LSA BIOPHYSICS
UNIVERSITY OF MICHIGAN

BIOPHYSICS NEWS FALL/WINTER '22-23

Understanding Antibiotic Resistance—Sometimes They Use A Village

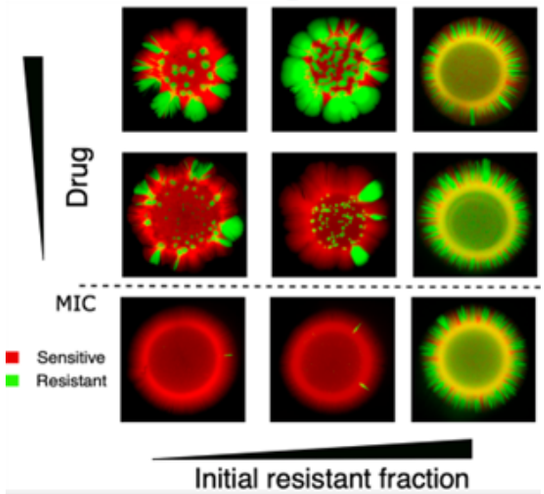


Figure 1: Bacterial colonies consisting of drug-sensitive (red) and drug resistant (green) populations exhibit a wide range of spatial patterns as drug concentration (vertical) and resistant fraction (horizontal) varies. The presence of resistant (green) cells in a community allows for survival of neighboring sensitive (red) populations, even at drug concentrations above the MIC (minimum inhibitor concentration) that would otherwise be fatal. Image modified from Sharma and Wood, ISME, 2021.

Antibiotic resistance is a growing threat to public health around the world. Bacteria are simple organisms, but when it comes to survival, they are agile tacticians. Microbes rely on a highly adaptable arsenal of molecular defenses—for example, drug-cleaving enzymes—to neutralize the effect of antibiotics. At the microscopic level, drug resistance is increasingly understood, yet we're faced with daunting questions about how the behavior of bacterial communities emerges from these microscopic details. Are microbial populations just amplified versions of single cells, an aggregate system where the whole is simply the sum of the parts? Or is community-level behavior—including the response to drugs—dominated instead by the intricate ways in which those cellular dynamics fit together?

Kevin Wood, Associate Professor of Biophysics and Physics, believes the answers to these questions may hold clues for slowing antibiotic resistance. Working with *E. faecalis*, an opportunistic human pathogen, scientists in his group have shown that microbial resistance—and survival—often hinges on the way bacterial cells interact with their neighbors. And these interactions can have surprising implications for how bacterial populations—and perhaps even human infections—can be controlled. For example, work from Wood and collaborators has shown that reducing or delaying drug treatment (*Hallinen, Karslake, et al, eLife, 2020*), or even adding more bacteria cells to the population (*Hansen, Karslake, et al, PLOS Biology, 2020*), can slow resistance in the lab. These counterintuitive strategies appear in simple mathematical models of interacting populations and emerge from ubiquitous features of microbial dynamics—things like competition for limited resources or metabolism-driven changes to the local environment.

Important interactions can also arise from the resistance mechanism itself. In resistant cells that make beta-lactamase, an enzyme that hydrolyzes many penicillin-like drugs, resistant cells can protect neighboring sensitive cells, which no longer require the enzyme to survive…as long as they choose their neighbors carefully. The push and pull of these different interactions can lead to dramatic spatial patterns (Figure 1), and researchers in Wood's group—in collaboration with biophysics professor Jordan Horowitz's group—are continuing to study the biophysical parameters that drive different patterns and may ultimately tip a population toward survival or extinction.

The work in Wood's lab is supported by NIH and driven by an interdisciplinary group of scientists, including many current and former Biophysics PhD students. "I've been lucky to work with an enormously talented group of students and postdocs," said Wood, who was originally trained as a theorist in physics. "Our work is built on a combination of mathematical models and microbiology lab experiments, and Biophysics offers students the unusually broad skillset that, in my view, leads to new perspectives on this classic and important problem."

Kevin (middle) is shown with two frequent collaborators, Emily (left) and Sam (right). Emily and Sam were not directly involved in the current work. But maybe one day

WELCOME FROM THE DIRECTOR

Greetings Alumni, Friends, and Prospective Students:

I am delighted to speak to you in this edition of the Biophysics Newsletter. We are very grateful to all of you for your continued support of Biophysics over the years, as many of you have watched the unit transform from a Research Unit within the Office of Research to a unique graduate and undergraduate program within the College of Literature, Science, and the Arts. Moving forward, finally leaving most of the restrictions that the COVID-19 pandemic imposed upon all of us, I am excited to share with you the recent news and events from Biophysics.

There has been a significant amount of activity within Biophysics since I last communicated with you. In November of 2021 we underwent an external review of our program. The committee of esteemed scholars who reviewed Biophysics — from our undergraduate program to our faculty, staff and graduate program - was composed of four Biophysicists: Professor Susan Marquese, from UC Berkeley, Vice Dean for Natural Sciences Bertrand Garcia-Moreno from Johns Hopkins University, Professor Anne McDermott from Columbia University and Professor Rama Ranganathan from the University of Chicago. During an extensive two-day review they explored many aspects of our program and plans for our future. We were very pleased to learn that they found our efforts to build a strong, diverse and inclusive unit looking to the future as a center of quantitative biological education, research and training to be on the mark. They noted the strength of our program faculty, the outstanding undergraduate majors in Biophysics and the impact of our graduate program within the university. As we move these initiatives forward we will keep you apprised of our exciting developments.

Biophysics has continued to expand its role in undergraduate education during the past few years, growing to match the interests of students in introductory programming in the sciences and in core physics pedagogy. Through a collaboration with our neighbor, the Physics Department, we revised and revamped the curriculum for the two-semester core Physics course structure "Physics for the Life Sciences." Playing a significant role in this effort, Professor Chris Meiners created a new course structure that consisted of lectures and studio sessions, and together with Professor Kevin Wood they are teaching in this new series and providing broader exposure about the quantitative thinking about biological problems that is a key focus of Biophysics. This new course structure complements the core physics training that was already part of Biophysics' one-semester "Physics of the Body and Mind".

Thus, our undergraduate program continues to thrive with an increasing number of majors and a significant increase in the number of students being taught by Biophysics faculty. As noted in our last newsletter, it is our strong goal to involve our undergraduate students in experiential learning through research and internships. Beyond the outstanding research opportunities offered to undergraduates in our laboratories, we continue to work to assist our undergraduates in identifying summer experiences that will help shape their future careers and goals through research experiences, for example summer research experiences for undergraduates (REU) programs and internships. Our faculty is playing a strong role in offering undergraduates outside of Michigan similar opportunities through our very successful NSF-sponsored summer REU program directed by Professor Michal Zochowski and newly appointed co-Director Professor Kevin Wood. We hosted six undergraduates for 10 weeks of research experience in our laboratories this summer.

Our graduate students are at the core of the outstanding research being carried out in our laboratories and are being recognized for their accomplishments through awards and recognitions, including NSF predoctoral fellowships, Rackham predoctoral fellowships, Rackham Merit Fellows and a host of other acknowledgments of their ongoing excellence in science and citizenry. In our efforts to maintain our strong and diverse graduate program, Biophysics continues to host its "preview visit" for diverse students to explore Michigan Biophysics as they move toward application for and matriculation into graduate school. We hosted an excellent group of students during our annual fall retreat to learn about our program, the process of applying for graduate school and to network with our students, faculty, postdocs and staff. The event was a great success, held at Matthaei Botanical Gardens and Nichols Arboretum this fall.

I continue to be amazed and awed by the outstanding research of our excellent faculty. We have tremendous faculty members addressing biophysical questions across the spectrum of scales – from the holistic system level, examining cells and their mutual interactions, to the molecular level, querying the structure-function relationships that govern cellular processes. Our faculty continues to be prosperous in their research and teaching endeavors and are being recognized for these efforts within the university, nationally and internationally with awards, grants and speaking invitations. In this newsletter, you will learn about the exciting efforts underway in the laboratory of Professor Kevin Wood to explore the role of antibiotics on bacteria at the community level, about advances by Professor Julie Biteen and her students in imaging molecules in live cells and by Professor Ajit Joglekar whose laboratory is exploring the factors that influence mitosis. Also notable are the efforts of Professor Ramamoorthy for overseeing a now long-running virtual seminar series on the molecular basis of proteinopathies, which has featured speakers from across the world and provides an ongoing update on research into diseases such as Alzheimer's dementia.

I am delighted that we have been able to feature the inspiring journey of one of our alumni in this issue of the newsletter, Dr. Eileen Sneeden. I had the honor of interacting with Dr. Sneeden this year and learned of her pathway from an undergraduate here at Michigan, into graduate school in Biophysics at Michigan and ultimately to pursue a lifetime interest in helping medical patients through Biophysics.

In closing, I note that it is truly my honor and pleasure to serve as the Director of our Biophysics Program. I remain extremely excited by the developments of my faculty colleagues and their coworkers, as well as the achievements of our students. I look forward to a new year that exceeds our expectations from the last. We benefit enormously from your help and support and encourage you to share with us what you are doing. Finally, if you find yourselves in Ann Arbor, please take a few minutes and visit us.

We look forward to hearing from you and seeing you in the future.
Charles L. Brooks III
Director and Professor of Biophysics
Cyrus Levinthal Distinguished Professor of Chemistry and Biophysics
Warner-Lambert/Parke-Davis Professor of Chemistry

BIOPHYSICS PROGRAM NEWS

Sam Krimm Graduate and Undergraduate Student Awards

We are pleased to offer these awards, made possible by the generous support of our friend and colleague Sam Krimm through the Krimm Endowment established by Sam in support of graduate students in Biophysics.

The **Krimm Exceptional Dissertation Award** recognizes a graduate student who defended their dissertation in the past academic year. The inaugural Krimm Exceptional Dissertation award is going to **Chris Macdonald** for his dissertation titled "Complexity in the Membrane: The Fluc Family of Fluoride Channels and Small Multidrug Resistance Family of Transporters as Models for Understanding Membrane Protein Structural and Functional Evolution." Chris layed new ground as the first student in Randy Stockbridge's lab while making valuable contributions to the graduate program.

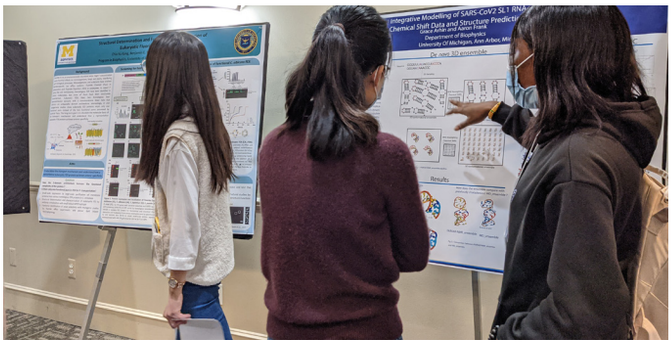
The **Krimm Exceptional Graduate Student Award** recognizes mid-career graduate students who are actively working on dissertation projects. The inaugural Krimm Exceptional Graduate student award is being shared this year by **Elizabeth Tidwell** and **Ziyuan Chen**. Liz's work in the Kutmos lab combines modeling,bioanalytical characterization, biochemical binding analysis, and structural methods to identify small molecule binding partners of structured RNAs. Ziyuan Chen's work in the Biteen lab develops experimental and analytical methods to quantify protein mobility in live bacterial cells, extracting information on their functional states.

The **Exceptional Undergraduate Student Award** recognizes graduating biophysics majors or minors. The inaugural Exceptional Undergraduate award is being shared by **Pujan Ajmera** and **RaghuRam Prasad.** Both students have made major contributions to research in their respective labs while being leaders in the Biophysics Club and other program activities.

Staff Profile - DaKayla Whitten

DaKayla Whitten, Events & Communications Coordinator, is new to the University of Michigan. She manages the Biophysics social media and events.

In her free time, she enjoys training/ coaching Brazilian JiuJitsu with her husband and playing with her two dogs, Albie and Newton.



UM Biophysics hosted its back in person Annual Retreat last year.

Joe & Kathleen's Service to the unit

Biophysics recently recognized the retirement of Joe Schauerte and Kathleen Wisser. We are grateful for their many years of service to Biophysics. We celebrated with a farewell picnic that was a wonderful last hoorah! Good luck to Joe and Kathleen on their next life adventures.

Zoominar series on the "Molecular Bases of Proteinopathies"

Organizers: Prof. Joan-Emma Shea (UCSB), Prof. Magda Ivanova (UM), Prof. (Rams) Ayyalusamy Ramamoorthy (UM), Dr. Bikash Sahoo (post-doctoral fellow, UM), and Samuel McCalpin (graduate student, UM).

This weekly zoominar series started in August 2020 to cover the breakthrough discoveries in this exciting multidisciplinary area of research through presentations from experts in the field. When conferences have been canceled around the world, these virtual presentations and discussions have been providing unique opportunities for everyone to learn about recent findings, new topics, and cutting-edge techniques. This virtual series also had mini-symposia to provide opportunities for young researchers (postdocs and students) to present their findings and theme-based sessions. More details on the list of speakers and topics covered can be found at: *rams.biop.lsa.umich.edu/symposium_1*. This series has >1000 registered participants from all over the world. Videos of the virtual presentations from this series are made available on a YouTube channel (search for the "amyloid symposium") for those who could not participate in the live session(s), and are also used for teaching.

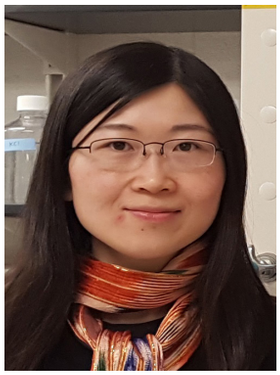
CORE FACULTY NEWS

Congratulations to **Sarah Keane** who was named Cottrell Scholar.
Sarah Keane is among 24 outstanding teacher-scholars in chemistry, physics, and astronomy named recipients of Research Corporation for Science Advancement's 2022 Cottrell Scholar Awards.

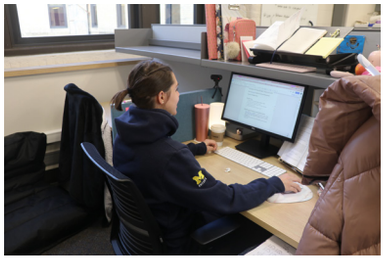
Each award is $100,000. Recipients are chosen through a rigorous peer-review process of applications from a wide variety of public and private research universities and primarily undergraduate institutions in the United States and Canada. Their award proposals incorporate both research and science education.

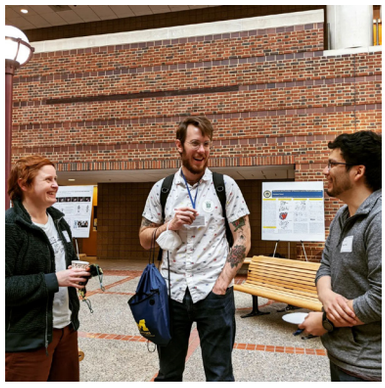
Research Corporation for Science Advancement, founded in 1912, is a private foundation that funds early stage, high-potential basic research in the physical sciences (astronomy, chemistry, physics, and related fields) at colleges and universities in the United States and Canada.

Qiong Yang awarded Teaching Award



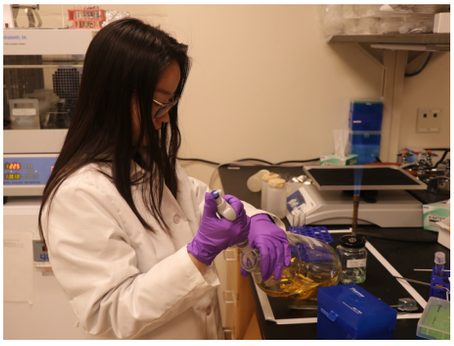
Congratulations to **Qiong Yang** for being recognized by the College of LSA with the 2022 Class of 1923 Memorial Teaching Award for outstanding teaching of undergraduates. This recognition is awarded each year by the College Executive Committee from among those recommended for promotion from assistant professor to associate professor, with tenure, who have demonstrated outstanding teaching during their first years on the faculty. In the Dean's letter to Qiong she notes that "While this award recognizes teaching, it is our belief that excellence in teaching goes hand in hand with excellence in research. Thus this award is only given to individuals whose achievements foretell a prolific career as a scholar, teacher, and mentor". Definitely well chosen words in Qiong's case.





Expanding Biophysics' Footprint in Undergraduate Physics Training

Of note has been our efforts in collaboration with our colleagues in Physics to revise the curriculum for "Physics for the Life Sciences" and share the instructional efforts in providing this two-semester sequence that serves as the base training of our undergraduate cohort focusing on degrees in the life sciences and in particular our pre-med directed undergraduates. This new initiative within Biophysics, combined with our growing enrollment in "Physics of the Body and Mind" have significantly increased the number of undergraduates being instructed by Biophysics faculty. We are excited to deepen our involvement in bringing quantitative tools to our life-sciences facing undergraduates.



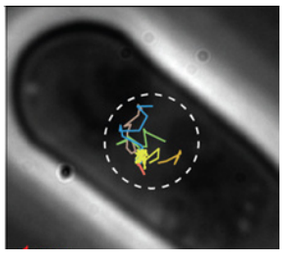
AFFILIATED FACULTY NEWS

Protein Society Award to Janet Smith

Affiliated Faculty **Janet Smith** was awarded the 2021 Dorothy Crowfoot Hodgkin award from the Protein Society. This award recognizes contributions to protein science that profoundly influence our understanding of biology. Professor Smith is recognized for exceptional contributions to our understanding of the biological function of proteins through knowledge of their 3D structures. In major studies of natural-product biosynthetic enzymes, she demonstrated how macrolactones form, how biosynthetic assembly lines function, and how nature has adapted enzymes from primary metabolism for surprising chemical transformations such as cyclopropane formation. Her recent investigations of viral proteins and host antiviral proteins led to an understanding of how the flavivirus NS1 protein increases the virulence of dengue and Zika viruses, and how the zinc-finger antiviral protein recognizes viral RNA.

Direct, Quantitative Measurements of DNA Packaging in Chromatin in Living Cells

Biophysics is leading efforts in the development of new approaches to quantitatively probe biological processes in living cells through high-resolution microscopy in the laboratory of Affiliated Biophysics Faculty Member Professor **Julie Biteen**. Ziyuan Chen, a Biophysics graduate student whose PhD research is directed to the development and application of new approaches for single-molecule fluorescence imaging to answer open questions inside microbial cells, collaborated with colleagues in the UM Medical School to track DNA-binding HP1 proteins in living fission yeast. This research, published in *Science Advances* (DOI: 10.1126/sciadv.abk0793), examined how HP1 proteins modify the packaging of DNA in chromatin to regulate gene expression. This research related the biophysical read-out of subcellular diffusion and binding to the biochemical properties of the protein. I and t led to the engineering of novel HP1 proteins with different localization patterns and allowed. the team to understand, for the first time, how HP1 proteins interact with DNA in the native cellular environment.



Affiliated Faculty Profile: Ajit Joglekar

Movement, Forces, and Signaling Directing the Choreography of Mitosis

In the laboratory of Professor Ajit Joglekar, two critical aspects of mitosis are being explored – how the dividing cell generates the mechanical force to move chromosomes and how it coordinates chromosome movement with the biochemical cell cycle. Both are responsible for accurately segregating the chromosomes and creating genetically identical daughter cells. One of their key objectives in studying mitosis is to advance our understanding of why cancer cells make frequent mistakes in chromosome segregation and whether they can be minimized.

The study of quantitative aspects of cell division in the Joglekar lab engages a diverse set of fluorescence techniques, from super-resolution principles and FRET to BiFC (Biomolecular Fluorescence Complementation), as well as approaches from DNA origami to engineered, ectopic activators of biochemical signaling cascades. In this research, the emphasis is always on observing living cells and understanding their biophysical and biochemical processes. Looking to the future of cell biology and biophysics research to establish a deeper understanding of how the extant machines involved in mitosis work, they have initiated a new and exciting area of study: reverse engineering cellular machines using de novo designed proteins.

Professor Joglekar comments on working with our amazing Biophysics graduate students that "one of the joys of running the lab is mentoring students and helping them prepare for bigger and better challenges" and seeing how these students, moving on from his laboratory, "have gone on to study diverse fields: virology (Pavi Aravamudhan), cell and molecular biology of plants (Alex Kukreja), and killifish aging (Chu Chen)."

We'd like to congratulate the following for joining our ranks as Biophysics Affiliated Faculty!

Professor David Sept, Biomedical Engineering
Professor Shyamal Mosalaganti, Assistant Professor, Cell and Developmental Biology

GRADUATE PROGRAM NEWS

Graduate Program General Updates

The Biophysics Graduate program currently has **38 students** who are doing research in 19 different labs within the departments of Chemistry, Physics, MCDB, CDB, Mechanical Engineering and Medicinal Chemistry.

This year we welcomed a first-year graduate student cohort of five new students. These students join us with a variety of scientific backgrounds, including Physics, Biochemistry, Biology and Chemical Engineering.

Grant for Diversity

This year the Biophysics Department is launching a Student Ambassador program to recruit applicants to the graduate program from Minority Serving Institutions. Our Student Ambassadors will be visiting their Alma Maters where they will have a unique opportunity to present their research, visit with the Faculty and Students, as well as talk about their experiences in the UMich Biophysics program. This program and training is led by a pair of Biophysics Faculty Members, who have secured financial support through the Rackham Faculty Allies Diversity Grant, an initiative of the Rackham Graduate School intended to support faculty-led activities to strengthen diversity, equity and inclusion in graduate programs.

Congratulations to our students who were first or second authors on publications this year!

Ziyuan Chen (Biteen Lab)
Minjun Jin (Yang Lab)
Sicong Ma (Keane Lab)
Franco Tavella (Yang Lab)
Logan Walker (Cai Lab)

Pictures from the 2022 Fall Biophysics Retreat at Matthaei Botanical Gardens

Graduate Student Highlight — Logan Walker

Grad student **Logan Walker** was inspired to study Biophysics after taking a class in undergrad that was taught by Ralf Bundschuh, who is the co-director of the OSU Interdisciplinary Biophysics Graduate Program. After that year, Logan joined Bundschuh working with Pearlly Yan in the OSU medical school working on RNA sequencing related research problems. When Logan applied for graduate school, he decided to apply for biophysics programs specifically because "it would let me leverage my quantitative training from undergrad to keep working on similar projects to what I did as an undergraduate student."

Originally from Oklahoma, but moved around a lot during youth. Logan attended Ohio State University for Physics, Astronomy and Astrophysics with a Computational Sciences minor. Logan plans on applying for staff scientist-type positions once he completes his PhD. From there, Logans ultimate goal would be to work in a role as core facility director or similar, where he would be able to design processes to assist other researchers in completing their experiments.

Logan's advice to future students: **keep a strict to do list and write everything you need to do as soon as it pops into your head. It is easy to forget small things when graduate school moves so fast.**

UNDERGRADUATE PROGRAM NEWS

Undergraduate Program General Updates

The Biophysics undergraduate class currently has **28 students** who are excelling not only in the classroom, but in their laboratory research as well. We are proud to have so many skilled undergraduate students in Biophysics and cannot wait to see what their future accomplishments will be!

We are currently working with our colleagues in Biology to create a new Quantitative Biology major that we hope to get started in 2024.

We'd like to recognize our Biophysics students who graduated this year:

Winter 2022

Chu Chen (Ph.D.)

Kevin Wu (Ph.D.)

Alumni Spotlight: Eileen Sneeden

Professor Brooks had the good fortune to engage one of our wonderful alumni during the past year, **Dr. Eileen Sneeden** (née Yu), and found her path through undergraduate and graduate studies at the University of Michigan and the life pathway chosen by her both engaging and inspiring. We were thus thrilled to convince Eileen to share her story with all of you in this issue of our Biophysics Newsletter. Dr. Eileen Sneeden wanted to be a biophysicist ever since attending a NY Jr Academy of the Sciences seminar in her sophomore year of high school, where she caught the vision for pioneering research in Biophysics, this highly interdisciplinary intersection of the sciences.

Dr. Sneeden arrived at the University of Michigan to pursue her undergraduate studies in Physics and Biophysics, finding Ann Arbor and the university a stimulating environment where she remained for graduate studies and completed her Ph.D. in Biophysics from the University of Michigan in 1999. During her years at Michigan, Dr. Sneeden was given ample opportunities to explore the biological universe through a physicist © lens: from tracking the effects of electromagnetic fields on cell motility with Professor Bill Parkinson, to positing positronium lifetime microscopy in biomatter as a unique probe for evidencing dental microcrack formation with Professor David Gidley and Dr. Bill Frieze.

Two and a half years into her doctoral program, Dr. Sneeden switched thesis research groups to be co-mentored by Professors Jim Penner-Hahn and Charlie Yocum, who patiently guided her through the perseverance-and-reward cycles of conducting scientifically complex, logistically challenging and time-sensitive projects at Department of Energy accelerator labs. Beyond the guidance in scientific matters, her mentors and the University fostered a diverse and enriching environment outside of the laboratory with activities that taught her the power of building trust through effective communication that balances objectivity with sensitivity and humor.

This impact and influence on Dr. Sneeden's early formation played a role in guiding her through a life and career that presented the need for both perseverance and reward. Her pathway, sculpted by experiences going back to her UM days, today finds Dr. Sneeden as a Medical Science Liaison at RayzeBio, a biotech startup, helping to pioneer the fast growing field of targeted radiopharmaceuticals for cancer treatment. Dr. Sneeden reflects that "Aside from an in-depth understanding of particle-biomatter interactions, the formative years at Michigan have equipped me for engaging the many stakeholders needed to take the therapy forward, from physicians to patients - to disseminate emerging data objectively, to optimize patient care and to ensure alignment in this rapidly evolving field." Dr. Sneeden is ever thankful for the Michigan years and blessed to pursue a life of passion and purpose, both then and now, however many pivots it may involve. "May the patients win! And their families.", she notes.

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Leela Ruckthong Graduated in 2016 from the Biophysics PhD program, and is now a lecturer at the King Mongkut's University of Technology Thonburi (KMUTT). They have also collaborated with the CCP4 Crystallographic Software Organization in the UK to organize International Macromolecular Crystallographic Workshops called SEA COAST (South-East Asian Crystallographic Overview And Systematic Training). SEA COAST is the first international macromolecular crystallophic workshop by CCP4 in Southeast Asia area.

Diversity, Equity & Inclusion Statement

Biophysics is an inherently integrative and inclusive endeavor: We use concepts and methods from a diverse array of disciplines to come to a more complete understanding of the natural world around us. As a department, we similarly value diversity, equity, and inclusion in its many forms in all aspects of our academic life, from the classroom to the research laboratory and beyond. We therefore strive to provide a safe and supportive environment for all our students, faculty and staff, where everyone is you are treated with respect and is are encouraged to contribute their your unique strengths and abilities to our shared mission, regardless of who you are. We commit to acting on these principles unwaveringly to improve our field, the department, the university, and our communities for a better future.

Thank you to those who participated in Giving Blueday last year! We great appreciate your support!

If you are still interested in giving to the Biophysics program, visit leadersandbest.umich.edu.

Join us for our upcoming events:

Giving Blueday - March 15th, 2023

Biophysics Graduation Reception - April 28, 2023

Want to be featured in an upcoming newsletter? We want to know what our alumni have been doing! Send us any recent publications, awards or family news to biophysics.events.communications@umich.edu and you could be featured in our publications, website or social media!

Just want to receive our e-newsletters and updates? Don't forget to update your alumni profile on our website!

Don't forget to follow us on social media!

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UM Biophysics Program Newsletter

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Associate Director for Undergraduate Studies:	Kevin Wood
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Chief Administrator:	Jan Malaikal (interim)
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Events & Communications/ Editor of Newsletter:	DaKayla Whitten