Homework questions. Please provide your answers on a separate sheet. These questions are mostly from lectures 15 and 16. Each question is worth one point unless stated otherwise.

1. (two points) Examine the following pedigree.

The A₁ alleles in the two brothers are identical by state (this just means that they are both A₁). The same is true of B₁. In either case can you infer that they are identical by descent? In other words, which alleles are identical by descent (neither, A₁, B₁, or both)?

(Questions 2-8, one point each): Consider two populations, 1 and 2, that differ at two unlinked loci, A and B. In each population a specific allele is fixed at each locus (all individuals in population 1 have the genotype A₁₁ B₁₁ while all individuals in population 2 have the genotype A₂₂ B₂₂).

First, you cross a single male from population 1 with a single female in population 2.

2. What is the expected frequency of each of the nine possible genotypes in the F₁ progeny? The possible genotypes are
   A₁₁ B₁₁ ; A₁₁ B₁₂ ; A₁₁ B₂₂ ;
   A₁₂ B₁₁ ; A₁₂ B₁₂ ; A₁₂ B₂₂ ;
   A₂₂ B₁₁ ; A₂₂ B₁₂ and A₂₂ B₂₂

3. Is locus A at Hardy-Weinberg equilibrium in the F₁ generation (your answer would be the same for locus B)?

4. Do the two alleles A₁ and B₁ show linkage disequilibrium (association) in this F₁ generation? (consider the haplotypes that are transmitted by this F₁ generation to the F₂ generation).

5. What is the expected frequency of each of the nine possible genotypes in the F₂ progeny (assuming random mating among the F₁)?
6. Is locus A at Hardy-Weinberg equilibrium in the F2 generation?

7. What is the frequency of each of the four possible haplotypes (A_1 B_1, A_1 B_2, A_2 B_1, and A_2 B_2) in gametes transmitted from the F2 generation to the F3 generation?

8. Do the two alleles A_1 and B_1 show linkage disequilibrium in this F2 generation? (again, consider haplotypes transmitted to the next generation, the F3).

Later (questions 9-11), you allow a large and equivalent number of individuals from the two populations -- for example, 500 males and 500 females from population 1 and 500 males and 500 females from population 2 -- to mate at random (and they do mate at random).

9. Is locus A at Hardy-Weinberg equilibrium in the "F1" generation?

10. Do the two alleles A_1 and B_1 show linkage disequilibrium in this F1 generation?

11. If the "F1" generation again mates randomly, do A_1 and B_1 show linkage disequilibrium in the resulting F2 generation?

This pedigree shows a family affected by an autosomal dominant genetic disease.

Genotypes for three linked markers, A, B and C, are shown.
The genotypes are:

I-1  A\textsubscript{1,2} B\textsubscript{1,2} C\textsubscript{1,2}
I-2  A\textsubscript{3,3} B\textsubscript{3,3} C\textsubscript{3,3}
II-1 A\textsubscript{1,3} B\textsubscript{1,3} C\textsubscript{1,3}
II-2 A\textsubscript{4,4} B\textsubscript{4,4} C\textsubscript{4,4}
III-1 A\textsubscript{1,4} B\textsubscript{1,4} C\textsubscript{1,4}
III-2 A\textsubscript{3,4} B\textsubscript{3,4} C\textsubscript{3,4}
III-3 A\textsubscript{1,4} B\textsubscript{1,4} C\textsubscript{3,4}
III-4 A\textsubscript{1,4} B\textsubscript{3,4} C\textsubscript{1,4}
III-5 A\textsubscript{3,4} B\textsubscript{3,4} C\textsubscript{4,4}
III-6 A\textsubscript{1,4} B\textsubscript{1,4} C\textsubscript{1,4}

12. Indicate the phase of alleles in individual II-1 by showing his haplotypes. There are four possibilities. They are

a) A\textsubscript{1} B\textsubscript{1} C\textsubscript{1} / A\textsubscript{3} B\textsubscript{3} C\textsubscript{3}
b) A\textsubscript{1} B\textsubscript{1} C\textsubscript{3} / A\textsubscript{3} B\textsubscript{3} C\textsubscript{1}
c) A\textsubscript{1} B\textsubscript{3} C\textsubscript{3} / A\textsubscript{3} B\textsubscript{1} C\textsubscript{1}
d) A\textsubscript{1} B\textsubscript{3} C\textsubscript{1} / A\textsubscript{3} B\textsubscript{1} C\textsubscript{3}

13. (3 points; one point per pair of markers) For each individual in the third generation (III-1, III-2, III-3, III-4, III-5 and III-6) indicate whether they are recombinant, nonrecombinant or indeterminate for each pair of markers in this pedigree (e.g. draw a 6 by 3 table with six individuals on one axis and the three pairs markers (A and B, B and C and A and C) on the other. Fill in all 18 squares with yes or no.

14. Ignoring all of the other loci, calculate a lod score for linkage to of the disease to A with $\theta = 0$

15. Now, assume that this disease is only 80% penetrant. What is the lod score for linkage to A with $\theta = 0$ under this revised model?

16. Now, assume that the penetrance is 100%, but there is a probability of 5% of phenocopy (i.e. 5% of people who are not at genetic risk show the trait).

Now, what is the lod score for linkage to A with $\theta = 0$?

17. Ignoring all other loci, what value of $\theta$ would give the highest lod score for linkage of the disease to B?