QUIZ 02 - KEY

Instructions: Download the quiz from Blackboard (in Quiz Questions Folder), print a copy and use the paper copy to work through the various questions and problems. Mark the correct answers on it. When you are ready to **submit** your answers, you will see the quiz posted under Quiz Answer Sheets.

Click the quiz name to launch the quiz. Enter your answers to each of the corresponding numbered questions onto the **blank answer sheet** (the questions will not be repeated, simply a blank page for your answers). The quiz may be saved if you do not finish entering your answers in one sitting. When you are finished with the quiz, make sure to **submit** your answers and they will be recorded.

For each question, select the one **best answer** from among those given (multiple choice). Each question is worth one (1) point.

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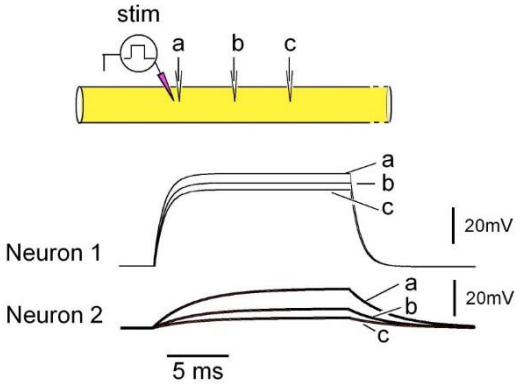
1. You inject identical (subthreshold) rectangular current pulses into axons of two different neurons, one of which is shown in the upper illustration. The injection site is near position "a" for each cell and the resulting voltages are recorded at position a, b, and c, separated by 100 microns each. The illustration below shows superimposed voltage traces from all three sites for Neurons 1 and 2. Based on these data we can say that the axon of Neuron 1 has a _____.



   a. Larger length constant, a smaller time constant, and larger membrane resistance than 2.
   b. Larger length constant, larger time constant, and smaller membrane resistance than 2.
   c. Smaller length constant, smaller time constant, and smaller membrane resistance than 2.
   d. Larger length constant, a smaller time constant, and smaller membrane resistance than 2.
   e. Smaller length constant, a larger time constant, and larger membrane resistance than 2.

   Answer key: Vmax of neuron 1 decays away less over positions a-c compared to the Vmax of Neuron 2, so it has a larger length constant. Neuron one rises and falls faster than neuron 2, so it has a smaller time constant. Vmax is greater in neuron 1 than two, so it has a larger membrane resistance (which indicates that less of the current injected into the cell flows back out).

2. What will happen if an axon is demyelinated (not surrounded by myelin anymore), as in case of some diseases?

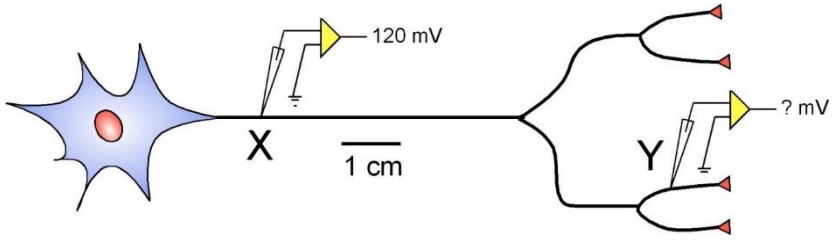
   a. threshold for triggering an AP will be more depolarized.
   b. threshold for triggering an AP will be more hyperpolarized

c. This axon will have a slower AP propagation speed.
d. This neuron will have a longer duration action potential.
e. Both c and d.

Answer key: Myelination will only affect the action potential propagation speed of neurons. Update: if "duration of action potential" is considered as "the total time that any part of the neuron is in action potential state" then D is possibly correct. Anyone who chose E or C is given 1 point for this question.

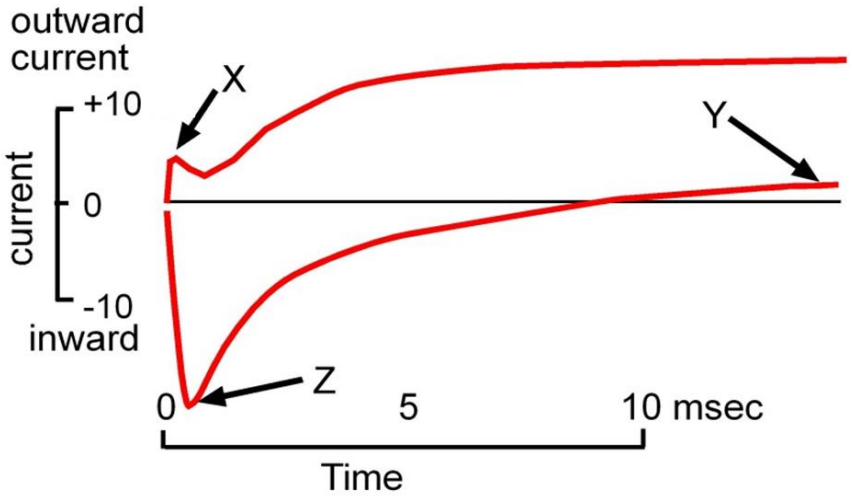
3. The microelectrode inserted into the axon at point X below records a propagating action potential that reaches a peak height of 120 mV above the resting potential. What will the peak amplitude be when the spike arrives at point Y? [The space constant of the neuron is 3 mm.]

a. 0 mV – it will not arrive at Y
b. 30 mV
c. 60 mV
d. 120 mV
e. more than 120 mV



Answer key: All or none.

4. The curves below are from two voltage clamp experiments with a squid axon with a resting potential of -75 mV. In the upper trace the clamp voltage was stepped from resting potential to +65mV since time 0. In the lower trace the clamp voltage was stepped from the resting potential to -20 mV since time 0. According to previous tests, we know that in this experiment the E_{Na+} = +55 mV, E_{K+} = -90mV, and the action potential threshold = -55mV. Only considering potassium and sodium, the **major** currents at X, Y, and Z are, respectively:
(Hint: The current you see on the figure is the current that is injected to counteract the natural flow of ions in the cell at a particular, constant voltage.)



a. inward sodium; inward potassium; outward potassium
b. inward potassium; inward sodium; outward sodium
c. outward potassium; outward potassium; inward sodium
d. inward sodium; outward potassium; outward sodium
e. outward sodium; outward potassium; inward sodium

Answer key: When you inject positive current, you are counteracting a negative (outward) current (positive ions flowing out *or negative ions flowing into* the cell). When you inject negative current, this means you are counteracting positive (inward) current (positive ions flowing into the cell *or negative ions flowing out of* the cell). Here, the bottom trace is using a voltage step above action potential threshold, but below E_{Na}. Therefore, you see a transient inward sodium current followed by a long lasting outward K current. In the above trace, which is above E_{Na}, sodium current is reversed so that sodium is leaving the cell (to try to get back to E_{Na}) rather than entering it, so you see an outward Na transient followed by a persistent outward K current (in both voltage steps, we are much higher than E_k, so it is outward in both cases.

5. Which of the following statements is **FALSE**? If all statements are true, pick e.

a. Opening chloride channels in a typical neuron would increase the ability of the neuron to fire action potentials.
b. The repolarization phase of an action potential is a consequence of both an inactivation of Na channels and a delayed opening of K channels.
c. The Nernst equation describes a situation in which there is no net current across the membrane for a particular ion, so if only one ion is permeable at rest, there is no need for ion pumps to maintain ion concentrations.
d. The threshold of an action potential depends on the relative amount of current flowing through Na and K channels.
e. All of the above are true.

Answer key: Opening chloride channels would reduce the ability to produce action potentials by decreasing the RMP (and decreasing membrane resistance).

6. You have found a toxin from the mamba snake that broadens the width of the action potential (for example, measured at half its height). Which of the following might explain the change?

   a. The voltage dependent Na+ channel activation (m) gates are not closing quickly enough.
   b. The voltage dependent Na+ channels are closing too quickly.
   c. The voltage dependent Na+ channel inactivation (h) gates are not closing quickly enough.
   d. The voltage dependent K+ channels are not opening quickly enough.
   e. Both c and d.

   Answer key: The venom makes the action potential last for longer than usual by delaying the return to normal. The venom has no effect on the speed it takes for the neuron to fire, which means that the Na+ channel activation (m) gates are unaffected. The venom could be affecting the Na+ channel inactivation (h) gates by delaying when they close, as this would broaden the width of the AP by slowing the depolarization of the cell. Another way to slow depolarization and widen the AP would be to delay the opening of the K+ channels. Therefore, both C and D are correct.

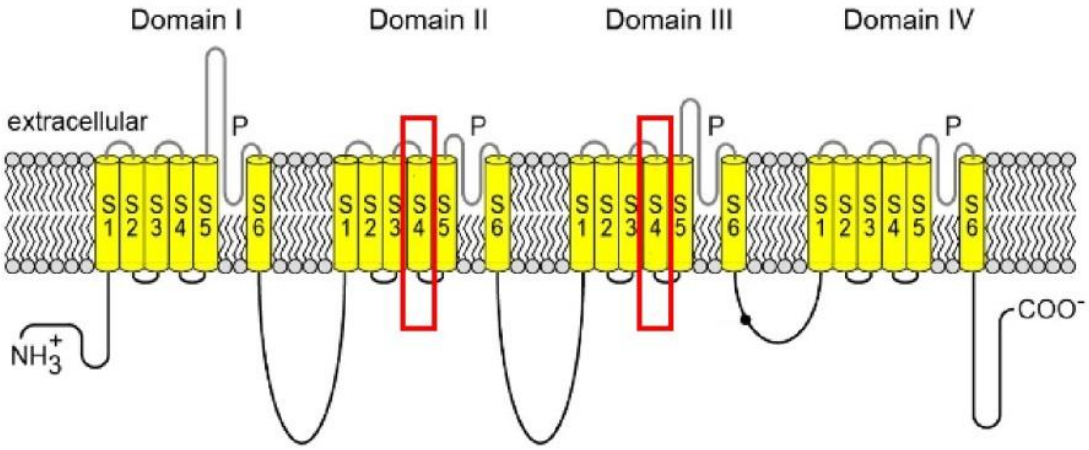
7. In response to a current step, the rate of change of the membrane potential over time is determined by the membrane capacitance and the membrane resistance. Why then does the equation for the length constant not contain any measure of capacitance, but only resistance measures?

   a. The length constant refers only to a time when the voltage is at the new steady state during current injection, when all of the membrane current is flowing through the resistance rather than through the membrane capacitance.
   b. The capacitance is the same along the neuron and so cancels out in the equations for the length constant.
   c. The capacitance only matters at the current injection site, but not at distances farther away from it.
   d. The membrane constant is constant, so capacitance does not matter.
   e. Both b and c are true.

   Answer key: Capacitance shapes the time course of a signal, but not the end voltage change, so it does not matter for the length constant.

8. A molecular biologist is exploring the physiological properties of voltage activated sodium channels by mutating specific sites in the voltage activated sodium channel gene. The first targeted sites in the resulting protein are located in the region of the **red rectangles** (marked by solid line) shown below and the mutations result in conversion a

charged arginine amino acid to a **neutral** alanine. What effect do you expect these mutations to have on the physiology of these sodium channels when they are expressed in a cell membrane studied under normal voltage clamp, during which a depolarization current was injected to the **inside** of the cell?

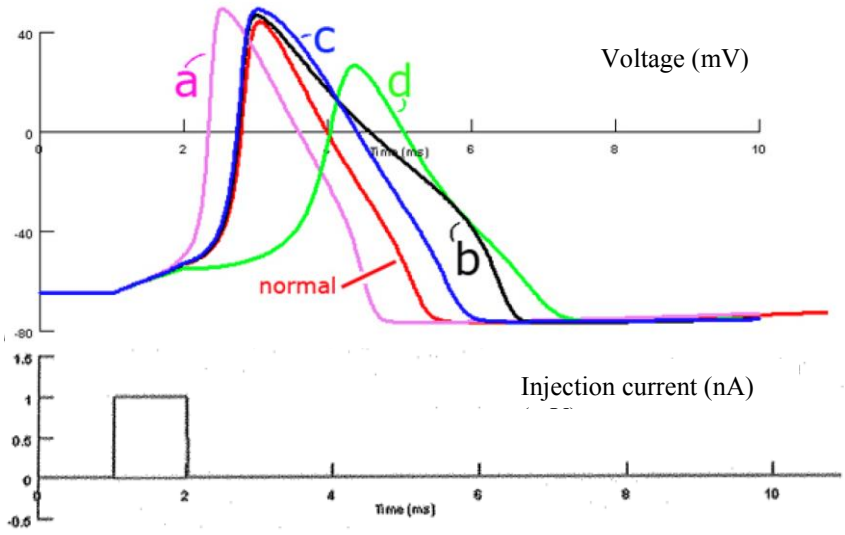


a. They will activate more rapidly than normal sodium channels.
b. They will require more depolarization to activate.
c. They will inactivate more rapidly than normal sodium channels.
d. They will inactivate more slowly than normal sodium channels.
e. They will not be affected by these mutations.

Answer key: The S4 loops contain positively charged residues which contribute to the voltage sensitivity, and the 'm' gate of the voltage-gated sodium channel. This would mean they would activate slower, or potentially not at all, depending on other factors.

9. The five action potentials shown below are all recorded from the same nerve cell axon in response to the identical current pulse shown below. The action potential is the curve labeled "normal" for this cell. The four other traces are action potentials under the influence of 4 different drugs, which alter the speed at which the m-gates and h-gates of the sodium channels and the n-gates of the potassium channels open and close. Each drug affects one gate only, either by slowing down, or speeding up the opening or closing of the gate. Which curve shows the effect of the drug that slows the opening of the m-gate, but has no effect on any other gate time constant?

a. Curve a
b. Curve b
c. Curve c
d. Curve d



Answer key: It must affect the activation of Na channels, but not its inactivation. A seems like it decreases it (by increasing the rate of activation of Na channels). B seems like it increases the n-gate time (decreasing the rate of activation and therefore also turning off K currents). C seems like it increases h-gate time (decreasing the rate of inactivation). Only D seems like it could be caused by increasing m-gate tome (thereby decreasing the rate of activation), since it delays the peak but doesn't affect the repolarization.

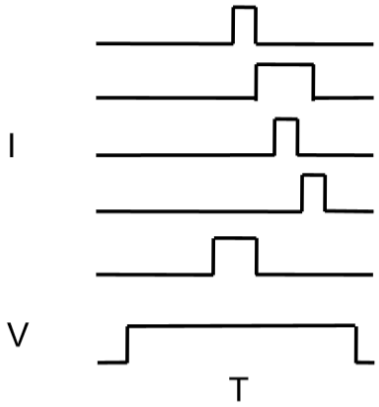
10. You have identified a patient with a genetic disorder that you have reason to believe might be a mutation in an ion channel. The neurons in the patient are excessively active. Which of the following mutations would NOT be a possible explanation for the excessive excitability?

    a. A mutation in the S4 region of the Na+ channel that increased how sensitive the m gate in the channel was to a membrane depolarization.
    b. A change in the pore region of the voltage dependent Na+ channel that increased the ion flow through the single channels.
    c. A mutation in the voltage dependent K+ channel pore that decreased the flow of K+ through the pore.
    d. A mutation of the Na+ channel h gate that increased its sensitivity to a membrane depolarization.
    e. A mutation in the promoter region of the voltage dependent Na+ channel gene that increased expression levels of the channel.

    Answer key: D would make it more probable for Na channels to turn off prematurely, making the neuron LESS active.

Thought questions (ungraded):

11. You collect the following single channel patch clamp recordings of an individual voltage dependent channel during repeated voltage steps from -70 to -30 mV. The baseline current is 0pA.



A) Propose an ion which could be permeable through the channel, and explain why you chose this ion.
B) Why does the channel not open at the same time on each voltage step?

Answer key:
A. You can see an OUTWARD current here (positive ions flowing out of the cell, or negative ions flowing in). Therefore, the two simplest is that this is a K+ or Cl- channel. Na+ or Ca++ would not be right, for example.
B. The channel does not open at the same time point (or for the same length of time, for that matter), because channel opening is probabilistic. This means that channels will open with increasing probability with more depolarized voltages.

12. What would happen to the action potential threshold of a particular neuron if the neuronal membrane had fewer voltage gated sodium channels. Why?

Answer key: If there were fewer voltage-gated sodium channels, the action potential threshold would depolarize. The action potential threshold is set because this is the point where depolarizing sodium current overtakes polarizing K (etc.) currents. If there are fewer Na channels to turn on, the cell will have to depolarize further to outweigh the resting potassium currents. The peak of the action potential may also be a bit less depolarized, but this may be a very subtle effect.