Biochemistry in the Age of Big Data

Meet our New Faculty

Letters from the Lab

And more
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Cover image: New experimental technologies generate large amounts of data that must be analyzed by computational methods. Mark Politz, a postdoctoral researcher in the lab of biochemistry professor Philip Romero, is fabricating a microfluidic chip in this close-up image. He is punching holes in the device to connect the small tubes inside. Data that’s generated from experiments like these are used to analyze structures, such as the one here of human Caspase 3, an enzyme involved in executing programmed cell death. Structure by Hridindu Roychowdhury, a graduate student in Romero's lab. Photo and design by Robin Davies.
Hello to everyone reading the 2018 edition of Biochemistry InVivo, where we keep current members of the department, our alumni, supporters, and friends up-to-date on the most exciting things happening in our research, teaching, and service to the world. It is our sincere hope you will find these newsletters engaging, enlightening, and inspiring.

The cover story, titled “Biochemistry in the Age of Big Data,” provides an intriguing image suggesting how stunning progress in high-throughput nucleic acid sequencing (both DNA and RNA), determination of high-resolution structures of biomolecules (proteins, nucleic acids, and complexes), and measurement of functional properties is leading to an integrative revolution in science. Our rapidly expanding ability to merge massive biological data sets and identify correlations among them lays the basis for systems biology, which is the study of the behavior of complex biological processes. Systems biology studies involve high-throughput quantitative measurement, modeling, reconstruction, and theory. The department embraces these integrative approaches.

Since our last edition, the College of Agricultural and Life Sciences under the leadership of Dean Kate VandenBosch completed a review and planning process to situate the college and its contributing departments for future success. The Department of Biochemistry enthusiastically engaged in this process and produced a five-year plan with new efforts proposed in research, teaching, and outreach. One of the most exciting aspects of our five-year plan is to hire 10 new faculty members in five years. This hiring will set the stage for the future, and we will seek innovators that will address basic and applied problems spanning human health, energy, bioproducts, ecosystem function, and others.

This edition includes research highlights from five faculty. Dr. Elizabeth Wright has now taken up residence in the Hector F. DeLuca Biochemistry Laboratories and is leading Biochemistry’s efforts in cryo-electron microscopy. Dr. Jason Cantor (new assistant professor) and Dr. David Pagliarini have labs in the Morgridge Institute for Research where they study metabolism, which is a long-standing theme in the department. Dr. Ophelia Venturelli is bringing engineering approaches to understanding the function of microbiomes, and Dr. Aseem Ansari is using chemical and synthetic biology approaches to design molecules that can selectively control gene expression. These compelling descriptions outline the success of our researchers and their future promise.

You will also find commentaries on three alumni covering their unique career directions and outstanding achievements: an undergraduate, Emily Baumann, B.S., ‘15; a graduate student, Dr. Lynne Maquat, Ph.D., ’79; and former postdoctoral fellow, Dr. Squire Booker, who was here from ‘95-’99.

Our department thrives on the diversity, skills, and commitment of its members, alumni, supporters, and friends. 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. If you are able, please consider becoming a donor to the Department of Biochemistry. Please contact us or the University of Wisconsin Foundation about your interests in supporting our new plans for research, teaching, and outreach.

We look forward to hearing from you.
Researchers and Students Push Boundaries of Science with High Throughput Methods and Big Data

The complexity of life makes it difficult to study. In biochemistry, there are often just too many processes and reactions taking place in a cell for humans to wrap their heads around. What helps biochemists make sense of it all?

Cue computational biology and biochemistry. Computation has been used in biology and biochemistry since the dawn of computers and is used today by many researchers in the University of Wisconsin–Madison Department of Biochemistry.

With the advent of high throughput technologies, researchers are able to collect more and more data — the era of “big data” is here to stay. Computational biochemistry can be defined as the use of computational methods and simulations to make sense of all of that data in order to predict and understand various biological processes.

“The main reason we use computers in biochemistry is because biological systems are composed of thousands of interacting components and predicting the behaviors of these complex systems becomes way too difficult to grasp within our brains,” says Assistant Professor Philip Romero, who uses computation in his lab. “Computers are much better at handling large amounts of information.”

Still Classic Biochemistry: Sequence Begets Structure Begets Function

One of the most important applications of computation in biochemistry is the prediction of the structure and function of a protein or other macromolecule.

“We investigate how proteins in the cell membrane come together to form complexes,” Associate Professor Alessandro Senes explains. “We use molecular modeling tools to study something that is often very hard to do with conventional experimental structural methods.”

The Senes Lab uses structural prediction to obtain an “educated guess” of what a certain membrane protein may look like. Often, the lab integrates the modeling with experimental information — such as the result of a mutation or data suggested by analyzing the evolutionary variation of the protein — which makes the prediction more reliable. The computation informs the experiments and vice versa. The prediction process can also go a step further and predict a protein’s function based on the sequence and structure in a similar way.

One project in the Senes Lab is the study of the bacterial divisome, a large complex of membrane proteins which helps bacterial cells divide — but that has an unknown structure. An understanding of how the complex’s mechanism functions could come in handy for other researchers looking for a way to prevent bacteria from dividing, and potentially lead to the discovery of new antibiotics. Another project in the lab focuses on the biophysics regulating how membrane proteins interact with each other.

“One of my favorite parts of learning how to program was looking at the physical code and then treating it like a puzzle and figuring out where things went wrong to make it work,” says Samantha Anderson, an Integrated Program in Biochemistry (IPiB) graduate student in the Senes Lab. IPiB is the joint graduate program of the Department of Biochemistry and Department of Biomolecular Chemistry.

“It’s fun because it’s a logic puzzle. A lot of people think computation and coding are very abstract but they are actually tangible things you can see and work with concretely, which makes them really rewarding.”

Using microfluidics. Hridindu Roychowdhury, an Integrated Program in Biochemistry (IPiB) graduate student in the Romero Lab, performs a microfluidic experiment to analyze the impact of mutations on human caspases. Caspases are enzymes involved in executing programmed cell death.
Computation is for Biochemistry what Pandora is for Music

Many often hear of algorithms when talking about social media platforms like Facebook or music streaming services like Pandora. These function by learning from the user what they want to see or listen to and tailoring what is presented. A lot of computational work in biochemistry functions in the same way.

“It’s actually really similar,” Romero says. “You have to teach the machine what is good and bad so you can make a prediction or design. We look at a sequence and know there are some parts that work poorly for what we want — we give those a thumbs down — and others that maybe produce something we are interested in — those we might give a thumbs up. The computer can then slowly learn what makes a good sequence good and a bad sequence bad. The examples allow the computer to extrapolate what makes a really good sequence good and deliver that to us.”

Like the Senes Lab, the Romero Lab’s broad interest is in trying to understand the relationships between protein sequence, structure, and function and how they can learn about these relationships from large data sets. They then apply those principles to design new proteins with optimized properties for applied uses in areas such as bioenergy, chemical production, or human health.

“Computer power is getting faster and faster and cheaper and cheaper,” Romero says. “This technology is only getting better and getting your foot in the door and investing in these tools and skills can be very valuable. They will play an increasingly important role in biological research. All of us, and the department as a whole, have a mission to stay ahead of this rapidly evolving technology.”

Using Computation to Design New Proteins with Novel Functions

While Assistant Professor Vatsan Raman also works on large scale experiments and protein design, he is exploring a third angle: precision medicine. He was recently awarded a $2.2 million-dollar grant from the NIH to support his research on allostery — the process by which a protein senses and conveys a signal that causes a change in a different part of itself.

“Another thing we can do is pick proteins relevant to disease and work to predict the pathogenic consequences of new mutations that may occur in those proteins,” he explains. “That is super important. If we could build this across the top ten or twenty highly mutated cancer genes that would be a repository worth its weight in gold.”

For example, if a physician finds an arbitrary mutation in a patient he or she could then use a kind of database to make an educated guess about what the mutation might do to the patient’s health and possibly how to treat it. A database of this size is only possible with high throughput methods and computation, Raman says.

“In my lab we are picking nuclear receptors that are highly relevant in disease and analyzing them to ask how we can figure out the rules that govern them so if we have a new mutation we can figure out what it does,” he says. “We are working to get enough data to be able to make predictions.”

Along with Senes, Romero, and Raman, many other labs use computational methods in their research. Professor Julie Mitchell, who is currently serving as deputy director of the biosciences division at Oak Ridge National Laboratory in Tennessee, and Assistant Professor Ophelia Venturelli work in this area. (See a story on Venturelli’s work on page 9.) Their expansion of these techniques is creating new opportunities, including coursework on quantitative approaches, for researchers and students interested in this area of biochemistry.

“Many students don’t come in with a lot of knowledge in this area but are able to learn on the job,” Raman says. “At this point computation is a necessity. Students might not come into the program knowing how to code but if you have a large dataset from a big experiment, you can’t just stare at it. You’ve got to start writing your own code to begin making sense of it. And so we dive in.”
Jason Cantor could describe himself as an engineer, biologist and biochemist, but don’t try to put his expertise into one box.

Cantor, a scientist exploring the environmental influences on cancer cell metabolism, launched a new lab in August as a Department of Biochemistry faculty member in the Metabolism Theme at the Morgridge Institute for Research. He is also affiliated with the Department of Biomedical Engineering.

“I have this half engineering, half fundamental biology background, and it’s a bit difficult to fit cookie-cutter style into one traditional department or one theme,” Cantor says. “Morgridge and UW–Madison embrace my hybrid training and accept that I’m trying to mix and match and merge these disciplines together in my work.”

Cantor earned his bachelor’s degree in chemical engineering at Cornell University. He went on to do doctoral work at the University of Texas at Austin where he came up with new strategies to engineer enzymes for cancer treatment.

At the time, there was a resurgence in the field of cancer metabolism, and for his postdoctoral work, Cantor decided to venture outside the scope of traditional engineering and join a fundamental biology group interested in cancer metabolism. This led him to the lab of cancer biologist David Sabatini, part of the Whitehead Institute at MIT, where Cantor helped develop a new method to study how environmental factors impact cancer metabolism.

Much of science relies on models — whether it’s animal or insect systems like mice and fruit flies or a colony of cells in a petri dish — to conduct and test experiments. Sometimes models are too far removed from reality to be useful, and it’s always a challenge in science to continually improve the models to close those gaps.

During his time at Whitehead, Cantor helped develop a new synthetic medium — a liquid that allows for the growth, storage or transport of cells in lab settings — that better reflected the composition of human blood. The synthetic medium, referred to as human plasma-like medium (HPLM), basically rewired the metabolism of the cultured cells. Not only did the medium have dramatic effects on the metabolic landscape of these cells, the scientists were able to discover an unexpected method of metabolic regulation.

Building off this foundation, the Cantor Lab will explore how environmental factors influence both cell biology from a fundamental aspect and from a translational aspect.

Cantor says he was drawn to Morgridge and UW–Madison because of the strong foundation of metabolism research and the opportunity to contribute to and collaborate with a thriving community.

“To take risks in science and move the field forward in meaningful ways, you need resources and personnel and the support to do that and the department and Morgridge exemplified this vision of doing big things,” Cantor says. “The exciting part for my work is we actually don’t know what we’re going to find because we’re studying these systems, whether it’s cancer or otherwise, in a way that no one has before.”

Improving cell culture media.

In an ode to Pink Floyd’s Dark Side of the Moon, Cantor illustrates the concept of an effort to shine light on the environmental conditions that help influence thousands of processes occurring inside the cells themselves. Through the design of culture media that more closely mimic conditions encountered by cells in the body, researchers can better model and ideally understand both normal and disease cell biology using isolated human cells growing in Petri dishes. Illustration by Steven Lee/Whitehead Institute. Image courtesy of Jason Cantor.
The University of Wisconsin–Madison Department of Biochemistry welcomed Elizabeth Wright in July as a faculty member and director of the department’s newly established cryo-electron microscopy (cryo-EM) facility.

Wright is an expert in cryo-EM, a technique able to obtain atomic or near-atomic level resolution images of biological molecules by imaging with electrons. It is a burgeoning technology that can help UW–Madison researchers make significant new contributions to many areas of structural biology, including enzymology, virology, cell biology, and medicine.

“I am very excited to be joining the department to develop this technology at UW–Madison,” says Wright, who will also be an affiliate of the Morgridge Institute for Research. “In the fields of fundamental biochemistry and structural biology, the department is one of the strongest in the country.”

Wright did her undergraduate education in biology and chemistry at Columbus State University and her Ph.D. in chemistry at Emory University. Following postdoctoral work at the University of Southern California and CalTech, she started as an assistant professor in the Department of Pediatrics in the Emory University School of Medicine. There she earned tenure and was the director of the Robert P. Apkarian Integrated Electron Microscopy Core at Emory University before joining UW–Madison.

Wright’s research interests are varied but all revolve around advancing and utilizing sophisticated light and electron microscopy imaging technologies. She works to push the limits of technology and methods development for cryo-EM.

On the biological side, she studies bacteria and how cells regulate interactions with the environment through their appendages, such as pili and flagella. Wright also studies the structures of enveloped viruses like HIV, measles, respiratory syncytial, and the flu.

“Broadly speaking, we are interested in how biological systems work,” Wright explains. “While much of our work focuses on fundamental biology, we also consider the translational aspects of our research. In order to help develop new therapeutics, antimicrobials, and antivirals we need to understand these basic structures at various levels of resolution.”

Besides her own research, Wright will build a community of researchers on campus that utilizes cryo-EM in their work. The upcoming facility is a cross-campus effort led by the Department of Biochemistry but will be available to all of campus and beyond. Some of the microscopes will arrive in the spring of 2019, allowing the facility to begin to take shape. For more information on the upcoming facility and how the technology works, see the Department of Biochemistry website.

Cryo-EM also offers a chance to advance the education of students in the department and across campus. Wright plans to teach both junior-level and advanced courses on the technology and its uses after spending time setting up the facility.

“In the broader scale, cryo-EM is going to help us to think more broadly about macromolecular complexes, viruses, bacteria, and mammalian cells and the manner in which they function,” she says. “It will enhance our capability to understand the structure and function of these systems now, but also provide that information to the next generations of scientists we’re training here at UW–Madison.”
Research News

Designer Molecule Points to Treatment for Diseases Caused by DNA Repeats

Professor Aseem Ansari’s research group in the Department of Biochemistry has designed a molecule that can precisely target a specific part of DNA and “switch on” a target gene located there. Specifically, their molecule targets short sequences of DNA that repeat many times (GAA1-GAA2-GAA3-...). These GAA repeats cause the rare but fatal disease Friedreich’s ataxia, and molecules that target such sequences would open doors for possible treatments of the disease and many others like it, such as Huntington’s disease, fragile-X syndrome, and myotonic dystrophy that are caused by other repeats.

Ansari’s group has tested many different synthetic genome readers (SynGR), how they bind DNA, and what changes would make binding to target DNA sequences more precise. They’ve harnessed a molecule that has the needed chemical complementarity to bind to the GAA repeats present in the genome of individuals who have Friedreich’s ataxia and then bring cellular machines to help the gene function properly. Their results were published in the journal Science.

“We asked, ‘could you control genes by making drug-like molecules that go to specific places in the genome?’” Ansari explains. “You can think of the molecule traveling along our DNA and reading it like braille, feeling the edges of the DNA to see if it can find the perfect fit. Once it locates its genomic zip code, the second half of the molecule functions like a homing beacon to precisely target the cell’s heavy machinery to fix the roadblock at that site and nowhere else.”

Friedreich’s ataxia is a fatal neurodegenerative disease with no known cure. It is caused by the massive expansion of GAA repeats within the gene coding for the protein frataxin, which mitochondria — the cell’s power supplier — need to process the body’s energy.

The lack of the protein causes developmental impairment as early as age five, particularly in places like the heart and brain that use a lot of energy. These repeats are passed on genetically and so can build over generations. Even though one American in 110 is a carrier, the severity of the disease is such that it only appears in approximately one in 50,000. In other words, severe silencing of the gene must be inviable.

While very precise, the molecule does bind to other parts of the DNA that also have GAA sequences. However, Ansari says the molecule causes little “collateral damage” in these areas in the patient cells they tested in the lab. This is because none of the other areas need the cellular machinery like the blocked frataxin gene in patients.

Their next step is ensuring their molecule is not toxic. Ansari would like to see the molecule tested in real patients down the road if further tests show that it is safe and effective in animal models of the disease.

“In medicine today, we fix the symptoms, but what we want to remedy is the underlying root of the disease,” Ansari says. “We want to correct problems that a person inherits via their genome, and along the way we are developing an exciting new approach to personalized and precision medicine.”

Friedreich’s ataxia targeted Synthetic Gene Reader/Regulator (SynGR). Friedreich’s ataxia is a progressive neurodegenerative disorder which has no therapy. The disease causes ataxia, scoliosis, cardiac hypertrophy, and diabetes. Silencing of frataxin (FXN) by GAA trinucleotide repeat expansions underlies the etiology of the disease in >96% of the patients. SynTEF1 is a first-in-class SynGR that targets GAA repeats via a polyamide composed of imidazoles (filled red balls) and pyrroles (open circles). The bi-functional molecule delivers JQ1 (blue ball) to the GAA repeats in FXN. The repurposed JQ1 functions as an “epigenetic mimic” of the acetyl-lysine on histone tails and recruits the transcription elongation machinery to FXN. This machinery modifies the stalled RNA polymerase II (Pol II) and enables it to transcribe across the repressive GAA microsatellite repeats and restore FXN expression in vivo (Erwin et al., Science 2017).
Dynamic Modeling Helps Predict the Behaviors of Gut Microbes

The human gut is teeming with microbes, each interacting with one another in a mind-boggling network of positive and negative exchanges. Some produce substances that serve as food for other microbes, while others produce toxins — such as antibiotics — that kill their neighbors.

Scientists have been challenged trying to understand how this collection of gut microbes — known as the microbiome — is formed, how it changes over time, and how it is affected by disturbances like antibiotics used to treat illnesses. A study out this year from Ophelia Venturelli, a biochemistry assistant professor at UW–Madison, and her collaborators at the University of California, Berkeley, may help alleviate some of that difficulty.

Published in *Molecular Systems Biology*, the study provides a platform for predicting how microbial gut communities work and represents a first step toward understanding how to manipulate the properties of the gut ecosystem. This could allow scientists to, for example, design a probiotic that persists in the gut or prevent an intestinal pathogen from invading the gut microbiome.

“We know very little about the ecological interactions of the gut microbiome,” Venturelli says. “Many studies have focused on cataloging all of the microbes present, which is a useful first step, but we wanted to try to understand the design rules governing their assembly into communities, how stability is achieved, and how they respond to perturbations.”

By learning these rules, researchers say they can better predict interactions between microbes using computational tools instead of performing laborious and time-consuming laboratory experiments. The data can also start to answer questions about how pathogens cause damage when they invade communities, and how to prevent it.

For the study, the researchers chose 12 different bacterial types present in the human gut. They represent the diversity of the gut microbiome, are highly prevalent across the individuals, and the majority have been shown to significantly affect human health. They have associations with diseases such as diabetes, irritable bowel syndrome, Crohn’s disease, and colon cancer.

The team collected data on what are called pairwise interactions, which means each bacterial species was paired with just one other to study how the two interacted, without worrying about what all of the others were doing. This was done for all pairs in the 12-member community.

The researchers fed data about the pairwise interactions, along with data on each individual species, into a dynamic model to predict how all community members would behave when combined. They found the individual and pairwise data alone was sufficient to predict how the larger community assembles. While still a big challenge to measure all the pairs of organisms in a complex microbial community, Venturelli says it will significantly reduce the number of measurements scientists need to make.

“Without a model, we are basically just blindly testing things without really knowing what we are doing and what the consequences are when we are, for example, trying to design an intervention,” she says. “Having a model is a first step toward being able to manipulate the gut ecosystem in a way that can benefit human health.”

*This work was supported by the Defense Advanced Research Projects Agency (DARPA) R0011516183.*
Heart disease is the number one killer in the United States, and high triglyceride levels in the blood are cited as just one of several risk factors. Millions of lipid panels, blood tests that look at cholesterol levels as well as triglycerides, are performed in clinics each year.

Two new studies from the lab of biochemistry and Morgridge Institute for Research professor Dave Pagliarini suggest the current tests, which measure the abundance of lipid classes, are insufficient. Rather, lipids identified and studied at the individual species level — instead of grouped in classes — may be better signatures of metabolic health.

The results were published in Cell Systems as open access papers, one focusing on plasma lipid species and the second on liver lipid species.

Lipids, or fats, are incredibly important to human health, yet one of the hardest biomolecules to study. Harnessing advances in mass spectrometry technology, the scientists measured almost 150 lipid species in the blood and liver of mice and identified some that can act as signatures of healthy or unhealthy metabolic states.

For patients getting a lipid panel, results will include a reference to triglyceride levels. These tests look at triglycerides in bulk, as a group, and measure how much is in the blood.

But Molly McDevitt, a biochemistry graduate student in Pagliarini’s Lab at Morgridge and co-first author on the papers, says looking at individual species of triglycerides provides a much more accurate picture.

“We don’t even know how many different triglycerides there are — hundreds, thousands,” says McDevitt. “We found that some triglycerides correlate positively with a fatty liver, while others correlate negatively with a fatty liver. Lumping all triglycerides into one class masks these subtler associations.”

In this study, the scientists identified seven triglyceride species in the blood that associated with either healthy or fatty liver.

Non-alcoholic fatty liver disease (NAFLD) — a disease in which the liver gets fat and cells start dying, eventually leading to organ failure — was a focus in this work, though the results also impact other diseases related to lipid metabolism like diabetes, obesity, and metabolic syndrome.

The work was co-led by Johan Auwerx’s team from EPFL in Switzerland, and Morgridge affiliate and UW–Madison professor Josh Coon contributed expertise in mass spectrometry to the studies.

One of the questions posed across the two papers: does measuring the lipids in plasma (a simple blood test) tell you something about what’s happening in an organ? Often, in order to identify a fatty liver, an invasive liver biopsy is required. Taking a blood sample would be a much simpler way to diagnose it.

The studies are still in the early stages, but the results look promising.

“As we move from measuring a bulk lipid class in serum to specific lipids, we’re finding that some do indeed predict what’s happening in the liver,” says Pagliarini, director of the Morgridge Metabolism Theme. “That gives us confidence that we might be able to discover biomarkers in plasma that report on what’s happening in organ metabolism.”

Story by Courtni Kopietz for the Morgridge Institute for Research.
For Pennsylvania State University professor Squire Booker, scientific inspiration comes from elucidating the “new chemical language” behind novel biochemical reactions. It’s inspiration he picked up during this time as a postdoctoral scholar in the Department of Biochemistry working with now-Emeritus Professor Perry Frey in the 1990s.

Booker, a Texas native, attended Austin College and went on to graduate studies at MIT and an NSF/NATO fellowship to study in Paris before writing a letter to Frey to request to join his lab as a postdoc.

“I wanted to get involved in bioinorganic chemistry and a blockbuster discovery by Perry in the late ‘80s sounded like a treasure trove of new and exciting chemistry,” says Squire, who joined the department in the fall of 1995. “Luckily Perry agreed to let me join his lab and I got to get in on this research area pretty much at the ground level. There was lots of great science going on and everyone, including the faculty, were very collegial.”

Perry’s research led to the development of an entirely new radical superfamily, called S-adenosylmethionine, of which there are now almost 114,000 unique sequences representing over 85 distinct reaction types. Booker learned to isolate these enzymes in the lab and characterize their oxygen-sensitive iron-sulfur cofactors with the help of now-Emeritus Professor George Reed. It started a line of research he continued into his independent career.

In 1999, Booker joined Penn State as an assistant professor of biochemistry and molecular biology and quickly grew in rank — getting tenure in 2005 — and amassed honors. Most recently he was named the Eberly Family Distinguished Chair in Science in 2017, and the Evan Pugh Professor of Chemistry, Biochemistry, and Molecular Biology in 2018. Being named an Evan Pugh Professor is the highest honor a faculty member can receive at Penn State.

At Penn State, Booker’s research program is broad but one important area is investigating how nature adds methyl groups to carbon atoms that would initially seem unable to receive them. Another area is researching how nature adds sulfur atoms to some compounds that are typically thought of as unreactive.

His approach is both basic and medicinal. He explains that some of the reactions his group studies provide bacteria a way to guard against and become resistant to many of the most common antibiotics in use. Understanding how these mechanisms work could point to a way to prevent the bacteria from doing this, for example.

Along with teaching undergraduates and graduate students, Booker is also very active in mentoring and performing outreach, especially to students from underrepresented backgrounds in science. He’s served as a mentor to numerous students and on minority affairs committees for professional organizations and groups.

“I’m also pretty good at networking so people across the country routinely email me to try to connect about different opportunities,” he says. “So I have students I look out for as their mentor. For postdocs specifically, some advice I’d give is to use a postdoc as an opportunity to explore a new area you’re unfamiliar with and learn something new.”

“Luckily Perry agreed to let me join his lab and I got to get in on this research area pretty much at the ground level. There was lots of great science going on and everyone, including the faculty, were very collegial.”
—Squire Booker, Biochemistry Postdoc ’95-99
Maquat Recognized as Trailblazer for RNA Research and Women in Science

Lynne Maquat says she was shy when she first started as a graduate student in the Department of Biochemistry, but since graduating with her Ph.D. in 1979, she’s become a force in the field of RNA research. The first person in her family to attend college, she’s earned numerous awards for groundbreaking research and mentoring prowess in her current post as a professor at the University of Rochester.

Maquat studied with now-Emeritus Professor William Reznikoff. After her Ph.D. she also performed postdoctoral work at the UW–Madison McArdle Laboratory for Cancer Research. Her lab currently studies the many roles RNA — particularly RNA processing and decay — plays in human health and disease.

“RNA is so important to our cells because it does so many critical things,” she says. “Most of our genetic material — our DNA — produces RNA. And, there are many types of RNA. One type contains information from which proteins are made; another type is the catalytic center of our protein synthesis machinery; still other types regulate either our DNA or other RNA molecules. All RNA molecules ‘self-regulate’ how long and where they reside in cells depending on their particular sequence and structure. RNA is a very versatile molecule.”

Today, her list of accolades is long. Two recent and highly competitive awards include the Vanderbilt Prize in Biomedical Science in 2017 and the Wiley Prize in Biomedical Sciences in 2018. While both honor scientists with a stellar record of research accomplishments, the first also honors those who have made significant contributions to mentoring other women in science. When compared to men, she explains, many fewer women who earn a Ph.D. go on and use that degree in a career, and so it is important to mentor women. One of the best ways to mentor, she believes, is through examples.

“As the first person in my family to go to college, I feel very fortunate and deeply humbled to receive the Wiley and other prizes,” she says. “I have changed a lot from my time as a shy and quiet graduate student in the Reznikoff Lab. Because of my temperament, Bill was a wonderful mentor and overt supporter of female graduate students at a time when many departments had few women faculty. I firmly believe that my rigorous training in basic biochemistry has served me well throughout my career.”

At Rochester, Maquat is the J. Lowell Orbison Endowed Chair in the Department of Biochemistry and Biophysics and the founding director of the university’s Center for RNA Biology, as well as founder and chair of the Graduate Women in Science program. She’s an international leader in the field and is credited with several major discoveries that are informing a new generation of therapies for a wide range of genetic disorders.

“I tell young scientists that it is important not to discourage yourself from taking the next step by looking too far into the future,” Maquat says. “For example, don’t look at someone like me and believe you can’t do it. Success doesn’t happen overnight but in small steps that, at the time, are manageable. This doesn’t mean they aren’t challenging, but they can be accomplished by working smart and getting help when you need it.”

“I tell young scientists that it is important not to discourage yourself from taking the next step by looking too far into the future. For example, don’t look at someone like me and believe you can’t do it. Success doesn’t happen overnight but in small steps that, at the time, are manageable.” —Lynne Maquat, Ph.D. Biochemistry ’79
Recent graduate Emily Baumann found a home for her University of Wisconsin–Madison biochemistry education, as well as her skills gained through working within the Office of Sustainability, in the field of clinical trials. The 2015 undergraduate alumna from Manitowoc, Wis. is now a medical monitoring associate for PRA Health Sciences in Raleigh, N.C.

During her undergraduate career, Baumann did research in the lab of biomolecular chemistry professor Jon Audhya but was also involved in lots of extracurricular activities, such as helping form a nonprofit with the Office of Sustainability, volunteering at UnityPoint Health - Meriter hospital, and tutoring at The Physics Learning Center. Through that work she learned management, networking, and leadership skills to complement her science education.

“Working as a Medical Monitoring Associate is a happy medium between doing traditional research and working more in a management position,” she explains. “I can still apply a lot of my biochem education but I’m not directly doing research. If you enjoy science but aren’t as interested in doing traditional lab work, that’s OK and there’s a place for you if you explore your many options. That’s what I did and it paid off.”

PRA Health Sciences is a contract research organization that provides research services to pharmaceutical companies. If a pharmaceutical company wants to bring a drug to market, they will get PRA Health Sciences to develop and run the required sophisticated clinical trials. Baumann helps on the medical side of the trials: getting patients enrolled and assisting PRA’s clinicians. She started in a project assistant position but has quickly ascended to her current role in the medical department.

“It really helped that I had a biochemistry degree and from UW–Madison because everyone knows about the university and the Wisconsin Idea,” she says. “It’s super cool because I can apply a ton of the course material I learned in Madison to understanding clinical trial protocols and determining if a patient meets the eligibility requirements for a trial.”

In her day-to-day work, she manages meetings between the pharmaceutical companies and PRA Health Sciences or reviews patient eligibility forms to narrow down patients that can participate in a clinical trial. It’s a global company so she often gets to interact with coworkers from all over the world. She also attends graduate school full time in the Executive MHA Program for Healthcare Administration through the University of North Carolina at Chapel Hill and will finish her master’s in August of 2019.

She adds that the size and breadth of a university like UW–Madison also allowed her to get involved in many extracurricular activities. These gave her the opportunity to pick up skills in organizing, writing, and coordinating.

“The work I do is important because it’s clinical trials that are cutting edge and trying to get new medicines to market that can help cure diseases,” Baumann says. “These pharmaceuticals are very important for the health of society and could really help people.”
<table>
<thead>
<tr>
<th>Degree</th>
<th>Name</th>
<th>Major Professor</th>
<th>Thesis Title</th>
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<tbody>
<tr>
<td>PhD</td>
<td>Elisa Frankel</td>
<td>Audhya</td>
<td>ESCRT-III regulation during multivesicular endosome biogenesis</td>
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<tr>
<td></td>
<td>(Jan 2018)</td>
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<tr>
<td>PhD</td>
<td>Funita Phan</td>
<td>Bertics &amp; Miyamoto</td>
<td>Investigating the role of DNA damage-NEMO-NF-κB signaling in vivo</td>
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<tr>
<td></td>
<td>(April 2018)</td>
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<tr>
<td>PhD</td>
<td>Gregory Reynolds</td>
<td>Bednarek</td>
<td>An investigation of the protein regulators underlying vesicular trafficking in Arabidopsis thaliana</td>
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<tr>
<td></td>
<td>(February 2018)</td>
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<tr>
<td>PhD</td>
<td>Elyse Freiberger</td>
<td>Coon</td>
<td>Methods for large-scale quantitative proteomics in systems biology</td>
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<tr>
<td></td>
<td>(February 2018)</td>
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<tr>
<td>PhD</td>
<td>Kanghyun Lee</td>
<td>Craig</td>
<td>Functional characterization of the ribosome-associated Zuol/Ssz1 chaperone complex</td>
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<tr>
<td></td>
<td>(November 2018)</td>
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<tr>
<td>PhD</td>
<td>Danielle Hamm</td>
<td>Harrison</td>
<td>Elucidating the mechanisms of Zelda that regulate cell fate during Drosophila development</td>
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<tr>
<td></td>
<td>(August 2018)</td>
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<tr>
<td>PhD</td>
<td>Katharine Schulz</td>
<td>Harrison</td>
<td>Defining the interaction of Zelda with chromatin</td>
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<tr>
<td></td>
<td>(July 2018)</td>
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<tr>
<td>PhD</td>
<td>Haley Brown</td>
<td>Holden</td>
<td>Biosynthesis of N-formylated sugars in Mycobacterium tuberculosis</td>
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<td>(August 2018)</td>
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<tr>
<td>PhD</td>
<td>Fima Zaltsman</td>
<td>Kiessling</td>
<td>The role of mechanical cues in guiding human pluripotent stem cell fate decisions</td>
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<td></td>
<td>(January 2018)</td>
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<tr>
<td>PhD</td>
<td>Michael Bellecourt</td>
<td>Landick</td>
<td>Movement of the Escherichia coli RNA polymerase clamp modulates intrinsic transcription termination</td>
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<td>(August 2018)</td>
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<tr>
<td>PhD</td>
<td>Keren Turton</td>
<td>Mosher</td>
<td>Case studies of cryptic proteins contributing to shape change in eosinophils</td>
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<td></td>
<td>(August 2018)</td>
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<tr>
<td>PhD</td>
<td>Michael Veling</td>
<td>Pagliarini</td>
<td>Assigning function to uncharacterized mitochondrial proteins using bioinformatics and biochemistry</td>
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<td>(November 2018)</td>
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<tr>
<td>PhD</td>
<td>John Crooks</td>
<td>Weibel</td>
<td>Signal integration in bacterial chemotaxis optimizes information transmission</td>
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<tr>
<td>PhD</td>
<td>Ti-Yu Lin</td>
<td>Weibel</td>
<td>Molecular mechanisms determining bacterial cell shape: Role of cardiolipin</td>
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<td></td>
<td>(May 2018)</td>
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<tr>
<td>MS</td>
<td>Elizabeth DeLeon</td>
<td>Merrins</td>
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<td></td>
<td>(May 2018)</td>
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Biochemistry Advisor Degrees 2018

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<tr>
<th>Degree</th>
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<th>Program</th>
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<tr>
<td>PhD</td>
<td>Steven Bruckbauer (Cox)</td>
<td>Microbiology</td>
<td>Foundations of experimentally-evolved ionizing radiation resistance in <em>Escherichia coli</em></td>
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<td>May 2018</td>
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<tr>
<td>PhD</td>
<td>Heather Hodges (Kiessling)</td>
<td>Chemistry</td>
<td>Probing bacterial signaling and cell envelope assembly with chemical reporters</td>
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<tr>
<td>Jan 2018</td>
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<tr>
<td>PhD</td>
<td>Erik Dean Jessen (Landick)</td>
<td>Genetics</td>
<td>Local- and genome-scale study of the interplay between <em>Escherichia coli</em> RNA polymerase and nucleoid-associated proteins</td>
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<td>May 2018</td>
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<tr>
<td>PhD</td>
<td>Sabrina Dumas (Ntambi)</td>
<td>Nutritional Sciences</td>
<td>The role of skin-specific Stearoyl-CoA desaturase-1 in whole-body metabolism</td>
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<td>March 2018</td>
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<tr>
<td>MS</td>
<td>Gurnimrat Sidhu (Butcher)</td>
<td>Biophysics</td>
<td></td>
</tr>
<tr>
<td>May 2018</td>
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**Degrees as of Nov. 30, 2018**

We heard from you!

Below are some notes we got after our last issue or some alumni news we spotted online. Have something you'd like to share with us? Contact: alumninews@biochem.wisc.edu.

Jerome Schultz, Ph.D. ’58 (Johnson), emailed us with many fun stories dating back to his time in the department. He is a biochemist who is in the National Academy of Engineers.

Roc Ordman, Ph.D. ’74 (Garver), has retired as a professor from Beloit College and is now a caregiver in Madison but continues his biochemical activities. He writes a nutrition newsletter and is submitting NIH proposals on a vitamin formulation.

John Burd, Ph.D. ’75 (Wells), wrote us with news of his company Lysulin, Inc. and its new product for the nutritional support of people with type 2 diabetes, prediabetes, or those at risk of developing diabetes.

Deneen Wellik, Ph.D. ’95 (DeLuca), is back on campus as the new Chair of the UW–Madison Department of Cell and Regenerative Biology.

Jeremy Johnson, Ph.D. ’07 (Raines), received an NSF grant to study a class of enzymes linked to cancer growth. He is an assistant professor at Butler University.

This year the department is honoring the 50th anniversary of UW–Madison biochemist Har Gobind Khorana receiving the Nobel Prize for contributions to deciphering the universal genetic code. He performed the work while a professor in the department from 1960 to 1970. Khorana passed away in 2011. This year also marks the 10th anniversary of the esteemed Khorana Scholars Program, a cultural exchange program run by UW–Madison biochemistry professor Aseem Ansari. Nearly 1,000 students have benefited from the Khorana Program and its parallel program called the Bose Program.
Honors & Awards

Faculty

Richard Amasino  WARF Named Professorship
Michael Cox  UW–Madison Award for Mentoring Undergraduates, in Research, Scholarly, & Creative Activities
Aaron Hoskins  CALS Pound Research Award
Robert Landick  Elected to the American Academy of Arts and Sciences
Ann Palmenberg  2018 WARF Innovation Awards: 1 of 7 finalist teams (with K. Watters)
Srivatsan Raman  Named to Biochemistry’s list of “Future of Biochemistry” NIH Director’s New Innovator Award
Philip Romero  Shaw Scientist Award from the Greater Milwaukee Foundation

Emeritus Faculty

Roland Rueckert  Who’s Who Marquis Nelson Lifetime Achievement Award 2018

Staff

Elle Kielar Grevstad  Optical Core “Image of Distinction” Award in Nikon’s 2018 Photomicrography Competition
Ryan H Hsu  Venturelli Best Poster Award Winner at the SEED Synthetic Biology Conference
Jean Prahl  DeLuca Awarded Emeritus Status
Rebecca Smith  Ralph American Society of Plant Biologists (ASPB) Robert Rabson Award
Kelly Watters  Palmenberg 2018 WARF Innovation Awards: 1 of 7 finalist teams (with A. Palmenberg)

Postdoctoral Staff

Kate Henderson  Record Sigrid Leirmo Memorial Award in Biochemistry
ChangHwan Lee  Kimble American Heart Association Postdoctoral Fellowship
Danielle Lohman  Pagliarini AAAS Science and Technology Policy Fellow
Alex Harwig  Landick Third place in Tufts New England Case Competition (with M. Chhabra)

Graduate Student Awards

Kasia Dubiel  Keck Denton Award for Graduate Student Excellence in Teaching & Mentoring
Sarah Hansen  Hoskins Denton Award for Graduate Student Excellence in Teaching & Mentoring
Beth Boudreau  Landick 2018 Best Poster Prize at the Biochemical Society Focused Meeting on Biology and Physics of Bacterial Chromosome Organization
Munish Chhabra  Record Third place in Tufts New England Case Competition (with A. Harwig)
Yanding Li  Ralph Invited to Marcus Wallenberg Prize Symposium in Stockholm, Sweden
Nathan Thomas  Henzler-Wildman Editors’ Pick Manuscript: Journal of Biological Chemistry

Graduate Student Training Grants

Jonathan Greenhalgh  Romero Biotechnology Training Program (BTP)
Susan Hromada  Venturelli Biotechnology Training Program (BTP)
Jacob Rapp  IPiB Rotator Biotechnology Training Program (BTP)
Gilbert Loiseau  Senes Chemistry-Biology Interface Training Program (CBI)
Sonali Gupta  Venturelli Molecular Biophysics Training Program (MBTP)
Zachary Romero  Cox Molecular Biosciences Training Grant (MBTG)
### Graduate Student Fellowships

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution/Fellowship Details</th>
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<tbody>
<tr>
<td>Ashley Cortes Hernandez</td>
<td>Bednarek Biochemistry Teaching Fellowship</td>
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<tr>
<td>Kelly Mitok</td>
<td>CALS Wisconsin Distinguished Graduate Student Fellowship</td>
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<tr>
<td>Samson Condon</td>
<td>Arthur B. Michael Fellowship</td>
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<td>Harriet Saunders</td>
<td>Arthur B. Michael Fellowship</td>
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<tr>
<td>Matthew Blackburn</td>
<td>Morgridge Wisconsin Distinguished Graduate Fellowship in Biotechnology</td>
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<tr>
<td>Abigail Bartlett</td>
<td>NSF Graduate Research Fellowship Program</td>
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<td>Brian Carrick</td>
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<td>Tina Lynch</td>
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<td>Nathan Murray</td>
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<tr>
<td>Delia Scoville</td>
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<tr>
<td>Jonathan Tai</td>
<td>Rath Wisconsin Distinguished Graduate Fellowship</td>
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<td>Jessica Heath</td>
<td>William H. Peterson Fellowship</td>
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<td>Michael Kelliher</td>
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<td>Zachary Kemmerer</td>
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<td>Nathan Thomas</td>
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<td>Gladys Diaz-Vazquez</td>
<td>Science and Medicine Graduate Research Scholars (SciMed GRS)</td>
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<td>Anthony Meza</td>
<td>Science and Medicine Graduate Research Scholars (SciMed GRS)</td>
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<td>Dana Dahhan</td>
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<td>Anne Schwarwalder</td>
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### Undergraduate Fellowships

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<td>Thomas Anderson</td>
<td>Hilldale Undergraduate Research Fellowship</td>
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<td>Cory Call</td>
<td>Hilldale Undergraduate Research Fellowship</td>
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<tr>
<td>Sarah Dyke</td>
<td>Hilldale Undergraduate Research Fellowship</td>
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<tr>
<td>Stephen Early</td>
<td>Hilldale Undergraduate Research Fellowship</td>
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<tr>
<td>Grant Hussey</td>
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<tr>
<td>Ryan Kempen</td>
<td>Hilldale Undergraduate Research Fellowship</td>
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<tr>
<td>Xiaoxuan Lin</td>
<td>Hilldale Undergraduate Research Fellowship</td>
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<tr>
<td>Maggie Liu</td>
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<tr>
<td>Gina Luu</td>
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<tr>
<td>Jack McCann</td>
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<td>Collin McFadden</td>
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<td>Brandon Nikolai</td>
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<td>Michael Palo</td>
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<td>Stephen Pan</td>
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<td>Steve Sacotte</td>
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<td>Cerise Siamof</td>
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<td>Andrew Suscha</td>
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<td>Johanna Virta</td>
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<tr>
<td>Tong Zhen Xie</td>
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<tr>
<td>Ke Xu</td>
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<tr>
<td>Sarah Dyke</td>
<td>SCORE Program Fellowship</td>
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<td>Jack McCann</td>
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<tr>
<td>Guanyu Liao</td>
<td>SUPER-G Program Fellowship</td>
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<tr>
<td>Thanh Phuong Nguyen</td>
<td>Sophomore Research Fellowship</td>
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<tr>
<td>Rachel Schneider</td>
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From Top: IPb graduate students Jessica Heath, Sam Condon, Harriet Saunders and Sarah Hansen with biochem undergrad Jack McCann. Left: Postdoc Kate Henderson with biochem undergrad Guanyu Liao.
Honors & Awards

Undergraduate Awards

Will Flanigan
Wenqi Shen
Ryan Risgaard
Bennett Bremer
Sarah Dyke
Jeff Harrington
Guanyu Liao
Gina Luu
Neema Mbele
Michael Palo
Ryan Risgaard
Wenqi Shen
Sarah Thimmesch
Dhruva Ajit Nair
Nick Bockhaus
Claire Evensen
Emma Groblewski
Garrett Gunderson
Grant Hussey
Artun Kadaster
Ryan Kempen
Grace Padgett
Paige Pistono
Rasika Ramanathan
Navid Shoaei
Alexios Staikos
Abby Stoltenburg
Katherine Vietor
Rezwana Karim
Sarah Dougherty
Jonathan Doenier
Clare Cimperman
Nathan Wang
Emma Groblewski
Evan Routhier
Ryan Kempen
Samantha Rider
Leah Johnson
Jorgo Lika
Claire Evensen
Stephen Halada

ASBMB Meeting Undergraduate First Place Poster
ASBMB Meeting Undergraduate Poster Honorable Mention
Autism Science Foundation Summer Scholar
Biochemistry Mary Shine Peterson Award
Biochemistry Mary Shine Peterson Award
Biochemistry Mary Shine Peterson Award
Biochemistry Mary Shine Peterson Award
Biochemistry Mary Shine Peterson Award
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Biochemistry Mary Shine Peterson Award
Biochemistry Mary Shine Peterson Award
Biochemistry Undergraduate Summer Research Award
Biochemistry Undergraduate Summer Research Award
Biochemistry Undergraduate Summer Research Award
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Biochemistry Undergraduate Summer Research Award
Biochemistry Undergraduate Summer Research Award
Biochemistry Undergraduate Summer Research Award
Chemistry Undergraduate Poster Session Award Winner
Chemistry Undergraduate Scholarship
College of Letters and Science Dean's Prize
Fulbright Scholarship
Goldwater Scholarship
Holstrom Environmental Scholarship
Holstrom Environmental Scholarship
Hormel Institute Summer Undergrad Research Experience
Trewartha Senior Thesis Award
Udall Scholarship
University Book Store Award
Welton L&S Sophomore Research Award
Welton L&S Sophomore Research Award


From Top: Biochem undergrads Sarah Dyke, Bennett Bremer, Neema Mbele, Garrett Gunderson, and Claire Evensen.
Letters from the Labs

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

Craig Lab

Greetings from the Craig Lab. We continue our efforts to understand how molecular chaperones (particularly, our favorite, Hsp70) do so many different things. It has been challenging (and fun) to mix “hard core” yeast genetics with NMR, X-ray crystallography, and site-specific crosslinking.

See-Yeun Ting graduated last year and is now a post-doc in Seattle — he reported that it was a looooong drive there with a young son and a cat! His eLIFE paper defining mitochondrial import motor architecture got accepted in the nick of time before his departure. Keeping us in the mitochondrial world, we welcome Zak Baker, a joint postdoc with the Pagliarini Lab. Zak will use mass spectrometry-based screening to identify cellular responses to disruption of mitochondrial proteostasis.

By the time you read this, Kanghyun Lee will have defended his thesis and begun his UCSF postdoctoral position. He, with Om Shrestha, Ruchika Sharma (who left us for a patent fellowship at NIH) and Tom Ziegelhoffer, have made good progress in understanding Zuotin, the J-protein of the complex, ribosome-associated Hsp70 machinery — involved in folding of nascent polypeptide chains AND translational fidelity through its 60S and 40S subunit interactions. Plus, Zuotin interacts with an “atypical Hsp70,” whose function Kanghyun has been unraveling over the past year.

Using a combination of yeast suppressor and NMR analyses, Brenda Schilke and Szymon Ciesielski continue to tackle how two very similar J-proteins (Sis1 and Ydj1) can be so different. Last, but not least, Jarek Marszalek is on his 20th lab visit from the University of Gdansk, Poland — keeping our Fe-S cluster biogenesis and evolution collaborations robust.

We are just beginning a five-year grant, so will be here working in the lab for a few more years — though Betty vows she will “never write another grant!” Keep in touch.

Hoskins Lab

Hello from the Hoskins Lab! Sarah Hansen is preparing to defend her thesis in December and is exploring postdoc opportunities. Her paper on splicing inhibition was accepted in Cell Chemical Biology and her magnum opus on U1 snRNA/5’ splice site interactions is nearing completion. Harpreet Kaur and Xingyang Fu have made fantastic progress studying spliceosome activation. Harpreet’s paper on the AGATHA software program is in revision. Clarisse van der Feltz is currently writing up her work on the Ecm2 protein and its role in structuring the spliceosome active site. The lab was also awarded funds to construct the CoSMoS 3.0 (or 4.0 depending on your counting) microscope. Harpreet, Clarisse, and Josh Paulson are busy figuring out how to move a 600lb optical table into the microscope room.

In undergrad news, David Beier’s paper on Prp5 has been submitted, and he is currently working at Vanderbilt and applying for medical school. Brent Groubert, Jack McCann, and Brandon Nikolai will all be graduating in the spring, and Brent and Jack will be traveling to the ASBMB meeting in Orlando in March. Charlie Schneider is currently busy memorizing glycolysis for 507 and learning how to carry out smFRET experiments. We also welcomed Cade Harkner into the lab this semester.

In alumni news, the tri-snRNPs (Tucker Carrocci, Josh Larson, Maggie Rodgers) will be reunited for Sarah’s thesis defense. Maggie was recently awarded a NIH NRSA postdoctoral fellowship (currently with Sarah Woodson at Johns Hopkins), and Josh received a Washington Research Foundation fellowship (currently with Chip Asbury at U. Washington).

Finally, Aaron received tenure this year and an affiliate appointment in the Chemistry Dept. He will also be on sabbatical at UCLA with Doug Black and Tracy Johnson in 2019 and can’t wait. He’d like to thank all his past and present lab members and colleagues who have made this possible.
Letters from the Labs

Markley Lab

Greetings from the Markley Lab. The big news from NMRFAM is that our new helium recovery system is finally operational. Paulo Cobra (pictured below), who took over the instrumentation position after Mark Anderson retired, did a great job pushing this to completion. Mark’s plans for retirement, now that he has a pilot’s license, are to build an airplane, and, just to be creative, he is also considering structural concrete. Our most recent Ph.D.s went to Hesam Dashti, who has left for a postdoc in bioinformatics at Harvard Medical School, and Kai Cai, who accepted a postdoctoral position in cryo-EM at UT Southwestern. Both were highly productive in the lab and will be missed. Upon leaving, Hesam had ten publications and Kai eleven. Jin Hae Kim (Daegu Gyeongbuk Institute of Science & Technology, Korea) participated in the 39th Steenbock Symposium on Iron-Sulfur Proteins — Biogenesis, Regulation and Function that John and Trisha Kiley organized in Madison last Spring. At the International Conference on NMR in Biological Systems held last August in Dublin, John was pleased to get to see Andrei Alexandrescu (University of Connecticut), Bin Xia (Peking University), Jasna Fejzo (University of Massachusetts-Amherst), and Andy Hinck (University of Pittsburgh). Andy was traveling with his portable bicycle that he planned to ride in between visits to collaborators in Europe. We recruited Pedro Romero as Director of the Biological Magnetic Resonance after Eldon Ulrich retired. Thankfully, Eldon still makes himself available to assist with the BMRB data dictionary and other issues. Jeff Hoch (University of Connecticut) joined John as Co-PI in the competitive renewal of the BMRB grant, which scored well. We always look forward to visits from former group members. We had a trifecta one recent week with Jikui Song (UC, Riverside) and Ian Lewis (University of Alberta) presenting seminars and Arash Bahrami (NetSeer, a startup in Silicon Valley) visiting for the football weekend.

Research in the Pike Laboratory over many years has focused on the molecular mechanisms through which steroid hormones, such as the vitamin D hormone, regulate the expression of genes. Currently, however, we are active in exploring the regulation of genes involved in the production and degradation of the vitamin D hormone and in a study of the regulation of expression of the new phosphaturic hormone FGF23, both of clinical interest. These studies are providing crucial new insight into how mineral regulating hormones control the output of the vitamin D hormone in the kidney and elsewhere — insight that has been lacking for more than 40 years. Importantly, these studies benefit strongly from the development of methods to examine the genome and from the discovery of methods that enable the rapid creation of mutant mouse strains useful in identifying the regulatory functions of the control regions of genes.

The major players in the work that has gone on over the past several years in the laboratory include Mark B Meyer, Ph.D., associate scientist, Seong Min Lee, Ph.D., assistant scientist, and Nancy A Benkusky, research associate. While Mark has been instrumental in the practical development of our genomic and in vivo approach, all three individuals have been involved in our most recent studies focused upon delineating mechanisms that control vitamin D hormone production. Since these studies are performed largely in the mouse, Mark, Nancy and Seong Min have become experts at animal husbandry and genomic analysis in addition to their biochemical prowess. The uniqueness of the work has been highlighted through Mark and Seong Min’s selection to present oral communications, seminars, and posters on the topics both locally and at national meetings, receiving multiple travel and young scientist awards for their work over the years as well. This work is currently supported by several NIH awards, including one that was received very recently, and we anticipate additional funding to continue exploration of FGF23 gene expression. Finally, Mark has submitted his first NIH grant application, so welcome to the world of science, Mark!
To reproduce and multiply, bacteria grow their cells and then split themselves into two halves. Our laboratory studies the molecular machine — the “divisome” — that makes this cell division process happen. The way the divisome works is still very mysterious. We know that many proteins are essential for the divisome to work properly, but their precise function is still unknown. We are interested in understanding these mechanisms not only because cell division is a fascinating and fundamental biological process, but also because a better understanding of cell division may lead to the discovery of new ways to prevent bacteria from multiplying and the development of new antibiotics. Specifically, we are studying the sub-complex formed by three divisome proteins: FtsQ, FtsL, and FtsB (or FtsQLB). Our goal is to understand their structure, which will provide important clues for understanding the exact function of the complex. At the end of 2017, we published an article on this topic in the Journal of Biological Chemistry, authored by graduate students Samson Condon, Deena-Al Mahbuba, and other members of our lab and collaborators. The article reported the structural characterization of the major domains of FtsL and FtsB. Although our structural work does not yet tell us the precise function of FtsQLB, the study reveals that the complex is much more complicated than initially thought, and that it contains some unusual structural features that must be important for the complex’s function. This structure is now guiding important follow up functional studies.

The second major project of the lab is understanding the fundamental principles that govern the interaction of membrane proteins, i.e. those proteins that are embedded in biological membranes. Because these proteins are in a strategic location between the outside and inside of the cell, they are involved in many essential functions, including the communication between the cell and the outside world. Our goal is to understand the rules that determine the association of a structural motif, i.e. a commonly found way for two proteins to come together and form a complex. At the beginning of 2018, we published a paper in the Journal of the American Chemical Society, authored by graduate student Samantha Anderson, former graduate student Benjamin Mueller, and undergraduate student Evan Lange. In this article, we show that two weak forces, the van der Waals forces and weak hydrogen bonding, cooperate to drive the stability of these membrane protein complexes.

In the past year, one member has joined the laboratory, IPiB graduate student Gilbert Loiseau, and another left us, postdoctoral researcher Kai Cai, who has moved to the UT Southwestern Medical Center to join Daniela Nicastro’s lab.
In Memoriam

Helga Ahrens  
M.S. 1974 — Prof. DeLuca  
January 2018

Laurens “Andy” Anderson  
M.S. 1947, Ph.D. 1950 — Prof. Lardy  
Professor 1951-1986  
Emeritus 1986-2018  
November 2018

John Asplund  
Ph.D. 1960 — Prof. PH Phillips  
February 2018

Claire Bailey  
B.S. 1947  
August 2018

Paul Boyer  
M.S. 1941, Ph.D. 1943 — Prof. PH Phillips  
June 2018

John Casida  
M.S. 1952 — Prof. Stahmann  
June 2018

Harriet Gorski  
Generous supporter  
August 2018

Alan Jones  
Dedicated staff member  
January 2018

Robert Kearl  
Generous supporter  
August 2018

William Leoschke  
M.S. 1952, Ph.D. 1954 — Prof. Elvehjem  
October 2018

Gladys Maley  
M.S. 1950, Ph.D. 1953 — Prof. Lardy  
February 2018

David McConnell  
Generous supporter  
May 2018

Lois Partridge  
Generous supporter  
May 2017

Alice Rohde  
M.S. 1952 — Prof. Elvehjem  
January 2018

Jack Snyder  
M.S. 1951, Ph.D. 1953 — Prof. Link  
August 2018

Fred Soltero  
M.S. 1952, Ph.D. 1954 — Prof. Johnson  
December 2017

Marcella Stewart  
M.S. 1962 — Prof. Stahmann  
August 2018

Kathryn Vaughan  
Generous supporter  
June 2018

Brian Wier  
B.S. 1978  
October 2018

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

Laurens ‘Andy’ Anderson — Dedicated Emeritus, Distinguished Alum, Mentor

University of Wisconsin–Madison Emeritus Professor of Biochemistry and Ph.D. alumnus Laurens “Andy” Anderson died on Nov. 6 at the age of 98.

Anderson was born in South Dakota, and he earned his undergraduate degree from the University of Wyoming in 1942. After college, he joined the Air Force and served as a bomber pilot in missions over southern Europe. In 1946, he began his graduate studies in biochemistry at UW–Madison.

As a graduate student he worked with esteemed biochemist Henry Lardy, an expert in carbohydrate structure and metabolism. After earning his Ph.D. in 1950, and following a yearlong postdoctoral position in Switzerland, Anderson returned to UW–Madison to join the biochemistry faculty. He became a world expert on the structure and chemical synthesis of cyclitols, including the inositols that proved to be central in biological signaling. Anderson served for many years an editor of Carbohydrate Chemistry.

Andy retired in 1986 but stayed involved in research and mentoring. His last paper, published when he was 92 years old, described his work with undergraduates and graduate students in the laboratory of Bassam Shakhashiri in the UW Chemistry Department. Anderson won many awards during his career, including the American Chemical Society’s Hudson Award in Carbohydrate Chemistry in 1984.

Paul Boyer — Distinguished Alum, Nobel Laureate, Generous Supporter

University of Wisconsin–Madison biochemistry Ph.D. alumnus and UCLA Emeritus Professor of Biochemistry Paul Boyer died on June 2 at the age of 99.

During his time at UW–Madison, he discovered the first known function for potassium. After earning his Ph.D. in 1943 he performed research at Stanford University, investigating how to stabilize blood plasma without refrigeration.

From Stanford he joined the University of Minnesota and after two decades there he joined UCLA in 1963. In his early years at UCLA, he helped start and lead their Molecular Biology Institute, which opened in 1965.

His most momentous achievement at UCLA came when he earned the Nobel Prize in chemistry in 1997 for his groundbreaking research on adenosine triphosphate, or ATP, which is the main energy source for biological reactions in the cell.

Boyer used a large portion of his Nobel Prize winnings to fund support for postdoctoral awards at several universities, including UW–Madison. The Boyer Award for Postdoctoral Excellence in Biochemistry recognizes a postdoctoral researcher in the UW–Madison Department of Biochemistry for his or her excellence in research. The postdoc also gives a lecture as part of the Boyer Lecture Series.
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Biochemistry Said Farewell to Beloved Elm Tree ‘Elmer’

The University of Wisconsin–Madison campus said goodbye to a beloved natural landmark. An elm tree that has stood for more than 100 years fell victim to Dutch elm disease and was removed from the Hector F. DeLuca Biochemical Sciences Complex by UW–Madison grounds staff.

The tree — often known informally as Elmer — had a rich past with the Department of Biochemistry and surrounding departments in the College of Agricultural and Life Sciences, such as the Department of Horticulture. Thousands of students who have taken biochemistry courses or frequented that area of campus have gazed up at the old elm or enjoyed breaks in the shade it provided.

“Diameter-wise, it was our largest tree on campus and I’d estimate it was 150 years old,” said UW–Madison Buildings and Grounds Superintendent Ellen Agnew.
Biochemistry steeped in history. UW–Madison biochemistry alumnus and professor Karl P. Link (1901-1978), is famous for his discovery of the anticoagulant warfarin in the 1940s. Depending on the strength and dose, it is effective to treat human heart attacks or to kill mice. Later, Link patented a mouse trap that contained the compound to use in rodent control. Rodents were a huge issue at the time, causing millions of dollars in damage each year, particularly in the agricultural industry. The name is a play on the Wisconsin Alumni Research Foundation (WARF), which held the patent. WARF serves as the dedicated patenting and licensing organization for UW–Madison and supports the university with millions of dollars each year.