Biostatistics 666
Problem Set 6
Due Thursday March 23

<u>Linkage Analysis of Affected Relative Pairs</u>

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?