Chapter 4

- Extensions to Mendelian Genetics
- Gene Interactions
Gene Interactions – Extensions to Mendelian Genetics

• Just as different alleles of 1 gene can interact in complex ways,

• 2 different genes can also act together to modify a phenotype:

  • 2 genes 1 phenotype (Additive Gene Action)
  
  Complementation (complementary gene action)

  Epistasis (recessive and dominant)

  Redundancy
Multifactorial Inheritance

- Vast majority of traits are determined by multiple factors:
  - genetic as well as environmental.

- Gene interactions between two or more genes
  - Example: Lentil Seed color.

- F1 all same, F2: 4 different phenotypes

- F2 phenotypic ratio is 9:3:3:1
  - (same as F2 dihybrids in Mendel’s original crosses).

- Difference:
  - in original crosses: 2 independent traits/phenotypes=2 independent genes;
    - Seed color and seed shape
  - here: multiple phenotypes of 1 trait=2 independent genes
    - Seed color only.
You can tell this genotype is caused by more than one gene:

• because there are 4 phenotypes not 3 in F2

• 1 gene F2 would have 3 phenotypes 1:2:1 ratio

(Additive Gene Action)
F2 phenotypes

• **Dominance Relationships:**
  – Tan is dominant to green
  – Gray is dominant to green
  – Brown is dominant to gray, green and tan.
  – Tan and Gray are incompletely dominant, giving rise to brown.

• **Genotypic classes:**
  – Brown: A_B_
  – Tan: A_bb
  – Gray: aaB_
  – Green: aabb
Complementary Gene Action

• Each genotypic class may not always dictate a unique phenotype

• A pair of genes can often work together to create a specific phenotype. We call this complementary interaction.

• With this type of interaction we see 2 different phenotypes instead of the 4 seen in 2 genes 1 phenotype

• Two or more genotypic classes may display an identical phenotype.
  – Example: Two lines of pure breeding white flowered pea plants falling into different genotypic classes: AAbb & aaBB

The must have a dominant allele in both genes to result in the purple flower phenotype
Complementary gene action

P
\[ AAbb \times aaBB \]
Gametes
\[ Ab \times aB \]

\[ F_1 \text{ (all identical)} \] ♀ AaBb

\[ F_2 \]

\[ \begin{array}{cccc}
AB & Ab & aB & ab \\
\hline
AB & AABB & AABb & AaBB & AaBb \\
Ab & AABb & AAbb & AaBb & aAbb \\
aB & AaBB & AaBb & aaBB & aAbb \\
ab & AaBb & Aabb & aaBb & aabb \\
\end{array} \]

<table>
<thead>
<tr>
<th>9</th>
<th>A_B_ (purple)</th>
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</table>

<table>
<thead>
<tr>
<th>7</th>
<th>3A_bb (white)</th>
</tr>
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<tbody>
<tr>
<td>3aaB_</td>
<td></td>
</tr>
<tr>
<td>1aabb</td>
<td></td>
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Colorless precursor 1

Pigment change catalyzed

Colorless precursor 2

Pigment change completed

Purple pigment
Genetic heterogeneity

(a) Genetic mechanism of complementation

P: AAbb × aaBB → F₁: AaBb

(b) Genetic mechanism of noncomplementation

P: AAbb × AAbb → F₁: AAbb
Epistasis

• One gene’s allele masks the phenotype of the other gene’s alleles.
• Four genotypic classes produce fewer than four phenotypes.
• Different types of epistasis:
  • **Recessive epistasis**: when the recessive allele of one gene masks the effects of either allele of the second gene.
  • **Dominant epistasis**: when the dominant allele of one gene masks the effects of either allele of the second gene.
Recessive Epistasis

• **Example 1**: Coat color of Labrador retriever

• **Example 2**: ABO blood groups: Bombay phenotype.

• Phenotypic ratios are 9:3:4 in F2.
Coat-Color Inheritance in Labrador Retrievers

P  golden  X  black  F1  black
Recessive Epistasis:
a recessive mutation in one gene masks the phenotypic effects of another

F1 X F2
9 : 3 : 4
Appears like incomplete dominance because some of the progeny look like neither parent, but the ratio is wrong.
### Dihybrid Cross:

**F2**

<table>
<thead>
<tr>
<th></th>
<th>BE</th>
<th>Be</th>
<th>bE</th>
<th>be</th>
</tr>
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<tbody>
<tr>
<td>BE</td>
<td>BBEE</td>
<td>BBEe</td>
<td>BbEE</td>
<td>BbEe</td>
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<tr>
<td>Be</td>
<td>BBEe</td>
<td>BBee</td>
<td>BbEe</td>
<td>Bbee</td>
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<tr>
<td>bE</td>
<td>BbEE</td>
<td>BbEe</td>
<td>bbEE</td>
<td>bbEe</td>
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<tr>
<td>be</td>
<td>BbEe</td>
<td>Bbee</td>
<td>bbEe</td>
<td>bbee</td>
</tr>
</tbody>
</table>

9 black: 3 brown: 4 golden

(9 B-E-: 3 bbE-: 3 B-ee: 1 bbee)
Molecular Explanation

Pigment production (B) and subsequent incorporation (E) into the hair shaft are controlled by two separate genes. To be black, both genes must function. Mutations in B (b) lead to brown pigment. Mutations in E (e) lead to no pigment in coat.
Recessive Epistasis

- Two genes involved in coat color determination.
- Gene B determines whether black (B) or brown (bb) pigment is produced.
- Gene E determines if pigment is deposited in hair
  - golden retrievers (ee) make either black (B-) or brown (bb) pigment (look at noses)… but not in fur
- The recessive allele is epistatic to (stands over) other genes when homozygous -- hence the name “recessive epistasis”
- Phenotypes do not segregate according to Mendelian ratios (the phenotypic ratios are modified Mendelian ratios).
- epistasis - (Greek, to stand upon or stop) the differential phenotypic expression of a genotype at one locus caused by the genotype at another, non allelic, locus. A mutation that exerts its expression by canceling the expression of the alleles of another gene.
Dominant Epistasis

• caused by the dominant allele of one gene, masking the action of either allele of the other gene.

• Ratio is 12:3:1 instead of 9:3:3:1

• Example: Summer Squash
Dominant epistasis
Petal color in snapdragons - if Mendel had used snap dragons for his experiments, he wouldn’t be famous!

\[ \begin{align*}
\text{P} &: AABB \\
\times &: aabb \\
\text{F1} &: A-B- \\
\downarrow & \\
\text{F2} &: 15/16 \text{ red; } 1/16 \text{ white}
\end{align*} \]
Whenever a dominant gene is present, the trait is expressed. One allele is sufficient to produce the pigment.
Hints for figuring out gene interactions:

**Look at the F2 phenotypic ratios!!**

- If one gene is involved in the trait, then the monohybrid phenotypic ratio is:
  
  3:1 or 1:2:1 or 2:1

- If two genes are involved in the trait, then the dihybrid phenotypic ratio is:
  
  9:3:3:1 or some permutation (9:4:3 or 9:7 or 12:3:1)

  → The 1/16 class is always the double homozygous recessive.

  → Look for internal 3:1 ratios, which will indicate dominance/recessive relationships for alleles within a gene.
Hints for figuring out gene interactions:

• **2 Genes 1 Phenotype (Additive Gene Action):** You can tell this genotype is caused by more than one gene because there are 4 phenotypes not 3 in F2 (9:3:3:1)
  – 1 gene F2 would have 3 phenotypes 1:2:1 ratio

• **Complementary Gene Action:** one good copy of each gene is needed for expression of the final phenotype
  – 9:7 ratio

• **Epistasis:** one gene can mask the effect of another gene
  – 9:3:4 ratio for recessive epistasis
  – 12:3:1 ratio for dominant epistasis

• **Duplicate genes:** only double mutant has mutant phenotype
  – 15:1 ratio
variations on Mendelian inheritance

<table>
<thead>
<tr>
<th>Gene interaction</th>
<th>Inheritance pattern</th>
<th>A-/B-</th>
<th>A-/bb</th>
<th>aa/B-</th>
<th>aabb</th>
<th>ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additive</td>
<td>Each genotype results in a unique phenotype</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>9:3:3:1</td>
</tr>
<tr>
<td>Complementary</td>
<td>At least one dominant allele from each of two genes needed for phenotype</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>9:7</td>
</tr>
<tr>
<td>Recessive Epistasis</td>
<td>Homozyous recessive genotype at one locus masks expression at second locus</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>9:3:4</td>
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<td>Dominant Epistasis</td>
<td>Dominant allele at one locus masks expression at second locus</td>
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<td>3</td>
<td>1</td>
<td>12:3:1</td>
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<td>Duplicate Genes</td>
<td>One dominant allele from either of two genes needed for phenotype</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>15:1</td>
</tr>
</tbody>
</table>
Sample Problem

true breeding brown dogs $X$ true breeding white dogs

F1 = all white

F2 = 118 white   12
    32 black   3
    10 brown   1

➢ Find the genotypes of the dogs in each class:
What is the ratio?

How many genes?   2

What is the ratio of white to colored dogs? $12:4 = 3:1$

This means that white is dominant to colored so let’s call one gene: $W$ = white  $w$ = colored
What is the ratio of black to brown dogs? \[3:1\]

So black must be dominant to brown. So we will call the second gene: \(B=\text{black}\) and \(b=\text{brown}\)

What class of dogs are the double recessive homozygotes and what is their genotype?

Brown - \(w\bar{w}bb\)

What is the genotype of the black dogs?

Must be \(w\bar{w}B-\)

What are the genotypes of the white dogs?

\(W_\_B_\_\) and \(W_bb\)

- This is an example of dominant epistasis (white).
Same Genotype may produce different Phenotypes

- **Penetrance**: Genotype does not necessarily define phenotype. The proportion of individuals with a given genotype express the phenotype determines penetrance.

- 100% penetrance = all individuals show phenotype.

- 50% penetrance = half the individuals show phenotype.
  - Example: retinoblastoma: only 75% individuals affected.

- **Expressivity**: the degree or intensity with which a particular genotype is expressed in a phenotype in a given individual.

  - Retinoblastoma: some have both eyes affected, some only one.
Modifier Effects

• **Modifier Genes**: they have a subtle, secondary effect which alters the phenotypes produced by the primary genes.

  – E.G. Tail length in mice. The mutant allele $t$ causes a shortening of the tail. Not all short tails are of the same length: another gene affects the actual length. (Variable expressivity).

• **Modifying environment**: The environment may influence the effect of a genotype on the phenotype.

  – E.G.: Siamese cats: temperature dependent color of coat. Color shows up only in extremities, where the temp is lower (enzyme for pigment formation is active only at lower temp.)
Modifying environment:
The environmental influence of a genotype on the phenotype = phenocopy
Modifying environment:
The environmental influence of a genotype on the phenotype = phenocopy
Homework Problems

– Chapter 4

– # 15, 16, 19, 26

DON’T forget to take the online QUIZ!!