

Joint Modeling of Survival Time and Longitudinal Data with Random Change points

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Joint models have been increasingly used in survival analysis to assess the relationship between time-to-event data and some time-fixed and time-dependent covariates that are measured longitudinally and often with error. A common framework consists of using the Cox regression model for the survival time data and a linear mixed-effects model for the longitudinal observations. However, individual covariates trajectories may reveal some nonlinearity with evidence of the presence of change points. We propose a joint model for survival time and longitudinal data assuming a mixed-effects model with random change point for the longitudinal covariates and the proportional hazards model for the survival times. The method is flexible as it leaves free the distribution of the random effects. The estimation of the parameters is made using the conditional score and the corrected score techniques to circumvent the measurement error that originates from the replacement of the true covariate process in the Cox model with an estimator obtained from the longitudinal data model. The resulting estimators are proven to be consistent, asymptotically normal and equivalent. Simulations are also carried out to investigate their finite-sample performance.