

Special Bioinformatics Faculty Search Seminar

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Using models of evolutionary history to understand human genetic variation

The study of genetic variation is fundamental to population and evolutionary genetics, as it provides the basis for understanding differences among individuals, populations, and species. My research focuses on discerning the demographic and adaptive processes that have shaped the current distribution of genetic variation in human populations. To address demographic processes, I investigated the extent to which models of human origins are consistent with observed patterns. I developed models of human demographic history to represent two main hypotheses for modern human origins, the "out-of-Africa" and "multiregional" hypotheses. Using simulations and analytical formulas under the coalescent process, I compared measures of genetic variation observed from human data to those predicted by our models. I found that the model representing the out-of-Africa hypothesis produces patterns that mimic those observed in human data, whereas the model representing the multiregional hypothesis generates opposite patterns, lending strong support to the out-of-Africa hypothesis. Next, I considered adaptive forces shaping human genetic variation. One force that was of great theoretical interest in the past but has received little attention recently, particularly in terms of method development, is balancing selection. I designed the first set of likelihood-based methods that explicitly model the genealogical process under balancing selection using a coalescent framework. Simulation results show that my methods for detecting balancing selection are robust to demography and are the most powerful developed to date. Application of these new methods to whole-genome sequencing data from human populations revealed evidence of balancing selection at previously-hypothesized regions such as the HLA locus, as well as at many novel candidate sites across the genome. Thus, mathematical models play an important role in understanding the demographic and adaptive processes that shape genetic variation in human populations