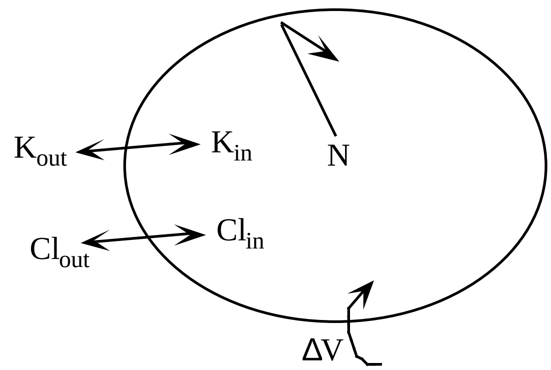
580.439 Midterm Exam

1.5 hour, closed book except for one sheet of standard-size (8.5”x11”) paper.

Problem 1

Part a) Consider a spherical cell of diameter 20 μm, with the usual intracellular and extracellular solutions inside and outside the cell. The cell has a membrane potential of -100 mV. This membrane potential is produced by a charge separation between the intracellular and extracellular space; that is, there must be a net negative charge inside the cell and a net positive charge outside the cell. Using the fact that the cell’s membrane has a capacitance of 1 μfd/cm^2, compute the amount of charge required for this membrane potential. Assuming, for simplicity, that the cell contains 140 mM KCl only, what fraction of the total charge contained in the cell (i.e. in the K^+ and Cl^- ions) is the charge separated on the membrane? In case you have forgotten, the volume of a sphere of radius r is $4\pi r^3/3$ and the surface area of the sphere is $4\pi r^2$. If you don’t remember other conversion factors you need, just write the equations.

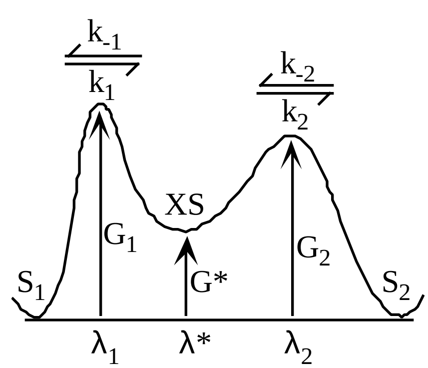
Part b) The Donnan equilibrium is a means by which a cell can maintain a membrane potential and substantial charge separation across the membrane, while still being at equilibrium. Consider the simplified situation at right. The cell contains K^+, Cl^-, and fixed negative charges (N); by fixed charges is meant a concentration N of negative charge on molecules, such as proteins, which cannot permeate the cell membrane. Assume that the cell is bathed in a medium containing K^+ and Cl^- only at fixed concentration $K_{out}=Cl_{out}$. Compute the concentrations K_{in} and Cl_{in} and the membrane potential ΔV at which both K^+ and Cl^- are at equilibrium (as functions of K_{out}, Cl_{out} and N). Of course, N will not be at equilibrium. From the results of Part a), you should be convinced that it is reasonable to assume that charge electroneutrality holds, i.e. that $K_{out}=Cl_{out}$ and $K_{in}=Cl_{in}+N$.



Part c) The equilibrium potential of a real cell is a steady state rather than an equilibrium. Explain the difference and tell what must be added to the cell of part b) to bring it to a steady state. Assume only that N and the concentrations in the external pool are fixed by external mechanisms that are not part of this problem.

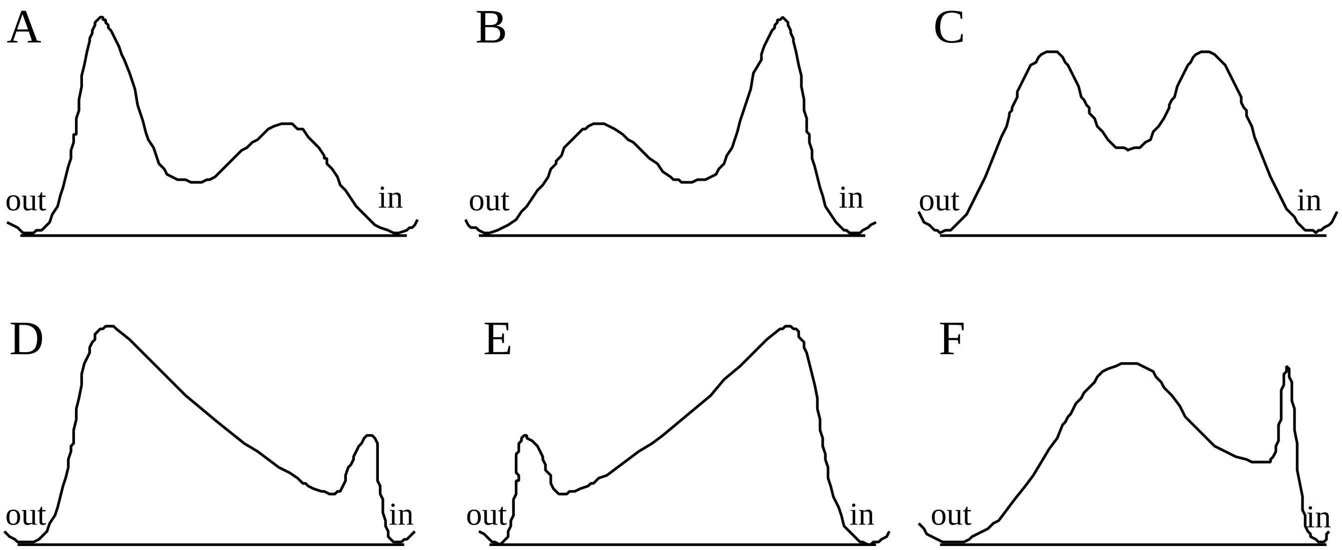
Problem 2

Part a) A certain sodium channel is blocked by H^+ ions. The block occurs when a proton enters the channel and binds at a site within the pore, thus blocking the channel. This process can be modeled with a barrier model like the one shown at right, which has a single binding site within the membrane. Work out an expression for the steady-state fraction of channels blocked. This will be the ratio XS/Q, the fraction of the total channels that have their site occupied by a proton, where XS is the concentration of occupied channels and Q is the total concentration of channels (i.e. take into account the fixed total amount of channel available).



Ignore Na^+ in answering this question (i.e. assume that only H^+ can enter the channel). Note: express the result in terms of the rate constants k_i, without evaluating the rate constants in terms of the parameters of the barrier model.

Part b) Suppose that when the pH inside the cell is changed, the degree of block changes hardly at all, whereas the degree of block is very sensitive to the pH outside the cell. Which of the barrier models sketched below are most consistent with this behavior? The answer can be more than one. Justify your answer in terms of the expression derived in part a); this will require working out the rate constants.



Part c) Assuming that the inner and outer barriers are exactly the same height in the vertical pairs of barrier diagrams above (i.e. in A and D, in B and E, and in C and F). How could you distinguish between the models in each vertical pair (e.g. between B and E), on the basis of channel block alone? (Hint, think about membrane potential)

Problem 3

Consider the system described by the following two equations:

$$\dot{x} = y - x^3 + x$$

$$\dot{y} = x - y$$

Sketch the phase plane for this system, showing the nullclines and the equilibrium points. Classify the equilibrium points according to their stability. Sketch the trajectories in the phase plane and comment on the likelihood that a stable limit cycle exists. (Hint: to make this easier, you may assume that if you have a saddle node in your phase plane, its unstable manifolds end in other equilibrium points and its stable manifolds extend to infinity.)