NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Honeymoon Havoc:

Action Potentials and Venom Pathophysiology

by
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Part I – The Heart of the Matter

Newlyweds Julien and Tanya Brahim were on a long flight to Australia for their honeymoon. Mr. Brahim looked out the small window of the plane and gazed at the ocean below. He was afraid of flying, and the sight of the water so far below him made his heart beat wildly. He commented on his rapid heartbeat to Tanya. She was a nursing student and had just covered cardiac function in her physiology course last semester. She excitedly explained to her husband that the heart has a unique conduction system involving two types of heart (myocardial) cells—contractile and autorhythmic. Both of these cell types are critical for proper heart contraction and relaxation (i.e., beating), and both rely on the separation of ions across their cells membranes to create an electrochemical gradient.

Questions

1. Use the words below to fill in the blanks in the paragraph that Tanya used to describe the heart. Words may be used once, more than once, or not at all.

Word Bank			
ATP	bundle of His	myosin	gap junctions
calcium (Ca^{2+})	Na^+/Ca^{2+} exchanger	tropomyosin	signal
Purkinje fibers	Golgi apparatus	sympathetic	autorhythmic
Na/K ATPase (pump)	sarcoplasmic reticulum	parasympathetic	contractile
spontaneously	sinoatrial node	acetylcholine	atrioventricular node
troponin	action potential	chordae tendineae	voltage-gated Na^+
internodal pathway	membrane potential	L-type calcium channel	

Anatomy and Organization of the Heart:
The heart has two types of myocardial cells: the (a) _____and (b) _____ In autorhythmic cells, an action potential is generated (c) _____; that is, no outside stimulation is necessary. The autorhythmic cells located in the (d) _____are considered the pacemakers for the heart. Once an (e) _____ (electrical signal) is generated in these cells, the signal spreads down the (f) _____ and reaches the (g) _____, located between the atria and ventricles. Then, the signal travels down the (f) _____and through the (h) _____, which make sure the signal reaches the apex of the heart. Once at the apex, the depolarizing signal makes its way back up the walls of the ventricles so that the ventricles can contract in a coordinated fashion.

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Modification of Heart Rate:
The action potential is also passed from autorhythmic cells to the contractile cells, first in the atria (they contract first) and then in the ventricles (they contract second). The autorhythmic cells of the heart set the intrinsic heart rate. While the heart does not require external stimulation to beat, it can be modified by hormones and neurotransmitters. The autonomic nervous system can increase or decrease heart rate; the (i) _____ nervous system, via norepinephrine and epinephrine, increases whereas the (j) _____ nervous system, via acetylcholine, decreases heart rate.

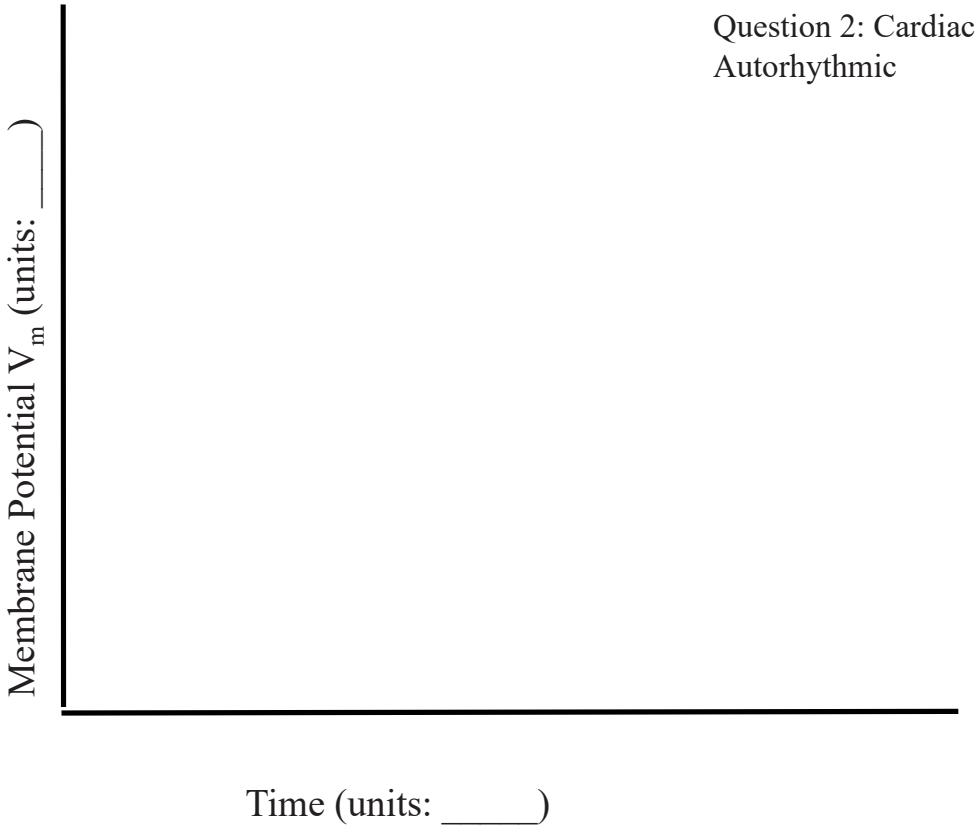
Going from Autorhythmic to Contractile Cells:
The action potential of contractile cells results in depolarization of the sarcolemma, which spreads down the t-tubules of an individual cell and spreads among cells via the (k) _____. Within a contractile cell, the action potential results in an influx of (l) _____ ions into the intracellular fluid/sarcoplasm via the opening of the (m) _____. Once in the cell, the calcium from the extracellular fluid aids in the release of (n) _____from the (o) _____. This creates a calcium spark. Several calcium sparks result in a calcium (p) _____. The Ca^{2+} ions bind to (q) _____ resulting in a conformational change. This conformational change moves (r) _____ thus exposing the actin binding sites on (s) _____, the motor protein behind contraction. These intracellular mechanisms are responsible for the mechanical contraction of the heart. In order for relaxation of contractile cells to occur, calcium ions need to be moved across the contractile cell membrane via the (t) _____or sequestered back into the (u) _____via the calcium ATPase. Thus, (v) _____ions and (w) _____ are required for contraction and relaxation of the heart.

Tanya was now on a roll and excited to continue the discussion of cardiac cell physiology. She grabbed an airplane napkin to draw a picture of the heart cells action potentials for Julien.

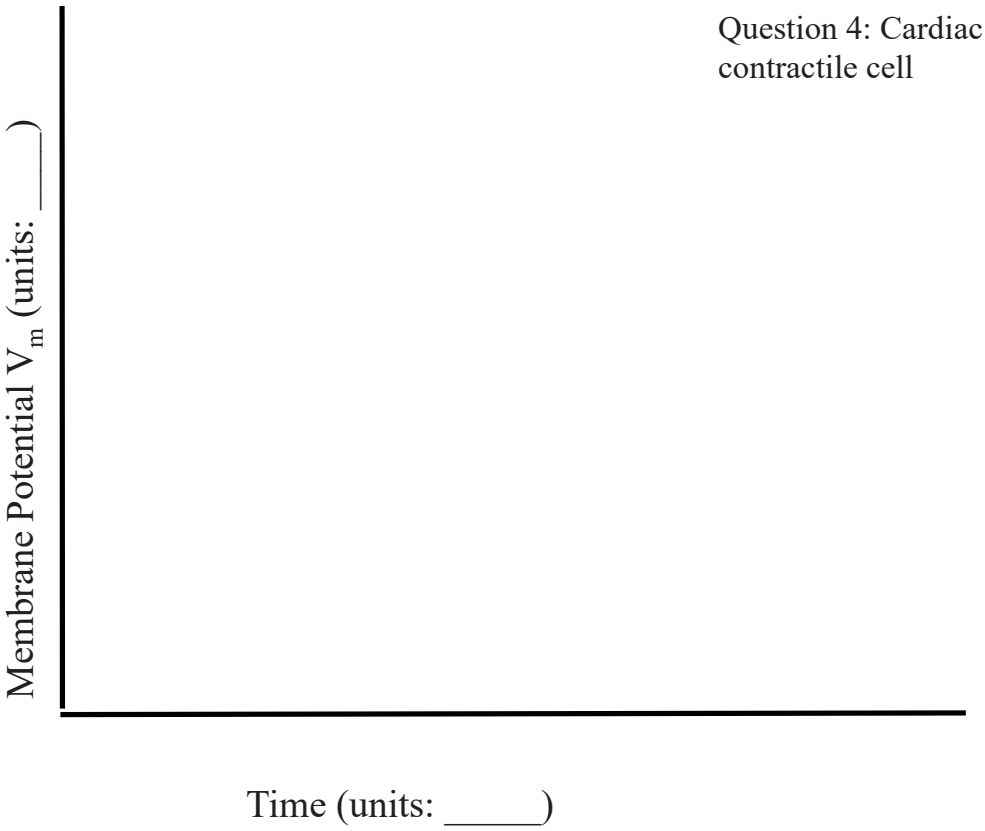
2. Use the provided figure (top of next page) to recreate Tanya's napkin image. Draw a graph depicting the typical action potential of an autorhythmic cell. Make sure to include a label and units for the *x* and *y* axes, the resting potential, the threshold potential, and make sure values drawn are representative of actual values.
3. Now write out a description of the ion movement and channel opening and closing that are responsible for the above graph in autorhythmic cells. Describe what happens in words. Then, add ion types and movement (in or out; influx or efflux) on the graph you drew.

4. Use the provided figure (bottom of next page) to recreate Tanya's napkin image. Draw the standard action potential of a myocardial (cardiac) contractile cell. Make sure to include a label and units for the *x* and *y* axes, the resting potential, the threshold potential, and make sure values drawn are representative of actual values.
5. Now, write out a description of the ion movement and channel opening and closing that are responsible for the above graph in myocardial contractile cells. Describe what happens in words. Then, add ion types and movement (in or out; influx or efflux) on the graph you drew.

Question 2: Cardiac Autorhythmic



Question 4: Cardiac contractile cell



Part II – A Day at the Pool

After a day of long flights and a good twelve hours of catch-up sleep, Tanya decided to lounge in a beach chair in the shallow end of the resort pool. Unbeknownst to her, a funnel-web spider had managed to get into the pool area and was beginning to crawl up her left leg. Suddenly Tanya screeched in pain and looked down in time to see a black spider clinging to her skin. She quickly flicked it off her leg. Luckily, there was a large party at the pool and one of the partiers was a trained emergency medical responder named Talei. Talei quickly ran to Tanya as she was jumping from her chair and asked her what was wrong.

"I think I just got bit by a spider!" Tanya cried. "It hurts so badly!" She pointed to the ground where the bug landed.

Talei grabbed a cup and scooped up the spider that had bitten Tanya. The spider was black and noticeably shiny with a midsection much smaller than the front and back; it also had fine hairs on its legs and was about 0.75 inches long. Upon inspection of the bite, Talei noticed some tenderness, swelling, and that Tanya was sweating profusely. It wasn't long until Tanya was complaining of dizziness and nausea. Talei recognized the spider as a funnel-web; her paramedic training in Fiji covered funnel-web spiders as part of the poisons and venoms section. Talei promptly told one of the other partiers to call for an ambulance and to inform the responder on the phone that funnel-web spider antivenom would be needed. While someone was calling, Talei gathered medical history details from Tanya.

Questions

6. What are the signs and symptoms that Tanya is experiencing?

7. Using the information provided by the NIH Medline website (<https://medlineplus.gov/ency/article/002844.htm>), determine what Talei should do to prevent rapid spreading of the venom until the paramedics arrive.

Part III – Waiting For EMS

As Talei and Tanya waited for the emergency personnel to arrive, Julien came running from the ocean as he noticed the group of people gathering around his new wife. Out of breath, Julien asked what was going on, and Talei explained that a funnel-web spider had likely bitten his wife.

"Is that serious?" asked Julien worriedly.

"It can be very serious," Talei replied, "but it's good that we caught this immediately after it happened. A team with antivenom is on the way."

Talei went on to explain that the toxin in the funnel-web venom is called atracotoxin. This specific chemical interacts with voltage-gated sodium channels; it slows the inactivation gate (e.g., in those channels with both activation and inactivation gates).

Questions

8. Using the below table, hypothesize if the atracotoxin would impact each of the below. Answer *Yes, No,* or *Possibly*.

	Nerve Cell	*Skeletal Muscle Cell*	*Autorhythmic Cell*	*Contractile Cell*
Resting potential				
Depolarization portion of AP				
Repolarization portion of AP				

9. Use the answers you came up with for Question 8 and sketch how the AP of each of the below cells would look after being exposed to atracotoxin. Then, beside each graph, briefly describe your reasoning. For this question, it is likely easiest to assume that the cell was at rest and then exposed to the toxin (but you are welcome to think about different scenarios for the answers; if you choose a different scenario, please state that in your answer).

   9a. *nerve cell:*

   9b. *skeletal muscle cell:*

   9c. *autorhythmic cell:*

   9d. *contractile cell:*

Part IV – Julien's No Good, Very Bad Day

Due to Talei's fast action and pool-side spider identification, Tanya was able to get the antivenom. She still didn't feel like herself, but she was expected to make a full recovery. After this traumatizing ordeal, Tanya decided to spend a quiet day at the beach. She was taking it easy and reading one of her favorite books on a chair in the sand enjoying the sun while her husband was out swimming in the ocean. Julien was closely following a native fish and failed to notice a sign warning for box jellyfish. Before he knew it, he felt a sharp pain on his leg and looked down into the water to see his leg being brushed by what looked like a jellyfish tentacle. Julien began to panic and swam quickly back to shore while suddenly feeling a breathlessness that was not brought on by his fright. His body felt heavy and his heart rate did not feel normal. His leg was swelling up around the sting site and a burning pain shot through his leg. He lethargically stumbled to his wife. With panic in his voice and labored breathing he said he had been stung.

"Is everything okay?" A lifeguard said as he approached Mr. and Mrs. Brahim. "I saw you running from an area that's sometimes occupied by box jellyfish."

He took a look at Julien's leg and immediately pulled out a small bottle from his fanny pack. He poured the contents onto Julien's sting site. "This is vinegar; it'll help until the ambulance gets here."

Julien was rushed to the same hospital his wife had visited the day before.

Question

10. What signs and symptoms is Julien experiencing?

After Julien was stabilized and had been given antivenom, the attending physician came to talk to the Brahims. She explained that the mechanism of action for *Chironex fleckeri*, commonly known as the box jellyfish, is not well understood. However, based on what is known, it seems the toxin has multiple effects. One component of the toxin is thought to function as a calcium pore-forming protein that is inserted into the membrane of autorhythmic cells (and possibly other cells). Tanya thought back to her physiology course and remembered that intracellular calcium concentrations are much lower than extracellular concentrations. She knew that this ion plays a large role in cardiac cells and in muscles. When stung, Julien had felt lethargic and was having trouble breathing, and noticed something off with his heart rate. Tanya started to wonder about the pathophysiology of this venom. While she sat next to Julien she began running through various physiological scenarios in her head.

Question

11. Based on what the physician stated, how do you think this toxin would impact the action potentials and function of autorhythmic cells and the activity of the heart? State your hypothesis, and then draw a graph to accompany your predicted outcome.

Once Julien was feeling better and the pain from his sting had dissipated, he and Tanya cut their honeymoon short and booked flights back to the States. The Brahim's had come to know the dangerous Australian wildlife a little too intimately and were ready to get home and start their life there. They boarded the plane wearing matching hospital bracelets and with a much greater appreciation of wildlife and cellular physiology.