

BASIC ELECTROPHYSIOLOGY

In this module we will see why the resting voltage of a neuron is negative, around -60mV to -70mV , and why neurons have a short memory. Book references that might be useful are

Theoretical Neuroscience, Dayan and Abbott. Chapter 5 p153-161. MIT Press

Spiking Neuron Models, Gerstner and Kistler. Chapter 2 p31-34. Cambridge University Press

Mathematical Physiology, Keener and Sneyd. Chapter 2 p52-59, Springer.

• CAPACITANCE OF A NEURON

The charge Q (in coulombs C) on a membrane of capacitance C (in farads F) is proportional to the potential difference across the membrane (membrane voltage) V_m measured in volts (V)

$$Q = CV_m \quad (1)$$

where $V_m = V^i - V^e$ with V^i the internal and V^e the external voltage. The cell membrane (a lipid bilayer) behaves as a capacitor with capacitance per unit surface area $c = 10\text{nF}/\text{mm}^2$. Injection of a current I (measured in Amperes, A) into a neuron will charge it up (by convention I is positive for charge flowing into the cell for injected current). Assume for now that the membrane is closed so no charge leaks out. Then

$$C \frac{dV_m}{dt} = I \quad \text{with a solution} \quad V_m(t) = \int_{-\infty}^t \frac{dt'}{C} I(t') \quad (2)$$

where $C = cA$ and A is the membrane surface area. Such a leakless neuron would be a perfect integrator. Neurons, however, also have channels on their membranes that allow ions to pass and are therefore leaky. The internal potential of a neuron is also lower than the external potential (so there is a resting charge on the membrane) - a feature that is also due to transmembrane ionic currents I_{ion} . By convention these are positive for current flowing out of the cell so that

$$C \frac{dV}{dt} + I_{ion} = I. \quad (3)$$

• THERMAL AND ELECTRIC POTENTIAL ENERGY

Thermal energy in Joules (J) of an ion at a temperature T in Kelvins ($T_K = T_{\circ C} + 273.15\text{K}$) per ion is set by the scale $k_B = 1.381 \times 10^{-23} \text{JK}^{-1}$. Electrical energy in a potential V is set by the scale q which is the charge on an electron $q = 1.602 \times 10^{-19} \text{C}$. By equating these scales a potential V_T can be identified which measures the typical potential difference that thermal energy can push an ion across

$$E_T = k_B T, \quad \text{and} \quad E_V = zqV \quad \text{so} \quad V_T = k_B T / q = 26.7\text{mV} \quad (4)$$

where z is the algebraic charge on the ion and body temperature $T = 37^\circ\text{C}$ (NB don't forget to convert to Kelvins!) was used. This is of the order of the resting potential of a neuron, and hence in understanding the flow of ions across the membrane both thermal and potential effects must be accounted for.

• DIFFUSION OF IONS IN A CHANNEL

Let the ionic density at a point x in a membrane-spanning channel of length a be N with N^e and N^i the external and internal densities (this could be measured in molarity M, which is moles per litre of fluid where a mole is $N_A = 6.02 \times 10^{23}$ ions). The ionic density in the channel obeys the continuity and diffusion equation with a flux J per unit area of channel:

$$\frac{\partial N}{\partial t} = -\frac{\partial J}{\partial x}, \quad \frac{\partial N}{\partial t} = D \frac{\partial^2 N}{\partial x^2} - \frac{\partial}{\partial x}(vN) \quad \text{and} \quad J = vN - D \frac{\partial N}{\partial x} \quad (5)$$

where D is the diffusion constant of the ion and $v(x)$ is the drift velocity which might be spatially dependent. From Einstein (1905) both the diffusion constant D and the average velocity v of the particle are related to the mobility of the ion μ .

$$D = \mu k_B T \quad \text{and} \quad v = -\mu z q \frac{\partial V}{\partial x} \quad (6)$$

where the mean drift velocity is proportional to the potential gradient (electric field strength). On substitution of these quantities the flux can be written

$$J = -\mu k_B T \left(N \frac{z}{V_T} \frac{\partial V}{\partial x} + \frac{\partial N}{\partial x} \right) \quad (7)$$

At some membrane voltage $V_m = V^i - V^e = E$ there will be an equilibrium and no net flux of the ion in question. Setting $J = 0$ and solving for the voltage yields

$$E = \frac{k_B T}{zq} \log \left(\frac{N^e}{N^i} \right) = \frac{V_T}{z} \log \left(\frac{N^e}{N^i} \right). \quad (8)$$

This is the famous Nernst equation; it can be used to calculate the equilibrium potentials E for different ionic species. The major ionic species are Sodium Na^+ , Potassium K^+ and Chlorine Cl^- . Typical values quoted are 50mV, -80mV and -70mV respectively.

• THE GOLDMAN CURRENT

If the membrane potential is not equal to the reversal potential of a particular ion, then an ionic current will flow. We first convert the flux J , which has units of ions $\text{m}^{-2} \text{s}^{-1}$, to an ionic current per unit area of membrane I , which has units Amperes m^{-2} . Thus $I = \rho \sigma z q J$ where the effective area of the channel openings is σ and the density of channels per surface area of membrane is ρ . We now combine the two differentials in (7) and write the current as

$$I = -\mu \rho \sigma z^2 q^2 \frac{V_T}{z} e^{-zV/V_T} \frac{\partial}{\partial x} \left(e^{zV/V_T} N \right). \quad (9)$$

We now bring the outer exponential form over to the LHS and integrate under conditions of constant, non-zero current throughout the channel. The potential is assumed to vary linearly with distance with $x=0$ internal at V^i and $x=a$ external at V^e

$$V = V^i + \frac{x}{a}(V^e - V^i). \quad (10)$$

We insert this linear form for the voltage change through the channel given in equation (10) and multiply by the exponential and z/aV_T

$$\frac{zI}{aV_T} \int_0^a dx e^{z(V^i + x(V^e - V^i)/a)/V_T} = -\frac{\mu \rho \sigma z^2 q^2}{a} e^{zV/V_T} N \Big|_{int}^{ext} \quad (11)$$

which on performing the integral on the LHS and rearranging yields

$$I = \frac{\mu \rho \sigma z^2 q^2}{a} V_m \left(\frac{N^e - N^i e^{zV_m/V_T}}{1 - e^{zV_m/V_T}} \right). \quad (12)$$

It proves convenient to write this in terms of a permeability P_s per unit area (units m s^{-1})

$$P = \frac{D \rho \sigma}{a} \quad \text{so that} \quad I = P z^2 q \frac{V_m}{V_T} \left(\frac{N^e - N^i e^{zV_m/V_T}}{1 - e^{zV_m/V_T}} \right). \quad (13)$$

This equation was derived in Goldman (1943). When V_m is equal to the equilibrium potential E of equation (8) the current vanishes, as expected.

• EXPANSION OF THE GOLDMAN CURRENT EQUATION

We now take equation (13) for some ion species (subscripted s) and expand it around the equilibrium potential E_s , where we know the current I_s vanishes. Given that it is the numerator that vanishes when $V = E_s$ (we drop the m subscript for the membrane voltage from now on) it is only this term that we need expand; in the rest of the terms we may replace $V \rightarrow E_s$. We can also use the Nernst equation (8) once again to replace the zE_s/V_T terms everywhere (except for the linear $V - E_s$ part) with $\log(N_s^e/N_s^i)$. This yields

$$I_s = g_s(V - E_s) + O((V - E_s)^2) \quad (14)$$

where we can identify a conductance per unit area g_s

$$g_s = \frac{P_s z_s^2 q}{V_T} N_s^e N_s^i \left(\frac{\log(N_s^e/N_s^i)}{N_s^e - N_s^i} \right). \quad (15)$$

The current-voltage relation (14) is ohmic, i.e. of the form $I = V/R$. If we make the further assumption, for simplicity, that all the ionic currents present can be well approximated by the ohmic form we can write the equation for the ionic currents as

$$I_{ion} = g_K(V - E_K) + g_{Na}(V - E_{Na}) + g_{Cl}(V - E_{Cl}). \quad (16)$$

As will be seen later, some of these conductances can be strongly voltage dependent, over and above that predicted by equation (13). But for now we consider only the passive case where the sum of the ionic currents may be considered ohmic and written

$$I_{ion} = g_L(V - E_L) \quad (17)$$

where g_L is the total conductance and E_L is the resting potential. A range for typical values of the leak conductance is $g_L = 0.2 - 1 \mu\text{S}/\text{mm}^2$.

• THE GOLDMAN-HODGKIN-KATZ EQUATION

We now derive an important equation for the resting potential (which we call here V^*) that does not assume ohmic forms for the currents, but which is only valid for charges $z = \pm 1$. We will label positively charged ions concentrations with N_{p+} and negatively charged concentrations with N_{n-} and it is assumed that the membrane permeability is different for each ion. For the neuron to be at equilibrium, all the currents must vanish. Hence,

$$I_{net} = \sum_p I_{p+} + \sum_n I_{n-} = 0. \quad (18)$$

The current (13) can be written to have the same denominator for the cases $z=1$ and $z=-1$

$$I_{p+} = P_{p+} q \frac{V^*}{V_T} \left(\frac{N_{p+}^e - N_{p+}^i e^{V^*/V_T}}{1 - e^{V^*/V_T}} \right) \quad \text{and} \quad I_{n-} = P_{n-} q \frac{V^*}{V_T} \left(\frac{N_{n-}^i - N_{n-}^e e^{V^*/V_T}}{1 - e^{V^*/V_T}} \right). \quad (19)$$

Note that the inner and outer concentrations are exchanged for the two cases. If we insert these forms into equation (18) and remove any common prefactors we have:

$$\left(\sum_k P_{p+} N_{p+}^e + \sum_n P_{n-} N_{n-}^i \right) - \left(\sum_k P_{p+} N_{p+}^i + \sum_n P_{n-} N_{n-}^e \right) e^{V^*/V_T} = 0 \quad (20)$$

Which on re-arranging for the voltage V_m yields

$$V^* = V_T \log \left(\frac{\sum_k P_{k+} N_{k+}^e + \sum_n P_{n-} N_{n-}^i}{\sum_k P_{k+} N_{k+}^i + \sum_n P_{n-} N_{n-}^e} \right) = V_T \log \left(\frac{P_K N_K^e + P_{Na} N_{Na}^e + P_{Cl} N_{Cl}^i}{P_K N_K^i + P_{Na} N_{Na}^i + P_{Cl} N_{Cl}^e} \right) \quad (21)$$

where the specific result for the ionic species crossing neuronal membranes has also been given. The equation appears in Goldman (1943) and is known as the Goldman-Hodgkin-Katz equation.

• THE VOLTAGE EQUATION FOR A PASSIVE MEMBRANE

Combining equation (17) with the membrane voltage equation (3) we have

$$C \frac{dV}{dt} + g_L (V - E_L) = I \quad \text{or more usually} \quad C \frac{dV}{dt} = g_L (E_L - V) + I. \quad (22)$$

On dividing this equation through by g_L a quantity with the units of time can be found $\tau_L = C/g_L$. The voltage can now be solved in terms of the current

$$V(t) = E_L + \int_{-\infty}^t \frac{dt}{\tau_L} \exp^{-(t-t')/\tau_L} \frac{I(t')}{g_L}. \quad (23)$$

The voltage is proportional to an exponentially-filtered current, with filter constant τ_L . Unlike equation (2) this model has a resting potential E_L that is negative, and a voltage that integrates recent current only over a time-scale of τ_L : it is a leaky integrator and also an input-coincidence detector over a timescale τ_L . The quantity τ_L typically takes values in the range 5 – 50ms. Generalisations of equation (22) are fundamental for the modelling of both simple and biophysically-detailed neurons.

References

- Einstein A (1905) Investigations on the theory of the brownian movement Dover edition, english translation.
Goldman DE (1943) Potential, impedance and rectification in membranes J. Gen. Physiol. 27, 37-60