Section 12. Mendelian Genetics
Gregor Mendel

Born 1822 in Heizenberg, Austria, son of a farmer. Very bright as a student, sent to gymnasium, but father was crippled and family couldn’t afford to keep him in school, so he joined monastery to get an education and to be teacher. 1843 joined Augustinian monastery at Brünn in Moravia. 1847 ordained into priesthood. 1849 assigned to teach in secondary school, took teaching examination, failed due to lack of knowledge. 1851 was sent to U. Vienna where got brief but extremely sound scientific education. 1856 failed teaching exam again; test anxiety? Began experiments with peas in 1850's. 1865 read paper on his results to Brunn Natural History Society.

1866 paper published in Proceedings of Brunn Natural History Society. (A date to remember!)

Besides studies on heredity, did other kinds of natural history. 1868 scientific career ended when became abbot of the monastery. 1884 died.
Mendel Was Not the First to Try: Why Did He Succeed in Deducing Laws of Heredity Where His Predecessors Failed?

He was really smart!

Better scientific background than those before him:
- cell theory; probably knew adult plant comes from egg by succession of cell divisions
- fertilization: pollen grain + egg -> zygote; knew, from his own experiments, that one pollen grain fertilized one egg
- took math including early probability theory; ready to see and understand random variation
- took physics from Doppler, saw power of quantitative data and mathematical laws

What Mendel did not know:
- Genes on chromosomes in nucleus
- Mitosis
- Meiosis

Simplified problem
Focused on discontinuous variation (either/or traits), usually controlled by one or two genes, instead of continuous variation controlled by many genes and the environment.
Good choice of experimental organism
Worked with plants, as did nearly all geneticists. Selected peas because:
• many different phenotypes; got $\geq 27$ varieties that differed in various phenotypic traits
• could do controlled crosses or selfing = self-fertilization, mating plant with itself
What Mendel Did

1. From commercial seed dealers, selected many pea strains differing in discrete characters. Chose some differing in 7 traits.

2. Subjected these to several generations of selfing. Bred true; e.g. plant green seeds, grow plants, self plants --> seeds all green.

We know, and Mendel deduced, that selfing (or any other form of inbreeding) produces pure lines, homozygous plants that produce only homozygous offspring.

3. Did crosses between strains differing in one or more traits. Monohybrid cross: parents differ in only one trait. Most of Mendel’s crosses were dihybrid or trihybrid.

Any cross can be analyzed as monohybrid crosse by following only one trait.
P₀
  ↘
  Self
    ↘
    P₁
      ↘
      Cross
        ↘
        F₁
          ↘
          Self or cross
            ↘
            inter se
              ↘
              F₂
                423 round 0.76 ≈ 3/4
                133 wrinkled 0.24 ≈ 1/4
                556 1.00

round wrinkled pure lines homozygous diploid

round wrinkled

round

heterozygous diploid

gametes

gametes

gametes

1.00
Two phenotypes produced by two different hereditary factors.
P₀  round  wrinkled  pure lines  homozygous diploid
                 R  r
Self  ↓  ↓  ↓  ↓
P₁  round  wrinkled  gametes
                 R  r
Cross  ↓  ↓  ↓  ↓
F₁  round  Rr  heterozygous diploid
                R  r
Self or Cross  ↓  ↓  ↓  ↓
Inter se  F₂  423 round  R  133 wrinkled  r

Two phenotypes produced by two different hereditary factors.
F₁ produces F₂ with both phenotypes so must have and transmit both hereditary factors.
Two phenotypes produced by two different hereditary factors.

F<sub>1</sub> must produce F<sub>2</sub> with both phenotypes so must have and transmit both hereditary factors.

If F<sub>2</sub> has two factors, all plants have to have two. Inbred parents only produce one kind of gamete, so have only one kind of hereditary factor.
Now Mendel can explain the ratio of phenotypes in the F$_2$. If the two kinds of F$_1$ gametes are paired randomly in all possible combinations, 1/4 will be RR, 1/2 Rr, and 1/2 rr. Rr will be round, as in the F$_1$. $R$ is dominant, so Rr is round.
How explain $F_2$? Mendel came up with a model:

- Mendel’s first law or law of segregation: Alleles segregate during formation of the gametes, 1/2 of the gametes get one allele and 1/2 the other.

$F_1$ gametes are 1/2 $R$ and 1/2 $r$.

- Fertilization is random with respect to genotype.

Make Punnett square to see different combinations of egg and pollen.

<table>
<thead>
<tr>
<th>Pollen</th>
<th>Eggs</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1/2 R</td>
<td>1/2 r</td>
</tr>
<tr>
<td>1/2 R</td>
<td>1/4 RR</td>
<td>1/4 Rr</td>
</tr>
<tr>
<td>1/2 r</td>
<td>1/4 rR</td>
<td>1/4 rr</td>
</tr>
</tbody>
</table>

Genotypic ratio 1/4 $RR$ : 1/2 $Rr$ : 1/4 $rr$
Phenotypic ratio 3/4 round : 1/4 wrinkled
Mendel didn’t know about meiosis or even about chromosomes so he couldn’t interpret his data in those terms.

Walter Sutton (1902), Theodore Boveri (1903): Chromosome theory of heredity:
• Genes are on chromosomes.
• Different chromosomes have different sets of genes.
• Different alleles are on different members of a pair of homologous chromosomes.
• Alleles segregate in meiosis because homologous chromosomes segregate.

Go back and look at notes about meiosis I.
Dihybrid Crosses

Mendel gave some data for one-factor crosses, but almost certainly most crosses actually had two or three factors differing, and he focused on one.

The above cross actually had at least two traits and two genes segregating:
• round and wrinkled seeds $R, r$
• yellow and green seeds $Y, y$
\[ P_1 \text{ round yellow } \times \text{ wrinkled green} \]

Cross

\[ F_1 \text{ round yellow} \]

Self or cross \ inter se 

\[ F_2 \]

\[
\begin{array}{lcl}
315 \text{ round yellow} & \approx & 9.6/17 \quad 9/16 \\
101 \text{ wrinkled yellow} & \approx & 3.1/17 \quad 3/16 \\
108 \text{ round green} & \approx & 3.3/17 \quad 3/16 \\
32 \text{ wrinkled green} & \approx & 1.0/17 \quad 1/16 \\
556
\end{array}
\]

Why did Mendel think of the 9:3:3:1 ratio instead of something else like 9.6 : 3.1 : 3.3 : 1.0?
Updated version of this will be put on web later today or tomorrow morning.
P₁  round yellow  wrinkled green
    \( RRYY \quad rryy \)

Cross  \( RY \times ry \)  gametes

F₁    round
    \( RrYy \)

Self or
cross  \( RY \quad ry \quad Ry \quad rY \)  gametes

inter se

F₂  315 round yellow  \( R^-Y^- \approx 9/16 \)
101 wrinkled yellow  \( rrY^- \approx 3/16 \)
108 round green  \( R^-yy \approx 3/16 \)
32 wrinkled green  \( rryy \approx 1/16 \)
556
First note that if we analyze the cross as two one-factor crosses, both give the 3:1 ratio in the F₂:

round/wrinkled alone: \[ 315 + 108 = 423 \text{ round} \approx 3/4 \]
\[ 101 + 32 = 133 \text{ wrinkled} \approx 1/4 \]

yellow/green alone: \[ 315 + 101 = 416 \text{ yellow} \approx 3/4 \]
\[ 108 + 32 = 140 \text{ green} \approx 1/4 \]

Test to see if are segregating completely independently. If they are, ratio round to wrinkled should be the same in yellow and green plants, and *vice versa*.

<table>
<thead>
<tr>
<th></th>
<th>yellow</th>
<th>green</th>
</tr>
</thead>
<tbody>
<tr>
<td>Round</td>
<td>315</td>
<td>108</td>
</tr>
<tr>
<td>Wrinkled</td>
<td>101</td>
<td>32</td>
</tr>
</tbody>
</table>

You do other combination.

Each locus shows 3/4:1/4 segregation regardless of what the other locus is doing.
Analysis as a two-factor cross requires two steps to predict $F_2$:

1. Use Punnett square to get all possible combinations of alleles in gametes:

<table>
<thead>
<tr>
<th></th>
<th>Y/y</th>
<th>1/2 Y</th>
<th>1/2 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>R/r</td>
<td>1/2 R</td>
<td>1/4 RY</td>
<td>1/4 Ry</td>
</tr>
<tr>
<td></td>
<td>1/2 r</td>
<td>1/4 rY</td>
<td>1/4 ry</td>
</tr>
</tbody>
</table>

Mendel’s second law (law of independent segregation: different pairs of alleles segregate independently of each other.)
2. Use Punnett square again to get all possible combinations of gametes:

<table>
<thead>
<tr>
<th>Eggs</th>
<th>1/4 R Y</th>
<th>1/4 R y</th>
<th>1/4 r Y</th>
<th>1/4 r y</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/4 R Y</td>
<td>RR YY</td>
<td>RR Yy</td>
<td>Ry YY</td>
<td></td>
</tr>
<tr>
<td>1/4 R y</td>
<td></td>
<td>RR yy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/4 r Y</td>
<td></td>
<td></td>
<td>rr Yy</td>
<td></td>
</tr>
<tr>
<td>1/4 r y</td>
<td></td>
<td></td>
<td></td>
<td>rr yy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1/16</td>
</tr>
</tbody>
</table>
Why do these two genes segregate independently of each other?
One answer, proposed by Sutton and Boveri: they are on different chromosomes which are segregating independently of each other.

Get four different genotypes of gametes in approximately equal numbers.
Reciprocal crosses: 

female $A \times$ male $a$

female $a \times$ male $A$

Mendel found that reciprocal crosses gave the same progeny in the same proportions.

Mendel did some crosses with other plants and probably saw incomplete dominance as well as complete dominance:

Flower color in four o' clock: $RR$ = red, $rr$ = white, $Rr$ = pink
Mendel’s Complete Model

• Alleles (alternative versions of a gene) segregate at
gametogenesis, one to each gamete, half receiving one allele
and half the other. ("Mendel's first law or law of
segregation").
• Different pairs of alleles segregate independently of each
other (‘Mendel’s second law or law of independent
segregation’).
• Genes in the zygote are transmitted to all the cells in the
plant as cells divide.
• Genes are inherited equally from both parents (biparental
inheritance) via the gametes when they fuse at fertilization.
(because reciprocal crosses gave same result)
• Fertilization is random with respect to genotype of the
gametes.

Textbooks refer to Mendel's two laws; I think all of these insights were probably
pretty new with Mendel and could be called laws, so Mendel really had five
laws, or one model with five parts.
Mendel Tested His Model

Mendel tested his conclusions in several ways:

1. Test by selfing $F_2$

progeny test
phenotypes genotypes self $\rightarrow$ $F_3$ phenotypes

1 wrinkled green $r$ $r$ $y$ $y$ $wg$
   (wrinkled green)

9 round yellow $4$ $R$ $r$ $Y$ $y$ $ry, rg, wy, wg$
   $2$ $R$ $r$ $Y$ $Y$ $ry, wy$
   $2$ $R$ $R$ $Y$ $y$ $ry, rg$
   $1$ $R$ $R$ $Y$ $Y$ $ry$

Exercise: you fill in rest.
2. Test by backcross and testcross

Two kinds of crosses are so common and important that they have special names:
• Backcross = cross of offspring to one parent
• Test cross = individual of unknown genotype X homozygous recessive

Test cross is especially important because phenotypic ratio of offspring = genotypic ratio of gametes from parent of unknown genotype.

e.g. $F_2$ round yellow could be any of four different genotypes. Look at two:

\[
\begin{align*}
rryy & \rightarrow \text{gametes } \ r\ y \\
RrYy & \rightarrow \text{testcross offspring} \\
1/4\ R\ Y & \quad R\ r\ Y\ y \quad \text{round yellow} \\
1/4\ R\ y & \quad R\ r\ y\ y \quad \text{round green} \\
1/4\ r\ Y & \quad r\ r\ Y\ y \quad \text{wrinkled yellow} \\
1/4\ r\ y & \quad r\ r\ y\ y \quad \text{wrinkled green} \\
\end{align*}
\]

\[
\begin{align*}
RRYY & \rightarrow \text{gametes } \ R\ Y \\
\text{testcross offspring} & \\
1/2\ R\ Y & \quad R\ r\ Y\ y \quad \text{round yellow} \\
1/2\ R\ y & \quad R\ r\ y\ y \quad \text{round green} \\
\end{align*}
\]

Exercise: You do the other two.
Ratios to memorize (as well as understand)

\[ \text{Aa} \times \text{Aa} \quad \frac{1}{4} \text{AA} \quad \frac{1}{2} \text{Aa} \quad \frac{1}{4} \text{aa} \quad 3/4 \text{ A-} \quad 1/4 \text{ aa} \]

\[ \text{Aa} \times \text{aa} \quad \frac{1}{2} \text{Aa} \quad \frac{1}{2} \text{aa} \]

\[ \text{AA} \times \text{Aa} \quad \frac{1}{2} \text{AA} \quad 1/2 \text{ Aa} \]

\[ \text{Aa Bb} \times \text{Aa Bb} \quad \frac{9}{16} \text{ A- } \text{B-} \quad \frac{3}{16} \text{ A- } \text{bb} \quad \frac{3}{16} \text{ aa B-} \quad \frac{1}{16} \text{ aa bb} \]
An aside about gene symbols:

All gene symbols are italicized when printed.

Different organisms use different naming conventions. Textbooks don’t always keep up with changes in conventions.

Peas:
Most textbooks use $R/r$ for round/wrinkled, and $Y/y$ for yellow/green. Your book uses $W/w$ and $G/g$ for these, maybe because in most organisms the gene is named after the mutant allele. Inconsistent: they use $P/p$ for purple/white flowers.

Real nomenclature given on web. To correct the textbook, change

$W/w$ to $R/r$
$G/g$ to $Y/y$ or $I/I$
$P/p$ to $A/a$ (easy to remember: $A$ stands for anthocyanin pigment, and the gene is called anthocyanin inhibition after the mutant allele).
Mendelian Genetics in Tetrads

Yeast cells (Saccharomyces cerevisiae)

Mating types a and α determined by alleles at the mating type locus

met = methionine auxotroph  \( MET = \) wild type allele

Both alleles segregate 2:2

\( MET \) and mating type genes are on different chromosomes, therefore segregate independently so the two-locus genotypes are

\[
\begin{align*}
1/4 & \ a \ met \\
1/4 & \ a \ MET \\
1/4 & \ \alpha \ MET \\
1/4 & \ \alpha \ met \\
1/4 & \ a \ MET
\end{align*}
\]
a met × α MET

diploid a/α met/MET

   sporulate

Tetrads
   All 2a:2α
   All 2MET:2met
   1/2  2 a met: 2 α MET
   1/2  2 a MET: 2 α met

Random spores
   1/4 a met  1/4 α MET parental genotypes
   1/4 a MET  1/4 α met recombinant genotypes

Cf. Peas:
   Parent diploid is heterozygous at two loci
   just like F1 R/r Y/y in Mendel’s cross.
   Genotypic ratio among random spores is
   1/4:1/4:1/4:1/4, same as in gametes from F1
   in dihybrid cross.
Note that all the preceding discussion has assumed there is no crossing-over or gene conversion. The only source of recombinant genotypes was independent assortment of genes on different chromosomes. Crossing-over and gene conversion will be added later.