

Exploring the Effects of Mutation Rate on Individuals

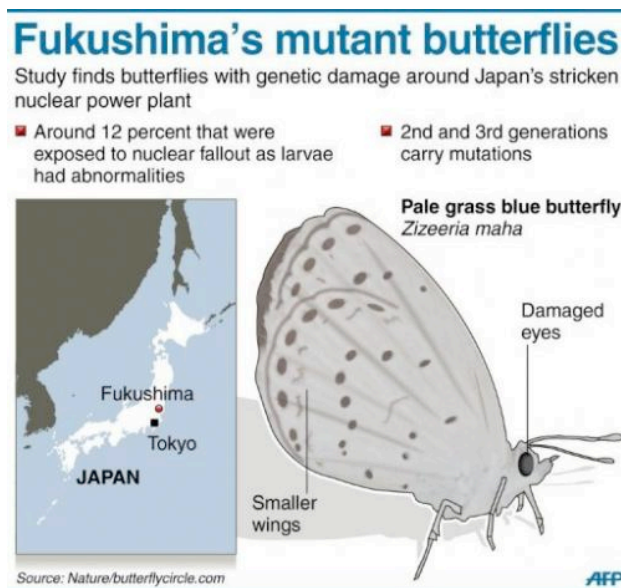
Lesson Overview

This lesson allows students to explore relationships between mutation rate and effects on the genomes of individual organisms. How variable are genetic sequences replicating at different mutation rates? To what degree are mutations harmful, and how might this be affected as mutation rates change? In addition, students will model an existing study to test claims made by other scientists.

Big Ideas

Mutations are changes to the genetic code of an organism as a result of random errors during genome replication. These changes can be beneficial or harmful, increasing or decreasing the individual's fitness relative to the rest of the population. Mutations can also be neutral, having no obvious fitness effect but still producing genetic variation in the population.

Harmful mutations tend to decrease an individual's relative fitness by reducing the ability to compete effectively for resources, producing inviability (e.g., sterility), or causing disabling or even lethal defects. Although mutations can be neutral or beneficial, the frequency of deleterious mutations is positively correlated with mutation rate. An example of this relationship can be seen in populations of butterflies in the vicinity of the compromised Fukushima nuclear power plant in Japan¹.



¹ Hiyama et al. (2012). The biological impacts of the Fukushima nuclear accident on the pale grass blue butterfly. *Scientific Reports* 2 (570). Retrieved from <http://dx.doi.org/10.1038/srep00570>.



Objectives for Student Learning

Through engagement in this lesson, students will:

- Explore, describe, and explain the relationship between mutation rate and the occurrence of adverse effects due to harmful mutations.
- Engage in science practices to test scientific claims.

Students' Prior Knowledge

- Students should be familiar with the idea of genetic variation and its origin (mutations).
- Students are likely to have several misconceptions regarding mutations. Some of these include:
 - “Mutations are always harmful, never beneficial.” While most mutations are neutral or deleterious, some are indeed beneficial (e.g., those contributing to antibiotic resistance in bacteria).
 - “All mutations have strong phenotypic effects.” Some mutations can cause large phenotypic changes, others small, and some not at all (e.g., “silent” mutations). Regardless, all mutations result in genetic variability.
- Students should have a basic understanding of probability. However, they may struggle with what is meant by a particular mutation rate. Rather than indicating that there will always be a 10% difference between the ancestor and offspring, a 10% mutation rate means that each site in the genome independently has a 10% chance of changing during replication. The actual number of mutations in a given replication event will vary.

Conceptual Connections

Biological Connections	Nature of Science Connections
Effects of exposure to radiation on DNA replication (increased mutation rate, higher incidence of cancers and birth defects)	Hypothesis development and testing

Activity

Materials

- Computers with Avida-ED installed
- Source article (Hiyama et al., 2012)
- Handout: Exploring the Effects of Mutation Rate on Individuals

Introduction

- Establish the problem: Introduce the Hiyama et al. (2012) report, summarizing the main patterns and claims. Ideally, students will have read this before coming to class.
- Introduce the model system: Explain that you’ll be using digital organisms in Avida-ED to model the conditions in the paper in order to test the claim that the phenotypic





abnormalities observed in the butterflies were caused by exposure to radiation from the damaged nuclear power plant. Briefly introduce Avida-ED, demonstrating in the Organism viewer how mutations occur during genome replication and explaining how natural selection of accumulated mutations by an environment can allow organisms to perform simple computational functions.

Main Teaching Activities (Estimated class time: 95 minutes)

- Think, Pair, Share (15 minutes): Ask students to predict what would happen to an individual Avidian's genome as it replicates at different mutation rates (low, medium and high). Will it change a little or a lot? How do they know? Will the resulting offspring be viable (able to replicate)? Why or why not? Students should take a few minutes to answer these questions on their own, and then consult with a neighbor before sharing with the entire class. The instructor should keep track of student predictions in a public place (board, overhead, etc.).
- Data Collection (60 minutes): In small groups, one per computer, students will replicate Avidians under four experimental conditions. In the Organism viewer, students will drag a provided² ancestor organism, capable of replicating and performing all nine metabolic functions, from the freezer into the viewing pane. Under the Settings tab they will set the per site mutation rate to 1%. They will then replicate the ancestor 10 times, setting up a new run each time. For each offspring organism, students will record on their data sheet the number of mutations in the offspring and then freeze the offspring (use a naming convention like "1%no01" or something similar). After saving all 10 offspring organisms, the students will drag each offspring, one at a time, into the Organism viewing pane, replicate it, and examine its genome to determine which of the 10 functions (9 metabolic functions plus the ability to replicate), if any, each organism can execute. Students should record the number of **lost** functions alongside the number of mutations for each replication event. This process will be repeated at mutation rates of 5%, 10%, and 15%. When the students are finished they may send their data to the instructor to be combined with data from the rest of the class.
- Exploring Class Data (20 minutes): Provide students with a graphical representation of the combined class data, showing the average number of mutations and abnormality rate – calculated as the percentage of functions lost from the total – for each of the four mutation rates (see sample data as an example). Students will decide which of their earlier predictions best matches the pattern shown by the data.

Conclusion

- Class Discussion: Discuss whether the data support the authors' claim that the adverse effects observed in the study can be explained by random mutations caused by exposure to radiation. This discussion can be for the purposes of formative assessment.

² A pre-evolved organism for this lesson is available for download from the Avida-ED website, but instructors may evolve one themselves or have students use one from some previous exercise—the only requirement is that the ancestor organism for this exercise is viable (able to replicate) and able to perform all nine metabolic functions.





- Extension (in class or as a homework assignment): Students will use class data to predict the effects of different mutation rates on populations. This can serve as a lead in to the exercise “Exploring the Effects of Mutation Rate on Populations”, which will explore this interaction in detail.

Variations and Supplemental Activities

- Variation: Instead of asking students to send their data, the instructor may choose to use the sample data provided.
- Variation: The instructor can give the collected class data (or sample data) to students/groups and ask them to decide how to analyze it, or provide them with directions on how to analyze it.
- Variation: The instructor can establish the problem as described (testing the scientists’ claim) and ask students to come up with an experimental protocol.
- Variation: The instructor can give the students just the initial problem (description of the disaster) and ask them to predict the effects on organisms in the vicinity of the nuclear power plant. They can then test their predictions in Avida-ED and later compare the results of their investigations to the findings in the Hiyama et al. (2012) report.
- Supplemental activity: In the Hiyama et al. (2012) article, the authors report that the effects of the initial exposure to radiation became increasingly pronounced in subsequent generations, even in butterflies that received low doses. They suggest that this is because mutations in the germ cell line are accumulating over time, and warn that the butterfly population will continue to deteriorate. Students can test these ideas in Avida-ED.
 - *Do harmful mutations accumulate over time?* Students can continue to replicate their frozen Avidians under various experimental conditions (i.e., mutation rates) and record the number of mutations and percentage of abnormalities in subsequent generations. How many generations does it take before there are no remaining viable offspring?
 - *What are the consequences of exposure to radiation at the population level?* This question could be a lead in to the exercise “Exploring the Effects of Mutation Rate on Populations”. Are the researchers’ concerns justified? Will a population that has been exposed to radiation continue to deteriorate, or can it recover? How is average population fitness affected over many generations?



Student Handout

Exploring the Effects of Mutation Rate on Individuals



Left: Pale grass blue butterfly (*Z. maha*) with normal fore and hind wings.
Right: Mutated butterfly with stunted wings.

Background

On March 11, 2011 the largest earthquake ever to hit Japan, and one of the five largest in recorded history, occurred 40 miles (70 km) off the coast of Tōhoku. The quake triggered a tsunami that produced waves with heights up to 133 feet (40.5 m) that traveled as much as 6 miles (10 km) inland, causing extensive damage to property and significant loss of human life. Among the infrastructure casualties was the Fukushima Daiichi Nuclear Power Plant complex. Three reactors sustained heavy damage, resulting in the worst nuclear accident since Chernobyl in 1986. The area within a 20-mile (~30 km) radius of the Fukushima plant was determined to have dangerously high levels of radiation, with the highest levels up to 2 miles (3 km) from the plant. The Japanese government prohibited access to this area and ordered the evacuation of anyone living between 2 and 12 miles (3 and 20 km) of the plant. People living between 12 and 20 miles (20 and 30 km) away were put on high alert and also encouraged to evacuate.

The disaster at Fukushima has provided scientists with an opportunity to investigate the biological impact of radiation on organisms. One species in particular, the pale grass blue butterfly (*Zizeeria maha*), is helping researchers pursue questions about the immediate and long-term effects of radiation at various doses (Hiyama et al., *Scientific Reports* **2** Article 570, 2012). Butterflies collected closer to the power plant experienced larger doses of radiation than those farther away, and the scientists found that larger doses were associated with increased infertility, mortality, and incidence of physiological abnormalities. Many of these abnormalities were inherited and amplified in offspring of butterflies that had been exposed to the radiation initially as overwintering larvae. The researchers concluded that “[I]t is most likely that the abnormal phenotypes observed are produced by random mutations caused by the exposure to radiation” (p. 8).

Using digital organisms as a model, your goal in this exercise is to test the scientists’ claim: assuming that higher doses of radiation are associated with increased mutation rates, can exposure to radiation account for the adverse biological effects reported in the study?





Assignment Tasks

Predict: What will happen to an individual Avidian's genome as it replicates at different mutation rates (low, medium and high)?

Test: Follow the instructions carefully. Use the table provided to record your data.

- 1.) Download the "All Functions" organism ("@allfunctions") from the Avida-ED website. Import this organism into the program.
- 2.) In the Organism viewer, drag the ancestor organism ("@allfunctions") into the viewing pane. Under the Settings, set the per site mutation rate to 1%.
- 3.) Click on the Run button and allow the ancestor to replicate.
- 4.) On your data sheet, record the number of mutations in the offspring (circled in green).
- 5.) Drag the offspring to the freezer. Name it in a way that will allow you to match it to your data (e.g., "1%no01"). *Note: You may have to create a new workspace before freezing your first organism. Name it something recognizable and save it to the Desktop.*
- 6.) Repeat steps 2 – 5 ten times, completely filling out the first "Mutations (n)" column of your data sheet.
- 7.) Drag your first saved offspring from the freezer into the Organism viewing pane. Click Run and record the number of functions (9 metabolic functions and the ability to replicate) it has **lost**. Repeat this for all remaining offspring until you have completely filled out the first "Abnormalities (n)" column of your data sheet.
- 8.) Repeat steps 2 – 7 at 5%, 10%, and 15% mutation rates, recording data in the appropriate spaces on your data table.
- 9.) Use your data to calculate the average number of mutations and percentage of abnormalities for each of the four mutation rates.



Results: Were your predictions confirmed or disconfirmed by the data you collected?

Discussion: What do your tests reveal about the relationships between mutation rate, frequency of mutations, and physiological abnormalities?

Does the evidence from your study support the researchers' claim that "it is most likely that the abnormal phenotypes observed are produced by random mutations caused by the exposure to radiation"? How?





Data Table. Keep track of your experimental observations in the table provided.

	Mutation Rate							
	1%		5%		10%		15%	
Offspring	Mutations (n)	Abnormalities (n)	Mutations (n)	Abnormalities (n)	Mutations (n)	Abnormalities (n)	Mutations (n)	Abnormalities (n)
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								
	Average number of mutations	Abnormality rate	Average number of mutations	Abnormality rate	Average number of mutations	Abnormality rate	Average number of mutations	Abnormality rate





Data Chart. Plot your data to reveal patterns.

