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2006 7.012 Problem Set 6

** Due before 5 PM on **WEDNESDAY**, November 22, 2006. **

Turn answers in to the box outside of 68-120.

PLEASE WRITE YOUR ANSWERS ON THIS PRINTOUT.

1. You create an artificial cell in a test tube. This artificial cell consists of a “cytoplasm” (i.e. the inside of the cell), a lipid bilayer, and the outside. The “cytoplasm” contains 150 mM NaCl, whereas the outside solution contains 15 mM NaCl. The only kind of proteins present in the membrane are Cl⁻ ion channels, but they are closed.

(a) Are any ions flowing across the cell membrane? If so, which ions are flowing and are they flowing inward or outward?

(b) Is there a membrane potential across the cell membrane? If so, is the membrane potential positive on the inside or negative on the inside?

(c) Are there concentration gradients across the cell membrane? If so, for which ions are there concentration gradients, and are those ions at higher concentrations or lower concentrations inside the cell?

Now assume that, all of the sudden, the Cl⁻ channels in the cell membrane open.

(d) Are any ions flowing across the cell membrane? If so, which ions are flowing and are they flowing inward or outward?

(e) Is there now a membrane potential across the cell membrane? If so, is the membrane potential positive on the inside or negative on the inside?

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(f) Are there concentration gradients across the cell membrane? If so, for which ions are there concentration gradients, and are those ions at higher concentrations or lower concentrations inside the cell?

You now create a different artificial cell in a different test tube. This artificial cell consists of a "cytoplasm" (i.e. the inside of the cell), a lipid bilayer, and the outside. The "cytoplasm" contains 150 mM NaCl, whereas the outside solution contains 15 mM NaCl. The only kind of proteins present in the membrane are H⁺/Na⁺ pumps, which simultaneously pump one H⁺ outside the cell for every one Na⁺ it pumps inside the cell, but these pumps are inactive. (Assume there is an excess of ATP both inside and outside of the cell that allows the pump to function. Also assume the NaCl is dissolved in water, which is where the H⁺ ions are coming from.)

Now assume that, all of the sudden, the pumps in the cell membrane become active.

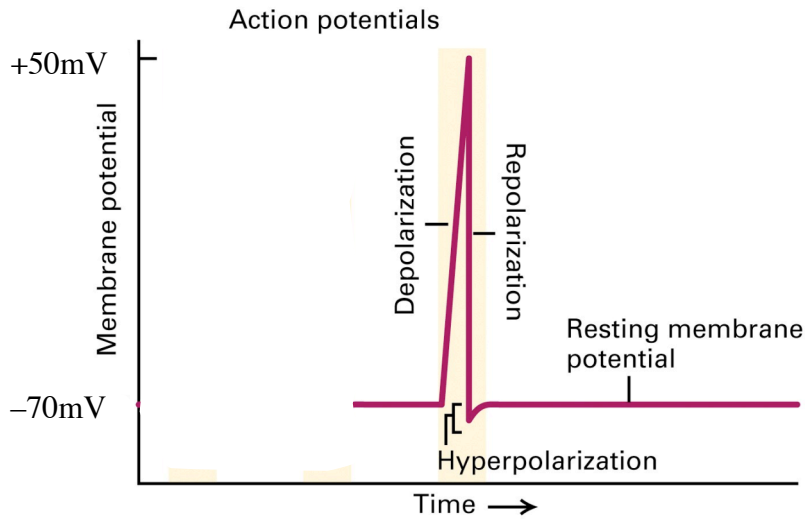
(g) Are any ions flowing across the cell membrane? If so, which ions are flowing and are they flowing inward or outward?

(h) Is there a membrane potential across the cell membrane? If so, is the membrane potential positive on the inside or negative on the inside?

(i) Are there concentration gradients across the cell membrane? If so, for which ions are there concentration gradients, and are those ions at higher concentrations or lower concentrations inside the cell?

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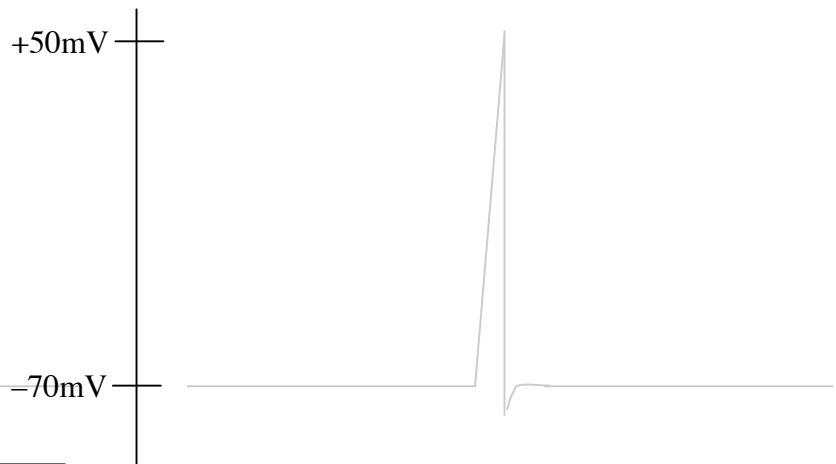
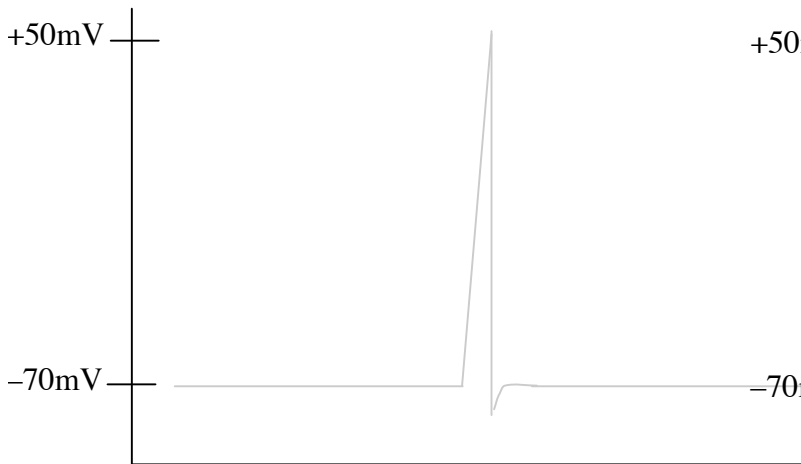
2. A normal action potential can be graphed as follows:



Draw what an action potential would look like if you **inhibited** the following voltage-gated channels in the following graphs. A normal action potential is drawn into each graph lightly, for comparison.

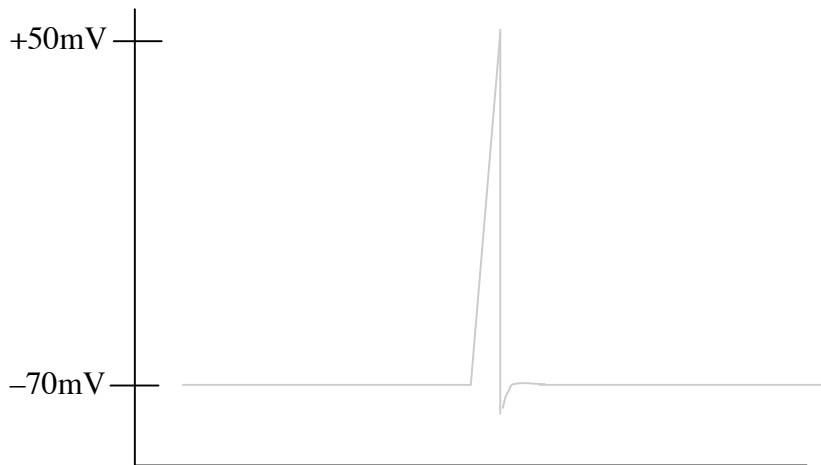
(a) ... voltage-gated K⁺ channels

(b) ... voltage-gated Ca⁺⁺ channels



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(c) ...voltage-gated Na⁺ channels



(d) After depolarization occurs during a normal action potential, is the concentration of sodium inside the cell high or low with respect to the concentration of sodium outside the cell?

(e) Do you think that action potentials in a neuron would cease immediately after one exposes the neuron to a drug that inhibits the Na⁺/K⁺ pump?

Loss of function mutations in some genes expressed in neurons cause flaccid paralysis (i.e. muscles cannot contract at all), while loss of function mutations in other genes cause rigid paralysis (i.e. muscles are permanently contracted).

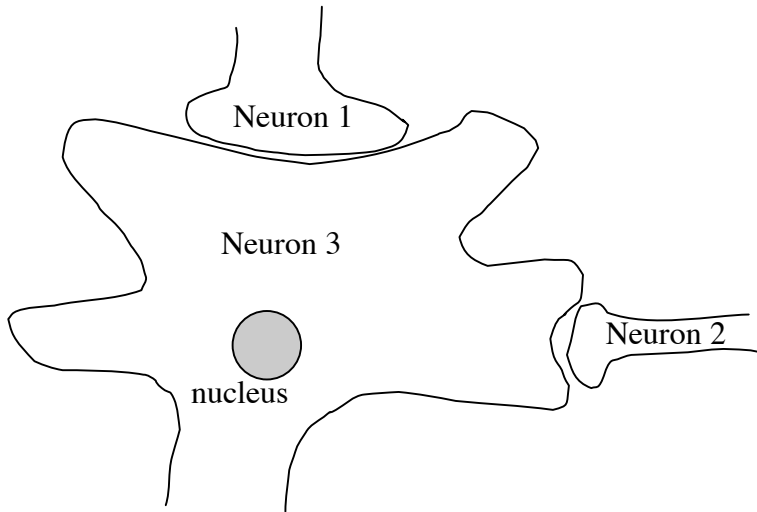
(f) Into which one of the two categories of mutants would the gene encoding the acetylcholine receptor found in muscle cells fall?

(g) Into which one of the two categories of mutants would the gene encoding acetylcholine esterase fall?

(h) Into which one of the two categories of mutants would the gene encoding the voltage-gated Ca²⁺ channel fall?

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In the schematic below, Neuron 3 receives signals from two different presynaptic cells, Neuron 1 and Neuron 2. The input from Neuron 1 is excitatory, whereas the input from Neuron 2 is inhibitory.



(i) Put an X in each box where the following proteins would be found.

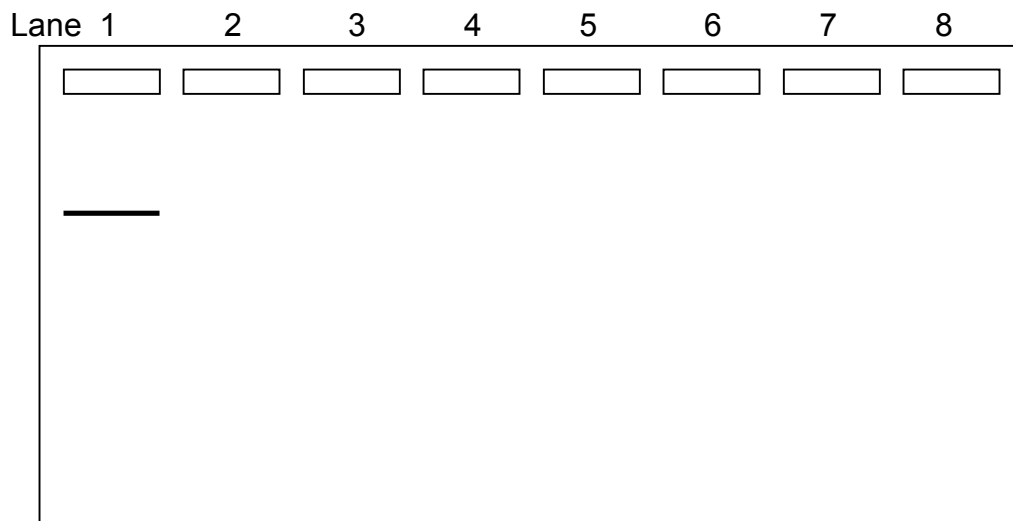
Proteins	Location				
	Terminal of Neuron 1	Axon of Neuron 1	Terminal of Neuron 2	Axon of Neuron 2	Dendrites of Neuron 3
Vesicle docking and fusion proteins (e.g. synapsin)					
Ligand-gated Cl ⁻ channels					
Voltage-gated Ca ⁺⁺ channels					
Ligand-gated Na ⁺ channels					
Voltage-gated K ⁺ channels					
Voltage-gated Na ⁺ channels					

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3. For the sake of this problem, assume that, during VDJ recombination, one allele of an antibody locus in every diploid B cell gets rearranged, and the other one doesn't (as is often true for B cells). Say you developed a PCR assay to test whether the two alleles of the antibody locus had been rearranged or not. You design primers to the regions of the genome directly flanking this gene. You do the PCR reaction on DNA extracted from the following cell populations:

- one skin cell (lane 1 of the gel below)
- a large population of skin cells (lane 2 of the gel below)
- one sperm cell (lane 3 of the gel below)
- a large population of sperm cells (lane 4 of the gel below)
- one mature B cell (lane 5 of the gel below)
- a large population of mature B cells (lane 6 of the gel below)

(a) You load each separate reaction into one lane of the gel below. In the gel below, draw all of the bands you would expect to see in lanes 2 - 6 of the gel. Lane 1 has been done for you, and lanes 7 and 8 will be filled in during part **(b)**.



(b) A patient with multiple myeloma has a clonal over-proliferation of one B cell that had been mature enough (at the time of cancer development) to secrete antibodies. Go back to Lane 7 of the gel and draw in the bands that you would see there if you had done your PCR reaction on a single cancerous B cell from the myeloma of a multiple myeloma patient. Go back to Lane 8 of the gel and draw in the bands that you would see there if you had done your PCR reaction on a population of B cells from that same patient with multiple myeloma.

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4. As we learned in the cancer unit, *myc* is one example of an oncogene. One way that *myc* can be mutated into its oncogenic cancer-causing form is by a translocation. A translocation is when two different chromosomes (e.g. chromosome #9 and chromosome #22) exchange segments at their ends. There is a specific translocation found in the tumor cells of Burkitt's lymphoma patients that places the coding region of *myc* (found on chromosome #8) under the promoter of an antibody-encoding gene (found on chromosome #14).

For part **(a)** only, assume that this translocation occurred early on in development (say at the 64-cell stage) in a cancer patient, such that lots of cells in the body contained this same translocation.

(a) Why would this patient get a lymphoma specifically, as opposed to any other type of cancer?

For parts **(b)** - **(d)**, assume that the translocation discussed occurred in only one developing B cell in each patient.

(b) Why does the *myc* open reading frame being under control of the antibody promoter lead to cancer?

There is a specific translocation found in the tumor cells of follicular B-cell lymphoma patients that places the coding region of *Bcl-2* (found on chromosome #18) under the promoter of an antibody-encoding gene (found on chromosome #14). The function of *Bcl-2* is to prevent apoptosis.

(c) Why does the *Bcl-2* open reading frame being under control of the antibody promoter lead to cancer?

(d) Why do you think that it is so common to have translocations involving chromosome #14 in cancers that are specifically cancers of B cells?

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5. When an activated helper T cell (T_H cell) binds to a B cell presenting the appropriate antigen on the B cell's Class II MHC molecules, the T_H activates the B cell. This stimulates the B cell to proliferate and make more antibodies to fight the invasion.

(a) Why must the T_H and B cells contact each other and specifically bind in order for this activation to occur? (i.e. What would be the problem if the activated T_H cells simply secreted an activating hormone into the blood without ever binding to a B cell?)

(b) After the antigen is cleared from the body, when the animal is no longer fighting the infection, many of the B cells die since they are no longer needed. Some however, continue to survive. What function do these cells provide?

(c) When a B cell is first generated, the antigen that it recognizes is determined based on whichever amino acid sequence and structure is possessed by the antibody that B cell produces. Many of these newborn B cells are selected to undergo apoptosis. Why might an autoimmune disorder result in a patient who is unable to properly select which B cells are supposed to undergo apoptosis and which B cells are not?

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6. Fill in the blocks in the following chart.

	macrophages	B cells	Helper T cells
Name a cell surface protein involved in immunology that they produce. Choose a different protein for each column.			
Name a protein that physically interacts with the protein listed above.			
Do they undergo genome rearrangements?			
Do they recognize specific antigens?			
Do they display antigens on MHC class II molecules?			
Do they undergo clonal expansion?			
Do they emit growth signals? If so, which cell types do they affect?			