Message From the President

By Justin Wilkins

I was going to start this column with “It’s been a very busy couple of months for ISoP”, but I just realized that that’s exactly what I wrote last time. That, of course, doesn’t make it any less true...

ACoP10 is full, having reached maximum capacity just a few days into August, barely after the Early Bird registration period had ended. This is a spectacular success and bodes very well for ACoP’s diamond anniversary! Congratulations to our Conference Chair, Mirjam Trame, and our pre-conference co-chairs, Navin Goyal and Liz Lakota, for what is looking like a program worthy of the occasion. I’m delighted that so many of you will be there; our 2019 theme, “Modeling Without Borders”, has clearly struck a chord.

As you read this, voting will have opened to select two new ISoP Board members, whose terms will begin on 1 January 2020. Members of the Board of Directors are elected for three years, and are responsible for overseeing the Society’s activities, administration and finances; members of the Executive Committee (the President, the President Elect, the Secretary, the Treasurer, and the Past President) are nominated and elected from the ranks of the Board. We had a tremendous slate of nominees this year – an embarrassment of riches – and we are very excited to find out who you’ll choose. We are proud that so many supremely capable candidates are willing to contribute their time and energy to serve our Society and our community by running for election to the Board. It’s fun, but it’s a lot of work, too.

Our Five-Year Strategic Plan is now well underway. The Working Groups have been very active, and I look forward to seeing where their leadership will take us over the next four and a half years. As a reminder of who our six Working Groups are, and what they’re doing, a brief summary: Scientific Expertise and Innovation, led by Five-Year Strategy originator and Past President Jin Jin, will focus on encouraging research and innovation in pharmacometrics; Influence, led by Heather Vezina, will work on increasing the impact of pharmacometrics on decision-making during drug discovery, development and clinical practice; Education, led by President-Elect Brenda Cirincione, will improve the consistency, quality and availability of educational resources for pharmacometricians through every stage of their careers; Tools and Resources, led by myself, will facilitate development of and access to pharmacometric software tools, both open source and commercial and promote open science; Internationalization, led by Siv Jönsson, will work to expand ISoP’s outreach to pharmacometric community members across the globe; and Operational Effectiveness, led by Pete Bonate, will ensure ISoP has the resources and staff to support and implement the plan. It’s a big job, and we’re always looking for help: you can find more information at go-isop.org/five-year-strategic-plan/, and you can volunteer at go-isop.org/volunteer-application/ (or contact the Working Group chairs directly).

Volunteering to serve on Committees and Working Groups and joining SIGs, I’ll remind you, is a wonderful way to get more involved with ISoP, and to meet and get to know other ISoP members from around the world!

We’ve been up to a lot more than that: we provided a joint consensus feedback statement in response to the draft FDA Guidance for Population Pharmacokinetics at the beginning of September, a wonderfully collaborative experience to which many of our members from industry and academia contributed, and the regional QSP Day held in New Jersey on July 16 and the ISoP New England-iPSP Symposium that took place in Boston on August 26 were both wonderful successes – congratulations to the organizers.

In closing, I’d like to remind everyone of the upcoming General Members’ Meeting, to be held as an online webinar at 12.00pm-13.30pm EST on September 18. It’s open to all our members and provides a way for us to tell you who we are, how we spend our money, recent and upcoming activities by the Society and its SIGs, Committees and Communities, and a range of other topics we think will be of interest. We’ll be recording the meeting and making it available online, and if enough of you are interested, we’ll be exploring holding a second later this year which will take place at a time better suited to our Eastern Hemisphere members. We intend to hold at least one every year. There’s more information at go-isop.org/general-members-meeting/, and you can register at zoom.us/webinar/register/WN_1ZMY3aflQKq7PBWBmDSCJg – we hope you’ll join us!
Registration is CLOSED for ACoP10 to be held October 20th to 23rd, 2019, at the Rosen Shingle Creek Hotel in Orlando, Florida!

ACoP10, being the largest ACoP to date, is promised to be a great meeting with exciting new events and features. You can find the most up-to-date information on our conference website and in our new conference app which will be live from mid-September, but here just a few highlights to pique your interest:

Main Conference (October 20th – 23rd, 2019 + free tutorials on October 24th, 2019): The main conference agenda is now available! 18 exceptional scientific sessions are lined up. We bet it will be difficult for you to choose between the parallel sessions. Main conference attendees can also register for free tutorials to be held on Thursday morning, October 24th. Please plan your travel accordingly and register ASAP – several tutorial sessions are already full and waitlisted. Multiple events throughout the entire main conference are specially designed and targeted towards our growing student and trainee community.

New this year is our Sponsored-Investigator-Session. We have invited three international speakers from low- and middle-income countries to share their research, goals, and their unique scientific perspective with us.

There will be ample opportunities to network with colleagues and friends, and all with late morning poster session start times (8AM)!

Stay tuned for details on our much-anticipated evening patio social event on Monday, October 21st, and remember to bring your dancing shoes!

Conference Abstracts:
We are excited about the many outstanding contributions we received! This year’s poster sessions are set up to be exceptional with many exciting cutting edge research. Soon all abstracts will be made available online on our conference website and in our conference app for the first time!
ACoP10 will offer two poster walks; one during the opening reception with special selected posters by the ACoP10 Abstract committee and one during the main conference to highlight and recognize outstanding scientific achievements in Mathematical and Computational Sciences (MCS).

Pre-conference (Sunday, October 20th, 2019): The Pre-Conference on, “Clinical Pharmacometrics: Bringing Models to Patients” will feature 4 exciting sessions presented by a diverse group of scientific experts from academia, research institutes, regulatory agencies, and pharmaceutical and technology industries. Presentations will focus on the application of pharmacometrics to direct patient care. The planned program is intended to bring together pharmacometricians with clinical interests and clinicians with an interest in pharmacometrics. Given the scope, this year’s Preconference has been developed in close collaboration with the Clinical Pharmacometrics Special Interest Group.

Pre- and Post-Conference Workshops (October 19th – 20th and 24th – 25th, 2019): ACoP10 provides many pre- and post-meeting workshops covering a range of topics for you to choose from. Space is limited and separate registration is required, so please be sure to secure your place at one or more training sessions.

3rd Annual ACoP Innovation in Communication Event: There is still time to register for our back by popular demand Innovation in Communication Event. There is no preparation needed this year! We are looking for 8 teams of 4-5 people to participate in a friendly competition with game show-like communication challenges! Our winning team will leave with bragging rights and a ‘fabulous’ trophy from your hostesses, Brenda Cirincione and Stacey Tannenbaum. A team can consist of students, university alums, company colleagues, or just a group of fun friends! Don’t have a team but are interested in participating? Register as an individual to be added to a team by the event organizers. Check out our ACoP10 conference website @ www.go-acop.org to register today!

Social Evening: We have planned a fun-filled evening. Enjoy a tasty dinner and drinks. DJ Matt will keep the party rocking through the night with eclectic dance music. The theme of the Social Event is “Masquerade and Costume Ball!” Attendees are encouraged to wear their favorite costume and mask. Don’t have a mask to wear? No problem! Many of our exhibitors will be giving away masks at their booths!

In addition, strike a pose with old new friends at the photo booth. NEW THIS YEAR- the ACoP10 Lip Sync Contest. Interested in showing off your lip sync skills? Email Mark Lovern, ACoP10 Social Event Chair (mark.lovern@certara.com), with the name of the song that you’ll be performing as well as the names of any co-performers.

We look forward to seeing you in Orlando!

Mirjam N. Trame, ACoP10 Conference Chair
On Behalf of the ACoP10 Planning Committee
ACoP10 QUALITY AWARD WINNERS

Yixuan Zou, Fei Tang, Chee M. Ng
Using Medical Claim Data and Modified Wald’s Approximated Covariate Selection Method to Develop a Population Disease Progression Model for Leuprorelin-treated Subjects with Hormone-sensitive Prostate Cancer

Fariba Khanshan, Alison Margolskee, Andy Stein, Yu-Yun Ho, Michael Looby
Exploratory Graphics (xGx): Promoting the purposeful exploration of PKPD data

Kyle Baron, Oliver Pohl, Matthew Riggs, Jonathan French, Jean-Pierre Gotteland, Ramon Garcia
Model-based Dose Selection for a GnRH Receptor Antagonist in Endometriosis and Uterine Fibroids (UF) to Reduce Symptoms While Preventing Lumbar Spine Bone Mineral Density (BMD) Loss

ACoP10 TRAINEE AWARD WINNERS

Freya Bachmann, Gilbert Koch, Marc Pfister, Johannes Schropp
OptiDose: Computing the optimal individual dosing regimen with constraints on model states to include side effects

Qunshu Zhang, James Travis, Rebecca Rothwell, Yaning Wang, Jian Wang
Developing Quantitative Methods to Compare Exposure-Response Relationships Between Pediatrics and Adults to Support Pediatric Extrapolation

Meera Varshneya, Xueyan Mei, Eric A Sobie
Combining Systems Pharmacology Modeling With Machine Learning Techniques To Identify Sub-Populations At Risk Of Drug-Induced Arrhythmias

ISoP QSP SIG STUDENT AWARD WINNER

Qingxiang Lin, Zhicheng Qian, Shichen Shen, William J. Jusko, Donald E. Mager, Wen Wee Ma, Jun Qu, Robert M. Straubinger
Mechanistic multi-scale models characterize drug synergism between BGJ398 and gemcitabine in pancreatic ductal adenocarcinoma

ISoP MCS SIG POSTER AWARD WINNER

Christopher Vincent Rackauckas, Vijay Ivaturi
Bayesian-Koopman Techniques for Optimization of Intervention With Respect to Uncertainty in PuMaS.jl

ISoP CLINICAL PHARMACOMETRICS SIG TRAINEE AWARD WINNER

Ly Minh Nguyen, Calvin Meaney, Mandip Panesar, and Wojciech Krzyzanski
An Adaptive Bayesian Method for the Development of Individualized Anemia Management Protocols in End-Stage Renal Disease Patients

ISoP SxP SIG STUDENT AWARD WINNER

Sihang Liu, Ziheng Cheng, Ziyi Yang, Alan Breier, Michael Francis, Robert Bies
Resolving Conflicting Results Arising from a Pharmacometric and a Statistical Analysis of the Cognitive Effects of a Selective Estrogen Receptor Beta Agonist (LY500307) in Schizophrenic Patients
ACOP10 Poster Walk

As an addition to our program this year, ACoP10 will offer two poster walk sessions during the main conference poster sessions to highlight and recognize significant and thought-provoking accomplishments in pharmacometrics and Mathematical Computational Sciences (MCS).

ACoP10 POSTER WALK PRESENTERS

Xiaomei Liu, Jeremiah Momper, Natella Rakhmanina, Tim R. Cressey, Mark Mirochnick, Brookie M. Best, John van den Anker, Dionna J. Green, Gilbert J. Burckart, Andr Dallmann
Application of physiologically based pharmacokinetic (PBPK) modeling to predict fetal exposure to dolutegravir

Linzhong Li, Dan Liu, Rachel Rose, Iain Gardner, Masoud Jamei
Mechanistic Modelling of Binding and Cell killing Events of Bispecific Antibodies in both in vitro Cytotoxicity Assay and within a PBPK Framework

Fiona Chandra, Andy Zhu
Optimizing Drug Antibody Ratio for Antibody Drug Conjugates Using a Mechanistic Model in Solid Tumor

Lyndsey Meyer, CJ Musante, Richard Allen
Modeling Fibrosis Progression in NAFLD and NASH

Franziska Kluwe, Monika Maas, Anita Hennige, Benjamin Weber, Charlotte Kloft
How predictive is short-term body-weight loss in the longer term for decision making during clinical drug development?

MCS POSTER WALK PRESENTERS

Ronny Straube, Brian J. Schmidt, Craig J. Thalhauser
An age-structured model for blasting T cell populations

Shuhua Hu
Incorporation of a time-dependent loss mechanism into the delay process

Florencio Serrano Castillo, Timothy E. Corcoran, Carol A. Bertrand, Monica E. Shapiro, Robert S. Parker

These abstract awards are an important way to recognize outstanding scientific contributions to our meeting. Thank you to the Award winners, and to all who contributed an abstract for presentation at ACoP10.

Also, thanks to the ACOP Abstract Review Committee:

Luning (Ada) Zhuang (Chair)
Kenta Yoshida (Chair-elect)
Daniel Gonzalez
Lian Ma
Sergey Aksenov
Christina Friedrich - ISoP QSP SIG
Wojciech Krzyzanski - ISoP MCS SIG
Amelia Deitchman - ISoP Clinical Pharmacometrics SIG
Jingtao Wu - ISoP SxP SIG
Download ISoPmx App to access ACoP10!

After installing the app, you can:

- Access ACoP10 by clicking on the respective tile and pressing “Install”
- Login with your Google account or create a Eureka account to view the participants list and interact with other participants
- Access the event program and speakers list
- Create your own daily schedule that will guide your through the day
- Stay informed and receive the latest messages and news
- Evaluate sessions and the conference
- Chat with other attendees and take part in our social feed
- Take notes during sessions

Do you have questions? Don’t hesitate to contact us!
connect@go-isop.org

How to download:

The easiest way to download our mobile app is to scan one of these barcodes.

You can also search for 'ISoPmx' in the Apple App Store or Google Play Store.

http://bit.ly/2yHABCr

After downloading the app, don’t forget to enable push notifications to stay up-to-date on the latest happenings and important news!
Tell me what you do at Novartis?

I’m a member of the pharmacometrics group where I focus on analyzing preclinical and clinical data to support dose selection, trial design, and decision making. I’ve primarily worked in oncology.

You were trained as an engineer and mathematician. How did you get into Pharmacometrics?

During my PhD, I had a “quarter-life-crisis” where I was stressing about what I was going to do when I finished school and since I loved biology and math, I spent a day googling “Pharma Company” + “Math” + “@” in order to try and figure out what the possibilities were. That led me to fellow mathematicians Anna Georgieva and Dean Bottino, and my first summer internship at Novartis.

We are starting to see more mathematicians enter the field. Do you think that gives you a different perspective on what we do? Do you feel like it’s an advantage or disadvantage, your background?

I think being a mathematician, physicist or engineer is an advantage. It’s given me a sense that I should always look for fundamental principles that govern a particular system (e.g. conservation of mass, mass-action binding kinetics, etc.). It’s also given me an instinct to try and understand all the key assumptions that are involved in any particular model. This helps a lot when understanding the key sources of uncertainty in our predictions. In my training, I also developed some intuition and analytical tools to help me understand how systems of differential equations behave. This insight helps me to find bugs in my code and helps me to find ways to simplify the models such that they’re both easier to fit and easier to explain to my collaborators.

We sometimes hear people complaining that they had more impact in their job. What do you think are the biggest impediments to success in the field?

Well, the biggest impediment is that biology is really complicated and we often don’t understand enough to make useful, quantitative models. Another impediment is that as a community, we rarely report our failures, and this makes it difficult for us to learn and grow. Bill Gates, highlighted in his blog that a critical step in the development of the steam engine was in constructing devices that measured incremental advances in power output. Developers could then easily tell if their new designs were improvements. [https://www.gatesnotes.com/Books/The-Most-Powerful-Idea-in-the-World] While the pharmacometrics and system pharmacology community widely reports successes, we do not always report failures or provide metrics for how accurate our predictions are. Since we don’t measure our predictive accuracy, it’s difficult for us to know if we’re improving over time. Philip Tetlock in “Super Forecasting” has shown how prediction accuracy can be measured and how “super predictors” can be identified. If the same rigor were applied to our drug development predictions, I think we would see greater improvement in our methods and greater impact of our work.

Where do you think we will be as a field in the next 10 years? What do you think will be the next big thing? And then I guess, what are you doing to prepare for it?

Drug development is changing so rapidly, with recent marketed products for chimeric antigen receptor T cells (CART), adeno-associated virus for gene therapy (AAV), and RNA inhibitors (RNAi). CRISPR has the potential to allow for even more accurate changes directly to the genome and more is being learned about the microbiome every day. The fundamental principles governing these new types of therapies are significantly different than for small molecules and biologics. And therefore, the types of models and analyses we use to understand these therapies are also different. To prepare for these changes, I try to find opportunities to work in these areas.

Is there any paper that you’ve read that you said, damn I wish I wrote that.

Alan Perelson’s mathematical model of HIV [1] is a powerful example of how very simple models can help to determine which biomarkers to collect and at what time points, in order to inform model-based analyses and provide deep biological insight into a system. It was his models that led us to realize that even though HIV has a 10-15 year latency period, it is replicating and mutating very rapidly during this time. Because of the rapid mutation, HIV can rapidly find mutations that are resistant to any single therapy. These insights helped lead to the combination era in HIV therapy.


Why did you join ISoP? What do you think is the best benefit to membership?

I joined ISoP because it’s free to join if you attend ACoP! And there are many benefits to attending ACoP: to keep up with the field, to connect with friends and colleagues, and to brainstorm ideas for how we might work together as a community.

Tell us something personal about you. What do you like to do for fun?

I have a ukulele webpage: www.ukeskywalker.com I can’t believe that domain name was still available back in 2010.
A Conversation With Dr. H.T. (Tom) Banks
MCS SIG Luncheon Speaker at ACoP10
By Patrick Hanafin and Zaid Temrikar

Dr. Harvey Thomas Banks is the LeRoy B Martin, Jr Distinguished Professor of Mathematics and Associate Director for the Center for Research in Scientific Computation at North Carolina State University. He spent 22 years working in the field of Applied Mathematics at Brown University. He has spent the last 27 years working as a Professor of Applied Mathematics at North Carolina State University. He has served on the board of trustees of the Society for Industrial and Applied Mathematics, has served as President of Sigma Xi, is a Fellow of the Institute of Physics, and is a Lifetime Fellow of the Institute of Electrical and Electronics Engineers. His current research focuses on inverse problems and control for partial differential equation and modeling in electromagnetics, strictures, fluids, and biology.

What is your educational background?
Undergraduate degree in Applied Mathematics 1963 from North Carolina State University. MS in Applied Mathematics 1965 from Purdue University. A PhD in Applied Mathematics 1967 from Purdue University. 1-year postdoc training at Brown University in Division of Applied Mathematics where I ended up staying for 22 years.

Can you give us an overview of the topic you will be speaking on?
I will be speaking about Optimal Control of Immunosuppressants in Renal Transplant Recipients Susceptible to BK virus (BKV) Infection.

Abstract:
Kidney transplant recipients are put on a lifelong regime of immunosuppressants to prevent the body from rejecting the allograft. Suppressing the immune system renders the body susceptible to infections. The key to a successful transplant is to ensure the immune system is sufficiently suppressed to prevent organ rejection but adequately strong to fight infections. Finding the optimal balance between over and undersuppression of the immune response is crucial in preventing allograft failure. In this paper we design a feedback control formulation to predict the optimal amount of immunosuppression required by renal transplant recipients in the context of infections caused by BK Virus. We use Receding Horizon Control methodology to construct the feedback control. Data as it is currently collected provides information for only some model states, so we use Non-Linear Kalman Filtering to estimate the remaining model states for feedback control. We conclude that using the presented methodology, an individualized adaptive treatment schedule can be built for renal transplant recipients.

What do you hope your audience will walk out of the room knowing?
I hope they come out with knowledge of the use of control theory and filtering in design of drugs.

What part of your current research is most relevant to drug development?
A major part of my current research concerns analysis and design of data collection to inform inverse problems procedures.

In your opinion, what mathematical work has had the most impact in the areas of human biology and physiology?
Control and design of data collection to support and inform modeling.

What advice would you give to mathematicians striving to understand the biology or biologists who are working to understand the math?
Pick an important problem and work in teams (biologists, applied mathematicians, medical scientists, entomologists, etc.). Repeat over and over on different problems!!
A systematic search for publications on real-world evidence of Benepali, the first etanercept biosimilar to obtain market authorization in Europe. Data regarding the effectiveness, safety and drug survival was undertaken using search terms (SB4 OR Benepali OR biosimilar etanercept OR innovator etanercept) in the BIOSIS® Toxicology, BIOSIS Previews®, Embase® and MEDLINE® databases up to 17 January 2019. The collected information included approximately 2500 etanercept-naïve patients initiated on benepali and outcomes are similar to those patients receiving reference etanercept. Overall the systematic review of real-world evidence provides additional reassurance that benepali is as effective and safe as etanercept (reference) in both switched and naïve patients.


A drug re-approval where M&S played a very important role as no new data was generated.


In an effort to improve the quality of statistics in the clinical urology literature, statisticians at European Urology, The Journal of Urology, Urology and BJU International came together to develop a set of guidelines to address common errors of statistical analysis, reporting, and interpretation.


As methods, tools and best practices for quantitative systems pharmacology (QSP) continue to evolve, it is critical that case studies are reported and shared broadly. The above cited work by Thiel et al, represents one such example published in a mainstream systems biology journal in partnership with the Systems Biology Institute.

In this paper a PBPK/QSP/PD model is used to investigate both a selective (celecoxib) and a non-selective (diclofenac) COX-2 inhibitor, as well as a selective 5-LOX inhibitor (zileuton) and a dual COX-2/5-LOX inhibitor (licofelone). The impact of pre-treatment with rifampicin on the clearances of the COX-2 and 5-LOX inhibitors is also investigated. The drug specific PBPK models are linked with existing QSP cellular models of arachidonic acid metabolism and rifampicin-induced CYP activation, to allow prediction of cellular biomarkers, including prostaglandins and leukotrienes, following treatment with the COX-2 and 5-LOX inhibitors. The model also predicts that the estimated decrease in prostaglandin formation over time following diclofenac and celecoxib treatment is correlated with pain relief observed in humans.

This work serves as a comprehensive case study illustrating the practical impact of pharmacometrically informed QSP modeling in advancing drug development and therapeutics.


It’s always nice to see pharmacometric methods highlighted in clinical journals. Colomban et al. used a population pharmacokinetic model of chemotherapy drugs linked to an indirect response model of cancer antigen 125 (CA-125), a protein biomarker secreted in ovarian cancer, and found that the CA-125 elimination rate (KELIM) was predictive of both overall survival and progression-free survival in ovarian cancer patients. The authors conclude that CA-125 decline over time may provide information about chemotherapy sensitivity and treatment-related benefits.
The authors also provide an online calculator that clinicians can use to estimate KELIM themselves with their own data (www.biomarkers-kinetics.org).

Noteworthy was the fact that the paper was deemed to warrant a commentary up-front at the beginning of the journal. Maitland, O’Cearbhaill, and Gobburu present a brief summary of the material and highlight the importance of the work. They created a really nice graphical representation of the model that is easily understood. We wanted to reprint it here in the newsletter but AACR wanted $264.00 to do so (I almost didn’t write this article review because I didn’t want to promote the journal after seeing that outrageous sum of money they wanted).

Nevertheless, having a pharmacometric model highlighted in a clinical journal is noteworthy. ISoP members should be encouraged to publish more in clinical journals so that clinicians and translational scientists start to become more familiar and accepting of our methods.

Cross-SIG Social at ACOP10

The Clinical Pmx, MCS, and SxP SIGs are hosting a joint social during ACOP10. The event will be held on Tuesday October 22 from 6 – 7:30 pm in Wekiwa 2. Take advantage of this opportunity to meet up with colleagues, learn about SIG initiatives, and network with SIG leadership, all in an informal setting with hor d’oeuvres and a cash bar. Attendees are strongly encouraged to find an ACOP10 abstract that encompasses components of all three SIGs prior to the event for a chance to win drink tickets. We look forward to seeing you there!

Did You Know?

Old versions of the newsletter are posted on the ISoP Web site:

http://go-isop.org/newsletters/

We are delighted to announce the RedIF 2019 Congress to be held from October 27th to 30th in Havana, Cuba: “Pharmacometrics in the Developing World: Translational M&S and Virtual Bioequivalence” Registration and abstract submission are now open (DEADLINE: August 25th, 2019). All info could be found in the following link: http://www.redifar.org/event

So please mark your calendars to join us in promoting the development of pharmacometrics in Latin America.

On behalf of the RedIF 2019 Scientific Committee,

Leyanis Rodriguez Vera, PhD.

The ISoP Newsletter Needs Contributors

Please contact Peter Bonate at peter.bonate@astellas.com if you are interested.

Registration and abstract submission for the 3rd World Conference on Pharmaco-metrics (WCoP) are now open. The scientific committee is hard at work reviewing the many programming submissions we received - more information on the WCoP program coming soon!

For more details, please visit https://wcop2020.org/ or email us at wcop2020@gmail.com.
Update from the Mathematical & Computational Sciences (MCS) SIG

By Helen Moore, MCS Chair

We are gearing up for ACoP!

Plans for the 2019 American Conference on Pharmacometrics (ACoP):

At our luncheon on Wednesday October 23, we will make announcements about the MCS SIG, and then present our 2019 MCS poster award. This year’s poster award winner is Christopher Rackauckas of MIT, and he will give a brief overview of the work in his poster. We will also have a longer talk by our featured speaker. We are excited to announce that Tom Banks, Distinguished University Professor of Mathematics at North Carolina State University will be this year’s featured speaker. His current research interests include the areas of optimal control, parameter estimation, and inverse problems. His presentation will be on optimization of post-kidney transplant therapeutics. See the interview with Dr. Banks in this ISoP Newsletter issue for more information.

In addition to the MCS poster award, we will also highlight three additional posters with significant mathematical and computational content during a poster walk, which will take place during the Monday afternoon poster session. Poster presenters this year will be Ronny Straube of Bristol-Myers Squibb, Shuhua Hu of Certara, and Florencio Serrano-Castillo of the University of Pittsburgh.

We will co-host an evening social event with the Clinical Pharmacometrics and the Statistics and Pharmacometrics SIGs the evening of Tuesday, October 22, 6 – 7:30 pm in the Wekiwa 2 Room. We will provide free food (hors d’oeuvres), and there will be a cash bar (everyone pays for their own drinks). We are promoting ties between the SIGs with a friendly competition: find a poster abstract that incorporates topics relevant to two or three of the SIGs, and get a chance to win a prize (a free drink of your choice!).

Additional information:

This year’s annual meeting of the Society for Mathematical Biology (SMB) was held in Montreal, Canada July 21-26, 2019. At least 14 biopharma industry modelers attended the conference this year, with two full sessions devoted to industry talks (a total of 8 speakers), and several additional industry talks in other sessions. Eleven of us gathered for a dinner, and started planning an Industry subgroup to support future participation and activities. Next year the SMB meeting will be in Heidelberg, Germany Aug 31-Sept 4, and the following year’s meeting will be at the University of California at Riverside July 11-14, 2021. See the SMB Life Sciences conference website for more information: https://www.smb.org/Conferences/CM/Conference/ls20.

We welcome Johannes Schropp of the University of Kostanz and Tongli Zhang of the University of Cincinnati as new members of the MCS Steering Committee, and Sinziana Cristea of Leiden University as our Student Community representative. We will hold an election for Secretary before ACoP. The secretary position is open to MCS members who are interested in getting more involved. The candidate elected to this position will serve one year as Secretary, then serve one year as Vice Chair, followed by a year as Chair. The current Vice Chair, Gilbert Koch of the
University Children’s Hospital Basel, will be transitioning to Chair this fall, and the current Secretary, Frank Gibbons of AstraZeneca, will transition to Vice Chair.

Join the MCS SIG to get advance notice of these and other opportunities. Click here for more information (membership link at the bottom of the page): [http://go-isop.org/special-interest-groups-sigs-and-communities/mathematical-and-computational-sciences-sig/](http://go-isop.org/special-interest-groups-sigs-and-communities/mathematical-and-computational-sciences-sig/)

Want to get more involved with the MCS SIG? Have questions or ideas? Contact the Chair, Helen Moore, at dr.helen.moore@gmail.com.

Update From the Statistics & Pharmacometrics (SxP) SIG

By Mike Smith and France Mentré

We have had a busy period in the SxP Special Interest Group over the last few months.

1/ The first ISoP SxP SIG local event was held at Université Paris Diderot on 11th July featuring talks from Prof Andrew Gelman, Prof Rob Bies, Mike K Smith, Sebastien Benzekry, Witold Wiecek, Francois Riglet, and Shan Pan. The event was well attended and the talks were engaging and interesting. More information is available on the SxP website with all the slides: [https://community.amstat.org/sxp/home.](https://community.amstat.org/sxp/home.)

2/ SxP also organized and supported a session at the recent ASA JSM meeting in Denver, Colorado. The session, entitled “Effective Application of Modelling, Simulation and Knowledge Sharing in Drug Development” was a reprise of the session from ACOP 8 (2018) meeting with presentations from Michael Heathman, Chyi-Hung Hsu, John Gibbs but also including a presentation by Neal Thomas on his meta-analysis of dose-response studies and implementation of Bayesian analysis of Emax dose response in his R package “clinDR”. Gary Rosner provided a discussion of the talks highlighting the impact of modelling and simulation, pharmacometrics and statistics in assisting decision making in clinical research with the use of Bayesian methodology and utility functions. Unfortunately with the session being scheduled on the last day of a 5 day conference, it was not terribly well attended but I encourage you to review these interesting presentations and the respective slides will appear on the SxP website shortly.

3/ But that’s not all! SxP will be making an impact at the upcoming ACOP 10 meeting in Orlando, FL. Stacey Tannenbaum and Jonathan French are representing SxP at the “You say to-mah-to, I say to-may-to” session where they aim to help pharmacometricians and statisticians reach a common understanding of some shared (and perhaps misused!) terminology. SxP will also be hosting a lunch meeting on 22nd October for you to meet the SIG, share ideas and hear a presentation from our SxP poster award prize winner. We will also be joining with the Clinical Pharmacometrics, Mathematical and Computational Sciences SIG to host a Social event also on 22nd October.

4/ We’re also VERY pleased to announce a new sub-team within the SxP SIG focusing on MBMA techniques, methodology and software under the leadership of Marion Bouillon-Pichault. ISoP recognizes that the number of pharmacometricians and statisticians actively engaged in MBMA within organizations may be small, so it is helpful to provide a network for these colleagues to discuss issues and to help move the discipline forward together. I encourage you to contact us if you’d like to be part of this subteam and contribute to the discussion.
Update From the Clinical Pharmacometrics SIG

By Marc Scheetz

The Clinical Pharmacometrics SIG has grown to a total of 123 active members, and we have new opportunities for engagement. We are excited to announce the launch of two Task Forces. The first, the **Education Task Force**, is focused on providing pharmacometric educational resources to non-pharmacometricians. The second, the **Outreach and Engagement Task Force**, will identify specific tasks to engage SIG membership and relevant scientific, clinical, and professional communities or organizations to advance pharmacometrics-based precision dosing in clinical and drug development settings. We are actively looking for volunteers for both Task Forces.

The SIG continues to be involved nationally/internationally. Dr. Michael Neely delivered a presentation on ways to overcome barriers to individualized dosing at the **FDA Precision Dosing Workshop**, while SIG Leadership is currently participating in ISoP’s response to the recently released FDA Population PK Draft Guidance, lending a clinical implementation perspective to model-based dose selection. Members from the SIG Leadership look forward to meeting you and discussing priorities at upcoming events.

Please connect with us at ACoP10 for a pre-conference event, **Clinical Pharmacometrics: Bringing Models to Patients** (Sunday, October 20th), the Cross-SIG Evening Social (Tuesday, October 22nd), and the Meet the SIG Luncheon on Wednesday, October 23rd. The SIG will also hold sessions at the ACCP Annual Meeting. Join us for a scientific session on Pediatric Therapeutic Drug Monitoring and Drug Development in the Age of Pharmacometrics (Sunday, September 15th) and the Meet the SIG Breakfast (Monday, September 16th).

Finally, the arrival of ACoP10 will mark the transition of Leadership positions within the SIG. Nik Onufak will serve as Chair, accompanied by Drs. Amelia Deitchein (Chair-Elect), Luning (Ada) Zhuang (Vice-Chair), and Marc Scheetz (Past-Chair). We thank Drs. Liz Lakota (Founding Chair), Michael Neely (Steering Committee Chair), and Sean Avedissian (Junior Secretary) as they complete their service to the SIG. Positions on the Leadership Team progress cyclically annually and are appointed (Steering Committee roles, Junior Secretary) or nominated and elected (e.g. Scientific Secretary). We are seeking nominations for a new member of the Leadership Team to fill the role of Scientific Secretary with the opportunity to advance within the Leadership Team at the end of the one-year term. If you are interested in becoming a member of the SIG Leadership Team, serving on one of the Task Forces, or simply becoming a SIG member, please contact us at clinical.pmx.sig@go-isop.org!

**ISoP Local Event Held in Paris**

By Julie Bertrand

The INSERM research group led by France Mentre, in Paris, held an ISoP SxP SIG Local event, on the 11th of July.

Program:

14:00-14:40 Prof Andrew Gelman (Columbia Univ.) - “We’ve Got More Than One Model: Evaluating, comparing, and extending Bayesian predictions”

14:40-15:20 Dr. Sebastien Benzekry (INRIA) - “Mechanistic modeling of metastasis: cancer at the organism scale”

15:20-15:40 Witold Wieck (Certara) - “Bayesian meta-analysis model for chemical risk assessment”

15:40-16:00 Francois Riglet (INSERM Paris Univ.) - “Bayesian individual dynamic predictions of biomarkers and risk of event in joint modelling (with uncertainty): a comparison between Stan, Monolix and NONMEM”

Coffee/tea/macarons break

16:30-17:10 Prof Rob Bies (Buffalo Univ.) - “A hybrid genetic algorithm for NONMEM structural model optimization”

17:10-17:50 Mike Smith (Pfizer) - “Dose-response, small data & big decisions”

17:50-18:10 Shan Pan (St John’s Institute of Dermatology) - “Real-world clinical effectiveness and utility of ustekinumab in adults with moderate to severe psoriasis: statistical and pharmacometric perspectives”

Prof France Mentre and Mike K Smith (Pfizer), co-chairs of SxP SIG, welcomed the audience to this first local event by SxP SIG. They handed the floor to Prof Andrew Gelman (Columbia Univ.) who gave an opinion piece (no slides) on how indeed all models are wrong but some are useful and certainly none are ridiculous. Then, Dr. Sebastien Benzekry (INRIA) illustrated how models of partial differential equations can help predict...
tumour metastasis development in breast and lung cancer. These two invited talks were followed by submitted abstracts: Dr. Wiecek Witold (Certara and LSE) on uncertainty factor meta-analysis and PhD student Francois Riglet (INSERM) on individual dynamic predictions. After a short macaroon break, Prof Robert Bies (Buffalo Univ.) presented the Single Objective Hybrid Genetic Algorithm and its implementation in a Shiny App using NONMEM. Then, Mike K Smith, guided the audience through 4 steps in drug development where statisticians and pharmacometricians work better together. Finally, PhD student Shan Pan (St John’s Institute of Dermatology) illustrated on ustekinumab how statisticians and pharmacometricians can benefit from working together. All presentation slides are to be uploaded on the ISoP website.

Update from the QSP SIG

By Eric Sobie, QSP SIG Chair

The last few months have been extremely busy for the QSP SIG, with several events and initiatives aimed at advancing the science of QSP and extending its reach. We are excited to notify the ISoP community of these recent events, as well as our plans for the upcoming ACoP10. We hope to see lots of you in Orlando!

Local ISoP QSP event in NJ. On July 16th, the SIG sponsored a “QSP Day” at Bristol-Myers Squibb (BMS) in Princeton, NJ. The day-long event featured presentations by leaders in the field, a lunchtime poster session, and opportunities for industry scientists and academic researchers to network and discuss potential collaborations. QSP Day had almost 90 attendees! Special thanks go to ISoP for providing logistical support, to Brian Schmidt, QSP SIG Chair-Elect, for taking the lead in organizing, and to BMS for providing meeting space and financial support. Congratulations to the poster award winner, Ronny Straube-Principal Scientist, BMS, who was honored for his work “Calibration of a Mechanistic Mini-Model of IL-2 induced Lymphocyte Proliferation.”

New Working Groups. The QSP SIG sponsors 8 working groups (WGs), which allow for small groups of scientists to focus on particular issues within the field. These can provide an excellent way to engage with other scientists, so please contact us for information on WGs that might fit your interests. Our two newest WGs are: (1) Uncertainty, Error, and Variability in QSP Models, led by Josh Apgar, Applied Biomath, and Michael Weis, Rosa & Co.; and (2) Integrating QSP and Machine Learning, led by Carolyn Cho, Merck, and Tongli Zhang, University of Cincinnati.

New Leadership Team Members. We are happy to announce that after ACoP10, Abhishek Gulati, Astellas Pharma, will succeed John Burke, Applied Biomath, as the SIGs first Communications Director, and Peter Bloomingdale, Merck, will assume the role of QSP SIG Secretary, taking over from Panteleimon Mavroudis, Sanofi. The new QSP Sig Vice-Chair will be determined by election – please watch for the announcement and make sure to vote!

ACoP10 plans. Conferences are a great way to connect, and the upcoming ACoP10 will provide opportunities for community members to learn more about the SIG. The annual Meet the SIG Lunch will take place at 11:45 AM on Tuesday, October 22. At this lunch, we will provide an update on SIG activities, introduce the new leadership team, and present the 4th QSP-SIG student award to Qingxiang Lin, for his work “Mechanistic multi-scale models characterize drug synergism between BGJ398 and gemcitabine in pancreatic ductal adenocarcinoma.” At 5:30 PM on Tuesday, October 22, we will host the QSP Sig Working Groups Poster Social, which will provide opportunities for both networking and learning about the activities of the WGs. We all hope to reconnect with old colleagues and meet new friends at these events!

ISoP NE Local Event

By Chris Penland (Chair), Andy Zhu (Chair Elect), and Hong Lu (Communications)

On August 26th 2019, ISoP New England was pleased to host a Symposium on integrated Pharmacometrics and Systems Pharmacology (iPSP) in collaboration with Dhananjay Marathe and Abhishek Gulati, members of the QSP SIG iPSP working group. Over 50 researchers from industry and academia gathered in Cambridge, MA to hear presentations and discuss the
benefits of, challenges to, and new methodologies for bringing the two disciplines more closely together. The intent of this symposium, working group (QSP-iPSP) and Trame et al. CPT: PSP 2019 was not to further define pharmacometrics and QSP; as doing so may serve only to divide the fields, but rather to demonstrate iPSP through compelling examples. The symposium highlighted use cases of iPSP and showcased some practical methodology enhancements and a cutting-edge new modeling environment (Pumas.jl).


Key Themes:

- Open source and open model informed drug development: the dividends of, and the efficiency and robust scientific learning enabled by model adaptation and reuse
- Model identification and advanced modeling & simulation methods for iPSP class models
- Model Verification, Validation, and Uncertainty Quantification – adopting/adapting practices from physics-based modeling and simulation of medical devices
- Regulatory perspective on the use of iPSP-class models in decision making
- Case studies in bone preservation, cardiorenal/metabolic disease, immunology, and hematology

Agenda and slides from the presenters at: https://sites.google.com/site/isopne/ipsp-august26-2019

Thank you to all of our speakers and attendees!

Acknowledgements: We would like to thank Michelle Johnson and Metrum Research Group for donating the meeting space and on-site coordination; and Enrico Smith and ISoP for registration support and meeting announcements.

Clockwise from top left, Chris Penland, Matt Riggs, Sietske Braaakman, Dhananjay Marathe
Growing the Community for Bay Area Mechanistic Modelers

By Jennifer Rohrs, jrohrs@vir.bio

A grassroots group of Bay Area mechanistic modelers held a networking event on Thursday, September 15th at Foundry and Lux in South San Francisco. This small meet-up, organized through word of mouth and personal contacts, had over twenty attendees from both academia and industry. Almost every company represented shared information on job openings, which were shared throughout the community. The event was a great opportunity for everyone involved to make connections and discuss future events to support Bay Area modelers:

“We were pleased to have modelers from a variety of companies and schools attending, including many students! We felt there is a need for events that bring together QSP modelers around networking activities, inspiring speakers, and learning opportunities. We hope to have more of such events in the future, and create a local community of mechanistic modelers in the Bay Area.”

− Vincent Lemaire, Genentech, event co-organizer

“It was exciting to see the strong interest in QSP in the Bay Area. The combination of seasoned modelers from industry and academic groups should make for some very interesting events and opportunities in the future.”

− Christina Friedrich, Rosa, event participant

We plan to continue building connections in the community by helping to organize cutting edge talks and education and networking events. We hope this event will be the first of many!

If you are want to get involved or attend the next event, contact Vincent Lemaire, lemaire.vincent@gene.com, or Helen Moore, helen.moore@appliedbiomath.com.

ISoP QSP Working Group on iPSP

In 2016, within ISoP, under the umbrella of Quantitative Systems Pharmacology (QSP) Special Interest Group (SIG), several different working groups (WGs) were established with the focus of compiling, developing and disseminating current state-of-the-art and futuristic strategies for the QSP stream. One of the WGs, the Integration of Pharmacometrics and Systems Pharmacology (iPSP) has the main goal of identifying, collecting & sharing useful information on best practices, examples, and approaches for integrating QSP & Pharmacometrics. The WG has good representation across industry, academia and the regulatory agency, with expertise spanning development and application of mechanistic and empirical models across the development/lifecycle of drugs/targets/biomarkers.

The current and former members in this WG are listed in the table below. The WG partakes monthly update calls involving all WG members to identify opportunities and implement them to drive the agenda forward. Over these last couple of years, the WG has successfully accomplished several tasks including developing several consensus proposals for scientific sessions in different conferences. Some of these are as follows:

• A session in PSWC 2017 titled, “Systems pharmacology – innovative approaches to drug safety”
• Session proposals for ASCPT 2017, ACOP 2017 and ASCPT 2018

• ISOP Study Group Webinar Series in 2017 titled, “Bridging and tackling the gap between Empirical and Systems Pharmacology Models: Where do we stand?” (Youtube links embedded below)
  ○ The semantics and terminology of Quantitative and Systems Pharmacology and Pharmacometrics to help enable bridging (Piet van der Graaf)
  ○ Understanding, incorporating, characterizing variability and uncertainty in Quantitative Systems Pharmacology models: Case studies and experiences from Drug Development (Richard Allen)
  ○ Fix vs Fit – The eternal debate (Matt Riggs)
  ○ Systems pharmacology models for understanding drug safety signals (Melissa Hallow)
  ○ Good Practices in MID3 – PM & QSP approaches informing decisions (Sandra Visser)
  ○ MatVPC: A User-Friendly MATLAB-Based Tool for the Simulation and Evaluation of Systems Pharmacology Models (Konstantinos Biliouris)
  ○ PK-Sim/Mobi – Open Systems Pharmacology Suite (Jan Schlender)
• Publication in CPT:PSP in 2018 titled, “Perspective on the State of Pharmacometrics and Systems Pharmacology Integration”
• A session in ACoP 2018 titled, “A Perspective on integrating Pharmacometrics and Quantitative Systems Pharmacology characteristics using examples”
• A dedicated symposium in Aug 2019 on iPSP in collaboration with New England chapter of ISoP (ISoP-NE) in Boston, MA (agenda and slides at: https://sites.google.com/site/isopne/ipsp-august26-2019)
• Two session proposals for ACoP 2019 (accepted) titled, “Integrated Pharmacometrics and Systems Pharmacology (iPSP) Modeling Without Borders: Opportunities and Challenges for Re-purposing iPSP Models” and “Curing Diseases Through Genetic Manipulation: Advancements and Potential of Gene and Viral Therapy and Their Optimization with Model-Based Analysis”

The WG is identifying and planning to work on more opportunities for the forthcoming future. There are a few membership positions that are open in the WG and any interested individuals, especially from organizations which are not already represented in the WG, are welcome to reach out to Abhishek (abhishek.gulati@astellas.com) or Dhananjay (Dhananjay.Marathe@merck.com).

<table>
<thead>
<tr>
<th>Current and Former Members (Affiliation; Role)</th>
<th>current members are designated with an asterisk (*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abhishek Gulati* (Astellas; Current Co-Chair)</td>
<td>Justin Earp* (FDA)</td>
</tr>
<tr>
<td>Anu Shilpa Krishnatry* (GSK)</td>
<td>Kevin Dykstra* (Simulations Plus)</td>
</tr>
<tr>
<td>Coen van Hasselt (Leiden Univ)</td>
<td>Kostas Biliouris (Novartis)</td>
</tr>
<tr>
<td>Cynthis Musante* (Pfizer; Former Co-Chair)</td>
<td>Matthew Riggs* (Metrum)</td>
</tr>
<tr>
<td>Dhananjay Marathe* (Merck; Current Co-Chair)</td>
<td>Matthew Rizk (Merck)</td>
</tr>
<tr>
<td>Jay Mettel (AstraZeneca)</td>
<td>Mirjam Trame* (Novartis; Former Co-Chair)</td>
</tr>
</tbody>
</table>

Inaugural ISoP General Members' Meeting

We believe it’s very important to provide regular feedback to you, our members, about ISoP’s activities, how we spend our money, and who our officers are and how they’re elected – and allow you the response to get to know us, ask us questions, and provide us with feedback. Up until now, the venue for us to do so has been our annual meeting, ACoP. This, we feel, isn’t really the best forum for this kind of meeting, so we’re starting something new: A General Members’ Meeting.

Our first General Members’ Meeting will take the form of a webinar on September 18, 2019, from 12.00pm to 1.30pm EST. All ISoP members are welcome to join. We’ll be talking about our finances, recent and upcoming activities by the Society and its SIGs, Committees and Communities, and a range of other topics we think will be of interest. We understand that this time may not be convenient for everyone, so we’ll be recording the meeting and making it available online. We’re also exploring holding a second GMM in Q4 2019 which will take place at a time better suited to our Eastern Hemisphere members, should there be interest in this.

We hope you’ll be able to join us! Information will be added to the GMM page at http://go-isop.org/general-members-meeting/ as it becomes available. The webinar details are as follows (we use Zoom – if you don’t have it, please allow a few minutes beforehand to set it up):

Register online at https://zoom.us/webinar/register/WN_1ZMY3aflQKq7PBWBmDSCJg to attend.

Best regards, Justin J. Wilkins
ISoP President
Two NONMEM Tutorials in August 2019 issue of PSP! Thank you Bob Bauer.

By Lena Friberg, PhD and France Mentrè, PhD, MD

NONMEM remains the most widely used software for population PK and PD analyses, both within academia and in the pharmaceutical industry. The August issue of PSP includes two tutorials on the NONMEM software – one for beginners and one for more advanced users.

**Part I** provides a comprehensive overview of the software and points to the most essential information to get started with NONMEM in a language that may be more easily accessible than the NONMEM user guides. For example, it explains how to set up the dataset, and the various components of the input and output files are described. Two basic PK modelling examples are discussed, step by step, and all necessary files to run the examples, as well as the user guide, are provided as supplementary material.

**Part II** focuses on the different estimation methods available in NONMEM, i.e. FO approximation methods, sampling-based methods, and MCMC Bayesian analysis. Their pros and cons are outlined from the perspective of the author. Moreover, the tutorial includes seven complete examples of more advanced models and common approaches that a user encounters, e.g. handling data below LOQ, inter-occasion variability, mixture models, interval collection data, categorical data, etc. All necessary input files, as well as the output files, are freely accessible as supplementary material (one zip-file per example).

These two tutorials and the associated examples will be a very welcomed resource to our pharmacometrics and QSP community and contribute to the curriculum in courses of population modelling. Thanks to Bob Bauer (ICON) for taking the effort to author these tutorials, which are nice complements to the earlier tutorials in our collection.

News from the Journal of PK and PD

By Peter Bonate, Associate Editor

Every year the journal publishes a themed clinical issue related to pharmacometrics. In the past we have done issues on infectious disease, immunology, and the central nervous system to name a few. This October’s issue will be The Application of Modeling and Simulation to the Development of Drugs For Rare Diseases.

In the United States, rare diseases affect fewer than 200,000 people, but there are estimated to be more than 7,000 of them. It’s also been estimated that in the United States, more than 7 million Americans have a rare disease. Drug development in such patients is challenging for many reasons: identification of patients that are spread over large geographic areas requires many study centers, the sparse numbers of patients available with the disease often leads to low statistical power, surrogate markers may not be available, and use of placebo controls can be unethical. Modeling and simulation could be used to help support dose recommendations and help fill in knowledge gaps in the label, such as identifying potential drug-interactions. Population pharmacokinetics, exposure-response, disease progression modeling, QSP, these are all tools that can be applied to rare diseases.

The October issue will consists of reviews and original articles. Patel and Needleman from the FDA kick things off with a discussion of the FDA’s Office of Orphan Products Development, followed by an overview of clinical pharmacology and modeling and simulation in orphan drug development from Ahmed et al. Das et al. and Serrano Castillo et al. show how QSP models can support drug development in patients with colonic motility disorders or cystic fibrosis, respectively. Conrado et al. presents a disease progression model for Duchenne Muscular Dystrophy. Schoemaker et al. present a joint longitudinal stroke scale-survival model in patients with intracerebral hemorrhage. Andrea Edginton’s group at the University of Waterloo present two papers related to the population pharmacokinetics for factor VIII in patients with hemophilia A. Chanu et al. used clinical trial simulation to examine the performance characteristics of a survival analysis in pediatric patients with pulmonary arterial hypertension treated with sildenafil. The journal’s editors would like to thank the author’s for the contributions.

Our themed issue for 2020, with Sara Quinney from Indiana University as co-editor, is planned to be the role of modeling and simulation in pregnancy and lactation.
PAGE 2019 Report

By Siv Jönsson

On 11 - 14 June, 2019, the 28th PAGE meeting was held at the Stockholm Waterfront Congress Centre, Stockholm, Sweden. As always, the scientific program was formed by selection from submitted abstracts with a few invited speakers. The full program, abstracts and in many cases also presentations/posters can be found at www.page-meeting.org.

The invited keynote speaker Dr. Jeff Sachs (MSD) gave a much appreciated talk entitled “Pharmacometrics: A shot in the arm for vaccine discovery and development ~or~ Vaccines are not immune to the charms of pharmacometrics”. Dr. Sachs detailed the pharmacometric opportunities in, and, impact on vaccine discovery and development, as well as he included vaccine history and anecdotes.

On 11 - 14 June, 2019, the 28th PAGE meeting was held at the Stockholm Waterfront Congress Centre, Stockholm, Sweden. As always, the scientific program was formed by selection from submitted abstracts with a few invited speakers. The full program, abstracts and in many cases also presentations/posters can be found at www.page-meeting.org.

The invited keynote speaker Dr. Jeff Sachs (MSD) gave a much appreciated talk entitled “Pharmacometrics: A shot in the arm for vaccine discovery and development ~or~ Vaccines are not immune to the charms of pharmacometrics”. Dr. Sachs detailed the pharmacometric opportunities in, and, impact on vaccine discovery and development, as well as he included vaccine history and anecdotes.

One of the highlights on the PAGE conference is The Lewis Sheiner Student Award session, featuring the Award recipients. This year we congratulate Drs. Moustafa Mahmoud Abdellatif Ibrahim (Uppsala University), Sebastiaan Goulooze (Leiden University) and Elena Tosca (University of Pavia). All three gave stellar presentations covering competing risks analysis, pharmacometric techniques to quantify and prevent iatrogenic withdrawal and Dynamic Energy Budget (DEB) based models.

The social top spot was Thursday night’s social event at the Stockholm City Hall where we enjoyed food, good company, entertainment and dancing!

An update on modelling and simulation involvement in the EU regulatory activities was given by Drs. Kristin Karlsson and Flora Musumba Tshinanu from the European Medicines Agency’s Modelling and Simulation Working Party. Related in the same session, Dr. Sylvie Retout (Roche) presented an illustrative example of a pediatric extrapolation application used that enabled labelling of emicizumab in haemophilia A pediatric patients <1 year old despite lack of clinical data.

The Stuart Beal Methodology session delivered a full plethora of topics from new model frameworks to model diagnostics to optimal design and included a brilliant talk challenging basic concepts of receptor pharmacology and the Emax model - thank you Xiao Zhu (University of Otago).

The local organizers – Thank you!

The 2019 Tutorial was a splendid talk on “Use of informative priors in model-informed drug development” given by Dr. Nicky Best (GSK). Dr. Best gave us a deepened insight in methods for constructing informative priors including elicitation from experts (not easy!), methods for weighting informative priors and for assessing and handling conflicts between prior and data. Finally, Dr. Best shared examples on how to introduce such priors in the model.

Xiao Zhu presenting a cohesive model framework of receptor pharmacology

On Friday finally we got to know where we will go next year.

To all of you - very welcome to Ljubljana, Slovenia, on 9-12 June, 2020!
Glimpses from the social event from PAGE 2019 at the Stockholm City Hall: dinner in Blue Hall (upper) and dancing in The Golden Hall (lower).

Group photo with guest speakers from ISoP Student Community Event @ Uppsala University
Can You Really Work on an iPad?

By Peter Bonate

Thanks to all of you that keep buying my books I had a little royalty money burning a hole in my pocket earlier this summer. I have an iPad mini, which I do a lot of reading on at night, but to read journal articles it’s just too small to be useful, so I decided to upgrade and buy a bigger iPad. My goals were simple: be able to read and edit journal articles. So I went out and bought a 10.5” iPad from Amazon. First thing I noticed was that it was not much bigger than my iPad mini. Papers still looked small on it. So I returned it and got the 3rd generation 12.9” iPad Pro. When I opened it, I was impressed by the size. The screen is huge. When I finally opened an article on it, I really felt like it was the right size for reading. The screen actually looks like size paper. The other big change is the iPad home button is gone – it’s all swipes now to access Apps. Swipe up. Swipe down. Left. Right. Corner. This is still hard to get used to.

I then went in search of a pdf editor. There are a lot of choices in the App store: PDF expert, PDF element, iLovePDF, GoodReader, Liquid Text, and many others. Many are free with in-app purchases, some are cheap ($2.99 thereabouts), and some are very expensive (Liquid Text was $29.99!). I did a lot of experimenting. Liquid Text had a lot of possibilities but editing files have to be saved in Liquid Text format, which can only be read by Liquid Text. When I converted it to pdf, my yellow highlighted text was so dark I could not read it. I finally settled on two: GoodReader and PDF expert. Of the two, I thought PDF expert interacted better with Dropbox so I mainly use that. I finally feel I can read and edit documents like using paper copies.

I soon realized this iPad was a lot more powerful than just a pdf editor. Could I do actual work on this? I found that Microsoft Office was available for download. This was great. I could edit documents in Word or Excel. But wait, there’s a catch. Apparently, Microsoft and Google are having a fight (I guess about their office products) and Microsoft does not allow access to files in your GoogleDrive. I am not kidding. They allow you access to sites I’ve never heard before, like HKT storage or Edmodo, but GoogleDrive is not on the list. A long time ago, I canceled Dropbox because of the problem it had freezing my computer (I have thousands of files to backup). This restriction forced me to reactivate my Dropbox account and move all my GoogleDrive files back to Dropbox. I now use Dropbox as my sync folder. That was a hassle that took an afternoon of my life.

But even once I solved this, these Microsoft products are not like PC versions. You don’t have the ribbon anymore and the amount of editing you can actually do in a document is not as extensive. But you can type with voice dictation easily and it’s quite accurate. You can also review documents (with comments), which makes it easy to review other’s work. In PowerPoint, trying to move things around without a mouse is not easy using the dragging you do on the iPad. I did find out you can add a mouse to an iPad but not on my version. Apparently with some other iOS versions you can pair a mouse through the Accessibility settings, but not with the latest version.

At this point, I bought a couple of external Bluetooth keyboards to try. They were so small I just never could get the hang of using them. They were also heavy. With the exception of the Apple keyboard, most of the external keyboards plus iPad weighed more than 2 kg, which after a while starts to feel heavy. So I returned them all and stopped trying to use a keyboard.

At this point, I could read/edit pdfs and I could review and edit (with some challenges) Microsoft documents. Could I go completely paperless and start taking all my meeting notes on my iPad? Like PDF readers there are many note-taking options in the App Store: Notability, GoodNotes, OneNote, NotePad+, and many others. After many false starts, I settled on GoodNotes because it is easy to organize documents into folders and you can search on hand-written text. One thing I could never get used to was the slickness of the screen. I installed a glass screen saver to protect my screen, but it was so slick that when I tried to write my notes, my normal chicken-scratch handwriting looked like I was also taking Quaaludes. Even after removing the screen save the regular screen of an iPad just didn’t feel right. While I was researching which screen saver to buy, I noticed a screen saver that advertised itself as having a paper-like feel (Bersem matte PET film, $33.99 for 2 on Amazon). After installing it I was amazed. It really did feel like paper and have the resistance of paper when you write. With the film installed, my handwriting became more readable. As an aside, I did buy the iPencil thinking it would help. Honestly I didn’t see any real benefit and it came with a hefty pricetag. Most apps don’t take advantage of the iPad-iPencil integration so I am not sure I would buy it again. The one good thing is that the pencil magnetically charges on the side of the iPad so I don’t ever have to worry about it staying charged.

Although I don’t use them, there are apps that allow you to run R, Python, and Jupyter notebooks; no way to run NONMEM though.

At this point, I started to use my iPad at work. I’ve gone completely paperless. I find I actually read more papers now. Those tiny fonts a lot of journals use to reduce paper are no longer an issue; I can just adjust them to any size. I don’t even have to wear my glasses any more. I now take more notes at work, I guess because it’s more fun this way. I also use the iPad for most of my teleconferences. Webex and Skype are no problem. And since the battery on the iPad Pro lasts more than 10 hours, I can go all day without a charge.

Going back to the question, can you actually do work on an iPad? You can, but it’s not easy and it takes some getting used to. Working with multiple windows is hard, although I’ve read that the next version of iOS (iOS 13), will have better support for multiple open windows. All in all, I’m glad I’ve made the change and I am also sure the environment is glad I made the change to go paperless.
ISoP Student Community Event
@ Uppsala University: “Life After Graduation - Your Guide to Success”

By Yi Ting (Kayla) Lien

On August 22nd 2019, a soft skill career event organized jointly by the ISoP Student Community and the Uppsala Pharmacometrics Group was held during Uppsala Pharmacometric Summer School in Sweden. The aim of the event was to introduce the ISoP Student Community to the student body attending the Summer School and to have an up-close and personal discussion session with speakers from different pharmaceutical sectors.

It was a well-attended event with over 30 students/trainees. The event kicked off with Ms. Yi Ting (Kayla) Lien (ISoP Student Community Chair), who gave a short overview of the ISoP Student Community and what the community does. Students who were interested to join were invited to be part of the Student Community Leadership Team and were provided with the respective information.

During the second part of the event, six invited speakers shared their career tracks and experience of their perspective job roles with the students/trainees. The six guest speakers were Dr. Johan Wallin (Industry, Eli Lilly), Dr. Kristin Karlsson (Regulatory, Swedish Drug Regulatory Authority Medical Product Agency), Dr. Maria Kjellsson (Academia, Uppsala University), Dr. Anders Viberg (Regulatory, The Dental and Pharmaceutical Benefits Agency), Dr. Anna-Karin Hamberg (Clinical, Academic Hospital Uppsala), and Dr. Anja Henningsson (CRO, qPharmetra).

This was followed by a 1.5 hour interactive panel discussion with the students/trainees, chaired by Kayla Lien. Students asked soft skill questions regarding challenges faced in their careers and what the one advice would be which they would give to students. The summarized response from the speakers was to learn how to communicate with non-modelers and to prepare a strategic thinking plan before your presentation to stakeholders. It was also highlighted that it is helpful to know who the key decision makers are to help or to convince for your pharmacometric tasks. Some other technical questions posed were around the challenge of (not) using pharmacometric models in clinical practice, what pharmacometric trends do they foresee being implemented in drug development over the next 5 years, how collaborations between academia and industry work, and which software are commonly used in industry.

The event ended off with a Swedish tradition called FIKA (coffee/tea break) with an assortment of lovely Swedish cookies where the students mingled with the guest speakers. The event turned out to be a great success and the ISoP Student Community would like to thank the Uppsala Pharmacometrics Group for the great support throughout the event and all the speakers for their time.

Far left: Kayla Lien (ISoP Student Community Chair) presenting on ISoP student community

From left to right: Johan Wallin, Kristin Karlsson, Anna-Karin Hamberg, Anders Viberg, Anja Henningsson, and Maria Kjellsson

Anders Viberg and Maria Kjellsson interacting with students during the coffee break

Student participants asking questions during the interactive panel discussion
Communication Corner

By Peter Bonate

YOU are the Brand!

The other day I was having an email exchange with a fellow ISoP-ian about communicating QSP models. He had some good ideas and I asked him if he would write this month’s column. He very politely declined and asked “Why? Why would I want to do this?” Journal articles last. These columns don’t; they’re ephemeral.” He couldn’t even remember what the last topic was about. Fair enough. But did he remember who wrote it? “You did”, he said. “Exactly.” Do I write these columns because I have all this free time on my hands and a huge altruistic streak? Well, I do somewhat, but I started these columns to maintain the Bonate Brand™!

A brand is an identifying symbol, logo, name, word and/or sentence that companies use to distinguish their product or themselves from others. How does Nike distinguish itself from Adidas? Or Coke differentiate itself from Pepsi? Nike has the Swoosh, Pepsi has a distinctive red, white, and blue wave within a circle. When you see these logos you immediately know who it is because of extensive advertising and years of building the brand.

You might be surprised to know that YOU are also a brand, just like I am. Jeff Bezos has said that your personal brand is how people describe you when you are not in the room. So how do I differentiate myself from other pharmacometricians? Early in my career there were a number of other pharmacokineticists (Pharmacometrician was not a word yet!) in my peer group: Marc Gastonguay, Bernd Meibohm, Holly Kimko, Paolo Vicini, and others. How was I going to stand out from them? They were all awesome in my view. I had to build the Bonate Brand™.

At the time, AAPS was the dominant professional society and the focus groups drove programming at the Annual Meeting. Programming chairs had huge networks since they operated with so many other groups and individuals within AAPS. I watched when the Population Pharmacokinetics focus group started the competition to be its Chair. It was heated and intense and provided immediate exposure to the winner. I also saw that to start a focus group you only needed 50 signatures; so I thought, why not start my own focus group? I differentiated myself by leading the Simulation Focus Group for 3 years, making a name for myself at AAPS, and then parlaying the recognition that I received into being elected as a section chair. And as my career developed, I started to differentiate myself further by writing. I started to write and edit books and book chapters. I never turned down an opportunity. Any time I was given an offer to write a chapter for a book I accepted. I was getting my name out there - I was building the Bonate Brand™.

If I were to ask “Am I a good pharmacometrician?”, I think (hope!) that most people would say yes. But why do you think that? You might say, “Because you’re Pete Bonate. You’ve written all those books. You’re famous! You’ve got groupies!” But unless you’ve worked with me, you have no idea whether I am actually any good or not. But because of my activities, and the things I’ve written, I have a level of authority that makes the things I say have credibility. I’ve turned the Bonate Brand™ into authority.

Today I am working to establish another component of the Bonate Brand™ – that of the great communicator. I got interested in public speaking because of my own failures as a modeler and not getting my models accepted by the teams that I worked with. To start my brand in this area I started preaching about communication and getting a proposal accepted into ACoP1 on Effective Communication. From there, I continued with such proposals and really advocating clear communication as a rate-limiting step to Pharmacometrician success. I think today my message has finally resonated through ISoP and I am seen as one of the pioneering champions in this area.

How do you go about building your brand? Is it necessary to volunteer at professional organizations like I did? Or write books? Or become a communications guru? Not necessarily. Start with identifying where you shine at work. For example, are you the resident expert in a particular methodology? If so, set a path to be seen as that person. This may require some self-promotion, which some people are uncomfortable with, but it is necessary to kick-start the process. Make sure people know you are using that methodology. Give an internal presentation or a tutorial on how to use the method. Submit posters and programming ideas to conferences on the method to give you that external visibility. Write an article on the method. Even try your hand at social media; maybe write a blog, or post something about the method on LinkedIn. Think about what your special set of skills are, and build your brand around it!

You might be asking yourself, why would I want to do this? This seems like total crap to me! The answer is that it sells you. Do you want that promotion? Do you want a raise? Do you want to get a better job? Who is a company going to hire? Who will the company promote? The nameless individual or the one they are aware of? All things being equal, it’s the one they are aware of. I can tell you that as a hiring manager, the first thing I do when I receive a CV is ask around: has anyone ever heard of this candidate? If so, what did they think of them? That’s their brand. Your brand matters!