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Quasi-complete separation in random effects of binary response mixed models

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Abstract: Clustered observations such as longitudinal data are often analysed with generalized linear mixed models (GLMM). Approximate Bayesian inference for GLMMs with normally distributed random effects can be done using integrated nested Laplace approximations (INLA), which is in general known to yield accurate results. However, INLA is known to be less accurate for GLMMs with binary response. For longitudinal binary response data it is common that patients do not change their health state during the study period. In this case the grouping covariate perfectly predicts a subset of the response, which implies a monotone likelihood with diverging maximum likelihood (ML) estimates for cluster-specific parameters. This is known as quasi-complete separation. In this paper we demonstrate, based on longitudinal data from a randomized clinical trial and two simulations, that the accuracy of INLA decreases with increasing degree of cluster-specific quasi-complete separation. Comparing parameter estimates by INLA, Markov chain Monte Carlo sampling and ML shows that INLA increasingly deviates from the other methods in such a scenario.

DOI: <https://doi.org/10.1080/00949655.2015.1129539>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-128140>

Journal Article

Accepted Version

Originally published at:

Sauter, Rafael; Held, Leonhard (2016). Quasi-complete separation in random effects of binary response mixed models. *Journal of Statistical Computation and Simulation*, 86(14):2781-2796.

DOI: <https://doi.org/10.1080/00949655.2015.1129539>

Supplementary material to "Quasi-complete Separation in Random Effects of Binary Response Mixed Models"

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24th February 2016

This supplementary material provides additional information to the main text of the paper "Quasi-complete Separation in Random Effects of Binary Response Mixed Models". The supplementary material contains additional information to the random intercept (RI) and the random intercept plus random slope (RI+RS) models, presented in the main text in Section 3. In Section 1 the marginal posterior distributions for the fixed effects and the hyperparameters obtained with integrated nested Laplace approximations (INLA) with the simplified Laplace approximation approach and with the full Laplace approximation are compared. Section 2 provides convergence diagnostics for the models parameters obtained with MCMC.

1 Simplified and full Laplace approximations in INLA

The following plots compare the marginal posterior distributions of the fixed effect parameters and hyperparameters obtained with INLA and MCMC. For the simplified Laplace approximation the `inla.control` option is set to

```
control.inla = list(  
  strategy = "simplified.laplace",  
  int.strategy = "grid",  
  h = 1e-5,  
  tolerance = 1e-6)}
```

which are the settings used also for the results reported in the main text. For the full Laplace approximation the `inla.control` option is set to

```
control.inla = list(  
  strategy = "laplace",  
  fast = FALSE,  
  int.strategy="grid",  
  h = 1e-5,  
  tolerance = 1e-6)
```

for which the results are reported in the following Figure 1 to 3. In general the full Laplace approximation in INLA is more accurate compared to the simplified Laplace approximation but in most cases nearly coincide according to ?. However, for the RI and RI+RS models of the toenail infection data we found substantial differences between the two approximation strategies and the simplified Laplace approximation was closer to the results obtained by MCMC, if the hyperparameters are not fixed. This differences may well be related to the problem of substantial cluster-specific quasi-complete separation. In the main text the reported results are always based on the simplified Laplace approximation.

1.1 Estimation with prior distribution

In Figure 1 the marginal posterior distributions for the fixed effects β based on INLA with simplified and with full Laplace approximation and with MCMC are shown with a prior distribution on the hyperparameters. The same prior distributions for the hyperparameters as described in the main text are used. Figure 2 shows the corresponding marginal posterior distributions for the hyperparameters.

Figure 1: Marginal posterior distributions of β by MCMC (histogram), INLA with simplified Laplace (INLA-SL, black line) and based on INLA with full Laplace (INLA-FL, red line).

Figure 2: Marginal posterior distributions of hyperparameters for the RI and RI+RS models by MCMC (histogram), INLA with simplified Laplace (INLA-SL, black line) and based on INLA with full Laplace (INLA-FL, red line).

1.2 Estimation with fixed hyperparameters

In Figure 3 the marginal posterior distributions for the fixed effects β based on INLA with simplified and with full Laplace approximation and with MCMC are shown with fixed hyperparameters. The hyperparameters are fixed at the same values as obtained by ML estimation and as indicated in the main text.

Figure 3: Marginal posterior distributions of β by MCMC (histogram), INLA with simplified Laplace (INLA-SL fix, black line) and based on INLA with full Laplace (INLA-FL fix, red line). Hyperparameters values are fixed at corresponding ML estimates.

2 Convergence diagnostics

In this section we provide convergence diagnostics of the MCMC run for the RI and RI+RS model based on the toenail dataset for which the results were presented in Section 3 in the main text. Convergence diagnostics are reported for all four models, the RI and the RI+RS model with a prior on the hyperparameters and with fixed hyperparameters. We show the convergence diagnostics for all fixed effects (β) of each model, of the hyperparameters if not fixed and for the random effect estimates of patient 233, who is one of the patients which always had a response value equal to one, plus two additional random effects of two patients in each model with the two highest autocorrelations at lag 1 in the MCMC run. For each reported parameter we show an excerpt of the traceplot, the autocorrelation as well as Geweke convergence diagnostics.

The excerpt for the traceplot covers the last 500 iterations of the MCMC run from iteration 1900 to 2400. We only report part of the MCMC run in the traceplot as the plot based on all 2400 kept iterations does not show any details about structures in the traceplot. Before reporting this excerpt, each traceplot based on all iterations was inspected to have possible jumps in the Markov chain. This was not the case for none of the reported parameters of the four models such that the shown excerpt is representative for the complete traceplot and thus the mixing of the Markov chain was found to be sufficient.

The autocorrelation was determined by the function `autcorr.diag` in the `coda` package and the maximum lag length was set to 10. The index in the autocorrelation plots and the Geweke diagnostic are values without thinning *e.g.* a autocorrelation for lag 1 has an index equal to iteration 200 in the plot. Except for the intercept, the time, the time treatment interaction and the hyperparameters in the RI+RS, there is no substantial autocorrelation in the MCMC run of the fixed effect parameters. Even for these coefficients in the RI+RS model the autocorrelation is modest and drops quickly to zero after six lags and if hyperparameters are fixed in the RI+RS model there is no autocorrelation present any more.

The Geweke diagnostics are computed by the function `geweke.plot` in the `coda` package in R. The Geweke statistic compares the posterior means computed based on the second half of the MCMC iterations with the means computed based on a decreas-

ing fraction of the first half of the MCMC iterations. The Geweke test statistic is a standardized z-score based on the difference between the two sample means divided by its estimated standard error. The standard error is estimated from the spectral density at zero and so takes into account any autocorrelation. The plot with the Geweke diagnostics shows what happens if successively larger numbers of iterations are discarded from the beginning of the chain. The first half of the Markov chain is divided into 7 segments, for which the Geweke's Z-score is repeatedly calculated. The first Z-score is calculated with all iterations in the chain, the second after discarding the first segment, the third after discarding the first two segments, and so on. The last Z-score is calculated using only the samples in the second half of the chain. The two horizontal dashed lines indicated the 2.5% and 97.5% quantile of the standard normal distribution. A Geweke Z-score which is far away from the dashed lines implies that the two means, of the first and the second part of the Markov chain, are probably not equal which implies that the stationary distribution was not reached. The presented plots with the Geweke statistics show that some of the Geweke Z-scores are outside the 2.5% or the 97.5% interval but all of them are still close to these quantiles and all of them have absolute values which are smaller than three.

From this analysis we would finally not reject the hypothesis of convergence to a stationary distribution of the MCMC run for the presented models. This was clearly not the case for MCMC runs with a smaller number of iterations, less thinning or based on different MCMC samplers.

2.1 Random intercept model (RI) with prior

Figure 4: Convergence diagnostics for fixed effects of RI model: traceplot, autocorrelation and Geweke diagnostics.

Figure 5: Convergence diagnostics for hyperparameters and selected random effects of RI model: traceplot, autocorrelation and Geweke diagnostics.

2.2 Random intercept model (RI) with fixed hyperparameters

Figure 6: Convergence diagnostics for fixed effects of RI model with fixed hyperparameters: traceplot, autocorrelation and Geweke diagnostics.

Figure 7: Convergence diagnostics for selected random effects of RI model with fixed hyperparameters: traceplot, autocorrelation and Geweke diagnostics.

2.3 Random intercept and slope model (RI+RS) with prior

Figure 8: Convergence diagnostics for fixed effects of RI+RS model: traceplot, autocorrelation and Geweke diagnostics.

Figure 9: Convergence diagnostics for hyperparameters of RI+RS model: traceplot, autocorrelation and Geweke diagnostics.

Figure 10: Convergence diagnostics for selected random effects of RI+RS model: traceplot, autocorrelation and Geweke diagnostics.

Figure 11: Convergence diagnostics for selected random effects of RI+RS model: traceplot, autocorrelation and Geweke diagnostics.

2.4 Random intercept and slope model (RI+RS) with fixed hyperparameters

Figure 12: Convergence diagnostics for fixed effects of RI+RS model: traceplot, autocorrelation and Geweke diagnostics.

Figure 13: Convergence diagnostics for selected random effects of RI+RS model: traceplot, autocorrelation and Geweke diagnostics.

Figure 14: Convergence diagnostics for selected random effects of RI+RS model: traceplot, autocorrelation and Geweke diagnostics.