Name: _____ **Student #: _____**

BIO 3305

Cellular Physiology

Prof: John Lewis

MIDTERM #2

November 5, 2018

- **4 Questions**
- **5 pages** total
- **40 marks** total

Please answer **ALL** questions.
Please write your name and student # on all pages.

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1. **(10 marks)** You are recording membrane potential from two neurons that are connected by a chemical synapse (i.e. transmitter binds to ligand-gated ionotropic receptor). The resting potential of the presynaptic neuron is -65mV but it spontaneously fires an action potential (AP) ten times per second. The resting potential of the postsynaptic neuron is also -65mV and every AP in the presynaptic neuron results in a postsynaptic potential (PSP). In this context, determine whether each of the following statements is TRUE or FALSE. **Please circle the correct answer.**

(a) [TRUE] or FALSE | If the depolarization phase of the AP in the presynaptic neuron involves voltage-gated Na^+ channels (as in the squid axon), then increasing extracellular Na^+ concentration should increase the AP amplitude (i.e. peak voltage during AP).

(b) TRUE or [FALSE] | If the presynaptic AP is mediated only by Na^+ and K^+ channels, then blocking voltage-gated Ca^{+2} channels in the presynaptic terminal will have no effect on the postsynaptic potentials.

(c) [TRUE] or FALSE | If the ionotropic postsynaptic receptors are permeable to Cl^- ions and the Cl^- equilibrium potential (E_{Cl}) is -60mV, then the PSPs should be depolarizing (i.e. excitatory).

(d) TRUE or [FALSE] | Because the presynaptic APs are separated by 0.1 seconds, it would be impossible for this synapse to exhibit any form of synaptic plasticity i.e. the postsynaptic potentials would always be identical in amplitude.

(e) [TRUE] or FALSE | If the PSPs are mediated by ionotropic receptors permeable to both Na^+ and K^+ ions, you could set the postsynaptic membrane potential to some value between E_K and E_{Na} for which the synaptic potentials would be eliminated.

2. **(4 marks)** Consider the factors that influence AP propagation along a single axon, and determine whether each of the following statements is TRUE or FALSE. **Please circle the correct answer.**

(a) TRUE or [FALSE] | Increasing the number of "leak" (or background) potassium channels will increase the membrane resistance and increase AP propagation velocity.

(b) TRUE or [FALSE] | Applying a drug that reduces myelination should increase the length constant of the axon.

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3. (8 marks) You are recording action potentials (APs) from a previously unidentified cell and have performed a number of experiments to study the control of membrane potential. In one experiment, you gradually decreased extracellular Na^+ concentration, $[Na^+]_{ex}$. You have assumed that the ionic basis of the AP is identical to that of the "classic" squid axon.

(a) Describe in detail the essential components of this classic AP mechanism and how they can lead to the production of an AP.

(b) Explain how the decreased $[Na^+]_{ex}$ should affect this AP and its production.

Please write your answers to both (a) and (b) within the box below

(a)

- ***Voltage/time dependent Na, K channels***
- ***Na channels activate fast at depolarized potential, V-dependence allows for positive-feedback activation of Na channels and the large increase in Vm***
- ***Na channels inactivate at depol potential with a slight delay, leading to repolarization***
- ***K channels activate at depolarized potential at slight delay and do not inactivate, and contribute to the repolarization and after hyperpolarization***

(b)

- ***decreased $[Na^+]_{ex}$ should decrease the AP peak/amplitude, and increase threshold, due to the decreased current through open Na channels. It could also result in a "narrower" AP, depending on the relative timing of Na+ channel activation-inactivation and K+ channel activation***

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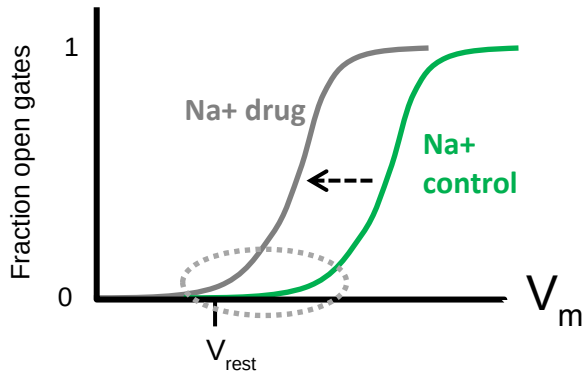
4. Assume that you are recording from a neuron that has a resting potential of -70mV and it produces action potentials with an ionic basis that is identical to that of the "classic" squid axon (with E_{Na}= +50mV, E_K= -90mV).

(a) (8 marks) You apply a drug that shifts the activation curve for voltage-gated Na^+ channels a few millivolts to the left. Briefly describe <u>two different effects</u> that this manipulation will have on the AP properties. Be sure to explain your reasoning.

Please write your answer within the box below

The largest impact here will likely be on the <u>threshold for AP generation</u> (the minimum stimulus amplitude at a given pulse duration that will produce an AP)
Assuming inactivation is not affected, more Na+ channels will be open at a given membrane potential, so it will be easier (require lower stimulus amplitude) to initiate the positive feedback required for an AP. If the shift in activation is far enough to the left, then it is possible that spontaneous APs will be produced.

In addition, <u>AP amplitude and/or duration could be increased</u>. Again, assuming Na channel inactivation is not affected, there will be more activation and less inactivation at a given Vm, allowing for a larger peak and depending on relative time-dependencies, <u>possibly</u> an AP with longer duration



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4. …cont'd

(b) (10 marks) After washing out the drug from part (a), you resume recordings in the control condition. You then discover a synaptic input to this neuron that is mediated by an ionotropic receptor permeable to Cl^- ions (E_{Cl}= -85mV). Surprisingly, a brief (5ms) postsynaptic potential due to this synaptic input can produce an AP. Describe in detail **an hypothesis** that could explain this observation. Then describe **two experimental manipulations** (along with **the associated predictions**) that would allow you to test your hypothesis.
(Feel free to use the back of this page if necessary)

E_{Cl} is -85mv, more hyperpolarized than resting potential, so opening Cl- channels will cause a hyperpolarization (hence the "surprise").

In terms of AP production, the hyperpolarizing PSP could deactivate Na+ channels (decrease the number of activated channels) but also remove inactivation of Na+ channels. After the PSP, the membrane potential will recover towards the resting potential. But inactivation would recover more slowly than activation, so there will be more Na+ channels available (i.e. open) when the membrane potential reaches its original resting level; thus the membrane will continue to depolarize. If the positive feedback cycle of Na+ activation occurs before Na+ inactivation "catches up", then an AP will be produced.

Testing this hypothesis could involve manipulations of:

- ***inactivation and/or activation time scales – if inactivation is not sufficiently slow relative to activation time scale…then hyperpolarization will not result in an AP***
- ***inactivation voltage dependence (i.e. inactivation curve) – shift to the left, so much less "removal of inactivation" for a given level of hyperpolarization…then no AP.***

Other hypotheses may be possible:
For example, an ion channel (with E_{ion} sufficiently above Vrest), that is activated at hyperpolarized voltages.

…but a valid hypothesis must be consistent with a hyperpolarization-induced AP; and the manipulation/prediction must directly relate to your hypothesis.