POPULATION GENETICS
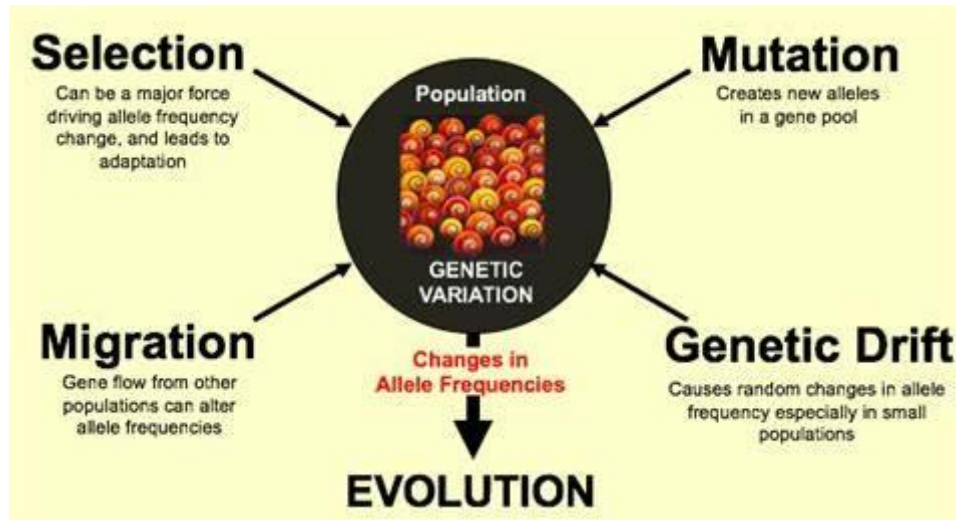

- The theory of evolution, proposed by Charles Darwin in 1859, was a strong motivating force in the field of genetics.

- Since evolution is based on gene frequency changes that occur in populations of freely inter breeding individuals, the application of mendelian principles of inheritance to populations of sexually reproducing organisms was essential for a complete under standing of the evolutionary process.

- Mendelism and the analysis of effects of inbreeding and cross breeding in randomly mating populations, coupled with the principles of quantitative genetics led first to the establishment of the discipline called population genetics and ultimately to the formulation of mechanisms that could account for the process of organic evolution.

- A population is usually defined as a community of sexually inter-breeding individuals.

- Since Mendelian laws apply to the transmission of genes among these individuals, a community has been termed by Wright as Mendelian population.

- A Mendelian population is defined as a group of sexually reproducing organisms with a relatively close degree of genetic relationship (such as species, strain

variety etc.) residing within defined geographical boundaries where inter-breeding occurs.

- In the Mendelian population each member has an equal chance of mating with any other member of the opposite sex.

- Within the population the set of genetic information carried by all inter breeding members is called gene pool.

- It can be considered as a gametic pool from which samples are drawn at random to form the zygote of the next generation.

- If a pair of alleles is considered, it can be found that the percentage of the gametes in the gene pool will depend upon the genotypic frequencies of the parental generation whose gametes form the pool.

- For example, if most of the population were of the recessive genotype, the frequency of recessive alleles in the pool would be relatively high.

- The term gene frequency is used to represent the proportions of the different alleles of a gene in a population.

- When mating between members of a population are completely at random i.e. when every male gamete in the gene pool has an equal opportunity of uniting with every female gamete the zygotic frequencies expressed in the next generation may be predicted from a knowledge of the gene frequencies in the gene pool of the parental population.

- One of the first attempts at utilizing the concepts of gene frequencies was made by G. Udney Yule and others when they argued that dominant alleles, no matter what their initial frequency would be, expected to reach a stable equilibrium frequency of three dominant individuals to one recessive, since this was the Mendelian segregation pattern for these genes.

- Although widely accepted at first, this argument was disproved in 1908 by Godfrey H. Hardy and Wilhelm Weinberg.

- They independently discovered the basic principles of population genetics, that an equilibrium is established for allelic frequencies in a freely inter breeding sexually reproducing population and that the frequency of each allele remains constant generation after generation.

- The constancy is maintained as long as the following conditions are met;

  · The population must be large enough so that sampling errors can be disregarded.
  · Mating within the population should occur at random.
  · There should be no selective advantage for any genotype in all genotypes produced by random mating are equally viable and fertile.
  · Other influencing factors like mutation, migration, selection and random genetic drift should be absent.

- If these conditions are met genetic equilibrium will be established. If not,gene frequencies will change. This change of gene frequencies over time is the basis of evolution.

- Let p be the frequency of a dominant allele 'A' and q the frequency of a recessive allele 'a' in a population. Because the sum of these frequencies represent 100 percent of the population, **p+q = 1.**

- If in a population 70% of the alleles are A and 30% are a then p = 0.7 and q = 0.3.

- A Punnet square shows that the distribution of genotypes produced by random mating in the next generation can be expressed as p2 + 2pq + q2.
  A (p=0.7)
  a (q=0.3)
  A (p=0.7)
  AA(p2=0.49) Aa(pq= 0.21)
  a (q=0.3)
  Aa (pq=0.21) aa (q2=0.09)

The Hardy-Weinberg Principle

frequency of homozygous dominant genotype

frequency of heterozygous recessive genotype

$$p^2 + 2pq + q^2 = 1$$

frequency of heterozygous genotype

- On the new generation the frequency of 'A' is p2 + ½ (2 pq) and the frequency of 'a' is q2 + ½ (2pq). [Only one half of the heterozygote 2pq is used because

Mendelian segregation is expected to add that fraction to the gametic pool of each allele among the parents.]

- Another example;

Allele frequencies: p=0.6, q=0.4

	A p=0.6	a q=0.4
A p=0.6	AA $G_{AA} = p^2$	Aa $G_{Aa} = pq$
a q=0.4	Aa $G_{Aa} = pq$	aa $G_{aa} = q^2$

Expected Genotype frequencies
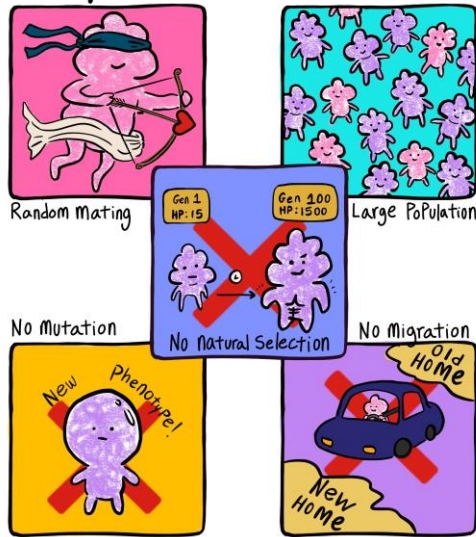
$$G_{AA} = p^2 = 0.36$$
$$G_{Aa} = 2pq = 0.48$$
$$G_{aa} = q^2 = 0.16$$

$$G_{AA} + G_{Aa} + G_{aa} = 1 \| 0.36 + 0.48 + 0.16 = 1$$

- A population in which the frequency of a given gene remains constant from generation to generation is said to be in a state of genetic equilibrium for that gene.

- Now the Hardy - Weinberg law can be stated as follows: - the gene frequencies and genotypic frequencies will remain constant from generation to generation infinitely in a large interbreeding population in which mating is at random and no selection, migration or mutation occurs.

- One important aspect of the genetic equilibrium thus established is that it maintains a state of genetic variability in a population.

- Once fixed in a population, allele frequencies remain unchanged during equilibrium – a factor important to the evolutionary process.

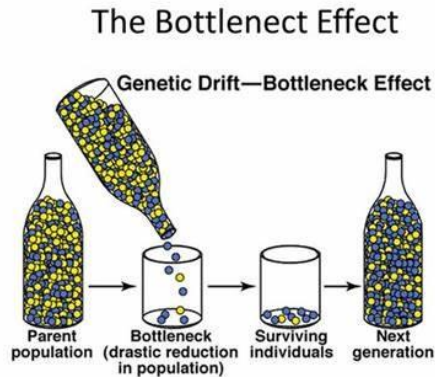**FACTORS INFLUENCING GENETIC EQUILIBRIUM**

- The Hardy-Weinberg equilibrium population is in a steady state-all alleles are maintained at a constant frequency-and this is precisely what Hardy and Weinberg intended to demonstrate. However, populations generally do not remain fixed.

- Gene frequencies change over time, thus forming the basis for evolution; the Hardy-Weinberg equilibrium model must therefore be expanded to include the forces that change or shift the equilibrium point, forces such as mutation, natural selection, genetic drift, meiotic drive, and migration.

Genetic Drift

- Each individual in a Mendelian population generates millions upon millions of gametes.

- From those millions, however, only one is involved in the formation of each offspring. If the number of offspring in a population is small, the number of gametes that go to form those offspring will also be small.

- Concomitantly, a large number of offspring means that a large number of gametes are involved.

- The smaller number of offspring will represent a smaller sample of parental gametes; and the smaller the sample of parental gametes, the greater are the chances for sampling errors.

- In small populations, the offspring may all be the same type simply by chance.

- Random genetic drift, then, is a random fluctuation in allele frequencies.

- Its effect on large populations is negligible.

The Bottlenect Effect

Genetic Drift—Bottleneck Effect

Parent population | Bottleneck (drastic reduction in population) | Surviving individuals | Next generation

- Consider a large population in which the frequency of A is $p = 0.4$ and the frequency of a is $q = 0.6$.

- In a random sample from this population the allele frequencies are expected to remain 0.4 and 0.6 respectively, with some expected deviation occurring because of sampling.

- The standard deviation (a) expected in a sample drawn from a large population is $= \sqrt{pq/2N}$
  where N = number of diploid individuals in the sample.

- In a sample of 10,000 individuals, the standard deviation would be = 0.6 X 0.4/20,000 = 0.0035

- This standard deviation means that for a normal distribution curve, the mean value plus or minus the standard deviation, takes in about two-thirds of the total area under the curve.

- For a sample size of 20,000 with $p = 0.4$ and $q = 0.6$, the frequency of A will lie within $0.4 \pm \sigma$, or between 0.3965 and 0.40035.

- However, if the sample is made up of only 20 individuals, the standard deviation will be = 0.6 X 0.4/40 = 0.077

- In this case, two-thirds of the time the frequency of A will lie within 0.4 ±σ, or between 0.323 and 0.477.

- If a new population is being established from a sample of a large parent population, a sample size of 20,000 will ensure that the gene frequencies-at least at the beginning-in both the old and the new populations will be essentially the same.

- However, if the new population is founded with a sample made up of only 20 individuals, chances are that the gene frequencies in the two populations will exhibit significant differences simply because of sampling error.

- The role of genetic drift in evolution has been actively debated, but no solid conclusions have resulted.

- In the human population there are instances of what appears to be genetic drift in operation.

- For example, the uneven distribution of the AB blood groups in different parts of the world could be the result of some areas having been settled by small migrant groups that were atypical of their populations.

- The high frequency of the A blood type among American Indians could stem from a small founding population of Asians crossing the Bering Strait and subsequently founding a series of populations throughout North and South America.

- The O blood type is uncommon in Asia, but the original migrants to North America may have been an atypical sample.

- Instances of drift are difficult to verify, though, because of the following restrictions which must be applied:

  ➢ The traits in question must be well understood genetically.

  ➢ The traits must be adaptively neutral.

  ➢ The population must be small, either at the time of origin or at some later time in its existence, and reproductively isolated

  ➢ The population's parent population and the population which now surrounds it must be genetically well defined with respect to the traits in

question.

- Migration of genotypes into the population either must not have occurred or be amenable to precise quantification so that its effects can be taken into account. Such populations are difficult to find.

- Bentley Glass has studied a population of "Dunkers" (German Baptist Brethren), numbering about 350, in south-central Pennsylvania.

- The Dunkers migrated from Germany early in the eighteenth century, and their communities have in large part remained reproductively isolated from each other and from the surrounding American population.

- The frequency of blood group A is 0.6 in the Dunkers but only 0.40 in the United States and 0.45 in the parent German population.

- The B and AB groups are almost entirely absent from the Dunkers (0.05) but comprise 0.15 of the United States and German populations.

- The same fluctuations hold for the M and N alleles and also for other presumably nonadaptive traits, such as attached ear lobes, "hitchhiker's thumb," and mid-digital hair.

- In all of these traits, the genes in the Dunkers have frequencies like neither the Germans nor the Americans surrounding them, nor like anything in between.

- Instead, the frequencies have fluctuated widely from one extreme to the other, suggesting that genetic drift has been at work.

Genetic load

- Genetic load is a measure of the number of disadvantageous genes in a population or of the damage done to the population by certain genetic factors.

- Disadvantageous genes reduce fitness by mortality, morbidity or sterility in **heterozygotes**, if the gene is dominant and in **homozygotes**, if it is recessive. Thus, it is related to **Darwinian fitness.**

- The genetic load can have two sources, one, **mutational** and the other, **segregational** and **recombination**.

- The mutational load is due to recurrent mutations.

- Most of the mutations are disadvantageous. It may be lethal also.

- While dealing with mutational load several factors like the number of deleterious genes, the nature of mutant alleles (recessive alleles, dominant alleles, partially lethal alleles etc.) and the occurrence of mutations are to be taken into consideration.

- The frequencies of mutant genes are, however, low. But there are possibilities of an increase of this type of load due to reduction of selection with the progress of civilization.

- Segregation leads to the formation of different **genotypes**, of which some are less fit.

- There may be a **heterozygous advantage** also as in balanced polymorphism.

- Blood group incompatibility is another component of genetic load.

- One should note the differential fitness of some genotypes under different environmental conditions.

- A comparative study of the offspring of **consanguineous** and **non-consanguineous** marriages can provide useful information on genetic load due to disadvantageous genes.

- The number and proportion of homozygous offspring are relatively high as a result of the first type of mating.

- The genetic load of disadvantageous recessive genes is usually expressed by **lethal equivalents**.

- A lethal equivalent is one deleterious gene that causes death in a homozygous state.

- Two genes, when each of them in a homozygous combination will lead to death in **50%** of the cases. It is said that the total genetic damage is **1.5** to **2.5** lethal equivalents per gamete and per zygote is **3** to **5**.