

A penalized likelihood approach for haplotype-based pharmacogenetic analysis

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Abstract

Haplotypes can hold key information to understand the role of candidate genes for pharmacogenetic responses. In this study, we present a penalized regression approach to evaluate haplotype effects and haplotype-treatment interactions. Unlike standard analysis where haplotype inference focuses on relative effects compared with an arbitrarily chosen baseline and does not depict the effect structure, the proposed method does not require the choice of a baseline haplotype, and reports haplotype-treatment group structure based on the effect sizes. By specifying an L1 penalty on the pairwise difference of the haplotype-by-treatment effects, the method simultaneously carries out the effect estimation and effect comparison of all haplotypes and haplotype-treatment interactions. Simulation studies reveal the better abilities of the proposed method to identify the effect structure compared with the traditional haplotype association methods, suggesting the informativeness and powerfulness of the proposed method.