The University of Chicago

Department of Statistics

Seminar Series

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"Nonparametric Tests of Association of Multiple Genes with Human Disease"

MONDAY January 17, 2005 at 4:00 PM
133 Eckhart Hall, 5734 S. University Avenue
Refreshments following the seminar in Eckhart 110.

ABSTRACT

The genetic basis of many common human diseases is expected to be highly heterogeneous, with multiple causative loci, and multiple alleles at some of the causative loci. Analyzing the association of disease with one genetic marker at a time can have weak power, due to relatively small genetic effects and the need to correct for multiple testing.

To overcome some of these limitations for case-control studies of candidate genes, we develop a new class of nonparametric statistics that can simultaneously test the association of multiple marker loci with disease. Our approach is based on U-statistics, which first measure the similarity over all marker loci for pairs of subjects, and then compares the averages of these similarities between cases versus controls.

Genetic similarity for a pair of subjects is measured by a "kernel" function, which we allow to be fairly general, and we provide guidelines on how to choose a kernel for different types of genetic effects.

Our global statistic has the advantage of having only one degree of freedom, and achieves its greatest power advantage when the contrasts of average similarities between cases and controls are in the same direction across all markers.

Simulations illustrate that our proposed methods have the anticipated Type-I error rate, and that they can be more powerful than single-locus tests. Application of our methods to a study of candidate genes for prostate cancer illustrates their potential merits, and offers guidelines for interpretation.