# **PAGE Meeting**

# Modeling Delays in Pharmacokinetics and Pharmacodynamics

## **Course Outline**

The course will provide an overview of biological systems exhibiting delays, of lifespan driven concepts pharmacodynamic response, modeling of cell maturation, and nonlinear mixed effect lifespan models. Delay differential equations (DDEs) will be introduced and implemented in PK/PD software such as NONMEM and Monolix. The course will consist of both lectures and hands-on computer exercises built in Berkeley Madonna. Source codes for DDE based PK/PD models will be provided to the participants.



## **Instructors**

pharmacology of growth factors, oncology and bone therapeutics.



Wojciech Krzyzanski, PhD, MA. Associate Professor at Department of Pharmaceutical Sciences, University at Buffalo. Holds PhD in applied mathematics and MA in pharmacology. Research focus on pharmacokinetics and pharmacodynamics of hematopoietic growth factors and pharmacometrics.

Gilbert Koch, PhD. Postdoctoral Associate at Department of Pharmaceutical Sciences, University at Buffalo. Holds PhD in applied mathematics. Research focus on delay and lifespan modeling, and anti-





cancer effects in combination therapy. Juanjo Jose Perez-Ruixo, PhD. Scientific Director in the Pharmacokinetics and Drug Metabolism Department at Amgen. Holds PhD in pharmaceutical sciences. Research focus on quantitative

Johannes Schropp, PhD. Professor at Department of Mathematics and Statistics, University of Konstanz. Research focus on PK/PD modeling and numerics of dynamical systems.

Sameer Doshi, BS. Senior Scientist in the Department of Pharmacokinetics and Drug Metabolism at Amgen. Holds a BS in biochemistry. Research focus on pharmacometrics and PK/PD of erythropoetins and oncology therapeutics.

Jérôme Kalifa, PhD. Lixoft CEO. Applied mathematician in data analysis, signal & image processing, inverse problems, wavelets, statistical estimation and scientific software. Holds PhD in applied mathematics.



### **Program**

#### June 10th Tuesday

9:00 - 9:15	Introduction	12:20 - 13:20	Lunch break			
Krzyzanski		13:20 - 14:1	Modeling of cell maturation			
9:15 - 9:50	Biological systems exhibiting delays	Koch	• Transit compartment models of cell aging			
Krzyzanski	Hematopoietic cascade	Krzyzanski	• Modeling of cytotoxic effects			
	• Immune system response		Hands-on III			
	Apoptotic cancer cells	14:10 - 14:50	Lifespan models of hematopoietic growth factors			
9:50 - 10:25 Koch	Concept of lifespan driven pharmacodynamic	Doshi Perez-Ruixo	<ul> <li>Implementation of DDEs in NONMEM</li> <li>PD models of rHuEPO</li> </ul>			
	response					
	Lifespan controlled cell loss		• PD models of PegTPO			
	• Distributions of lifespan	14:50 - 15:05 15:05 - 15:45	Coffee break New modeling software for DDE systems			
	• Lifespan PD models with delays					
10:25 - 11:15	Basic lifespan based indirect response models	Kalifa	• DDE in Monolix for population analysis			
Krzyzanski	• Drug effect on response production		Mixplore for DDE model exploration			
	Drug effect on lifespan distribution		• DDE model simulator for R and Matlab			
	• Hands-on I	15:45 - 16:00	Final comments and remarks			
11:15 - 11:30	Coffee break	Koch				
11:30 - 12:20	Introduction to delay differential equations					
Schropp	Overview of DDE systems					
	Categories of DDE models					
	• Hands-on II					

# **Registration**

**Course location:** The course will be held at Palacio de Congresos de Alicante, Av de Dénia, 47, 03013 Alicante, Spain, 7.7 km from the Cruise Terminal of Alicante. Phone: +34 965 26 99 62. Fax: +34 965 26 37 97. Website: <u>http://www.palaciocongresosalicante.com</u>

Fee: Individual fee: €180. This includes course documentation, midsession refreshments and lunch. Students may enroll at a fee of €30.

**Registration:** Please register ASAP in view of the limited course capacity of 30 participants. Confirmation of registration will be returned upon receipt, together with an invoice for the course fee. Registration will not be final until payment is received.

**Cancellations:** Cancellations with a full refund may be made until April 17, 2014. No refund is possible on cancellations received after this date. Substitutions may be made at any time.

#### Payment: University at Buffalo Foundation Inc. Bank transfers and credit card payments are accepted as well as checks.

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Please return to: Wojciech Krzyzanski, Department of Pharmaceutical Sciences, 370 Kapoor Hall, Buffalo, NY, 14214, USA; Phone: (716) 645-4847; Fax: (716) 829-6569; Email: wk@buffalo.edu.