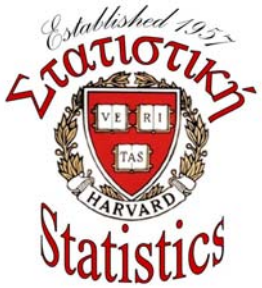

Statistical Methods for Detecting Expression Quantitative Trait Loci (eQTL)

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Treating mRNA transcript abundances as quantitative traits and mapping gene expression quantitative trait loci for these traits has been studied in many species from yeast to humans. There has been significant success in finding associations between gene expression and genetic markers. These eQTL studies have been used to identify candidate causal regulators, to construct gene regulation networks, to identify hot spot regions, and to better understand clinical phenotypes. Because of the large number of genes and genetic markers in such analyses, it is extremely challenging to discover how a small number of eQTLs interact with each other to affect mRNA expression levels for a set of (most likely co-regulated) genes.

We present a Bayesian method to facilitate the task, in which co-expressed genes mapped to a common set of markers are treated as a module characterized by a latent indicator variable. The latent variable represents a combination of the genetic and phenotypic effect, conditional on which the markers and expression of genes are independently distributed. A Markov chain Monte Carlo algorithm is designed to search simultaneously for the module genes and their linked markers. We show by simulations that this method is much more powerful for detecting true eQTLs and their target genes than traditional QTL mapping methods.

We applied the procedure to a data set consisting of gene expression and genotypes for 112 segregants of *S. cerevisiae* previously described by Brem and Kruglyak (2005). Our method identified modules containing genes mapped to previously reported eQTL hot spots, and dissected these large eQTL hot spots into several modules corresponding to different causal regulators or primary and secondary responses to causal perturbations. In addition, we identified nine modules associated with pairs of eQTLs, of which two have been previously reported, including the mating module (Brem *et al.* 2005) and the *ZAP1* target module (Lee *et al.* 2006). We demonstrated that one of the novel modules containing many daughter-cell expressed genes is regulated by *AMN1* and *BPH1*.