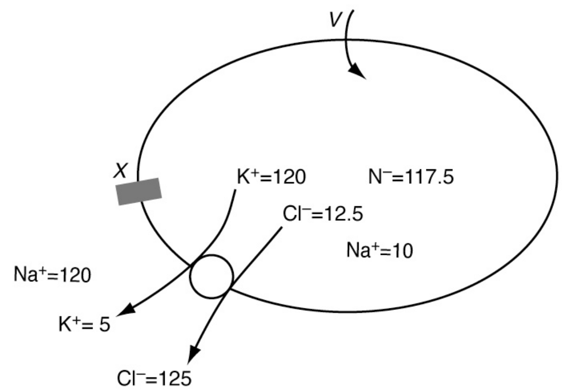
580.439/639 Midterm Exam, 2009

One hour, closed book except for one sheet of paper, do all problems.

Problem 1



This problem is about steady-state conditions for membranes. Consider the cell sketched at right. This cell contains a KCl transporter which moves one K^+ and one Cl^- ion through the membrane, both in the same direction. Ions only move through this molecule in pairs, i.e. one K^+ or one Cl^- cannot be transported separately, only together as a pair. Ignore the gray rectangle (*X*) for the time being. The concentrations of ions inside and outside the cell are given (in mM). The N^- are impermeable anions inside the cell of unknown identity. They are only there to provide charge electroneutrality, i.e. the total positive and negative charge concentrations are equal.

In doing this problem, remember that the charge transferred by a small flux of ions is very large, so typical membrane potentials are maintained by charge separations (on the membrane capacitance) that are several orders of magnitude smaller than the total amount of charge present in the cell. Thus, it is reasonable to always assume charge electroneutrality. Moreover, if ions move through the membrane in steady state, they must do so in an electroneutral way, i.e. a net zero flux of charge through the membrane.

Part a) For the situation diagrammed, i.e. the concentrations given and ONLY the KCL transporter in the membrane, which way will KCl move through the membrane (in or out)? Explain why the membrane potential *V* does not matter to your answer here.

Part b) Suppose the KCl transporter is the only ion transport mechanism in the membrane. Suppose the concentrations are initially as given in the diagram and that the <u>extracellular</u> concentrations are fixed, but that the intracellular ones can vary. Assume that KCl is transported in the direction you predicted in part a), thus lowering or raising the intracellular concentrations of K^+ and Cl^- by the same number of mM. Will this system come to a steady-state of no transport? If so, at what intracellular concentrations of K^+ and Cl^-?

Part c) Suppose that *X* is a non-gated K^+ channel, like a leak channel. Does the existence of the K^+ channel change your answer to part b)? Explain why or why not. What will be the membrane potential in the steady state derived in part b)?

Part d) Suppose that *X* contains both a K^+ and a Cl^- leak channel and the channels' permeabilities (or conductances) are equal. Will the existence of the channels change your answer to part b)? What will the membrane potential be in the steady state now? Show that both K^+ and Cl^- are at equilibrium across the membrane in this steady state (just computing E_K and E_{Cl} is not sufficient). HINT: check whether the steady state of part b) a steady state here also?

Part e) Suppose that X contains both a K^+ and a Na^+ channel (but no Cl^- channel). Write the equations that have to be satisfied for a steady-state in this case and solve for the internal concentrations given fixed external concentrations (K_{out} = 5 mM, Na_{out} = 120 mM, and Cl_{out} = 125 mM) and N_{in} = 117.5 mM. This is not hard, but it will require some thought, so DO THIS AS THE LAST THING ON THE TEST. You should get an unphysiological answer.

Problem 2

Consider the following 2-dimensional system (from Kaplan and Glass)

$$\frac{dx}{dt} = y - \frac{5x^3}{8} + \frac{9x}{4}$$
$$\frac{dy}{dt} = \begin{cases} -y & \text{for } x<0 \\ -y + \dfrac{x^3}{x^3+8} & \text{for } x \geq 0 \end{cases} \qquad (1)$$

Part a) To see what the terms in Eqns. (1) might represent, consider the Fitzhugh-Nagumo (FN) equations.

$$\frac{dV}{dt} = 1 - \left[V^3 - (a+1)V^2 + aV\right] - w$$
$$\frac{dw}{dt} = bV - w$$

The FN equations are polynomial approximations to the Morris-LeCar (ML) equations and have similar properties. The state-variable names of the FN system are chosen to correspond to those of the ML equations. Tell what the analogies are between the terms of the FN equations and those in the ML equations (e.g. I_{inj}, calcium current, potassium current, leakage current, $w_\infty(V)$, etc). As a hint, the leading 1 in the *dV/dt* equation is the injected current. Don't worry about the fact that the constants have been simplified in various ways. Treat the polynomial in brackets in the *dV/dt* equation as one entity in making this analogy.

Part b) Now what analogies can be made between between the terms in Eqn. (1) and the ML or FN equations? That is, which of *x* and *y* is membrane potential, which is analogous to *w*, etc?

Part c) Sketch the *x* and *y* isoclines for Eqns. (1) over the range x=[-3,3] and y=[-3,3]. HINT: the dx/dt=0 isocline is N-shaped.

Part d) Give the values of *x* and *y* at the equilibrium points. Because this is a bit hairy, you should choose the values from the following list of (*x*, *y*) values, only some of which are equilibrium points.

$-(18/5)^{1/2}$, 0	0, 1/8	2, 1/2
$-(18/5)^{1/2}$, 2	0, 0	2, 1
-8/5, 1	1, ½	1, 2
-1, 0	1, 0	2, 2

Part e) Write the Jacobian of the system at the equilibrium points found in part d) and classify the stability of one of the equilibrium points (you pick which one).

Part x) EXTRA CREDIT On the r.h.s. of the first equation (for dx/dt) in Eqn. (1) there is a term $+y$ where we might have expected $-y$. Based on your knowledge of ion channels, what channel might this represent (not a potassium channel).