MULTIPOINT LINKAGE ANALYSIS UNDER LINKAGE DISEQUILIBRIUM

I. S. Chang, President's Laboratory, National Health Research Institutes, Taipei, Taiwan, ischang@nhri.org.tw.
W. C. Wang, Division of Biostatistics and Bioinformatics, National Health Research Institutes, Taipei, Taiwan.
Y. C. Chuang, Department of Applied Statistics and Information Science, Ming Chuan University, Taipei, Taiwan.
W. C. Chen, Division of Biostatistics and Bioinformatics, National Health Research Institutes, Taipei, Taiwan.
C. A. Hsiung, Division of Biostatistics and Bioinformatics, National Health Research Institutes, Taipei, Taiwan.

This paper presents a new Monte Carlo approach to the problem of calculating the conditional probability of inheritance patterns given sibship genotype data. By limiting the study to sibships, we propose a linkage analysis method that allows linkage disequilibrium among relevant genetic loci, can incorporate general crossover process model, and is computationally feasible. The cruxes of this approach are systematic ways to introduce probability distributions on the space of legal ordered parental genotypes and on the space of legal inheritance patterns so as to apply importance sampling techniques for calculating various relevant probabilities. Using the three generation genotype data of CEPH families, we examine the performance of our method in terms of the accuracy in calculating the conditional probability of IBD sharing for sib-pairs given the sibship genotype data on chromosome 19. It seems that our method performs very well and outperforms GENEHUNTER, and the advantage comes from the possibility of utilizing population haplotype frequencies derived without the assumption of linkage equilibrium.