1 Problems NS3

Topic of this homework: Neuron and synapse terminology; Postulates of systems; Analysis of a diffusion transmission line.

History

Problem *# 1: Provide a brief discussion of the following individuals:*

– 1.1: Albert Einstein

Sol: In 1905 he published four key papers. The one relevant to neuroscience (and many other fiels) is that he was the first to provided the quantitative relation between the diffusion constant D and the mobility constant μ (p. 56, 59)

$$D = \frac{kT}{q}\mu,$$

now known as the *Einstein relation*. This relation is equally important to the semiconductor industry where it allows one to find the nonlinear relation of the current conducted through the diode, as a function of voltage across a diode. ■

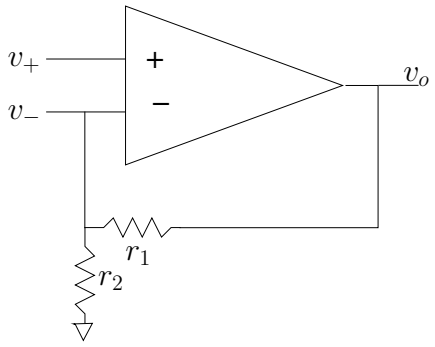
– 1.2: Hodgkin and Huxley

Sol: H–H were the first to work out the mechanism between spike propagation in nerve fibers. ■

– 1.3: Hermann Helmholtz

Sol: Helmholtz was the first to measure the speed of a spike in a frog nerve, which he found to be ≈27 [m/s], around 1850. ■

Problem *# 2: Set up the equations and solve for various properties of the OpAmp.*



– 2.1: In qualitative terms, what is the ratio of the input to output impedance.

Sol: The input impedance of a FET amplifier can be G-ohms (i.e., 10^9 [Ohms]). The output impedance is typically less than 1 ohm, and determined by the current limit of the output transistors, not v_o. ■

– 2.2: Describe the purpose and setup for the space-clamp *circuit.*

Sol: For the space-clamp a wire is pushed down into the plasma core of the squid axon. The low output impedance of the amplifier drives the wire, which holds the internal voltage of the axon constant over several space-constants Δ. This keeps spikes from propagating. When the output voltage of the amplifier is set to the rest voltage of the axon, the displacement current $J_d = C_o dv_o/dt = 0$. This is because the voltage drop across the membrane is zero. ■

– 2.3: Find the formula for the transfer function $H = V_o/V_+$.

Sol: The basic equations are

$$V_o = G(v_+ - v_-) \text{ with } G = 10^6$$

$$v_- = \frac{r_2}{r_1 + r_2} v_o$$

$$v_+ - v_- = v_o/G \approx 0 \text{ thus } v_+ \approx v_-$$

$$H \equiv \frac{v_o}{v_+} \text{ thus } H \approx \frac{v_o}{v_-} = 1 + \frac{r_1}{r_2}.$$

■

Problem *# 3: Thermodynamics of the cell membrane. Set up the equations to estimate the equilibrium sodium and potassium concentrations.*

– 3.1: Define the three membrane currents that re the most important to action potentials (spikes).

$$J_{\mathtt{disp}} = C_o \frac{d}{dt} v(t)$$

$$J_c(s) = q\mu_{\mathtt{Na}}[\mathtt{Na}^+]E = -q\mu_{\mathtt{Na}}[\mathtt{Na}^+]\frac{dV}{dx}$$

$$J_d = -qD_{\mathtt{Na}} \frac{d}{dx}[\mathtt{Na}^+]$$

Sol: the displacement current J_{disp}, the conduction current J_c and the diffusion current J_d. ■

– 3.2: What is the relation between the conduction and diffusion currents under equilibrium conditions?

Sol: The two currents sum to zero. ■

– 3.3: Derive the relation between the voltage and $\lfloor \mathtt{Na}^+ \rfloor$ when the system is in the equilibrium condition?

Sol: When the two currents are equal $J_c + J_d = 0$, thus

$$q\mu_{\mathtt{Na}}[\mathtt{Na}^+]\frac{dV}{dx} = -qD_{\mathtt{Na}}\frac{d[\mathtt{Na}^+]}{dx}.$$

■

– 3.4: Integrate the differential equation and derive the relation between the $\mathtt{Na}^+$ concentrations on the two sides of the membrane and the voltage across the membrane $V = V_o - V_i$. Hint: see pp. 57-59.

Sol: Rewriting and consolidating the equilibrium equation gives

$$\frac{1}{\mathtt{Na}^+}\frac{d[\mathtt{Na}^+]}{dx} = -\frac{\mu_{\mathtt{Na}}}{D_{\mathtt{Na}}}\frac{dV}{dx}$$
$$\int_i^o d\ln[\mathtt{Na}^+] = \ln[\mathtt{Na}^+]\Big|_i^o = -\frac{\mu_{\mathtt{Na}}}{D_{\mathtt{Na}}}\int_i^o dV$$

Thus finally we find

$$\frac{[\mathtt{Na}^+]_o}{[\mathtt{Na}^+]_i} = e^{-\frac{\mu_{\mathtt{Na}}}{D_{\mathtt{Na}}}(V_o - V_i)}.$$

■

Problem *# 4: Analyize a Δ long patch of membrane. Set up the equations to estimate the properties of a mylinated nerve fiber.*

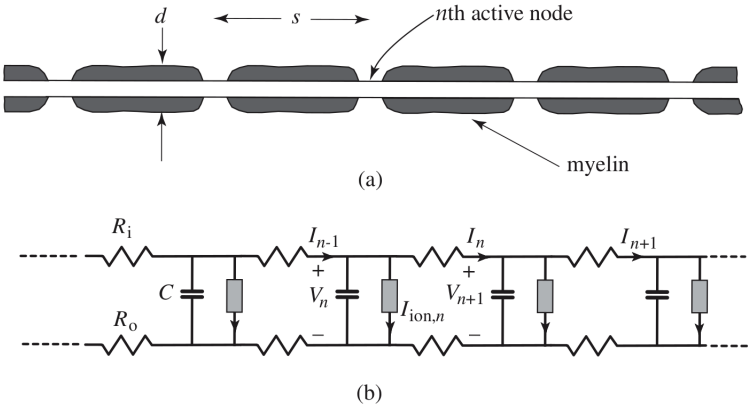


Figure 1: *Diagram of the Frog axon showing the physical and electrical circuit (Scott, p. 142).*

Standard frog axon

Distance between nodes $(s) = 2$ mm.

Outside fiber diameter $(d) = 14$ μm.

Internal resistance/length $(r_{\mathrm{i}}) = 140$–145 megohm/cm.

External resistance/length $(r_{\mathrm{o}}) \ll r_{\mathrm{i}}$.

Capacity of myelin/length $(c_{\mathrm{m}}) = 10$–16 pF/cm.

Capacity of active node $(C_{\mathrm{n}}) = 0.6$–1.5 pF.

Experimental impulse speed $v_{\mathrm{e}} = 23$ m/s.

Figure 2: *Parameters measured for the Frog axon (Scott, p. 142)*

– 4.1: Assume the following

$$\lambda_o f_{\max} = v_e = 23 \text{ [m/s]}$$
$$= \lambda_o/2 \text{ [mm]}$$

From a previous homework we assumed that $\Delta = \lambda/2$ and $\tau = RC$. Here $\Delta = s$ is taken to be the distance between nodes. Find $f_{\max}$.

Sol: Since $f_{max} = v_e/\lambda_o$ with $v_e = 23$ [m/s] and $\lambda_o = 2s = 4 \times 10^{-3}$ [m]. Thus $f_{max} = 23/4 = 5.75$ [kHz]. ■

– 4.2: Find the time constant ($\tau = RC$) and the cutoff frequency $f_c = 1/2\pi\tau$. Compare f_c to $f_{\max}$.

Sol: The internal $R = 142 \times 10^8$ [Ω/m] and the membrane capacitance is $C = 1,300$ [pF/m]. Thus $\tau = 142 \times 10^8 \times 1300 \times 10^{-12}$ [F/cm], thus $\tau = RC = 18.46 \times 10^{-6}$ [s/m^2]. Expressed in terms of the area $s^2 = 4 \times 10^{-6}$ this is $\tau \cdot s^2 = (4 * 18.46) * 10^{-6} = 73.84$ [μ s].

The corresponding cutoff frequency is $\omega = 1/\tau \cdot s^2$, which in [Hz] is $f_c = 1/2\pi\tau \cdot s^2 = 2.155$ [kHz] which is 37.5% of $f_{max} = 5.75$ [kHz]. ■

– 4.3: The two figures below show the parameters $n(t), m(t), h(t)$ used in Hodkins–Huxley's model of spike generation. Their equation for the current is :

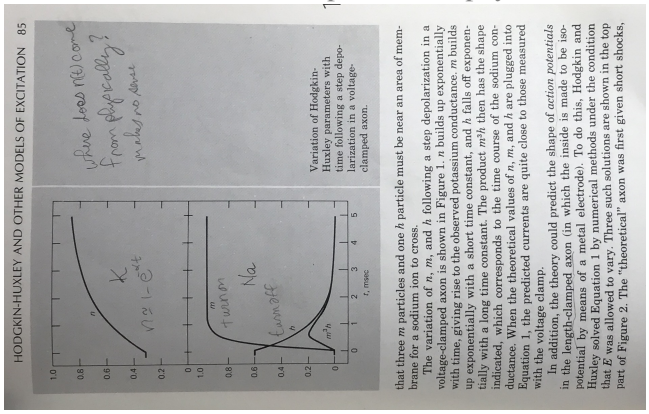
$$I(t) = C_m \frac{d}{dt} V + g_{\mathrm{K}} n^4(t)(V - V_{\mathrm{K}}) g_{\mathrm{Na}} m^3(t) h(t)(V - V_{\mathrm{Na}}).$$

The generally accepted but unproven form of the spike voltage is the solution to the linear wave equation

$$V(t) = S(x - v_e t),$$

where x is the axial distance down the fiber and c_s is the spike velocity. A number of models have attempted to replace the phenomenological H–H model with a physical model into closer agreement with the data, however H–H is still the generally accepted explaination.

Explain in your own words why the nonlinear model would have the same properity as the wave equation, where the spikes travel at the fixed velocity v_e (see the above equation). **Sol:** See the relevant discussion from Scott in §4.5. These two attached pages from Cole's book (p. 84-85) (Scott's ref. 8, p. 92) give the HH view of spike propagation. The model described in class using Matlab's similink with three diodes, seems to provide the physical model we need.



g_l = leak conductance, mho/cm²
E_{Na} = sodium equilibrium potential, V
E_K = potassium equilibrium potential, V
E_l = leak equilibrium potential, V

This equation describes the current across a nervous structure whose interior is isopotential (no longitudinal spread of current). The conductances g_{Na} and g_K are assumed to vary with potential and time in a deterministic way. The leak conductance is assumed constant. Under voltage-clamp conditions, the rate of change of potential is zero, and the membrane currents are purely ionic and should be given by the last three terms of Equation 1. In order to see if the model can predict real membrane currents, it is first necessary to write expressions for g_{Na} and g_K as functions of potential and time.

THEORETICAL POTASSIUM AND SODIUM CONDUCTANCES

The potassium conductance is described by

$$g_K = \bar{g}_K n^4 \tag{2}$$

where $\bar{g}_K$ = maximum potassium conductance, a constant
n = a dimensionless variable which varies from 0 to 1 as a function of voltage and time

The fourth power of n is needed to describe the slow buildup of g_K following a step depolarization. The physical analogue of such a process is that four particles must be near a certain area of the membrane at once in order for a potassium ion to cross, where the probability of each particle being there is proportional to n. Hodgkin and Huxley worked out an equation for n as a function of potential and time, which need not be derived here. This allowed them to calculate g_K versus the time following a step depolarization.

The sodium channel is a little more complicated because it inactivates. In order to include this in their theory, Hodgkin and Huxley assumed that

$$g_{Na} = \bar{g}_{Na} m^3 h \tag{3}$$

where $\bar{g}_{Na}$ = maximum sodium conductance, a constant
m = an activation parameter like n, which varies from 0 to 1 as a function of voltage and time
h = an inactivation parameter which varies from 0 to 1 as a function of voltage and time

The physical analogue of the activation and inactivation processes is