Bayesian non-linear PK modelling applied to dose escalation studies using WinBUGS

Foteini Strimenopoulou
Ruth Oliver
Miren Zamacona

Making Bayesian inference from a simple linear PK model has been well studied and applied in the past through the use of software like WinBUGS. However in some situations, for example for monoclonal antibodies, it is common to observe some degree of non-linear clearance. To accommodate this, a two-compartment model with linear and nonlinear elimination clearance can be assumed. The addition of the nonlinear part of the model considerably complicates the fitting. The reason for this is that the full posterior of this hierarchical model is composed of a likelihood that requires solving ordinary differential equations (ODE).

In this talk, we will present the case study and a 'simple' way to overcome the complexity induced by the inclusion of ODEs using WinBUGS and its differential interface. In particular, we will use the *ode.block* function from WBDiff which solves ODEs and allows blocking by time. The latter is critical in situations when the second derivatives, with respect to time, are not continuous (e.g. multiple subcute dosing). Our experience in how to fit and build this model in WinBUGS will be presented and discussed. Application of this nonlinear PK model to describe plasma-concentration time data observed in a FIM dose escalation study will be presented.