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An Efficient Method for Global Gene Regulatory Network Construction

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Constructing gene regulatory networks is crucial to unraveling the genetic architecture of complex traits. On the basis of transcriptomic profiles, many methods have been proposed to construct undirected networks by calculating the pairwise correlation between gene expressions. However, constructing directed networks with genome-wide genes remains a challenge. Taking advantage of both transcriptomic and single nucleotide polymorphism data, we proposed a two-stage penalized least squares method to build large systems of structural equations for directional network construction. A large system of structural equations via optimal prediction of a set of surrogate variables was established at the first stage, and lasso was employed to obtain consistent selection of regulatory effects at the second stage. The proposed method can simultaneously investigate all the genes across the entire genome and the computation is fast due to the parallel implementation. Such unbiased network construction will enable the determination of the causal relationship between genes, and facilitate our understanding of disease mechanisms. We demonstrate the superior performance and effectiveness of the method using Monte Carlo simulation studies. With application to real data, the method has successfully detected genes that are coordinately controlled by transcription factors driven by trans-acting expression quantitative trait loci.