### **Activity 1: Connections**

Based on video content

15 minutes (10 minutes before and 5 minutes after the video)

### Setup

Neurobiology is all about connections. So, to begin this unit, try making connections between some of the topics that will be covered in the video. Work in pairs on the diagram with terms for this unit. Draw a line between terms that have a connection. As you draw the line, explain to your partner what the connection is between the terms. If you don't know the meaning of a term, either leave it out of the network until after the video or see if you can deduce how it is connected.

After viewing the video, look at your diagram and see if there are any new connections you would make between the terms.

#### **Materials**

• One copy of the Diagram of Terms per person (master copy provided)

# **Diagram of Terms**

memory	stem cells
glutamate	synaptic plasticity
vesicle	exocytosis
neurogenesis	dopamine
long-term potentiation (LTP)	pre-synaptic terminal
post-synaptic neuron	action potential

### **Activity 2: Penny for Your Thoughts**

Based on video content

10 minutes, during a break in watching the video

### Setup

We handle coins nearly every day, but the features of a common coin (like a penny) can be difficult to recall if those particular details have not been placed in long-term memory. In the video, we'll see a little about neural connections and the molecular basis of memory. But just for fun, before watching the video try this exercise: Working in pairs, take one set of the parts of a penny and, from them, put together a replica of the front and back of a penny from memory. The sets contain extra parts, so you will not use them all.

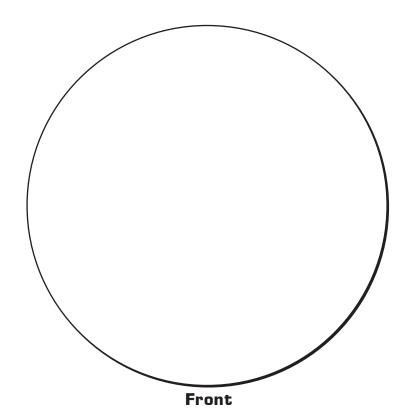
As you make your replicas, think about why it is easy or difficult for you to recall details about an object you've seen many times. Are the details that you remember connected with the memory of a specific event? Is it hard to remember details because you've never really paid attention to the features of a penny? Are facts like the details of a coin important to remember? When you and your partner are finished, check your replicas against a real penny.

#### **Materials**

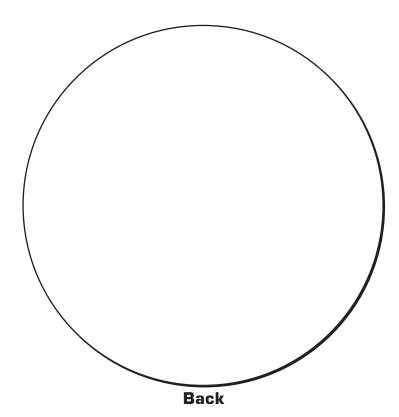
- One set of the Parts of a Penny per two people (master copy provided; to make a set, cut on the dotted lines after copying)
- One penny per two people (as the answer key)

## Parts of a Penny

STATES OF AMERICA	COD BLESS AMERIC	SCOO WE TRUSS
		ONE CENT
FREEDOM	LIBERTY	E PLURIBUS UNUM
	2003	
		* * * * * * * * * * * * * * * * * * *



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### **Activity 3: Action Potentials**

Based on video and online text content

### 60 minutes

### Setup

Action potentials are the key to neural activity. Within a few milliseconds of receiving a chemical or physical stimulus, a neuron responds by changing the balance of ions across its cell membrane. This change in membrane potential is propagated along the neuron and ultimately leads to a response that might be the stimulation of another neuron, a gland, or a muscle.

In this activity, you will simulate an action potential using a box to represent the neuron, and small colored objects to represent the ions that generate the resting membrane potential and move across the membrane during an action potential. The purpose is not to build a realistic model of a neuron, but rather to illustrate key principles about action potentials. This activity is quite involved, so please read over all of the instructions carefully before starting. This activity will be done in teams of four: one person acts as a scorekeeper, one as gatekeeper, and two as ball handlers.

#### **Materials**

- One copy of the Instructions per four people (master copy provided)
- One copy of the Neurobiology online text chapter per four people (available online at http://www.learner.org/channel/courses/biology)
- One copy of the Discussion Questions per person (master copy provided)
- One set of 100 small colored objects per four people. (The objects can be balls, chocolate-covered candies, jellybeans, coins, or gumdrops. Each set should have 30 blue, 49 red, and 21 green objects.)
- One box for every four people. The boxes should be open at the top to allow visualization and manipulation of the colored objects. Make two panels in the sides of each box that can be opened and closed, and are sufficiently large that they permit the addition and removal of the objects. For Exercise 2, have at least three boxes.
- One piece of graph paper per person
- Tips and Suggested Answers

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### Instructions

### Exercise 1: Simulating a Neuron and an Action Potential

### 1. Reviewing action potentials

Briefly review the membrane potential of a resting neuron and the changes that occur during an action potential by reading the appropriate section in the chapter text.

### 2. Setting up the neuron

In this exercise, colored balls are used to represent ions of potassium (blue), sodium (green), and chloride (red). If colored balls are not available, use colored candies, coins, or other small objects. The boxes represent neurons. Each ball will contribute enough of the ion to change the voltage in a neuron by 5 mV. Potassium and sodium ions are positively charged and will increase the voltage by 5 mV each, while chloride is negatively charged and will decrease the voltage by 5 mV.

The neuron itself will be represented by the open box. The box should be constructed so that the 100 balls representing the ions can be visualized and manipulated. The box has two panels that open and close to permit addition and removal of the balls. One represents the sodium channels and the other represents the potassium channels.

The "resting potential" of the neuron is -70 mV. We will represent this in our simulated neuron as 30 potassium ion balls, 5 sodium ion balls, and 49 chloride ion balls. Check that this results in a net voltage of -70 mV.

#### 3. The rules of the simulation

Sodium channels open when the potential of the neuron is above -50 mV; they close when the potential is above +25 mV. They are otherwise closed.

Potassium channels open when the potential reaches +25 mV and they remain open until the concentration is below -75 mV.

The gatekeeper of each group is responsible for determining whether the sodium and potassium channels should be open or closed. The ball handlers are responsible for adding and removing the sodium and potassium ions. The scorekeeper is responsible for determining and recording the potential of the neuron at each time unit.

### 4. The simulation

- a. At a signal provided by the facilitator, five sodium balls are added to each box to represent an increase in positive charge. (These do not go through the sodium channels, but have entered through another channel, for example a neurotransmitter-gated channel.)

  What is the charge now inside the neuron? The scorekeeper should record the charge and mark this as time period one.
- b. Because the charge is now above the threshold for the sodium channels to open, they do so. The opening of the sodium channel permits three sodium balls to enter the neuron for each time period. What is the voltage within the neuron now? Record that value as the potential at time period two.
- c. For each time period, continue adding two sodium balls, unless the potential goes above +25 mV.
- d. When the potential goes above +25 mV, the sodium channels close and no further sodium balls are added to the neuron. Moreover, the potassium channels open when the potential goes above +25 mV. In our simulation of a neuron, the opening of the potassium channels results in the removal of three potassium balls for as long as the potassium channels remain open. The potassium channels will close when the potential goes below -75 mV.

#### 5. The results

Once the data have all been collected, graph the changes in potential as a function of time and discuss the discussion question for this exercise.

### **Exercise 2: Propagating an Action Potential**

### 1. The background

An action potential must be propagated down the length of the neuron, from its input source at the dendrites, to the cell body, and then down the axon to the synaptic terminals. How is this achieved? This propagation also involves the movement of ions. When the sodium channels in one part of the neuron are opened, sodium ions rush in. Once inside, they cause nearby regions of the neuron to become depolarized by moving laterally through the axon. This in turn causes the opening of more voltage-gated sodium channels in those regions. Thus, the sodium channel activation moves in a wave-like fashion down the neuron.

### 2. Setting up the neuron

We can simulate the propagation by arranging the boxes in a linear array. Now, each box represents part of the neuron. A box at one end will be designated the dendrite of the neuron.

As before, each box will start with 30 potassium ion balls, 5 sodium ion balls, and 49 chloride ion balls, giving an initial potential of -70 mV.

### 3. The simulation

The rules of this simulation will be the same as the one above except in every time period that one box has more than 20 sodium ion balls, it will pass one sodium ball to its nearest neighbor away from the dendrite. This is how we will simulate the lateral movement of sodium ions. At some point, these additional sodium ion balls will cause the potential of that region of the neuron to rise above the threshold that will open the sodium channel.

At time period one, the dendrite will receive 5 sodium balls which will cause its potential to rise above the -50 mV threshold and will open the sodium channel.

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### **Discussion Questions**

See the Tips and Suggested Answers.

### After finishing Exercise 1:

1. Although the membrane potential of the neuron has returned to near the resting potential, there is much more sodium and much less potassium inside the neuron than before the action potential. How does the neuron return to having low sodium and high potassium concentrations?

### After finishing Exercise 2:

- 2. Compare the amount of time it took your team to simulate or propagate an action potential with the time required for a neuron to perform this task. What mechanisms increase the speed at which action potentials are relayed?
- 3. After finishing the propagation exercise, consider what happens when the action potential reaches the end of the neuron. List the effects on the neuron and on cells with which the neuron may communicate.

### **Discussion Question Answers**

#### Exercise 1:

1. Although the membrane potential of the neuron has returned to near the resting potential, there is much more sodium and much less potassium inside the neuron than before the action potential. How does the neuron return to having low sodium and high potassium concentrations?

The sodium-potassium pump, which actively transports potassium in and sodium out, restores the ionic balance.

#### Exercise 2:

2. Compare the amount of time it took your team to simulate or propagate an action potential with the time required for a neuron to perform this task. What mechanisms increase the speed at which action potentials are relayed?

Besides the propagation along the axon demonstrated in this exercise, gaps in the myelin insulation of myelinated neurons allow the action potential to jump from one gap to another, resulting to signal speeds of over 100 meters per second.

3. After finishing the propagation exercise, consider what happens when the action potential reaches the end of the neuron. List the effects on the neuron and on cells with which the neuron may communicate.

From neuron to neuron, the signal may be transferred electrically through a gap junction or chemically by a neurotransmitter. Neurons may also communicate chemically with muscles or other cells.

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Neurobiology: Activity 4 Page 1 of 5

### Activity 4: Sex, Drugs, and Neurobiology

Based on video and online text content 25 minutes

### Setup

We have all witnessed or experienced the effects of alcohol, nicotine, and other drugs on the central nervous system. As we learn more about the nervous system, we learn more about the mechanisms and effects of these drugs. However, knowing how the drugs affect neurons and synapses does not answer questions about how the drugs should be used, if they should be used at all, and who should decide these issues. In this discussion, read a few paragraphs from the online text about the action mechanisms of different drugs. Then, in teams of three, discuss some of the physiological and societal aspects of the drugs and their use.

#### **Materials**

- One copy of the Neurobiology Online Text Chapter Excerpts per person (master copy provided)
- One copy of the Discussion Questions per person (master copy provided)

### **Neurobiology Online Text Chapter Excerpts**

### Section 1: Neurotransmitters, Psychoactive Drugs, and the Reward Pathway

Drugs that have effects on the central nervous system are known as psychoactive drugs. The mode of actions of both therapeutic drugs (e.g., Ritalin, Prozac, and Paxil) and recreational drugs (e.g., alcohol, cannabis, cocaine, and nicotine) affect the firing of certain neurons by changes in various neurotransmitters or receptors. Not all drugs have specific modes of action; alcohol, for example, has many and varied effects. We will focus, however, on a few examples of those drugs that have specific effects.

Humans and many other animals engage in many activities from which they derive pleasure. Researchers working with various animals have shown that there are regions of the brain, such as the ventral tegmental area, that are more active when animals engage in pleasurable acts. When researchers stimulate these areas experimentally, the animals will perform various tasks in order to receive further stimulation. Hence, the neural pathway comprised of those regions has been called the **reward pathway**.

Like many drugs, nicotine from tobacco products acts on the reward pathway. This drug, however, is unusual in that it directly affects the dopamine receptor in the reward pathway's neurons. Unlike the action of most drugs, no intermediary steps are involved: nicotine binds to the receptor and stimulates the postsynaptic neuron. The overstimulation of the postsynaptic cell, however, also has effects at the cellular level. Over time, it leads to a decrease in the number of dopamine receptors being expressed and inserted to the membrane, as well as a change in the shape of the cell. The reduction of receptors is referred to as "desensitization." When the nicotine is removed, because there are fewer receptors on the postsynaptic cell, more dopamine than normal is required for proper stimulation of postsynaptic neuron. Addiction can result because nicotine becomes needed just to maintain the normal stimulation of the postsynaptic cells.

Allelic variation at the dopamine receptor gene appears to affect one's likelihood of becoming addicted to nicotine. Individuals who have the A1 allele have fewer dopamine receptors than those that do not have the allele. These individuals also have more difficulty in quitting smoking and are more likely to exhibit other addictive and compulsive behaviors. The genetic components of many types of addiction are the topic of intensive research—and often heated debate.

Cocaine also works on dopamine and the reward pathway but does so in a different way. Recall that some neurotransmitters are normally taken up by the presynaptic neuron by reuptake receptors, or transporters, in the presynaptic membrane. The molecular structure of cocaine is such that it can block the binding site for dopamine on its reuptake receptor. Because this cell is now impaired in the reuptake of dopamine, an excess of dopamine builds up in the synapse. This excess leads to overstimulation of the postsynaptic neuron. Because the action is occurring in the reward pathway, overstimulation leads to euphoria. The effects of overstimulation of the postsynaptic cell by cocaine are much the same as those of nicotine: the reduction of the number of receptors leads to desensitization and the possibility of addiction.

There have been concerns that Ritalin (methylphenidate), used for treatment of attention deficit and hyperactivity disorder (ADHD), is chemically similar to cocaine. Indeed, Ritalin increases dopamine levels by interfering with reuptake. Moreover, Ritalin and cocaine compete for the same receptor site. One crucial difference between these two drugs is that Ritalin acts much more slowly than cocaine. While cocaine's effects on dopamine levels occur within seconds, the response from Ritalin (when administered in pill form) takes about an hour. Some studies suggest that, far from leading to addiction, Ritalin treatment in childhood may be associated with *decreased* risk of drug and alcohol use later on. Other studies, however, suggest that Ritalin may be a gateway drug: by using it, teens may be more willing to experiment with other drugs. As of 2003 the consequences of Ritalin treatment remain unresolved.

Before reading further, discuss the questions for Section 1.

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### Section 2: Cannabis, the Cannabinoid Receptors, and Endocannabinoids

The active ingredient of marijuana, from the cannabis plant, is THC (delta-9-tetrahydrocannabinol). This chemical exerts its effects on the brain by binding to receptors called the cannabinoid receptors. Scientists have identified two cannabinoid receptors (CB1 and CB2), and evidence suggests that there may be others. Although CB1 is found in many regions of the brain, CB2 is present only in certain cells of the immune system. Because the receptor is present in several brain regions, THC can have manifold effects. For instance, THC may affect memory formation. CB1 is prevalent in the **hippocampus**, a region of the brain strongly associated with memory. By binding to and activating CB1, THC decreases activity of neurons in the hippocampus and interferes with the proper function of that region, which may translate to an interference with memory formation.

The human body does not produce THC, so why would there be receptors that can bind it? During the 1990s, researchers discovered that the body makes chemicals, such as anandamide, that can bind to the cannabinoid receptors. The function of these chemicals, called endocannabinoids, and their receptors is still unknown. To investigate the role of the CB1 receptor, scientists have studied mutant mice that lack the receptor. Compared with normal mice, these mice have a decreased appetite, are less active, and have a reduced lifespan; however, the mice have an enhanced memory.

The CB receptors have recently been associated with some beneficial actions, such as pain relief and extinguishing some fear behaviors. THC has even been prescribed as medication in some states for pain relief for various diseases, including glaucoma, AIDS, and cancer.

Discuss the questions for Section 2.

### **Discussion Questions**

### **Questions for Section 1:**

- 1. For what purpose might a plant like tobacco or coca make a chemical compound that acts on the reward pathway of animals?
- 2. All three of the drugs discussed here—nicotine, cocaine, and Ritalin—operate on the same basic dopamine receptor and reuptake system. Why is nicotine legal, but cocaine is not? Why is Ritalin a prescription drug, while the others are not? What societal and historical factors determine which drugs are used socially, which are used medically, and which are forbidden? What makes one type of drug acceptable for medical use while others are not?
- 3. Compare the use of the three drugs with two other legal and socially acceptable drugs, alcohol and caffeine. Of the five substances, which do you think has the greatest negative effect on society? What kind of solutions can you think of to reduce the negative effects of these drugs on individuals and on society?
- 4. Who should decide which drugs may be legally used and which should be illegal?
- 5. In your opinion, how much of addictive behavior is genetically determined, and how much is determined by environmental or other factors? If a large portion is genetically determined, how should we perceive and treat people with addiction problems?

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#### **Ouestions for Section 2:**

- 1. For what purpose would the cannibis plant make a chemical compound that interferes with the memory function of animals?
- 2. Why do we have the system of endocannabinoids and receptors that interferes with memory formation? What might it be an advantage to forget? Think of the Penny for your Thoughts activity, for example. Do you need to remember all the details of the structure of a penny?
- 3. As you did with the dopamine system drugs, compare cannabinoids with alcohol and caffeine. Which do you think is the most damaging or dangerous to individuals? Which has the greatest negative effect on society? What factors have made alcohol and caffeine legal but marijuana illegal?
- 4. What arguments can you think of in favor of legalizing marijuana? What arguments can you think of against it?
- 5. Are there additional arguments for or against legalizing marijuana only for medical purposes? If marijuana were legalized for medical use, would it be possible to regulate its use effectively? Would it be acceptable to use synthetic forms of marijuana for medical treatment?

### **Activity 5: Fountain of Youth**

Based on video and online text content

10 minutes

### Setup

Our image of the brain as fully developed and unchanging by the end of childhood is being replaced by a new model. Recent research has discovered neural stem cells that can differentiate into neurons and make new connections, even in adulthood. The research by Dr. Fred Gage (described in the video) and Dr. Elizabeth Gould (described in the online text) suggests that environmental factors are critical for neurogenesis.

#### **Materials**

• One copy of the Discussion Questions per person

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### **Discussion Questions**

- 1. In mice and in monkeys, the animals studied by the researchers in this unit, areas with toys provided the stimulating environment that led to increased neurogenesis. What do you think would provide this environment for humans?
- 2. Do you know of any anecdotal evidence that supports the correlation between stimulating environments and adult neurogenesis? Have you seen evidence for it in your classroom or your personal experiences?
- 3. How might you use this information to make your efforts in education more effective?

# Notes