1. Nernst Potentials and Equilibrium Resting Potential: Consider the following simplified circuit model for a Hodgkin-Huxley neuron at body temperature (37 °C), with membrane conductance densities $g_K = 40 \mu S/cm^2$, $g_{Na} = 3 \mu S/cm^2$, and $g_{Cl} = 30 \mu S/cm^2$, and with membrane capacitance density $C_m = 1 \mu F/m^2$.

(a) With the intracellular and extracellular concentrations given in the table below, calculate the Nernst potentials for each of the ionic species: $E_K$, $E_{Na}$, and $E_{Cl}$.

<table>
<thead>
<tr>
<th>Ionic Species</th>
<th>Intracellular concentration</th>
<th>Extracellular concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K^+$</td>
<td>392 mM</td>
<td>14 mM</td>
</tr>
<tr>
<td>$Na^+$</td>
<td>45 mM</td>
<td>422 mM</td>
</tr>
<tr>
<td>$Cl^-$</td>
<td>38 mM</td>
<td>578 mM</td>
</tr>
</tbody>
</table>

(b) Using the circuit model with Nernst potentials $E_K$, $E_{Na}$, and $E_{Cl}$ and the conductances given above, find the membrane potential $V_m$ at steady-state.

*Hint:* At DC steady-state, any capacitance reduces to an open circuit connection.

(c) Now find the equilibrium resting potential $V_m$ using the Goldman-Hodgkin-Katz equation. Compare the two values of the membrane potential. Which value is more reasonable for a typical resting potential of a cell?

*Hint:* Membrane conductance (the reciprocal of membrane resistance) for any ion type is directly proportional to membrane permeability for that ion type.

(d) Find the time constant for the membrane potential $V_m$ of the cell to recover from a transient and settle to its steady-state value.

2. Cardiac Action Potential Ionic Current: Consider a cylindrical model of cardiomyocytes with length $L = 100 \mu m$ and radius $r = 5 \mu m$. The Nernst potentials at body temperature (37 °C) for potassium and sodium are $E_K = -96 \text{ mV}$ and $E_{Na} = +52 \text{ mV}$, and the extracellular concentrations are $[K^+]_o = 4 \text{ mM}$ and $[Na^+]_o = 145 \text{ mM}$. The membrane capacitance density is $C_m = 1 \mu F/m^2$. During the action potential upstroke, the membrane becomes permeable to sodium, and the flux of sodium ions into the cardiomyocyte causes the intracellular voltage to rise by $\Delta V = 100 \text{ mV}$ in $\Delta t = 2 \text{ ms}$. 

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1
(a) Find the equilibrium intracellular concentrations \([K^+]_i\) and \([Na^+]_i\).

(b) Calculate the amount of current flowing through the membrane during the upstroke. 

*Hint*: \(C \frac{dV}{dt} = -I\), where \(C = AC_m\) is the cell capacitance and \(A\) is the cell membrane surface area.

(c) Calculate the total number of sodium ions traversing the membrane during the upstroke.

(d) Estimate the intracellular concentration of sodium \([Na^+]_i\) immediately following the upstroke. How does the concentration return to its equilibrium value?

3. **Muscle Fiber Action Potential Propagation and Electromyogram Volume Conduction**: Consider the propagation of an action potential along a muscle fiber bundle in the thigh as shown below. The action potential travels at a velocity \(v = 10\) m/s. Model the net current entering the muscle from the extracellular medium at the action potential onset as a current monopole \(-I = -1\) mA traveling at \(v\), and a second net current exiting the muscle at repolarization as a current monopole \(+I = 1\) mA following at a distance \(d = 2\) mm. An electrode on the thigh surface at a distance \(D = 2\) cm from the muscle measures the EMG signal relative to body ground. The extracellular medium has a volume conductivity \(\sigma = 1\ \Omega^{-1}\text{m}^{-1}\). At time \(t = 0\), the EMG current dipole is perpendicular to the electrode as shown below.

(a) Estimate the peak voltage magnitude of the EMG signal.

(b) Plot the EMG signal as a function of time as the action potential goes by.

4. **Design Problem: FitzHugh–Nagumo Neuron**. The FitzHugh–Nagumo (FN) model is a simplified mathematical model of spiking neuronal dynamics of the giant squid axon, given by the following set of coupled differential equations:

\[
\frac{dV}{dt} = f(V) - W + I \\
\frac{dW}{dt} = a (V + b - cW)
\]

where \(V\) is the neuron membrane potential (accounting for sodium-mediated excitation), \(W\) is the accommodation variable (accounting for potassium-mediated refraction), \(I\) is the current injected into the neuron, \(f(V) = V - V^3/3\) is a nonlinear activation function (modeling sodium excitability), and \(a = 0.08\), \(b = 0.7\) and \(c = 0.8\) are fixed FN model parameters.
The purpose of this design problem is to instantiate the above dynamics of the FN model using a circuit driven by an external current $I$, and producing the voltage $V$ and the current $W$ as shown in the circuit diagram below. The tunnel diode in the circuit diagram is a type of nonlinear resistor, i.e., it carries a current $I_{td}$ that is a nonlinear function of the voltage $V$ across it.

(a) Identify the functional form $I_{td} = g(V)$ for the current-voltage characteristic of the tunnel diode, and values for the capacitance $C$, resistance $R$, and inductance $L$, in order to align the dynamics of the circuit with that of the FN model, for the given nonlinearity $f(V)$ and given parameters $a$, $b$, and $c$ in the FN model.

(b) Plot the tunnel diode current-voltage characteristic $I_{td} = g(V)$, i.e., the current through the tunnel diode $I_{td}$ as a function of the membrane voltage $V$ across it. Identify the voltage region over which the tunnel diode has negative resistance, i.e., where the current decreases with increasing voltage. Explain the role of this negative resistance in making the circuit “spike”.

*Background reading:* See [http://www.scholarpedia.org/article/FitzHugh-Nagumo_model](http://www.scholarpedia.org/article/FitzHugh-Nagumo_model) and the references therein for the background and further details on the FN model.