

# Modeling Delays in Pharmacokinetics and Pharmacodynamics

## Course Outline

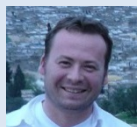
The course will provide an overview of biological systems exhibiting delays, concepts of lifespan driven PD response, modeling of cell maturation, and nonlinear mixed effect lifespan models. Delay differential equations (DDEs) will be introduced and implemented in PK/PD software such as NONMEM, Monolix,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



## Instructors



**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.



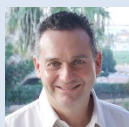
**Johannes Schropp, PhD.** Professor at Department of Mathematics and Statistics, University of Konstanz. Research focus on PK/PD modeling and numerics of dynamical systems.



**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 erythropoietins 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.



**Serge Guzy, PhD.** President, and CEO of POP\_PHARM, Senior Consultant Pharsight. Holds PhD in bioengineering and MS in biomathematics and chemistry. Co-developer of the MC-PEM algorithm for Mixed Effect Modeling.

# Program

## October 12<sup>th</sup> Sunday

9:00 - 9:15	Introduction	12:20 - 13:20	Lunch break
Krzyzanski		13:20 - 14:10	Transit compartment models
9:15 - 9:50	Biological systems exhibiting delays	Koch	<ul style="list-style-type: none"><li>• Signal transduction</li><li>• Cell maturation and senescence</li><li>• Hands-on III</li></ul>
Krzyzanski	<ul style="list-style-type: none"><li>• Hematopoietic cascade</li><li>• Immune system response</li><li>• Apoptotic cancer cells</li></ul>	14:10 - 14:50	Lifespan models of hematopoietic growth factors
9:50 - 10:25	Concept of lifespan driven pharmacodynamic response	Doshi	<ul style="list-style-type: none"><li>• Implementation of DDEs in NONMEM</li><li>• PD models of rHuEPO and PegTPO</li><li>• Hands-on demonstration</li></ul>
Koch	<ul style="list-style-type: none"><li>• Lifespan controlled cell loss</li><li>• Distributions of lifespan</li><li>• Lifespan PD models with delays</li></ul>	14:50 - 15:05	Coffee break
10:25 - 11:15	Basic lifespan based indirect response models	15:05 - 15:45	New modeling software for DDE systems
Krzyzanski	<ul style="list-style-type: none"><li>• Drug effect on response production</li><li>• Drug effect on lifespan distribution</li><li>• Hands-on I</li></ul>	Kalifa	<ul style="list-style-type: none"><li>• DDE in Monolix for population analysis</li><li>• Mlxplore for DDE model exploration</li><li>• DDE model simulator for R and Matlab</li><li>• Hands-on demonstration</li></ul>
11:15 - 11:30	Coffee break	15:45 - 16:25	Modeling DDEs with Phoenix NMLE
11:30 - 12:20	Introduction to delay differential equations	Guzy	<ul style="list-style-type: none"><li>• Graphical tools to describe delays in PD response</li><li>• Asymmetric dosing at steady state</li><li>• Hands-on demonstration.</li></ul>
Schropp	<ul style="list-style-type: none"><li>• Overview of DDE systems</li><li>• Categories of DDE models</li><li>• Hands-on II</li></ul>	16:25 - 16:40	Final comments and remarks
		Krzyzanski	

# Registration

**Course location:** The course will be held at The Mirage, 3400 Las Vegas Blvd South, Las Vegas, NV 89109, US, which is the venue for the ACoP meeting. Phone: 702-791-7444 Fax: 702-791-7414 / 702-862-1857. Website: <http://www.mirage.com>.

**Fee:** Regular fee \$500. This includes course documentation, breakfast and lunch. Students/Academia/Government/Non-profit employees may enroll at a fee of \$200.

**Registration:** This is a pre-meeting workshop that requires registering for the ACoP 2014 meeting <http://www.acop5.org/registration>. Please register ASAP in view of the limited course capacity of 30 participants.

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