Multivariate partial linear varying coefficients model for gene-environment interactions with multiple longitudinal traits

Abstract: Correlated phenotypes often share common genetic determinants. Thus, a multi-trait analysis can potentially increase association power and help in understanding pleiotropic effect. When multiple traits are jointly measured over time, the correlation information between multivariate longitudinal responses can help to gain power in association analysis, and the longitudinal traits can provide insights on the dynamic gene effect over time. In this work, we propose a multivariate partially linear varying coefficients model to identify genetic variants with their effects potentially modified by environmental factors. We derive a testing framework to jointly test the association of genetic factors and illustrated with a bivariate phenotypic trait, while taking the time varying genetic effects into account. We extend the quadratic inference functions to deal with the longitudinal correlations and used penalized splines for the approximation of nonparametric coefficient functions. Theoretical results such as consistency and asymptotic normality of the estimates are established. The performance of the testing procedure is evaluated through Monte Carlo simulation studies. The utility of the method is demonstrated with a real data set from the Twin Study of Hormones and Behavior across the Menstrual Cycle project, in which SNPs associated with emotional eating behavior are identified.

Keywords: Partial linear model, Genetic association; Gene-environment interaction; Longitudinal traits; Multi-trait analysis