

Quasi-likelihood Methods for Statistical-Genetic Inference in Founder Populations

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Abstract: This work is motivated by ongoing genetic studies in the Hutterites, an isolated founder population in the northern U.S. and western Canada, in which the approximately 1100 sampled individuals are virtually all related through multiple lines of descent, with the relationships characterized by a known, 13-generation, 1,623-person pedigree with only 64 founders. One reason isolated founder populations such as the Hutterites are of interest is that it is believed that they may be particularly useful for complex trait mapping. Major presumed advantages include (i) that the small number of founders would tend to reduce the genetic heterogeneity in the population, (ii) that the environment is usually more homogeneous, reducing the potential confounding effects of non-genetic risk factors, and (iii) that linkage disequilibrium would exist over greater distances than in outbred populations, so that a less dense marker map would be required for successful detection of association than would be needed in outbred populations. The problem of allele frequency estimation (estimation of the frequency distribution of types at a genetic locus) is relatively straightforward in the context of an infinitely-large, randomly-mating population. In this talk, the problem is treated in a founder population, and from this starting point, I will move on to discuss the problems of case-control association testing and Hardy-Weinberg testing in a founder population. I plan to discuss the meanings of the relevant parameters and hypotheses in the founder population context, propose quasi-likelihood-based methods of inference, treat the computational issues, and discuss applications of all methods to genetic studies in the Hutterites. This is joint work with Carole Ober, Catherine Bourgain, Tim Thornton, and Xiaodong Wu.