Epistasis

Epistasis is when multiple genes interact to influence a single trait (not to be confused with scenarios where different alleles of the same gene influence a trait, such as incomplete dominance or co-dominance). In order for a trait to be the result of epistasis, multiple genes must be involved. Thus traits resulting from epistasis are not **monogenic** (encoded by a single gene), and such traits are Non-Mendelian (because they violate the one gene = one trait rule). In this section we will examine how multiple genes can influence a trait; such traits are **polygenic**.

1 One trait, two genes?

William Bateson ("Mendel's Bulldog) coined the therm "epistasis", which is greek for "standing upon". Bateson hypothesized that the status of one gene could "mask" (i.e., "stand upon") another gene and mask its effect. For example, imagine a population of flowers (Pop I) where petal color is a trait that exhibits complete dominance and is encoded by a single gene (gene 1), with the dominant allele ('P') encoding 'enzyme P' that synthesizes violet coloration and the recessive allele ('p') encoding no enzyme and thus no violet coloration (leaving the petals white). If a monohybrid cross is performed ('Pp' x 'Pp'), you end up with the typical Mendelian ratio of 3 : 1 (violet : white). This ratio provides no evidence of epistasis- and we cannot reject the hypothesis that petal coloration is a Mendelian trait.

Now let's consider a scenario in a different population (Pop II) where variation at another gene (gene 2) affects the phenotype. Gene 2 encodes 'enzyme B'. Pop I also possesses gene 2, but there is no variation at this gene in Pop I (i.e., all of the individuals have the 'BB' genotype). However, in Pop II individuals can be of genotype 'BB', 'Bb', or 'bb'. 'BB' and 'Bb' individuals have 'enzyme B' and 'bb' individuals have no 'enzyme B'. The presence/absence of 'enzyme B' affects the function of 'enzyme P' (from gene 1)- without 'enzyme B', 'enzyme P' cannot synthesize the violet coloration in petals (Figure , left). The 'bb' genotype at gene 2 "masks" the effect of the genotype at gene 1 (it doesn't matter if an individual is of genotype 'PP' or 'Pp' at gene 1- because the 'bb' genotype at gene 2 prevents the violet coloration from being created). Therefore, gene 1 (which encodes 'enzyme P') and gene 2 (which encodes 'enzyme P') interact with each other to create the flower color phenotype. Because flower color is determined by the interaction of multiple genes, this trait is **epistatic**.

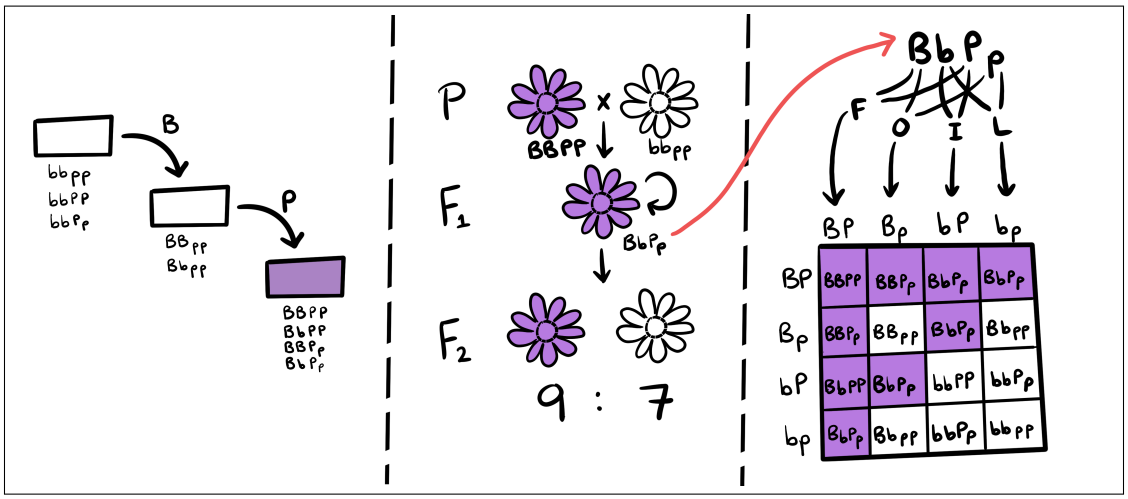

Figure 1: Epistasis example where two genes control petal coloration. **Left-** Pathway that leads to purple phenotype (enzyme B and enzyme P both needed, each of which is controlled by a dominant allele for their respective genes (the 'B' allele for enzyme B and the 'P' allele for enzyme P). **Center-** Phenotypic ratio results from dihybrid cross. **Right-** Genotypic and phenotypic ratios in Punnet square.

A dihybrid cross (two genes, both heterozygous) can identify (1) if a trait is a result of epistasis between the two genes and (2) what kind of epistatic interaction between the genes controls the trait. In the flower scenario described in this section, a dihybrid cross would consist of crossing two individuals with genotype 'PpBb' (Figure , center). In this case, we see a phenotypic ratio of 9 : 7 (violet : white) in the F_2 generation. If the trait was only controlled by one of these genes, we would have seen the Mendelian 3: 1 ratio in the F_2 generation. Epistasis where the interaction of two genes creates a 9 : 7 ratio in the F_2 generation is called "Double Recessive" epistasis. However, this isn't the only type of epistasis between two genes. Figure shows several other outcomes of a dihybrid cross.

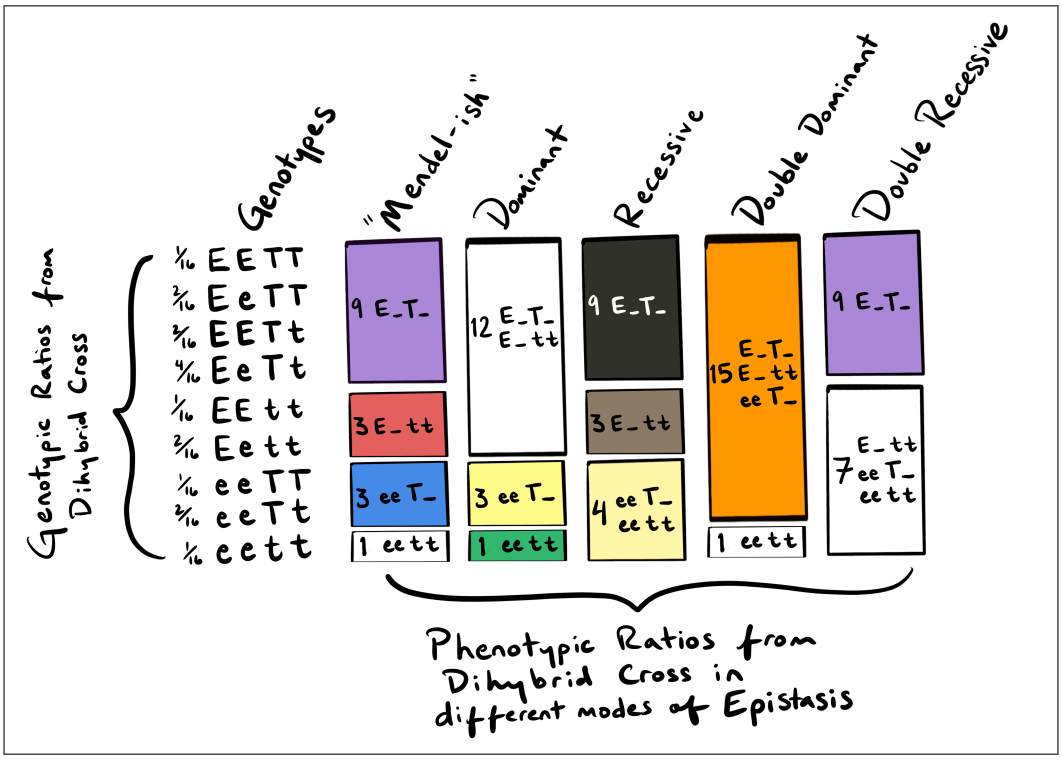

Figure 2: Results of dihybrid cross for five epistatic scenarios. Far left shows genotypes and their frequencies (shown as fractions) from a dihybrid cross. Under each epistatic scenario, the phenotypic ratio is shown (each block is a phenotype). The phenotypic blocks correspond to the genotypes on the far left.

NOTE: While you'll notice that the different modes of epistasis each have names, the way the names connect to the inheritance patterns is not intuitive. Therefore, rather than attempting to understand why a pattern may have a certain name, it is more helpful to simply understand the pathway that leads to the phenotypic ratio. These names are seldom used outside of textbooks, so memorizing them is essentially pointless.

2 Incomplete/Co-dominance or epistasis?

While the previous example of flower petal coloration examined a trait with two phenotypes (violet and white), it is possible for a trait to have more than two phenotypes due to epistasis. For this reason, it is easy to confuse epistasis for incomplete dominance and/or codominance (where more than two phenotypes are observed for a single trait). However, incomplete dominance and co-dominance are inheritance patterns for a trait controlled by a single gene that will show the 1 : 2 : 1 phenotypic ratio for a monohybrid cross (or a dihybrid cross, since only one gene controls

the trait).

As a second example, we will consider Labrador Retriever coat color, which is a trait with three phenotypes (yellow, chocolate [brown], and black) that is controlled by two genes. At Gene 1, enzyme E is encoded by the dominant allele 'E'. Individuals with the homozygous recessive genotype ('ee') don't express enzyme E, and they have a yellow coat color. Individuals that express enzyme E enzyme have chocolate fur color– unless they also have enzyme B. At Gene 2, enzyme B is encoded by the dominant allele 'B' (individuals with the homozygous recessive genotype ('bb') don't express enzyme B). Individuals that express enzyme E *and* enzyme B have black fur color. However, individuals that are homozygous recessive at Gene 1 (genotype 'ee') are yellow regardless of their genotype at Gene 2. See Figure 3 for pathway schematic.

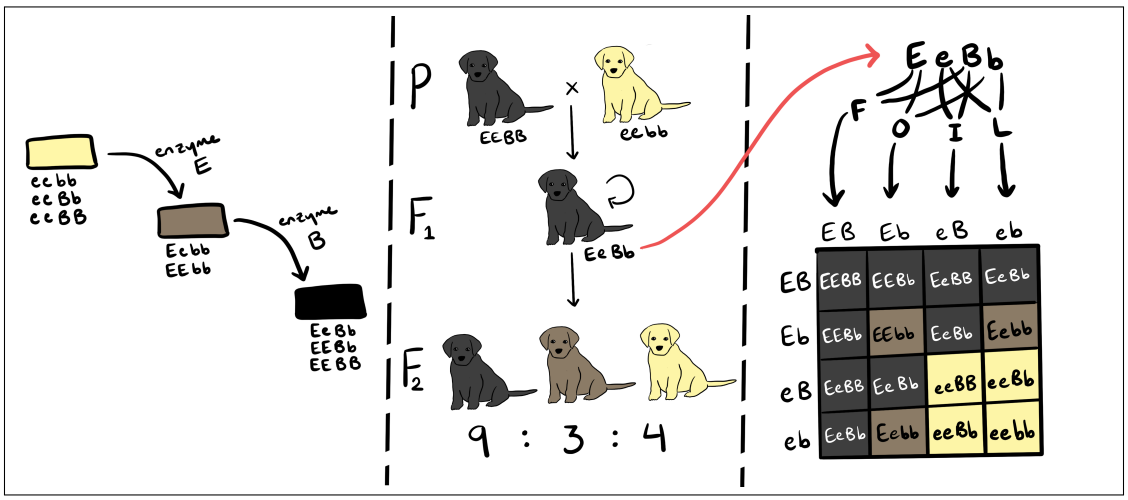

Figure 3: Epistasis example where two genes control Labrodor Retriever coat coloration. **Left-** Pathway that leads to chocolate and black phenotypes. **Center-** Phenotypic ratio results from dihybrid cross. **Right-** Genotypic and phenotypic ratios in Punnet square.

A dihybrid cross for these genes gives a phenotypic ratio of 9 : 3 : 4 (black : chocolate : yellow). Without being aware of the type of epistasis (or the gene pathway), the deviation from the 1 : 2 : 1 ratio that occurs in monogenic traits with three phenotypes suggests epistasis. To best understand the epistatic scenario responsible for this phenotypic ratio, writing out the genotypes associated with phenotypes (e.g., using a Punnet square) can be helpful (Figure 3, right).