Bayesian Association-Based Fine Mapping in Small Chromosomal Segments

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Abstract

A Bayesian method for fine mapping is presented, which deals with multi-allelic markers (with ≥ 2 alleles), unknown phase, missing data, multiple causal variants, and both continuous and binary phenotypes. We consider small chromosomal segment spanned by a dense set of closely linked markers and putative genes only at marker points. Locus-specific indicator variables are used to control inclusion or exclusion of marker contributions from the phenotypic model. To account for covariance between consecutive loci and to control fluctuations in association signals along candidate region we introduce joint prior for the indicators which depends on genetic or physical map distances. The potential of the method, including posterior estimation of trait-associated loci, their effects, linkage disequilibrium pattern due to close linkage of loci, and the age of causal variant (time to most recent common ancestor), is illustrated with the well known cystic fibrosis and Friedreich ataxia data sets by assuming that haplotypes

were not available. In addition, simulation analysis with large genetic distances is shown. Estimation of model parameters is based on Markov chain Monte Carlo sampling and is implemented using WinBUGS. The model specification code is freely available for research purposes from the URL: http://www.rni.helsinki.fi/∼mjs/.