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المرحلة الاولى للدراستين الصباحية والمسائية

الفصل الدراسي الثاني

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المرحلة الاولى- الدراسة الصباحية والمسائية

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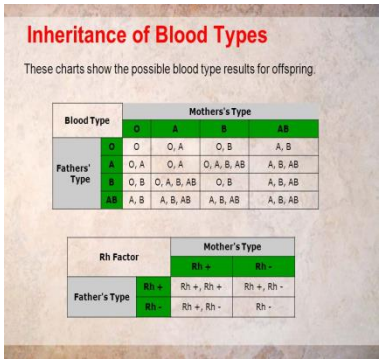
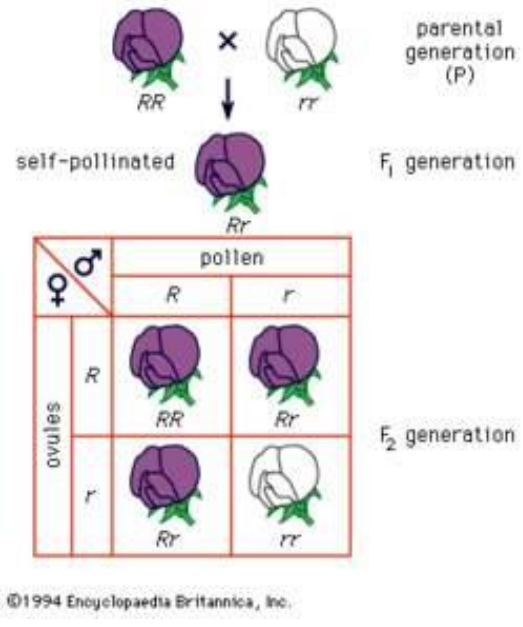
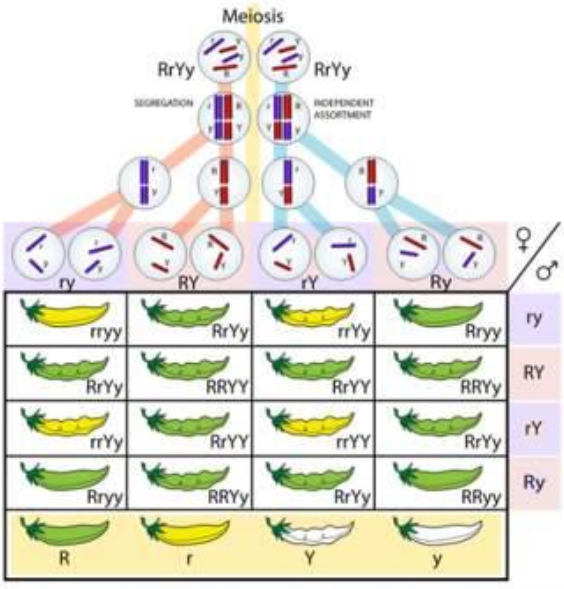






Lab 1 *Drosophila*

1.1- ***Drosophila melanogaster****:* Is a small, common fly found near ripe and rotted fruit. It has been in use for over a century to study genetics. **Thomas Hunt Morgan** was the preeminent biologist study Drosophila early 1900s. **Morgan** was the first to discover **sex-linkage and genetic recombination**, which place the small fly in forefront of genetic research.

Drosophila is one of the few organisms whose entire genome is known and many genes have been identified.

1.2- Why use *Drosophila*?

1- Its care and culture requires little equipment and uses little space even when using large cultures and the overall cost is low.

2- It is small and easy to grow in the laboratory and its morphology is easy to identify once anesthetized (usually with **ether, carbon dioxide gas, by cooling, or with products like FlyNap).**

3- It has a short generation time (about 10 days at room temperature), so several generations can be studied within a few weeks.

4- It has a **high fecundity** (female lay up to 100 eggs per day, and perhaps 2000 in a lifetime).[2]

5- Males and females are readily distinguished and virgin females are easily isolated, facilitating genetic crossing.

6- The mature larvae show giant chromosomes in the salivary glands called **polytene chromosomes** indicate regions of transcription and hence gene activity.

7- It has only **four pairs** of chromosomes: **three autosomes**, and **one pair of sex chromosomes.**

1.3- Classification of *Drosophila*

Kingdom: Animalia

Phylum: Arthropoda

Class: Insecta

Order: Diptera

Family: Drosophilidae

Genus: Drosophila ("dew lover")

Species: melanogaster ("dark gut")

1.4- Breeding (culturing) of *Drosophila*

The age of *Drosophila* is depended on the:

1. Type of manipulation**.**
2. Culture conditions**.**
3. Race of flies**.**

The wild type found to have long lifespan reach to **100 days**. In order to incorporate *Drosophila* in the laboratory, it will be necessary to maintain culture of flies for manipulation in crosses and as backup for any mishaps (حوادث) which may occur. Culturing is very easy and it is recommended.

Equipments:-

1-Breeding Bottles and Vials:

Thomas Morgan used glass milk bottle for his experiments. However uniform bottles and vials are the best approach (both can be purchased from a biological supply store).

Bottles are used mainly for the maintenance a large population of flies whereas culture vials are used mainly for the maintenance smaller population and are preferred container for constructing student crosses. If there is a desire to maintains stock culture for long period of time. It is important completely clean and sterilized bottles and vials. This to prevent outbreak of pest and diseases.

Bottles and vials are variety of size and material. Glass is effected (plastic vials are available and preferable for students use).

Vials size ranges 96*25 mm to larger sizes. There are a variety of plugs available from soft cotton to rubber plugs.

Figure1-1: Breeding Bottles and Vials

2- Media (feeding):

The first step in preparing culture vials is adding food media. There are variety types of food available for the flies; some require cooking and others are bought already prepared and dehydrated.

Cooking media can be stored in a refrigerator for several weeks. Be sure to allow media to warm to room temperature before adding flies. Don't allow media to dry out. Media should fill the culture vial, bottle or vial $1/5^{th}$ to $2/5^{th}$ full. Keep the media out overnight to cure, being sure completely cover the vials with cloth to keep flies from laying eggs in them. **The next day add yeast** (several grains but not more) and plugs before adding flies. Refrigerate any unused media vials. Unused media can last up to two weeks.

Cooking media consist of:

20g agar (for hardening the media)

100g dry yeast (consumed as file's food)

100g flour

100g sugar

1000ml distil water

0.3ml propionic acid (to prevent fungi outbreak)

Agar put in the cold distils water and mixed gently after that the mixture put on the heater. Then add the sugar, yeast and flour with continuous mixing for 5-10 min until reached to the boiling mixture. The mixture (media) put away until be cool. After that the media fill culture vial and bottle.

1.5- ***Drosophila melanogaster*** **(Wild Type "W.T")**

A wild type phenotype is the most common expression of particular allele combination in population. Fruit flies have red eyes, gray (yellow-brown) body, and have transverse black rings across their abdomen. They exhibit sexual dimorphism: female about 2.5mm (0.1 inches) long; males are slightly smaller.

1.6- Male and Female ***Drosophila*** **characteristics:**

Use the following characteristics to distinguish male from female flies among the anesthetized flies provided by your instructor:

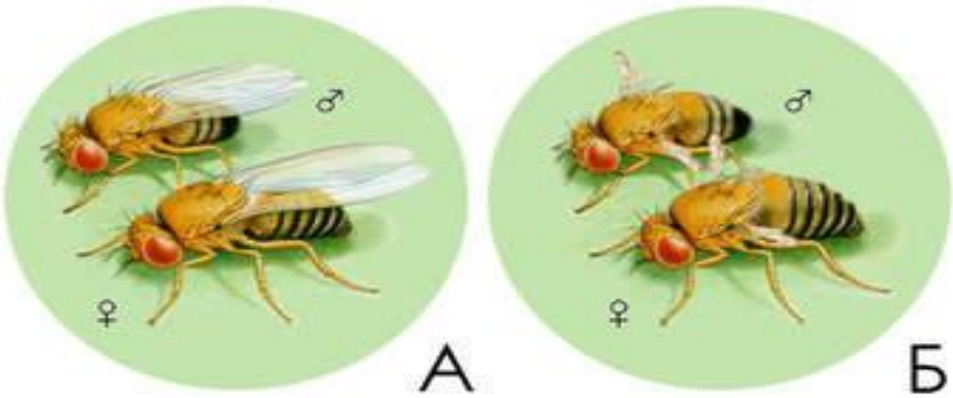
The male is generally smaller.

The male has a more rounded abdomen than female. The female has a pointed abdomen.

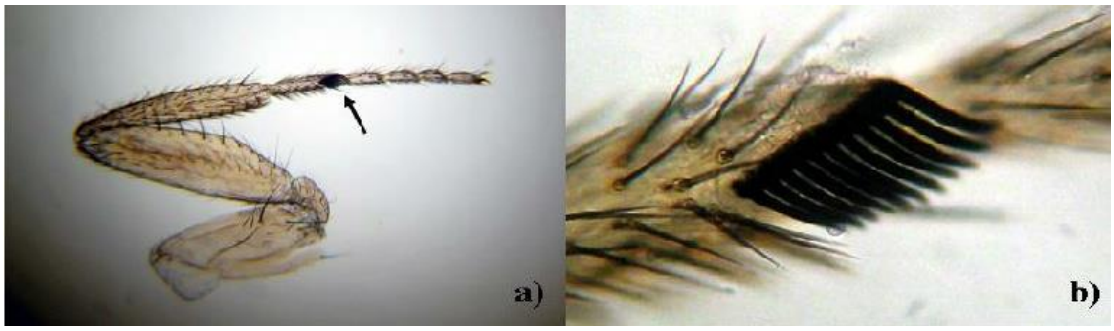
The male has **sex combs** on the forelegs.

Dorsally, the male is seen to have a black-tipped abdomen. Whereas the female appears to have dark lines only at the tip**.**

Ventrally, the abdomen of the male has a dark region at the tip due to the presence of claspers, this dark region is lacking in female.



1.2 Male and Female *Drosophila*



1.3 Sex comb

1.6- Life cycle of *Drosophila*

D. melanogaster exhibits complete metamorphism, meaning includes an egg, larva (worm-like) form pupa and finally emergence (eclosure) as a flying adult. This is the same as the well-known metamorphism of butterflies and many other insects. The larval stage has three instars or molts.

Life cycle by days:

Day 0: female lays eggs contain pairs of spike helps attach the media surface.

Day 1: eggs hatch

Day 2: first instar (one day in length)

Day 3: second instar (one day in length)

Day 5: third and final instar (two day in length)

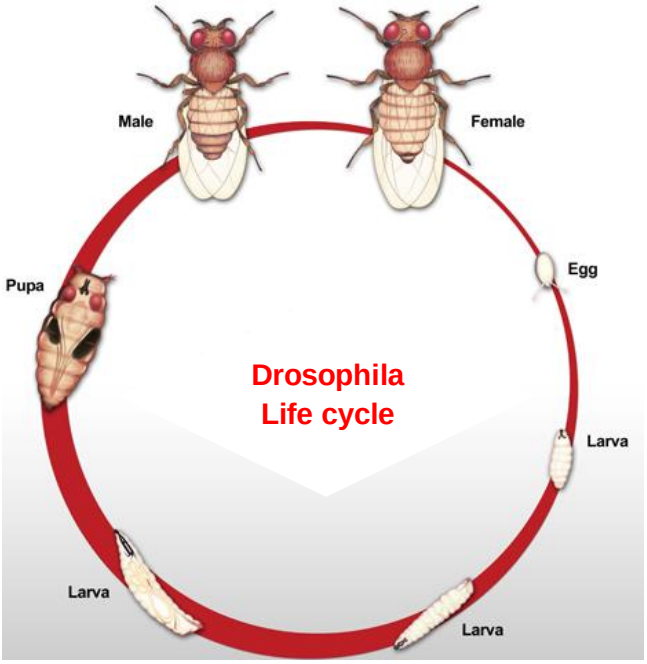
Day 7: larvae begin roaming stage puparation (pupal stage) occur 120 hrs after egg lying.

Day 11-12: eclosin (adult emerage from the pupa case). Females become sexually mature 8-10 hrs after eclosion.

The time from egg to adult is temperature- dependent. The above cycle is for temperature range of 21-23**C**°. The higher temperature cause faster generation time. Whereas a lower (to 18**C**°) temperature causes a longer generation time. After the egg hatch, small larvae should be visible in the growing medium.

1.7- Collecting virgin female

Remove all flies 8-10 hrs before collecting. Visually inspect surface of food to ensure complete removal of flies. After 8-10 hrs collects all females that are present. All will be virgins. Place in a fresh culture vial and wait 2-3 days look for larvae. Virgin females can lay eggs, but they will be sterile. Since they are photoperiod sensitive, females tend to eclose early in morning. Therefore early collections will ensure the greatest number of virgins for experimentation. However collection is possible later in the day.



Lab 2: *Drosophila* mutations

2.1- Mutation: is a change: is a change in **gene nucleotide base** sequence. It can occur at **DNA base** for anther or adding or deleting few bases, or **at chromosomal level**. Chromosomes can exchange parts, and genetic material can even jump from one chromosome to another. These events can cause mutation**.**

2.2- **Types of mutations**

1. **Spontaneous mutation**: that just happens in Nature. **Achondroplasia** is a common cause of **dwarfism**. It occurs as a sporadic mutation in approximately 80% of cases (associated with advanced paternal age) or it may be inherited as an autosomal dominant genetic disorder. People with **achondroplasia** have short stature, with an average adult height of 131 centimeters for males and 123 centimeters for females. Achondroplastic adults are known to be as short as 62.8 cm (24.7 in) fig 2-1. If both parents of a child have achondroplasia, and both parents pass on the mutant gene, then it is very unlikely that the homozygous child will live past a few months of its life.

2. **Induced Mutation**: Those that result from the influence of any artificial factors. Researchers can sometimes interfere with normal genes function. Spontaneous mutation rate is far too low to be practical source of genetic variation, fig 2-2.

Chemicals (EMS, ect.)

Physical (X-RAY, GAMA RAY, UV-radiation).

2-1

2-2

3.Conditional mutation: Affect the phenotype only under certain conditions. Organisms can be protected by avoiding the exposure to these trigger symptoms. For example X-linked that encoded to Glucose-6-phosphate dehydrogenase. **Glucose-6-phosphate dehydrogenase (G6PD)** deficiency is a genetic disorder that occurs most often in males. This condition mainly affects red blood cells, which carry oxygen from

the lungs to tissues throughout the body. In affected individuals, a defect in an enzyme called glucose-6-phosphate dehydrogenase causes red blood cells to break down prematurely. This destruction of red blood cells is called **hemolysis**. **Hemolytic anemia** is most often triggered by bacterial or viral infections or by certain drugs (such as some antibiotics and medications used to treat malaria). Hemolytic anemia can also occur after eating **fava beans** or **inhaling pollen** from fava plants (a reaction called **favism**).

Glucose-6-dehydrogenase deficiency is also a significant cause of mild to severe jaundice in newborns. Many people with this disorder, however, never experience any signs or symptoms.

2.3: Drosophila mutation

Table 1.2**: Drosophila mutation**

Characteristic	**Mutation type**	**Chromosome number**	**Mutation symbol**	**Wild type**	
Vestigial wing	Recessive	II	vg	**vg^+**	Single mutation
Dumpy wing	Recessive	II	dp	**dp^+**	
Ebony body	Recessive	III	e	**e^+**	
White -eye	Recessive	I	w	**w^+**	
Ebony-vestigial	Recessive	II, III	evg	**ev^+g^+**	Double mutation
Ebony-dumpy	Recessive	II, III	edp	**ed^+p^+**	

Drosophila melanogaster has been important in mutation studies **because this organism has very low chromosome number.** The haploid (n) number of chromosome is 4, and the chromosomes are designed X (1), 2, 3, and 4 (figure 2-3).

The **2, 3, and 4** chromosomes are the same in both sexes and are referred to as **autosomes** to distinguish them from the **X and Y sex chromosomes**. XDrosophila females are characterized by two **X chromosomes XX**, while males have an **X and Y chromosome.**

Chromosome **4 and the Y** chromosome **contain so few genes that for all practical purpose, they can be ignored.** Thus, almost the entire genetic content of drosophila genome resides on only three chromosomes**: X, 2, and 3.**

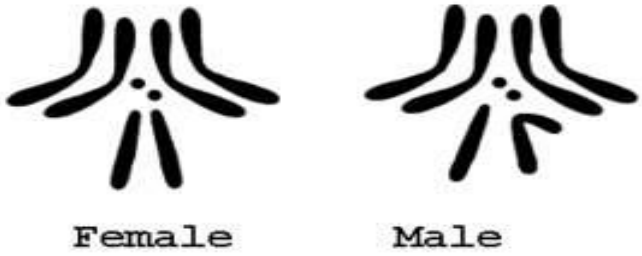


Figure 3-3 *Drosophila melanogaster* Chromosomes**.**

2-4: **Phenocopy**

Is a variation in phenotype (generally referring to a single trait) which is caused by environmental conditions (often, but not necessarily, during the organism's development), such that the organism's phenotype matches a phenotype which is determined by genetic factors. It is not a type of mutation, as it is non-hereditary.

Example: 1-**AgNo3** its effect on the **color of body** for drosophila insect its effect on the mechanism of the enzyme **tyrosinase.** If larva of normal flies were fed with silver salts, they develop into **yellow bodied** flies irrespective of their genotype. The yellow bodied flies which are genetically **brown** is a variant of the original yellow bodied fly.

Tyrosine (yellow) **tyrosinas**e melanin (gray)

AgNo3 ⟹ **yellow**

2-Another chemical factor is **sodium metaborate** its effect on the **color of eyes for drosophila**

LAB 3: Mendelian inheritance

Publishing papers are the primary means to communicate scientific discoveries. One of the most famous of these papers, entitled "Experiments in Plant Hybridization" was written in 1866 by **Gregor Mendel**, an Austrian monk. Although his paper later becomes the basis for genetics and inheritance, it went largely unnoticed until it was rediscovered independently by several European scientists in 1990. The experiments and conclusions in Mendels paper now from the foundation of **Mendelian genetics,** the topics of today exercise. **Mendel, sometimes called "father of genetics".**

3-1: Particulate theory

Inherited characters are determined by factors called (**genes**).

These factors occur in **pairs** (genes on maternal and paternal homologous chromosomes.

When gametes form, these genes segregate so that only **one** of the homologous pairs is contained in a particular gamete.

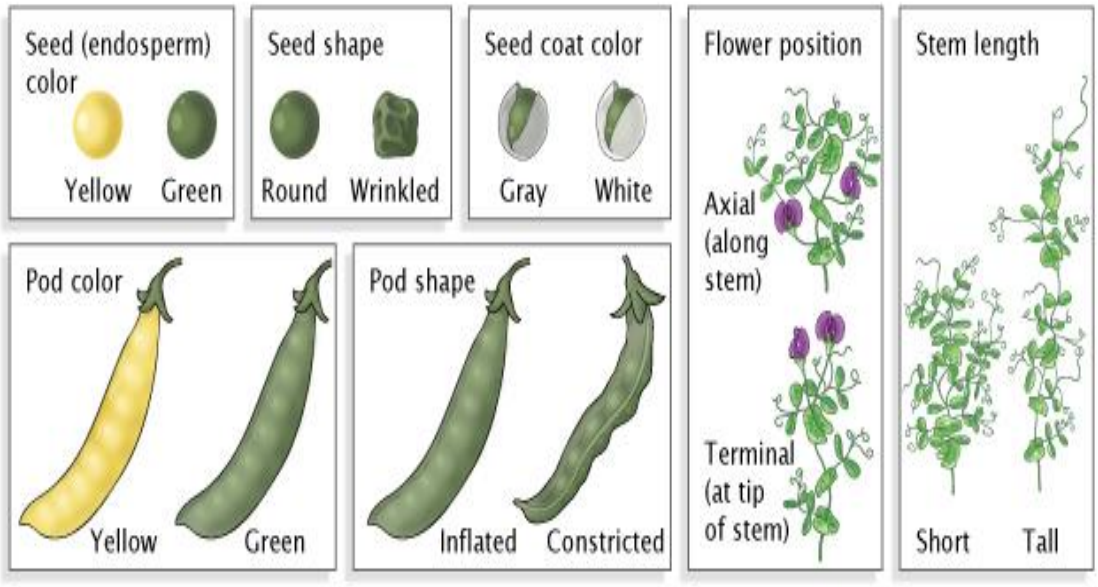
3-2: Mendel's experiment

Mendel's approach centered on the use of **pea plant *Pisum sativum* L. a model organism. It is unlikely that Mendel was truly interested in the genetic of pea's plant, but he recognized that organism had the characteristics necessary to study genetics:**

First: It was relatively easy to grow, develop quickly.

Second: It had easily identifiable variants of trait.

Third: He could easily self-fertilize the plant and produced true-breeding lines. Figure 3-1.



3-1: *Pisum sativum* L. Traits Mendel studied

3-3 Law of Segregation of genes (the "First Law")

The Law of Segregation states that every individual organism contains **two alleles** for each **trait,** and that these alleles segregate (**separate**) during **meiosis** such that each gamete contains **only one of the** alleles. An offspring thus receives a **pair of alleles** for a trait by inheriting homologous chromosomes from the parent organisms: **one allele for each trait from each parent.**

***Before you start the exercise, briefly review some principles and terms:**

- **Gene** is an unit of heredity on a chromosome.
- **Gene** has an alternate state called allele.
- **Allele** for particular gene occurs in pairs. Why?
- **Alleles** that **mask expression** of other alleles but are themselves expressed are **dominant**; this allele is usually designated by capital letter (for exp., T).
- **Alleles** whose expression is **masked by dominant** alleles are **recessive**, and they are designated by a lowercase letter (for exp., t).
- **The genotype** of an organism includes all alleles present in the cell, whether they are dominant or recessive. Tt, TT, tt, ee, dpdp
- **The physical** appearance of the trait is **the phenotype**.
- Thus if **tallness (T)** is dominant to **dwarfness (t)**, a tall plant can have a genotype **TT or Tt.**

- **A dwarf** plant can only have a genotype **tt.**
- When the paired alleles are **identical** (**TT or tt**), the genotype is **homozygous.**
- **Heterozygous** refer to a pair of alleles that are **different (Tt)**. Figure 3-2.

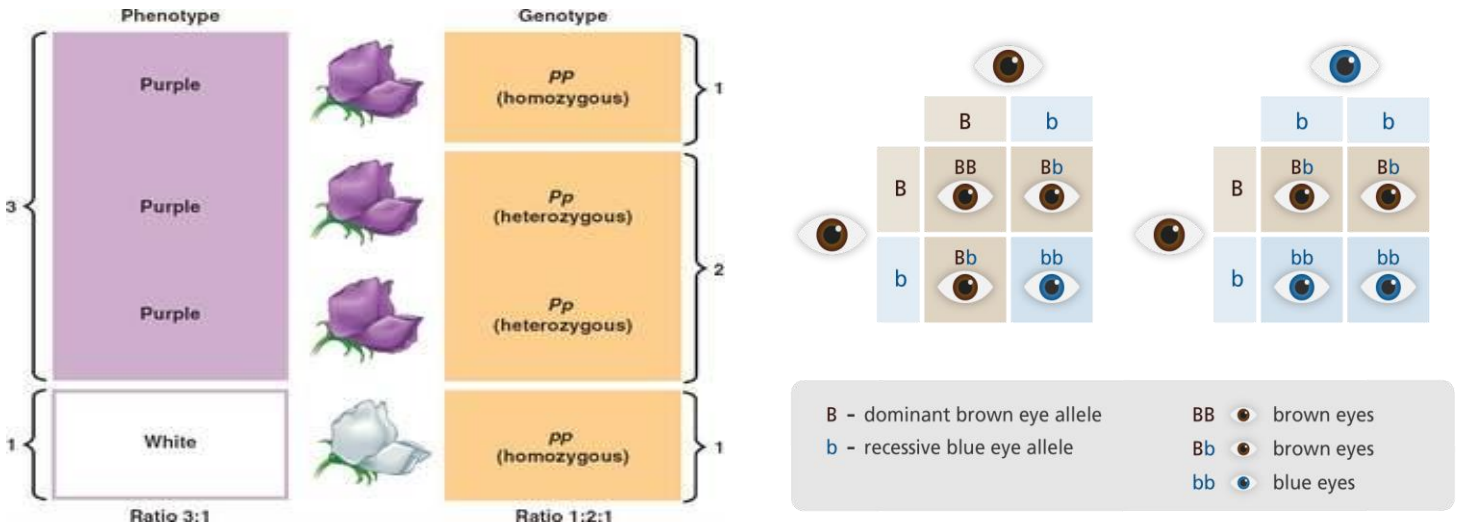


Figure 3-2 (Heterozygous and homozygous)

3-4: Monohybrid Crosses

Mendel found that reproduction between **two heterozygous monohybrid individual (Aa**) result in both dominant and recessive phenotypes among the offspring. **The phenotype ratio** among the offspring was **3:1; three offspring had the dominant phenotype for every one that had the recessive phenotype.** Mendel realized that these results were obtainable only if the allele of each parent segregated during meiosis. Figure 3-3.

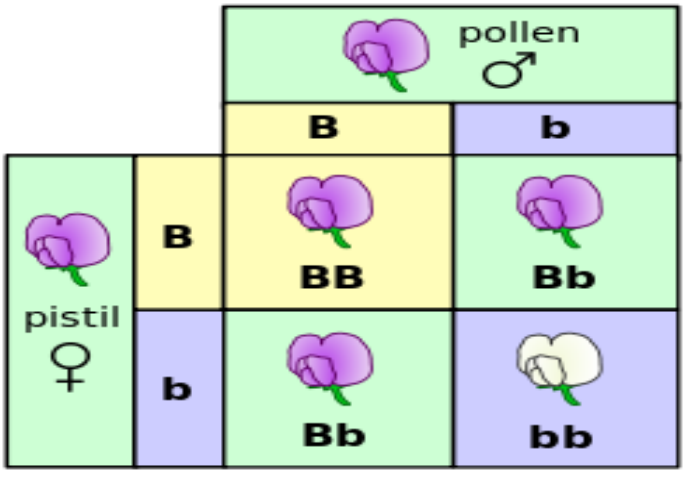


Figure 3-3: Monohybird cross (its ratio 3:1)

3-5 Test cross

- Used to **determine** whether or not an individual with the dominant trait has two dominant factors for a particular trait. Figure 3-4.

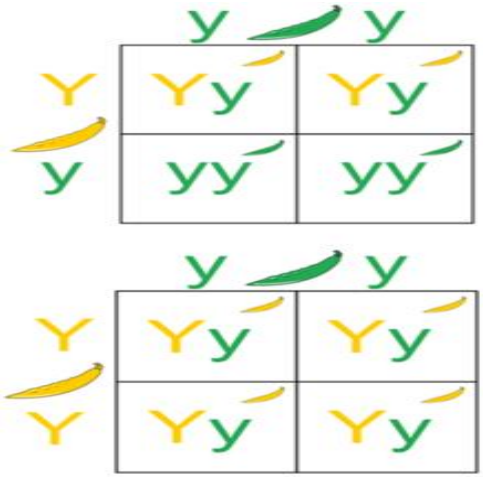


Figure 3-4 Test cross (its ratio 1:1)

Exercises:-

1. A man with **brown eyes** (his father had **blue eyes**) marries a **brown-eyed** women (her mother had **blue eyes**), what is the proportion of children would be expected to have blue eyes? (The brown color is **dominant**).

2. A **right** handed man marries a **left** handed women and produce **left** handed children. Write the complete cross (**right** hand is **dominant**).

3. A mating between *Drosophila* fly **wild type** and **dumpy winged** fly, what is the possible result of this mating?

LAB 4: Data analysis

4-1: Chi-Square Analysis x2

Geneticists typically use the Chi-Square Analysis (X^2) statistical test to determined whether experimentally obtained data are a satisfactory approximation of the expected data . This test expresses the difference between **(hypothetical**) and **observed (collected**) numbers as a single value, **X^2.**

The formula for the test is:

$$\chi^2 = \sum \frac{(o-e)^2}{e}$$

— **o =** the observed value

— **e** = the expected value

— =The sum of all values of $(o-e)^2/e$ for various categories of phenotypes.

— Probability level

—

—

—

—

Df	0.5	0.10	0.05	0.02	0.01	0.001
1	0.455	2.706	3.841	5.412	6.635	10.827
2	1.386	4.605	5.991	7.824	9.210	13.815
3	2.366	6.251	7.815	9.837	11.345	16.268
4	3.357	7.779	9.488	11.668	13.277	18.465
5	4.351	9.236	11.070	13.388	15.086	20.517

— **Df=n-1**

— **In mendelian first law df=1 , but in mendelian second law df=3**

— **The critical value of $\chi 2$ with 1 degree of freedom is 3.841.**

— **The critical value of $\chi 2$ with 3 degree of freedom is 7.815.**

— If calculated **X^2** value is **less than** 3.841, it is likely that variation in the observed and expected is the result of chance, and our hypothesized outcome is correct (**the differences not significant).**

— A value **greater than** 3.841, however would indicate that chance alone, cannot explain the deviation between observed and expected, and would reject our hypothesis (**the differences are significant). Calculated X^2** value exceeds the

critical value in the table for a 0.05 probability level, and then we can reject the null hypothesis.

— **Example 1**: In garden peas, tall plants are dominant over short plants. If there were in the second generation offspring **F2 64** tall plants and **17** short plants write the complete cross, and make certain of results statistically.

— Observation is: 64+17=81

— Our hypothesis (expectation) is: ¾ of them will be tall:-

— E for tall plants = ¾ x 81=60.75

— E for short plant= ¼ x 81= 20.25

— O-E FOR TALL = (64-60.75)2/60.75=0.174

— O-E FOR SHORT= (17-20.25)2/20.25= 0.696

— X^2=(0.174+ 0.522)= 0.696

Phenotype	Observation	Ratio	Expected	O-E	$(O-E)^2/E$	X^2	
Tall	64	3	60.75	64-60.75	(64-60.75)2/60.75	— 0.174	
Short	17	1	20.25	17-20.25	(17-20.25)2/20.25	0.522	
2	81	4	81			— 0.696	

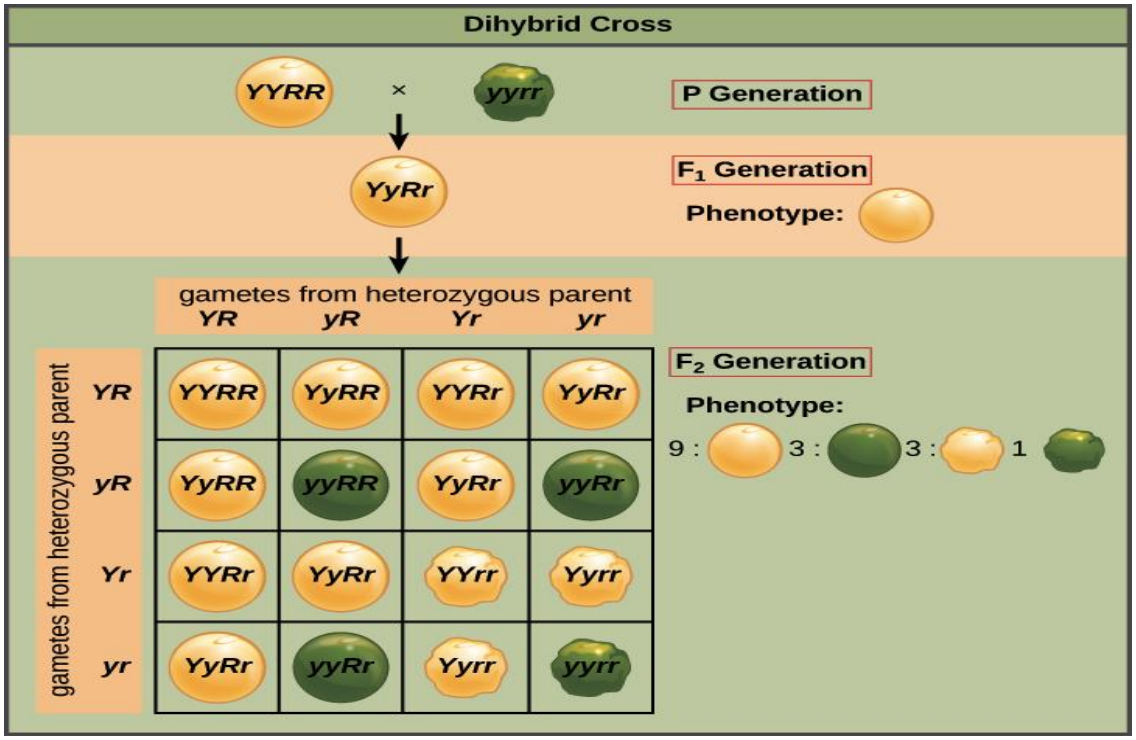
If calculated $\mathbf{X^2}$ value is **less than** 3.841, it is likely that variation in the observed and expected is the result of chance, and our hypothesized outcome is correct (the **differences not significant**).

Lab 5: Mendelian Second Law- the Law of Independent Assortment

During gamete formation the segregation of alleles of one allelic pair is independent of the segregation of the alleles of another allelic pair.

1-Genes for different traits are inherited independently from each other.

2- This is why Mendel found all the different combinations of traits



— **Q1:** In ***Drosophila***, gray body colour is dominant to ebony body colour, while long wings are dominant to vestigial wings. Assuming that the P1 individuals are homozygous, work the following crosses through the F2 generation, and determine the genotypic and phenotypic ratios for each generation.

— (a) Gray, long X ebony, vestigial

— (b) Gray, vestigial X ebony, long

— (c) Gray, long X gray, vestigial

Example-2: Let us examine Mendel's F2 data for the **Round/wrinkled** and **Yellow/green** dihybrid cross. He counted a total of **556** peas with this observed ratio: **315: 108: 101: 32**. We will use to test Mendel's data by the χ^2 method?

Other Mendelian Genetics Problems and Answers

PROBLEM 1.

You have an individual who is totally heterozygous for 2 genes that are not linked (i.e., not on the same chromosome). One gene is for ear size (AA or Aa being big ears whereas aa is for small ears) and the other gene is for buggy eyes (BB and Bb for buggy eyes whereas bb represents normal eyes). If you testcross this individual, what are the resulting genotypes and phenotypes?

Answer: Remember that a testcross represents a cross with a totally recessive individual. These types of crosses are useful in weeding out hidden recessive alleles from your unknown. Remember the information on recessives if you don't remember anything else. By knowing the recessive, you automatically know both the phenotype and genotype. In the monohybrid cross, a testcross of a heterozygous individual resulted in a 1:1 ratio. With the dihybrid cross, you should expect a 1:1:1:1 ratio!

AaBb x aabb

	ab	ab	ab	ab
AB	AaBb	AaBb	AaBb	AaBb
Ab	Aabb	Aabb	Aabb	Aabb
aB	aaBb	aaBb	aaBb	aaBb
ab	aabb	aabb	aabb	aabb

Thus, you get the following...

PERCENTAGES	GENOTYPE	PHENOTYPE
25%	AaBb	Big ears, buggy eyes
25%	Aabb	Big ears, normal eyes
25%	aaBb	Small ears, buggy eyes
25%	aabb	Small ears, normal eyes

PROBLEM 2.

Now then, after you've completed the problem above, lets ignore the Punnett's square and simply look at the 4 types of offspring from the above cross. What if the actual ratios in your testcross were not 1:1:1:1, but were as follows. What would this represent?

PERCENTAGES	GENOTYPE	PHENOTYPE
48%	AaBb	Big ears, buggy eyes
2%	Aabb	Big ears, normal eyes
2%	aaBb	Small ears, buggy eyes
48%	aabb	Small ears, normal eyes

Answer: Whenever you know that you have a totally heterozygous individual, and you get this type of lopsided percentage during the testcross, you have discovered that the A and B genes are linked (i.e. they occur on the same chromosome). Thus, they are NOT assorting independently as Mendel states in his second law. If they were, you would get the 1:1:1:1 ratios. The genotypes and phenotypes with the small percentages (Aabb and aaBb) represent outcomes that were produced due to "crossing over" (during Meiosis I, some homologous chromosomes broke between the 2 genes and DNA was exchanged). Because the percentage of these oddball recombinants was low, then it is likely that the genes are fairly near one another. If the percentages of these middle two combinations were 10-12% each, then the distance between the genes would be greater. In this case, "A" and "B" are on the same chromosome whereas "a" and "b" occur on the other chromosome (except for the ones that just crossed over).

PROBLEM 3.

The following is a genetic linkage problem involving 4 genes. You want to determine which of the genes are linked, and which occur on separate chromosomes. You cross two true breeding (i.e., remember that this means that they are homozygous) plants that have the following characteristics:

PLANT 1	PLANT 2
Red flowers	White flowers
Spiny seeds	Smooth seeds
Long pollen grains	Short pollen grains
Late blooming	Early blooming

Following the above cross, all of the offspring have red flowers, spiny seeds, long pollen grains, and early blooming (meaning, that these traits are dominant). You then testcross the F1 generation, which you should realize by now are totally heterozygous individuals, and obtain the ratios below. What's going on?

49% red-spiny	25% red-long	25% red-early	25% long-early
1% red-smooth	25% red-short	25% red-late	25% long-late
1% white-spiny	25% white-long	25% white-early	25% short-early
49% white-smooth	25% white-short	25% white-late	25% short-late

Answer: A little more difficult, but still something you should be able to figure out. Obviously from the above, the red/white flowers and the spiny/smooth seed traits are not assorting independently. If they were, we would see the 1:1:1:1 ratios (25%:25%:25%:25%) represented for the other sets of genes. Therefore, the flower color gene and seed texture are linked. Because of the high percentage of red-spiny and white-smooth, the allele for red flowers and the allele for spiny seeds are on the same homologue (except for 2% of the offspring, which are a result of the crossover). Conversely, the allele for white petal color and the allele for smooth seeds are on the same chromosome (again, except for the 2% of the offspring that are a result of crossing over). Since all of the other crosses are 1:1:1:1, then all other genes are on chromosomes separate from the first 2. Therefore, 3 separate chromosomes are involved.

PROBLEM 4.

The following is a genetic linkage problem also involving 4 genes. You want to determine which of the genes are linked, which occur on separate chromosomes, and the distances between the linked genes. You cross 2 true breeding (i.e. homozygous) plants that have the following "unusual" characteristics:

PLANT 1	PLANT 2
Red flowers	White flowers
Long pollen grains	Short pollen grains
Dumb backtalk	Smart backtalk
Mean disposition	Nice disposition

All of the offspring have red flowers, long pollen grains, give smart backtalk, and have a nice disposition (meaning, that these traits are dominant). You then testcross the F1 generation, and obtain the ratios below. How many chromosomes are involved in the linkages, and what are the positions of the linked genes relative to one another?

45% red-long	25% red-dumb	25% long-dumb	48% red-mean	43% long-mean
5% red-short	25% red-smart	25% long smart	2% red-nice	7% long-nice
5% white-long	25% white-dumb	25% short-dumb	2% white-mean	7% short-mean
45% white-short	25% white-smart	25% short-smart	48% white-nice	43% short-nice

Answer: As you can see from the above, some characteristics between genes do not assort in the 1:1:1:1 fashion. Therefore, they are linked. In the first column, one can see that red/white and long/short are on the same chromosome and are 10 (5 + 5) units apart (see below). Also, red/white and mean/nice in the third column are linked and are 4 (2 + 2) units apart (see below). Since mean/nice and short/long are on the same chromosome as red/white, they too are linked as can be seen in column five and are 14 (7 + 7) units apart (see below). The gene for smart/dumb must exist on a second, separate chromosome by itself.

PROBLEM 5.

In the ABO blood system in human beings, alleles A and B are codominant and both are dominant to the O allele. In a paternity dispute, a type AB woman claimed that one of four men was the father of her type A child (the child would be type A with a genotype of either be AA or AO). Which of the following men could be the father of the child on the basis of the evidence given?

A. The Type A father? Answer: In this case, a type A person would have one of the following genotypes: AA or AO. A man with either of these genotypes could be the father as the mother would donate the A allele to the child and either an A allele from the father or an O allele from the father would produce a child with Type A blood.
B. The Type B father? Answer: In this case a type B father would have either the genotype BB or BO. A man with the genotype BO could be the father as the mother would donate the A allele to the child and an O allele from the father would produce a child with Type A blood.
C. The Type O father? Answer: In this case a type O person would have the genotype OO. A man with this genotype could be the father as the mother would donate the A allele to the child and an O allele from the father would produce a child with Type A blood.
D. The Type AB father? Answer: In this case a type AB person would have the genotype AB. A man with this genotype could be the father as the mother would donate the A allele to the child and an A allele from the father would produce a child with Type A (i.e. AA) blood.

NOTE: In this case, none of the men can be excluded from possible paternity. I guess they'll need to do genetic testing.

PROBLEM 6.

A brown-eyed, long-winged fly is mated to a red-eyed, long-winged fly. The progeny are: 51 long, red ; 53 long, brown ; 18 short, red ; 16 short, brown Using solely the information provided, what are the genotypes of the parents?

Answer: In this case, it is easier to look at each locus separately. At the wing locus, we have two long-winged flies crossed to yield 104 long-winged flies and 34 short-winged flies. This is very close to a 3:1 ratio that we would expect from a monohybrid cross. Thus, the parents must be heterozygous (Ll) at the wing-length locus and long wings must be dominant. At the eye color locus, we have a red-eyed fly crossed with a brown-eyed fly to yield 69 brown-eyed flies and 69 red-eyed flies. This is a 1:1 ratio, which is what we would expect from a monohybrid testcross. However, we do not know which is dominant, red eyes or brown eyes. Thus one parent is heterozygous (Rr) and the other parent is homozygous recessive (rr) at the eye color locus. Combining the information from the two loci, possible genotypes for the parents are LlRr for the brown-eyed, long-winged parent and Llrr for the red-eyed, long-winged parent. The other possibility is Llrr for brown-eyed, long-winged and LlRr for red-eyed, long-winged.

PROBLEM 7.

A strange woman has a bizzare condition known as "Cyclops" syndrome, where she has a single eye in the middle of her forehead. The allele for the normal condition (i.e. NO "Cyclops" syndrome) is recessive (cc). Her father is a Cyclops, as well as her mother. Her father's mother was normal. What is the genotype of the strange woman's father?

Answer: Because the woman's father was a Cyclops, he had to have at least one big C. However, it is unknown if his other allele was big C or little c. But, interestingly enough, her father's mother was normal. Since normal is recessive (cc), then she could only donate a little c to her son. Thus, the bizzare woman's father is heterozygous (Cc).

PROBLEM 8.

In calico cats, there is an X-linked gene with 2 alleles that control fur color. BB is a black female; B'B' is a yellow female; B'B (heterozygous) is a calico female; B' is a yellow male; and B is a black male. You have recently taken over judge Wapner's job on the People's Court and a woman brings in a black female cat that has given birth to 4 calico female kittens and 2 black male kittens. You must decide which of the defendent's male cats is guilty: the black one or the yellow one.

Answer: Note first that the mother, a black female, only has big Bs to offer. The black male kittens are of no help in the problem as they got their B alleles (each a single B on a single X-chromosome) from their mother. However, the female kittens are calico, and thus are B'B. They couldn't receive the B' allele from their mother since their mother was black; thus, they had a yellow (B') father.

PROBLEM 9.

A common form of red-green color blindness in humans is caused by the presence of an X-linked recessive allele. Given simply that, please answer the following:

A. Can two color-blind parents give birth to a normal son or daughter? Answer: No. 100% of the parental alleles are recessive; thus, there are no normal alleles to give to the offspring.
B. Can two normal parents produce a color-blind daughter? Answer: No. Dad will give all of his daughters a normal allele. Thus, even if Mom has a hidden recessive allele, the worst case senario is that the daughter would be heterozygote.
C. Can two normal parents produce a color-blind son? Answer: Yes. If Mom has a hidden recessive allele, 50% of the sons will be color-blind. The other 50% will get her normal allele and be normal.

PROBLEM 10.

In an epistasis situation, PP or Pp is purple and pp is yellow. CC and Cc encode the ability to produce color whereas cc prevents color production resulting in an albino (i.e., the C allele either allows, or prevents, P from functioning to produce color). Given the following parental matings, provide the ratios of the offspring that are either purple, yellow, or albino. Remember: all offspring must have at least one big C to produce color or they will be albino.

	OFFSPRING RATIOS			
PARENTAL CROSSES	**purple**	**yellow**	**albino**	**PROVIDE EXPLANATIONS FOR EACH OF YOUR ANSWERS**
PPCC x PPCC	**1**	**0**	**0**	**all offspring PPCC and will have at least one big C and one big P**
PPCC x ppcc	**1**	**0**	**0**	**all offspring PpCc and will have at least one big C and one big P**
ppcc x ppCc	**0**	**1**	**1**	**one-half ppCc and one-half ppcc**
Ppcc x PpCc	**3**	**1**	**4**	**6 different possibilities. See below***

*Out of 16 gametes, 2 will be PPCc (purple); 2 will be PPcc (albino); 4 will be PpCc (purple); 4 will be Ppcc (albino); 2 will be ppCc (yellow); and 2 will be ppcc (albino).

Lab6: Sex Linkage Inheritance

5-1: The chromosome theory of inheritance

The fact that genes **are located on chromosomes** and the segregation of these chromosomes during meiosis was finally worked by **Sutton and Boveri, in 1903, figure 1-5.**

States that genes are found at specific locations on chromosomes, and that the behavior of chromosomes during meiosis can explain Mendel's laws of inheritance.

Figure 5-1:**Sutton and Boveri, in 1903**

5-2: Holandric Inheritance: Found only in males, such as traits inherited through genes on the Y chromosome **(hairy pinna**).

5-3: SEX LINKAGE INHERITANCE

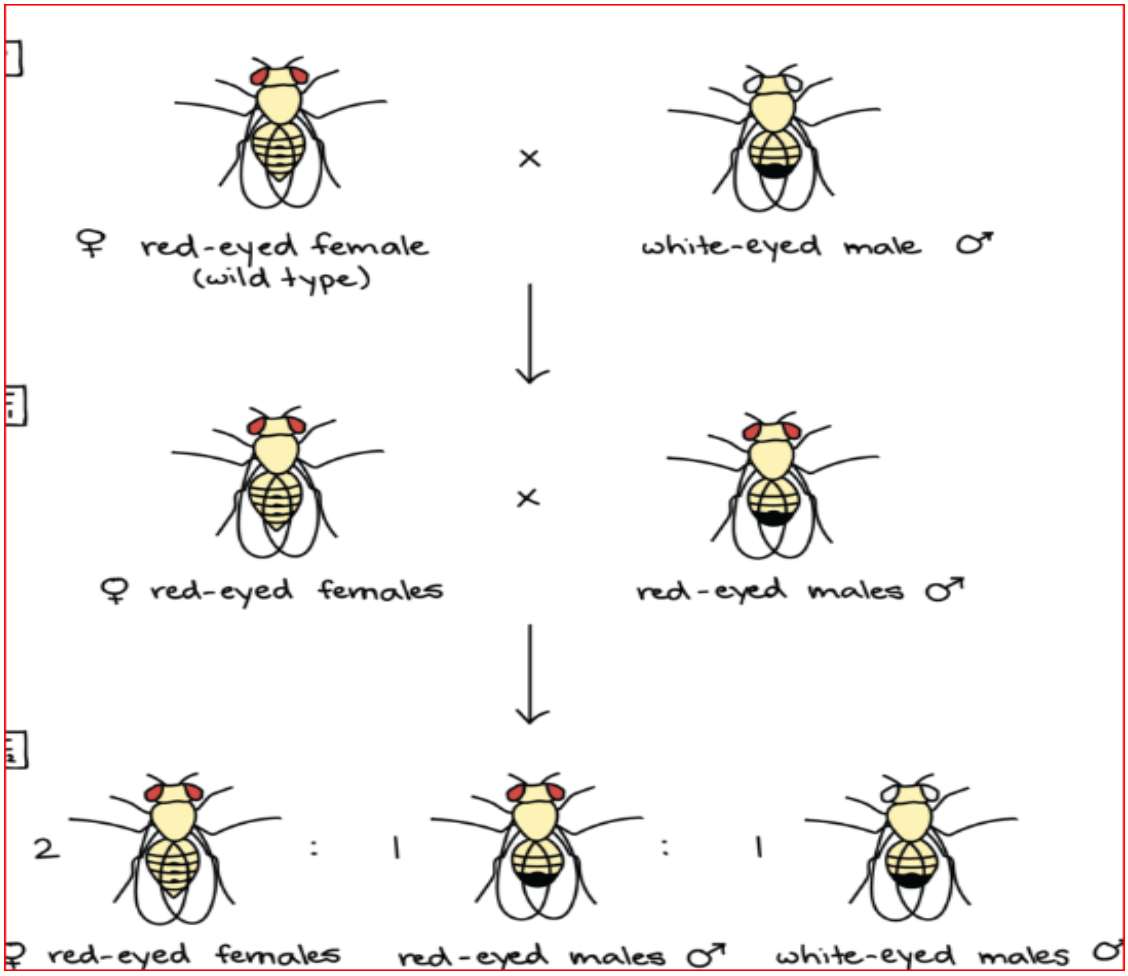
About **1910, T.H. Morgan** and his students at Columbia University began to study inheritance in ***Drosophila***. Among the first mutants found were flies that had **developed white eyes instead of normal red eyes.**

The researchers noticed that **eye color** inherited as if the causative gene were located on the **X chromosome**, and missing from the Y chromosome.

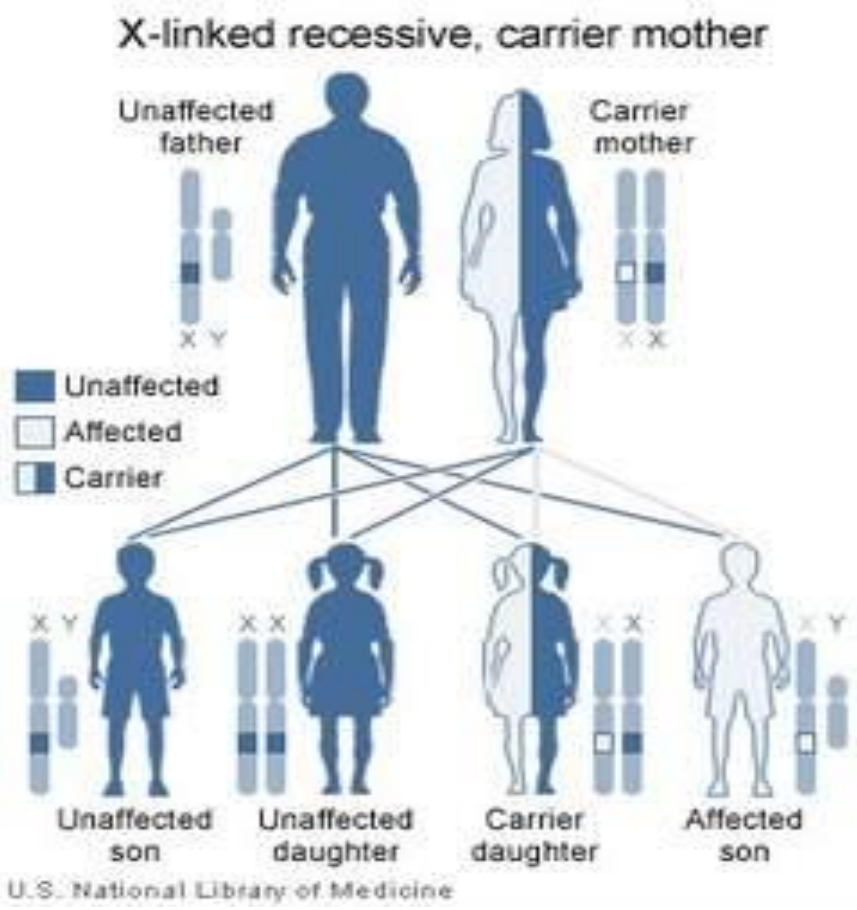
Red was dominant to white

Thomas Hunt Morgan

- If **homozygous** red-eyed female was mated to a white eyed male, all the offspring had red eyes; but if a **white eyed female** was mated to a **red-eyed male**, the **males** had white eyes.
- When a **heterozygous red-eyed female** was crossed to a **red-eyed male**, half the sons (male) were white-eyed.
- The results were compatible with the hypothesis that the color eyes gene is located on the **X chromosome**, **but not on the Y.**
- Characters that inherited in this way are called **sex linked, or X- Linked.**
- The female, since she has **two X chromosomes** may be either **homozygous or heterozygous** for an X-linked gene.
- A male having one **X-chromosome,** is said to be **hemizygous.**



5-4: X-linked inheritance



- The best known example of **X-linked** inheritance in human species are color blindness and Hemophilia.
- **5-4-1: Color Blindness**
- **Color blindness** caused by recessive gene (c) on X-chromosome.
- Most color blind people are able to see things as clearly as other people but they unable to fully 'see' **red, green or blue** light.

♀**Female genotype/phenotype**	**Male ♂ genotype/phenotype**
C||C normal vision	**C| ⌠ normal vision**
C||c carrier	**----------**
c||c affected	**c| ⌠ affected male**

5-4-2: Hemophilia

- **Hemophilia** is a deficiency in a **protein** necessary for normal blood-clotting. The famous pedigree with **Queen Victoria**, who was a heterozygous carrier. She had one hemophilic son and two daughters. Because of the royal custom to exporting daughters, the hemophilia gene was passed to the royal families of Europe from Spain to Russia. The present British family, which is descended through a normal son, is free of this disease.

- **Hemophilia caused by recessive gene (h) located on X-chromosome.**

♀Female genotype/phenotype	♂Male genotype/phenotype
H||H normal female	**H| normal male**
H||h carrier	**----------**
h||h affected	**h| affected male**

5-5: Criteria for an X-Linked recessive trait:-

1. Always expressed in male
2. Expressed in female homozygous
3. Passed from heterozygous or homozygous to affected sons.
4. Affected female has an affected father and a mother who is affected or heterozygous.

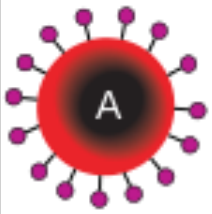
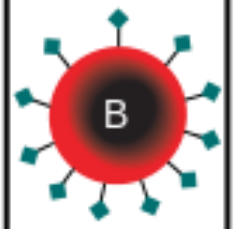
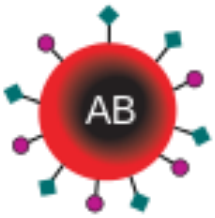
5-6: Criteria for an X-Linked dominant trait:-

1. Expressed in female in one copy
2. Much more sever effect in males.
3. High rate of miscarriage due to early lethality in males.
4. Passed from male to all daughters but no sons.

Criss-cross inheritance: inheritance of sex-linked characters transmitted from fathers to daughters or from mothers to sons.

Lab7: Blood groups

- A blood type (also called a blood group) is a classification of blood based on the presence and absence of antibodies and also based on the presence or absence of inherited antigenic substances on the surface of red blood cells (RBCs).
- These antigens may be proteins, carbohydrates, glycoprotein's, or glycolipids, depending on the blood group system. Some of these antigens are also present on the surface of other types of cells of various tissues.
- Several of these red blood cell surface antigens can stem from one allele (or an alternative version of a gene) and collectively form a blood group system. Blood types are inherited and represent contributions from both parents.
- Blood serum is blood plasma without clotting factors**.**

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in Red Blood Cell	 A antigen	 B antigen	 A and B antigens	None

The ABO Blood Group System

- There are four major blood groups determined by the presence or absence of two antigens – A and B – on the surface of red blood cells:
- **Group A** – has only the A antigen on red cells (and B antibody in the plasma)
- **Group B** – has only the B antigen on red cells (and A antibody in the plasma)
- **Group AB** – has both A and B antigens on red cells (but neither A nor B antibody in the plasma) (**universal recipient).**

☐ **Group O** – has neither A nor B antigens on red cells (but both A and B antibody are in the plasma) (**universal donor).**

Genotypes	Antibodies in serum	Antigens on RBCs	Blood group
I^AI^A **or** I^{Ai}	**Anti-B**	**A**	**A**
I^BI^B **or** I^Bi	**Anti-A**	**B**	**B**
I^AI^B	**Neither**	**A and B**	**AB**
ii	**Anti-A and Anti-B**	**Neither**	**O**

The Rh system

☐ **The Rh** blood group system (including the Rh factor) is one of thirty-five known human blood group system. It is the second most important blood group system, after ABO.

☐ **Rh antigens** are transmembrane proteins with loops exposed at the surface of red blood cells. They be used for the transport of carbon dioxide and/ or ammonia across the plasma membrain.

☐ They are named for the **rhesus monky** in which they were first discovered. The commonly used terms Rh factor, **Rh positive and Rh negative** refer to the **D antigen** only.

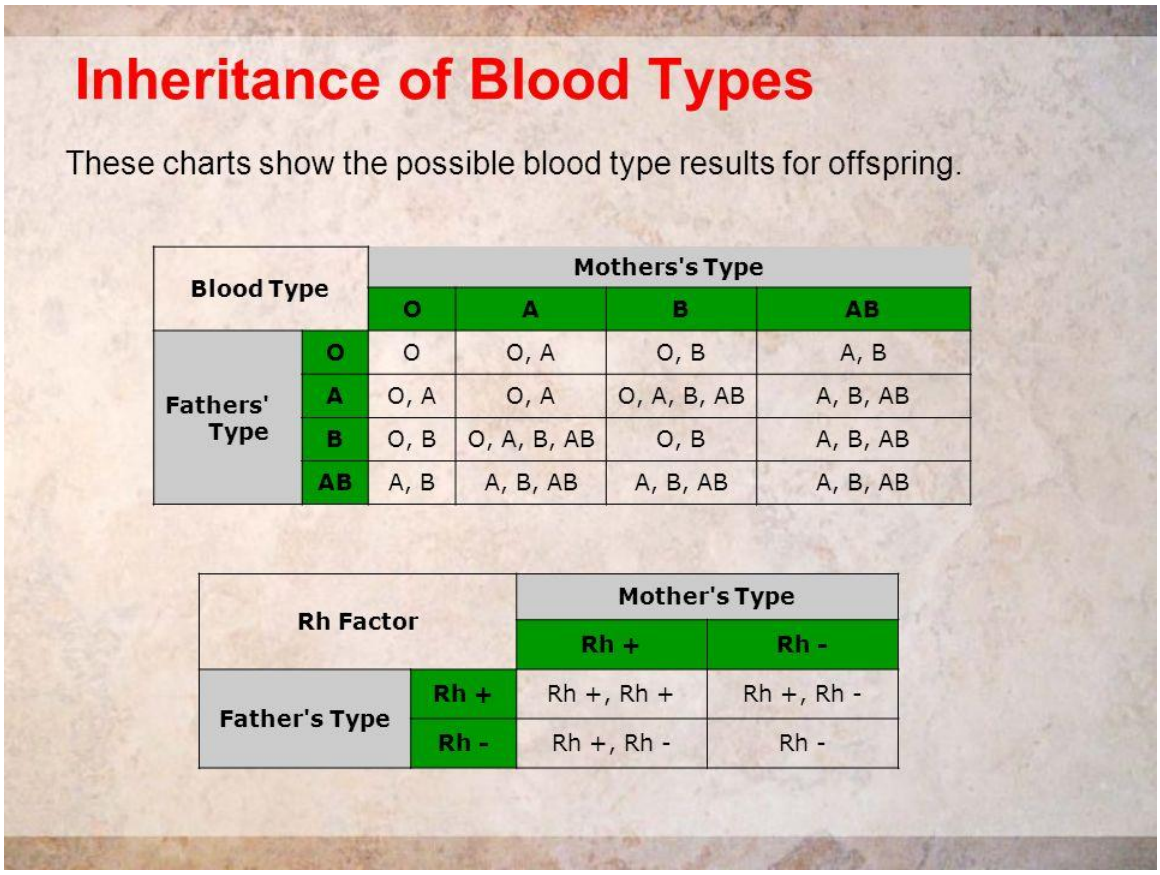
☐ Besides its role in **blood transfusion**,

☐ The **D antigen** is used to determine the risk of hemolytic disease of the new born (or **eryrthroblastosis fetalis**) for Rh disease management.

☐ The hemolytic condition occurs when there is an **incompatibility** between the blood types of the **mother and the fetus**. There is also potential **incompatibility** if the **mother is Rh nega**tive and the **father is positive**.

☐ When any incompatibility is detected, the mother often receives an injection at 28 weeks gestation and at birth to avoid the development of antibodies toward the **fetus**. (**Rh immune globulin injection).**

- The disorder in the fetus due to **Rh D incompatibility** is known as ***erythroblastosis fetalis*.**



Inheritance of Blood Types

These charts show the possible blood type results for offspring.

Blood Type		Mothers's Type			
		O	A	B	AB
Fathers' Type	O	O	O, A	O, B	A, B
	A	O, A	O, A	O, A, B, AB	A, B, AB
	B	O, B	O, A, B, AB	O, B	A, B, AB
	AB	A, B	A, B, AB	A, B, AB	A, B, AB

Rh Factor		Mother's Type	
		Rh +	Rh -
Father's Type	Rh +	Rh +, Rh +	Rh +, Rh -
	Rh -	Rh +, Rh -	Rh -

Mother's Rh factor	Father's Rh factor	Baby's Rh factor	Precautions
Rh positive	Rh positive	Rh positive	None
Rh negative	Rh negative	Rh negative	None
Rh positive	Rh negative	Could be Rh positive or Rh negative	None
Rh negative	Rh positive	Could be Rh positive or Rh negative	Rh immune globulin injections

Exercises

- ☐ ***If one of your parents is blood type A and the other is type B, which of the following blood types would you likely are?***
- ☐ ***Can these parents have a child with blood group O? How?***
- ☐ ***A man is blood group A was get married from a women is blood group B, the Rh factor for each other was Rh+, they have two children one of them is blood group O- , and the other is blood group A+; now:***
- ☐ ***What are the genotypes for these parents and children?***

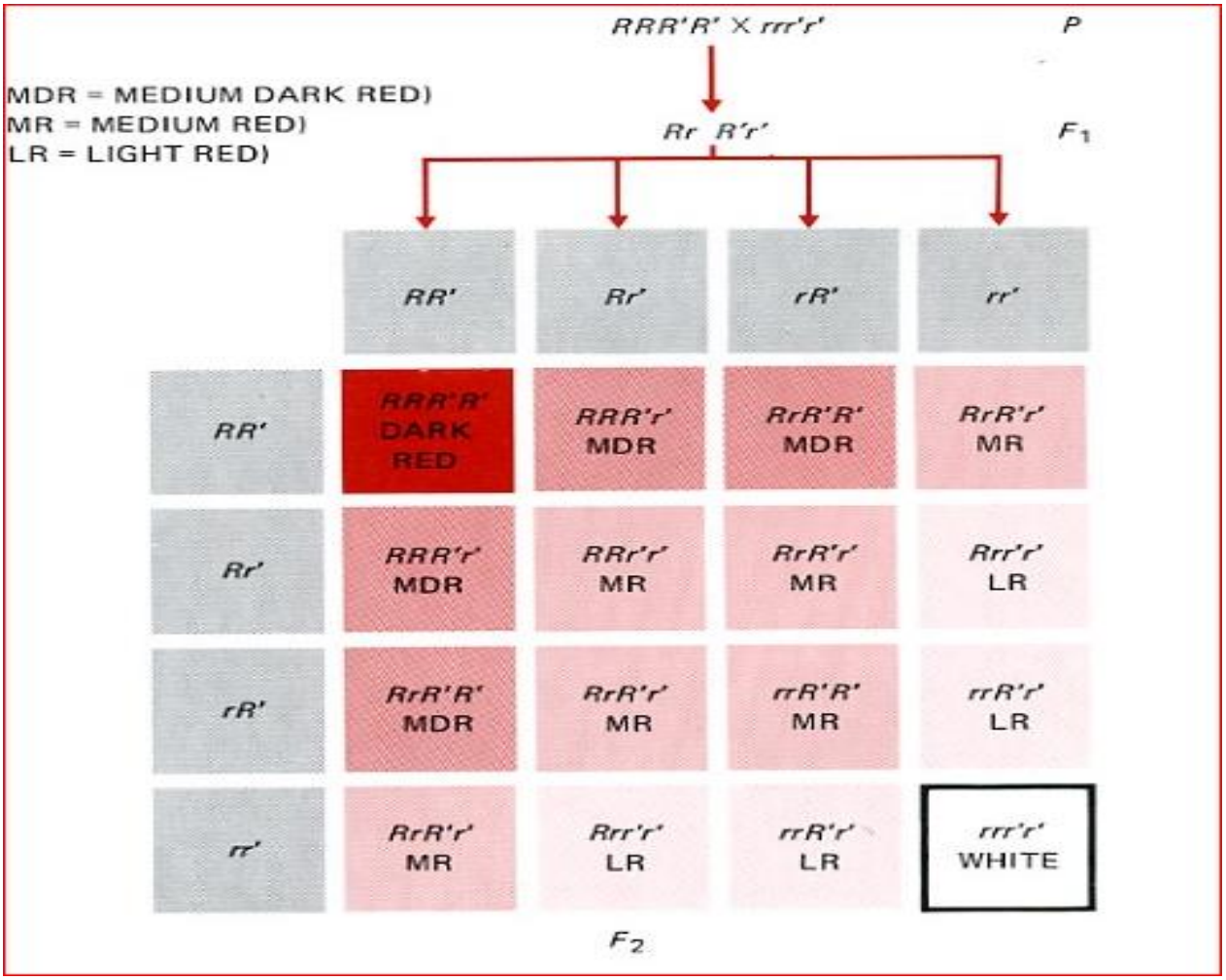
- ☐ A man with **unknown** blood group and **Rh-** get married from **two women**, the first is blood group **O+** she has one child is blood **group A+**, but the second women is blood group **A+** she have two children one of them **B-** and the other **B+**, What are the genotypes of parents and children?

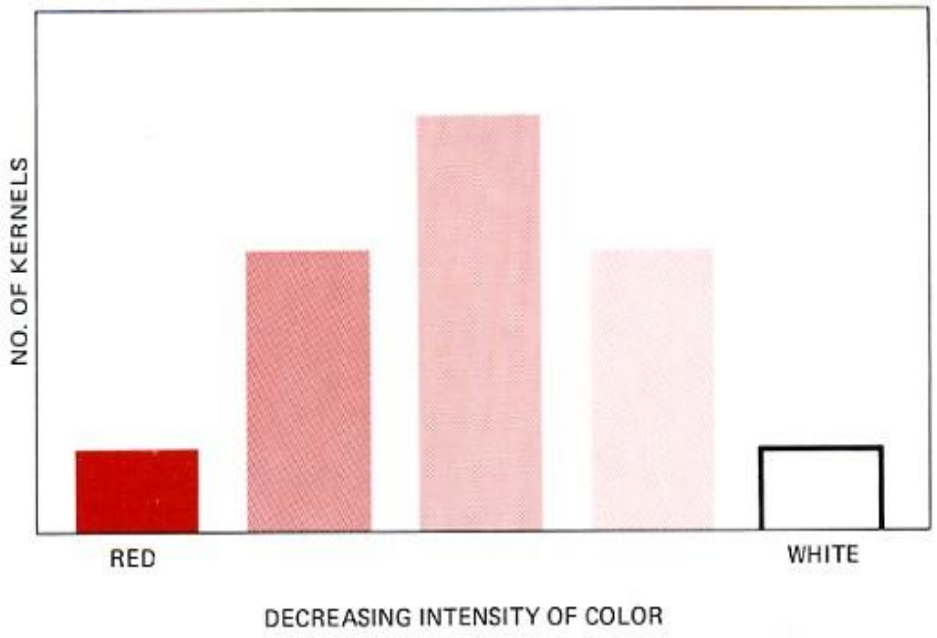
Lab 8: Quantitative Inheritance

Quantitative Inheritance: Are described numerically examples include **(height, weight, speed and metabolic rate).** In a population, a trait may be given a mean value, and the degree of may be described by the variance and standard deviation. Often exhibit a **continuum of phenotype** variation because they are usually influenced by multiple genes that exist as multiple allele.

Mendel considered **a single gene** to be responsible for a single trait, this type of inheritance called **Qualitative inheritance discontinuous traits**.

— **Quantitative inheritance**	**Qualitative inheritance**
1. **A continuous** trait is one that does not fall into discrete categories. Examples include height in human and fruit weight in tomatoes. 2. Occurs when **two or more different genes** influenced the outcome of a single trait (**no dominant principle**). 3. Depends on the **accumulative or additive action of several or many genes**, each of which produces a small proportion of the total effect. **4.** Environmental influence is especially important in the analysis of **Quantitative traits.**	1. **A discontinuous** trait is one that falls into discrete categories. Example includes brown eyes versus black eyes in human. 2. Occurs when a single gene to be responsible for a single trait (**dominant** principle). 3. Such this effect doesn't found.


MDR = MEDIUM DARK RED)
MR = MEDIUM RED)
LR = LIGHT RED)
RRR'R' × rrr'r'
P
Rr R'r'
F1
RR'
Rr'
rR'
rr'
RR'
RRR'R' DARK RED
RRR'r' MDR
RrR'R' MDR
RrR'r' MR
Rr'
RRR'r' MDR
RRr'r' MR
RrR'r' MR
Rrr'r' LR
rR'
RrR'R' MDR
RrR'r' MR
rrR'R' MR
rrR'r' LR
rr'
RrR'r' MR
Rrr'r' LR
rrR'r' LR
rrr'r' WHITE
F2


NO. OF KERNELS
RED
WHITE
DECREASING INTENSITY OF COLOR

Example

— We have length of 30 leaves of plant and they are: [54, (39), 48, 55, 60, 56, 47, 61, 57, 63, 67, 58, 45, 50, 55, 62, 55, (70), 63, 57, 68, 56, 58, 69, 49, 66, 51, 52, 49, 53]

— Are the results belonging to quantitative inheritance?

— Range (R) = **Maximum value- Minimum value**

70-39= 31

Class number (C.N)= 2.5 $\sqrt[4]{n}$

= $2.5\sqrt[4]{30}$

= 5.85

Class inter (C.I)= R/C.N = 31/5.85= 5.3 ~ 5

Each group contain 5 measures

C.I	F	X	FX	$X-\bar{X}$	$(X-\bar{X})^2$	$F(X-\bar{X})^2$
39-43	1	41	41	-15.33	235.01	235.01
44-48	3	46	138	-10.33	106.71	320.13
49-53	6	51	306	-5.33	28.41	170.46
54-58	10	56	560	-0.33	0.109	1.09
59-63	5	61	305	4.67	21.81	109.05
64-68	3	66	198	9.67	93.51	280.53
69-73	2	71	142	14.67	215.21	430.42
	30		1690			1546.68

—

X= maximum value+ minimum value/2

Mean $(\bar{x})$ **= fx/n = 1690/30= 56.33**

— **Variance** (s^2)= $F(X-\bar{X})^2/ n-1$

— = 1546.68/29 = 53.47

— **Standard deviation (s)**= √ s^2

— = √53.47

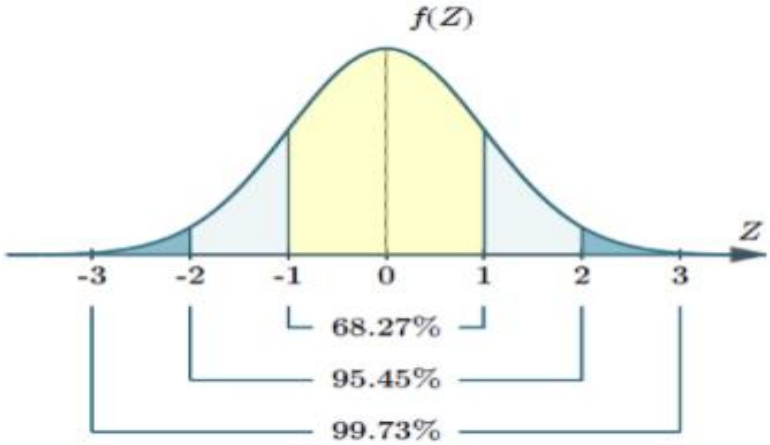
— =7.303

— $\bar{X}$±s= 68.27%

— $\bar{X}$+s= 56.33+7.303= 63.633 **~ 64**

— $\bar{X}$-s= = 56.33-7.303= 49.027 **~ 49**

— The measurements (49-64) must be ≥ 68.27 to have quantitative inheritance and normal distribution



The number of plants between (49-64) is 21

— 21x100/30 =70%

— 70% > 68.27%

— **Quantitative inheritance and normal distribution.**

— **Note:**

— If the result < 68.27% that mean the experiment not belong to quantitative inheritance and there is experimental or distribution error.

— **Correlation variance (C.V)=(s/x)*100**

— **7.303/56.33*100= 12.69% length**

— **C.V. of width = 18.82% given in the question**

— **Correlation variance:** using to compare between two traits belong to quantitative inheritance such as the length and width of leaves, however if the c.v. for the study trait less than mean of the trait don't effected by the environmental changes and the result is best.

Lab9: Cytogenetics and Karyotyping

Overview and objectives

The object of this lab is to learn how cytogeneticists use karyotyping to understand chromosomal abnormalities.

Karyotyping is a technique where chromosomes are stained and visualized during the metaphase stage of cell division (mitosis or meiosis).

In this lab, you will take on the role of a medical cytogeneticist and use human karyotypes to diagnose various diseases and abnormalities in patients. Upon completion of the lab, you should be familiar with what chromosomes are, what a karyotype is and how it is constructed, the different ways in which chromosomal abnormalities might arise, and the basic terminology used to describe chromosomes.

Background information

Overview

DNA is packed into units called **chromosomes**. In many species, DNA is closely associated

with several types of proteins called histones that are used to tightly pack the DNA into the cell nucleus (in eukaryotes). In eukaryotes, we say that the chromosomes are linear, whereas most bacteria contain a single circular chromosome. All eukaryotes also contain a second genome inside their cells called mitochondrial DNA (mtDNA). Genes in mtDNA help regulate the process of cellular respiration. In addition, plants and several protists contain a third genome in their chloroplasts called chloroplast DNA (cpDNA), which is involved with photosynthesis. In this lab we will focus exclusively on **eukaryotic nuclear chromosomes**.

Human somatic cells contain 46 chromosomes. As humans are a diploid species, half of the complement of chromosomes (23) originated from a sperm cell and half (23) originated from the egg cell. These are called **homologous chromosomes**. For example, each person has two copies of Chromosome 1, one copy inherited from the father and one copy inherited from the mother. Portions of homologous chromosomes

can exchange segments during meiosis in a process called recombination. During cell division, each homolog is also duplicated, forming sister chromatids (Figure 1). The region where sister chromatids attach during cell division is called the **centromere**.

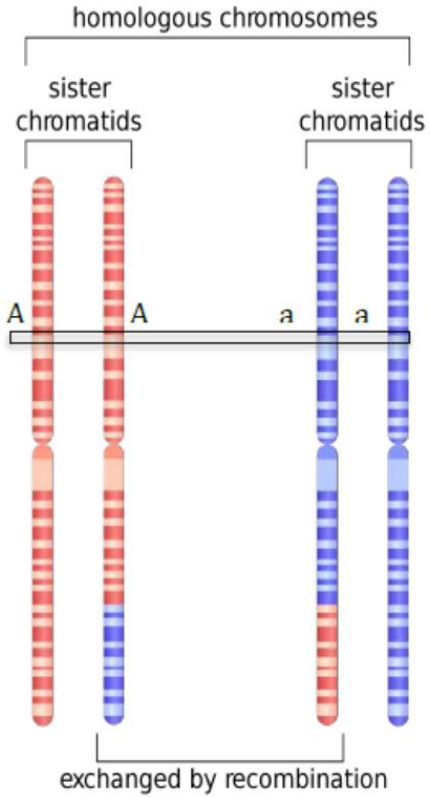


Figure. 1. Homologous chromosomes and sister chromatids. Note that recombination has taken place. Box and letters illustrate heterozygosity at the 'A' gene.

Telomeres are regions at the tips of chromosomes that consist of highly repetitive sequences that form a protective cap to the ends of chromosomes. Telomeres tend to shorten with each cell division, leading to cell aging and eventually cell death. Much research has focused on techniques decrease the propensity of telomere shorting to counteract the aging process. Therapeutic-related work has also focused on the role of telomeres in the proliferation of cancer cells.

Human sex is determined genetically through the XY system—human females are XX and human males are XY. Research has shown that human "maleness" is determined by a gene that sits on the Y chromosome. In several other species, sex is not determined by genes and chromosomes, but by environmental temperature though what is called temperature- dependent sex determination. For example, in many

crocodilian species, males are only produced if eggs are incubated at intermediate temperatures. In contract, females are produced if eggs are incubated at either extreme.

Chromosome classification

Chromosomes are generally classified using multiple criteria. First, they are number from largest to smallest. For example, human chromosome 1 would be the largest chromosome, which contains 2,100 protein-coding genes and 249 million bp. The sex chromosomes are labelled appropriately as either XX in females or XY in males. Note that the X-chromosome is much larger than the Y-chromosome. Therefore, the X- and Y- chromosomes are considered nonhomologous (although there are a few homologous regions that are needed for proper pairing during cell division).

The relative position of the centromere can also differ between chromosomes. Centromeres that are placed in the center of a chromosome are called **metacentric chromosomes**, resulting in equal length chromosomal arms. When the centromere is not found in a central position, different chromosomal arm lengths result. These arms are referred to as **p arms (short arms)** and **q arms (long arms)**. In addition to metacentric chromosomes, chromosomes can be **submetacentric, acrocentric, and telocentric**, all varying in the relative position of the centromere (Figure 2).

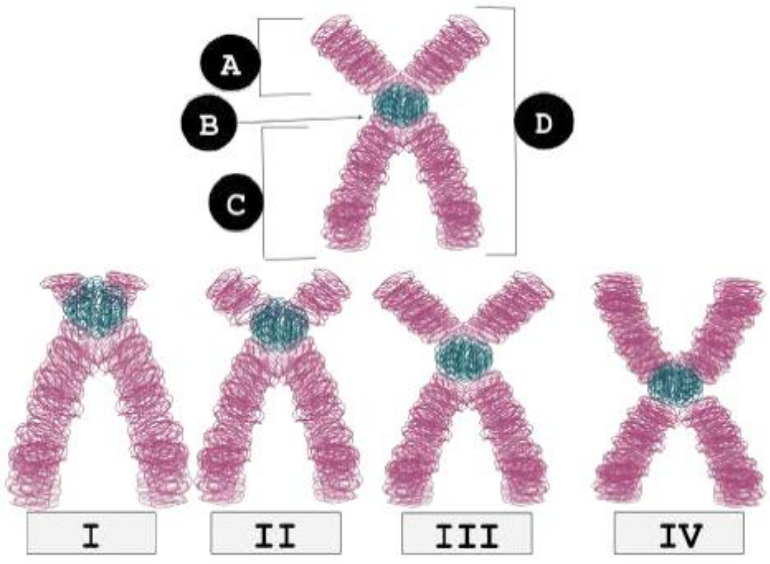


Fig. 2. Alternative means of classifying chromosomes based on the relative position of the centromere. I= telocentric; II = acrocentric; III = submetacentric; IV= metacentric. A = p arm; B = centromere; C = q arm; D= sister chromatid

A final way that cytogeneticists can differentiate and classify chromosomes is to stain them with dyes that produce diagnostic banding patterns. Note that bands on a stained chromosome are not indicative of genes. In general, there can be dozens or hundreds of genes within a single band. A common stain used by cytogeneticists is called the **Giemsa stain**, also known as the G-banding technique.

Following the staining procedure, AT-rich regions of the chromosome appear dark whereas transcriptionally active GC-rich regions incorporate less of the dye and thus appear lighter. The differential banding patterns can be used to identify homologous chromosomes and look for chromosomal alterations.

Procedure for creating karyotype

1. Obtain cells (e.g. white blood cells, skin cells, cancer cells, cells from amniotic fluid).

Obtaining cells from amniotic fluid (amniocentesis) can be used to detect genetic abnormalities in the fetus.

2. Treat cells with chemical to promote cell division.

3. Treat cells with a second chemical that halts cell division at metaphase. This is the stage when chromosomes are highly condensed and easily visualized.

4. Immerse cells in a hypotonic solution and place on glass slide.

5. Stain chromosomes with Giemsa stain and observe under microscope.

6. Prepare digital images and analyze results.

Genetic abnormalities observed by G-banded karyotyping

In general, chromosome abnormalities can include both **numerical changes** and **structural changes**. Numerical changes can involve an irregular number of a particular chromosome (**aneuploidy**). For example, a diploid individual possessing

three copies of a chromosome instead of the usual two copies would be called **trisomy**, whereas an individual with one copy would be called **monosomy**. Trisomy 21 would mean three copies of chromosome 21 and is characteristic of individuals with Down syndrome (Figure. 3)

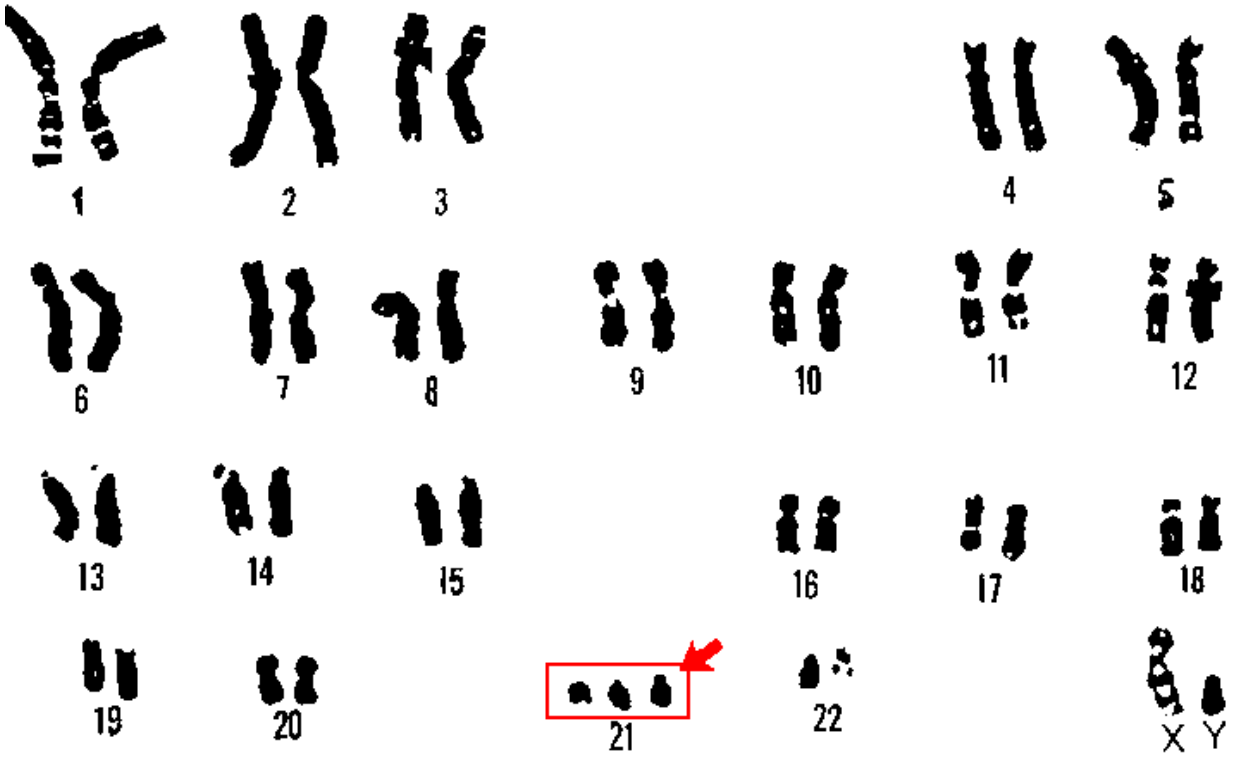


Figure 3. Karyotype of a human male with Trisomy 21 (Down syndrome). Note the three copies of Chromosome 21. Homologous chromosomes were determined by size and banding pattern.

In addition to abnormalities in the number of specific chromosomes, an individual can have an incorrect number of the complete set of chromosomes. A gain in one or more complete sets of chromosomes is termed **euploidy**, whereas a loss of an entire set of chromosomes is called **monoploidy**. Monoploidy is usually fatal due to recessive mutations (many of which are lethal) being phenotypically expressed.

In addition to numerical changes, chromosomes can also exhibit the following structural changes involving either one or two chromosomes (Fig. 4):

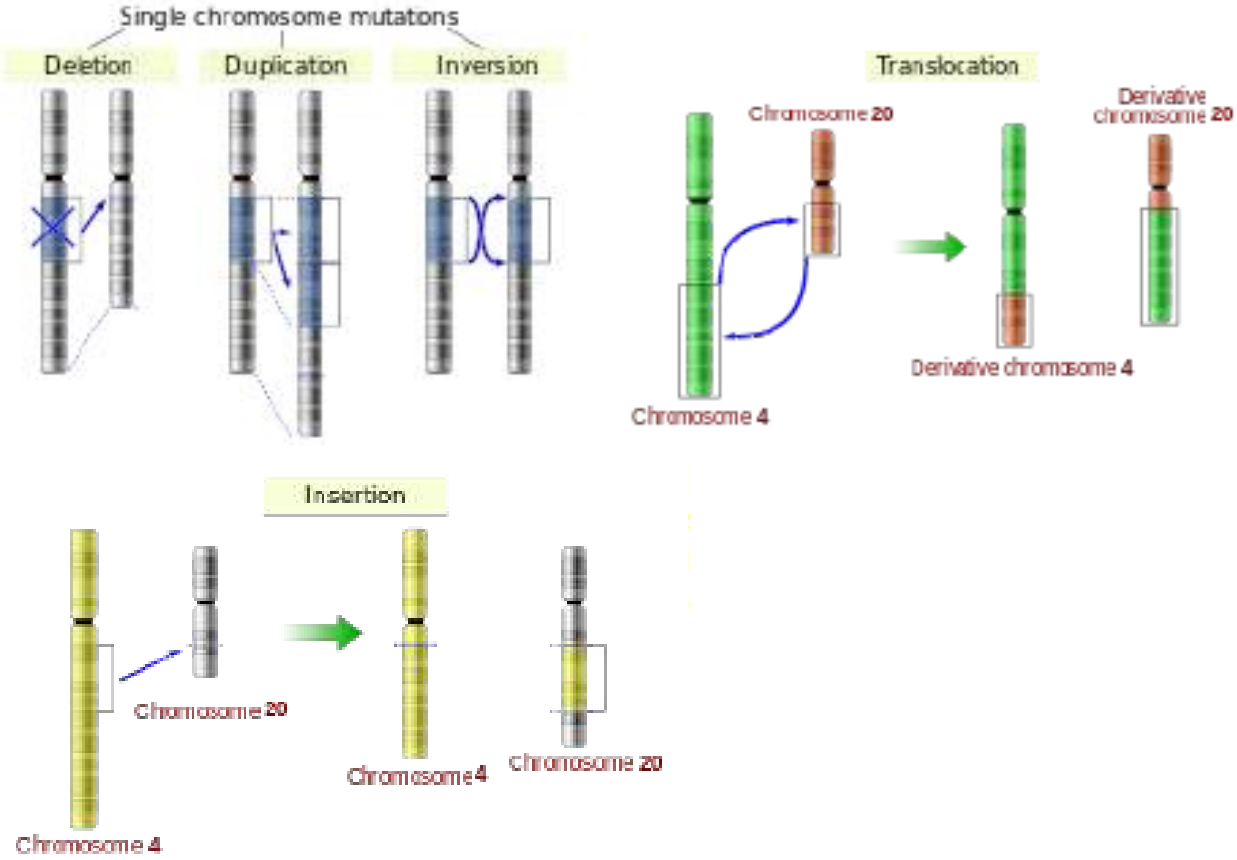
a. Translocations (two chromosomal change) – two non-homologous chromosomes fuse or swap segments.

b. Insertions (two chromosomal change) – one region of one chromosome removed and inserted into a different chromosome.

c. Inversions (single chromosomal change) – certain regions of a chromosome are placed in an incorrect orientation with respect to the remainder of the chromosome.

d. Duplications (single chromosomal change) – one segment of a chromosome is duplicated.

e. Deletions (single chromosomal change) – removal or loss of a particular region or segment of a chromosome. Commonly occurs in telomeric regions during cell division.



Although standard karyotyping can provide a powerful approach to diagnosing various genetic diseases, it is considered a wide resolution technique, meaning that it is unable to detect genetic abnormalities below a certain number of base pairs (~1 million). In these cases, other techniques such as fluorescent in situ hybridization (FISH), array comparative genome hybridization (CGH), and direct DNA sequencing can be used, the latter of which can be used to detect single nucleotide changes or polymorphisms (SNPs).

Lab 10: Allele frequency

An individual's genotype is the combination of alleles found in that individual at a given genetic locus. If there are two alleles in a population at locus A (*A* and *a*), then the possible genotypes in that population are *AA*, *Aa*, and *aa*. Individuals with genotypes *AA* and *aa* are homozygotes (i.e., they have two copies of the same allele). Individuals with genotype *Aa* are heterozygotes (i.e., they have two different alleles at the A locus). If the heterozygote is phenotypically identical to one of the homozygotes, the allele found in that homozygote is said to be dominant, and the allele found in the other homozygote is recessive.

Most phenotypic variation among individuals and organisms is **quantitative** rather than **qualitative** in nature. Quantitative characteristics have a **continuous distribution** among different individuals. This differs from **monogenic traits** displaying a Mendelian mode of inheritance, which can be assigned to separate, distinct categories.

Examples of common quantitative genetic characteristics in humans are **height**, **weight**, **eye** and s**kin color**, **blood pressure**, **p**lasma **c**oncentrations of **glucose**, lipids, **intellectual abilities**, behavioral patterns, and others. A primary goal of quantitative genetics is to distinguish the **genetic** and **environmental contributions to a trait**. The underlying genetic variation (**genotypic variation**) is **interchangeably** called **polygenic** (many genes), **multigenic** (several genes), or **multifactorial** (many factors).

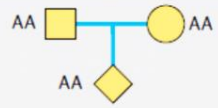
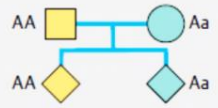
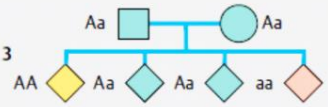
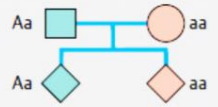
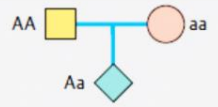
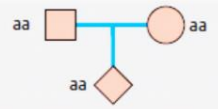
Allele frequency

The allele frequency (often called gene frequency) designates the proportion of a given allele at a given locus in a population. If an allele accounts for 20% of all alleles present (at a given locus) in the population, its frequency is 0.20. The allele frequency determines the frequencies of the individual genotypes in a population.

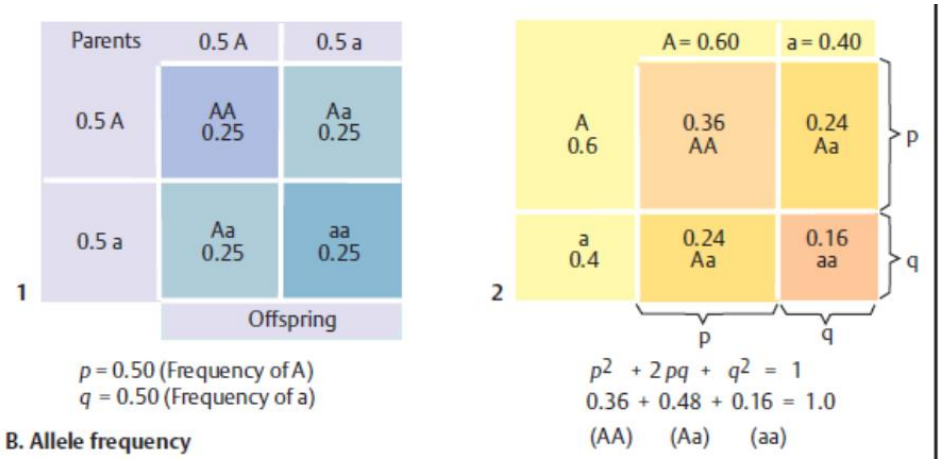
For example, for a gene locus with two possible alleles **A** and **a,** three genotypes are possible: **AA**, **Aa** , or **aa**. The frequency of the two alleles together (p the

frequency of A and q the frequency of a) is 1.0 (100%). If two alleles A and a are equally frequent (each 0.5), they have the frequencies of p = 0.5 for the allele A and q = 0.5 for the allele a (1). Thus, the equation p + q = 1 defines the population at this locus. The frequency distribution of the two alleles in a population follows a simple binomial relationship**: (p + q)2 = 1**. Accordingly, the distribution of genotypes in the population corresponds to **p2 +2pq+q2 = 1.0.** The expression **p2** corresponds to the frequency of the genotype **AA**; the expression 2pq corresponds to the frequency of the heterozygotes **Aa**; and **q2** corresponds to the frequency of the homozygotes **aa**.

When the frequency of an allele is known, the frequency of the genotype in the population can be determined. For instance, if the frequency p of allele A is 0.6 (60%), then the frequency q of allele a is 0.4 (40%, derived from q = 1 – p or 1 – 0.6). Thus, the frequency of the genotype AA is 0.36; that of Aa is 2 0.24 = 0.48; and that of aa is 0.16 (2).And conversely, if genotype frequency has been observed, the allele frequency can be determined. If only the homozygotes aa are known (e.g., they can be identified owing to an autosomal recessive inherited disease), then q2 corresponds to the frequency of the disorder. From p=1-q, the frequency of heterozygotes (2pq) and of normal homozygotes (p2) can also be determined.

		Genotype of parents	Genotype of offspring
1		AA and AA	1.0 AA
2		AA and Aa	0.50 AA 0.50 Aa
3		Aa and Aa	0.25 AA 0.50 Aa 0.25 aa
4		Aa and aa	0.50 Aa 0.50 aa
5		AA and aa	1.0 Aa
6		aa and aa	1.0 aa

A. Expected frequency of genotypes in children of parents with different genotypes



Hardy–Weinberg Equilibrium Principle

The Hardy–Weinberg equilibrium principle states that in certain circumstances, the frequency of alleles will **remain constant** in a population from one generation to the other. This principle was formulated independently by the English mathematician G. F. Hardy and the German physician W. Weinberg in 1908. It assumes that any allele that causes a severe genetic disease incompatible with reproduction will be replaced by a new mutation, as long as the rate of mutations at this locus remains constant.

Constant allele frequency

An autosomal recessive allele (here referred to as allele a) that leads to a severe disorder in the **homozygous state** remains undetectable in the **heterozygous state** in a population. Only the homozygotes (aa) can be recognized because of their disease. The frequency of affected individuals (homozygotes aa) depends on the frequency of allele a (corresponding to q). The frequency of the three genotypes is determined by the binomial relationship **(p+q)2 = 1**, where **p** represents the frequency of allele A and **q**, the frequency of allele a (see previous page). The homozygous alleles (aa) eliminated in one generation by illness are replaced by new mutations. This occurs in each generation, and results in equilibrium between elimination due to illness and frequency of the mutation.

Calculating Frequencies for Multiple Alleles in Hardy–Weinberg Populations

We commonly find several alleles of a single gene in a population. The ABO blood group in humans is such an example. Recall that the locus I (isoagglutinin) has three alleles I^A, I^B, and i, yielding six possible genotypic combinations (I^AI^A, I^Bi , ii , I^AI^B, I^Ai , I^Bi). Remember that in this case I^A and I^B are codominant alleles and that both of these are dominant to i. The result is that homozygous I^AI^A and heterozygous I^Ai individuals are phenotypically identical, as are I^BI^B and I^Bi individuals, so we can distinguish only four phenotypic combinations.

By adding another variable to the Hardy–Weinberg equation, we can calculate both the genotype and allele frequencies for the situation involving three alleles. Let p, q, and r represent the frequencies of alleles I^A, I^B, and i, respectively.

Note that because there are three alleles

p + q + r = 1

Under Hardy–Weinberg assumptions, the frequencies of the genotypes are given by **(p + q + r)2 = p2 + q2 + r2 + 2pq + 2pr + 2pq = 1**

If we know the frequencies of blood types for a population, we can then estimate the frequencies for the three alleles of the ABO system. For example, in one population sampled, the following blood-type frequencies are observed: A = 0.53, B = 0.13, O = 0.26. Because the i allele is recessive, the population's frequency of type O blood equals the proportion of the recessive genotype r^2. Thus,

$$r^2 = 0.26$$
$$r = \sqrt{0.26}$$
$$r = 0.51$$

Using r, we can calculate the allele frequencies for the IA and IB alleles. The IA allele is present in two genotypes, I^AI^A and I^Ai. The frequency of the I^AI^A genotype is represented by p^2 and the I^A i genotype by 2pr. Therefore, the combined frequency of type A blood and type O blood is given by

$p^2 + 2pr + r^2 = 0.53 + 0.26$

If we factor the left side of the equation and take the sum of the terms on the right

$$(p + r)^2 = 0.79$$
$$p + r = \sqrt{0.79}$$
$$p = 0.89 - r$$
$$p = 0.89 - 0.51 = 0.38$$

Having calculated p and r, the frequencies of allele I^A and allele i, we can now calculate the frequency for the I^B allele:

p + q + r = 1

q = 1 - p - r

= 1 - 0.38 - 0.51

= 0.11

Calculating Genotype Frequencies for Multiple Alleles in a Hardy–Weinberg Population Where the Frequency of Allele I^A = 0.38, Allele I^B = 0.11, and Allele i = 0.51

Genotype	Genotype Frequency	Phenotype	Phenotype Frequency
$I^A I^A$	$p^2 = (0.38)^2 = 0.14$	A	0.53
$I^A i$	$2pr = 2(0.38)(0.51) = 0.39$		
$I^B I^B$	$q^2 = (0.11)^2 = 0.01$	B	0.12
$I^B i$	$2qr = 2(0.11)(0.51) = 0.11$		
$I^A I^B$	$2pr = 2(0.38)(0.11) = 0.084$	AB	0.08
ii	$r^2 = (0.51)^2 = 0.26$	O	0.26