

## Crossing Over and Genetic Mapping

During meiosis, the two chromosomes in each homologous pair exchange segments, through a process called *crossing over*. This process of crossing over and the resulting *recombination*, (exchange of gene alleles across the chromosomes in a pair) enables us to reason about *genetic mapping* - that is, about the order of genes on a chromosome and the distances among the genes. The next section provides a brief description of crossing over and recombination. The section that follows introduces the logic that allows us to reason about genetic mapping.

### Crossing Over and Recombination

When a chromosome replicates early in meiosis, the two duplicate copies (called *chromatids*) are joined at a point called the *centromere*, as shown in Figure 1.

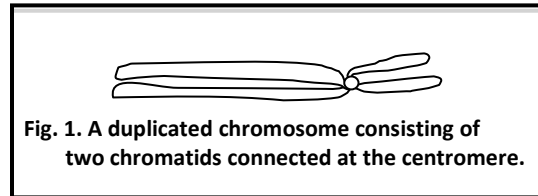


Fig. 1. A duplicated chromosome consisting of two chromatids connected at the centromere.

After the chromosomes duplicate but before cell division, the two homologous chromosomes in each homologous pair align as shown in Figure 2.

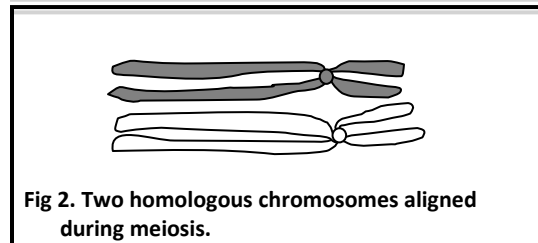


Fig. 2. Two homologous chromosomes aligned during meiosis.

Crossovers occur when homologous chromosomes are aligned: chromatids from two different chromosomes can exchange segments as in Fig. 3. In Fig. 3a, chromatids from two homologous chromosomes come in contact at an equivalent point along their lengths. In Fig. 3b, the two chromatids have separated after exchanging the segments between the contact point and the tips of the chromatids.

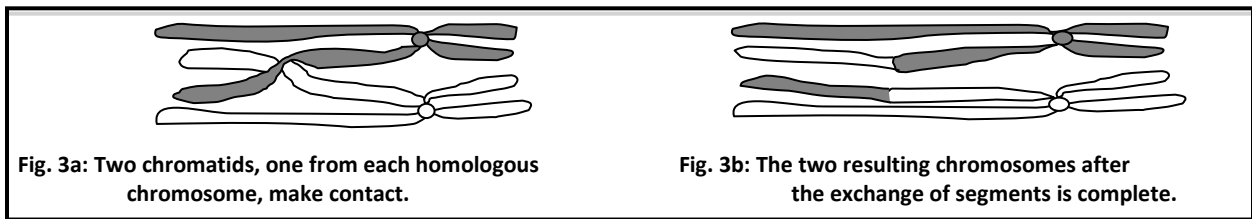


Fig. 3a: Two chromatids, one from each homologous chromosome, make contact.

Fig. 3b: The two resulting chromosomes after the exchange of segments is complete.

Occasionally a **double crossover** can occur, as shown in Figure 4. In Figure 4a, chromatids from two homologous chromosomes come in contact at two points. In Figure 4b, the two chromatids have separated, after exchanging the segments between the two points of contact.

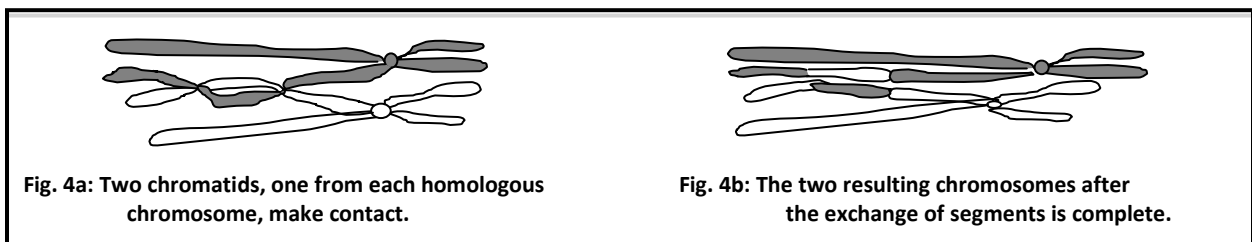


Fig. 4a: Two chromatids, one from each homologous chromosome, make contact.

Fig. 4b: The two resulting chromosomes after the exchange of segments is complete.

Suppose an organism is heterozygous for a set of linked genes as shown in Figure 5a, and the crossover shown in Figure 5b occurs. Notice that the copies of the A / a, B / b and C / c gene alleles have crossed over the chromatids.

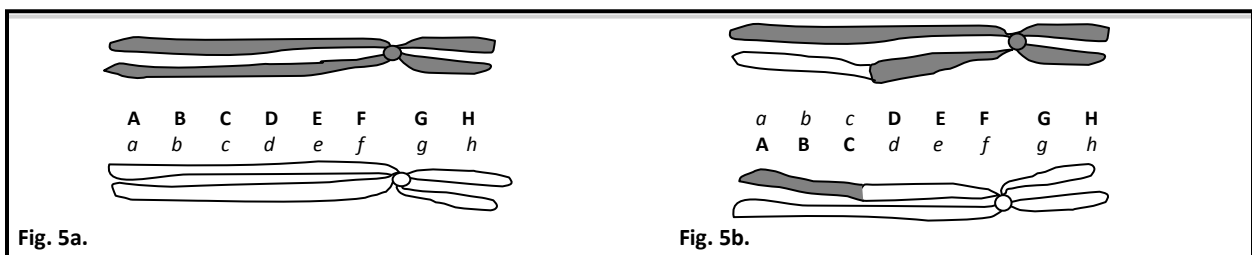


Fig. 5a.

Fig. 5b.

In Figure 5b a crossover occurred between genes C and D. During meiosis the probability of a single crossover between any two genes that are relatively close together on the chromosome is low – and the probability of a double crossover between nearby genes is very low!

## Crossover Frequency and Genetic Mapping

We can use the phenomenon of crossovers described above to reason about the order of genes along a chromosome and about the distances between those genes. This reasoning depends on this basic principle:

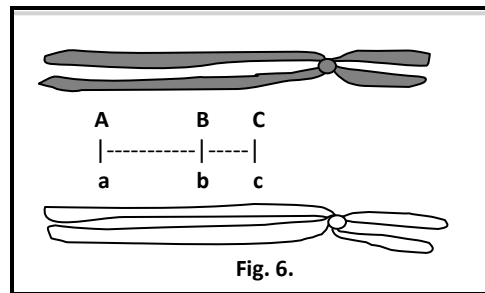
- To a first approximation, crossovers are **equally** likely to occur at any point along the length of a chromosome.

It follows that:

- the probability of a crossover between two genes is proportional to the distance between the two genes.

That is, the greater the distance between the two genes, the greater the probability that a crossover will occur between them during meiosis.

In Fig. 6, the probability of a crossover occurring somewhere between A and B is twice the probability of a crossover occurring between B and C – because there is twice as much space on the chromosome between A and B as there is between B and C.



It also follows that:

- The greater the frequency of crossovers between two genes, the greater the distance between them.

and, as discussed in the following sections, we use this principle to draw gene mapping conclusions based on empirical observations. If we observe that twice as many crossovers occur between genes A and B as between genes C and D, then we conclude that the distance between A and B on the chromosome must be twice the distance between C and D.

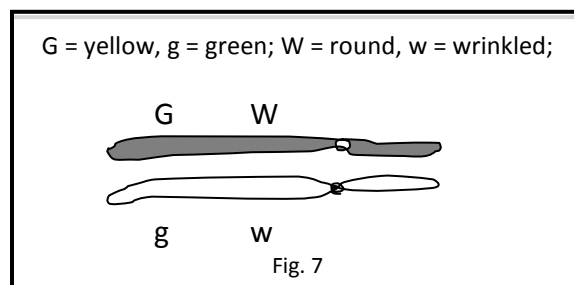
### Reasoning about Gene Mapping: Two Factor Cross

In real life, we do not directly observe the crossovers occurring as they are depicted in Figs. 3-5. Instead we perform a **test cross** between two individuals (e.g., pea plants) to look for evidence of crossovers. In these crosses

- One individual is heterozygous for the genes in question.
- One individual is homozygous recessive for these genes.

The different offspring phenotypes that result from a test cross reveal the gene alleles in different gametes from the heterozygous parent, and these allow us to infer the probability (or frequency) of recombination between the genes in question.

For instance, suppose we have an individual that is heterozygous for two genes:



(1) We perform a test cross by crossing the heterozygous individual shown above with a homozygous recessive individual ( $gw/gw$ ). If there are NO crossovers, then the heterozygous parent will generate only two types of gametes:  $GW$  and  $gw$ , while the homozygous recessive parent only generates  $gw$  gametes.

50% of the offspring would be yellow and round (heterozygous  $GW/gw$ ), and  
50% of the offspring would be green and wrinkled (homozygous recessive  $gw/gw$ ).

(2) But if crossovers occur in between the two genes during meiosis, then the heterozygous parent will generate all four possible gametes: GW, gw, Gw and gW, and we will see all four offspring phenotypes, perhaps:

- 45% of the offspring yellow and round (GW/gw),
- 45% of the offspring green and wrinkled (gw/gw),
- 5% of the offspring yellow and wrinkled (Gw/gw),
- 5% of the offspring green and round (gW/gw).

Since crossovers are rare, there are many more offspring with parental phenotypes (GW and gw), than with the crossover phenotypes (Gw and gW).

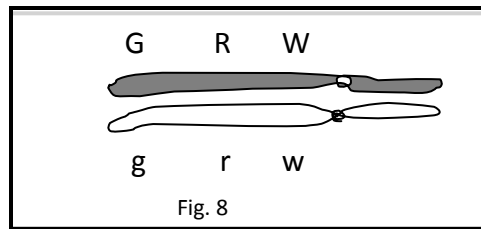
We use the unit **centimorgan** (cM) to measure distance between genes based on offspring phenotype frequency. A centimorgan = 100 times the frequency of crossovers in the offspring. In this example, the frequency of crossovers is 10/100 and the distance between the genes is  $100 * 1/10 = 10$  centimorgans.

### Reasoning about Gene Mapping: Three Factor Cross

The hypothetical study we just discussed is called a two-factor cross because it focuses on two genes. A two-factor cross can tell us about the distance between two genes, but cannot tell us anything about the order of the two genes.

In contrast, a three-factor cross study focuses on three linked genes and can tell us about the order of the three genes on their chromosome and the distances between each pair of genes.

In a three factor cross study we perform a test cross with an individual that is heterozygous for three genes, as shown in Fig, 8.



When this individual is crossed with individual that is homozygous recessive for the three genes (gsw/gsw), the frequency of the phenotypes among the offspring of this cross reveal the probability (frequency) of recombination among the three genes.

Let's consider the recombination possibilities for the individual that is heterozygous for the three genes depicted on the homologous chromosomes in Fig. 8.

- |   |  |
|---|--|
| If no crossovers in during meiosis:                                     | One of the gametes formed will have the genotype G R W<br>And the reciprocal gamete will have the genotype g r w |
| When a crossover occurs between G and R:                                | One of the gametes formed will have the genotype g R W<br>And the reciprocal gamete will have the genotype G r w |
| When a crossover occurs between R and W:                                | One of the gametes formed will have the genotype G R w<br>And the reciprocal gamete will have the genotype g r W |
| If two crossovers occur, between G and R:<br><u>and</u> between R and W | One of the gametes formed will have the genotype g r w<br>And the reciprocal gamete will have the genotype G r W |

Now consider the possible phenotypes for the resulting offspring. If no crossovers occurred,

- 50% of the offspring would have the dominant phenotype for all 3 traits,
- 50% of the offspring would have the recessive phenotype for all 3 traits.

But when crossovers occur between G and R, we'll observe

- Offspring with the dominant R & W phenotypes and the recessive g phenotype;
- Offspring with the recessive r & w phenotypes and the dominant G phenotype;

When crossovers occur between R and W, we'll observe

- Offspring with the dominant G & R phenotypes and the recessive w phenotype;
- Offspring with the recessive g & r phenotypes and the dominant W phenotype;

And on the rare occasions that crossovers occur between G and R, and between R and W we'll observe

- Offspring with the dominant G & W phenotypes and the recessive r phenotype;
- Offspring with the recessive g & w phenotypes and the dominant R phenotype;

In summary, when we perform this test cross, we're likely to see all 8 of these phenotype classes:

Offspring Phenotypes	Number of Offspring	
G R W	340	(parental)
g r w	340	(parental)
g R W	50	(GR crossover)
G r w	50	(GR crossover)
G R w	100	(RW crossover)
g r W	100	(RW crossover)
G r W	10	(GR and RW crossover)
g R W	10	(GR and RW crossover)

The second column in the table shows the number of offspring out of 1000 with each of the 8 phenotypes. (These numbers are idealized; the two numbers within each of the four groups are only approximately equal in real life.)

The offspring group with no crossovers, called the **parental** genotype group, is the most frequent, because crossovers between any two genes are rare.

Note that the phenotype group with a crossover between G and R is half the size of the group with a crossover between R and W, so we can conclude that R and W are twice as far apart as G and R.

Finally, a double crossover, between both G and R and between R and W is extremely rare, so the offspring phenotype group that reflects such double crossovers is very small compared to the other groups.

*In the Cognitive Genetics Tutor activities you will use this logic to reason through three-factor cross gene mapping studies.*