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***Identifying Human Genomic Variation
by Optical Mapping******Abstract:***

The study of human genomic variation has led to fundamental advances in our understanding of human biology. As the sequencing of the human genome nears completion, novel methods for discerning human variation are being developed while classical methods are being refined. These methods span a wide range in resolution and often incorporate sequence information in critical ways. The Optical Mapping System, pioneered at the Laboratory for Molecular and Computational Genomics, is ideal for studying genomic variation because it produces a genome-wide view of variation at a dense set of markers from high-throughput data. The primary data obtained is a collection of ordered restriction maps from single molecules of DNA, redundantly covering the genome. We have recently collected optical mapping data from four human genomes: three cell lines and a tumor tissue sample. Within these data is a wealth of information about each of the genomes in particular and about human genomic variation in general.

Our basic strategy for extracting that information involves comparing restriction maps to the in silico map obtained from the human sequence. In this talk, I will give an overview of the algorithmic and statistical methods we use to overcome the challenges posed by the error-prone nature of the primary data and highlight a few of the results of the analysis. I then will describe a novel method for discerning variation using a Hidden Markov Model. In the conserved regions of a genome, we model the coverage by the Lander-Waterman process and, in the variable regions, we use the hidden states of the Markov chain to model the degrees of deviation from the expected coverage, thereby reflecting the degrees of aberrancies in the genome.

**Tuesday, September 14th
4:00 p.m.**

Genetics/Biotechnology Center Auditorium
425 Henry Mall