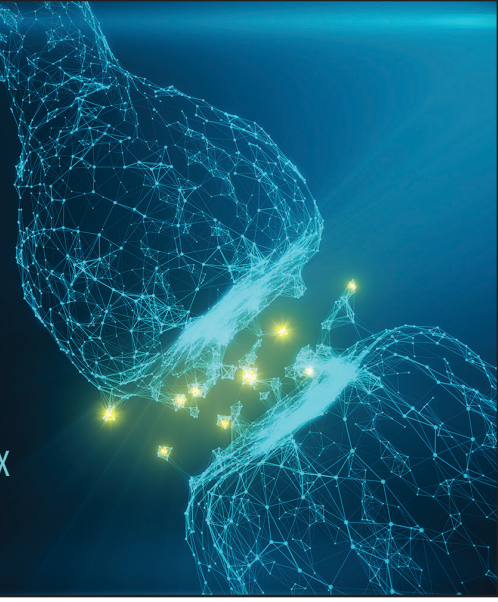
NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

A Nervous Night in the ER: Stings, Poisonings, and More



by
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Introduction

Sari walked into the San Diego ER for her second week of shadowing. Her first week consisted of paperwork and training videos, but she was excited for the coming weeks. She was also a little nervous; she had been waiting for this opportunity since she was a child and throughout her study of biology in college for three years. Sari walked to the nurses' station to sign in and wait for her preceptor, Dr. Mendez.

Dr. Mendez came to the station and began to tell Sari about the few cases the ER had handled earlier that day. Suddenly, the sound of sirens grew louder, the sliding doors opened, and the paramedics wheeled in a man in his thirties who was moaning on a stretcher (Patient 1 – Jerome Robinson). Then, not two minutes later, another ambulance pulled up, this time carrying a young girl on a stretcher. The girl's right arm was red and swollen and she was crying (Patient 2 – Ximena Cruz). Suddenly, the previously quiet ER came alive; patients were being wheeled to exam rooms while paramedics, nurses, and physicians exchanged patient stats.

Sari ran to follow Dr. Mendez who was tending to Patient 1, the moaning man. Then, almost to Sari's disbelief, a third ambulance pulled up, this time with a woman in her late twenties wearing a shorty wetsuit who was also having trouble breathing and seemed to be quite limp and lethargic (Patient 3 – Nguyen Tran).

Just as the team was getting the details for Patient 1, a young man (Patient 4 – Nick Lee) arrived, driven by his friend, complaining of fatigue and sporadic paralysis.

At this point Sari was completely engaged, and information from her physiology course started running through her head. It seemed that all of these patients exhibited some sort of neurological issue. Her professor had just covered the nervous system last week in class and the information was fresh in Sari's mind. Additionally, just this morning Sari had listened to a Science Friday podcast with the award-winning scientist, Dr. Mande Holford, and her work with marine snail venom and its impacts on ion channels. She was ready for this!

In the following sections of this case study, use what you have learned in class to review material about neuron physiology and then apply that information to the patients described.

Review

Before determining how the nervous system has been impacted in the patients, use this section to review basic neuronal anatomy and the physiology of membrane potentials. You will also focus on how the structure and function of ion channels contributes to the stereotypical pattern of an action potential.

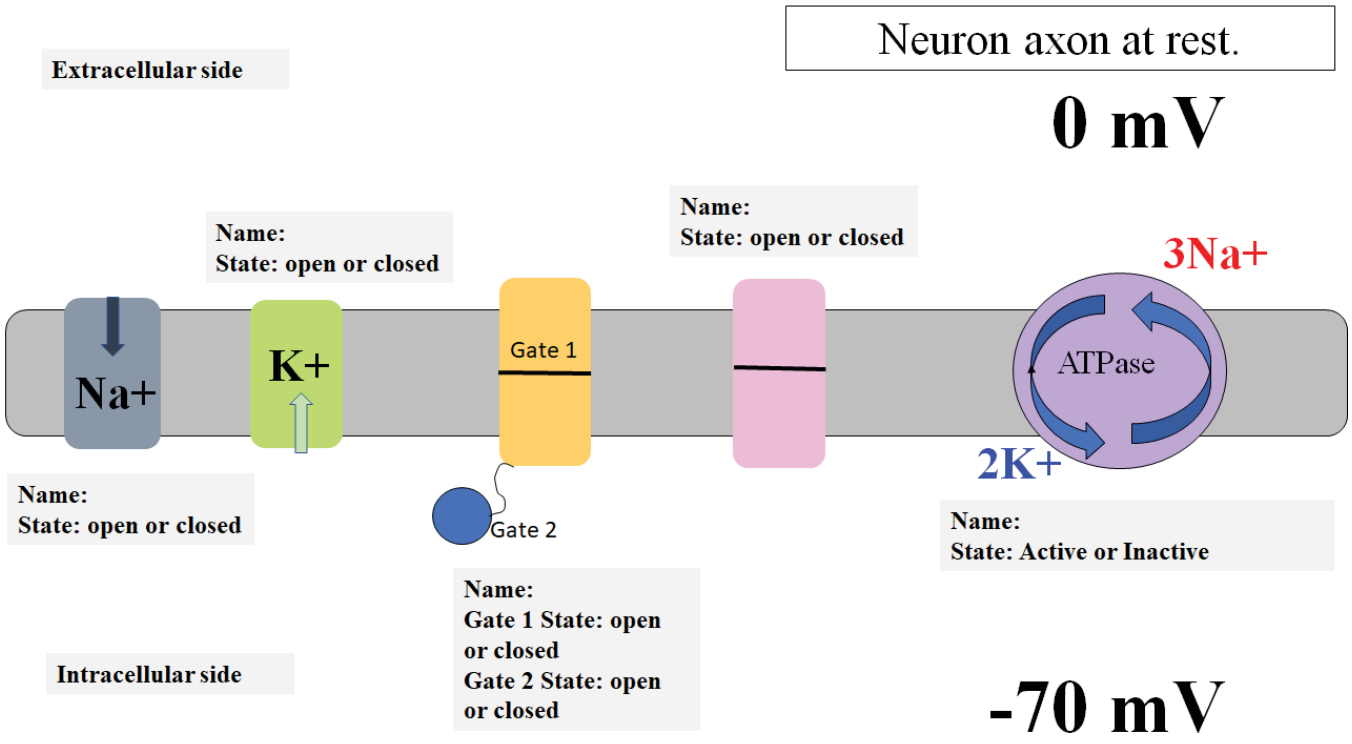
Questions

1. Use the following terms to complete the table below (each term used once): *Membrane Potential (Difference); Threshold Potential; Graded Potential; Action Potential; Depolarize; Hyperpolarize; Leak Channel; Voltage-Gated Channel; Sodium Potassium Pump.*

Term	*Definition*
	A channel in the plasma membrane that allows a specific ion to flow through, down its concentration gradient. No energy expended to use this type of channel.
	Electrical potential difference between the inside and outside of a cell; exists in all living cells. Results from the uneven distribution of ions across a living membrane. Passive and active forces help determine this value.
	A pump located in the cell membrane; uses ATP to move sodium out of the cell and potassium into the cell. Critical for maintaining ion concentrations.
	When the membrane potential difference increases (the inside of the cell becomes less similar to the outside); typically this means the inside of the cell is becoming more negative.
	When the membrane potential difference decreases (the inside of the cell becomes more similar to the outside); typically this means the inside of the cell is becoming more positive.
	A channel that opens in response to a change in membrane potential.
	A change in membrane potential, with varying amplitude that is proportional to the stimulus.
	A rapid, stereotyped series of changes in membrane potential that is conducted along the axon of a neuron or the membrane of a muscle fiber.
	The membrane potential necessary to initiate an action potential.

2. Draw a typical neuron. Make sure to include the dendrites, the axon, the axon hillock, myelin sheath, nodes of Ranvier, soma, and axon terminal.

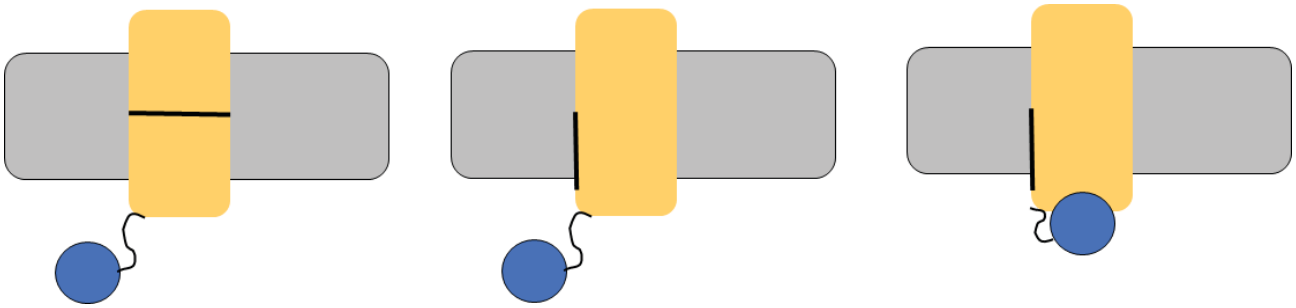
3. Next, label on your drawing where you would generally find sodium-potassium pumps, chemically gated channels, mechanically gated channels, voltage-gated Na^+ and voltage-gated K^+ channels.
4. The figure below is an image of the neuronal axon at rest. Label the five structures (i.e., fill in "Name:") and underline their state (open or closed; active or inactive) at rest. Use each of the following terms once:
   - *Na^+ leak (sodium leak channel)*
   - *K^+ leak (potassium leak channel)*
   - *Vg Na^+ (voltage-gated sodium channel)*
   - *Vg K^+ (voltage-gated potassium channel*
   - *Na^+/K^+ pump (sodium-potassium pump)*



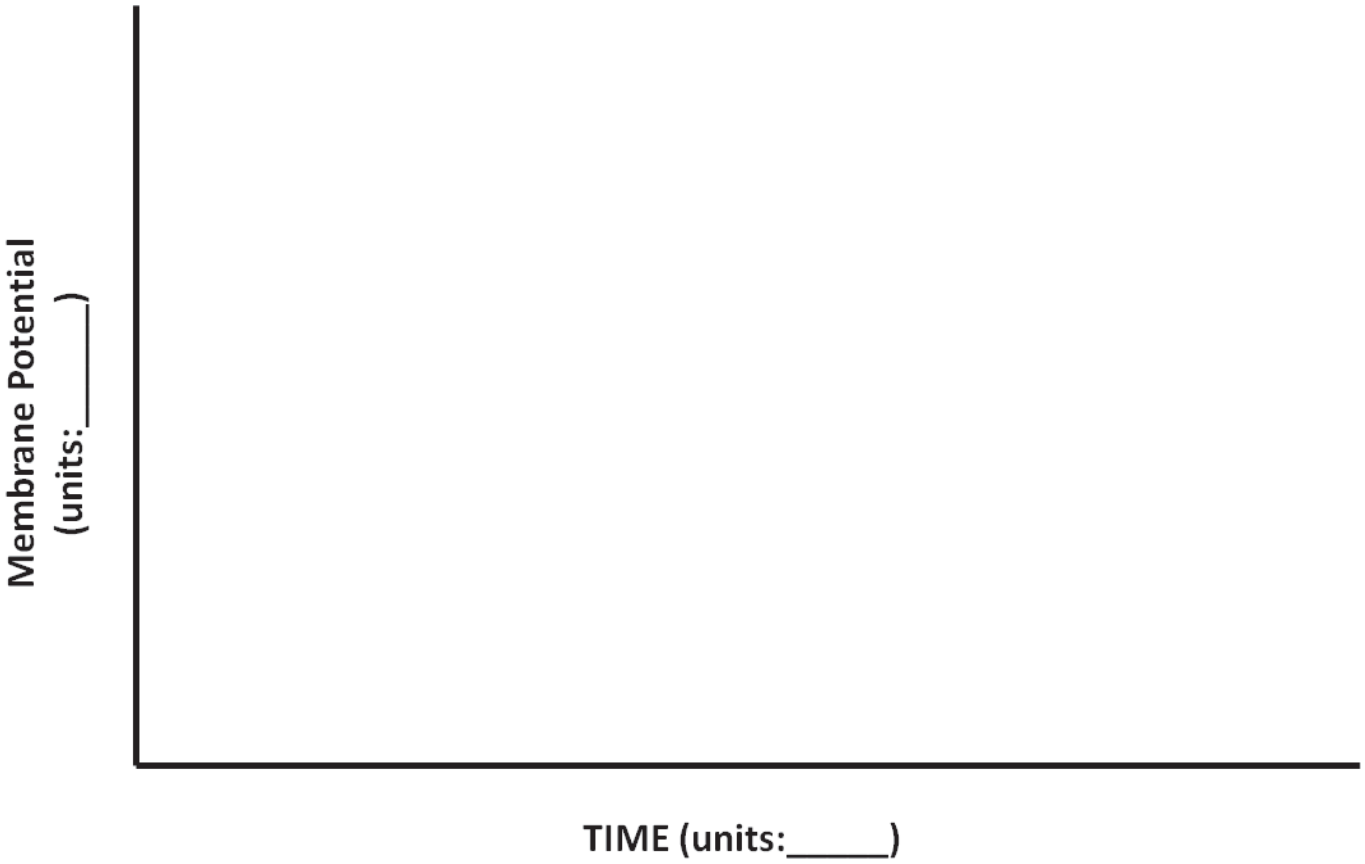
5. Using what you know about membrane potentials fill in the chart below. Put either "yes" or "no" in the boxes.

	Does the structure play a direct role in …	
	… resting membrane potential?	*… action potential?*
Na^+ Leak Channels		
K^+ Leak Channels		
Na^+/K^+ Pump (Na^+/K^+ ATPase)		
Voltage-Gated Na^+ Channels		
Voltage-Gated K^+ Channels		

6. Below is an image of the neuronal voltage-gated sodium channel. In each panel, label Gate 1 (activation gate) and Gate 2 (inactivation gate), and then choose the image that represents the channel at rest.



7. Draw a typical action potential using the graph below. Make sure to include the following:
   - properly labeled x- and y-axes
   - values for resting membrane potential and threshold
   - the point at which voltage-gated Na^+ activation gates open
   - the point at which voltage-gated Na^+ inactivation closes
   - the point at which voltage-gated K^+ channels would normally open and close
   - the movement of sodium and potassium ions and their direction (into or out of cell)
   - accurate timing of key events

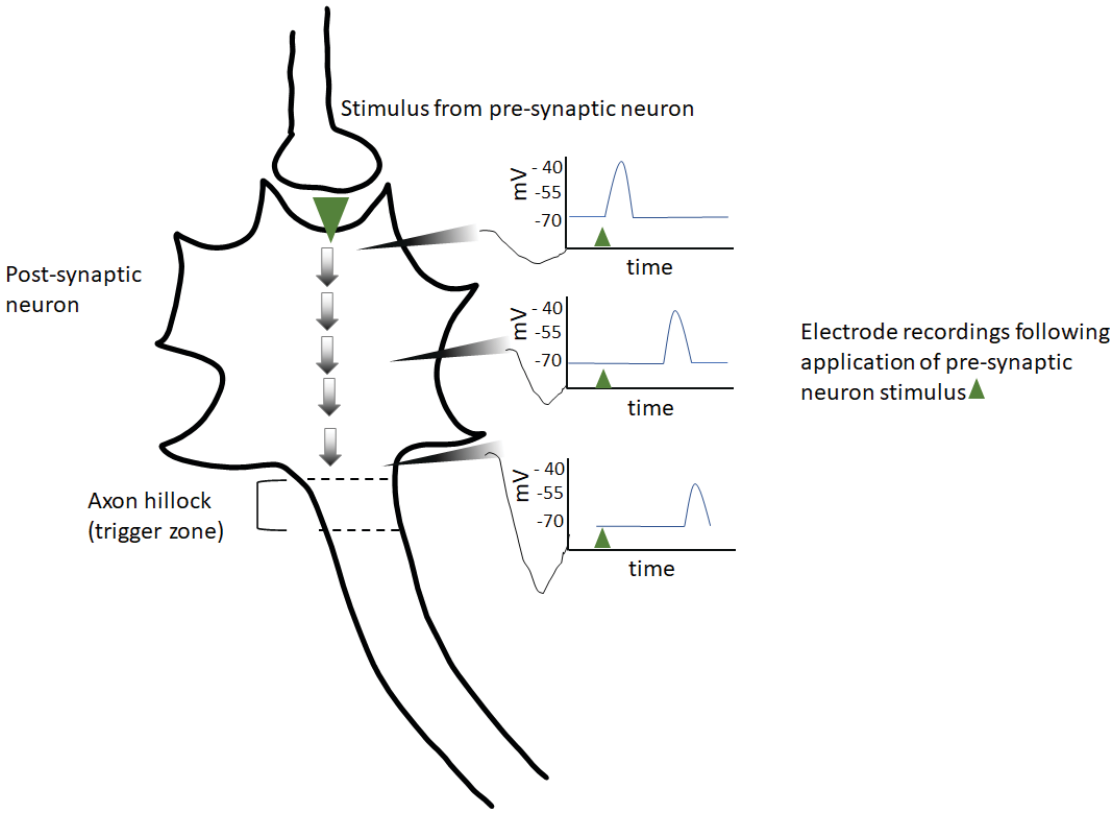


8. What allows a neuron to go from resting potential to threshold potential? (In other words, what triggers an action potential to begin at the hillock?)

9. At what membrane potential are the neuronal voltage-gated Na^+ and voltage-gated K^+ triggered to open?

10. What is the voltage difference from typical resting potential to threshold?

11. Refer to the following figure to answer the questions below.



a. What is the resting potential of the post-synaptic neuron in the picture?

b. What type of stimulus (depolarizing or hyperpolarizing) was initiated by the presynaptic neuron? How do you know?

c. What would we call the change in membrane potential traveling through the soma of the post-synaptic neuron?

d. Would the post-synaptic neuron fire an action potential (yes or no)? Explain your reasoning.

12. What is the absolute change in membrane potential from threshold to peak of a typical action potential?

13. If a cell's resting potential was more depolarized than normal, do you think it would be easier or harder to fire an action potential? Why?

14. If a cell's resting potential is more hyperpolarized than normal, but the threshold potential remains the same, do you think it would be easier or harder to fire an action potential? Why?

Patient 1 – Jerome Robinson

Dr. Mendez and her team were busy hooking Mr. Robinson up to the monitors to gain more information. At that same time, Mr. Robinson's partner, Connor Pham, rushed into the ER and told the medical team that they were having dinner at a fancy sushi restaurant for their anniversary when Jerome began acting drunk (even though they only had a few sips of sake with their first two courses) and then complained about tingling in his lips and tongue. Vitals were stable: heart rate was 82 beats per minute, the patient was conscious and alert. The electrocardiogram taken on arrival was normal, with no arrhythmias noted. Electrolytes were also within normal limits. However, he was having some trouble breathing and his limbs felt weak.

According to Jerome, Mr. Robinson was a previously healthy, 30-year-old male with no significant past medical history. He did not show any gastrointestinal symptoms at dinner, such as nausea, vomiting or diarrhea. One of the courses consumed was fugu sashimi. At that note, Dr. Mendez perked up and said, "I think I know what happened!"

Fugu is a puffer fish. Puffer fish are from the family Tetraodontidae, and like other fish from that family, can contain tetrodotoxin. Tetrodotoxin (TTX) is a potent neurotoxin that blocks voltage-gated sodium channels in most nerves and some muscle cell membranes. TTX is produced by bacteria within the puffer fish and is concentrated in the liver, gonads, intestines, and skin. Thus, if the fish is not prepared properly, TTX could be present in the dish (chefs require special training to serve fugu).

Questions

15. How would application of tetrodotoxin affect resting membrane potential? Why? (In other words, if you had a neuron in a dish and poured TTX over it, what would happen?)

16. How would application of tetrodotoxin affect an action potential? Write out your answer, and then make a graph similar to the one you drew for Question 7 to diagram what your predicted action potential would look like.

Patient 2 – Ximena Cruz

After finishing the above case with Dr. Mendez, Sari found out what happened to the other patients admitted to the ER that night.

Ximena was 6 years old and had been with her parents at their research lab where they were working on isolating various components of scorpion venom for research on their therapeutic properties. The research lab contained multiple vials of toxins found in a diverse set of scorpion species. Somehow, before anyone knew what happened, Ximena had put a vial of one of the toxins in her mouth. Her parents removed it from her mouth, but noted that the vial contained maurotoxin and had just been prepped. Soon after, Ximena began experiencing symptoms from maurotoxin exposure, including, pain, numbness, swelling, nausea, slight difficulty breathing, and inconsolable crying. Maurotoxin blocks neuronal voltage-gated potassium channels.

Questions

17. How would exposure to maurotoxin affect resting membrane potential? Why?

18. How would exposure to maurotoxin affect an action potential? Write out your answer, and then make a graph similar to the one you drew for Question 7 to diagram what your predicted action potential would look like.

Pateint 3 – Nguyen Tran

Nguyen had been out snorkeling with friends in one of her favorite San Diego Bay spots. After a day of swimming, fish watching, and fun, they stopped by a seafood place known for serving shellfish from all regions. They had a post-snorkel meal and watched the sunset. About an hour after eating, as they were all heading home, Nguyen felt unwell. She had abdominal pain, diarrhea, headache, tingling in her mouth and face, and vertigo.

The hospital team concluded that Nguyen had consumed seafood which contained algal toxins. Marine dinoflagellates and algae can produce toxins and these toxins build up in the flesh of fish that consume them. There are various classes of the toxins (e.g., ciguatoxins, brevetoxins), and several can affect neuronal voltage-gated Na^+ channels.

Assume that the toxin Nguyen consumed causes the inactivation gate of the voltage-gated Na^+ channels to close in half the amount of time as unaffected neurons (inactivation gate closes faster than normal).

Questions

19. How would application of this toxin affect resting membrane potential? Why?

20. How would application of this toxin affect an action potential? Write out your answer, and then make a graph similar to the one you drew for Question 7 to diagram what your predicted action potential would look like.

Patient 4 – Nick Lee

Nick Lee arrived with fatigue and sporadic paralysis; this occurred after a workout at the gym. The team ran some tests and determined that Mr. Lee was hypokalemic and likely had thyrotoxic periodic paralysis (TPP). TPP is a rare condition in which increased production of thyroid hormones can lead to episodes of severe muscle weakness. Thyroid hormones increase the activity of the sodium-potassium pump. For each turn, the pump moves 3 Na^+ out and 2 K^+ into the cell. Increasing activity of this pump can result in decreased extracellular potassium. Exercise exacerbates this situation as the epinephrine released during exercise also increases Na/K pump activity.

Questions

21. How would this change in blood potassium concentration impact the resting membrane potential?

22. How would this change in blood potassium concentration impact an action potential? Explain your answer.