Genetics &
The Work of Mendel
Problem: Is inheritance blending or particulate?

Blending gives rise to uniform populations but Evolution needs variation.
Gregor Mendel

- Modern genetics began in the mid-1800s in an abbey garden, where a monk named Gregor Mendel documented inheritance in peas
  - used experimental method
  - used quantitative analysis
    - collected data & counted them
  - excellent example of scientific method
Mendel chose peas wisely

- Pea plants are good for genetic research
  - available in many varieties with distinct heritable features with different variations
    - flower color, seed color, seed shape, etc.
  - Mendel had strict control over which plants mated with which
    - each pea plant has male & female structures
    - pea plants can self-fertilize
    - Mendel could also cross-pollinate plants: moving pollen from one plant to another
Mendel chose peas luckily

- Pea plants are good for genetic research
  - relatively simple genetically
    - most characters are controlled by a single gene with each gene having only 2 alleles,
      - one completely dominant over the other
True breeding PP

Hybridization – crossing two pure breeding PP x pp
Mendel’s work

- Bred pea plants
  - cross-pollinate true breeding parents (P)
    - P = parental
  - raised seed & then observed traits (F₁)
    - F = filial
  - allowed offspring to self-pollinate & observed next generation (F₂)

Pollen transferred from white flower to stigma of purple flower

P

F₁

F₂

P = parental

F = filial

F₁

F₂

all purple flowers result

self-pollinate
Mendel collected data for 7 pea traits

<table>
<thead>
<tr>
<th>Character</th>
<th>Dominant Form</th>
<th>×</th>
<th>Recessive Form</th>
<th>F₂ Generation</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purple flowers</td>
<td>×</td>
<td></td>
<td>White flowers</td>
<td>705:224</td>
<td>3.15:1</td>
</tr>
<tr>
<td>Yellow seeds</td>
<td>×</td>
<td></td>
<td>Green seeds</td>
<td>6022:2001</td>
<td>3.01:1</td>
</tr>
<tr>
<td>Round seeds</td>
<td>×</td>
<td></td>
<td>Wrinkled seeds</td>
<td>5474:1850</td>
<td>2.96:1</td>
</tr>
<tr>
<td>Green pods</td>
<td>×</td>
<td></td>
<td>Yellow pods</td>
<td>428:152</td>
<td>2.82:1</td>
</tr>
<tr>
<td>Inflated pods</td>
<td>×</td>
<td></td>
<td>Constricted pods</td>
<td>882:299</td>
<td>2.95:1</td>
</tr>
<tr>
<td>Axial flowers</td>
<td>×</td>
<td></td>
<td>Terminal flowers</td>
<td>651:207</td>
<td>3.14:1</td>
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<tr>
<td>Tall plants</td>
<td>×</td>
<td></td>
<td>Dwarf plants</td>
<td>787:277</td>
<td>2.84:1</td>
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</tbody>
</table>
Mendel’s 1\textsuperscript{st} law of heredity

- Law of \textbf{segregation}
  - during \textit{meiosis}, \textit{alleles segregate}
    - homologous chromosomes separate
  - each allele for a trait is packaged into a separate gamete
Law of Segregation

- Which stage of meiosis creates the law of segregation?

Whoa! And Mendel didn’t even know DNA or genes existed!
Looking closer at Mendel’s work

P

true-breeding purple-flower peas

X

ture-breeding white-flower peas

F_1

generation (hybrids)

100%
purple-flower peas

F_2

generation

75%
purple-flower peas

25%
white-flower peas

100%

3:1

self-pollinate
Traits are inherited as discrete units

- For each characteristic, an organism inherits 2 alleles, 1 from each parent.

  - **diploid** organism
    - inherits 2 sets of chromosomes, 1 from each parent
    - homologous chromosomes
    - like having 2 editions of encyclopedia
      - Encyclopedia Britannica
      - Encyclopedia Americana

What are the advantages of being diploid?
What did Mendel’s findings mean?

- **Traits come in alternative versions**
  - purple vs. white flower color
  - **alleles**
    - different alleles vary in the sequence of **nucleotides** at the specific **locus** of a gene
      - some difference in sequence of A, T, C, G

**purple-flower allele** & **white-flower allele** are two DNA variations at **flower-color locus**

different versions of gene at same location on homologous chromosomes
What did Mendel’s findings mean?

- Some traits mask others
  - purple & white flower colors are separate traits that do not blend
    - purple x white ≠ light purple
    - purple masked white
  - dominant allele
    - functional protein
      - affects characteristic
    - masks other alleles
  - recessive allele
    - no noticeable effect
    - allele makes a malfunctioning protein

I'll speak for both of us!
Genotype vs. phenotype

- Difference between how an organism “looks” & its genetics
  - **phenotype**
    - description of an organism’s trait
  - **genotype**
    - description of an organism’s genetic makeup

Explain Mendel’s results using...
...**dominant** & **recessive**
...**phenotype** & **genotype**
Making crosses

- Can represent alleles as letters
  - flower color alleles → P or p
  - true-breeding purple-flower peas → PP
  - true-breeding white-flower peas → pp
**Genotypes**

- **Homozygous** = *same* alleles = **PP**, **pp**
- **Heterozygous** = *different* alleles = **Pp**

### Diagram

- **Homozygous dominant**
  - **PP** (homozygous)
    - **Ratio 1:** Purple
  - **Pp** (heterozygous)
    - **Ratio 2:** Purple
- **Heterozygous**
  - **Pp** (heterozygous)
    - **Ratio 2:** Purple
  - **pp** (homozygous)
    - **Ratio 1:** White

**Ratio:** 1:2:1
**Phenotype vs. genotype**

- 2 organisms can have the same phenotype but have different genotypes

<table>
<thead>
<tr>
<th>purple</th>
<th>PP</th>
<th>homozygous dominant</th>
</tr>
</thead>
<tbody>
<tr>
<td>purple</td>
<td>Pp</td>
<td>heterozygous</td>
</tr>
</tbody>
</table>

How do you determine the genotype of an individual with a dominant phenotype?  

*Can’t tell by lookin’ at ya!*
Looking closer at Mendel’s work

- **P**: true-breeding purple-flower peas
- **pp**: true-breeding white-flower peas

**F1** generation (hybrids):
- **PP**: 100% purple-flower peas
- **Pp**: 100% purple-flower peas
- **pp**: 25% white-flower peas

**F2** generation:
- 75% purple-flower peas
- 25% white-flower peas

**Phenotype**: 3:1
**Genotype**: 100%
Punnett squares

F<sub>1</sub> generation (hybrids)

male / sperm

P
p

Pp x Pp

female / eggs

P
p

PP
Pp
Pp
pp

% genotype

PP
25%
Pp
50%
pp
25%
pp
25%

% phenotype

25%
50%
25%

1:2:1
3:1

Aaaaah, phenotype & genotype can have different ratios
Test cross

- Breed the dominant phenotype — the unknown genotype — with a homozygous recessive (pp) to determine the identity of the unknown allele.

How does that work?

is it PP or Pp?

pp
How does a Test cross work?

100% purple

50% purple:50% white or 1:1
Monohybrid cross

- Some of Mendel’s experiments followed the inheritance of single characters
  - flower color
  - seed color
  - monohybrid crosses
Dihybrid cross

- Other of Mendel’s experiments followed the inheritance of 2 different characters
  - seed color and seed shape
  - dihybrid crosses

*Mendel was working out many of the genetic rules!*
Dihybrid cross

true-breeding
yellow, round peas

true-breeding
green, wrinkled peas

\[ YYRR \times yyrr \]

\[ F_1 \]
generation (hybrids)

\[ YyRr \]

\[ F_2 \]
generation

9/16 yellow round peas
3/16 green round peas
3/16 yellow wrinkled peas
1/16 green wrinkled peas

9:3:3:1
What’s going on here?

- If **genes** are on different chromosomes…
  - how do they assort in the gametes?
  - **together** or **independently**?

YyRr

Is it this? Or this?

YyRr

YR yr

YR Yr yR yr

Which system explains the data?
Is this the way it works?

YyRr x YyRr

9/16 yellow round
3/16 green round
3/16 yellow wrinkled
1/16 green wrinkled

Well, that's NOT right!
Dihybrid cross

YyRr x YyRr

<table>
<thead>
<tr>
<th></th>
<th>YR</th>
<th>Yr</th>
<th>yR</th>
<th>yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>YR</td>
<td>YYRR</td>
<td>YYRr</td>
<td>YyRR</td>
<td>YyRr</td>
</tr>
<tr>
<td>Yr</td>
<td>YYRr</td>
<td>YYrr</td>
<td>YyRr</td>
<td>Yyrr</td>
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<tr>
<td>yR</td>
<td>YyRR</td>
<td>YyRr</td>
<td>yyRR</td>
<td>yyrr</td>
</tr>
<tr>
<td>yr</td>
<td>YyRr</td>
<td>Yyrr</td>
<td>yyRr</td>
<td>yyrr</td>
</tr>
</tbody>
</table>

9/16 yellow round
3/16 green round
3/16 yellow wrinkled
1/16 green wrinkled

BINGO!
Mendel’s 2nd law of heredity

- **Law of independent assortment**
  - different loci (genes) separate into gametes independently
    - non-homologous chromosomes align independently
    - classes of gametes produced in equal amounts
      - \( YR = Yr = yR = yr \)
    - only true for genes on separate chromosomes or on same chromosome but so far apart that crossing over happens frequently
Law of Independent Assortment

- Which stage of meiosis creates the law of independent assortment?

**Metaphase 1**

**EXCEPTION**
- If genes are on the same chromosome & close together
  - will usually be inherited together
  - rarely crossover separately
  - “linked”

Remember Mendel didn’t even know DNA—or genes—existed!
The chromosomal basis of Mendel’s laws...

Trace the genetic events through meiosis, gamete formation & fertilization to offspring
Review: Mendel’s laws of heredity

- **Law of segregation**
  - monohybrid cross
    - single trait
  - each **allele** segregates into separate gametes
    - established by Metaphase 1

- **Law of independent assortment**
  - dihybrid (or more) cross
    - 2 or more traits
  - **genes** on separate chromosomes assort into gametes independently
    - established by Metaphase 1

- **Exception**
  - linked genes
Probability & Genetics
Probability

Probability is the likelihood that a specific event will occur.

\[
\text{Probability} = \frac{\text{number of times an event is expected to happen}}{\text{number of opportunities for an event to happen}}
\]

Probability scale runs from 0 to 1.
Genetics & Probability

- Mendel’s laws:
  - segregation
  - independent assortment

reflect same laws of probability that apply to tossing coins or rolling dice
Probability & genetics

- Calculating probability of making a specific gamete is just like calculating the probability in flipping a coin
  - probability of tossing heads?
  - probability making a B gamete?
Probability & genetics

- Outcome of 1 toss has no impact on the outcome of the next toss
  - probability of tossing heads each time? 50%
  - probability making a B gamete each time? 50%
Calculating probability

\[ Pp \times Pp \]

<table>
<thead>
<tr>
<th>sperm</th>
<th>egg</th>
<th>offspring</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>P</td>
<td>PP</td>
</tr>
<tr>
<td>1/2</td>
<td>1/2</td>
<td>1/4</td>
</tr>
<tr>
<td>P</td>
<td>p</td>
<td>Pp</td>
</tr>
<tr>
<td>1/2</td>
<td>1/2</td>
<td>1/4</td>
</tr>
<tr>
<td>p</td>
<td>P</td>
<td>Pp</td>
</tr>
<tr>
<td>1/2</td>
<td>1/2</td>
<td>1/4</td>
</tr>
<tr>
<td>p</td>
<td>p</td>
<td>pp</td>
</tr>
<tr>
<td>1/2</td>
<td>1/2</td>
<td>1/4</td>
</tr>
</tbody>
</table>
Rule of multiplication

- Chance that 2 or more independent events will occur together
  - probability that 2 coins tossed at the same time will land heads up
  
  \[
  1/2 \times 1/2 = 1/4
  \]

  - probability of \( Pp \times Pp \rightarrow pp \)
  
  \[
  1/2 \times 1/2 = 1/4
  \]
Rules of Probability

The Rule of Multiplication

Multiply the probability of each separate event

\[ Ff \times Ff \quad ff = \frac{1}{4} \]

\[ RrTt \times RrTt \quad RRTT = \frac{1}{16} \]

The Rule of Addition

The probability of an event is the sum of the probabilities of the separate events that could make it happen.
Calculating probability in crosses

Use rule of multiplication to predict crosses

YyRr \times YyRr

\[ \frac{1}{4} \times \frac{1}{4} = \frac{1}{16} \]

yy rr

1/4  1/4

1/16
Apply the Rule of Multiplication

AABbccDdEEFf \times AaBbccDdeeFf

\Rightarrow AabbccDdEeFF

\begin{align*}
AA \times Aa &\rightarrow Aa & 1/2 \\
Bb \times Bb &\rightarrow bb & 1/4 \\
cc \times cc &\rightarrow cc & 1 \\
Dd \times Dd &\rightarrow Dd & 1/2 \\
EE \times ee &\rightarrow Ee & 1 \\
Ff \times Ff &\rightarrow FF & 1/4
\end{align*}

1/64
Rule of addition

- Chance that an event can occur 2 or more different ways
  - sum of the separate probabilities
  - probability of $Bb \times Bb \rightarrow Bb$

<table>
<thead>
<tr>
<th>sperm</th>
<th>egg</th>
<th>offspring</th>
</tr>
</thead>
<tbody>
<tr>
<td>$B$</td>
<td>$b$</td>
<td>$Bb$</td>
</tr>
<tr>
<td>$1/2$</td>
<td>$1/2$</td>
<td>$1/4$</td>
</tr>
<tr>
<td>$b$</td>
<td>$B$</td>
<td>$Bb$</td>
</tr>
<tr>
<td>$1/2$</td>
<td>$1/2$</td>
<td>$1/4$</td>
</tr>
</tbody>
</table>

$1/4 + 1/4 = 1/2$
The Rule of Addition
The probability of an event is the sum of the probabilities of the separate events that could make it happen.

Round Yellow: could be be

SSYY 1/16
SsYy 4/16
SSYy or 2/16
SsYY 2/16
So it is 9/16
Fish tail method

Traits
Flower color Plant height

Offspring (F2) phenotypes

Tall
Purple
P = 3/4

Tall
White
P = 3/4

Purple
Q = 1/4

Short
White
Q = 1/4

Purple
Short
3/4 * 1/4 = 3/16

Purple Tall
3/4 * 3/4 = 9/16

White Tall
1/4 * 3/4 = 3/16

White Short
1/4 * 1/4 = 1/16

Short
1
Beyond Mendel’s Laws of Inheritance
Complete Dominance – mendelian

Incomplete Dominance - Traits “blend” to an intermediate
Red does not dominate white they blend and make pink.

RR is red
RW is pink
WW is white
Extending Mendelian genetics

- Mendel worked with a simple system
  - peas are genetically simple
  - most traits are controlled by a single gene
  - each gene has only 2 alleles, 1 of which is completely dominant to the other

- The relationship between genotype & phenotype is rarely that simple
Incomplete dominance

- Heterozygote shows an intermediate, blended phenotype

  example:
  - RR = red flowers
  - rr = white flowers
  - Rr = pink flowers
    - make 50% less color
Incomplete dominance

**P**

true-breeding red flowers

**F₁**

100% pink flowers

**F₂**

25% red

50% pink

25% white

It's like flipping 2 pennies!

1:2:1

true-breeding white flowers
Incomplete dominance

**Genotype vs. Phenotype**

**Parentage:**
- **Male** (sperm): $C^R C^W$
- **Female** (eggs): $C^R$, $C^W$

**Gamete Formation:**
- **Male** gametes: $C^R$, $C^W$
- **Female** gametes: $C^R$, $C^R$, $C^W$, $C^W$

**Possible Offspring:**
- $C^R C^R$
- $C^R C^W$
- $C^R C^W$
- $C^W C^W$

**Phenotype Distribution:**
- Red ($C^R C^R$): __
- Red ($C^R C^W$): __
- White ($C^R C^W$): __
- White ($C^W C^W$): __
**Codominance** - Both alleles are expressed at the same time.

- **BB** – black chicken
- **BW** – black and white striped feather
- **WW** – white chicken
- **RR** – red horse
- **RW** – Roan horse
- **WW** – white horse
Multiple Alleles

- more than two alleles for a trait
- ABO blood type

<table>
<thead>
<tr>
<th>(a) Phenotype (blood group)</th>
<th>(b) Genotypes (see p.258)</th>
<th>(c) Antibodies present in blood serum</th>
<th>(d) Results from adding red blood cells from groups below to serum from groups at left</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>( I^A I^A ) or ( I^A i )</td>
<td>Anti-B</td>
<td><img src="image" alt="A group results" /></td>
</tr>
<tr>
<td>B</td>
<td>( I^B I^B ) or ( I^B i )</td>
<td>Anti-A</td>
<td><img src="image" alt="B group results" /></td>
</tr>
<tr>
<td>AB</td>
<td>( I^A I^B )</td>
<td></td>
<td><img src="image" alt="AB group results" /></td>
</tr>
<tr>
<td>O</td>
<td>( ii )</td>
<td>Anti-A Anti-B</td>
<td><img src="image" alt="O group results" /></td>
</tr>
</tbody>
</table>
Co-dominance

- 2 alleles affect the phenotype equally & separately
  - not blended phenotype
  - example: ABO blood groups
  - 3 alleles
    - $I^A$, $I^B$, $i$
    - $I^A$ & $I^B$ alleles are co-dominant to each other
      - both antigens are produced
    - both $I^A$ & $I^B$ are dominant to $i$ allele
  - produces glycoprotein antigen markers on the surface of red blood cells
## Genetics of Blood type

<table>
<thead>
<tr>
<th>phenotype</th>
<th>genotype</th>
<th>antigen on RBC</th>
<th>antibodies in blood</th>
<th>donation status</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td>antigens on surface of RBC</td>
<td>antibodies</td>
<td>___</td>
</tr>
<tr>
<td>B</td>
<td></td>
<td>antigens on surface of RBC</td>
<td>antibodies</td>
<td>___</td>
</tr>
<tr>
<td>AB</td>
<td></td>
<td>antigens on surface of RBC</td>
<td>antibodies</td>
<td></td>
</tr>
<tr>
<td>O</td>
<td></td>
<td>on surface of RBC</td>
<td>antibodies</td>
<td></td>
</tr>
</tbody>
</table>
Blood compatibility

- Matching compatible blood groups
  - critical for blood transfusions
- A person produces antibodies against antigens in foreign blood
  - wrong blood type
    - donor’s blood has A or B antigen that is foreign to recipient
    - antibodies in recipient’s blood bind to foreign molecules
    - cause donated blood cells to clump together
    - can kill the recipient
# Blood donation

<table>
<thead>
<tr>
<th>(a) Phenotype (blood group)</th>
<th>(b) Genotypes</th>
<th>(c) Antibodies present in blood serum</th>
<th>(d) Results from adding red blood cells from groups below to serum from groups at left</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>$I^A I^A$ or $I^A i$</td>
<td>Anti-B</td>
<td><a href="clotting">A-B clotting</a> <a href="clotting">AB clotting</a> <a href="clotting">O clotting</a></td>
</tr>
<tr>
<td>B</td>
<td>$I^B I^B$ or $I^B i$</td>
<td>Anti-A</td>
<td><a href="clotting">B clotting</a> <a href="clotting">AB clotting</a> <a href="clotting">O clotting</a></td>
</tr>
<tr>
<td>AB</td>
<td>$I^A I^B$</td>
<td>—</td>
<td><a href="clotting">AB clotting</a> <a href="clotting">O clotting</a> <a href="clotting">O clotting</a></td>
</tr>
<tr>
<td>O</td>
<td>$ii$</td>
<td>Anti-A Anti-B</td>
<td><a href="clotting">O clotting</a> <a href="clotting">O clotting</a> <a href="clotting">O clotting</a></td>
</tr>
</tbody>
</table>
Pleiotropy

- One gene can affect an organism in numerous ways.

Two copies of the sickle-cell allele

All hemoglobin is the sickle-cell (abnormal) variety

Abnormal hemoglobin crystallizes when oxygen content of blood is low, causing red blood cells to become sickle-shaped

Normal cells

Sickled cells

Breakdown of red blood cells

Clumping of cells and clogging of small blood vessels

Accumulation of sickled cells in spleen

Physical weakness

Anemia

Heart failure

Pain and fever

Brain damage

Damage to other organs

Spleen damage

Impaired mental function

Paralysis

Pneumonia and other infections

Rheumatism

Kidney failure
Pleiotropy

- Most genes are **pleiotropic**
  - one gene affects more than one phenotypic character
    - wide-ranging effects due to a single gene
    - dwarfism (achondroplasia)
    - gigantism (acromegaly)
Acromegaly: André the Giant
Epistasis

When one trait hides another

red hair tint is hidden by hair color, red heads are really blondes
Epistasis

- **One gene completely another gene**
  - coat color in mice = 2 separate genes

- **C,c:**
  - pigment (C) or no pigment (c)

- **B,b:**
  - more pigment (black=B) or less (brown=b)

- **cc** = albino, no matter B allele

- 9:3:3:1 becomes 9:3:4

How would you know that difference wasn’t random chance? Chi-square test!
Polygenic inheritance

- Some phenotypes determined by additive effects of 2 or more genes on a single character
  - phenotypes on a continuum
  - human traits
    - skin color
    - height
    - weight
    - eye color
    - intelligence
    - behaviors
Quantitative Characters Variations exist in a population along a continuum.
Skin color: Albinism

- However albinism can be inherited as a single gene trait

melanin = universal brown color

<table>
<thead>
<tr>
<th>tyrosine</th>
<th>enzyme</th>
<th>melanin</th>
<th>albinism</th>
</tr>
</thead>
</table>

Johnny & Edgar Winter

albino Africans
Nature vs. nurture

- Phenotype is controlled by both environment & genes

Human skin color is influenced by both genetics & environmental conditions

Color of Hydrangea flowers is influenced by soil pH

Coat color in arctic fox influenced by heat sensitive alleles
Nature versus Nurture

Multifactorial: means trait is affected by the environment as well as genes
Studying Inheritance in Humans
Pedigree analysis

- Pedigree analysis reveals Mendelian patterns in human inheritance
  - data mapped on a family tree

= male  = female  = male w/ trait  = female w/ trait
Genetic counseling

- Pedigree can help us understand the past & predict the future
- Thousands of genetic disorders are inherited as simple recessive traits
  - from benign conditions to deadly diseases
  - albinism
  - cystic fibrosis
  - Tay sachs
  - sickle cell anemia
  - PKU
Genetic testing
Karyotype: a photomicrograph of chromosomes used to detect genetic abnormalities.

http://www.medindia.net/interactives/Amniocentesis.asp
Recessive diseases

- The diseases are recessive because the allele codes for either a malfunctioning protein or no protein at all
  - Heterozygotes (Aa)
    - carriers
    - have a normal phenotype because one “normal” allele produces enough of the required protein
Recessive diseases

- Cystic Fibrosis
- Tay-Sachs
- Sickle Cell Anemia
Heterozygote crosses

- Heterozygotes as carriers of recessive alleles

<table>
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<tbody>
<tr>
<td><strong>Aa x Aa</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>female / eggs</td>
<td><strong>AA</strong></td>
<td><strong>Aa</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Aa</strong></td>
<td><strong>aa</strong></td>
</tr>
</tbody>
</table>

- male / sperm

- A
- a

- A
- a

- A
- a

- A
- a

- A
- a
Cystic fibrosis

- Primarily whites of European descent
  - strikes 1 in 2500 births
    - 1 in 25 whites is a carrier (Aa)
  - normal allele codes for a membrane protein that transports Cl\(^-\) across cell membrane
    - defective or absent channels limit transport of Cl\(^-\) (& H\(_2\)O) across cell membrane
    - thicker & stickier mucus coats around cells
    - mucus build-up in the pancreas, lungs, digestive tract & causes bacterial infections
  - without treatment children die before 5; with treatment can live past their late 20s
Normal Lungs

Chloride channel
Transports chloride through protein channel out of cell
Osmotic effects: $\text{H}_2\text{O}$ follows $\text{Cl}^-$

- $\text{Cl}^-$
- $\text{Na}^+$

airway

cells lining lungs

mucus secreting glands
Cystic fibrosis

Cl⁻ Na⁺

airway

cells lining lungs

damaged lung tissue

bacteria & mucus build up

thickened mucus hard to secrete
DELETED IN MANY PATIENTS WITH CYSTIC FIBROSIS
Tay-Sachs

- Primarily Jews of eastern European (Ashkenazi) descent & Cajuns
  - strikes 1 in 3600 births
    - 100 times greater than incidence among non-Jews or Mediterranean (Sephardic) Jews
  - non-functional enzyme fails to breakdown lipids in brain cells
    - symptoms begin few months after birth
    - seizures, blindness & degeneration of motor & mental performance
    - child usually dies before 5yo
Sickle cell anemia

- Primarily Africans
  - strikes 1 out of 400 African Americans
  - caused by substitution of a single amino acid in hemoglobin
  - when oxygen levels are low, sickle-cell hemoglobin crystallizes into long rods
    - deforms red blood cells into sickle shape
    - sickling creates pleiotropic effects = cascade of other symptoms
Sickle cell anemia

- Substitution of one amino acid in polypeptide chain

(a) Normal red blood cells and the primary structure of normal hemoglobin

(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin
Two copies of the sickle-cell allele

All hemoglobin is the sickle-cell (abnormal) variety

Abnormal hemoglobin crystallizes when oxygen content of blood is low, causing red blood cells to become sickle-shaped

Normal cells

Sickled cells

- Breakdown of red blood cells
- Clumping of cells and clogging of small blood vessels
- Accumulation of sickled cells in spleen

- Physical weakness
- Anemia
- Heart failure
- Pain and fever
- Brain damage
- Damage to other organs
- Spleen damage

- Impaired mental function
- Paralysis
- Pneumonia and other infections
- Rheumatism
- Kidney failure
Sickle cell phenotype

- 2 alleles are **codominant**
  - both **normal** & **mutant** hemoglobins are synthesized in heterozygote (Aa)
  - carriers usually healthy, although some suffer some symptoms of sickle-cell disease under blood oxygen stress
    - exercise
Heterozygote advantage

- **Sickle cell frequency**
  - high frequency of heterozygotes is unusual for allele with severe detrimental effects in homozygotes
    - 1 out of 400 African Americans

- **Suggests some selective advantage of being heterozygous**
  - sickle cell: resistance to malaria?
  - cystic fibrosis: resistance to cholera?
Heterozygote advantage

- **Malaria**
  - single-celled eukaryote parasite spends part of its life cycle in red blood cells

- **In tropical Africa, where malaria is common:**
  - *homozygous dominant* individuals die of malaria
  - *homozygous recessive* individuals die of sickle cell anemia
  - *heterozygote carriers* are relatively free of both

- **High frequency of sickle cell allele in African Americans is vestige of African roots***
Malaria

mosquitos
Sucked up from the bloodstream, malaria parasites mate and move from the mosquito gut to salivary glands. When the bugs next bite man, their saliva passes the parasites on.

liver
The invaders make straight for the liver where they mature and reproduce. This generation then migrates to the blood.

red blood cells
Replicating in red blood cells, the parasites eventually burst them open. This damage leads to characteristic malaria fever and sometimes death.
Prevalence of Malaria

Prevalence of Sickle Cell Anemia
Huntington’s chorea

- Dominant inheritance
  - on end of chromosome 4
    - one of 1st genes to be identified
    - mutation = CAG repeats = glutamine amino acid
  - build up of protein “huntingtin” in neurons (brain) causing cell death
    - memory loss
    - muscle tremors, jerky movements = “chorea”
    - early death (10-20 years after onset)
- onset age 30-50
Woody Guthrie & Arlo Guthrie
Genetics & culture

- Why do all cultures have a taboo against incest?
  - laws or cultural taboos forbidding marriages between close relatives are fairly universal

- Fairly unlikely that 2 unrelated carriers of same rare harmful recessive allele will meet & mate
  - but matings between close relatives increase risk
    - “consanguineous” (same blood) matings
  - individuals who share a recent common ancestor are more likely to carry same recessive alleles
A hidden disease reveals itself

AA x Aa

AA x Aa

male / sperm
A
A

female / eggs
A
a

female / eggs
A
a

Aa

Aa

AA
AA

Aa
Aa

AA
AA

Aa
aa
Chapter 15

The Chromosomal Basis of Inheritance
Chromosome Theory of Inheritance

Mendelian Genes have a specific loci on chromosomes and it’s the chromosomes that undergo segregation and independent assortment.
Classes of chromosomes

autosomal chromosomes

sex chromosomes
Remember: Law of Independent Assortment gave a 9:3:3:1 ratio of phenotypes in offspring?

What happens when the ratio is 1:1:1:1 or something close?
Sex linked traits

- Genes are on **sex chromosomes**
  - as opposed to **autosomal** chromosomes
  - first discovered by T.H. Morgan at Columbia U.
- *Drosophila* breeding
  - good genetic subject
    - prolific
    - 2 week generations
    - 4 pairs of chromosomes
    - XX=female, XY=male

1910 | 1933
Parents in testcross

Most offspring
**P Generation** (homozygous)

Wild type (gray with normal wings)

\[ b^+ b^+ vg^+ vg^+ \]

Double mutant (black with vestigial wings)

\[ b b vg vg \]

**F1 dihybrid** (wild type) (gray with normal wings)

\[ b^+ b vg^+ vg \]

**TESTCROSS**

**Double mutant** (black with vestigial wings)

\[ b b vg vg \]

**Offspring of testcross**

Wild type

\[ b^+ b vg^+ vg \]

Black-vestigial

\[ b b vg vg \]

Gray-vestigial

\[ b^+ b vg vg \]

Black-normal

\[ b b vg^+ vg \]

**Expected (independent assortment)**

<table>
<thead>
<tr>
<th>Parental phenotypes</th>
<th>Recombinant phenotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>575</td>
<td>575</td>
</tr>
<tr>
<td>575</td>
<td>575</td>
</tr>
</tbody>
</table>

**Observed**

<table>
<thead>
<tr>
<th>Wild type</th>
<th>Black-vestigial</th>
<th>Gray-vestigial</th>
<th>Black-normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>965</td>
<td>944</td>
<td>206</td>
<td>185</td>
</tr>
</tbody>
</table>
(a) Production of recombinant gametes by a dihybrid female

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(a) Meiosis, as in (a)

Testcross parents
- F₁ dihybrid (gray with normal wings)
- Meiosis

Gametes
- Ova: $b^+ vg^+$, $b vg$, $b^+ vg$, $b vg^+
- Sperm: $b vg$

Testcross offspring
- Wild type: $b^+ vg^+$
- Black-vestigial: $b vg$
- Gray-vestigial: $b^+ vg$
- Black-normal: $b vg^+$

Recombinant offspring
- 965 Wild type
- 944 Black-vestigial
- 206 Gray-vestigial
- 185 Black-normal

Recombination frequency = \(\frac{391 \text{ recombinants}}{2,300 \text{ total offspring}} \times 100 = 17\%\)

(b) Production of recombinant offspring

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Genetic Map - ordered listing of the genetic loci along a chromosome.

Linkage Map – Is a genetic map based on recombination frequencies.

Map units are equivalent to percentage of recombinations.
Genetics of Sex

- In humans & other mammals, there are 2 sex chromosomes: X & Y
  - 2 X chromosomes
    - develop as a female: XX
    - gene redundancy, like autosomal chromosomes
  - an X & Y chromosome
    - develop as a male: XY
    - no redundancy
Some Chromosomal Systems of sex inheritance

Two months
Discovery of sex linkage

P

true-breeding red-eye female  X  true-breeding white-eye male

100% red eye offspring

F₁ generation (hybrids)

100% red-eye female

F₂ generation

50% red-eye male  50% white eye male

Huh! Sex matters?!
What’s up with Morgan’s flies?

RR × rr → Rr

100% red eyes

Rr × Rr → 3 red : 1 white

 Doesn’t work this way!
What’s up with Morgan’s flies?

- 100% red eyes
- 50% red males; 50% white males
Genes on sex chromosomes

- **Y chromosome**
  - few genes other than **SRY**
    - sex-determining region
    - master regulator for maleness
    - turns on genes for production of male hormones
      - many effects = pleiotropy!

- **X chromosome**
  - other traits beyond sex determination
    - mutations:
      - hemophilia
      - Duchenne muscular dystrophy
      - color-blindness
Sex-linked usually means “X-linked” more than 60 diseases traced to genes on X chromosome
Map of Human Y chromosome?

< 30 genes on Y chromosome

- Sex-determining Region Y (SRY)
- Channeling Flipping (FLP)
- Catching & Throwing (BLZ-1)
- Self confidence (BLZ-2)  
  note: not linked to ability gene
- Devotion to sports (BUD-E)
- Addiction to death & destruction movies (SAW-2)
- Air guitar (RIF)
- Scratching (ITCH-E)
- Spitting (P2E)  
  linked
- Inability to express affection over phone (ME-2)
- Selective hearing loss (HUH)
- Total lack of recall for dates (OOPS)
Sex-linked traits summary

- **X-linked**
  - follow the X chromosomes
  - males get their X from their mother
  - trait is never passed from father to son

- **Y-linked**
  - very few genes / traits
  - trait is only passed from father to son
  - females cannot inherit trait
Queen Victoria and Descendants
Hemophilia

sex-linked recessive

Hh x H

male / sperm

X^H Y

female / eggs

X^H

X^H X^H

X^H Y

X^h

X^H X^h

X^h Y

carrier
disease

X^H

X^H X^H

X^h Y

X^H

Y
Sex linked traits are traits found on sex chromosomes.
  X-linked are on the X chromosome.
  Y-linked are on the Y chromosome.

Color blindness is on the X so females get 2 copies and only one.
X-inactivation

- Female mammals inherit 2 X chromosomes
  - one X becomes inactivated during embryonic development
    - condenses into compact object = Barr body
    - which X becomes Barr body is random
  - patchwork trait = “mosaic”
X-inactivation & tortoise shell cat

- 2 different cell lines in cat
Male pattern baldness

- **Sex influenced trait**
  - autosomal trait influenced by sex hormones
    - age effect as well = onset after 30 years old
  - dominant in males & recessive in females
    - B_ = bald in males; bb = bald in females
Genomic Imprinting: Methyl groups are added to cytosine nitrogen bases to silence them. In the gonads, the imprinting from parents is deleted (reset).

Most important in genes used for embryonic development where two genes are lethal.

Fragile X Syndrome the tip of the X is held on by a thread of DNA.
Maternal imprint on chromosome in egg

Paternal imprint on chromosome in sperm

Inherited imprinting affects the development of the individual

Zygote

Somatic cells

Original imprints erased in gamete-producing cells

Copyright © Pearson Education, Inc., publishing as Benjamin Cummings.
Maternal imprint on chromosome in egg
Paternal imprint on chromosome in sperm

Inherited imprinting affects the development of the individual

Zygote

Somatic cells

Original imprints erased in gamete-producing cells

New imprints made, differing in male and female

Meiosis

All sperm have paternal imprint
All eggs have maternal imprint
Mutations a sudden change in the structure or amount of genetic material.

Mutagens cause mutations, chemical, radiation, viral.
Chromosomal Mutations

A. Translocation – transfer of a part of a chromosome to a nonhomologous chromosome

B. Inversion – a piece of a chromosome is inverted, reversing the order of the genes.

C. Deletion – a piece of a chromosome breaks off.
D. Addition – a piece breaks off and attaches to a homologous chromosome

E. Nondisjunction - the addition or loss of a whole chromosome when they don’t separate.
(a) A **deletion** removes a chromosomal segment.

(b) A **duplication** repeats a segment.

(c) An **inversion** reverses a segment within a chromosome.

(d) A **translocation** moves a segment from one chromosome to another, non-homologous one.
Also, sometimes, the chromosomes do not separate completely and an egg gets a second chromosome in a pair. When fertilized this leads to TRISOMY.
(a) Nondisjunction of homologous chromosomes in meiosis I
(b) Nondisjunction of sister chromatids in meiosis I
Down Syndrome
Klinefelter syndrome

Turner Syndrome
Cri Du Chat
A rooster with gray feathers is mated with a hen of the same phenotype. Among their offspring, 15 chicks are gray, 6 are black, and 8 are white. A) What is the simplest explanation for the inheritance of these colors in chickens? B) What offspring would you predict from the mating of a gray rooster and a black hen?

A. Incomplete dominance
B. ½ Black ½ Gray
In some plants, a true-breeding, red-flowered strain gives all pink flowers when crossed with a white-flowered strain: RR (red) x rr (white) x Rr (pink). If flower position (axial or terminal) is inherited as it is in peas (see Table 14.1, p. 250 in the textbook), what will be the ratios of genotypes and phenotypes of the F₁ generation resulting from the following cross: axial-red (true-breeding) x terminal-white? What will be the ratios in the F₂ generation?
Flower position, stem length, and seed shape were three characters that Mendel studied. Each is controlled by an independently assorting gene and has dominant and recessive expression as follows:

If a plant that is heterozygous for all three characters is allowed to self-fertilize, what proportion of the offspring would you expect to be as follows? (Note: Use the rules of probability instead of a huge Punnett square.)
A) homozygous for the three dominant traits
B) homozygous for the three recessive traits
C) heterozygous
D) homozygous for axial and tall, heterozygous for seed shape
A black guinea pig crossed with an albino guinea pig produces 12 black offspring. When the albino is crossed with a second black one, 7 blacks and 5 albinos are obtained. What is the best explanation for this genetic situation? Write genotypes for the parents, gametes, and offspring.
In sesame plants, the one-pod condition (P) is dominant to the three-pod condition (p), and normal leaf (L) is dominant to wrinkled leaf (l). Pod type and leaf type are inherited independently. Determine the genotypes for the two parents for all possible matings producing the following offspring:

A) 318 one-pod normal, 98 one-pod wrinkled
B) 323 three-pod normal, 106 three-pod wrinkled
C) 401 one-pod normal
D) 150 one-pod normal, 147 one-pod wrinkled, 51 three-pod normal, 48 three-pod wrinkled
E) 223 one-pod normal, 72 one-pod wrinkled, 76 three-pod normal, 27 three-pod wrinkled

A) PPLL x PPLL, PpLI, or ppLI
B) ppLI x ppLI
C) PPLL x any of the 9 possible genotypes or PPll x ppLL
D) PpLI x PpII
E) PpLI x PpLI
A man with group A blood marries a woman with group B blood. Their child has group O blood. What are the genotypes of these individuals? What other genotypes, and in what frequencies, would you expect in offspring from this marriage?

Man I^A i; woman I^B i; child ii. Other genotypes for children are 1/4 I^A I^B, 1/4 I^A i, 1/4 I^B i.
Color pattern in a species of duck is determined by one gene with three alleles. Alleles H and I are codominant, and allele i is recessive to both. How many phenotypes are possible in a flock of ducks that contains all the possible combinations of these three alleles?

Four
Phenylketonuria (PKU) is an inherited disease caused by a recessive allele. If a woman and her husband are both carriers, what is the probability of each of the following?

A) All three of their children will be of normal phenotype.

B) One or more of the three children will have the disease.

C) All three children will have the disease.

D) At least one child will be phenotypically normal.

(Note: Remember that the probabilities of all possible outcomes always add up to 1.)

A) \( \frac{3}{4} \times \frac{3}{4} \times \frac{3}{4} = \frac{27}{64} \)

B) \( 1 \times \frac{27}{64} = \frac{37}{64} \)

C) \( \frac{1}{4} \times \frac{1}{4} \times \frac{1}{4} = \frac{1}{64} \)

D) \( 1 \times \frac{1}{64} = \frac{63}{64} \)
The genotype of individuals in a tetrahybrid cross is AaBbCcDd. Assuming independent assortment of these four genes, what are the probabilities that offspring will have the following genotypes?

A) aabbccdd  
B) AaBbCcDd  
C) AABBCCDD  
D) AaBBccDd  
E) AaBBCCdd

A) 1/256  
B) 1/16  
C) 1/256  
D) 1/64  
E) 1/128
What is the probability that each of the following pairs of parents will produce the indicated offspring? (Assume independent assortment of all gene pairs.)

A) $\text{AABBCC} \times \text{aabbcc} \rightarrow \text{AaBbCc}$
B) $\text{AABbCc} \times \text{AaBbCc} \rightarrow \text{AAbbCC}$
C) $\text{AaBbCc} \times \text{AaBbCc} \rightarrow \text{AaBbCc}$
D) $\text{aaBbCC} \times \text{AABbccc} \rightarrow \text{AaBbCc}$

A) $1$
B) $\frac{1}{32}$
C) $\frac{1}{8}$
D) $\frac{1}{2}$
A man with hemophilia (a recessive, sex-linked condition) has a daughter of normal phenotype. She marries a man who is normal for the trait. What is the probability that a daughter of this mating will be a hemophiliac? That a son will be a hemophiliac? If the couple has four sons, what is the probability that all four will be born with hemophilia?
0; 1/2, 1/16
Pseudohypertrophic muscular dystrophy is a disorder that causes gradual deterioration of the muscles. It is seen only in boys born to apparently normal parents and usually results in death in the early teens. Is this disorder caused by a dominant or a recessive allele? Is its inheritance sex-linked or autosomal? How do you know? Explain why this disorder is seen only in boys and never in girls.

Recessive. If the disorder were dominant, it would affect at least one parent of a child born with the disorder. For a girl to have the disorder, she would have to inherit recessive alleles from both parents. This
Red-green color blindness is caused by a sex-linked recessive allele. A color-blind man marries a woman with normal vision whose father was color-blind. What is the probability that they will have a color-blind daughter? What is the probability that their first son will be color-blind? (Note: The two questions are worded a bit differently.)

1/4 for each daughter (1/2 chance that child will be female x 1/2 chance of a homozygous recessive genotype); 1/2 for first son.
A wild-type fruit fly (heterozygous for gray body color and normal wings) is mated with a black fly with vestigial wings. The offspring have the following phenotypic distribution: wild type, 778; black-vestigial, 785; black-normal, 158; gray-vestigial, 162. What is the recombination frequency between these genes for body color and wing type?

17%
What pattern of inheritance would lead a geneticist to suspect that an inherited disorder of cell metabolism is due to a defective mitochondrial gene?

The disorder would always be inherited from the mother.
An aneuploid person is obviously female, but her cells have two Barr bodies. What is the probable complement of sex chromosomes in this individual?
Determine the sequence of genes along a chromosome based on the following recombination frequencies: A-B, 8 map units; A-C, 28 map units; A-D, 25 map units; B-C, 20 map units; B-D, 33 map units.

D-A-B-C
About 5% of individuals with Down syndrome are the result of chromosomal translocation in which one copy of chromosome 21 becomes attached to chromosome 14. How does this translocation lead to Down syndrome?

In meiosis, the combined 14-21 chromosome will behave as one chromosome. If a gamete receives the combined 14-21 chromosome and a normal copy of chromosome 21, trisomy 21 will result when this gamete combines with a normal gamete.
9. More common than completely polyploid animals are mosaic polyploids, animals that are diploid except for patches of polyploid cells. How might a mosaic tetraploid-an animal with some cells containing four sets of chromosomes-arise from an error in mitosis? At some point during development, one of the embryo's cells may have failed to carry out mitosis after duplicating its chromosomes. Subsequent normal cell cycles would produce genetic copies of this tetraploid cell.
Assume that genes A and B are linked and are 50 map units apart. An animal heterozygous at both loci is crossed with one that is homozygous recessive at both loci. What percentage of the offspring will show phenotypes resulting from crossovers? If you did not know that genes A and B were linked, how would you interpret the results of this cross? Fifty percent of the offspring would show phenotypes that resulted from crossovers. These results would be the same as those from a cross where A and B were not linked. Further crosses involving other genes on the same chromosome would reveal the linkage and map distances.