INTRODUCTION
The tiny rock pocket mouse weighs just 15 grams, about as much as a handful of paper clips. A typical rock pocket mouse is 172 millimeters long from nose to rump, which is shorter than an average pencil. Its impact on science, however, has been enormous. What’s so special about this little mouse?

Populations of rock pocket mice are found all over the Sonoran Desert in the southwestern United States. Two varieties occur widely in the area—a light-colored variety and a dark-colored variety. Similarly, there are two major colors of substrate, or surface material, that make up the rocky desert floor. Most of the desert landscape consists of light-colored sand and granite. Here and there, however, separated by several kilometers of light-colored substrate, are patches of dark volcanic rocks that formed from cooling lava. These areas of dark volcanic rock range in age from 1,000 to more than 1 million years old.

Dr. Michael Nachman of the University of Arizona and his colleagues have spent many years researching the genetics of fur color in rock pocket mice. In particular, they were interested in understanding the forces that shape genetic variation in natural populations.

Investigating the adaptive value of different coat colors in rock pocket mice is an example of how scientists are attempting to connect genotype with phenotype for fitness-related traits. In this type of research, investigators try to find the underlying gene or genes for a given adaptation. Examples of other fitness-related traits that researchers are currently investigating are resistance to the pesticide warfarin in rats, tolerance to heavy metals in plants, and antibiotic resistance in bacteria.

MATERIALS
calculator
computer and the Selection Coefficient file found under the “Survival of the Fittest—Battling Beetles” activity at http://www.hhmi.org/biointeractive/classroom-activities-battling-beetles.

PROCEDURE
1. Watch the short film The Making of the Fittest: Natural Selection and Adaptation. As you watch, record the following information.
   a. What specific trait did researchers study in this investigation?

   ____________________________________________________________

   b. How does this trait affect the survival of the mice in different environments?

   ____________________________________________________________

   ____________________________________________________________

   ____________________________________________________________

   c. What is the genetic basis of the trait?

   ____________________________________________________________

   ____________________________________________________________

2. After watching the film, complete Parts 1–3 that follow.
PART 1: REVIEWING THE PRINCIPLES OF THE HARDY-WEINBERG THEOREM

The genetic definition of “evolution” is “a change to a population’s gene pool.” “Gene pool” is defined as “the total number of alleles present in a population at any given point in time.” According to the Hardy-Weinberg theorem, a population is in equilibrium (and is therefore not evolving) when all of the following conditions are true:

1. The population is very large and well mixed.
2. There is no migration.
3. There are no mutations.
4. Mating is random.
5. There is no natural selection.

To determine whether a population’s gene pool is changing, we need to be able to calculate allelic frequencies. Suppose, for example, a gene has two alleles, A and a. Each individual has one of three genotypes: AA, Aa, or aa. If the population is in equilibrium, the overall number of A alleles and a alleles in the gene pool will remain constant, as will the proportion of the population with each genotype. If allele frequencies or genotype frequencies change over time, then evolution is occurring.

Two equations are used to calculate the frequency of alleles in a population, where \( p \) represents the frequency of the dominant allele and \( q \) represents the frequency of the recessive allele:

\[
p + q = 1.0
\]

and

\[
p^2 + 2pq + q^2 = 1.0.
\]

The first equation says that if there are only two alleles for a gene, one dominant and one recessive, then 100% of the alleles are either dominant \( (p) \) or recessive \( (q) \).

The second equation says that 100% of individuals in the population will have one of these genotypes: AA, Aa, and aa. Let’s look at each genotype one by one to understand the equation:

- If \( p \) represents the frequency of the A allele, then the frequency of the genotype AA will be \( p \times p \), or \( p^2 \).
- If \( q \) represents the frequency of the a allele, then the frequency of the genotype aa will be \( q \times q \), or \( q^2 \).
- For heterozygotes, we must allow for either the mother or the father to contribute the dominant and recessive alleles. You can think of it as allowing for both genotypes Aa and aA. So, we calculate the frequency of the heterozygous genotype as \( 2pq \).

In rock pocket mice, several genes code for fur color. Each gene has several possible alleles. That’s why there is a range of fur color from very dark to light. For simplicity, we will work with two alleles at one gene. The allele for dark-colored fur \( (D) \) is dominant to the allele for light-colored fur \( (d) \). In this scenario, individual rock pocket mice can have one of three genotypes and one of two phenotypes, as summarized in the table below.

<table>
<thead>
<tr>
<th>Rock Pocket Mice Genotypes and Phenotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
</tr>
<tr>
<td>Homozygous dominant</td>
</tr>
<tr>
<td>Heterozygous</td>
</tr>
<tr>
<td>Homozygous recessive</td>
</tr>
</tbody>
</table>
So, applying Hardy-Weinberg, we have the following:

- \( p \) = the frequency of the dominant allele \( (D) \)
- \( q \) = the frequency of the recessive allele \( (d) \)
- \( p^2 \) = the frequency of \( DD \)
- \( 2pq \) = the frequency of \( Dd \)
- \( q^2 \) = the frequency of \( dd \)

We can also express this as

the frequency of the \( DD \) genotype + the frequency of the \( Dd \) genotype + the frequency of the \( dd \) genotype = 1.

SAMPLE PROBLEM

In a hypothetical population consisting of 100 rock pocket mice, 81 individuals have light, sandy-colored fur. Their genotype is \( dd \). The other 19 individuals are dark colored and have either genotype \( DD \) or genotype \( Dd \).

Find \( p \) and \( q \) for this population and calculate the frequency of heterozygous genotypes in the population.

It is easy to calculate \( q^2 \).

\[ q^2 = \frac{81}{100} = 0.81, \text{ or } 81\% \]

Next, calculate \( q \).

\[ q = \sqrt{0.81} = 0.9 \]

Now, calculate \( p \) using the equation \( p + q = 1 \).

\[ p + 0.9 = 1 \]

\[ p = 0.1 \]

Now, to calculate the frequency of heterozygous genotypes, we need to calculate \( 2pq \).

\[ 2pq = 2(0.1)(0.9) = 2(0.09) \]

\[ 2pq = 0.18 \]

QUESTIONS

1. If there are 12 rock pocket mice with dark-colored fur and 4 with light-colored fur in a population, what is the value of \( q \)? Remember that light-colored fur is recessive.

2. If the frequency of \( p \) in a population is 60% (0.6), what is the frequency of \( q \)?

3. In a population of 1,000 rock pocket mice, 360 have dark-colored fur. The others have light-colored fur. If the population is at Hardy-Weinberg equilibrium, what percentage of mice in the population are homozygous dominant, dark-colored mice?
PART 2: APPLYING HARDY-WEINBERG TO ROCK POCKET MOUSE FIELD DATA

Dr. Nachman and his colleagues collected rock pocket mice across 35 kilometers of the Arizona Sonoran Desert, which included both dark, rocky lava outcrops and light, rocky, granite areas. They recorded substrate color and coat-color frequencies for each location. Each site was separated from any of the others by at least eight kilometers. The researchers trapped a total of 225 mice. Their data are summarized below.

**Field Data Summary**

<table>
<thead>
<tr>
<th>Collecting Site</th>
<th>Substrate Color</th>
<th>Number of Mice</th>
<th>Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Light</td>
<td>6</td>
<td>Light 6</td>
</tr>
<tr>
<td></td>
<td>Light</td>
<td>85</td>
<td>Light 80</td>
</tr>
<tr>
<td></td>
<td>Dark</td>
<td>7</td>
<td>Dark 7</td>
</tr>
<tr>
<td></td>
<td>Dark</td>
<td>5</td>
<td>Dark 5</td>
</tr>
<tr>
<td></td>
<td>Dark</td>
<td>45</td>
<td>Dark 42</td>
</tr>
<tr>
<td></td>
<td>Light</td>
<td>77</td>
<td>Light 43</td>
</tr>
</tbody>
</table>


**QUESTIONS**

   frequency = number of mice of one color/total number of mice
   Frequency of light-colored mice ________ Frequency of dark-colored mice ________

2. Calculate the overall frequencies of light-colored mice and dark-colored mice caught on dark-colored substrates.
   frequency = number of mice of one color/total number of mice
   Frequency of light-colored mice ________ Frequency of dark-colored mice ________

3. Using the Hardy-Weinberg equation and data from the table above, determine the number of mice with the **DD** and **Dd** genotypes on the light, rocky, granite substrate.
   Frequency of mice with the **dd** genotype on light-colored substrate ________
   Frequency of mice with the **DD** genotype on light-colored substrate ________
   Frequency of mice with the **Dd** genotype on light-colored substrate ________

4. Using the Hardy-Weinberg equation and data from the table above, determine the number of mice with the **DD** and **Dd** genotypes on the dark, rocky lava substrate.
   Frequency of mice with the **dd** genotype on dark-colored substrate ________
   Frequency of mice with the **DD** genotype on dark-colored substrate ________
   Frequency of mice with the **Dd** genotype on dark-colored substrate ________
5. Which fur color seems to have the greatest overall selective advantage? Use data collected from both dark-colored and light-colored substrates to support your answer.

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6. According to the film, what environmental change gave a selective advantage for one coat color over another?

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7. In a separate study, 76 rock pocket mice were collected from four different, widely separated areas of dark lava rock. One collecting site was in Arizona. The other three were in New Mexico. Dr. Nachman and colleagues observed no significant differences in the color of the rocks in the four locations sampled. However, the dark-colored mice from the three New Mexico locations were slightly darker than the dark-colored mice from the Arizona population. The entire Mc1r gene was sequenced in all 76 of the mice collected. The mutations responsible for the dark fur color in the Arizona mice were absent from the three different populations of New Mexico mice. No Mc1r mutations were associated with dark fur color in the New Mexico populations. These findings suggest that adaptive dark coloration has occurred at least twice in the rock pocket mouse and that these similar phenotypic changes have different genetic bases. How does this study support the concept that natural selection is not random?

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8. To determine if the rock pocket mouse population is evolving, explain why it is necessary to collect fur color frequency data over a period of many years.

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PART 3: HARDY-WEINBERG EXTENDED
We can adapt the Hardy-Weinberg equations to investigate what happens to gene frequencies in a population that is evolving. To do this, it is necessary to introduce a new term, selection coefficient. It is defined as “the relative advantage or disadvantage of a genotype with respect to survival and reproductive success.” You can also think of it as the relative selection advantage of a specific allele. For example, if there are two alleles present in a population for a particular trait and one allele is 10% more likely to survive than the other allele, then the selection coefficient for that allele is +0.1.
QUESTIONS

1. Use the spreadsheet to determine how the selection coefficient (s) influences the phenotype of future generations. Substitute increasingly large numbers for s. Record each new value and describe what happens to the frequencies of $p$ and $q$ over the next five generations.

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2. Explain how the selection coefficient and natural selection are related.

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3. In areas with primarily dark-colored substrate, dark-colored mice have a selective advantage over light-colored mice. Therefore, mice with one or more copies of the dominant $Mc1r^D$ allele have a selective advantage over mice with two copies of the $Mc1r^d$ allele.

In the film, Dr. Sean Carroll says that with a 1% selection advantage, it takes 1,000 years for 95% of the mice to have the dominant phenotype. With a 10% selection advantage, it would take just 100 years. Use the spreadsheet to verify these facts.

   a. Find out how many generations following the first appearance of a dark-colored mutation it would take for 95% of the mice to express the dominant dark-colored phenotype, given a 1% advantage ($s = 0.01$). Rock pocket mice have approximately one litter of pups a year, so the number of generations will be equal to the number of years. You will not be able to use the graph on the Main Page tab since it only goes up to 100 generations. So, you will need to look at column D of the worksheet called Main Worksheet. Scroll down until the value is greater than 0.95. Record your answer below.

   It would take about ____________ generations.

   b. Repeat the process for a 10% advantage ($s = 0.1$).

   It would take about ____________ generations.

   c. What would the selection coefficient need to be for 95% of the mice to have the dominant phenotype in just 50 years? Record your answer below.

   The coefficient would need to be about ________________________________.

AUTHOR
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