Modeling Pleiotropy and Epistasis to Understand Genetic Complexity

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Understanding the genetic basis of complex disease will require network models of how multiple genes combine to affect phenotypic outcomes. These networks will likely involve epistasis, or gene-gene interaction, and pleiotropy, in which one gene affects multiple phenotypes. Here we introduce a combined analysis of pleiotropy and epistasis (CAPE) that integrates information from multiple related phenotypes to constrain models of epistasis, thereby enhancing the detection of interactions that simultaneously describe all phenotypes. The networks inferred are readily

individual genetic variants on other variants, which in turn account for the variance in quantitative

genetic effects. We demonstrate the utility of this approach for a variety of data types in multiple model systems. CAPE is implemented in an R package that can be applied to data from both genetic screens and segregating populations.