



EDVO-Kit: AP02

Mathematical Modeling: Hardy-Weinberg

See Page 3 for storage instructions.

EXPERIMENT OBJECTIVE:

In this experiment, students will examine the effects of mutations, genetic drift and natural selection on gene frequency in a population by the Hardy-Weinberg law of genetic equilibrium. Using computer and Internet access, students will explore how a hypothetical gene pool changes from one generation to the next.

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Experiment Components

- PTC taste paper
- Control taste paper

Store the entire experiment at room temperature.

This experiment is designed for 10 lab groups.

Requirements

- Computer with spreadsheet software (Microsoft® Excel)
- Calculator with square root function

Background Information

Population genetics deals with analysis of gene frequencies in a population over many generations. The concept of describing frequencies of inherited traits owes its origin to scientific works published at the beginning of the 20th century. A 1908 paper, "Mendelian Proportions in a Mixed Population" published in *Science* 28 (49-50) by British mathematician G.H. Hardy, and a separate independent study also published in 1908 by the German physician W. Weinberg, both suggested that gene frequencies were not dependent upon dominance or recessiveness but may remain unchanged from one generation to the next under a set of "idealized conditions." These classic papers describe an equation which has come to be called the Hardy-Weinberg theorem of genetic equilibrium. This theorem has become the basis for population genetics.

The Hardy-Weinberg theorem is used to determine the frequencies of individual alleles of a pair of genes, and the frequency of heterozygotes and homozygotes in the population. The theorem states that in the absence of outside forces such as mutation, selection, random genetic drift, and migration, gene frequencies remain constant over many generations in a large population. It is important to remember that in natural populations, events such as gene mutation, selection of genotypes which confer enhanced viability, presence of lethal homozygous recessive genes, nonrandom mate selection, and immigration and emigration of individuals of a population, are events that do occur. Nevertheless, the Hardy-Weinberg theorem is useful since unexpected deviations can point to the occurrence of evolutionary significant events such as speciation.

Distribution frequencies of two alleles for a given gene at a single locus, one being dominant, the other recessive, will follow a binomial distribution in the population. Consider the case of two alleles for a gene, one dominant and the other recessive.

Let p = the frequency of one allele and q = the frequency of the other. If gene frequencies are expressed as decimals, the following must be true,

$$\text{Equation \# 1: } p + q = 1$$

and,

$$\text{Equation \# 1a: } p = 1 - q$$

therefore,

$$\text{Equation \# 2: } (p + q)^2 = 1.$$

Expanding equation #2 generates,

$$\text{Equation \#3: } p^2 + 2pq + q^2 = 1.$$

When equation 3 is applied to an ideal population, it follows that the frequency of homozygous dominant individuals is p^2 , the frequency of the heterozygotes is $2pq$, and the frequency of homozygous recessives is q^2 .



Background Information

As an example, consider the following hypothetical situation. The famous European geneticist, Professor Ed V. Otek, tested his rather large genetics class for the ability to taste the chemical phenylthiocarbamide, PTC. He knew that the gene for this ability to taste PTC had two alleles, the dominant allele for tasting called T, and the recessive allele called t. He found that out of 1000 students, there were 700 students with the ability to taste PTC and 300 who lacked the ability to taste PTC. He used the Hardy-Weinberg equation to determine the gene frequencies for the T and t alleles of the gene for the ability to taste PTC. His notes show the following analysis:

A Converted raw data to decimals.

- Frequency of two genotypes for tasting, TT and Tt, was $700/1000 = 0.7$.
- Frequency of genotype for inability to taste PTC, t t, was $300/1000 = 0.3$.

B Determined gene frequency of the unique allele.

- From the Hardy-Weinberg equation # 3, ($p^2 + 2pq + q^2 = 1$), the frequency of non-tasters, tt = $0.3 = q^2$.
- Taking the square root of 0.3, $q = 0.5477$, and 0.5477 is the frequency of the t allele in Dr. Otek's student population.

C Determined gene frequency of other allele, p:

From equation # 1a, ($p = 1 - q$), the frequency of p is 0.4523.

D. Determined frequency of homozygous TT and heterozygous Tt individuals in the population. Using equation #3:

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

$$(0.4523)^2 + 2(0.4523 \times 0.5477) + (0.5477)^2 = 1$$

- The frequency of homozygous tasters is,
TT = $p^2 = 0.4523^2 = 0.2046$.
- The frequency of heterozygous tasters is
Tt = $2pq = 2(0.4523 \times 0.5477) = 0.4954$.

A computer spreadsheet allows students to build and test their own models to see how a gene pool of a population changes over time. Most spreadsheets have a "Random" function that can generate random numbers to model stochastic events. The computer can generate thousands of samples in a very short time. In this investigation, students will build a spreadsheet that models how a hypothetical gene pool changes from one generation to the next. Students will utilize the Hardy-Weinberg equation to analyze population data from the class.

Experiment Overview and General Instructions

EXPERIMENT OBJECTIVE

In this experiment, students will examine the effects of mutations, genetic drift and natural selection on gene frequency in a population by the Hardy-Weinberg law of genetic equilibrium. Using computer and Internet access, students will explore how a hypothetical gene pool changes from one generation to the next.

WORKING HYPOTHESIS

If there is no selection for any allele in a large randomly-mating population, then the gene frequencies will remain constant over many generations. However, if there are outside forces such as selection for an allele, heterozygote advantage, and genetic drift working in a population, then the gene frequencies will change over time.

LABORATORY SAFETY GUIDELINES

1. Wear gloves and goggles while working in the laboratory.
2. Exercise caution when working in the laboratory – you will be using equipment that can be dangerous if used incorrectly.
3. DO NOT MOUTH PIPET REAGENTS - USE PIPET PUMPS.
4. Always wash hands thoroughly with soap and water after working in the laboratory.
5. If you are unsure of something, ASK YOUR INSTRUCTOR!



LABORATORY NOTEBOOKS:

Scientists document everything that happens during an experiment, including experimental conditions, thoughts and observations while conducting the experiment, and, of course, any data collected. Today, you'll be documenting your experiment in a laboratory notebook or on a separate worksheet.

Before starting the Experiment:

- Carefully read the introduction and the protocol. Use this information to form a hypothesis for this experiment.
- Predict the results of your experiment.

During the Experiment:

- Record your observations.

After the Experiment:

- Interpret the results – does your data support or contradict your hypothesis?
- If you repeated this experiment, what would you change? Revise your hypothesis to reflect this change.

Investigation I:

Estimation of Gene Frequency for the Trait to Taste PTC Within a Small Sample Population

This experiment deals with the determination of the gene frequency of a human trait amongst students with no known selective advantage. The ability to taste the chemical phenylthiocarbamide, PTC, is one such human trait.

The ability to taste PTC is due to the presence of a dominant allele, T. Therefore, all tasters will either be homozygous, TT, or heterozygous, Tt. Non-tasters will be homozygous for the recessive gene, tt.

1. Students groups should obtain a PTC taste strip and a control strip.
2. Every member of the group should first taste the control strip of paper.
3. Every person should taste the PTC impregnated strip of paper. Compare the taste of the control and the PTC paper.

If you are a taster, the PTC paper strip will be bitter. Non-tasters will not notice a difference between either strip of paper.

4. For the class, record the total number of tasters and the total number of non-tasters on the blackboard. Also record the results in your lab notebook.
5. Determine decimal value by division for tasters ($p^2 + 2pq$), and likewise the decimal value for non-tasters (q^2).
 - For example, there are 100 people in your class. 25 are non-tasters and 75 are tasters.
 - Then 25/100, or 0.25, is the frequency of non-tasters, and 75/100, or 0.75, is the frequency of tasters.
6. Record your values in Table 1. Use Hardy-Weinberg as described above to determine the value of p and q for your class.

TABLE 1: Phenotypes and Gene Frequencies for Trait to Taste PTC				
	CLASS PHENOTYPES		ALLELE FREQUENCY CALCULATED BY THE HARDY WEINBERG EQUATION	
	% TASTERS	% NON-TASTERS	p	q
	$p^2 + 2pq$	q^2		
CLASS POPULATION				
NORTH AMERICAN POPULATION	0.55	0.45		

TABLE I: Phenotypes and Gene Frequencies for Trait to Taste PTC

Investigation II:**Testing Your Mathematical Model to Explore the Behavior of Allele Frequencies from Generation to Generation**

Use the Excel file for Deme 1.0 to investigate a minimum of 5 different questions related to Hardy-Weinberg equilibrium. For each one...

- a. Write a question that you would like to answer.
- b. Make a hypothesis to predict your answer to that question.
- c. Run a Hardy-Weinberg analysis using Deme 1.0.
- d. Review, interpret, and print your data.
- e. Determine whether or not your hypothesis was correct.
- f. Draw conclusions as to why your hypothesis was correct or incorrect.

Experimental Results and Study Questions

Address and record the following in your laboratory notebook or on a separate worksheet.

Before starting the experiment:

- Write a hypothesis that reflects the experiment.
- Predict experimental outcomes.

During the Experiment:

- Record (draw) your observations, or save the results on your computer or flash drive.

Following the Experiment:

- Formulate an explanation from the results.
- Determine what could be changed in the experiment if the experiment were repeated.
- Write a hypothesis that would reflect this change.