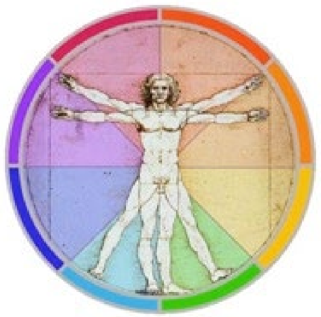
HUBS 191 Lecture Material

This pre-lecture material is to help you prepare for the lecture and to assist your note-taking within the lecture,
it is NOT a substitute for the lecture !



Please note that although every effort is made to ensure this pre-lecture material corresponds to the live-lecture there may be differences / additions.

HUBS 191

Jeff Erickson – Department of Physiology

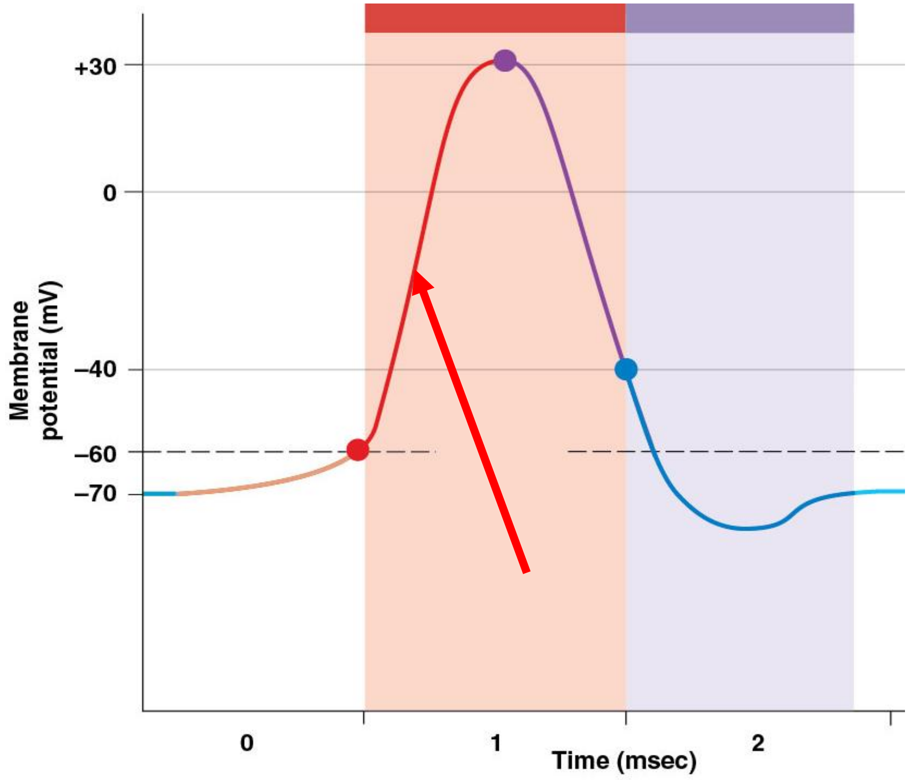
Lecture 19
Neurophysiology 2: Propagation and Synaptic Transmission

Example exam question

At the point indicated by the red arrow:

A. the neuron is hyperpolarizing.
B. voltage-gated Na^+ channels have opened.
C. the neuron is waiting for sufficient summation at the axon hillock.
D. the rapid repolarization phase has begun.

Changes in membrane potential during an action potential



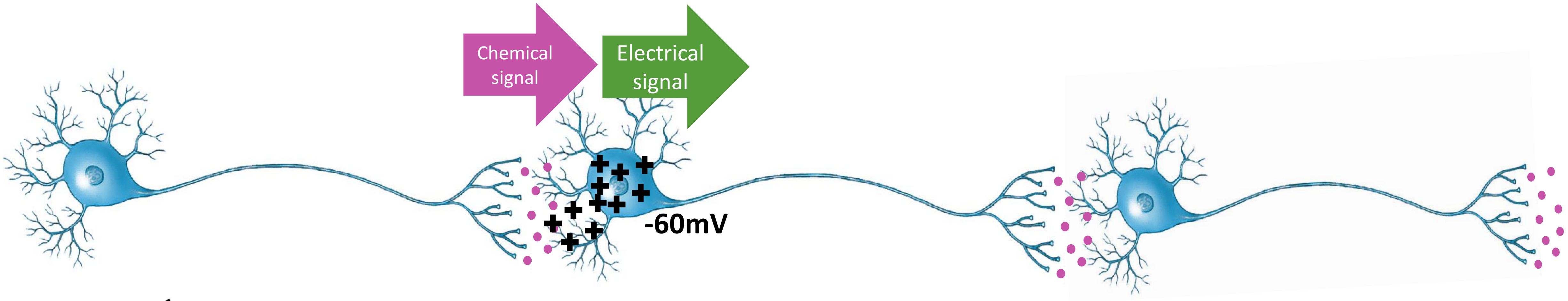
Objectives and Study Guide

After this lecture you should be able to:

- Contrast the absolute and relative refractory periods of an action potential
- Describe the movement of an action potential down the axon of a neuron
- Describe the process of synaptic transmission at the axon terminal

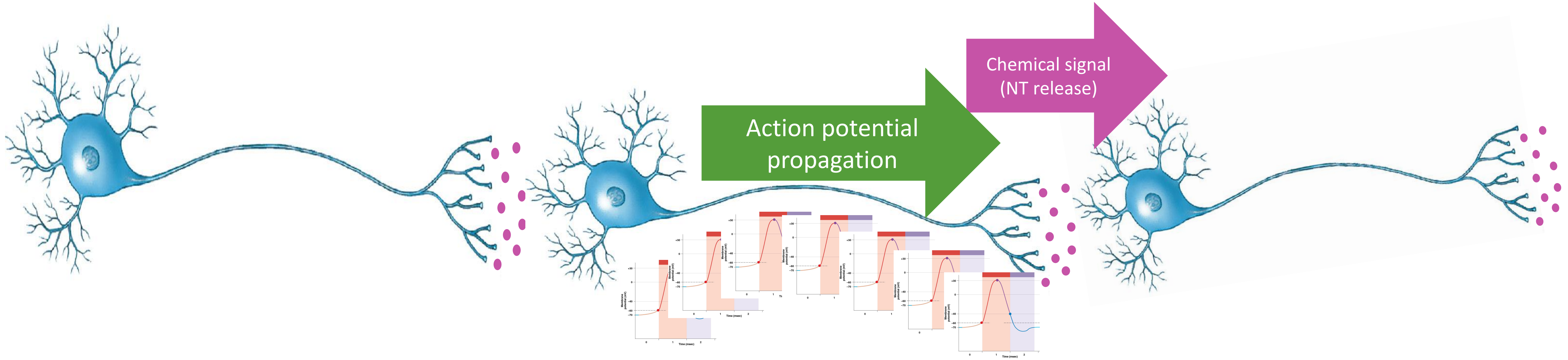
Related reading: Martini et al. Modules **9.6** (p. 366-67) and **11.11-11.14** (p. 464-470)

How does a chemical signal get converted into an electrical signal?



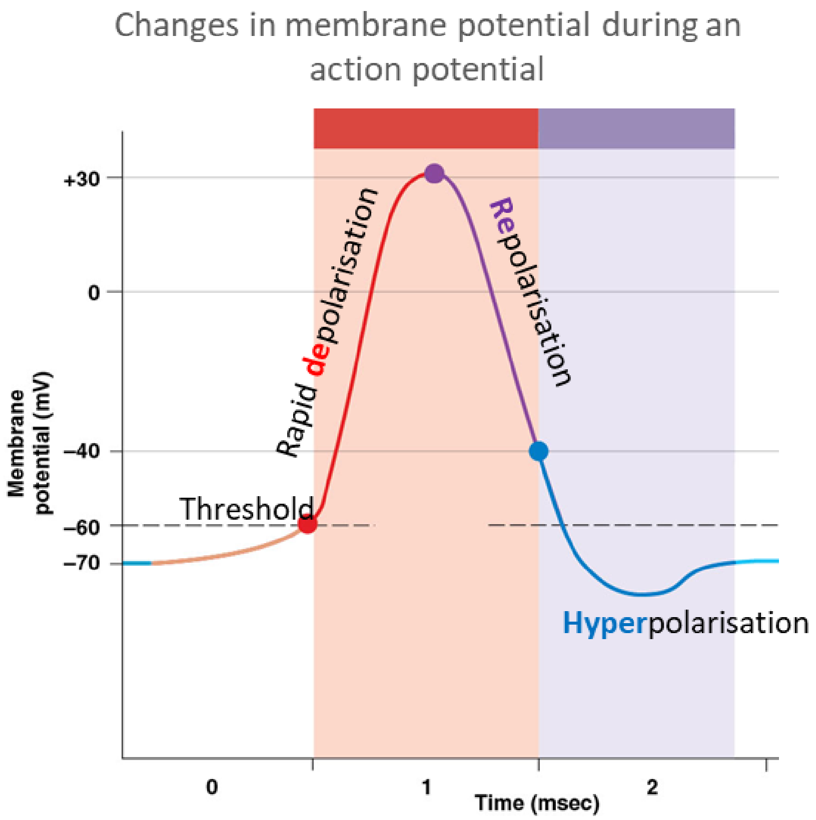
- A chemical signal (neurotransmitter) binds to and opens chemically-gated ion channels.
  - Can be inhibitory or excitatory
- Ions flow in or out, changing the voltage at a localized area of membrane.
  - Adding these ion movements together is called summation
- If the membrane voltage reaches -60mV at the axon hillock…
  - The axon hillock contains lots of voltage-gated Na^+ channels
- …an electrical signal (action potential) begins.
  - Coordinated movement of ions leads to depolarization, repolarization, and hyperpolarization

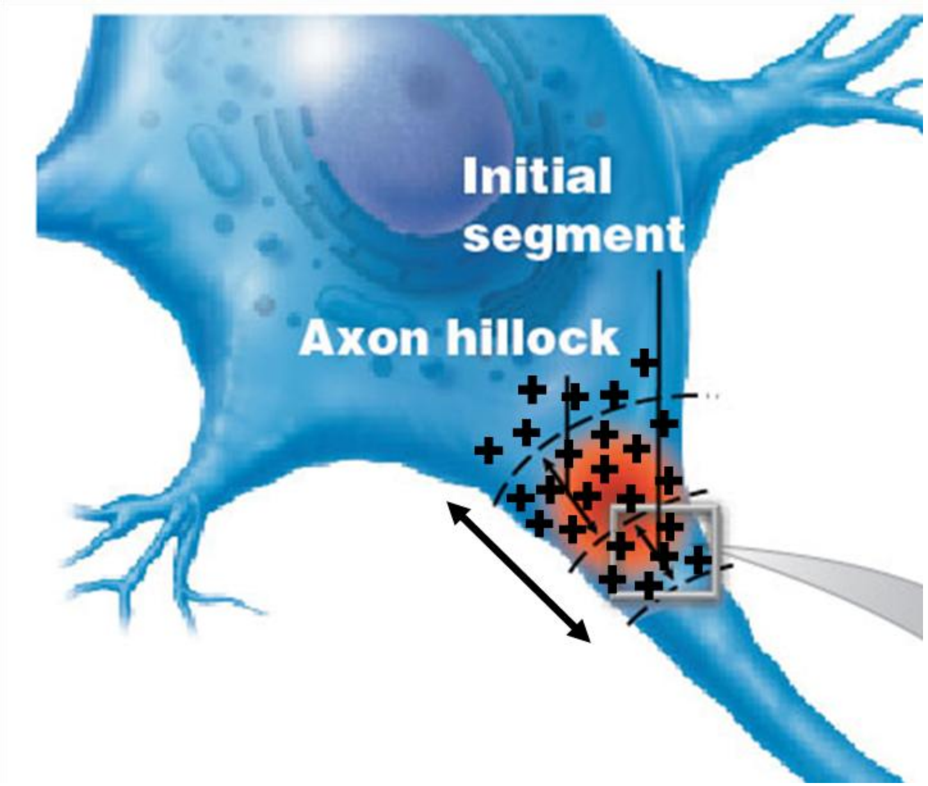
How does an electrical signal (action potential propagation) trigger a chemical signal (neurotransmitter release)?



- Na^{+} diffuses from the axon hillock to initiate an AP in the initial segment of the axon
- AP propagates to each neighboring axon segment (unmyelinated axon) or node (myelinated axon) in one direction.
- The AP arrives at the axon terminals, causing VG Ca^{2+} channels to open
- Ca^{2+} enters terminals, causing release of neurotransmitter into synaptic cleft to activate the post-synaptic cell

Action potential propagation is the movement of the action potential down the axon to the terminal





- During rapid depolarization, a ‘flood’ of Na^+ enters the axon hillock
- Na^+ diffuses from the points of entry
- We’ll ignore backwards diffusion…only diffusion down the axon towards the terminal matters for our purposes!

Martini - Visual Anatomy and Physiology (2018) Module 11.10 p. 462-3.

A refractory period is a period of rest after a stimulus during which another stimulus won't have an effect

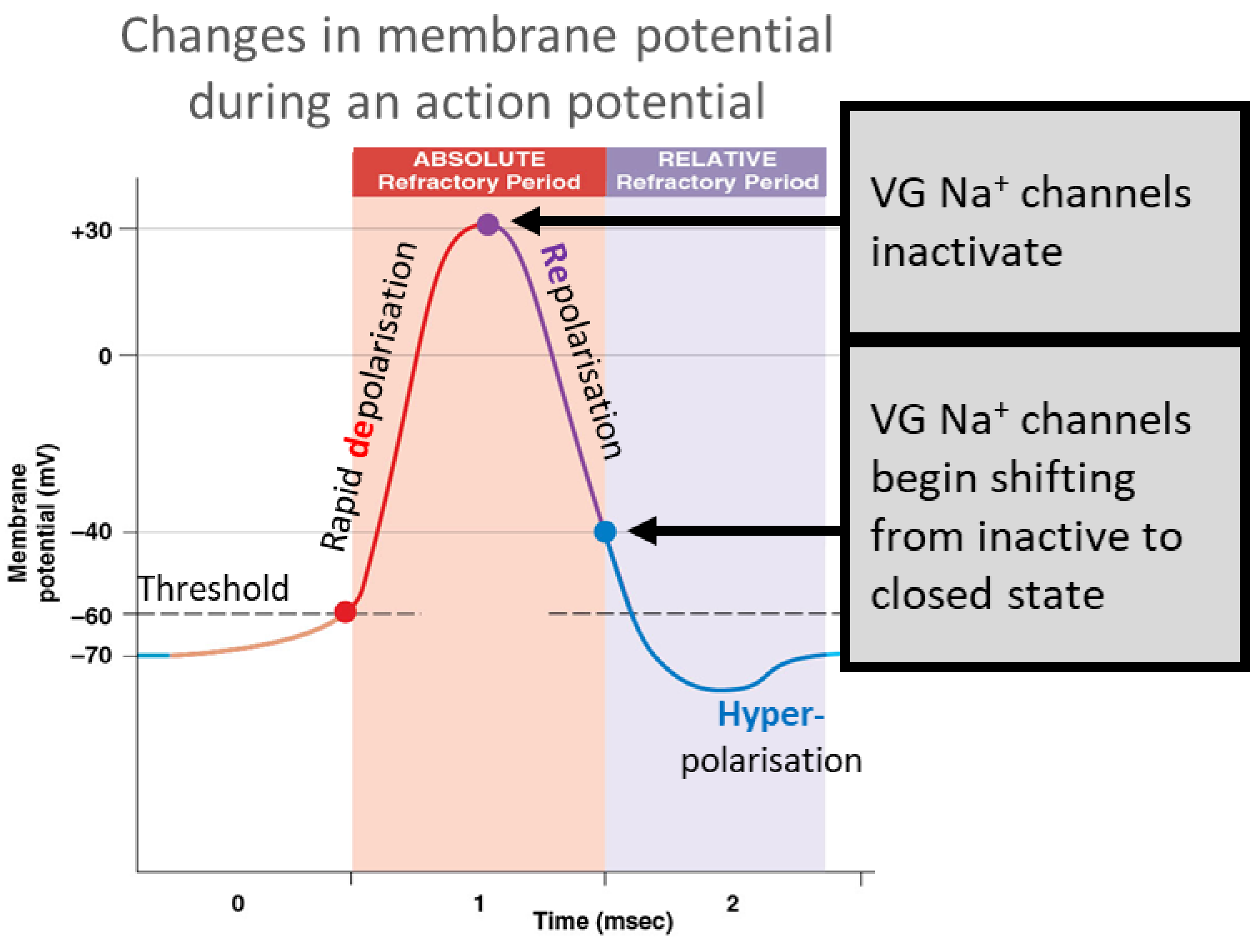
Absolute refractory period

- A 2nd AP cannot be generated
- Occurs when VG Na^+ channels are already open or become inactive.

Relative refractory period

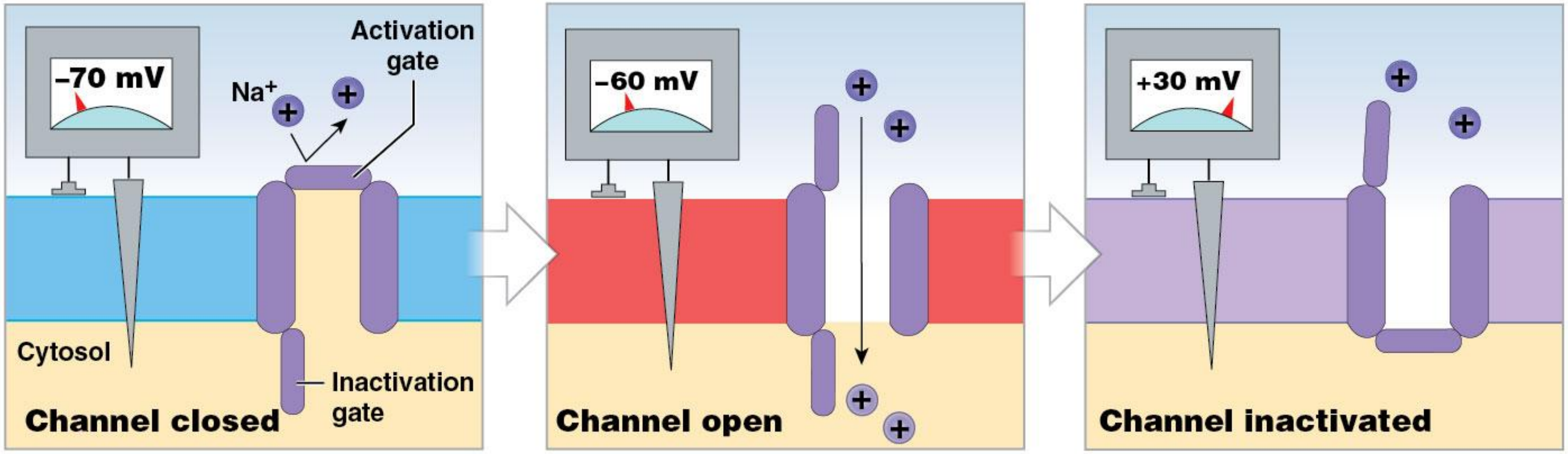
- A 2nd AP can be generated only if the stimulus is much larger than normal.
- Occurs when some VG Na^+ channels begin to shift from an inactive to closed state.

Note: VG Na^+ channels cannot open when inactive. They only open from a closed state.



Martini - Visual Anatomy and Physiology (2018) Module 11.10 p. 462-3.

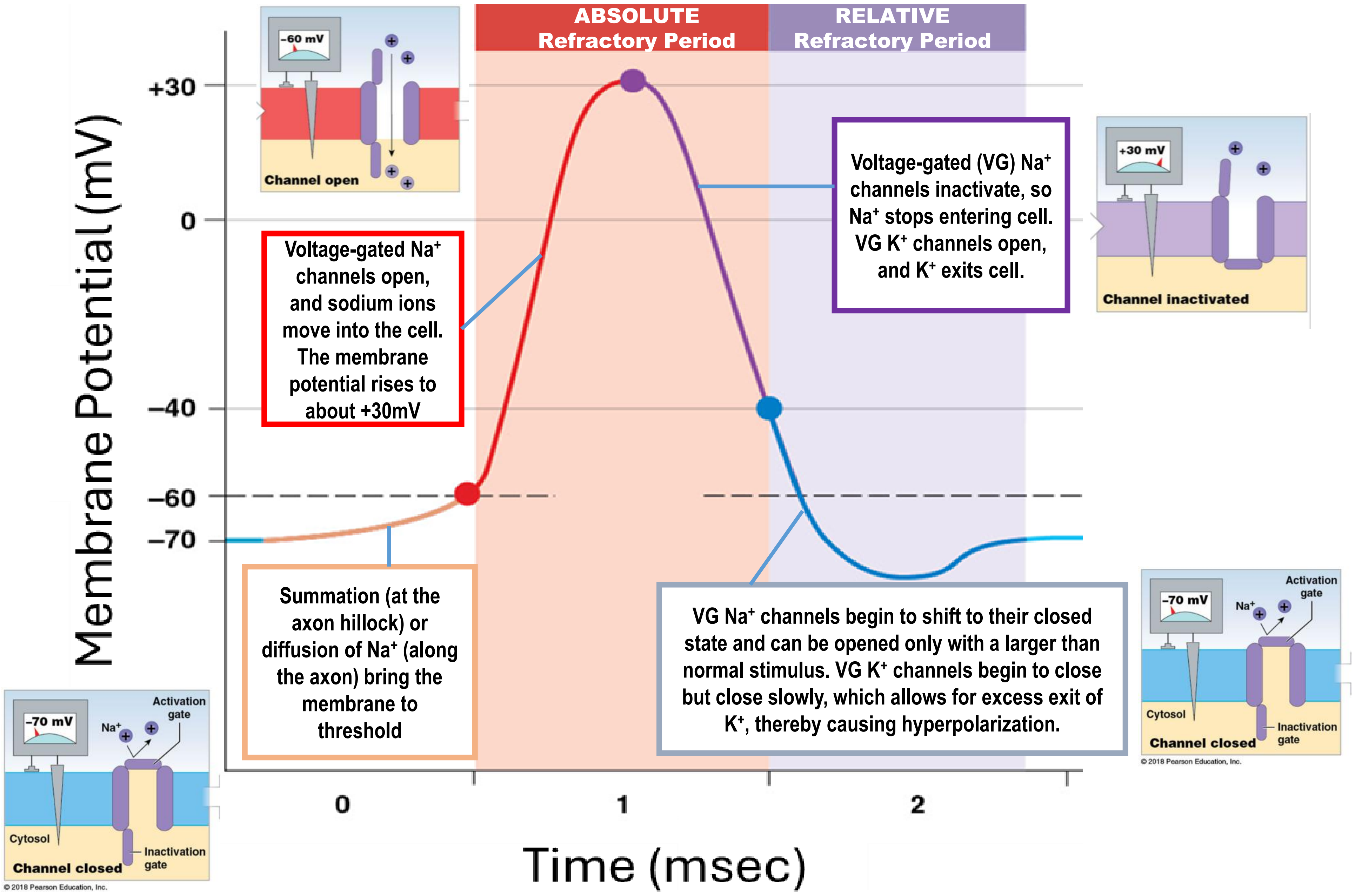
Voltage-gated ion channels open when they sense a (sufficiently large) change in voltage



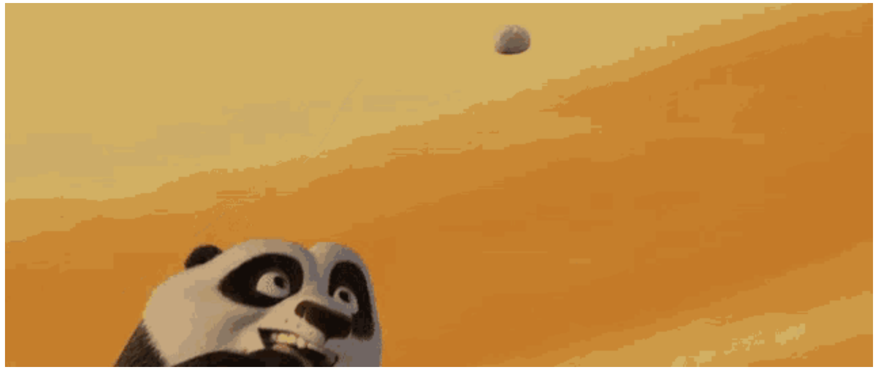
1. **Stimulus = membrane depolarizes to threshold voltage (e.g. -60mV)**
2. Channel changes shape (i.e opens)
3. Ions cross the membrane driven by their electrochemical gradient
4. **Membrane potential changes** will cause the channel to inactivate or close

Martini - Visual Anatomy and Physiology (2018) Module 11.8 p. 458.

Action potential cheat sheet



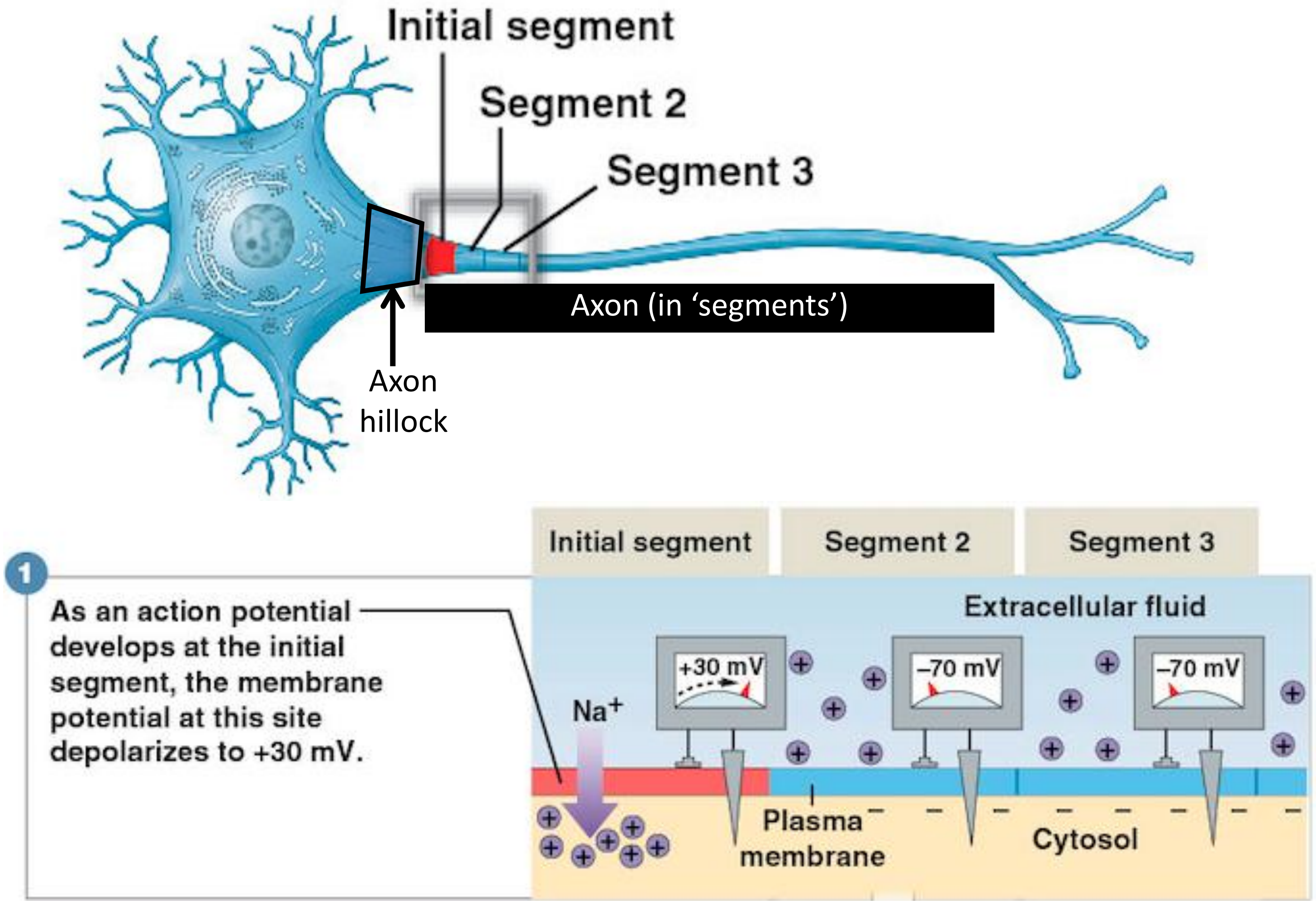
Did you catch it?

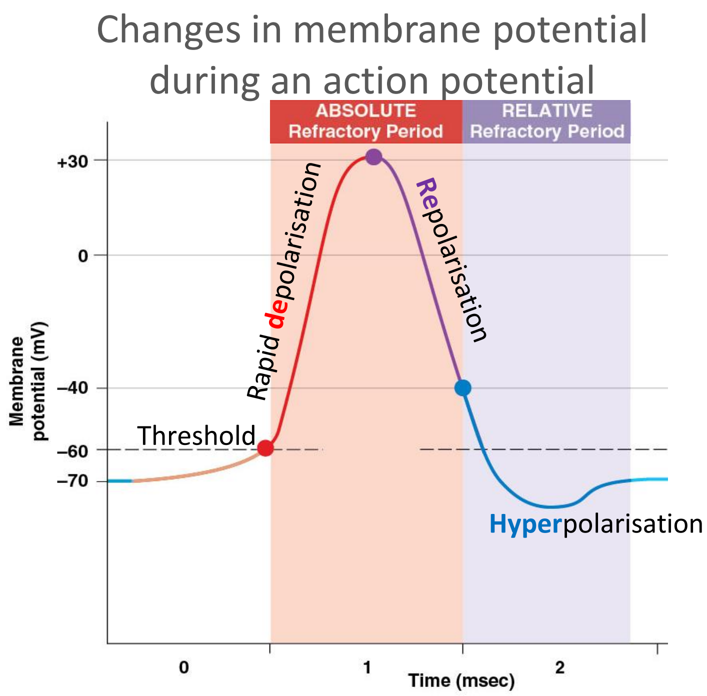


DreamWorks Animation

- What is a refractory period in neurons?
- What is the difference between the absolute refractory period and the relative refractory period?
- What is the state of voltage-gated Na^+ channels in the absolute and relative refractory periods?

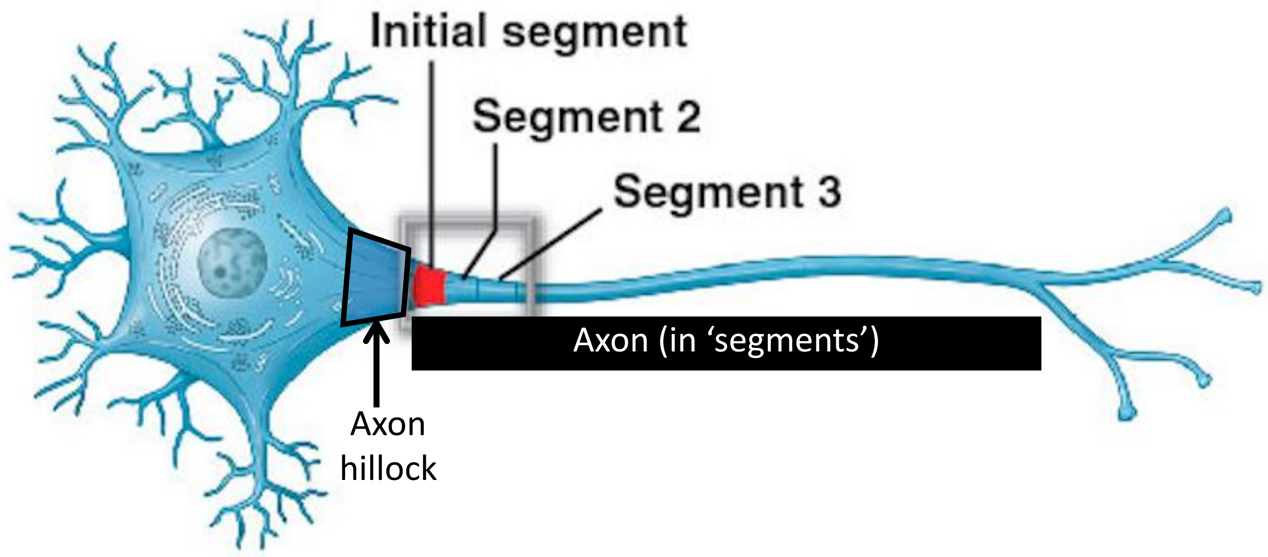
In an unmyelinated axon, an influx of Na^+ at the axon hillock leads to diffusion of Na^+ into the initial segment, triggering depolarization

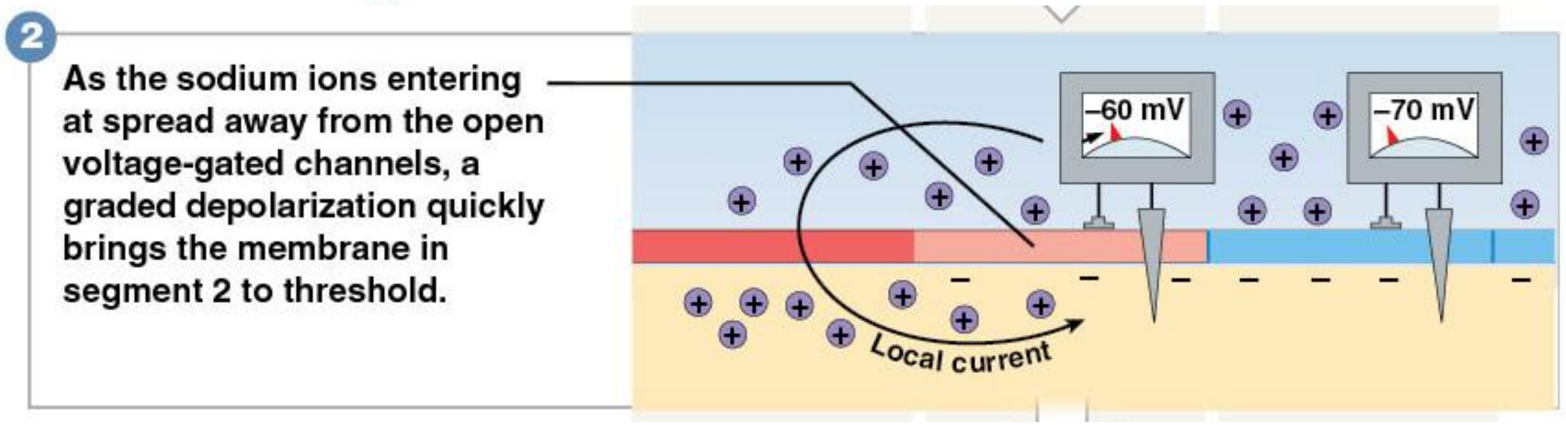


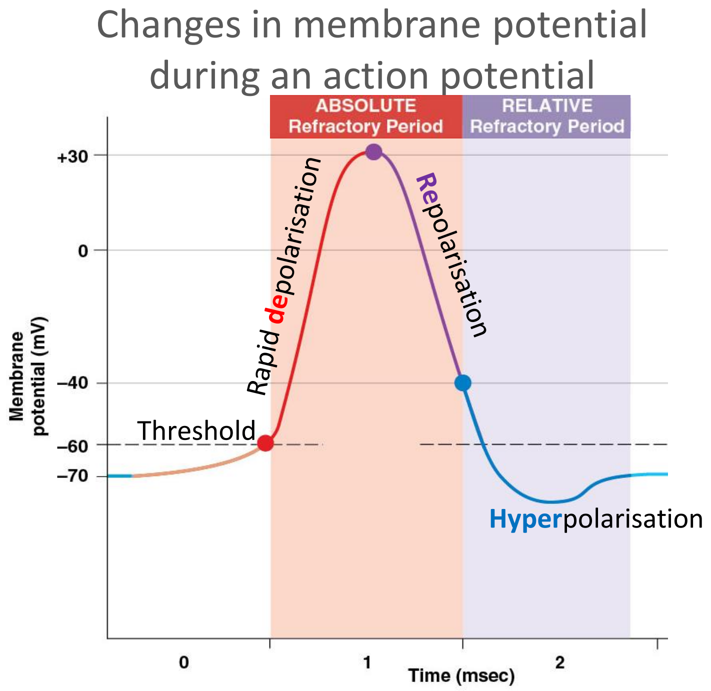


Martini - Visual Anatomy and Physiology (2018) Module 11.11 p. 464.

The Na$^+$ continues to spread to segment 2, moving it from -70mV to -60mV (threshold)

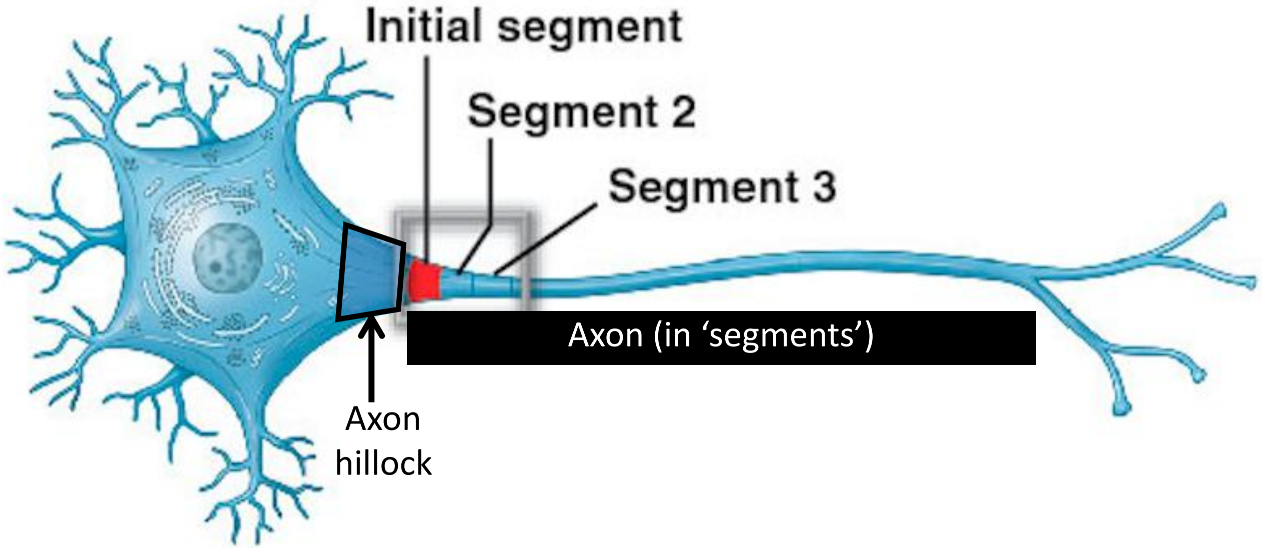


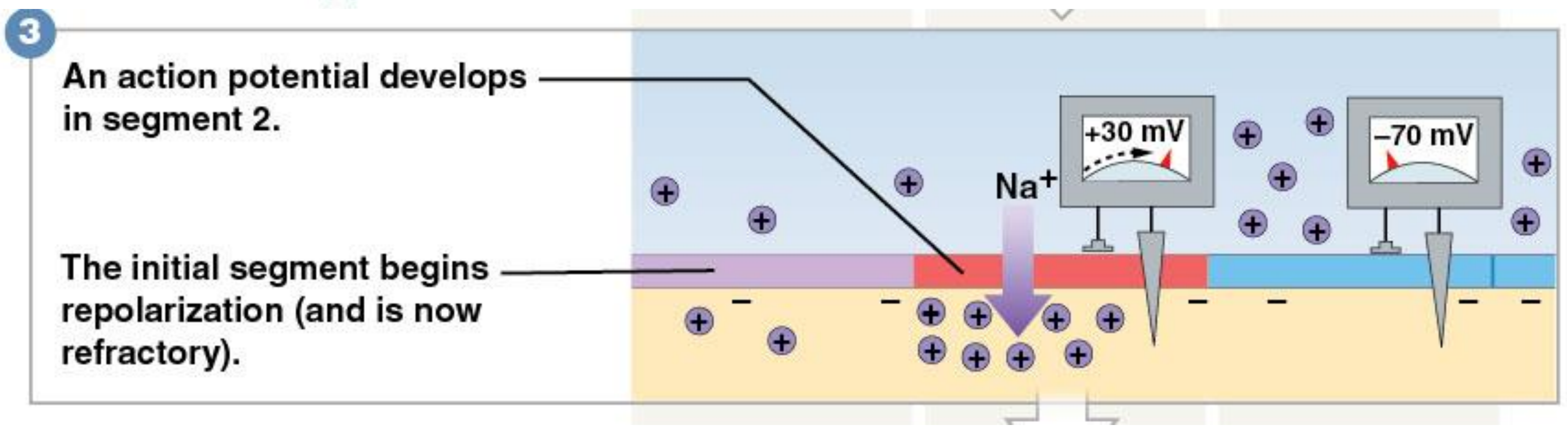




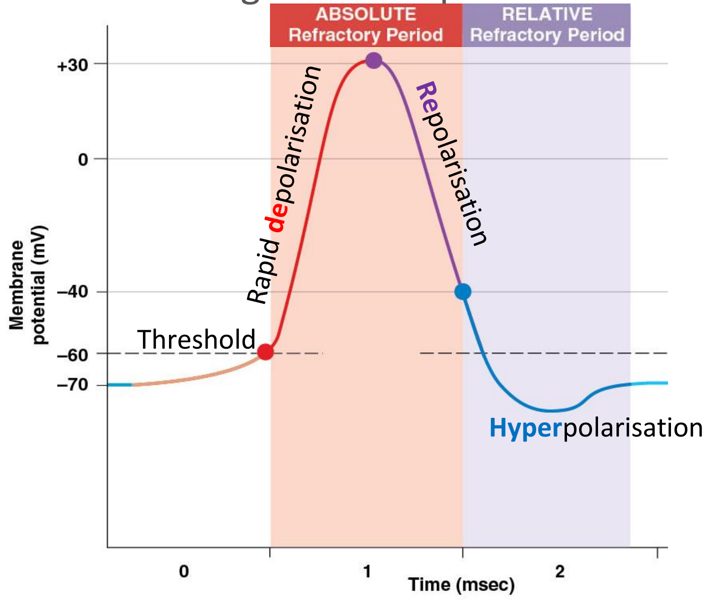
Martini - Visual Anatomy and Physiology (2018) Module 11.11 p. 464.

As we move past threshold, an action potential is triggered in segment 2. Back in the initial segment, VG Na^+ channels are closing and VG K^+ channels are opening…it's time to repolarize!





Changes in membrane potential during an action potential



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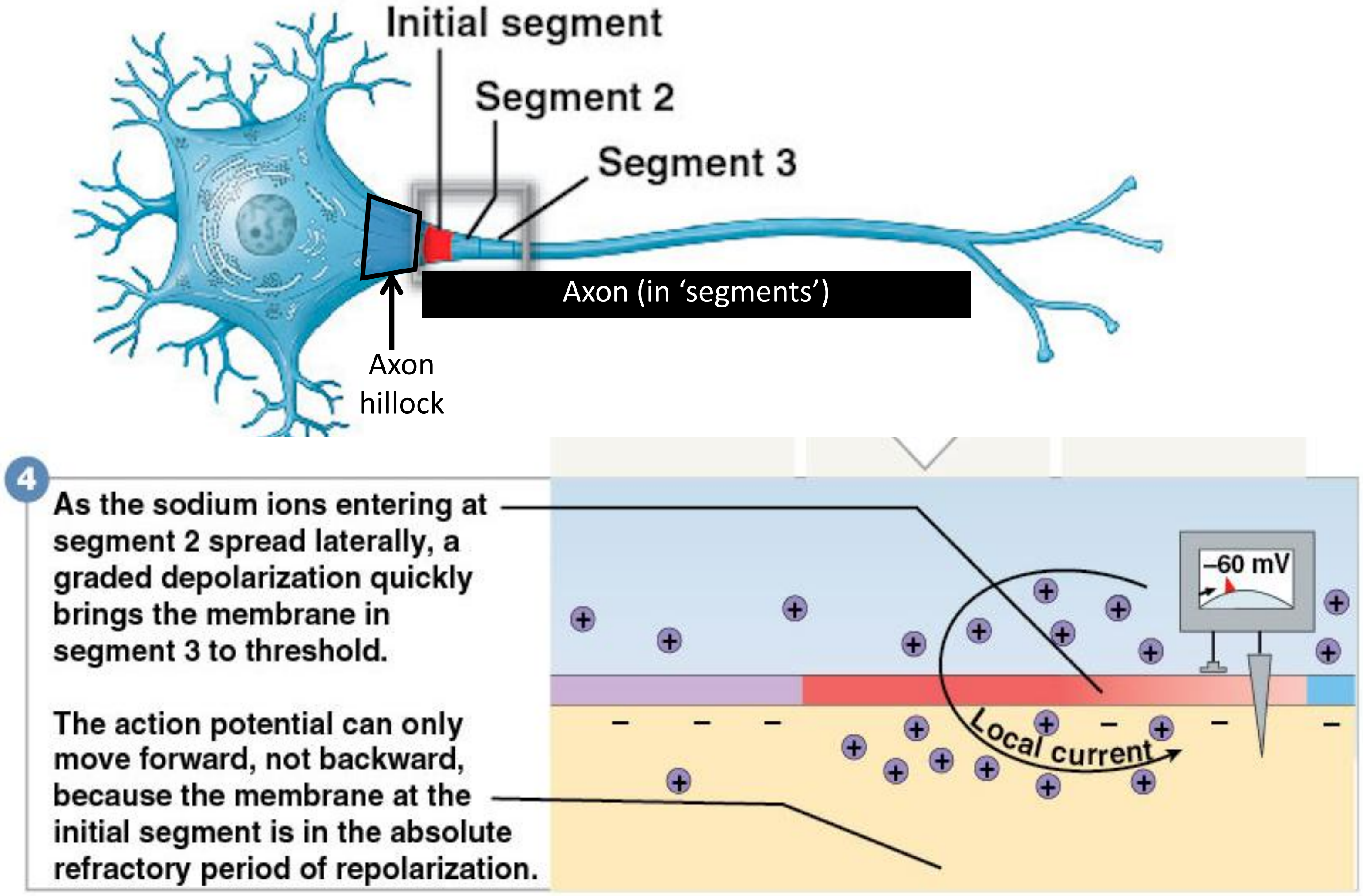
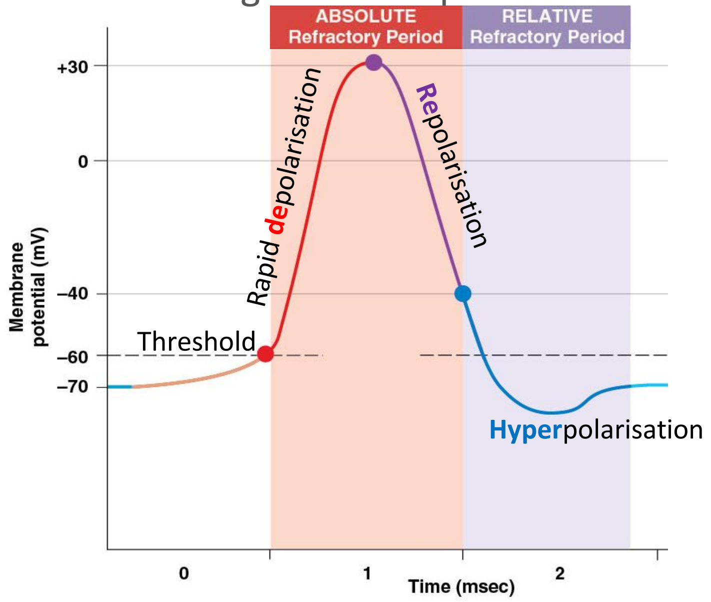
Segment 2 is rapidly depolarizing, and the movement of Na^+ into the cell is now spreading to segment 3, which is nearing threshold. The initial segment is well on its way to hyperpolarization.



Changes in membrane potential during an action potential



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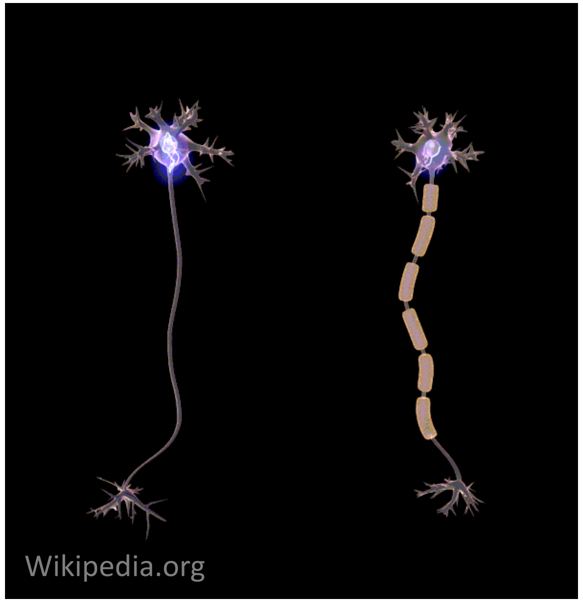
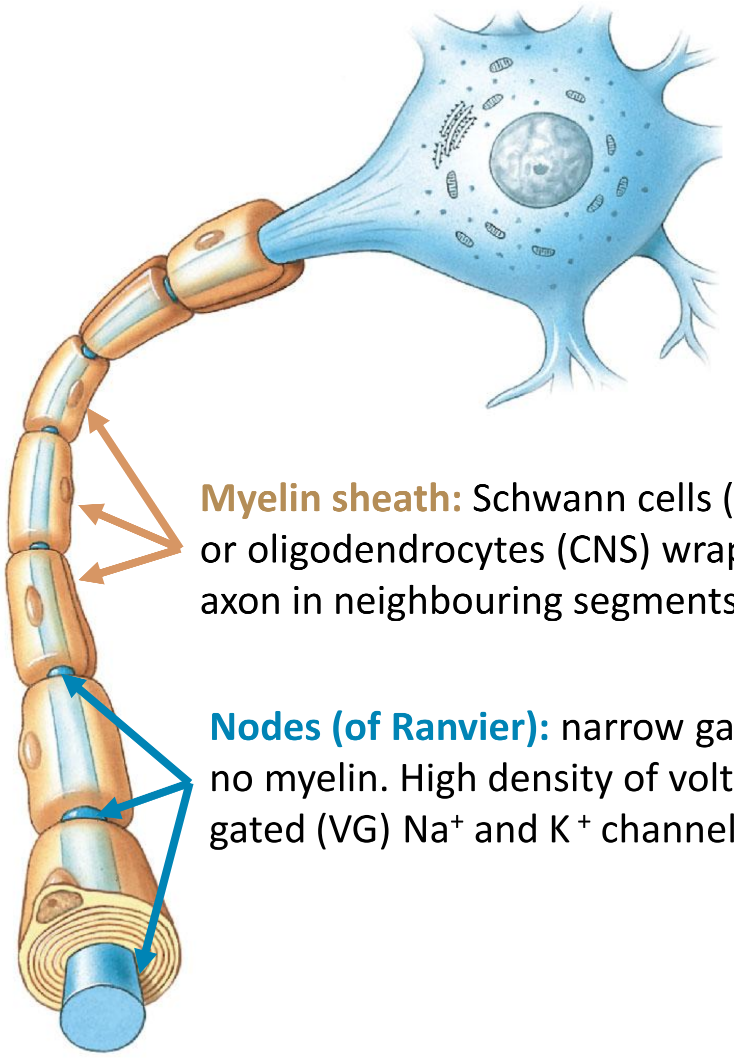
Unmyelinated vs Myelinated axons



- Action potentials (APs) propagate along unmyelinated axons relatively slowly (e.g. ~ 1 to 5 meters per second - m/s)
- Some axons can be ~1 m long (e.g. to lower limbs), so slow AP conduction is not adequate for all our needs.
- Myelination dramatically increases AP conduction velocity
- Ion movement is restricted to the areas without myelin (nodes), so conduction appears to jump from one node to the next. This is called **saltatory conduction** (from the Latin saltus: to leap)



Myelin sheath: Schwann cells (PNS) or oligodendrocytes (CNS) wrap the axon in neighbouring segments

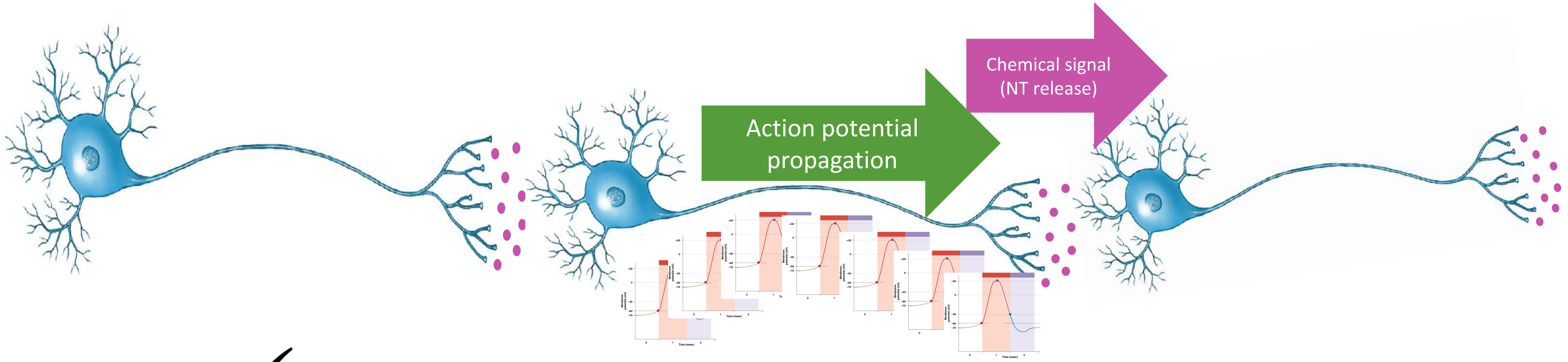
Nodes (of Ranvier): narrow gaps with no myelin. High density of voltage-gated (VG) Na^+ and K^+ channels.

Example exam question

When a segment of a neuronal axon is undergoing rapid depolarization:

A. Na^+ is moving from inside to outside the neuron in that segment.
B. that segment is in a relative refractory period.
C. the next segment is about to move directly from its resting membrane potential to repolarization.
D. that segment is in an absolute refractory period.

How does an electrical signal (action potential propagation) trigger a chemical signal (neurotransmitter release)?



- ✓ Na^+ diffuses from the axon hillock to initiate an AP in the initial segment of the axon
- ✓ AP propagates to each neighboring axon segment (unmyelinated axon) or node (myelinated axon) in one direction.
- The AP arrives at the axon terminals, causing VG Ca^{2+} channels to open
- Ca^{2+} enters terminals, causing release of neurotransmitter into synaptic cleft to activate the post-synaptic cell

Key features of the chemical synapse

Presynaptic axon terminal
- VG Ca^{2+} channels
- Synaptic vesicles filled with neurotransmitter

Synaptic cleft
- A space neurotransmitter diffuses across
- Enzymes that inactivate neurotransmitter are present in the cleft

Postsynaptic cell
- Chemically-gated ion channels

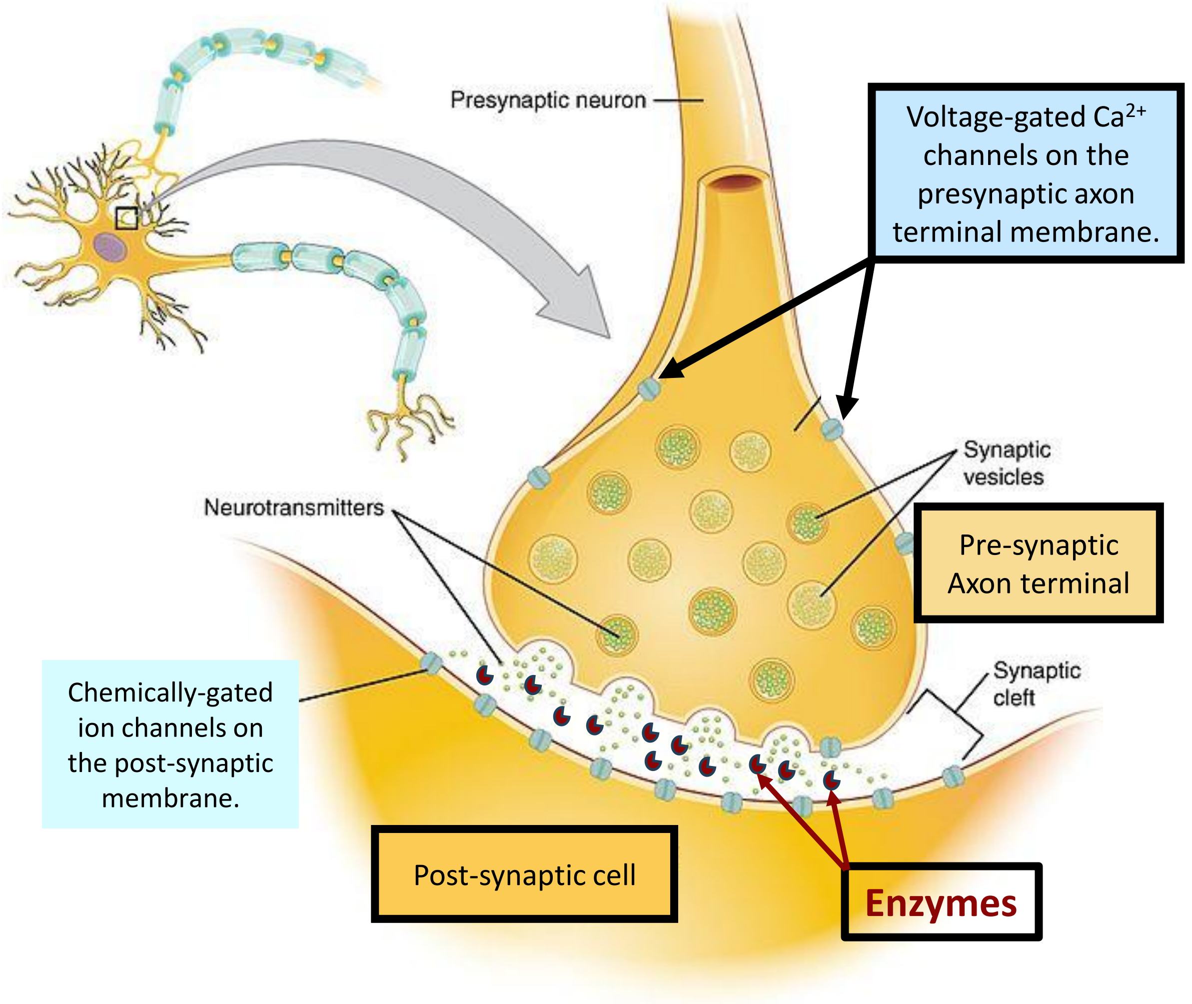
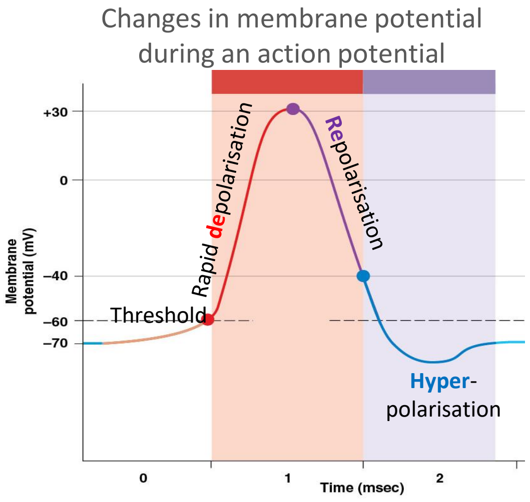
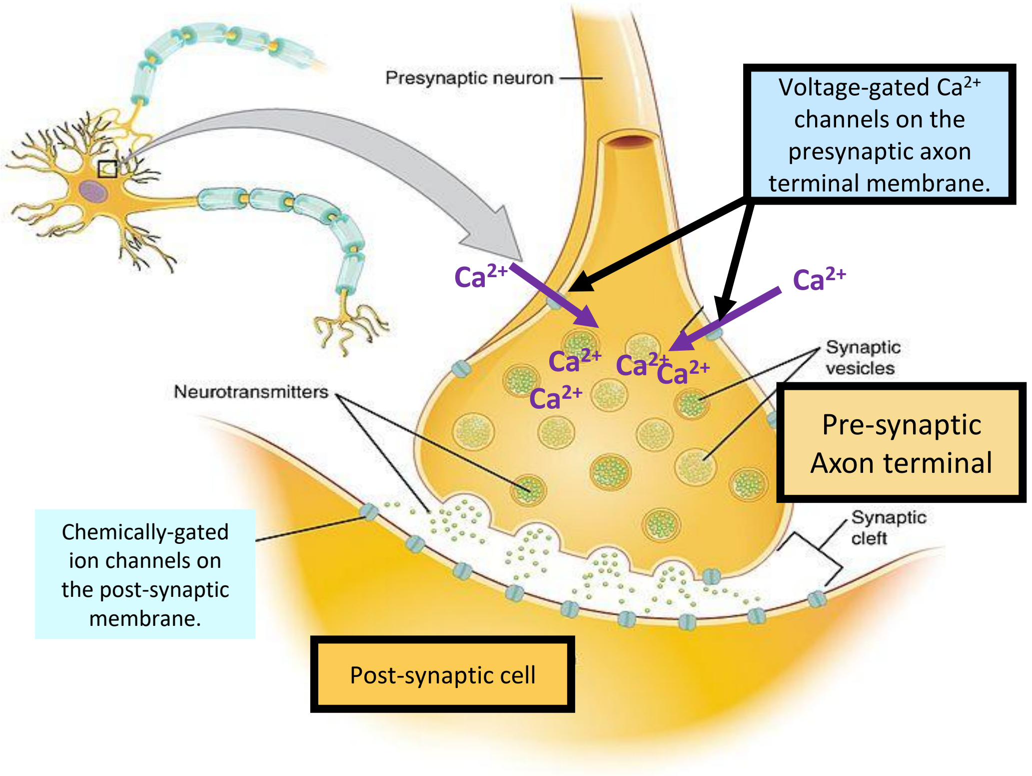


Image credit: Chemical synapse. Commons.Wikimedia.org

Synaptic transmission step 1: The axon terminal is depolarized



- When the action potential arrives at the axon terminal, the change in voltage causes VG Ca^{2+} channels to open
- Ca^{2+} moves down its electrochemical gradient into the axon terminal



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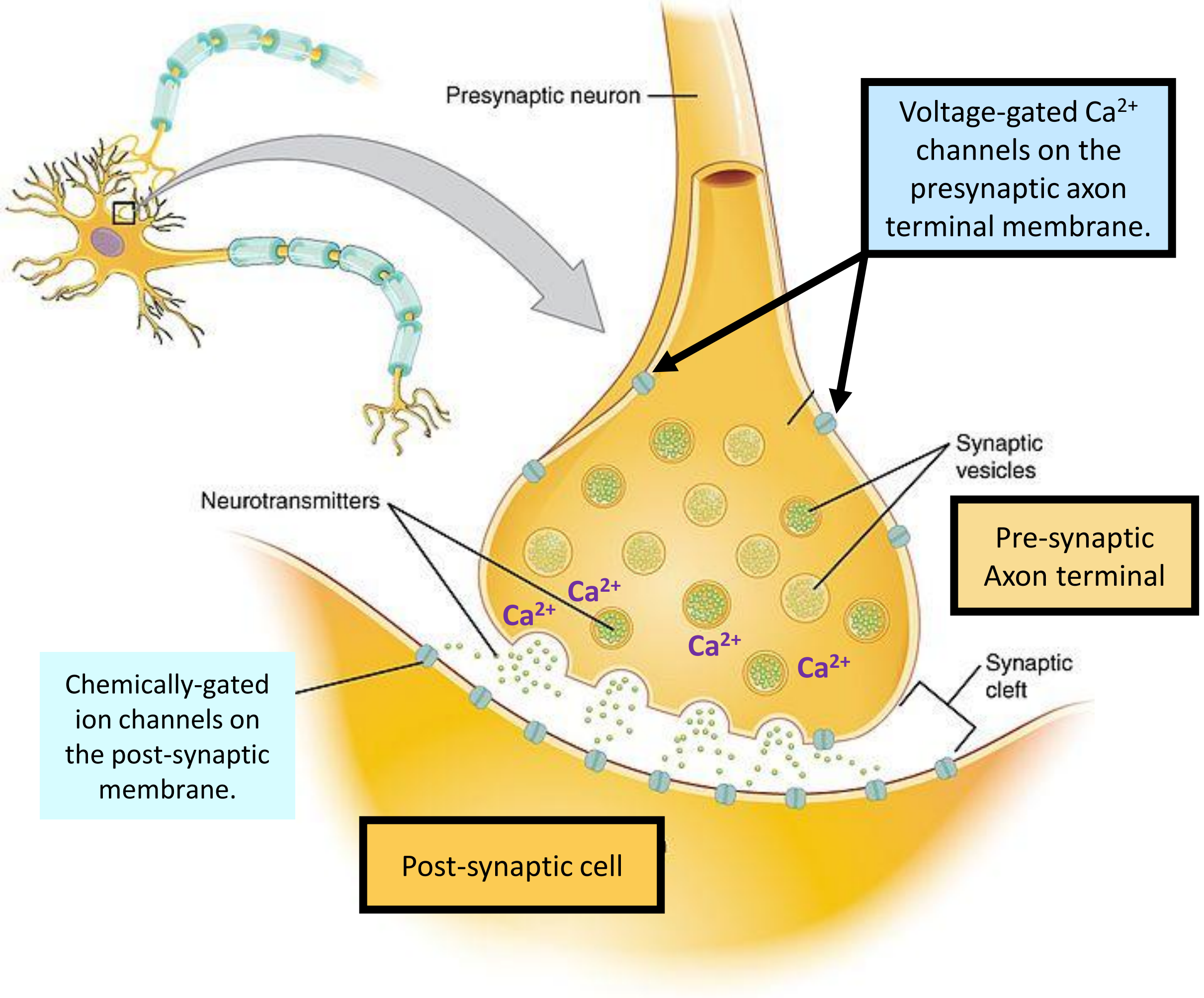
Synaptic transmission step 2: Neurotransmitters are released

- Ca^{2+} interacts with vesicles
- …causing them to fuse with the membrane and release neurotransmitter into the synaptic cleft
- Neurotransmitter diffuses across the synaptic cleft



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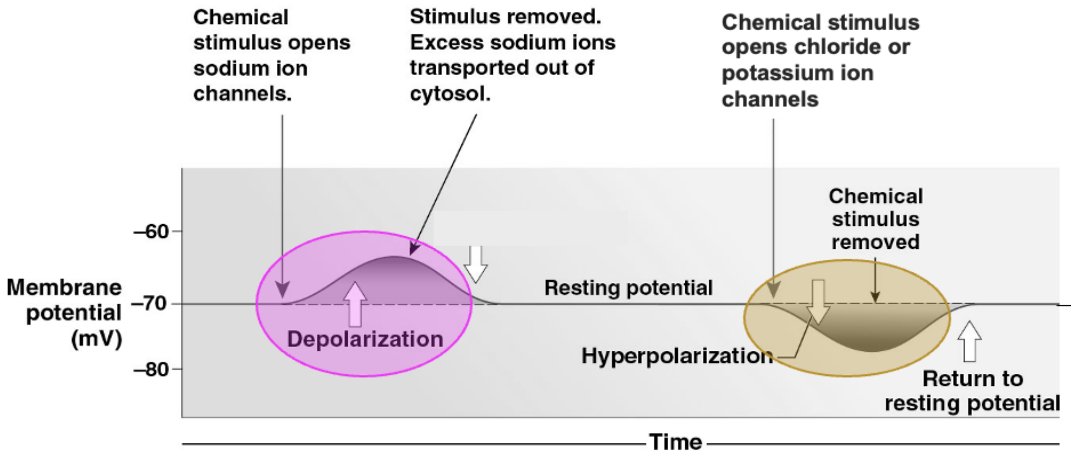
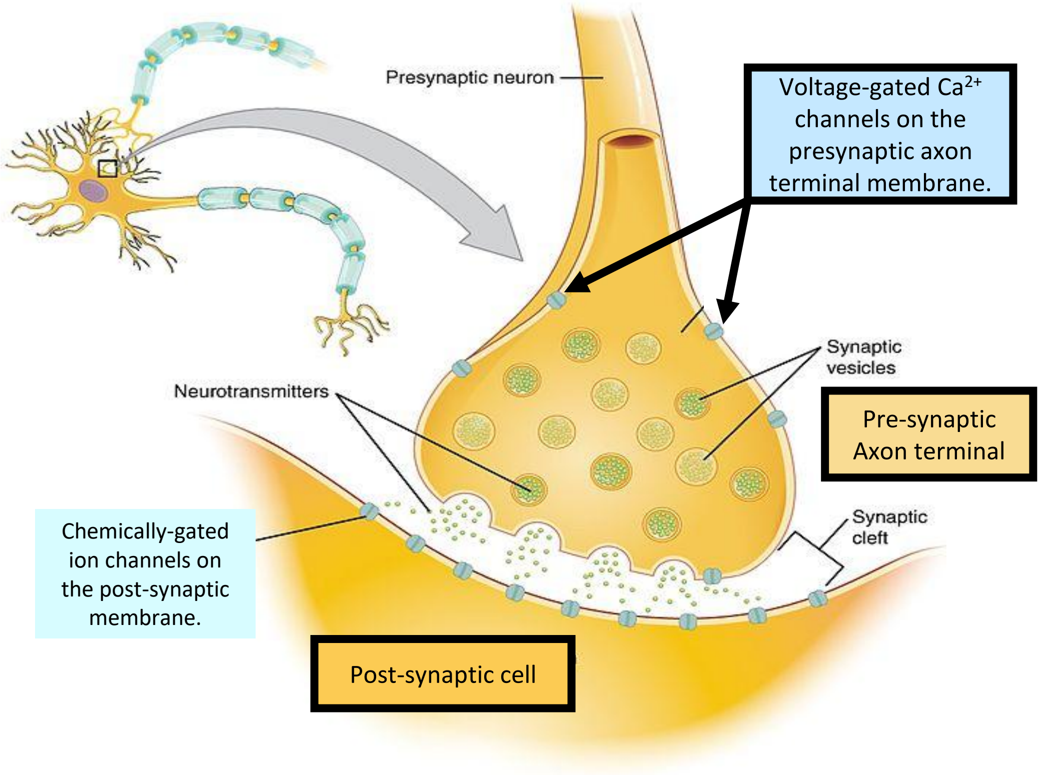
Synaptic transmission step 3: Formation of local potentials

Neurotransmitter binds to chemically-gated ion channels on the post-synaptic cell

- Excitatory neurotransmitter (ex. ACh) opens Na^+ channels to cause EPSPs
- Inhibitory neurotransmitter (ex. GABA) opens Cl^- or K^+ channels to cause IPSPs





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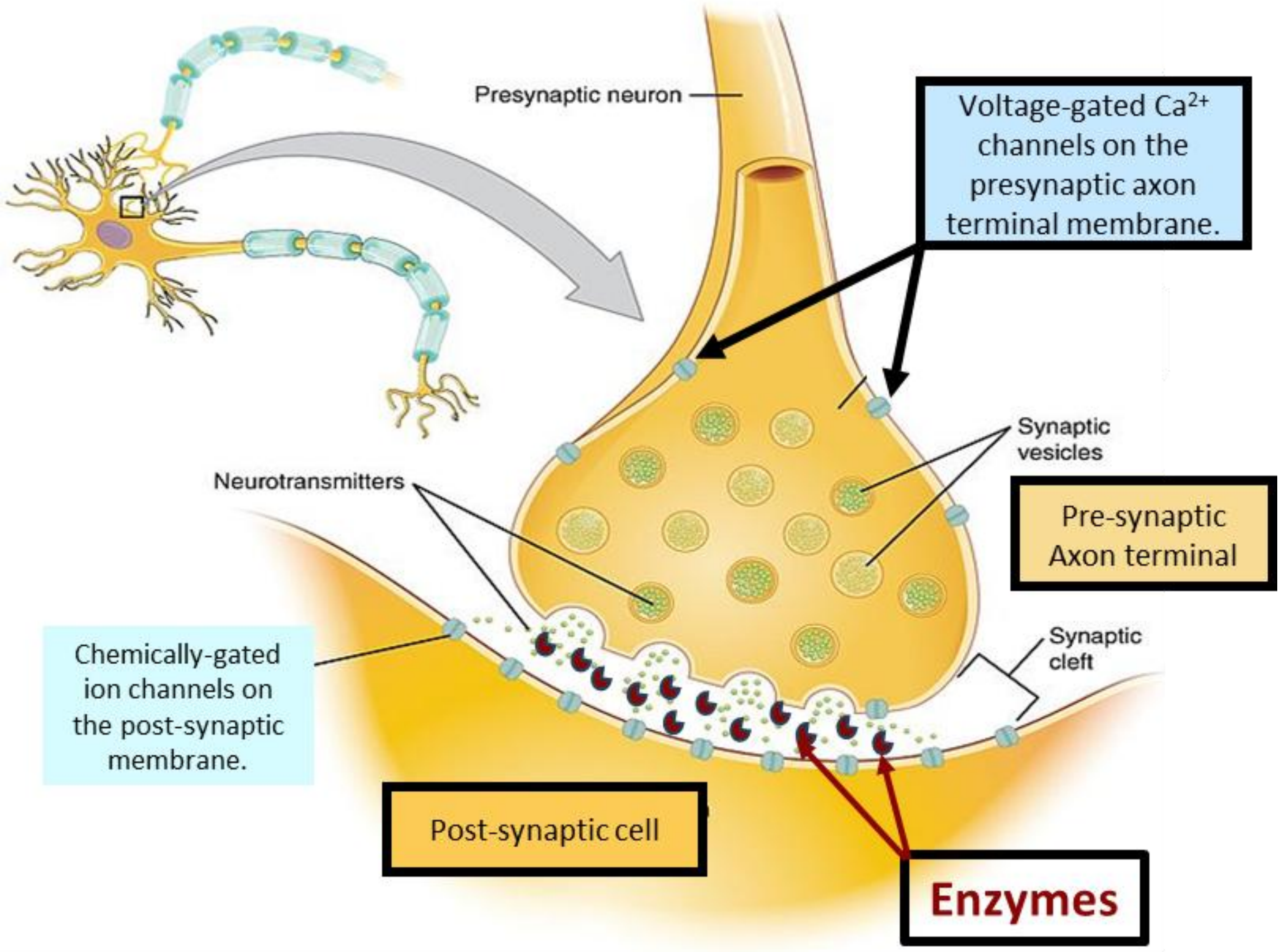
How do we terminate synaptic transmission?

Synaptic transmission ends when:

- Neurotransmitter unbinds from chemically-gated channels
- Enzymes in the synaptic cleft degrade neurotransmitter
- Portions of the degraded neurotransmitter are recycled back into the axon terminal



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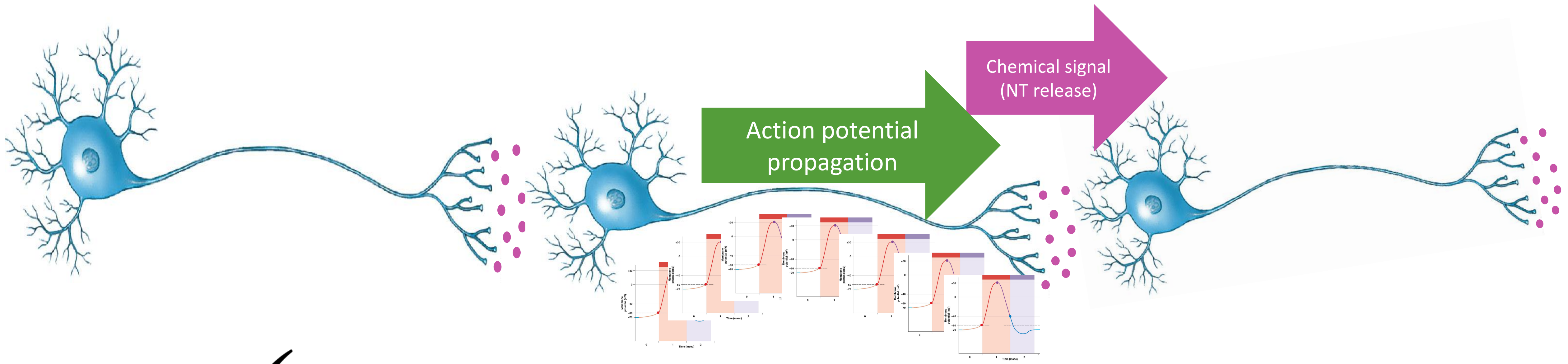
How does an electrical signal (action potential propagation) trigger a chemical signal (neurotransmitter release)?



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Example exam question

Which of the following statements about neurotransmitters is NOT correct?

A. Neurotransmitters are stored in synaptic vesicles.
B. Neurotransmitters are released into the synaptic cleft when calcium levels rise.
C. Neurotransmitters are degraded by enzymes to terminate synaptic transmission.
D. Neurotransmitters are transported into the post-synaptic cell through chemically-gated channels.

HUBS191