Model Organisms: Fly School

Lesson Overview

Students conduct a series of online experiments that use model organisms to better understand genes that influence human learning and memory.

Description of Activity

Model Behavior engages students in a series of experiments using the *Fly School* training maze simulation. In Part 1, students become familiar with experimental variables and controls. They conduct their first training session using wild-type fruit flies. The *Fly Training Matrix* provides students with an organized way to record their results. One of the experiments measures short-term memory while the other measures long-term memory in fruit flies.

In Part 2, students are asked to build on their understanding by researching fruit-fly variants and then conducting, recording, and interpreting their designed experiments.

In the final set of activities, students are asked to research other model organisms as candidates for studying learning and memory through amino acid alignment and protein percentage comparisons.

Background

Model Behavior is based around a series of experiments designed to investigate the genes for learning and memory. The key experiment concerns the *shibire* mutant, which was the focus of an experiment by Cold Spring Harbor Laboratory scientist Josh Dubnau and colleagues in 2001.

Shibire is a gene in fruit flies that is heat sensitive, and is blocked when the temperature exceeds 29˚C. Dubnau *et al.* engineered the gene to selectively express in the mushroom bodies of flies. The mushroom body is a brain structure involved in learning and memory. It has been conceptualized as a model for the cerebral cortex of mammals. Flies with this mutation can learn at any temperature, but can only remember when the temperature is below 29˚C. This experiment provides a neat way of dissociating learning from memory and confirms the role of the mushroom body in memory formation.

CREB mutations are also critical, as they provide a way to selectively enhance or block memory formation. CREB A mutants essentially develop a photographic memory, and require very little training to form long-term memories. The ethical ramifications of giving humans a similar capacity can lead to a stimulating class discussion.

In comparing the performance of groups of flies, it is important to note that in a T-maze training paradigm (such as in *Fly School*), only 85-90% of the group will ever choose the correct option. As such, if ~85% do choose the correct option, we can conclude that the group, as a whole, has successfully learned. Chance performance (no learning) is 50%.

Goals and Objectives

Students will be able to:

- explain the value of model organisms in scientific research.
- formulate and test hypotheses.
- design and conduct controlled experiments.
- analyze and interpret the results of a series of experiments.
- apply the findings of experiments with model organisms to human learning.
- Describe how the molecules of learning and memory have been conserved by evolution across several species.

Assumptions of Prior Knowledge

Students should have some knowledge of experimental design and model organisms. Also, students should have a basic understanding of DNA, transcription, translation, and protein formation.

Common Misconceptions

Students often think:

- Short-term memory is the same as long-term memory.
- Learning and memory are not dependent upon genetics.
- Designing and conducting experiments involves few variables to consider.
- Different organisms have unique DNA and proteins, and do not share similarities with other species.

Implementing the Lesson

Time Allotment:

Parts 1 & 2:	1 x 50-minute class
Part 3:	1 x 50-minute class

Before Class

Become familiar with *Genes to Cognition* (*G2C*) *Online* (www.g2conline.org). It may be useful to pay particular attention to the *Model Systems* section.

Photocopy the following student worksheets:

Model Organisms – Introduction to Fly School
Part 1: *Model Organisms*
Part 2: *Model Organisms*
Part 3: *Model Organisms*

Students may be paired or work independently.

During Class

Begin the lesson by asking students how they prepare for tests. Inquire if cramming the night before an exam works as well for them as reviewing several times over a period of several days. Next, ask those who play sports if running a play many times in one day works as well as running the new play several times over many days. How does a coach address this? Discuss that in both cases, they are learning something new, and the goal is to commit the new information into long-term memory so that it will be there when they need it later – on a test or in an athletic competition.

Use the student worksheet *Model Organisms – Introduction to Fly School* to introduce students to the concept of model organisms, the fruit fly, and the T-maze training chamber that they will utilize to conduct online experiments.

Use the student worksheet *Part 1: Model Organisms* to guide students through the training session variables. Further information on each of the variables can be found by rolling over the relevant icon. Variables include fly type, number of training sessions, odor type, and electric shock. Students will conduct a series of training sessions to examine effects on short- and long-term memory, after which they are asked to hypothesize about the implications of their experiment on human memory and learning.

Using the *The Fly Training Matrix* in *Part 1*, students will follow prescribed variables in preparing, conducting, and interpreting the training sessions. Students use this worksheet to record the results of comparing fly strains on different short- and long-term memory training paradigms.

Using the student worksheet, *Part 2: Model Organisms*, students are asked to compare different fly strains on the different training paradigms. Students can design and analyze a series of experiments comparing the mutants across different set-ups.

In *Part 3: Model Organisms*, students use the *Model Center* (#548) tool to explore protein alignment in other model organisms.

Note: Before engaging with the tool, it is recommended that students view *Model Organisms* (#555), which is part of the GENES content of Model Systems.

The *Model Center* protein alignment tool allows students to compare genes in different species. Once a gene is selected from a drop-down menu, the tool lines-up the amino acid sequences of selected organisms. This provides a rather striking example of how well genes are conserved across species. Students can also click to see the *"% of protein the same"* which further emphasizes the point. Students may be surprised at the proportion of proteins shared between humans and yeast.

Recommendations for Evaluation

Have students use the *DNALC Simple Mapper* to construct individual concept maps or ask students to build a concept map using the terms: gene, protein, hypothesis, model organism, data, learning, T-maze, short-term memory, long-term memory, conservation of function, and *Drosophila melanogaster*.

Use the *G2C Online Test Items* to construct an assessment based on this lesson.

Suggestions for Extended Learning

Researchers in the pharmaceutical industry are currently trying to develop drugs that can replicate the CREB A mutation (i.e. create a photographic memory). A number of interesting theoretical issues are related to this research, for example:

- Is it fair to those who would not be able to afford the drug?
- Could this drug lead to a smarter human race?
- Would you take this drug while studying for an exam?
- Post-traumatic stress disorder can be considered a form of photographic memory. Clearly, it is not always preferable to remember.
- Some individuals with autism have an incredible photographic memory, which is a form of savantism. Might there be a trade-off between photographic memory and social functioning?

Many animals can be trained to perform a wide variety of tasks – dogs can "shake hands," roll over, and beg. Working dogs are trained to herd sheep, sniff for drugs, and perform rescues. How is this done? Are most of these behaviors natural (but performed on cue), or are they learned?

- To learn the answers to these questions, check a variety of sources for information about training animals. Interview an animal trainer at a zoo or aquarium. If there is a canine police training facility nearby, interview a dog handler.
- Determine if some or all of the tricks/tasks these animals perform are learned or natural. How are animals trained to perform them? What are acceptable training practices? Based on what you have learned about the brain and learning, explain why these practices work.

Glossary

Conclusion: A conclusion is a summary of the results of a scientific study that confirm or refute the hypothesis.

Drosophila melanogaster: *Drosophila melanogaster* is the common fruit fly.

Gene: Genes are the basic units of heredity. A gene is a section of DNA on a chromosome that codes for the production of a protein. It can also code for RNA.

Hypothesis: A hypothesis is a prediction of how two or more quantifiable phenomena are related.

Learning: Learning is a relatively permanent change in behavior resulting from experience.

Long-term memory (LTM): Long-term memory is a relatively permanent form of memory. It involves new protein synthesis that gives rise to new synaptic connections.

Memory: Memory is an organism's ability to register, retain, and retrieve information over time.

Model organism: Model organisms are particular species of animal that substitute for humans or other animals.

Protein: A protein is a complex organic molecule composed of one or more chains of amino acids. The order of the amino acids is determined by the sequence of bases in DNA. Some examples include enzymes, structural proteins, transport proteins and receptors.

Short-term memory: Short-term memory is a relatively temporary form of memory. Short-term memory involves alterations in preexisting proteins and alterations in the strength of preexisting connections. Unlike long-term memory, it does not give rise to new synaptic connections.

T-maze: A T-maze is an apparatus often used in scientific studies of animals to measure learning and memory. It is shaped like a “T” and requires the animal to travel down the long arm and then chose to go either to the left or to the right.

Theory: A theory is a statement or set of statements explaining the relationship between two or more phenomena.

Resources

Articles:

Dubnau J, Grady L, Kitamoto T, Tully T. (2001). Disruption of neurotransmission in *Drosophila* mushroom body blocks retrieval but not acquisition of memory. *Nature*, May 24; 411 (6836), 476-80.

Dudai, Y., Jan, Y., Byers, D., Quinn, W., and Benzer, S. (1975). dunce, a mutant of *Drosophila* deficient in learning. *Proc. Natl. Academy Sci.* (73)5, 1684-1688.

Foer, J. (2007). Remember: Why We Remember, Why We Forget. *National Geographic,* (212)5.

Greenspan, R.J., and Dierick, H.A. (2004). Am I not a fly like thee? From genes in fruit flies to behavior in humans. *Human Molecular Genetics, 13*(2).

Books:

Restak, R. (2001). *The Secret Life of the Brain.* Co-publication of the Dana Press and the Joseph Henry Press.

National Science Education Standards

Content Standard A: Science as Inquiry

- Identify questions and concepts that guide scientific investigations
- Design and conduct scientific investigations
- Use technology and mathematics to improve investigations and communications
- Formulate and revise scientific explanations and models using logic and evidence
- Recognize and analyze alternative explanations and models
- Communicate and defend a scientific argument
- Understand about scientific inquiry

Content Standard C: Life Science

The Cell

- Most cell functions involve chemical reactions.
- Cells store and use information to guide their functions. The genetic information stored in DNA is used to direct the synthesis of the thousands of proteins that each cell requires.
- Cell functions are regulated. Regulation occurs both through changes in the activity of the functions performed by proteins and through the selective expression of individual genes. This regulation allows cells to respond to their environment and to control and coordinate cell growth and division.

The Behavior of Organisms

- Organisms have behavioral responses to internal changes and to external stimuli. Responses to external stimuli can result from interactions with the organism's own species and others, as well as environmental changes; these responses either can be innate or learned. The broad patterns of behavior exhibited by animals have evolved to ensure reproductive success. Animals often live in unpredictable environments, and so their behavior must be flexible enough to deal with uncertainty and change. Plants also respond to stimuli.
- Like other aspects of an organism's biology, behaviors have evolved through natural selection. Behaviors often have an adaptive logic when viewed in terms of evolutionary principles.
- Behavioral biology has implications for humans, as it provides links to psychology, sociology, and anthropology.

The Molecular Basis for Heredity

- In all organisms, the instructions for specifying characteristics of the organism are carried in the DNA

Content Standard E: Science and Technology

Understandings about Nature and Technology

- Creativity, imagination, and a good knowledge base are all required in the work of science and engineering.
- Science and technology are pursued for different purposes. Scientific inquiry is driven by the desire to understand the natural world, and technological design is driven by the need to meet human needs and solve human problems. Technology, by its nature, has a more direct effect on society than science because its purpose is to solve human problems, help humans adapt, and fulfill human aspirations. Technological solutions may create new problems. Science, by its nature, answers questions that may or may not directly influence humans. Sometimes scientific advances challenge people's beliefs and practical explanations concerning various aspects of the world.

Content Standard G: History and Nature of Science

Nature of Scientific Knowledge

- Science distinguishes itself from other ways of knowing and from other bodies of knowledge through the use of empirical standards, logical arguments, and skepticism, as scientists strive for the best possible explanations about the natural world.
- Scientific explanations must meet certain criteria. First and foremost, they must be consistent with experimental and observational evidence about nature, and must make accurate predictions, when appropriate, about systems being studied. They should also be logical, respect the rules of evidence, be open to criticism, report methods and procedures, and make knowledge public. Explanations on how the natural world changes based on myths, personal beliefs, religious values, mystical inspiration, superstition, or authority may be personally useful and socially relevant, but they are not scientific.
- Because all scientific ideas depend on experimental and observational confirmation, all scientific knowledge is, in principle, subject to change as new evidence becomes available.

APA National Standards for High School Psychology Curricula

Standard Area IA: Introduction and Research Methods

CONTENT STANDARD IA-3: Research strategies used by psychologists to explore behavior and mental processes.

Students are able to (performance standards):

IA-3.1 Describe the elements of an experiment.
IA-3.2 Explain the importance of sampling and random assignment in psychological research.

CONTENT STANDARD IA-5: Ethical issues in research with human and other animals that are important to psychologists
Students are able to (performance standards):

IA-5.1 Identify ethical issues in psychological research.

Standard Area IIA: Biological Bases of Behavior

CONTENT STANDARD IIA-6: How heredity interacts with environment to influence behavior
Students are able to (performance standards):

IIA-6.1 Assess the effects of heredity and environment on behavior.

CONTENT STANDARD IIA-7: How psychological mechanisms are explained by evolution

Students are able to (performance standards):

IIA-7.1 Explain how evolved tendencies interact with the present environment and culture to determine behavior.

Answer Key

Part 1: Model Organisms

1. After reading the information, explain why your first round of experiments should be done with wild-type flies and not with a variant.

   These flies are the typical type occurring in nature and are often used as controls to measure normal responses.

2. Click on the *wild-type* fly icon to load your flies in the training device. They are now ready to learn.

   d. Now the moment of truth! Did you train your flies? Do they remember which odor is associated with the electrical shock? Click on *Results*. Were you successful? Explain.

   Yes. The flies were trained. They knew which way to go.

6. The flies were learning to avoid a specific odor because it was associated with receiving an electrical shock. What variable(s) directly influenced the formation of long-term memory? Support your answer with evidence from your series of experiments.

   The variables are the number of training sessions (1 or 10) & the type of training (massed vs. spaced).

7. What does Experiment 7 tell you about the CREB A fly strain?

   The flies from the CREB A strain essentially have photographic memories; they require only one training session to form long-term memories. You can use this finding to introduce an interesting ethical discussion (see Suggestions for extended learning, *above).*

8. If learning in fruit flies and humans is similar, describe what this experiment indicates about the ideal combination of variables when studying for a science test, learning a new dance step, or memorizing lines for a play?

   A person should review the material or repeat the dance step multiple times over an extended period of time. The flies learned best with 10 spaced training sessions.

Fly Training Matrix: After 30 minutes

Experiment	**Exp. 1**	**Exp. 2**	**Exp. 3**
Fly variant	wild type	wild type	wild type
No. of training sessions	1	10	10
Type of training	n/a	massed	spaced
Training session 1	OCT & shock	OCT & shock	OCT & shock
Training session 2	MCH & No shock	MCH & No shock	MCH & No shock
When to test	After 30 minutes	After 30 minutes	After 30 minutes
Results	*Trained*	*Trained*	*Trained*

Fly Training Matrix: After 1 day

Experiment	**Exp. 4**	**Exp. 5**	**Exp. 6**	**Exp. 7**
Fly variant	wild type	wild type	wild type	CREB A
No. of training sessions	1	10	10	1
Type of training	n/a	massed	spaced	n/a
Training session 1	OCT & shock	OCT & shock	OCT & shock	OCT & shock
Training session 2	MCH & No shock	MCH & No shock	MCH & No shock	MCH & No shock
When to test	After 1 day	After 1 day	After 1 day	After 1 day
Results	*Not trained*	*Not trained*	*Trained*	*Trained*

Published Data from All Fly Strains

	STM (30m) Mean (%)*	LTM x 1 (24h) Mean (%)*	LTM x 10 (24h) Massed Mean (%)*	LTM x 10 (24h) Spaced Mean (%)*
wild type	84	52	60	79
CREB A	84	85	83	87
CREB B	84	52	60	60
rutabaga	66	52	Not Available**	Not Available**
shibire (PT)	84	52	Not Available**	Not Available**
shibire (RT)	60	52	Not Available**	52
notch (PT)	84	52	60	79
notch (RT)	84	52	60	60

PT = Permissive Temperature STM = Short-term Memory
RT = Restrictive Temperature LTM = Long-term Memory
* Proportion of flies choosing correctly – NOTE, chance is 50%
** Results hint at likely outcome that flies will perform no better than chance.

Part 2: Model Organisms

2. Formulate a hypothesis about the ability of one of the variants to learn as compared to wild-type flies. Record your hypothesis.

   Student hypotheses will vary. Allow any hypothesis that is correctly formulated and can be tested using the Fly School simulation.

3. Do the results of your experiment support your hypothesis? Explain.
   You will need to examine the results of the experiment and determine if the results do or do not support the student hypothesis using Published data from all fly strains, above. You will also need to determine if the student conducted a scientifically controlled experiment.

Part 3: Model Organisms

6. Explain why knowing the proportion of protein that is common across species would be important in selecting new model organisms for your research.

   The proportion of a protein that is the same in different species indicates that the genetic code for the protein is similar…that the genetic information has been conserved. If the protein is similar, what it does in the different species is also very likely similar.

7. Based on your observation, which three species would you select to research the role of the *CREB1* gene in human learning and long-term memory formation?

   The chimp (100%), Dog (100%) and Mouse (99.7%)

8. For each of the three you selected, list two positives and two negatives that would influence your final decision. Indicate which species you would recommend for use.

   Appropriate responses include, but are not limited to those below:

Animal	**Positive**	**Positive**	**Negative**	**Negative**
Chimp	CREB protein is 100% the same as human CREB protein.	They are primates and closely related to humans.	There are many ethical issues.	They are expensive.
Dog	CREB protein is 100% the same as human CREB protein.	Its genome is similar in size to the human genome.	There are many ethical issues. They are pets.	They are large.
Mouse	CREB protein is 99.7% same as human CREB protein.	They are small and easy to keep.	They smell.	They do not live very long.

   Students may select any one of the three species. Their choice will depend on what they list for positives and negatives. Ethical issues may play a large role in their selections. This could set the stage for an ethical issues activity.

9. Would the same species be the best model organism to use when you investigate the influence of the rut gene on learning and memory formation in humans? Explain why or why not.

   If students selected the chimp, they will have to decline using it for an investigation of the rut gene because there is no information posted. They could look elsewhere. If they do, consider their explanation. It should not be merely because chimps are primates and closely related to humans. There must be more.

   If they selected the dog or the mouse above, either would be equally qualified to serve as a model organism for their investigation of the rut gene. For both species, the % of the rut protein that is the same as in humans is 95.6.

Test Items Answer Sheet

1. The primary reason biologists often use model organisms when researching human disorders is that…

    c. it is unethical to do many kinds of experiments on humans.

2. A student conducted an original, well-designed experiment, carefully following proper scientific procedure. In order for conclusions to become generally accepted, the experiment must…

    c. be repeated to support the reliability of the experiment.

3. Which statement best explains how proteins and genes are related?

    a. Genes are segments of DNA. They code for proteins.

4. CREB and ataxin-1 are proteins found to be important in learning and memory. In fruit flies, chimps, chickens, humans, and many other animals, segments of these proteins have exactly the same amino acid sequences. This is evidence that these animals…

    a. share a common ancestor.

5. In fruit flies with the curly wing mutation, the wings will be straight if the flies are kept at 16˚ Celsius. The most probable explanation for this is that…

    b. the environment influences wing phenotype in these fruit flies.

6. A scientist is performing an investigation funded by a company researching how people learn. The company is interested in developing a product that would help people learn faster. Which action would be the least likely to produce biased data?

    b. Repeating each trial multiple times.

Please use the information below to respond to questions 7 and 8.

Four groups of students designed and conducted experiments that investigated learning in fruit flies. All four groups placed their flies in a simple T-maze. They then exposed the flies to two different odors – odor X and odor Y. Each time the flies traveled in the direction of odor X, they received a weak electric shock. They received no electric shock if they traveled toward odor Y. In this way, the students hoped to train the flies to go in the direction opposite odor X and toward odor Y.

7. The dependent variable in this experiment is…

    d. the direction the flies take.

8. Each group of students conducted their fly training experiment in a slightly different way. Which combination of variables most likely resulted in long-term learning in the flies?

    d. Spaced trials and ten training sessions

Please use the information below to respond to question 9.

CREB is one of several proteins found to be involved in long-term memory formation. Below is the amino acid sequence for a segment of CREB protein synthesized in humans and in three other organisms.

Human:	M-T-M-E-S-G-A-E-N-Q
Animal X:	M-T-M-E-S-G-A-D-N-Q
Animal Y:	M-T-M-E-S-G-A-E-N-Q
Animal Z:	M-T-M-D-S-G-A-D-N-Q

9. Using only the information provided, would animal X, Y, or Z be the best model organism to use in studies of long-term memory formation in humans? Support your answer with a one or two sentence explanation.

    Animal Y would be the best because the sequence aligns directly with that of the humans.