Genetics II: Linkage and the Chromosomal Theory

An individual has two copies of each particle of inheritance (gene). These two copies separate during the formation of gametes and come together when the two gametes combine to from a zygote.

A <u>locus</u> (plural = loci) is a place on a chromosome where a gene resides. Traits assort independently when the R and G gene loci are on different chromosomes.
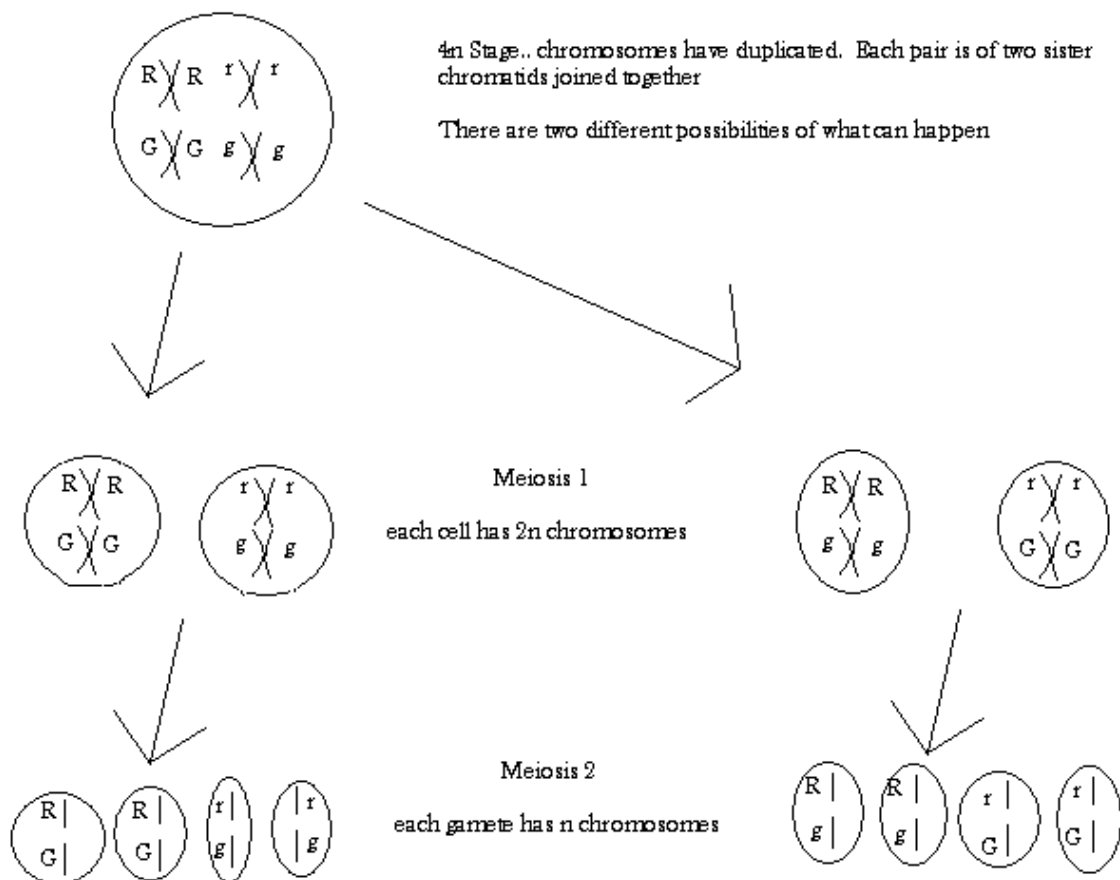
Based on these results, the chromosomal theory predicts that the gene for the round trait and the gene for the green trait are on separate chromosomes.

§1. The Chromosomal Theory of Inheritence

According to the chromosome theory...
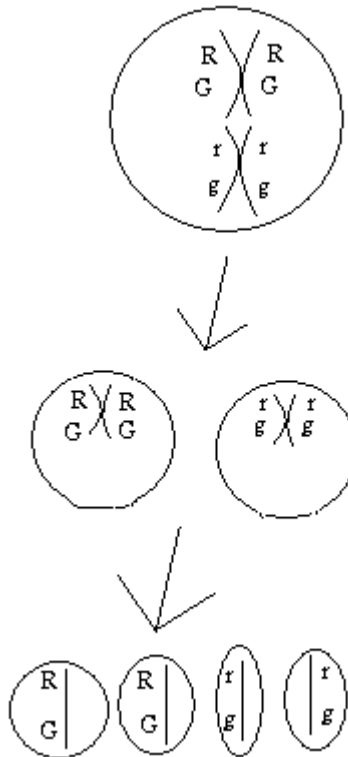
<u>If the R and G genes are on different chromosomes:</u>

Look at F1 hybrid cells nucleus: RrGg

If genes are on different chromosomes, when you look at the products of many meioses you seethe following gametes: RG 25% : rg 25% : Rg 25% : rG 25%

But if the R and G genes are on the same chromosome

If genes are on the same chromosome, when you look at the products of many meioses you seethe following gametes: RG 50% : rg 50% : Rg 0% : rG 0%

According to Mendel the traits should assort independently:
RG 25% : rg 25% : Rg 25% : rG 25%

According to chromosomal theory, the traits should assort with chromosomes
RG 50% : rg 50%

So, what is the actual mode of inheritence?
Actually, a third result occurs when the two genes are on the same chromosome. You see results somewhere in between the two predictions. You also see progeny resulting from RG and rg gametes at higher frequency then you see progeny resulting from the Rg or rG gametes.
In the case as diagramed above, RG, rg are parental type gametes (the chromosome in the gamete is the same as it is in the parent) while Rg and rG are non-parental gametes.

How does this happen??

The Rg and rG are non-parental gametes are formed through a process called
recombination

§2. Recombination

Recombination was first studied using the fruit fly <u>Drosophila Melanogaster</u> by Thomas Morgan (~1910)

Look at cross of two pure breeding strains of flies

$$F_0 \ : \ \text{male} \ \frac{+\ +}{+\ +} \qquad X \qquad \text{female} \ \frac{b\ vg}{b\ vg}$$

$$\downarrow$$

+ = wild type phenotype (body and wings)

$$F1: \text{All} \ \frac{b\ vg}{+\ +}$$

b = allele for black body

vg = allele for vestigial (short) wings

Take F1 heterozygote and do a testcross:

$$\frac{b\ vg}{+\ +} \qquad X \qquad \frac{b\ vg}{b\ vg}$$

$$\downarrow$$

EXPECT :

$$\frac{b\ vg}{b\ vg} \qquad \frac{+\ +}{b\ vg} \qquad \frac{b\ +}{b\ vg} \qquad \frac{b\ vg}{b\ vg}$$

A   1 : 1 : 1 : 1   ratio

However, the progeny was found in the following ratios:

944 : 965 : 206 : 185

The flies represented by the numbers 944 and 965 are the parental types. The flies represented by the numbers 206 and 185 are the non-parental types (recombinants).

-If the b and the vg genes were on different chromosomes, you would expect a 1 : 1 : 1 : 1 ratio for the genotypes
-If the b and the vg genes were on the same chromosome, you would expect a 1:1:0:0 ratio of the genotypes.

These results; however, indicate that some recombination must have taken place to produce the
<u>non-parental</u> (recombinant) types. <u>Recombination</u> occurs during <u>Meiosis</u> when gametes are being produced.

Recombination occurs during metaphase of meiosis I, (cell is 4n, each chromosome is duplicated and homologous chromosomes are aligned). Parts of each homologous chromosome cross over, effectively exchanging genetic material.

leads to a "b +" and "vg +" ganetes
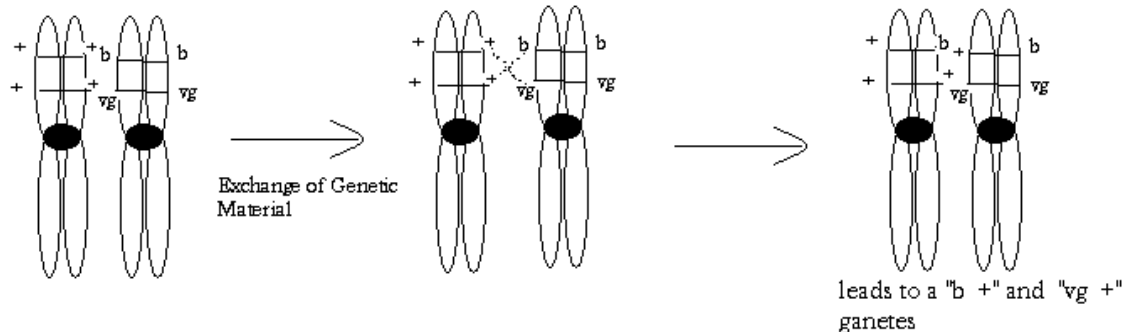
-Recombination (cross-over event) occurs at some frequency. The non-parental types (recombinants) are produced when recombination occurs.

-Examined cells undergoing meiosis and saw chromosomes touching each other to form a chiasma (cross over). But, was this proof that recombination occurred?

To prove that recombination occurred had to look at number of recombinants produced.

Recombination frequency (RF) is a measure of the probability of genetic exchange

$$\text{Frequency of Recombination} \ = \ \frac{\#\,nonparentals}{Total\,\#\,progeny} \qquad \frac{recombinants}{recombinants + parentals}$$

From the data : RF $= \ \dfrac{206+185}{944+965+206+185} = \dfrac{39}{2300}\,x100 = 17\%$

This means that 17% of the time, there is recombination between the *b* and the *vg* loci on a chromosome.

If two genes are close recombination frequency is low - ~ 0%
If two genes are far apart, recombination frequency is high ~ 50%

-Genes are said to be linked on the same chromosome if RF is less than 50%
-Genes are said to be unlinked if RF ~ 50%. They could be very far apart on a chromosome or they could be on different chromosomes.

§3. Genetic Maps

A Genetic Linkage Map shows the order of genes on a chromosome. The order is based on the recombination frequency data between the genes
~1911 Alfred Sturtevant, a student in T. H. Morgan's lab, used recombination frequency data to construct genetic linkage maps.
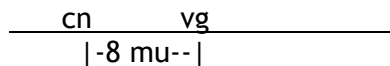
-He used RF values to assign distances between the genes in map units (m.u)

Example: *b* and *vg* genes on a chromosome show a recombination frequency of 17%

```
     b              vg
      |----17 mu----|
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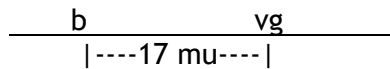
Therefore the RF value tells us that the *b* and the vg genes are 17 map units apart on the same chromosome

Sturtevant knew that the RF between the *vg* gene and another gene called *cinnabar* (*cn*) was 8 %

```
   cn        vg
     |-8 mu--|
```

Now Sturtevant realized that if chromosomes where linear entities then there were two possibilities:

```
1)      b              vg        cn            where the RF between b and cn is
expected to be 25%
          |--------17mu---|---8mu--|
```

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2)      b        cn          vg            where the RF between b and cn is
expected to be 9%
          |---9mu---|---8mu---|
          |--------17mu--------|
```

Sturtevant examined the data and found that the recombination frequency between *b* and the *cn* genes was 9 % therefore assumed map #2 was correct.

Sturtevant the compiled all the linkage data and made a more extensive genetic linkage map. He inferred that genes resided on chromosomes and was able to map genes on chromosomes by looking at RF data between genes.

§4. Sex-determination and Sex Linkage

Most plants and animals are diploid (2n) – have two copies of each chromosome.
        N = # of chromosomes.

In the nucleus of the cells, the chromosomes are found in sets of identical pairs with the exception of 1 set of chromosomes.
Matched chromosomes are called <u>autosomes.</u>
Unmatched chromosomes are called <u>sex chromosomes</u>.

Humans have 22 pairs of <u>autosomes</u> and 1 pair of <u>sex chromosomes</u> (XX or XY).
In most organisms, the type of sex chromosome found in the cell determines the sex of the individual.

Look at Different Organisms

	Humans	Flies	Chickens	Worms
Males	XY	XY	ZZ	XO
Females	XX	XX	ZW	XX

In most cases the males are <u>heterozygotes</u> (XY) while females are <u>homozygotes</u> (XX). Exception is in chickens

So, what makes a male a male?
>   Does XX cause femaleness or does Y cause maleness?
Depends on the organism.
>   In humans: XXY   -phenotypically male
>   In flies :   XXY   -phenotypically female

In humans Y chromosome is the male determining factor.
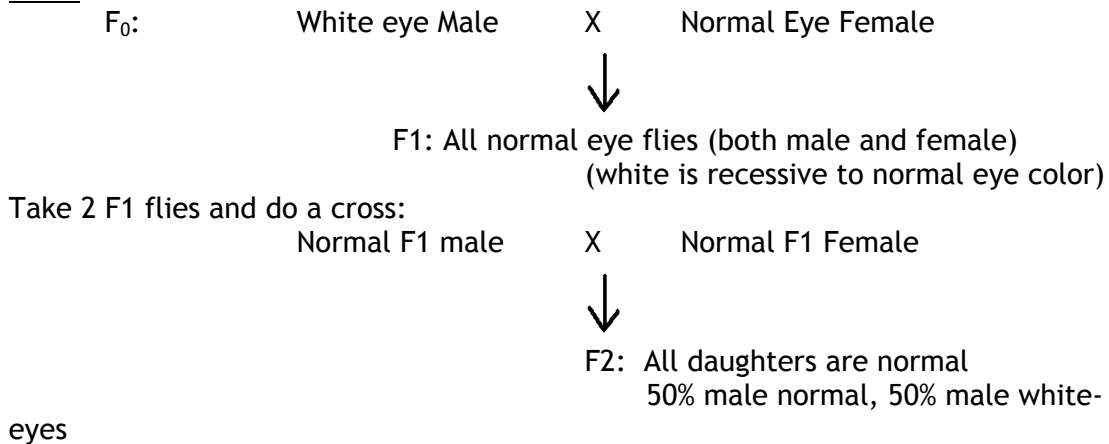
<u>Sex-linkage</u>
Genes are found not only on <u>autosomes</u> but also on the <u>sex-chromosomes</u> (mainly on the X).
Connection between sex chromosomes and sex determination was strengthened by experiments on sex linkage.

<u>Studies on Sex-Linkage</u>

<u>Flies:</u>
> F_0:   White eye Male   X   Normal Eye Female

>   ↓

>   F1: All normal eye flies (both male and female)
>   (white is recessive to normal eye color)
Take 2 F1 flies and do a cross:
>   Normal F1 male   X   Normal F1 Female

>   ↓

>   F2: All daughters are normal
>   50% male normal, 50% male white-
eyes

Conclusion: Gene for eye color is on X chromosome – results cannot be explained by simple dominance/recessiveness. Therefore the trait is Sex-linked.