RANDOM MATING AND THE HARDY-WEINGBERG METHOD

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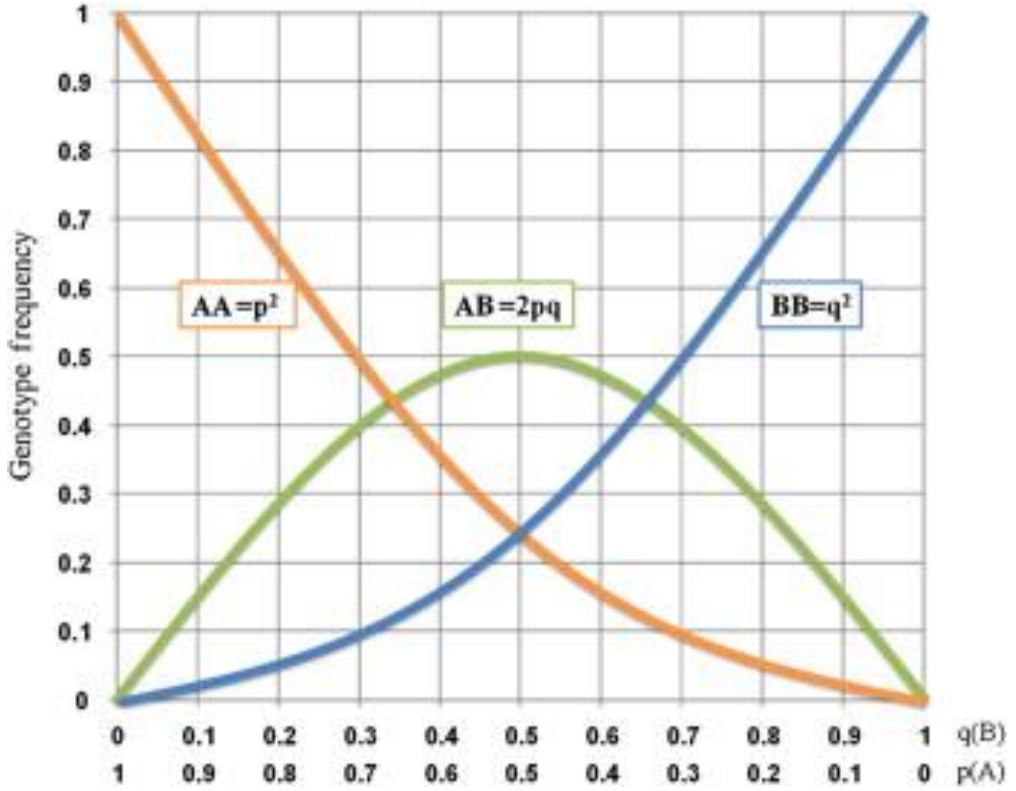
Hardy-Weinberg Principle

The Hardy-Weinberg is a principle stating that the genetic variation in a population will remain constant from one generation to the next in the absence of disturbing factors. When mating is random in a large population with no disruptive circumstances, the law predicts that both genotype and allele frequencies will remain constant because they are in equilibrium.

The Hardy-Weinberg equilibrium can be disturbed by a number of forces, including mutations, natural selection, nonrandom mating, genetic drift, and gene flow. For instance, mutations disrupt the equilibrium of allele frequencies by introducing new alleles into a population.

When a population meets all the Hardy-Weinberg conditions, it is said to be in Hardy-Weinberg equilibrium (HWE). Human populations do not meet all the conditions of HWE exactly, and their allele frequencies will change from one generation to the next, so the population evolves. How far a population deviates from HWE can be measured using the “goodness-of-fit” or chi-squared test ($\chi 2$)

- The distribution of genotypes in a population in Hardy-Weinberg equilibrium can be graphically expressed as shown in the accompanying graph. The x-axis represents a range of possible relative frequencies of A or B alleles. The coordinates at each point on the three genotype lines show the expected proportion of each genotype at that particular starting frequency of A and B.



- Consider a single biallelic locus with two alleles A and B with known frequencies (allele A = 0.6; allele B = 0.4) that add up to 1.

- Possible genotypes: AA, AB and BB

- Assume that alleles A and B enter eggs and sperm in proportion to their frequency in the population (i.e., 0.6 and 0.4)

- Assume that the sperm and eggs meet at random (one large gene pool).

Calculation of Genotypic Frequency

- The probability of producing an individual with an AA genotype is the probability that an egg with an A allele is fertilized by a sperm with an A allele, which is 0.6 × 0.6 or 0.36 (the probability that the sperm contains A times the probability that the egg contains A).

- Similarly, the frequency of individuals with the BB genotype can be calculated (0.4 × 04 = 0.16).

- The frequency of individuals with the AB genotype is calculated by the probability that the sperm contains the A allele (0.6) times the probability that the egg contains the B allele (0.4), and the probability that the sperm contains the B allele (0.6) times the probability that the egg contains the A allele. Thus, the probability of AB individuals is (2 × 0.4 × 0.6 = 0.48).

Genotypes of the next generation can be given as shown in the accompanying table.

Allele	Allele Frequency	Genotype	Frequency	Counts for 1000
A (p)	0.6	AA	0.36	360
B (q)	0.4	AB	0.48	480
General formula of HW equation: $p^2 + 2pq + q^2 = 1$		BB	0.16	160
		Total	1	1000

Conclusion of Hardy-Weinberg

- Allele frequencies in a population do not change from one generation to the next only as the result of assortment of alleles and zygote formation.
- If the allele frequencies in a gene pool with two alleles are given by p and q, the genotype frequencies is given by p2, 2pq, and q2.
- The HWE principle identifies the forces that can cause evolution.
- If a population is not in HWE, one or more of the five assumptions is being violated.

Assumptions

- Random selection: When individuals with certain genotypes survive better than others, allele frequencies may change from one generation to the next.
- No mutation: If new alleles are produced by mutation or if alleles mutate at different rates, allele frequencies may change from one generation to the next.
- No migration: Movement of individuals in or out of a population alters allele and genotype frequencies.
- No chance events: Luck plays no role in HWE. Eggs and sperm collide at the same frequencies as the actual frequencies of p and q. When this assumption is violated and by chance some individuals contribute more alleles than others to the next generation, allele frequencies may change. This mechanism of allele change is called genetic drift.
- Individuals select mates at random: If this assumption is violated, allele frequencies do change, but genotype frequencies may.

Applications of the Hardy-Weinberg Law

- **Complete Dominance**

When Hardy-Weinberg equilibrium exists, allele frequencies can even be found out in presence of complete dominance where two genotypes cannot be distinguished. If two genotypes AA and Aa have the same phenotype due to complete dominance of A over a the allele frequencies can be determined from the frequencies of individuals showing the recessive phenotype aa.

When aa phenotype is 0.25 in the population, then it follows that the frequency of the recessive allele a is $\sqrt{0.25} – 0.5$. The frequency of the dominant allele A would be $1 – q$ or $1 – 0.25 = 0.75$.

- **Frequencies of Harmful Recessive Alleles**

The Hardy-Weinberg Law can also be used to calculate the frequency of heterozygous carriers of harmful recessive genes. If there are two alleles A and a at an autosomal locus with frequencies p and q in the population and p + q = 1, then the frequency of AA, Aa, and aa genotypes would be p2 + 2pq + p2.

If the aa genotype expresses a harmful phenotype such as cystic fibrosis, then the proportion of affected individuals in the population would be q2, and the frequency of the heterozygous carriers of the recessive allele would be 2pq.

- **Multiple Alleles**

The Hardy-Weinberg Law permits calculation of genotypic frequencies at loci with more than two alleles, such as the ABO blood groups. There are 3 alleles I^A, I^B and I° with frequencies p, q and r. Here p + q + r = 1. The genotypes of a population with random mating would be $(p + q + r)^2$.

- **Sex-Linked Loci**

It is possible to apply Hardy-Weinberg Law for calculating gene frequencies in case of sex-linked loci in males and females. Red green color blindness is a sex-linked recessive trait. Let r denote the recessive allele which produces affected individuals, and R the normal allele. The frequency of R is p and of r is q where p + q = 1. The frequencies of females having RR, Rr, rr genotypes would be p2, 2pq, q2 respectively.

- **Linkage Disequilibrium**

Consider two or more alleles at one locus and another locus on the same chromosome with two or more alleles. Due to genetic exchange by recombination occurring regularly over a period of time, the frequencies of the allelic combinations at the two syntenic loci will reach equilibrium.

If equilibrium is not reached, the alleles are said to be in linkage disequilibrium. The effect is due to tendency of two or more linked alleles to be inherited together more often than expected. Such groups of genes have also been referred to as supergenes.

Reference

- https://www.youtube.com/watch?v=NNPU4Ozul9U
- https://www.youtube.com/watch?v=chkd8-aqWaI
- https://www.youtube.com/watch?v=xPkOAnK20kw