

# Workshop Lecturers and Trainers



### Qiang Zhang, M.D., Ph.D., Course Director

Starting as a biomedical scientist, Dr. Zhang is a computational biologist interested in using simulations to understand how biological systems behave in response to perturbations. His research has focused on the nonlinear dose response behavior arising from cellular homeostatic control and the genetic toggle switch underlying irreversible binary cell fate decisions.



### Melvin E. Andersen, Ph.D., CIH, D.A.B.T.

Dr. Andersen pioneered the use of PBPK modeling in toxicology and in safety and risk assessments. In recent years, his research emphasis has been on developing mathematical descriptions of the control of genetic circuitry and the dose response and risk assessment implications of these control processes.



### Sudin Bhattacharya, Ph.D.

With a background in particle-based modeling in materials science and engineering, Dr. Bhattacharya is currently developing computational models of signal transduction and gene regulatory networks underlying terminal differentiation of B lymphocytes into plasma cells and inflammatory response in the liver, and investigating how dioxin-like toxicants perturb these cellular pathways.



### Courtney Woods, Ph.D.

With educational training in Chemical Engineering and Toxicology, Dr. Woods has used genomics techniques to study the mechanism of hepatotoxicity of environmental and pharmaceutical compounds in mouse models. Her current research focuses on identifying molecular mediators involved in transcriptional regulation of anti-oxidant response to chlorine and developing computational models of the anti-oxidant response pathway in mammalian cells.

### Course Advisors

We wish to thank our advisors: Dr. Rory B. Conolly, National Center for Computational Toxicology, US Environmental Protection Agency, and Dr. Harvey J. Clewell, III, Director, Center for Human Health Assessment, The Hamner Institutes for Health Sciences for continuing direction and contributions to course content.

# General Information

## Workshop Fee

General . . . . .	\$1,600
Government Employee . . . . .	\$1,200
Graduate Student and Postdoctoral Fellow . . . . .	\$1,000

## Workshop fee includes:

- Tuition and computer laboratory
- Comprehensive take-home course materials
- Continental breakfast
- Daily lunch
- Refreshment breaks
- Certificate of attendance

## Registration and Payment Policy

Class size is limited to 40 attendees. Reservations will be accepted on a first-come, first-served basis upon receipt of the registration form with full payment. Please fill out the attached registration form and return it with full payment in U.S. funds to Ms. Jeanne Galbo by mail no later than **August 22, 2008**. Only payment by check is accepted.

Please make check payable to: The Hamner Institutes for Health Sciences.

Return to:  
Ms. Jeanne Galbo  
The Hamner Institutes for Health Sciences  
6 Davis Drive  
P. O. Box 12137  
Research Triangle Park, NC 27709-2137 USA

All requests for substitutions or cancellations must be made in writing and received by **August 29, 2008**. Substitutions may be made with an additional charge. Cancellations made on or before August 29, 2008 will be issued a refund of 80%. Cancellations received after August 29, 2008 will be issued a refund of 50%. Please contact Ms. Jeanne Galbo (jgalbo@thehamner.org) for questions regarding registration and payment policy.

**Please contact Dr. Qiang Zhang (qzhang@thehamner.org) for course-specific questions and to obtain a reading list.**

## Suggested Accommodations

Please note that you should make your own reservation directly with the hotel. The Hamner Institutes has reserved a limited number of rooms at a conference rate of \$139 per night (plus tax) at the Radisson Hotel Research Triangle Park. When you contact the hotel, please ask for "The Hamner Dose Response Modeling Workshop" rate. The rate will be reserved until 5:00 p.m. September 12, 2008.

Radisson Hotel Research Triangle Park  
NC54 & I-40 at Davis Drive (Exit 280)  
Research Triangle Park, NC 27709  
Phone: (919) 549-8631

# Computational Systems Biology and Dose Response Modeling Workshop

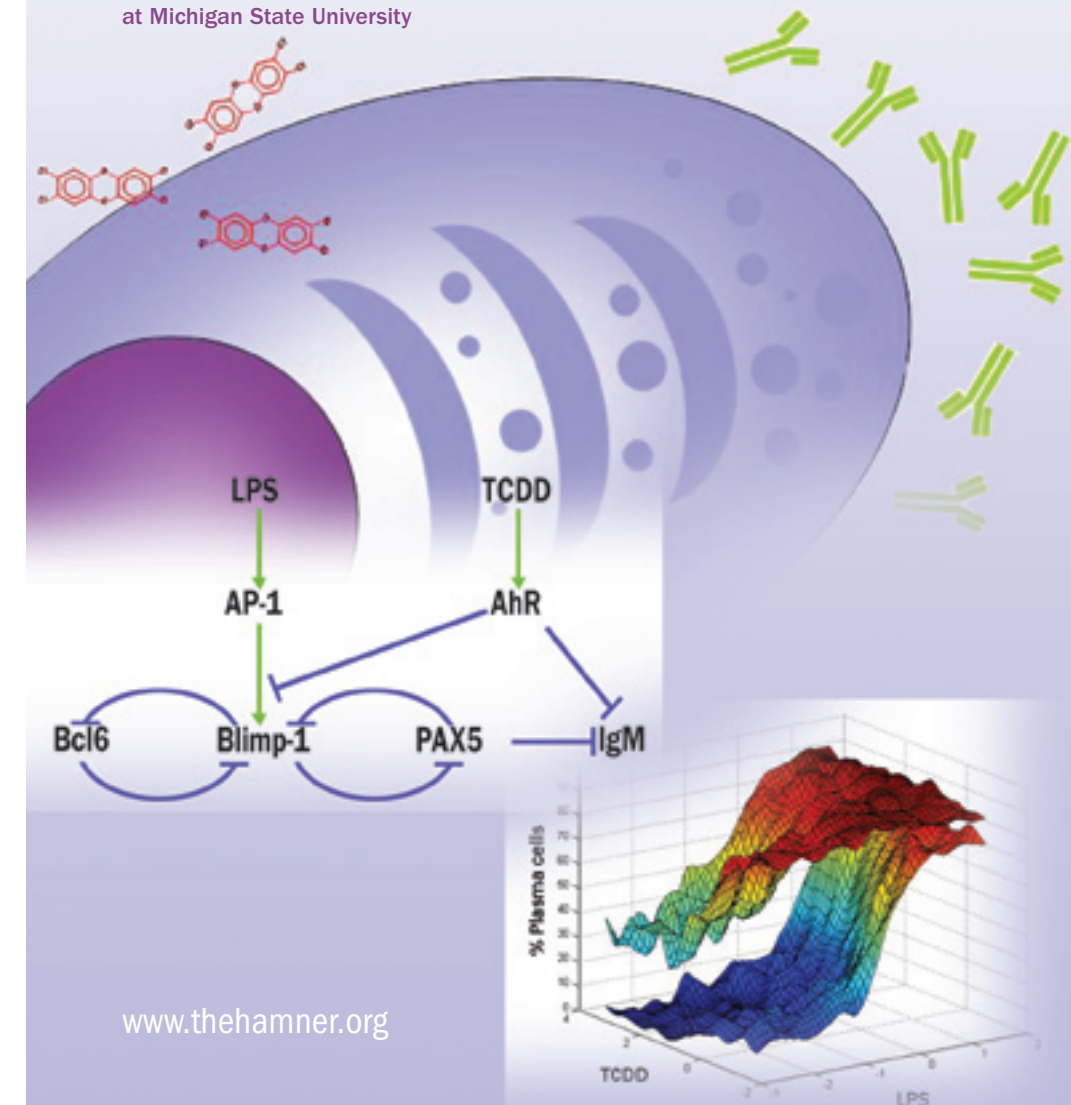
September 22 – September 26, 2008

In this course you will learn:

- Current computational modeling techniques for the quantitative investigation of how biological systems respond to perturbations at the cellular level
- Common themes in signal transduction and gene regulatory networks that underlie systems-level cellular behaviors including homeostasis, adaptation, threshold response, binary cell fate decisions, and irreversible differentiation
- To use these techniques to develop computational models for understanding and predicting dose response behaviors of drugs and environmental agents

Division of Computational Biology  
The Hamner Institutes for Health Sciences

With support from the Superfund Basic Research Program  
at Michigan State University



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# Agenda

## Monday, September 22

<b>Morning</b>	Welcome, introductions and course overview Computational dose response modeling – background Response motifs in quantitative cell signaling and dose response
<b>Afternoon</b>	Introduction to Berkeley Madonna® Exercise 1: Synthesis/degradation motif Exercise 2: Reversible binding motif Exercise 3: Homo-multimerization Exercise 4: Zero-order ultrasensitivity Exercise 5: Hill function

## Tuesday, September 23

<b>Morning</b>	Binary decision-making in biological systems MAPK-mediated ultrasensitivity and bistability
<b>Afternoon</b>	Exercise 1: A bistable gene auto-regulation model Exercise 2: MAPK ultrasensitivity and bistability – modeling <i>Xenopus</i> oocyte maturation

## Wednesday, September 24

<b>Morning</b>	Response motifs – repeating components controlling biological function Exercise 1: Type I coherent feedforward Exercise 2: Type I incoherent feedforward Exercise 3: Sequential gene activation
<b>Afternoon</b>	The eukaryotic cell cycle and checkpoint control Exercise: Modeling a simple cell cycle circuit and checkpoint control

## Thursday, September 25

<b>Morning</b>	Cellular homeostasis, adaptation and steady-state dose response Oxidative/electrophilic stress response
<b>Afternoon</b>	Exercise 1: Negative feedback and homeostasis (Part I) Exercise 2: Negative feedback and homeostasis (Part II)

## Friday, September 26

<b>Morning</b>	Stochasticity in gene expression and its implication for dose response Computational biology, dose response modeling and risk assessment: where to from here?
<b>Afternoon</b>	Optional Exercise: Switching through activation of cellular circuits and biological consequences (with demonstration of stochastic modeling tool)

## What you will learn:

- The quantitative concepts underlying cell signaling and gene regulation
- How molecular circuits comprising genes, proteins, and their interactions give rise to different dose response behaviors
- The shapes of dose response curves in feedback/feedforward-mediated cellular homeostatic systems
- The molecular engine driving the cell cycle and checkpoint control, and its implications for modeling dose responses with respect to cell proliferation
- How binary (either/or) decisions are made and how cells remember the results of these decisions
- The noisy (stochastic) nature of gene expression and its implications for the shapes of dose response curves
- Approaches to modeling signal transduction and gene regulatory networks
- To use programs such as Berkeley Madonna for computational modeling of cellular response to perturbations

## Who should attend?

- Researchers interested in applying computational systems biology to modeling dose response behaviors of drugs and environmental agents, and understanding the underlying cellular mechanisms
- Risk and safety assessment professionals who would like to link dosimetry models to biologically-based cellular response models
- Toxicologists and pharmacologists interested in applying quantitative simulation tools to interpreting *in vitro* cellular response data

## Course Registration Form

Name		
Degree		
Title		
Organization		
Department		
Address		
City	State	Zip
Work Phone	Fax	Email
Workshop Fee		
<input type="checkbox"/> \$1,600 (General)	<input type="checkbox"/> \$1,200 (Government Employee)	<input type="checkbox"/> \$1,000 (Graduate Student/Postdoctoral Fellow)
<b>Only payment by check or money order is accepted. Please make check payable to: The Hamner Institutes for Health Sciences. Return payment and registration form to: Ms. Jeanne Galbo The Hamner Institutes for Health Sciences 6 Davis Drive, P.O. Box 12137 Research Triangle Park, NC 27709-2137</b>		