

**Linkage Analysis of Affected Relative Pairs**

1. Consider a polymorphism with three alleles, with frequencies  $p_1 = 0.50$ ,  $p_2 = 0.30$  and  $p_3 = 0.20$ .
  - a) If a sample of affected sibling pairs were collected, what proportion of sib-pairs would you expect to share zero, one and two alleles IBS if the marker were not linked to any susceptibility genes?
  - b) Repeat the previous analysis, but considering a sample of half-sibling pairs.
  - c) Calculate the LOD score using the IBS test of Bishop and Williamson (1990) if 20 sib-pairs who share genotype 3/3 are collected (this is the rare allele).
  
2. Now consider the MLS approach of Risch (1990)
  - a) For the same polymorphism as in 1.c) above, calculate the MLS score using the E-M algorithm to maximize the likelihood.
  - b) Re-calculate the LOD score assuming the 20 sib-pairs share genotype 1/1. Can you explain the difference?
  - c) Would your answers to a) or b) above change if you imposed the possible triangle constraint?