

MI250: Introduction to Bayesian PK-PD Modeling & Simulation (3 CR)

MI250 provides an introduction to Bayesian modeling theory and the practical use of WinBUGS and R for PK-PD applications. In addition to basic concepts, this course includes instruction on BUGSModelLibrary, an open-source tool developed by Metrum Institute. This library facilitates the implementation of population PK-PD models in WinBUGS for compartmental models described by algebraic or differential equations. Participants may apply the 3 credit hours from this course to the Metrum Institute Certificate Program in Pharmacometrics.

Instructors

Bill Gillespie, Marc Gastonguay, and Metrum Institute staff

Prerequisites

Experience with PK-PD modeling and some familiarity with nonlinear regression, mixed-effects modeling and R (or S-Plus) is required. Applicable MI courses include: MI210 and MI212, or contact us: info@metruminstitute.org.

Computer Hardware/Software

This course requires a Windows laptop computer with an available USB 2.0 port. All required software used for hands-on examples will be freeware/open-source software and simple instructions will be provided for users to configure their computers before the course.

Spring 2010 Schedule

Tuesday, April 27	8:30am-4:30pm
Wednesday, April 28	8:30am-4:30pm
Thursday, April 29	8:30am-4:30pm

Location

Children's Hospital of Philadelphia
Colket Translational Research Building
3501 Civic Center Boulevard
Philadelphia, PA 19104

Accommodations

Metrum Institute does not provide hotel accommodations for students. All travel accommodations must be arranged independently.

Fees

Regular registration: \$3000 USD / Academic & government registration: \$1500 USD

Course Outline

1. Overview of the current and potential role of Bayesian methods in clinical drug development
2. Introduction to Bayesian statistical principles and methods
 - Bayes Rule
 - Bayesian modeling & inference process
3. Computation for Bayesian modeling
 - Key challenge of Bayesian modeling and inference: high-dimensional multiple integration
 - General computational approach: posterior simulation
 - Brief intro to Markov chain Monte Carlo simulation
4. WinBUGS basics
 - What is it?
 - How do I get it?
 - How do I run it?
 - WinBUGS demo: Linear regression

5. Introduce PK-PD modeling case study to be used throughout the course
6. Hands-on example 1: Simple nonlinear regression, e.g., a PK-PD model relating a single exposure metric to a single continuous PD outcome
7. Topics in Bayesian model development using WinBUGS I
 - Using WinBUGS scripts
 - R tools for running WinBUGS and analyzing MCMC simulations
 - Assessing convergence
 - Programming hierarchical models (aka mixed effect or population models)
8. Hands-on example 2: Nonlinear mixed effects, e.g., a PK-PD model relating observed drug concentrations to continuous PD measurements at the same time.
9. Topics in Bayesian model development using WinBUGS II
 - Model evaluation and comparison
 - BUGSModelLibrary for pharmacometric modeling: Introduction & demonstration
 - Dealing with censored data in WinBUGS
10. Hands-on example 3: Population PK.
11. Topics in Bayesian model development using WinBUGS III
 - Informative prior distributions in clinical pharmacology applications
 - Assessing sensitivity to prior distributions
 - Using the cut function in WinBUGS
 - Programming models in terms of differential equations
 - Hands-on example 4: Population PK-PD using an indirect action model
12. Additional topics & closing discussion
 - Selected published examples of Bayesian applications
 - Considerations in deciding whether to use Bayesian modeling with WinBUGS versus maximum likelihood modeling with NONMEM[®] (or other ML tools)
 - What didn't we cover?