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Some Recent Work in Family-based Association Studies

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3:30pm - 4:30pm, CHS 33-105A

Refreshments served at 3:00 PM in room 51-254 CHS

ABSTRACT: In this talk I will discuss how to address two challenges in family-based association studies of complex diseases.

In genetic studies it is critical to develop methods that can efficiently analyzing multiple genetic markers, as complex diseases are caused by multiple risk factors. For family-based association studies, we address this challenge by evaluating two pseudosibship methods: the 1:1 matching, which matches each affected offspring to the pseudo sibling formed by the alleles not transmitted to the affected offspring; the exhaustive matching, which matches each affected offspring to the pseudo siblings formed by all the other possible combinations of parental alleles. We prove that the two matching strategies use exactly and approximately the same amount of information from data under additive and multiplicative genetic models, respectively. This result paves the way for many existing multi-locus analysis methods developed for the case-control (or matched case-control) design to be applied to case-parents data with minor modifications. As an example, we apply an L1 regularized regression to a Crohn's disease dataset using the 1:1 matching.

Another significant challenge in family-based association studies is the reduced power due to conditioning on parental data to prevent confounding caused by population stratification. Here we propose to improve power by learning mode of inheritance from parental data. Specifically, we propose a novel statistic to test whether the underlying true genetic model is additive, dominant, or recessive. We then develop a model-selection-elimination strategy to incorporate the information in the statistic into family-based association tests. The application of our proposed methods to a candidate-gene study of type 1 diabetes successfully detects a recessive effect in MGAT5 that would otherwise be missed by conventional family-based association tests.