

POPULATION GENETICS, SELECTION, AND EVOLUTION

OVERVIEW

This hands-on activity, used in conjunction with the short film *The Making of the Fittest: Natural Selection in Humans* (<http://www.hhmi.org/biointeractive/making-fittest-natural-selection-humans>), teaches students about population genetics, the Hardy-Weinberg principle, and how natural selection alters the frequency distribution of heritable traits. It uses simple simulations to illustrate these complex concepts and includes exercises such as calculating allele and genotype frequencies, graphing and interpreting data, and designing experiments to reinforce key concepts in population genetics.

KEY CONCEPTS AND LEARNING OBJECTIVES

Students will be able to

- calculate the allele and genotype frequencies of populations using the Hardy-Weinberg equations,
- explain the concept of Hardy-Weinberg (genetic) equilibrium and interpret data that does not show Hardy-Weinberg equilibrium; and
- construct and interpret graphs and tables to deduce the effect that natural selection has on allele and genotype frequencies in populations over time.

CURRICULUM CONNECTIONS

Curriculum	Standards
NGSS (April 2013)	HS-LS2-1, HS-LS2-6, HS-LS3-1, HS-LS3-2, HS-LS3-3, HS-LS4-2, HS-LS4-3, HS-LS4-4 LS2.A, LS2.C, LS3.A, LS3.B, LS4.B, LS4.C
Common Core (2010)	ELA-Literacy.RST.9-10.7, ELA-Literacy.RST.11-12.4, ELA-Literacy.RST.11-12.7 Math.Content.HSS-IC.A.1, Math.Content.HSS-IC.A.2, Math.Content.HSS-IC.B.3, Math.Content.HSS-IC.B.4, Math.Content.HSS-IC.B.5, Math.Content.HSS-MD.B.6
AP Biology (2012–13)	1.A.1, 1.A.2, 1.A.4, 1.C.3, 3.A.3, 3.C.1, 3.C.2, 4.C.1, 4.C.3
IB Biology (2009)	4.1, 4.3, 5.4, D.2, D.4, G.1

KEY TERMS

allele frequencies, evolution, genotype frequencies, Hardy-Weinberg principle, hemoglobin, heterozygous advantage, malaria, natural selection, population genetics, red blood cells, sickle cell disease

TIME REQUIREMENTS

This hands-on activity was designed to be completed within two to three 50-minute class periods, depending on whether students complete a portion of the activity as homework. You may wish to show the film outside of class. See “Teaching Tips.”

SUGGESTED AUDIENCE

This hands-on activity is appropriate for high school biology (all levels including AP and IB) and introductory college biology.

PRIOR KNOWLEDGE

Students should have prior knowledge of the Hardy-Weinberg principle, including the five conditions that must hold true for a population to remain at Hardy-Weinberg (genetic) equilibrium. Students should also understand that when these five conditions do not hold true, the population is evolving and therefore the allele and genotype frequencies change over time.

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MATERIALS

- two colors of beads (These can be pop beads, pony beads, marbles, or even two similar-sized dry beans of different colors. These beads will be the alleles in the simulations. For example, red beads could represent normal hemoglobin, and yellow beads could represent mutant sickle cell hemoglobin. Color is not important. We recommend about 100 beads of each color per student group. If you have substantially more beads of one color than the other, tell students to make this color the normal [A] hemoglobin allele color.)
- container for the parent population (This should be large enough to hold 120 beads and could be a plastic cup, a plastic storage container, a beaker, or a brown paper bag. One container is required per student group.)
- calculator
- felt-tipped marking pen
- colored pencils
- graph paper (Optional; graphing grids are provided within the student handout, but if you prefer your students to have a larger space, consider providing graph paper. Plan for a maximum of three sheets per student.)

TEACHING TIPS

- We recommend that this hands-on activity be completed in groups of 2–3 students.
- To minimize the amount of class time devoted to this activity, have the groups of students focus on collecting the data, filling out the tables, and completing necessary calculations to simulate subsequent generations for each simulation during class time. Students can complete any or all of the questions as homework.
- To save time, you may wish to have each group do a different simulation and share the data with the class.
- Students may also graph Question 2 using spreadsheet software that has graphing capability.
- If you are teaching AP Biology, you can do this activity before completing the computer modeling in the new AP Biology *Population Genetics Lab*. Alternatively, if your students have access to computers, they can use the data collected in these simulations to complete the computer modeling.

ANSWER KEY

PROCEDURE PART 1

1. *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?*

The order is not important for these answers.

- a. **Large population size**
- b. **No gene flow (isolated population)**
- c. **Random mating**
- d. **No natural selection**
- e. **No new mutations**

2. *Before beginning the activity, answer the following general Hardy-Weinberg problems for practice (assume that the population is at Hardy-Weinberg equilibrium).*

- a. *If the frequency of a recessive allele is 0.3, what is the frequency of the dominant allele?*

$$p = 0.7 \quad (q = 0.3, p + 0.3 = 1)$$

- b. *If the frequency of the homozygous dominant genotype is 0.36, what is the frequency of the dominant allele?*

$$p = 0.6 \quad (p^2 = 0.36, p = \sqrt{0.36})$$

- c. *If the frequency of the homozygous recessive genotype is 0.49, what is the frequency of the dominant allele?*

$$p = 0.3 \quad (q^2 = 0.49, q = \sqrt{0.49} = 0.7, p + 0.7 = 1)$$

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Natural Selection in Humans*

**HANDS-ON ACTIVITY
TEACHER MATERIALS**

- d. In a certain population, the dominant phenotype of a certain trait occurs 87% of the time. What is the frequency of the dominant allele?

$p = 0.64$ (If the dominant phenotype frequency is 0.87, then the recessive phenotype frequency is 0.13. $q^2 = 0.13$. $q = \sqrt{0.13} = 0.36$, $p + 0.36 = 1$)

- e. If the frequency of the homozygous dominant genotype is 0.49, what is the frequency of the homozygous recessive genotype?

$q^2 = 0.09$ (Since $p^2 = 0.49$, then $p = 0.7$ and $q = 0.3$; therefore $q^2 = 0.09$.)

- f. 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?

$p = 0.974$, $q = 0.026$, $p^2 = 0.949$, $2pq = 0.051$, $q^2 = 0.00067$

PROCEDURE PART 2

4. Perform simulation 1, which examines the Hardy-Weinberg principle.

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	15	60	0.25	A	60	120	0.50
AS	30	60	0.50	S	60	120	0.50
SS	15	60	0.25				

- i. Using the allele frequencies in 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 your work.)

Students should show their work.

Since p (A) = 0.50, q (S) = 0.50; then p^2 (AA) = 0.25, $2pq$ (AS) = 0.50, and q^2 (SS) = 0.25.

Table 1.2. First Generation of Offspring: Sample Data

Genotype	Tally Marks for Offspring	Number of Individuals	Total Number of Individuals in the Offspring Population	Genotype Frequency	Allele	Number of Alleles	Total Number of Alleles in the Offspring Population	Allele Frequency
AA		13	60	0.22	A	57	120	0.475
AS		31	60	0.52	S	63	120	0.525
SS		16	60	0.27				

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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 that you calculated in the parent population and in the first generation of offspring the same? (yes or no) **The answer is No. However, there is a slight chance that your students will answer yes and obtain frequencies in Table 1.2 that equal the frequencies in Table 1.1. Students may then answer below that no conditions of the Hardy-Weinberg principles were violated and that the population is at genetic equilibrium. This is an acceptable answer.)**

i. If yes, then the population is said to be at **genetic equilibrium, or Hardy-Weinberg equilibrium**, and all five conditions were followed.

If no, then at least one of the conditions of the Hardy-Weinberg principle was violated. In this simulation, which condition or conditions were violated? **The simulation does not have a large enough population. (Strictly speaking, the Hardy-Weinberg principle applies only to infinitely large populations. For finite populations, there will be deviations from the predicted frequencies because of chance. The larger the population, however, the more likely the population will approach Hardy-Weinberg equilibrium if the other four conditions are met.)**

ii. If a million more offspring were produced from this parent population, predict how the genotype and allele frequencies would compare with the frequencies calculated in Table 1.1. **As the population increases in number, we would expect that the allele and genotype frequencies would approach Hardy-Weinberg equilibrium, equaling those frequencies found in Table 1.1.**

5. Perform simulation 2 to examine a 100% negative selection pressure.

(Note: For this and all subsequent simulations, students should not have any individuals with the SS genotype.)

Table 2.1. First Generation of Offspring: Sample Data

Genotype	Tally Marks for Offspring	Number of Individuals	Total Number of Individuals in the Offspring Population	Genotype Frequency	Allele	Number of Alleles	Total Number of Alleles in the Offspring Population	Allele Frequency
AA		24	60	0.40	A	84	120	0.70
AS		36	60	0.60	S	36	120	0.30
SS		0	60	0.00				

Table 2.2. Second Generation of Offspring: Sample Data

Genotype	Tally Marks for Offspring	Number of Individuals	Total Number of Individuals in the Offspring Population	Genotype Frequency	Allele	Number of Alleles	Total Number of Alleles in the Offspring Population	Allele Frequency
AA		37	60	0.62	A	97	120	0.81
AS		23	60	0.38	S	23	120	0.19
SS		0	60	0.00				

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- 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 = 0.5 and S = 0.5

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

The specific numbers in the answers will vary. In the sample data, the frequency of S decreased from 0.50 to 0.30 and then to 0.19 in each successive generation. Students should note the significant decrease of the S allele from generation to generation. There is 100% selection against those with the SS genotype (those who have sickle cell disease). This quickly reduces the frequency of the S allele over time.

- 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.

The specific numbers in the answers will vary. In the sample data, the frequency of S decreased approximately 20% in each successive generation of offspring. The successive decrease results from the strong selection against the sickle cell disease (SS) genotype.

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

No

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

No

If the population were at equilibrium, the genotype frequencies would remain constant from one generation to the next.

(Note: Students may also use the Hardy-Weinberg equation to calculate expected genotype frequencies from the known allele frequencies in Table 2.2. They may say that the population is not in Hardy-Weinberg equilibrium because the expected genotype frequencies, calculated by the Hardy-Weinberg equation, do not equal the genotype frequencies from Table 2.2. This is an acceptable answer.)

- l. If this population is not at Hardy-Weinberg equilibrium, which Hardy-Weinberg condition or conditions were violated in simulation 2?

No natural selection and small population size

(Note: Simulation 2 models the lethality of sickle cell disease. Because of the 100% selection against the SS genotype in the simulation, this model violates the no natural selection condition of the Hardy-Weinberg principle. Also, as in simulation 1, the population of 60 is still small and, because of chance, will cause deviations in genotype frequencies.)

6. Perform simulation 3, which examines heterozygous advantage.

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

Table 3.1. First Generation of Offspring: Sample Data

Genotype	Tally Marks for Offspring	Number of Individuals	Total Number of Individuals in the Offspring Population	Genotype Frequency	Allele	Number of Alleles	Total Number of Alleles in the Offspring Population	Allele Frequency
AA		22	60	0.37	A	82	120	0.68
AS		38	60	0.63	S	38	120	0.32
SS		0	60	0.00				

Table 3.2. Second Generation of Offspring: Sample Data

Genotype	Tally Marks for Offspring	Number of Individuals	Total Number of Individuals in the Offspring Population	Genotype Frequency	Allele	Number of Alleles	Total Number of Alleles in the Offspring Population	Allele Frequency
AA		13	60	0.22	A	73	120	0.61
AS		47	60	0.78	S	47	120	0.39
SS		0	60	0.00				

- f. *What happened to the frequency of the sickle cell allele (S) with each successive generation? Remember to refer to the parent population established in simulation 1 when interpreting your data.*

Answers will vary. In the sample data, the frequency of S decreased from the first generation to the next, but then it increased slightly from the first generation of offspring to the second.

- g. *Was the change in the frequency of the sickle cell allele (S) from the parent to the first generation of offspring the same as the change from the first to the second generation of offspring? Explain your answer.*

Answers will vary. No, the change was not the same. In the sample data, because of the negative selection of the SS genotype, the sickle cell allele is selected against. However, it did not continue to decrease over the two generations, as in simulation 2. The slight increase in the S allele frequency is due to the selective advantage of the AS genotype; this selective advantage results in the retention of the sickle cell allele in the population.

- h. *Do the genotype frequencies of the parent population equal the genotype frequencies calculated in Tables 3.1 and 3.2? (yes or no)*

No

- i. *Is this population at Hardy-Weinberg equilibrium? (yes or no) Explain your answer.*

No

If the population were at equilibrium, the genotype frequencies would remain constant from one generation to the next.

(Note: Students may also use the Hardy-Weinberg equation to calculate expected genotype frequencies from the known allele frequencies in Table 2.2. They may say that the population is not in Hardy-Weinberg equilibrium because the expected genotype frequencies, calculated by the Hardy-Weinberg equation, do not equal the genotype frequencies from Table 2.2. This is an acceptable answer.)

- j. *If this population is not at equilibrium, which Hardy-Weinberg condition or conditions were violated in this simulation?*

No natural selection and large population size

(Note: Simulation 3 also models the lethality of sickle cell disease. Additionally, the homozygous genotype for normal hemoglobin (AA) had a 50% selection against it because the AA individuals are not resistant to malaria. Both violate the no natural selection condition. Also, as in simulation 1, the population is small.)

QUESTIONS

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

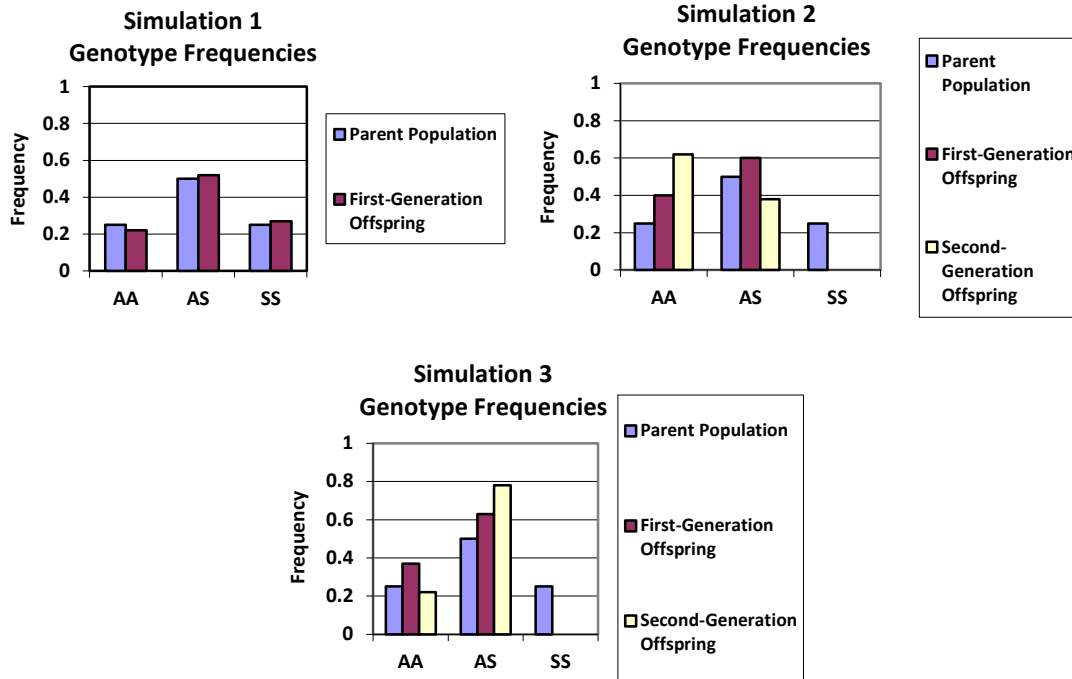
Table 4.1. Genotype Frequencies for All Simulations: Sample Data

Simulation Stage	AA Genotype Frequency (p^2)	AS Genotype Frequency ($2pq$)	SS Genotype Frequency (q^2)
Simulation 1: Parent population	0.25	0.50	0.25
Simulation 1: First-generation offspring	0.22	0.52	0.27
Simulation 2: Parent population	0.25	0.50	0.25
Simulation 2: First-generation offspring	0.40	0.60	0.00
Simulation 2: Second-generation offspring	0.62	0.38	0.00
Simulation 3: Parent population	0.25	0.50	0.25
Simulation 3: First-generation offspring	0.37	0.63	0.00
Simulation 3: Second-generation offspring	0.22	0.78	0.00

2. *Using colored pencils and the graphing grids provided below, 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, or on graph paper if your teacher provides it, before drawing your final graphs here.*

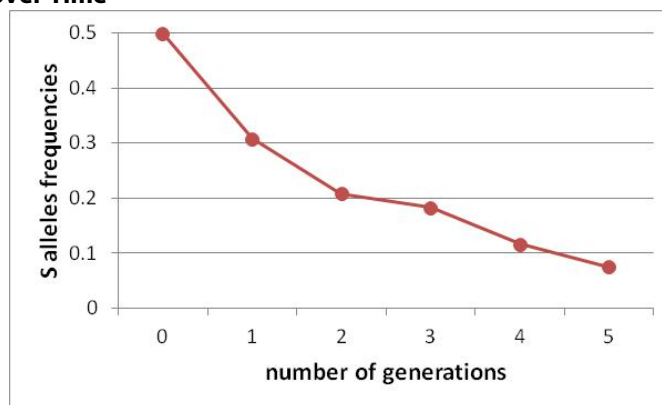
(Note: There are several ways students can set up the bar graphs. Below is one interpretation. Another common approach would be for students to place the generations on the x-axis. Then, for each generation, the students would draw bars for each genotype within that generation.)

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3. You 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.

Frequency of the S Allele over Time



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

First, there may not have been enough time for the allele to be completely eliminated from the population. Many more generations may be required. Second, in simulation 2, even though individuals with the sickle cell disease genotype (SS) were 100% selected against, individuals who were heterozygous (AS) had neither a selective advantage nor a selective disadvantage. The S allele can “hide” in the heterozygotes from generation to generation and persist in the population.

4. If you continued both simulation 2 and simulation 3 for three more generations (up to five generations), do you predict that the frequency of the S allele in simulation 2 would be greater, less than, or equal to the S allele frequency in simulation 3? Explain your answer.



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

**HANDS-ON ACTIVITY
TEACHER MATERIALS**

The frequencies of the *S* allele at generation five will be less in simulation 2 than in simulation 3. This is because simulation 3 illustrates the concept of heterozygous advantage, in which individuals who are heterozygous for a particular locus are selected for 100% of the time and have a greater fitness than either of the homozygotes do. Because the *AS* genotype is selectively advantageous, the *S* allele will be maintained at a higher frequency in the population than in simulation 2. In simulation 2, there is no selective advantage for maintaining the *S* allele.

5. Which simulation might represent a population of people who live in the moist lowlands of East Africa? Use data to explain why you chose this simulation.

Simulation 3; individuals who live in the moist lowlands of East Africa would be exposed to the mosquitoes that carry the malaria parasite present in these areas. Individuals who are carriers of the sickle cell allele (*AS*) would have a genetic advantage over the homozygous normal (*AA*) individuals because of their resistance to malaria parasite infection. According to the data, the *SS* individuals would be strongly selected against, while the *AA* genotype individuals would have a slight disadvantage when compared with the *AS* genotype individuals, who would survive 100% of the time.

6. Which simulation might represent a population of people living in a remote village in the dry highlands of Africa? Use data to explain why you chose this simulation.

Simulation 2; this population would suffer from severe sickle cell disease because of the limited health care options, so we would see a significant decrease in the *SS* genotype from generation to generation. The dry highlands of Africa do not have many mosquitoes that carry the malaria parasite, so there is no selective advantage for the *AS* genotype. We would not expect any increase in the *AS* genotype in each successive generation. Because of the selective advantage of the *AA* genotype, we would likely observe an increase in the *AA* genotype in subsequent generations.

7. Design a simulation that models equal selection for the two homozygous genotypes and selection against the heterozygous genotype. Start with the original parent population as established in Table 1.1. Design your simulation to have 60 parents and 60 offspring in each successive generation. Feel free to vary the survival percentage of particular genotypes, as in simulation 3; however, be sure to incorporate selection for the two homozygous genotypes and selection against the heterozygous genotype. Explain your simulation in the space provided.

Answers will vary. Students should design a simulation that increases the frequency of the *AA* and *SS* genotypes over time and decreases the *AS* genotype over the same time period.

Design

Sample answer: "Using the same mixing and selecting procedure as in simulation 1, produce 60 offspring from this population by randomly picking two alleles to represent an individual offspring. If the offspring is *AS*, place a tally mark every third time *AS* is selected and return the alleles to the population. (You will need to keep track of this 33% chance of survival.) If the offspring is *AA* or *SS*, place a tally mark every time it is selected. Each time, return the alleles to the population and mix. Repeat the selection process until 60 offspring have been produced."

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.

(Note: Students should get credit for any prediction showing a decrease in the *AS* genotype. You can award extra points for students who collect their own data.)

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Natural Selection in Humans*

Predicted of Number of Offspring Per Genotype Per Generation: Sample Data

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	17	18	21
AS	30	21	19	14
SS	15	22	23	25

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

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

Number of Alleles in Each Generation

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	55	55	56
S	60	65	65	64

Calculated Frequencies

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

Genotype and Allele Frequency Changes over Three Generations: Sample Data

Genotype	Initial Parent Population Frequencies	Predicted First-Generation Frequencies	Predicted Second-Generation Frequencies	Predicted Third-Generation Frequencies
AA	0.25	0.28	0.30	0.35
AS	0.50	0.35	0.32	0.23
SS	0.25	0.37	0.38	0.42
Allele				
A	0.50	0.49	0.49	0.47
S	0.50	0.51	0.51	0.53

Explanation

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

Both of the homozygous genotypes (AA and SS) increase over time. Because of the selection against the heterozygous (AS) genotype, it decreases over time.



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

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

The sickle cell allele (S) increases slightly, and the normal allele (A) decreases slightly. However, for the most part, the alleles remain close to their initial values.

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

Sample answer: "This simulation was designed to select for the two homozygous genotypes; therefore, neither allele was selected against, as in simulation 2. The data suggest that the homozygous genotypes did increase over time and that both alleles were maintained in the gene pool. Therefore, it is not surprising that the two alleles remained close to their initial values of 0.5, because they are equally represented in the two homozygous genotypes (AA and SS). In addition, there was selection against the heterozygous genotype (AS). This slight selection would equally select against both the A and S alleles, since they are both present in this genotype. In conclusion, it makes sense that the heterozygous genotype frequency will decrease over time, while the allele frequencies will remain approximately the same."

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