

Inferring Genetic Architecture of Complex Biological Processes

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Abstract:

Gene mapping infers the relationship between genotype and phenotype in a segregating population. We map thousands of mRNA expression phenotypes, or expression QTL, using dimension reduction methods to uncover correlated genetic architecture, including number and location of genomic regions as well as gene action and epistasis. We show a novel blending of principal components and discriminant analysis with functional information to detect multiple expression QTL that together may affect the expression of many correlated mRNA. These common patterns of gene action are largely overlooked by simple interval mapping when conducted separately for each mRNA. In our current study with 60 F2 mice from a B6-BTBR ob/ob model of diabetes and over 40,000 mRNA transcripts measured with Affymetrix chips, we find three pairs of genomic regions of particular interest associated with signal transduction, apoptosis, and lipid metabolism. We propose to join genetic architecture with graphical models of biochemical activity. Our approach is directly applicable to gene mapping for other “omic” measurements on the horizon.

