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The Hardy Weinberg Principle and Equation: Understanding Genetic Equilibrium

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Abstract

The Hardy-Weinberg principle, named after G.H. Hardy and Wilhelm Weinberg, is a cornerstone concept in population genetics, elucidating the relationship between allele and genotype frequencies within a population. This review delves into the principle's significance within population genetics, its underlying assumptions, applications in fields like medicine and forensics, as well as its limitations. By the conclusion of this article, a comprehensive comprehension of the Hardy-Weinberg principle and its critical role in genetic research will be attained

Introduction

In 1908, the English mathematician G.H. Hardy and the German physician W. Weinberg made independent revelations about a principle centered on allele frequencies in populations. This principle suggests that genotypes within a Mendelian population naturally gravitate towards an equilibrium, resulting in consistent allele and genotype frequencies across successive generations. Known as the Hardy-Weinberg law, this concept stands as a fundamental pillar in the study of population genetics

"The Hardy-Weinberg principle relies on five essential assumptions to elucidate its dynamics:

1) equivalent reproductive fitness among individuals of each genotype in the population
2) an infinitely large population
3) random mating throughout the population
4) no migration into or out of the population
5) a mutation equilibrium
6) the absence of natural selection.

These assumptions form the foundation for understanding the stability of allele and genotype frequencies within a population over successive generations, as outlined by the Hardy-Weinberg law."

Principle

The Hardy-Weinberg principle asserts that in the absence of evolutionary influences, such as mutation, migration, natural selection, and genetic drift, allele frequencies within a population remain consistent across generations. This principle is applicable to sizable populations engaged in random mating without exposure to these forces. In population genetics, the Hardy-Weinberg principle serves as a valuable null hypothesis, allowing the assessment of deviations in allele and genotype frequencies. Such deviations suggest the presence of evolutionary forces at play. This principle, defined by the Hardy-Weinberg equilibrium, is a mathematical framework describing the anticipated allele and genotype frequencies in a population unburdened by evolutionary mechanisms. The equilibrium assumes a large, randomly mating population that is not affected by mutation, migration, natural selection, or genetic drift

Equation

Thus, if mating is random, & no other factor disturb the reproductive abilities of any genotype, the equilibrium genotypic frequencies are given by sequence of allelic frequency.

If there are only two alleles A & a with frequencies p & q respectively the frequencies of three possible genotype are-

$$(p+q)^2 = p^2 + 2pq + q^2$$

Also sum of allelic frequencies & all of the genotypic frequencies must always be one.

- $p^2 + 2pq + q^2 = 1$.
- p represents the frequency of the dominant allele.
- p^2 represents the frequency of the homozygous dominant genotype.
- q^2 represents the frequency of the homozygous recessive genotype.
- 2pq represents the frequency of the heterozygous genotype.

This equation allows us to calculate the expected frequencies of alleles and genotypes in a population under the assumptions of the Hardy-Weinberg equilibrium

If there are two alleles p & q then p+q = 1 & therefore, $p^2+2pq+q^2 = (p+q)^2 + 1$

If there are three alleles with frequencies p,q & r, then p+q+r = 1 as well as $(p+q+r)^2 = 1$

Allelic frequency square = genotypic frequency.

If we consider two alleles (Aa) are present in X-chromosome then the genotypic values at equilibrium will be –

1) For females: p^2 + 2pq + q^2 i.e, AA + 2Aa + aa
   (due to double dose of X-Chromosome)
2) For Males: p+q i.e., A + a
   (Due to single dose of X-Chromosome)

Factors Upsetting Hardy - Weinberg Equilibrium

The disruption of balance is orchestrated by a dance of evolutionary influences:

- Genetic mutations.
- The discerning hand of natural selection.
- Selective mating patterns.
- The whims of genetic drift.
- The interplay of migration and the flow of genes

Non- random matting

Nonrandom mating happens when there is a difference between the chances that any two individuals in a population will mate.

Two different kinds of non-random mating exist.

Assortative reproduction/mating

- Assortative mating unfolds when an increased number of paired individuals share a common phenotype, exceeding the expectations of chance.
- Mating partners possess akin genetic compositions, exemplified by inbreeding, where close kin engage in mating and self-pollination.

Discordant mating/disassortative

- Disassortative mating is the union of people with various phenotypes.
- Mates differ genetically from one another.

Forces or Agencies Changing Gene And Genotype Frequencies

In the absence of influencing forces, a sizable population engaging in random mating maintains stability in its gene and genotype frequencies. Two distinct processes have the potential to induce frequency shifts or changes:

1. Systematic processes: These operate predictably on gene frequencies in terms of quantity and direction. They affect both large and small populations. Three such systematic mechanisms exist: migration, mutation, and selection.

2. The dispersal procedure: This emerges within small populations due to sampling effects. While the amount of change is predictable, the direction is not. Due to the sampling effect, this process primarily impacts smaller populations.

Migration

Migration is the term used to describe the movement of individuals from one breeding population to another. When individuals move into a population, it's called immigration, whereas emigration refers to the outward movement of individuals from a population. These movements impact the size of the gene pool, leading to a reduction. The migration of breeding animals to or from a population can led to shifts in the population's composition. This has direct implications for the frequency of genes within the population.

Let us suppose that a large population consists of a proportion of "*m*" of new immigrants in one generation then the remainder (*1-m*) being natives.

- o Number of natives = n1
- o Number of immigrants = n2

$$m = \frac{n_2}{n_1 + n_2}$$

$$1 - m = \frac{n_1}{n_1 + n_2}$$

- Let the frequency of a certain allele (A) be *qm* among the immigrants and *q0* among the natives.
- Then the frequency of the allele in the mixed population *q1* will be
  $q1 = m\,qm + (1 - m)\,q0$
  $q1 = m\,qm + q0 - m\,q0$
  $q1 = m\,qm - m\,q0 + q0$
  $q1 = m\,(qm - q0) + q0$
- The gene frequency in mixed population will depend on the original gene frequency of the population and the difference in gene frequency between the immigrants and native (*qm – q0*) and the proportion of immigrants.
- The change of gene frequency Δq brought about by one generation of immigration is the difference between the frequency before immigration and the frequency after immigration.
  $\Delta q = q1 - q0$
  $\Delta q = m\,(qm - q0) + q0 - q0$
  $\Delta q = m\,(qm - q0)$
- Thus, the rate of change of gene frequency in a population subject to immigration depends on the immigration rate and the difference in gene frequency between the immigrants and the natives.

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Mutation

A mutation can introduce new alleles, causing changes in the gene pool of a population. These changes can impact an individual's ability to survive, either positively or negatively. If the mutations provide an advantage, the new alleles are more likely to thrive and be selected within the population.
If the wild allele A1 mutates to A2 with a frequency of u per generation.

- u is the fraction of all A1 alleles that mutate to A2 during one generation to Next
- Then, If the frequency of A1 within a generation is p0
- , Frequency of newly mutated gene A2 in the next generation = u p0
- Frequency of new gene A1 in the mutant population = p0- u p0
- Therefore, change in gene frequency = -u p0

Assume it mutates. Both orientations and original alleles (genes) then the frequencies are p(A1), q(A2)

$$A_1 \underset{v}{\overset{u}{\rightleftharpoons}} A_2$$

- Change in gene frequency in one generationo $\Delta q = up - vq$
- This situation results in an equilibrium gene frequency at which no further changes occur. The equilibrium point can be found by equating the variation of frequency Δq to Zero
  o pu - qv = 0
  o qv = pu
  qv = (1-q)u
  qv = u – qu
  qv + qu = u
  q(v+u)=u
  q = u / (u + v)
- Similarly, *p = v / (v + u)*
  If the mutational rates of *A1* to *A2* (u*)* and *A2* to *A1* (v) are known at equilibrium

then the frequency of *A1* allele and *A2* allele can be calculated directly without using conventional method of estimating gene frequency

Selection

Selection constitutes the process of differential reproduction and is pervasive across various scenarios. Individuals within a population reproduce at distinct rates, driven by differences in viability, fertility, and contributions to the next generation. The term used to quantify this contribution is "fitness" (denoted as "W"), which encompasses both the adaptive and selected values of an individual.

When there's a preference for a specific genotype, the frequency of the corresponding allele should increase, and vice versa. The strength of selection is quantified by the coefficient of selection, denoted as "s." This coefficient signifies the proportionate reduction in the gametic contribution of a particular genotype when compared to the standard genotype, which is usually the most favored one. Assuming a default genotype fitness of 1, the fitness of the selected genotypes can be represented as 1 - s.
W = 1-s

Complete selection against dominant gene

* The selection coefficient is 1, or the fitness is 0.
* One selection generation is sufficient to remove all dominant genes. Only if fully penetrated.
In the next generation, all individuals become recessive homozygotes,
The frequency of recessive allele (q) has a frequency of 1.

Selection against recessive homozygote (partial selection against recessive)

	genotypes			
	A1A1	A1A2	A2A2	total
initial frequency	p_0^2	$2p_0q_0$	q_0^2	1
coefficient of selection	0	0	s	
fitness	1	1	1-s	
gametic contribution	p_0^2	$2p_0q_0$	$q_0^2(1-s)$	$1-sq_0^2$

$$q_1 = \frac{q_0 - sq_0^2}{1 - sq_0^2}$$

- The change in gene frequency of a recessive allele as a result of selection

Complete selection against recessive:
It will not be possible because we can eliminate only those recessive alleles which are present in recessive homozygote, leaving the heterozygote undetected.

- Number of generations required
- The number of generations required to change the gene frequency from *q0* to *qt* is

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$$\Delta q = q_1 - q \quad t = \frac{1}{q_t} - \frac{1}{q_0}$$

where t = number of generations
qt is the frequency after t generations of complete elimination of recessives

$q0$ is the initial (recessive) gene frequency

Selection favoring heterozygote (Overdominance)

- If the fitness of the heterozygote is superior to the respective homozygote, then selection will favor heterozygote.

	genotypes			
	A1A1	A1A2	A2A2	TOTAL
INITIAL FREQUENCY	p_0^2	$2p_0q_0$	q_0^2	
COEFFICIENT OF SELECTION	s_1	0	s_2	
FITNESS	$1-s_1$	1	$1-s_2$	
GAMETIC CONTRIBUTION	$p_0^2(1-s_1)$	$2p_0q_0$	$q_0^2(1-s_2)$	$1-s_1 p_0^2-s_2 q_0^2$

- When selection favors the heterozygote, the gene frequency of the two alleles *A1* and *A2* tend towards equilibrium at an intermediate value, both alleles remaining in the population.
- The condition for equilibrium is that $\Delta q = 0$ and is fulfilled in generation when $s1p = s2\,q$

$$q = \frac{s_1}{s_1 + s_2} \text{ and similary } p = \frac{s_2}{s_1 + s_2}$$

Dispersive Process

Dispersive processes are distinct from systematic processes due to their inherent randomness in both direction and their quantitative predictability.

- When systematic factors are present, particularly in very large populations, gene frequencies tend to reach equilibrium and remain stable until external conditions change.
- This property of stability observed in large populations does not apply to small populations. In such cases, gene frequencies are susceptible to random fluctuations caused by the sampling of gametes.
- The gametes responsible for transmitting genes to the next generation carry a sample of genes from the parent generation.
- If the sample size is not sufficiently large, gene frequencies are prone to change from one generation to the next due to stochastic sampling effects.

Causes

- Small population size
- Founder effects – occurs when a population is initially established by small number of breeding individuals
- Bottleneck effect – occurs when a population is dramatically reduced in size

Effects

- Random drift
- Differentiation between sub-populations
- Uniformity within sub-populations
- Increased homozygosity

Applications of the Hardy-Weinberg Principle

The versatile Hardy-Weinberg principle finds its place in diverse domains, particularly medicine and forensics:

In the realm of medicine, this principle becomes a powerful tool, enabling the estimation of carrier frequencies for genetic disorders within a population. Picture this: armed with the knowledge of the frequency of a disease-causing allele, we can wield the Hardy-Weinberg equation to calculate the prevalence of carriers in the population. This not only sheds light on the genetic health landscape but serves as a compass guiding healthcare strategies and empowering genetic counselors to navigate the intricate genetic terrain.

Stepping into the world of forensics, the Hardy-Weinberg principle turns into a strategic asset, deftly calculating the probability of a match between enigmatic DNA samples from a crime scene and those from a suspect. Imagine the scene: meticulously comparing the frequencies of specific alleles in both samples with the expected frequencies under the elegant equilibrium of Hardy and Weinberg, we

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unravel the likelihood of a match. This forensic ingenuity amplifies our ability to decipher the truth, providing an invaluable instrument in the pursuit of justice, where complex criminal puzzles are pieced together with greater precision.

Limitations of the Hardy-Weinberg Principle

While the Hardy-Weinberg principle stands as a valuable tool for comprehending genetic diversity within populations, it is not without its limitations. One significant drawback lies in its reliance on simplifying conditions, which often diverge from reality in complex populations. A noteworthy example is the assumption of random mating, a premise that crumbles when faced with strong social or cultural barriers to reproduction.

Moreover, the Hardy-Weinberg principle confines its scope to a single genetic locus, rendering it unable to factor in the intricate dance of interactions between genes or the nuanced influence of environmental factors on trait expression. This restriction can lead to an incomplete understanding of the multifaceted nature of genetic inheritance.

Furthermore, the principle assumes the absence of evolutionary forces, yet in the real world, these forces perpetually mold the genetic fabric of populations. The dynamic interplay of mutation, natural selection, migration, and genetic drift orchestrates a continuous evolutionary symphony, fundamentally altering gene frequencies over time. As a result, the Hardy-Weinberg principle, while an essential stepping stone, offers only a limited glimpse into the intricate complexities of real-world genetic dynamics.

Conclusion

While the Hardy-Weinberg principle serves as a valuable tool for grasping genetic diversity within populations, it has notable limitations. A significant drawback arises from its reliance on oversimplified conditions, which often diverge from the intricate reality of complex populations. A striking example is the assumption of random mating, a premise that crumbles when confronted with strong social or cultural barriers to reproduction.

Furthermore, the Hardy-Weinberg principle confines its purview to a single genetic locus, thus neglecting the intricate choreography of gene interactions or the subtle impact of environmental factors on trait expression. This constraint can lead to an incomplete understanding of the multifaceted nature of genetic inheritance.

Additionally, the principle presupposes the absence of evolutionary forces, yet in the real world, these forces perpetually shape the genetic tapestry of populations. The dynamic interplay of mutation, natural selection, migration, and genetic drift orchestrates a continuous evolutionary symphony, fundamentally reshaping gene frequencies over time. As a result, the Hardy-Weinberg principle, though a foundational element, provides merely a limited glimpse into the intricate complexities of real-world genetic dynamics.

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