D) Gene Interaction Takes Place When Genes at Multiple Loci Determine a Single Phenotype.

In the dihybrid crosses, each locus had an independent effect on the phenotype. When Mendel crossed a homozygous round and yellow plant (*RR YY*) with a homozygous wrinkled and green plant (*rr yy*) and then self-fertilized the F1, he obtained F2 progeny in the following proportions:

9/16 *R_ Y_* round, yellow
3/16 *R_ yy* round, green
3/16 *rr Y_* wrinkled, yellow
1/16 *rr yy* wrinkled, green

In this example, the genes showed two kinds of independence. First, the alleles at each locus are independent in their *assortment* in meiosis, which is what produces the 9 : 3 : 3 : 1 ratio of phenotypes in the progeny, in accord with Mendel's principle of independent assortment. Second, the genes are independent in their *phenotypic expression*, the *R* and *r* alleles affect only the shape of the seed and have no influence on the color of the seed; the *Y* and *y* alleles affect only color and have no influence on the shape of the seed.

In many cases, the effects of genes at one locus depend on the presence of genes at other loci. This type of relation between the effects of genes at different loci (genes that are not allelic) is termed **gene interaction**. With gene interaction, the products of genes at different loci combine to produce new phenotypes that are not predictable from the single-locus effects alone. In the following section we will discuss some examples of gene interaction. For simplicity, we will refer to the two couples of alleles as A & a and B & b. We shall study two types of gene interaction: the first is that produces novel phenotypes while the second is called epistasis.

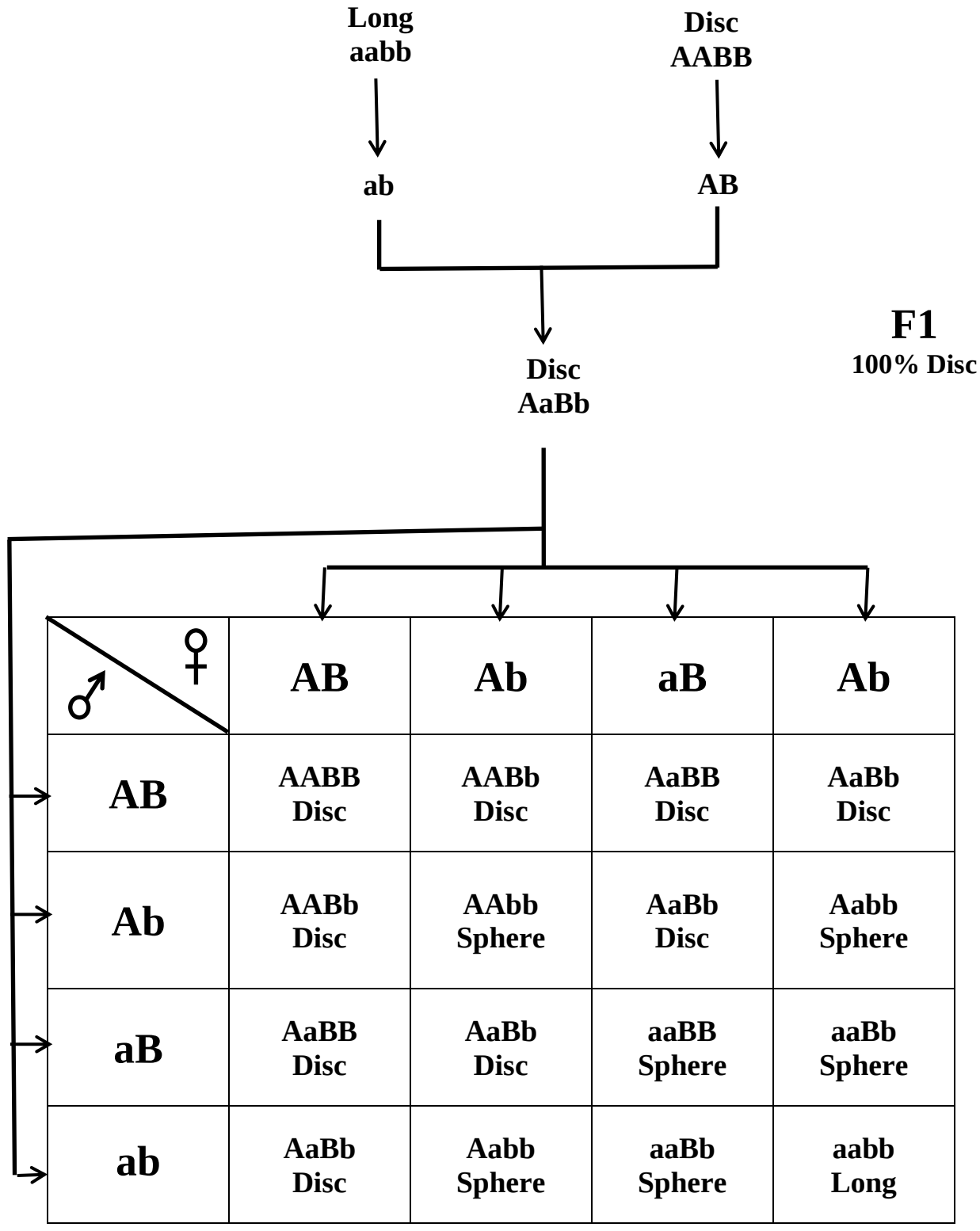
1) Gene interaction that produces novel phenotypes

Let's first examine gene interaction in which genes at two loci interact to produce a single characteristic. Two genes in different loci affect the same character, either equally or in different ways. The presence of dominant allele(s) of both genes produces a novel phenotype.

Fruit shape in the summer squash *Cucurbita pepo* is controlled with 2 couples of alleles (*A* & *a* and *B* & *b*). Presence of at least one copy of *A* or At least one copy of *B* results in sphere-shaped fruits while the genotypes *A-B-* result in disc-shaped fruits. Finally, plants carrying *aabb* genotype have long fruit.

Genotype	**Phenotype**
*A_B_*	Disc
*aaB_*	Sphere
A_bb	
aabb	Long

When a homozygous plant that produces discoid fruits is crossed with a homozygous plant that produces long fruits F1 plants carried discoid fruits. Self-crossing of F1 plants produced discoid, spherical and long fruits in 9 : 6 : 1 ratio.



F2 (9 Disc : 6 Sphere : 1 Long)

2) Epistasis

Sometimes the effect of gene interaction is that one gene masks (hides) the effect of another gene at a different locus, a phenomenon known as **epistasis**. Epistasis is similar to dominance, except that dominance entails the masking of genes at the *same* locus (allelic genes). In epistasis, the gene that does the masking is called an **epistatic gene**; the gene whose effect is masked is a **hypostatic gene**. Epistatic genes may be recessive or dominant in their effects.

- **Recessive epistasis**

Recessive epistasis is seen in the genes that determine coat color in Labrador retrievers. These dogs may be black, brown, or yellow; their different coat colors are determined by interactions between genes at two loci. One locus determines the type of pigment produced by the skin cells: a dominant allele *B* encodes black pigment, whereas a recessive allele *b* encodes brown pigment. Alleles at a second locus affect the *deposition* of the pigment in the shaft of the hair; dominant allele *B* allows dark pigment (black or brown) to be deposited, whereas recessive allele *a* prevents the deposition of dark pigment, causing the hair to be yellow.

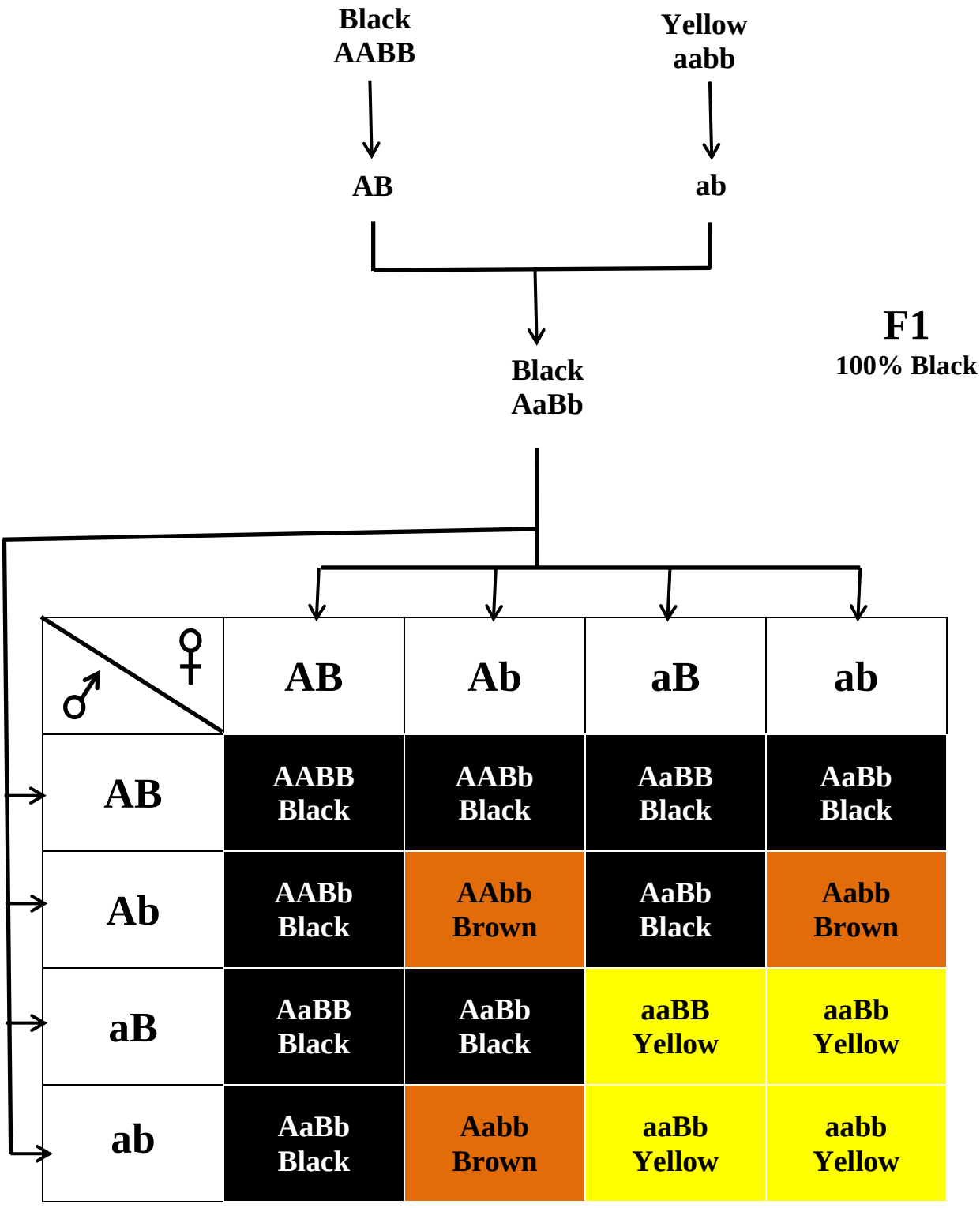
The presence of genotype *aa* at the second locus therefore masks the expression of the black and brown alleles at the first locus. The genotypes that determine coat color and their phenotypes are:

Genotype	Phenotype
A_B_	Black
A_bb	Brown
aa_ _	Yellow

If we cross a black Labrador homozygous for the dominant alleles (*AA BB*) with a yellow Labrador homozygous for the recessive alleles (*aa bb*) and then intercross the F1, we obtain progeny in the F2 in a 9 : 3 : 4 ratio.

Notice that yellow dogs can carry alleles for either black or brown pigment, but these alleles are not expressed in their coat color. In this example of gene interaction, allele *a* is epistatic to *B* and *b*, because *a* masks the expression of the alleles for black and brown

pigments, and alleles *B* and *b* are hypostatic to *a*. In this case, *a* is a recessive epistatic allele, because two copies of *a* must be present to mask the expression of the black and brown pigments.



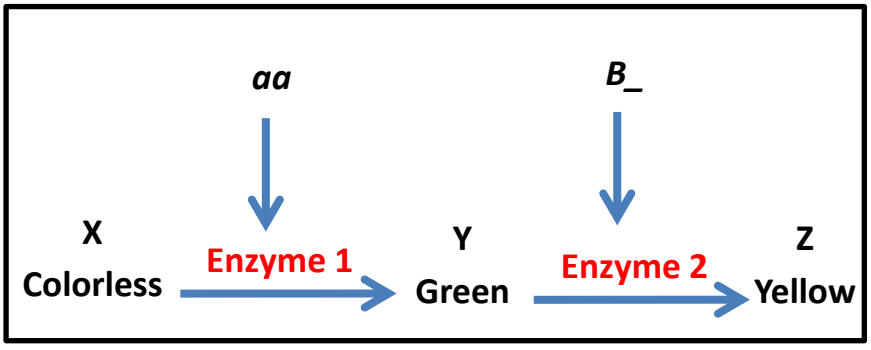
F2 (9 Black : 4 yellow : 3 Brown)

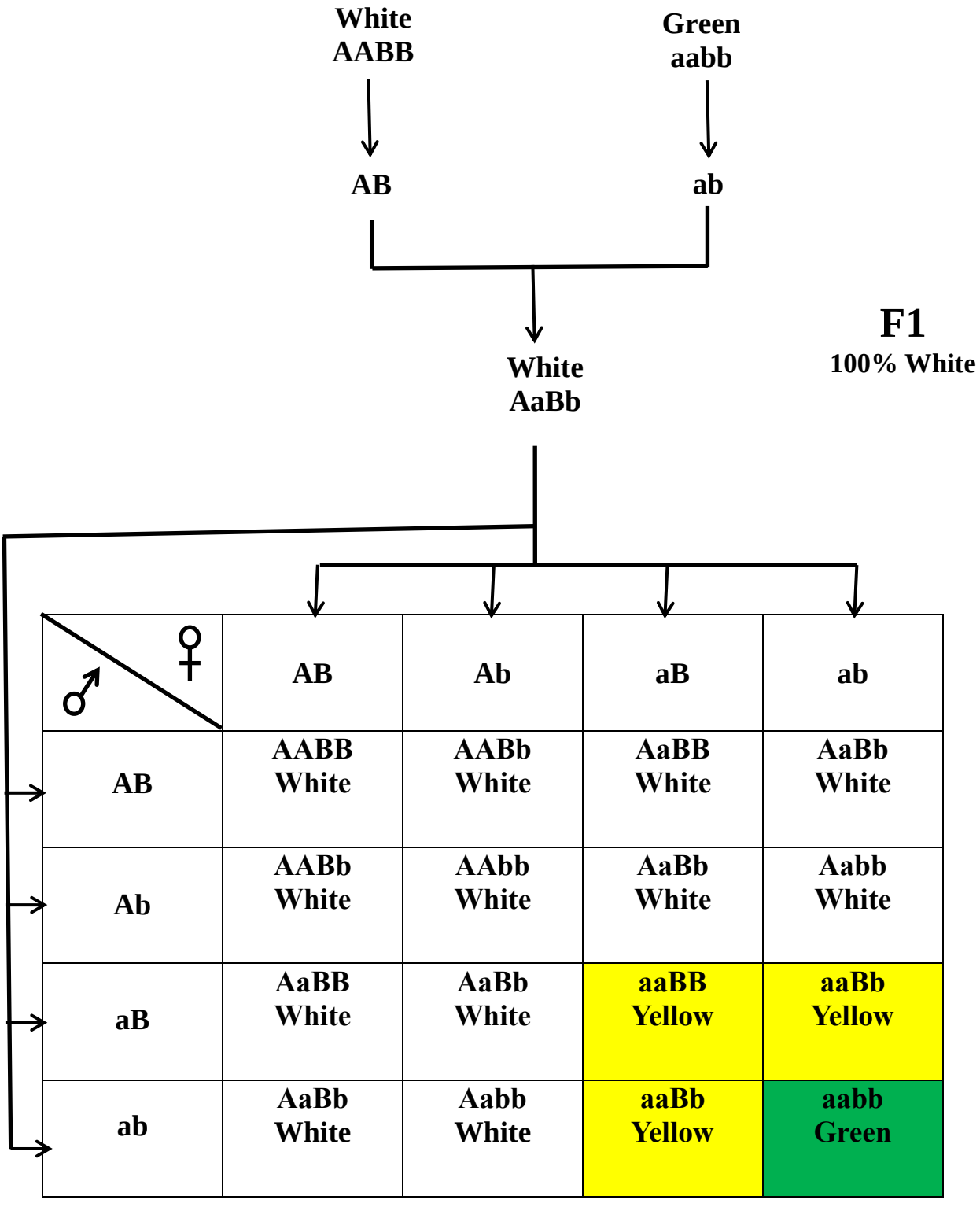
- **Dominant epistasis**

In *recessive* epistasis, which we just considered, the presence of two recessive alleles (the homozygous genotype) inhibits the expression of an allele at a different locus. In *dominant* epistasis, only a single copy of an allele is required to inhibit the expression of the allele at a different locus. Dominant epistasis is seen in the interaction of two loci that determine fruit color in summer squash, which is commonly found in one of three colors: yellow, white, or green. When a homozygous plant that produces white squash is crossed with a homozygous plant that produces green squash and the F1 plants are crossed with each other, the following results are obtained: 12/16 plants with white squash 3/16 plants with yellow squash1/16 plants with green squash.

Yellow pigment in the squash is most likely produced in a two-step biochemical pathway. **X** is a colorless (white) compound is converted by enzyme I into green compound **Y**, which is then converted into yellow compound **Z** by enzyme II. Plants with the genotype *aa* produce enzyme I and may be green or yellow, depending on whether enzyme II is present. When allele *B* is present at a second locus, enzyme II is produced and compound **Y** is converted into compound **Z**, producing a yellow fruit. When two copies of allele *b*, which does not encode a functional form of enzyme II, are present, squash remain green. The presence of *A* at the first locus inhibits the conversion of compound **X** into compound **Y**; plants with genotype *A*_ do not make compound **Y** and their fruit remains white, regardless of which alleles are present at the second locus.

Genotype	Phenotype
*A*_ *B*_	White
*A*_ *bb*	
*aa B*_	yellow
aa bb	green





♂ \ ♀	AB	Ab	aB	ab
AB	AABB White	AABb White	AaBB White	AaBb White
Ab	AABb White	AAbb White	AaBb White	Aabb White
aB	AaBB White	AaBb White	aaBB Yellow	aaBb Yellow
ab	AaBb White	Aabb White	aaBb Yellow	aabb Green

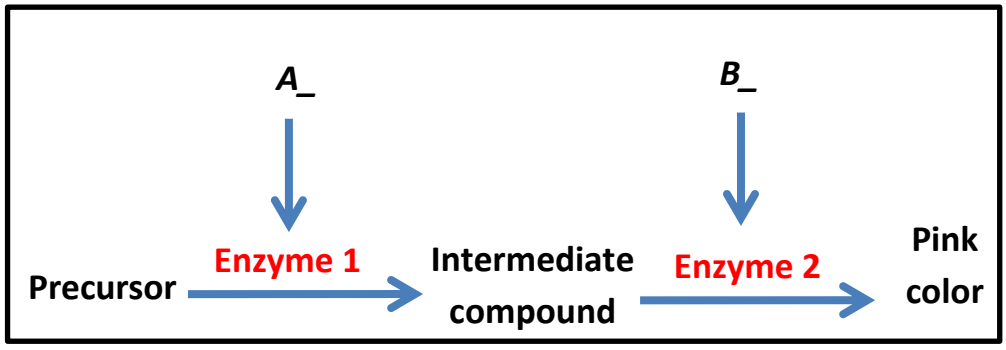
F2 **(12 White : 3 Yellow : 1 Green)**

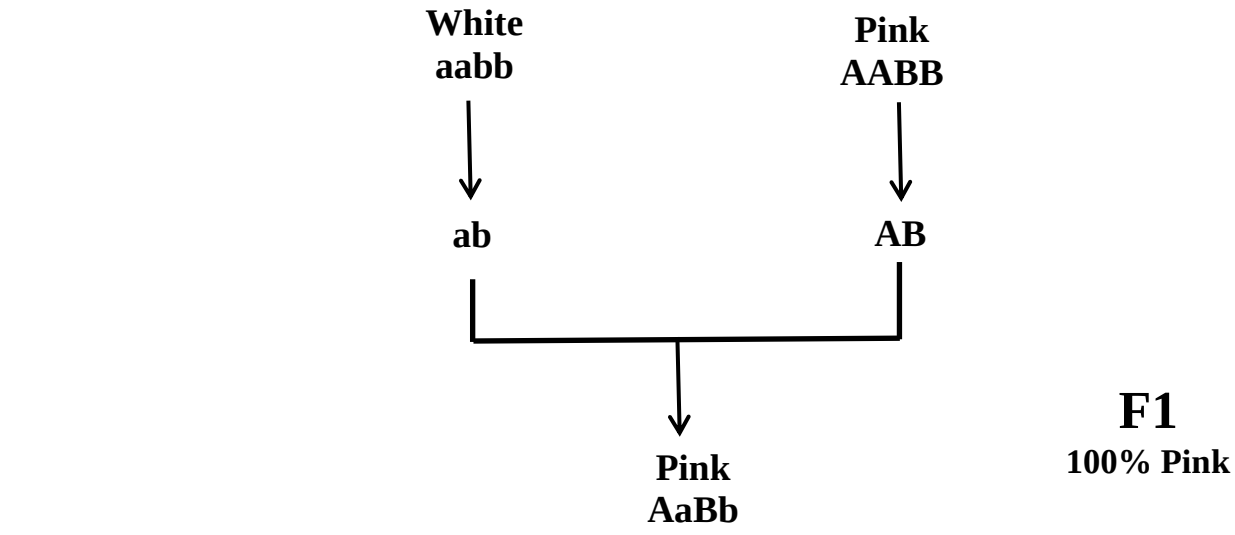
Notice that white fruits can carry alleles for either yellow or green pigment, but these alleles are not expressed. In this example of gene interaction, allele *A* is epistatic to *B* and *b* and alleles *B* and *b* are hypostatic to *A.* In this case, *A* is a dominant epistatic allele, because one copy of *A* is enough to inhibit the expression of the *B* & *b* alleles.

- **Duplicate recessive epistasis (complementary genes)**

In some cases, alleles of each gene exhibit an epistatic effect on alleles of the other gene. Duplicate recessive epistasis is an example of this mutual effect. Two recessive alleles of any gene are capable of suppressing a phenotype. Flower color in sweet pea is controlled with alleles of 2 genes (A & a and B & b). Pink flowers are produced through two steps; each step is controlled by an independent gene. At least one dominant allele of each gene is required to produce pink flowers. When a homozygous plant that produces pink flowers is crossed with a homozygous plant that produces white flowers F1 plants carried pink flowers. Self-crossing of F1 plants produced pink and white flowers in 9 : 7 ratio. This case is also called duplicate recessive epistasis where 2 copies of the recessive allele of any of the genes prevent pigment formation.

Genotype	Phenotype
*A_B_*	Pink
*aaB_*	White
A_bb	
aabb	





♂ \ ♀	AB	Ab	aB	Ab
AB	AABB Pink	AABb Pink	AaBB Pink	AaBb Pink
Ab	AABb Pink	AAbb White	AaBb Pink	Aabb White
aB	AaBB Pink	AaBb Pink	aaBB White	aaBb White
ab	AaBb Pink	Aabb White	aaBb White	aabb White

F2 (9 Pink : 7 White)

Additional extensions of Mendelian ratios (eg: 15:1, 13:3, 10:3:3 and 6:3:3:4) were recorded and proved to be as a result of gene interaction. In interpreting the genetic basis of modified ratios, we should keep several points in mind:

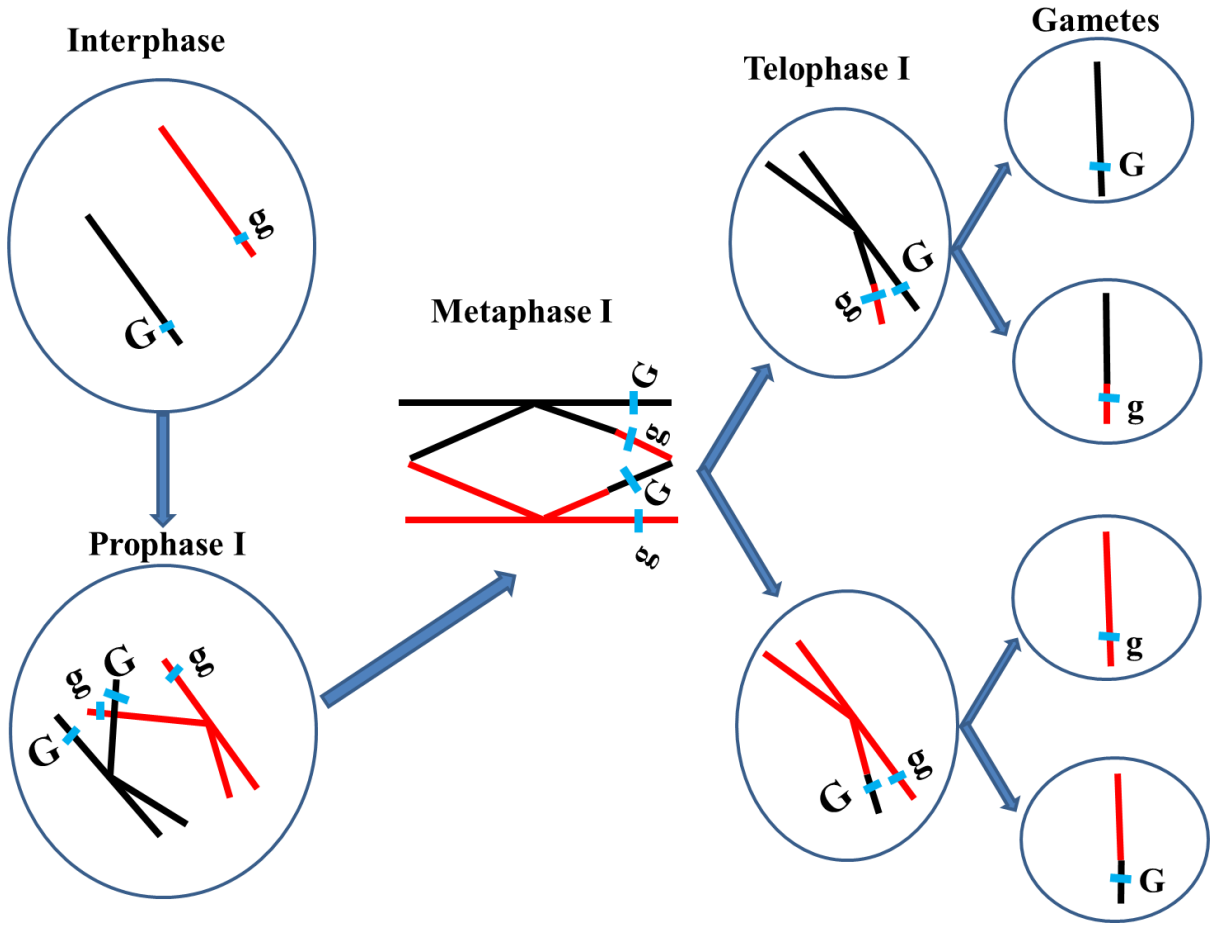
- The inheritance of the genes producing these characteristics is no different from the inheritance of genes encoding simple genetic characters (characters controlled with single couple of alleles). Mendel's principles of segregation and independent assortment still apply; each individual organism possesses two alleles for each gene, which separate during gametes formation, and alleles of different genes assort independently. The only difference is in how the *products* of the genotypes interact to produce the phenotype. Thus, we cannot consider the expression of genes at each locus separately; instead, we must take into consideration how the genes at different loci interact.

- The phenotypic proportions were always in sixteenths because, in all the crosses, pairs of alleles segregated at two independently assorting loci. The probability of inheriting one of the two alleles at a locus is 1/2. Because there are two loci, each with two alleles, the probability of inheriting any particular combination of genes is $(1/2)^4 = 1/16$.

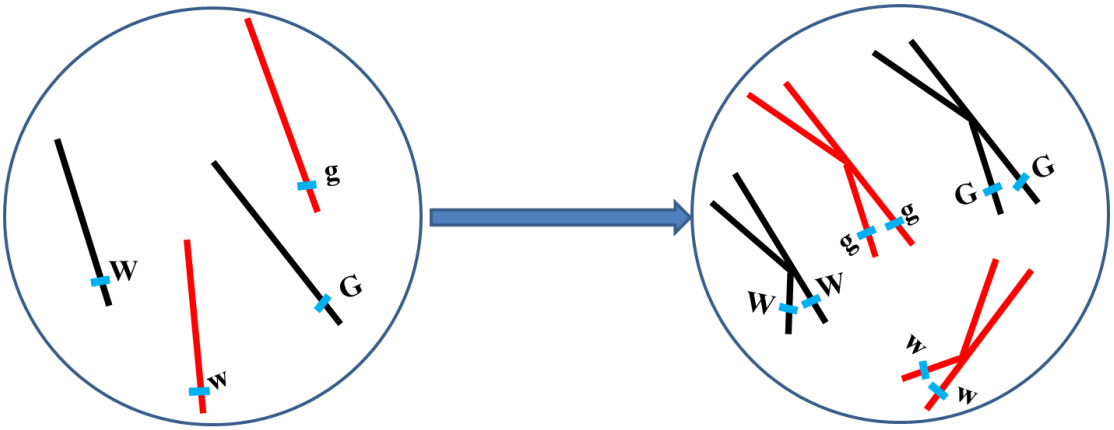
Chromosome theory of heredity

In 1900, when Mendel's work was rediscovered and biologists began to apply his principles of heredity, the relation between genes and chromosomes was still unclear. The theory that genes are located on chromosomes (the **chromosome theory of heredity**) was developed in the early 1900s by Walter Sutton, then a graduate student at Columbia University. Through the careful study of meiosis in insects, Sutton documented the fact that each homologous pair of chromosomes consists of one maternal chromosome and one paternal chromosome. Showing that these pairs segregate independently into gametes in meiosis, he concluded that this process is the biological basis for Mendel's principles of heredity.

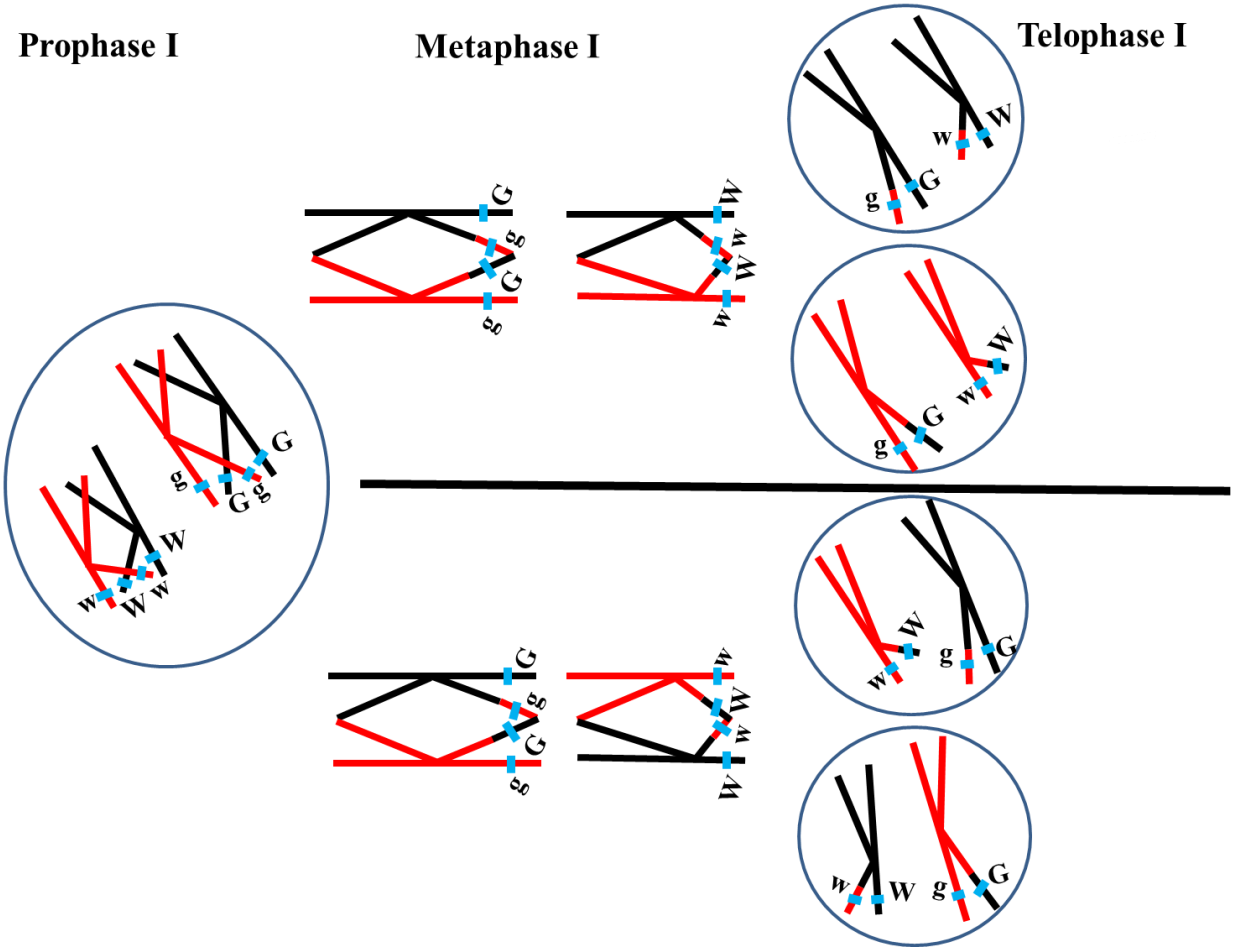
For the law of segregation, the two alleles of a genotype are found on different but homologous chromosomes. One chromosome of each homologous pair is inherited from the mother and the other is inherited from the father. In the S phase of meiotic interphase, each chromosome replicates, producing two copies of each allele, one on each chromatid. The homologous chromosomes segregate in anaphase I, thereby separating the two different alleles. This chromosome segregation is the basis of the principle of segregation. In anaphase II of meiosis, the two chromatids of each replicated chromosome separate; so each gamete resulting from meiosis carries only a single allele at each locus, as Mendel's principle of segregation predicts. The result is not affected with occurance of crossing over.

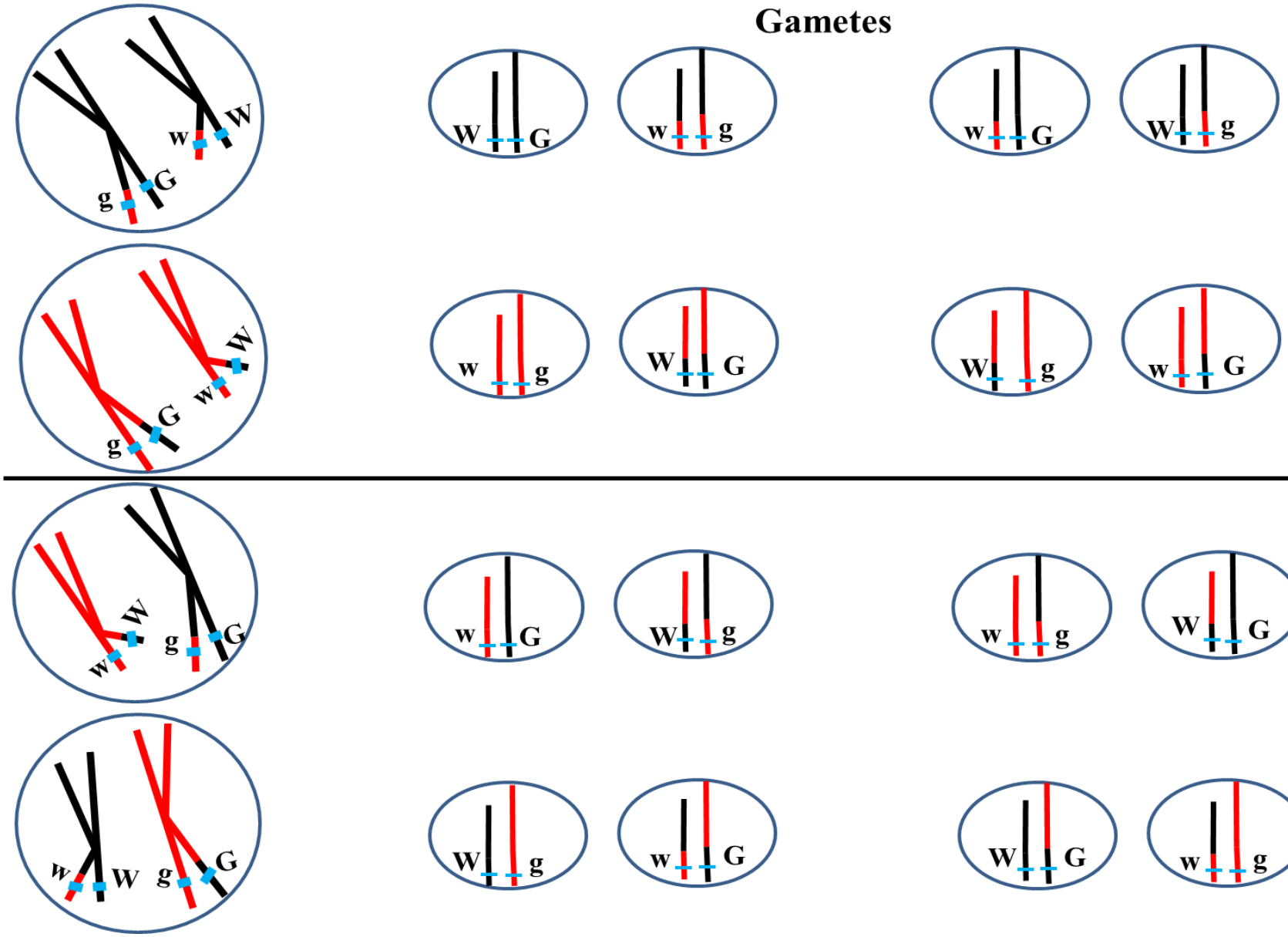


The principle of independent assortment states that alleles of the same gene assort independently of alleles of other genes. It is easy now to see that the number of chromosomes in most organisms is limited and that there are certain to be more genes than chromosomes; so some alleles belonging different genes must be present on the same chromosome and should not assort independently.



Interphase Prophase I

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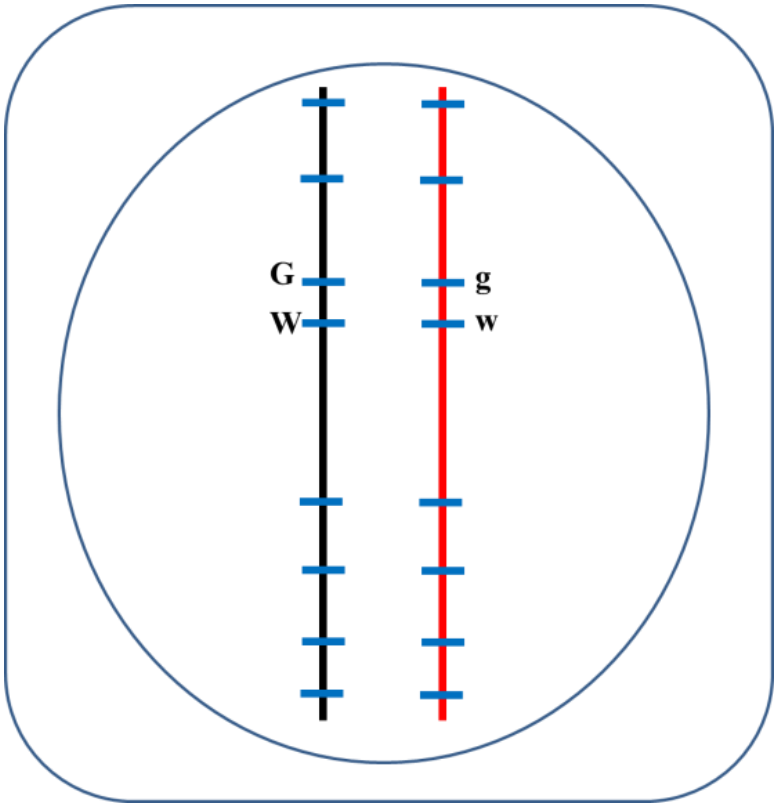
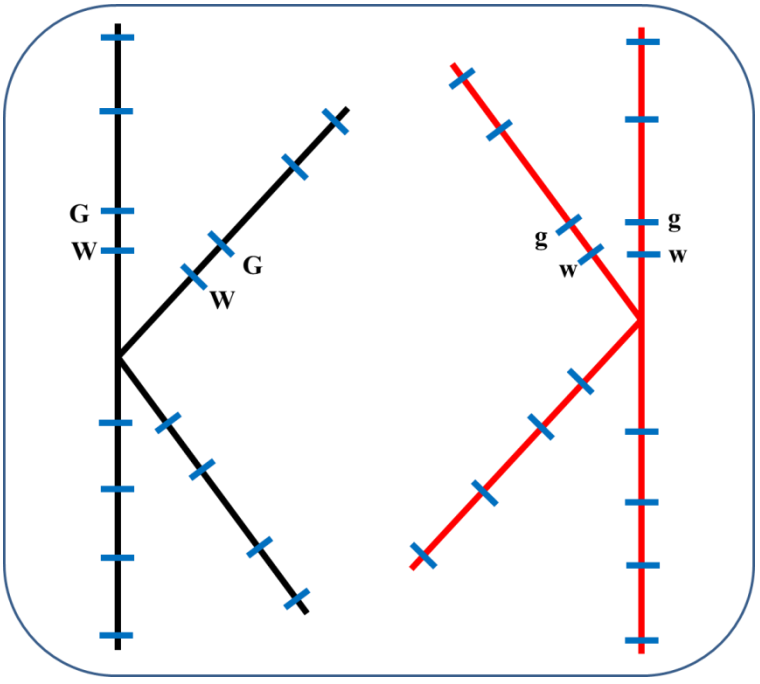
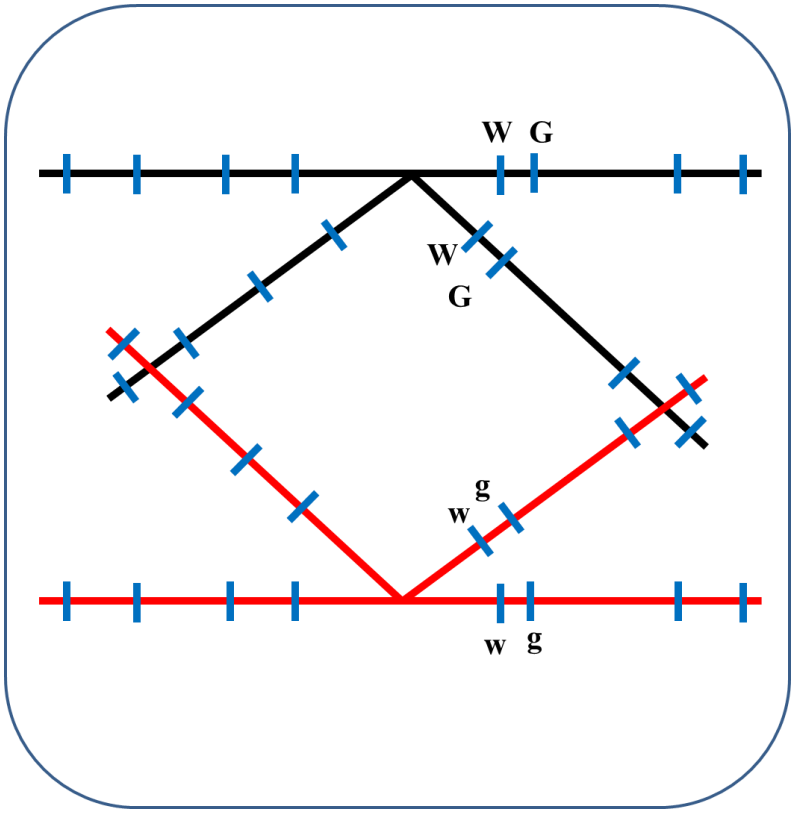
Genes located together on the same chromosome are called **linked genes**. Linked genes travel together in meiosis, eventually arriving at the same destination (the same gamete), and are not expected to assort independently.



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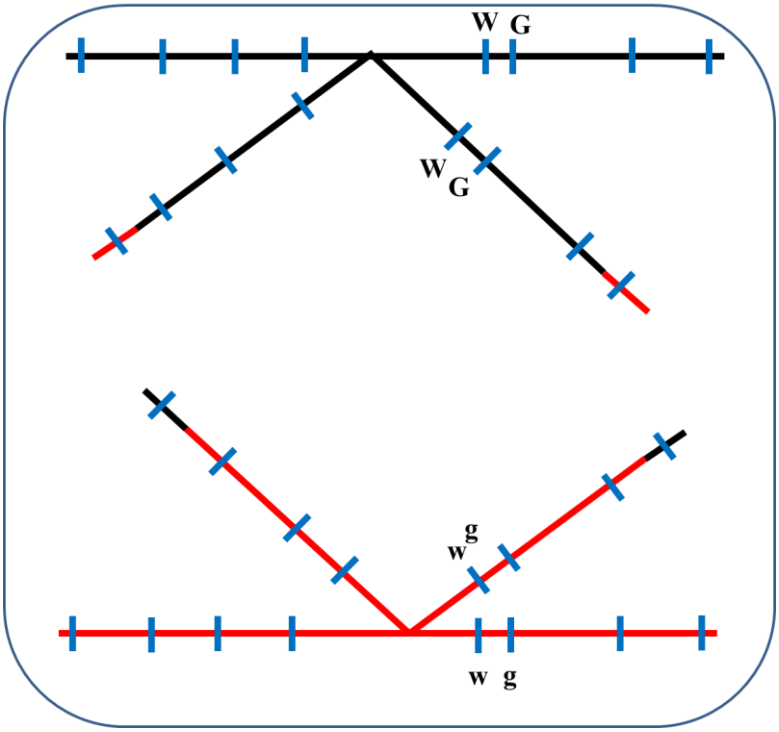
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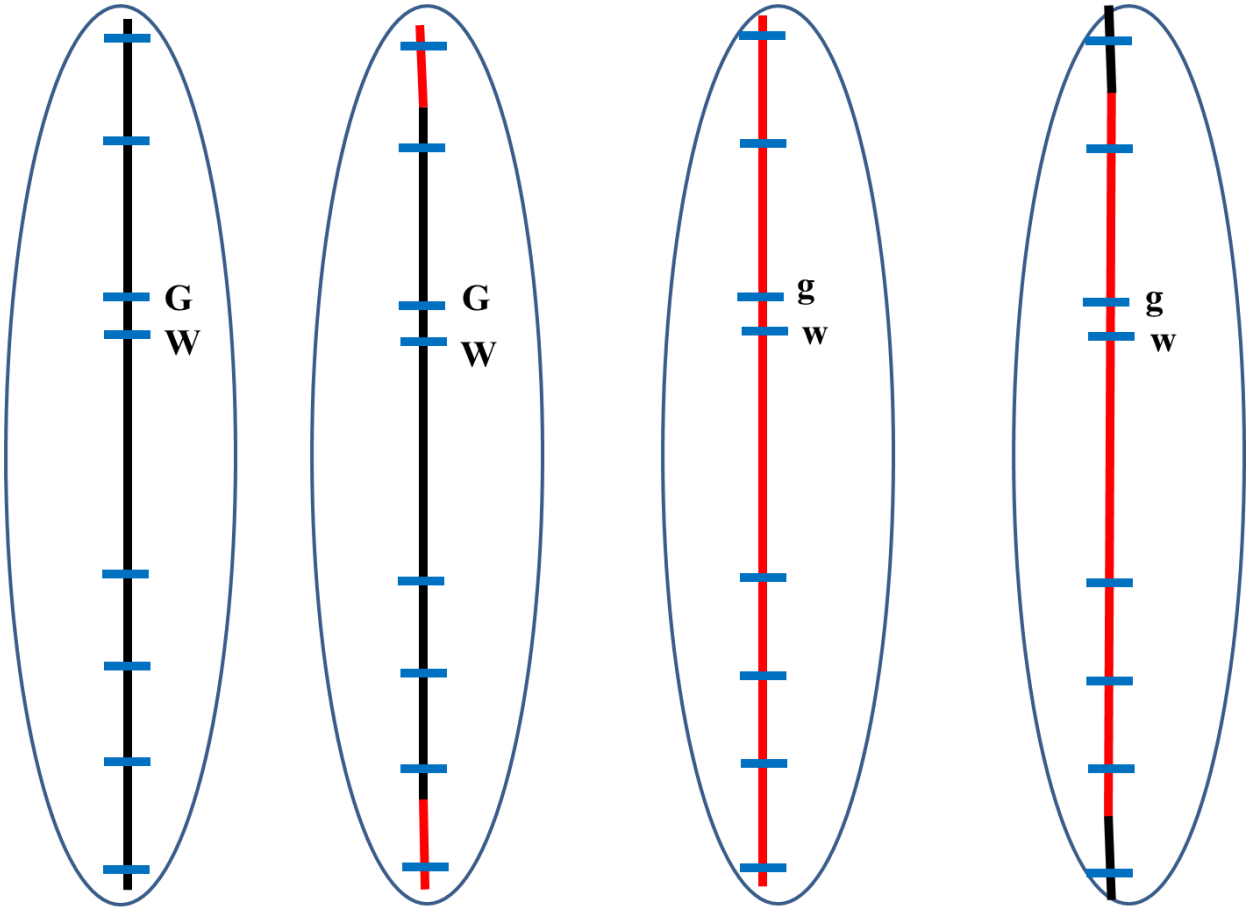
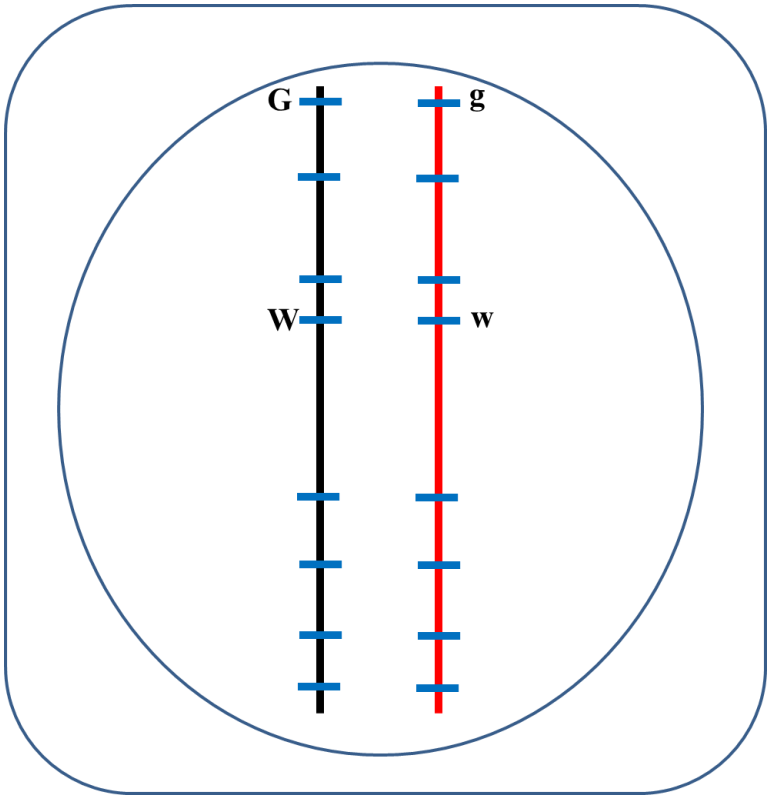
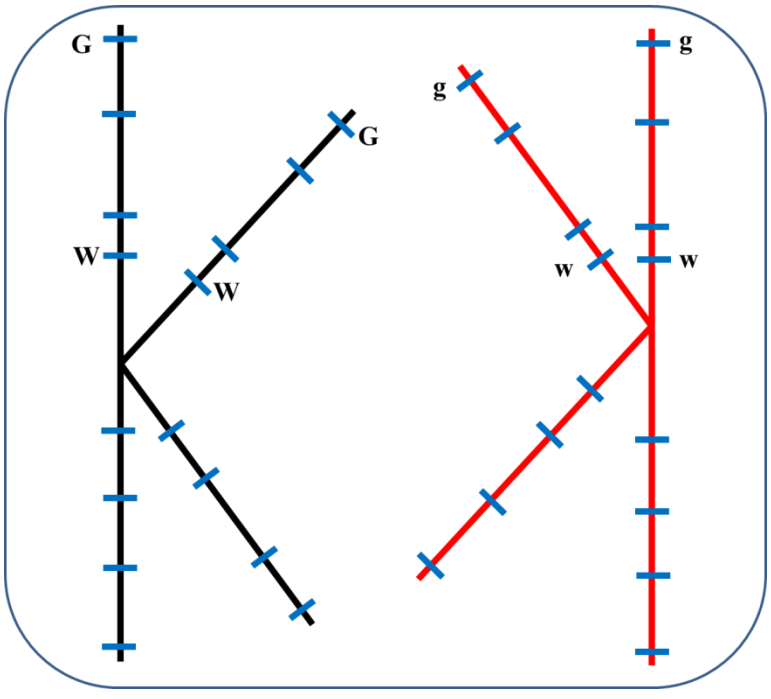
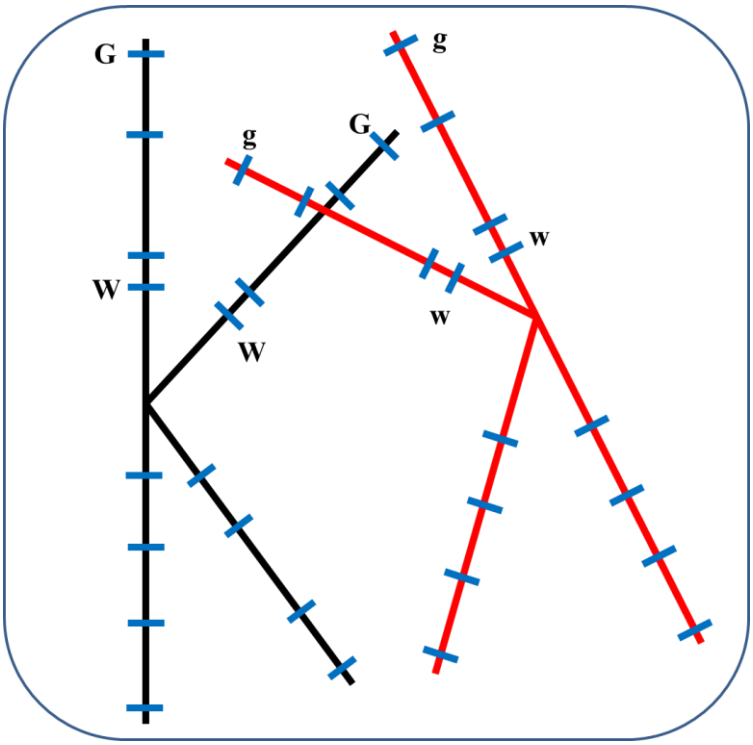


Genes that are close together on the same chromosome usually segregate as a unit and are therefore inherited together. However, alleles occasionally switch from one homologous chromosome to the other through the process of crossing over. Crossing over results in recombination; it breaks up the associations of alleles on the same chromosome. Linkage and crossing over can be seen as processes that have opposite effects: linkage keeps particular alleles together, and crossing over mixes them up. Consider alleles of 2 linked genes (G & g and W & w) and a dihybrid has G and W on a homologous chromosome and consequently g and w on the other homolog. In absence of crossing over, this individual produces 2 types of gametes (all carrying either G and W or g and w). Crossing over results in 4 types of gametes:

- Two types receive chromatids that did not share in crossing over and carry the same association of alleles present in the dihybrid (G and W or g and w) that are called nonrecombinant gametes, or parental gametes.
- Another 2 types receive chromatids that shared in crossing over and carry G and w or g and W that are called recombinant gametes.



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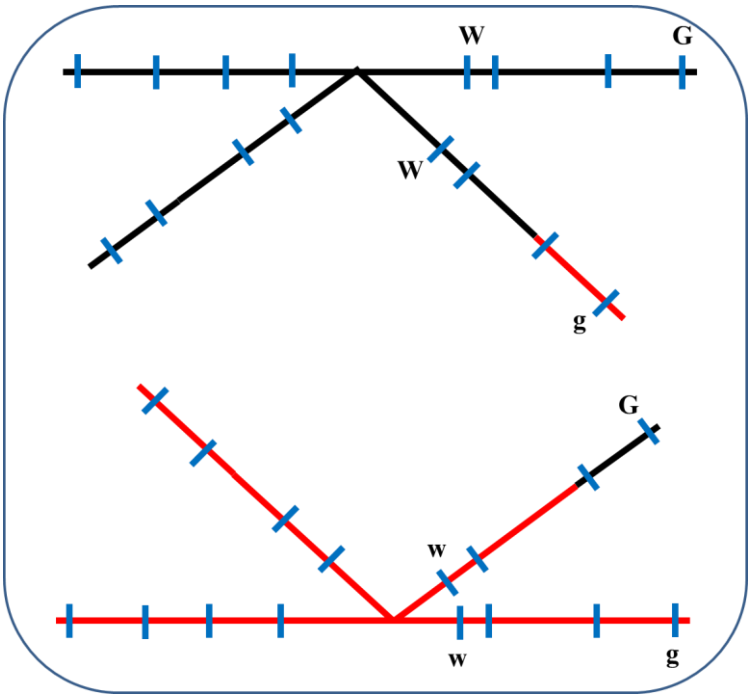
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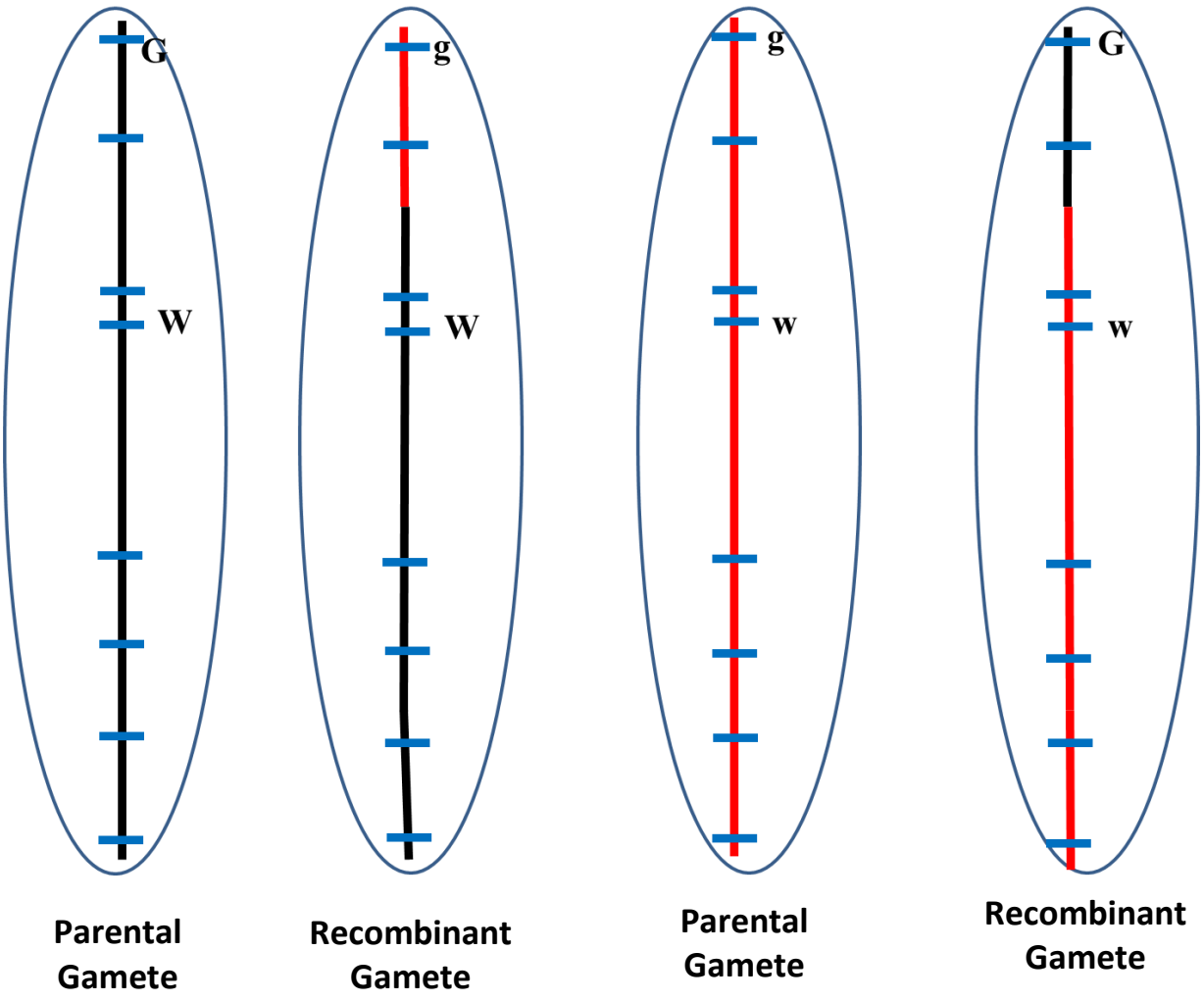

Thus, if crossing over occurred in all gametes producing cells; only 50% of gametes will carry parental combinations of alleles and the remaining 50% of gametes will carry new combinations. However, this is not always observed where crossing over does not always occur in the same position for all dividing cells. The probability for crossing over to occur between 2 loci depends on the distance between them; the greater the distance between loci the greater the chance for crossing over to occur between them and vice versa.

Test cross (cross with individual carrying recessive alleles ggww that produces one type of gametes gw) for a dihybrid (GgWw) results in 4 types of offspring; 2 of which result from parental gametes and called parental progeny while the remaining 2 types result

from recombinant gametes and called recombinant progeny. The ratios of different types of offspring equal to the ratios of different types of gametes produced by the dihybrid.

The percentage of recombinant progeny produced in a cross is called the **recombination frequency**, which is calculated as follows:

$$\text{Recombinant frequency} = \frac{\text{Number of recombinant progeny}}{\text{Total number of progeny}} \text{ X } 100$$

Thomas Hunt Morgan and his students developed the idea that physical distances between genes on a chromosome are related to the rates of recombination. They hypothesized that crossover events occur more or less at random up and down the chromosome and that two genes that lie far apart are more likely to undergo a crossover than are two genes that lie close together. They proposed that recombination frequencies could provide a convenient way to determine the order of genes along a chromosome and would give estimates of the relative distances between the genes. Distances on genetic maps are measured in **map units** (abbreviated m.u.); one map unit equals 1% recombination. Map units are also called **centiMorgans** (cM), in honor of Thomas Hunt Morgan; 100 centiMorgans equals 1 **Morgan**. Thus, if a dihybrid having 2 linked genes produced 10% recombination progeny for these 2 genes following test cross; it means that the distance between loci of these genes = 10 m. u. or 10 centimorgan