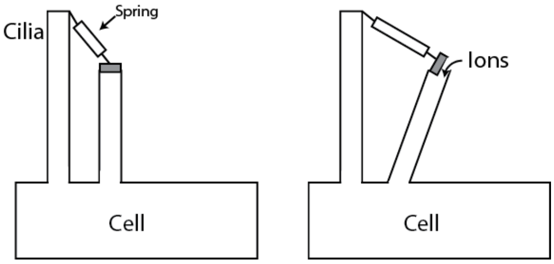
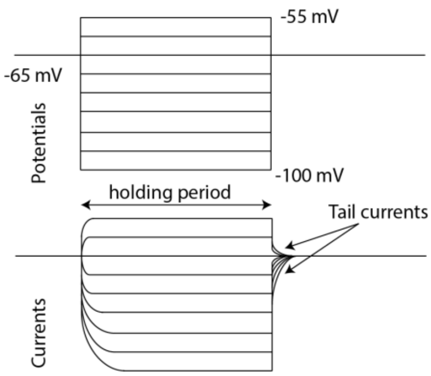
COMPUTATIONAL NEUROSCIENCE (EC60007) ASSIGNMENT I (DUE: 23/09/23 along with Midsem answerscripts)

Problem-1 (Mechano transduction by cochlear hair cells)



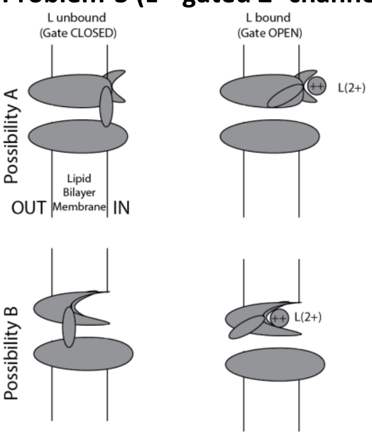
The mechano-transduction by hair cells in the vertebrate cochlea is hypothesized to work as represented in the diagram to the left. The channel is at the tip of the cilium and is opened the by mechanical movement that extends the spring connecting it to the previous cilium. The probability of the channel being open increases with the force exerted on the spring. If channels can be in 2 states (Open or Closed) construct a single barrier model with 2 possible energy states. Modify the barrier model by the spring's extension as appropriate. Derive an equation for the probability that the channel is open expressed in terms of the energy barrier, the mechanical properties of the spring, and the separation *x* of the cilia. Assume that the system is in a steady-state. Make additional assumptions needed. Suppose the cilia have been held at a separation of x_0 for a long time and suddenly the separation is increased to x_i. What is the rate of opening of channels at the moment the separation is increased? (*Hint: As the length increases new channels must open*).

Problem-2 (Tail current analysis)



In developing a Hodgkin-Huxley type model for a channel current, the analysis is often based on tail currents, which are the currents which flow after the offset of a voltage clamp. An example is shown to the left. It is the current for a particular type of ion, called H-current (I_H: hyperpolarization activated current), whose HH-type model is: $I_H = \bar{g}_H h(V,t)(V - E_H)$.
h is the inactivation gate which is the only gate for this type of channel. Dynamics of *h* follows the same kind of differential equation with $h_\infty(V)$ and $\tau_h(V)$ as HH gating variables. Voltage clamp in 5 mV steps from -55 mV to -100 mV are done with the resting potential of -65 mV as the starting point. Before during and after the clamp the holding is for long enough duration such that *h* reaches h_∞.
The objective is to find the parameters in the model based on the above kind of data.
Write an equation for the current during the hold period and another for the tail current, in terms of the parameters of the HH model and the parameters of the voltage clamp.
For the H-current, the equilibrium potential E_H is about -43 mV. Explain why the voltage-clamp current appears to reverse polarity at -65 mV in the figure above. Show how E_H can be determined experimentally from the tail currents. Show how the other parameters may be obtained: $h_\infty(V)$ and $\tau_h(V)$.

Problem-3 (L^{2+} gated Z^+ channel)



Consider the cartoon structure of a (Ligand L) L^{2+} gated (ion Z) Z^+ channel (ligand gated ion channel) to the left. The channel opens when one L^{2+} ion binds to the binding site on the channel. Two possibilities are given: A) L^{2+} binding site is in the inner side of the cell but outside the membrane and B) L^{2+} binding site is halfway into the membrane. With appropriate barrier models show how you would be able to tell apart which of the cases A or B is likely. (*Hint: Effect of membrane potential*)

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Problem-4 (Gates as barrier models and small signal analysis - resonance)

Consider a membrane with only potassium channels and leakage channels as follows:

$$C\frac{dV}{dt} = I_{ext} - \bar{g}_K n^4(V - E_K) - g_L(V - E_L)$$

$$\frac{dn}{dt} = \alpha(V)(1 - n) - \beta(V)n$$

PART (A)

Note the different form of the dynamics of *n* compared to what has been developed in class. Represent the differential equation with $\frac{dn}{dt}$ in its usual form and get expressions for $n_\infty(V)$ and $\tau_n(V)$.

Based on the $\frac{dn}{dt}$ equation show how the gating process can be represented with a barrier model – between open and closed states. What are the rate constants? Now show how the entire K^+ channel with 4 gates can be represented in terms of a barrier models. Pay careful attention to the rate constants when coming up with the full model.

PART (B)

Neural membranes can behave like a resonant electrical circuit under certain conditions. In the above model we will consider the small signal behaviour to show resonance. Consider the variables *V*, I_{ext} and *n* to be represented around their resting state values V^o, I^o_{ext} and n^o by $V^o + v$, $I^o_{ext} + i_{ext}$ and $n^o + \eta$. v, i_{ext} and η represent extremely small changes around their respective resting state values: $v \ll V^o$, $i_{ext} \ll I^o_{ext}$ and $\eta \ll n^o$. Consider any second and higher order terms of the small signals to be negligible (including cross terms).

Represent the above model in terms of the small signals as:

$$\begin{bmatrix} \dot{v} \\ \dot{\eta} \end{bmatrix} = \begin{bmatrix} a & b \\ c & d \end{bmatrix} \begin{bmatrix} v \\ \eta \end{bmatrix} + \begin{bmatrix} i_{ext}/C \\ 0 \end{bmatrix}$$

Approximate $\alpha(V)$ and $\beta(V)$ as linear functions of *V* around resting value of $V = V^o$.

What is the small signal relationship between v and i_{ext}. (Eliminate η from the above equation) Show that the system behaves like an RLC circuit and hence can show resonance.

Problem-5 (Phase plane analysis)

Consider the system of equations:

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

$$\frac{dv}{dt} = bu - au^2v$$

Find the null clines and equilibrium points of the system. What is the nature of the equilibrium points (note that it depends on *a* and *b*) in the *a*-*b* plane? Comment on the feasibility of presence of limit cycles in the system (consider different regions in the *a*-*b* plane).

These problems are slight modifications of problems from a similar course that I had taken.