Description:

My emphasis is to teach physiologically-based pharmacokinetic (PBPK) modeling at a very basic level. The ultimate goal is that, at the end of the Workshop, participants can do their own PBPK modeling work using their own software (acquired for this Workshop as detailed below) and computers. For those of you whose primary interest is to understand application of PBPK modeling to risk assessment rather than to become PBPK modelers, my line-by-line detailed explanation and instruction of the code, as well as hands-on exercises, will enhance tremendously your appreciation of PBPK modeling and your risk assessment capability. Most of the lectures will be integrated with hands-on computer simulation exercises. The exercises will illustrate different modeling techniques. Participants needs only beginning background in calculus (don’t be afraid of calculus; we use relatively little of that and I will review it slowly and clearly at the beginning). As biology and toxicology are the “drivers,” participants are expected to have more thorough and advanced understanding in biology and toxicology. However, principles and concepts in mathematics, chemical engineering, biology, chemistry, toxicology, etc., will be conveyed slowly and clearly with plain English to achieve the learning objectives. Throughout the years, we have improved the design of this Beginners’ Workshop in such a way that it is very user friendly. Thus, in this Workshop, participants will learn how to create, modify, and utilize PBPK models for a number of chemicals and a nanoparticle using
Berkeley Madonna as a software. Participants will obtain these skills through extensive “hands-on” practice with simple models that grow in complexity as the Workshop progresses. Berkeley Madonna is a user-friendly and inexpensive software ($49 to $299/each depending on your professional status and whether or not ordering as a group) that can nevertheless handle most PBPK modeling needs. Each participant will need to bring a laptop with Berkeley Madonna installed prior to the first day of Workshop. It is important for each participant to have access to the modeling software for the tutorial modeling exercises in order to get the most out of the Workshop. The software may be downloaded at www.berkeleymadonna.com. The license fee is a one-time fee only and you will own this software for your modeling needs henceforth. Two other software, a data-capturing tool for digitizing figures in published papers (GetData Graph Digitizer; http://www.getdata-graph-digitizer.com/ USD$30) and an open-source dose-response modeling software [Benchmark Dose Software (BMDS) Version 2.2; http://www.epa.gov/NCEA/bmds/dwnldu.html] from the USEPA, will be used in our Workshop as well. These software should be installed on your laptop as well prior to coming to the Workshop. All the class material, in PDF format, will be given to the participant during the Workshop. Prior to the start of the Workshop, some introductory papers on PBPK modeling will be provided so the participants may obtain some basic background. During the Workshop, there will be debugging exercises. Please note that you will get more out of the Workshop if you are willing to put in more effort.

Instructor:

Raymond S. H. Yang, Ph.D., is Professor Emeritus of Toxicology and Cancer Biology, Quantitative and Computational Toxicology Group, Department of Environmental and Radiological Health Sciences, Colorado State University. Dr. Yang has more than 40 years of experience in academic, industrial and government research settings including the National
Institute of Environmental Health Sciences/National Toxicology Program (NIEHS/NTP), Union Carbide Corporation, North Carolina State University, Cornell University, Albany Medical College, Colorado State University, and the USEPA National Center for Environmental Assessment (NCEA) at Cincinnati. His research interests include toxicology of chemical mixtures, toxicologic interactions, carcinogenesis, developmental toxicology, and physiologically-based pharmacokinetics/pharmacodynamics (PBPK/PD) and other biologically-based computer modeling. He has had extensive experience in training and mentoring graduate students, postdoctoral fellows, junior and senior faculty members and he created and developed an interdisciplinary research program on Quantitative and Computational Toxicology at Colorado State University. Since 1992, Dr. Yang has organized 22 national and international workshops on PBPK/PD Modeling and Risk/Safety Assessment at Colorado State University (1992, 1994, 1996, 1999, 2001, 2003, 2005, 2008, 2009, 2010, 2011, 2012, 2013), Pfizer Inc., Groton, CT (October 2002), California Environmental Protection Agency/OEHHA, Oakland, CA (September 2000), the National Health Research Institutes, Zhunan, Taiwan (August-November, 2006), and USEPA, National Center for Environmental Assessment (NCEA), Cincinnati (April-May 2008; March-August 2009), and British American Tobacco, Southampton, UK (November 2009), California Environmental Protection Agency/Department of Pesticide Regulation, Sacramento, CA (two Workshops in May and September, 2011), California Environmental Protection Agency/OEHHA, Sacramento, CA (August-September, 2011).

Workshop Schedule:

This Workshop is a one-week concentrated effort starting 8:00 am and ending 5:00 pm Monday through Friday with two coffee breaks and a lunch break daily.

Monday, August 04, 2014
Tuesday, August 05, 2014

8:00 am     PBPK Modeling: Numerical Integration and a Three-compartment PBPK Model (Fat, Richly and Poorly Perfused Compartments)
9:45 am     Break
10:15 am    PBPK Modeling: The Liver and Metabolism
12:00 pm    Lunch
1:00 pm     PBPK Modeling: Experimental Issues and Data
2:45 pm     Break
3:15 pm     PBPK Modeling: An Oral PBPK Model (Gavage/Bolus)
4:30 pm     Debugging Exercise
5:00 pm     End of Day 2

Wednesday, August 06, 2014

8:00 am     PBPK Modeling: An Oral PBPK Model (Drinking Water)
9:45 am     Break
<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
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<tbody>
<tr>
<td>10:15 am</td>
<td>PBPK Modeling: Protein Binding and Related Issues</td>
</tr>
<tr>
<td>12:00 pm</td>
<td>Lunch</td>
</tr>
<tr>
<td>1:00 pm</td>
<td>Recreate a PBPK Model Published in the Literature I (1,1,1-Trichloroethane; Adapted from an actual project from the USEPA/NCEA-DC )</td>
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<tr>
<td>2:45 pm</td>
<td>Break</td>
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<tr>
<td>3:15 pm</td>
<td>Recreate a PBPK Model Published in the Literature II (1,1,1-Trichloroethane; Adapted from an actual project from the USEPA/NCEA-DC )</td>
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<tr>
<td>4:30 pm</td>
<td>Debugging Exercise</td>
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<tr>
<td>5:00 pm</td>
<td>End of Day 3</td>
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</tbody>
</table>

Thursday, August 07, 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00 am</td>
<td>Recreate a PBPK Model Published in the Literature III (1,1,1-Trichloroethane; actual project from USEPA/NCEA-DC; Non-cancer Risk Assessment Applications)</td>
</tr>
<tr>
<td>9:45 am</td>
<td>Break</td>
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<tr>
<td>10:15 am</td>
<td>Sensitivity, Variability, and Monte Carlo Simulation</td>
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<tr>
<td>12:00 pm</td>
<td>Lunch</td>
</tr>
<tr>
<td>1:00 pm</td>
<td>Methylene Chloride as an Example for Cancer Risk Assessment and PBPK Applications</td>
</tr>
<tr>
<td>2:45 pm</td>
<td>Break</td>
</tr>
<tr>
<td>3:15 pm</td>
<td>Bayesian Population PBPK Modeling/Markov Chain Monte Carlo Simulation: Methylene Chloride as an Example (Risk Assessment Applications)</td>
</tr>
<tr>
<td>4:30 pm</td>
<td>Debugging Exercise</td>
</tr>
<tr>
<td>5:00 pm</td>
<td>End of Day 4</td>
</tr>
</tbody>
</table>
6:00 pm Class dinner/outing downtown Fort Collins

**Friday, August 08, 2014**

8:00 am PBPK Modeling of Human Lactational Transfer of PCB153 Comparing to Worldwide Biomonitoring Results (Public Health Applications)
9:45 am Break
10:15 am Reverse Dosimetry Modeling: PBPK Modeling of Human Lactational Transfer of PCB153 from Canadian Inuit Biomonitoring Results and Case Study (Public Health Applications)
12:00 pm Lunch
1:00 pm PBPK Modeling of a Nanoparticle: Quantum Dot 705
2:45 pm Break
3:15 pm Future Perspectives: Computational Toxicology and Risk Assessment
4:30 pm Wrap Up
5:00 pm End of Day 5

**Registration and Fees:**

Class size is limited to 15 attendees; the small size of the class would enhance personal attention and accommodate questions, solutions, and discussions. You will be able to register on-line at [https://conferencereg.colostate.edu/PBPK2014](https://conferencereg.colostate.edu/PBPK2014) The registration fee of $2,500.00 covers the full one-week course including: lectures, computer laboratories, class materials, refreshment breaks, and Class Dinner/Outing on Thursday evening. A limited number of Fellowships at USD$1,250 (thus reduced registration fee of $1,250.00) are available for full-time graduate students from
other Institutions worldwide. To apply, please send letter stating your research interest to: raymond.s.h.yang@gmail.com

Cancelling and Refund Policy:

The Workshop will be cancelled if a minimum of five registrants is not reached. Cancellation by Dr. Yang: 100% refund.
Cancellation by the registrants: 50% refund before 31 May 2014; 25% refund before 30 June 2014; beyond 30 June 2014, there will be no refund but credit will be given for either a substitute, or for 2015 Workshop minus the expenses already incurred.

**Colorado and Fort Collins:**

August in Colorado is absolutely beautiful and comfortable. Depending on the consensus of the participants, Dr. Yang is open to re-arranging the Workshop such that we may visit the Rocky Mountain National Park on Friday afternoon.

Fort Collins is a community of more than 126,000 located 65 miles north of Denver and 45 miles south of Cheyenne, Wyoming. At the foot of the Rocky Mountains, Fort Collins is within an hour’s drive of such major recreation areas as Estes Park, Red Feather Lakes, Cache la Poudre River (“Colorado’s Trout Route”), and several mountain peaks including the 790,000-acre Roosevelt National Forest and Rocky Mountain National Park. Horsetooth Reservoir, a man-made boating and recreation area, is a 10-minute drive from campus. At an elevation of 5,000 feet, Fort Collins enjoys a clear, cool, dry climate. For more information, please go to [http://www.ci.fort-collins.co.us/](http://www.ci.fort-collins.co.us/)

**Testimonials of the Workshop:**

The testimonials below are mostly from individuals without any prior modeling background:

“...The quality of this Workshop was simply superb...Your passion for teaching others was evident. Thank you for balancing the hard core stuff with historical descriptions...”

“...This Workshop contains so many excellent lectures that is difficult to select only one as best overall...”
“...The course was excellent! It was great to be able to actually perform the hands-on modeling & write our own codes, instead of using models that were already created for us and just ‘playing’ with them...”

“...Excellent course. Lectures were designed such that it was not difficult to stay focused on this difficult material for long periods of time...”

“...It was one of the best courses that I have ever taken...”

“...Very clear, very good course for beginners...”

“...The materials were presented in such a basic level that, literally, people walk off the street could follow the lectures...”

“...Exactly what I needed to get started...”

“...Perfect for me...”

“...The Workshop was everything I expected...”

“...The first two days were very informative – great background info...”

RSHY/02/Feb/2014