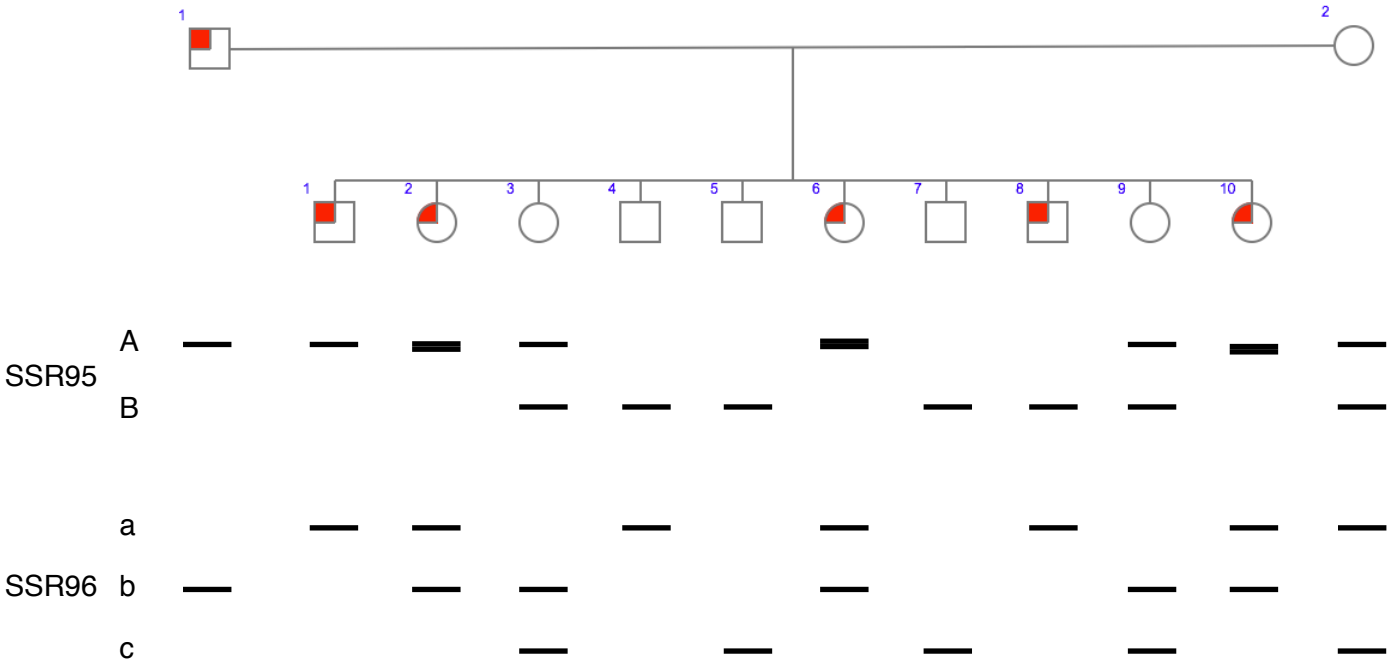
Bio393: Biomedical Genetics **Name:**_____
Problem Set #6
Due on Friday, May 17, 5 PM

Question 1:
You set out to genetically map color blindness with respect to short-sequence repeat (SSR) markers. Color blindness shows X-linked recessive inheritance and therefore is usually found in males. However, the mutant allele frequency is sufficiently high that colorblind females do occur.

Alleles: + (normal) cb (associated with color blindness)

Here is a family in which some individuals are affected:



(a) Diagram the two possible phase relationships between the SSR95 and SSR96 alleles in the mother.

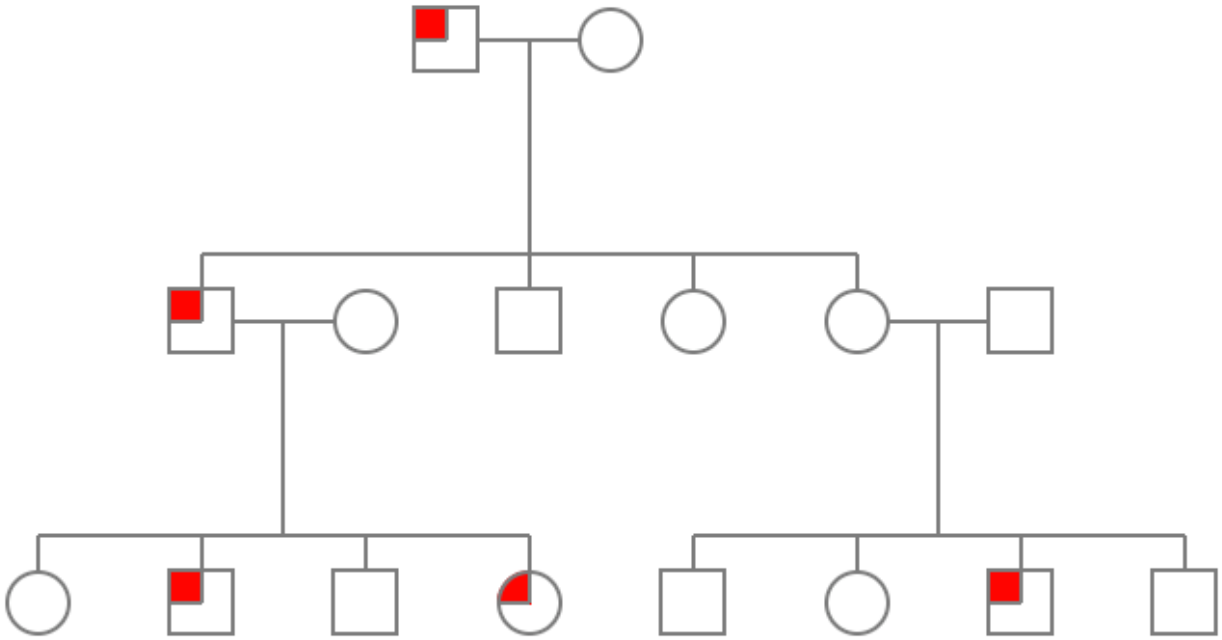
(b) Calculate the LOD score for linkage at $\theta = 0.1$ between SSR95 and SSR96 in this family.

(c) Identify a value of θ at which this family will yield a higher LOD score for linkage between SSR95 and SSR96. Calculate the LOD score for linkage between SSR95 and SSR96 at that new θ value.

(d) Diagram the two possible phase relationships between the SSR95 and color blindness alleles in the mother.

(e) Calculate a LOD score for linkage at $\theta = 0.1$ between SSR95 and color blindness in this family.

Question 3:
Syndactyly is a rare genetic condition inherited as an autosomal dominant trait. Unusually however, a person who has the defective allele responsible for syndactyly (N) does not always express the trait. The diagram below shows a pedigree of a family with syndactyly.



You find no history of syndactyly in the ancestors of individual I-2, II-2, and II-6. Assuming no new mutations exist, explain why or why not it is reasonable to conclude the following:

(a) Individual II-5 has the genotype nn at the syndactyly locus

(b) Individuals II-4 and II-5 may have the same genotype at the syndactyly locus

(c) Individual II-2 has the genotype Nn at the syndactyly locus

(d) Individuals III-2 and III-7 have different genotypes at the syndactyly locus

Question 4:
You are studying a dominant Mendelian disease via linkage analysis and are focusing on a single marker. Two large families have been genotyped at the same marker and scored for the disease.

In Family I, ten offspring are genotyped: eight children inherited a marker allele and a disease-causing allele without recombination; two children appear to be recombinants. You test many values of the recombination fraction (theta) and discover that theta = 0.2 gives the maximum odds ratio, which is 6.87 (LOD = 0.837).

In Family II, 20 offspring are genotyped: 17 children inherited a marker allele and a disease-causing allele without recombination; three children appear to be recombinants. You test many values of theta and discover that theta = 0.15 gives the maximum odds ratio, which is 223.4 (LOD = 2.34).

To combine data across Family I and Family II, you multiply odds ratios (add LOD scores). The final estimate of the odds of linkage relative to the null as 1534.8 (LOD = 3.18). Explain what is wrong with this calculation.