TEACHER RESOURCES—ELECTRICAL AND CHEMICAL COMMUNICATION IN THE NERVOUS SYSTEM WORKSHEET

LEARNING OBJECTIVES

At the end of this activity, students should be able to:

1. Describe chemical communication in the nervous system including the role of calcium upon neurotransmission at a synapse.
2. Explain electrical communication in the nervous system including the effects of neuronal stimulation below and above a threshold value.
3. Predict outcomes of the experimental manipulation of one neuron upon a second neuron in a two-neuron pathway.
4. (Extension section) Locate and describe the functions of different gated-ion channels in a neuronal cell.

PREREQUISITE KNOWLEDGE

Students should:

1. know the general structure and function of a neuron.
2. be familiar with the resting membrane potential of a neuron.
3. have a knowledge of the semipermeable nature of the plasma membrane and the methods for molecules to cross a plasma membrane, for example, by facilitated diffusion.

ACTIVITY FACILITATION

In the face-to-face classroom:

During a 50-minute class period, I provide a brief 10-minute introduction to the nervous system and the activity before having students break off into teams of three. After introducing themselves to each other, students sign-up for a specific activity role. These roles include:

- **Reader:** reads the activity to the group out loud during the activity session. This helps keep everyone in the group together and on-track.
- **Recorder:** writes the group consensus answers to questions on the worksheet following group discussion.
- **Reporter:** reports to the whole class when the group is called upon. Reporters also periodically respond to activity questions that are presented to the entire class using a classroom response system.

My undergraduate learning assistants and I circulate throughout the classroom to answer questions and monitor progress during the activity period. I also present a subset of questions from the activity to the entire class using a classroom response system called "LearningCatalytics" (https://www.pearson.com/us/higher-education/products-services-teaching/learning-engagement-tools/learning-catalytics.html) and ask reporters to respond with the consensus answer from their group. This allows me to detect any sticking points during the activity in real-time and to provide clarification or hints if needed.

During the final 10 minutes of class, I call the class back together and address any commonly asked questions. If time allows, I also pose the assessment questions below to the class and discuss the class responses. Worksheets are collected at the end of class and scored for class participation.

In the online class:

I have used this activity both in my 100-level introductory biology class and 300-level human physiology class in an online format. A detailed description of the adaptation and facilitation of this activity in an online introductory biology class is available from the *CourseSource* website here:

Cafferty, P. (2021) Adaptation and facilitation of small group activities in an online introductory biology class. *CourseSource.* https://doi.org/10.24918/cs.2021.9

A detailed description of my online human physiology course is found here:

Cafferty, P. (2020) Teaching a flipped, fully online class using small group work. *HAPS Educator*. Special Edition:55-61. https://doi.org/10.21692/haps.2020.100

ASSESSMENT QUESTIONS

1. To study the role of Ca^{2+} in regulating biological processes, Roger Tsien and colleagues developed highly selective Ca^{2+} indicators, for example, the dye "Fura-2." Fura-2 becomes fluorescent in the presence of Ca^{2+}. When ________ are loaded with Fura-2, an increase in cytoplasmic fluorescence is expected when the neuron is ________.

- A) axons; at rest
- B) synaptic terminals; at rest
- C) synaptic terminals; firing action potentials
- D) cell body; firing action potentials
- E) dendrites; at rest

2. You are studying a sensory neuron that forms a synaptic connection with an interneuron in culture. When you stimulate the sensory neuron, you do not record a change in voltage in the interneuron. Which of the following can explain this result?

- A) the sensory neuron was stimulated below the threshold value
- B) stimulation of a sensory neuron can never generate a change in voltage in an interneuron
- C) the interneuron was stimulated below the threshold value
- D) the interneuron was stimulated above the threshold value
- E) the sensory neuron was stimulated above the threshold value

3. The puffer fish, an expensive gourmet delicacy in Japanese cuisine, produces a potent neurotoxin called Tetrodotoxin (TTX). A chef must remove the tissues that produce TTX carefully before serving. When neurons are treated with TTX, graded potentials in the treated neurons are unaffected, but action potentials are blocked. What kind of gated-ion channels are inhibited by TTX?

- A) Ligand-gated ion-channels
- B) Voltage-gated ion-channels
- C) Mechanically-gated ion-channels

ASSESSMENT TARGET RESPONSES

1. **C.** When action potentials arrive at the synaptic terminal, voltage-gated calcium channels in the plasma membrane open and allow calcium entry. Fura-2 becomes fluorescent in the presence of calcium.

2. **A.** Subthreshold stimulation of the sensory neuron does not result in action potential firing and subsequent neurotransmitter release. Consequently, no change in voltage is generated in the plasma membrane of the interneuron.

3. **B.** TTX blocks the voltage-gated sodium channels responsible for the rising phase of an action potential. Students are not responsible for knowing that TTX specifically blocks sodium-voltage gated ion channels based on the information in this activity.

TEACHER TIPS AND RESOURCES

- The extension questions of this worksheet introduce ligand, mechanical, and voltage gated ion-channels but do not elaborate upon the sub-types of gated ion-channels, for example voltage-gated sodium and voltage-gated potassium channels. Thus, the underlying mechanism of an action potential is not addressed in this worksheet.

- The activity *Action Potential* from "Fifteen POGIL Activities for Introductory Anatomy and Physiology Courses" (by Jensen, Loyle, and Matthesis (August 25, 2014) 1st edition available from Wiley) introduces the mechanics of an action potential.

- In question #8, students are asked to predict the outcome of an experiment not shown in the corresponding "click-and-learn." This question may be useful to facilitate class discussion as student responses are expected to vary. The justification of any given answer to this question is more important than the specific answer provided.

- More detail about use of *Aplysia californica* as a model to study synaptic plasticity by Eric Kandel and colleagues is available on pages 181-185 in the textbook entitled "Neuroscience" (Purves *et al.* (July 31, 2008) 4th edition available from Sinauer Associates, Inc.).

- More information about Nobel Prize laureates can be found on the nobelprize.org website including Eric R. Kandel (https://www.nobelprize.org/prizes/medicine/2000/kandel/facts/) and Roger Y. Tsien (https://www.nobelprize.org/prizes/chemistry/2008/tsien/facts/). (Both accessed May 2019)

WORKSHEET ANSWERS

Slide 1 animation:

1. How many neurons are shown in the circuit in this animation? (select one)

A) One neuron.
B) Two neurons.
C) Three neurons.
D) Four neurons.
E) Unable to answer.

2. What are represented by the white "flashes" that move along the neurons?

The white flashes include electrical signals such as graded potentials (see the extension questions 23-26 below) and action potentials.

3. Information moves from one neuron to another across a structure called the synapse.

4. Two types of synapses exist:
(i) Electrical synapses pass electrical signals directly between the cytoplasm of two cells.
(ii) Chemical synapses pass chemical signals called neurotransmitters from one cell to another across an extracellular space called the synaptic cleft.

What kind of synapses are shown in this animation? (select one)

A) Only electrical synapses.
B) Only chemical synapses.
C) Both electrical and chemical synapses.

5. Information transfer at the type of synapse shown in this animation occurs (select one):

A) in a single direction from dendrite to synaptic terminal.
B) back-and-forth between dendrite and synaptic terminal.
C) in a single direction from synaptic terminal to dendrite.

6. What triggers calcium entry into the synaptic terminal?

Calcium enters the synaptic terminal when an action potential stimulates calcium channels (green discs) in the membrane to open.

7. Describe the role of calcium in information transfer from one neuron to another across the synapse in this animation.

Calcium ions enter the synaptic terminal to activate small packets of neurotransmitter to release their contents into the gap of the synapse. Put another way, an increase in calcium concentration in the synaptic terminal stimulates the fusion of vesicles with the plasma membrane, releasing neurotransmitters into the synaptic cleft. Some neurotransmitters activate receptors on target neurons.

8. Chemicals called chelators can be introduced to the body experimentally to bind specific ions and remove these ions from solution. For example, BAPTA is a calcium-specific chelator that binds to and prevents normal calcium functioning. Predict the outcomes upon neurotransmission in the synapses of this animation immediately following the injection of BAPTA into the structures/regions below and *justify your answers*.

a. Synaptic terminal.

Blocking calcium signaling in the synaptic terminal in the synapse shown in this animation will prevent neurotransmitter release, and thus communication between neurons across the chemical synapse.

b. Dendrite.

Blocking calcium signaling in the dendrite will have no effect on detection of neurotransmitter in the synapse shown in this animation.

c. Extracellular fluid.

Answers may vary. When an action potential reaches the axon terminal, calcium channels (green in this animation) open to allow calcium entry and, consequently, neurotransmitter release. If the calcium concentration was lowered by addition of BAPTA to the extracellular fluid, less calcium would be available to enter the synaptic terminal to promote neurotransmitter release.

Some alternative responses:

- Adding a high enough concentration of BAPTA to the extracellular fluid to chelate a significant proportion of calcium in the solution may not be possible. In this case, no effect on neurotransmitter release will be observed.
- Given BAPTA is membrane permeable, negative effects upon neurotransmitter release may result from calcium chelation inside the presynaptic terminal rather than from lowering the calcium concentration of the extracellular fluid when a high concentration of BAPTA is added to the extracellular fluid.

9. According to the animation, what happens to neurotransmitters that are released from the synaptic terminal?

Some neurotransmitters diffuse away while others activate receptors on target neurons that allow sodium entry.

Slide 2:

10. **Model organisms** are species that have been widely studied and are used in neuroscience research because they can be kept in a laboratory setting, have specific experimental advantages, and the knowledge gained from studies of these organisms provides insight into the biological processes of other species. Thus, studies of model organisms with simpler nervous systems can provide insight into the function of more complex nervous systems with a greater number of neurons and synapses.

In this click-and-learn, *Aplysia,* a marine mollusk commonly referred to as a "sea slug," is used as a model organism to study neuronal activity. Based on the information above, and from **slide 2**, which of the following statements about studies of the electrical activity of *Aplysia* neurons is/are **correct**? Choose all that apply.

A) Scientists who study *Aplysia* are solely interested in learning about the neurobiology of mollusks.
B) *Aplysia* cannot survive in a laboratory setting.
C) *Aplysia* have large neurons that allow for ease of inserting a recording electrode.
D) Knowledge gained from studies of *Aplysia* is only applicable to mollusk neurobiology.
E) Knowledge gained from studies of *Aplysia* is only applicable to nervous systems with a similar number of neurons and synapses.
F) Knowledge gained from studies of *Aplysia* can provide insight into the electrical activity of neurons from more complex species.
G) The cost of maintaining *Aplysia* in a laboratory setting is prohibitive.
H) Recording from neurons of mammalian species, such as the mouse, is easier than recording from *Aplysia* neurons.

Responses C and F are correct while responses A, B, D, E, G, and H are incorrect.

11. Neuroscientists typically show electrical activity as a graph of <u>time</u> on the X-axis and <u>voltage</u> on the Y-axis.

Slide 3:

12. What types of neurons are visible on the culture dish?

A sensory neuron and a motor neuron.

13. Under the pictured conditions, can the sensory neuron be stimulated to fire an action potential?

Yes, an electrode is placed in the sensory cell that can be used to inject electrical current and stimulate an action potential.

14. Under the pictured conditions, is there evidence that action potentials can be recorded in the motor neuron?

No, no electrode is visible in the motor neuron.

Slides 4 and 5:

15. Based on the information on slides 4 and 5, which of the following statements about the generation of an action potential is **false**? (select one)

A) Under natural conditions, stimuli such as touch can trigger action potentials.
B) Electrical stimulation of a neuron can trigger action potentials.
C) Stimulation below the threshold value does not change the voltage of a neuron.
D) Stimulation below the threshold value does not stimulate a neuronal action potential.
E) Stimulation above the threshold value stimulates a neuronal action potential.

16. Sub-threshold changes in membrane potential can be either:
i) Excitatory – changing the neuronal membrane potential closer to the threshold value.
ii) Inhibitory – changing the neuronal membrane potential further away from the threshold value.

a) How many sub-threshold stimuli are shown in the video of this recording?

A) 1
B) 2
C) 3
D) 4
E) Too many to count.

b) Are these sub-threshold stimuli excitatory or inhibitory?

Excitatory

Slide 6:

17. Under the pictured conditions, can the sensory neuron be stimulated to fire an action potential? Justify your answer.

Yes, electrode #1 in the sensory neuron can be used to inject current.

18. Under the pictured conditions, can action potentials be recorded in the motor neuron? Why or why not?

Yes, electrode #2 in the motor neuron can be used to record electrical activity.

Slide 8:

19. Under the conditions in this video, is neurotransmitter released from the sensory neuron? Why or why not?

No, neurotransmitter is not released from the sensory neuron. An action potential is required for calcium entry into, and subsequent neurotransmitter release from the sensory neuron axon terminal. The sub-threshold stimulation of the sensory neuron did not result in an action potential in the sensory neuron.

Slide 9:

20. Under the conditions in this video, is neurotransmitter released from the sensory neuron? Why or why not?

Yes, an action potential was generated in the sensory neuron that led to neurotransmitter release into the chemical synapse between the sensory and motor neuron. This neurotransmitter release resulted in an excitatory sub-threshold potential visible in the motor neuron.

21. Was an action potential generated in the motor neuron? Why or why not?

An action potential was not generated in the motor neuron because the membrane potential change that was generated in the motor neuron, following sensory neuron stimulation, was sub-threshold.

22. Under the conditions in this video, what can you do to stimulate the firing of an action potential in the motor neuron?

You can provide a greater stimulus to the sensory neuron by injecting more current and triggering more action potentials. This will result in greater neurotransmitter release at the chemical synapse and generate a strong enough change in the motor neuron membrane potential to reach the threshold voltage.

Extension questions:

Under living conditions, excitatory and inhibitory sub-threshold changes in membrane potential are called **graded potentials** or **synaptic potentials.** Graded potentials are generated by opening either ligand-gated or mechanically-gated ion channels in the plasma membrane of the dendrites and/or cell body of a neuron.

When the threshold voltage of a neuronal plasma membrane is reached by the addition, or summation, of graded potentials, voltage-gated ion channels are stimulated to open and generate an action potential.

23. Complete the table below comparing the three types of gated ion channels. You may need to look up some of the answers.

Gated ion-channel type	**Location of gated ion-channel in a neuron**	**Stimulated (opened) by**	**Membrane potential change generated when open** (graded or action potential)
Ligand-gated	Cell body and dendrites	neurotransmitter (ligand) binding to channel	Graded potential
Mechanically-gated	Dendrites of a sensory neuron (also found in sensory receptor cells)	pressure of touch or mechanical vibration, for example, sound waves	Graded potential
Voltage-gated	Axon hillock and axon	changes in membrane voltage	Action potential

24. Which of the following statements regarding the voltage recordings in the video of **slide #5** is/are **correct**? Choose all that apply. In this video:

A) sub-threshold graded potentials are generated by opening mechanically-gated ion channels.
B) voltage-gated ion channels are stimulated to open by injection of any electrical current resulting in an action potential.
C) sub-threshold graded potentials are generated by adding neurotransmitter to the dendrites and cell bodies of the sensory neuron.
D) the electrical current injected into the sensory neuron at the end of the video was strong enough to raise the membrane voltage above a threshold value.
E) The electrical current injected into the sensory neuron at the end of the video was strong enough to open ligand-gated ion channels.
F) The electrical current injected into the sensory neuron at the end of the video was strong enough to open voltage-gated ion channels.

Responses D and F are correct while responses A, B, C, and E are incorrect.

25. Consider the video of ***slide #8***.

a) What kind of gated ion channels open in the motor neuron when the sensory neuron is stimulated? (select one)

A) Only ligand-gated ion channels opened in the motor neuron.
B) Only mechanically-gated ion channels opened in the motor neuron.
C) Only voltage-gated ion channels opened in the motor neuron.
D) No gated ion channels opened in the motor neuron.
E) All of these gated ion channels opened in the motor neuron.

b) Explain your answer to part "a" above.

The sub-threshold membrane potentials in the sensory neuron do not generate an action potential. Consequently, neurotransmitter is not released from the sensory neuron and no gated ion channels are stimulated to open in the motor neuron.

26. Consider the video of ***slide #9***.

a) What kind of gated ion channels open in the motor neuron following the sensory neuron action potential? (select one)

A) Only ligand-gated ion channels opened in the motor neuron.
B) Only mechanically-gated ion channels opened in the motor neuron.
C) Only voltage-gated ion channels opened in the motor neuron.
D) No gated ion channels opened in the motor neuron.
E) All of these gated ion channels opened in the motor neuron.

b) Explain your answer to part "a" above.

The sensory neuron action potential allowed calcium entry into, and subsequent neurotransmitter release from, the sensory neuron axon terminal. Some of this neurotransmitter bound to and activated ligand-gated ion channels on the motor neuron membrane to generate a subthreshold graded potential.

27. Based on the information in ***slide #10***, is the following statement true or false? If false, correct the statement.

"Single graded (or synaptic) potentials are sufficient to generate action potentials in a neuron."

This statement is false. Corrections to the statement will vary but should identify the additive quality of graded potentials, for example:

"Multiple graded (or synaptic) potentials can summate to reach a threshold value."

or

"Single graded (or synaptic) potentials are not sufficient to generate action potentials in a neuron."