580.439/639 Midterm Exam, 10/27/08

1 hour, closed book except for one sheet of paper. Answer all questions.

10 points per part plus 10 points for writing your name on the answer sheet.

Problem 1

Short answers:

Part a) It is not clear which active transport molecule is working in a cell. The possibilities are 1) Na-K ATPase (which transports 3 Na out and 2 K in); 2) NaKCC cotransporter (1 Na, 1 K, and 2 Cl in); or 3) KCl cotransporter (1 K and 1 Cl out). Explain how the following tests would differentiate them. Assume that the only the K flux can be measured, so the alternatives can't be identified by measuring the three possible fluxes.

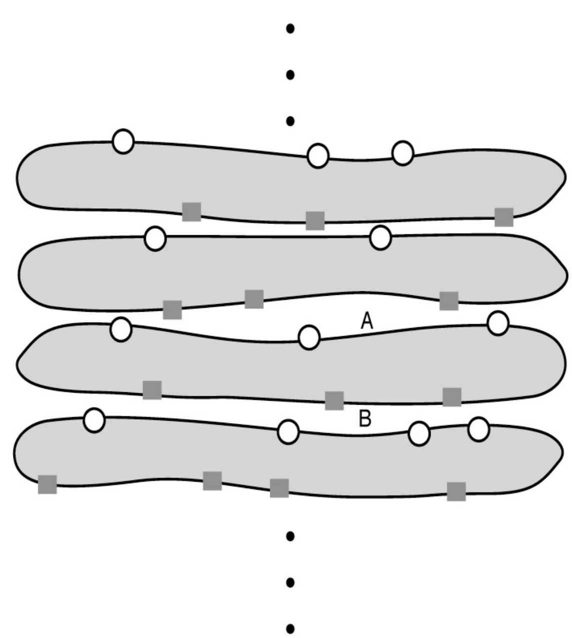
1) Changing the membrane potential by 20 mV.
2) Eliminating the ATP in the system.
3) Removing the Na in the extracellular space.
4) Removing the Cl in the extracellular space.

Explain what provides the energy for each of the three transport mechanisms.

Part b) Make a sketch of a cross-section of the bacterial KcsA channel. Using this as the pore structure of a general potassium channel, point out the parts that are responsible for 1) selectivity between K and Na ions; 2) gating when it is present; 3) the anomalous flux ratio behavior, in which K ions seem to move through the channel in packets of 2-3 elementary charges; 4) use-dependent block in which some molecules only block the channel when the gate is open. Explain each effect with one sentence.

Part c) Explain why hyperpolarizing a neuron from a rest potential of -60 mV to -70 or -80 mV can increase the activity of T-type Ca channels but not the other types, whereas depolarizing a neuron from the same rest potential activates the L/P/Q/N/R type channels but not the T-type channels.

Problem 2



This problem is based on the electric organ of electric fish, which acts as a voltage source controlled by the nervous system. The diagram at right shows how cells are stacked in the organ. The ellipsis at top and bottom represent the fact that many cells are stacked in such an organ, many more than the 4 drawn. The cells are identical. Their membranes are asymmetric as indicated by the unfilled circles, which represent nicotinic acetylcholine receptor channels (nAChR) and the gray squares which represent ion channels (IC) in the opposite membrane. The nAChRs are in the innervated membrane and are innervated by cholinergic neurons from the spinal cord. The other membrane (with the IC) is uninnervated.

Assume for this problem that there are appropriate transporters that maintain the usual intracellular environment (high K, low Na concentrations) and that the extracellular solutions are high Na, low K as usual. Extracellular Cl has its usual value and intracellular Cl is at equilibrium across the uninnervated membrane (except for Part c) below). The electrical effects of the transporters can be ignored. The resting potential of the cells (with no activation of the nAChRs) is negative as usual.

The organ produces a large potential (typically 10s to 100s of volts) in the extracellular space from top to bottom when the nAChRs are activated. No potential is produced when the receptors are not activated.

Of course there are capacitors in all the membranes in this system. Include them in the circuit diagrams requested, but <u>not in the potential or current calculations</u>.

Part a) Draw an electric circuit for one cell assuming that the open circles contain only nAChRs and that the IC box contains only a potassium leak channel (which is not voltage or ligand gated). The circuit should represent current flows in the vertical direction in the diagram (assume there are only small horizontal currents that can be ignored) and should connect nodes *A* and *B* in the diagram above. What is the resting potential between A and B, i.e. the potential when the nAChRs are not activated? In doing this, assume that the innervated and uninnervated membranes are two separate membranes with different membrane potentials. This is true if horizontal currents are small.

Part b) Suppose the nAChRs are activated simultaneously throughout the entire organ. What will be the potential between A and B? Assume the current that flows through the entire organ (in the vertical direction) in this case is I_{active}. In which direction will this current flow (positive charge from *A* to *B* or vice versa)? Give an expression for I_{active} assuming that there is an external resistance R_E between the top and bottom of the whole organ (i.e. R_E is the external resistance through which the organ drives current, the fish's body, the external environment, etc.).

Part c) Suppose there is a chloride channel in the gray box along with the potassium channel. Again the channel is not voltage or ligand gated. Assume that there is no active transport of Cl^- in this system. Answer the following questions:

1) Redraw the circuit from part a).
2) What is E_{CL} when the nAChRs are not activated?
3) What is the potential between *A* and *B* when the nAChRs are not activated?
4) What happens to E_{Cl} and the potential from *A* to *B* when G_{nAhR} is turned on and left on until a new steady state is established? Give both the potentials at time 0 when the nAChRs are turned on and in the steady state.

Problem 3

Consider a membrane containing a HH-type Na channel with a fast *m* activation gate and an inactivation *h* gate, along with a fixed-conductance K channel that behaves like a leak channel. That is, the K channel has conductance G_K a constant. Assume the *m* gate is fast enough that *m* can be assumed to be instantaneous, i.e. $m = m_\infty(V)$. Thus the system has two state variables, *V* and *h*. Such a system can produce action potentials with the right parameters.

Part a) Write the differential equations for this system.

Part b) Write equations for the nullclines of this system in a phase plane with axes V and h.

Part c) Three phase planes are sketched below, computed from the parameter functions of the HH equations. Pick the correct one for this system and label the V and h nullclines. Explain your choice (lucky guess won't count). The dashed and solid line styles just serve to separate the functions.