg	Romero	Hilldale Undergraduate Research Fellowship
Anika Gupta		Hilldale Undergraduate Research Fellowship
Paige Hill	Craig	Hilldale Undergraduate Research Fellowship
Aadhishre Kasat	Buller	Hilldale Undergraduate Research Fellowship
William Langholz	Record	Hilldale Undergraduate Research Fellowship
Alex (Ximian) Li		Hilldale Undergraduate Research Fellowship
Renxi Li		Hilldale Undergraduate Research Fellowship
Qianyun (Lexi) Luo		Hilldale Undergraduate Research Fellowship
Jarod Moyer	Butcher	Hilldale Undergraduate Research Fellowship
Evelyn Okal	Romero	Hilldale Undergraduate Research Fellowship
Alejandro Onate		Hilldale Undergraduate Research Fellowship
Qiuwen Quan		Hilldale Undergraduate Research Fellowship
Chloe Stevens		Hilldale Undergraduate Research Fellowship
Anton Tung		Hilldale Undergraduate Research Fellowship
Lukas Voigts	Hoskins	Hilldale Undergraduate Research Fellowship
Caleb Carlsen		Sophomore Research Fellowship
Allison Czora	Landick	Sophomore Research Fellowship
Jasmine Machhi	Cavagnero	Sophomore Research Fellowship
Gordon Winkler	Cavagnero	Sophomore Research Fellowship

2021 Biochemistry Undergraduate Summer Research Awards sponsored by
Henry A. Lardy Undergraduate Research Fund, Floyd C. McIntire Biochemistry Award Fund, Dr. Shang-Chen Pan Fund in Biochemistry, E.W. Hopkins Fund, Jerome J. Stefaniak Biochemistry Scholarship Fund, Eric Bey and Amanda Boley Scholarship Fund, and Carl Krieger Memorial Fellowship Fund.

We Heard About You

Below are some updates we received from the faculty and other sources.
Have something you'd like to share with us? (You don't need to wait for someone else to tell us.)
Contact: alumninews@biochem.wisc.edu.

Amasino Lab
Kevin Mayer now at the Promega Corporation working as a Senior Research Scientist.

Butcher Lab
Allison Didychuk (Ph.D. 2017, Biophysics) is a Damon Runyun postdoctoral Fellow at UC Berkeley and will be joining the faculty at Yale University as an Assistant Professor in Molecular Biophysics and Biochemistry in 2022.
Sam Hayes (postbaccalaureate research intern 2020) is a medical student at UW–Madison.
Johanna Virta (postbaccalaureate research intern 2020) is a Ph.D. student at UCSF in the Department of Chemical Biology.

Craig Lab
See-Yeun Ting (IPiB 2017 grad) has joined the faculty of the Institute of Molecular Biology at Academia Sinica in Taipei, Taiwan.
Syzmon Ciesielski joined the Dept. of Chemistry at the University of North Florida as an Assistant Professor of Biochemistry this fall.

Frey Lab
Squire Booker (former postdoc) is among the 2021 inaugural class of ASBMB fellows.

Hoskins Lab
Yichen Sun is now working as a video game developer in San Francisco.
Clarisse van der Feltz is now an Assistant Professor of Biology at Northwest U. in Kirkland Washington.
Matt Ashton graduated from medical school at Tulane and will soon begin his residency in emergency medicine at Mt. Sinai in New York.

Ludden Lab
Paul Ludden recently retired as professor and provost emeritus from Southern Methodist University. Paul and his wife Linda have returned to Wisconsin and live in Middleton. Paul also just completed a term as a member of the CALS Board of Visitors.
Priya Rangaraj was recently promoted to Director, Global Market Development - Electron Microscopy, at Thermo Fisher Scientific.

Ntambi Lab
Sabrina Dumas (Ph.D. 2018) is a Clinical Research Liaison at Imbed Biosciences, Inc, where she identifies, develops, and maintains professional relationships with wound healing clinicians to provide comprehensive medical and scientific support on novel bioresorbable antimicrobial wound healing matrices.
Lucas O'Neill (Ph.D. 2021) moved back to Fort Worth to teach science at the I.M. Terrell Academy for STEM and VPA. I.M. Lucas is ecstatic to be back in the classroom and enjoys attending the many visual and performing arts activities his students participate in.
After graduating, John (Zhaojin) Liu joined the Interdisciplinary Biomedical Graduate Program at University of Pittsburgh. He is currently working on cancer research and pursuing his doctorate degree in pharmacology.

Pagliarini Lab
Danielle Lohman (Ph.D. 2017) is now a Foreign Affairs / Science Officer, Biological Policy Staff in the Bureau of International Security and Nonproliferation, U.S. Department of State in Washington, D.C.
Mile Veling (Ph.D. in 2019) is now a postdoctoral fellow at Harvard Medical School studying synthetic biology with Pam Silver.
Zack Kemmerer (Ph.D. in 2021) is now a Patent Agent, Morrison & Foerster in San Diego, CA.
Kyle Robinson (Ph.D. in 2021) is now an ADME/MetID Study Director at Labcorp Drug Development in Madison, WI.

Raines Lab
Jin-Soo Kim (Ph.D. 1994) is a Professor and the Director of the Center of Genome Engineering at Seoul National University in South Korea.
Jed Thompson (Ph.D. 1995) now works for LifeMine Therapeutics in Cambridge, Massachusetts.
Marcia Haigis (Ph.D. 2002) has been promoted to Professor with tenure in the cell biology department at Harvard Medical School.
Jeremy Johnson (Ph.D. 2007) has been promoted to Professor with tenure in the chemistry and biochemistry department at Butler University.
Jeet Kalia (Ph.D. 2008) is now an Associate Professor at the IISER in Bhopal, India.
Kelly Gorres (Ph.D. 2009) has been promoted to Associate Professor with tenure in the chemistry and biochemistry department of UW–La Crosse.
Chelcie Eller (Ph.D. 2014) is now working for Abcam in Eugene, Oregon.
Trish Hoang (Ph.D. 2016) and Jim Vasta (Ph.D. 2015) work for Promega in Fitchburg, Wisconsin.
Kalie Mix (Ph.D. 2017) is working for Sanofi Genzyme in Framingham, Massachusetts.

Raman Lab
Megan Leander (Ph.D. 2021) now works at Pfizer Inc. in St Louis.

Reznikoff Lab
Lynne Maquat, (Ph.D. 1979) was awarded the 2021 Wolf Prize in Medicine.

Simcox Lab
Charlie Kirsh a former postbaccalaureate in the Simcox Lab promoted to Research Associate II at A2 Biotherapeutics.
Jenna Rogalinski a former Biochem Scholar in the Simcox Lab is now a sales intern at ibidi GmbH.
Ayren McGahee a former undergraduate in the Simcox Lab is now a postbaccalaureate in the Ntambi lab.

Venturelli Lab
Ryan Clark (former postdoc) is now a senior scientist at Nimble Therapeutics.
Jin Wen Tan (grad) is a Research Associate at Metagenomi.
Zhengyi Chen (undergrad) is now at Vanderbilt Ph.D. program.

Wildonger Lab
Mike Kelliher is in his second year of a Clinical Chemistry Fellowship at Dartmouth-Hitchcock.

Letters from the Labs

Butcher Lab

The Butcher lab has been on a roll and couldn't be better, thanks to the hard work from staff scientist **Dr. Yuichiro Nomura**, postdoc **Dr. Cristian Escobar**, Ph.D. students **Saeed Roschdi** (IPiB), **Riley Petersen** (Chemistry) and **Rahul Vivek** (IPiB), our undergraduate extraordinaire **Jarod Moyer**, and a revolving cohort of outstanding rotators from IPiB and Biophysics: **Mikaela Seeman**, **Kylie Kawisza**, **Takuma Kume** and **Dhaval Ghone**. This year we celebrated the 5-year renewal of our NIH R35 grant that supports our biophysical investigations of RNA structure. Jarod received a Hilldale Award, and **Sam** was named the Steenbock Professor of Biomolecular Structure. Sam supports technology development and the user program for the NMR facility (NMRFAM), which is expanding and doing great under the leadership of **Professors Katherine Henzler-Wildman** and **Chad Rienstra**. With the help of **Dr. Craig Bingman**, we have a couple of amazing new X-ray crystal structures that "fell" out of conversations with **Professor Marv Wickens**, and these will be submitted soon. Thanks to our outstanding colleagues, the lab is busier than ever and moving in exciting new directions that we never could have imagined!

Left to right, Sam Butcher, Saeed Roschdi, Riley Petersen, Cristian Escobar Bravo, Rahul Vivek, Yuichiro Nomura.

Weeks Lab

Greetings from the Weeks lab! We celebrated the two-year anniversary of opening our doors in 2021, and it's been an exciting adventure! Our lab's main focus is on engineering enzymatic tools for mapping biological signals across space and time and living cells. Spatial organization and temporal dynamics are essential properties of cellular signaling. However, current technologies are unable to provide a systems-level experimental mapping of the dynamic subcellular localization of proteins involved in these processes. We are initially focusing on two types of signaling processes, proteolysis and phosphorylation, both of which play critical roles in myriad biological signaling pathways relevant to human health and disease.

Our efforts in developing tools for subcellular mapping of proteolysis are led by **Clara Frazier** and **Aspasia (Aspa) Amiridis**, who are engineering enzymes for capture of proteolytic neo-C and neo-N termini, respectively. Clara's review article on peptide ligase enzymes was recently published in *Biochemical Society Transactions*, and she continues to make amazing progress toward developing a C-terminal bioconjugation enzyme for mapping proteolytic cleavage events. She was also recently awarded a traineeship in the NIH-funded Biotechnology Training Program. Aspa is focused on enzymatic capture of proteolytic neo-N termini, and her methods paper on labeling cell surface N termini was recently accepted for publication in *Methods in Molecular Biology*. Aspa was recently awarded a traineeship in the NIH-funded Chemistry-Biology Interface Training Program.

Spatiotemporal mapping of phosphorylation events is another major focus in the lab. Based on their unique chemistries, we are developing separate enzymatic tools for capture phosphoserine/phosphothreonine (pSer/pThr) and phosphotyrosine (pTyr). **Katarzyna (Kasia) Radziwon** is leading the charge on pSer/pThr. Her review article on protein engineering for selective proteomics was recently published in *Current Opinion in Chemical Biology*. **Haley Penkala** is spearheading the pTyr project and making excellent progress. She's also been moonlighting on another project focused on developing new technologies to map protease specificity and is busy preparing a manuscript.

Lauren Mazurkiewicz is leading a new project that aims to uncover the biological function of the unusual post-translational modification diphthamide, a histidine modification that is presently only known to occur on one protein, and for which there are no enrichment or identification tools. In support of this work, she was recently awarded a traineeship in the NIH-funded Biotechnology Training Program.

All of our projects have relied on assists from talented undergraduate students. **William (Will) DeAngelis** and **Alexis (Lexi) Klomhaus** were the first undergraduates in the lab. Lexi graduated in 2020 and moved on to an exciting position at Abbott, while Will graduated in 2021 and is currently working at Labcorp Drug Development. In 2021, two new undergraduates, **Izzy Eppinger** and **Brendyn Ramos**, joined the lab.

Finally, **Amy** was awarded a Packard Fellowship in Science and Engineering in 2021. She is incredibly grateful to all past and present members of the Weeks lab for their hard work and creativity (and for taking a chance on a new lab!).

Left to right, Amy Weeks, Haley Penkala, Katarzyna Radziwon, Clara Frazier, Lauren Mazurkiewicz, Aspasia Amiridis.

Kaye Apollo
Generous Supporter
May 2021

Takis Apollo
Generous Supporter
May 2021

Shirley Aprison
Generous Supporter
January 2021

Robert Baldwin
Generous Supporter
April 2021

Anastasia & Peter Basdavanos
Generous Supporters
May 2021

Norman Beachley
Generous Supporter
June 2021

Brent Behrens
B.S. 1971
May 2021

Robert Bingham
Ph.D. 1964 — Prof. Strong
June 2021

John Blanchard
Ph.D. 1979 — Prof. Cleland
November 2021

Lyda Boyer
Generous Supporter
January 2021

James Chen
Generous Supporter
April 2021

David & Louise Clark
Generous Supporters
May 2021

Gregory Duke
Ph.D. 1989 — Prof. Rueckert
April 2021

David Filmer
Ph.D. 1961 — Prof. Kaesberg
June 2021

Andrew Heffernon
Generous Supporter
March 2021

Irene Ilgen
Generous Supporter
January 2021

Richard Jacobs
Ph.D. 1975 — Prof. Hoekstra
December 2020

Kenneth Johnson
Instrument Technician at
the Institute for Enzyme Research
June 2021

Neal Jorgensen
Generous Supporter
January 2021

Marjorie & John Losse
Generous Supporters
March 2021

Colleen Marion
Ph.D. 2004 — Prof. Amasino
June 2021

Eloise Marsh
Generous Supporter
March 2021

Lafayette Noda
Generous Supporter
September 2021

Edmund Overton
B.S. 1979
June 2021

Marilyn Prouty
Generous Supporter
October 2021

John Reed
Generous Supporter
March 2021

Marjorie Reynolds
Ph.D. 1964 — Prof. DeLuca
Generous Supporter
June 2021

Helen Roberts
Generous Supporter
December 2020

Donald Schuette
Generous Supporter
August 2021

Earl Shrago
Generous Supporter
January 2021

Ward Smith
Generous Supporter
July 2020

Philip Stansly
Generous Supporter
September 2021

John Suttie
B.S. 1957, M.S. 1958,
Ph.D. 1960 — Prof. PH Phillips
Professor 1961-2001
Emeritus 2001-2020
December 2020

Jack Towne
M.S. 1952, Ph.D. 1955 — Prof. Burris
September 2021

Willard Visek
Generous Supporter
October 2021

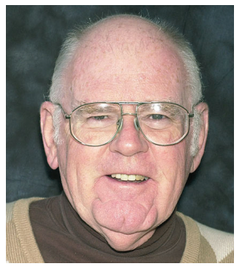
Robert Weaver
Generous Supporter
October 2021

Robert Wohlhueter
Ph.D. 1970 — Prof. Harper
January 2021

Our thoughts are with the families of any others in the Biochemistry community who recently passed.

In Memoriam

John Suttie — Nutritional Biochemistry Professor, Vibrant Person



University of Wisconsin–Madison Professor Emeritus of Biochemistry and Nutritional Sciences alumnus John Suttie died on Monday, Dec. 21, 2020 at 86. For four decades, he was a faculty member with expertise in the metabolism and mode of action of vitamin K and fluoride toxicity. He made seminal contributions to both departments, and his advocacy and helping to establish national nutrition policy raised the national visibility of the College of Agricultural and Life Sciences and UW–Madison. He retired from the university as professor emeritus in 2001.

Suttie was born and raised on a dairy farm in Galesville, Wisconsin, where the foundation for his long career in science was laid in a one-room schoolhouse. He obtained his bachelor's (1957), master's (1958), and doctoral (1960) degrees in biochemistry under Paul H. Phillips. After completing a year-long postdoc as an NIH Postdoctoral Fellow at the National Institute for Medical Research in England, Suttie returned to UW–Madison in 1961 as a professor.

Throughout his career, Suttie influenced generations of student scientists, training 45 graduate students and 27 postdoctoral scientists, and serving as lead instructor of Biochemistry 501, a key course in the Biochemistry undergraduate curriculum. He authored the highly regarded "Introduction to Biochemistry" textbook for undergraduates and also played a key role in reorganizing Biochemistry's graduate curriculum.

Among other significant contributions, his lab's research provided a baseline for assessing hazards, defining emission standards, and enacting regulations of fluoride emissions across the country. He himself served as a world expert on vitamin K and the anticoagulants dicumarol and Warfarin. Suttie's career was filled with awards and service to the fields of nutrition and biochemistry. He became chair of the Department of Nutritional Sciences, held both national and international positions, published many research articles, and received numerous awards of distinction.

"Because of his great sense of humor, John made life pleasurable for everyone around him," says Hector DeLuca, a biochemistry professor emeritus. "Yet he was strong and resolute when required. John Suttie is a largely unsung championof the University of Wisconsin–Madison at all levels...Both I and the university will forever miss him."

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Biochemistry
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Innovation

```
train_thermo_X, train_thermo_y = zip(*thermo_seqs.values())
gpr = GPR(kernel=kernel)
gpr.fit(train_thermo_x, train_thermo_y)

if len(func_seqs) - len(thermo_seqs) > 0:
    gpc = GPC(kernel=kernel)
    train_func_X, train_func_y = zip(*func_seqs.values())
    gpc.fit(train_func_X, train_func_y)
    probs = {ID: gpc.predict_proba([seq])[0][1] for ID, seq
             in unexplored_seqs.items()}
else:
    probs = {ID: 1 for ID in unexplored_seqs}

y_means = {}
y_stds = {}
for ID, seq in unexplored_seqs.items():
    y_mean, y_std = gpr.predict([seq], return_std=True)
    y_means.update({ID: y_mean})
    y_stds.update({ID: y_std})
```

Designing proteins with tailor-made functions

Philip Romero, Bennett Bremer, Jacob Rapp

Proteins perform complex chemical and biological functions and present tremendous potential for solving challenging problems in medicine, agriculture, environmental protection, and industrial chemistry. Yet, designing proteins with tailored functions is impeded by our limited understanding of these complex molecules. The lab of biochemistry professor Philip Romero is using a robot and machine learning to design enzyme sequences with improved activity, driving our understanding of the relationships between protein sequence, structure, and function. The robot is used to express and test proteins for given properties, while a machine learning model uses this information to tell the robot which proteins of thousands possible to test. The codes above show how the computer decides which sequences to test using the robot. The patent application for this work was filed by the Wisconsin Alumni Research Foundation (WARF).