Genetic Interactions and Linkage

Lecture 3
Applied Animal and Plant Breeding
GENE 251/351

School of Environment and Rural Science (Genetics)
Topics

– Relating Genotype to Phenotype

– Mendelian genetics and the single locus model
– Interactions between alleles at one locus
– Interactions between alleles at different loci
– Sex specific traits

– Linkage
– Comparative mapping of genes

– Polyploidy
Remember

Parents pass on only 1 allele of a pair
Parents transmit 50% of their genes
Progeny receive 2 alleles (chromosome sets)
  one from each parent

Recombination occurs in the gametes to give rise to new combinations of alleles

Chromosome number is halved in the gametes
Gene interactions

Interactions between alleles at one locus

- Dominant/recessive
- Co-dominant
- Incomplete dominance

Interaction between alleles at different genes (loci) can result in Epistasis

- Can have varying effects on the phenotype
Examples of inheritance model

• dominance/recessive model
  • polledness in cattle, 2 alleles: P and p
    PP = polled
    Pp = polled
    pp = horned

• co-dominant
  • (ABO blood groups)
  • phenotypes are: A, AB and B (and O)

• sex linked
  – females
    CC
    Cc
    cc
  – males
    C-
    c-

example: sex linked genetic defects
Additional Examples of Co-dominant traits

Colour in Carnations

White carnations crossed with red carnations results in pink carnations

Feather colour in birds

White feathered chickens crossed with black feathered chickens gives chickens with black and white feathers
Dominant and Recessive Alleles

- For example: Two heterozygous dogs with black coats are crossed. What would their pups look like? (Alternative is brown coat)

<table>
<thead>
<tr>
<th>Parents</th>
<th>Phenotype</th>
<th>Black</th>
<th>x</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Genotype</td>
<td>Bb</td>
<td></td>
<td>Bb</td>
</tr>
<tr>
<td></td>
<td>Gametes</td>
<td>½ B,</td>
<td></td>
<td>½ B,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>½ b</td>
<td></td>
<td>½ b</td>
</tr>
</tbody>
</table>
### Offspring

<table>
<thead>
<tr>
<th>Female gametes</th>
<th>Male Gametes</th>
<th>Phenotype Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>BB</td>
<td>¾ Black dogs : ¼ Brown dogs or 3 Black dogs : 1 Brown dog</td>
</tr>
<tr>
<td>B</td>
<td>Bb</td>
<td>Black</td>
</tr>
<tr>
<td>b</td>
<td>Bb</td>
<td>Black</td>
</tr>
<tr>
<td>b</td>
<td>bb</td>
<td>Brown</td>
</tr>
</tbody>
</table>

**Punnett Square**

- **Genotype summary**
  - $\frac{1}{4}$ BB : $\frac{1}{2}$ Bb : $\frac{1}{4}$ bb

- **Phenotype summary**
  - $\frac{3}{4}$ Black dogs : $\frac{1}{4}$ Brown dogs

**Evidence of learning:**

- Use of Punnett Square to illustrate genetic inheritance.
Sex determination

- In mammals
  - Females are the homogametic sex, i.e. XX
  - Males are the heterogametic sex, i.e. XY

- In birds,
  - Females are the heterogametic sex, ZW
  - Males are the homogametic sex, ZZ.
How would we discover the model of inheritance?

- Red Bull x Black Cow $\rightarrow$ ?
- Red Bull x Red Cow $\rightarrow$ ?
- Black Bull x Black Cow $\rightarrow$ ?

What to expect when

1. black is dominant
2. red is dominant
Autosomal vs Sex Linked

• Genes located on the sex chromosomes are said to be sex-linked, usually X-linked and they display a different inheritance pattern to autosomal genes.

• In humans most of these genes are on the X chromosome.

• Only 27 genes so far have been identified on the Human Y chromosome.
### X-linked inheritance, e.g. deleterious recessive mutations

Cross between heterozygous female for X-linked trait and a particular male

**e.g. Recessive genetic defect:** $HH = $ healthy, $Hh = $ healthy, $hh = $ sick, $H^- = $ healthy, $h^- = $ sick

<table>
<thead>
<tr>
<th>Normal male</th>
<th>Carrier Female</th>
<th>Male Gametes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$\frac{1}{2} X^H$</td>
</tr>
<tr>
<td>Female Gametes</td>
<td>$\frac{1}{2} X^H$</td>
<td>$\frac{1}{4} X^H X^H$</td>
</tr>
<tr>
<td></td>
<td>$\frac{1}{2} X^h$</td>
<td>$X^H X^h$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Female offspring</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>All normal</strong></td>
</tr>
</tbody>
</table>
Sex-limited genes

• The sex of an organism can influence the expression of autosomal genes via hormonal feedback systems. These are called *sex-limited* genes.

• Examples:
  – milk production genes, genes for reproductive traits

• Individuals of both sexes carry copies of all of these genes even if they are not expressed in a particular sex!
Sex-influenced genes

- The dominance relationship of alleles for these autosomal genes change depending on the sex of the individual.

- Example:
  - horned Dorset sheep crossed with hornless Suffolk
    Dorset $h^+h^+$ x Suffolk $hh$
    Females $h^+h = $ hornless
    Males $h^+h = $ horned
Epistasis - interactions between different loci

• Alleles for one gene can influence the expression of alleles for another gene

• Complex biochemical pathways determine production of various chemicals / phenotypes eg hair or coat colour

• For every step at least one gene product is needed

• Epistasis results when genes are involved in the same biochemical pathway
Numerous biochemical pathways for epistasis to be present
Summary of Epistatic ratios

When epistasis is operative between two gene loci, the number of phenotypes appearing in the offspring from dihybrid parents will be less than four. Reference only

<table>
<thead>
<tr>
<th>Genotypes</th>
<th>A-/B-</th>
<th>A-/bb</th>
<th>aa/B-</th>
<th>aa/bb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical Ratio</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Dominant epistasis</td>
<td>12</td>
<td></td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Recessive epistasis</td>
<td>9</td>
<td>3</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Duplicate genes with cumulative effect</td>
<td>9</td>
<td></td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Duplicate dominant genes</td>
<td></td>
<td>15</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Duplicate Recessive genes</td>
<td>9</td>
<td></td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Dominant and Recessive interaction</td>
<td></td>
<td>13</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>
Epistasis example

In European Simmentals coat colour is either deep red or yellow, both with white face and markings.

\[ \text{Red} = E^r E^r DD; \quad \text{Yellow} = E^r E^r Dd \quad \text{or} \quad E^r E^r dd \]

Here D – the dilution allele shows epistasis and dilutes the expression of the red allele even though the individuals are all homozygous for that allele.
The alternative to the red phenotype is black – $E^{D}$-

$D$ is a diluter gene where

$DD=$ dark, $Dd=$ medium colour, and $dd=$ pale colour

Red and black calves

Diluted red = yellow

diluted black = ‘mouse’
Linkage, Recombination and Mapping

Parent animal

\[
\begin{array}{c}
A \\
a
\end{array}
\begin{array}{c}
B \\
b
\end{array}
\]

Non-recombinant gametes
Frequency: \((1 - r)\)

- AB
- ab

Recombinant gametes
Frequency: \(r\)

- Ab
- aB
**Classical Mapping: Using a test cross**

Parent 1 \( \text{AABB} \) × Parent 2 \( \text{aabb} \)

<table>
<thead>
<tr>
<th>Parent 1 AABB</th>
<th>Parent 2 aabb</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>F1</strong></td>
<td>AaBb (100%)</td>
</tr>
</tbody>
</table>

**F1-gametes**:  

<table>
<thead>
<tr>
<th></th>
<th>AB</th>
<th>Ab</th>
<th>aB</th>
<th>ab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>frequencies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A and B are unlinked:</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>A and B linked:</td>
<td>35</td>
<td>15</td>
<td>15</td>
<td>35</td>
</tr>
<tr>
<td>A and B tightly linked</td>
<td>48</td>
<td>2</td>
<td>2</td>
<td>48</td>
</tr>
</tbody>
</table>
Classical Mapping: Using a test cross

<table>
<thead>
<tr>
<th>Parent 1</th>
<th>AABB</th>
<th>x</th>
<th>aabb</th>
<th>Parent 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>AaBb (100%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>F1-gametes</th>
<th>AB</th>
<th>Ab</th>
<th>aB</th>
<th>ab</th>
</tr>
</thead>
<tbody>
<tr>
<td>frequencies</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>A and B are unlinked:</td>
<td>35</td>
<td>15</td>
<td>15</td>
<td>35</td>
</tr>
<tr>
<td>A and B linked:</td>
<td>48</td>
<td>2</td>
<td>2</td>
<td>48</td>
</tr>
<tr>
<td>A and B tightly linked</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Recombinants

Recombination Frequency
Genetic linkage maps

- Genetic distances determined according to recombination fraction between each pair of loci

- The unit of measure is Morgans (or centimorgans, cM)

Length of chromosomes vary from 50 - 350 cM
Sheep map–microsatellite markers

Distribution and informativeness of markers on SheepMap v4.4 (sex averaged)

Marker informativeness is indicated by the colour (red > orange > green > blue > purple > grey) and the length of the vertical line.
Bovine

A culturally important animal for beef and milk production.

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Perissodactyla; Bovinae; Bos; Bos taurus

Photo: courtesy of Terri Hobbs (www.crazyforcows.com)
Synteny of Human chromosome 17

Indian
Human  Pig  Cattle muntjac  Horse  Cat  Mouse

Synteny of entire chromosomes conserved
Synteny of Human chromosome 2.

Synteny of large chromosome segments conserved.
Synteny of Human chromosome 3 and 21

Segments of chromosomes combine to produce new synteny.
**Polyploidy**

- Majority of animals are diploid = 2n

- A lot of plants (and a small number of animals) can tolerate having multiple copies of the chromosome set therefore are = 3n, 4n, 6n
Polyploidy

• This can either occur due to pollination by a closely related species and subsequent doubling of the chromosomes because the mitotic spindles don’t form properly.

• The cell’s own mitotic spindle formation fails and you get doubling of the chromosome set.

• Most species survive because they can reproduce vegetatively.
**Polyploidy**

- If chromosome sets are doubled it means pairing can happen properly at meiosis and so these can reproduce sexually. These are tetraploids (at least).

Examples:
  - roses, chrysanthemums, tulips, coffee, bananas, cotton, wheat.

---

Octoploid  
![Octoploid Image]

Tetraploid  
![Tetraploid Image]

Triploid  
![Triploid Image]
Polyploidy

• Individuals with multiple copies of the same genome set are AUTOPOLYPLOIDS

• and those with genome sets from different species are ALLOPOLYPLOIDS.
Wheat – a hexaploid

- Wheat, *Triticum aestivum*, is hexaploid (6n) and is called an allopolyploid

**AA** \(x\) **BB**

\(n=7\) \(n=7\)

T. urartu \(x\) A. searsii

**AB**

\(n=14\)

Emmer wheat

\[\text{1 Two diploid species cross to produce a hybrid with two different sets of chromosomes in its genome.}\]

\[\text{2 The chromosomes in the hybrid double to form a tetraploid.}\]

\[\text{3 The tetraploid hybrid crosses with another diploid species to produce a plant with three sets of chromosomes in its genome.}\]
Wheat – a hexaploid

4 The chromosomes in the triple hybrid double to form a hexaploid.

5 Modern bread wheat is a hexaploid – a hybrid of three different species.