Lec. 4

Epistasis

If the two allelic pairs in the dihybrid cross affect the same phenotypic characteristics, there is a chance for interaction of their gene products to give novel phenotypes, and the result may or may not be modified phenotypic ratios, depending on the particular interaction between the products of the non-allelic genes.

Epistasis is a form of gene interaction in which one gene masks the phenotypic expression of another. No new phenotypes are produced by this type of gene interaction. A gene that masks another gene's expression is said to be *epistatic*, and a gene whose expression masked is said to be *hypostatic*.

(Another definition of epistasis: - A double mutant where one mutation masks the phenotype of another mutation).

Epistasis is interaction between different genes (non-allelic), while dominance is the interaction between different allele of the same gene.

Epistasis= inter-allelic interaction= intergenic interaction (more than one locus).

Dominance= Intra-allelic interaction= intragenic interaction (at one locus).

*Note that epistasis is not the same thing as dominance. With epistasis a mutation in one gene masks the expression of a different gene. With dominance, one allele of a gene masks the expression of another allele of the same gene.

A gene or locus which suppressed or masked the action of a gene at another locus was termed *epistatic gene*. The gene or locus suppressed called *hypostatic gene*.

Dominance involves intra-allelic gene interaction, while epistasis involves inter-allelic gene suppression or the masking affecting which one gene locus has upon the expression of another gene locus.

Types of epistasis

1- Dominant epistasis (12:3:1)

With this interaction, color is recessive to no color at one allelic pair. This recessive allele must be expressed before the specific color allele at a second locus is expressed. At the first gene white colored squash is dominant to colored squash, and the gene symbols are W=white and w=colored. At the second gene yellow is dominant to green, and the symbols used are G=yellow, g=green. If the dihybrid is selfed, three phenotypes are produced in a 12:3:1 ratio. The following table explains how this ratio is obtained.

Fruit color of Squash Fruit

Genotype	Fruit Color	Gene Actions
9 W_G_	White	Dominant white allele negates effect of G allele
3 W_gg	White	Dominant white allele negates effect of G allele
3 wwG_	Yellow	Recessive color allele allows yellow allele expression
1 wwgg	Green	Recessive color allele allows green allele expression

Because the presence of the dominant W allele masks the effects of either the G or g allele, this type of interaction is called *dominant epistasis*.

2- Recessive epistasis (9:3:4)

C gene in mouse coat color
There are several loci that affect coat color in mice.
B/b locus B = Black pigment b = brown pigment
C dominant = permits coat color expression (of other gene loci)
c recessive = prevents coat color expression
cc, homozygous recessive lack any coat pigmentation - called albinos - white hair.
Because they have white hair (no pigment) they prevent (preclude) the expression of any other hair color loci
Labrador retrievers coat color
B/b locus B = Black pigment b = brown pigment
E/e locus E = permit deposition e = prevent deposition

Example Cross

Mice:

Interaction between the B locus and C locus in
B=Black color (dominant)
b=brown color (recessive)
(albino) (brown)
BBcc x bbCC P1
BbCc (Black) F1
Cross F1 x F1
F2: ratios modified ratio
B_C_ black 9
bbC_ brown 3
B_cc albino-white
bbcc albino-white 4

Result:

The cc homozygote is said to be epistatic to the other coat colour genes
The albino phenotype prevents one from "seeing" the phenotype from the other loci

Dogs:

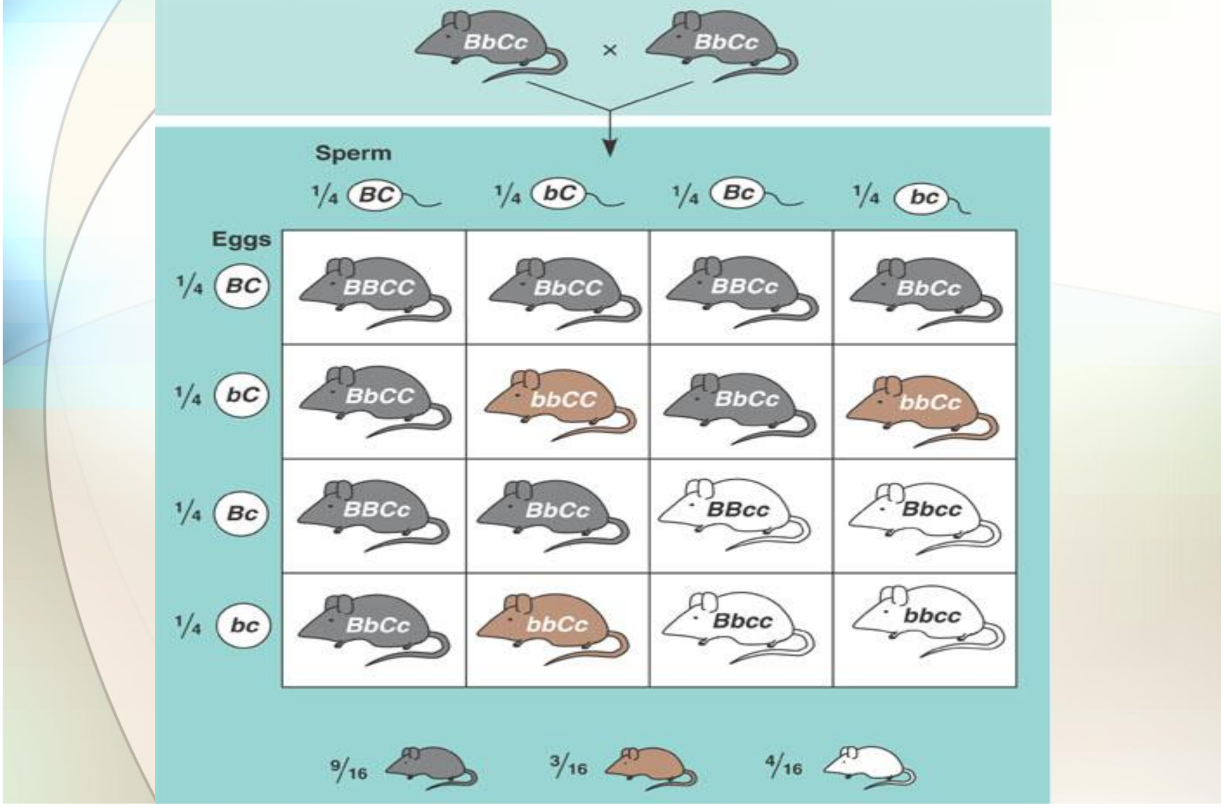
Interaction between the B locus and E locus in
(golden) (brown)
BBee x bbEE P1
BbEe (Black) F1
Cross F1 x F1
F2: ratios modified ratio
B_E_ black 9
bbE_ brown 3
B_ee golden
bbee golden 4

Result:

The ee homozygote is said to be epistatic to the other coat colour genes
The golden phenotype prevents one from "seeing" the phenotype from the other loci
Opposite of epistatic is hypostatic Bb locus is hypostatic to the ee alleles.

Epistasis example

- **Mice (and many other mammals) - coat color depends on two genes**
- **One (epistatic gene), determines whether pigment will be deposited in hair**
  - **Presence (*C*) is dominant to absence (*c*)**
- **Second determines whether pigment deposited is black (*B*) or brown (*b*)**
  - **The black allele is dominant to the brown allele**
- **Individual with *cc* has a white (albino) coat regardless of the genotype of the 2nd gene**



3- Duplicate genes with cumulative effect (9:6:1)

If the dominant condition (either homozygous or heterozygous) at either locus (but not both) produces the same phenotype, the F2 ratio becomes 9:6:1. For example where the epistatic genes are involved in producing various amounts of a substance such as pigment, the dominant genotypes of each locus may be considered to produce one unit of pigment independently. Thus genotypes *A-bb* and *aaB-* produce one unit of pigment each and therefore have the same phenotype. The genotype *aabb* produces no pigment, but in the genotype *A-B-* the effect is cumulative and two units of pigment are produced.

Example (1): Fruit shape in summer squash.

Spherical, elongated and disc shaped.

A- for spherical
B- for spherical
aa for elongated
bb for elongated

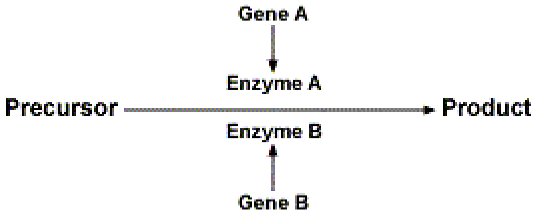
AAbb X aaBB (Spherical)
Ab aB
F_1 AaBb (100% disc shape)
AaBb X AaBb
F_2 9 A-B- disc shape 3 aaB- spherical
3 A-bb spherical 1 aabb elongated

Example (2): Pig color

Sand color RRss X rrSS Sand color
F_1 RrSs Red
F_2 9 R-S- Red 3 rrS- Sand
3 R-ss Sand 1 rrss White

4- Duplicate dominant genes (15:1)

The 9:3:3:1 ratio is modified into a 15:1 ratio if the dominant alleles of both loci each produce the same phenotype without cumulative effect.
Example: Kernel color in wheat



For this type of pathway a functional enzyme A or B can produce a product from a common precursor. The product gives color to the wheat kernel. Therefore, only one dominant allele at either of the two loci is required to generate the product.

Thus, if a pure line wheat plant with a colored kernel (genotype = AABB) is crossed to plant with white kernels (genotype = aabb) and the resulting F1 plants are selfed, a modification of the dihybrid 9:3:3:1 ratio will be produced. The following table provides a biochemical explanation for the 15:1 ratio.

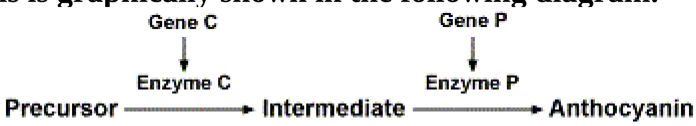
Genotype	Kernel Phenotype	Enzymatic Activities
9 A_B_	colored kernels	functional enzymes from both genes
3 A_bb	colored kernels	functional enzyme from the A gene pair
3 aaB_	colored kernels	functional enzyme from the B gene pair
1 aabb	colorless kernels	non-functional enzymes produced at both genes

If we sum the three different genotypes that will produce a colored kernel we can see that we can achieve a 15:1 ratio. Because either of the genes can provide the wild type phenotype, this interaction is called duplicate gene action.

5- Duplicate recessive genes (9:7)

In the case where identical phenotypes are produced
Example: Flower color in sweet pea

If two genes are involved in a specific pathway and functional products from both are required for expression, then one recessive allelic pair at either allelic pair would result in the mutant phenotype. This is graphically shown in the following diagram.



If a pure line pea plant with colored flowers (genotype = CCPP) is crossed to pure line, homozygous recessive plant with white flowers, the F1 plant will have colored flowers and a CcPp genotype. The normal ratio from selfing dihybrid is 9:3:3:1, but epistatic interactions of the C and P genes will give a modified 9:7 ratio. The following table describes the interactions for each genotype and how the ratio occurs.

Genotype	Flower Color	Enzyme Activities/TH>
9 C_P_	Flowers colored; anthocyanin produced	Functional enzymes from both genes
3 C_pp	Flowers white; no anthocyanin produced	p enzyme non-functional
3 ccP_	Flowers white; no anthocyanin produced	c enzyme non-functional
1 ccpp	Flowers white; no anthocyanin produced	c and p enzymes non-functional

Because both genes are required for the correct phenotype, this epistatic interaction is called complementary gene action.

6- Dominant and recessive interaction (13:3)

Example: Malvidin production in Primula

Certain genes have the ability to suppress the expression of a gene at a second locus. The production of the chemical malvidin in the plant Primula is an example. Both the synthesis of the chemical (controlled by the K gene) and the suppression of synthesis at the K gene (controlled by the D gene) are dominant traits. The F1 plant with the genotype KkDd will not produce malvidin because of the presence of the dominant D allele. What will be the distribution of the F2 phenotypes after the F1 was crossed?

Genotype	Phenotype and genetic explanation
9 K_D_	no malvidin because dominant D allele is present
3 K_dd	malvidin productions because dominant K allele present
3 kkD_	no malvidin because recessive k and dominant D alleles present
1 kkdd	no malvidin because recessive k allele present

The ratio from the above table is 13 no malvidin production to 3 malvidin production. Because the action of the dominant D allele masks the genes at the K locus, this interaction is termed dominant suppression epistasis.

Gene Interactions (non-epistatic interaction):

The genes of an individual do not operate isolated from one another, but obviously are functioning in a common cellular environment. Thus, it is expected interactions between genes would occur.

Bateson and Punnett performed a classical experiment that demonstrated genetic interactions. They analyzed the three comb types of chicken known to exist at that time:

Chicken Varieties	Phenotype
Wyandotte	Rose Comb
Brahmas	Pea Comb
Leghorns	Single Comb

Rose Pea Single Walnut

Parental Cross — Rose Comb (Wyandotte) x Pea Comb (Brahama)
(Both parents were pure lines.)

↓

F1 Result — All Walnut Combs
(This is a new phenotype not previously seen.)

↓

F2 Result — 9 Walnut : 3 Rose : 3 Pea : 1 Single

Result: The F1 differed from both parents and two new phenotypes not seen in the parents appeared in the F2. How can this result be explained? The first clue is the F2 ratio. We have seen this ratio before when the F1 from a dihybrid cross is selfed (or intermated). This observation suggests that two genes may control the phenotype of the comb. The gene interactions and genotypes were determined by performing the appropriate testcrosses.

A series of experiments demonstrated that the genotypes controlling the various comb phenotypes are as follows.

Phenotypes	Genotypes	Frequency
Walnut	R_P_	9/16
Rose	R_pp	3/16
Pea	rrP_	3/16
Single	rrpp	1/16

It was later shown that the genotypes of the initial parents were:
Rose = RRpp
Pea = rrPP
Therefore, genotypically the cross was:

Parental Cross RRpp x rrPP

F1 Genotypes RrPP

F2 Genotypes See above table

The development of any individual is obviously the expression of all the genes that are a part of its genetic makeup. Therefore, it is not an unexpected conclusion that more than one gene could be responsible for the expression of a single phenotype.

Summary of Epistatic Ratios

Genotypes	*A-B-*	*A-bb*	*aaB-*	*aabb*	Ratio
Classical ratio	9	3	3	1	9:3:3:1
Dominant epistasis	12		3	1	12:3:1
Recessive epistasis	9	3	4		9:3:4
Duplicate genes with cumulative effect	9	6		1	9:6:1
Duplicate dominant genes	15			1	15:1
Duplicate recessive genes	9	7			9:7
Dominant and recessive interaction	13		3		13:3

Questions:

Q1/ A wheat variety with colored seeds is crossed to a colorless strain producing an all F1. In the F2, 1/64 of the progeny has colorless seeds.

(a) How many pairs of genes control seed color?

(b) What were the genotypes of the parents and the F1 (use your own symbols)?

Answer:

(a) 3 (b) P: AABBCC X aabbcc ; AaBbCc

Q2/ Listed below are 7 two-factor interaction ratios observed in progeny from various dihybrid parents. Suppose that in each case one of the dihybrid parents is testcrossed (instead of being mated to another dihybrid individual). What phenotypic ratio is expected in the progeny of each testcross? (a) 9:6:1 (b) 9:3:4 (c) 9:7 (d) 15:1 (e) 12:3:1 (f) 9:3:3:1 (g) 13:3.

Answer:

(a) 1:2:1 (b) 1:1:2 (c) 1:3 (d) 3:1 (e) 2:1:1 (f) 1:1:1:1 (g) 3:1.

Q3/ Two white flowered strains of the sweet pea were crossed, producing an F1 with only purple flowers. Random crossing among the F1 produced 96 progeny plants, 53 exhibiting purple flowers and 43 with white flowers. (a) What phenotypic ratio is approximated by the F2? (b) What type of interaction is involved? (c) What were the probable genotypes of parental strains?