



Understanding the Introduction of Genetic Variations by Random Mutation

Lesson Overview

The focus of this lesson is on mutations as a source of genetic variability and what it means to say that mutations occur randomly at a particular rate. Students will make predictions about and observe the random mutations in the genomes of Avidians.

Big Ideas

The basic components of the Darwinian evolutionary mechanism are variation, inheritance, natural selection and time (aka VIST). Genetic variation is produced by mutations—changes in an organism’s genome caused by random replication errors. These errors occur at a relatively constant rate within broad groups of organisms and may be expressed probabilistically in various ways (e.g. mutation rate per base pair or per genome per replication).¹ Because each site in the genome is equally susceptible to replication errors, the actual number of mutations occurring during a given replication event is variable, with higher mutation rates increasing the likelihood that mutations will occur. Random mutations produce the raw materials that are shaped by non-random selection into complex adaptive features.

Objectives for Student Learning

Through engagement in this lesson, students will:

- Learn that mutations may occur at random in a genome at various rates
- Observe how random mutations introduce genotypic variability in a population
- Explain what mutation rates imply about the distribution of genotypic changes
- Test hypotheses via a cycle of Hypothesis, Prediction, Testing, and Evaluation.

Students’ Prior Knowledge

Students should have a basic understanding of probability. However, they may struggle with what is meant by a particular mutation rate. Students may think, for instance, that a 10% mutation rate means that there will always be a 10% difference between the ancestor and offspring, instead of recognizing that each site in the genome independently has a 10% chance of changing during replication. The actual number of variations in a given replication event will vary.

Conceptual Connections

Biological Connections	Nature of Science Connections
Background mutation rate Luria-Delbrück experiment (for extension): mutations are random rather than directed	Hypothesis development and testing; replication of experiments; sample size

¹ Drake, J.W. et al (1998) Rates of Spontaneous Mutations. *Genetics* 148 (1667-1686).



Activity

Materials

- Handout: Understanding the Introduction of Genetic Variations by Random Mutation

Introduction

- Interactive introductory lecture: What comes to mind when someone says “mutant”? What is a mutation (*in vivo* and in Avida-ED)?
 - Genetic mutations in Avida-ED occur during replication at whatever rate is set.
 - The default @ancestor genome is 50 instructions long and there are 26 possible instructions in the basic set. Any instruction in the genome may randomly change to some other at the given rate.
 - In real organisms, a *point mutation* is a change in a single nucleotide in its DNA, such as a *substitution mutation* (e.g. a change from adenine to thymine). A substitution mutation determines which of the 20 amino acids is produced (it may be “silent”, because of redundancy in the genetic code). Substitution mutations occur in Avidians in a similar manner—any of the 26 basic instructions may be replaced with any other. For simplicity, in this version of Avida-ED insertion mutations and deletion mutations are not allowed, though we plan to allow that in a future release in an advanced mode option.
 - In real organisms, mutation rate varies between species. In bacteria, for instance, the mutation rate is roughly 5×10^{-10} per base pair per generation (Ochman 2003). Mutation rate may also vary between different regions within a genome of the same individual (by as much as several orders of magnitude) or change as a function of environmental stress. In Avida-ED, mutation rate may be set from 0% - 100% per site per generation, but for simplicity it is constant across the genome and over the course of any given run.
- Demonstration: Show an Avidian genome before and after replication at two mutation rates (e.g., 0%, 5%).

Main Teaching Activities (Estimated class time: 30 minutes)

- Observing mutations (20 minutes): Working in pairs or small groups², students will follow the outline provided on their lesson handout. Using the Organism Viewer in Avida-ED, they will set the per site mutation rate to 10% and allow the ancestral organism to replicate, observing and recording any differences in the offspring, paying particular attention to the specific mutations and how many there are. The students will then make predictions about what will happen with regard to the specific mutations and number of mutations that will occur if this process is repeated, providing a rationale for their answer. They will then repeat the experiment with the same settings three more times, recording their observations each time.

² Alternatively, this activity could be assigned individually as homework.





- Class discussion (10 minutes): In groups or as a whole class, students will discuss what their tests reveal about how genotypic variations arise in a population. The goal is for students to understand that variation arises from mutations that are random and what this means about the predictability of *specific* changes in a genome vs. a distribution of possible *number* of changes.

Conclusion

Extension (to be completed as homework): Thinking about possible follow-up research, students should develop a hypothesis about what patterns would be expected in the data as the number of runs is increased. They should also try to come up with a way to graph their data to make any patterns that might emerge easier to see. (*Note: You may or may not have them actually conduct the experiment, depending on your objectives and time constraints.*)

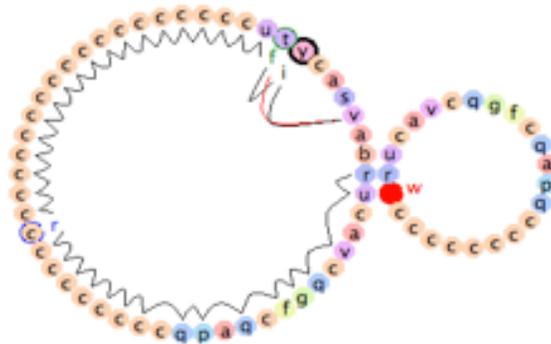
Variations and Supplemental Activities

- *Probability*: Before starting students on the main activity, use coin tossing to discuss probability. This can be done as a short demonstration or mini-activity during the lesson introduction. Explain that the probability of obtaining either heads or tails on a given coin toss is 50% because you can only have one of two possible outcomes. Next, ask the students to predict the number of heads you will observe in 10 consecutive tosses. As a whole class, in groups or individually, ask students to justify their prediction in terms of probability (for example, they may predict that 5 tosses will result in heads and 5 in tails because 5 is 50% of 10). Conduct the experiment by flipping the coin 10 times and recording the outcome of each toss. Ask students to explain the results: did they differ from what was predicted? Why?
 - To further connect this activity with the main lesson, ask students if they can predict, in 10 consecutive coin tosses, the exact number and sequence of heads or tails. Discuss whether this is possible in terms of probability and random chance.
- *Relating probability and mutation rate*: After students have recorded their observations in Avida-ED, pool class data of the number of mutations per replication event at a 10% mutation rate. (Ideally, do this only *after* they have completed the Future Research section on their own.) Graph these data to show that there is a regular distribution. Identify the range and calculate the mean. Ask students how their data compare to the class data and explain any differences in terms of probability. They should be able to see that although it is not possible to predict the specific number of mutations it is possible to predict a distribution.
 - NOS connection: Ask students why increasing the sample size (number of data points) causes the actual mean to converge on the theoretical mean. What implications does this have for the design of scientific investigations?



Student Handout

Understanding the Introduction of Genetic Variations by Random Mutation



An Avidian creating a copy of itself

Background

The basic components of the Darwinian evolutionary mechanism are variation (V), inheritance (I), natural selection (S) and time (T). This exercise focuses on variation and one basic way it can arise.

Natural selection acts upon phenotypic variations in a population of organisms. Variations can arise in a population in several different ways. Here we will look only at variations that may be introduced by genetic *mutations*—random changes in an organism’s genome—and not at other processes such as recombination, horizontal transfer, etc. Genetic mutations may be substitutions (changes from one instruction to a different one), insertions (additions of an instruction into the genome), or deletions (deletions of an instruction from a genome).

As in nature, a population of Avidians—the model organisms in Avida-ED—can vary both phenotypically and genotypically. Like plasmids, Avidians have a circular genome composed of simple genetic instructions. Different genetic sequences can produce different phenotypic functions. Each instruction in the sequence is represented by a colored dot. During genome replication, point mutations may occur at random in the sequence. [Note: For simplicity, this version of Avida-ED allows only substitutions, not insertions or deletions.]

Your goal in this exercise is not to look at what exactly makes a sequence of instructions functional, but just to understand *how* mutations produce varieties of genetic sequences. Specifically, you will explore what it means to say that mutations occur at random at a particular rate.



Assignment Tasks

Pilot Study: Use the Organism Viewer to see how substitution mutations change the genomes of organisms.

- (i) In the Organism viewer, go to settings. Set the per site mutation rate to 10%. Keep repeatability mode set to Experimental. Flip back to the viewer.
- (ii) Drag in the @ancestor from the freezer and click Run to watch it replicate.
- (iii) Record the position and total # of any changes in the offspring's genome after replication. (Do this in clockwise order starting from the 3 o'clock position on the circular genome, which is the origin of replication).

- Run #1: Mark differences from ancestral genome below.

Wzcgagcczcvcaxgab Total#

Predict: What do you expect to see if you repeat your Pilot Study several times using the same ancestor with the same mutation rate?

- (1) Will the *specific* mutations always be the same? Yes / No
- (2) Why, or why not?
- (3) Will the *number* of mutations always be the same? Yes / No
- (4) Why, or why not?

Test: Repeat steps (ii) and (iii) from the Pilot Study at least three times (but not until AFTER you have written down your predictions above).

- Run #2: Mark differences from ancestral genome below.

Wzcgagcczcvcaxgab Total#

- Run #3: Mark differences from ancestral genome below.

Wzcgagcczcvcaxgab Total#

- Run #4: Mark differences from ancestral genome below.

Wzcgagcczcvcaxgab Total#

Results: Were your predictions confirmed or disconfirmed?

Discussion: Explain your results. What do your tests above reveal about how random mutations introduce genotypic variations in a population? (Use back of sheet.)

Future research: What patterns, if any, in the sequences and total number of mutations would you expect to see if you increased the number of runs (replicates)? How would you graph your data to better see whether your predictions are correct?