

Joint modeling for the prediction of exacerbation events in patients with COPD

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Abstract

This work is motivated by the AERIS study, a two-year longitudinal non-interventional study which aimed to assess the contribution of bacterial pathogens to acute exacerbations in adults aged 40 to 85 years old with Chronic Obstructive Pulmonary Disease (COPD), in Southampton, UK. COPD causes persistent airflow limitation that is often progressive and associated with intensified chronic inflammatory response in the airways and the lung. Patients with COPD are in high risk of suffering from exacerbations which increase the severity of the disease and may lead to medication changes. Patients were followed up monthly and when experiencing exacerbations. 16S ribosomal RNA gene amplicon sequencing was performed on sputum samples to determine the relative abundance of bacteria. One of the research questions was to better understand if, how, and which bacteria are associated to the risk of exacerbation and predict future exacerbations.

Joint models of longitudinal and time-to-event data are a popular choice for such objectives. Although there has been a lot of work towards extensions of the classic joint modeling framework, the performance of joint models in high-dimensional settings with multivariate longitudinal outcomes and recurrent events has not been studied. Moreover, the performance of Bayesian shrinkage priors for feature selection in highly correlated settings has not been well investigated.

We propose a flexible multivariate joint model for multiple longitudinal outcomes and recurrent exacerbation events with various association structures between the evolution of the relative abundance of bacteria and the hazard of future exacerbations. To select the most predictive bacteria and association structures, we applied horseshoe and ridge global-local shrinkage priors on the regression coefficients that define the association between relative abundance and the exacerbation hazard.

The results suggest that the use of Bayesian shrinkage priors may help in the identification of bacteria features that are predictive for the exacerbation hazard.