

Detection of gene-gene interactions using multistage sparse and low-rank regression

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Abstract

Finding an efficient and computationally feasible approach to deal with the curse of high-dimensionality is a daunting challenge faced by modern biological science. The problem becomes even more severe when the interactions are the research focus. To improve the performance of statistical analyses, we propose a low-rank interaction model, where the interaction effects are modeled using a low-rank matrix. With parsimonious parameterization of interactions, the proposed model increases the stability and efficiency of statistical inferences. To detect gene-gene interactions, we further propose an Extended Screen-and-Clean approach, built upon the low-rank model and based on the Screen-and-Clean method (Wasserman and Roeder, 2009; Wu *et al.*, 2010). In the screen stage of the proposed approach, a combination of a low-rank structure and a sparsity constraint are utilized to achieve higher power and higher selection-consistency probability. We use simulations to demonstrate the effectiveness of the proposed method and apply the new procedure to a Warfarin dosage study. The data analysis identified main and interaction effects that would have been omitted by conventional methods.