

Solutions for 580.439/639 Midterm Exam 2008

Problem 1

Part a)

- 1) Only the NaK ATPase is voltage sensitive, the others are neutral.
- 2) Only the ATPase depends on ATP in the short run. If ATP is removed, the concentrations in the cells will begin to decline, so a delayed effect on the other transports would be observed.
- 3) Only the KCl transporter is independent of extracellular Na.
- 4) Only the NaK ATPase is dependent on extracellular chloride.

Energy for the ATPase is provided by ATP; energy for the NaKCC transporter is provided by the Na electrochemical gradient; energy for the KCl transporter is provided by the K, and perhaps also the Cl electrochemical gradients.

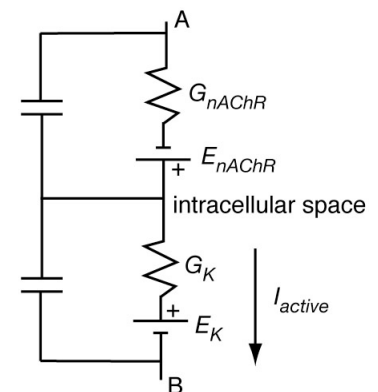
Part b) See class notes for the structure.

- 1) Selectivity is due to the selectivity filter on the outside of the pore where K^+ ions are coordinated by carbonyl oxygens in the peptide chains making up the walls of the filter.
- 2) Gating occurs in these channels by opening and closing of the teepee shape of the S5-6 segments at the inside of the pore. (Gating may also occur by collapse of the selectivity filter or by the ball and chain mechanism at the inside of the membrane.)
- 3) Potassium ions have to pass through the selectivity filter in single file, with 2 ions in the filter and a third in the aqueous cavity in the middle of the membrane.
- 4) Some blocking molecules bind to sites in the aqueous cavity, which they can only reach when the S5-6 gate is open.

Part c) T channels have a low threshold voltage inactivation that closes its inactivation gate at -60 mV. Thus the cell must be hyperpolarized to de-inactivate T channels and make opening them possible. The other Ca channels do not have this V-dependent inactivation, but are activated by depolarization to potentials above -60 mV.

Problem 2

Part a) The circuit is shown at right. This circuit repeats in series (connecting A_1 to B_2 , ...) through the whole organ. As discussed in class, the nAChR fluxes both Na and K and therefore $E_{nAChR} \sim 0$. As usual, $E_K \sim -90$ mV or similar. NOTE that the two batteries face opposite directions, consistent with the convention across the two opposite-facing membranes. When the nAChR is not activated, $G_{nAChR} \sim 0$ and V_{AB} is not defined. In practice, $V_{AB} \sim 0$ because of small horizontal currents.



Part b) In this case there will be a current I_{active} driven by the batteries. Because $E_{nAChR} \sim 0$, the batteries will push charge in the downward direction, consistent with the membrane potential of the uninnervated membrane (outward potassium current). Ignoring the capacitors,

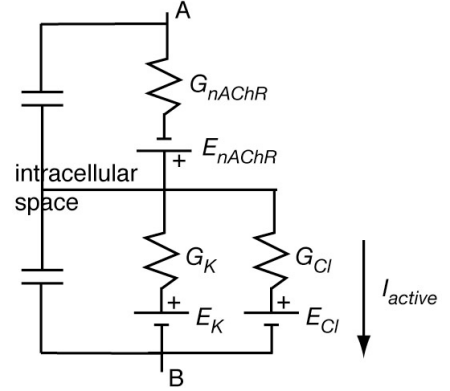
$$V_{AB} = V_A - V_B = -E_{nAChR} + I_{active} / G_{nAChR} + E_K + I_{active} / G_K \quad (*)$$

Also

$$I_{active} = \frac{E_{total}}{R_E + 1/G_{total}} \quad \text{where} \quad E_{total} = n(E_{nAChR} - E_K) \quad \text{and} \quad 1/G_{total} = n(1/G_{nAChR} + 1/G_K) \quad (**)$$

For the situation drawn here, this current will be positive (because E_K is negative and $E_{nAChR} \sim 0$) as drawn.

Part c) 1) The modified circuit is at right. The chloride channels have been added in parallel with the potassium channels
 2) If there is no active transport of Cl^- , then chloride will distribute across the membrane so that E_{Cl} equals the membrane potential across the uninnervated membrane, E_K . 3) The value of V_{AB} will be undefined (or zero) again in the resting state. 4) When the nAChRs are activated, V_{AB} will be similar to Eqn. (*) (ignoring capacitors):



$$V_{AB} = \frac{G_K E_K + G_{Cl} E_{Cl}}{G_K + G_{Cl}} + \frac{I_{active}}{G_K + G_{Cl}} - E_{nAChR} + \frac{I_{active}}{G_{nAChR}}$$

The membrane potential of the uninnervated membrane will change from E_K because of I_{active} to equal the first two terms in the equation above. Because E_{Cl} is now different from the uninnervated membrane potential, the chloride concentration inside the cells will change with time until a new steady state is established with E_{Cl} equal to membrane potential. Because E_{Cl} will be equal to the membrane potential of the uninnervated membrane in the new steady state, there will be no current flow through G_{Cl} and Eqn. (*) will apply in the new steady state.

Problem 3

Part a) The differential equations:

$$C \frac{dV}{dt} = I_{ext} - \bar{G}_{Na} m_{\infty}^p(V) h(V - E_{Na}) - \bar{G}_K (V - E_K)$$

$$\frac{dh}{dt} = \frac{h_{\infty}(V) - h}{\tau_h(V)}$$

where p is either 1 or 3. There was some uncertainty about this during the test and either is acceptable.

Part b) The nullclines are where the time derivatives of the state variables are zero:

$$h_V = \frac{I_{ext} - \bar{G}_K (V - E_K)}{\bar{G}_{Na} m_{\infty}^p(V) (V - E_{Na})} \quad h_h = h_{\infty}(V)$$

Part c) C is the correct phase plane (it is the only one with a nullcline $h_h = h_{\infty}(V)$). The dashed line is h_h the solid line is h_V . These nullclines were computed with $p=1$.