2. (15 points) From Wake et al., "Control of local protein synthesis and initial events in myelination by action potentials". H. Wake, P.R. Lee, R.D Fields, *Science* **333**, 1647 (2011), available on Canvas with this exam.

A. Please read the abstract and 1st paragraph of this paper. What was the authors' big question and why is it interesting? **3 pts**

B. How did they make their measurements? **4 pts**

C. Explain in your own words what is shown in Figure 1B and 1C and what this signifies. BnTX is botulinum toxin A and TnTX is tetanus toxin; both block transmitter vesicle exocytosis. **4 pts**

D. Explain what is shown in Figure 2H and 2I. GCaMP2 is a genetically encoded Ca^{2+} reporter. Other, later figures show that activation of OPC glutamate receptors is required for synthesis of myelin protein. **4 pts**

3. (20 points) You are studying the properties of a giant axon from an alien creature discovered by the Perseverance Rover on Mars. From your experiments you know that the membrane is only permeable to potassium ions when at rest and that the threshold for generating an action potential is -20 mV.

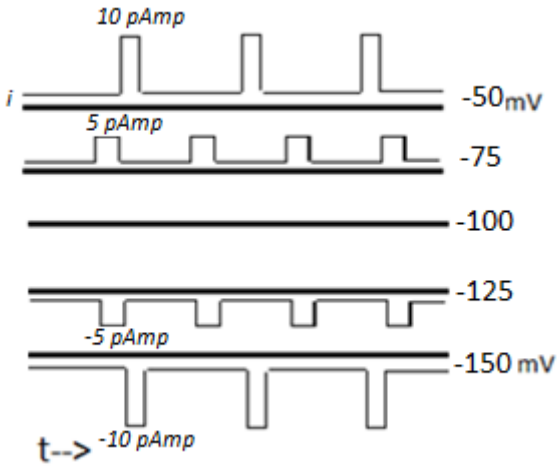
A. During one experiment, you accidentally spill a solution of KCl into the dish holding the axon. After the spill, your recording electrode tells you that V_m is at -58 mV. From your notes, you know that you filled the axon with a solution containing 100 mM NaCl and 700 mM KCl. Assuming the intracellular solution did not change during your unfortunate accident, what is the concentration of K+ in the extracellular solution after the spill? Please show relevant equation(s) and intermediate steps for full credit. Label the units of your answer. **10 pts**

B. When you perfuse the axon with the solutions from the table below, you are able to elicit action potentials! Not only that, but the overshoot is a staggering +144 mV.

Ion	Intracellular solution (mM)	Extracellular solution (mM)
Li+	20	200
K+	700	30
F-	500	50
Cs+	10	3200
Na+	100	200
Cl-	330	3580

Which ion is responsible for the overshoot of the action potential? State your reasoning and show calculations to support your conclusion. **10 pts**

4. (15 points). You are conducting experiments on a monkey COS cell, in which you have expressed a K^+ leak channel in order to study the K^+ current. The cell has a resting potential of -70 mV, and you measure the K^+ current for a single channel at various membrane potentials, as shown in the following graph:



A. Draw the i-V plot for this channel; assume that K^+ channels have a constant conductance at all voltages. Be sure to label both axes. **5 pts**

B. Using the values above, calculate the single channel conductance, [?] for this K^+ channel. Please show relevant equation(s) and intermediate steps for full credit. Label the units of your answer. **5 pts**

C. You make whole-cell recordings of your COS cells, and at a voltage command of -50 mV you find that you record a current of 1 mAmp. Assuming that all K^+ channels are open at all voltages, how many K^+ channels are there in this cell? Please show relevant equation(s) and intermediate steps for full credit. Label the units of your answer. **5 pts**

5. (20 points) You find a giant purple monster stranded on the beach at low tide below the glider port and you are curious about the properties of its axons. You cut a slice from what appears to be the head of the beast, hoping that you'll be able to record from its neurons. Upon examination you observe an odd feature: the axon of the neuron you have isolated is half myelinated and half unmyelinated! You cut off a piece of axon 20 cm in length that is 10 cm myelinated and 10 cm unmyelinated and perform several experiments.

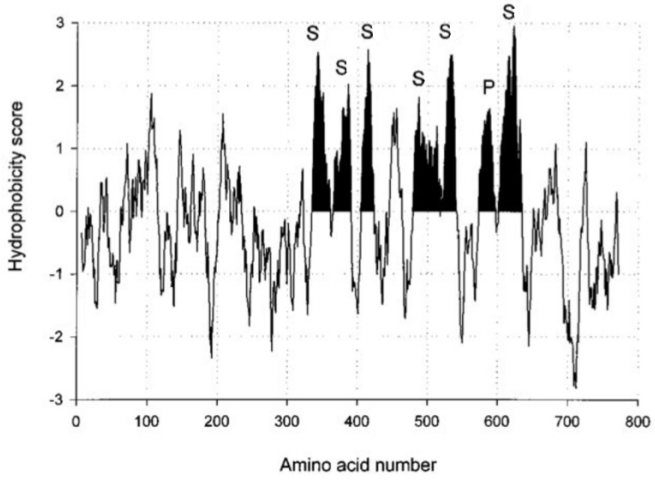
You determine that its resting potential is -60 mV and its threshold potential is -45 mV. You inject a depolarizing current into the middle of the axon you have isolated, where the myelinated and unmyelinated regions meet, until the neuron reaches a steady state of -30 mV. The specific

resistance of the axon membrane is 300 ohms*cm^2, the specific capacitance is 1μFarad/cm^2, the axon radius is a staggering 2 mm, the internal resistance is 72 ohms/cm, and the distance between the nodes of Ranvier is 5 cm.

A. Is it possible to elicit an action potential in this manner? If yes, how long does it take to do so? Show your calculations and state your conclusions. Label the units of your answer. **8 pts**

B. Since you stimulate at the middle of an isolated axon you may suspect the AP to be propagate bidirectionally along the unmyelinated and myelinated parts of the axon. Is that the case with this neuron? Explain your answer mathematically and label the units of your answer. **12 pts**

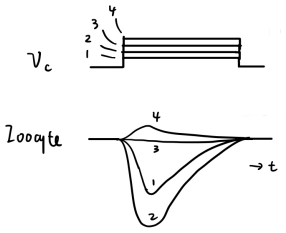
6. (15 points**)** You obtain a Kyte-Doolittle hydrophobicity plot of a subunit of an unknown channel, X (below). The putative transmembrane segments (S) and pore loop (P) regions are labeled. This plot reminds you of the voltage-gated sodium channel that you have learned about in your UC San Diego neurobiology course.



A. Briefly describe the structure of the Na channel ? subunit (a labeled sketch is sufficient) **4 pts**

B. What pattern in the amino acid sequence do you expect to see in each segment 4? Why is this significant? **3 pts**

C. You construct the mRNA to express this channel in *Xenopus* oocytes and then apply a series of voltage commands and record the current. The command voltages are (1) -20 mV, (2) 0 mV, (3) +85 mV, and (4) +150 mV. In your experimental recording solutions, the concentrations of ions are: [K+] in = 140 mM, [K+] out = 5 mM, [Na+] out = 145 mM, [Na+] in = 5 mM, [Cl-] in = 15 mM, [Cl-] out = 115 mM. The records from your recording are shown below. Calculate the reversal potential of each ion and decide if the channels you expressed are Na channels. **8 pts**



7. (15 points)
A. What are pacemaker neurons? **3 pts**

B. Name the two additional conductances involved in generating their firing pattern, in addition to the ones that generate an action potential, and briefly summarize their time course and function. **7pts**

C. Describe the effects of increasing and of decreasing each of these two additional conductances separately. **5 pts**

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