580.439/639 Midterm Exam, 2005

1.5 hours, answer all questions, closed book except for one sheet of paper. 9 points for each question part, 1 point for your name.

Problem 1:

Part a) The ion concentrations in two extracellular fluid spaces of the mammalian cochlea, the endolymphatic and perilymphatic spaces, are shown below. There is an endolymphatic potential of +90 mV between these two spaces, endolymph positive w.r.t. perilymph (which is at the normal 0 mV extracellular reference potential). Tell which ions are at equilibrium between these spaces and which ions must be actively transported. For the actively transported ions, tell which direction the ions must be transported (out of or into the endolymph).

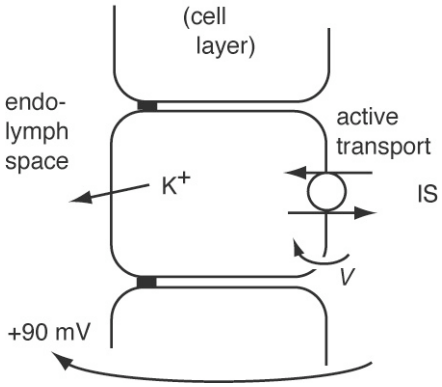
Ion	perilymph	endolymph	
Na^+	145 mM	2 mM	
K^+	5	157	
Ca^{++}	1	0.02	
Cl^-	120	132	
HCO_3^-	20	31	
urea	5	5	(urea is uncharged)

Part b) A Na-2 Cl-K transporter moves one Na^+, one K^+, and 2 Cl^- ions through a membrane in the same direction on each transport step. Usually, it uses the energy in the sodium electrochemical potential gradient to transport K^+ and Cl^- against their electrochemical gradients (into a cell, for example). Given the ion concentration gradients described in part a), is there enough energy in the Na^+ gradient to allow this transporter to move potassium and chloride into the endolymph?

Suppose this transporter only moved 1 Cl^- each time (i.e. each transport step moved 1 Na^+, 1K^+, and 1 Cl^-, all in the same direction). Is your answer different? Why?

Part c) Ion X is not at equilibrium between perilymph and endolymph. The anatomy of the epithelium between these spaces is quite complex, despite the simple discussions above; suppose that there is a third compartment, called interstitial space (IS), between perilymph and endolymph (so that endolymph exchanges only with IS, perilymph exchanges only with IS, and transport from perilymph to endolymph must go through IS). A claim is made that the concentrations of ion X can be maintained in this system by adjusting its concentration X_{IS} in the interstitial space and adjusting the potentials V_{IS}-V_{peri} and V_{endo}-V_{IS} between the spaces so that X is at equilibrium between perilymph and interstitial space and also between interstitial space and endolymph. Prove that this is not possible. (This is a really easy question!)

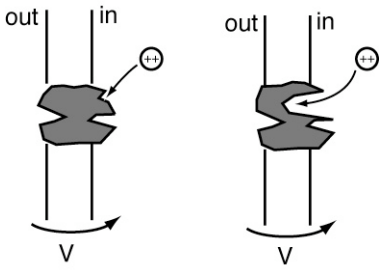
Part d) Experimental evidence favors the arrangement at right for maintaining the ion concentrations in the endolymph. In this model, K^+ diffuses passively (down its electrochemical gradient) into the endolymph from the intracellular space of the cells lining the endolymphatic space; the perilymphatic space is not relevant here and is not shown. The active transport takes place in the basal membranes of these cells, i.e. on the side away from the endolymph. Assuming that the concentration of K^+ inside the cells is a typical value of 150 mM, what is the range of membrane potentials *V* of these cells, w.r.t. a 0-mV reference in the IS, that will allow passive electrodiffusion of K^+ into the endolymph? Remember that the endolymph is at +90 mV w.r.t. the IS, as shown.



Problem 2:

Suppose that a Ca^{++}-gated K^+ channel has no voltage sensitivity as such but is gated exclusively by binding of intracellular Ca^{++} to the channel. That is, when Ca^{++} binds, the channel opens.

Part a) Consider the two conceptual models sketched at right for the binding of Ca^{++} to the channel. In the left one, the Ca^{++} binds to the channel just inside the membrane; in the right one, the Ca^{++} binds to a site that is about half-way through the membrane. In one of the two, the gating will appear to be voltage-dependent in voltage-clamp studies and in one it will not. Tell which one and explain why in words, no diagrams or equations. (One or two sentences)



Part b) As a basic model of gating in these channels, sketch two barrier diagrams for binding of a Ca^{++} ion to the channel, one diagram for each channel. Clearly show the role of membrane potential in both models.

Part c) Compute the $n_\infty(V,Ca)$ functions for the two channels (i.e. the steady-state fraction of open channels, with Ca bound). Note that this is potentially a function of both calcium concentration *Ca* and membrane potential *V*.

Problem 3 (from Kaplan and Glass, Chapt. 5):

Consider the differential equations below for the "Brusselator", a chemical oscillator.

$$\frac{du}{dt} = 1 - (b+1)u + au^2 v$$
$$\frac{dv}{dt} = bu - au^2 v$$

where $a, b>0$ and $u, v \geq 0$.

Part a) Find the equilibrium point or points algebraically. This looks hairy, but turns out to be simple.

Part b) Find the characteristic equation(s) used to solved for the eigenvalues at the equilibrium point(s) and compute the eigenvalues of the linearized system(s).

Part c) Under what conditions is the equilibrium point a spiral? This is a little hairy. It will help to make a sketch of the locus of points in the (a,b) plane where the equilibrium point is a spiral. Remember that $a,b>0$.

Under what constraints on a and b is the spiral stable?

Part d) For what values of a and b are the eigenvalues 1) stable and real; 2) unstable and real; and 3) a saddle?

(5 points extra credit) Part e) Sketch a phase-plane for this system and discuss the possibility of limit cycle(s). (What values of a and b? Where in the phase plane?)