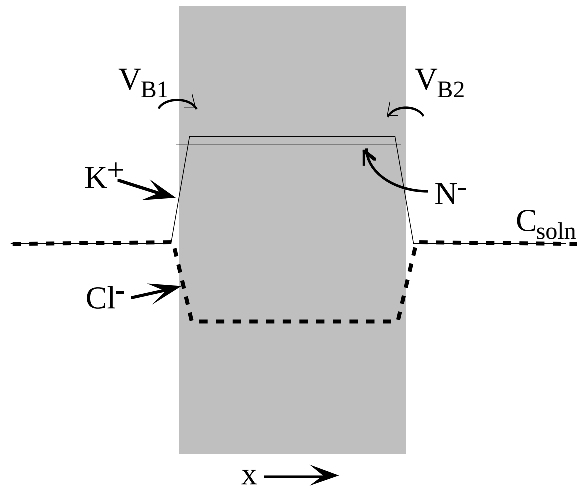
# 580.439 Midterm Exam, 1999

**1.5 hours; answer all questions; closed book, except for one 8.5” x 11” piece of paper**

**Problem 1:**




Consider the membrane drawn at right. The membrane contains a concentration $N$ of fixed negative charges but is otherwise a diffuse barrier that is well-modeled by the Nernst-Planck equation. The membrane is bounded by solutions containing equal concentrations ($C_{soln}$) of KCl. Because of the fixed negative charges, the concentration of potassium (thin solid line) in the membrane is higher than the chloride concentration (thick dashed line) and both concentrations are different in the membrane than in solution. The concentration gradients at the edges of the membrane cause barrier potentials $V_B$ to exist at both membrane interfaces. For this problem, assume that the barrier regions are very thin compared to the rest of the membrane, so that the transitions in concentration occur over a small region, as in the sketch above.

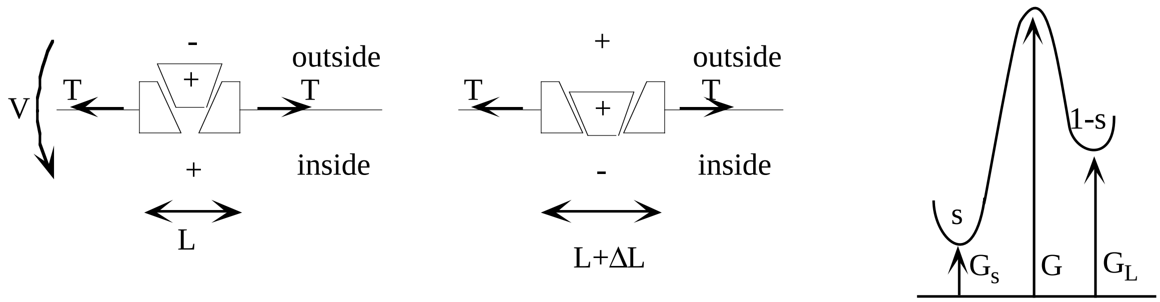
12 pts **Part 1:** Assume that potassium and chloride are at equilibrium between the membrane and the bounding solutions. Write equations for $V_B$ in terms of the potassium and chloride concentrations in solution and in the membrane, so that both ions are at equilibrium across the membrane interface (ignore the details of what happens within the actual barrier region).

12 pts **Part 2:** Assume that charge electroneutrality (equal concentrations of positive and negative charge) holds in both the membrane and solutions. Write equations that express charge electroneutrality for both regions. From these equations and the equations of Part 1, solve for the potassium and chloride concentrations in the membrane and the barrier potentials in terms of $C_{soln}$ and $N$..

14 pts **Part 3:** Assuming that ion flow through the interior of the membrane follows the Nernst-Planck equation, compute the resistance to current flow of this membrane. Compute the resistance for potassium separately from the resistance for chloride and argue that the membrane has a smaller resistance for potassium than chloride. For this calculation, assume that the barrier regions at the edges of the membrane do not contribute to the resistance, i.e. the resistance arises from the interior of the membrane only. You may need some additional parameters of the membrane, like its thickness $d$, the mobility of potassium and chloride in the membrane $u_K$ and $u_{Cl}$, etc.

**Problem 2:**

The mammalian outer hair cell has a specialized protein in its membrane which serves to transduce membrane potential into movement. When the cell is depolarized, this protein changes its cross sectional area; the collective action of a large number of such proteins changes the length of the hair cell. A simple one-dimensional model of the process is shown in the figure below. The sketches at left show the protein in the membrane (horizontal line) with the inside and outside solutions marked. The protein has a plug which contains a charge +. The plug serves as the voltage sensor and moves in or out of the membrane under the influence of the membrane potential *V*. When the membrane potential is positive (left drawing), the plug is repelled and the width of the channel is *L*. When the membrane potential is negative (middle drawing), the plug is attracted inward and the width of the channel is $L+\Delta L$. The membrane connected to the protein is under tension and exerts a force *T* on the channel, as indicated in the drawings. For this problem, assume that *T* does not change when the plug moves.

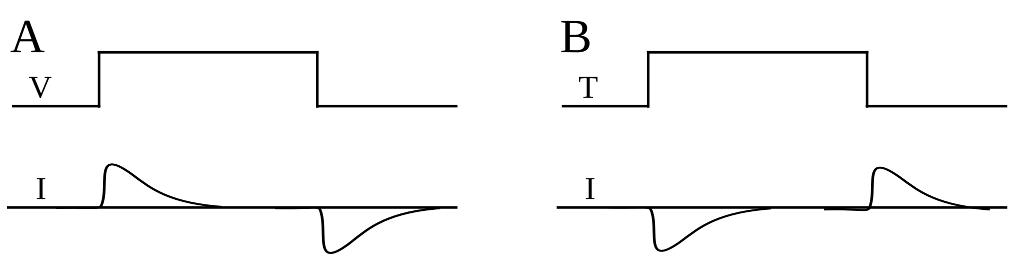



14 pts **Part 1:** Assume that the movement of the plug is characterized by the barrier diagram at right above, where *s* represents the fraction of the proteins in the short (*L*) configuration and 1-*s* is the fraction in the long ($L+\Delta L$) configuration. The energy diagram does not take into account the tension in the membrane or the membrane potential. Modify the barrier diagram to include the mechanical energy change of the protein plus membrane when the plug moves and the electrical energy change when the plug moves.

12 pts **Part 2:** Write a differential equation for *s* using the rate constants predicted by the barrier system.

12 pts **Part 3:** Find the steady-state ($ds/dt=0$) value of *s* in terms of *T*, *V*, and the parameters of the barrier system.

12 pts **Part 4:** Suppose the cell has no ion channels in its membrane (or that all the ion channels have been pharmacologically blocked). When a voltage clamp is applied to the cell without changing *T*, substantial current transients, like those drawn in Fig. A below, are observed. Alternatively, when the tension *T* in the cell membrane is changed suddenly, holding the membrane potential fixed, currents are also observed (Fig. B below). Explain these observations (Hint: gating current). Write an expression for the time constant of the currents.




12 pts **Part 5:** Could a simultaneous voltage clamp and tension change be applied for which there would be no current transient? If so, give the necessary relationship between *T* and *V*.