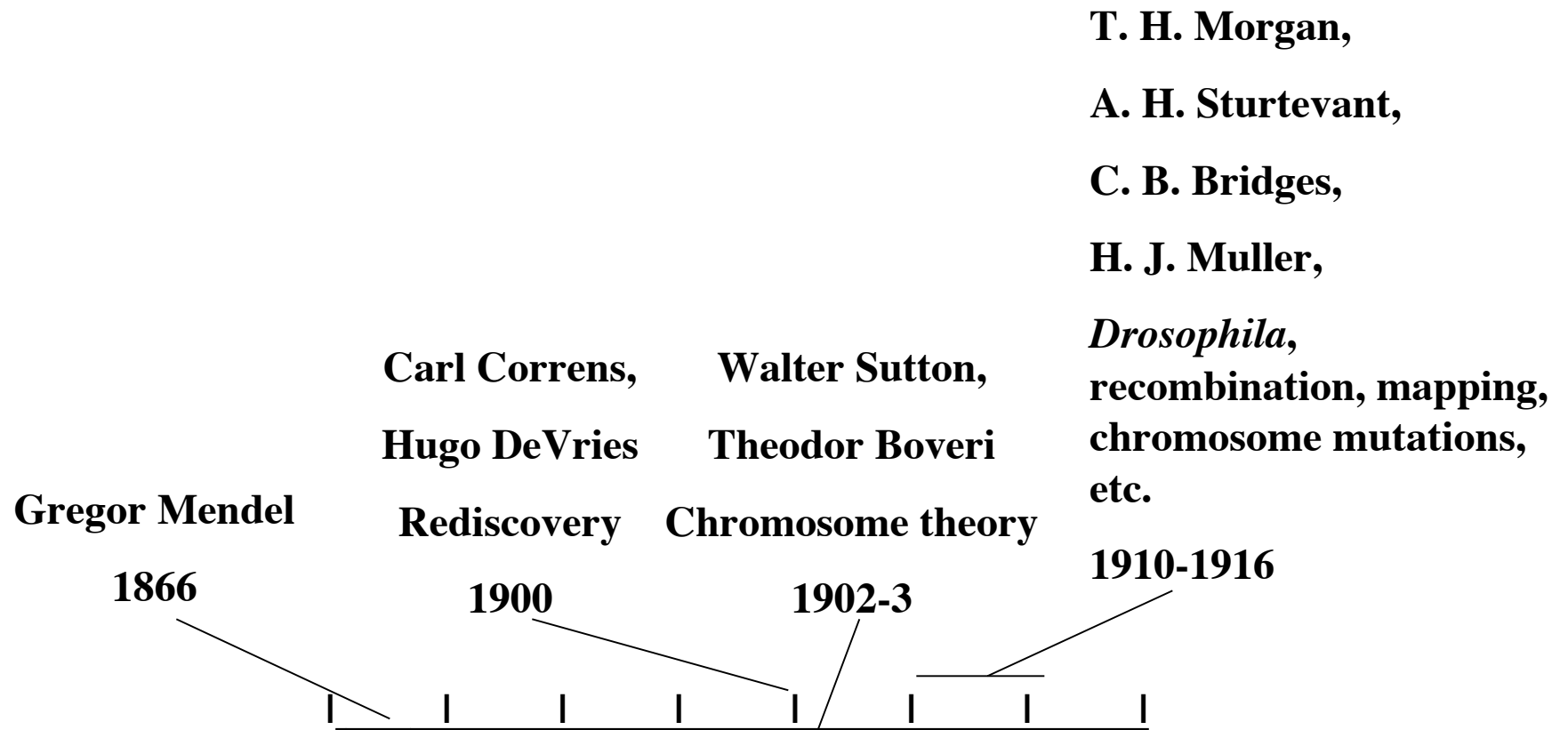


Update: Time Line of Revolutions in Genetics



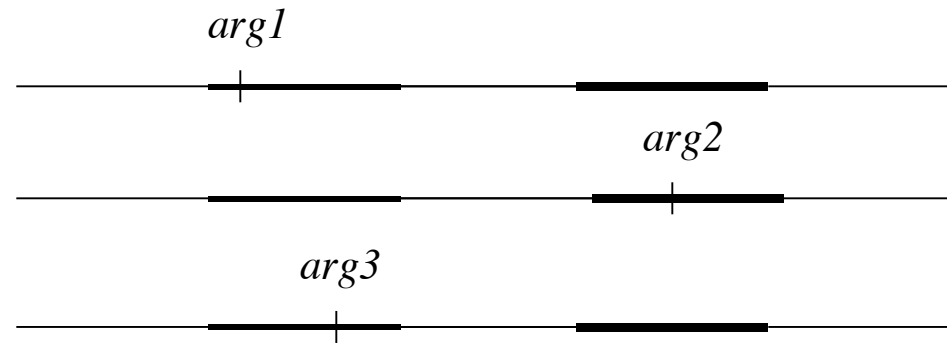
Complementation groups, genes, and alleles.

Object:

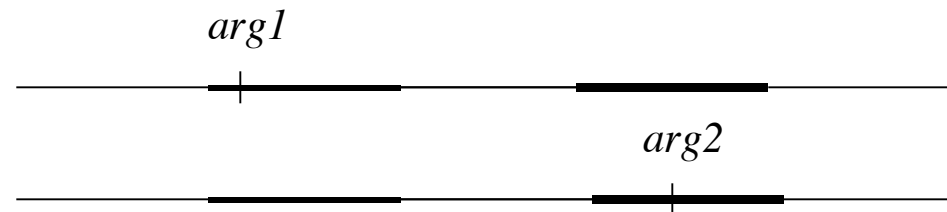
Determine if two mutations are in the same or different genes.

e.g. isolate three arginine auxotrophic mutations in haploid yeast strains:

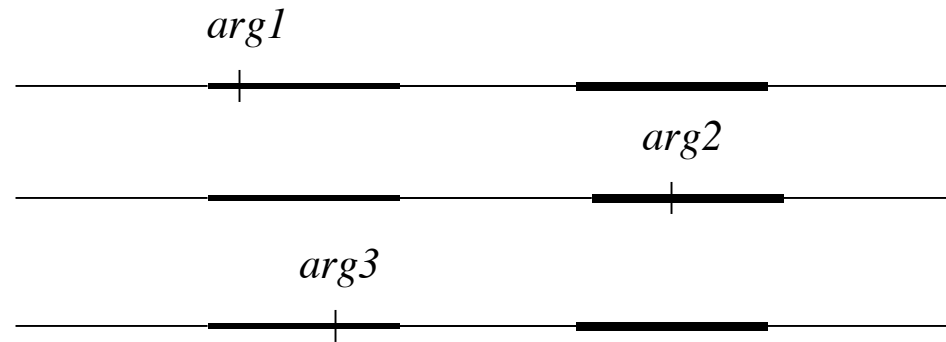
arg1, *arg2*, *arg3*



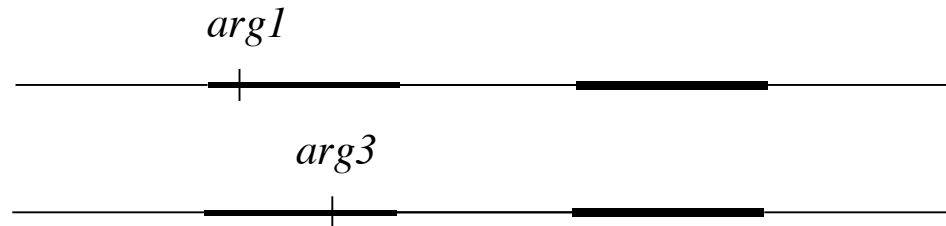
Cross α *arg1* \times α *arg2*, look at diploid phenotype:



The diploid grows on minimal medium because each mutant came with the wild type allele of the other gene, thereby complementing it. So *arg1* and *arg2* are in different genes, and they are not alleles.



Cross $a\ arg1 \times \alpha\ arg3$, look at diploid phenotype:



The diploid does *not* grow on minimal medium because each mutant is in the same gene and there is no wild type copy of that gene in the diploid. *arg1* and *arg3* do not complement each other, so they are different mutations of the same gene, and they are alleles.

We have identified two genes, which we might call *ARGA* and *ARGB*.
ARGA has three alleles: *ARGA*, *argA1*, and *argA3*.
ARGB has two alleles: *ARGB* and *argB2*.

Isolate two more *arg* auxotrophs, test growth of diploids on MM:

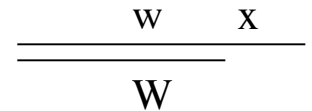
	<i>arg1</i>	<i>arg2</i>	<i>arg3</i>	<i>arg4</i>	<i>arg5</i>
<i>arg1</i>		+	-	+	+
<i>arg2</i>			+	+	+
<i>arg3</i>				+	+
<i>arg4</i>					-
<i>arg5</i>					

arg4 and *arg5* are in another complementation group, so we now have three complementation groups and have identified three genes. Each one may encode an enzyme for a different step in the biosynthesis of arginine.

Can you explain hw # 5.8 [I did this in Discussion] and 8.12 as well as another example of physical and genetic maps?

8.12 Recessive genes $a, b, c, d, e,$ and f are are closely linked but their order is unknown. Three deletions in the region are examined. One deletion uncovers $a, d,$ and e ; another uncovers $c, d,$ and f ; and the third uncovers b and c . What is the order of the genes?

“Uncovers” means that in a heterozygote that has one chromosome with a deletion but is otherwise wild type and the other chromosome has recessive alleles, one sees the recessive phenotype for the gene that is “uncovered”.



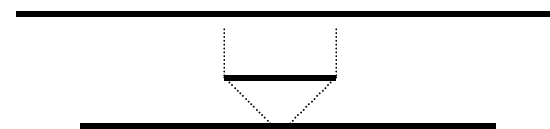
Deletion 1 uncovers $a, d,$ and $e,$ so these are in a cluster that includes none of the others: $a d e$ or $a e d$ or $d a e$.

Deletion 2 uncovers $c, d,$ and $f,$ so they are also clustered: $c d f$ or $c f d$ or $d c f$. But d must be at the end because it is also uncovered by deletion 2, so we have $a e d c f$ or a similar order.

The third uncovers b and $c,$ so these are adjacent to each other. We also know that b is not in any of the other clusters, so c must be at the end of the combined cluster identified by deletions 1 and 2.

The order must be as shown below, with the three deletions shown in order below it. Note that for mapping purposes, deletions are shown as lines where the deleted segments are, not chromosomes missing certain regions.

$a e d$ $f c$ b (or $e a d f c b$)

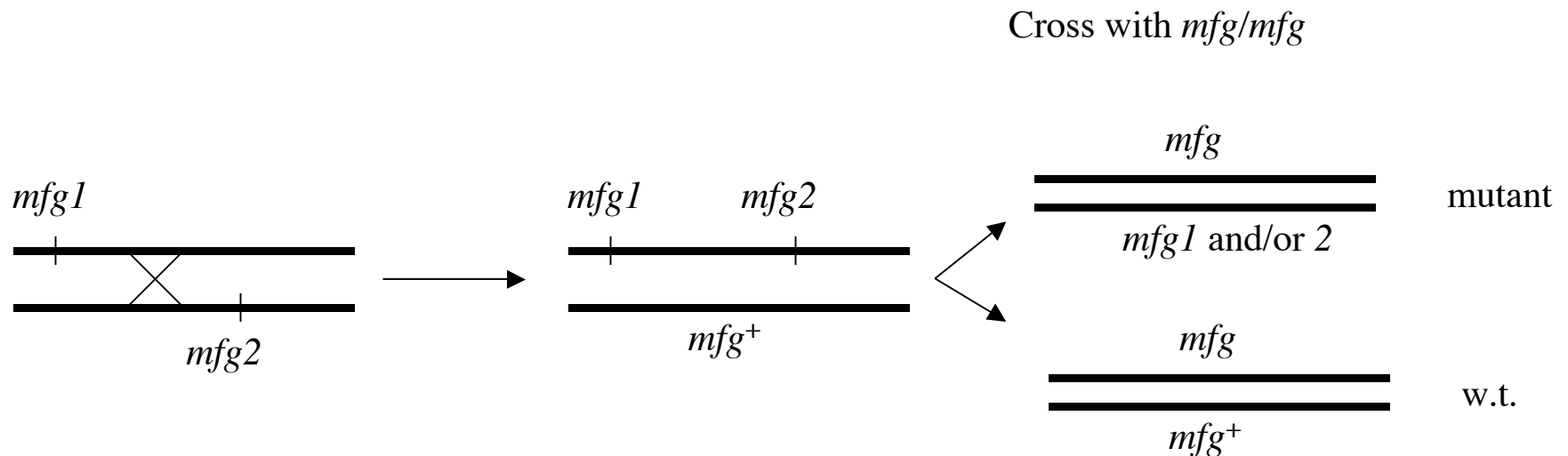


w.t.
deleted
deletion

Intragenic recombination

This simply means recombination between two mutations in the same gene. It is detected by making a heterozygote for the two mutations and finding wild type recombinant chromosomes.

We would also have to do a complementation test to know that the mutations are in the same gene. Finding a wild type recombinant merely shows that *mfg1* and *mfg2* are not two cases of the same mutation (in the same base pair).



During our review tomorrow can you explain how to do problems 2 and 3 from homework 2

[I reviewed these in Discussion.]

You won't be required to do a complete analysis, but might be asked to do part of it.

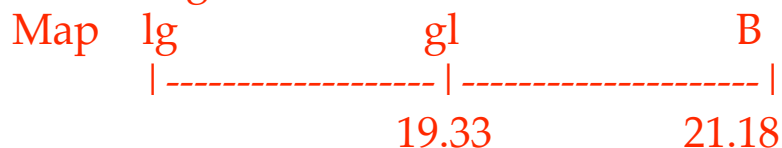
2. In maize, a strain homozygous for two recessive mutations, *liguleless* (*lg*) and *glossy* (*gl*), was crossed to another strain homozygous for a dominant allele, *Booster* (*B*). An F1 plant was backcrossed to the *liguleless glossy* parent strain. The progeny phenotypes and numbers are shown below. (For example, *lg + gl* 172 means that 172 plants were liguleless glossy.) Make a map with these three genes. Carry calculations to two decimal places.

<i>lg + gl</i>	172	F1 had <i>lg B⁺ gl</i> on one chromosome
<i>+ B +</i>	162	and <i>lg⁺ B gl⁺</i> on the other.
<i>lg B gl</i>	56	This has <i>B</i> and <i>gl</i> together, so it is a recombinant for these loci.
<i>+ + +</i>	48	
<i>lg B +</i>	51	
<i>+ + gl</i>	43	
<i>lg + +</i>	6	
<i>+ B gl</i>	<u>5</u>	
	543	

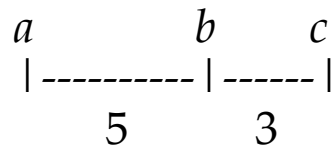
By comparing the double crossover genotypes to the parental genotypes, we can tell that *gl* is in the middle.

$$\text{Distance } lg-gl = 51 + 43 + 6 + 5 = 105 \quad 105/543 = 0.1933 = 19.33 \text{ cM}$$

$$\text{Distance } gl - B = 56 + 48 + 6 + 5 = 115 \quad 115/543 = 0.2118 = 21.18 \text{ cM}$$

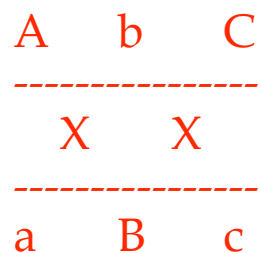


3. In dragons, three genes (a, b, c) have been mapped on a chromosome as shown below, with distances between the loci in centimorgans:



Suppose a dragon of genotype $A A b b C C$ was mated to one of genotype $a a B B c c$ and the offspring were testcrossed. What is the expected frequency of $a a b b c c$ dragons in the progeny from the test cross? Give answer to 5 decimal places.

Offspring had one chromosome with $A b C$ and the other with $a B c$. So the only way to get $a a b b c c$ is by a double crossover.



Answer: $(0.05)(0.03) = 0.0015 = P(\text{double crossovers}) = f(\text{aabbcc} + \text{AABBCC})$

$$f(\text{aabbcc}) = 0.0015 / 2 = \mathbf{0.00075}$$

1.) What do we need to know about the Chi squared test for the exam?

You won't have to do one on an exam.

Should we be able to recognize what is statistically acceptable according to this test?

Yes

2.) I understand what n , w , and x represent individually, but what exactly does $n!/(w!x!)$ without $(p^w)(q^x)$ represent?

It calculates the number of orders.

3.) On slide 4 of the 15th lecture is a time line of scientific discoveries, are these all the names, dates, and events we need to know for the exam?

See first slide.

4.) On slide 19 of the 3/2/07 discussion, in the very bottom right corner, you have the distance from lz to gl as 24.7. I thought that this distance should instead be the result of the addition between lz-su (10.7) and su-gl (14.7), which is 25.4. Could you please explain why it is actually 24.7?

My error, now fixed.

Could you discuss:

1. problem 3 from homework sheet 2.

Similar problem done earlier.

2. problem 10 from Practice problems 4

Similar problem done earlier.

3. problem 4.10, 4.16, 4.28

4.10 X-linked recessive color blindness. Normal couple have normal daughter and color blind son. What is the probability that the daughter is heterozygous?

Color blind son got X from mother and it had the recessive allele b , so mother is Bb .

Father is normal so is BY . Daughter gets B from father and could get B or b from mother, probability $1/2$ either way.

4.16 Draw a pedigree and fill it in. Then do the problem as usual; the description in the book should help.

4.28 Did Chi-square in Discussion and I have nothing to add to that.

1) Will we likely face a multinomial equation? **Maybe but it would have to be a very simple one.** Also, could you review a binomial problem similar to the problem describe on slide 17 of the probability lecture? **I have nothing to add to what was already said.**

2) I was digging around for an updated time line, what specific names/dates should we know, and do what extent should we understand their work/ lives? **Names and dates and general description of what they did on time line. Details of what they did are in lectures.**

3) Why/how do tandem repeats act as molecular markers? **The number of copies of the repeat can increase or decrease. You can view a set of repeats as having many alleles that differ in number of repeats. The number of alleles is very high because the “mutation” rate is high, so everybody has a unique set of alleles if one looks at the standard set of repeat regions. Each repeat region can be amplified by a unique set of PCR primers and repeats of different lengths can be separated by electrophoresis so we can get a profile of of the alleles for an individual.**

4) On slide 20 of the chromosome variation lecture - if you know d was not in 6 could one infer it is in 5? **Yes, if we assume that it is not in the interband region. We used to think all genes were in the bands, but last I heard this was no longer clear.**

5) Can you explain the $p^s q^t$ section of the equation for homework problem 24 in chapter 4? I understand the rest of the solution listed in the back of the book, but not the $(1/2)^8$. **The answer is to sum up the binomial probabilities of all the possible ways of getting an even number of males and of females. Each one is multiplied by $(1/2)^4(1/2)^4$ which is $(1/2)^8$.**

