

Population designs evaluation and optimization in R: the PFIM function

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Keywords: Nonlinear mixed effects models; Fisher information matrix; Population design; Pharmacokinetics;

Nonlinear mixed effect model or population approach has been developed for the analyses of biological processes described by longitudinal data. It allows estimation of the mean value of the parameters in the population studies and their interindividual variability.

Population analyses often involve a limited sampling strategy in the data collection, mainly due to ethic or financial concerns. To face with the risk of unreliable results in such limited samples studies, efforts have been given since a decade to the development of a methodology for population designs evaluation and optimization based on the expression of the Fisher information matrix for nonlinear mixed effects models (Mentré et al. 1997; Retout et al. 2002; Bazzoli et al. 2007). In this context, we have proposed PFIM (Retout et al. 2003), a R function for population design evaluation and optimization.

PFIM evaluates population designs for single or multiple response models and thus returns the expected standard errors, defined as the square roots of the diagonal elements of the inverse of the Fisher information matrix, on the population parameters with the design evaluated. To use PFIM, some prior information has to be supplied by the user such as the structural model, its parameterization and a priori values of the parameters. PFIM can also optimize population designs with different optimization options, based on the D_optimality criterion, i.e. to maximize the determinant of the Fisher information matrix or minimize its inverse.

Since 2003, several releases of PFIM have been proposed. Currently, two main versions now are implemented in parallel: a graphical user interface package using the R software (PFIM Interface) and a direct R version. The latter requires knowledge in R programming but benefits of the latest methodological developments performed in our research team.

Examples of the use of both versions of PFIM will be presented. They are performed in the context of pharmacokinetics and pharmacodynamics data. Pharmacokinetics deals with the time-course of drug concentration, whereas pharmacodynamics refers to the time-course of drug action in the body (Retout et al. 2007).

PFIM versions and their extensive documentation are freely available on the PFIM website (Retout et al. 2007).

References

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