BIOCHEMISTRY *In Vivo*

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

2020 Education | Research | Innovation

For our alumni, supporters, and friends

Open for Research: Essential Workers

Meet our New Faculty
Research Updates
And more

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Light tango. Biochemical Sciences Building, *Helical Tango* art by Nori Sato.

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***Cover image:* Open for Research: Essential Workers.**

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by Robin Davies

From the Chair

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Professor Brian G. Fox

Biochemistry In Vivo has the purpose of keeping our current members, alumni, supporters, and friends world-wide up to date on happenings in the department. It is our sincere hope you will find these newsletters engaging, enlightening, and inspiring. The 2020 edition is a presentation of resilience, our commitment to each other, and achievements and continued success in the face of tremendous challenges caused by the SARS-CoV-2 pandemic and social outrage brought to light by the tragic killings of George Floyd, Breanna Taylor and many others.

The cover, titled *Open for Research: Essential Workers*, emphasizes the reality of a year in the SARS-CoV-2 pandemic. Following mounting concerns arising in early March, the UW-Madison closed all non-essential research activities on March 19, 2020. The entire department heard the call, arranged to quickly stow all research in progress and move to remote work. Although I can safely say we didn't like it, everyone quickly adapted to entirely on-line operations: no classes or research group meetings held in person; all members of the department at home beyond only a few essential researchers performing COVID-related research (**Robert Kirchdoerfer, Phillip Romero**), maintaining living animals, caring for expensive research equipment, and assuring continued receipt of critical supplies and equipment. The Department of Biochemistry staff (**David Parker, Julie Kennedy** and **Max Noltner**) rounded up our excess stores of cleaning supplies, sanitization reagents, face masks and gowns that were urgently needed in the University Hospitals and Clinics and provided them to the campus to help others. I worked remotely throughout the remainder of the spring semester, including three meetings a week with the best administrative team that one could ever ask for: **Rick Amasino; Dustin Irving;** Julie Kennedy; **Conor Klecker; Cathy Michael; Sarah Traver-Saunders; Kerry Tobin;** and **Kris Turkow.**

As the efficacy of mitigating risk of transmission by wearing a face mask, keeping physical distance, and including careful attention to personal behavior and hygiene became understood, the University called for a restart to research in a phased way. The Biochemistry Department organized itself by research floor in each building. Rick Amasino, **Sam Butcher, Aaron Hoskins, Judith Kimble, Wes Pike, Vatsan Raman, Ivan Rayment, Ophelia Venturelli** and **Amy Weeks** led the effort to define how the department would reopen and carry out research safely. I would like to express my deepest appreciation for their efforts. I also want to emphasize the enthusiastic and conscientious actions of every other member of the Department during this time.

The Department was reopened for on-site research on June 8, 2020 and has operated safely and successfully since then. Through careful planning and continued diligence, the Department is supporting on-site research for undergraduates, graduate students, postdoctoral fellows, staff and faculty.

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Please read the other details contained in one of the highlight articles of this issue.

The Department has continued to sustain our hiring campaign for new faculty members. We seek innovators who will address basic and applied problems spanning human health, energy, bioproducts, ecosystem function and others. In this newsletter, you will be able to read about three new hires: Assistant Profs. **Tim Grant** and **Ci Ji Lim**, and Prof. **Chad Rienstra**.

The Department continues to build and expand our research frontiers. Please read about the new successes of Prof. Chad Rienstra and Associate Prof. **Katherine Henzler-Wildman**, who are Co-Directors of the Nuclear Magnetic Resonance Facility at Madison (NMRFAM). There is a short summary of a fascinating new finding on protein and enzyme allostery, where Prof. Vatsan Raman and co-author **Megan Leander** have shown that the molecular determinants are considerably more adaptable than the popular conception of this critically important phenomenon. There is also a highlight on exciting new work from Prof. Ophelia Venturelli's lab on tools to enhance our understanding of the dynamics of microbiomes.

Prof. **John Markley**, the Steenbock Professor of Biomolecular Structure and Function, retired in May 2020, after 35 years at the helm. John's insight and eye for scientific problems and talent has helped assure a bright future for NMRFAM. Prof. **Colleen Hayes** also retired this year with accolades for a comprehensive review of the impacts of lipids, lymphocytes and vitamin D on multiple sclerosis, co-authored by Prof. **James Ntambi**.

Just two years ago, *Biochemistry In Vivo* introduced Prof. **Elizabeth Wright**, who came to UW-Madison to lead our efforts in cryo-electron microscopy. Four microscopes were successfully installed during the COVID-19 pandemic, and the first research data are now being collected. The investments of the Department, Morgridge Institute for Research, Office of the Vice Chancellor for Research and Graduate Education, College of Agricultural and Life Sciences and campus set the stage for Prof. Wright's recent selection by the National Institutes of General Medical Sciences (NIGMS) to lead a national cryo-electron tomography center housed in the DeLuca Biochemistry building at UW-Madison. Remarkable achievements in three short years.

The Department also celebrates the success of Prof. **Alan Attie**, who has been awarded an RC2 grant through the National Institute of Diabetes and Digestive Kidney Disease (NIDDK) to explore the role of genetic variation in the response to two popular human diets. The RC2 grant is a collaboration with Distinguished Scientist **Mark Keller**, Biochemistry Assistant Prof. **Judith Simcox** and Bacteriology Associate Professor **Federico Rey** at UW-Madison, along with **Richard Kibbey** (Yale) and **Gary Churchill** (Jackson Lab). Simcox was also named a Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Scholar at UW-Madison for her studies on lipids as predictive markers for metabolic diseases such as diabetes in African American women. These new efforts strengthen the departmental commitment to basic research needed to address major human health challenges.

There is a story on the 2020 Packard Fellowship, won this year by Assistant Prof. **Scott Coyle**. Also noted, and celebrated here, Prof. Sam Butcher won the Chancellor's Distinguished Teaching Award this year. In just a couple of years, Biochemistry 501, taught by Sam, Rick Amasino and **Mario Pennella** has become one of the 5 largest classes taught in Summer session across the whole university. We look forward to having students from all over the world taking this course, either on-line or here in Madison in the future. You will also find 90th birthday celebrations of the achievements of emeritus Profs. **Julius Adler** and **Hector DeLuca** as seen through the eyes of their former students and staff. Indeed, one must be intrigued by the evidence associating messy floors with clear minds.

Our Department thrives on the diversity, skills and commitment of its members, alumni, supporters and friends. If you are able, please consider becoming a donor to the Department of Biochemistry, or a fan of our next Crowdfunder campaign. Our need for your support in these challenging times is greater than ever, and so we request your consideration of generosity. The Department wishes to expand our named fellowships for support of students and provide named endowments for professorships for our faculty and our nationally recognized facilities.

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 at the end. We encourage all of you to interact with us and look forward to receiving your comments, advice and referrals as we continue along this path and affirm our commitment to excellence. Also let us know if there is something you would like to see featured in future editions.

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

Biochemistry Research and Restart in COVID-19 Times

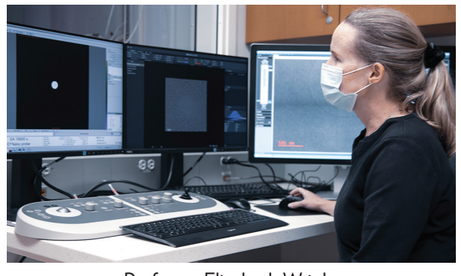
The halls of the Hector F. DeLuca Biochemistry buildings look a little different these days. They're quiet, like much of campus, but slowly and surely seeing more activity than they have since the start of the pandemic, when in late March, on-site access to campus was restricted to essential personnel.

Harriet Saunders (above), a graduate student in the lab of Associate Professor Jill Wildonger, is one of few who have been in the buildings for the duration, from the closure of campus through Phase 1 and now Phase 2 of its Research Reboot. Saunders was cleared for access during the initial closure in order to care for the lab's fruit flies, which are critical to their research.

"When I was coming in during lockdown, there was nobody here," said Saunders, who entered the buildings for about two hours each week. "I would go into the fly room and do whatever I needed to do, and by the time I'd come out, the lights in the corridor would [time] out. There was nobody."

But there were a few.

"It was definitely quiet and empty in the buildings for months," said Professor Elizabeth Wright, director of the department's new Cryo-Electron Microscopy Research Center (CEMRC), which was permitted to continue operations during campus closure. Wright remained on-site throughout to supervise a critical phase of the new center's construction and orchestrate complicated staffing needs during this time of heavily-restricted activity.



Professor Elizabeth Wright

Essential staff both on- and off-site played key roles in ensuring safe and productive progress on the project. In particular, center manager Eric Montemayor was "instrumental in efforts to roll out the CEMRC resources to the research community," said Wright. Biochemistry IT and DoIT also worked closely with center staff member Matt Larson to install complex IT infrastructure. Biochemistry shipping & receiving facilitated the deliveries of well over 50 crates and large boxes of equipment.

Careful coordination between CEMRC staff, CALS, FP&M, and microscope engineers from ThermoFisher Scientific ensured the commissioning of four high-end electron microscopes: a Titan Krios, Talos Arctica, and Talos L120C for negative stain and cryo transmission electron microscopy experiments; and an Aquilos cryo-microscope for scanning electron microscopy and *in situ* focus ion beam (FIB) milling of intact cells.

Ronnie Fredrick, NMRFAM

The result: continued operations during campus closure means CEMRC is nearing readiness to support research for the broader UW community.

Associate Professor Katie Henzler-Wildman also continued operations during the early months of the pandemic. As co-director of the National Magnetic Resonance Facility at Madison (NMRFAM) with Professor Chad Rienstra, and as PI of her own lab, Henzler-Wildman experienced the evolution of campus closure and restart on multiple levels.

NMRFAM was approved to remain open for essential operations at the start of campus closure. Magnets can't simply be switched off – shutting down and restarting would cost hundreds of thousands of dollars – so they must be filled with cryogens on a weekly basis.

Shortly after campus closure, Henzler-Wildman and Rienstra were awarded an EAGER grant to study coronavirus proteins of direct relevance to COVID-19, research carried out in collaboration with Assistant Professor Robert Kirchdoerfer. This award moved NMR from essential

Restart *Continued on next page*

Andrea Wegrzynowicz, Henzler-Wildman

operations only to essential operations and research.

Then in early June, Henzler-Wildman's lab was approved to resume research as part of Phase 1, along with 32 other faculty labs and facilities in all three buildings.

"It's been an avalanche of paperwork," said Henzler-Wildman. "The challenge is how to reasonably capture what's actually happening in a way that fits onto a semi-standardized form. Research is not set up the way paperwork is set up." Schedules and operations don't fit the same way into a form for one lab the way they might for another. Coordinating across common spaces is another challenge, as scheduling and sanitizing must be organized at the floor-level, across labs and PIs. Nevertheless, said Henzler-Wildman, "Overall, it's gone reasonably smoothly."

In order to resume research operations, labs and facilities submitted detailed plans, identifying essential personnel, outlining schedules, ensuring plans for PPE and density of population, use of common spaces and equipment, and so on in compliance with campus regulations. Plan coordination and oversight was provided by department leadership and team leaders from each floor of the buildings, including Brian Fox, Rick Amasino, Sam Butcher, Aaron Hoskins, Judith Kimble, Wes Pike, Vatsan Raman, Ivan Rayment, Ophelia Venturelli, and Amy Weeks, and approval was ultimately obtained from CALS and campus.

Jill Wildonger's lab was also approved to move from essential operations to resuming research. "I've never been so excited to fill out paperwork!" said Wildonger. She and her lab members worked closely together to develop a plan for resuming safe and effective research within their group. "Lab members were instrumental in giving suggestions and providing feedback that shaped these guidelines. We talked about various risk factors and scenarios (riding the bus, for example), trying to anticipate anything that we might encounter."

Schedules within the buildings are deliberately arranged to ensure partial capacity in compliance with Smart Restart, but the lights don't time out nearly as often these days. Saunders still works by herself in the Wildonger lab most of the time, but there may be multiple members on site depending on the day of the week.

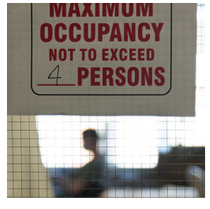
Masks were not new to many lab personnel, but are a new sight in hallways and other common areas. As part of the restart, the department supplied masks and hand sanitizer for each lab, and stationed additional supplies throughout the building. Individual bottles of sanitizer were also provided to all personnel who returned to the building. Signage on each floor reminds occupants of distancing guidelines, and each floor has its own method of ensuring safety in common spaces.

"We have a sign to flip on the bathroom when it is occupied to make sure there's only one person in there at a time," said Josie Mitchell, a graduate student in the Wildonger lab. "There are a lot more signs around reminding

people to wash their hands. Many doors have paper towel and ethanol spray for cleaning handles."

Campus custodians are not entering labs or offices at this time, so departmental staff have extra work to do in ensuring spaces remain clean and trash free. Building operations staff are considered essential personnel and have continued to work on site since the initial closure. Among other duties, they routinely walked the buildings to ensure alarms, leaks, equipment failures and other issues were promptly identified and resolved. They were also on site to oversee operations approved to continue during campus closure, including the delivery of infrastructure critical to the CEMRC, and, on a smaller scale, to empty breakroom refrigerators of food that was abandoned when campus was vacated.

Distancing guidelines have allowed research to resume, but as in so many public arenas, these behavioral shifts have altered interpersonal dynamics. "While everyone was generally excited to get back to the bench, there was a tinge of sadness in realizing that we wouldn't have the same in-person interactions that we had previously," said Wildonger.



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The department maintains a comprehensive vetting process at the floor, building, and department-levels, though the initiation of Phase 2 in mid-July introduced less stringent spacing requirements, allowing for more flexibility in scheduling of in-person research and the careful use of common spaces.

Throughout the evolution of the pandemic and the careful planning of campus leadership, the department has remained attentive and responsive to its new and evolving normal.

"There's more work to be done to stay safe and open for business," said Biochemistry Chair Brian Fox, "but I'm encouraged by the vigilance and compliance I see when I walk through our buildings. I applaud the efforts of everyone involved in our restart on all levels – it's been a herculean effort."

Research continues.....
Top: Ahlan Ferdous, Brian Carrick; Middle: James Corban, Gina Wade; Bottom: Liz Wood, Job Grant

Grant Research to Refine and Expand the Reach of Cryo-EM

Professor Timothy Grant

You may have missed Tim Grant's arrival on campus earlier this year: he joined the Biochemistry faculty and the Morgridge Institute for Research at a historic time, on the brink of campus-wide shutdown due to COVID-19.

In fact, Grant's first day of work was also the first day of shutdown. "I came into the building and it was largely empty. There were a few people who kindly came in to say welcome and so that I could fill out my starting paperwork," said Grant. "I've mainly been working from home ever since."

And he's made it work. Grant's field of research is in advancing Cryo-EM technology to improve the results of the technique, and to extend its use to more and more samples. Cryo-EM has been at the forefront of research in recent days, perhaps most notably in terms of understanding the structure of the SARS-CoV-2 virus which causes COVID-19. Cryo-EM as a tool has played a substantial role in contributing structures of these proteins to the research community, providing valuable insight into the way the virus works.

One of Grant's first collaborations on campus is with Professor Ivan Rayment and his team studying the structure of the yeast spindle pole body central plaque, which is expected to provide insight into the control of cell division. The central plaque samples form two-dimensional crystals, which are difficult to study using current Cryo-EM techniques.

"As the crystal is a sheet, the only way to get three-dimensional information is to tilt the sample," said Grant, "and this leads to a number of problems when trying to process them, so we're working on new computational methods to enhance the results."

Better images mean better structures and a better understanding of how molecules work, which can help researchers interact with molecular processes more effectively. If, as in the case of COVID-19, the molecules being studied are important to a specific disease, the structural information can be used to help design therapeutics for that disease.

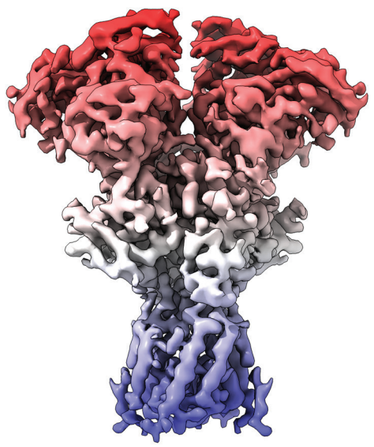
This is key for Grant: "The underlying reason for doing the research I do is to better understand biology and disease."

Grant joins the Department of Biochemistry and the John W. and Jeanne M. Rowe Center for Research in Virology at the Morgridge Institute for Research most recently from Janelia Research Campus, an HHMI research institute just outside of Washington D.C., where he worked as a Bioinformatics Research Specialist. Prior to his time at Janelia, he was in London at Imperial College, where he completed his undergraduate and Ph.D. degrees and developed a passion for Cryo-EM.

"My undergraduate degree was in Biochemistry, but I've always had a strong interest in computation," says Grant. "Cryo-EM is a great mix of the two. It requires a large amount of sophisticated computation to get a result, but the ultimate aim is to understand molecular structure and mechanisms and therefore further our understanding of biology."

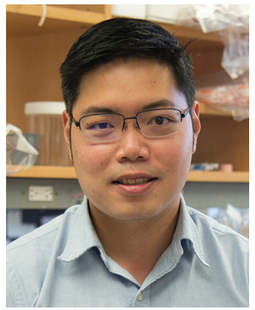
Grant was inspired by those courses he took as a student that were led by teachers who had a passion for the subject that they were able to instill into their teaching. He looks forward to emulating this model, and is driven to inspire similar passion in his own students in the years ahead.

And he looks forward to hiking, cooking, and making beer here in Madison – as well as identifying a winter hobby. "I came for an interview in late February," said Grant. "Apparently it was relatively warm for that time of year, but being from the UK — which rarely gets below freezing — it was still the coldest I have ever been. Something tells me I need to find an outdoor winter hobby I like soon!"



Single-particle cryo-EM structure of rat NMDA receptor.
Image courtesy of Tim Grant

Lim to Use Cryo-EM to Study Telomere Biology



Professor Ci Ji Lim

Ci Ji Lim's first impression of UW-Madison's campus: "amazing!" He was struck not only by the surrounding lakes – in stark contrast to the mountains in Colorado he was used to – but even moreso by the deeply meaningful interactions he had with UW-Madison's people, its faculty, staff, and students.

Now he'll be among them as the Department of Biochemistry's newest faculty member.

Lim, who goes by CJ, will use Cryo-EM technology to study how mammalian telomeres are regulated and how they achieve homeostasis. Telomeres act as protective caps at the ends of chromosomes, holding genetic information in place. Without telomeres, some of that information is lost every time a cell undergoes division. This loss of genetic information at the cellular level can lead to cancer and age-related diseases.

Lim developed an interest in telomere biology during his undergraduate research work in Singapore, where he grew up. This work led him to a Ph.D. in single-molecule biophysics at the National University of Singapore, and from there to Colorado, where he pursued postdoctoral training in biochemistry and Cryo-EM in the Cech lab at the University of Colorado, Boulder.

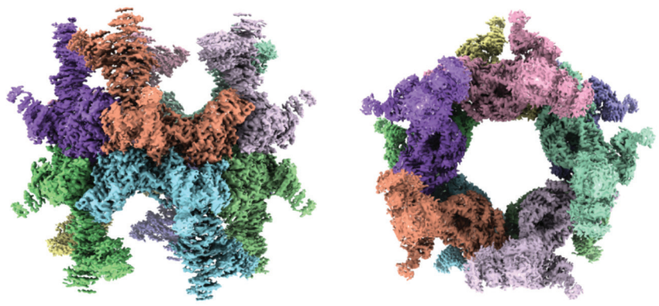
The thriving structural biology research community and state-of-the-art new Cryo-EM Research Center within the Department of Biochemistry at UW-Madison were a powerful lure for Lim. The cutting-edge facility was established by the Department and key partners including The Morgridge Institute for Research, with whom Lim will hold affiliate status, and can help researchers make significant new contributions to many areas of structural biology.

"Cryo-EM is a microscope technique that allows us to observe and take pictures of our samples frozen in thin ice," Lim explained. "Cryo-EM requires samples to embed in amorphous ice (also called vitreous ice) for imaging, which unlike crystalline ice (the kind of ice you would find in soft drinks or glaciers), is optically transparent. Amorphous ice is achieved by rapid cooling of water, so one would think this form of ice is rare, but in fact is likely the dominant form of ice in our universe!"

Lim's research has important implications for biomedical research, such as having the ability to develop specific drugs to target cancer and age-related illnesses.

Lim is eager to contribute to the University's long-standing tradition of the Wisconsin Idea, training and mentoring the next generation of scientists in his field. "I believe the benefits derived from research and education should not be confined within a laboratory or classroom, and should instead be applicable to a broader practicality," said Lim. "Studying how human telomeres are regulated will help us understand how related diseases come about, and find specific ways to combat these diseases. This involves training students and postdoctoral fellows through a key phase of their career development – and beyond."

The draw of the department's long-standing reputation in basic research excellence and commitment to establishing a leading Cryo-EM research facility excites Lim, who arrived in Madison in early August. When he finds the time, he also enjoys hiking, soccer and fishing.



Cryo-EM model of human CST decamer with telomeric ssDNA.
Image courtesy of Ci Ji Lim

Rienstra Joins Department as New Co-Director of NMRFAM

Professor Chad Rienstra

Chad Rienstra's scientific career was jump started by four years of undergraduate research, where he developed a broad interest in biology, chemistry, physics, mathematics, and engineering. It's this commitment to interdisciplinary research and education that he brings to bear years later as he joins the University of Wisconsin–Madison Department of Biochemistry as a professor.

After his undergraduate experience at Macalester College in St. Paul, Minn., he attended MIT for graduate school, followed by a postdoc at Columbia University. In 2000 he started at the University of Illinois, was tenured in 2008 and promoted to full professor in 2013, before joining UW–Madison this year.

Throughout this journey there has been one common thread — his interest in nuclear magnetic resonance (NMR), a scientific technique that allows scientists to measure the unique properties and structures of proteins, as well as other biomolecules and chemicals.

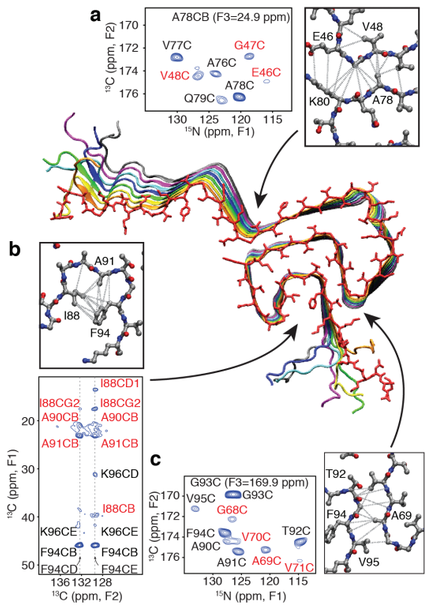
"I had an experience when I was an undergraduate, and then again in my postdoc, where my institution was getting a new magnet to use in NMR and I was tasked with helping with the installations," Rienstra says. "It was so fascinating and formative for me to follow around the engineers to learn about the instruments and how they work. NMR had seemed like magic to me — you push a button and get a result — but the more I learned, the more interested I became in the guts of how NMR spectrometers work and how they can work better."

In NMR experiments, samples of interest are placed in a probe and then placed inside a powerful magnet. The probe contains a special type of antenna, or "sample coil", to communicate with the nuclei inside the powerful magnetic field. Radiofrequency signals are sent to the sample through the probe in a series of magnetic pulses (so-called "pulse sequences"), which cause the nuclei of sample atoms to respond. "It's sort of like a game of 20 questions," Rienstra says, "the more precise questions you ask, the more you learn about the sample."

These answers are also picked up by the probe and stored in the receiver, where they carry vital information that allows scientists to learn about the molecules in the sample. In the specific experiments Rienstra performs — called solid-state NMR — the probe also spins the sample very rapidly at a "magic angle" to collect better data.

It is these probes that are at the heart of Rienstra's research. His lab performs experiments and collects and analyzes data using solid-state NMR, as well as engineers new probes, pulse sequences, and computational programs that help them better collect, analyze, and make use of data.

"The probe is the part of the instrument that interfaces the sample with the magnet," he explains. "Probes have critical effects on performance in every possible way and really determine the quality of NMR data you can get in an experiment."



Alpha-synuclein is a protein that forms fibrils in the brains of patients with Parkinson's disease (PD) and related disorders such as Lewy body dementia (LBD). Using solid-state NMR, the Rienstra group determined the first high-resolution structure of alpha-synuclein fibrils shown here. The figure illustrates the relationship between various types of solid-state NMR data and the molecular coordinates of the protein. Ongoing studies at NMRFAM are applying this technology to develop improved diagnostics for PD and LBD.

Image courtesy of Chad Rienstra

The structural data and other information that NMR supplies researchers is essential for understanding and finding treatments for many diseases. For example, Rienstra's lab studies aggregates of a protein (named alpha-synuclein) believed to be a cause of Parkinson's disease. Since solving the structure of a form of the protein, they have been working with a neurologist to study patients with different types of Parkinson's and other related diseases to see how the protein structures differ among them. The resulting structures could hold the key to better diagnosing and treating the diseases.

In another area of research in the lab, they are focused on the development of anti-fungal drugs, in collaboration with researchers at Illinois. One drug they are investigating (called amphotericin B) binds to fungal cells and extracts compounds (sterols) they need to survive. The problem is, it does the same with healthy human cells. Through their work they want to make it more effective but also less toxic to cells they don't want to kill.

A final part of his lab is devoted to developing better NMR technologies, including tools and techniques for obtaining data as well as computer algorithms and software to analyzing the data more effectively. He says the two areas feed off each other. Necessity is the mother of invention so when they need to gather specific data using a method not yet developed, they take on the task.

"I'm constantly fascinated by this discipline and how many ways it can be applied, from MRI in the human body all the way down to studying small drug molecules and even how to make better batteries," Rienstra says. "It's amazing that on a given instrument there might be a biochemist, an organic chemist, a materials scientist, and a physicist, all of whom can use NMR to accomplish very important yet very different research objectives."

During his career, Rienstra has been awarded a Howard Hughes Medical Institute predoctoral and postdoctoral fellowship, a National Science Foundation Faculty Early Career Development Program (CAREER) Award, among others. He is a fellow of the American Association for the Advancement of Science and a Cottrell Scholar from the Research Corporation for Science Advancement.

At UW–Madison, Rienstra will co-direct, along with biochemistry professor Katherine Henzler-Wildman, UW–Madison's world-renowned National Magnetic Resonance Facility at Madison (NMRFAM), which is housed in Biochemistry and serves as both a campus and national resource. He already brought in three 600 MHz magnets that were installed early this year, and a 750 MHz magnet moved from Illinois this fall. He is also expanding the number and types of probes to allow for a larger variety of experiments in NMRFAM, including for chemistry, materials, physics and engineering applications.

"This is one of the top NMR facilities in the world," he says. "It strikes a great balance between having state-of-the-art instrumentation and being highly accessible to researchers, a difficult feat. There are multiple faculty members doing NMR research and a world-class staff of experts. It's the type of environment that supports great research, where you can learn and collaborate with great colleagues. I've envied it for a long time and it's my dream job to be leading NMRFAM well into the future."

Installation of Varian 750 MHz magnet.

To read more about the department's new faculty go to *biochem.wisc.edu/faculty*

New National Imaging Center has Potential to Transform Medicine

A national research initiative announced in September will place the University of Wisconsin–Madison at the forefront of a revolution in imaging fostered by cryo-electron microscopy and cryo-electron tomography — technologies that can illuminate life at the atomic scale.

The National Institutes of Health will provide $22.7 million over six years to create a national research and training hub at UW–Madison that will give scientists across the country access to this game-changing technology.

Cryo-electron microscopy (cryo-EM for short) is a method used to make images of biological molecules that are flash-frozen to capture them in their native state. No dyes or other alterations are needed to view the structures, which gives scientists a highly accurate picture of true biological function. Scientists can peer into the very surfaces where drugs and proteins interact, where diseases occur, and where viruses orchestrate their attacks. Cryo-EM has the potential to impact every corner of medicine, from Alzheimer's disease to vaccine development, protein and cellular engineering and many other areas across all aspects of life sciences research.

One important specialization and focus of the national center, cryo-electron tomography (cryo-ET), dramatically extends the atomic scale illumination of cryo-EM by making images of the precise three-dimensional molecular locations where diseases and potential therapies interact with cells. This combination provides an unprecedented level of detail about the structure of living organisms.

Professor Elizabeth Wright

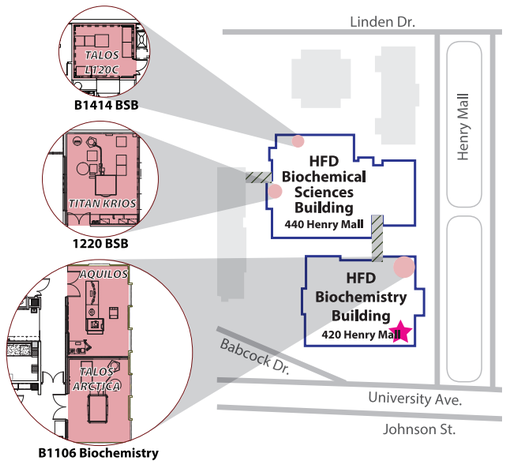
"One of the most exciting parts of the project will be bringing new investigators into the cryo-ET field," says lead investigator Elizabeth Wright, a UW–Madison professor of biochemistry and affiliate with the Morgridge Institute for Research. "This will help everyone in biological science research because discoveries made here will have the potential to be translated into new therapeutics and drug targets that benefit humanity."

One major aim of the NIH initiative is to bring more scientists into the game. Cryo-EM and cryo-ET are still young technologies with a limited workforce and very low access to the necessary equipment and expertise. The creation of four new centers — others will be at Stanford University, the University of Colorado-Boulder, and the New York Structural Biology Center — are meant to provide access to advanced instrumentation for cryo-ET, train a new workforce, and continually improve the technology while also providing new research discoveries.

The UW–Madison center will serve as a central hub for the national initiative, helping direct participating scientists to the right cryo-ET network resource.

"The goal is to help people become independent practitioners of the routines such as cryo-ET specimen preparation, data collection, and image analysis," Wright says. "Whenever appropriate, the UW–Madison center will support researchers as they solve interesting and technically challenging problems."

UW–Madison became a cryo-EM leader thanks to a decade-long investment beginning around 2010. The Department of Biochemistry in the College of Agricultural and Life Sciences (CALS) took the lead and the Morgridge Institute joined with significant financial and organizational support. The investment attracted partnerships with the Office of the Vice Chancellor for Research and Graduate Education (OVCRGE), the School of Medicine and Public Health (SMPH) and several other campus units. The fruits of this partnership will debut later this year with the grand opening of the UW–Madison Cryo-EM Research Center (*map left star*) in the Biochemical Sciences and DeLuca Biochemistry Buildings.



While the campus has already installed four high-powered cryo-EM instruments, the NIH initiative will pave the way for at least three more microscopes to accommodate the national demand. Installation is expected to be complete by early 2022. The grant also provides funding for training, computation and personnel.

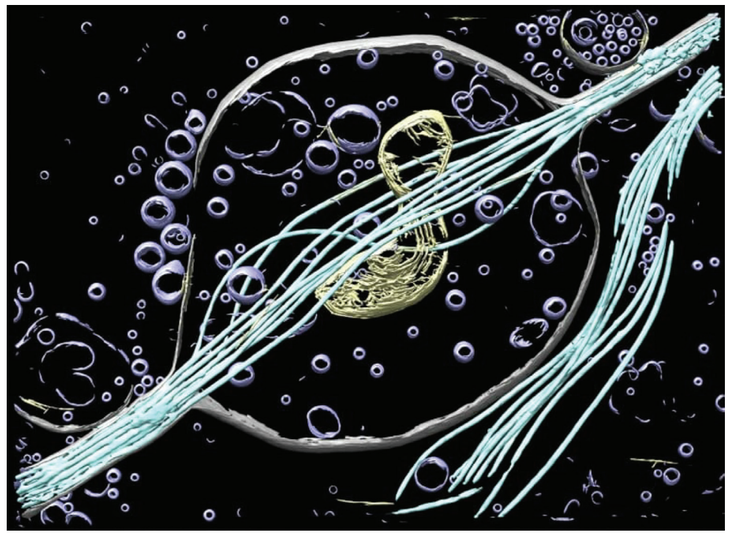
Recognizing the importance of cryo-EM to the future of structural biology, the Biochemistry Department and Morgridge Institute have already begun to assemble a team of investigators to advance the science. In addition to Wright, the Department of Biochemistry and CALS hired professors Robert Kirchdoerfer, who has expertise in cryo-EM applications in virology, and Ci Ji Lim, who has expertise in cryo-EM applications in DNA biology. The Morgridge Institute hired investigator Tim Grant (also a UW–Madison professor of biochemistry), who develops computer programs to improve cryo-EM and cryo-ET data collection and analysis, and investigator Brian Bockelman, who is an expert in research computation.

Wright's research experience in cryo-ET and cryo-EM was critical to securing the NIH hub. Prior to joining UW–Madison in 2018, Wright oversaw the development of an entire cryo-EM program at Emory University in Atlanta. She was intrigued with the same ground-up project development taking place in Madison, with added advantages of being associated with a powerhouse research university.

"There's no way we could have built a facility like this without Prof. Wright's vision, leadership, and scientific expertise," says Biochemistry Chair Brian Fox. "This initiative will push the understanding at a scientific level and has great potential for basic discoveries leading to translation from the lab to the clinic and transformative applications in many other important areas."

"UW–Madison has a long history of developing and perfecting imaging technologies that help biologists see, and therefore better understand, life," says Kate VandenBosch, CALS dean. "I am proud of our researchers' applications of these tools, as well as their efforts to make them available to the research community. Great discoveries will result."

Spinoffs have already emerged from cryo-ET. A colleague of Wright at Emory developed a vaccine for respiratory syncytial virus — a highly contagious infection that afflicts infants and young children — based on cryo-ET structures that has now advanced into a commercial venture. Investigators expect similar results here as new compounds, vaccines and drug targets are identified.



This three-dimensional view made by UW–Madison's Joseph Kim and Tanner Tenpas with cryo-electron tomography shows microtubules (in cyan) and mitochondria (yellow) — essential cellular components — of an individual neuron from the cortex of a mouse brain.

The Morgridge Institute, a private nonprofit research institute affiliated with UW–Madison, served as an important early catalyst in bringing cryo-EM tools and talent to Madison. Morgridge virology investigator Paul Ahlquist led the effort by bringing Morgridge, Biochemistry, OVCRGE and SMPH together to put UW–Madison on the map as a cryo-EM leader.

"As a basic research nonprofit, we have the ability to act quickly and make these kinds of strategic partnerships and investments in new frontiers of science," says Morgridge CEO Brad Schwartz.

Steven Ackerman, UW–Madison vice chancellor for research and graduate education, says the new cryo-ET hub will contribute to a great tradition of shared research facilities at UW–Madison, which is eighth in the nation for total volume of research conducted.

"The national status of this new center will serve as a powerful magnet for attracting top scientific talent to Wisconsin," Ackerman says.

The OVCRGE has provided key contributions from the annual Wisconsin Alumni Research Foundation gift to purchase instruments and provide start-up packages for new faculty, and its UW2020 program to hire new staff contributing to the advances in cryo-EM and cryo-ET on campus.

NIH's support for the cryo-ET center includes grant No. 1 U24 GM139168-01.

Story by Brian Mattmiller
Chief Communications Officer for Morgridge Institute for Research

Scott Coyle Awarded 2020 Packard Fellowship

Assistant Professor Scott M. Coyle has been named a 2020 Packard Foundation Fellow in Science and Engineering.

Coyle, whose research focuses on understanding and engineering microscale molecular and cellular machines, is one of 20 early career scientists from across the United States to be awarded this year's Packard Fellowship. The fellowship provides $875,000 in flexible funding over five years.

Coyle's project will develop models for how the structure and behavior of single cells — which he likes to think of as microscopic robots that move through, interact with, and respond to their environment — are encoded and programmed by their smaller components: the motors, filaments, signaling molecules, and so on, that are used to build and control the physical machinery of the cell. His goal is to reveal strategies for building and organizing molecules into complex machines that scientists can one day use to engineer new cell behaviors.

What Coyle learns could have broad-reaching applications, from expanding the scope and utility of cell-based therapies deployed inside the human body to fight human disease to developing smart micro-technologies that could scavenge damaged environmental sites to be used for bioremediation. The work could even lead to potential computing systems powered by biochemistry instead of electricity.

"To do this we explore a broad range of cellular systems," says Coyle, "from human cells that crawl around your body to single celled protozoans that can jump, forage, and hunt for prey like tiny animals. Despite how different these cells appear, they are all built from a similar toolbox of molecular components, but ones which are deployed in different ways — not so unlike how you can make a whole bunch of different electronic devices out of resistors, capacitors, and transistors."

Professor Scott Coyle

Coyle was drawn to apply for the fellowship in part because of its support of collaborative and creative approaches to research. The Packard Fellowship's flexible funding allows scientists the freedom to pursue research in innovative ways. In Coyle's case, this flexibility provides the resources for his lab to obtain and work with materials and biological systems, such as protozoan cells, which may otherwise be difficult to secure with traditional funding streams.

"Dr. Coyle is an extraordinary young scientist with a rich array of academic and industry research experiences," says Biochemistry Chair Brian Fox. "He is uniquely poised to integrate his training and break new ground with an exciting research program that will redefine how we understand the systems biology of cell behavior."

For Coyle, the fellowship is about a big-picture research vision. Collaboration and innovation will drive Coyle's project, as he works with researchers across disciplines at UW–Madison, including computer science for technologies in machine vision and deep learning as applied to cell biology and limnology to study Madison's lakes, a source of myriad understudied protozoan cells.

"We are entering an era in which the extraordinary biology of living systems will provide us a foundation upon which to build an exciting new class of molecular technologies," says Coyle. "Getting to interact with physicists, ecologists, and engineers will provide invaluable new perspectives and help me approach my own research questions from a fresh and inspired point of view."

Coyle is UW–Madison's 16th Packard Fellowship winner, chosen from among 100 other nominees from 50 universities across the country by an advisory panel of distinguished scientists and engineers.

The Coyle Lab mines the morphology dynamics of human cells as well as protozoan cells, like these Lacrymaria, to look for the design principles that govern complex cell behaviors.

Photo courtesy of Scott Coyle

NMRFAM Co-directors Awarded EAGER Grant to Study COVID-19

Professors Katie Henzler-Wildman and Chad Rienstra, co-directors of the National Magnetic Resonance Facility at Madison (NMRFAM), were awarded a grant in early June to study coronavirus proteins of direct relevance to COVID-19. The research is funded by a National Science Foundation EArly-concept Grants for Exploratory Research (EAGER) award, and carried out in collaboration with Assistant Professor Robert Kirchdoerfer.

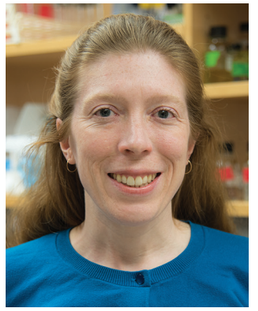
The research quickly contributes new insights into the structure and function of two important SARS-coronavirus-2 proteins: nsp8 and the membrane protein M. These proteins are key participants in genetic replication, translation, assembly and budding, and could provide vital insight into critical functions in the viral life cycle.

The protein nsp8 joins with other proteins to form larger complexes necessary for the replication of genetic material and the accuracy of that replication.

Membrane protein M mediates the viral assembly and budding of new material; there is no structural data currently available for M.

The immediate goal of the research is to understand the structure and dynamics of these proteins in relation to COVID-19 and other coronaviruses. In particular, the role they play in the replication process, why that role is important, how they interact with other proteins and molecules, and how they contribute to the overall form of the virus.

"These are the core processes of a much larger machine," said Henzler-Wildman. "We think that the conformational changes undergone by these proteins are important for this machinery to be able to function. Getting a better handle on the core functions of this family of virus will benefit our long term ability to control them."



Professor Katie Henzler-Wildman

Professor Chad Rienstra

Professor Robert Kirchdoerfer

This research is part of an organized international effort by the NMR community to understand the structure and function of the RNA and protein structures of SARS-CoV-2. Data from NMRFAM is being made available to other research groups as quickly as possible in order to further COVID-19 and related research. These data, and those of other NMR contributors, is shared online at COVID19-NMR (https://covid19-nmr.de).

NMRFAM has a long history of supporting activities such as remote data collection, so research contributing to this project can be performed by Madison personnel and remote collaborators despite evolving restrictions on physical access to the facility.

The EAGER grant funds a new direction for NMRFAM and leverages new instrumentation purchased as part of the recruitment of co-director Rienstra, who joined the Department of Biochemistry in early 2020. This solid state NMR equipment allows researchers to study molecules too large for liquid state NMR and too small for Cryo-EM. It expands the range of molecules that can now be studied through NMR technology, which has broad applications for studying the structure, dynamics and interactions of small molecules across a wide range of projects.

NMR sample tubes.

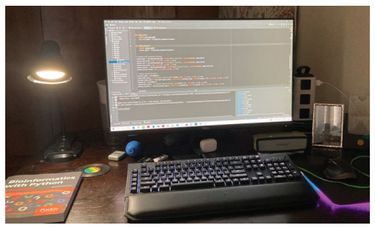
Undergraduate Research Continues Despite COVID-19 Restrictions

Despite COVID-19 restrictions on in-person campus operations, undergraduate students continue to carry out research with Biochemistry faculty. In particular, computational work is well-suited to being conducted remotely.

This brand of telecommuting, coined "tele-science" by Associate Professor Aaron Hoskins and carried out largely by undergraduate students across the department, is vital to research in biochemistry.

"All of my undergraduates are given their own, independent research projects – all of which are exciting and make contributions to my lab and the field at large," said Hoskins. "I don't think COVID-19 has changed this; however, it is has allowed us to prioritize computational projects for the moment.

Students conducting this type of research play a key role in taking large quantities of data and making those data accessible to scientists and researchers who need the information, but may not have the computer programming background necessary to gather and analyze it effectively.

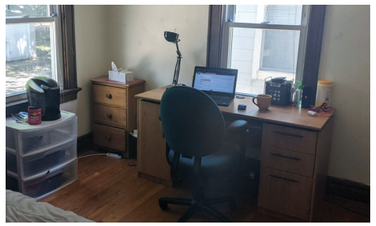


Yichen Sun, a rising senior majoring in statistics, works in the Hoskins lab. Hoskins's lab members, in particular, Drs. Harpreet Kaur and Clarisse van der Feltz, have developed a new way to evaluate the structures of complex cellular machines like the ribosome, spliceosome, or even the COVID-19 RNA dependent RNA polymerase. But to make their method more generally useful, they needed a way for it be used by non-computer-programming experts.

"That's where Yichen's summer tele-science project comes in," said Hoskins. "Using Python and his computer programming skills, he has created a graphical user interface (GUI) that allows anyone to carry out these evaluations."

Sun is writing a computer program which calculates the surface areas of intermolecular interactions between proteins from Protein Data Bank (PDB) files. These files contain information comprising RNA chains, and provide calculations on interactions within those chains. The aggregate information is then used to create network-theory based models of the structure.

The Hoskins lab is also interested in understanding how mutations in the spliceosome can change its function and cause diseases like cancer. "DNA sequencing of tens of thousands of tumor samples have revealed many different mutations in the spliceosome that are frequently associated with one cancer or another," said Hoskins. "What we need is an easy way to map these mutations onto cryo-EM structures of spliceosomes."



And that's where Lukas Voigts comes in. Voigts, a third year student majoring in biochemistry, is working on a project mapping these mutations. Specifically, he's mapping thousands of these mutations – found in 33 different types of cancers – onto spliceosome structures. He then uses PyMol to create a viewing platform which allows anyone to easily see how these mutations can impact spliceosome structure.

Sarah Fahlberg is a rising sophomore studying biochemistry and computer science. She works in Assistant Professor Phil Romero's lab, which studies the design principles of proteins and how they can be applied to engineer new molecular functions. Her project aims to understand how different methods of encoding protein sequences can be used for machine learning driven protein engineering.

Better methods mean more efficient processes for researchers studying the data. Protein sequences contain long chains of amino acids, which are indicated by letters. Computers need numbers to perform computations, so the protein sequences need to be coded accordingly. Falhberg's project examines how well different protein coding methods perform so that researchers can use machine learning to better predict sequences, and ultimately learn more about their questions by doing fewer experiments.

When campus shut down most on-site research operations earlier this year, these students, and their peers across the department, were able to steadily continue contributing to research.

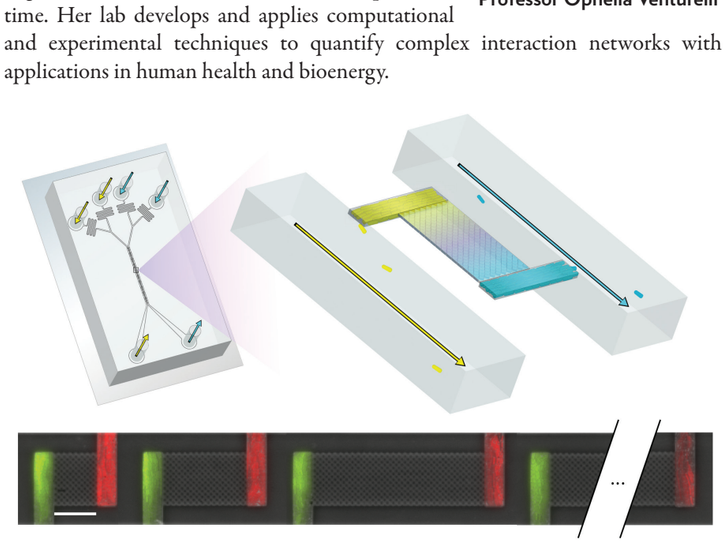
The arrangement is mutually beneficial, providing the lab with important research, and the students with hands-on experience, professional connections, and continued learning opportunities. Both technical and more nuanced types of learning have continued to progress for students off-site during the pandemic, thanks in part to the attentive support of mentors and colleagues, with whom students connect formally and informally through virtual lab meetings and via chat platforms.

Undergraduate *Continued on next page*

Scientists Develop and Apply New Tool for Studying the Dynamics of Microbial Communities

Microbial communities perform diverse chemical and physical transformations in every environment on Earth. These communities exhibit tremendous spatial and temporal variability. Abiotic (e.g. nutrient, pH) and biotic interactions shape the spatial distribution of microbes in natural environment such as the gut microbiome and plant rhizosphere. However, we do not fully understand how spatial arrangements influence microbial community metabolic activities, diversity or stability, or how to manipulate these spatial and temporal parameters to program community properties.

Biochemistry Assistant Professor Ophelia Venturelli and her team of researchers have developed and applied an experimental platform to quantify the impact of spatial and temporal parameters on synthetic microbial communities, according to a study published May 15 in *Nature Communications*.



Investigating spatiotemporal effects in microbial consortia using a microfluidic device that enabled precise control of spatial positioning and temporal inputs. We applied this method to study the role of spatial and temporal parameters in metabolic interactions in microbial consortia and bacterial signal communication.

Image courtesy of Ophelia Venturelli

In this study, the team applied MISTiC (Mapping Interactions across Space and Time in Communities) to identify key parameters that impact community stability and quality of information transmission within microbial communities. The platform enables real-time quantification of the net impact of one strain on another's growth rate, gene expression or other cellular phenotype and could be used to study diverse natural and synthetic communities.

Professor Ophelia Venturelli

Venturelli's lab seeks to understand and engineer microbial communities across space and time. Her lab develops and applies computational and experimental techniques to quantify complex interaction networks with applications in human health and bioenergy.

Undergraduate *Continued from previous page*

Fahlberg in particular cited enthusiasm for her developing skills in navigating the programming side of software development, as well as considering the needs of the end user; the constituents on these opposite ends of the software spectrum often speak different technical languages and exist in two different technical worlds, which she now bridges.

Sun has been learning Python, a program critical for a data scientist; the experience working with Python has broadened his thinking about potential careers: "I'd been thinking of only data science or consulting, but now bioinformatics looks pretty interesting."

Voigts's work with PyMOL and R "will be incredibly useful regardless of the area of study" he pursues.

And each of these projects continues to move research forward in the department, pandemic or no. Sun's GUI will be part of the research manuscript the Hoskins lab will submit on this project later this year. Voigts's work was released as a resource for the RNA community at the end of the summer.

"These computational projects are just as critical and important for our scientific research as would be purifying a protein or synthesizing a new ligand," said Hoskins. "Overall, I think our dynamic is as good as can be expected, but we all eagerly await the day when we can be in lab together!"

Attie Awarded RC2 Grant to Study Genetic Variation in Response to Diet

Professor Alan Attie has been awarded an RC2 grant through the National Institute of Diabetes and Digestive Kidney Disease to explore the role of genetic variation in the response to two popular human diets.

Obesity and related metabolic disorders have reached a historic high worldwide. While health experts have long debated the benefits of two disparate diets, high-fat/low-carb vs. low-fat/high-carb, clinical studies have not determined which diet achieves optimal metabolic health.

"Despite many years of research in humans and model organisms," said Attie, "there remains no clear consensus about which diet is most compatible with human health. But the premise of this statement is that a single diet is ideal for everyone. We know from our work in mice that different mouse strains respond differently to different diets, thus they harbor genetic variants that favor particular diets."

Professor Alan Attie

Attie's study investigates the genetic variants that determine this metabolic flux.

"Our collaborator, Dr. Richard Kibbey," said Attie, "has developed a method that uses stable isotope tracers to simultaneously interrogate many metabolic pathways. We will be able to genetically map the drivers that modify metabolic flux in response to the two extreme diets." Identifying these markers is the first step toward matching diets to individuals.

The RC2 award provides a total of $8.2M over five years to fund the discovery of genes and pathways that mediate diet responsiveness, and will be carried out in collaboration with Biochemistry researchers Attie, Distinguished Scientist Mark Keller, and Assistant Professor Judith Simcox, and Bacteriology Associate Professor Federico Rey at UW-Madison, along with Richard Kibbey (Yale) and Gary Churchill (Jackson Lab).

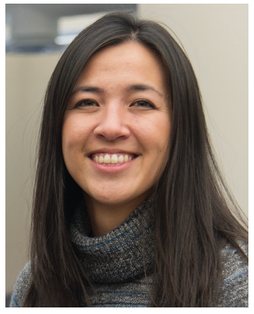
Simcox Named BIRCWH Scholar

Assistant Professor Judith Simcox has been named a Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Scholar at UW-Madison. The BIRCWH program supports highly-qualified early-career faculty whose research focuses on women's health or sex and gender differences.

Simcox's lab uses liquid chromatography mass spectrometry (LC/MS) analysis to characterize lipids and understand their role in metabolic diseases. In particular, Simcox studies lipids as predictive markers for metabolic disease in African American women.

In the 1950s and 1960s, medical doctors used lipids in the blood stream, including levels of LDL cholesterol and triglycerides, to develop a set of predictive markers for metabolic diseases such as type 2 diabetes. These markers were only validated in Caucasian males.

"Since the 1980s," said Simcox, "it was found that these are poor predictive markers for metabolic disease in African Americans, Latinxs, and Native Americans. By performing lipidomics on the Midlife in the US (MIDUS) and Survey of the Health of Wisconsin (SHOW) population studies, we've identified lipids that serve as predictive markers for metabolic disease in African American women, and will work to validate these results across multiple populations."



Professor Judith Simcox

Simcox is working with mentors Alan Attie, Biochemistry Professor and expert in lipid metabolism; Chris Coe, a psychologist and core leader for the MIDUS study; and Kristen Malecki, director of the SHOW population study, epidemiologist and bioinformatician.

"Being selected for this grant means that I have guided training in grant writing and mentoring," said Simcox. "It also allows me to connect my research with personal passions of addressing issues of health equity, inclusion, and diversity – as well as being part of an inspiring cohort of BIRCWH scholars I can turn to for support."

The UW-Madison BIRCWH program is funded by the NIH. The program seeks to improve women's health by developing a scientific network of independent research programs.

The term of the BIRCWH award for scholars is a minimum of two years.

Study from the Raman Lab Reveals Plasticity in Allosteric Signaling

Assistant Professor Vatsan Raman and IPiB graduate student Megan Leander have published findings in the *Proceedings of the National Academy of Sciences* (PNAS) on how proteins work. The findings are key to allostery, a property of proteins which is central to biology. Allosteric proteins play critical roles in cellular function, including signal transduction, metabolism, and gene regulation. Understanding how allostery works is a fundamental question in protein biophysics, and has high relevance to disease.

For instance, cancer genomes contain mutations in allosteric proteins that disrupt communication. And together, G-protein coupled receptors, nuclear receptors, ion channels and kinases – all allosteric proteins – account for 44% of all human protein drug targets.

But what is allostery?

"Perhaps a good analogy for allostery that most people can relate to is a Rube Goldberg machine," said Raman. "Most of us have seen a Rube Goldberg machine in real life or on TV. If you move a lever at one end, the lever rolls a ball, the ball falls into a balance, the balance tilts over, so on and so forth until some action happens at the other end far from the origin."

Imagine instead of a Rube Goldberg machine, a protein. When a protein is perturbed at one end, say by binding to another molecule, that perturbation is communicated through a network of amino acids within the protein resulting in a response at the other end. Depending on the protein, the response could be binding to DNA, binding to a different protein, catalysis and so on. The long-distance coupling between perturbation at one end and response at another end is allostery.

In the PNAS publication, Raman, Leander and their collaborators at Boston University show two things: first, that allostery is "plastic." This means that when allosteric communication is broken by a mutation, function can be restored easily by a compensatory mutation far away from the mutation that breaks function.

"It turns out there are many, many compensatory mutations for every breaking mutation," said Raman. Our results suggest that evolution has figured out multiple solutions to allostery, which is in contrast to the traditional notion that allostery is a brittle and finely-tuned network."

They also show that residues critical for these allosteric communications are poorly conserved, which also seems counterintuitive given that allostery is essential for function. Instead, residues required for structural integrity are highly conserved, suggesting evolutionary pressure to preserve fold over function.

"Once nature gets the fold right," said Raman, "there are many ways to create and preserve function."

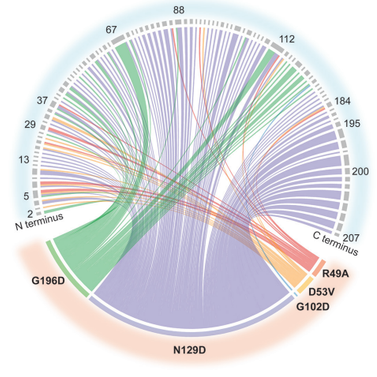
These unexpected findings offer a better biophysical understanding of allostery and has important implications for how natural proteins evolve.

"Our longer term goal is two-fold: First, to more broadly understand how mutations affect disease-relevant proteins. Can we predict what a mutation does without having to do laborious experiments? We think we can by learning from large datasets. Second, we want to identify allosteric sites for drug targeting," said Raman.

Professor Vatsan Raman

Megan Leander

"In fact," said Raman, "a major focus in pharmaceutical sciences is targeting drugs to the allosteric site instead of the active site to enhance target selectivity and reduce side effects. Our approach in the PNAS paper shows that allosteric sites in a protein can be systematically identified."

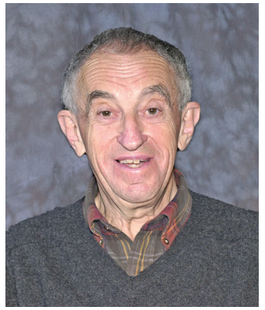


Protein wide mutational scanning reveals allosterically coupled residue pairs in TetR transcription factor.

Shaded mutations inactivate allosteric signaling. Each line indicates a residue that restores allostery by long-distance coupling.

Image courtesy of Vatsan Raman

To read more about the department's research go to ***biochem.wisc.edu/news***



Dr. Julius Adler

Emeritus Professors

The year 2020 marked an important and impressive occasion for two Emeritus Professors in the Department of Biochemistry. Both Julius Adler and Hector DeLuca celebrated their 90th birthdays.

Adler received his Ph.D. under Henry Lardy and then became a faculty member in 1960. In 1996 he became Emeritus.

When Julius accepted me as a graduate student, I was an immature boy who had never before lived away from home, who wanted desperately to be a great scientist, but who had little, if any, idea how to go about it. Fortunately for me, Julius had the patience of a saint, the temperament of a rabbi, and the knowledge of a first-class scientist. Oscar Wilde once said, "With age comes wisdom, but sometimes age comes alone." When I look back on the past 60 years, I realize that it was Julius who made my career in science possible. Thank you, Julius.

Patience: I loved to work late into the night. Julius tried to explain to me why it was important to be present during the day, as well, but I countered all his arguments, until – out of frustration – he said, "Someday I will have to write a letter of recommendation for you, and..." From then on, I was in the lab bright and early.

Temperament: Late one night I looked into the electron microscope and became the first person ever to see the basal bodies on bacterial flagella. Success! I needed to tell somebody that my experiment actually worked, but I was alone. So, I phoned Julius at his home (~11 PM). He answered the phone with a sleepy voice. "Julius, I cried, it worked! It worked! What worked, he replied? We've discovered the basal body on bacterial flagella! That's nice, you can tell me all about it in the morning."

Knowledge: Julius and I wrote several manuscripts together. He often asked me questions for which I thought the answers were obvious, but he insisted on solid experimental evidence. "Mel, there are two parts to research. First, you convince yourself of the truth. That's the easy part. Then you have to convince everyone else. That's the hard part!"

– Melvin L. DePamphilis, Ph.D. 1970, 1996 – present, Lab Head, National Institute of Child Health & Human Development, National Institutes of Health, Bethesda, MD

This is Julius' first lab group, ~1965. Julius Adler, Vera Waska Scott (technician), John Armstrong, Marjorie Dahl (research assistant), Melvin DePamphilis & Sylvia Zottu Schade.

Sylvia, John and Melvin were Julius' first graduate students.

I was a postdoc with Julius from 1986 to 1990. At the time, the lab consisted of several smallish rooms along the hallway in the basement of the Biochemistry Building on Henry Mall. All the doors of these small rooms were always kept open. Julius's office was nearby, with its door open as well, and one could hear him laugh at times. When you heard his bright and loud laughter, you could not help but smile! Every morning, he would "make his rounds": he would go in each one of these rooms and say Good Morning to whomever had arrived before him. In the afternoon, we would see him go to McDonalds across the street. He made no qualms about it! In front of his office outside, there was a beautiful large tree. I had heard that he fought for this tree not to be cut down a few years prior, when they were making additions to the building. Julius loves Nature. He loves birds, and flowers and *E. coli*! We had very lengthy group meetings. He just liked to hear people brainstorm. He wanted to hear your interpretations, your opinions, your plans, in details. He is very thorough and detail-oriented, but at the same time has a wonderful ability to tell a story, as we have all appreciated form his papers, lectures and talks. I always felt valued and welcome any time I interacted with Julius.

Happy Birthday, Julius!!

– Anne Delcour, Professor of Biology & Biochemistry and Associate Dean for Graduate Studies in the College of Natural Sciences and Mathematics, University of Houston, Houston, TX

Dr. Hector DeLuca

Celebrate 90th Birthdays

The Department was hoping to celebrate Adler and DeLuca with a reception earlier this year, but COVID-19 halted those plans. Instead, we've asked former lab members and alumni to help us honor them by sharing some of the anecdotes and messages of appreciation you would have heard in person.

DeLuca earned his Ph.D. under Harry Steenbock and became a faculty member in 1959. He became an Emeritus Professor in 2011.

Sometimes in life brief impromptu conversations have lasting impact. One morning after the very early Friday morning DeLuca Lab Meeting, I lingered with a few other graduate students over breakfast talking about the value of basic science and how critical it was to society. Someone in the group opined on how frustrating it was that the public did not understand true basic science. Overhearing a few youthful, somewhat disparaging comments over the public's lack of appreciation for basic science, Hector joined the conversation. He passionately told us that we as scientists must be able to clearly articulate to those supporting the research why it is important. He continued...the farmers in Wisconsin that support UW deserve to understand how the research at the University will benefit their farms, the state, and society. As I have progressed in my career in both basic science and pharmaceutical research, this memorable conversation became a guidepost to continually reflect on who are the key stakeholders and making sure I am keeping patients as the center of my scientific work. I know that I am one of many who have been profoundly impacted by Hector. I am grateful for the privilege of being trained and coached by Hector while I was a graduate student in the biochemistry department.

– Tom Brown, Ph.D. 1989, Medical Director, Alnylam Pharmaceuticals

I remember Hector's 65th birthday. We had buttons made that said Happy 65th birthday. I was on the elevator when someone entered, saw my button and asked if it was my birthday. I was 44 at the time. My mouth literally dropped open. Here it is a quarter of a century later and I am wondering where the time has gone. I spent more than a third of my life working for Hector and want to express my appreciation to Hector for that opportunity. Hector was, and I am confident continues to be, a very supportive leader and boss -- as evidenced by the loyalty and longevity of many of his former and current staff members. Thank you, Hector. I wish you many more years of health and satisfaction in your work.

– Wendy Hellwig, Nearly 26 years as Lab Manager in the Hector DeLuca lab.

I started working for Hector when I was pregnant with my second child, Gabriella who is now 25. A few years after that Margaret was pregnant with Martin and we had a funny conversation about child birth. I told Hector that in the 1990s, he would need to be present in the delivery room for the birth and not in a bar waiting to hear the outcome. We had a good laugh. Working with Hector was a lot of fun and there was much laughter. What has stuck with me over the years is if you make work fun, success is more likely. Hector and I did not always agree on the interpretation of the data. Those discussions made me better and were part of the fun. Happy birthday to my mentor, colleague and friend. Love and hugs, Margherita

– Margherita T. Cantorna, 1994-1998, Distinguished Professor Pennsylvania State University

The DeLuca lab was an exciting place for me as a graduate student. The isolation and identification of 25-OH-D had occurred shortly before I joined the lab. While I pursued my graduate work, 1,25(OH)2D was isolated, identified, and its biological properties explored.

This group of folks, who worked hard and played hard, created many memorable times. One fall day all of us, including Hector, collected chicken intestines at a processing plant in central WI. On another, we braved a WI blizzard to help isolate intestinal mucosa from chickens dosed with a radioactive tracer for the isolation of what would prove to be 1,25(OH)2D.

Everyone shared in the challenges and excitement of advancing Hector's vision for the basic science and for the application of vitamin D metabolism.

During this time, Hector was frequently gone, giving invited lectures or accepting awards and prizes. We 'lab rats' decided, in fun, that Hector's office could be put to better use in his absence. We put a 'For Rent' sign on the door. Before he returned, we filled the office with balloons and put a scarecrow in a lab coat at his desk with a mug of coffee. I am very pleased that Hector has subsequently made good use of his office, and he was there to celebrate his 90th birthday milestone. I still remember his 40th celebration! Many thanks for the memories, Hector, and all my best wishes.

– Joyce Clark Knutson, Ph.D. 1973, Wonderfully retired.

Julius Adler

My fondest memories of my time with Julius are his kindness to everyone, his passion for "Elmer" outside his office, and many interesting conversions that we had or in group settings. His yearly "Equinox" parties were fun and was never afraid to have these moments. In my office, I still have a picture of Julius with a kid's paper crown on head enjoying his 65th birthday party. My best wishes are to him on his 90th birthday.
– Louis S. Tisa, 1989-1994 Research Associate, Professor of Microbiology and Genetics; Chair of the Department of Molecular, Cellular and Biomedical Sciences, University of New Hampshire, Durham, NH

The impressive record of Julius in science speaks for itself. Therefore, I will not touch this aspect. Instead, I will mention two of the many things that caused me to be so highly fond of him.

One is the humane side and caring of Julius. I was touched to see how much he and Hilde cared for the wellbeing of me and my family in Madison when I did in his lab my second postdoc. We felt it from the moment of landing in Madison, finding Julius waiting for us at the airport with a named signboard in his hand and warmly welcoming us. Both Julius and Hilde made every effort to make us feel at home and miss nothing throughout our stay in Madison.

The other thing is Julius' unique, creative way of thinking. Julius and I occasionally used to stroll in the beautiful campus of Madison, discussing a variety of issues, not necessarily science-related. During these strolls, he sometimes surprised me with questions such as "Do you think that plants sense pain?" or "How come that the physical appearance of Jews (for example, the tint of the skin, eyes and hair) is not different from that of non-Jews in a given geographical location, even though Jews have refrained from intermarriages for many generations?", pointing out that the time elapsed since the beginning of the exile was too short for mutations to occur. We discussed such questions at length, and Julius always had original, interesting ideas about them. I also remember when, in one of our strolls, Julius demonstrated to me taxis other than bacterial chemotaxis. We passed by a *Mimosa pudica* plant and Julius touched one of its leaves. The leave immediately closed, and Julius explained that this is thigmotaxis, movement in response to touch. As can be imagined, these strolls and discussions were pure delight for me, and I very much cherish them and Julius.
– Michael Eisenbach, Postdoc 1978-1980, Professor emeritus, Weizmann Institute of Science, Israel

I have so many great memories of Julius; we hiked and ice skated and went canoeing together. I have kept in touch since I left his lab and my husband and I visit Julius and Hilde every so often. I remember one day, that Julius was telling a bunch of us in the lab, that there were prickly pear cactus in WI. We were filled with disbelief! So we all piled into Julius' car and he drove all over back roads west of Madison, looking for a certain hill. Those of us stuffed into his car were still doubters. Then he stopped and we started hiking up the sharp hill and suddenly, there were flowering prickly pear cactus all over!! We were all amazed. Julius taught me as much about nature, as he taught me about science!
– Mary L Hedblom, Ph.D., Postdoc 1978-1983, Happily retired now; Assistant Professor of Chemistry at Lafayette College for 2 years, then technical manager at Abbott Laboratories for 25 years.

Julius met with students at least weekly; we sat on his spartan green couch with bony wooden arms, while he asked questions about our data from the thick wooden swivel chair at his desk. His floor was often completely covered with research papers. The wall of reprints next to his desk was intimidating, but Julius put us at ease with his genuine curiosity and deep, resonating full-bodied laugh. Julius guided gently, but could let you know that you were on the wrong track – after I went off on some wild train of thought with little evidence, Julius simply responded "That's a very idiosyncratic idea." When Julius was intrigued, he was eager to discuss possible experiments. Once I brought some fresh result to Julius in the hallway. He said "Let's talk," plopped onto the floor with his legs out, and patted the floor to have me do the same. We sat there going over data for over an hour, with undergrads and faculty walking over us between their classes.

Julius introduced me at my dissertation defense with: "He has been in my lab.....forEVER. He is here in a futile attempt to get his degree with a talk on...". Julius planned on holding a sit-down dinner in his home that evening. Alas, my wife went into labor that afternoon. Hilde took formal photographs of the long table stretching into their living room, all empty, except for Julius and David eating soup as if the room were full.

More than any other scientist I've ever met, Julius had boundless curiosity, optimism, and genuine exuberance for students and living creatures. I've tried to bring that same exuberance to my own teaching.
– Matthew Buechner, Ph. D. 1990, Program Director, National Science Foundation, starting Sept. 2020, Associate Professor, University of Kansas until Dec. 2020

Anyone who's interacted with Julius Adler knows that he's a very methodical thinker. This was apparent to me in the small science sessions Julius held in his office when we brainstormed interpretations of perplexing results and what experiments to do next. But Julius' unique data-processing style really hit home to me one late November day as we walked along the shore of Lake Mendota, watching it freeze, as Julius loved to do. There were three or four of us strolling with Julius and someone asked him a question along the lines of "Do you know anyone who has a cabin in the Baraboo Mountains?" Julius continued walking, and walking, and walking. Five minutes passed and the questioner finally said "Julius, I asked..." and Julius instantly replied, "I'm thinking..." We kept walking, and walking, and walking. Another five minutes passed, then Julius turned to the questioner and said, "No".

I've tried to incorporate Julius' methodical, linear-logic approach in my own scientific endeavors and in my interactions with students and postdocs in my group. It's always served me well, as it did Julius.
– John S. (Sandy) Parkinson, NSF/NIH Postdoctoral fellow July, 1970-August, 1972, Distinguished Professor of Biological Sciences, University of Utah, Salt Lake City, UT

Hector DeLuca

Doing my doctoral work with Hector provided the foundation for my scientific career. I learned so many things from my time in his lab at UW Madison. Most importantly, I learned how to do science: how to identify important questions, how to think about them, and how to plan experiments, including the needed controls. Perhaps most of all, Hector taught me that science is always changing and that to keep up, it was important to embrace new challenges. As one example, Margaret Dame and I wanted to make antibodies to the 1,25–dihydroxyvitamin D3 receptor, but we weren't able to purify the protein to homogeneity. Hector arranged for us to work with Colleen Hayes to be trained in how to make monoclonal antibodies, which was a hot new technique at the time. We wound up with several great antibodies that catalyzed our research. I've tried to convey this spirit of being open to new things to the students and postdocs in my group since I started my own lab. In addition to being a great mentor, Hector also became a good friend. I am thrilled to wish him a happy 90th birthday.
– Eric Pierce, Ph.D. 1986, Chatlos Professor of Ophthalmology, Director, Ocular Genomics Institute, Harvard Medical School, Mass Eye and Ear, Boston, MA

One piece of scientific advice that he spouted continually in my memory:
"If you ask small questions, it's very likely you'll get small answers. If you ask big questions, you are much more likely to get big answers." He always encouraged scientific risk with reason - and to dream big in this endeavor.

An anecdote:
I had my first child in graduate school and found out I was pregnant shortly after my prelims. I was very nervous about telling him because it was extremely uncommon then, more than even now, to have a child as a graduate student. I told many lab mates and they shared my fear about telling him, with wagers going out on how badly and in just what manner he would explode when I told him. I chose a time right after it had been my turn to present lab meeting. I felt like I had produced a lot of data and he would be happy about that, and I knew there would be time alone after others had left and he stayed to give feedback, as he always did. I mustered up great courage and plowed into the news. About half-way through my pre-planned discussion, he started smiling then laughing, congratulating me and finding humor in that I was so afraid to tell him. He said quite a few things, but what I remember the most is his comment on my future in science (something I did not bring up and may not have thought through completely at that point). He said that, in his view, some people make it in science and some don't, but that he did not think it would have much to do with when you have a family; that one either perseveres or one does not and this was very unlikely to be the factor that mattered. That always stuck with me in my years of training and beyond.
– Deneen M Wellik, Ph.D. 1995, Professor and Chair of Cell & Regenerative Biology here at SMPH (UW-Madison)

While in grad school, I never wore a skirt or dress (because why would one dress up to be in lab???), and Hector noted that. He offered to wear a kilt for a day if I would wear a dress for a day. I agreed, bought a dress, and showed up to lab. Terry Meehan, another grad student, had two "kilts" (basically plaid skirts) made, one for him and one for Hector. They changed over the lunch hour, and we went out by Elmer the tree for a photo op. Most of biochemistry showed up for a photo op of Hector in a kilt.
– Beth Werner, Ph.D. 2001, Director Intellectual Property, Life Science WARF, Madison, WI

I started my PhD in Hector's lab in 1991, and initially I had little understanding of the stature of the man that was about to shape me into not only the scientist, but also the person I am today. Eventually I understood.

I had a passion for research, I was determined, and I was independent so I very much appreciated Hector's off-hand mentoring style. I would diligently conduct experiments until I hit dead-ends, and all it took was just short conversations with Hector for him to come up with the ideas to propel me into the next phase. To me they were always brilliant ideas and I marveled how they would come so easily.

Some of my colleagues referred to Hector as "the God of vitamin D" many years later, that's the kind of impact he had made to the field but his large research group of >30 people had open doors for just about anyone that needed an opportunity. He could have been elitist and chosen only the best for his lab, but instead he gave everyone a chance and generated excellence. His humbleness was exemplary.

In addition to providing me with an environment conducive to learning, teaching me how to undertake well-designed experiments, giving me confidence to undertake leadership roles, teaching me to write scientific papers (I take particular pleasure when reviewers comment that "this manuscript is well written"), Hector has been a friend: he has lent me a shoulder to cry on when needed, and has always helped and supported not only me, but also my family.

I'm lucky that I still get to work with Hector in my present job many years after I left the lab. Happy 90th Hector, I hope you can visit me in Switzerland soon.
– Claudia Zierold, Ph.D. 1995, in lab from 1991 to 2006, Technology Scouting and Scientific Affairs for DiaSorin

Julius Adler

I first met Julius Adler in November 1967. I was a second-year graduate student at Case Western Reserve University on a visit to UW to find a new Ph.D. advisor. The faculty member whose laboratory I had joined at Case Western had gotten very sick and I was advised that I needed to identify a new thesis lab. There were reasons to look beyond Case Western.

As I entered Julius' office, he explained that he had no extra funds or space for an additional graduate student, but he was happy to explain his research in what was scheduled to be a 30-minute meeting. Over the next hour and a half, as I listened to the amazing new areas he was investigating, we both got more and more excited. When I finally departed, Julius indicated that, if interested, I could join his research group but I should go back to Cleveland, consider all my options and write him if I were interested in joining his laboratory.

I did just that and received in return a quintessential "Julius letter". It read more or less as follows:

Dear Jerry,
Fine.
Best regards,
Julius

I have tried to emulate but never achieved that combination of brevity and content.
– Gerald L. Hazelbauer, Ph.D. (genetics) 1971, Active researcher, retired faculty member (Curators' Distinguished Professor and Biochemistry Chair Emeritus, University of Missouri)

In the late 80s and early 90s, I was a graduate student in Julius' lab studying the behavioral response of *E. coli* to blue light. Back then there was another student, Congyi Li, who was a very talented artist. He could convert any serious scientific discovery into a funny cartoon. After we discovered a mutant *E. coli* that had an enhanced tumbling response to blue light, Congyi produced a cartoon version entitled "Phototaxis Mutant". The character he drew looked like the Chinese mythological god Erlang Shen (二郎神), a deity with a magical third eye on his forehead. Just like our mutant *E. coli* , the Phototaxis Mutant had a mutation that enhanced its light perception ability.

In Julius' lab, my desk was the second one from the door, next to Mike's desk. My desk was always covered with research notebooks, research papers, and other miscellaneous items.... As embarrassing as this is to admit, my desk was probably the messiest in the whole lab. Julius must have noticed this, because one day he handed me a note that said, "Messy desk, clean mind." While I was thinking back on my time with Julius, this memory stood out to me. Even though it was a small gesture, I remember feeling really encouraged by his message.
– Hanjing Yang, Ph. D. 1992, Research associate, Molecular and Computational Biology, Department of Biological Sciences, University of Southern California

Hector DeLuca

Congratulations on your 90th birthday and successful career in vitamin D research. I also want to celebrate your longevity with the appreciation for your lifelong friendship. I spent two years and seven months (from July 1968 to January 1971) as a postdoctoral fellow in your laboratory. It was indeed an unforgettable time. While I was in Madison, I worked on the isolation and identification of vitamin D metabolites including 25(OH)D2, 25,26(OH)2D3, 1α,25(OH)2D3, and 24,25(OH)2D3. I enjoyed lab work with wonderful colleagues including Mike Holick, Heinrich Schnoes, John Blunt, Yoko Tanaka, Gerard Ponchon, Bob Cousins, Maryka Horsting, Tai Chen, Jack Omdahl, Ian Boyle, and many other excellent colleagues. After I came back to Tokyo, we synthesized 1α(OH)D3 as a synthetic analog of 1α,25(OH)2D3 and reported that 1α(OH)D3 is rapidly and quantitatively converted into 1α,25(OH)2D3 in the liver. 1α(OH)D3 has been used as a therapeutic drug for treating metabolic bone diseases such as renal osteodystrophy and osteoporosis in Japan. In 1998, we discovered osteoclast differentiation factor (ODF) as a key molecule for osteoclast formation, which was induced by 1α,25(OH)2D3. Hector kindly communicated this paper for publication in PNAS, USA (95: 3597-3602). The citation of this paper attained over 4,600. Hector taught me not only "biochemistry of vitamin D", but also "how science is fun". On this occasion, I would like to thank you for your lifelong collaboration and heartfelt friendship.
– Tatsuo Suda, D.D.Sc., Postdoc 1968-1971, Emeritus Professor of Showa University, Japan, Member of the Japan Academy

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On April 1st, 1983 I accepted a position in Hector DeLuca's laboratory to work in his lab as a cell biologist. I began my 35 years as an employee somewhat proficient in cell culture. Hector was always willing to discuss our research, and explore new ideas. After some time Hector put me in charge of cell culture in his laboratory. I began working primarily with two of his outstanding graduate students (Margaret Dame, and Eric Pierce), then eventually the entire lab followed by many graduate students and scientists.

Anyone who knows Hector, knows he likes his wine, so with my experience in cell culture, I soon began to culture yeast for wine fermentation, and always being grateful, he repaid me with wine. Hector was also known for his legendary "Pig Roasts", with many families and friends. We all had fun, playing games, and experiencing new foods.

During my time in the DeLuca lab, I was given opportunities to expand my knowledge in Biotechnology, stem cells, clinical trial monitoring. Hector is always appreciative of honest work and good results! – Jean Prahl, Research Program Manager, retired 2017

Around the Department

New Joint Advising Hub to Support Biochemistry and Microbiology Majors

Biochemistry and Microbiology Advising Hub advisors left to right: Amy Betzelberger, Jolijn Nagelkerke, Morgan Reidinger, and Katy France.

To continue to improve the student experience, the Departments of Biochemistry and Bacteriology are combining their undergraduate advising services to form the Biochemistry and Microbiology Advising Hub. With support from the College of Agricultural and Life Sciences (CALS), the hub will have a team of four advisors in a new space.

The hub will provide biochemistry and microbiology majors with expanded advising support, including shorter wait times, more flexible drop-in hours, and overall increased access to an academic advisor. It will also build a professional community among the advising staff, who can work closely together to continually improve student services. The location of the new Biochemistry and Microbiology Advising Hub is in Room 1315 of the Hector F. DeLuca Biochemical Sciences Building at 440 Henry Mall.

"The first of its kind in our college, this pilot collaboration will allow us to provide a professional community for our advisors and continue to better the student experience in these two excellent majors in our college," says Karen Wassarman, the CALS Associate Dean for Academic Affairs. "We've identified this as an area where we could do things more collaboratively, efficiently, and effectively and really serve our students in the best way possible, which is our top priority."

In addition to traditional academic advising on courses and degree completion, the increased staff will continue to explore other critical areas — such as mental health and wellness, career services, student organizations, recruitment, and programmatic improvements — to guide students or point them toward campus resources.

Katy France, who has been serving as the microbiology advisor, will be one of the hub advisors, as well as the recently hired Jolijn ("Yo-line") Nagelkerke and Morgan Reidinger. Amy Betzelberger, who served as the biochemistry advisor, will manage the hub and also advise students.

"Our goal is to best serve our students and also facilitate increased enrollment and diversity in both majors by expanding our services," Betzelberger says. "First-generation students, for example, might not come in with as much knowledge about college, and being able to assist those students as best we can will ensure they stay with us and finish their degree. We hope to continue our commitment to those students."

France is excited to work with Betzelberger in being part of a core group of advisers. Her knowledge of the microbiology major will be extremely valuable as all of the hub staff learn the requirements and post-graduation opportunities for both majors.

"In the long run, we hope to be able to offer more convenient and creative services to students," France says. "I am excited to transition to the hub because, in addition to continuing to work directly with students, I will get to work with a team of advisors on a day-to-day basis. We may also have the opportunity to develop expertise in new areas since we'll have more support."

The chairs of both departments, bacteriology professor Charles Kaspar and biochemistry professor Brian Fox, are excited for the opportunity to share advising resources between two large CALS majors that focus on molecular and fundamental biological processes.

"The new advising hub will benefit microbiology majors with a team of professional advisors available to help guide students through their four-year degree plan," says Kaspar, whose department offers the microbiology major. "The advisers will answer questions and concerns in a timely manner and help our great students meet the goals of both their major and budding professions."

To Fox, the hub is an example of what CALS and its departments excel at, which is uncovering areas of partnership with the ultimate goal of moving the entire college forward.

"We are excited for the opportunities this hub will provide our undergraduate students and advising staff," Fox says. "This initiative is at the heart of what we do as departments and a college: find creative and effective ways to serve our students in the best way possible."

Wassarman says the hub will also build community among the student support staff, allowing them to foster new ideas and initiatives that will better serve students. In addition, she says she'd like to see the college broadly move toward this model of collaboration, which was inspired by CALS Organizational Redesign efforts.

"By providing this professional community, they will have backup support and ways to troubleshoot and brainstorm new ideas," says Wassarman, who is also a professor in the Department of Bacteriology. "It is important to recognize the professional and unique skill set required for our undergraduate services. I have every confidence that this is going to be a success and others will be able to see how this idea of community building can support both students and professional staff."

She adds that the hub is not meant to replace student-faculty relationships. Students and faculty are still encouraged to connect for mentorship. The hub's advisors hope that it can also serve as a resource for faculty and instructors who identify students who need extra help.

"Students are going to experience a greater quantity and quality of advising services as we continue our commitment to their education," Betzelberger says. "We are very excited about the possibilities this collaboration opens for us and the students in these majors."

IPiB Degrees 2020

Degree	Name (Major Professor)	Thesis Title
PhD April 2020	**Samuel Craven** (Senes)	Structural and functional analysis of the *E. coli* cell division proteins FtsL and FtsB
PhD April 2020	**Kelly Mitok** (Attie)	Mutation in Sortilin identified in an Amish population results in hypercholesterolemia and insulin resistance in mice and humans
PhD May 2020	**Samson Condon** (Senes)	Understanding membrane protein association through molecular modeling and evolution
PhD July 2020	**Zachary Romero** (Cox)	Critical roles for *E. coli* DNA repair proteins Uup and RadD
PhD Aug 2020	**Valeriu Bortnov** (Mosher)	Myeloid-derived growth factor (MYDGF): investigations of structure and function
PhD Aug 2020	**Megan Dowdle** (Sheets)	Defining the RNA binding functions of the translational repressor Bicaudal-C
PhD Sept 2020	**Evan Glasgow** (B. Fox)	Discovery, analysis, and modification of multifunctional glycoside hydrolases
PhD Oct 2020	**Mark Klein** (Denu)	Mechanisms of enhanced catalysis for the histone deacetylase SIRT6
PhD Oct 2020	**Stephanie Maciuba** (Martin)	Characterizing the roles of CAPS proteins in secretory cells

IPiB Graduates

Biochemistry Advisor Degrees 2020

Degree	Name (Major Professor)	Program	Thesis Title
PhD Dec 2019	**Jeremy D. Volkening** (Sussman)	CMB	Development and application of mass spectrometric technologies for plant molecular biology
PhD June 2020	**Sihui Z. Yang** (Wildonger)	CMB	*In vivo* genetic analysis of golgi outposts' role in microtubule organization in Drosophila sensory neurons
PhD Oct 2020	**Leland Hyman** (Romero)	CMB	Integrating DNA logic circuits and isothermal amplification methods: novel tools for single-cell tanscriptional profiling and diagnostics
PhD Oct 2020	**Sarah Robinson-Thiewes** (Kimble)	Genetics	The role and regulation of ERK/MAPK in the *C. elegans* germline
MS Aug 2020	**Ashley M. Cortés Hernández** (Bednarek)	CBMS	
MS Aug 2020	**Apoorv Saraogee** (Romero)	CBE	

****Degrees Dec. 1, 2019 - Nov. 30, 2020****

CBE: Chemical & Biological Engineering
CBMS: Comparative Biomedical Sciences
CMB: Cellular & Molecular Biology

Honors & Awards

Faculty

Samuel Butcher	2020 Distinguished Teaching Award
Scott Coyle	2020 Packard Foundation Fellow in Science and Engineering
John Ralph	2020 Groupe Polyphénols Scientific Grand Prize 2020 Clarivate Analytics Highly Cited Researcher
Judith Simcox	Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Scholar at UW-Madison UW2020: WARF Discovery Initiative Awardee Washington University at St. Louis Diabetes Research Center Pilot Grant University of IL at Chicago 8th Annual Diabetes & Obesity Research Day Emerging Investigator Award
Jill Wildonger	Jean V. Thomas Professorship in Biochemistry

Emeritus Faculty

William Reznikoff	2020 Fellow of the American Association for the Advancement of Science (AAAS)

Staff

Amy Betzelberger	Advising Hub	2020 Early Career Excellence in Undergraduate Advising Award
Hoon Kim	Ralph	Senior Scientist Distinguished UW–Madison Job Title
Megan Pierce	Dept. Office	Light of Well-being Recognition (with Bre Sinotte Wang) Platinum certification Green Office Program (with Morgan Wendt)
Bre Sinotte Wang	Dept. Office	Light of Well-being Recognition (with Megan Pierce)
Morgan Wendt	Dept. Office	Platinum certification Green Office Program (with Megan Pierce)

Postdoctoral Staff

Samantha Anderson	Senes	Biophysical Society/AAAS Congressional Fellow
Ryan Clark	Venturelli	Genomic Sciences Training Program (GSTP)
Christopher Emfinger	Attie	Metabolism and Nutrition Training Program MANTP Fellowship
Gisela Geoghegan	Simcox	UW-Madison Comprehensive Diabetes Center Pilot Award
Daniel Parrell	Wright	Cover artwork for Molecular Microbiology Volume 114, Issue 4 (October 2020)
Bryan Sibert	Wright	Microscopy Society of America 2020 meeting Invited Platform Presentation
Jae Yang	Wright	Microscopy Society of America 2020 meeting Postdoctoral Scholar Award for Platform Presentation

Graduate Student Awards

Megan Dowdle	Sheets	Denton Award for Graduate Student Excellence in Teaching & Mentoring
Harriet Saunders	Wildonger	Denton Award for Graduate Student Excellence in Teaching & Mentoring
Josephine Mitchell	Wildonger	Sigrid Leirmo Memorial Award in Biochemistry
Raghav Jain	Simcox	Center for Demography of Health and Aging (CDHA) Pilot Grant
Joseph Kim	Wright	Microscopy Society of America 2020 Student Award for Platform Presentation
Juan Sanchez	Wright	Student Spotlight in the November 2020 Microscopy Society of America Newsletter
Lainy Von Bank	Simcox	Hatch Award

Graduate Student Fellowships

Matthew Blackburn	Sussman	Biochemistry Teaching Fellowship
Josephine Mitchell	Wildonger	Biochemistry Teaching Fellowship
Evan Glasgow	Fox	CALS Thomsen WI Distinguished Graduate Fellowship
Dana Dahhan	Bednarek	Arthur B. Michael Fellowship
Harriet Saunders	Wildonger	Arthur B. Michael Fellowship
Abigail Bartlett	Pagliarini	NSF Graduate Research Fellowship Program
Christine Hustmyer	Landick	NSF Graduate Research Fellowship Program
Nathan Murray	Pagliarini	NSF Graduate Research Fellowship Program
Kyle Robinson	Pagliarini	NSF Graduate Research Fellowship Program
Katherine Senn	Hoskins	NSF Graduate Research Fellowship Program
John Ah	Coyle	NSF Graduate Research Fellowship Program Honorable Mention
Karli Lipinski	Hoskins	NSF Graduate Research Fellowship Program Honorable Mention
Jacob Rapp	Romero	NSF Graduate Research Fellowship Program Honorable Mention
Jonathan Tai	Pagliarini	National Institute of Health Fellowship
Brian Carrick	Kimble/Wickens	William H. Peterson Fellowships in Biochemistry
Megan Leander	Raman	William H. Peterson Fellowships in Biochemistry
Dylan Plaskon	Record	William H. Peterson Fellowships in Biochemistry
Ashley Cortes Hernandez	Bednarek	Science and Medicine Graduate Research Scholars (SciMed GRS)
Christiana Binkley	Landick	Science and Medicine Graduate Research Scholars (SciMed GRS)
Matthew Blackburn	Sussman	Sam C. Smith Graduate Fellowship
Miguel Osorio Garcia	Cox	William R.& Dorothy E. Sullivan WI Distinguished Graduate Fellowship in Biochemistry
Peyton Spreacker	Henzler-Wildman	Steenbock Predoctoral Fellowship in Biochemistry
Nathan Thomas	Henzler-Wildman	Steenbock Predoctoral Fellowship in Biochemistry

Graduate Student Training Grants

Jackie Chen	Raman	Biotechnology Training Program (BTP)
Clara Frazier	Weeks	Biotechnology Training Program (BTP)
Andrea Killian Wegrzynowicz	Henzler-Wildman	Biotechnology Training Program (BTP)
Jacob Rapp	Romero	Biotechnology Training Program (BTP)
Johnson Saba	Landick	Biotechnology Training Program (BTP)
Juan Sanchez	Wright	Biotechnology Training Program (BTP)
Aspasia Amiridis	Weeks	Chemistry-Biology Interface Training Program (CBI)
Christine Hustmyer	Landick	Chemistry-Biology Interface Training Program (CBI)
Laura Steenberge	Pagliarini	Chemistry-Biology Interface Training Program (CBI)
Sierra Love	Hoskins	Genetics Training Program (GTP)
Juan Diaz Rodriguez	Romero	Genomic Sciences Training Program (GSTP)
Max Frenkel	Raman	Genomic Sciences Training Program (GSTP)
Kimberly Huggler	Cantor	Genomic Sciences Training Program (GSTP)
Mark Mahnke	Romero	Molecular Biophysics Training Program (MBTP)
Tyler Peterson	Senes	Molecular Biophysics Training Program (MBTP)

Undergraduate Awards

Jessica Liu	Cox	Alpha Helix Scholarship Award
Takahiro Ishikuri	Record	Biochemistry Mary Shine Peterson Award
Eric Leisten		Biochemistry Mary Shine Peterson Award
Claudia Liu	Markley	Biochemistry Mary Shine Peterson Award
Jessica Liu	Cox	Biochemistry Mary Shine Peterson Award
Stella Ma		Biochemistry Mary Shine Peterson Award
Saveda Majety		Biochemistry Mary Shine Peterson Award
Anuchit Rupanya	Record	Biochemistry Mary Shine Peterson Award

Undergraduate Awards continued

Jiayin Tang		Biochemistry Mary Shine Peterson Award
Connie Wang	Fox	Biochemistry Mary Shine Peterson Award
Mingyu Xue	Kimble	Biochemistry Mary Shine Peterson Award
Alana Caldwell	Pagliarini	Biochemistry Undergraduate Summer Research Award
Xi Chen	Cavagnero	Biochemistry Undergraduate Summer Research Award
Gregory Francis		Biochemistry Undergraduate Summer Research Award
William Langholz	Record	Biochemistry Undergraduate Summer Research Award
Jihua Liu		Biochemistry Undergraduate Summer Research Award
Steven Martell		Biochemistry Undergraduate Summer Research Award
Najhee Purdy		Biochemistry Undergraduate Summer Research Award
Alex Taylor		Biochemistry Undergraduate Summer Research Award
James Wang	Romero	Biochemistry Undergraduate Summer Research Award
Abigail Watson	Cox	Biochemistry Undergraduate Summer Research Award
Wei Wanting	Cavagnero	Biochemistry Undergraduate Summer Research Award
Stella Ma		Barry Goldwater Scholarship
Elizabeth Sumiec		Barry Goldwater Scholarship
Sarah Doughty	Record	Phi Beta Kappa Honor Society
Seamus McWilliams		Phi Beta Kappa Honor Society
Jacob O'Hearn		Phi Beta Kappa Honor Society
William Raskopf		Phi Beta Kappa Honor Society
Jinan Sous		Phi Beta Kappa Honor Society
Elizabeth Sumiec		Phi Beta Kappa Honor Society

Undergraduate Fellowships

Anna Allen	Cavagnero	Hilldale Undergraduate Research Fellowship
Owen Erpelding		Hilldale Undergraduate Research Fellowship
Sarah Ertmer	Venturelli	Hilldale Undergraduate Research Fellowship
Gregory Francis		Hilldale Undergraduate Research Fellowship
Fang Hao	Bednarek	Hilldale Undergraduate Research Fellowship
Tiancheng Hu		Hilldale Undergraduate Research Fellowship
Takahiro Ishikuri	Record	Hilldale Undergraduate Research Fellowship
Jaitri Joshi		Hilldale Undergraduate Research Fellowship
Bridget Kaiser	Rayment	Hilldale Undergraduate Research Fellowship
Eric Leisten		Hilldale Undergraduate Research Fellowship
Jessica Liang	Wildonger	Hilldale Undergraduate Research Fellowship
Erin McCann		Hilldale Undergraduate Research Fellowship
Geet Pandya		Hilldale Undergraduate Research Fellowship
Kayleigh Pignato		Hilldale Undergraduate Research Fellowship
Kunal Sondhi		Hilldale Undergraduate Research Fellowship
Jiayin Tang		Hilldale Undergraduate Research Fellowship
Mingyu Xue	Kimble	Hilldale Undergraduate Research Fellowship
Michael Gilpin	Simcox	NSF Undergraduate Research Fellowship
Pak Lun Kevin Cheung	Venturelli	Sophomore Research Fellowship
Sarah Fahlberg	Romero	Sophomore Research Fellowship
Zoe Zanella	Kirchdoerfer	Sophomore Research Fellowship
Anna Christenson		Sophomore Research Fellowship
Asha Jain		Sophomore Research Fellowship
Xi Chen		Sophomore Research Fellowship Honorable Mention
Hailee Morrison		Sophomore Research Fellowship Honorable Mention
Qiuwen Quan		Sophomore Research Fellowship Honorable Mention
Alexandra Steinberg		Sophomore Research Fellowship Honorable Mention

2020 Biochemistry Undergraduate Summer Research Awards sponsored by

Carl Krieger Memorial Fellowship Fund, Department of Biochemistry Fund, Eric Bey & Amanda Boley Fund, EW Hopkins Fund, Floyd C McIntire Biochemistry Award Fund, Henry A Lardy Undergraduate Research Fund, Kimberly Clark Undergrad Fund, Telander Research Fund.

We Heard About You

Below are some updates we got from the faculty.
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.

Attie Lab
Melkam Kebede, former post-doc, earned tenure at the University of Sydney, Australia.
Jeremy Lavine, former graduate student, is now an Assistant Professor at Northwestern University.

Butcher Lab
Dr. Eric Montemayor is now Manager of the UW-Madison Cryo-EM Facility.
Dr. Allison Didychuk (PhD 2017) is a Damon-Runyon Postdoctoral fellow at UC-Berkeley and currently interviewing for faculty positions.

Frey Lab
Professor Squire J. Booker of Penn State University, a past postdoctoral associate, has been elected to the National Academy of Sciences in 2020.

Hoskins Lab
Harpreet Kaur and her husband welcomed Aroha Rooh into the world on October 17 at 7:27am.
Clarisse van der Feltz is now an Assistant Professor of Biology and Biochemistry at Northwest University.
Margaret Rodgers published some of her postdoctoral work in a tour-de-force manuscript in Cell.
Tucker Carrocci received a NIH F32 postdoctoral fellowship.
Both Tucker and Sarah Hansen published chapters in the same book--RNA Control and Regulation from CSHL Press.
Jack McCann started graduate school at UC Berkeley in Chemistry.
David Beier is now in grad school at U. Michigan.
Doug Zoerner is now a neurosurgery resident at U. Kentucky.

Ludden Lab
Sandra Grunwald, former graduate student, is Professor of Chemistry and the Associate Vice Chancellor for Academic Affairs at UW LaCrosse.

Ntambi Lab
Harini Sampath PhD, Assistant Professor, Rutgers University.
Maggie Burhans PhD, Scientist on biomarkers in cardiometabolic diseases at Amgen in South San Francisco.
Laura Bond PhD, Postdoctoral Research Associate, Farese and Walther Laboratories, Harvard School of Public Health.
Sabrina Dumas PhD, Clinical Research Liaison at Imbed Biosciences Inc.

Record Lab
Kate Henderson, former post-doc, is now a research scientist at Illumina.
Claire Evensen, former undergrad & 2020 summer intern, has started her Marshall Fellowship at Oxford. She added a few more awards to her already impressive CV before leaving: 2020 Berkeley Fellowship for Graduate Study, Hertz Fellowship Finalist & NSF Graduate Research Fellowship Honorable Mention.

Reznikoff Lab
Cathy and I have moved to St. Paul, MN. We have a great apartment that overlooks the Mississippi. We are near all of our kids - with Charlie being 15 min away. When the pandemic disappears we will be making regular trips to Mad City. I NEED to check on all the Biochem folks.

Simcox Lab
Jenna Rogalinski, former undergrad, has a job as a Quality Assurance Auditor at Covance. She worked in the Simcox lab as part of the Biochem Scholars.
Charlie Kirsh, former postbac, currently working as a research associate I at A2 Biotherapeutics in LA.

Wickens Lab
Amy Cooke is now an Assistant Professor at Haverford College.

Wright Lab
Lab well represented at Microscopy Society of America (MSA) 2020 Microscopy & Microanalysis Meeting: grad students Joseph Kim*, Juan Sanchez and postdocs Jae Yang*, Bryan Sibert, Daniel Parrell, & Juleen Dickson all gave Platform Presentations at the meeting. (*won award for presentation).
Joseph Kim was appointed Communications Chair for the MSA Student Council, and elected to MSA Student Council Biological Sciences Co-Chair for PMCx60 Meeting.
Daniel Parrell & Jae Yang each presented a poster at EMSL Integration 2020 (Environmental Molecular Sciences Laboratory).

Letters from the Labs

We'll be including a selection of faculty members each issue of *Biochemistry InVivo*.

Fox Lab

I can hardly remember the simple life before March 8, 2020. However, it is awe-inspiring to reflect on how the lab rose to the challenge of the COVID-19 pandemic. We closed the lab, moved to remote research, planned for the reopening, and then brought our research enterprise back to life starting in June 2020. We are now operating safely and carrying out our mission of research, teaching and service.

Our lab brings together researchers from the Biochemistry and Chemistry departments and the Great Lakes Bioenergy Research Center. Here are a few highlights.

Kirk Vander Meulen (PhD from the Butcher lab) manages my lab and has done an exemplary job guiding us throughout the COVID-19 operations. When he is not keeping us safe and productive, Kirk has continued to develop his programming skills and has brought quantitative analyses to a new level in our enzyme assay methods. Kirk is also creating new ways to visualize our extensive functional assignments to phylogenetic trees of glycoside hydrolases, transferases and ligases. Kirk is the mentor to undergraduates **Connie Wang** (Mary Shine Peterson fellowship) and **Eric Heffernan** (Biochemistry Scholars Program) who have projects that take full advantage of the biophysical capabilities of the lab and department research core facilities.

Evan Glasgow completed his PhD in September 2020 and moved to Promega shortly after. Evan was a Trainee of the Biotechnology Training Grant. During his graduate training, Evan was a mentor of **Jenna Amro, Kaylee Findseth, Eli Kemna** and **Niall Ellias**, who came to the lab from the Dane County Youth Apprentice Program and **Jesslyn Park**, who came from an NSF REU program; they all made great contributions. With this outstanding mentorship effort, Evan was a recipient of the Denton Teaching Award and a Wisconsin Distinguished Graduate Fellowship. Evan made significant advances in understanding the structural basis for broad substrate specificity observed in glycoside hydrolase family GH5_4. Best wishes to Evan; we hope to see him at BTP Winter Banquets in the future as a sponsor of new BTP interns.

Nate Kuch is also a Trainee of the BTP. He completed the required internship at Promega in 2019 and is working on a collaborative bioenergy project with the Dumesic lab from the Chemical & Biological Engineering department as part of the Great Lakes Bioenergy Research Center. Nate is the mentor to UW-Madison undergraduates **Alex Parker** and **Mark Kutschke**, who have been helping us write an invited review on the use of cell-free biosynthesis methods in systems biology research. This team is also researching a processive endocellulase with high reactivity with GVL cellulose produced in the Dumesic lab.

John MacDonald worked with us for about two years and then entered Pharmacy School in Fall 2019. Congratulations to John for achieving his next career step after undergraduate studies.

Rebeca Fernandez, Rebecca Schultz and **Joshua Miller** join us from the lab of Thomas Brunold in Chemistry. In exchange for their gentle teaching about spectroscopy and density functional theory, we help them with protein expression problems and crystal structure determination. Their topics of study are the structure and mechanism of mononuclear iron enzymes involved in cysteine metabolism: cysteine dioxygenase and cysteamine dioxygenase. Each has made impressive advances. In her race toward the dissertation finish line Rebeca made a hero's effort along with **Bob Smith** and **Craig Bingman** to obtain a high-resolution crystal structure of human cysteamine dioxygenase. Equally impressive, Bob carried this structure to the goal-line as one of his last projects before retirement. His skills and insights have been so valuable to us over many years, and we wish success in his search for best methods to obtain *Esox masquinongy*.

Emily Beebe moved to Illumina in 2017 after 6 years working with me. Emily is one of the best people that I have ever worked with. She helped make the first discoveries in the work described in the next paragraph. I am very happy for her and wish continued success.

In 2019, I joined forces with **John Ralph** from Biochemistry and **Shawn Mansfield** from the University of British Columbia to apply bioinformatics, cell-free translation, and good-old biochemical reasoning to the problem of biosynthesis of ester-linked precursors to lignin biosynthesis. This effort led to discovery of new enzymes and ultimately, a DOE-funded project to engineer the composition of lignin in bioenergy crops to make them more easily digestible while maintaining all desirable aspects of plant viability. We are joined in this venture by Kirk, Craig, **Rebecca Smith** and **Steve Karlen** in the Wisconsin Energy Institute, and **Debayan Chaudhury** who joined the project as a first-year graduate student. Rebecca is a plant biochemist and Steve is an analytical chemist. They bring new great skills, insight and energy to the project.

The lab has been fortunate to receive funding from the Great Lakes Bioenergy Research Center and an additional grant from the US DOE to work on lignin engineering. Prof. **Taichi Takasuka** and I were recipients of a Japan Society for the Promotion of Science grant to study enzymatic deconstruction of kelp. This work is proceeding by Zoom, which at present is a pale substitute for the 2x per year trips I have made to Sapporo each year since 2017.

DOE called on me to help write workshop reports on 'Technologies for Characterizing Molecular and Cellular Systems Relevant to Bioenergy and Environment (2017)' and 'Genome Engineering for Materials Synthesis (2019)' and I just completed a comprehensive review of 'Diiron Enzyme Structure and Catalysis (2021)' for Coordination Chemistry Reviews.

Fox Lab *continued*

On an ending note, the UW Madison Biotechnology Training Grant, managed with excellence by **Cheri Stephens**, was funded for another 5 years starting in July 2020. I am happy to be the Director of this project, which supports 20 trainees per year from 4 schools and colleges and over 10 departments and graduate programs.

There are a few comments on being Chair of the Department on page 3. I look forward to every day because of the outstanding people I get to interact with, all of the successes I see, and your enthusiasm and willingness to help each other to move forward. To you, the reader of these brief comments, please accept my best wishes for the future. Be safe and smart in these challenging times.

Ralph Lab

As always, the last few years have been pretty exciting in the Ralph Lab, where students, postdocs, and researchers are involved in a range of studies on plant cell wall chemistry and biochemistry.

We are lucky enough to work with some amazing collaborators and inconceivably publish a paper on average every 2 weeks – some of them are even quite good! We've been lucky enough to get some nice cover articles (see the picture below) again, so the vanity wall in the office is getting a little crowded.

We work on lignin, the phenolic polymer that holds plant cell wall fibers together, and is important for enabling plant growth, water transport, defense, UV protection, etc.

Highlights? Oh my gosh, it is hard to pick, but among them would be...

- Discovering phenolics from well outside the monolignol biosynthetic pathway that are used as monomers and incorporated into the lignin polymer, opening new avenues in plant engineering for improved processing and enhanced value.
- Discovering new ways that plants 'decorate' their lignins with an array of components that are also useful. We even got local and international press for a patent on making Tylenol® from one such component on poplar lignin (instead of from fossil fuels). (https://biochem.wisc.edu/news/2019/news-relieving-two-headaches-one-process-2019-07-02)
- Discovering (or helping to discover) lots of new genes and characterizing the functions of their produced proteins.
- Discovering new natural antifungals that are now undergoing promising field trials.
- Showing that plants engineered to have lignins that more easily fall apart during processing have value in a variety of processes, including in wood pulping for paper.
- Homing in on ideas, compatible with Nature, for making 'ideal lignins' – lignins that can be cleanly depolymerized to one or a few simple phenolic commodity chemicals.
- Finding new enzymes that can depolymerize lignins, and detailing the mechanisms by which they work.
- Developing new or improved tools and analytical methods to aid plant researchers.
- Understanding mechanisms of chemical depolymerization of lignin, again to simple phenolic commodity chemicals.
- And on and on. Along the way, we develop new organic synthetic methods to produce compounds for authenticating metabolites and cell wall components, for accurate analysis, and for determining mechanisms.

The group has seen wonderful people leave and other wonderful people arrive – it is simply exciting to be part of a group that is innovating and making discoveries at such a pace. COVID-19 restrictions have hit us hard, like many other groups, as we struggle to maintain the pace of collaborative obligations, and experimental work and that simply isn't amenable to the working remotely model.

Wright Lab

Hello from the Wright Lab! This year we celebrated our 12th anniversary as an independent laboratory and our 2nd anniversary as part of the Biochemistry department and Morgridge/UW-Madison family. It has been a busy few years as we continued to establish our lab in Madison and build the cryo-EM Research Center, a unique experience within the context of the pandemic! Scientifically, we have made progress in our major emphasis areas of bacteriology, virology, cell biology, and methods development. Let's take a closer look

Eric Montemayor, **Nicoleta Ploscariu**, **Daniel Parrell**, and **Juan Sanchez** have been exploring bacterial flagella in several species to better understand flagellum structure and its impact on motility regulation and bacteriophage predation. Our favorite model organism, *Caulobacter crescentus*, has a flagellum composed of six individual flagellin proteins that assemble together to form the flagellar filament. To visualize the surface residues that may be recognized by flagellotropic φCbK, we determined two high-resolution structures of the FljK-only filament, with (3.2 Å) and without (3.4 Å) an amino acid substitution that straightens the filament. We observed post-translational modifications on conserved surface threonine residues of FljK that are likely O-linked glycans, which may support φCbK adsorption. We also determined the structure of a heterogeneous filament of FljK and FljL, at ~4.6 Å resolution. This molecular level detail provides us with a sharper view of how phage φCbK infects *C. crescentus*!

Bryan Sibert, **Jae Yang**, and **Joseph Kim** have begun to unlock the order of the respiratory syncytial virus (RSV) matrix protein. Viral matrix proteins form organized lattices that regulate virus assembly and structure, and coordinate with surface glycoproteins and the internal ribonucleoprotein (RNP) complex. Our cryo-ET data of intact, filamentous RSV particles show that the matrix protein persists as a helical 'checkerboard' lattice that regulates the periodic placement of the fusion (F) glycoprotein, M2-1, and the RNP. This is significant progress towards understanding the structure of this and related pathogenic viruses, which may lead to the development of drug and vaccine targets.

Joseph Kim and **Juleen Dickson** have explored new cellular worlds by imaging primary neurons and platelets. Their cryo-ET studies will be used to better our understanding of healthy and diseased cell morphologies and how cell-state impacts the structure and organization of organelles, the cytoskeleton, and macromolecular complexes.

Top: Juleen Dickson, Joe Kim, Matt Larson
Middle: Eric Montemayor, Vicky Pappas, Dan Parrell
Bottom: Juan C Sanchez, Bryan Sibert, Jae Yang

Along with our biological targets, we have been developing many tools and methods to improve cryo-EM and correlative imaging pipelines. **Jae Yang** and **Matthew Larson** have engineered a new software package, *CorRelator*. This user-friendly program provides a simple environment for investigators to bridge between light microscopy and electron microscopy at room-temperature and under cryo-imaging conditions. Efforts are underway to further integrate the pipeline with the Aquilos cryo-FIB-SEM.

We were awarded an NIH U24 Grant to build the National Cryo-Electron Tomography Network Hub (page 10 of this newsletter or https://news.wisc.edu/new-national-imaging-center-has-potential-to-transform-medicine-2/). This is a new research center that will expand the scope of cryo-microscopy at UW-Madison to support local, regional, national, and international investigators who would like to learn and apply cryo-imaging technologies to their research questions.

Several members of the group were recognized for their research and research accomplishments. These include an MSA M&M 2020 Student Scholar Award (**Joseph Kim**) and MSA M&M 2020 Postdoctoral Scholar Award (**Jae Yang**). One traineeship was awarded this year to **Juan Sanchez** (Biotechnology Training Program (BTP) T32). And a Zoom wave welcome to our rotator / soon to be newest lab member, **Vicky Pappas**.

For more news and updates from the Wright research lab, Cryo-EM Research Center (CEMRC), and the Midwest Center for Cryo-Electron Tomography (MCCET), check out our websites: **https://biochem.wisc.edu/faculty/wright** and **https://cryoem.wisc.edu**

In Memoriam

Edward Appelbaum
Ph.D. 1976 — Prof. Rowind
April 2020

Susan Becker
Generous supporter
March 2020

David Berg
M.S. 1961, Ph.D. 1964 — Prof. Link
March 2020

Susanne Clee
Postdoc 2000 - 2007 — Prof. Attie
July 2020

John Cramer
M.S. 1952, Ph.D. 1955 — Prof. Steenbock
September 2017

George Drysdale
M.S. 1950 — Prof. Baumann,
Ph.D. 1952 — Prof. Lardy
March 2020

Henry Ehrlich
Ph.D. 1951
May 2020

Leonard Fahien
Generous supporter
January 2018

Eugene Goldsmith
B.S. 1969
July 2020

Minette Goldsmith
Generous supporter
July 2020

Thomas Higgins
Ph.D. 1970 — Prof. Johnson
March 2019

John Kelley
M.S. 1956, Ph.D. 1959 — Prof. Anderson
September 2020

Hirochika Komai
Generous supporter
August 2020

Ralph Kurtzman
Ph.D. 1959 — Prof. Burris
October 2015

David McCarthy
B.S. 1981
March 2020

Ina Mirviss
M.S. 1949 — Prof. Steenbock
April 2020

Sylvia Robertson
Research Technician — Prof. Kenealy
November 2019

Alice Sievert
M.S. 1952, Ph.D. 1958 — Prof. PH Phillips
April 2020

H William Sievert
M.S. 1952, Ph.D. 1958 — Prof. PH Phillips
November 2019

Marlys Sloup
Generous supporter
June 2018

Connie Smith
Research Specialist — Prof. DeLuca
July 2018

Howard Sprecher
Ph.D. 1964 — Prof. Strong
December 2019

Chester Underwood
M.S. 1962 — Prof. Link
October 2020

Malcom Von Saltza
Prof. Strong
July 2020

Eugene Wegner
M.S. 1957, Ph.D. 1962
December 2019

Fay Yin
M.S. 1956, Ph.D. 1960 — Prof. Bock
July 2020

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

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Innovation

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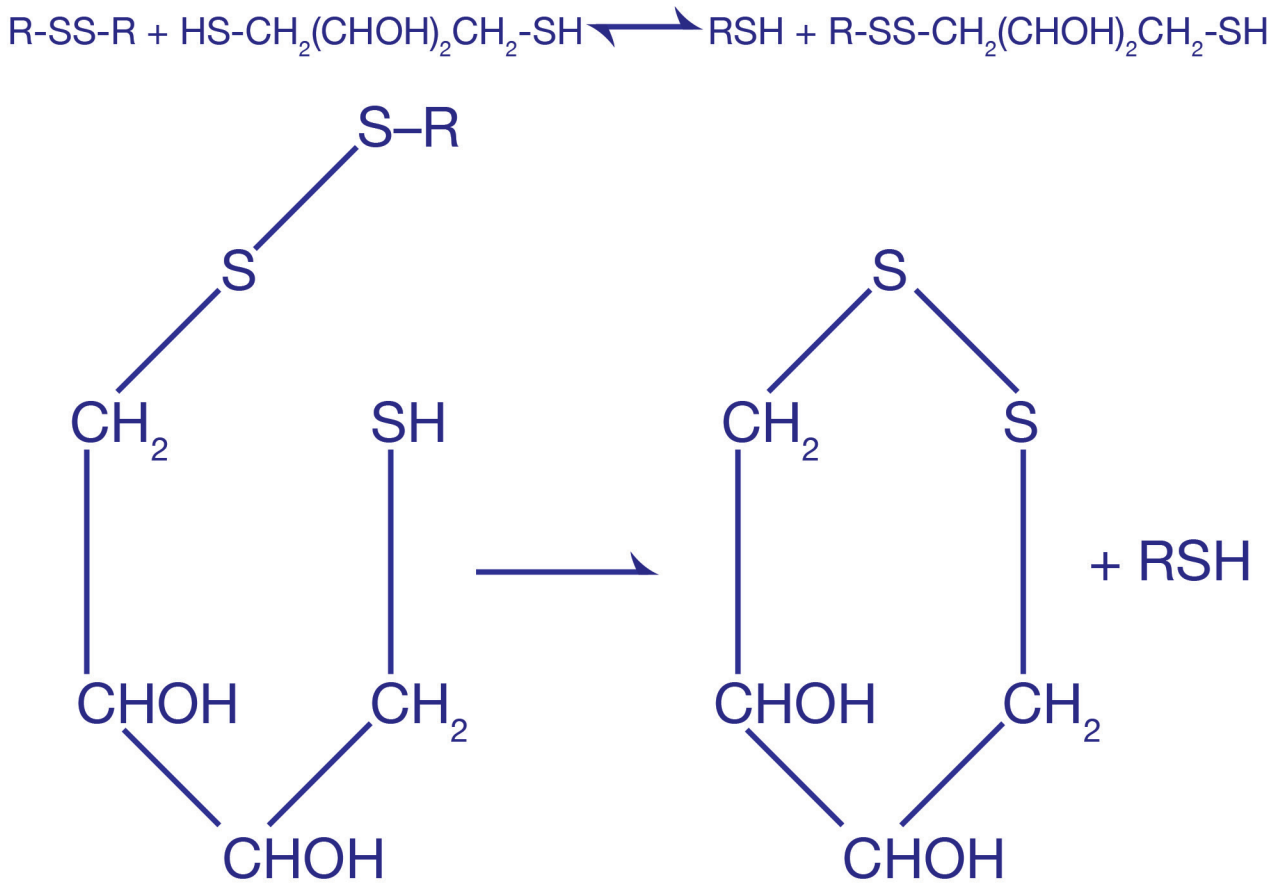

Dithiothreitol, a New Protective Reagent for SH Groups
W. W. Cleland

Because of its low redox potential (—0.33 volts at pH 7), dithiothreitol (and its isomer, dithioerythritol) is capable of maintaining monothiols completely in the reduced state and of reducing disulfides quantitatively. Since this compound is a highly water-soluble solid with little odor and little tendency to be oxidized directly by air, it should prove much superior to the thiols now used as protective reagents for sulfhydryl groups.

Biochemistry 3:480-2, 1964