

# Estimation of compartment model parameters by combining genetic algorithm and jackknife method

Özlem Türkşen<sup>1</sup> and Müjgan Tez<sup>2</sup>

<sup>1</sup>Ankara University, Turkey, turksen@ankara.edu.tr

<sup>2</sup>Marmara University, Istanbul, Turkey, mtez@marmara.edu.tr

**Keywords:** compartment models, generalized nonlinear least squares, genetic algorithm, jackknife method

Modeling the pharmacokinetic behavior of a particular drug is a valuable tool in the drug development process. A well-known and commonly used model is two-compartment model which provides good insight into the underlying behavior of most drugs [1]. The model can be described analytically in the form of a system of ordinary differential equations. The solution of equation system is nonlinear form of the model parameters. Furthermore, compartments are correlated across the equations. In this case, generalized nonlinear least squares (GNLS) estimator is more efficient than nonlinear least squares (NLS) estimator [2]. The GNLS approach minimizes the Minkowski metric with respect to model parameters in which the covariance structure is not ignored.

In this study, estimation of two-compartment model parameters is considered in case of correlated equations. It is aimed to estimate the unknown model parameters based on GNLS minimization. For this purpose, genetic algorithm (GA), a well-known population based search algorithm [3], is used as optimization tool. In order to reduce the bias of the estimators, Jackknife delete-one algorithm [4] is used. The suggested approach is applied on simulated data set. It is seen from the results that bias of parameter estimates is reduced by using Jackknife method which helps to get statistical inference about the parameters.

## References

- [1] Bonate, P.L. (2011). *Pharmacokinetic-Pharmacodynamic Modeling and Simulation*. Springer, New York.
- [2] Seber, G.A.F. and Wild, C.J. (2003). *Nonlinear Regression*. Wiley, New York.
- [3] Michalewicz, Z. (1996). *Genetic Algorithms + Data Structures = Evolution Programs*. Springer, New York.
- [4] Obiora-Ilouno H.O. and Mbegbu J.I. (2013). A jackknife approach to error-reduction in nonlinear regression estimation. *American Journal of Mathematics and Statistics* **3**, 32–39.