

A MULTIVARIATE SHRINKAGE APPROACH TO EXPRESSION QUANTITATIVE TRAIT LOCI MAPPING

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Abstract: This paper provides an investigation of the univariate methods commonly used to search for expression Quantitative Trait Loci (eQTL), and presents a multivariate method based on the Lasso as a superior alternative. We show that the Lasso is equivalent to univariate methods in assessing evidence for the existence of one or more eQTL at a transcript, but gives improved performance in terms of locating eQTL. More precisely, simulation studies show that the Lasso has higher power for a given false positive rate than univariate methods, because Linkage Disequilibrium between markers generate false positive signals which damage the performance of univariate methods. Further simulation studies examine properties of methods which construct confidence intervals for location of QTL. These suggest, with the typical effect sizes simulated here, that precise estimates of location are difficult. Finally we apply these methods to experimental data to produce a list of genes with evidence of genetic regulation; for a subset of these, large effect sizes means a precise estimate of location *is* possible. Properties of these eQTL imply that this subset is under monogenic control, and multiple eQTL proposed by univariate methods are false positives induced by marker correlation.