Mathematical Biology 5120-S07: Problem Set 3

Due Tuesday April 17, before class.

Some of the problems below refer to pages in a set of notes on the Hodgkin-Huxley equations that are posted at the course website (`http://www.math.utah.edu/~fogelson/5120_s07`). You should download those notes before doing the problems.
After trying the problems yourself, I encourage you to talk to each other about how to solve them. If you cannot work a problem out, don't leave it — be sure to come and ask for help.

1. Consider the phase plane for the (V, m) 'fast'-subsystem of the Hodgkin-Huxley equations with n and h held fixed at their resting values. A drawing of this is shown on page 9 of the notes referred to above. (In the notes E_K, E_L and E_{Na} refer to what we have denoted V_K, V_L and V_{Na} in class.) Imagine that the two ODEs are written in the form

$$\frac{dV}{dt} = F(V, m),$$

and

$$\frac{dm}{dt} = G(V, m).$$

Then, $F > 0$ above the V-nullcline and $F < 0$ below this nullcline, while $G < 0$ above the m-nullcline and $G > 0$ below this nullcline.

Use the following facts (without making use of the specific formulas for the nullclines or ODEs) to show that the equilibrium points labeled R and E are stable nodes and the equilibrium point labeled T is a saddle point.

Fact 1: On the V-nullcline and the m-nullcline, m is a monotonically increasing function of V.

Fact 2: a) At R, the slope of the V-nullcline is greater than that of the m-nullcline. b) At T, the slope of the m-nullcline is greater than that of the V-nullcline. c) At E, the slope of the V-nullcline is greater than that of the m-nullcline.

Fact 3: An equilibrium point is a stable node if at that point the Jacobian matrix J has negative trace ($\mathrm{Tr(J)} < 0$), positive determinant ($\det(\mathrm{J}) > 0$), and positive discriminant ($(\mathrm{Tr(J)})^2 - 4\det(\mathrm{J}) > 0$). An equilibrium point is a saddle point if at that point J has negative determinant.

Hint: Think about how the slopes of the nullclines are related to the first partial derivatives of F and G?

2. *Relative refractory period* For this problem, make use of the (V, n) phase-plane shown in the notes on pages 13-16. Following an action potential, a second stimulus is given during the recovery phase (between point 4 and the return to point 0 in the diagrams on page 16 of the notes). What can you say about (a) the threshold voltage that must be reached to achieve an action potential, (b) the size of the voltage step required to reach threshold, (c) the peak voltage achieved during the action potential, and (d) the duration of the action potential. (Do not just use words, draw pictures to discuss these issues.)

3. *Anode-break excitation* For this problem, make use of the (V, n) phase-plane shown in the notes on pages 13-16. From $t = -\infty$ until $t = 0$, the transmembrane potential V is clamped at some value V_* which is sufficiently negative that $n_\infty(V_*) < n_1$. (Recall that n_1 is the smallest value of n reached by the R branch of the slow manifold, see page 13 of the notes.) At $t = 0$, the voltage clamp is removed. What happens? Would the result be the same if a membrane at rest were *suddenly* stepped to the voltage V_*? Explain the difference between the two situations. Hint: Think about n. (Again, do not just use words, draw pictures to discuss these issues.)

4. Consider the Fitzhugh-Nagumo ODEs:

$$\frac{dv}{dt} = v(a - v)(v - 1) - w + I,$$

and

$$\frac{dw}{dt} = bv - gw.$$

Let $a = 0.3$, $b = 0.002$ and $g = 0.002$.

Write a Matlab program to solve the initial value problem for these equations for $0 \leq t \leq 2000$ with initial conditions $v(0) = 0$ and $w(0) = 0$. Solve the system for several (constant in time) values of the applied current I: I=0.05, 0.10, 0.15, 0.16, 0.20, 0.30. For each current, plot $v(t)$ and $w(t)$ vs t. Also plot $(v(t), w(t))$ in the vw-phase plane along with the w and v nullclines. Describe the different features of the solution for the different values of the applied current I and use the phase plane to explain these features.