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Topic: Genetic linkage

Genetic linkage

Linkage:

Linkage is the phenomenon of certain genes staying together during inheritance through generations without any change or separation due to their being present on the same chromosome.

Linkage was first suggested by Sutton and Boveri (1902-1903) when they propounded the famous "chromosomal theory of inheritance."

Bateson and Punnet(1906) while working on Sweet Pea found that the factors for certain characters do not show independent assortment.

They then argued that since Sweet Pea has only a few pairs of homologous chromosomes, a chromosome must possess several factors which should be transmitted together.

It was Morgan (1910) who clearly proved and defined linkage on the basis of his breeding experiments in fruitfully Drosophila melanogaster.

In 1911, Morgan and Castle proposed chromosome theory of linkage. It states that-

(i) Linked genes occur in the same chromosome:

(ii) They lie in a linear sequence in the chromosome.

(iii) There is a tendency to maintain the parental combination of genes except for occasional crossovers.

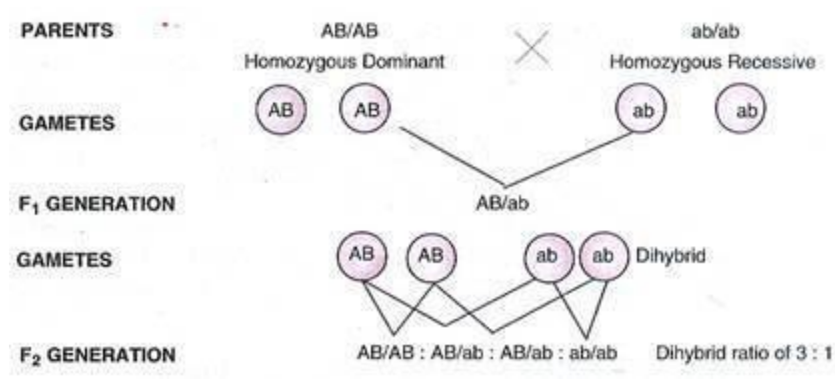
(iv) Strength of the linkage between two genes is inversely proportional to the distance between the two, i.e., two linked genes show higher frequency of crossing over if the distance between them is higher and lower frequency if the distance is small.

Linked genes are those genes which occur on the same chromosome while unlinked genes are the ones found on different chromosomes. Linked and unlinked genes can be easily known from breeding experiments.

Unlinked genes show independent assortment, a di-hybrid ratio of 9: 3: 3: 1 and the di-hybrid or double test cross ratio of 1: 1: 1: 1 with two parental and two recombinant types.

The linked genes do not show independent assortment but remain together and are inherited en block producing only parental type of progeny. They give a di-hybrid ratio of 3: 1 and a test cross ratio of 1: 1.

Di-hybrid ratio of two Linked genes:



Types of Linkage:

Linkage is of two types, complete and incomplete.

1. Complete Linkage (Morgan, 1919):

The genes located on the same chromosome do not separate and are inherited together over the generations due to the absence of crossing over.

Complete linkage allows the combination of parental traits to be inherited as such. It is rare but has been reported in male Drosophila and some other heterogametic organisms.

2. Incomplete Linkage:

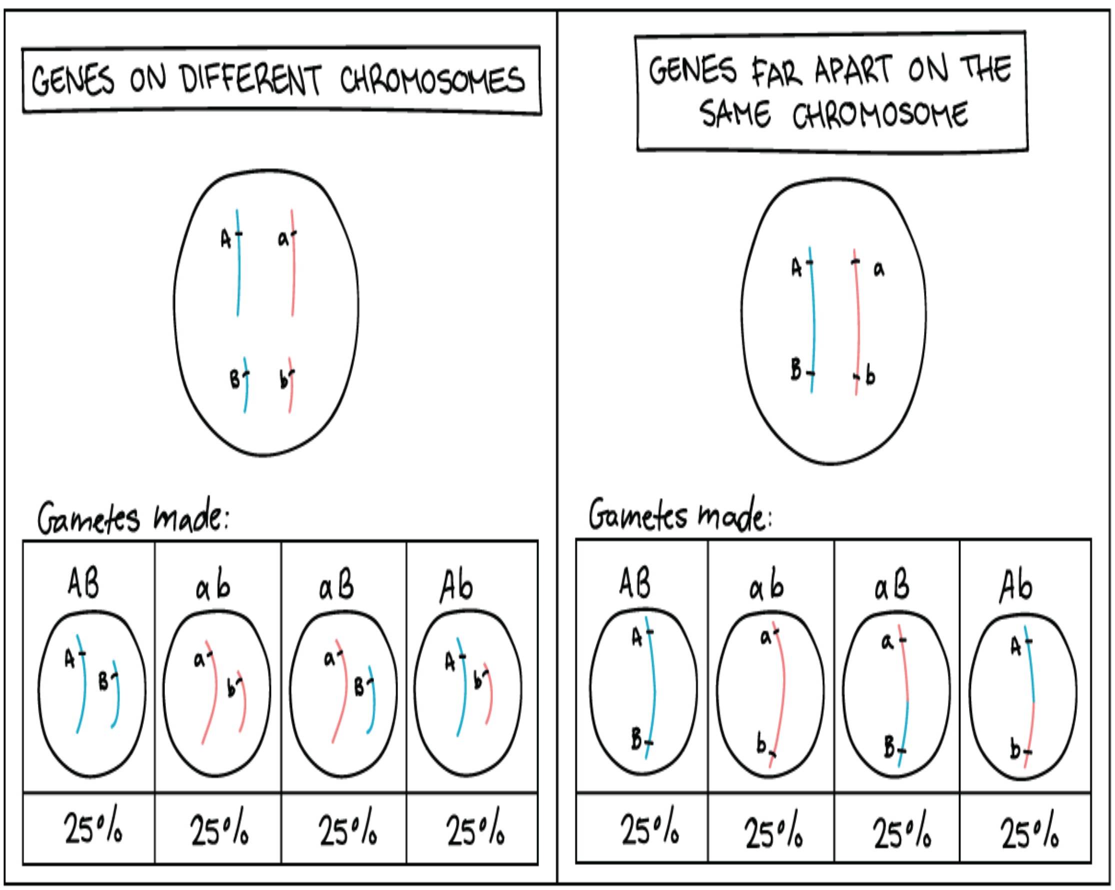
Genes present in the same chromosome have a tendency to separate due to crossing over and hence produce recombinant progeny besides the parental type.

The number of recombinant individuals is usually less than the number expected in independent assortment.

In independent assortment all the four types (two parental types and two recombinant types) are each 25%. In case of linkage, each of the two parental types is more than 25% while each of the recombinant types is less than 25%.

When genes are on separate chromosomes, or very far apart on the same chromosomes, they assort independently. That is, when the genes go into gametes, the allele received for one gene doesn't affect the allele received for the other.

In a double heterozygous organism (*AaBb*), this results in the formation of all 4 possible types of gametes with equal, or 25\%25%25, percent, frequency.

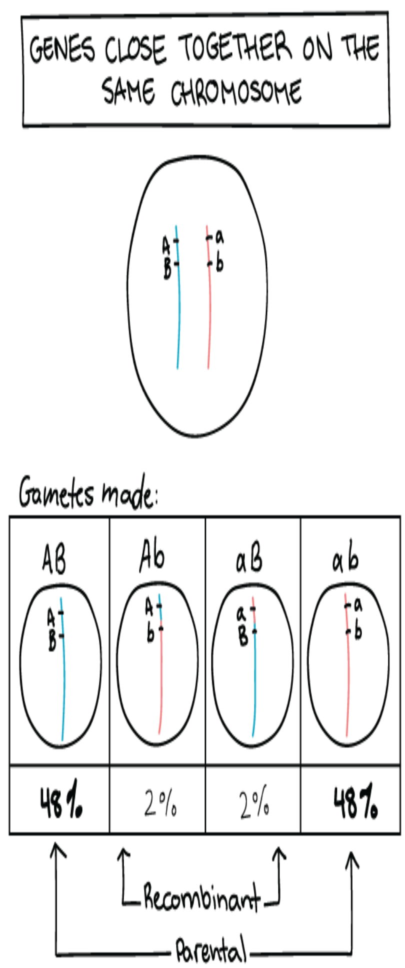


Genes on separate chromosomes assort independently because of the random orientation of homologous chromosome pairs during meiosis.

When genes are very close together on the same chromosome, Instead of assorting independently, the genes tend to "stick together" during meiosis.

That is, the alleles of the genes that are already together on a chromosome will tend to be passed as a unit to gametes. In this case, the genes are linked.

For example, two linked genes might behave like this:



The common types of gametes contain parental configurations of alleles—that is, the ones that were already together on the chromosome in the organism before meiosis (i.e., on the chromosome it got from its parents).

The rare types of gametes contain recombinant configurations of alleles, that is, ones that can only form if a recombination event (crossover) occurs in between the genes.

Finding recombination frequency:

Let's suppose we are interested in seeing whether two genes in the fruit fly (*Drosophila*) are linked to each other, and if so, how tightly linked they are.

- The *purple* gene, with a dominant *pr^++start superscript, plus, end superscript* allele that specifies normal, red eyes and a recessive *pr* allele that specifies purple eyes.
- The *vestigial* gene, with a dominant *vg^++start superscript, plus, end superscript* allele that specifies normal, long wings and a recessive *vg* allele that specifies short, "vestigial" wings.

If we want to measure recombination frequency between these genes, we first need to construct a fly in which we can observe recombination. That is, we need to make a fly that is not just heterozygous for both genes, but where we know exactly which genes are together on the chromosome. To do so, we can start by crossing two homozygous flies as shown below.

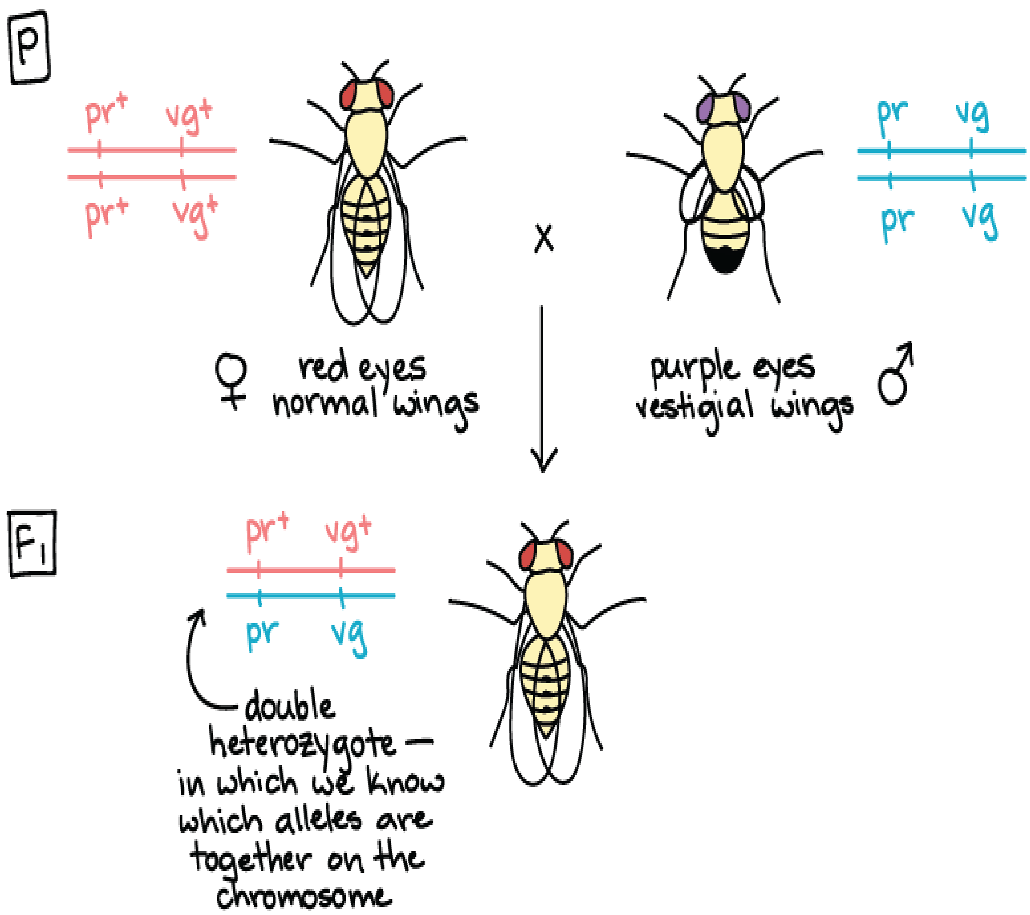


Fig: Drosophila melanogaster

This cross gives us exactly what we need to observe recombination: a fly that's heterozygous for the *purple* and *vestigial* genes, in which we know clearly which alleles are together on a single chromosome.

Now, we need a way to "see" recombination events. The most direct approach would be to look into the gametes made by the heterozygous fly and see what alleles they had on their chromosomes. Practically, though, it's much simpler to use those gametes in a cross and see what the offspring look like!

To do so, we can cross a double heterozygous fly with a tester, a fly that's homozygous recessive for all the genes of interest (in this case, the *pr* and *vg* alleles). The purpose of using a tester is to ensure that the alleles provided by the non-tester parent fully determine the phenotype, or appearance, of the offspring. When we cross our fly of interest to a tester, we can directly "read" the genotype of each gamete from the physical appearance of the offspring.

Below, we can see a modified Punnett square showing the results of the cross between our double heterozygous fly and the tester fly. Four different types of eggs are produced by a double heterozygous female fly, each of which combines with a sperm from the male tester fly.

Four different phenotypic (appearance-based) classes of offspring are produced in this cross, each corresponding to a particular gamete from the female parent:

The four classes of offspring are *not* produced in equal numbers, which tells us that the *purple* and *vestigial* genes are linked.

As we expect for linked genes, the parental chromosome configurations are over-represented in the offspring, while the recombinant chromosome configurations are under-represented.

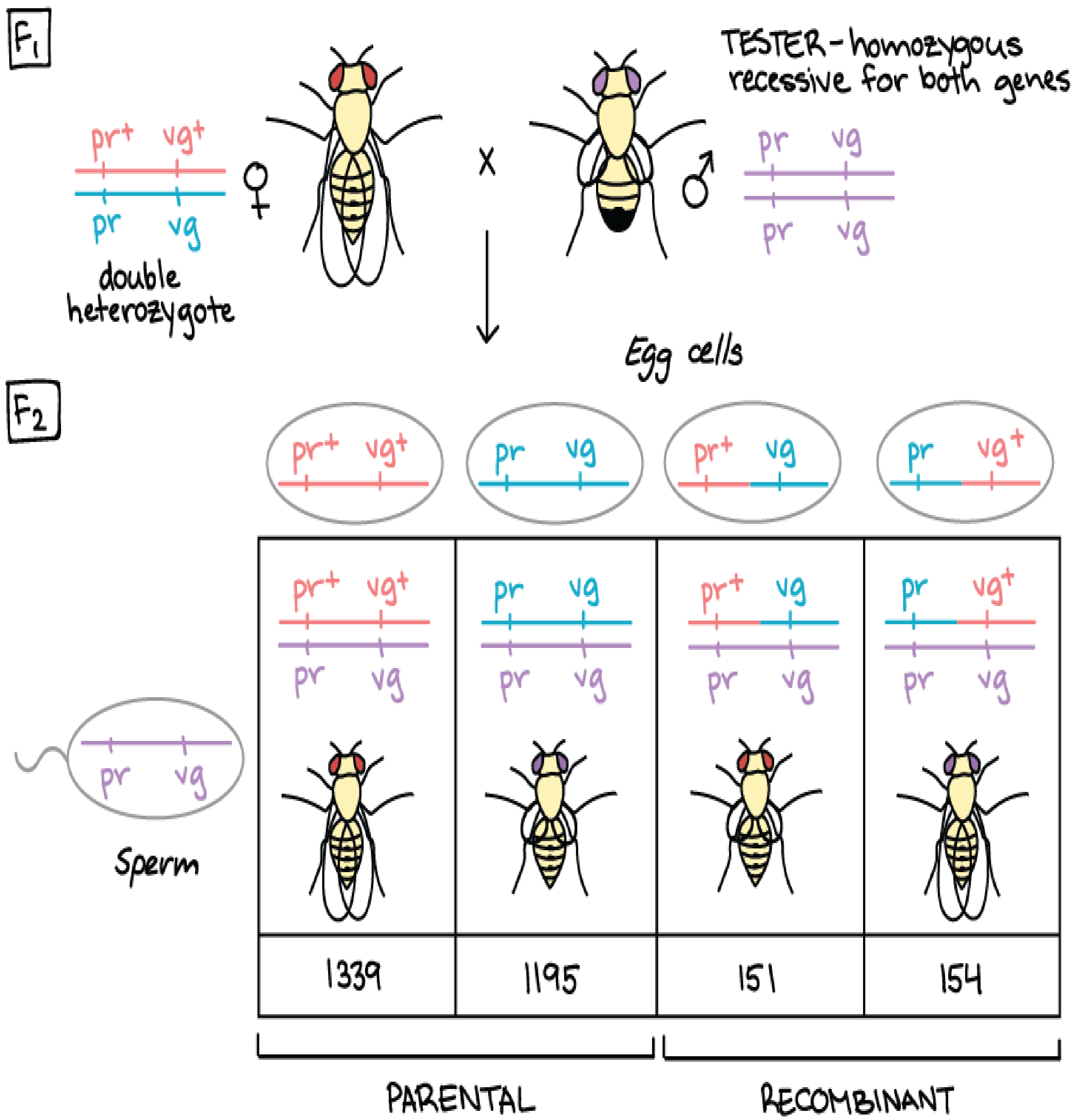


Fig: Drosophila melanogaster

Characteristics of Sex Linked Inheritance:

1. It is criss-cross inheritance. Father does not pass the sex-linked allele of a trait to his son. The same is passed to the daughter, from where it reaches the grandson, i.e., diagynic. It is because the males have only one X-chromosome which is transferred to the female offspring. Only Y-chromosome of the father is

transferred to the male offspring but this sex chromosome does not carry many alleles.

2. Mother passes the alleles of sex-linked traits to both sons and daughters.

3. Majority of the sex linked traits are recessive.

4. Sex linked traits are more apparent in males than in females.

5. As many sex-linked traits are harmful, males suffer more from sex-linked disorders.

6. Females generally function as carriers of sex-linked disorders because recessive genes can express themselves in females only in the homozygous state.