Applied Neuroscience

Columbia Science Honors Program

<u>Spring 2017</u>

Mid-Term Review

Review

Circle whichever is greater, A or B. If A = B, circle both:

I.

A. permeability of a neuronal membrane to Na^+ during the rise phase of an action potential

B. permeability to K^+ at the same time

II.

A. permeability of the resting membrane to K^+

B. permeability of the membrane to K^+ during the falling phase of the action potential

III.

A. concentration of K^+ in the intracellular fluid before the action potential

B. concentration of K^+ in the intracellular fluid immediately after the action potential

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Circle whichever is greater, A or B. If A = B, circle both:

I.

A. speed of conduction of nerve impulse in neuron with diameter of 10 microns

B. speed of conduction of nerve impulse in neuron with diameter of 5 microns

II.

A. number of directions action potential will travel if stimulated at axon hillock

B. number of directions action potential will travel if stimulated at dendrite

III.

A. Na^+ ions moved out by the Na/ K pump

B. K^+ ions moved in by the Na/ K pump

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A. Na^+ ions moved out by the Na/ K pump

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Review

Suppose a nerve cell membrane is made less permeable to passive diffusion of K^+ ions, without affecting the Na^+/K^+ ATPase pump.

A. What will happen to the amount of K^+ within the cell?
B. What will happen to the resting potential of the cell?
C. Will it be harder or easier to elicit an action potential?
D. How can a substance produce such an effect on the cell?

Review

Suppose a nerve cell membrane is made less permeable to passive diffusion of K^+ ions, without affecting the Na^+/K^+ ATPase pump.

A. What will happen to the amount of K^+ within the cell?
   Increase, Less K+ would diffuse out of the cell down its concentration gradient
B. What will happen to the resting potential of the cell?
   Increase, More K+ stays in and the potential becomes less negative
C. Will it be harder or easier to elicit an action potential?
   Easier, Potential is closer to threshold
D. How can a substance produce such an effect?
   Block K^+ leak channels

Review

Suppose a nerve cell membrane is made more permeable to passive diffusion of Na^+ ions, without affecting the Na^+/K^+ ATPase pump.

A. What will happen to the amount of Na^+ and the amount of K^+ within the cell?
B. What will happen to the resting potential of the cell?
C. Will it be harder or easier to elicit an action potential?
D. How could a substance produce such an effect on the cell?

Review

Suppose a nerve cell membrane is made more permeable to passive diffusion of Na^+ ions, without affecting the Na^+/K^+ ATPase pump.

A. What will happen to the amount of Na^+ and the amount of K^+ within the cell?

    Na^+ inside the cell increases, K^+ inside the cell decreases (less electrical “pull” back in)

B. What will happen to the resting potential of the cell?

    More positive, Net Na^+ in will be greater than net K^+ out

C. Will it be harder or easier to elicit an action potential?

    Easier

D. How could a substance produce such an effect on the cell?

    Increase the number of ligand-gated channels for Na^+

Review

Hodgkin and Huxley conducted an experiment in which they removed sodium from the fluid surrounding a neuron, and replaced it with choline, a positively charged molecule that doesn't penetrate the membrane. They found that when the neuron was stimulated electrically to threshold, there was no action potential, but after a small delay (about 3 msec) an increase in positive charge could be measured on the outside of the stimulated membrane.

Explain these findings in terms of our current knowledge of neuron function.

Review

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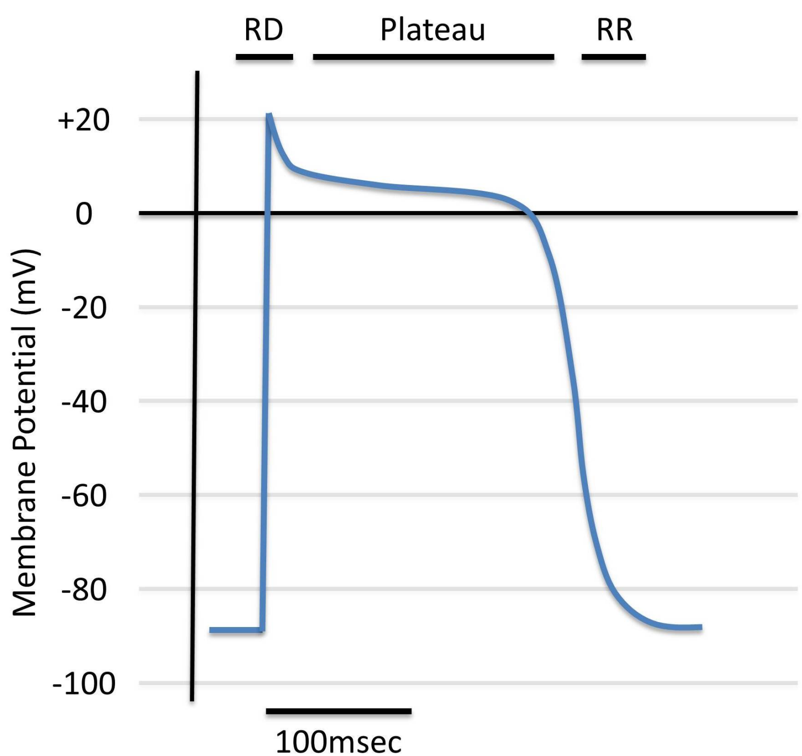
Explain these findings in terms of our current knowledge of neuron function.

There was no action potential at first because there was no Na^+ available to enter the cell. An action potential is caused by an influx of Na^+. When the neuron is electrically stimulated, Hodgkin and Huxley increase the membrane potential to threshold. This causes voltage-gated K^+ channels to open after a delay and leave the cell. This resulted in a positive charge outside of cell, which was measured.

Review

The membrane of the heart develops a resting potential just like a neuron does. The membrane depolarizes due to the movement of Na^+ but <u>stays</u> at this potential for a while, due to changes in membrane permeability.

A. Assume Ca^{++} is responsible for this plateau. How would a change in membrane permeability to Ca^{++} account for this plateau?



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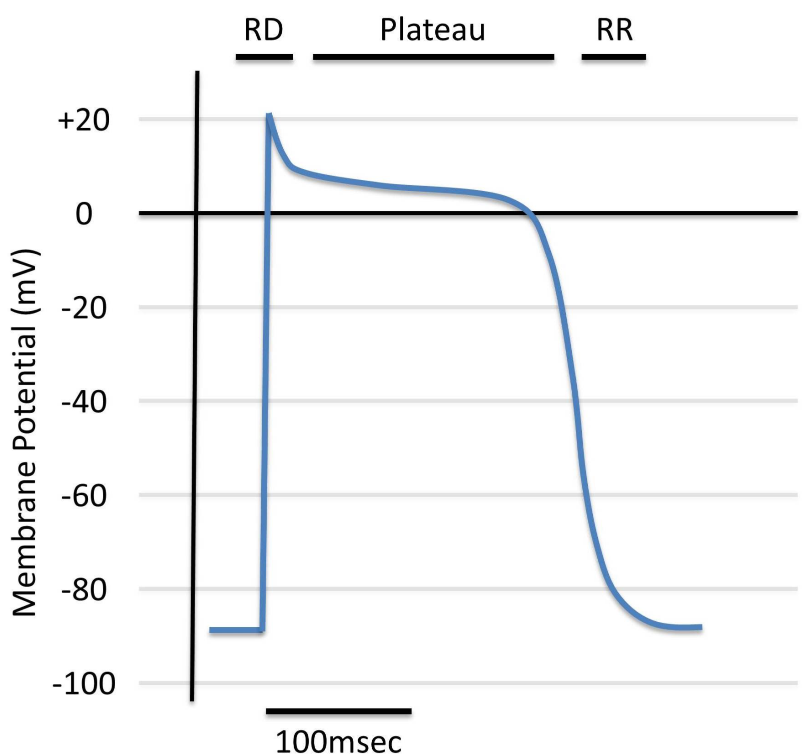
A. Assume Ca^{++} is responsible for this plateau. How would a change in membrane permeability to Ca^{++} account for this plateau?

Increased permeability to Ca^{++}. Ca^{++} is higher outside the cell. If permeability to Ca^{++} increases, the ions will flow in and maintain the inside at a positive potential, relative to the outside.

Review

The membrane of the heart develops a resting potential just like a neuron does. The membrane depolarizes due to the movement of Na^+ but stays at this potential for a while, due to changes in membrane permeability.

B. Assume K^+ is responsible for this plateau. How would a change in membrane permeability to K^+ account for this plateau?



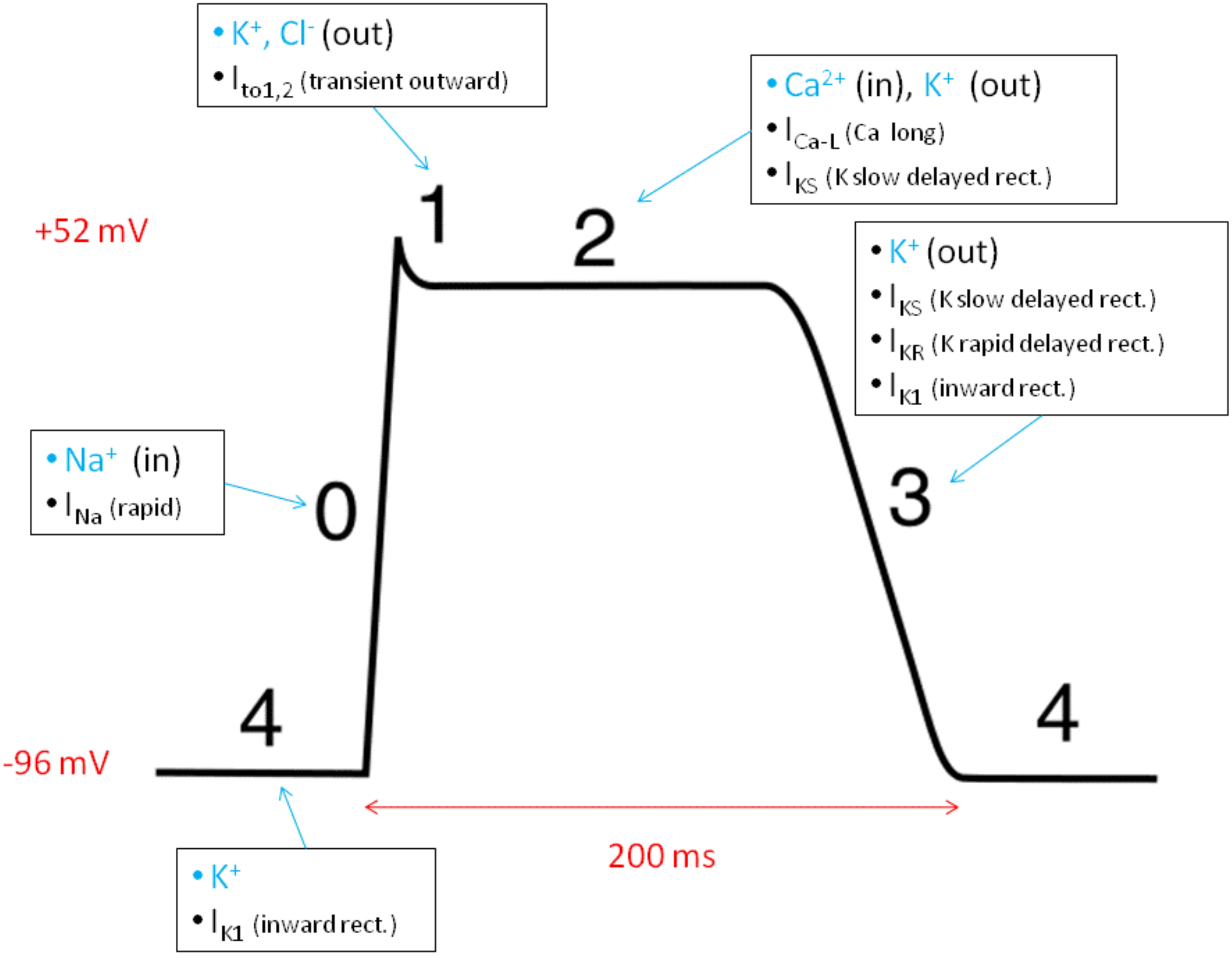
Review

The membrane of the heart develops a resting potential just like a neuron does. The membrane depolarizes due to the movement of Na^+ but stays at this potential for a while, due to changes in membrane permeability.

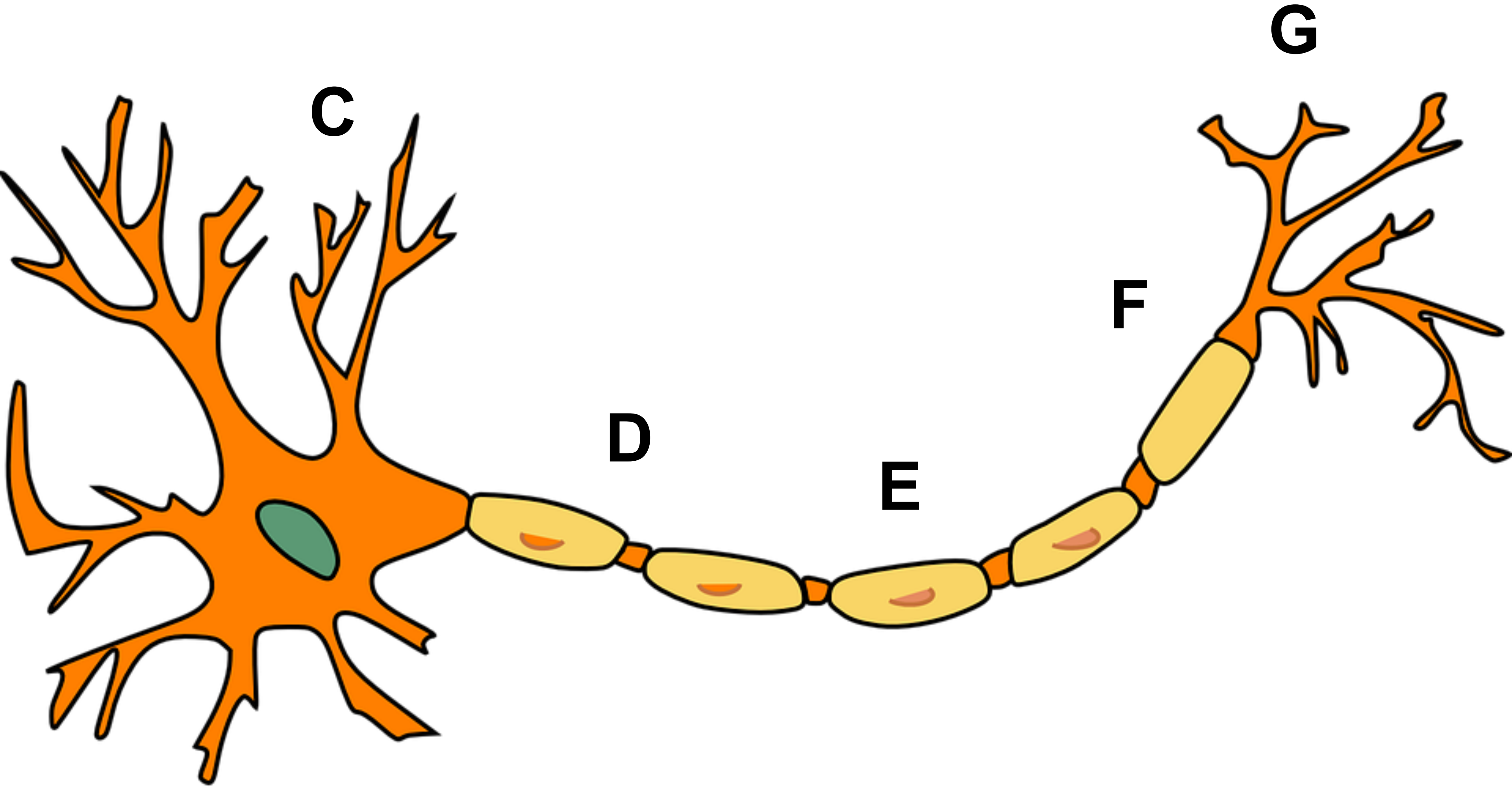
B. Assume K^+ is responsible for this plateau. How would a change in membrane permeability to K^+ account for this plateau?

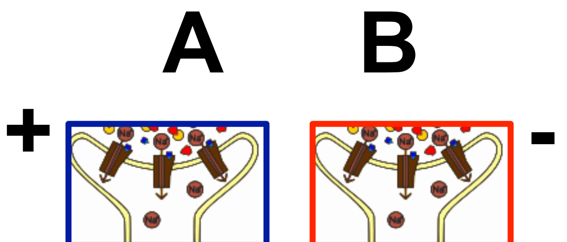
Decreased permeability to K^+ or a delay in opening of K channels. In neurons, the membrane repolarizes after peak of action potential due to opening of voltage-gated K^+ channels. If these channels remain closed, the membrane will stay depolarized.

Cardiac Action Potential



Review





Review

Based on the nerve cell and synapses drawn in the previous slide, fill in the blanks below. Use all letters that apply for each case:

A. Ligand-gated ion channels
B. Voltage-gated ion channels

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Based on the nerve cell and synapses drawn in the previous slide, fill in the blanks below. Use all letters that apply for each case:

A. Ligand-gated ion channels
B. Voltage-gated ion channels

A. The ligand of the pre-synaptic neuron, also known as a neurotransmitter, binds to receptors on the post-synaptic neuron. Those receptors are ligand-gated ion channels. The answer is thus **A and B.**

B. Voltage-gated ion channels are present along the axon. There are voltage-gated Na^+ and K^+ channels at **D, E, and F.** There are voltage-gated Ca^{++} channels at **G.**

Review

Based on the nerve cell and synapses drawn in the previous slide, fill in the blanks below. Use all letters that apply for each case:

C. Graded local potentials

D. Action potentials should be initiated at

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Based on the nerve cell and synapses drawn in the previous slide, fill in the blanks below. Use all letters that apply for each case:

C. Graded local potentials
D. Action potentials should be initiated at

C. Graded local potentials occur at the soma and dendrites, so **A, B, C, and D** (generated at A and B, but spread passively to C and D).

D. Action potentials begin at the axon hillock, so **D.**

Review

Based on the nerve cell and synapses drawn in the previous slide, fill in the blanks below. Use all letters that apply for each case:

E. IPSP is expected at

F. If you electrically stimulate the cell at (E), and initiate an action potential, the action potential should be propagated to

____

Review

Based on the nerve cell and synapses drawn in the previous slide, fill in the blanks below. Use all letters that apply for each case:

E. IPSP is expected at

F. If you electrically stimulate the cell at (E), and initiate an action potential, the action potential should be propagated to __________

G. Synaptic vesicles should be found mostly at

E. IPSP at **A**

F. AP should go towards **F and G**

G. Synaptic vesicles should be at **G**

Review

Based on the nerve cell and synapses drawn in the previous slide, fill in the blanks below. Use all letters that apply for each case:

H. Gated ion channels that generate potentials without a refractory period should be found at __________

I. If the cell shown is a motor neuron, then the synapse to the right of point G should be (excitatory) (inhibitory) (either one)

Review

Based on the nerve cell and synapses drawn in the previous slide, fill in the blanks below. Use all letters that apply for each case:

H. Gated ion channels that generate potentials without a refractory period should be found at __________

I. If the cell shown is a motor neuron, then the synapse to the right of point G should be (excitatory) (inhibitory) (either one)

H. Gated ion channels without a refractory period are K^+ or Cl^- channels. These are located at **A.** There are gated ion channels at **G** also but these do not generate potentials.

I. **Excitatory**: The neuromuscular junction is always excitatory. This question refers to motor neurons that innervate skeletal muscles.

Review

Circle whichever is greater, A or B. If A = B, circle both:

I.

A. time it takes for voltage-gated potassium channels to open after threshold is reached

B. time it takes for voltage-gated sodium channels to open after threshold is reached

<u>Note</u>: Assume the threshold is -50 mV and the action potential has not yet begun.

II.

A. force pushing sodium into neuron at resting potential

B. force pushing potassium out of neuron at resting potential

III.

A. voltage-gated Ca^{++} channels in axon hillock

B. voltage-gated Ca^{++} channels in nerve terminals

Review

Circle whichever is greater, A or B. If A = B, circle both:

I.

A. time it takes for voltage-gated potassium channels to open after threshold is reached

(K^+ channels open more slowly)

B. time it takes for voltage-gated sodium channels to open after threshold is reached

II.

A. force pushing sodium into neuron at resting potential

(Na^+ has both electrical and chemical gradients pushing it in)

B. force pushing potassium out of neuron at resting potential

III.

A. voltage-gated Ca^{++} channels in axon hillock

B. voltage-gated Ca^{++} channels in nerve terminals

(Ca^{++} channels in nerve terminals needed for neurotransmitter release)

Review

Circle whichever is greater, A or B. If A = B, circle both:

I.

A. number of axon K+ channels open the threshold potential

B. number of axon K+ channels open at the resting potential

II.

A. chance of finding a graded potential at the pre-synaptic membrane

B. chance of finding a graded potential at the post-synaptic membrane

III.

A. number of neurotransmitter receptors on post-synaptic membrane

B. number of neurotransmitter receptors on pre-synaptic membrane

Review

Circle whichever is greater, A or B. If A = B, circle both:

I.

A. number of axon K+ channels open the threshold potential

B. number of axon K+ channels open at the resting potential

Depolarization is due to opening of Na^+ channels, not closing of K^+ channels.

II.

A. chance of finding a graded potential at the pre-synaptic membrane

B. chance of finding a graded potential at the post-synaptic membrane

There is no graded potential on the pre-synaptic side.

III.

A. number of neurotransmitter receptors on post-synaptic membrane

B. number of neurotransmitter receptors on pre-synaptic membrane

Neurotransmitter release is unidirectional.

Review

Circle whichever is greater, A or B. If A = B, circle both:

I.

A. potassium channels open during an EPSP

B. potassium channels open during an IPSP

II.

A. rate of substance moving down axon through the cytoplasm by simple diffusion

B. rate of substance moving down axon by vesicular transport

III.

A. sodium ions crossing the membrane during an EPSP

B. sodium ions crossing the membrane during an IPSP

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A. sodium ions crossing the membrane during an EPSP

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Review

Serotonin is a neurotransmitter that can be either stimulatory or inhibitory, depending on the particular receptor on the post-synaptic membrane. For each of these serotonin receptors, indicate whether it will be inhibitory (produces IPSP) or stimulatory (produces EPSP).

Stimulation of the receptor…

A. Increases levels of the cAMP, leading to an increase in K^+ permeability
B. Increases levels of IP3, leading to a decrease in K+ permeability
C. Increases levels of IP3, leading to an increase in Cl- permeability
D. Is directly coupled to an ion channel that leads to increase in permeability to both Na^+ and K^+

Review

Serotonin is a neurotransmitter that can be either stimulatory or inhibitory, depending on the particular receptor on the post-synaptic membrane. For each of these serotonin receptors, indicate whether it will be inhibitory (produces IPSP) or stimulatory (produces EPSP).

Stimulation of the receptor…

A. Inhibitory. K+ is higher inside cell than outside. If you increase permeability to K+, more K+ leaks out of the cell. The inside of the membrane becomes more negative (hyper-polarized) and further from threshold.
B. Stimulatory. K+ is high inside and membrane depolarizes.
C. Inhibitory. Cl- is higher outside than inside. Cl- will flow in, and the membrane becomes more negative than usual (hyper-polarized).
D. Stimulatory. Na+ is higher outside cell than inside. If you increase permeability to both, Na+ will enter and K+ will leave.

Review

Consider two nerve cells that produce action potentials.
Cell #1 is a post-ganglionic cell of the parasympathetic nervous system.
Cell #2 is a sensory receptor in the olfactory cell.

Note: Pre-ganglionic cells are from brainstem or spinal cord. Post-ganglionic cells are from outside the central nervous system.

A. Which cell moves toward the central nervous system?

Review

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Cell #2 is a sensory receptor in the olfactory cell.

Note: Pre-ganglionic cells are from brainstem or spinal cord. Post-ganglionic cells are from outside the central nervous system.

A. Which cell moves toward the central nervous system?
   Cell #2, Sensory neurons move toward the CNS.

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B. Which cell should have voltage-gated Na+ channels?
   - Cell #1
   - Cell #2
   - Both
   - Neither

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B. Which cell should have voltage-gated Na+ channels?
   - Cell #1
   - Cell #2
   - Both
   - Neither

Review

You are studying a synapse in a newly discovered worm species, and you want to determine whether it is a chemical or an electrical synapse. You don’t have an electron microscope, so you can’t visualize the synapse directly. Describe an experiment you could do to determine which kind of synapse is involved here.

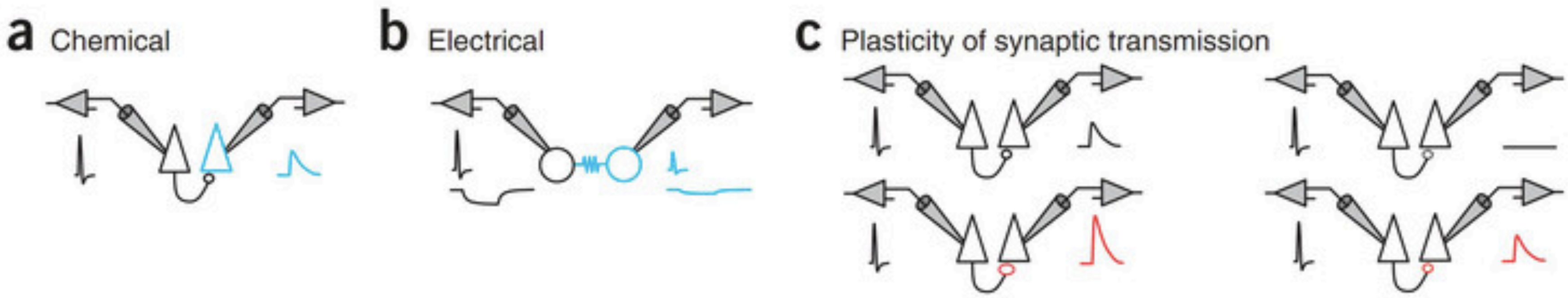
Review

You are studying a synapse in a newly discovered worm species, and you want to determine whether it is a chemical or an electrical synapse. You don't have an electron microscope, so you can't visualize the synapse directly. Describe an experiment you could do to determine which kind of synapse is involved here.

Stimulate the pre-synaptic neuron and measure the time it takes for depolarization to occur in the post-synaptic neuron. Signal conduction is slower in chemical synapses than in electrical synapses.

Alternative: Apply a Ca^{++} channel blocker to synapse. Opening of calcium channels is necessary for release of neurotransmitters, but not necessary for transmission across electrical synapses.

Overview of Electrophysiology

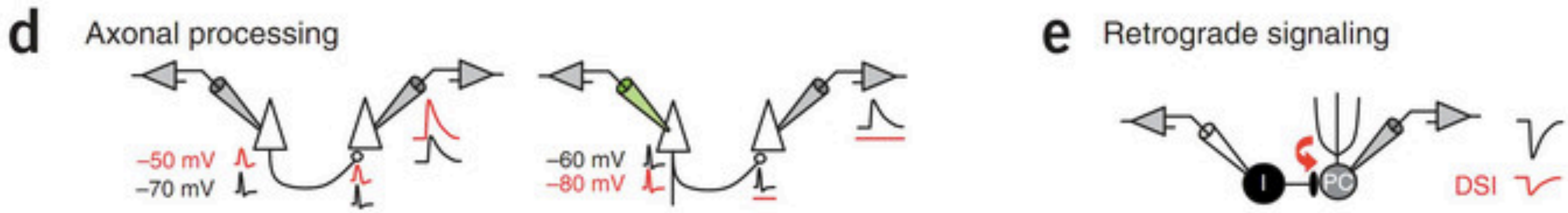


A. Chemical Synapse
Action potential (**black**) triggered in pre-synaptic neuron evokes an EPSP (**blue**) in post-synaptic neuron.

B. Electrical Synapse
Action potential (**black**) in first neuron produces attenuated voltage signals (**blue**) in second cell.

C. Plasticity of Synaptic Transmission
In control, pre-synaptic neuron evokes an EPSP in post-synaptic cell (left) or no response (right) in case of silent synapse. After **potentiation** (**red**), the efficacy of synaptic transmission is enhanced.

Overview of Electrophysiology



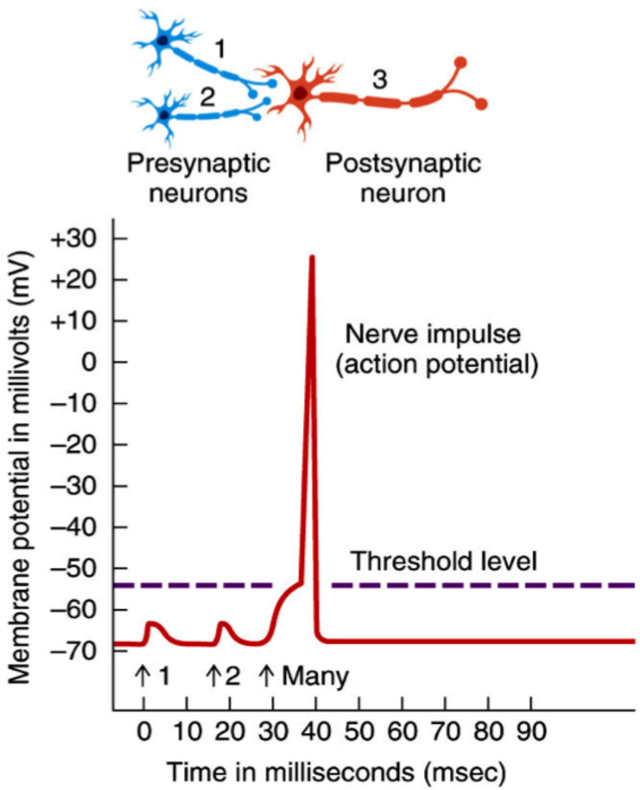
D. Axonal Processing

Pre-synaptic membrane potential-dependent axonal integration (left) and conduction failure (right). *Pre-synaptic spike fails to propagate in axon when it is evoked from a hyper-polarized potential (-80 mV).*

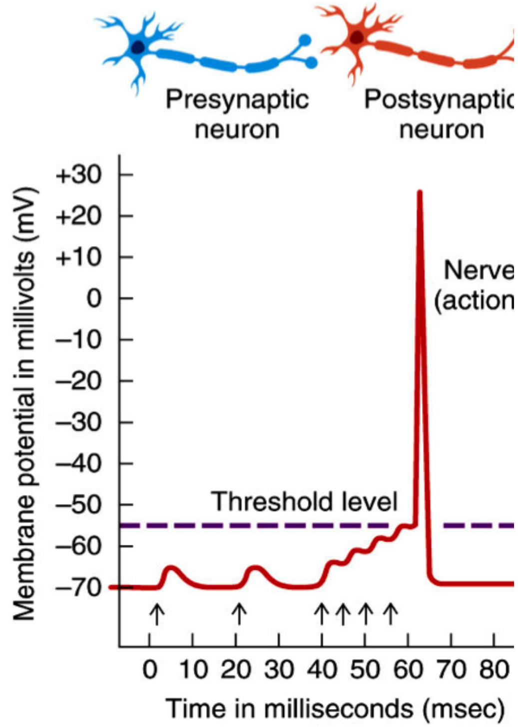
E. Retrograde Signaling

Retrograde signaling established between an interneuron (I) and a Purkinje cell (PC). **Depolarization-Induced Suppression** (DSI) of inhibition. Red arrow indicates the release of endocannabinoids from PC to pre-synaptic terminal of interneuron.

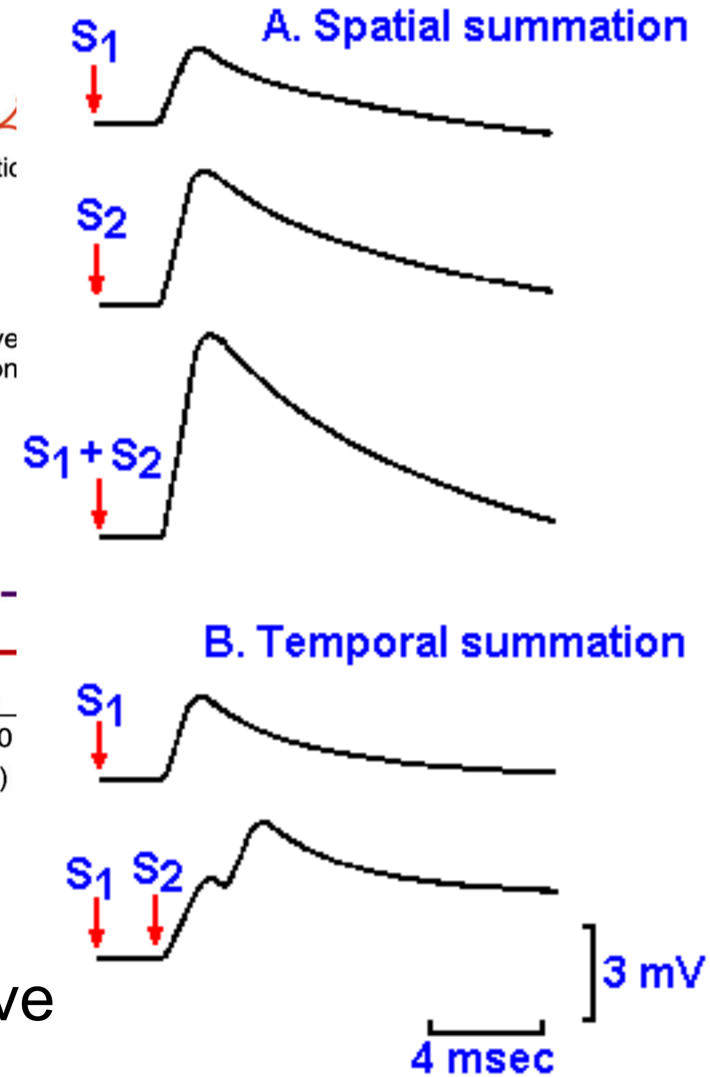
Summation



(a) Spatial summation



(b) Temporal summation



Spatial Summation:

Occurs when post-synaptic potentials arrive near same location

Temporal Summation:

Occurs when post-synaptic potentials arrive near same time

Next Time:

Guest Lecture by Roger Traub

(IBM Watson)