Meta analysis of genetic association studies with different sets of markers

Claudio J. Verzilli, Paul Newcombe and John C. Whittaker

Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, UK

Genetic effects underlying complex traits and disorders are small and their detection requires comprehensive typing of single nucleotide polymorphisms (SNPs) in large samples. Quantitative synthesis of evidence from available studies remains vital, even in the era of genome-wide analyses. However, a major obstacle is that studies of the same gene, region, or even the genome as a whole, may type a different repertoire of SNPs, yielding partially overlapping genotypic data. The meta-analysis of results from each marker in isolation would exclude those studies that did not type the marker in question, with a potential loss of power; moreover, multiple single-SNP analyses are difficult to interpret. Here we present Bayesian hierarchical models for evidence synthesis that incorporate prior information on pairwise LD measurements between markers to make posterior inference on adjusted effects. In addition, a reversible jump algorithm enables the selection of the most promising associations. The methods we describe, which use the freely available software WinBUGS, are likely to be of substantial value both to the emerging networks of investigators engaged in synthesis of evidence on genetic associations of complex quantitative traits and disorders, and to those applying and extending findings from genome wide association studies.