Basic Genetics (SQBS 2753)

Mendelian Inheritance

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Mendel and The Laws Of Inheritance

- Gregor Johann Mendel (1822-1884) - father of genetics
- Austrian monk
- Conducted landmark studies from 1856-1864, - thousands of crosses
- Kept meticulously accurate records that included quantitative analysis

Mendel Chose Pea Plants as His Experimental Organism

- Hybridization
  - The mating or crossing between two individuals that have different characteristics
    - Tall plant X dwarf plant
- Hybrids
  - The offspring that result from such a mating
  - Presumed to be a blending of the parent traits
  - Often observed to be different than either parent (hybrid vigor)
- Mendel observed them to be like one of the parents with respect to some traits – no blending

Mendel studied the inheritance of alternative traits in pea plants

- Mendel inferred laws of genetics that allowed predictions about which traits would appear, disappear, and then reappear
  - This work was done in his garden at a monastery
- Mendel's paper "Experiments in plant hybrids" was published in 1866 and became the cornerstone of modern genetics

Keys to the success of Mendel's experiments

- Pure-breeding lines of peas (*Pisum sativum*)
  - Breeding could be done by cross-fertilization or selfing
  - Large numbers of progeny produced within a short time
  - Traits remained constant in crosses within a line
- Inheritance of alternative forms of traits
  - Antagonistic pairs of "either-or" traits: e.g. purple or white, yellow or green
- Brilliant experimentalist
  - Planned experiments carefully
  - Controlled the plant breeding
  - Analyzed results mathematically

Mendel Studied Seven Traits That Bred True

- The morphological characteristics of an organism are termed characters or traits
- A variety that produces the same trait over and over again is termed a true-breeder

Seven traits studied by Mendel

Trait	Dominant	Recessive
Flower colour	Purple	White
Flower position	Axial	Terminal
Seed colour	Yellow	Green
Seed shape	Round	Wrinkled
Pod shape	Inflated	Constricted
Pod colour	Green	Yellow
Height	Tall	Dwarf

MONOHYBRID CROSSES

The Principles of Dominance and Segregation

Mendel's Experiments

- Crossed two variants differing in only one trait
  - a monohybrid cross

Monohybrid cross:

Tall plant × Dwarf plant

	Experimental			Conceptual
P plant:	Tall	×	Dwarf	*TT* × *tt*
Gametes:		↓		*T* and *t*
F_1 plants:	All Tall			*Tt*
	- SELF-FERTILIZATION -			*Tt* × *Tt*
F_2 plants:				↓
Phenotypic ratio	Tall: dwarf 3:1			T- : tt
Genotypic ratio				TT: Tt : tt 1 : 2 : 1

Parent plants: **Purple flower PP** X **White flower pp**

Gametes: P p

F_1 generation: **Purple flower Pp**

Self-fertilization: **Purple flower Pp** X **Purple flower Pp**

F_2 generation:

	P	*p*
P	*PP*	*Pp*
p	*Pp*	*pp*

DATA FROM MENDEL'S MONOHYBRID CROSSES

P Cross	F_2 progeny	Ratio
Tall X dwarf plants	787 tall, 277 dwarf	2.84:1
Round X wrinkled seeds	5,474 round, 1,850 wrinkled	2.96:1
Yellow X Green seeds	6,022 yellow, 2,001 green	3.01:1
Purple X white flowers	705 purple, 224 white	3.15:1
Axial X terminal flowers	651 axial, 207 terminal	3.14:1
Smooth X constricted pods	882 smooth, 229 constricted	2.95:1
Green X yellow pods	428 green, 152 yellow	2.82:1

Interpreting the Data

- For all seven traits studied
  1. The F_1 generation showed only one of the two parental traits
  2. The F_2 generation showed an ~ 3:1 ratio of the two parental traits

- These results refuted a blending mechanism of heredity

Summary

1. A pea plant contains two discrete hereditary factors, one from each parent
2. The two factors may be identical or different
3. When the two factors of a single trait are different
   - One is **dominant** and its effect can be seen
   - The other is **recessive** and is masked
4. During gametogenesis (meiosis), the paired factors segregate randomly so that half of the gametes received one factor and half of the gametes received the other

The Principle of Dominance

- *In a heterozygote, one allele may conceal the presence of another*

The Principle of Segregation

- *In a heterozygote, two different alleles segregate from each other during the formation of gametes*

Definitions of commonly used terms

- Phenotype is an observable characteristic (e.g. yellow or green pea seeds)
- Genotype is a pair of alleles in an individual (e.g. YY or Yy)
- Homozygote has two identical alleles (e.g. YY or yy)
- Heterozygote has two different alleles (e.g. Yy)
  - The heterozygous phenotype defines the dominant allele (e.g. Yy peas are yellow, so the yellow Y allele is dominant to the green y allele)
  - A dominant allele with a dash represents an unknown genotype (e.g. Y− stands for either YY or Yy)

Back Cross

- **The F1 progeny are mated back to one of their parents** (or to individuals with a genotype identical to parents).

Example

P:	***RR*** ♀ **Round seeds** **X** ***rr*** ♂ **wrinkled seeds**
F1:	*Rr* ♂ and ♀ **Round seeds -males and female plants**
F1 Back cross :	***Rr*** ♂ Round male X ***RR*** ♀ Round mother
Backcross progeny	***½ RR, ½ Rr*** All- Round progenies

Testcross

a cross to determine between a homozygous dominant genotype and heterozygous genotype which has the same phenotype parent is always homozygous recessive *for all the genes*

Example: Testcross of a tall plant which only produced tall progeny

P :	***T -*** **Tall female (genotype unknown)** **X** ***tt*** **dwarf male (testcross parent)**
Gamete :	***T, ?*** ***t***
F1:	All progenies are **tall**
Conclusion:	*The female parent must be producing only one kind of gamete, hence she is homozygous dominant **TT**.*

DIHYBRID CROSSES

The Principle of Independent Assortment

Mendel's Experiments

- Mendel also performed dihybrid crosses
  - Crossing individual plants that differ in two traits
- For example
  - Trait 1 = Seed texture (round vs. wrinkled)
  - Trait 2 = Seed color (yellow vs. green)
- There are two possible patterns of inheritance for these traits

Dihybrid cross:

Yellow, Round × Green Wrinkled Seeds

	Experimental			Conceptual
P plant:	Yellow, Round	×	Green, Wrinkled	*YYRR* × *yyrr*
Gametes:	↓			*YR* and *yr*
F_1 plants:	All yellow and round seeds			*YyRr*
	- SELF-FERTILIZATION -			*YyRr* × *YyRr*
F_2 plants:				↓
Phenotypic ratio	9 Yellow, round 3 Yellow, wrinkled 3 Green, round 1 Green, wrinkled			*Y – R –* *Y – rr* *yyR –* *yyrr*

F_2 Generation

Male gametes

Female gametes	*YR*	*Yr*	*yR*	*yr*
YR	*YYRR*	*YYRr*	*YyRR*	*YyRr*
Yr	*YYRr*	*YYrr*	*YyRr*	*Yyrr*
yR	*YyRR*	*YyRr*	*yyRR*	*yyRr*
yr	*YyRr*	*Yyrr*	*yyRr*	*yyrr*

Genotypes	Genotypic ratio	Phenotypes	Phenotypic ratio
YYRR *YYRr* *YyRR* *YyRr*	*1* *2* *2* *4*	*Yellow, round*	*9*
Yyrr *Yyrr*	*1* *2*	*Yellow, wrinkled*	*3*
yyRR *yyrr*	*1* *2*	*Green, round*	*3*
yyrr	*1*	*Green, wrinkled*	*1*

DATA FROM ONE OF MENDEL'S DIHYBRID CROSSES

P Cross	F_1 generation	F_2 generation
Round, Yellow seeds X wrinkled, green seeds	All round, yellow	315 round, yellow seeds 101 wrinkled, yellow seeds 108 round, green seeds 32 green, wrinkled seeds

Interpreting the Data

- The F_2 generation contains seeds with novel combinations not found in the parentals
  - Round and Green
  - Wrinkled and Yellow
- These are nonparentals
- Occurrence contradicts the linkage model

Principle of Independent Assortment

- If the genes,assort independently the predicted phenotypic ratio in the F_2 generation would be 9:3:3:1

P Cross	F_1 generation	F_2 generation	Ratio
Round, Yellow seeds X wrinkled, green seeds	All round, yellow	315 round, yellow seeds	9.8
		101 wrinkled, yellow seeds	3.2
		108 round, green seeds	3.4
		32 green, wrinkled seeds	1.0

- Mendel's data was very close to segregation expectations
- Thus, he proposed the law of Independent assortment
  - During gamete formation, the segregation of any pair of hereditary determinants is independent of the segregation of other pairs

The Principle of Independent Assortment

- The alleles of different genes segregate, or as we sometimes say, assort, independently of each other

Applications of Mendel's Principles

To predict the outcomes of crosses between different traits of organisms

(A) The Punnett Square Method

- A Punnett square is a grid that enables one to predict the outcome of simple genetic crosses
- Proposed by the English geneticist, Reginald Punnett

Punnett Squares

Axial flowers X Axial flowers Cross of heterozygotes

1. Write down the genotypes of both parents
   - Male parent = *Aa*
   - Female parent = *Aa*

2. Write down the possible gametes each parent can make.
   - Male gametes: *A* or *a*
   - Female gametes: *A* or *a*

3. Create an empty Punnett square

Male gametes

	A	*a*
A	*AA*	*Aa*
a	*Aa*	*aa*

Female gametes

4. Fill in the Punnett square with the possible genotypes of the offspring

5. Determine the relative proportions of genotypes and phenotypes of the offspring

- Genotypic ratio

  AA : *Aa* : *aa*

  1 : 2 : 1

- Phenotypic ratio

  Axial : terminal

  3 : 1

Mendel's results and the Punnett square reflect the basic rules of probability

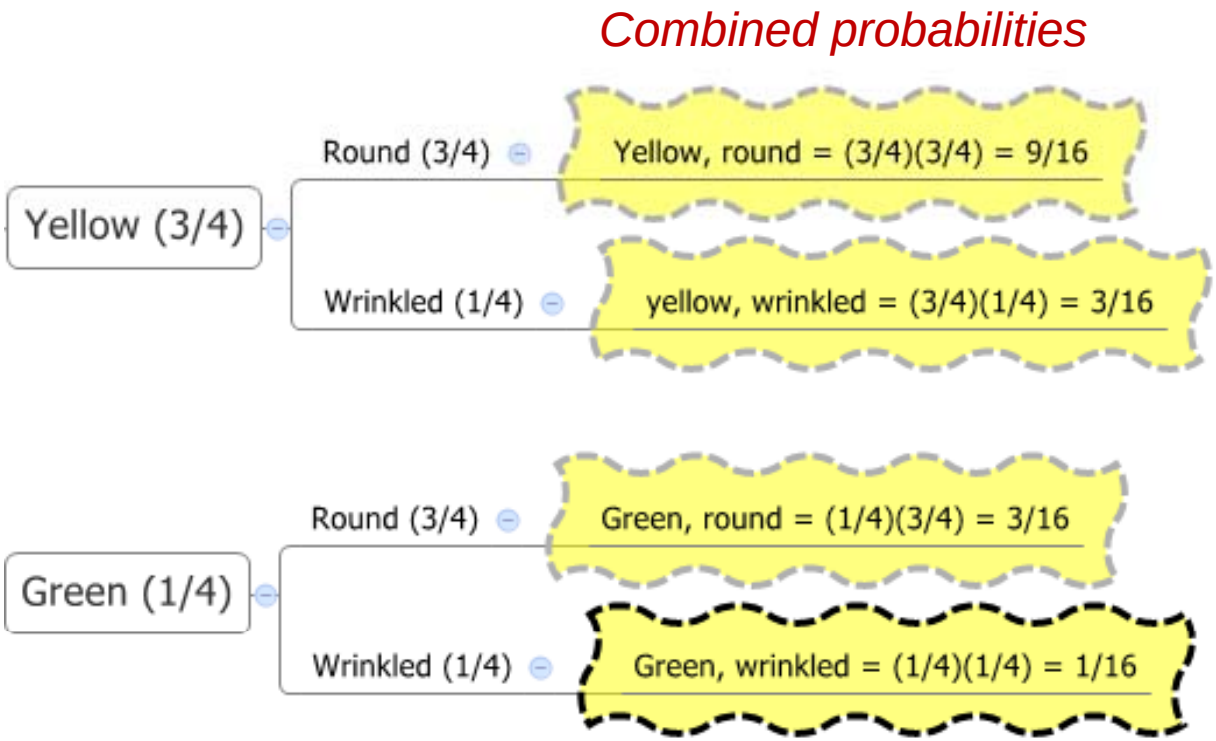
- Product rule: probability of two independent events occurring together is the product of their individual probabilities
  - What is the probability that event 1 AND event 2 will occur?
  - P(1 and 2) = probability of event 1 X probability of event 2
  -
- Sum rule: probability of either of two mutually exclusive events occurring is the sum of their individual probabilities
  - What is the probability that event 1 OR event 2 will occur?
  - P(1 or 2) = probability of event 1 + probability of event 2

Applying probability to Mendel's crosses

- From a cross of **Gg x Gg** peas:
  - What is the chance of getting ***GG*** offspring?
    - Chance of G pollen is 1/2
    - Chance of G ovule is 1/2
    - Chance of G pollen and G ovule uniting is 1/2 x 1/2 = ¼
  - What is the chance of getting ***Gg*** offspring?
    - Chance of G pollen uniting with g ovule is 1/2 x 1/2 = 1/4
    - Chance of g pollen uniting with G ovule is 1/2 x 1/2 = 1/4
    - Chance of either event happening is 1/4 + 1/4 = 1/2

(B) Forked-line Method (fork diagram)

- Calculate predicted ratios of offspring by multiplying probabilities of independent events
- Cross: yellow, round x yellow, round



The Probability Method

Dihybrid Cross: **CcDd** × **CcDd**

Segregation of D gene

Segregation of C gene	*D* - (3/4)	*dd* (1/4)
C - (3/4)	*C- D* - (1/4)	*C - dd* (1/4)
cc (1/4)	*D- cc* (1/4)	*ccdd* (1/4)

F_2 generation

Genotype	Frequency	Phenotype	Frequency
C – D -	9/16	Dominant for both genes	9/16
C – dd *ccD –* *ccdd*	3/16 3/16 1/16	Recessive for at least one gene	7/16

(C) The Probability Method

Monohybrid Cross: **Dd × Dd**

Male gametes

Female gametes	*D* (1/2)	*d* (1/2)
D (1/2)	DD (1/4)	Dd (1/4)
d (1/2)	Dd (1/4)	Dd (1/4)

F_2 generation

Genotype	Frequency	Phenotype	Frequency
DD	1/4	Dominant	3/4
Dd	1/2		
dd	1/4	Recessive	1/4

Probability

- To compute probability, we can use three mathematical operations
  - Sum rule
  - Product rule
  - Binomial expansion equation

Sum rule

- The probability that one of two or more mutually exclusive events will occur is the sum of their respective probabilities

- Consider the following example in mice
- Gene affecting the ears
  - *De* = Normal allele
  - *de* = Droopy ears
- Gene affecting the tail
  - *Ct* = Normal allele
  - *ct* = Crinkly tail

***Example**: What is the probability that an offspring of the above cross will have normal ears and a normal tail **or** have droopy ears and a crinkly tail?*

- If two heterozygous (*Dede Ctct*) mice are crossed
- Then the predicted ratio of offspring is
  - 9 with normal ears and normal tails
  - 3 with normal ears and crinkly tails
  - 3 with droopy ears and normal tails
  - 1 with droopy ears and crinkly tail
- These four phenotypes are mutually exclusive
  - A mouse with droopy ears and a normal tail *cannot* have normal ears and a crinkly tail

- Applying the sum rule
  - Step 1: Calculate the individual probabilities

$$P_{(\text{normal ears and a normal tail})} = 9/(9 + 3 + 3 + 1) = 9/16$$

$$P_{(\text{droopy ears and crinkly tail})} = 1/(9 + 3 + 3 + 1) = 1/16$$

  - Step 2: Add the individual probabilities

    9/16 + 1/16 = 10/16

- 10/16 can be converted to 0.625
  - Therefore 62.5% of the offspring are predicted to have normal ears and a normal tail *or* droopy ears and a crinkly tail

Product rule

- The probability that two or more independent events will occur is equal to the product of their respective probabilities

- Note
  - Independent events are those in which the occurrence of one does not affect the probability of another

Example:

Two heterozygous individuals plan to start a family What is the probability that the couple's first three children will all have congenital analgesia?

- Consider the disease congenital analgesia
  - Recessive trait in humans
  - Affected individuals can distinguish between sensations
    - However, extreme sensations are not perceived as painful
  - Two alleles
    - *P* = Normal allele
    - *p* = Congenital analgesia

- Applying the product rule
  - Step 1: Calculate the individual probabilities
    - This can be obtained via a Punnett square

$$P_{(\text{congenital analgesia})} = 1/4$$

  - Step 2: Multiply the individual probabilities

$$1/4 \times 1/4 \times 1/4 = 1/64$$

- 1/64 can be converted to 0.016
  - Therefore 1.6% of the time, the first three offspring of a heterozygous couple, will all have congenital analgesia

Binomial Expansion Equation

- Represents all of the possibilities for a given set of unordered events

$$P = \frac{n!}{x!\,(n-x)!}\, p^{x}\, q^{n-x}$$

- where
  - p = probability that the unordered number of events will occur
  - n = total number of events
  - x = number of events in one category
  - p = individual probability of x
  - q = individual probability of the other category

- Note:
  - p + q = 1
  - The symbol ! denotes a factorial
    - n! is the product of all integers from n down to 1
      - 4! = 4 X 3 X 2 X 1 = 24
      - An exception is 0! = 1

- Question
  - Two heterozygous brown-eyed (*Bb*) individuals have five children
  - What is the probability that two of the couple's five children will have blue eyes?

- Applying the binomial expansion equation
  - Step 1: Calculate the individual probabilities
    - This can be obtained via a Punnett square

$$P_{(\text{blue eyes})} = p = 1/4$$

$$P_{(\text{brown eyes})} = q = 3/4$$

  - Step 2: Determine the number of events
    - n = total number of children = 5
    - x = number of blue-eyed children = 2

  - Step 3: Substitute the values for *p*, *q*, *x*, and *n* in the binomial expansion equation

$$P = \frac{n!}{x!\,(n-x)!}\, p^{x}\, q^{n-x}$$

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

$$P = \frac{5 \times 4 \times 3 \times 2 \times 1}{(2 \times 1)\,(3 \times 2 \times 1)}\, (1/16)\,(27/64)$$

$$P = 0.26 \quad \text{or } 26\%$$

- Therefore 26% of the time, a heterozygous couple's five children will contain two with blue eyes and three with brown eyes

Problems

- A family with six children.
  i. What is probability that at least four will be girls?
  ii. What is probability that at least one but no more than four of the children will be girls?

Solution (i)

The probability that it will be a girl (p) is ½, boy (q) = ½

Event	Binomial Formula	Probability
4 girls and 2 boys	$[(6!)/(4!\ 2!) \times (1/2)^4(1/2)^2$	15/64
5 girls and 1 boy	$[(6!)/(5!\ 1!) \times (1/2)^5(1/2)^1$	6/64
6 girls and 0 boys	$[(6!)/(6!\ 0!) \times (1/2)^6(1/2)^0$	1/64

Therefore, the answer is (15/64) + (6/64) + (1/64) = **22/64**

Solution (ii)

The probability that it will be a girl (p) is ½, boy (q) = ½

Event	Binomial Formula	Probability
1 girl and 5 boys	$[(6!)/(1!\,5!) \times (1/2)^1(1/2)^5$	6/64
2 girl and 4 boys	$[(6!)/(2!\,4!) \times (1/2)^2(1/2)^4$	15/64
3 girls and 3 boys	$[(6!)/(3!\,3!) \times (1/2)^3(1/2)^3$	20/64
4 girls and 2 boys	$[(6!)/(4!\,2!) \times (1/2)^4(1/2)^2$	15/64

Therefore, the answer is (6/64) +(15/64) + (20/64) + (15/64) = 56/64

The Chi Square Test

- A statistical method used to determine goodness of fit
  - Goodness of fit refers to how close the observed data are to those predicted from a hypothesis
- Note:
  - The chi square test does not prove that a hypothesis is correct
    - It evaluates whether or not the data and the hypothesis have a good fit

The Chi Square Test

- The general formula is

$$\chi^2 = \Sigma \frac{(O - E)^2}{E}$$

- where
  - O = observed data in each category
  - E = observed data in each category based on the experimenter's hypothesis
  - Σ = Sum of the calculations for each category

- Consider the following example in *Drosophila melanogaster*
  - Gene affecting wing shape
    - c^+ = Normal wing
    - c = Curved wing
  - Gene affecting body color
    - e^+ = Normal (gray)
    - e = ebony
  - Note:
    - The wild-type allele is designated with a + sign
    - Recessive mutant alleles are designated with lowercase letters

- The Cross:
  - A cross is made between two true-breeding flies ($c^+c^+e^+e^+$ and *ccee).* The flies of the F_1 generation are then allowed to mate with each other to produce an F_2 generation.

- The outcome
  - F_1 generation
    - All offspring have straight wings and gray bodies
  - F_2 generation
    - 193 straight wings, gray bodies
    - 69 straight wings, ebony bodies
    - 64 curved wings, gray bodies
    - 26 curved wings, ebony bodies
    - 352 total flies

- Applying the chi square test
  - Step 1: Propose a hypothesis that allows us to calculate the expected values based on Mendel's laws
    - The two traits are independently assorting

– **Step 2**: Calculate the expected values of the four phenotypes, based on the hypothesis

- According to our hypothesis, there should be a 9:3:3:1 ratio on the F_2 generation

Phenotype	Expected probability	Expected number
straight wings, gray bodies	9/16	9/16 X 352 = 198
straight wings, ebony bodies	3/16	3/16 X 352 = 66
curved wings, gray bodies	3/16	3/16 X 352 = 66
curved wings, ebony bodies	1/16	1/16 X 352 = 22

– Step 3: Apply the chi square formula

$$\chi^2 = \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2} + \frac{(O_3 - E_3)^2}{E_3} + \frac{(O_4 - E_4)^2}{E_4}$$

$$\chi^2 = \frac{(193 - 198)^2}{198} + \frac{(69 - 66)^2}{66} + \frac{(64 - 66)^2}{66} + \frac{(26 - 22)^2}{22}$$

$$\chi^2 = 0.13 + 0.14 + 0.06 + 0.73$$

$$\chi^2 = 1.06$$

- Step 4: Interpret the chi square value
  - Low chi square values indicate a high probability that the observed deviations could be due to random chance alone
  - High chi square values indicate a low probability that the observed deviations are due to random chance alone
  - If the chi square value results in a probability that is less than 0.05 (ie: less than 5%)
    - The hypothesis is rejected

- **Step 4**: Interpret the chi square value
  - Before we can use the chi square table, we have to determine the degrees of freedom (*df*)
    - The *df* is a measure of the number of categories that are independent of each other
    - $df = n - 1$
      - where n = total number of categories
    - In our experiment, there are four phenotypes/categories
      - Therefore, df = 4 – 1 = 3

TABLE 2.1

Chi Square Values and Probability

Degrees of Freedom	$P = 0.99$	0.95	0.80	0.50	0.20	0.05	0.01
1	0.000157	0.00393	0.0642	0.455	1.642	**3.841**	**6.635**
2	0.020	0.103	0.446	1.386	3.219	**5.991**	**9.210**
3	0.115	0.352	1.005	**1.06**	2.366	4.642	**7.815**	**11.345**
4	0.297	0.711	1.649	3.357	5.989	**9.488**	**13.277**
5	0.554	1.145	2.343	4.351	7.289	**11.070**	**15.086**
6	0.872	1.635	3.070	5.348	8.558	**12.592**	**16.812**
7	1.239	2.167	3.822	6.346	9.803	**14.067**	**18.475**
8	1.646	2.733	4.594	7.344	11.030	**15.507**	**20.090**
9	2.088	3.325	5.380	8.343	12.242	**16.919**	**21.666**
10	2.558	3.940	6.179	9.342	13.442	**18.307**	**23.209**
15	5.229	7.261	10.307	14.339	19.311	**24.996**	**30.578**
20	8.260	10.851	14.578	19.337	25.038	**31.410**	**37.566**
25	11.524	14.611	18.940	24.337	30.675	**37.652**	**44.314**
30	14.953	18.493	23.364	29.336	36.250	**43.773**	**50.892**

From Fisher, R. A., and Yates, F. (1943) *Statistical Tables for Biological, Agricultural, and Medical Research.* Oliver and Boyd, London.

- Step 4: Interpret the chi square value
  - With *df* = *3*, the chi square value of 1.06 is slightly greater than 1.005 (which corresponds to P= 0.80)
  - A P = 0.80 means that values equal to or greater than 1.005 are expected to occur 80% of the time based on random chance alone
  - Therefore, it is quite probable that the deviations between the observed and expected values in this experiment can be explained by random sampling error

Modern Genetic Terminology

- Recessive
  - Null – no functional protein is produced
    - genetic null – gene is lost
    - functional null – no protein function
- Dominant
  - Gain-of-function (GOF)
    - protein functions is a new way
    - more protein is made than in wildtype
    - protein can not be regulated as in wildtype

MENDELIAN INHERITANCE IN HUMANS

- Many heritable traits in humans are caused by interaction of multiple genes
- Even with single-gene traits, determining inheritance pattern in humans can be tricky
  - Long generation time
  - Small numbers of progeny
  - No controlled matings
  - No pure-breeding lines

Some of the most common single-gene traits caused by recessive alleles in humans

Disease	Effect	Incidence of Disease
Thallassemia (chromosome 16 or 11)	Reduced amounts of hemoglobin; anemia, bone, and spleen enlargement	1/10 in parts of Italy
Sickle-cell anemia (chromosome 11)	Abnormal hemoglobin; sickle-shaped red cells, anemia, blocked circulation; increased resistance to malaria	1/625 African-Americans
Cystic fibrosis (chromosome 7)	Defective cell membrane protein; excessive mucus production; digestive and respiratory failure	1/2000 Caucasians
Tay-Sachs disease (chromosome 15)	Missing enzyme; buildup of fatty deposit in brain; buildup disrupts mental development	1/3000 Eastern European Jews
Phenylketonuria (PKU) (chromosome 12)	Missing enzyme; mental deficiency	1/10,000 Caucasians

Some of the most common single-gene traits caused by dominant alleles in humans

Disease	Effect	Incidence of Disease
Hypercholesterolemia (chromosome 19)	Missing protein that removes cholesterol from the blood; heart attack by age 50	1/122 French Canadians
Huntington disease (chromosome 4)	Progressive mental and neurological damage; neurologic disorders by ages 40 - 70	1/25,000 Caucasians

PEDIGREES

- In the study of human traits, there are not controlled parental crosses
- Rely on information from family trees or pedigrees
- Pedigree analysis is used to determine the pattern of inheritance of traits in humans

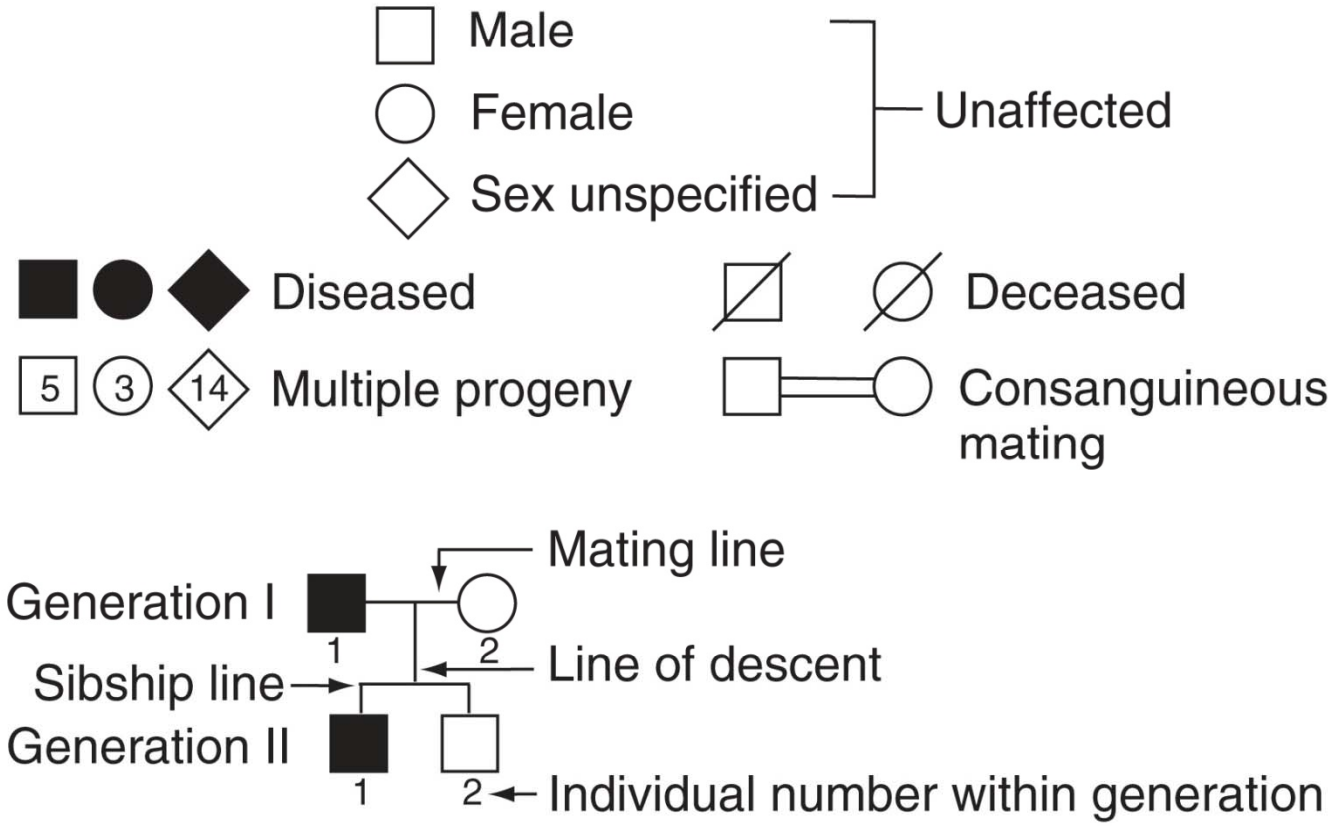
Pedigree Analysis

- Pedigree analysis is commonly used to determine the inheritance pattern of human genetic diseases
- Genes that play a role in disease may exist as
  - A normal allele
  - A mutant allele that causes disease symptoms
- Disease that follow a simple Mendelian pattern of inheritance can be
  - Dominant
  - Recessive

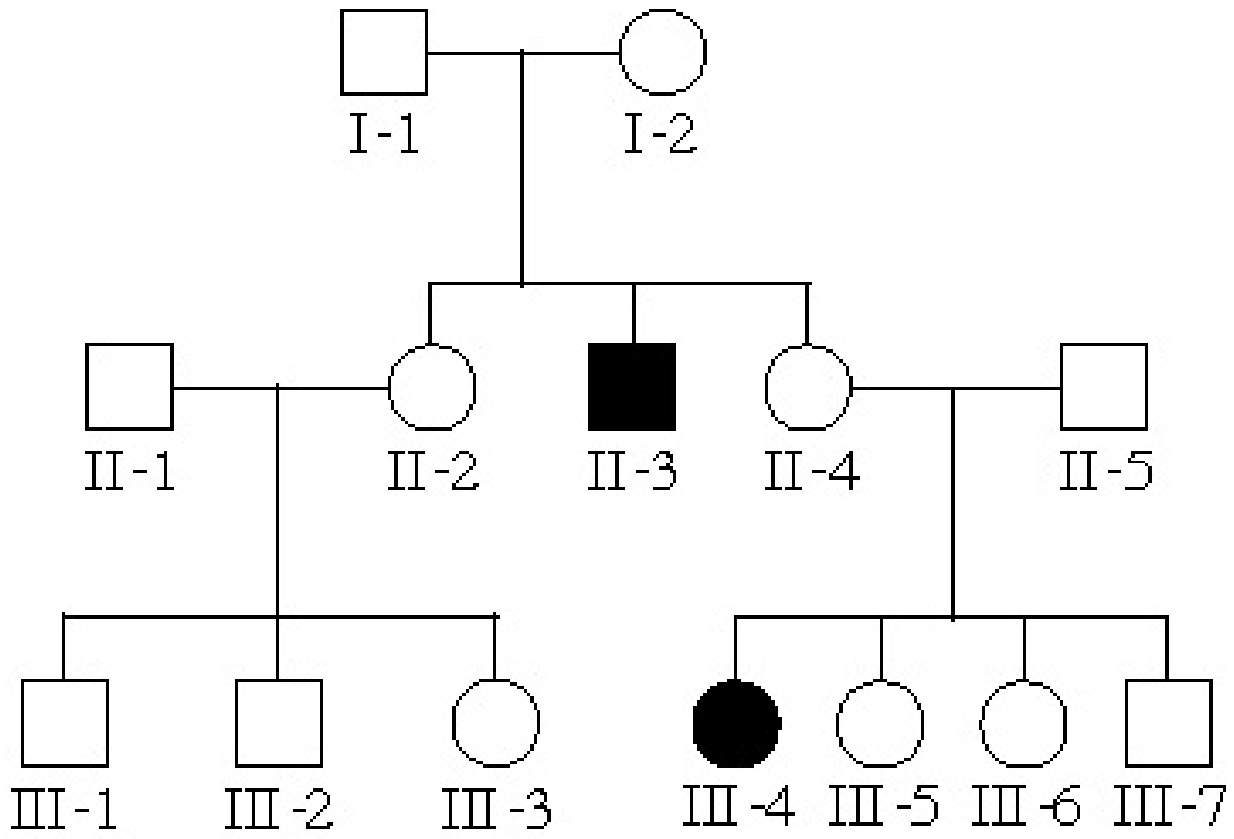
In humans, pedigrees can be used to study inheritance

- Pedigrees are orderly diagrams of a family's relevant genetic features
- Includes as many generations as possible (ideally, at least both sets of grandparents of an affected person)
- Pedigrees can be analyzed using Mendel's laws
  - Is a trait determined by alternate alleles of a single gene?
  - Is a trait dominant or recessive?

Symbols used in pedigree analysis



Human pedigree showing cystic fibrosis



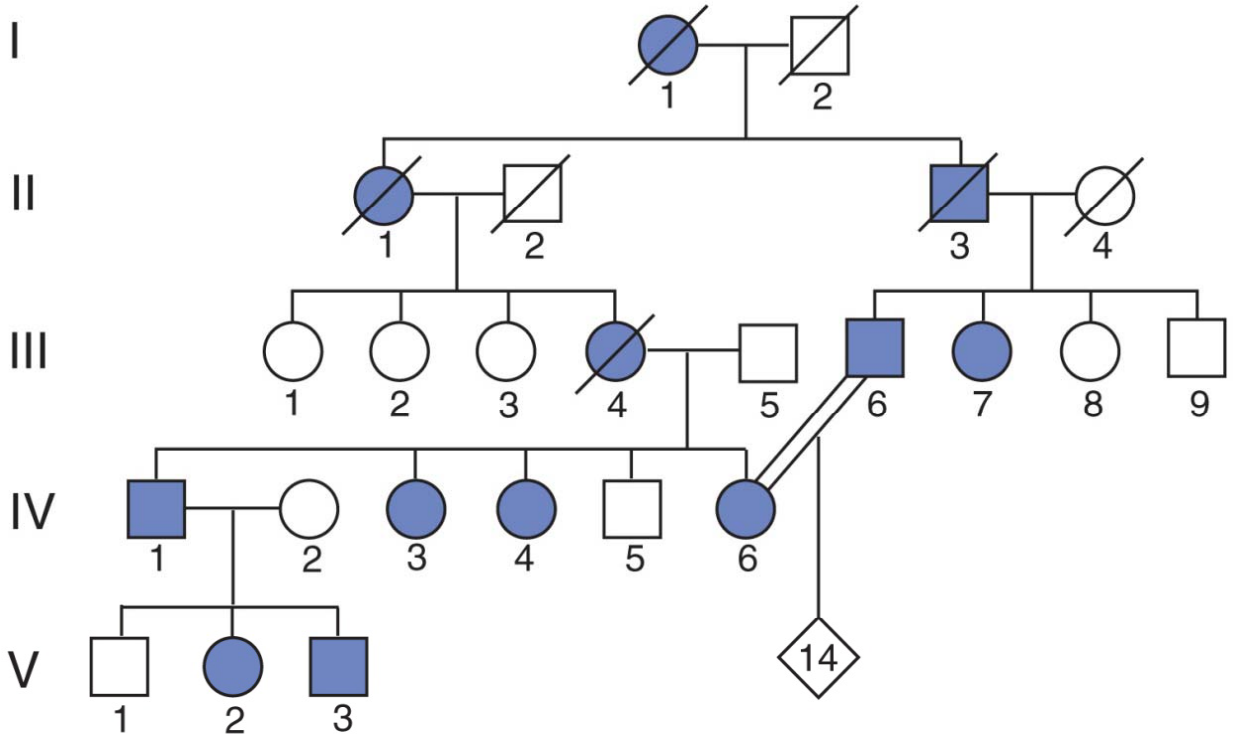
Dominant traits in pedigrees

- Three key aspects:

1. Affected children always have at least one affected parent
2. As a result, dominant traits show a vertical pattern of inheritance
3. Two affected parents can produce unaffected children, if both parents are heterozygotes

A vertical pattern of inheritance indicates a rare dominant trait; e.g Huntington disease

- Every affected person has at least one affected parent
- Mating between affected person and unaffected person is effectively a testcross



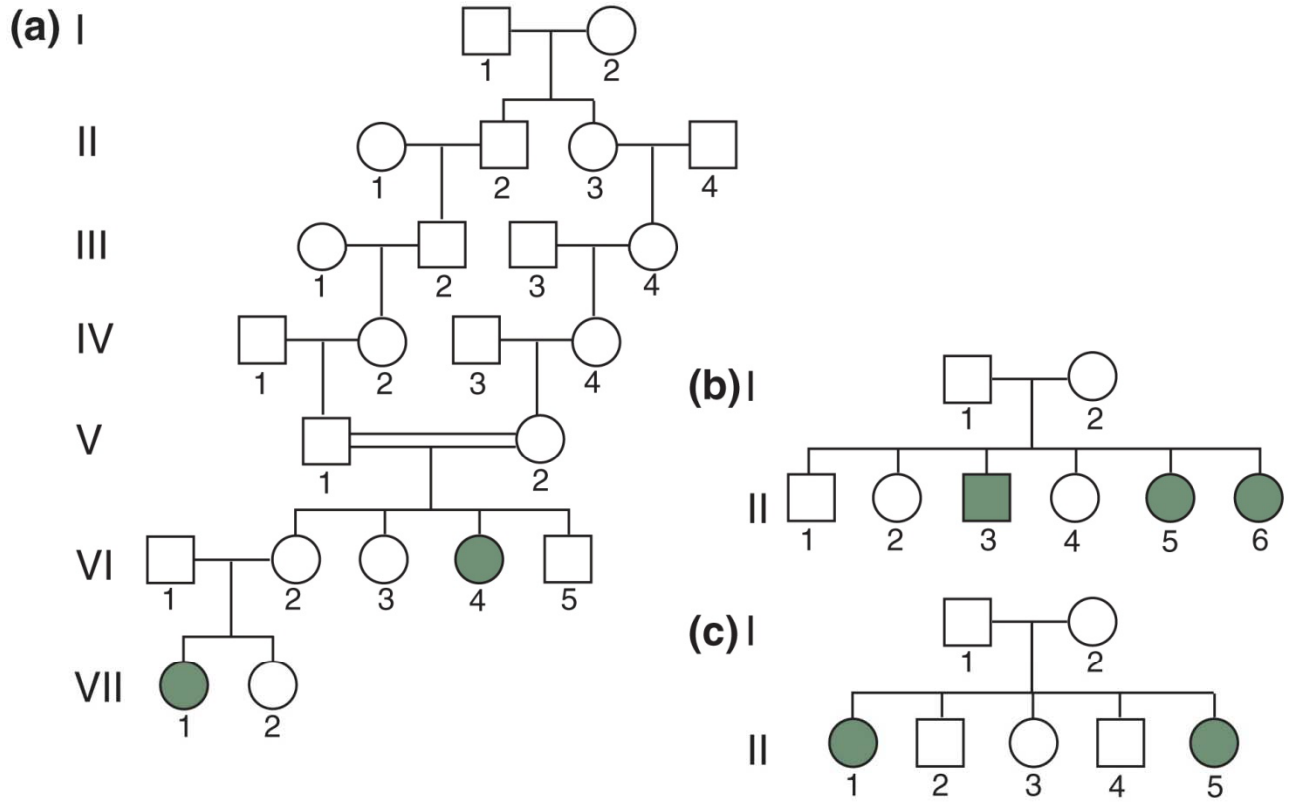
Recessive traits in pedigrees

- **Four** keys aspects:

1. Affected individuals can be the children of two unaffected carriers, particularly as a result of consanguineous matings
2. All the children of two affected parents should be affected
3. Rare recessive traits show a horizontal pattern of inheritance

A horizontal pattern of inheritance indicates a rare recessive trait; e.g. cystic fibrosis

- Parents of affected individuals are unaffected but are heterozygous (carriers) for the recessive allele



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