

# Introduction to Computational Neuroscience (Fall 2023)

## The Basis of Electrical Activity in the Neuron

---

### The Nernst-Planck equation

- **Fick's law of diffusion** (1855) states that “The molar flux due to diffusion is proportional to the concentration gradient”. Also, diffusion of the substance is down the gradient. Thus, in one dimension, if  $X$  is the concentration of the diffusing substance:

$$(1) \quad J_{\text{diff}} = -D \frac{dX}{dx}$$

where  $D$  is the **diffusion constant**.

- If the diffusing substance is charged, and there is an electric field, then the particles will drift in response to the field. The flux is

$$(2) \quad J_{\text{drift}} = -\frac{DF}{RT} z_X X \frac{dV}{dx}$$

where  $F$  is **Faraday's constant**,  $R$  is the **gas constant**,  $T$  is **temperature** (in kelvins), and  $z_X$  is the **valence** (charge) of the ion that is drifting in the field.

- When both processes happen, i.e., electrodiffusion, then the total flux of particles is the sum of  $J_{\text{diff}}$  and  $J_{\text{drift}}$ :

$$(3) \quad J_X = J_{\text{diff}} + J_{\text{drift}} = -D \left( \frac{dX}{dx} + \frac{z_X F}{RT} X \frac{dV}{dx} \right)$$

This equation was developed by Nernst (1888) and Planck (1890) and is called the **Nernst-Planck equation**.

### Current and flux

- The amount of positive charge flowing per unit time through a conductor such as an ion channel is the **current**, measured in amperes (A). The **current density** is the current flow per unit of cross-sectional area, and will be denoted as  $I$ . (Note that  $I$  is often used to also denote the current, so there is ambiguity. In the text,  $I$  means current density.) The typical units are  $\mu\text{A cm}^{-2}$ .
- The relationship between current density and flux of substance X is

$$(4) \quad I_X = F z_X J_X$$

The sign of the current for positive ions flowing out of the cell through channels is positive (note that  $x = 0$  inside the cell and  $> 0$  outside the cell). So **outward currents are positive**. Positive ions flowing into the cell through channels is negative. So **inward currents are negative**. Negative ions flowing into the cell generate a positive, outward current!

- If  $K^+$ ,  $Na^+$ , and  $Cl^-$  are moving through ion channels, then

$$(5) \quad I_i = I_{Na} + I_K + I_{Cl}$$

$$(6) \quad = Fz_{Na}J_{Na} + Fz_KJ_K + Fz_{Cl}J_{Cl}$$

where  $I_i$  is the total current through the channels.

The Nernst equation

Nernst (1888) derived an equation for the equilibrium voltage for a single type of ion subject to electrodiffusion. This equilibrium voltage is called the **Nernst potential**, and it is given by the **Nernst equation**:

$$(7) \quad V_X = \frac{RT}{z_X F} \ln \frac{X_{out}}{X_{in}}$$

The Goldman-Hodgkin-Katz equations

- If there is more than one type of ion flowing across the membrane, then an equilibrium potential will be reached such that the flux due to concentration gradients equilibrates with that due to electrical drift for the different ion types combined. (The fluxes won't be equilibrated for each ionic species separately.) The equilibrium voltage, called the **resting membrane potential** in the case of neurons, is given by the **Goldman-Hodgkin-Katz voltage equation**:

$$(8) \quad V_m = \frac{RT}{F} \ln \frac{P_K K_{out} + P_{Na} Na_{out} + P_{Cl} Cl_{in}}{P_K K_{in} + P_{Na} Na_{in} + P_{Cl} Cl_{out}}$$

where  $P_X$  is the permeability to ion X, and  $X_{in}$  is the concentration of the ion inside the cell, while  $X_{out}$  is the concentration outside. This reduces to the Nernst equation when there is only one type of ion.

- The **Goldman-Hodgkin-Katz current equation** relates the current generated by an ion X when it crosses a semipermeable membrane and when there is an ion concentration difference. This is:

$$(9) \quad I_X = P_X z_X^2 \frac{F^2 V}{RT} \left( \frac{X_{in} - X_{out} e^{-z_X FV/RT}}{1 - e^{-z_X FV/RT}} \right).$$

Note that the relationship between voltage  $V$  and current  $I$  is nonlinear in this equation.

- A linear approximation is often used to relate current and voltage. This is similar to Ohm's law, so is called an **Ohmic approximation**. It is

$$(10) \quad I_X = g_X(V - V_X)$$

where the parameter  $g_X$  is the **conductance** and  $V - V_X$  is the **driving force**. This approximation is typically quite good, except in the case of  $\text{Ca}^{2+}$ , where it deviates a lot from the GHK curve at higher voltages (this is because the intracellular concentration of  $\text{Ca}^{2+}$  is extremely small). The resulting linear  $I - V$  relation is called **quasi-ohmic**.

The capacitive current

- How do the currents flowing across a semipermeable membrane affect the voltage? This is what the capacitive current equation tells us. The strength of the electric field set up through the separation of ions between plates of a capacitor is proportional to the magnitude of the excess charge  $q$  on the plates. The constant of proportionality is called the **capacitance** ( $C$ ) and is measured in farads. It indicates how much charge can be stored on a capacitor for a given potential difference:

$$(11) \quad q = CV.$$

Said another way, the capacitance  $C$  is a measure of how much charge  $q$  needs to be transferred from one conductor to another to create a given potential difference  $V$ .

- As the charge  $q$  changes, due to flow through ion channels for example, so too will  $V$ . For neural membranes,  $C \approx 1 \mu\text{F cm}^{-2}$ . Differentiating w.r.t.,

$$(12) \quad I_C = C \frac{dV}{dt}$$

which is called the **capacitive current**. It tells how voltage changes due to an electrical current.

Equivalent circuit and Kirchoff's current law

- The ionic currents across a patch of neural membrane can be represent by an electrical circuit, called an **equivalent circuit**. This represents the membrane as a capacitor, and the current through each ion channel as a resistor in series with a battery. The resistor reflects the ion channel while the battery reflects the driving force due to the Nernst potential.
- **Kirchoff's current law** states that the sum of the current flowing through a parallel circuit is conserved. Recalling that  $I_i$  is the current through the

ion channels. If there is an electrode attached to the patch of membrane that introduces an applied current  $I_e$ , then

$$(13) \quad I + I_e/a = I_i + I_C$$

where  $I$  is the total current flowing through the membrane and  $a$  is the area of the patch of membrane. (This is needed because the applied current is not a current density, while other currents are really current densities.)

- For an isolated membrane patch (not connected to more membrane)  $I = 0$ . Putting in other terms and rearranging,

$$(14) \quad C \frac{dV}{dt} = -(I_{Na} + I_K + I_L - I_e/a)$$

where the **leak current**  $I_L$  may be a  $Cl^-$  current or a current due to a mix of ions flowing through **non-specific channels**. This is the **voltage equation**.

- **Thévenin's theorem** states that any combination of voltage sources and resistances across two terminals can be replaced by a single voltage source and a single resistor. If the voltage sources are due to  $Na^+$ ,  $K^+$ , and leak, then according to this theorem,

$$(15) \quad V_m = \frac{g_{Na}V_{Na} + g_KV_K + g_LV_L}{g_m}$$

where  $g_m$  is the **specific membrane conductance**,

$$(16) \quad g_m = g_{Na} + g_K + g_L.$$

The reciprocal of this is the **specific membrane resistance**,

$$(17) \quad R_m = \frac{1}{g_m}.$$

The word “specific” is included since the conductance (or resistance) is per unit area of membrane.

Neural dynamics of a passive membrane

- The voltage equation can be written as:

$$(18) \quad C \frac{dV}{dt} = g_m(V_m - V) + I_e/a$$

or

$$(19) \quad C \frac{dV}{dt} = \frac{V_m - V}{R_m} + I_e/a.$$

- Because the voltage equation is linear we can solve it. Assuming that the system is at rest at equilibrium ( $V_m$ ) when the external current is applied, the solution is

$$(20) \quad V(t) = V_m + \frac{R_m I_e}{a} (1 - e^{-t/\tau})$$

where  $\tau \equiv R_m C$  is called the **membrane time constant**. The equilibrium with the external current on is

$$(21) \quad V_\infty = V_m + \frac{R_m I_e}{a},$$

so one could rewrite Eq. 20 as

$$(22) \quad V(t) = V_m + (V_\infty - V_m) (1 - e^{-t/\tau}).$$

The membrane time constant ( $\tau$ ) is the time to go approximately 2/3 (actually  $1 - 1/e$ ) of the way from the original equilibrium to the new equilibrium. A large  $\tau$  means it takes a long time to go from the old to the new equilibrium.

- **Ohm's law** says that  $\Delta V = IR$ . Applying this, where  $\Delta V = V_\infty - V_m$  (the new equilibrium minus the old one) and  $I = I_e$ , gives an equation for the **input resistance**:

$$(23) \quad R_{\text{in}} = \Delta V / I_e.$$

This tells how much an applied current will change the equilibrium. A big input resistance means an applied current will have a large effect on the equilibrium voltage.

### Compartmental model

- In the single-compartment model, the total current was 0, reflecting conservation of charge. In a compartment within a compartmental neuron model, the membrane current is equal to the sum of the leftward and rightward axial currents. The axial resistance is proportional to the length  $l$  of the compartment (approximated as a cylinder), and inversely proportional to its cross-sectional area,  $\frac{\pi d^2}{4}$ . So the axial resistance is

$$(24) \quad \text{axial resistance} = \frac{4R_a l}{\pi d^2}$$

where  $R_a$  is the **specific axial resistance**. For compartment  $j$ , using Ohm's law, the total membrane current is

$$(25) \quad I_j = \frac{V_{j+1} - V_j}{4R_a l / \pi d^2} + \frac{V_{j-1} - V_j}{4R_a l / \pi d^2}$$

where the first term is the current into compartment  $j + 1$  and the second is the current into compartment  $j - 1$ .

- Replacing Eq. 25 into Eq. 13 and replacing the patch area  $a$  with the surface area of the compartment cylinder,  $a = \pi dl$ , one gets the **fundamental equation of a compartmental model**:

$$(26) \quad C \frac{dV_j}{dt} = \frac{V_m - V_j}{R_m} + \frac{d}{4R_a} \left( \frac{V_{j+1} - V_j}{l^2} + \frac{V_{j-1} - V_j}{l^2} \right) + \frac{I_{e,j}}{\pi dl}$$

There would be an equation like this for each compartment, so  $j = 1, \dots, N$  where  $N$  is the number of compartments.

- **Boundary conditions** are need at the left and right boundaries. There are several options. At the left end, for example,  $V_1 = 0$  and Eq. 26 is not used in the first compartment if a **killed end** condition is applied. If the **sealed end** condition is used, then Eq. 26 is used in compartment 1, with  $V_0 = V_2$  in the calculation of  $V_1$ .

The cable equation

- In the limit of a large number of very short compartments, the compartmental model converges to a partial differential equation called the **cable equation**:

$$(27) \quad C \frac{\partial V}{\partial t} = \frac{V_m - V}{R_m} + \frac{d}{4R_a} \frac{\partial^2 V}{\partial x^2} + \frac{I_e}{\pi d}$$

in which the contributions of current from left and right of a point in the cable is through the second partial derivative, which is the diffusion operator, and  $I_e$  is the injected current per unit length.

- For a semi-infinite cable with a current source of  $I_e$  applied at  $x = 0$  and a sealed end boundary condition, the steady state voltage is

$$(28) \quad V(x) = V_m + R_\infty I_e e^{-x/\lambda}$$

where  $\lambda$  is called the **length constant**. This determines the rate of decay of the voltage with distance from the current source. A large  $\lambda$  means a slow decay with distance. The formula for the length constant is

$$(29) \quad \lambda = \sqrt{\frac{R_m d}{4R_a}}$$

Thick neural processes have large length constants.

- The input resistance of a semi-infinite cable,  $R_\infty$  tells how much the voltage changes in response to an applied current. It's value is

$$(30) \quad R_\infty = \frac{R_m}{\pi d \lambda}$$

The thicker neural processes have smaller input resistance, so are not as sensitive to applied currents as are thin processes.