Name: ___________________________   **Student #: ______________**

BIO 3305

Cellular Physiology

Prof: John Lewis

MIDTERM #1

October 1, 2018

- **4 questions**
- **4 pages** total
- **40 marks** total

Please answer **ALL** questions.

Please write your name and student # on all pages.

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1. **(6 marks)** Determine whether each of the following statements is TRUE or FALSE. **Please circle the correct answer.**

(a) TRUE or FALSE | A distinguishing feature of *primary* active transport is the requirement of energy from the hydrolysis of ATP.

(b) TRUE or FALSE | An active transporter that is *electrogenic* will generate a charge difference across the membrane.

(c) TRUE or FALSE | The direction of transport through membrane ion channels is independent of the concentration gradient of the ion involved.

(d) TRUE or FALSE | At a depolarized membrane potential, individual voltage-gated ion channels are always open.

2. **(8 marks)** You are investigating the ionic basis of the resting membrane potential of a newly-discovered sensory cell in the gut. You have established that these cells are permeable to K^+, Cl^-, Ca^{+2}, Na^+ ions, and **only** these ions contribute to the resting potential (i.e. no other ions are involved in the membrane potential). The equilibrium potentials are E_K= -100mV, E_{Cl}= -90mV, E_{Ca}= +30mV, E_{Na}= +100mV. Given these observations, determine whether each of the following statements is TRUE or FALSE. **Please circle the correct answer.**

(a) TRUE or FALSE | If K^+ and Na^+ permeabilities are equal, the resting potential must be between -90mV and +30mV.

(b) TRUE or FALSE | If Cl^- and Ca^{+2} permeabilities are equal, the resting potential must be between -90mV and +30mV.

(c) TRUE or FALSE | Blocking K+ channels will result in a depolarization of the membrane.

(d) TRUE or FALSE | If K^+ and Na^+ permeabilities are equal and all Cl^- channels are blocked, then the membrane potential will be negative.

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3. **(10 marks)** While recording from your favorite cell, you observe spontaneous depolarization events lasting about 200ms; they occur about once every second. The resting potential of this cell is -75mV and the membrane potential depolarizes to -70mV during these events. You know that Cl^- is **not** involved in the resting potential, but you hypothesize that Cl^- channels are solely responsible for the depolarization events. Unfortunately, there are no specific drugs that block these channels. In the space below, describe **two distinct experimental manipulations** that will allow you to test your hypothesis (i.e. one manipulation must involve ion concentrations and the other must involve the membrane potential directly). Be sure to include a specific discussion of the **predicted outcomes for each of your proposed experiments**, along with any assumptions you are making.

1. Manipulate membrane potential (Vm) above and below E_{Cl}.

In this case, you must make an assumption about E_{Cl}. Since the resting potential does not involve Cl, then the depolarizing events must be due to opening Cl channels (i.e. closing Cl channels would mean that some are open at the resting potential).
Therefore, E_{Cl} must be above (or equal to) -70mV (i.e. less negative than -70mV).

Then you change Vm so that it is above E_{Cl} , equal to E_{Cl} and below E_{Cl}.
The predicted outcomes of this experiment will be such that when Cl- channels open, Vm will go towards E_{Cl}. i.e. hyperpolarizing, no change, and depolarizing respectively

2. Manipulate ECl or Cl concentrations.

Similar to above, you must assume an initial value of ECl (above -70mV).
And then the experiment is to change ECl to a value more negative than -75mV (then predict hyperpolarizing events) and equal to -75mV (predict no change in membrane potential when the channels open)

Note that two distinct experiments are required here i.e. manipulating E_{Cl} and Vm. In other words, increasing E_{Cl} and decreasing E_{Cl} (or increasing and decreasing extracellular Cl) are not two distinct experiments, because only one variable is manipulated.

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4. You have recently made recordings from a previously unknown cell in the mouse auditory system and found that it has a resting membrane potential of -20mV. You would like to identify the ionic basis of this resting potential. Your initial experiments have allowed you to rule out all but three ions: K^+, Cl^-, Na^+ (i.e. only these ions, and no others, could possibly be involved in the resting potential).

(a) (6 marks) Given these observations, **state your hypothesis** (in the space below) for the ionic basis of the resting potential in this cell. Be sure to include any necessary assumptions.

The resting potential is based on <u>at least two of the three ions</u>, with the following equilibrium potentials: at least one above -20mV and the other below -20mV.

If only one ion is chosen then the equilibrium potential must be equal to -20mV

(b) (10 marks) From additional experiments you now know that **all three** ions (K^+, Cl^-, Na^+) are definitely involved in determining the resting potential. You then find that after blocking all Na^+ channels the membrane potential depolarizes to -10mV. Given these new observations, **outline a new hypothesis** for the ionic basis of the resting potential in this cell (or explain why the original one still holds**).** Then describe at least **one experimental manipulation,** along with **the associated prediction(s),** that would allow you to test this hypothesis. (You can use the back of this page if necessary)

The following outlines one solution; others involving different combinations of equilibrium potentials etc are also possible:

<u>Hypothesis:</u> The resting membrane potential is determined by all three ions, with specific conditions on the equilibrium potentials: $E_{Na} << -20mV$ ***and*** $E_K > -10mV > E_{Cl}$
You have to consider that Vrest= -20mV is when the effects of all ions are in equilibrium. Then when you block Na channels, the new membrane equilibrium (or "balance point") of -10mV is between K and Cl alone (EK and ECl)

<u>Expt test:</u> manipulate E_{ion} ***directly by increasing/decreasing extracellular/intracellular concentration of this ion, then apply the Na+ channel blocker***
Prediction: the resting potential should go towards the new E_{ion} ***and after the blocker the membrane potential should also move in the direction of the new*** E_{ion} ***(relative to the original result)***

Could also (in principle) apply another drug to block a specific channel, but assumptions must be stated very clearly (drug is specific, with the effects on membrane potential explicitly stated)

Again, other hypotheses involving different specific details may be possible, but a valid hypothesis must be consistent with all observations and supported by any necessary assumptions