Biological Modeling Specialty Section Newsletter

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President's message

Welcome to the BMSS newsletter. First, I would like to introduce you to the officers whose names are located on the right-hand side of this page and pictures can be found on the last page. We have been working to increase student/postdoctoral involvement in BMSS. Read about the new Best Trainee-Abstract Award in this newsletter. We have updated our website with the expert help of Dr. Nan-Hung Hsieh, a postdoctoral fellow at Texas A&M. We thank Nan-Hung for his service to BMSS and bringing our website into the 21st Century. This newsletter contains personal stories from BMSS members. This idea was suggested by Dr. Pankajini Mallick from ScitoVation. Pankajini also helped to create this newsletter along with the talented Dr. Miyoung Yoon, our Vice President-Elect, from ToxStrategies. We thank Pankajini for her service. Many thanks to those who were brave and told their story!

We have one more volunteer, Dr. Patricia Ruiz, from the Agency for Toxic Substances and Disease Registry, who has agreed to be our endowment fund steward and will work with our new Treasurer, Tammie Covington, from Henry M. Jackson Foundation for the Advancement of Military Medicine. You may hear from us later in the year.

Thank you all of your participation and continued support of our specialty section.

Jeff Fisher

BMSS President

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Interested in joining BMSS?

Apply today!

Newly Launched BMSS Best Trainee Abstract Award

Would you like to make your research highlighted and got attention from your peer toxicologists? Would you like to get connections and collaborations with biological modelers? A best trainee abstract award, newly launched this year by the Biological Modeling Specialty Section (BMSS), will be your choice. This award only focuses on highlighting trainees' research. Besides the best abstract awards, a list of selected top trainee abstracts will also be highlighted and honored.

In order to emphasize the postdoctoral and graduate trainees' research, this brand new award will be available for the coming SOT meeting in Baltimore. All SOT graduate and postgraduate members are eligible to apply. Besides selections by the award committee, trainees can also nominate themselves by sending a copy of the submitted abstract via email to Miyoung Yoon. The BMSS best trainee abstract award is emphasized but not limited to biologically-based computational modeling research. All relevant experimental and computational research aimed to contribute to the fields of biological modeling, risk assessment, and improve our knowledge for toxicological mechanisms are eligible for this award.

The Best Abstract Award Committee will be composed of BMSS member volunteers and led by the BMSS Vice President. The candidate abstracts will be judged based on innovation, quality of modeling, potential or realized impact on the field, utility in toxicology/risk assessment, and other criteria deemed important to the Committee. BMSS will present the Best Trainee Abstract Award and all other selected top abstract awards to the lead author at the BMSS Business Meeting and Reception during the SOT Annual Meeting.

For other awards offered by BMSS, please send us email at Miyoung Yoon or Brad Reisfeld, or refer to the link below:

LEARN MORE

Stories from BMSS members

Miao Li, PhD

Postdoctoral Fellow, Kansas State University

Nobody is an outsider in BMSS

How can I be a biological modeler? Is it possible for me to find a training position in the biological modeling area with limited experiences? These were the questions that always bothered me before I joined BMSS.

I have my bachelor's degree in pharmaceutics, so the terms of QSAR, PK and PKPD modeling are not strange to me. But I did not realize modeling is also well used in toxicology, until the final stage of my PhD journey….(continue on Page 4)

Marc Verner, PhD

Assistant professor, University of Montréal

It all started in my third year of elementary school

It all started in my third year of elementary school when I won a math contest called Mathemathlon. I thought it would be smooth sailing from there. Oh boy, was I wrong!

College. That's where my love affair with math wore off. Would you believe that I failed my integrals class? Yes, that thing PBPK modelers use all of the time….(continue on Page 5)

Christopher D. Ruark, PhD

Scientist/Toxicologist, Procter and Gamble Company

Be open to new ideas, push yourself into challenging situations, collaborate with others and build relationships.

"Deciding where to focus my career and where to go for my education after high school probably drove my parents crazy. I recall having interests in architecture, engineering, chemistry, biology and even medicine." …….Finally after careful consideration (or so I'd like to think), I settled on….(continue on Page 6)

Anne E. Loccisano, PhD, DABT

Senior Scientist/Toxicologist at Exponent, Inc

I still don't know what I want to "be," but I do know that I love what I do.

I had no idea what I wanted to do when I started my undergraduate education. My father told me to major in something practical; that was the guidance I had. I had always liked my biology, chemistry, and calculus courses in high school, so I focused on taking those classes during my freshman year. When it came time to declare a major during my sophomore year, I had all the credits needed to major in…(continue on Page 7)

Nobody is an outsider in BMSS (continued from page 3)…

By talking with Dr. Babasaheb Sonawane, I learned the application of PBPK modeling in toxicological risk assessment in EPA IRIS. With the support from SOT STEP award, I got training in risk assessment from TERA "Dose Response Assessment Boot Camp." The training made me more interested in biological modeling, and more into using mechanistic research data for making public policies.

As I had my heart all into the field of biological modeling, I was so eager to find a training position in this area. However, with no experiences I always considered myself as an outsider in biological modeling. Two questions in the first paragraph bothered me when I tried to get training in this field, and I even had nobody to ask. During 2015 SOT meeting, I talked with Dr. Harvey Clewell at the RASS trainee luncheon. He told me I should get more involved in BMSS and know people working in the area first, and generously invited me to the BMSS mentoring luncheon and reception. I thought I must feel awkward for attending these activities as barely knowing anyone in BMSS. However, all those BMSS activities were like family get-togethers to me. People were all friendly and extremely nice to the young generation and new faces as me, just as taking care of the young kids in the family. I talked with senior members about my interests in biological modeling. They not only gave me suggestions but also remembered me and forwarded me training opportunities. I started to get interviews for the postdoctoral training positions in biological modeling.

During the 2016 Annual Meeting, I had more chances to talk with PIs who had openings or potential openings during BMSS activities. I met and talked with Dr. Zhoumeng Lin during the BMSS trainee luncheon. Couple weeks after the Annual Meeting, I got the job post sent by Dr. Lin. The thing impressed and moved me most is Dr. Cecilia Tan, Dr. Annie Lumen, and some other BMSS members also forwarded me this opportunity. As a BMSS family member, I have never been forgotten. I started my postdoctoral position focusing on the PBPK modeling of veterinary medicines in Dr. Lin's lab later 2016. Co-mentored by Dr. Jim Riviere and Dr. Ronette Gehring, now I can proudly say I'm a biological modeler. This is the end of my current story, but the beginning of my career as a biological modeler.

My words are too limited to express my appreciation to all help and support from BMSS, and I have no chance to list everyone helped me before. Once I was an outsider for biological modeling, but I have never been an outsider for BMSS. Everyone is welcomed to join BMSS as nobody was born as a modeler.

by Miao Li, PhD

Postdoctoral fellow, Kansas State University

It all started in my third year of elementary school

(continued from page 3)…

Anyhow, biology sparked an interest in me and I decided to do a bachelor degree in this field. The program had a two-year general program during which we would learn anything from optimal foraging in wolves to C4 photosynthesis, followed by a third year in either biotechnology, ecology, or toxicology. Throughout the first two years, I was determined to do my third year in ecology. However, during the Summer before my third year, I was trekking in the Canadian Rockies, and did not feel like coming back on time to start the Fall semester in ecology which started a few weeks before the two other options. So I called the University and asked to be registered in toxicology instead. That's right, toxicology, you got the gold medal because ecology failed its drug test.

I wasn't sure about pursuing graduate studies, but I saw an ad about a Master's project on metabolic interactions between drugs and environmental chemicals, and decided to apply. This is how I ended up in Sami Haddad's laboratory. Sami had just started as a Professor, and the lab was this wide open space with two test tubes and a desktop computer… while we were waiting for the material to arrive, Sami suggested I start working on a project he and Michel Charbonneau had been discussing for a while, and that they secretly called Epi-Bashing. Basically, that project entailed building a lifetime PBPK model of exposure to persistent organic pollutants in women to show that retrospective case-control studies of PCBs and breast cancer had important exposure misclassification. This project made it clear that PBPK modeling could be a valuable tool in environmental epidemiology, and decided to do a PhD on that subject.

At the end of my PhD, I flew across the pond to do a postdoctoral training with Gunnar Johanson where I worked on using PBPK models for exposure assessment in the occupational setting. After a year of PBPK modeling between crayfish parties and rotten fish challenges, I crossed the pond again to do a second postdoctoral training with Susan Korrick on early-life exposure to PCBs and neurodevelopment in a contaminated area. While I enjoyed learning about confounding factors, section bias and the wide variety of IPAs at the Sunset Grill and Tap, it was time for me to go back to Montreal and start a career/family.

Back home, I worked for a year as a consultant on a project on PBPK modeling to quantify bias assessment in epidemiologic studies. However, I was determined to get back to academia, and got a salary grant to work at the Department of Occupational and Environmental Health (Université de Montréal). So here I am, fourth year into my academic career, with my own laboratory and team of graduate students. **The path leading me here was winding, but it's all these little detours that made it fun and convinced me to keep coding my way forward.**

by Marc Verner, PhD

Assistant professor, University of Montréal

Be open to new ideas, push yourself into challenging situations, collaborate with others and build relationships. (continued from page 3)…

chemistry as my degree of choice. After my first day of undergraduate I switched my major to Biochemistry (a two for one deal!). I graduated from Miami University (Oxford, OH) with a major in Biochemistry and a minor in Molecular Biology. I worked in the laboratory of Dr. Christopher A. Makaroff as an undergraduate student where I learned to utilize RNA interference (RNAi) as a tool to study the proteins involved in chromosome adhesion within the plant Arabidopsis thaliana. Using RNAi, my goals were to knock out the genes involved in chromosome adhesion so that we could elucidate the roles of these proteins in meiosis. During my undergraduate studies I became fascinated with pharmacology and the way chemicals interact with the human body. I credit an elective pharmacology course with enlightening me to this passion.

Upon graduation, I pursued this passion and was employed at Wright Patterson Air Force Base (WPAFB) as a contractor with The Henry M. Jackson Foundation for the Advancement of Military Medicine (HJF) under the direction of Dr. Jeffery Gearhart. My role as a contractor was to develop Quantitative Structure-Activity Relationship (QSAR) and Physiologically-Based Pharmacokinetic (PBPK) models for chemicals relevant to the Department of Defense. Here is where I first learned of the toxicology field, and more specifically, computational toxicology. I remember Dr. Gearhart joking with me about my first few weeks on the job: "Where is my pipette?" I would ask. Of course, my computer became my pipette!

After a year on the job I began attending Wright State University (Dayton, OH) in pursuit of a Master's degree in Pharmacology and Toxicology. Dr. Gearhart encouraged me to pursue a PhD at the same university and 8 years after starting work at WPAFB, a marriage to my wife and the birth of our first child, I graduated with a PhD in Biomedical Sciences. My PhD was full of challenges and opportunities and I credit much of the knowledge I have today to the employees that I worked with on a daily basis. I learned everything from how to program a PBPK model in acslX and MatLab to discovering new modeling techniques such as agent based modeling, to figuring out what each organ should be colored in a PBPK model diagram for publication. I developed QSAR models for predicting acetylcholinesterase inhibition, physio-chemical models for predicting partition coefficients, PBPK models for oximes and even spent time in a wet laboratory developing high throughput in vitro screening assays and protein purification strategies for guinea pig acetylcholinesterase.

Upon graduation I left WPAFB for The Hamner Institute for Health Sciences in North Carolina to work with Drs. Miyoung Yoon and Matthew Longnecker on a PBPK PFOA and PFOS reverse causality project as well as to learn about the importance and future direction of *in vitro* to *in vivo* extrapolation (IVIVE) in the field of Toxicology. (continue on the next page)

Be open to new ideas, push yourself into challenging situations, collaborate with others and build relationships. (continued from page 6)…

At this point, my family had grown by one with the birth of our daughter, I became the BMSS post-doctoral representative and also helped to initiate a webinar series on behalf of the BMSS. Miyoung, Matt, Mel Andersen, Harvey Clewell and the rest of the Hamner staff taught me about life-stage PBPK models whereby an individual's exposure could be calculated from early childhood, through adolescence and into adulthood. I was also a part of The Hamner's transition to ScitoVation, a wholly owned subsidiary of SciMetrika.

My postdoc experience next led me to the Procter & Gamble Company, back to my home town of Cincinnati, OH and to the addition of our third child to the family. I am now a toxicologist in our Fabric Care business, providing global toxicology and safety support to a number of multi-billion dollar brands. I am an active member of our Pharmacokinetic expert team, currently led by Dr. Corie Ellison. These opportunities have shown me the importance of people in our lives, in how they shape you as an individual, in both your personal character and in your career. Here at P&G I see firsthand the importance of our biological modeling expertise. As you complete your education and move into your career, be open to new ideas, push yourself into challenging situations, collaborate with others and build relationships. One of the great future challenges I envision for this field will be obtaining regulatory acceptance and properly validating PBPK models developed in the absence of *in vivo* data. I have full faith that the current and future generation of modelers will be up for the challenge.

by Christopher D. Ruark, PhD

Scientist/Toxicologist, Procter and Gamble Company

I still don't know what I want to "be", but I do know that I love what I do. (continued from page 3)…

chemistry (and graduate in 4 years), so that was what I did. While I liked organic chemistry on paper (i.e., all those reverse synthesis exercises), I quickly found out that I had no patience for synthesis in the lab during my undergraduate research experience. I'd go through all the steps to make something, work it up, do the GC-MS, all to find out I had starting material. The lab was not for me.

I graduated in 2001 with a major in chemistry and double minor in German and psychology from Allegheny College in Meadville, PA. I did not feel prepared to actually get a job, so I thought graduate school would be a good idea. I had absolutely no idea what I wanted to do and I didn't have much guidance on choosing a graduate program; I thought because my bachelor's degree was in chemistry that I had to enter a graduate program for chemistry. I started graduate school in the fall of 2001 at Duquesne University in Pittsburgh, PA. As I had no patience for the lab, computational chemistry was the area I chose. I felt a lot more comfortable with the computer than expensive laboratory equipment (it's a lot harder to break a computer), and I learned how to code, set up and run quantum mechanical and molecular dynamics simulations, and also how data from laboratory experiments could feed into computational studies and vice versa. My graduate work involved the use of molecular dynamics simulations to examine the effects of drug binding on DNA and various proteins, including retinoid-binding proteins, myoglobin, and hemoglobin. I graduated in 2007 with a PhD in physical chemistry and again, had absolutely no idea what I wanted to do. All I knew was that a career in academics was not for me. I'm sure a pattern is becoming evident here—I have no idea what I'm doing so I just do whatever seems like a good idea at the time, and it just happens to work out.

After I defended my dissertation, I was exhausted. I took about 4 months off before looking for a postdoc. I applied to anything and everything—fellowships, postdocs, and even academic positions. I went to one interview for an academic postdoc, which confirmed that academics would not work for me. I was also looking to leave Pittsburgh as I grew up there and was tired of cold weather. In my searching, I discovered the Hamner Institute. I had never heard of Hamner, I knew nothing about toxicology or risk assessment at that point, and although I knew a lot about computational models in the chemistry arena, I had never even heard of pharmacokinetic or dose-response models. I went for an interview, and few months later, I moved to Durham, NC and started my postdoc at the Hamner. And that's where my career really started.

At the Hamner, I worked with Drs. Harvey Clewell and Melvin Andersen to develop physiologically-based pharmacokinetic (PBPK) models for perfluorinated compounds (perfluorooctanoic acid; PFOA and perfluorooctane sulfonate; PFOS). I learned everything from how to code in acslX to principles of toxicology and risk assessment, and about the utility of pharmacokinetics and PBPK models in risk assessment. I don't think I can express how much I loved doing my postdoc. I worked with great people, figured out that I liked toxicology and biology a lot more than chemistry, and most important, I found something that I was really interested in. (continue on the next page)

I still don't know what I want to "be", but I do know that I love what I do. (continued from page 8)…

During my 3 years at Hamner, I developed PBPK models for PFOA and PFOS in the rat, monkey, and human, which I extended to describe PK during pregnancy and lactation. When my contract was up, something was different—I actually found an area I wanted to work in—career decisions based on something logical could be made.

After Hamner, I did an ORISE fellowship in the USEPA IRIS program in Arlington, VA. While at US EPA, I worked on chemical assessment teams for various chemicals. I did PBPK work but I also evaluated toxicological data and learned about EPA guidelines and policies and how the EPA does risk assessment. At this point, I considered myself a toxicologist and no longer a chemist. Although I liked the EPA, about a year into my fellowship, I figured I better find a more permanent position or people were going to be asking why I kept running around doing postdocs.

In November 2012, I went to Reynolds American Incorporated in Winston-Salem, NC and worked in the product integrity group. At RAI, I performed risk and exposure assessments on consumer products and learned about FDA regulations as well as learned how to work with other scientists in R&D, including engineers and chemists. I mention this as this experience truly taught me the importance of good communication! I also obtained my board certification while at RAI (Diplomate of the American Board of Toxicology; DABT). After three years at RAI, I was ready to move on. I liked working there, but I needed a change (and I wanted to move out of Winston).

I liked the variety that consulting offered; I came to Exponent in 2015, where I am a senior toxicologist. My work ranges anywhere from assisting clients with regulatory support to working with attorneys for litigation support. The diverse projects I work on not only allow me to use my expertise in pharmacokinetics/PBPK modeling and risk assessment but I have gained knowledge with specific chemical classes, regulatory guidelines, and also about serving as an expert witness. The modeling work I perform has allowed me to see how important our expertise is to anything from regulatory submissions to litigation matters. Every project challenges me to think about a problem from a different perspective or how to expand my thinking about the problem. I never thought I'd get paid to do such interesting work.

As you move through your education and career, realize that you don't always have to have some specific path or end goal in mind. Do what seems right for you at the time and it will all work itself out. At this point, I still don't know what I want to "be", but I do know that I love what I do. Be open to taking on challenges, get out of what you're familiar and comfortable with, and know that you will be constantly learning. I always wonder what I'm getting myself into and it always turns to be not only a learning experience but I am amazed at what I can do—you're a lot stronger than you think you are.

by Anne E. Loccisano, PhD, DABT

Senior Scientist/Toxicologist at Exponent, Inc

Other BMSS Announcement!

We are co-sponsoring a webinar with Risk Assessment Specialty Section (RASS) on December 12, 2018. Stay tuned for more details!

In vitro to *in vivo* extrapolation (IVIVE) to support new approach methods (NAMs)-based safety assessment –
A tiered approach with a focus on the consideration of kinetics and metabolism

Miyoung Yoon, PhD
Managing Scientist
The Center of Excellence for 21st Century Toxicology, A Division of ToxStrategies, Inc.

We are looking for volunteers who are willing to contribute to selecting the paper of the year for BMSS Best Paper Award!

Please contact Brad Reisfeld if you are interested in becoming a review team.

Meet our 2018-2019 officers!

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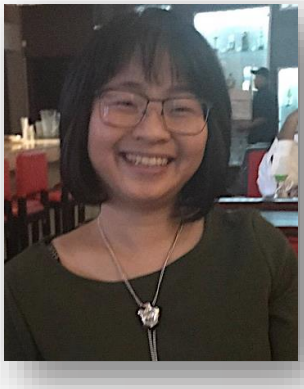
Jeffrey W. Fisher

Vice President
Brad Reisfeld



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