

Lecture 5 Linkage and gene mapping

- 1. Linkage**
- 2. Cross-over**
- 3. Meiotic recombination**
- 4. Gene mapping by a 2-point cross**

Thomas Morgan: a dihybrid testcross in *Drosophila* that involved two autosomal genes:

eye color - *pr*, purple, *pr*⁺, red

wing length - *vg*, vestigial, *vg*⁺, normal

Wild type alleles are dominant

P: *pr* / *pr* · *vg* / *vg* X *pr*⁺ / *pr*⁺ · *vg*⁺ / *vg*⁺

Gametes: *pr* *vg* pr⁺ *vg*⁺

F₁ *pr* *pr*⁺ *vg* *vg*⁺

testcross of F₁ ♀: *pr* *pr*⁺ *vg* *vg*⁺ X ♂ *pr* *pr* *vg* *vg*

Gametes of ♀	Gametes of ♂	Classes of F ₂	Observed results
<i>pr</i> <i>vg</i>	<i>pr</i> <i>vg</i>	<i>pr</i> <i>pr</i> <i>vg</i> <i>vg</i>	1195
<i>pr</i> ⁺ <i>vg</i> ⁺	"	<i>pr</i> ⁺ <i>pr</i> <i>vg</i> ⁺ <i>vg</i>	1339
<i>pr</i> ⁺ <i>vg</i>	"	<i>pr</i> ⁺ <i>pr</i> <i>vg</i> <i>vg</i>	151
<i>pr</i> <i>vg</i> ⁺	"	<i>pr</i> <i>pr</i> <i>vg</i> ⁺ <i>vg</i>	154

A reciprocal cross:

P: *pr*⁺ / *pr*⁺ · *vg* / *vg* x *pr* / *pr* · *vg*⁺ / *vg*⁺

Gametes: *pr*⁺ *vg* *pr* *vg*⁺

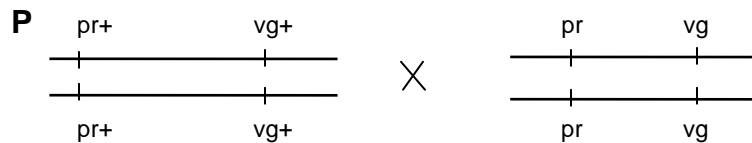
F₁: *pr*⁺ *pr* *vg*⁺ *vg*

Testcross of F₁ ♀: *pr*⁺ *pr* *vg*⁺ *vg* x ♂ *pr* *pr* *vg* *vg*

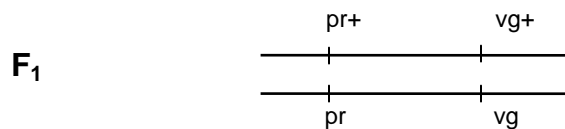
Gametes of ♀	Gametes of ♂	Classes of F ₂	Observed results
<i>pr</i> <i>vg</i>	<i>pr</i> <i>vg</i>	<i>pr</i> <i>pr</i> <i>vg</i> <i>vg</i>	146
<i>pr</i> ⁺ <i>vg</i> ⁺	"	<i>pr</i> ⁺ <i>pr</i> <i>vg</i> ⁺ <i>vg</i>	157
<i>pr</i> ⁺ <i>vg</i>	"	<i>pr</i> ⁺ <i>pr</i> <i>vg</i> <i>vg</i>	965
<i>pr</i> <i>vg</i> ⁺	"	<i>pr</i> <i>pr</i> <i>vg</i> ⁺ <i>vg</i>	1067

Morgan noticed that in both cases the most abundant classes in the testcross corresponded to the original parental gametic type. Morgan suggested that they are located on the same chromosome: each gene occupies a certain position which is called a **locus** (pl - **loci**).

The original cross is then represented as follows:

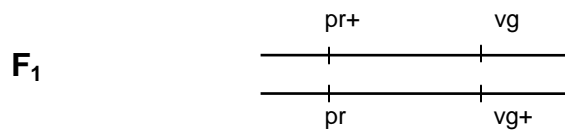
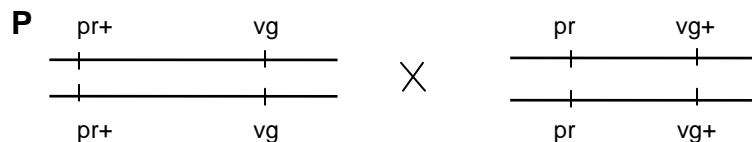


Gametes:



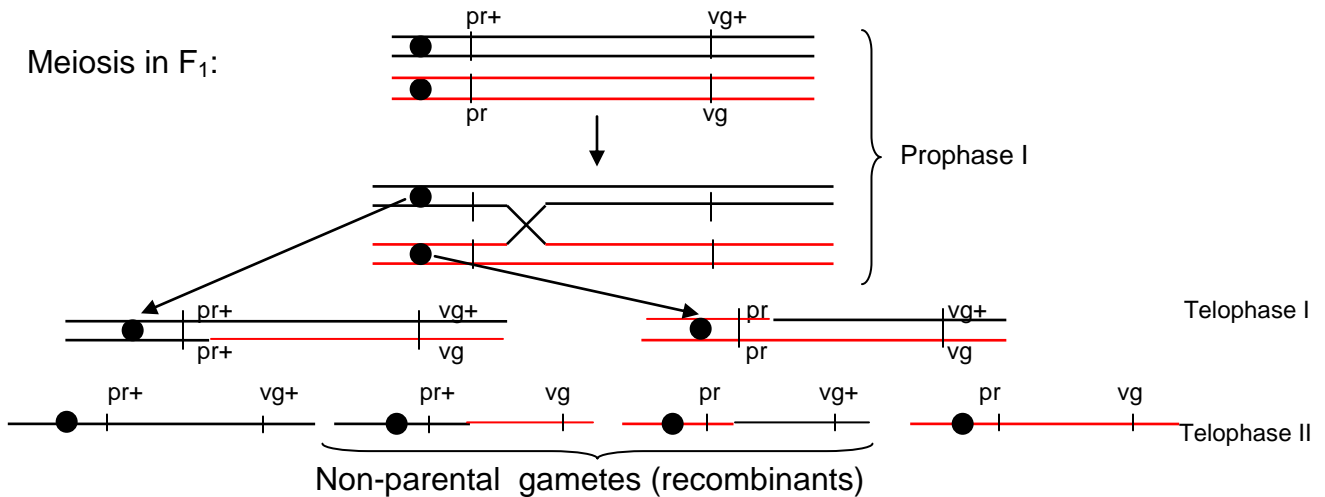
This was a coupling conformation (the wild type alleles on the same chromosome).

In the second cross, there was a repulsion conformation:



A preferential reappearance of parental combinations in both crosses is explained by linkage. But what about a smaller number of classes produced by gametes with non-parental combinations?

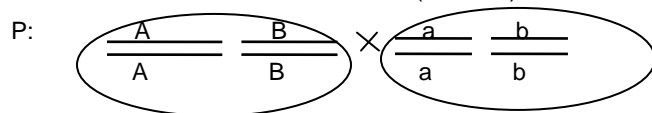
Morgan suggested that when homologous chromosomes (dyads) pair up during meiosis (Prophase I), the nonsister chromatids occasionally exchange their parts:



This is called a recombination by a **cross-over** (*crossing-over*). Recombination is a process which generates genotypes different from the parental genotypes.

Meiotic recombination

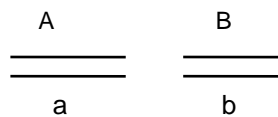
Interchromosomal recombination (Mendel)



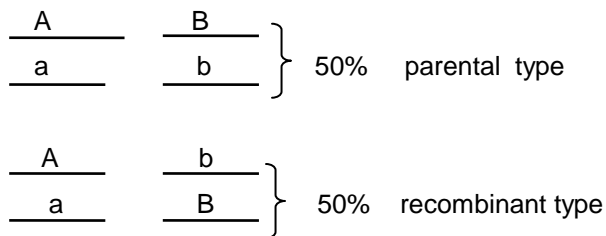
Gametes:



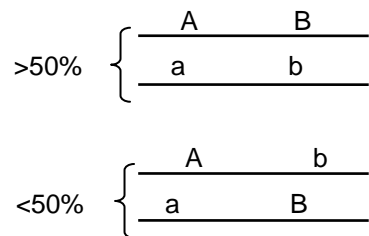
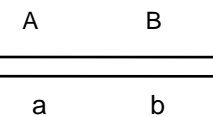
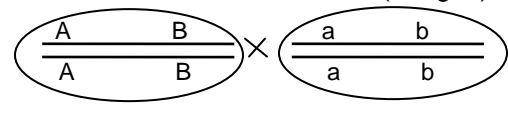
F1



Gametes:



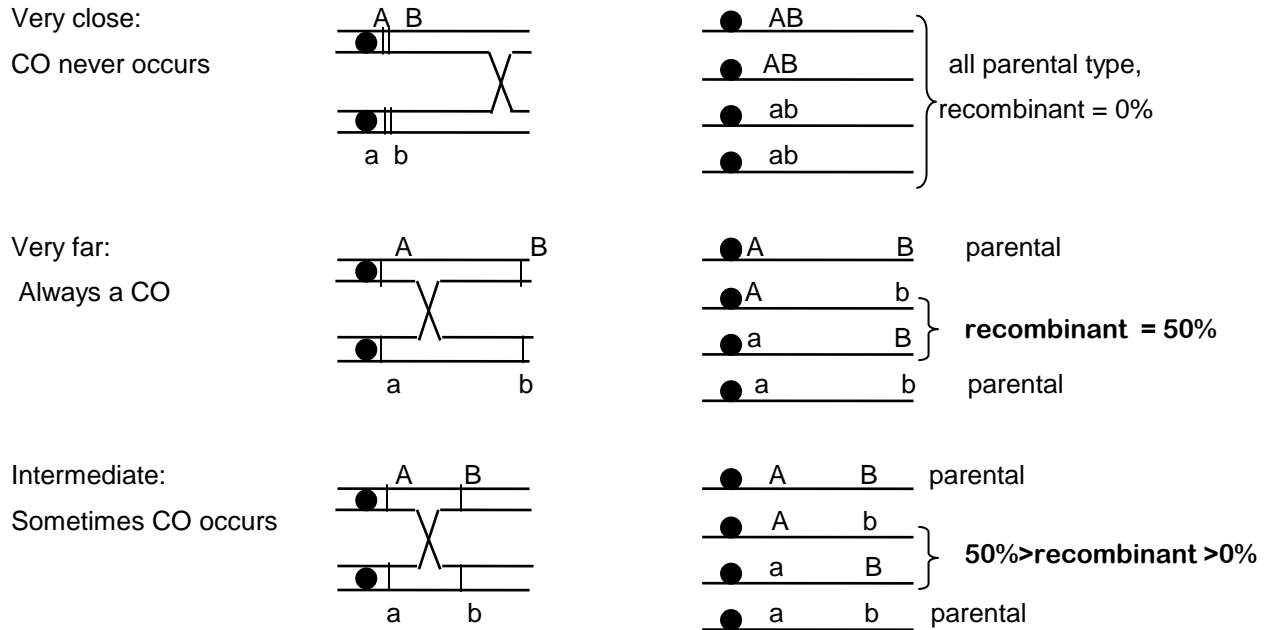
Intrachromosomal recombination (Morgan)



Interchromosomal recombination occurs between unlinked genes and is due to independent assortment.

Intrachromosomal recombination occurs between linked genes and is due to cross-over.

Recombination frequency depends of the distance between the loci:



If A and B too close → recombination frequency between them is almost zero

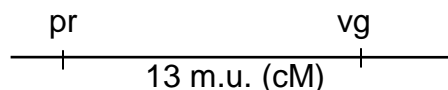
If A and B are far apart → recombination frequency between them is 50%

If there are linked → recombination frequency between them is between 0% and 50%

Frequency of recombination between two genes reflects to the physical distance between them on a chromosome.

For example, if we look at the second Morgan’s experiment, the number of recombinants is 157+146=303. RF (recombination frequency) = the number of recombinant progeny over the total number of progeny = 303/2335= 13%.

Maps drawn on the basis of this analysis are called **linkage maps**. 1% of RF corresponds to 1 map unit (m.u.) or centimorgan (cM):



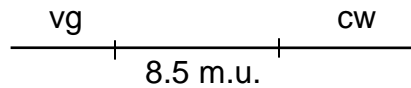
We can also map another allele (cw) in respect to vg:

P: $vg^+ vg^+ cw^+ cw^+$ cross to $vg vg cw cw$

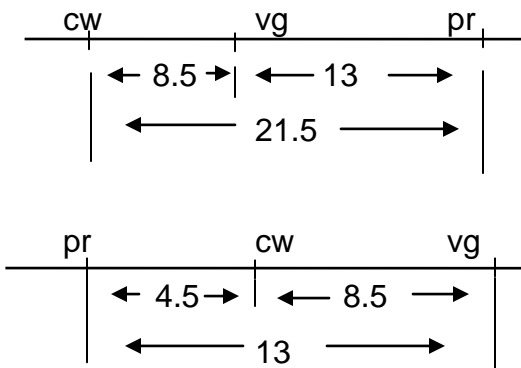
Then test-cross F_1 to a double recessive homozygote $vg vg cw cw$

Count the recombinant progeny: $vg^+ vg\ cw\ cw$
 $vg\ vg\ cw^+ cw$ } **8.5%**

Let's assume, that these represent 8.5%. Then the map is:



Now, what is the distance between *pr* and *cw* loci? Two situations are possible:



In order to distinguish between these two possibilities, we will determine the recombination frequency directly between *pr* and *cw*:

P: $pr^+ pr^+ cw^+ cw^+$ cross to $pr\ pr\ cw\ cw$

Test-cross F_1 to double recessive homozygote $pr\ pr\ cw\ cw$

Count recombinant progeny: $pr^+ pr\ cw\ cw$
 $pr\ pr\ cw^+ cw$ } **20.0%**

Let's assume that these represent 20.0%

Then the first map order is correct, although the obtained map distance is less than the value (21.5 m.u.) expected.