580.439/639 Midterm Exam

1.5 hours, answer all questions, closed book except for one sheet of paper

Problem 1

Suppose that a membrane in its resting state (i.e. at steady state with $\Delta V = V_{RP}$, the resting potential) contains a potassium channel, a sodium channel, and a chloride channel. The membrane also contains the active transporter Na-K-ATPase and no other passive or active transport mechanisms. Assume that the passive transport currents are described by the current-voltage equations derived from Nernst-Planck theory.

Part a) Write the equations that specify the steady-state, in terms of the active and passive transport currents for K, Na, and Cl. Assume that Na-K-ATPase transports r sodium ions for each potassium ion in the usual fashion (usually r=3/2). In the steady-state, there should be no charge transfer and no net transport of any ion.

Part b) Write an equation for the resting potential V_{RP}. Base this on the current-voltage equation derived from Nernst-Planck theory. State if it is necessary to make the constant-field assumption. Explain what happens to chloride in this situation. Ignore channel gating.

Part c) A number of equations for the current-voltage relationship of a channel were derived under various assumptions about the barrier diagram for the channel. Under what conditions would the result of Part b) hold for these barrier-diagram models?

Part d) Suppose the steady state of parts a) and b) are disturbed by adding the drug ouabain, which blocks the active transport of Na and K. Consider the steady state of zero charge transfer through the membrane that might occur immediately after ouabain application. Of course there would be net non-zero transport of individual ions, but assume that that process is slow enough that the ion concentrations can be assumed to be approximately constant. This turns out to be reasonable, as the membrane potential changes very fast, but ion concentrations may change over minutes or hours. What is the resting membrane potential in this new steady state, using the same method as part b)? Consider again the status of chloride and whether you need to make the constant-field assumption to get a closed-form solution.

Part e) Will the membrane hyperpolarize or depolarize when the ouabain is applied? You must justify your answer.

Problem 2

Give short answers to the following questions.

Part a) Gating variables are usually taken to a power in HH models, e.g. n^4 for the HH potassium channel. Provide a justification for this practice based on the structure of ion channel molecules.

Part b) The leakage channel in a certain cell is shown experimentally to consist of a conductance G_M in series with a battery E_M. In fact, the leakage is actually a sodium channel (G_{Na},

E_{Na}) in parallel with a potassium channel (G_K, E_K). Assuming that E_K and E_{Na} are given, write expressions for the sodium and potassium conductances that make up this leakage channel (i.e. solve for G_K and G_{Na} in terms of the other parameters)?

Part c) Name two kinds of bifurcations in phase-plane systems, defining them in terms of the behavior of the eigenvalues at equilibrium points.

Part d) Explain why there is a hyperpolarization following the depolarization of the action potential.

Part e) Supppose that, among the usual complement of channels, a cell has a persistent sodium channel and a delayed-rectifier type potassium channel, both described by $I_i = \bar{G}_i m(V - E_i)$, i.e. with a single activation gate. Assume that the HH variable m is identical for the two channels, i.e. with the same m_∞ and τ_m functions, so that the gating would be identical during an action potential. Would these two channels together serve to hyperpolarize the cell or depolarize it at the resting potential? . . . during an action potential? Assume the usual values for resting potentials, E_{Na}=45, E_K=-90 and assume that $G_K \geq G_{Nap}$.

Problem 3 (from Izhikevich, 2007)

The Jacobian matrix of a system at its equilibrium point is

$$\mathbf{J} = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$$

where *a, b, c, d* are real scalars. In this problem, we show that the classification of the equilibrium point, in terms of stable, unstable, saddle, spiral, etc., can be specified in terms of trace[**J**] = a+d and det[**J**] = ad-bc. In fact, it is useful to divide up a two-dimensional graph with abscissa=determinant and ordinate=trace into regions having different kinds of stability.

Part a) Show the regions of the determinant-trace plane where the equilibrium points are the following: 1) saddle; 2) stable e.p.; 3) stable spiral; 4) unstable e.p.; 5) unstable spiral. Hint: the locus of points where

$$trace^2 - 4\ determinant = 0$$

will be useful. You should be able to divide the entire plane into these five regions.

Part b) The boundaries of the regions may correspond to bifurcations. Indicate where bifurcations lie in the plane of part a).