



THE UNIVERSITY OF
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DEPARTMENT OF STATISTICS

PHD DISSERTATION PROPOSAL PRESENTATION

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Association Analysis of Phenotypes Jointly Influenced by a Pair of Organisms

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Jones 111, 5747 S. Ellis Avenue

ABSTRACT

The virulence of an infectious disease is usually affected by a combination of a host and at least one pathogen organism, so it is influenced by all of their genomes. Previous experiments have divulged that combining genetic information from all organisms involved has enabled to identify more relevant genetic variants than just individually performing an association analysis on each organism. Conducting genetic mapping on a pathogen organism usually presents some challenges of its own. Random insertions and deletions in the pathogen genome can lead to the existence of multiallelic genetic variants, which are often associated with the presence of some alleles with particularly small frequencies. We build upon existing work to construct a pathogen genetic relatedness matrix which aggregates information across genetic variants with different numbers of alleles and accommodates small allele frequencies without introducing numerical instability by applying some form of regularization. When considering interaction tests between the genotypes of different organisms, the fact that the phenotype is held fixed while the genotypes are allowed to vary among tests may often lead to significant departures from the known null distribution of the test statistic. We present diagnostic tools to detect such departures and a method to correct for them under a wide range of scenarios. We demonstrate the applicability of our methodology on data from a Hepatitis C clinical trial and simulated data.