Quantitative Biology > Quantitative Methods

Two General Methods for Population Pharmacokinetic Modeling: Non-Parametric Adaptive Grid and Non-Parametric Bayesian

Tatiana Tatarinova, Michael Neely, Jay Bartroff, Michael van Guilder, Walter Yamada, David Bayard, Roger Jelliffe, Robert Leary, Alyona Chubatiuk, Alan Schumitzky

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Population pharmacokinetic (PK) modeling methods can be statistically classified as either parametric or nonparametric (NP). Each classification can be divided into maximum likelihood (ML) or Bayesian (B) approaches. In this paper we discuss the nonparametric case using both maximum likelihood and Bayesian approaches. We present two nonparametric methods for estimating the unknown joint population distribution of model parameter values in a pharmacokinetic/pharmacodynamic (PK/PD) dataset. The first method is the NP Adaptive Grid (NPAG). The second is the NP Bayesian (NPB) algorithm with a stick-breaking process to construct a Dirichlet prior. Our objective is to compare the performance of these two methods using a simulated PK/PD dataset. Our results showed excellent performance of NPAG and NPB in a realistically simulated PK study. This simulation allowed us to have benchmarks in the form of the true population parameters to compare with the estimates produced by the two methods, while incorporating challenges like unbalanced sample times and sample numbers as well as the ability to include the covariate of patient weight. We conclude that both NPML and NPB can be used in realistic PK/PD population analysis problems. The advantages of one versus the other are discussed in the paper. NPAG and NPB are implemented in R and freely available for download within the Pmetrics package from www.lapk.org.

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