

Hierarchical likelihood estimation in non linear mixed models

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The classical approach for estimating parameters in a non linear mixed model is to compute the maximum likelihood estimators. However, the computation of the likelihood involves multiple integrals with a dimension equal to the number of random effects that can largely complicate the estimation procedure. In this work, we propose to adapt the hierarchical likelihood developed by Lee and Nelder in the Generalized Linear Modelling context [2]. This approach avoids any computation of multiple integrals by focusing on the estimation of individual parameters rather than random-effect variances.

Maximization of the hierarchical likelihood can be performed using a Newton-Raphson-like algorithm. This algorithm requires an approximation of the Hessian of the hierarchical likelihood but we noticed that this matrix had a particular structure and we developed an algorithm well-adapted to this special form.

We apply our hierarchical approach to a complex non linear mixed model describing HIV dynamics [1]. This model is built from a system of non linear ordinary differential equations (ODE) which are especially adapted to model some biological phenomenons.

References

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