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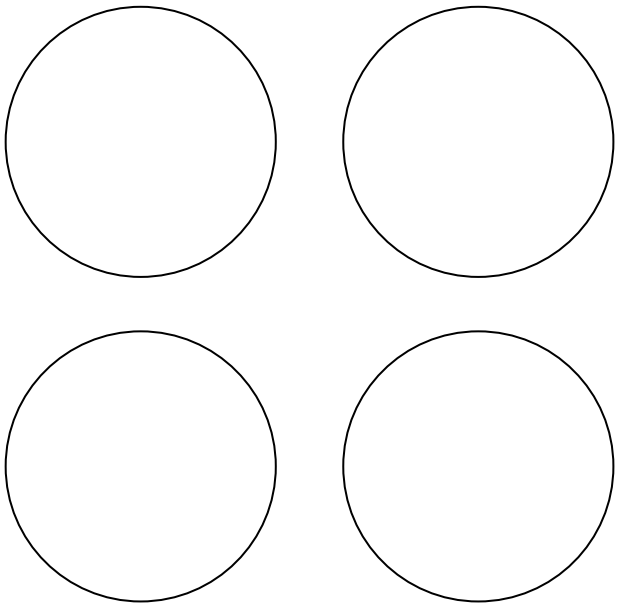
7.03 Problem Set 2
Due Monday, March 2, 2015 by 3 PM

1. You have identified some yeast mutant strains that, when performing meiosis to transition from a diploid state to a haploid state (**sporulation**), end up with daughter spores with abnormal chromosome number (also known as **ploidy**).

a) Through whole-genome sequencing, you discover that one of your mutant strains has a mutation in the gene *SMC1*, which encodes a subunit of the cohesin complex. Briefly explain how this mutant strain might result in abnormal ploidy in daughter cells.

b) As it turns out, you are able to copy the mutation of *SMC1* in your yeast strains in mice, and observe the germ cells that result. Let also assume that we are able to selectively induce this mutation during specific stages of meiosis. Considering the case where **only one** of the homologous chromosomes experiences non-disjunction, draw the resulting daughter cells after this mutation is activated just prior to meiosis II, and explain your answer briefly:



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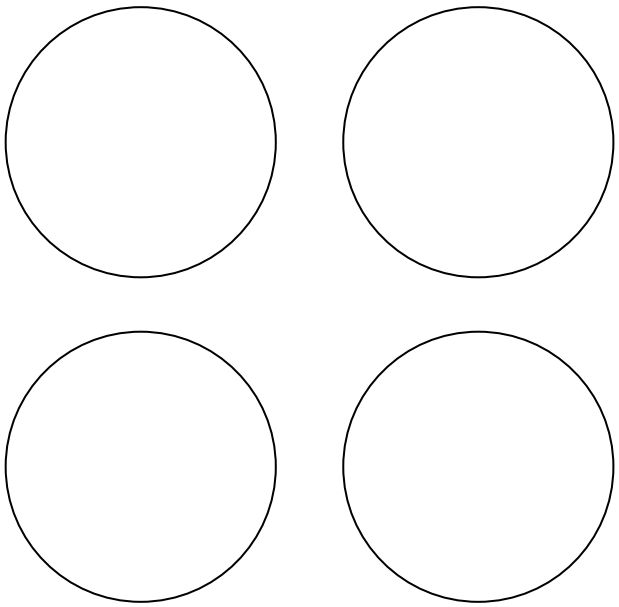
c) Now draw the resulting daughter cells after this mutation is activated **only during** meiosis I, and explain your answer:



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2. You have isolated three novel Drosophila mutants in the lab and want to map them to the Drosophila genome. **cr** makes flies fly in circles, **lg** causes them to grow an extra set of legs and **ye** mutants have yellow eyes. After some preliminary work you determine that these mutant traits are each caused by a single gene and are recessive. You also suspect they might be linked to each other, and to a known recessive fly marker – **eb** (ebony body).

a) Design a set of crosses that will allow you to score offspring with both parental and recombinant genotypes for all four genes. You have in the lab true breeding wild type flies and a true-breeding strain of flies that have extra legs, ebony bodies, yellow eyes and fly in circles. Explain briefly why you chose these crosses.

b) You carry out your crosses and find that you obtain offspring with the following phenotypes (+ denotes wild type). Calculate the genetic distances between the four genes of interest and draw a map of their positions relative to each other. Please show your work.

	Phenotype	**Number of Offspring**
1	ye lg cr eb	70
2	+ + + eb	10
3	ye lg cr +	13
4	ye + cr eb	80
5	+ lg + +	75
6	+ + cr eb	2
7	ye lg + +	3
8	ye + + +	2
9	ye lg + eb	22
10	+ lg + eb	13
11	ye + cr +	11
12	+ + + +	74
13	+ lg cr +	20
14	+ + cr +	24
15	ye + + eb	17
16	+ lg cr eb	4
	Total	

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c) Explain why some distances between genes do not add up and any other ambiguities you may come across.

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d) A few months later, you discover another dominant mutant phenotype, **Pi,** that causes your flies to have pink eyes. After attempts to place this gene onto the map you created in (b) you find that out of 500 offspring you only get one offspring that is recombinant for ye and Pi.

What is the genetic distance between these two mutations? If the **ye** gene is 0.09 Mbps and given a recombination rate of 3.3 cM/Mbp in Drosophila, do you think **Pi** & **ye** are alleles of the same gene?

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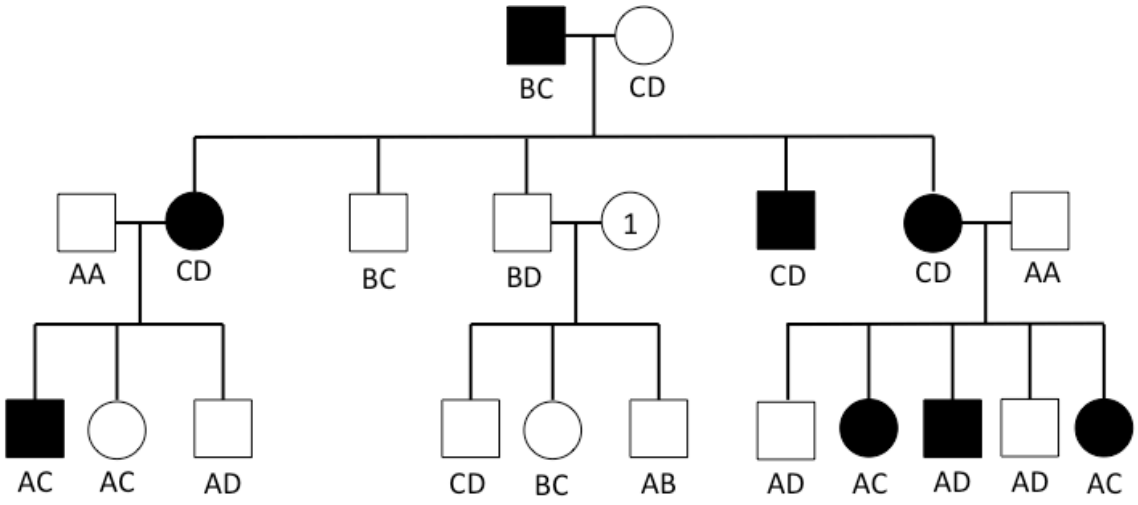
3. You are a geneticist who has been asked to help pinpoint the inheritance of a newly discovered disease (maybe they will name it after you, if you can figure out its inheritance). Your work has led you to believe that this disease is linked to alleles of a simple sequence repeat (SSR). Based on this, your collaborators have painstakingly collected samples from families and sequenced them, resulting in the following pedigree, where A, B, C, and D are alleles of the SSR of interest:



a) What is the most likely mode of inheritance of this disease? (autosomal or sex-linked? dominant or recessive?) Briefly explain your answer.

b) What can you infer about the genotype of the individual marked 1?

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c) Is it likely that this SSR is completely linked to the disease? Explain briefly. What would the LOD score be for this scenario (i.e. calculate the LOD score for $\theta = 0$)?

d) Estimate a recombination frequency between the trait and this SSR (Estimate θ). Calculate the LOD score based on only the individuals in the second generation for this estimated frequency (θ).

e) Calculate the LOD score for the individuals in the third generation with the same estimate from part (d).

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f) Calculate the LOD score for this entire pedigree. Based on this calculation, can you infer that this SSR is linked to the disease from this pedigree alone?

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4. You have isolated four different yeast mutants by mutagenesis that can not grow on medium lacking leucine. You cross each of these haploid mutants to wild type yeast and observe the following diploids.

Haploid genotype	**Diploid genotype**	**Diploid phenotype**
leu1		WT
leu2		leu-
leu3		WT
leu4		WT

a) What are the diploid genotypes of these crosses (Please fill in the table)? What can you deduce about your four mutants based on these crosses?

You then obtain *MAT*a and *MAT*α strains of each of these mutants and cross them to each other to obtain diploids. You sporulate the resulting diploids and obtain 120 tetrads each. You observe the following phenotypes:

Diploid	**Tetrads**	**Tetrad #**	**Tetrad Type**
leu1/leu2	4 leu-	120	
leu1/leu3	4 leu- 2 leu- , 2 leu+ 3 leu- , 1 leu+	18 22 80	
leu1/leu4	3 leu- , 1 leu+ 4leu-	14 106	

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b) Identify the tetrad types observed in the table above. What can you deduce about the relationship between these four mutant alleles based on the tetrads observed?

c) Calculate the genetic distance between these genes and draw a map.