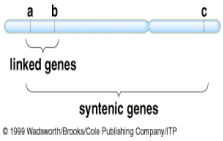
Lectures 9 and 10

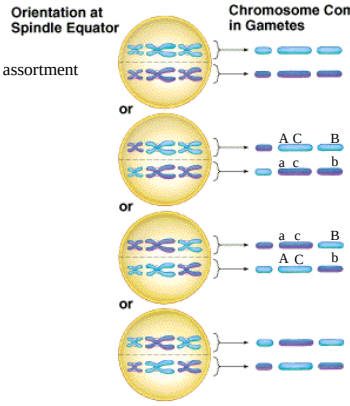
Chapter 7: Linkage, Recombination, and Eukaryotic Gene Mapping, Parts 1 and 2

1. Linked genes: located close together on same chromosome

Syntenic genes: located on same chromosome



2. Independent assortment versus linkage.



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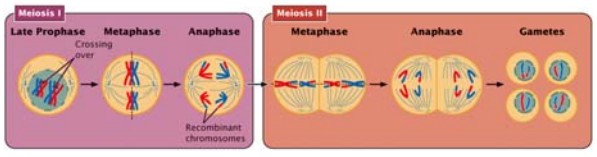

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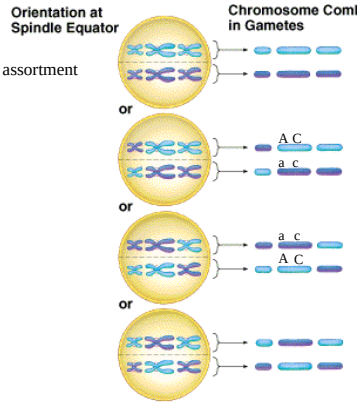
3. Independent assortment versus linkage.



before: AaCc

now: AC/ac

4. Genetic maps show the relative locations of genes on chromosomes.

A. If genes are unlinked, their recombination rate is 50%.
Recombination rate cannot exceed 50%.

B. If recombination rate is <50%, the genes can be seen to be linked.

Before: AaBb x aabb = genotypes in a test cross

Can write as: AB/ab x ab/ab

--If want to look at recomb. in 1st individual, 2nd individual's alleles can not mask expression of 1st one's alleles.

--Thus looking at phenotype of offspring lets us "see" what genotype of gametes was in the first individual.

Also lets us "see" what alleles are on that chromosome.

Phenotypes of progeny:

Unlinked: 1/4 A,B 1/4 a,b 1/4 A,b 1/4 a,B

(Completely) Linked: 1/2 A,B 1/2 a,b

(Partially) Linked:

>1/4 A,B >1/4 a,b <1/4 A,b <1/4 a,B

5. Map units = % recombination

One map unit: the distance between gene pairs for which one product of meiosis out of 100 is recombinant.

Map units usually, but not always proportional to physical distance.

1 mu = 1% recombination = 1cM (centimorgan)

6. Calculating recombination frequencies.

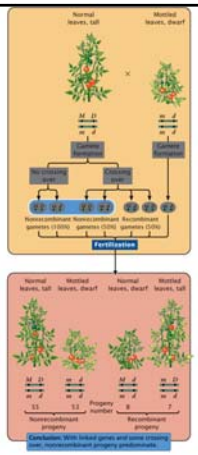
CD/cd x cd/cd

phenotype	frequency	
c,d	478	nonrecombinant
C,D	482	nonrecombinant
C,d	19	recombinant
c,D	21	recombinant
Total	1000	

Recombination frequency = 19+21/1000 = 40/1000 = 0.04 or 4 %

C and D are 4 map units apart on the chromosome.

7. Crossing over betweeen linked genes produces nonrecombinant and recombinant offspring



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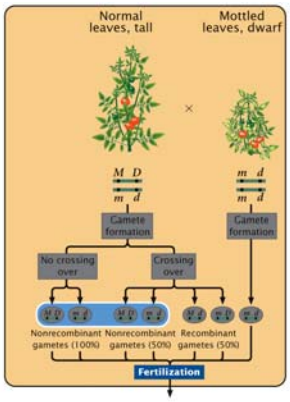
MD/md x md/md



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Two point cross
(two loci)

Four kinds of progeny

Recombination frequency:

# of cross-overs/
total # of progeny =

8+7/55+53+8+7 = 0.12
=12%

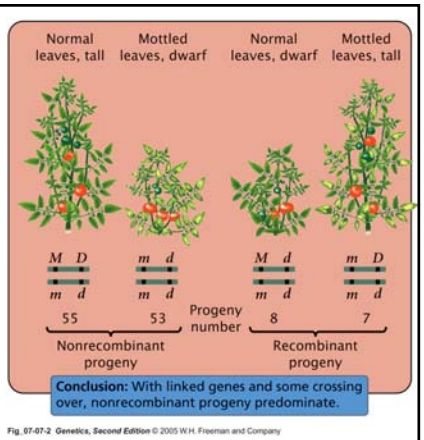
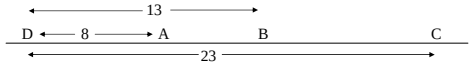
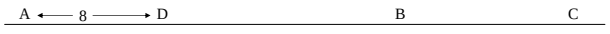


Fig. 07-07-2 *Genetics, Second Edition* © 2005 W.H. Freeman and Company

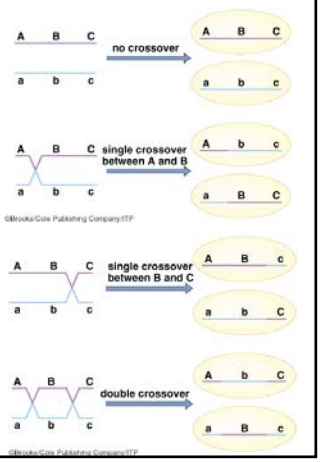
8. Gene Mapping with Recombination Frequencies

Gene Pair	% Recombination
A and D	8
B and D	13
C and D	23





9. Linkage and Recombination between Three Genes
(three point crosses)



10. Calculating recombination frequencies in 3-factor crosses.

Step 1: Look at the numbers. What do they tell you?
Are the genes linked?

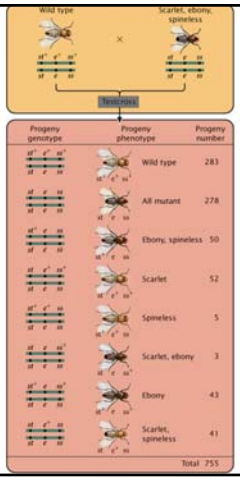
Step 2: Determine which phenotypes represent the nonrecombinant chromosomes.

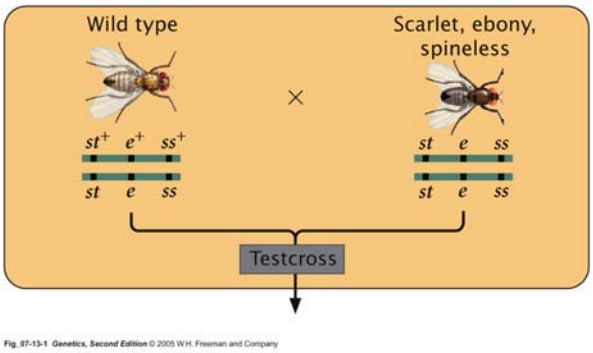
Step 3: Determine which phenotypes represent the double recombinant chromosomes. What is the gene order?

Step 4: Write the phenotypes in their gene order.

Step 4: Calculate the map distances.

dominant traits	recessive traits
red eyes	scarlet eyes
grey body	ebony body
normal bristles	spineless





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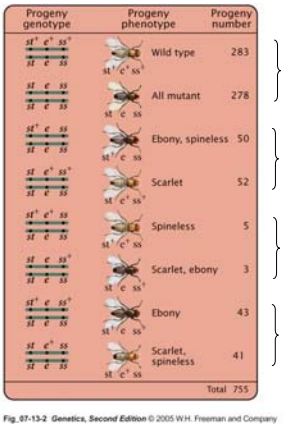

Progeny genotype	Progeny phenotype	Progeny number	
$st^+\ c^+\ ss^+$ / $st\ c\ ss$	Wild type	283	No cross-overs
$st\ c\ ss$ / $st\ c\ ss$	All mutant	278	
$st^+\ c\ ss$ / $st\ c\ ss$	Ebony, spineless	50	Single cross-overs in one region
$st\ c^+\ ss^+$ / $st\ c\ ss$	Scarlet	52	
$st^+\ c^+\ ss$ / $st\ c\ ss$	Spineless	5	Double cross-overs
$st\ c\ ss^+$ / $st\ c\ ss$	Scarlet, ebony	3	
$st^+\ c\ ss^+$ / $st\ c\ ss$	Ebony	43	Single cross-overs in other region
$st\ c^+\ ss$ / $st\ c\ ss$	Scarlet, spineless	41	
		Total 755	

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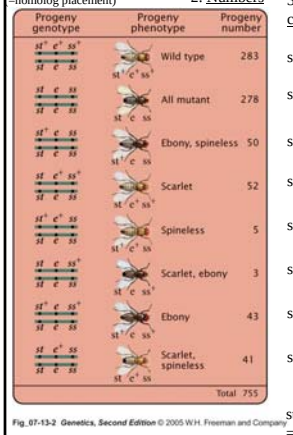
1. Phenotypes (=homolog placement)
2. Numbers
3. Phenotypes in correct order
4. Region getting crossover



Progeny genotype	Progeny phenotype	Progeny number	3. Phenotypes in correct order	4. Region getting crossover
$st^+\ c^+\ ss^+$ / $st\ c\ ss$	Wild type	283	st+ ss+ e+	none
$st\ c\ ss$ / $st\ c\ ss$	All mutant	278	st ss e	none
$st^+\ c\ ss$ / $st\ c\ ss$	Ebony, spineless	50	st+ ss e	st –ss (region 1)
$st\ c^+\ ss^+$ / $st\ c\ ss$	Scarlet	52	st ss+ e+	st –ss (region 1)
$st^+\ c^+\ ss$ / $st\ c\ ss$	Spineless	5	st+ ss e+	(region 1&2)
$st\ c\ ss^+$ / $st\ c\ ss$	Scarlet, ebony	3	st ss+ e	(region 1&2)
$st^+\ c\ ss^+$ / $st\ c\ ss$	Ebony	43	st+ ss+ e	ss—e (region 2)
$st\ c^+\ ss$ / $st\ c\ ss$	Scarlet, spineless	41	st ss e+	ss—e (region 2)
	Total 755			

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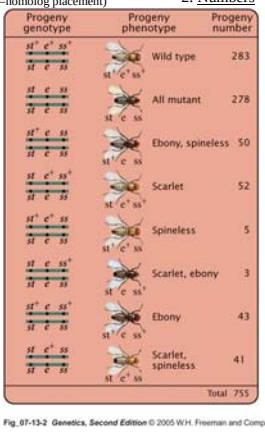
st-ss rec. freq. = 50+52+5+3/755 = 0.146
= 14.6% Map distance: 14.6cM

1. Phenotypes (=homolog placement)
2. Numbers
3. Phenotypes in correct order
4. Region getting crossover



Progeny genotype	Progeny phenotype	Progeny number	3. Phenotypes in correct order	4. Region getting crossover
$st^+\ c^+\ ss^+$ / $st\ c\ ss$	Wild type	283	st+ ss+ e+	none
$st\ c\ ss$ / $st\ c\ ss$	All mutant	278	st ss e	none
$st^+\ c\ ss$ / $st\ c\ ss$	Ebony, spineless	50	st+ ss e	st –ss (region 1)
$st\ c^+\ ss^+$ / $st\ c\ ss$	Scarlet	52	st ss+ e+	st –ss (region 1)
$st^+\ c^+\ ss$ / $st\ c\ ss$	Spineless	5	st+ ss e+	(region 1&2)
$st\ c\ ss^+$ / $st\ c\ ss$	Scarlet, ebony	3	st ss+ e	(region 1&2)
$st^+\ c\ ss^+$ / $st\ c\ ss$	Ebony	43	st+ ss+ e	ss—e (region 2)
$st\ c^+\ ss$ / $st\ c\ ss$	Scarlet, spineless	41	st ss e+	ss—e (region 2)
	Total 755			

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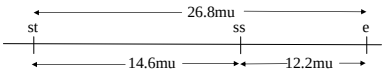
ss--e rec. freq. = 43+41+5+3/755 = 0.122
= 12.2% Map distance: 12.2cM

Map:



11. **Requirements of 3-point crosses:**

A. One parent must be heterozygous for all traits under consideration.

B. The genotypes of gametes produced by the heterozygote must be evident from phenotypes of the offspring.

C. Must look at sufficient numbers of progeny.

12. Interference: <u>Usually</u> one cross-over will interfere with formation of another crossover near it.

Leads to: reduction (or increase) in observed number of double cross-overs versus the number expected, when genes are close.

observed DCO = 8/755 = 0.0105

expected DCO = (Prob. of st--ss CO)(Prob. of ss--e CO) =
= 0.146 x 0.122 = 0.0178

A. Coefficient of coincidence = C = Observed DCO / Expected DCO
C usually <1 = positive interference

B. Interference: I = 1-C = 1- Obs. DCO/Exp. DCO)

Usually positive interference: I > 0

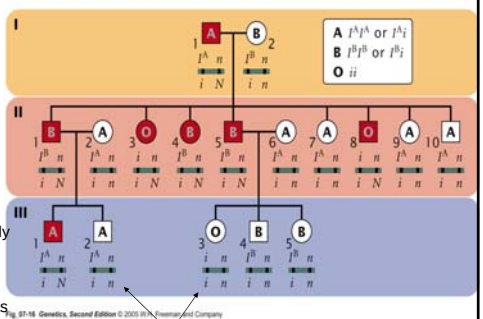
Mapping can be done even when large numbers of crosses can't be done.

13. Linkage can be determined by analyzing pedigrees

i and N cosegregate in all the children of this generation

Lod scores: a measure of how likely two loci are to be linked.

Pedigree linkage was used to locate at least two of the genes involved in familial Alzheimer's.



Only these children were produced by cross-over events

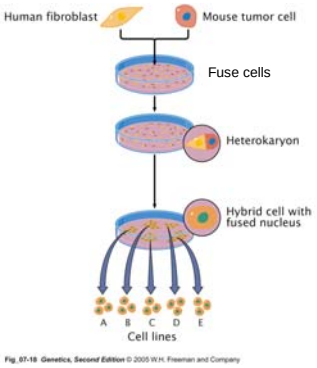
14. Mapping with molecular markers: later in the course. Variations in the DNA sequence at each allele can be the “phenotypes” that are seen.

15. Deletion mapping: Mapping of the Testis Determining Factor gene.

See worked problem 4, p. 192

16. Mapping with somatic cell hybrids

Example: Mouse/human somatic cell hybridization leads to cell lines with mainly mouse chromosomes and only a few human chromosomes.



Which chromosome encodes the gene for the gene product being found?

Human

Human chromosomes present

Cell line	Gene product present	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	X
A	+		+		+			+	+															
B	+	+	+		+				+	+	+	+	+	+										
C	–															+		+		+			+	
D	+		+		+		+	+	+															
E	–												+								+			
F	+				+															+	+			

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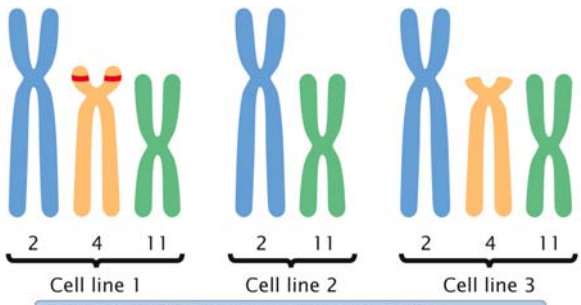
Use of deletions in somatic cell hybrids

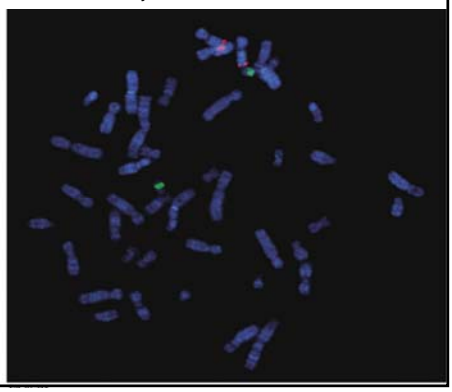


Conclusion: If the gene product is present in a cell line with an intact chromosome but missing from a line with a chromosome deletion, the gene for that product must be located in the deleted region.

17. Mapping by *in situ* hybridization

FISH: Fluorescence *in situ* hybridization
DNA probe is labeled with a fluorescent dye.

18. Mapping by
DNA sequencing



Chromosome Painting with chromosome-specific FISH probes causes each chromsome to appear a specific color.