Midwest Regional Chapter
Society of Toxicology

Fall 2018

The MRC-SOT
Proudly Presents the
Annual Fall Meeting

October 12, 2018
University of Wisconsin-Madison Pyle Center
Madison, WI

Using Artificial Intelligence and Machine Learning to Advance Toxicology Research

Sponsored by:
University of Wisconsin-Madison / UMASS Boston
George M. O'Brien Center for Benign Urologic Research

Registration Information

The Midwest Regional Chapter of the Society of Toxicology is proud to present the 2018 Fall Meeting and career outreach event. The meeting will take place on Friday, October 12th from 12:00 pm to 4:00 pm at the Pyle Center, University of Wisconsin-Madison. The topic will focus on using artificial intelligence and machine learning to advance toxicology research.

Prior to the meeting, students and postdocs will also have the opportunity to gain first-hand knowledge of the drug discovery and development process by attending a tour of the Covance facility from 9 to 11:30 am on October 12. The event will be open to 30 students and postdocs on a first-come-first-served basis.

Link to online registration: https://www.aim-hq.com/netForumSOT/eweb/DynamicPage.aspx?Site=SOT&Webcode=EvtRedirector&RegPath=EventRegFees&REg_evt_key=7dfd144e-c380-42cf-8d72-e0c252bc3ffa&evt_title=MRC2018SP

On-line registration open: Now
On-line registration close: October 4, 2018

Registration Cost
Midwest Regional Chapter of the Society of Toxicology Members: $50
Non-members: $75
Graduate Students: $10
Undergraduates: $0

President's Message

Hello MRC-SOT members,

The Midwest Regional Chapter is proud to present the 2018 Fall meeting and career outreach event. The meeting will take place on Friday, October 12th from 12:00 pm to 4:00 pm at the Pyle Center, University of Wisconsin-Madison. The topic will focus on using artificial intelligence and machine learning to advance toxicology research. Students and postdocs will also have the opportunity to gain first-hand knowledge of the drug discovery and development process by attending a tour at Covance at 9 am to 11:30 am on Oct 12th. The event will be open to 30 students and postdocs on a first-come-first-serve basis. The detailed information, including meeting registration, directions, and scientific program can be found in the newsletter. Many thanks to our President-Elect/Program Chair, Chad Vezina, and Dr. Lisa Biegel (Covance) for their efforts in coordinating the fall meeting and the career outreach event.

On behalf of the executive committee, I would like to thank you for the continued support of our regional chapter.

Thanks again,
Wei Xu

Want to know more about the Midwest Regional Chapter?

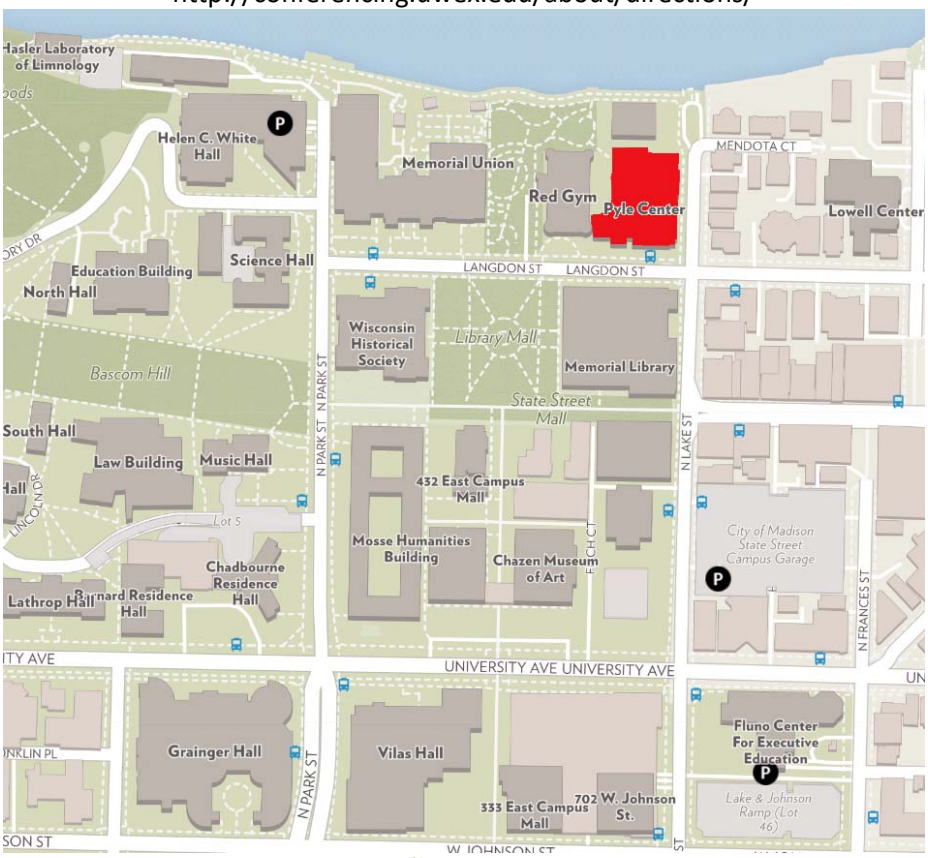
Regional Chapter newsletters, information pertaining to membership, MRC-SOT awards, and nomination/application forms may be viewed or printed from our website:
http://www.toxicology.org/groups/rc/midwest/index.asp

Meeting Location

University of Wisconsin-Madison Pyle Center, 702 Langdon St, Madison, WI 53706
Phone: (608) 262-1122
http://conferencing.uwex.edu/about/pyle-center/

Map of Meeting Location (The Pyle Center is in Red)

http://conferencing.uwex.edu/about/directions/



Parking

Lot 6 – Helen C. White Garage ($14/day/vehicle)
600 N Park St, Madison, WI 53706

Lot 83 – Fluno Garage ($12/day/vehicle)
601 University Ave, Madison, WI 53715

City of Madison State Street Garage ($1.50/hr/vehicle)
430 N. Frances St. (Frances St. side) Madison, WI

For parking inquiries, please contact the Pyle Center front desk at 608-262-1122.

Covance Labs Tour

Limited to 30 applicants, first come, first serve

Covance East Side Lab, 3301 Kinsman Boulevard, Madison, WI 53704

Phone: (608) 241-4471

Tour Meeting Location and Instructions

Participants should come to the Main Visitor entrance of the Lab (East Side Lab on the map; it is a big building with lots of glass). There are a limited number of parking spots (including handicap parking) in the circle in front of the main entrance and additional visitor parking in the lot just to the right of the building as you enter the site. Security will have name tags and confidentiality forms in the main entrance. **Please meet at 9am. The tour will conclude at 11:30 am.**

MRC-SOT Fall Meeting

October 12, 2018

"Using Artificial Intelligence and Machine Learning to Advance Toxicology Research"

Career Outreach (RSVP Required)
9:15 – 11:30 am

Registration & Luncheon
12:00 – 1:00 pm

Welcome and Introductions
Wei Xu, President, University of Wisconsin-Madison
Chad Vezina, President-Elect
UW-Madison
1:00 – 1:15 pm

Presentations

Charles David Page Jr, PhD
University of Wisconsin-Madison
Machine Learning for Phenotyping and -Omics Data
1:15 - 2:00 pm

Hao Zhu, PhD
Rutgers University at Camden
Big data in computational toxicology: predictive animal toxicity modeling using data-driven profiling and mechanism-driven read-across
2:00 - 2:45 pm

Refreshment Break
2:45 – 3:00 pm

Robert Tanguay PhD, Keynote
Oregon State University
Tackling the 'mixtures problem' using zebrafish
3:00 – 3:45 pm

Concluding Remarks
Chad Vezina, President-Elect
University of Wisconsin-Madison

Machine Learning for Phenotyping and -Omics Data

Charles David Page, PhD
Professor
Department of Biostatistics and Medical Informatics
and Department of Computer Sciences
School of Medicine and Public Health
University of Wisconsin-Madison
Wisconsin Institute of Discovery (WID)

Abstract

Machine Learning is in the news frequently and already has a history in toxicology. This talk will introduce machine learning, sample a bit of its history in toxicology, and then illustrate machine learning with two recent lines of work. One line of work uses machine learning from RNA-seq data taken from a 3D model of developing neural tissue exposed to neurotoxins or non-neurotoxins, with a goal of determining if a new compound is a neurotoxin from the gene expression signature it elicits in this tissue model. Another line of work uses electronic health records to do "electronic phenotyping" of patients, with potential applications to assessing response to chemical exposures.

Biosketch

David Page has over thirty years' experience in machine learning research and twenty years' experience in bioinformatics and clinical research informatics, especially in applying machine learning to biomedical data. He has been faculty lead for the UW Carbone Cancer Center's Cancer Informatics Shared Resource for fifteen years. He directed the data analysis for the International Warfarin Pharmacogenetics Consortium's *NEJM* publication on Warfarin dosing, served on the scientific advisory boards for the Observational Medical Outcomes Partnership and the Wisconsin Genomics Initiative, directed the EHR project in UW-Madison's NIH BD2K Center, and served as a management committee member in UW-Madison's NLM-funded training program in biomedical informatics. He has experience applying machine learning to a wide variety of biomedical data types including electronic health records (EHR), changes in gene expression with disease or treatment exposure, mass spectrometry proteomics, and genome sequence data.

Big data in computational toxicology: predictive animal toxicity modeling using data-driven profiling and mechanism-driven read-across

Hao Zhu, PhD
Associate Professor
Graduate Program Director
Department of Chemistry
The Rutgers Center for Computational & Integrative Biology
Rutgers University at Camden

Abstract

We aimed to develop an automated method to extract useful biological data from a public repository (i.e. PubChem) as bioprofiles for target compounds and incorporate both chemical structure information and bioprofiles into a read-across study to assess chemical toxicity. To achieve this goal, we used a database containing 7,385 compounds with diverse animal acute toxicity results (i.e. rat oral acute toxicity) to search against PubChem for their bioprofiles. Using a novel subspace clustering algorithm, we identified several groups of PubChem assays which may reflect similar biological mechanisms. We used these assay groups to perform read-across for acute toxicity. Assays relevant to toxicity predictions were identified by a cross-validation procedure within the modeling set. Then, a set of over 600 new compounds obtained from a new resource was used to validate the predictivity of the resulted models. Nineteen assay clusters showed high predictivity for chemical toxicants (positive prediction rates range from 62.19% to 100.00%) through a cross validation process. Incorporating individual clusters into a consensus model, we were able to prioritize chemical toxicants in the validation set (positive prediction rate as 76%). Additionally, we show that imputing data gaps for compounds lacking bioassay data high predictivity can still be obtained for compounds with certain chemical features. Furthermore, the chemical-in vitro-in vivo relationships existing within clusters can be used to illustrate toxicity mechanisms for animal acute toxicity. In this study, we developed a new data-driven profiling method to automatically extract and optimize biological data from the public big data landscape for target compounds. The read-across was performed not only to accurately predict and prioritize potential chemical toxicants for future animal studies but also to reveal toxicity mechanisms. This read-across strategy can be applied to develop predictive models for other complex toxicity endpoints.

Biosketch

Dr. Zhu has dedicated 10 years to developing predictive toxicology models to assess chemical toxicity in vitro, in vivo and in human beings. With the research background across chemistry, informatics, and toxicology, his toxicology research is driven by progressively more available public data, two papers he published in 2014 were recognized as the pioneering research effort to demonstrate the value of using big data in computational toxicology. The originality of his current research is to construct dynamic predictive models built upon all available public big data sources, rather than fixed models based on in-house data. Since 2014, he has developed the Chemical In vitro-In vivo Profiling (CIIPro) web portal (ciipro.rutgers.edu) as a depository tool. This effort will benefit the whole toxicology community by sharing modeling approaches and optimized toxicity databases from public big data sources. Currently the CIIPro is being used to evaluate the chemical toxicity by National Center for Computational Toxicology (NCCT) at US EPA.

Tackling the 'mixtures problem' using zebrafish

Robert Tanguay
Distinguished Professor of Research
Department of Environmental and Molecular Toxicology
Director, Oregon State University Superfund Research Program
Director, Sinnhuber Aquatic Research Laboratory
Director, OSU Environmental Health Sciences Center
Director, NIEHS training program in toxicology
Oregon State University, Corvallis, OR

Abstract
Human exposures always occur as mixtures, yet most toxicological investigations continue to evaluate the risk of one chemical at a time and increasingly evaluations are performed in simple biological systems. Polycyclic aromatic hydrocarbons (PAHs) are widespread environmental contaminants that occur in dynamic mixtures. Several PAHs are carcinogens, but there is increased human data indicating that PAH exposures produce other adverse health effects. For example, recent epidemiological data indicates strong associations between early life stage PAH exposures and increases in neurobehavioral deficits. It is not yet possible to predict developmental outcomes following PAH exposures forcing decision makers to assume that PAHs share common mechanisms of developmental action. We have taken systems approaches using the zebrafish model to begin to evaluate, classify and define the mechanisms of PAH toxicity. Our research platform uses high throughput screening where developmental morphological and behavioral endpoints are assessed following developmental exposures to PAHs and mixtures. A large set of PAHs including parent, nitrated, oxygenated, hydroxylated, methylated, heterocyclic, and aminated structures produced complex biological response patterns. To begin linking PAH structure to underlying adverse outcome pathways, we have obtained genome-wide gene expression profiles using RNA-sequencing. Distinct patterns of gene expression have emerged providing finer resolution to help classify PAHs. Finally, we have determined that a number of PAHs produce later life stage effects following short-term developmental exposures. This presentation will summarize our current understanding of PAH developmental toxicity and suggest that surrogate zebrafish data may provide the foundation for predicting the toxicity of mixtures of PAHs.

Biosketch
Dr. Tanguay received his BA in Biology from California State University-San Bernardino in 1988, his PhD in Biochemistry from the University of California-Riverside in 1995 and postdoctoral training in Developmental Toxicology from the University of Wisconsin-Madison 1996-1999. He serves on a number of academic, commercial and federal advisory boards and is on the editorial board for several scientific journals. He has authored more than 250 manuscripts and book chapters across numerous disciplines. Over the past several years, he has pioneered the use of zebrafish as a systems toxicology model and recently developed automated high throughput instrumentation and workflow to accelerate discoveries in zebrafish. A major focus in on identifying chemicals and mixtures that produce neurotoxicity. Phenotypic anchoring coupled with the inherent molecular and genetic advantages of zebrafish are used to define the mechanisms by which chemicals, drugs and nanoparticles interact with and adversely affect vertebrate development and function. These tools are also now routinely used to assist in the development of inherently safer chemicals and nanoparticles.

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