

Population and ODE-based models using Stan and Torsten

Instructors: Charles Margossian and Yi Zhang

Length: 1 day

Description:

This class focuses on fitting models in pharmacometrics. We consider the following challenges when building such models: (i) the data generating process involves solutions to ODE systems, (ii) these ODEs are embedded in a complicated event schedule, and (iii) the data comes from various sources, for instance various patients and studies, and the resulting models are hierarchical. Note that these properties are not specific to pharmacometrics, and arise in other fields such as epidemiology, geology, and econometrics. To accommodate a broad audience, we will keep the core concepts general, and review basic notions of pharmacometrics, so that participants from all fields can do the exercises.

The course covers elementary techniques to solve ODEs in Stan, the efficient parametrization of hierarchical models, and within-chain parallelization. We also introduce *Torsten*, an extension of Stan for pharmacometrics, which allows us to seamlessly combine the above methods.

Prerequisites:

Participants should be familiar with Bayesian statistics and basic Stan. The requisite material is covered in the introductory tutorial and the tutorial on hierarchical modeling at Stan Con 2019, which participants can attend before coming to this workshop.

Outline:

1. Introduction

- Modeling framework: build, fit, and criticize
- Review: diagnosing inference
- Review: criticizing the model

2. Models in pharmacometrics

- Compartment models
- The event schedule
- Torsten: a library of Stan functions for pharmacometrics
- *Exercise 1: build, fit, and diagnose a two compartment model*

3. Ordinary differential equations in Stan

- Arsenal of tools to solve ODEs
- Matrix exponential solution for linear ODEs
- Numerical integrators for nonlinear ODEs
- *Exercise 2: write, fit, and diagnose a two compartment model with the ODE integrator*
- Combining analytical and numerical integrators
- *Example: the Friberg-Karlsson model*

4. Population models

- Review of hierarchical models
- *Exercise 4: write, fit, and diagnose a population two compartment model*
- Divergent transitions and where they come from
- *Exercise 5: re-parametrize the population two compartment model*

5. Within chain parallelization

6. Open discussion and concluding remarks