LECTURE 2: MENDELIAN GENETICS JULY 6, 2011

1. Genetic Terminology
2. Monohybrid Crosses
   - The principle of segregation
   - The concept of dominance
3. Predicting the Outcome of Genetic Crosses
   - Simple Crosses: the Punnett Square
   - More complicated crosses: Probability calculations
   - Incomplete Dominance
   - Ratios in simple crosses – memorize these!
4. Dihybrid Crosses
   - The principle of independent assortment
5. Mendel, meiosis, and the chromosome theory of heredity
6. Use of statistics to analyze the results of a genetic cross

GREGOR MENDEL (1822 - 1884)

- Austrian monk, botanist, and physicist
- "Hybridization" experiments with pea plants
- Excellent example of the scientific method

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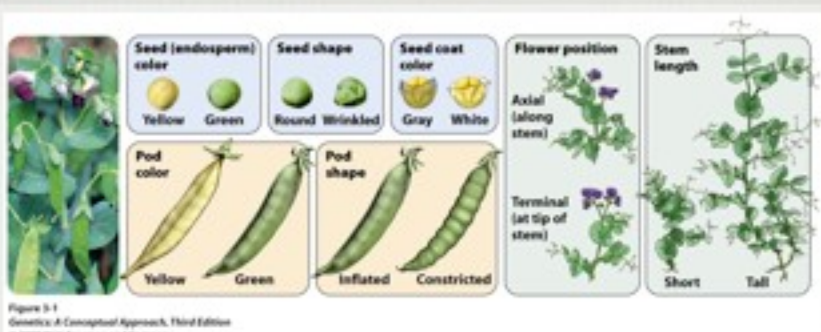
THE SCIENTIFIC METHOD

1. MAKE OBSERVATIONS
2. FORMULATE A HYPOTHESIS
3. USE HYPOTHESIS TO MAKE PREDICTIONS
4. TEST THOSE PREDICTIONS EXPERIMENTALLY/ MATHEMATICALLY

MENDEL'S PEAS (*PISUM SATIVUM*)



- COMPARATIVELY SHORT GENERATION TIME (1 YEAR)
- EASY TO CULTIVATE AND INTERCROSS
- MANY OFFSPRING
- NUMEROUS TRAITS THAT ARE DISCONTINUOUS AND BINARY ("EITHER/OR, NOT "MORE OR LESS"

TWO HYPOTHESES:

1. BLENDING: OFFSPRING ARE A BLEND/MIX OF PARENTAL TRAITS
2. ONE TRAIT OR THE OTHER "WINS" - OFFSPRING DISPLAY ONE OF THE TWO TRAITS, NOT A COMBINATION OF BOTH

- WHY DOES "DISCONTINUOUS AND BINARY" HELP TO DISTINGUISH THESE HYPOTHESES?

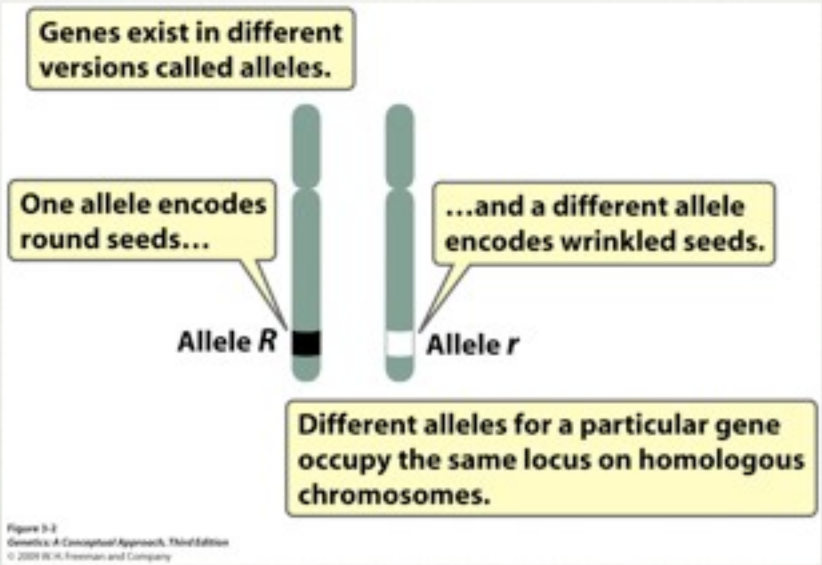
IMPORTANT GENETIC TERMS

Table 3.1 Summary of important genetic terms

Term	Definition
Gene	A genetic factor (region of DNA) that helps determine a characteristic
Allele	One of two or more alternate forms of a gene
Locus	Specific place on a chromosome occupied by an allele
Genotype	Set of alleles possessed by an individual organism
Heterozygote	An individual organism possessing two different alleles at a locus
Homozygote	An individual organism possessing two of the same alleles at a locus
Phenotype or trait	The appearance or manifestation of a character
Character or characteristic	An attribute or feature

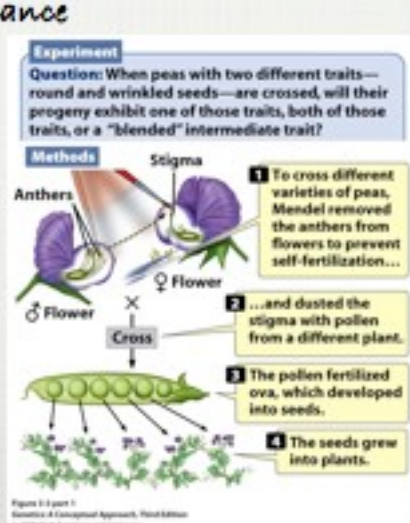
Table 3-1
Genetics: A Conceptual Approach, Third Edition

DIPLOID ORGANISMS POSSESS TWO ALLELES AT EACH LOCUS



The First Experiment: Monohybrid Crosses

- Monohybrid crosses: reveal the principle of segregation and the concept of dominance



MONOHYBRID CROSS

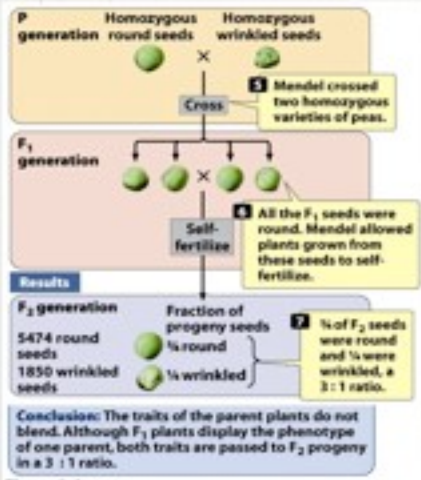


Figure 3-3
Genetics: A Conceptual Approach, Third Edition

1. Cross involves only one varying trait
2. "Pure-breeding" strains (homozygous - bearing only one type of allele)
3. First conclusion: blending?

MONOHYBRID CROSS

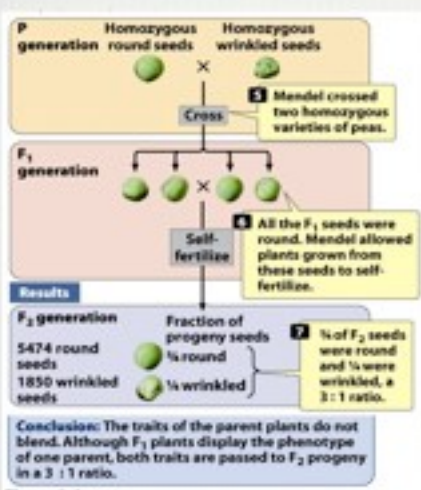


Figure 3-3
Genetics: A Conceptual Approach, Third Edition

- Second conclusion: "round" is dominant to "wrinkled"
- Third conclusion: the recessive allele still exists in the F1 generation, though it isn't expressed
- So: The recessive allele passed unchanged through the F1 generation

THE PRINCIPLE OF SEGREGATION (MENDEL'S FIRST LAW)

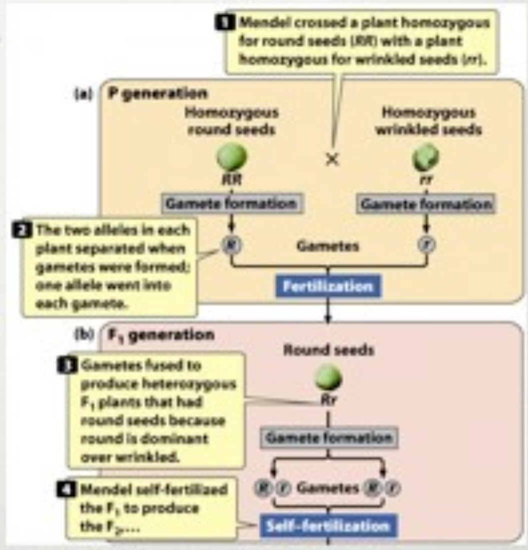
- Diploid organisms possess two alleles for each characteristic.
- These two alleles segregate (separate) when gametes are formed.
- One allele goes into each gamete.
- The two alleles segregate into gametes in equal proportions.

THE CONCEPT OF DOMINANCE

- When two different alleles are present in a genotype, only the trait encoded by one of them is observed in the phenotype.
- This allele is defined as the "dominant" allele.

SO, TO RECAP:

1. PRINCIPLE OF SEGREGATION

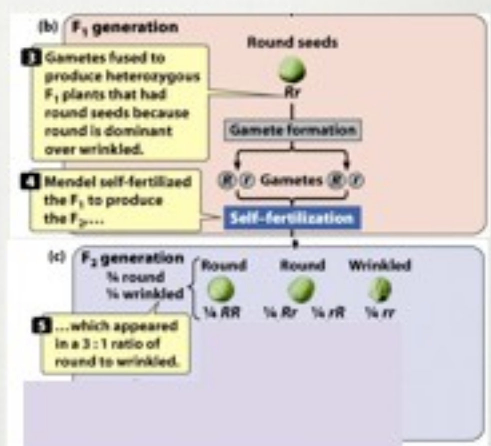


2. CONCEPT OF DOMINANCE

- F1 progeny are heterozygotes
- When they self-fertilize, you get an F2 generation....

THE F2 GENERATION

- F1 progeny produce two types of gametes in equal proportions
- These combine at random to generate the F2 generation
- Which results in a 3:1 ratio of round to wrinkled - why?



Predicting outcomes of a genetic cross: The Punnett Square

1. Determine the gametes that will be produced.
2. Put gametes from one parent along the upper edge of a Punnett square and those from the other down the left side.
3. Combine the gametes in each square to get the genotype of each class of progeny.
4. Write the phenotype of each class of progeny.

	R	*r*
R	*RR* Round	*Rr* Round
r	*Rr* Round	*rr* Wrinkled

3 ROUND: 1 WRINKLED

SLIGHT DETOUR (BUT IMPORTANT): THE TESTCROSS

- How do you determine the genotype of an organism that is displaying the dominant phenotype?
- <u>Testcross</u>: an individual of unknown genotype is crossed with a homozygous recessive individual to reveal the unknown genotype (Rr or RR).
- Recessive alleles "unmask" any dominant alleles present in the other parent

EXAMPLE:

- We have a plant that produces round seeds
- What are the possible genotypes?

THE TESTCROSS

- Cross the round-seeded parent to a wrinkled-seeded "test parent" (genotype rr)
- Possible result 1: All round progeny
- What was the genotype of the parent?

	R	?
r	RR Round	?r Round
r	Rr Round	?r Round

THE TESTCROSS

- Cross the round-seeded parent to a wrinkled-seeded "test parent" (genotype rr)
- Possible result 1: 1/2 round progeny, 1/2 wrinkled progeny
- What was the genotype of the parent?

	R	?
r	RR Round	?r Wrinkled
r	Rr Round	?r Wrinkled

USING PROBABILITY TO PREDICT THE OUTCOME OF CROSSES

- Probability expresses the likelihood of the occurrence of a particular event
- Probability = $\frac{\text{Number of times that an event occurs}}{\text{Number of all possible outcomes}}$
- e.g. The probability of randomly drawing the king of hearts from a deck of cards is 1/52
  - There is only one card that is the king of hearts (1 event)
  - There are 52 cards that could be drawn (52 possible outcomes)

PROBABILITY, CONTINUED

- Probability can be expressed as either a fraction (1/52 in this case) or a decimal number (0.019 in this case)
- Two rules are useful for predicting ratios of offspring produced in genetic crosses:
  - <u>The multiplication rule</u>
  - <u>The addition rule</u>

MULTIPLICATION RULE

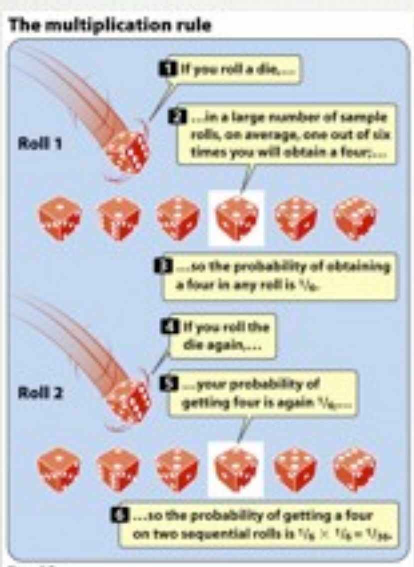


Figure 3.7a
Genetics: A Conceptual Approach, Third Edition

- The probability of two or more <u>independent</u> events occurring together is calculated by multiplying their independent probabilities.
- The key indicator for using the multiplication rule is the word "and".
- Cannot use the multiplication rule with dependent events

ADDITION RULE

- The probability of any one of two or more <u>mutually exclusive</u> events is calculated by adding the probabilities of these events.
- The indicators for using the addition rule are the words "either" and "or".

APPLYING PROBABILITY TO GENETICS

Rr x Rr

Gametes: 1/2 R, 1/2 r   1/2 R, 1/2 r

Probability R = 1/2, Probability r = 1/2 (in both cases)

- Use multiplication rule to determine the probability of each possible type of progeny:

	Phenotypes
Probability RR progeny = 1/2 x 1/2 = 1/4	round
Probability Rr progeny = 1/2 x 1/2 = 1/4	round
Probability rR progeny = 1/2 x 1/2 = 1/4	round
Probability rr progeny = 1/2 x 1/2 = 1/4	wrinkled
	3/4 round: 1/4 wrinkled

APPLYING PROBABILITY TO GENETICS

Rr x Rr

Gametes: 1/2 R, 1/2 r   1/2 R, 1/2 r

Probability R = 1/2, Probability r = 1/2 (in both cases)

- Use addition rule to determine the overall phenotypic ratios:

Probability of round progeny = 1/4 + 1/4 + 1/4 = 3/4
Probability of short progeny = 1/4

BREAK

- BACK IN 10 MINUTES....

USING PROBABILITY TO ANSWER MORE COMPLEX QUESTIONS

- Example: Two parents are heterozygous for albinism, a recessive condition (Aa x Aa)
- Probability of an aa child with albinism = 1/2 x 1/2 = 1/4

  Probability of an unaffected AA or Aa child = 3/4
- What is the probability of these parents having a total of three children, all with albinism?
  - Probability = 1/4 x 1/4 x 1/4 = 1/64

USING PROBABILITY TO ANSWER MORE COMPLEX QUESTIONS

- What about the probability of this couple having one child with albinism and two with normal pigmentation?

  a) #1 albinism, #2 unaffected, #3 unaffected, Probability = 1/4 x 3/4 x 3/4 = 9/64

  b) #1 unaffected, #2 albinism, #3 unaffected, Probability = 3/4 x 1/4 x 3/4 = 9/64

  c) #1 unaffected, #2 unaffected, #3 albinism, Probability = 3/4 x 3/4 x 1/4 = 9/64

  - We then apply the addition rule (why?):
  - 9/64 + 9/64 + 9/64 = 27/64

USING PROBABILITY TO ANSWER MORE COMPLEX QUESTIONS

- What about the probability of this couple having five children, two with albinism and three with normal pigmentation?
- Would require figuring out MANY different combinations - too many for an exam (or a reasonable person with another option).
- The solution: the probability equation...

THE PROBABILITY EQUATION

$$P = \frac{n!}{s!t!} p^s q^t$$

P = overall probability of event X
with probability p
occurring s times
and event Y
with probability q
occurring t times

! stands for factorial, the product of all integers from n to 1

THE PROBABILITY EQUATION

$$P = \frac{n!}{s!t!} p^s q^t$$

In this example:

Event X is the occurrence of a child with albinism, so p = 1/4
Event Y is the occurrence of an unaffected child, so q = 3/4
s = number of children with albinism, 2
t = number of unaffected children, 3
n = number of events, 5 children

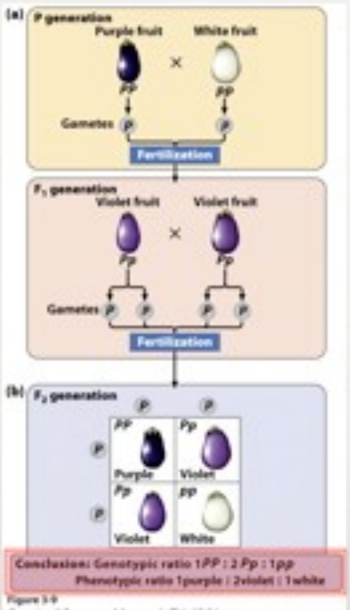
Plugging in the numbers:

$$P = \frac{5!}{2!3!} (1/4)^2(3/4)^3 = \frac{5 \times 4 \times 3 \times 2 \times 1}{(2 \times 1) \times (3 \times 2 \times 1)} (1/4)^2(3/4)^3 = 0.26$$

INCOMPLETE DOMINANCE

- Not all phenotypes have traits that exhibit true dominance:
  - Mendel crossed two homozygous varieties that differed in their flowering time by an average of 20 days.
    - The F_1 plants had an intermediate flowering time between those of the two parents.
  - When a heterozygote has a phenotype intermediate between the phenotypes of the two homozygotes, the trait is said to display <u>incomplete dominance.</u>

EXAMPLE: FRUIT COLOR IN EGGPLANT



- With incomplete dominance, genotypic and phenotypic ratios of the offspring are the same.
- Could you obtain eggplants that are pure breeding for violet fruit?

GENETICS SYMBOLS

- In genetic crosses, italicized symbols are used to designate alleles
  - Lowercase letters traditionally represent recessive alleles
  - Uppercase letters represent dominant alleles
  - 1-4 letters can be used to designate an allele

GENETICS SYMBOLS

- The common allele for a character is called the wild type allele.
  - Symbolized with 1-4 letters and a plus sign.
  - The letters are usually chosen based on the mutant phenotype.
  - For example:
    - The recessive allele for white eyes in Drosophila is represented as w
    - The wild type allele is represented by w^+, or just +

GENETICS SYMBOLS

- A slash may be used to distinguish alleles present in an individual genotype.
  - e.g. The genotype of a w heterozygote can be written:

    w/w^+, or simply w/+
  - Genotypes at more than one locus can be represented with a space or semicolon between the loci: $w/w^+; y/y^+$

RATIOS IN SIMPLE CROSSES

Table 3.2 Phenotypic ratios for simple genetic crosses (crosses for a single locus)

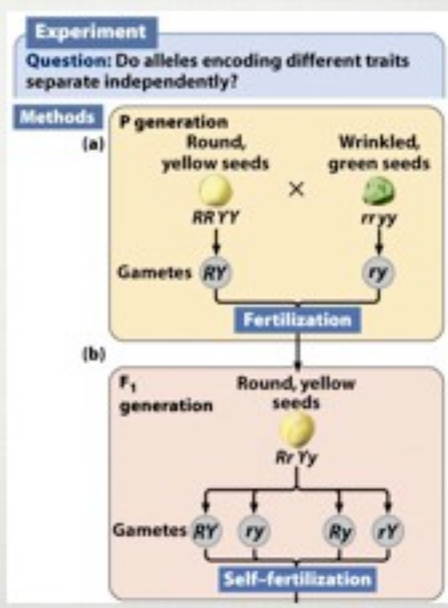
Ratio	Genotypes of Parents	Genotypes of Progeny	Type of Dominance
3 : 1	*Aa* × *Aa*	$^3/_4$ *A_* : $^1/_4$ *aa*	Dominance
1 : 2 : 1	*Aa* × *Aa*	$^1/_4$ *AA* : $^1/_2$ *Aa* : $^1/_4$ *aa*	Incomplete dominance
1 : 1	*Aa* × *aa*	$^1/_2$ *Aa* : $^1/_2$ *aa*	Dominance or incomplete dominance
	Aa × *AA*	$^1/_2$ *Aa* : $^1/_2$ *AA*	Incomplete dominance
Uniform progeny	*AA* × *AA*	All *AA*	Dominance or incomplete dominance
	aa × *aa*	All *aa*	Dominance or incomplete dominance
	AA × *aa*	All *Aa*	Dominance or incomplete dominance
	AA × *Aa*	All *A_*	Dominance

Note: A line in a genotype, such as *A_*, indicates that any allele is possible.

Table 3-2
Genetics: A Conceptual Approach, Third Edition

MORE THAN ONE GENE: DIHYBRID CROSSES

- Dihybrid crosses involve parents with different alleles at two loci.
- Such crosses result in a 9:3:3:1 ratio in the F_2 progeny
  - 9/16 have both dominant traits
  - 3/16 have the one dominant trait and one recessive trait
  - 3/16 have the other dominant trait
  - 1/16 have both recessive traits



Dihybrid crosses reveal the Principle of Independent Assortment

- Where do these ratios come from?
- We're now dealing with two independent genes
  - alleles will segregate without regard for one another
  - Four equally likely combinations (one allele at each locus from each parent):

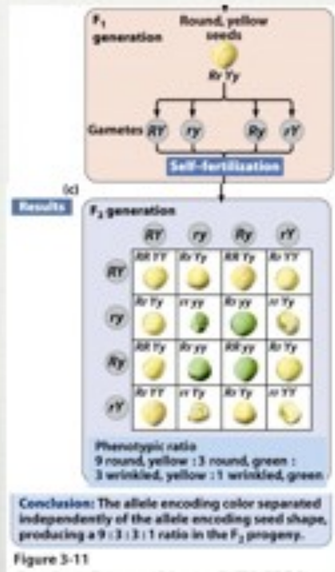


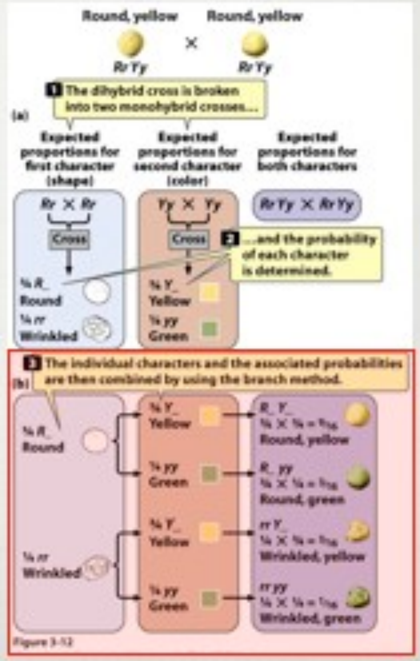
Figure 3-11

INDEPENDENT ASSORTMENT

- The principle of independent assortment is an extension of the principle of segregation
  - Principle of Segregation: Two alleles of a locus separate when gametes are formed.
  - Principle of Independent Assortment: When two alleles separate, their separation is independent of the separation of alleles at other loci.
    - Applies only to loci on different chromosomes due to independent segregation of homologous chromosomes during anaphase I of meiosis.

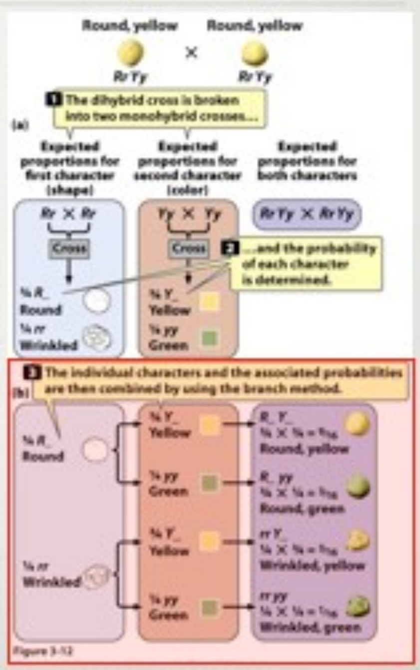
PROBABILITY AND THE BRANCH DIAGRAM

- Branch diagrams simplify dihybrid crosses, by treating them as two monohybrid crosses.
- Column 1: list the proportions of the phenotypes for one character (e.g. 3/4 round and 1/4 wrinkled).
- Column 2: list the proportions of the phenotype for the second character (e.g. 3/4 yellow and 1/4 green) twice.



PROBABILITY AND THE BRANCH DIAGRAM

- Multiply the probabilities for each trait along that branch.
- Particularly useful
  - if we need the probability of only a particular phenotype or genotype.
  - If there are different alleles at more than 2 loci.

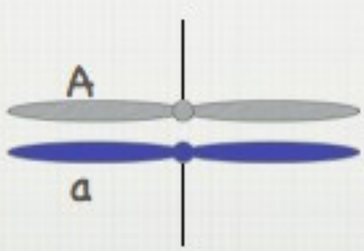


MENDEL, MEIOSIS, AND THE CHROMOSOME THEORY OF HEREDITY

- ☐ How does chromosome behavior in meiosis explain Mendel's Laws?

THE LAW OF SEGREGATION

The two alleles at each genetic locus segregate from one another in the formation of gametes.

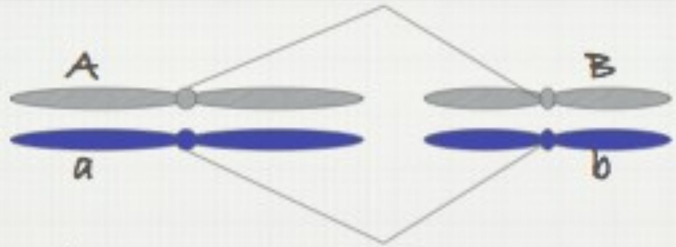


GAMETES:

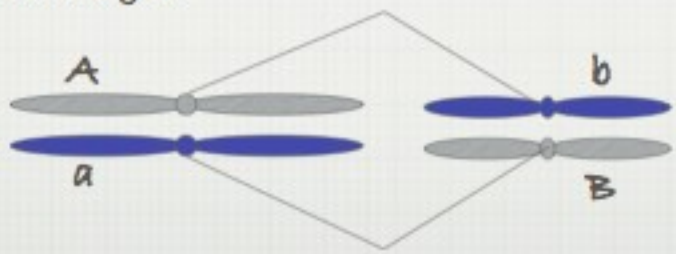
- 50% A
- 50% a

In meiosis, homologous chromosomes segregate, taking their alleles with them.

INDEPENDENT ASSORTMENT



Is as likely as:



Ab or aB gametes are as likely as AB or ab gametes

PROGENY RATIOS MAY DIFFER FROM EXPECTED RATIOS BY CHANCE

- The outcome of genetic crosses is governed by probability
- When you flip a coin 10 times, you EXPECT a 5:5 ratio of heads to tails
  - You may, however, OBSERVE a 6:4 ratio…or 3:7.
  - This is explained by chance (and by low sample size)
  - The results of meiosis are similarly affected by random chance
  - How do we tell if the deviation is based on chance or an actual difference in the biology?

THE CHI-SQUARE TEST

- Gives the probability that the difference between observed and expected values is due to chance.

Example: Bb x Bb
black black

↓

Expected Ratio:	3/4 black	1/4 gray	
If n=50, Expect:	37.5	12.5	
Observed #1:	39	11	Chance?
Observed #2:	30	20	Complex inheritance or reduced viability of bb animals?

THE CHI-SQUARE TEST

- Null hypothesis:
  - Chance is responsible for the difference between observed and expected values.
- High probability → Null hypothesis true / Chance produced deviation
- Low probability → Null hypothesis false / Another factor produced deviation

Step 1: Determine the chi-square (χ^2) value

If n=50, Expect:	37.5	12.5	
Observed #1:	39	11	Chance?
Observed #2:	30	20	Complex inheritance or reduced viability of bb animals?

Formula: $\chi^2 = \Sigma \dfrac{(\text{observed - expected})^2}{\text{expected}}$

Case #1

$$\chi^2 = \frac{(39 - 37.5)^2}{37.5} + \frac{(11 - 12.5)^2}{12.5} = 0.06 + 0.18 = 0.24$$

Step 1: Determine the chi-square (χ^2) value

If n=50, Expect:	37.5	12.5	
Observed #1:	39	11	Chance?
Observed #2:	30	20	Complex inheritance or reduced viability of bb animals?

Case #1

$$\chi^2 = \frac{(39 - 37.5)^2}{37.5} + \frac{(11 - 12.5)^2}{12.5} = 0.06 + 0.18 = 0.24$$

Case #2

$$\chi^2 = \frac{(30 - 37.5)^2}{37.5} + \frac{(20 - 12.5)^2}{12.5} = 1.5 + 4.5 = 6.0$$

STEP 2: DETERMINE THE PROBABILITY (*P*)

Goal: Determine the probability the deviation between the observed and expected results could be due to chance.

- Compare calculated chi-square values (0.24 and 6.0) with theoretical values that have the same degrees of freedom in a chi-square table.

- <u>Degrees of freedom</u>
  - Number of ways in which the expected classes are free to vary
  - Degrees of freedom (df) = $n - 1$
    - n is the number of expected phenotypes
    - $n = 2$ (black and gray)
    - $df = n - 1 = 2 - 1 = 1$

STEP 2: DETERMINE THE PROBABILITY (*P*)

Table 3.4 Critical values of the χ^2 distribution

df	0.995	0.975 > P1 >	0.9	0.5	0.1 > P2 >	0.05	0.025	0.01	0.005
1	0.000	0.000	0.016	0.455	2.706	3.841	5.024	6.635	7.879
2	0.010	0.051	0.211	1.386	4.605	5.991	7.378	9.210	10.597
3	0.072	0.216	0.584	2.366	6.251	7.815	9.348	11.345	12.838
4	0.207	0.484	1.064	3.357	7.779	9.488	11.143	13.277	14.860
5	0.412	0.831	1.610	4.351	9.236	11.070	12.832	15.086	16.750
6	0.676	1.237	2.204	5.348	10.645	12.592	14.449	16.812	18.548

<u>Case 1:</u> $0.9 > P > 0.5$

- Probability of chance being responsible for deviation is between 0.5 and 0.9, so chance is likely responsible for the slight deviation.

<u>Case 2:</u> $0.025 > P > 0.01$

- Probability of chance being responsible for deviation is between 0.025 and 0.01, so chance is not likely to be responsible. Another factor!

If <u>$P \geq 0.05$</u>, most scientists accept that chance may be responsible

If $P < 0.05$, chance is not likely responsible and a <u>significant difference</u> exists

FOR NEXT TIME:

- READ CHAPTERS 4 AND 5 (SEX DETERMINATION AND SEX-LINKED CHARACTERISTICS/EXTENSIONS AND MODIFICATIONS OF BASIC PRINCIPLES)
- PROBLEMS FOR THIS WEEK ARE AVAILABLE ON D2L. YOU SHOULD BE ABLE TO DO ALL OF THESE IN PREPARATION FOR EXAM 1