Linear and Nonlinear Mixed-Effects Models, with applications in R

José C. Pinheiro,
Biostatistics, Johnson & Johnson PRD

Abstract:

Mixed-effects models provide a powerful extension of traditional regression models for independent data. They are particularly useful for data with heteroscedasticity and/or correlation structures induced by grouping according to one or more classification factors. Examples of such "grouped data" include: repeated measures, longitudinal data, and multilevel data, being collected in a wide variety of application areas. This course will provide an overview of the theory and application of linear and nonlinear mixed-effects models in the analysis of grouped data, using capabilities in the nlme package in R to illustrate different stages of model fitting. A unified model-building strategy for the different types of mixed-effects models will be presented and applied to the analysis of real datasets from a variety of areas, including pharmacokinetics, clinical trials, agriculture, and manufacturing. Strong emphasis will be placed on the use of graphical displays at the various phases of the model-building process, starting with exploratory plots of the data and concluding with diagnostic plots to assess the adequacy of a fitted model.

Outline:

1) Fitting linear mixed-effects models
  - brief review of linear models for independent data
  - the linear mixed-effects (LME) model
  - using the lme function in R
  - confidence intervals, hypothesis tests, and predictions
  - fitting LME models to multilevel data

2) Extending the basic LME model
  - modeling the random effects covariance structure
  - variance functions to model unequal within-group variances
  - serial and spatial within-group correlation structures
  - an extended linear model with no random effects: the gls function

3) Fitting nonlinear mixed-effects models
  - brief review of nonlinear regression for independent data
  - obtaining starting estimates: self-starting regression functions
  - nonlinear mixed-effects (NLME) models for grouped data
  - the nlme function in R
  - extending the basic NLME model: variance functions and correlation structures