AMS 332/BIO 332/NEU 536
– Homework for Module 4 –

Part I: Defining concepts (15/30 points)

Answer 5 **of the following questions (your choice)**. Be concise but make sure to write down full answers with relevant details. *Please include the question in your answer.*

> EXAMPLE: Explain the difference between *resting potential* and *reversal potential*.
>
> ANSWER: The resting potential is the equilibrium potential of the membrane in the absence of input. The reversal potential is the equilibrium potential for a single, specific ion species, as if it were the only ion species present (or as if the membrane were selective to that ion species only). The reversal potential is given by the Nernst equation. The resting potential is approximately given by the Goldman equation.

1. Explain the difference between activation and inactivation gate. Include a sketch as appropriate.
2. Define the leak current and explain the origin of its name.
3. Sketch the kinetic model of the delayed-rectified potassium channel studied in class. Make sure to label appropriately the transition rates and to define the quantities in the sketch.
4. An ion channel comprises 5 independent subunits, 3 activation gates and 2 inactivation gates. How many gates must be open for the channel to be open? Explain.
5. Sketch the equivalent circuit of the Hodgkin-Huxley model. Make sure to label correctly every element of the circuit and write down the corresponding differential equation for the membrane potential V.
6. Is the Hodgkin-Huxley model a deterministic or stochastic model? Explain.
7. Describe all relevant phases of an action potential.
8. What is the order of magnitude of the range of change in membrane voltage during an action potential?
9. True or false: "the ion pumps are responsible for the repolarization of the membrane after an action potential". Justify your answer.
10. Describe the boundary conditions for the leaky integrate-and-fire (LIF) neuron model and explain why boundary conditions are required in this model.
11. Does the LIF model neuron have a threshold for spike emission? Is this threshold un unstable equilibrium of the membrane potential dynamics?
12. Describe the type of bifurcation taking place in the quadratic integrate-and-fire model neuron.
13. We have seen that the QIF model neuron can generate the upstroke of a spike but not its downstroke. Is it possible to write down a more complex 1D non-linear ODE that generates both the upstroke and the downstroke of the action potential? Why or why not?
14. Is the f-I curve of the LIF neuron continuous or discontinuous at the rheobase current? Can you think of a way in which your answer could be linked to a bifurcation at rheobase in this model? (Hint: how does the input current modify the $\dot{V} - V$ plot of this model? Include the boundary conditions.)

Part II: Applying concepts (15/30 points)

Solve 2 **of the following problems (your choice)**. Be concise but make sure to write down the essential steps of your derivations. *Please include the question in your answer.*

EXAMPLE: Solve the differential equation of the passive membrane:

$$\tau \dot{V} = -V + V_\infty, \quad V(t_0) = V_0, \tag{1}$$

where τ, V_∞ are constants.

SOLUTION: The solution can be obtained via separation of variables: assuming that $V = V_0$ at initial time t_0, we can separate variables and integrate:

$$\int_{V_0}^{V(t)} \frac{dV}{V_\infty - V} = \frac{1}{\tau} \int_{t_0}^{t} dt. \tag{2}$$

Performing the integrations on each side gives

$$-\ln \frac{V(t) - V_\infty}{V_0 - V_\infty} = \frac{t - t_0}{\tau}. \tag{3}$$

Now exponentiate both sides to get the solution:

$$V(t) = V_\infty + (V_0 - V_\infty)\, e^{-\frac{t-t_0}{\tau}}, \quad t \geq t_0. \tag{4}$$

1. Find the change in reversal potential for Ca^{2+} ions caused by a two-fold increase in extracellular concentration. Assume a temperature of $T = 37\,^\circ$C and initial concentrations of 1 and 0.0001 mM per unit volume outside and inside the cell, respectively.
2. <u>Derive</u> the master equation for a single subunit of the potassium channel: $\dot{n} = \alpha(V)(1-n) - \beta(V)n$, where n is the probability that the subunit is open.
3. Let p_1 be the probability that a potassium channel has all 4 subunits closed p_2 the probability that it has exactly one subunit open. The master equation for p_1 is

   $$\dot{p}_1 = \beta\, p_2 - 4\alpha\, p_1. \tag{5}$$

   Knowing that $p_1 = (1-n)^4$ and $p_2 = 4n(1-n)^3$, replacing these functions into Eq. 5 you obtain a differential equation for n, i.e., an equation of type $\dot{n} = f(n, \alpha, \beta)$. Derive this differential equation for n.
4. Find the mathematical expressions for $\tau^* = \tau^*(V)$ and $V^* = V^*(V)$ so that HH model,

   $$C\frac{dV}{dt} = -G_L(V - E_L) - \bar{G}_K n^4 (V - E_K) - \bar{G}_{Na} m^3 h\,(V - E_{Na}) + I_e, \tag{6}$$

   can be written as

   $$\frac{dV}{dt} = -\frac{V - V^*}{\tau^*}, \tag{7}$$

   where both V^* and τ^* depend on V.
5. Write down an equation for the equilibrium potential for the following membrane model:

   $$C\frac{dV}{dt} = -G_L(V - E_L) - G_K(V - E_K) - G_{Na}(V - E_{Na}) + I_e, \tag{8}$$

   where the G_X are *voltage-dependent* conductances, the E_X are reversal potentials, and I_e is an input current. Assume I_e and the reversal potentials to be constant. *Note:* you will get no closed-form solution for V_{eq}.
6. Find the formula for the equilibria of the membrane potential of the QIF neuron,

   $$C\frac{dV}{dt} = \frac{(V - V_L)(V - \theta)}{R_m V_u} + I_e, \tag{9}$$

   as a function of the neuron parameters and the value of the input current, I_e.
7. Show that the rheobase current (=the bifurcation point) of the QIF neuron (Eq. 9) is given by

   $$I_e^* = \frac{(\theta - V_L)^2}{4 V_u R_m}. \tag{10}$$

   Hint: At the bifurcation, the two equilibria coalesce, hence the equation $CdV/dt = 0$ has a single solution.

8. Assume a zero absolute refractory period, $\tau_{arp} = 0$, and show that, for a large input current I, the firing rate of the LIF neuron,

$$f_{LIF}(I) = \begin{cases} \left(\tau_{arp} + \tau \ln \frac{\mu - V_r}{\mu - V_{spk}}\right)^{-1} & \text{if} \quad \mu \doteq V_L + RI > V_{spk} \\ 0 & \text{otherwise,} \end{cases} \tag{11}$$

is linear in I:

$$f \approx \frac{I}{C(V_{spk} - V_r)} \quad \text{for} \quad I \gg \frac{V_{spk} - V_L}{R} = I_{rh}. \tag{12}$$

Hint: recall that $\ln(1 + x) \approx x$ to leading order in x when $x \to 0$.