

## SEMINAR ANNOUNCEMENT

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**Title:** Maximum Likelihood Estimation of Haplotype Effects and Haplotype-Environment Interactions in Genetic Association Studies

**Speaker:** Danyu Lin, Ph.D.  
Dennis Gillings Distinguished Professor  
Department of Biostatistics  
University of North Carolina at Chapel Hill

**Date:** Friday, April 1, 2005

**Time:** 11:00 am – 12:00 pm

**Location:** Monroe Hall (2115 G Street NW), Room B02

**Abstract:** A haplotype is a specific sequence of nucleotides on a single chromosome. The population associations between haplotypes and disease phenotypes provide critical information about the genetic basis of complex human diseases. Standard genotyping techniques cannot distinguish the two homologous chromosomes of an individual so that only the unphased genotype (i.e., the combination of the two homologous haplotypes) is directly observable. Statistical inference about haplotype-phenotype associations based on unphased genotype data presents a very interesting and difficult missing-data problem, especially when the sampling depends on the disease status. We provide a comprehensive and rigorous treatment of this problem. All commonly used study designs, including cross-sectional, case-control and cohort studies, are considered. The phenotype can be a disease indicator, a quantitative trait or a potentially censored time to disease variable. The effects of haplotypes on the phenotype are formulated through flexible regression models, which can accommodate a variety of genetic mechanisms and gene-environment interactions. We construct appropriate likelihoods, which usually involve high-dimensional nuisance parameters. The identifiability of the parameters, and the consistency, asymptotic normality and efficiency of the maximum likelihood estimators are established. Efficient and reliable numerical algorithms are developed. Simulation studies show that the likelihood-based procedures perform well in practical settings. An application to the Finland-United States Investigation of NIDDM Genetics Study is provided. Areas in need of further development are discussed.

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**Directions:** Foggy Bottom-GWU Metro Stop on the Orange and Blue Lines. The campus map is at <http://www.gwu.edu/~map>.

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