BIOL 230: Cell & Molecular Biology

Fall 2019 17-205 MW, Nov. 25-27ff

http://accounts.smccd.edu/staplesn/biol230/

1. **Find Anastasia & Alien GEL DATA under *ADDITIONAL MATERIALS*.**
2. **LAB: Finish Expt. 15 Data and Discussions today. Wed. – Review for next Monday's LAB Practical Exam!!!**
   - ***NOTE: Lab PRACTICAL will be given ONCE, ON-TIME, and absolutely NO Makeup Tests well be given!!***
3. **Final Research Report is Due on Wednesday, Dec. 4th.**
   - **The assignment will -- if you REALLY need the extra 2 days!! close PERMANENTLY on Friday, Dec. 6th**
   - **PROOFREAD, do NOT PLAGIARIZE any information, and EXPLAIN all of your learning in detail, & entirely in your OWN WORDS!!!**
4. **NOTE: All Exams and Reports are the KEY ASSIGNMENTS of this course. If you miss any one or any part of one, it may result in automatic failure of the course!! ☹**
5. **FINAL Objectives & Study Guide questions due THIS WED.!! NO MORE late assignments will be accepted after Wed. afternoon.**
6. **FINAL EXAM is Wednesday, Dec. 11th , 11:10AM-1:40PM**
   - **(Note: We stil have Lecture and Lab on Monday, Dec. 9th!!).**
   - **DO NOT MISS ANY CLASSES thru the Final Exam.**

1

REVIEW

1. Describe and diagram how **meiosis** generates **diversity** in gametes.
2. Define and explain the function of **Apoptosis**.

TODAY's Objectives: Students should be able to ......

1. Describe Mendel's experiments, their results, and how these lead him to formulate the Laws of **Segregation** and **Independent Assortment**.
   – *His methods, choice of organism, choice of characters, Monohybrid & Dihybrid Crosses.*
2. Define & give examples of ***gene, allele, dominant, recessive, homozygote, heterozygote, Genotype, Phenotype, monohybrid, dihybrid, true-breeding/purebred***, and ***locus***.
3. Calculate the probabilities of both the genotypic and the phenotypic outcomes of monohybrid and dihybrid crosses. Define ***test cross***.
4. Predict inheritance patterns in **human pedigrees** for recessive, dominant, X-linked recessive, and X-linked dominant traits.
5. Define and compare non-Mendelian phenotypic ratios produced by different **allelic interactions**: ***multiple alleles, incomplete dominance, codominance, pleiotropy***.
6. Describe and give examples of **Complementary genes** and **Epistasis**.
7. Distinguish between **sex determination** chromosomal patterns in birds, flies, and mammals. Define & describe the usefulness of a ***Reciprocal Cross***.
8. Define & explain the significance of **Cytoplasmic Inheritance**. *(Maternal or Non-Nuclear Inheritance)*
9. Calculate **genetic distances and orders** of **linked genes**.

❖ ***LAST Objectives & Study Guide Questions are your HOMEWORK between classes!!! DUE THIS WED. at the END of LECTURE!!***

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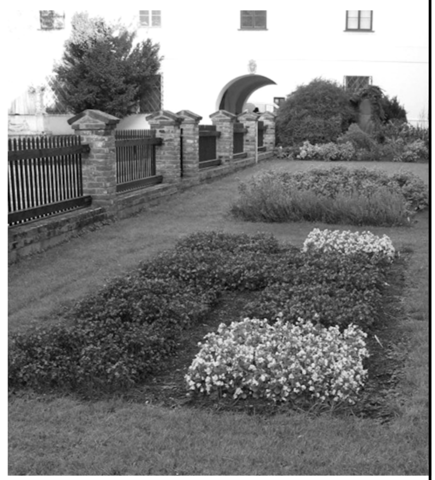
A. Mendel's Monohybrid Experiments

1) When the F_1 offspring were self-pollinated, **F_2 generation** showed a **3:1 phenotypic ratio.**

2) the recessive phenotype was present in 1/4 of the offspring.
   – ***Reappearance of the recessive phenotype refuted the blending hypothesis!!***



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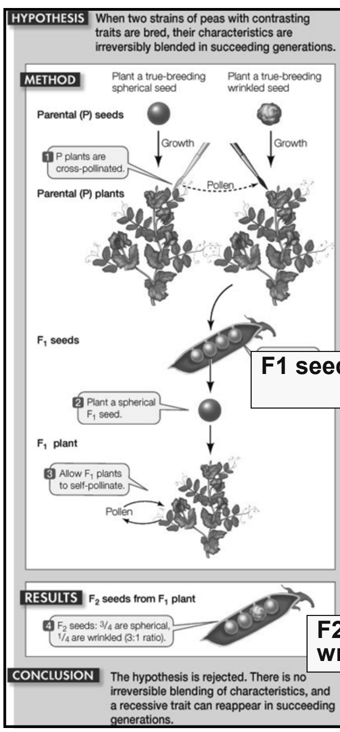

F1 seed = spherical
<u>= dominant</u>!

F2 seeds = ¼ wrink, ¾ spher.

<u>Monohybrid Cross:</u>

- Reappearance of **recessive** wrinkled trait in F2 *disproved blended inheritance*!!
- As did the LACK of an intermediate phenotype in F1
  - (no "slightly wrinkled" phen)

- **<u>P</u>** = parental generation.
- **<u>F1</u>** = first filial gen.
- **<u>F2</u>** = second filial gen.

4

Zygosity

- Because some alleles are dominant and some are recessive, ***the same phenotype can result from different genotypes***.

1. **Homozygous genotypes** have two copies of the same allele (AA or aa);
2. **Heterozygous genotypes** have two different alleles (Aa).
   - Heterozygous genotypes yield phenotypes showing the dominant trait.
   - AA or Aa show dominant phen.; only aa shows recessive (homozygous recessive)

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Mendel's First Law of Inheritance

❖ On the basis of many crosses using different characters, Mendel proposed his ***First Law, The Law of Segregation:***

1) the units of inheritance (**genes**) are ***particulate***,
2) there are two copies/versions (**alleles**) of each gene in every parent, &
3) during gamete formation (meiosis!) the two alleles for a character segregate from each other.
   - ***"Particulate Inheritance"* – NOT blending!!**

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1. The Law of Segregation:

- ❖ **During gamete formation, <u>alleles separate</u> so that <u>each gamete receives only one</u> member of the pair of alleles.**
  - **<u>MONOHYBRID CROSS:</u>**
  - **Traits = <u>separable/particulate</u>**
    - **= distinct!**

- <u>Punnett Squares</u>: consider all possible gametes from each parent.

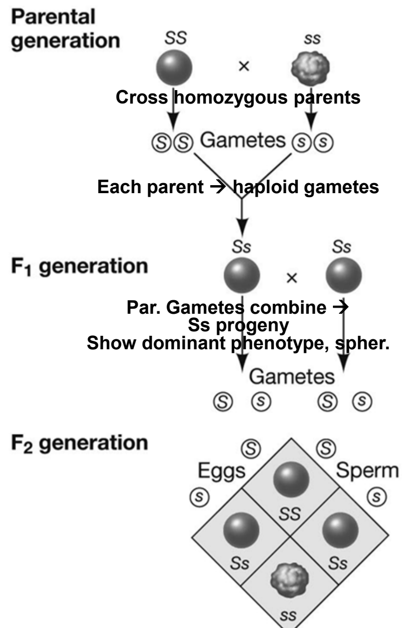

Figure 10/12.4

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Modernized Mendelian Genetics:

Meiosis Accounts for Segregation of Alleles!

- Geneticists who followed Mendel showed that

1. ***<u>Genes</u> are carried on <u>chromosomes,</u> and that***
2. ***<u>Alleles</u> are segregated during meiosis I.***
   - = modern restatement of Law of Segregation!
   - 1 gene = at 1 ***<u>locus</u>***
     - several alleles may be possible at each locus (for each gene)

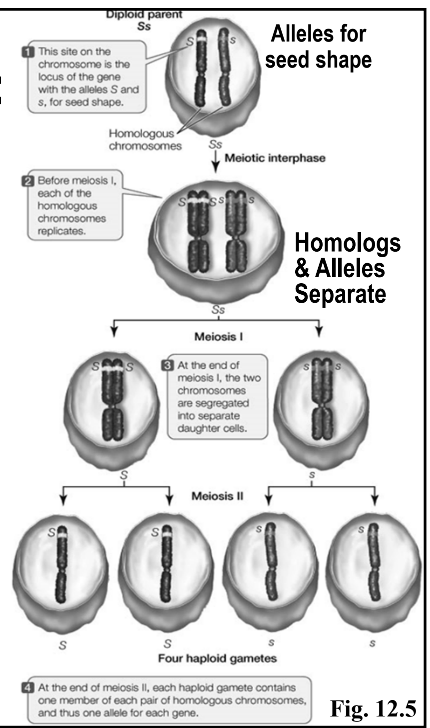

Fig. 12.5

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The Test Cross: Homo- or Heterozygous?

- Using a ***Test Cross:*** **(unknown dominant phenotype x homozygous recessive "tester")**
  - → determine *whether a plant showing the* ***dominant*** *phenotype was* ***homozygous*** ***or*** ***heterozygous*****.**

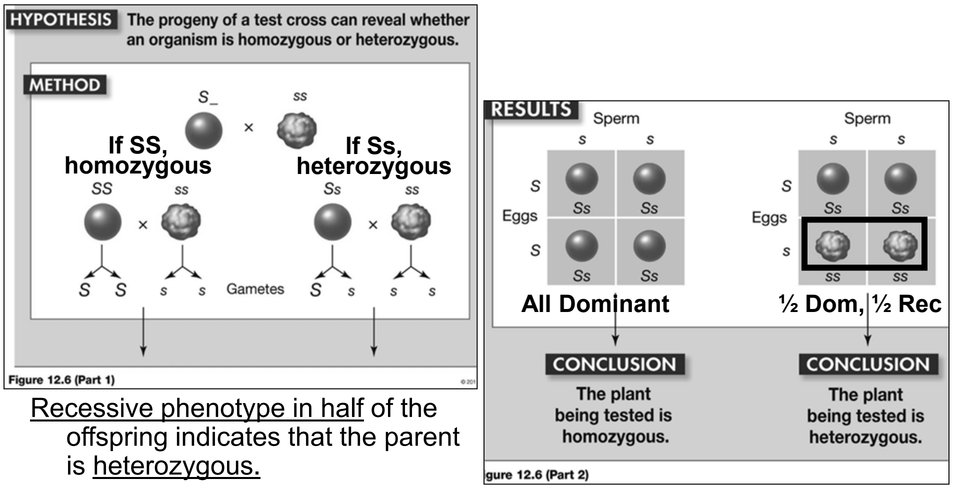

Figure 12.6 (Part 1)

Figure 12.6 (Part 2)

Recessive phenotype in half of the offspring indicates that the parent is heterozygous.

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B. Mendel's Experiment #2: The DIHYBRID CROSS:

- From studies of the simultaneous inheritance of two characters (genes), Mendel concluded that alleles of different genes assort independently.
- ***The Law of Independent Assortment***

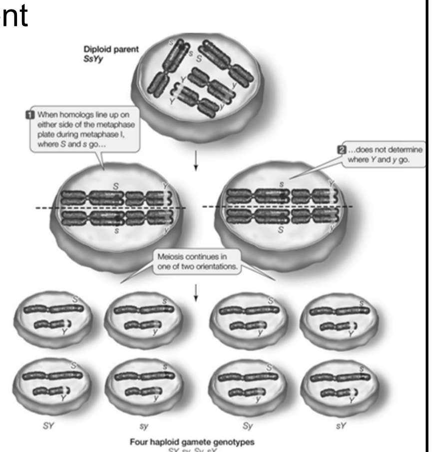

Fig. 12.8: Meiosis Accounts for Independent Assortment of Alleles

12.8

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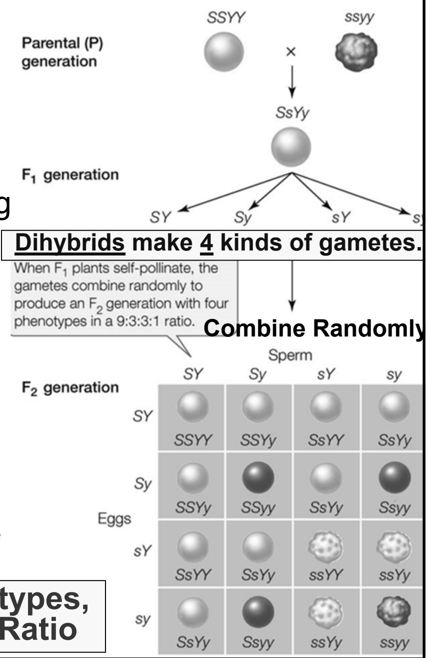
2. <u>Law of Independent Assortment:</u>

figure 12.7

❖ **<u>Dihybrid Cross</u> –**

- Alleles of different genes assort independently of one another during gamete formation.
  - **(Not "linked"; Lucky for Mendel!!)**
  - **Genes on different chromosomes!**



- **9:3:3:1 = Like two 3:1 ratios superimposed upon each other!!**
  - Each gene's pair of alleles separated & were distributed independently from the other's.
  - Each pair of alleles still segregates normally!

4 Phenotypes, 9:3:3:1 Ratio

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12.3) Genetic <u>Probabilities</u>

- We can predict the results of hybrid crosses by using a <u>Punnett square</u> or by <u>calculating probabilities</u>.

1. ***<u>Product Rule:</u>*** To determine the joint probability of independent events, individual probabilities are multiplied. **("and", "also")**

2. ***<u>Sum Rule:</u>*** To determine the probability of an event that can occur in two or more different ways, they are are added. **("or", "either")**

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A. Product Rule

Fig. 12.9

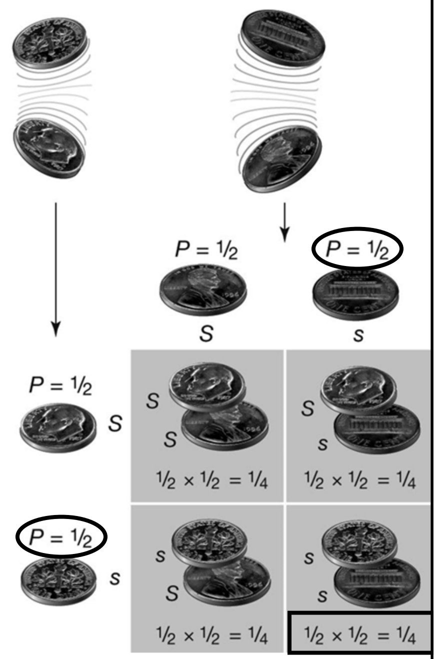
What is the probability that two coin tosses will both give "s" (tails)?

OR

What is the prob. that both a tossed dime and a tossed penny will give tails?

P (ss) = P (s dime) x P (s penny)
= ½ x ½ = ¼.

Product / Multiplication Rule!!



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B. SUM Rule

- Eg: What is the probability that the progeny of a hybrid self-cross will show the dominant phenotype?
  - *Reword: What's the probability that Aa x Aa will produce AA **or** Aa? (abbr. **A_**)*
  - **P(A_) = P(AA) + P(Aa) = 1/4 + 2/4 = 3/4**

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12.4) Human Pedigrees & Mendel's Laws of Inheritance

- Analysis of **pedigrees** reveals that humans exhibit Mendelian Inheritance.
  - Can't control human matings (legally ☺), and
  - not many progeny
  - ***Must look at large family trees = Pedigrees!***

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A. Dominant Autosomal Inheritance

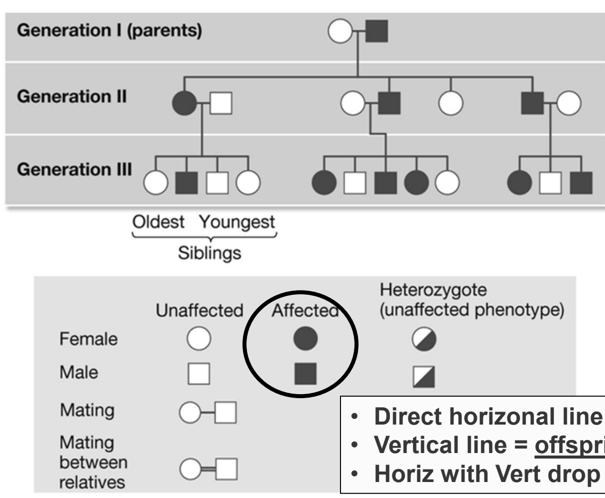

Fig. 12.10a

- **Direct horizonal line = mating**
- **Vertical line = offspring**
- **Horiz with Vert drop = siblings**

Rare Dominant Phenotype:

1. Every affected person has an affected parent (affects every generation)
2. ~1/2 offspring of an affected person are also affected
3. Phenotype occurs equally in both sexes

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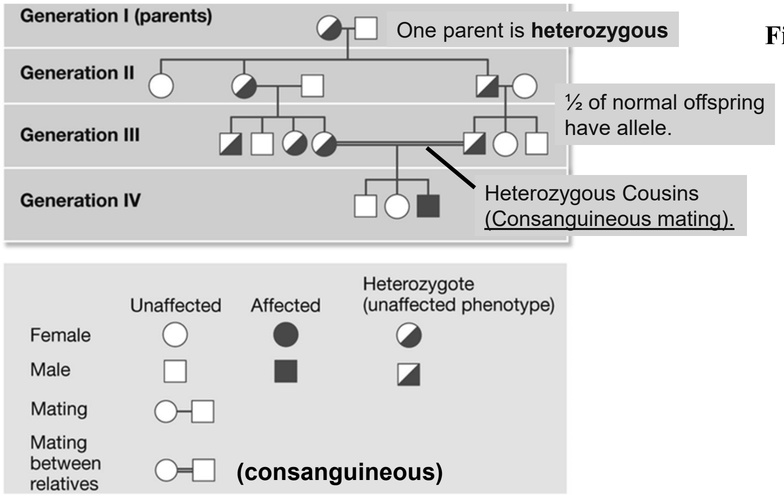
B. Recessive Autosomal Inheritance

Fig 12.10b



Rare Recessive Phenotype:

1. Parents of affected people may not be affected (skips generations)
2. 1/4 of the children of unaffected parents can be affected
3. Phenotype occurs equally in both sexes

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12.5) Alleles & Their Interactions

- **(A.)** New alleles arise by mutation, & many genes have **Multiple Alleles** **of the same Gene.**
- **(*Locus*** = position of a gene on a chromosome**)**.

Possible genotypes	CC, Cc^{ch}, Cc^{h}, Cc	$c^{ch}c^{ch}$	$c^{ch}c^{h}$, $c^{ch}c$	$c^{h}c^{h}$, $c^{h}c$	cc
Phenotype	Dark gray	Chinchilla	Light gray	Point restricted	Albino

Fig 12.11

- Eg: Rabbit coat color
  - ***Dominance Hierarchy***: **$C>c^{ch}>c^{h}>c$**
    - **C_ = Dark gray, c^{ch} _= chinchilla,**
    - **c^{h}_=Himalayan (~Siamese), cc = albino (no pigment!)**
- ***Dominance is usually not complete***, ***since both alleles in a heterozygous organism may be expressed in the phenotype.***

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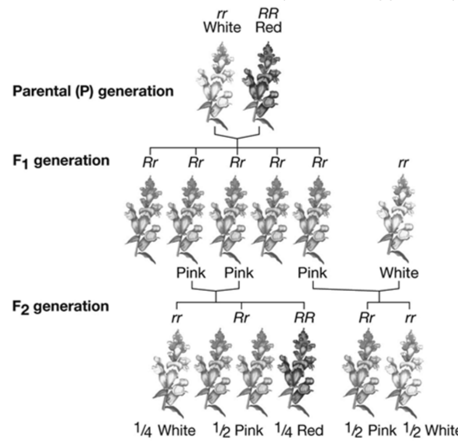
B. Incomplete Dominance:

Snapdragons!!
(see also: egg plants)

- **Heterozygote has an intermediate phenotype!**
  - ❖ **STILL follows Mendel's Laws!**
- **NOT Blended inheritance**, because the Homozygous phenotypes reemerge in the F2 Generation!!
  - **1:2:1 Phenotypic Ratio**
  - (matches Genotypic Ratio!!)
    - Heterozygotes distinguishable from homozygous dominant!
    - "Gene Dosage" (enzyme activity), Rr < RR
    - Don't need a Test Cross!! Heterozygotes are phenotypically distinct.



e 12.12

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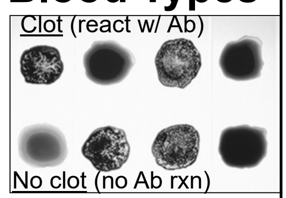
C. Codominance: Human Blood Types

- both alleles are expressed simultaneously!!

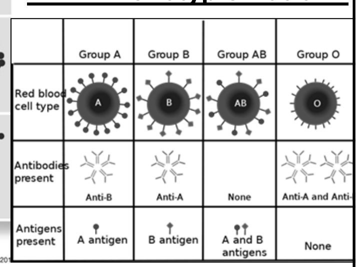


Blood type of cells	Genotype	Antibodies made by body	Reaction to added antibodies: Anti-A	Reaction to added antibodies: Anti-B
A **A = dominant to O**	I^AI^A or I^Ai^O	Anti-B		
B **B = dominant to O**	I^BI^B or I^Bi^O	Anti-A		
AB **A & B = codominant**	I^AI^B	Neither anti-A nor anti-B **Universal Recipient**		
O **Recessive** (actually = null allele)	i^Oi^O	Both anti-A and anti-B **Universal Donor**		

9e, **Figure 12.13**

$$I^A = I^B > i$$

1:2:1 Phenotypic Ratio …



http://nobelprize.org/educational_games/medicine/landsteiner/

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D. Pleiotropy

- ***A single gene has more than one phenotypic effect.***
  - **Siamese cats**
    - body coloration gene also affects eyes (crossed).
  - **Cystic Fibrosis Mutation** (change in single gene, membrane transporter).
    - damages lungs and pancreas.
    - ***CFTR- =*** *defective chloride channel in secretory cells.*
  - **Melanin Gene** – color in skin, eyes, hair.
  - **Hormonal Disorders** ……

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12.6) Gene Interactions

(1.) In **Epistasis**, the products of different genes interact to produce a phenotype; *one gene affects the expression of another.*

- ee genotype is Yellow, no matter what B genotype is (BB, Bb, bb). **In EeBb x ….**
  - **Produces variation on the 9:3:3:1 dihybrid ratio**
    - **9 E_B_ = Black lab**
    - **3 E_bb = Chocolate**
    - **3 eeB_ = Yellow**
    - **1 eebb = Yellow**
  - **= 9:3:4 Ratio!!**

Eggs \ Sperm	*BE*	*Be*	*bE*	*be*
BE	Black *BBEE*	Black *BBEe*	Black *BbEE*	Black *BbEe*
Be	Black *BBEe*	Yellow *BBee*	Black *BbEe*	Yellow *Bbee*
bE	Black *BbEE*	Black *BbEe*	Brown *bbEE*	Brown *bbEe*
be	Black *BbEe*	Yellow *Bbee*	Brown *bbEe*	Yellow *bbee*

(A) Black labrador (*B_E_*) (B) Chocolate labrador (*bbE_*) (C) Yellow labrador (*_ _ee*)

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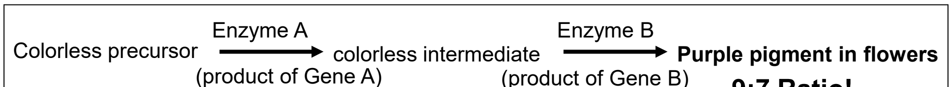
Gene Interactions

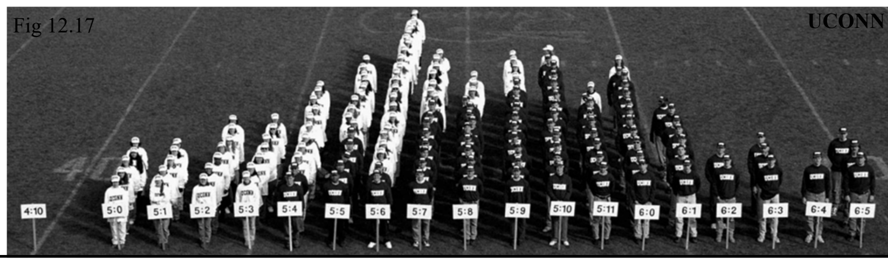
(2.) Also, **Complementary genes:** two genes are both required to produce a given phenotype. (eg: biochemical pathway)



9:7 Ratio!

(3.) Phenotype may be the result of additive effects of **multiple genes,** and inheritance is ***quantitative***.

- ***Continuous Variation***
- Interactions between separate genes & environment produces continuous variation



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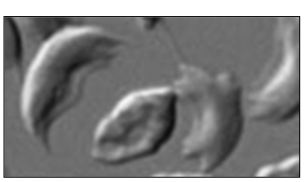
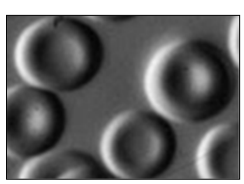
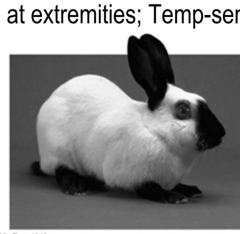
Gene Interactions with Environment

- ***Environmental variables* such as temperature, nutrition, and light affect gene action.**

1. ***Penetrance*** = proportion of individuals in a *group* with a given genotype that actually show the expected phenotype.
2. ***Expressivity*** = the degree to which a genotype is expressed as a phenotype in an *individual*

- ***Both types of interactions are affected by environment, eg:***
  - **Sickle cell anemia:** heterozygotes = OK at sea level, but exhibit Sickle Cell disease at high altitude!
  - **Height in Identical twins:** one well-nourished = tall, like parents; but malnourished one = short
  - **Himalayan rabbit/Siamese Cat:** only melanin at extremities; Temp-sensitive!

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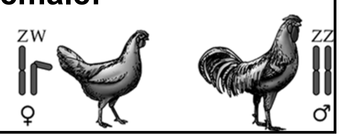
12.7) Sex Determination

- Sex chromosomes carry genes that determine whether male or female gametes are produced.
- Specific functions of X and Y chromosomes differ among species, but
  - ***all ensure that progeny are ~1/2 male and ~1/2 female!***

1. **<u>Mammals</u>: Y chromosome → Male; Need ≥ 1 X**
   - ***XXY = <u>Klinefelter</u>, male; XO = <u>Turner's</u>, female.***
   - ***<u>SRY</u>*** **<u>gene</u>** on **Y chromosome** → Determines Maleness
     - ***<u>S</u>ex-determining <u>R</u>egion on <u>Y</u> chromosome***
     - Inhibits the maleness inhibitor gene on X, ***<u>DAX1</u>*** (anti-testes factor)
2. **<u>Flies</u>:** Ratio of Autosomes to X; ≥ 2X = Female!
   - **<u>XO</u> = sterile male; <u>XXY</u> = fertile female!**
3. **<u>Birds</u>: <u>ZZ</u>** = Male, **<u>ZW</u>** = Female
   - mother/egg determines sex of progeny!



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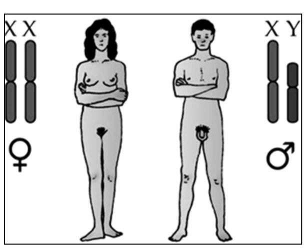
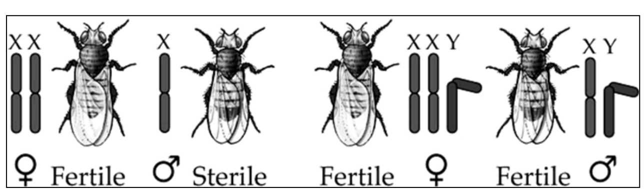
12.8) Sex-Linked Inheritance

- In fruit flies and mammals, the X chromosome carries many genes, but the Y chromosome has only a few.
- Males have only one allele for most X-linked genes ***(<u>HEMIZYGOUS!</u>),*** so rare alleles appear phenotypically more often in males.





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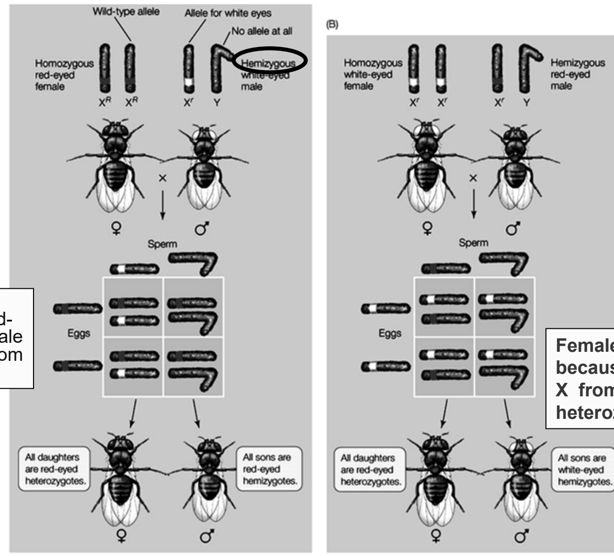
Unequal Reciprocal Cross!



Females and Males both red-eyed, since male gets "red" X from mother

Females Red-eyed, because get only "red" X from father (dom in heteroz)

Males white-eyed, since only "white" X from mother

Figure 12.23

"<u>Wild Type" Allele</u> = most common ("normal") allele in nature; often dominant, but NOT always!!

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X-Linkage Punnett Square

(re: Fig 12.23b)

		Red-eyed Dad (X^RY)	
		X^R	**Y**
White-eyed Mom (X^rX^r)	**X^r**	**X^RX^r** Red Females	**X^rY** White males
	X^r	**X^RX^r** Red Females	**X^rY** White males

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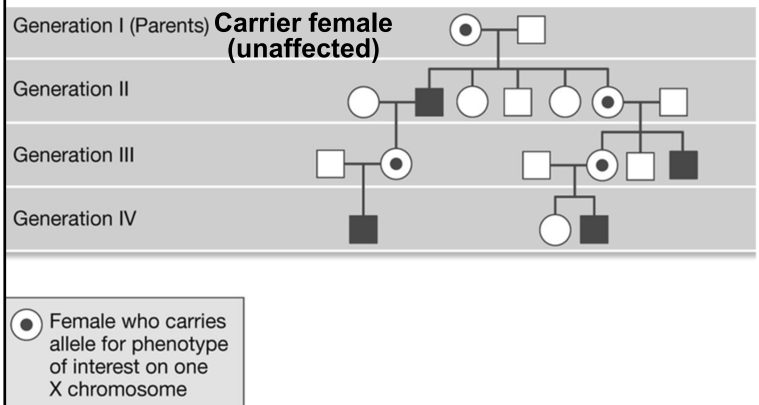
Sex Linkage Pedigree (X-Linkage)

Figure 12.24



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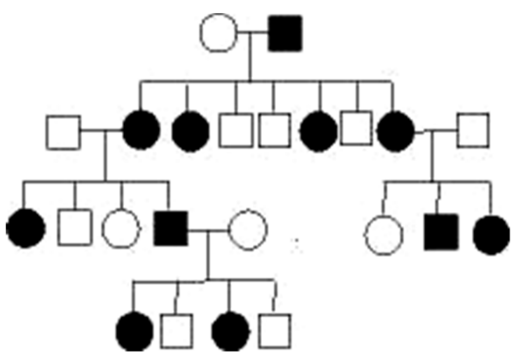
Can you identify this mode of inheritance?



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Special Case of X-linkage

- **<u>Calico Cats</u>**…….
  - ***X-linked coloration gene***
  - Affected by ***X-inactivation***
    - Males have only one X, so either all **<u>Orange (*O*)</u>** or all **<u>Black (*o*)</u>**
    - **<u>Female Heterozygotes (*Oo*)</u>** = patches of **black** with patches of **orange**
      - depending upon which X (with <u>*O*</u>, or <u>*o*</u>) was inactivated in the embryonic precursor cells to each region of skin
        - » [White = determined by a different gene.]

❖ ***Therefore: <u>X-linkage</u>, <u>heterochromatin</u> transcriptional silencing, <u>embryonic X-inactivation</u>, "<u>codominance</u>", & <u>XX sex determination</u> all displayed by this 1 animal!***

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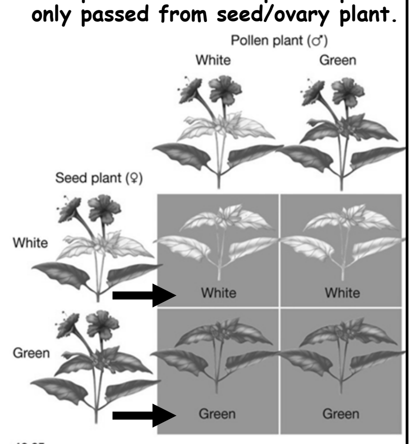
12.9) Non-Nuclear Inheritance

- Cytoplasmic organelles such as **plastids** and **mitochondria** contain some heritable genes.
- ***<u>Cytoplasmic Inheritance:</u> is generally by way of the egg (mother),***
  - male gametes contribute only their nucleus (and a centriole) to the zygote.
  - ***Your mitochondria are inherited only from your mother!***
    - ***"Eve" Hypothesis –*** *re: human mitochondrial inheritance*
  - Mitochondrial mutations primarily affect organs that require high energy: **<u>muscles</u>, <u>nerves</u>, <u>kidneys</u>**
    - *<u>Greg Lemond</u> (champion bicyclist) – muscle weakness, due to mitochondrial mutation, led to early retirement.*

Chloroplast mutation in parent plant: only passed from seed/ovary plant.



4-o'-Clock Plants

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12.10) Genes & Chromosomes

- Each chromosome carries many genes.
- ***Linked Genes*** are located on the same chromosome, and are often inherited together. (= ***"Linkage Group"***)

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EXPERIMENT

Figure 12.18

HYPOTHESIS: Alleles for different characteristics always assort independently.

METHOD

Parent: *BbVgvg* Wild type ♀ × *bbvgvg* ♂ **(Dihybrid Testcross!)**

F1

RESULTS

	P	**P**	**R**	**R**
Genotypes	*BbVgvg* Wild type	*bbvgvg* Black vestigial	*Bbvgvg* Gray vestigial	*bbVgvg* Black normal
Expected phenotypes	575	575	575	575
Observed phenotypes	965	944	206	185
	Parental phenotypes		Recombinant phenotypes	

Expected phenotypes ← **Mendelian**

Observed phenotypes ← **Actual**

RF < 50%
= Linked Genes!!

CONCLUSION: The hypothesis is rejected. These two genes do not assort independently, but are linked (on the same chromosome).

'E 8e, **Figure 10.18**

<u>Recombination Frequency</u> = 206 + 185 = 391 recomb/2,300 total = 0.17
0.17 x 100 = <u>17 map units (= % recombination)!!</u>

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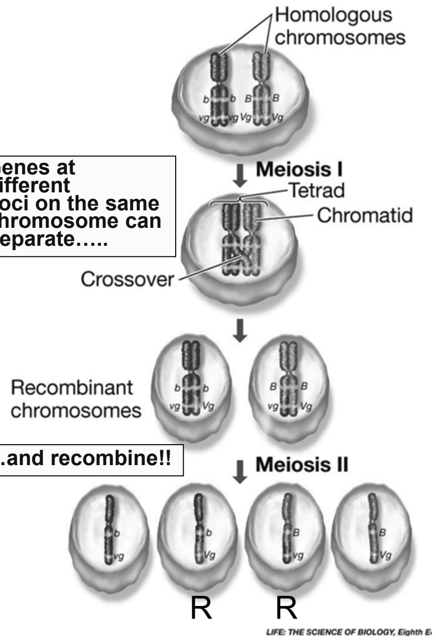
Genes & Chromosomes: Meiosis



Genes at different Loci on the same chromosome can Separate…..

…and recombine!!

Figure 12.19: Crossing Over Results in Genetic Recombination

- ***Linked genes recombine by crossing over in prophase I*** of meiosis, resulting in ***recombinant gametes***, which have new combinations of linked genes.

Result = 2 recombinant gametes from each crossover event (reciprocal process!!)

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T.H. Morgan & Alfred Sturtevant 1911

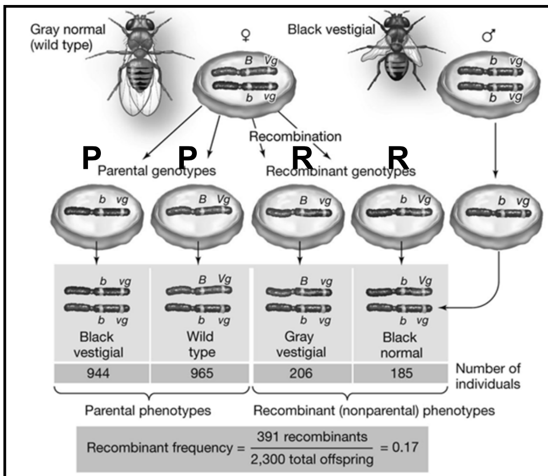

Figure 12.20

Recombination Frequency = 391 recomb/2,300 total = 0.17

0.17 x 100 = **17 *map units*** (= ***% recombination*** = ***centiMorgans*** / cM)!!

Recombination Frequencies:

- **The farther apart two loci are on a chromosome, the more likely a recombination event will occur!!**
  1. Use to calculate relative distance on a “Genetic Map”.
  2. **RF = # recombinant progeny/ # total progeny.**
  3. **RF < 50% = LINKED genes/loci !!**

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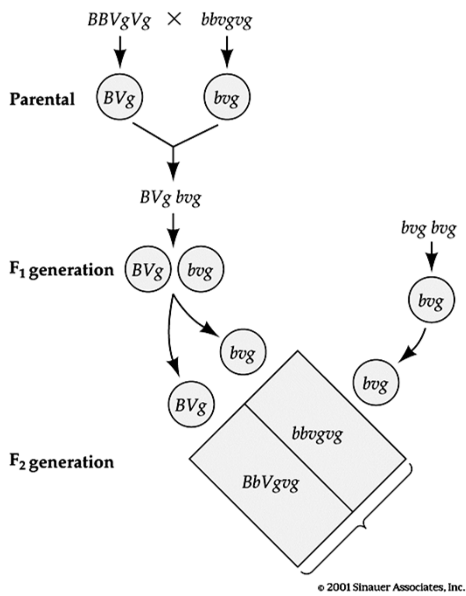

<u>Test Cross: (dihybrid)</u>

- ❖ B (body color) and Vg (wing Size) genes would not separate if <u>linkage</u> were <u>absolute</u>
- ❖ The two genes would act as if they were ONE!

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Genes & Chromosomes: Linkage Maps!

- The ***distance between genes*** on a chromosome is ***proportional to the frequency of crossing over***.
- <u>Genetic maps</u> are based on recombinant frequencies.

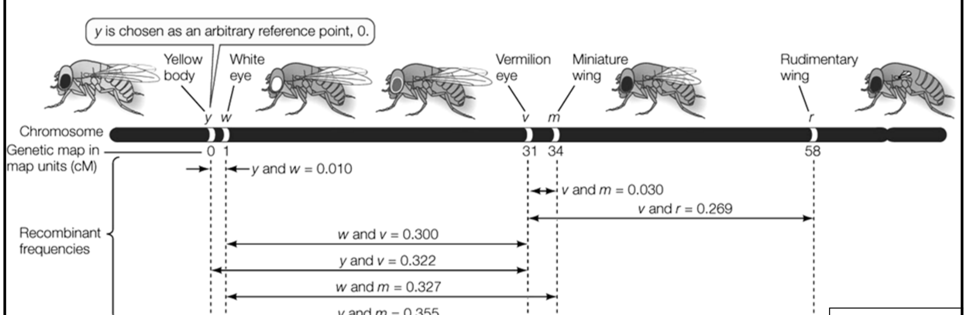

Figure 12.21

→ Practice Figure 12.22

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A Genetic Mapping Problem (Fig 12.22)

1. **What are the distance and orders of three loci *a, b & c* on a chromosome?**
   - **No idea of order: *a-b-c, a-c-b, or b-a-c*?**
   - **Start with *A and B***
2. Cross 1: P, *AABB x aabb* → *AaBb*
3. Cross 2: **Test-cross** F1, *AaBb* x *aabb*
   - F2: (1000 progeny) 450 *AaBb*, 450 *aabb*, 50 *Aabb*, 50 *aaBb*
4. How far apart are ***A & B*?**
   - **RF = #Rec/#Total** = 100/1000 = 0.1, (x 100) = **10 cM**
5. How far apart are ***A & C*?** *AACC* x *aacc* → *AaCc* x *aacc*
   - 460 *AaCc*, 460 *aacc*, 40 *Aacc*, 40 *aaCc*; RF = 80/1000 = **8 cM**
6. How far apart are ***B & C*?** *BBCC* x *bbcc* → *BbCc* x *bbcc*
   - 490 *BbCc*, 490 *bbcc*, 10 *Bbcc*, 10 *bbCc*; RF = 20/1000 = **2 cM**

- ***Therefore, since A and B are farthest apart, they must be on the outside; C must be in the middle.***

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Review GENETICS Concepts:

1. **Mitosis**= exact copies of parent cell; → constancy!
2. **Meiosis**= (esp M1) → diversity: pairing & crossing over, reduction for gamete production, random assortment of parents' chromosomes (from mom or dad) into gametes
3. **Mendel**: trait, character, gene, allele, dominant, recessive, homozygous, heterozygous, monohybrid, dihybrid,
   a) **Segregation:** alleles are particulate/distinct and can be separated.
   b) **Independent Asst:** unlinked genes are distributed independently at meiosis.
4. **Allele interactions:** multiple, codom, incomp. Dom., pleiotropy
5. **Gene interactions**: multiple, complementary, epistasis
   - *Continuous variation; penetrance, expressivity*
6. **Pedigrees** – human trait-tracking; consider genders affected, if skips generations (unaffected parents?), passed mostly from mothers to sons…
7. **Sex Linkage**= on X-chromosome; girls = carriers, boys = affected more.
8. **Cytoplasmic Inheritance** = Maternal Inheritance. Mitochondria, chloroplasts…
9. **Linkage** = percentage RECOMBINATION (less than 50%)
   - cM = genetic map unit; for genes that do not Assort Independently!

Keep working Hard, Good luck, & have a great Break!!
Thank you all for a really FUN semester!! ☺

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Practice Pedigrees…..

http://www.mhhe.com/biosci/genbio/biolink/j_explorations/ch12expl.htm
http://www.biology.arizona.edu/human_bio/problem_sets/human_genetics/human_genetics.html
http://www3.telus.net/howerton/human_pedigree_analysis_problem.htm
https://rowan.biology.ualberta.ca/courses/biol207/uploads/winter07/lecture/b2/good/lecture_notes/Human_Pedigree_Problems.pdf

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Ch. 10 (*8e*) problem #4

Bay Scallops

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