Nematod-ally: How and why we use model organisms

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Abstract: Biomedical research is an integral part of science research. Frequently, to gather information about a disease, model organisms must be used. *C. elegans*, a soil nematode, is one such organism. To teach a zoology course with students from grades 9-12, I will be using a 5E lesson based on a lab given at the Bench to Bedside institute at the University of Florida. Students will use live nematode worms to make observations and infer the usefulness of this organism as a model for human physiology and disease. The class will discuss the characteristics of a good model organism and how the worms meet these criteria. I will use a pre and post assessment as well as a longer term post assessment to measure the effectiveness of the lesson and long term retention of content. Overall, students achieved higher test scores both short term and long term after the lesson. Timing of the lesson should be modified in the future to make it an application lesson instead of an introductory lesson.

Rationale: I am a high school teacher, teaching grades 9-12. I teach a course, zoology, which involves a great deal of comparative anatomy as well as many standards in animal diversity. The students in this class usually vary in terms of achievement level on standardized tests, from the top end of the range to the bottom. Additionally, I have a mix of general population, gifted and ESE students in this course.

Throughout the course, I introduce students to the major animal phyla and to the major vertebrate classes. In most cases, I have not given phylum Nematoda much time in class, as I thought it was difficult to obtain live or preserved organisms. Usually in my class we would spend maybe one class period discussing this phylum, one of the most biodiverse in the animal kingdom. One member of this phylum, *Caenorhabitis elegans*, is very commonly used in biomedical research as a model organism. (Bolker 2012).

I wanted to expand my treatment of this very important phylum and give my students a chance to see real world uses of their content knowledge on the various animal phyla. Because of this, I developed a lesson based on *C. elegans* being used as a model organism. In addition to the content knowledge for the lesson, I will also be teaching on the usefulness of models in biomedical research. Developing models of phenomena is one of the core science and engineering concepts, based on the National Research Council's Next Generation Science Standards (2013).

I expect to collect data from students based on a pre and post assessment given immediately before and after the lesson, as well as a longer term post assessment that will follow approximately nine weeks after the lesson, to show success at retention of the content knowledge. Follow up lessons not included in this plan would also include the biology of nematodes, using *C. elegans* as a representative organism.

Intervention: I will deliver this lesson in my zoology class during the unit on phylum Nematoda. This is usually the fifth unit of the course, falling some time toward the end of the first quarter of the school year.

In this lesson, I have developed a 5E style lesson that educates students on the reasons for using model organisms in biological research and why *C. elegans* is a commonly used organism. Students will observe live nematodes using a dissecting microscope. I begin the lesson with an engaging conversation about genetic diseases. I probe for the students' ideas on why we cannot always use humans in biomedical research. Once we have discussed, the students will then do a lab involving the nematode worms. During the lab, they will take observations of the organisms, answering questions throughout using a guided lab worksheet. Using these observations, I expect my students to infer the usefulness of the worms as model organisms. After the students have finished the lab exercise, we will discuss the characteristics of a good model organism and what makes *C. elegans* useful for biomedical research even though they are very different than humans in many ways. Afterward I will elaborate on the model organism theme by introducing students to other frequently used model organisms and their benefits and drawbacks. See appendix 1 for the complete lesson plan.

Connections to Bench to Bedside summer institute: This lesson is based on the model organisms lesson at the Bench to Bedside summer institute. The lab activity is heavily based on the one performed during the institute with Dr. Keith Choe. It incorporates many of the conceptual ideas that the lesson at the institute included.

Changes to Action Research Intervention: Between the initial writing of the proposal and the current version, I did not change anything about the lesson or the assessments.

Data collection and analysis: Before the lesson, I will give the students a pre test designed to assess my learning objectives for the lesson (Appendix 1). I will calculate mean scores for each of the questions as well as tally the particular distractors students chose, if applicable. Immediately following the lesson, I will give the students the same assessment to measure growth in content knowledge. Using these data, I will then determine difference in total scores on the assessments, which will provide me a good measure on student growth. I will use a paired sample t-test to determine if this growth was statistically significant. Later in the year, I will give the students the same questions mixed in their first semester exam, and then use those questions to determine long term retention of the content knowledge.

In October 2016, I delivered the lesson, as written, to my two zoology classes. Before the lesson began, I gave a pre test using the three questions that I would be using again for my short term post test and my long term post test. At this point, the students, on the whole, seemed to know that there were distinct advantages to using non-human subjects in science (question 3, 65 percent correct responses). Otherwise, the other two questions indicated that they were not aware of the subjects we were going to cover, as the responses were no better than random guessing (questions 1 and 2, 22 and 25 percent correct, respectively). For the lesson itself, we began with the discussion of using organisms other than humans for scientific study, then did the lab on nematode worms. We had a discussion and an explanation of the content I wanted my students to know. The first assessment, given immediately after the lesson, showed near universal correct responses on question 3 (97 percent correct), while there was a very large increase of correct responses for questions 1 and 2 (67 percent increase and 63 percent increase, respectively). This suggests the lesson was a success at addressing the concepts of using non-human subjects for scientific experimentation.

In December 2016, the students took their semester exam, a cumulative exam covering all aspects of the course that semester, including evolution and the animal groups we had covered thus far, including sponges, cnidarians, flatworms, round worms, segmented worms, mollusks, and arthropods. Embedded in the semester exam were the three questions from the lesson. On these questions, there was considerable retention of the information after two months, although there was some loss. 72 percent of my students got question 1 correct, 85 percent got question 2 correct and 89 percent. got question 3 correct. Overall, I found this lesson to be quite successful, although there are a few changes I would make. I used this lesson as an introductory lesson and omitted the mutant-type worms from the lesson. I would change the timing of the lesson to be an application lesson, with students having the knowledge of the group first, and also include the mutant-type as originally written by Choe and Portuallo.

Permissions: As this involves a standard lesson with nothing unusual for a science classroom, I am not anticipating needing any special permission for the methods of collecting and analyzing data for my students. I may have to get special permission from the principal or the district science resource teacher to use the nematode worms.

Literature Cited:

Bolker, J. (2012, November 1). Model organisms: There's more to life than rats and flies. *Nature, 491*(7422), 31-33. doi:10.1038/491031a

Choe, K., & Portuallo, M. (2016, June 13). *What can worms do for you?* Lecture presented at CPET Biomedical Explorations: Bench to Bedside, Gainesville, Florida.

Next Generation Science Standards. (n.d.). Retrieved June 22, 2016, from http://www.nextgenscience.org/

Appendix 1: Lesson Plan

Nematod-ally: How and why we use model organisms

Author: Jeff Higginbotham

Key questions: Why do we use model organisms in science research? What makes a good model organism?

Science Subject: Zoology, but can be used for biology, experimental science or biotechnology course.

Grade and ability level: Grade level 9-12. It is assumed in the lesson that students have had experience using dissecting light microscopes, have a general understanding of experimental design, and a general understanding of genetics, inheritance, and genetic disease.

Science Concepts: Model organisms, *C. elegans*, nematode biology, scientific research, biotechnology.

Overall time estimate: One 50 minute class period, plus homework assignment.

Learning styles: Strongly kinesthetic, however visual and auditory are included

Vocabulary: model organism, nematode, biotechnology

Objectives: Students will be able to:

1. Explain the need for the use of model organisms in biomedical research
2. Identify the characteristics of *C. elegans* that makes it a good model organism in many cases

Next Generation Science Standards addressed:

HS-LS1-2. Develop and use a model to illustrate the hierarchical organization of interacting systems that provide specific functions within multicellular organisms

Materials List and Advanced Preparations: Make sure you have the worms plated following instructions given by the distributor of the worms. Make sure each groups' lab stations have the following on them:

- 1 dissecting microscope per group of 2
- 1 sharp dissecting probe
- 1 plate of mixed stage N2 wildtype worms per group
- Copies of the student worksheet (attached)

Background: Model organisms, organisms that are widely used in science research because they are well studied, easy to maintain and provide an experimental advantage, are important for use in biomedical research, as many of the things scientists want to know are too dangerous to research on humans, at least at first. Using a model organism allows a scientist to study things on an organism that would be impractical or unethical on humans. *Caenorhabitis elegans*, a common soil **nematode** (roundworm) is frequently used as a model organism for studies with genetics, since its genome is very well known and its cell development has been completely mapped out. They are cheap, easy to care for, have a similar genome size to humans and are very well characterized, which make them ideal candidates for biomedical research. **Biotechnology** is the exploitation of living systems for industrial, medical or other purposes. Biomedical research frequently uses biotechnology.

Safety: Dissecting scope can get hot depending on the light source. Dissecting probes are sharp and pose a puncture and cutting hazard

Procedure and Discussion Questions:

Before lesson (5 minutes)
Administer a pre test (attached). Allow students about 5 minutes to complete this, and collect before starting the lesson.

1. **Engage (5 minutes)**

What the teacher will do	Probing/eliciting questions
Set up the scenario for the exploration. Tell students to pretend that they work for a university and they are trying to study a particular genetic disease in humans.	What information would we need to do this study? Why is that important?
Tell the students that if they wanted to develop a treatment for this disease, they would need to better understand how it works.	Would we start doing tests on this disease on humans immediately after we received approval? Why or why not?
Tell the students that scientists would not necessarily want to start using humans immediately at the most basic stage of	

research. Tell the students that in science we frequently use model organisms to do initial testing, and even in later stages. Tell them that today we are going to explore why we use these organisms and what makes a good model organism. Tell students that we are going to be observing one particular kind of organism that is frequently used in biomedical research: a roundworm (nematode) called *C. elegans*. Show a picture of a light micrograph of *C. elegans*.	 Why do you think we don't use humans at the beginning stages of research? So if we can't use humans, what do you think we can use?

2. **Explore (20-25minutes)**

What the teacher will do	**Probing/eliciting questions**
Make sure the materials are prepared for the students. Have the students follow along with the worksheet's instructions (see attached). Tell students that they should find at least 5 different looking individuals and infer the life cycle from their observations. Project a micrograph with all of the anatomy on question 3 labeled. As students are working circulate around the room, asking them questions about some of the things they are observing about the worms.	

Look at their papers. Ask students to elaborate verbally on answers you feel are too shallow in depth. Once students have finished, or enough time has elapsed, have students return to their seats. Begin a discussion of the observations students have made by asking them questions from the worksheet.	

3. **Explain (10 minutes)**

What the teacher will do	**Probing/eliciting questions**
Remind the students that *C. elegans* is very commonly used as a model organism in biological research. Explain to the students that we use model organisms in biomedical research for a number of reasons including: • Cost (working on humans is very expensive) • Time (in general, model organisms have a much higher reproduction rate and time to reproductive maturity than humans do) • Ethical concerns (still exist for model organisms, especially vertebrates, but many things we can do with model organisms, like modify the genome, would be unethical in humans) • Understanding of organisms (we have sequenced the genome of *C. elegans* and mapped the development of every cell in its body) Explain that when we use *C. elegans*, we achieve all of these goals. Worms are very cheap to produce. Also, they become reproductively mature after	Why do you think we use *C. elegans* in research? What characteristics of this organism do you think are useful for this purpose? Why do you think it is important that we get organisms that can produce many generations quickly? Why do you think this is important?

2-3 days of life. We remove any ethical concerns that we would have for vertebrate models (like mice). Vertebrates have more considerations because it is thought that they experience the world in a more similar way to humans than worms do. We also have a great understanding of the worms' genome, we have sequenced the genome of *C. elegans* and mapped the development of every cell in its body, and their genes are very easy to manipulate using inexpensive and straightforward techniques. This allows us to better understand how genes work in the body.	

4. **Elaborate (5 minutes)**

What the teacher will do	Probing/eliciting questions
Show students a photo slideshow of various model organisms. For each one, ask students how they think these organisms fulfill most or all of the requirements for a good model organism. Use the following organisms: • Mouse/rat • Fruit fly • Zebrafish • Daphnia	For each: How do you think this organism fulfills the requirements for a good model organism? Do you think there are any requirements they don't fulfill? Explain.

5. **Evaluate (5 minutes)**

Assessment Suggestions: The pre test and post test are identical. Each question assesses each objective in order. The third question assesses an extension of the lesson. This may be done for homework, or a bell ringer for the next class period if you run out of time.

Extensions: Continue to experiment 2 of the Choe lab's *C. elegans* lesson sequence

Resources/References: "Introduction to *C. elegans* life cycle, anatomy, and behavior", developed by the Choe lab, University of Florida. Lesson plan format based on 5E lesson plan template from FSU-Teach, Florida State University.

Name:____ Date:______________ Period:_________

Pre/Post Assessment

Instructions: This assessment is being given to evaluate your gains in content knowledge. Please only spend 1-2 minutes per question, using only the knowledge in your head (closed book, no help from a partner).

1. Which of the following are NOT an advantage of using a model organism like *C. elegans* in studying biology?
    a. They are inexpensive and simple to culture, with little animal welfare or ethical concerns
    b. They have a short lifespan, making them a good model to study reproduction, aging, and over multiple generations
    c. Their genome is very well studied and defined
    d. These are all advantages for using *C. elegans*

2. Why do we use model organisms in biology instead of humans?
    a. Humans are too smart and would unintentionally invalidate the study's data
    b. There are many ethical considerations when using humans, and some experiments may even be harmful when performed on humans
    c. Model organisms in general are not alive, while humans are, which makes them useful for study
    d. It is inexpensive to get humans to participate in studies

3. Why are there fewer ethical considerations when using *C. elegans* versus a vertebrate organism like a mouse?
    a. Worms are not alive, which removes any ethical considerations
    b. Worms do not have senses
    c. Worms do not have as developed a nervous system as vertebrates, which makes them experience the environment in a less "sophisticated" way
    d. There aren't fewer considerations, worms have the same protections as vertebrate organisms do

Experiment #1 - Introduction to *C. elegans* life cycle, anatomy, and behavior

Developed by the Choe Lab, University of Florida

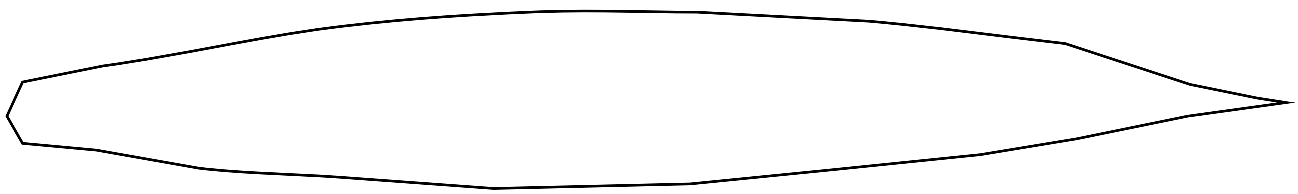
Use observations of the worms and discussions with your group members to answer the following questions. Write your observations in your worksheet and be prepared as a team to present and discuss your conclusions with the rest of the class.

Remember to first locate your worms on low power, then switch to a higher power once you have a group located. When you finish observing one field of view, carefully move your dish around to see nematodes in other areas of the dish.

1. How many developmental stages were you able to observe? Based on your observations, what do you think are the main differences between each stage?

2. Try to diagram the life cycle of *C. elegans* from inferences based on your observations, starting with an adult, progressing though larval stages, and then back to the adult. Hint, it should form a circle and label each stage.

3. Using the highest magnification, draw the anatomy of the adult stage worms (the largest stage); you can also take images if you have a camera attached. Can you tell which end is head and tails, if so, how? Label the following: head, pharynx, intestine, cuticle, gonad, eggs, tail. List the functions of the pharynx, intestine, cuticle, and gonad. Use the diagram on the board to help you with the labels.



4. *C. elegans* has two sexes, hermaphrodite and male, but males are very rare and you are unlikely to see one. Do hermaphrodites reproduce sexually or asexually? Given its preferred environment (rotting fruit) and life history of feasting and then searching for a new food source (famine), why do you think it is an advantage for *C. elegans* to be a hermaphrodite?

5. Watch individual worms carefully for ~1-2 minutes each. You may have to move the plate to keep them in view. Describe any behaviors that you see. Try touching (gently) a few worms on the head and tail with a sharp dissecting probe; what happens when you do this and why do you think worms respond this way?

6. Gently touch a few worms repeatedly on the head over ten times. Do you observe a difference in the response as you repeat the stimulus? If so, why do you think this happens? Believe it or not, you have just trained the worm.

If you are done early, you can begin reading the second C. elegans experiment and watch the video on osmolarity - https://www.youtube.com/watch?v=IaZ8MtF3C6M