BIOCHEMISTRY & CELLULAR AND MOLECULAR BIOLOGY

DISCOVERIES

DEPARTMENT NEWS

Computing Power at Our Fingertips

Computational sciences represent a strategic and transformative axis of development for UT, and our department is on the cutting edge in teaching and research in this field. Five research groups in the department specialize in computational biophysics and systems biology and virtually all BCMB research groups utilize these approaches for intradepartmental collaboration. The supercomputers owned and operated by UT/ORNL computational scientists within the Joint Institute for Computational Sciences offer BCMB faculty and students a computing power that is, without question, unrivaled. Today, the TITAN supercomputer (#4 in the world), located in Oak Ridge, is available to our students and researchers and is one of the most powerful supercomputers in the world. Titan debuted as number one in the world in 2012 and has maintained the top four position for the last five years.

Until a few years ago, UT also operated the Kraken supercomputer, the most powerful academic supercomputer on the planet at the time. Kraken is now replaced with a newer and more powerful machine, STAMPEDE2 (#12 in the world, located at University of Texas Supercomputer Center), which is accessible for our research. Supercomputing resource consortium XSEDE built and now manage both Kraken and STAMPEDE2. UT computer scientists at NICS are a part of it.

In order to grasp the power of a supercomputer, think of Neyland Stadium entirely filled with spectators. Even if each of these spectators had a computer on their knees, and if they were all working at the same time on the same task, it would still represent only about a fifth of the supercomputing power available to us.

With such computing power at our fingertips, we can address research questions and grand challenges within molecular and cellular biology that are far more complex and realistic than what was previously achievable. For instance, scientists led by BCMB Professor and Governor's Chair Jeremy Smith and BCMB faculty member Jerome Baudry have used Titan to virtually test tens of millions of drug candidates as potential agents for protein targets associated with a wide variety of diseases and human pathologies, and also, remarkably, to test for potential unwanted side effects of these compounds.

"The supercomputer Deep Thought in the *Hitchhiker's Guide to the Galaxy* was rumored to have predicted the existence of the baguette and the Archbishop of Lyon from the Big Bang in under a millisecond," Smith says. "Buoyed by that concept, the BCMB computational scientists have thrown themselves onto TITAN at ORNL, the nation's most powerful machine, which is capable of doing 19,000,000,000,000,000 (19 quadrillion) calculations a second. They use this monster to design drugs, understand bacterial membranes, and improve bioenergy. Predicting the genesis of the Archbishop of Lyon is on the list of future activities."

In addition to these applications, BCMB scientists are using the power of petascale computing in systems biology inquiries, which integrate large complex datasets to simulate, understand, and predict the behavior of entire cells, organisms, and populations.

These research opportunities provide unique and powerful training experiences for BCMB graduate and undergraduate students and have spearheaded the development of computation laboratories within the evolving BCMB curriculum. There are not many departments in the nation that can offer their seniors a class with a lab project on "Top-10 in the world" supercomputers. It is, to paraphrase one student's comment, like "using the Saturn V rocket to learn how to fly."

Willy Evangelista, PhD student, with the TITAN supercomputer at ORNL.

Fall 2017

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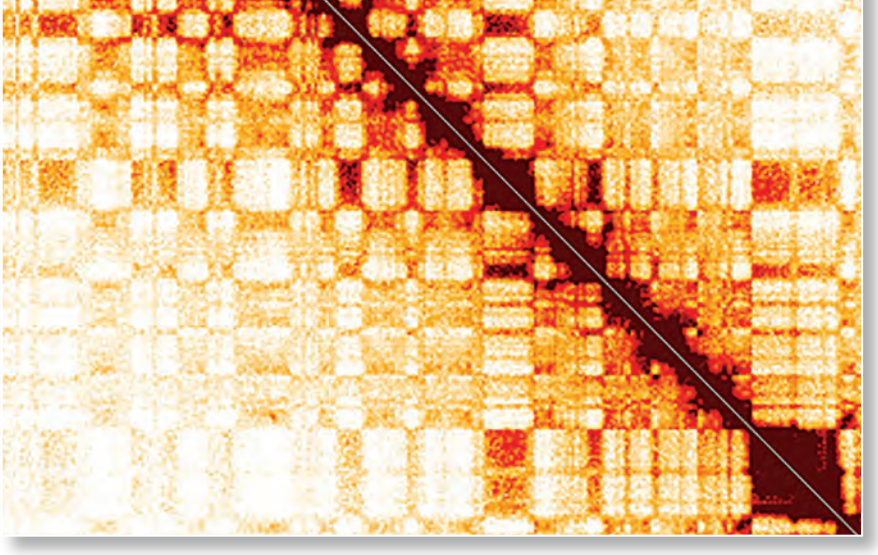


A *Diverse* & *Interdisciplinary* DEPARTMENT

DANIEL ROBERTS
Professor and
Department Head

As I enter my fifth year as department head and 31st year as a faculty member and research biochemist, I marvel at how diverse and interdisciplinary our field has become. In BCMB in particular, we have developed considerable strength at the interface between molecular and cellular biosciences and computational/mathematic approaches. In the new era of "Big Data," we have witnessed the emergence of "Systems Biology" that leverages large datasets of gene expression, proteomics, and metabolic information to understand and predict how molecule networks interact to give rise to emergent properties and behaviors of cells and organisms. These approaches take innovative collaborations between the physical and biological sciences, as well as robust and high-powered computational resources. In this edition of *Discoveries*, we feature how BCMB faculty are utilizing the high-powered supercomputing resources at ORNL.

In addition, we highlight one of our new talented faculty members, Rachel McCord, who uses systems biology approaches to construct 3-D models of genomes associated with normal and disease states (image above). While we celebrate our departmental growth and evolution, we also honor and recognize the pioneers of the early biochemistry department without whom BCMB would not exist. In this edition, we highlight one of our first PhD graduate alumni, Bill Albritton, as well as his work in assisting us with ongoing efforts to provide recognition and awards for our very best graduate students. I hope you enjoy reading these, as well as our other highlights of outstanding BCMB graduate and undergraduate students!

Focusing on the Neurological Pathways

Growing up, Ronald Dean Franz learned a lot about how the human body worked from his dad, who was an ER physician.

"He always emphasized how amazing the human body was and explained to me how the body worked together in perfect homeostasis," Dean says. "Ever since then, I have taken it upon myself to learn as much as I can about how all life functions on this planet."

Over the past six months, Dean has worked in Keerthi Krishnan's lab researching the neurological pathway that is altered in individuals with Rett's Syndrome in hopes of expanding the research to all different types of autism. He has contributed to our understanding of perineuronal net formation after behavioral experience using whole brain microscopy. This work is important for laying the groundwork on mapping these structures in the whole brain and then determining how they are misregulated in neurodevelopmental disorders.

> "While going through images for perineuronal net analysis, Dean found a special region of interest for our study," Krishnan says. "We wouldn't have thought to look for this region. Now we are planning on focusing on this region, and Dean will lead that study."

For Dean, the most exciting part of being in the lab was to learn how to perform a variety of different lab techniques and procedures. Conducting research has also been a valuable learning experience for Dean, who wants to pursue a career in medicine.

"While this is not the clinical side of medicine, research plays a very important role in medicine," Dean says. "Research is how new drugs, techniques, and procedures are discovered every single day. This insight will one day help me with my medical career because of my general understanding on how the scientific process works."

Growth in Newborn Cells

Julie Rich joined the lab of Maitreyi Das as an undergraduate student researcher and published an honors thesis on describing the basic principles of cell polarity establishment. Julie expressed her interest in pursuing a PhD degree in biology, and Das was so impressed with her acumen for science and her strong critical thinking skills that she encouraged Julie to join the graduate program in BCMB.

"My interest in biology was sparked by my high school AP biology class," Julie says. "It was my first-in-depth exposure to complex biological topics."

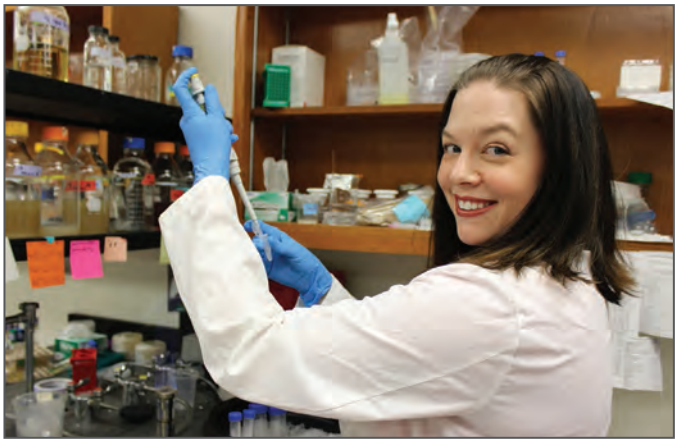
In the Das lab, Julie has initiated a novel line of research where she is exploring the signaling mechanisms that allow a cell to resume growth at the end of division.

"My research aims to explain how a cell achieve its shape," Julie says. "A cell's function often depends on its shape. Cells come in many different shapes, providing some difficulty in teasing apart the mechanisms governing establishment of cell shape via polarized growth. Our research is helping to establish the basic principles of Cdc42 regulation in relation to cell polarity, which are applicable to higher eukaryotes."

Julie was awarded a prestigious graduate research fellowship by the National Science Foundation to pursue her research. Das is very confident that Julie will be very successful in her endeavor and is excited to see where her research takes her in the future.

"For me, the value in conducting research has been in learning how to ask good scientific questions," Julie says. "I have also learned that gathering relevant data and communicating findings effectively are critical elements of putting together a convincing scientific story."

Fighting Infectious Diseases



A native of Texas, **Jessica Gullett** graduates with her PhD in fall 2017 and will do her postdoc work at St. Jude Children's Research Hospital in the Department of Infectious Diseases.

Growing up, Jess was the model literary student, always excelling in English classes, but not really enjoying any of her science classes. Getting a PhD in a scientific discipline was not on her radar. A chance opportunity to participate in an undergraduate research project led her to discover she enjoyed the power of scientific inquiry and especially how experimental design can lead to often unexpected yet insightful answers.

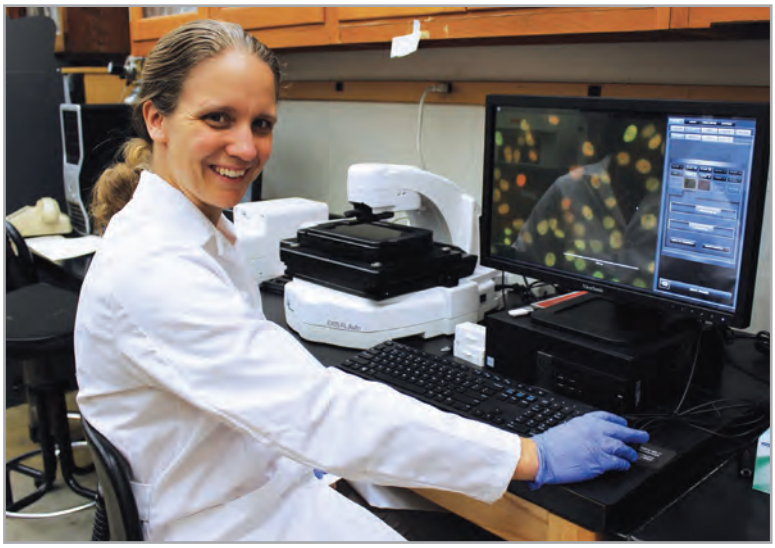
Her work focuses on deciphering how bacteria monitor their surroundings, including the characterization of a universal membrane protein that could represent a novel antimicrobial target. Bacterial antibiotic resistance is a growing global health concern because an increasing number of pathogenic bacterial strains have developed resistance to antibiotics, making treatment more invasive and costlier for patients. Various clinically relevant antibiotics used to treat pathogenic bacteria specifically target bacterial membranes.

Membranes, which form barriers between the inside of the cells and the outside environment, are essential to cell viability. Jess identified a protein that contributes to the cell's ability to modulate its membrane's permeability to various molecules and chemical agents. Because of its role in bacterial membrane permeability, this protein could be a potential drug target to aid efforts in the fight against antibiotic resistant "superbugs."

Jess views her scientific contribution as a puzzle where each scientific discovery contributes a piece, of various size, to a big puzzle.

"Usually the answer you find leads to the next exciting question," Jess says.

Folding Genes for Tight Spaces



Rachel McCord's interest in science is in her genes. She learned how to be curious about the natural world and how it works from her parents, who were both scientists.

"I always loved puzzles and solving problems," says Rachel, a new assistant professor in the department. "Some of my favorite TV shows growing up were math and science PBS shows like "Newton's Apple" and "Square One." I loved other classes like literature, history, and music, but during my time at Davidson College it became clear that I wanted science to be my main focus while continuing other interests in the background."

The problem Rachel faced, however, was what kind of science she wanted to pursue. When explaining this dilemma to her advisor, he opened her eyes to the field of biophysics. With this revelation, Rachel designed her own major in biophysics through the Center for Interdisciplinary Studies at Davidson and work with both biology and physics advisors.

"I had the opportunity to build optical tweezers and use them to trap swimming single celled algae called *Chlamydomonas*," Rachel says. "This amazing independent research experience as an undergraduate has continued to influence my desire to involve undergraduates in meaningful research. It also showed me how asking one question in biology can lead to another and another seemingly endlessly, which convinced me that I wanted to keep pursuing this kind of science research in graduate school."

Rachel went on to earn a PhD in biophysics from Harvard University and was a postdoc in systems biology at the University of Massachusetts before joining the BCMB faculty. In her lab, Rachel has continued her research in 3-D genomic structures.

> "We start by considering the basic problem that the six-foot long human DNA sequence must fold into a microscopic space, and this compact folding must still allow it to do its basic functions of regulating genes at the right time, replicating itself before cell division, and repairing itself after damage," Rachel says.

"We are then investigating how this 3-D genome folding is affected by stress on the nucleus caused by X-ray irradiation, or when the nucleus has to squeeze through tight spaces."

Rachel involves both undergraduate and graduate students in her research and hopes to provide them with confidence in interpreting, critiquing, and using the vast array of new tools available.

"There are so many analysis tools available now that it is more important that students learn how to ask the right questions than it is for them to know how to write a computer program," Rachel says. "Now that there is such a flood of biological data coming from these kinds of techniques, I also want the students to learn to think critically about how to interpret these data, and what kinds of pitfalls you can run into during research."

Rachel is excited about returning to Knoxville and the UT community where her parents began her quest for scientific discovery many years ago.

"I love the diversity of research going on at UT," Rachel says. "Even within BCMB, I have learned so much about fascinating areas of biology outside my own focus."

Founders Give Back with New Endowment

BCMB had its genesis at UT in 1963 as the biochemistry department. Prior to 1963, the chemistry department offered one biochemistry class, available to graduate students or advanced undergraduates. When the biochemistry department opened in 1963, it brought together an initial faculty of four with diverse scientific backgrounds under the leadership of the first department head, Ken Monty. BCMB was formed in 1995 when the biochemistry department was combined with cell biologists and geneticists of the zoology department. In 2017, BCMB has grown into a vibrant multidisciplinary department with 26 tenure line faculty, 58 graduate students, and 400 undergraduate majors.

In 2011, a group of the original biochemistry departmental alumni returned to UT for a reunion to revisit and celebrate their careers, and to share in BCMB's success that would not have been possible without their early efforts. Among these alumni was **Bill Albritton**, a distinguished PhD graduate of the program ('68). Bill received his undergraduate education at the University of Alabama, and first became familiar with the Knoxville area and university through a summer program offered by the Oak Ridge National Laboratory. There he decided to attend graduate school at UT in the nascent Department of Biochemistry and carry out his dissertation research under the guidance of one of the founding biochemistry faculty, Al Levin.

After obtaining his PhD from UT in 1968, Bill went on to earn an MD from the Medical College of Alabama in 1970 on an American Cancer Society fellowship. Following a pediatric residency at Stanford and two years with the CDC in Atlanta, he immigrated to Canada in 1975, where he joined the faculty of the University of Manitoba in Winnipeg. He has had a distinguished career in public and private medicine in Canada and the United States and served as the dean of the College of Medicine at the University of Saskatchewan before his retirement last year.

While attending the 2011 reunion, the attendees came up with a creative idea to "give back" to the department that they pioneered.

"We had a reunion that Ken Monty set up back in 2011, and when we were talking about it, we thought maybe if we created the fund we would allow people to donate to it in the name of anybody that they wanted to – it wouldn't be just Al Levin's students or colleagues, it could be open to the entire department," Bill says.

The result was the creation of the Biochemistry Alumni Graduate Assistant Award Endowment. Through their generous gift, the department recognizes one outstanding PhD student based on excellence both in teaching and research scholarship with the Biochemistry Alumni Graduate Assistant Award and $1,000. (Note, last year's winner Jessica Gullet is featured in this year's newsletter).

Ken Monty provided oversight of this endowment in the name of the early biochemistry alumni until his untimely passing in 2016. Bill, who is a strong supporter of this fund, has graciously agreed to take up the mantle where Ken left off and will spearhead the effort to engage alumni and others to continue to raise support for this critical effort to attract and retain deserving graduate students.

"For me it was a way of acknowledging my mentor Al Levin. You kind of think when you first graduate that you don't have to thank people for what they did for you," Bill says. "It was a way for me to say thank you. When it was first created, the department did not have an undergraduate program; it was only a graduate department. I think focusing on graduate student support was a logical outcome of what we were trying to do with the fund."

As he looks back on his career and time at UT, he has one piece of advice for current graduate students.

"Find your passion in life – hopefully it's in science – and pursue that passion," Bill says. "Keep that sense of inquiry; that sense of yearning to discover."

If you are interested in donating to the **Biochemistry Alumni Graduate Assistant Award Endowment,** please contact **Don Eisenberg at 865-770-1913** or by email at **BCMBalumni@utk.edu**.

A POPULAR MAJOR

BIOCHEMISTRY & CELLULAR AND MOLECULAR BIOLOGY

BCMB remains the home of the most popular undergraduate major in the natural sciences with 142 students (38 percent of all natural science majors in the college) receiving their BS in the 2016 academic year.

More than 60 undergraduate students each semester participated in research in BCMB labs. Twenty-two undergraduate students from the BCMB department participated in the 21st Exhibition of Undergraduate Research and Creative Achievement (EUReCA) that took place April 17-21, 2017. Congratulations to Gold and Silver Undergraduate Research Excellence Awards winners Jeremiah Holt (Albrecht VonArnim, mentor) Emily Miller (Elena Shpak, mentor), and Madeline Davis (Andreas Nebenfuehr, mentor). Jeremiah Holt, Emily Miller, and Avery Sukienik (Andreas Nebenfuehr, mentor) were College of Art and Sciences winners with the first place in Cellular and Molecular Biology category.

MOVING ON

Congratulations to the following PhD and MS graduates in 2016!

PhD Graduates:
Kristen Holbrook, postdoc with Sabeeha Merchant, UCLA
Randy Lacey, postdoc fellowship at Sandia National Labs
Meng Li, postdoc with Helmut Kirchhoff at Washington University
Sudershana Nair, postdoc with Nicholas Baker, Albert Einstein College of Medicine
Khoa Nguyen, postdoc, Environmental Protection Agency
Letitia Puster, adjunct instructor of chemistry, Maryville College
Yufei Yue, The Medicines Company

Master's Graduate: **Tiffany Thomas**

Faculty and Student Achievements

Last year BCMB faculty received seven big grants from NIH, NSF, and Intel Corporation.

Elias Fernandez received an NIH grant for "Role of Allostery in CAR Transactivation." **Fran Barrera** is a co-PI on a grant from NIH for "Labeling of Lipid Products Using Synthetic Tagged Metabolite Probes to Analyze Lipid Biosynthesis and Trafficking." **Jeremy Smith** received a grant from Intel Corporation for "Porting and Optimization of the General Purpose Molecular Dynamics Code GROMACS on Next Generation Intel Based Computers."

The grants from NSF include grants to **Andreas Nebenfuehr** for "Mechanisms of Cytoplasmic Streaming," **Gladys Alexandre** for "Chemotaxis sensing preference in plant-microbe associations," **Brad Binder** for "Ethylene Signaling and Transcriptional Networks that Control Root Development." **Jeremy Smith** received a grant to organize a workshop titled "Progress and Prospects for Neutron Scattering in the Biological Sciences."

Zach Beamer, a graduate student in Dan Roberts' lab, received a Department of Energy Office of Science Graduate Student Research (SCGSR) award to study the functional basis of transport selectivity by nodulin 26 intrinsic protein.

Julie Rich, a graduate student in Maitreyi Das Lab received an NSF Graduate Research Fellowship Program (GRFP) award to study the signaling mechanisms that allow a cell to resume growth at the end of division.

To see more faculty accolades and notable publications visit **bcmb.utk.edu**.

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Department of Biochemistry & Cellular and Molecular Biology
M407 Walters Life Sciences
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The University of Tennessee
Knoxville, TN 37996-0840

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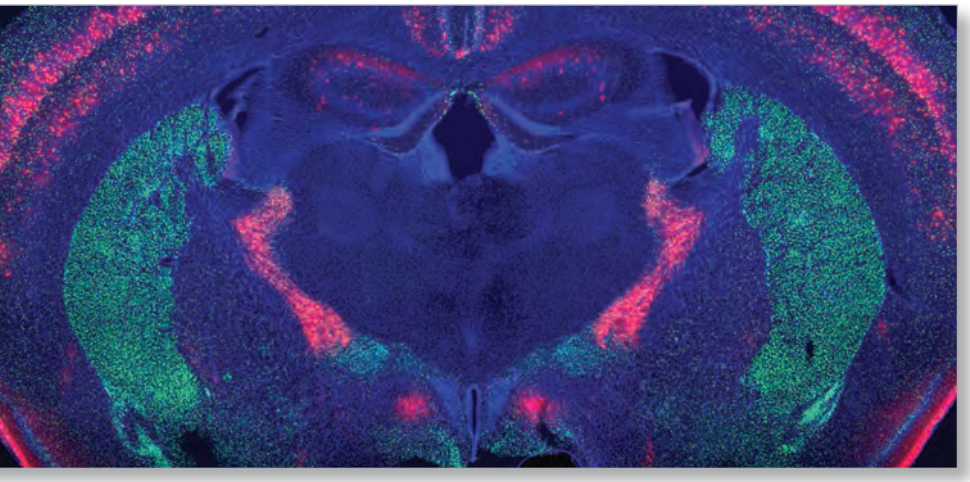

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Neurological Pathways

Dean Franz is researching the neurological pathway that is altered in individuals with Rett's Syndrome in hopes of expanding the research to all different types of autism. He has contributed to our understanding of perineuronal net formation after behavioral experience using whole brain microscopy.

Your gifts make a difference!

Over the years, we have been fortunate to receive generous donations from a variety of supporters, including former graduates. These gifts have made it possible for us to offer undergraduate and graduate scholarships. Other donations have been used for Research Incentive Awards to faculty who propose pilot projects that promise to lead to extramural grant funding from national agencies. Our generous donors have made all of these things possible.

To contribute online, please visit:
bcmb.utk.edu/support-the-department and click on **"Give to UT."**

DISCOVERIES

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Department Head: **Daniel Roberts**
Associate Department Head: **Gladys Alexandre**
Phone: 865-974-5148 • Fax: 865-974-6306
E-mail: bcmb@utk.edu • Web: bcmb.utk.edu