

Network hub-node prioritization of gene regulation with intra-network association

Chuhsing Kate Hsiao

National Taiwan University
E-mail: ckhsiao@ntu.edu.tw

Abstract: To identify and prioritize the influential hub genes in a gene-set or biological pathway, most analyses rely on calculation of marginal effects or tests of statistical significance. Such procedures may be inappropriate if dependence between gene nodes exists, and if the hub nodes require more attention than others. The dependence may manifest itself in correlation between the nodes or in the topology of the pathway network. The highly connected hub genes may play a more important role for the whole network to function properly. Here we develop a pathway activity score incorporating the local effect of gene nodes as well as intra-network affinity measures. This score summarizes the expression levels in a gene-set/pathway for each sample, with weights on local and network information, respectively. The score is next used to examine the impact of each node through a leave-one-out evaluation. Two cancer studies, one involving RNA-Seq from breast cancer patients with high-grade ductal carcinoma in situ and one microarray expression data from ovarian cancer patients, and simulation analysis are used to assess the performance of the procedure, and to compare with existing methods with/without consideration of correlation and network information. The identified hub genes have reproduced previous findings; some are currently undergoing clinical trials for target therapy. The results show that the proposed procedure can provide a useful and complementary list of recommendation for prioritizing causal hubs.