7.03 - Genetics - Fall 2004
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1. Consider an autosomal recessive trait that occurs at a frequency of 10^{-6} in a specific population that is at Hardy-Weinberg equilibrium (ie. random mating is occurring). When answering the following parts, show all of your calculations.

(a, 7 pts) Draw a pedigree below that shows a mating between two relatives that would correspond to an inbreeding coefficient that equals 0.007813. Denote the mating between relatives with a double-bar connecting the two related parents. Start your pedigree with the common pair of ancestors and end your pedigree with the two related parents who are mating.

(b, 8 pts) Now say that all matings in Generation X of the given population are either between unrelated individuals, or have the same inbreeding coefficient as the mating described in part **(a)**. If the incidence of the trait in Generation "X+1" increases to a frequency of 2×10^{-6}, what percentage of matings in Generation X must have been between **unrelated** individuals?

(c, 4 pts) Now assume that this autosomal recessive trait causes lethality in childhood. If a constant percentage of matings are between related parents for many generations, would you predict that q would increase OR decrease?

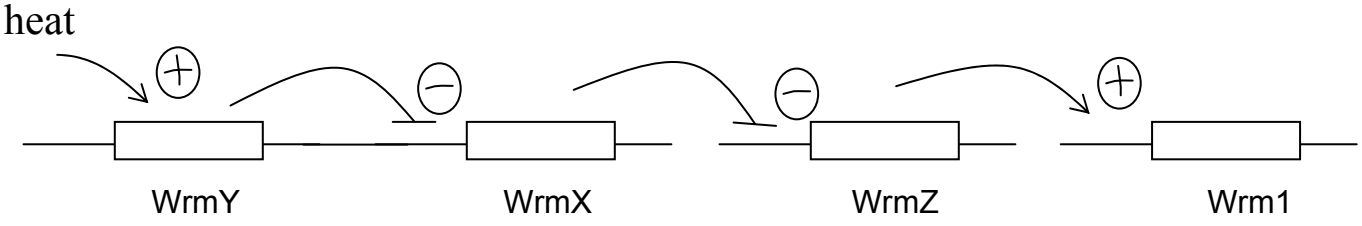
(d, 9 pts) A constant percentage of matings has occurred between related parents for many generations, and yet you find experimentally that q has not changed. Of the three choices below, circle **ALL** that could potentially act against the effect you chose in part **(c)** in order to keep q constant. Explain in one sentence why you chose or did not choose <u>each</u> option.

Choice A: migration

Choice B: heterozygote advantage (Aa over AA)

Choice C: mutation

2. You are studying regulation of the Wrm1 gene, a yeast gene that is expressed in response to heat. You isolate a wrm1::lacZ strain that expresses β-galactosidase when Wrm1 is normally expressed (which is at 36°C but not at 24°C). You use this wrm1::lacZ strain to perform a genetic screen looking for mutants that do not properly regulate expression of Wrm1. In your screen, you isolate a series of mutant strains that either show constitutive or uninducible expression of wrm1::lacZ.
Your results indicate that the following is the correct pathway for regulation of Wrm1 expression. Note that WrmY and WrmX are on the same chromosome, and that WrmX, WrmZ, and Wrm1 are all on different chromosomes.



One of the mutant strains you isolate contains a mutation called WrmX⁻, which is in the **coding region** of WrmX. You mate a WrmX⁻ wrm1::lacZ haploid strain to a wrm1::lacZ haploid strain. The resulting diploids are white on X-gal plates that are incubated at 24°C, and are blue on X-gal plates that are incubated at 36°C.

(a, 3 pts) Classify the WrmX⁻ mutation as constitutive OR uninducible.

(b, 3 pts) Classify the WrmX⁻ mutation as dominant OR recessive.

(c, 3 pts) Classify the WrmX locus as cis-acting OR trans-acting with respect to Wrm1.

You next isolate a mutant strain containing a mutation called WrmY⁻, which is in the **coding region** of WrmY. You mate a WrmY⁻ wrm1::lacZ haploid to a wrm1::lacZ haploid. The resulting diploids are white on X-gal plates, regardless of the temperature at which the plates are incubated.

(d, 6 pts) Classify WrmY⁻ by the type(s) of mutation it could be **with respect to Wrm1**. (Your choices are: repressor –, activator –, UAS–, URS–, super activator, super repressor, dominant negative repressor, dominant negative activator.)

You create diploid yeast by mating WrmX$^-$ WrmY$^-$ wrm1::lacZ haploid yeast to wrm1::lacZ haploid yeast. Sporulation of these diploids yields two types of tetrads, and you correctly conclude (given the number of each type of tetrad) that the WrmX and WrmY loci are linked at a distance of 2.22 cM.

(e, 14 pts) Depicted below are the two types of tetrads that resulted when you sporulated the above diploids. For each type of tetrad, state **how many** you found of that tetrad (out of a total of 90 tetrads), **classify** the tetrad as PD, NPD, or TT, and **color in** all of the spores that would be blue on each of the following Petri plates.

Tetrad Type A
Number of these tetrads out of a total of 90: _____
Classification of these tetrads (PD, NPD, or TT): _____

Color in the spores that would be blue in color when growing on the following plates:

X-gal, 24°C	X-gal, 36°C
○	○
○	○
○	○
○	○

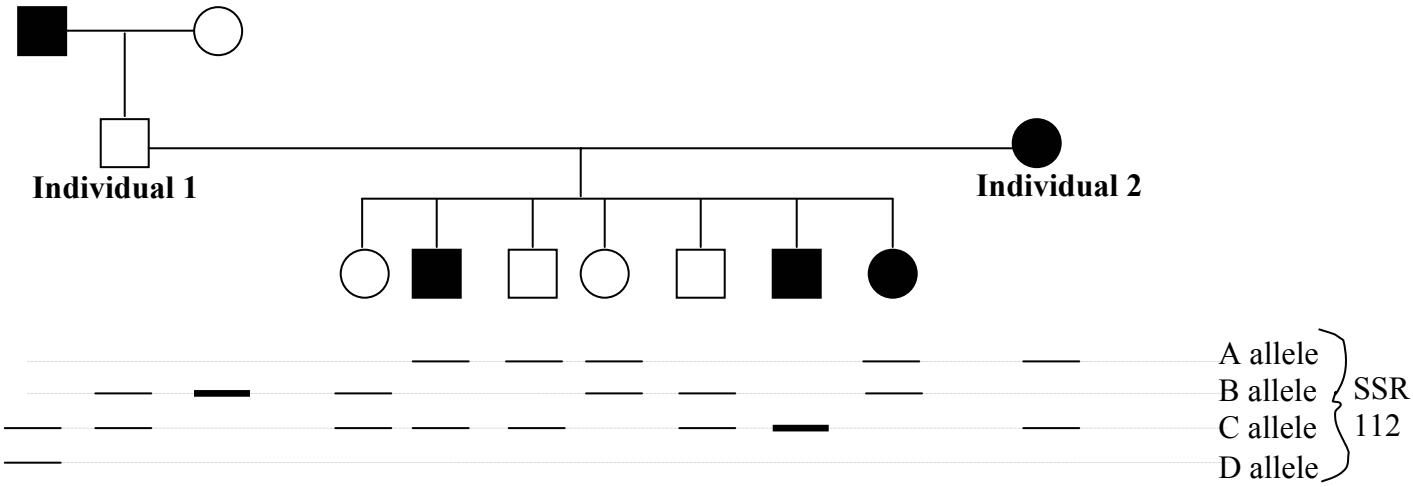
NOTE that the two plates are replicas, so the top spore on the left plate has the same genotype as the top spore on the right plate.

Tetrad Type B
Number of these tetrads out of a total of 90: _____
Classification of these tetrads (PD, NPD, or TT): _____

Color in the spores that would be blue in color when growing on the following plates:

X-gal, 24°C	X-gal, 36°C
○	○
○	○
○	○
○	○

3. You are mapping a certain disorder that is caused by an allele at the N locus. You suspect that the N locus is linked to SSR112 on human chromosome #17. You analyze the following family for these two loci. You will fill in the charts below in subsequent parts of the problem.



maternally inherited allele at SSR112							
paternally inherited allele at SSR112							

maternally inherited allele at the N locus							
paternally inherited allele at the N locus							

IF the condition is autosomal recessive [parts **(a)** and **(b)**] (Individual 2 is "nn")

maternally inherited allele at the N locus							
paternally inherited allele at the N locus							

IF the condition is autosomal dominant [parts **(c)** - **(e)**] (Individual 2 is "Nn")

Answer parts **(a)** and **(b)** as if the disorder is autosomal recessive and caused by the "n" allele, so that Individual 2 is "nn."

(a, 9 pts) Fill in the upper four rows of the chart using autosomal recessive inheritance for the disorder. Then answer below: **which parent's** alleles will you follow to correctly calculate a LOD score between the N locus and SSR 112 -- Individual 1 or 2?

(b, 3 pts) Draw all phases of the parent you chose in part **(a)** with respect to SSR 112 and the N locus that are possible given everything you know about that parent. Make sure to draw the phases using the proper notation.

Answer parts **(c)** through **(e)** as if the disorder is autosomal dominant and caused by the "N" allele, so that Individual 2 is "Nn.".

(c, 6 pts) Fill in the lower two rows of the chart using autosomal dominant inhertance for the disorder. Then answer below: **which parent's** alleles will you follow to correctly calculate a LOD score between the N locus and SSR 112 -- Individual 1 or 2?

(d, 3 pts) Draw all phases of the parent you chose in part **(c)** with respect to SSR 112 and the N locus that are possible given everything you know about that parent. Make sure to draw the phases using the proper notation.

(e, 7 pts) How many times more likely is it that the data from this family arose because of linkage between the SSR 112 and N loci at $\theta = 0.2$ than because the two loci were unlinked? Show all calculations.

4. The scenario on the next page asks a biological question that can be addressed by creating genetically engineered mice. When creating engineered mice, the following 8 steps need to be considered. **For each mouse you make** in this problem, please state:

i) whether you are using pronuclear injection or gene targeting techniques
ii) what DNA you would introduce into the mouse cells (also draw the DNA)
iii) whether you would put the DNA into a fertilized egg or ES cells
iv) from what genotype of mouse would you get the fertilized egg or ES cells
v) where in the mouse genome the DNA you introduced would integrate
vi) whether creating the mouse should involve the generation of a chimera or not
vii) which additional breeding steps you would do to make the mouse you wanted
viii) two possible phenotypic results you could get from the newly made mice, and the corresponding conclusions you would make based on each result

(15 pts) "Non-homologous end joining" is the process by which a DNA sequence gets inserted into a chromosomal region to which it is not homologous. Having a functional copy of the gene "NheJ" is necessary for this process to occur in mice. A mouse with no copies of the NheJ gene is sensitive to irradiation as an adult, but a heterozygote is not sensitive.

You decide to test whether one copy of the *Drosophila* "d-Nhe" gene could fully compensate for the absence of the mouse NheJ gene. You have wild-type homozygous mice (NheJ+/NheJ+), heterozygous mice (NheJ+/NheJ^{-}), and homozygous mutant mice (NheJ^{-}/NheJ^{-}) readily available to you.