## DIFFERENTIAL EVOLUTION MARKOV CHAIN FOR BAYESIAN ANALYSIS OF NONLINEAR MIXED EFFECTS MODELS

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Convergence of nonlinear mixed effects models (nlme) in WinBugs may be very slow, because subject-specific parameters may be highly correlated, WinBugs cannot do block updates and has to resort to one-dimensional Metropolis updates. Here we propose Differential Evolution Markov chain (DE-MC) to speed up convergence. In DE-MC multiple chains are run in parallel; proposals are generated by adding to the current state of a chain a multiple of the difference of two other randomly chosen chains. Such proposals are reversible and adapt automatically to the correlation structure of the posterior. By applying DE-MC as a Metropolis-within-Gibbs step to the parameters of each subject in turn, efficient block updates are generated. The number of parallel chains does not need to be higher than two or three times the maximum block size. The approach is illustrated by comparing block DE-MC with WinBugs using literature data on the pharmacokinetics of Theophylline.