

POPULATION GENETICS, SELECTION, AND EVOLUTION

INTRODUCTION

It is a common misconception that individuals evolve. While individuals may have favorable and heritable traits that are advantageous for survival and reproduction, the impact of selection is only apparent in the changes in phenotypes and genotypes observed in the population over time. The study of population genetics determines allele and genotype frequency distributions to deduce whether the population is evolving or not and, if it is, to what extent it is evolving. In 1908, two researchers independently derived the Hardy-Weinberg principle, which states that the allele and genotype frequencies in a population will remain constant from generation to generation only if Mendelian segregation and recombination of alleles are at work. If the major conditions of the Hardy-Weinberg principle are not met, then there is a departure from Hardy-Weinberg equilibrium, which indicates that the population is evolving.

In this activity, you will apply what you have learned about the Hardy-Weinberg principle and population genetics to understand how a deadly genetic disease—sickle cell disease—can be maintained in a population.

PRE-ACTIVITY QUESTIONS

- The Hardy-Weinberg principle and its equations predict that frequencies of alleles and genotypes remain constant from generation to generation in populations that are not evolving. What five conditions does this prediction assume to be true about such a population?
 - _____
 - _____
 - _____
 - _____
 - _____
- Before beginning the activity, answer the following general Hardy-Weinberg problems for practice (assume that the population is at Hardy-Weinberg equilibrium).
 - If the frequency of a recessive allele is 0.3, what is the frequency of the dominant allele? _____
 - If the frequency of the homozygous dominant genotype is 0.36, what is the frequency of the dominant allele? _____
 - If the frequency of the homozygous recessive genotype is 0.49, what is the frequency of the dominant allele? _____
 - In a certain population, the dominant phenotype of a certain trait occurs 87% of the time. What is the frequency of the dominant allele? _____
 - If the frequency of the homozygous dominant genotype is 0.49, what is the frequency of the homozygous recessive genotype? _____
 - If the frequency of an autosomal recessive disease is 1 in 1,500 births, what are the allele and genotype frequencies in a population of 3,000?
 $p = \underline{\hspace{1cm}}$, $q = \underline{\hspace{1cm}}$, $p^2 = \underline{\hspace{1cm}}$, $2pq = \underline{\hspace{1cm}}$, $q^2 = \underline{\hspace{1cm}}$



*The Making of the Fittest:
Natural Selection in Humans*

HHMI
BioInteractive.org
HANDS-ON ACTIVITY
STUDENT HANDOUT

MATERIALS:

- Container for parent population
- Container of stock population beads
 - 100 beads of one color
 - 100 beads of a second color
- Calculator
- Colored pencils
- Graph paper (optional)

PROCEDURE, DATA COLLECTION, AND QUESTIONS

3. Watch the film *The Making of the Fittest: Natural Selection in Humans*. Pay close attention to the genetics of sickle cell disease and the connection to malaria infection.

From the film, you learned that sickle cell disease is caused by a mutation in the gene that encodes hemoglobin. Hemoglobin, a protein found in red blood cells, transports oxygen throughout the body. Individuals who are homozygous for the normal hemoglobin allele are designated AA. Individuals who receive one normal hemoglobin allele from one parent and one mutant hemoglobin, or sickle cell, allele from the other parent are heterozygous and are said to have the “sickle cell trait.” Their genotype is AS. People with sickle cell disease are homozygous for the sickle cell allele (SS genotype).

4. Simulation 1: Examining the Hardy-Weinberg Principle

- Label a container “Parent Population.”
- Designate one color of bead as “Allele A” and the other color as “Allele S.” Write this information here. (Example: A = Red, S = White)
Allele A: _____
Allele S: _____
- From the stock population container, select 15 homozygous individuals for normal hemoglobin (AA). Place them in your parent population container. Be sure to count one bead per allele per individual. (For example, in this step you will need 30 beads of the Allele A color.)
- From the stock population container, select 30 heterozygous individuals for the sickle cell trait (AS). Place them in your parent population container. (Be sure to count one bead per allele.)
- From the stock population container, select 15 homozygous individuals for sickle cell disease (SS). Place them in your parent population container. (Be sure to count one bead per allele.)
- Record the number of individuals with each genotype in this population in Table 1.1. For example, there are 15 AA individuals.
- Count the number of alleles (A and S) in this population. Record this information in Table 1.1. For example, there should be 60 Allele A beads in the parent population.
- Calculate the genotype and allele frequencies of your parent population directly from the number of individuals you recorded in parts 4f and 4g, respectively. (To calculate the genotype frequencies, you will need to take the number of individuals with a specific genotype and divide by the total number of individuals in the population. To calculate allele frequencies, you will use the number of each allele, A or S, and divide by the total number of alleles [beads] in the population.) Record these in Table 1.1.

Table 1.1. Parent Population

Genotype	Number of individuals	Total number of individuals in parent population	Genotype frequency	Allele	Number of alleles	Total number of alleles in parent population	Allele frequency
AA				A			
AS				S			
SS							

- i. Using the allele frequencies from Table 1.1 (allele frequencies of A and S in the shaded boxes), use the Hardy-Weinberg equation to calculate the expected frequencies of each genotype for the parent population (show work).

$p^2 = \text{_____}$, $2pq = \text{_____}$, $q^2 = \text{_____}$

As you can see, the observed genotype frequencies (Table 1.1) and the expected genotype frequencies calculated using the Hardy-Weinberg equation (part 4i) agree. This indicates that the parent population could be in Hardy-Weinberg equilibrium.

If the population is in Hardy Weinberg equilibrium, each subsequent generation should maintain the genotype and allele frequencies calculated above.

- j. For this simulation, let's assume that the A and S alleles have **no** selective advantage or disadvantage; they each survive 100% of the time. Using the parent population established in steps 4c through 4e, simulate random mating of individuals in the population by randomly selecting two beads (alleles) from the parent population container. These two beads represent the first offspring. Determine the genotype of the individual by looking at the color of the two beads. Record the genotype of this individual by entering a tally mark in Table 1.2 under "Tally marks for offspring." Once you have entered the result, return the two beads (alleles) to the parent population container and mix.
- k. Repeat step 4j until 60 offspring are produced.
- l. Convert the tally marks to numbers and record the result in the "Number of individuals" column. Next, calculate the genotype frequencies based on the number of individuals you recorded and the total population. Record the calculations in Table 1.2.
- m. Calculate the number of alleles. You will need to count each individual allele (bead) in the population. For example, in order to calculate the number of A's, use the following equation: (number of AA x 2) + (number of AS x 1). To calculate total number of alleles in the offspring population, use the following equation: total number of individuals in the first offspring population x 2.

Table 1.2. First Generation of Offspring

Genotype	Tally marks for offspring	Number of individuals	Total number of individuals in the first offspring population	Genotype frequency	Allele	Number of alleles	Total number of alleles in the offspring population	Allele frequency
AA					A			
AS					S			
SS								

n. The Hardy-Weinberg principle predicts that the genotype frequencies of the offspring will be the same as those of the parent population if the population is not evolving. Were the allele and genotype frequencies calculated in the parent population and in the first generation of offspring the same? ____ (yes/no)

i. If so, the population is said to be at _____ and all five conditions were followed.

If not, then at least one of the conditions of the Hardy-Weinberg principle was violated. In this simulation, which condition or conditions were violated?

ii. If a million more offspring are produced from this parent population, predict how the genotype and allele frequencies would compare with the frequencies calculated in Table 1.1.

5. Simulation 2: Examining a 100% Negative Selection Pressure

- a. In the parent population container, establish the same population that you used in Simulation 1, Table 1.1.
- b. For this simulation, let's assume that the SS genotype represents individuals who have sickle cell disease. Sickle cell disease is a lethal disease caused by a genetic mutation. In East Africa, children born with sickle cell disease often die. In this simulation, we will assume that sickle cell disease is 100% selected against. This means that all children born with this disease die before reproductive age and do not pass their genes on to the next generation.
- c. Using the same mixing and selecting procedure as in Simulation 1, produce offspring from this population by randomly picking two alleles to represent an individual offspring. If the offspring is AA or AS place a tally mark in Table 2.1 in the appropriate genotype row. Return the alleles to the population and mix. If the offspring is SS, do **not** place a tally mark in the table. Simply return the alleles to the population and mix. This procedure simulates 100% lethality of sickle cell disease in this population. To keep the population size consistent from generation to generation, you must repeat step 5c until **60 viable offspring** have been produced (the tally marks should total 60).

- d. Calculate the genotype frequencies for this first population of offspring directly from the number of individuals you recorded in parts 5b and 5c. Record the calculations in Table 2.1. If you need help, refer back to Simulation 1.
- e. Calculate the number of alleles and the allele frequencies. Remember, to calculate the number of alleles, you will need to count each individual allele (bead) in the population. Refer to calculations provided in Simulation 1 if needed. Record the calculations in Table 2.1.

Table 2.1. First Generation of Offspring

Genotype	Tally marks for offspring	Number of individuals	Total number of individuals in the first offspring population	Genotype frequency	Allele	Number of alleles	Total number of alleles in the offspring population	Allele frequency
AA					A			
AS					S			
SS								

- f. In order to produce the next generation of offspring, change the number of beads in the container to reflect the gene pool of the first generation of offspring (Table 2.1). In other words, the number of alleles (beads) in the container should match the numbers calculated in Table 2.1 (number of alleles). For example, if the number of alleles in Table 2.1 were A = 76 and S = 44, place 76 beads of Allele A and 44 beads of Allele S into the container. You may need to obtain more beads from the stock population.
- g. Repeat steps 5b and 5c above to produce the second generation of 60 offspring. Tally the results and fill in Table 2.2.

Table 2.2. Second Generation of Offspring

Genotype	Tally marks for offspring	Number of individuals	Total number of individuals in the first offspring population	Genotype frequency	Allele	Number of alleles	Total number of alleles in the offspring population	Allele frequency
AA					A			
AS					S			
SS								

*The Making of the Fittest:
Natural Selection in Humans*

**HANDS-ON ACTIVITY
STUDENT HANDOUT**

h. You began Simulation 2 with the same parent population as in Simulation 1. What were the frequencies of the A and S alleles of the parent population in Simulation 1? A = _____ and S = _____.

In Simulation 2, what happened to the frequency of the sickle cell allele (S) with each successive generation of offspring? Explain your observation.

i. In Simulation 2, was the change in frequency of the sickle cell allele (S) from the parent generation to the first generation of offspring similar to the change from the first generation to the second generation of offspring? Explain your answer.

j. Do the genotype frequencies of the parent population equal the genotype frequencies calculated in Table 2.2? _____ (yes/no)

k. Is this population at Hardy-Weinberg (genetic) equilibrium? _____ (yes/no) Explain your response.

l. If this population is not at Hardy-Weinberg equilibrium, which Hardy-Weinberg condition(s) were violated in Simulation 2? _____

6. Simulation 3: Examining Heterozygous Advantage

a. Establish the same parent population that you used in Simulation 1.

b. Using the same mixing and selecting procedure as in Simulation 1, produce offspring from this population by randomly picking two alleles to represent an individual offspring. Follow the instructions below:

i. If the offspring is AS, place a tally mark in Table 3.1, return the alleles to the population, and mix. Individuals who are AS have two genetic advantages: they do not have sickle cell disease and they are resistant to malaria infection. Therefore, in this simulation, the sickle cell trait (the heterozygous state) is selected for, and individuals with the AS genotype survive 100% of the time.

ii. If the offspring is AA, place a tally mark **every other time** one of these individuals is selected. You will need to develop a system to keep track of this 50/50 chance of survival. Individuals with the AA genotype do not have sickle cell disease but are more susceptible to malaria. This simulation models a 50% selection against this trait: people with the AA genotype have a 50% chance of surviving and passing on their genes to the next generation of offspring.

iii. If the offspring is SS, do **not** place a tally mark in the table; simply return the alleles to the population and mix as you did in Simulation 2. The SS genotype represents individuals who have sickle cell disease. Sickle cell disease is a lethal disease caused by a genetic mutation. In East Africa, children born with sickle cell disease often die. We will assume that sickle cell disease is 100% selected against. This means that all children born with this disease die before reproductive age.

Make sure that you return the alleles to the population and mix each time before drawing another two beads.

- c. In order to keep the population size consistent from generation to generation, you must repeat step 6b until **60 viable offspring** have been produced (the tally marks should total 60). Record the tallies and calculate the frequencies in Table 3.1.

Table 3.1. First Generation of Offspring

Genotype	Tally marks for offspring	Number of individuals	Total number of individuals in the first offspring population	Genotype frequency	Allele	Number of alleles	Total number of alleles in the offspring population	Allele frequency
AA					A			
AS					S			
SS								

- d. In order to produce the next generation, change the number of beads in the container to reflect the gene pool of the first generation of offspring, as you did in Simulation 2. In other words, the number of alleles (beads) in the container should match the numbers calculated in Table 3.1 (number of alleles). Again, you can obtain more alleles from the stock population if you need them.
- e. Repeat steps 6b and 6c above to produce the second generation of 60 offspring. Record the tallies and calculate the frequencies in Table 3.2.

Table 3.2. Second Generation of Offspring

Genotype	Tally marks for offspring	Number of individuals	Total number of individuals in the first offspring population	Genotype frequency	Allele	Number of alleles	Total number of alleles in the offspring population	Allele frequency
AA					A			
AS					S			
SS								

- f. What happened to the frequency of the sickle cell allele (S) with each successive generation? Remember to refer back to the parent population established in Simulation 1 when interpreting your data.
- _____
- _____
- g. Was the change in the frequency of the sickle cell allele (S) from the parent population to the first generation of offspring the same as the change from the first to the second generation of offspring? Explain your answer.
- _____
- _____
- h. Do the genotype frequencies of the parent population equal the genotype frequencies calculated in Tables 3.1 and 3.2? _____ (yes/no)
- i. Is this population at Hardy-Weinberg equilibrium? _____ (yes/no) Explain your answer.
- _____
- _____
- j. If this population is not at equilibrium, which Hardy-Weinberg condition(s) were violated in this simulation?
- _____
- _____

POST-ACTIVITY ANALYSIS AND QUESTIONS

From the simulations, it is easy to see that natural selection can alter the frequency distribution of heritable traits. Using the information and data from the simulations, along with your knowledge from the film, complete the following analysis questions.

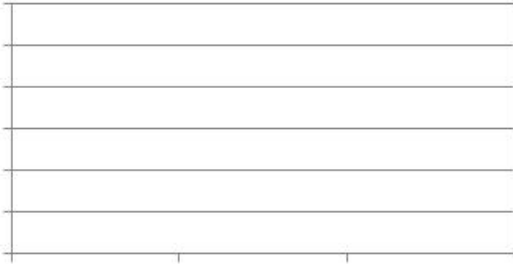
7. From the tables in all three simulations, record the calculated genotype frequencies in Table 4.1 below.

Table 4.1

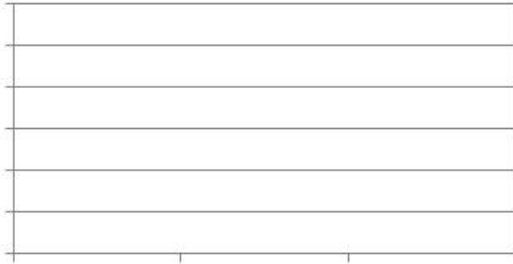
	AA genotype frequency (p^2)	AS genotype frequency ($2pq$)	SS genotype frequency (q^2)
Simulation 1: Parent Population			
Simulation 1: First-Generation Offspring			
Simulation 2: Parent Population			
Simulation 2: First-Generation Offspring			
Simulation 2: Second-Generation Offspring			
Simulation 3: Parent Population			
Simulation 3: First-Generation Offspring			
Simulation 3: Second-Generation Offspring			

8. Using colored pencils and the graphing grids provided, sketch a bar graph representing genotype frequencies in each generation for **all three** simulations. Clearly and neatly label the axes and the bars with their respective variables. You may want to sketch practice graphs on another piece of paper before drawing your final graphs here. If you need additional graph paper, more will be provided.

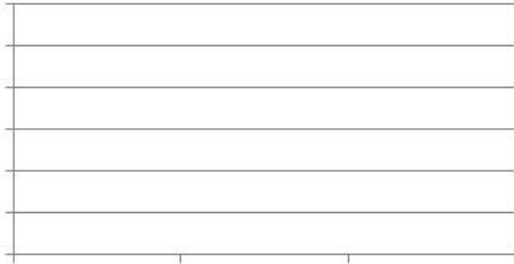
Simulation 1



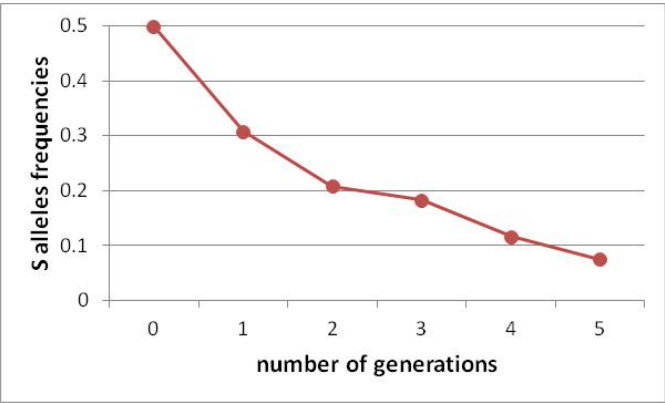
Simulation 2



Simulation 3



9. We collected data from Simulation 2 over five generations. The frequency of the S allele over time is graphed below. The graph shows a rapid decrease in the sickle cell allele frequency in the first generation but a slower decrease in later generations. By the fifth generation, the allele is not completely eliminated from the population.



Provide two explanations for why the S allele persists after five generations.

*The Making of the Fittest:
Natural Selection in Humans*

Predicted Data

Based on 60 offspring in each generation, predict the number of offspring of each genotype in each generation of the simulation you designed. Use the table below to record your predictions.

Genotype	Initial number of individuals in the parent population	Predicted number of first-generation offspring	Predicted number of second-generation offspring	Predicted number of third-generation offspring
AA	15			
AS	30			
SS	15			

Based on the predicted genotype numbers above, count the number of each allele found in each generation.

Example: Parent population A allele calculation = $(AA \times 2) + AS = (15 \times 2) + 30 = 60$ A alleles

Allele	Initial number of alleles in the parent population	Predicted number of alleles in the first generation of offspring	Predicted number of alleles in the second generation of offspring	Predicted number of alleles in the third generation of offspring
A	60			
S	60			

Calculated Frequencies

Based on the predicted numbers above, calculate the genotype and allele frequencies to illustrate how the frequencies will change over the three generations of offspring.

Genotype	Initial parent population frequencies	Predicted first-generation frequencies	Predicted second-generation frequencies	Predicted third-generation frequencies
AA	0.25			
AS	0.50			
SS	0.25			
Allele				
A	0.50			
S	0.50			

Explanation

a. How do the genotype frequencies change over time? Be sure to address all three genotypes.

b. How do the allele frequencies change over time? Address both alleles.

c. Based on how this simulation was designed, explain why these changes in allele and genotype frequencies make sense in terms of selection and evolution.

AUTHOR

Ann Brokaw
AP Biology Teacher
Rocky River High School
Rocky River, Ohio