Efficient estimation of joint models for multivariate longitudinal and survival data using INLAjoint

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Abstract: Joint models for longitudinal and survival outcomes have recently gained a lot of interest in clinical research. These complex models involve multiple likelihoods (i.e. for each longitudinal and survival outcome), usually linked through correlated or shared random-effects. In this context, inference methods reach limitations due to long computation times and convergence issues. We introduce a Bayesian approximation for these joint models based on the INLA algorithm implemented in the R package INLAjoint, which is a user-friendly interface to fit joint models that relies on the R package INLA, to alleviate the computational burden and allow the estimation of multivariate joint models with less restrictions. Our simulation studies show that INLA reduces the computation time substantially as well as the variability of the parameter estimates compared to alternative strategies such as Bayesian inference via Markov Chain Monte Carlo. We further apply the methodology to analyze 5 longitudinal markers (3 continuous, 1 count, 1 binary, and 16 random effects) and competing risks of death and transplantation in a clinical trial on primary biliary cholangitis. INLAjoint provides a fast and reliable inference technique with an easy to use interface for applying joint models to the complex multivariate data encountered in health research.

Key words: Bayesian inference; Competing risks; Efficient estimation; Joint modeling; Multivariate longitudinal markers.