Gene Linkage

Up to this point we have considered whether a single trait is Mendelian. However, Mendel himself also looked at the inheritance of two traits together in his second experiment (the dihybrid cross). Although dihybrid crosses were revisited in the unit on epistasis, the focus was still on a single trait (and how multiple genes influenced that trait). In this unit we will examine the inheritance patterns of multiple traits together and introduce techniques for testing whether traits are linked using approaches to quantify recombination.

1 When genes assort independently, and when they don't

Mendel's dihybrid cross experiment crossed individuals heterozygous for two genes ('RrYy'), each of which controlled a different trait (seed shape ['R' = round, 'r' = wrinkled] and seed color ['Y' = yellow, 'y' = green]). This resulted in a $9:3:3:1$ ratio (round/yellow : round/green : wrinkled/yellow : wrinkled/green). This allowed Mendel to describe the Law of Independent Assortment– the idea that genes are inherited independent of each other. However, Mendel was fortunate to have traits whose genes are located on different chromosomes (Figure 1, left).

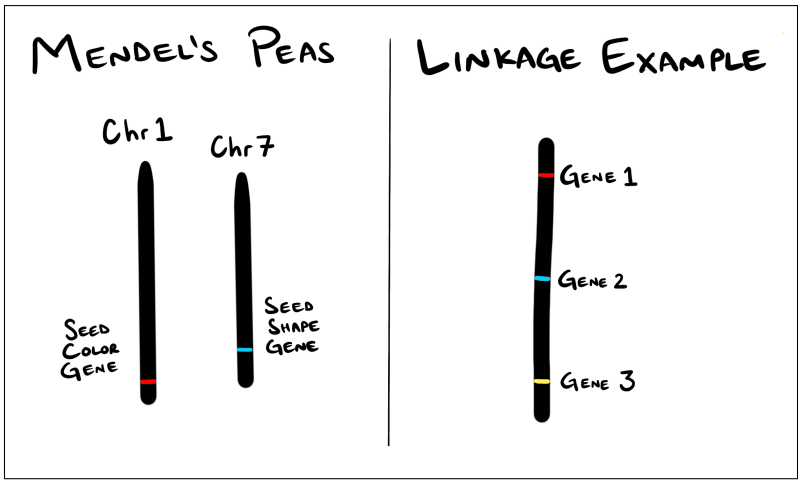

Figure 1: Depiction of Mendel's seed shape and seed color genes on different chromosomes in the garden pea genome (left) and depiction of three hypothetical genes that we look examine in this unit located on the same chromosome (right).

What would have happened if the genes were on the same chromosome (Figure 1, right)? For the sake of simplicity, first we will assume there is no crossing over (i.e., no recombination between homologous chromosomes). This would mean that the genes would be **linked**. Linked genes are inherited together more frequently than would be expected given independent assortment. **Complete linkage** occurs when genes are *always* inherited together. For example, if the genes for seed shape and seed color were completely linked, then Mendel would have observed a 3:1 ratio resulting from his dihybrid cross (Figure 2).

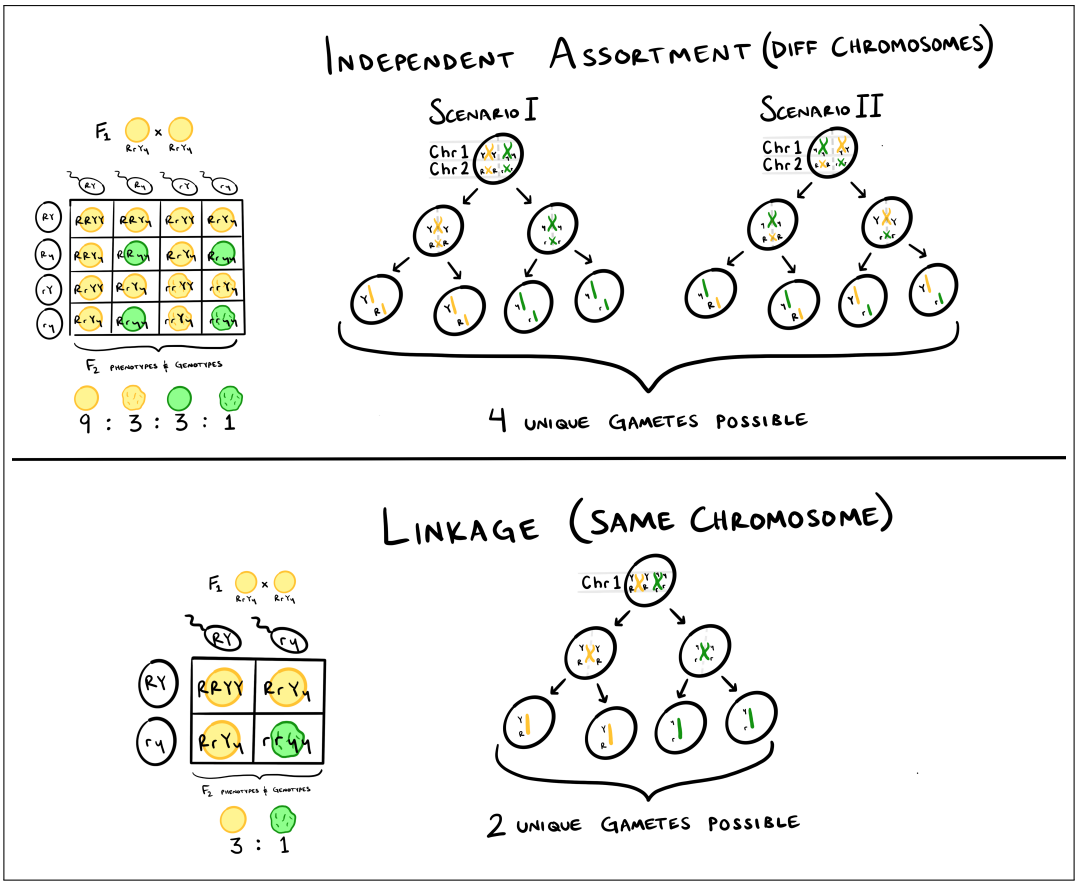

Figure 2: Depiction of Mendel's second experiment (dihybrid cross) in scenarios where genes were unlinked and assorted independently- which is the actual genetic structure and results of Mendel's cross (top) and where genes were linked on the same chromosome- which is a hypothetical scenario and not actually what happened in Mendel's cross (bottom).

Incomplete linkage occurs when genes are inherited together more frequently than would be expected given independent assortment, but sometimes recombination between homologous chromosomes during Prophase I breaks them up and they are inherited separately. There are varying levels of incomplete linkage, and linkage is quantified using **recombination frequency**, which is an approximation for the distance between genes.

2 Linkage terms

Recombination is the rearrangement of genetic material during Meiosis I. Technically this includes both crossing over (resulting in genetic material being exchanged between homologous chromosomes) and independent assortment (resulting in a haploid set of chromosomes that have different parental ancestry), however in this class when we refer to recombination we will generally be referring to the exchange of genetic material between homologous chromosomes via crossing over (which results in a DNA molecule with diverse ancestry). "Diverse ancestry" simply means that a chromosome has multiple "parents" for its genetic material. For example, look at the chromosomes in the pink boxes of Figure **??**. These recombinant chromosomes contain alleles from both P_d and P_r. When crossing over leads to the exchange of genetic material (i.e., recombination between homologous chromosomes), the resultant DNA is called **recombinant DNA**.

NOTE: Recombinant DNA (rDNA) is also a common term in molecular biology that refers to DNA that has been artificially altered to include novel genetic material using lab techniques. In this unit we are not referring to lab-produced rDNA, rather we are referring to natural recombination that occurs during Meiosis I in eukaryotes

3 Testing for linkage

3.1 Testing for linkage between two genes

In this section we will examine a simple approach to test for gene linkage between two genes. This approach has a few requirements:

1. **Variation at both genes.** Each gene must have two alleles.
2. **Complete dominance at both genes.** For each gene the heterozygote shows the phenotype encoded by the dominant allele.
3. **A strain that is heterozygous at both genes.** Just like the F_1 generation in Mendel's second experiment (e.g., 'AaBb').
4. **In the heterozygous strain (the F_1), you must know the allele ancestry.** In other words, you must know where each allele came from. This is why the F_1 from Mendel's cross is a great design, because you know where each allele came from (there were two original parents, one that was true-breeding for the dominant alleles at both genes (P_r: 'AABB') and one that was true-breeding for the recessive alleles at both genes (P_d: 'aabb'). For the F_1 ('AaBb'), we know where each allele came from ('A' and 'B' came from P_d; 'a' and 'b' came from P_r).

   Note: While knowing the ancestry of the alleles is important for estimating gene linkage, you'll see that if you don't know the ancestry you can infer it from the **progeny** (offspring) numbers. This is explained in section 3.2.1 below.

5. **A strain that is homozygous recessive at both genes.** Just like the recessive true-breeding parent in Mendel's second experiment (e.g., aabb).

In order to test for gene linkage, the genes of interest must have genetic variation (i.e., there must be alleles). If there is no genetic variation for a gene, there is no way to know if recombination occurs (Figure 3. This is because the recombinant DNA will look the exact same as the non-recombinant DNA. The F_1 generation from Mendel's experiment, which is heterozygous, possesses variation at both genes. The F_1s (AaBb) can then be crossed with the strain that homozygous recessive for both genes (aabb)- this type of cross is known as a **test cross** (where a heterozygous individual is crossed with a homozygous recessive individual).

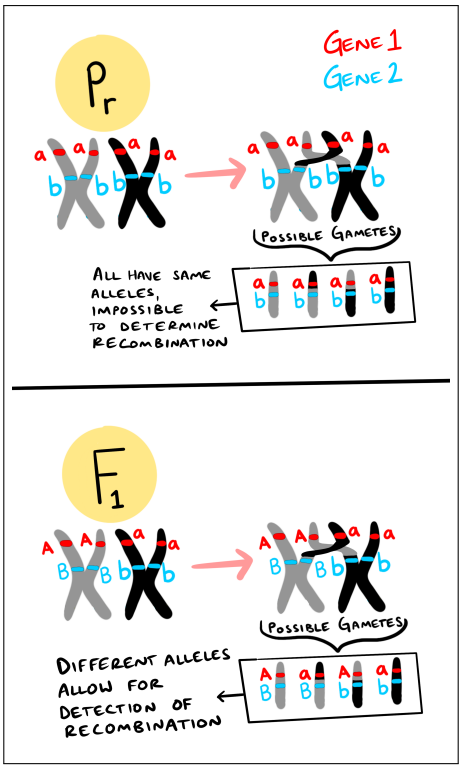

Figure 3: Visual explanation of why variation in genes is needed to detect recombination. Recombination in the P_r individual (homozygous 'aabb' genotype - no variation) results in the same gamete (this is true for any homozygous genotype, such as that of the P_d ('AABB'). Recombination in the F_1 individual (heterozygous 'AaBb' genotype - variation for both Gene 1 and Gene 2) results in 4 unique gametes (two of which are the result of recombination).

Why a test cross? The homozygous recessive parent (P_r) will always provide the same gamete (e.g., ab). This gamete will possess the two recessive alleles, which will act as a "background" in the offspring of the test cross (we'll call these offspring F_T for "test cross" offspring). In other words, the phenotype you observe in the F_T is the result of the alleles given by the heterozygous parent (the F_1), because the gametes of (P_r) are always the same recessive alleles. Therefore, if the dominant phenotype of a trait is observed it is because the F_1 gave a dominant allele, and if the recessive phenotype for a trait is observed it is because the F_1 gave a recessive allele. The F_1 can give four possible gametes (AB, Ab, aB, and ab). Thus the offspring of the test cross will have four possible phenotypes (AaBb, Aabb, aaBb, or aabb), each of which will exhibit the phenotype of the gamete provided by the F_1 (Figure 4).

Performing a test cross allows for the estimation of **genetic distance**, which is the physical distance between two genes. Early approaches to estimating genetic distance used **recombination frequency** (f), which is the proportion of recombination events in meiosis that occur between two genes. In other words, recombination frequency is a measure of how often recombination occurs. It can be calculated by taking the data from the experimental cross and dividing the number of offspring that resulted from recombination events (R) by the total number of offspring (T):

$$f = \frac{R}{T} \tag{1}$$

The value of f ranges from 0 (completely linked genes) to 0.5 (completely unlinked genes);

f cannot be greater than 0.5. The recombination frequency is a function of distance between the genes (while it doesn't provide an exact physical distance, it is an approximation of physical distance between genes). Genetic distance is sometimes reported in centimorgans (cM), which is the f x 100.

3.1.1 Completely linked genes

If genes are completely linked (due to being in very close proximity on the same chromosome), then you will only see the original parental phenotypes in the F_T generation. This is because when the gametes were formed in the F_1, the inability of genes to recombine resulted in the parental alleles always ending up in the same gamete (Figure 3). Because the genes are completely linked, $R = 0$, and thus $f = 0$.

3.1.2 Completely unlinked genes (a.k.a., independent assortment)

If genes are completely unlinked (as occurs with genes that are on different chromosomes), then they independently assort during Metaphase I in Meiosis (see Mendelian Genetics unit for details of independent assortment). This results in an equal proportion of all possible phenotypes in the F_T generation, since the alleles of different genes segregate independently of one another (Figure 4). Because the genes assort completely randomly of each other, $R = \frac{T}{2}$ and $f = 0.5$. This is always the value of f in genes that assort independently, because the equal proportion of all possible phenotypes means that 1/2 of those scenarios are from recombination events.

3.1.3 Incompletely linked genes (a.k.a., partial linkage)

If genes are partially linked (due to being on the same chromosome, but far enough apart as to allow for recombination between them), then all possible phenotypes will be observed in the F_T generation at unequal proportions. The partial linkage means that parental phenotypes will occur more frequently than the recombinant phenotypes, so you will not see the equal proportions expected under the assumption of independent assortment (Figure 4). The value of f for incompletely linked genes is between 0 and 0.5.

- Watch this youtube video to learn more about linkage between two genes and be introduced to three gene linkage (which we will cover in the next section): `https://www.youtube.com/watch?v=wrtLyLwt51o`

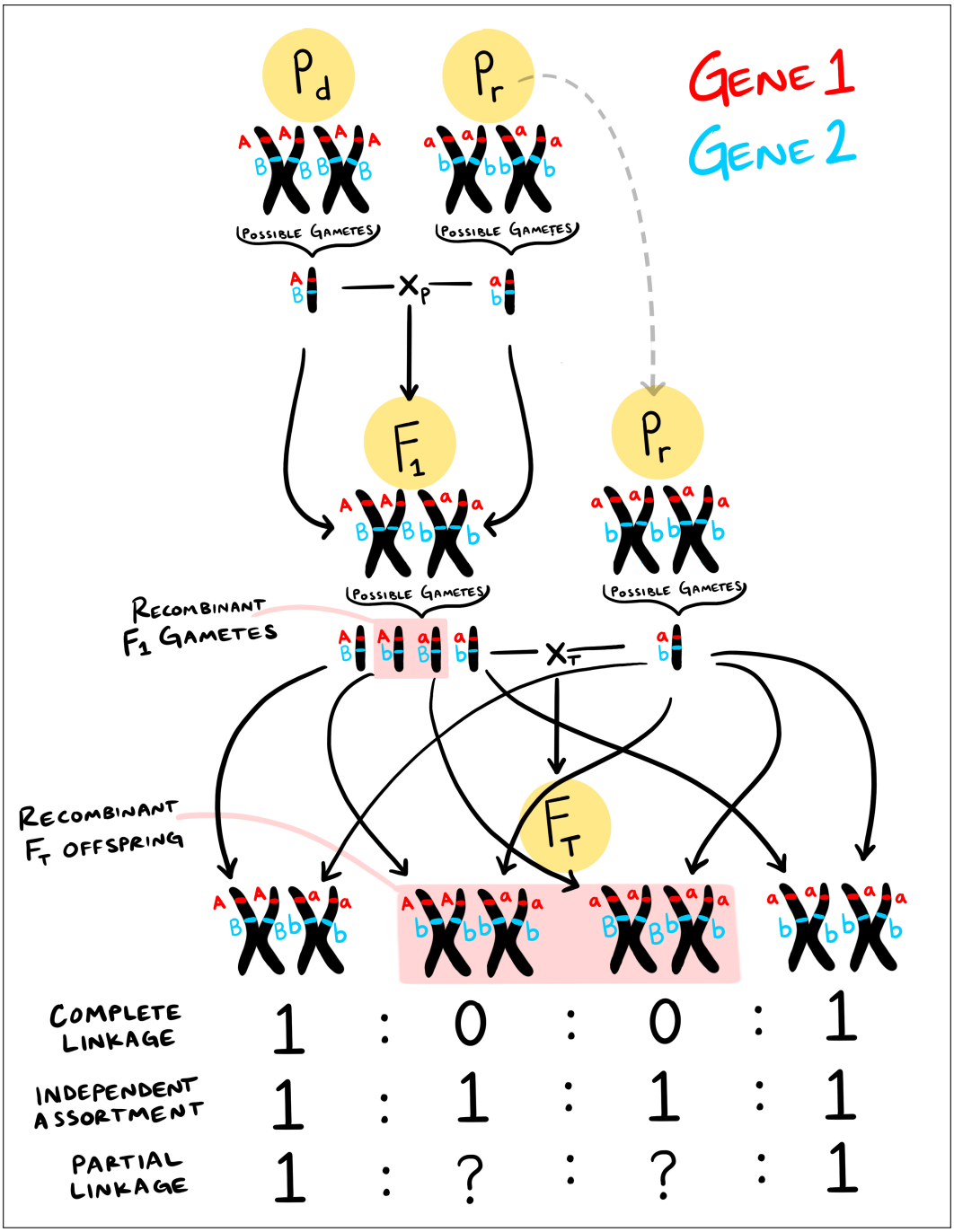

Figure 4: Experimental design to test for linkage between two genes. Two crosses are depicted: First a parental cross between two homozygous parents (dominant P_d (genotype 'AABB') and recessive P_r (genotype 'aabb'); cross marked X_P) and second a test cross between the F_1 (genotype 'AaBb') and the homozygous recessive parent (cross marked X_T). The possible gametes for all individuals are shown, along with the possible offspring produced from the crosses. Recombinant gametes/individuals are shown in the pink boxes. Ratios for different linkage scenarios are shown at the bottom. The question marks for partial linkage indicate values that can range from 0-1. Keep in mind that **these are ratios, not proportions**. A ratio of 1 : 1 : 1 : 1 has proportions of 0.25, 0.25, 0.25, 0.25 (respectively). A ratio of 1 : 0 : 0 : 1 has proportions of 0.5, 0, 0, 0.5 (respectively)

Practice Problem: You want to determine if two genes (Gene 1 and Gene 2) are linked. Each gene has two alleles ('A' and 'a' for Gene 1; 'B' and 'b' for Gene 2), with one allele being dominant (uppercase) to the other (lowercase). Design an experiment to determine if these genes are linked in a diploid organism.

Solution: You should have set up an experiment where a true-breeding parent homozygous dominant for both genes ('AABB'; P_d) is crossed with a true-breeding parent homozygous recessive for both genes ('aabb'; P_r). This means that the F_1 will be heterozygous, with the dominant alleles ('A' and 'B') both being inherited from P_d and the recessive alleles ('a' and 'b') both being inherited from P_d. For an example of this parental cross, see the cross marked X_P in Figure 4. Then you should have performed a test cross, where you cross the F_1 with the P_r. For an example of this test cross, see the cross marked X_T in Figure 4.

Practice Problem: You want to determine the recombination frequency between Gene 1 and Gene 2. Using the experimental design described in the solution of the previous practice problem, you obtain the following offspring in the F_T generation: 50 'AaBb', 50 'aabb', 24 'Aabb', and 26 'aaBb'. What is the genetic distance (in cM) between Gene 1 and Gene 2?

Solution: The recombinant genotypes in the F_T are 'Aabb' and 'aaBb' (because these required 'Ab' and 'aB' genotypes from the F_1, see 4). To calculate genetic distance, we add up the number of offspring with these genotypes and divide by the total number of offspring:

$$\frac{24 + 26}{50 + 50 + 24 + 26} = 0.333$$

The genetic distance between Gene 1 and Gene 2 is 33.3 cM.

3.2 Testing for linkage between three genes

When the genetic distance for more than two genes is of interest, it is possible to determine the gene order and genetic distance for these genes using a test cross in a single experiment. An example of this is the **three-point test cross**, which is similar to what we did above to estimate genetic distance between two genes but this time we will examine three genes. We'll call these Gene 1 ('A' and 'a' alleles), Gene 2 ('B' and 'b' alleles) and Gene 3 ('C' and 'c' alleles).

Using a three-point test cross, you can estimate genetic distance for all three genes and their order on a chromosome (e.g., 123, 132, or 213). To do this, the experiment needs the same criteria described above for a test of linkage in two genes (variation at all three genes, complete dominance at all three genes, strain that is heterozygous for all three genes, strain that is homozygous recessive for all three genes). Using the results from the test cross, you can determine the genetic distance and gene order. This process is known as **gene mapping**.

To perform gene mapping, it is important to use the data from the test cross in the following sequential order:

1. **Identify the parental genotypes** by finding the most frequent phenotypes in the F_T generation.

2. **Identify the double crossover genotypes** by finding the most infrequent phenotypes in the F_T generation.

3. **Determine the gene order** by using the double crossover information to place the middle gene.

4. **Calculate the peripheral-central recombination frequency** by dividing the number of offspring resulting from crossover between the genes by the total number of offspring.

These steps are described in more detail below.

- To learn more about gene mapping using these steps, watch this youtube video: `https://www.youtube.com/watch?v=ZeATszO-6e0`

3.2.1 Identify the parental genotypes

If the parental cross was between homozygous dominant (P_d 'AABBCC') and homozygous recessive (P_r 'aabbcc') genotypes, then the most frequent phenotypes in the F_T generation will show the phenotype of the dominant allele at each trait (these will have genotype 'AaBbCc') and the recessive allele at each trait (these will have genotype 'aabbcc'). That is because the gametes from the F_1 that created these F_T individuals did not require any recombination (and thus were more likely to occur; (Figure **??**).

NOTE: Remember, the F_T generation is a result of a cross. A test cross is a cross between the F_1 and a homozygous recessive strain ('aabbcc')

However, sometimes you may not know the genotypes of the parents (in the P generation). In other words, they may not be P_d ('AABBCC') and P_r ('aabbcc'). Even if you don't know the parental genotypes, you can infer them by identifying the phenotypes that are the most abundant in the F_T generation. For example, if the most abundant genotypes in the F_T generation were 'AabbCc' and 'aaBbcc', then you would know, assuming the parents of the F_1 were true breeding, that the parental genotypes were 'AAbbCC' (we'll call that parent P_1) and 'aaBBcc' (We'll call that parent P_2). Keep in mind that the F_T genotype consists of a chromosome from the F_1 and a chromosome from P_r (which is homozygous recessive for each allele).

3.2.2 Identify the double crossover genotypes

Double crossover events occur on both sides of the gene that is in the middle. Because these events require two crossovers, they are more rare than single crossover events (and thus the phenotypes resulting from double crossover events are less frequent). For example, If our gene order was truly '123', and our parental cross was between P_d ('AABBCC') and P_r ('aabbcc'), then the most infrequent genotypes in the F_T generation would be 'AabbCc' and 'aaBbcc'. These genotypes are the result of fertilization between 'AbC' and 'aBc' F_1 gametes with the 'abc' P_r gamete. These F_1 gametes are the result of a double crossover, where the middle gene (Gene 2) switched between the P_d and P_r chromosomes during Prophase I in the F_1 (Figure **??**.

3.2.3 Determine the gene order

Once you identify the double crossover events, you can use that information to place the middle gene.

Practice Problem: You want to know the order of three genes: Gene α ('X' and 'x' alleles, Gene β ('Y' and 'y' alleles), and Gene γ ('Z' and 'z' alleles). After performing a parental cross between homozygous dominant (P_d 'XXYYZZ') and homozygous recessive (P_r 'xxyyzz') individuals, you performed a test cross between the F_1 ('XxYyZz') and P_r individuals. If the most infrequent genotypes in the F_T generation are 'xxYyZz' and 'Xxyyzz'. What is the order of these three genes?

Solution: The two chromosomes in the F_1 have alleles 'XYZ' (chromosome from P_d) and 'xyz' (chromosome from P_r). You need to identify the F_1 gametes that created the infrequent genotypes of the F_T generation. Because the infrequent genotypes are 'xxYyZz' and 'Xxyyzz', and you know that the P_r gametes in the test cross must have been 'xyz' (since these are the only alleles this strain has), then the gametes from the F_1 must have been 'xYZ' and 'Xyz' for the respective infrequent genotypes. The 'x' and 'X' alleles switched between the parental chromosomes, meaning that Gene α is in the middle (between Gene β and Gene γ). So the gene order is '$\beta\alpha\gamma$' (or '$\gamma\alpha\beta$'; this is the same order, just reversed).

3.2.4 Calculate the peripheral-central recombination frequency

You can't do this until you have the gene order. Once you know the gene order, calculate the recombination frequency (f) between the peripheral genes (those on the outside) and the central gene (the gene on the inside). For example, if you determined the gene order to be '123', in this step you would calculate f between Genes 1 & 2 (f_{1-2}) and then calculate f between Genes 2 & 3 (f_{2-3}). To calculate f between two genes, divide the total number of offspring resulting from a crossover between those two genes (including the double crossovers) by the total number of offspring (see equation 1 above). For example, for f_{1-2}, you would add up the number of offspring where recombination happened between Genes 1 & 2 and divide it by the sum total of all offspring:

$$f_{1-2} = \frac{`aBC' + `Abc' + `aBc' + `AbC'}{`ABC' + `abc' + `aBC' + `Abc' + `aBc' + `AbC' + `abC' + `ABc'} \tag{2}$$

Notice that we included the double crossovers as well, since they consist of a crossover event between our two genes of interest. The same approach is used to calculate f_{2-3}:

$$f_{2-3} = \frac{`abC' + `ABc' + `aBc' + `AbC'}{`ABC' + `abc' + `aBC' + `Abc' + `aBc' + `AbC' + `abC' + `ABc'} \tag{3}$$

a

To calculate f_{1-3}, simply take the sum of f_{1-2} and f_{2-3}.

$$f_{1-3} = f_{1-2} + f_{2-3} \tag{4}$$

- For a different walkthrough of a three-point test cross, watch this video: `https://www.youtube.com/watch?v=JndROGIEeVY`

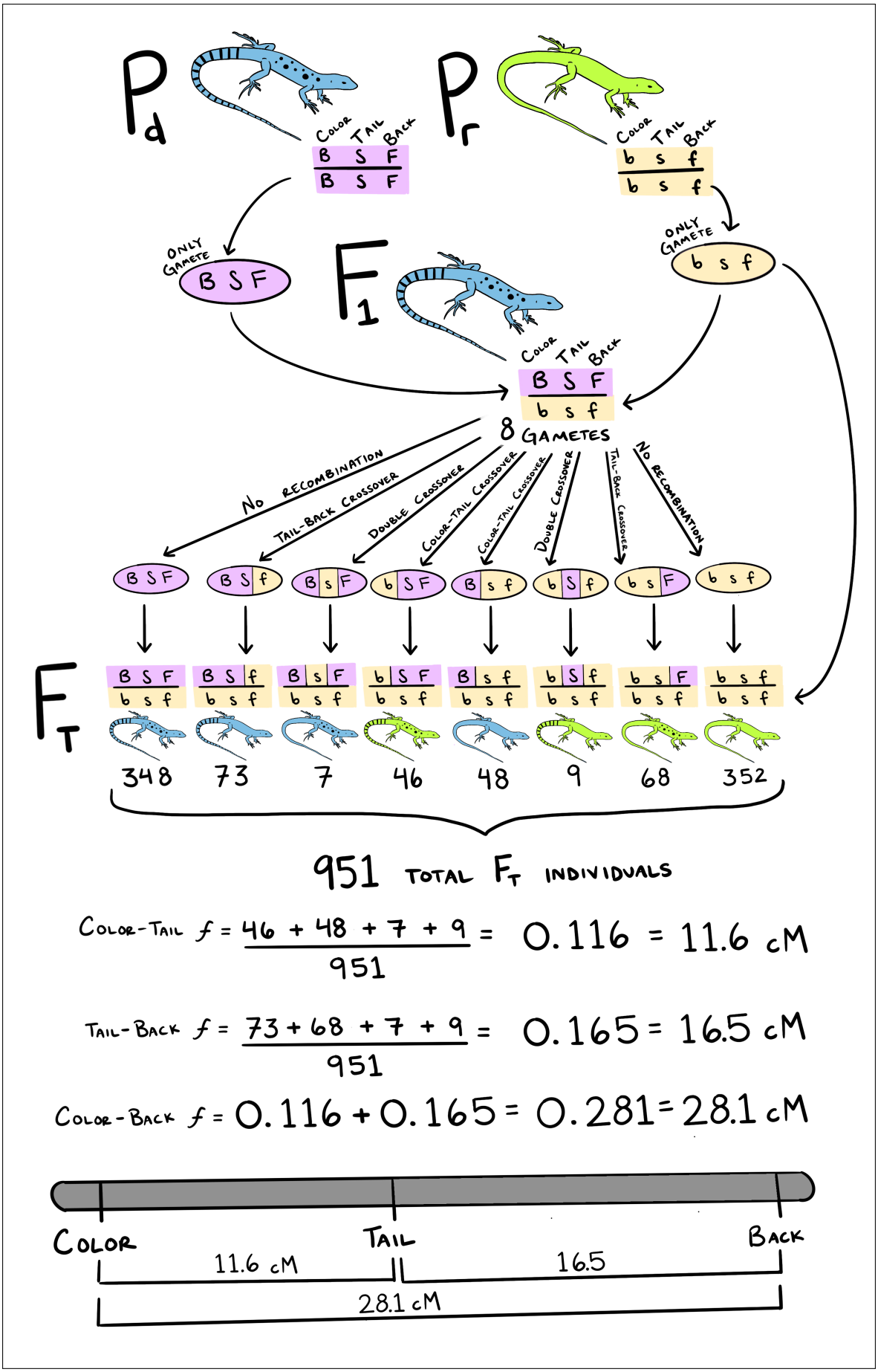

Figure 5: Visual depiction of a three-point test cross with genotypic and phenotypic information for three genes (Color, Tail, and Back). This depiction includes the parental cross (P_d x P_r) and the test cross (F_1 x P_r). The possible gametes and resultant progeny for each cross are depicted.

Practice Problem: You want to know the genetic distance between genes α, β, and γ (see allele information in previous practice problems). In the previous practice problem you determined the gene order to be '$\beta\alpha\gamma$'. The genotypes of the F_T are as follows: 302 'YyXxZz', 298 'yyxxzz', 112 'yyXxZz', 108 'Yyxxzz', 78 'YyXxzz', 82 'yyxxZz', 7 'YyxxZz', 13 'yyXxzz'. Calculate the recombination between each gene.

Solution:

$$f_{\beta-\alpha} = \frac{112+108+7+13}{302+298+112+108+78+82+7+13} = 0.24 = 24cM$$

$$f_{\alpha-\gamma} = \frac{78+82+7+13}{302+298+112+108+78+82+7+13} = 0.18 = 18cM$$

$$f_{\beta-\gamma} = 0.3 + 0.225 = 0.42 = 42cM$$

3.3 Estimating interference

While you may think that crossover events happen independently, it is possible for a crossover event affecting the probability of a second event (in the case of a double crossover). We can calculate the **interference** (I), which is the frequency at which one crossover prevents the occurence of a second crossover. To do this, first the **coefficient of coincidence** (coc) must be calculated. This is the number of double crossovers divided by the number of expected double crossovers:

$$coc = \frac{d}{(f_{1-2})(f_{2-3})(T)} \tag{5}$$

Where d = the number of F_T offspring that are the result of a double crossover and T = the total number of F_T offspring. Interference (I) can then be calculated by taking 1 - coc.

$$I = 1 - coc \tag{6}$$

Practice Problem: Calculate interference for the data from the previous practice problem.

Solution:

$$coc = \frac{7+13}{(0.24)(0.18)(302+298+112+108+78+82+7+13)} = 0.46$$

$$I = 1 - 0.46 = 0.54$$

4 Test crosses: Inferring genotypes using phenotypes

Up to this point only genotypes have been mentioned (not phenotypes) because following genotypes can be more intuitive when talking about linkage vs following phenotypes. However, in a true test cross you only see the phenotypes (you can prove the genotypes using techniques in molecular genetics that we will discuss in the future, but this takes more lab work and equipment). The beauty of a test cross is that you can determine the genotype just by looking at the phenotype!

Practice Problem: Genes S, E, & B are three new genes you discovered on the same chromosome in the silkmoth genome. Gene I encodes the trait 'stripes' ('S' = stripes, 's' = no stripes). Gene II encodes the trait 'eye color' ('E' = black, 'e' = red). Gene III encodes the trait 'body color' ('B' = Dazao [light], 'b' = melanistic [dark]).

You perform a parental cross between two true-breeding strains: One is stripes, black, Dazao and the other is no stripes, red, melanistic. What are the genotypes of these parents? What is the expected phenotype(s) of their offspring (the F_1)? What is the expected genotype of the F_1?

Solution: Because the parents are true-breeding for each trait, we know that they are homozygous. We can determine their genotype by recalling which alleles are dominant (see the question description). The first parent has all of the phenotypes encoded by the dominant allele (we'll call this parent P_d), so their genotype is 'SSEEBB'. The second parent has all of the phenotypes encoded by the recessive alleles (we'll call this parent P_r), so their genotype is 'sseebb'.

The F_1 will all be expected to have the phenotypes of the dominant alleles for each gene, so they will have the same phenotypes as P_d. However, they also inherited the recessive alleles from P_r, so their expected genotype will be 'SsEeBb'.

Practice Problem: Continuing with the previous problem, you want to discover the gene order for genes S, E, and B. What kind of experiment would you set up?

Solution: A three-point test cross would be the best experiment to set up. This would be performed by taking the F_1 and backcrossing them with P_r.

Practice Problem: Continuing with the previous problem, you obtain the following F_T data from your three-point test cross:

stripes, black, Dazao : 402
no stripes, red, melanistic: 398
no stripes, black, Dazao : 16
stripes, red, melanistic: 20
stripes, red, Dazao : 106
no stripes, black, melanistic: 104
stripes, black, melanistic : 148
no stripes, red, Dazao: 152

What are the genotypes for all of these F_T phenotypes?

Solution:

We can find out the genotypes for these offspring by thinking about the characteristics of the test cross: We crossed the F_1 (genotype 'SsEeBb') with the P_R (genotype 'sseebb'). The possible gametes from the F_1 are 'SEB', 'SEb', 'SeB', 'sEB', 'Seb', 'sEb', 'seB', and 'seB'. The only possible gamete from the F_T is 'seb'. The P_r gamete provides an all recessive 'background'- meaning that any phenotype we see in the F_T is representative of the alleles the F_1 gamete provided.

Practice Problem: Using the same F_T data from the previous practice problem, can you infer the parental genotypes (i.e., the genotypes of the individuals in the original parent generation)?

Solution:

Remember- when we refer to parental genotypes we are referring to the parents of the F_1. We know the parental genotypes (because we performed the cross), but we can confirm their genotypes by looking at the numbers. The most frequent phenotypes in the F_T are stripes, black, Dazao (402) and no stripes, red, melanistic (398). **These are the offspring from F_1 gametes that did not experience any recombination**. Therefore, we know that the alleles encoding each of these traits ('S', 'E', and 'B' for the 402; 's', 'e', and 'b' for the 398) make up the genotypes of the alleles from the original parents. The parent that gave 'S', 'E', and 'B' alleles to the 402 F_T individuals must have been of genotype 'SSEEBB' (this was P_d), and the parent that gave 's', 'e', and 'b' alleles to the 398 F_T individuals must have been of genotype 'sseebb' (this was P_r). These genotypes match with what we know to be correct, since we performed the cross!

Practice Problem: Using the same F_T data from the previous practice problem, can you infer the gene order for genes I, II, and III?

Solution:

To identify the gene order, we need to first identify the parental phenotypes (we did this in the previous practice problem). Next, we need to identify the double crossover events. We do this by finding the most infrequent phenotypes in the F_T. These are no stripes, black, Dazao (16) and stripes, red, melanistic (20). When we compare these infrequent phenotypes to the parental phenotypes (stripes, black, Dazao (P_d) and no stripes, red, melanistic (P_r), we see that in the infrequent events the 'stripes' phenotype switched. This means that Gene I (which encodes the 'stripes' trait) is in the middle. The gene order, therefore, is II-I-III.

Practice Problem: Using the same F_T data from the previous practice problem, can you infer the genetic distance between genes I, II, and III?

Solution:

Because Gene I is in the middle, we will start by getting the distance between genes II and I and then distances between genes I and III.

Use equation 1 to calculate genetic distance between two genes. Examples are available in the other equations (2, 3, 4).

$$\text{Distance between Gene II \& Gene I} = \frac{106+104+20+16}{402+398+16+20+106+104+148+152} = 0.183 = 18.3 \text{ cM}$$

$$\text{Distance between Gene III \& Gene I} = \frac{148+152+20+16}{402+398+16+20+106+104+148+152} = 0.250 = 25.0 \text{ cM}$$

Distance between Gene II & Gene III = 0.183 + 0.250 = 0.433 = 43.3 cM

Practice Problem: Using the same F_T data from the previous practice problem, can you estimate the amount of interference occuring? Can you describe what this value means?

Solution:

Because Gene I is in the middle, we will start by getting the distance between genes II and I and then distances between genes I and III.

Use equations 5 and 6 to calculate interference.

$$T = 402 + 398 + 16 + 20 + 106 + 104 + 148 + 152 = 1346$$

$$coc = \frac{16+20}{(0.183)(0.250)(1346)} = 0.585$$

$$I = 1 - 0.585 = 0.415$$

This means that 41.5% of single crossovers inhibit (interfere) with the occurence of a second crossover event.

5 Genetics naming conventions

While up to this point we have used the traditional Mendelian convention of uppercase letters for dominant alleles ('A') and lowercase letters for recessive alleles ('a'), this convention does not consider which of these alleles is the original form. In other words, the convention doesn't indicate whether 'A' or 'a' was the first allele. When Mendel originally described the convention of using upper/lower-case letters there was little/no understanding of mutation.

Thomas Hunt Morgan was interested in mutation, so he exposed colonies of fruit flies to **mutagens** (things that cause mutations) to see if he could create new phenotypes. And he did- the first thing he noticed was a change in eye color. The **wild-type** (typical) eye color in the flies was red. Morgan found a **mutant** (variant) with white eyes. Rather than referring to the alleles as 'R' (red) and 'r' (white), it is common to refer to them as '+' (wild type red) and 'w' (mutant white). You may notice the '+' convention in referring to wild-type alleles. Be careful, not all wild-type alleles are dominant (sometimes the mutant allele is dominant).