Considering Instructional Approach & Question Design with the Hardy-Weinberg Principle

**ABSTRACT**

The Hardy-Weinberg principle (HWP) is an application of the binomial expansion theorem that is foundational to the field of population genetics. Because of the important history of the HWP in answering how variation is preserved during evolution, and the ability of Hardy-Weinberg equilibrium (HWE) to detect natural and sexual selection acting on a trait, the HWP is a staple of the introductory biology undergraduate curriculum in the United States. Introductory courses often cover a wide range of topics in ecology and evolution, and it is important that students have enough time during the semester to grasp the foundations of population genetics. At the same time, information needs to be presented clearly to ensure that the student gains a correct understanding of the HWP. This article discusses the importance of the HWP to undergraduate education in biology and describes misconceptions from the instructor’s perspective. These misconceptions are pervasive and risk undermining a proper understanding of the HWP. We provide examples adapted from university- and AP-level standardized tests.

**Key Words:** Hardy-Weinberg; population genetics; introductory biology; mathematics; evolution.

○ The HWP: Historical Perspective

A critical link between Darwin’s theory of evolution and Mendelian genetics was provided by G. H. Hardy and Wilhelm Weinberg’s analyses of the segregation of trait variants following Mendelian inheritance rules (Hardy, 1908; Weinberg, 1908), contributing what is known as the Hardy-Weinberg principle (HWP). Darwin’s theory had not fully accounted for the preservation of diversity through direct inheritance (Vorzimmer, 1968). “Blending inheritance,” a leading theory in the late 19th century, attacked Darwinian evolution by pointing out the impossibility of preserving diversity if traits inherited from each parent led to intermediate offspring (Jenkin, 1867). The rediscovery of Mendel’s findings illustrated an inheritance pattern where parental phenotypes were preserved through generations without necessarily being expressed (Mendel, 1866; Druery & Bateson, 1901). The HWP, a form of the binomial expansion theorem, provided the mathematical rationale for Mendelian inheritance, rendering blending inheritance obsolete.

In its simplest form, Hardy-Weinberg equilibrium (HWE) assumes a Mendelian inherited gene with only two alleles A and a, with respective frequencies p and q. Given only two variants in the population, these proportions must add to one (p + q = 1). Two binomials are generated, representing the probability of inheriting either allele from the father, (p_m + q_m), and from the mother, (p_i + q_i). The product of the probabilities, (p_m + q_m)(p_i + q_i), analogous to the binomial probability of flipping a coin twice in succession, equates to one representing the whole population. Multiplying the terms (“FOIL” mnemonic) then gives the Hardy-Weinberg equation, p^2 + 2pq + q^2 = 1, where the frequency of receiving two A alleles is p^2, two a alleles is q^2, and one of each is 2pq (the heterozygote genotype occurs twice, representing alternative inheritance of each allele from each parent, p_m q_i and p_i q_m). Provided that allele frequencies do not change between generations (HWE conditions), the genotypic and phenotypic frequencies remain the same. This resolves Darwin’s predicament and explains why diversity is maintained across generations.

○ Present-Day Context of the HWP in the Undergraduate Classroom

Appropriately, the HWP is a gateway into the application of evolutionary theory to populations in biology undergraduate curricula (Journet, 1986). The HWP helps students understand the connection between evolution in a single pedigree and evolution in a population, highlighting changes in allelic frequencies over time (Mertens, 1992). Once the background and significance of the HWP is presented, the math behind the HWP is typically introduced. In HWP math problems, students are often given the number of homozygotic and heterozygotic individuals in a population and asked to calculate allele frequencies to determine whether the original genotypic frequencies provided match genotypic frequencies generated from the Hardy-Weinberg equation. To determine whether the genotypic frequencies from the given population are statistically significant from the genotypic frequencies at HWE, students may

**References**

Hardy, G. H. (1908). “Weanbergs Faktor-Theorem.” Annalen der Physik, 34, 571-573.

Weinberg, W. (1908). “On the Law of Heredity.” Biometrika, 6, 36-56.

Jenkin, R. (1867). “On the Inheritance of Characters.” Philosophical Transactions of the Royal Society of London, 157, 403-413.

Druery, G. S., & Bateson, J. (1901). “The Inheritance of Characters.” Cambridge University Press.

Mertens, A. (1992). “Population Genetics.” In R. C. Lewontin & J. A.讯 (Eds.), Evolution: Theory and Methods (pp. 351-380). Oxford: Blackwell Science.

Journet, J. E. (1986). “Population Genetics.” In R. C. Lewontin & J. A.讯 (Eds.), Evolution: Theory and Methods (pp. 333-350). Oxford: Blackwell Science.
employ a chi-square test and compare values. This also serves as an introduction to biological statistics for undergraduates.

Upon calculating a $p$-value from the chi-square test, students will find that the population either matches the values from the Hardy-Weinberg equation (is in HWE) or does not match the genotypic frequencies from the equation (is not in HWE). As a final step, students then relate their findings back to the biology of the population. If the genotypic frequencies in question do not match HWE, what does that tell us about the population with respect to that locus? The HWP describes how variation persists when allele frequencies remain constant (population is not evolving with respect to the trait). In natural populations evolving with respect to a trait, allele frequencies change over time. To understand why a locus may not be in HWE, students learn about the assumptions of the HWP. HWE requires populations to have a very large size, so as to negate the effects of genetic drift. At HWE, neither selection nor nonrandom mating can give one genotype a fitness advantage over the other. Finally, no migration into the population and no mutation can impact the neutral attributes of either allele. Students can hypothesize about which of these forces may be in play in a given example.

Despite the importance of the HWP, students may have difficulty solving problems and grasping the connection between the math and the biology. The math itself can be intimidating to students, and common pitfalls can be avoided with innovative teaching techniques (Ortiz et al., 2000; Masel, 2012; Brewer & Gardner, 2013). However, to make sure that students gain a thorough understanding of the HWP, biology instructors must also be adept at working through problems and addressing student concerns. Unfortunately, common misconceptions are propagated through instructor error (even at the university level) as well as on standardized tests. Given the fundamental nature of the HWP in population genetics and evolution generally, failing to teach the HWP correctly can lead to long-lasting confusion for biology majors, particularly with concepts that build upon the implications of the HWP. Below, we address misconceptions derived from teaching materials and questions from standardized tests, and suggest how to present information to students so as to build an understanding of evolution in populations.

Issues & Solutions

Solution 1: Make Sure Equilibrium Is Not Stated

One important goal for students learning the HWP is to understand how an evolving population differs from one under HWE. This concept is conveyed to students in part by determining whether or not a given population is in HWE. Therefore, it is important that sample problems do not specify whether a population is in HWE, but to allow the student to come to this conclusion themselves (Figure 1). The decision of whether the population mathematically meets HWE conditions allows the student to connect a biological interpretation of evolution with statistical methods. By contrast, in problems where HWE is assumed, the count of each genotype and genotypic frequencies of the population are often not given, thereby preventing the possibility of working through the problem with a biological context. Particularly at issue is that questions specifying populations at HWE enable students to find allele frequencies by taking square roots of homozygote genotype frequencies. This shortcut backfires on problems where given allelic frequencies are not in HWE, thereby confusing the student by introducing an entirely different set of methods than what are necessary for solving a biologically meaningful HWP problem (Figure 2).

Solution 2: Genotype Counts (or Frequencies) Must Be Provided if HWE Is Not Specified

We do not recommend that an instructor use a problem where HWE is assumed, but if this does occur, then genotype counts must be provided (Figure 3). This is because a problem that does not specify HWE and also does not specify genotype counts or frequencies cannot be solved. Students need to compare the genotype frequencies in the sample population to a population in HWE. If a problem specifies HWE, but does not give genotype counts, then students can still conclude that the population is in HWE, because this information is given. However, if students are not given genotype counts or information about HWE, then the problem cannot be solved. Students can try to solve the problem using incorrect means by either assuming that the population is in HWE or inventing their own genotype counts for the population, in which case answers for each student would be different. In these problems that do not specify HWE or genotype counts, the allelic frequencies $p$ and $q$ are provided, allowing the student to figure out the genotypic frequencies if the population were in HWE, through the Hardy-Weinberg equation.
Asking the student to assume that HWE is met encourages the student to always make this assumption, even when it is incorrect to do so in biologically meaningful HWP problems. These problems may also ask the question of how the HWP can be used to determine whether the example population is evolving (Figure 3). It is only possible to obtain expected genotypic frequencies assuming HWE, so the student will have nothing to compare these frequencies to. If taught to use this incorrect strategy to solve this type of problem, the student is also likely to use the same strategy in HWP problems with a biological context and conclude erroneously that the genotypic frequencies generated by the Hardy-Weinberg equation are the only values relevant to this concept. This undermines efforts to correctly work through an HWP problem.

Solution 3: Be Sure That Wording Accurately Reflects the HWP

To gain the interest of students pursuing medicine, HWP examples often use genetic conditions with deleterious alleles (Figure 4). Although biological information about the relevant locus in an HWP problem is superfluous to solving the problem, it is beneficial to include when students consider HWE assumptions that may be violated. Therefore, we recommend adding information about the locus that an HWP problem is focused on, as it helps relate the question to the real world. Language can describe the phenotypic effects or the cellular pathways that the protein functions in. However, it is important to consider that alleles specifically described to have major fitness costs should not, in turn, be defined as experiencing HWE. If the student is thinking about the biology of the problem, an allele causing cancer (Figure 4) should present a selective disadvantage and not be in HWE. Additionally, it is important to remember that the HWP works independently on each locus across the genome, and so different loci will vary in the degree to which they violate the HWP. Problems should ask whether a single locus is in HWE, as opposed to populations (Figure 4). Describing populations as under HWE takes away from the student’s understanding that the HWP can be applied independently to any locus and gives the impression that all loci behave in the same way.

Conclusions

The HWP enables us to understand how diversity is preserved and how evolution operates on allelic frequencies over the course of generations. The concept allows students to think about how loci violate HWE assumptions and enables them to think creatively when reconciling the impact of genotype on phenotype. It also introduces the application of statistics in a biological framework. We describe three solutions to misconceptions of the HWP and provide examples of each adapted from standardized tests. We encourage faculty and graduate students teaching introductory biology courses to seek out population geneticists or evolutionary biologists in their departments to help ensure that all instructors leading students through the HWP understand the concept properly and
apply best practices in teaching it. We hope that misleading HWP problems will be removed from standardized tests in the future and be replaced by ones that enhance student understanding.

References

Brewer, M.S. & Gardner, G.E. (2013). Teaching evolution through the Hardy-Weinberg principle: a real-time, active-learning exercise using classroom response devices. American Biology Teacher, 75, 476–479.

Druery, C.T. & Bateson, W. (1901). Experiments in plant hybridization. Journal of the Royal Horticultural Society, 26, 1–32.

Hardy, G.H. (1908). Mendelian proportions in a mixed population. Science, 28, 49–50.

Jenkin, F. (1867). Review of ‘The Origin of Species.’ North British Review, 46, 277–318.

Journey, A.R.P. (1986). Population genetics: a fishy process. American Biology Teacher, 48, 478–482.

Masel, J. (2012). Rethinking Hardy-Weinberg and genetic drift in undergraduate biology. Bioessays, 34, 701–710.

Mendel, J.G. (1866). Versuche über Pflanzenhybriden. Verhandlungen des naturforschenden Vereines in Brünn, Bd. IV für das Jahr. Abhandlungen, 3–47.

Mertens, T.R. (1992). Introducing students to population genetics & the Hardy-Weinberg principle. American Biology Teacher, 54, 103–107.

Ortiz, M.T., Taras, L. & Stacoulakis, A.M. (2000). The Hardy-Weinberg equilibrium: some helpful suggestions. American Biology Teacher, 62, 20–22.

Vorzimmer, P.J. (1968). Darwin and Mendel: the historical connection. Isis, 59, 77–82.

Weinberg, W. (1908). Über den Nachweis der Vererbung beim Menschen. Jahreshefte des Vereins für vaterländische Naturkunde in Württemberg, 64, 368–382.

Robert Driver (driverr16@students.ecu.edu) is a graduate student and Susan B. McRae is a Teaching Professor in the Department of Biology, East Carolina University, Greenville, NC 27858. Funding provided by National Science Foundation awards RCN-1457541 and IOS-1456612.