BIOLOGICAL MODELING SPECIALTY SECTION NEWSLETTER

President's Message

Welcome to a new year of biological modeling and participation in the Biological Modeling Specialty Section (BMSS) of SOT. Our discipline is playing a key role in implementing the National Research Council's recommendations for "Toxicity Testing in the 21st Century". Research programs are underway in the U.S. and other nations that will be transforming the practice of risk assessment. Keeping up with the rapid pace of new developments and the data generated will require more efficient communication, collaborations and development of new information sources. ToXchange was initiated some 2 years ago by SOT to help meet this need. I encourage you to log-in to ToXchange and explore the information sources now available there to SOT/BMSS members. Let's continue to increase the use of this resource to communicate about events, funding sources, planned and ongoing research projects, open modeling positions and related announcements. Please contact me (bruckner@rx.uga.edu) or Hisham El-Masri (el-masri.hisham@epa.gov) with information you would like to have included on ToXchange or communicated directly to the BMSS membership. Hisham is our Web Site Liaison and ToXchange Site Administrator.

Inside this newsletter are: results of election of BMSS officers; selection of the 2011 Best Paper of the Year Award and the 2012 Perry J. Gehring Student Award winner; announcement of BMSS-sponsored/endorsed SOT events; details on the upcoming BMSS reception at the 2012 SOT meeting; and announcement of an upcoming international symposium.

Jim Bruckner
BMSS President

BMSS Reception – Monday March 12

This year's annual BMSS reception will be held on Monday, March 12, from 6:00 – 7:30 pm in Yuerba Salon 2 of the Marriott Marquis Hotel. Early on there will be ample time to renew acquaintances, catch up on the latest news and gossip, meet new people and enjoy yourself. Food, soft drinks and bottled water will be provided *ad libitum.* A cash bar and bartender will also be available. Your current BMSS Council members will be introduced, as will the new Vice President-Elect, Secretary/Treasurer, and Councilor. The winner of the 2012 Perry J. Gehring Student award will be recognized and her research poster displayed. Each author (in attendance) of the manuscript selected as the Best Paper of 2011 will be recognized and receive a plaque. Their work will be on display at the reception. To "top off" the evening, Dr. Nicole C. Kleinstreuer has kindly agreed to give an overview of agent-based multicellular computational modeling for predictive toxicology. Her Biosketch is provided below.

Biosketch of Dr. Nicole C. Kleinstreuer

Nicole's research focuses on mathematical and computational modeling of biological systems and their susceptibility to environmental and genetic perturbations that may result in disease outcomes. At the University of Canterbury, Christchurch, NZ, she developed a multi-scale mathematical model of renal blood flow autoregulation which was used to investigate the effects of hypertension and diminished nitric oxide production on kidney function. As a member of the National Center for Computational Toxicology at the U.S.EPA, she analyzes high-throughput data sets on large numbers of environmental chemicals and has developed *in vitro* bioactivity-based signatures from these data for toxicity mechanisms such as embryonic vascular disruption. As a member of the Virtual Embryo project, she uses computational systems biology approaches to link relevant information about molecular pathways and cellular processes into a cellular-agent-based model of embryonic vascular plexus formation that may serve as an *in silico* assay for predictive toxicology. This group is also applying similar computational techniques to other developing systems including limb-bud formation, lens invagination and neural crest migration.

2012 Election Results for the BMSS Council

Congratulations to: Harvey Clewell, our new Vice President-Elect; Eva McLanahan, our new Secretary-Treasurer; and Brad Reisfeld, our newest Councilor. Council members who will rotate to new positions include: Jim Bruckner, who will become Past President; Hisham El-Masri, who will become President; and Cecilia Tan, who will be Vice-President. Retiring from the Council, with many thanks for the great job he did over the past 4 years, is Rob Dewoskin. Thanks also to Jerry Campbell for serving faithfully as Secretary-Treasurer and to John Wambaugh for his contributions as a Councilor. The new BMSS Council will officially take office in May, 2012.

On behalf of the entire membership, our sincere thanks to the other BMSS members who volunteered to be on the ballot this year. These members included Andy Nong, Nina Ching Wang and Miyoung Yoon. The election was very close this year. We encourage you and other BMSS members to continue your interest in the BMSS Council and your active involvement in our section's activities.

For further information about the roles and responsibilities of each position, go to the BMSS By-Laws available at the SOT/BMSS Web site or feel free to contact current Council members.

2012 Perry J. Gehring Student Award for Excellence in Biological Modeling

This year's winner of the Gehring Student Award is Kathleen Holm for her research project entitled "Identifying the Sources of Uncertainty in the Process of Reconstructing Exposures to Carbaryl Using Exposure-to-Dose Modeling". Kathleen is a postdoctoral fellow working at the U.S.EPA National Exposure Research Laboratory under the supervision of Cecilia Tan. Co-authors of the study included Cecilia Tan, Miyoung Yoon, Bruce Young, Harvey Clewell, Rogelio Tornero-Velez, Rocky Goldsmith, Daniel Chang, Christopher Grulke, and Curtis Dary. The poster will be displayed at the BMSS reception. Kathleen will receive a plaque and $500, from the Endowment fund, in recognition of her award.

Other applicants for the Gehring Award included Michelle Carroll, Susie Crowell, Yen Low, Raja Settivari, Marc-Andre Verner, Li Zhenhong and Chi Zhang. A number of the research projects were excellent, resulting in tight scoring.

2011 Best Modeling Paper Award

The Best Modeling Paper Award goes to Paul Hinderliter, Paul Price, Michael Bartels, Chuck Timchalk and Torka Poet for their work entitled "Development of a Source-to-Outcome Model for Dietary Exposures to Insecticide Residues: An Example Using Chlorpyrifos". Their manuscript described a PBPK/PD model that linked differences in dietary exposure with inhibition of erythrocyte and brain acetylcholinesterase (AChE) activity in 3- and 30-year old humans. A description of variation in individual physiology, metabolism, and activity levels was included to account for their impact on AChE. Interestingly, the influence of population variability on AChE activity was relatively minor at low chlorpyrifos exposure levels. This source-to-outcome model demonstrates the utility of merging different types of models in toxicology and risk assessment.

The other finalists for best 2011 modeling paper were:

Jack, J., Wambaugh, J.F. and Shah, I. (2011). Simulating quantitative cellular responses using asynchronous threshold Boolean network ensembles. *BMC Systems Biol* 5: 109.

Price, P.S., Schnelle, K.D., Cleveland, C.B., Bartels, M.J., Hinderliter, P.M., Timchalk, C. and Poet, T.S. (2011). Application of a source-to-outcome model for the assessment of health impacts from dietary exposures to insecticide residues. *Regul. Toxicol. Pharmacol.* 61: 23-31.

Low, Y., Uehara, T., Minowa, Y., et al. (2011). Predicting drug-induced hepatotoxicity using QSAR and toxicogenomics approaches. *Chem. Res. Toxicol.* 24: 1251-1262.

Judson, R.S., Mortensen, H.M., Shah, I., Knudsen, T.B. and Elloumi, F. (2012). Using pathway modules as targets for assay development in xenobiotic screening. *Mol. Bio. Syst* 8: 531-542.

Wang, N.C.Y., Venkatapathy, R., Bruce, R.M. and Moudgal, C. (2011). Development of quantitative structure-activity (QSAR) models to predict carcinogenicity potency of chemicals. II. Using oral slope factor as a measure of carcinogenic potency. *Regul. Toxicol. Pharmacol.* 59: 215-226.

The committee that selected the best paper was formed from volunteer members of BMSS. Members were Hugh A. Barton (Chair), Jim Bruckner, Ravi Dugyala, Sudin Bhattachara, Eva McIanahan, Ted Simon, and Marc Verner. Papers published either electronically or in hard copy from January to December, 2011, were considered. The review process included an initial screening of hundreds of abstracts obtained by electronic searching and nominations from BMSS members, followed by reading and ranking of the top six papers according to a number of criteria. The selection process was difficult, due to the wide range of topics and modeling approaches considered.

BMSS Sponsored and Endorsed Sessions at the 2012 Annual SOT Meeting

Discovering Novel Hypotheses for Mechanisms of Toxicity from High-Content Data Sets
Wednesday 3/13/2012 ~ 1:30 PM to 4:15 PM
Workshop Session
Characterizing Toxic Modes of Action and Pathways to Toxicity
Sponsor: Biological Modeling Specialty Section
Endorsed by: Molecular Biology Specialty Section

The Use of Physiologically Based Pharmacokinetic Modeling to Inform Early Life Sensitivity to Chemical Toxicity
Sunday 3/11/2012 1:15 PM to 5:00 PM
Continuing Education
Drug Metabolism
Sponsor: Risk Assessment Specialty Section
Endorsed by: Biological Modeling Specialty Section and Regulatory and Safety Evaluation Specialty Section

Upcoming Workshop on Integration of Human Health & Environmental Data

I recently sent everyone an announcement of a workshop/conference organized by SOT's Risk Assessment Specialty Section (RASS). RASS and BMSS are co-sponsoring this international conference, which is entitled "Building Better Decisions: Multi-Scale Interpretation of Human Health and Environmental Data". The event is partially funded by the SOT Contemporary Concepts in Toxicology (CCT) Meeting Initiative.

The major focus of the conference is exploring new approaches to integration of exposure and dose-response modeling outputs. It is being held May 8 – 11, 2012, at the U.S.EPA in Research Triangle Park, NC. The Advanced Registration Deadline is February 1 – April 15, 2012. The Abstract Deadline has been extended to March 23, 2012. Specific information may be obtained at: https://www.toxicology.org/ai/meet/cct_b4bd.asp

Contribute to the Perry J. Gehring Biological Modeling Student Award Fund

This is a "net asset restricted" endowment fund, which means that the net asset base cannot be spent. Only a percentage of the base is available each year to support and recognize students. In 2010 – 2011, SOT's Endowment Fund Board (EFB) authorized use of up to 4% ($1,312) of the net assets of $32,789. The most current balance is $29,656, down from $33,321 in July of 2011. The EFB authorized expenditure of $1,332.83 in 2012. Kathleen Holm will receive $500 from this authorized amount for winning the Perry J. Gehring Student Award.

The good news is that SOT/BMSS members can make tax deductible contributions to the fund to increase its net asset base, and thereby increase the funds available each year for student awards and support. As you review your tax

deductible charitable contributions, please consider donating to this very worthwhile fund and to the future of our biological modeling graduate and postdoctoral students.

The 2012 BMSS Numbers Corner (as of 02/16/12)

Number of active members: 145 (increase of 5 over last year)
Operating Funds: $11,783 (~ same as last year)
Gehring Fund Net Assets: $29,656
Gehring Funds Available: $1,332.83