Model neurons

The membrane equation

Suggested reading:

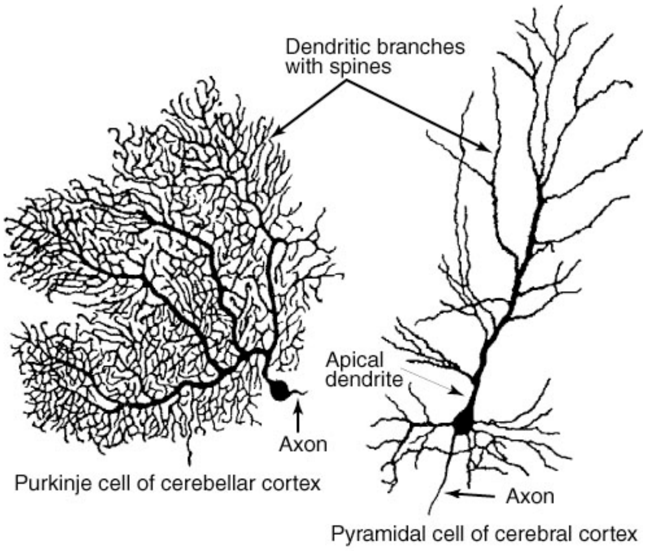
Chapter 5.1-5.3 in Dayan, P. & Abbott, L., Theoretical Neuroscience, MIT Press, 2001.

Model neurons: The membrane equation

Contents:

- Ion channels
- Nenst equation
- Goldman-Hodgkin-Katz equation
- Ion concentrations
- Membrane capacity
- RC-circuit

The neurons in the brain

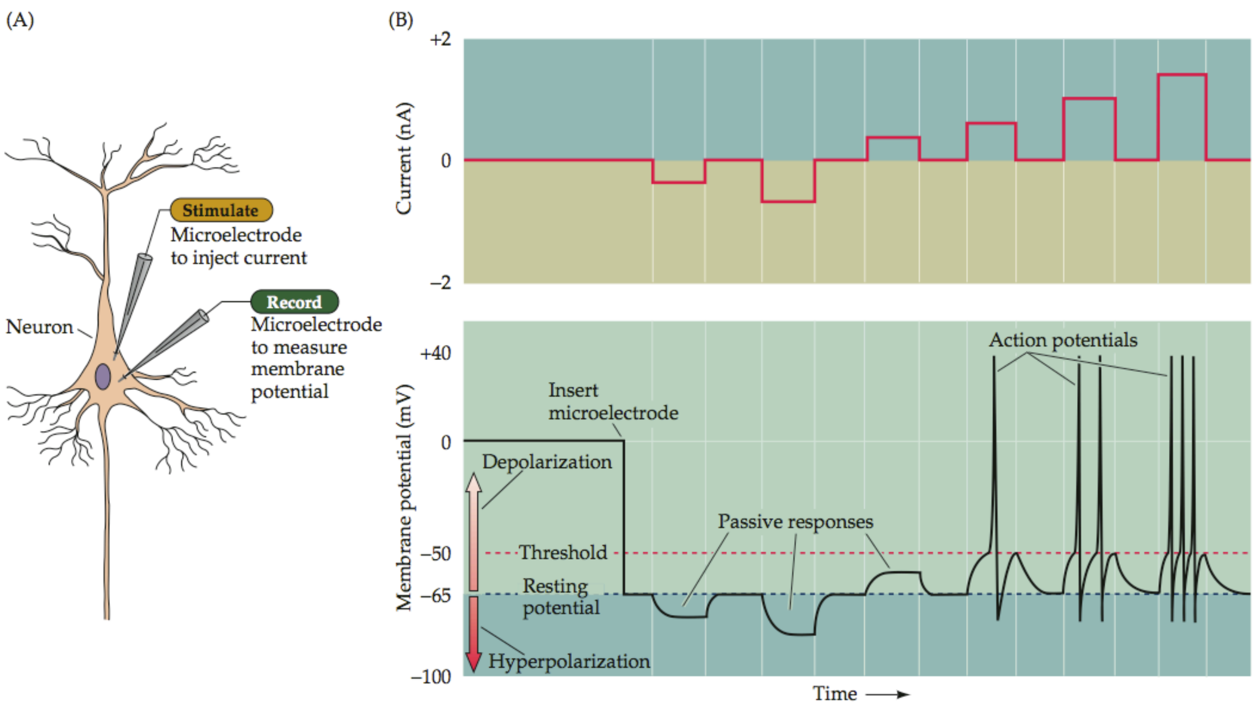


Examples of neurons in the brain.

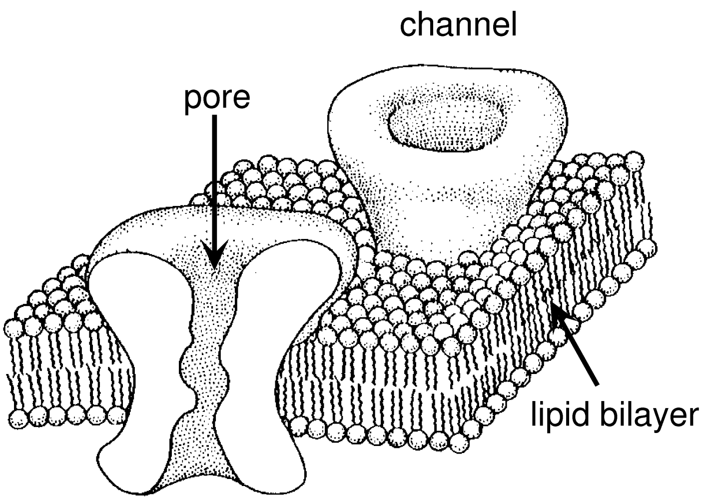
Neurons are already extremely complicated devices.

They transfer signals by means of ion exchanges through channels made of proteins.

Terms and definitions



Cell membrane with ion channels



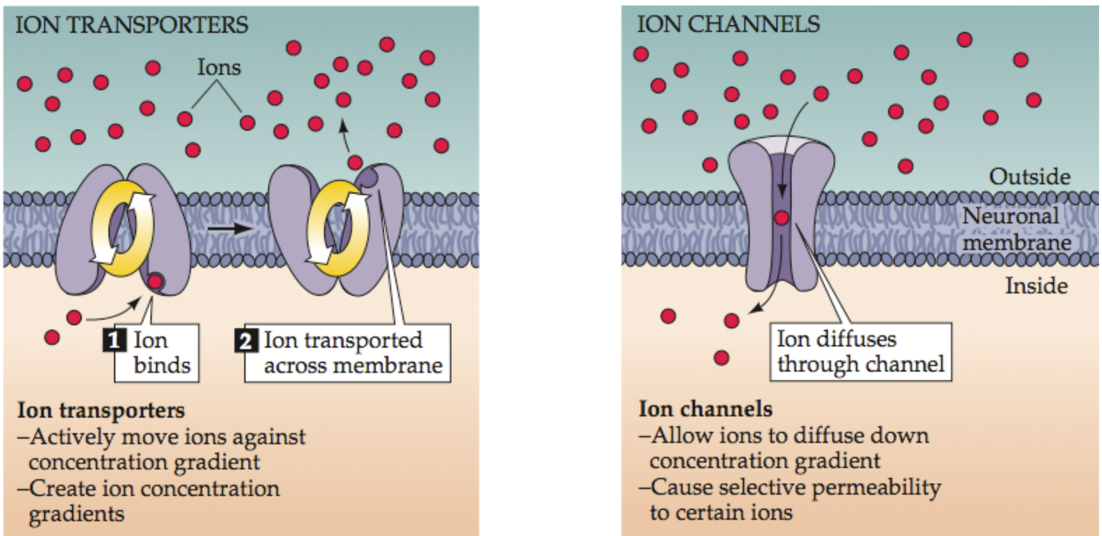
The cell membrane keeps a voltage difference between the cell and the surrounding by selectively allowing different ions in and out of the cell.

Typical ions:
Calcium [Ca^{2+}]
Potassium [K^{+}]
Sodium [Na^{+}]
Cloride [Cl^{-}]
Magnesium [Mg^{2+}]

Membrane Potential:

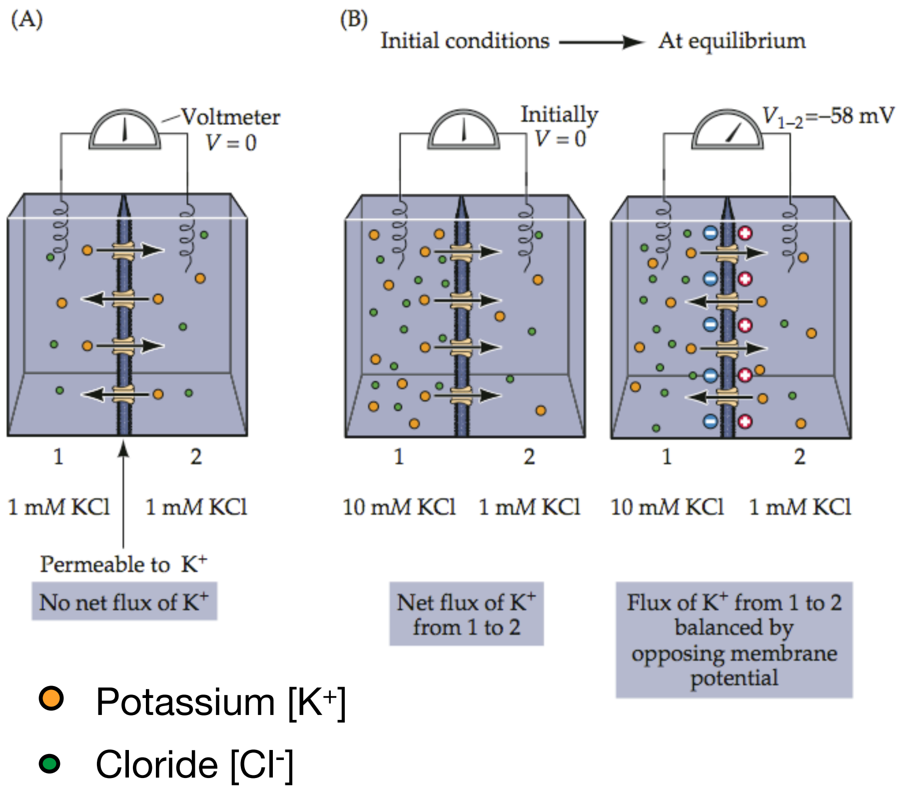
$$V_m = V_i(t) - V_e(t)$$

Ion transporters and ion channels



Ion transporters and ion channels are responsible for ionic movements across membranes. **Transporters** create ion concentration differences by actively transporting ions against their chemical gradients. **Channels** take advantage of these concentration gradients, allowing selected ions to move, via diffusion, down their chemical gradients.

Electrochemical equilibrium



(A) A membrane permeable only to K+ separates compartments 1 and 2, which contain the indicated concentrations of KCl.

(B) Increasing the KCl concentration in compartment 1 to 10 mM initially causes a small movement of K+ into compartment 2 until the electromotive force acting on K+ balances the concentration gradient, and the net movement of K+ becomes zero.

Nernst equation

Each ion has an equilibrium potential associated with whereby the diffusive forces and the electrical forces balance. This can be expressed by equal probabilities of an ion to cross the membrane:

$$P_{\text{concentration gradient}} = P_{\text{thermal energy}}$$

$$V_{eq} = V_i - V_e = \frac{RT}{zF} \ln \frac{[C]_{out}}{[C]_{in}} = \frac{k_B T}{qz} \ln \frac{[C]_{out}}{[C]_{in}}$$

T: the absolute temperature (273.16 + °C)
R: the universal gas constant (8.31451 joules/mol K°)
F: Faraday constant (96485.3 C/mol)
z: valence of the ion
k_B: Boltzman constant

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The Nernst equation only applies when the channels that generate a particular conductance allow only one type of ion pass through them.

Explanation of the Nernst equation

From the theory of thermodynamics, it is known that the probability that a molecule takes a state of energy E is proportional to the Boltzmann factor.

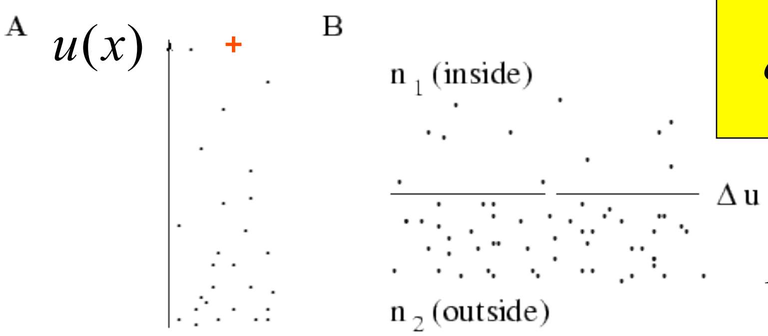
$$p(E) \propto e^{\frac{-E}{k_B T}}$$

Electrical energy:

$$E(x) = zqu(x)$$

Interpret probability as ion density:

$$e^{-\frac{zqu(x_1) - zqu(x_2)}{k_B T}} = \frac{[C]_{in}}{[C]_{out}}$$



$$E = \Delta u = u(x_1) - u(x_2)$$

Goldman-Hodgkin-Katz equation

The Nernst equation only applies when the channels that generate a particular conductance allow only one type of ion pass through them. In the presence of several different ions, the equilibrium of the cell depends on the relative permeability *P* of the ions.

Potassium Sodium Chloride

$$V_{eq} = \frac{RT}{F} \ln \frac{P_K[K^+]_{out} + P_{Na}[Na^+]_{out} + P_{Cl}[Cl^-]_{in}}{P_K[K^+]_{in} + P_{Na}[Na^+]_{in} + P_{Cl}[Cl^-]_{out}}$$

The permeability of an ion depends on a number of factors such as the size of the ion, its mobility, etc.
E.g. Squid giant axon: $P_k : P_{Na} : P_{Cl} = 1 : 0.03 : 0.1$

$$V_{eq} = 58 \log \frac{1(10) + 0.03(460) + 0.1(40)}{1(400) + 0.03(50) + 0.1(540)} = -70mV$$

The Goldman-Hodgkin-Katz equation can be linearized using conductances and individual ion potentials.

$$V_{eq} = \frac{g_K E_K + g_{Na} E_{Na} + g_{Cl} E_{Cl}}{g_K + g_{Na} + g_{Cl}}$$

Often this equilibrium potential is not computed explicitly but defined as an independent leakage potential E_L and determined by the resting potential given the experimental data (free parameter).

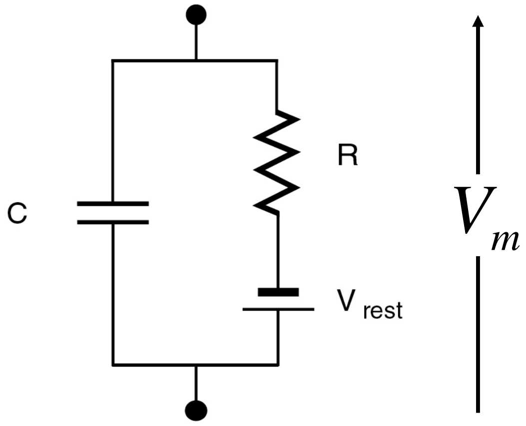
$$I_L = g_L (V - E_L)$$

Extracellular and intracellular ion concentrations

Ion	Concentration (mM) Intracellular	Extracellular
Squid neuron		
Potassium (K^+)	400	20
Sodium (Na^+)	50	440
Chloride (Cl^-)	40–150	560
Calcium (Ca^{2+})	0.0001	10
Mammalian neuron		
Potassium (K^+)	140	5
Sodium (Na^+)	5–15	145
Chloride (Cl^-)	4–30	110
Calcium (Ca^{2+})	0.0001	1–2

E_{Na} pos.

Simplified membrane capacity



$$Q = CV_m$$

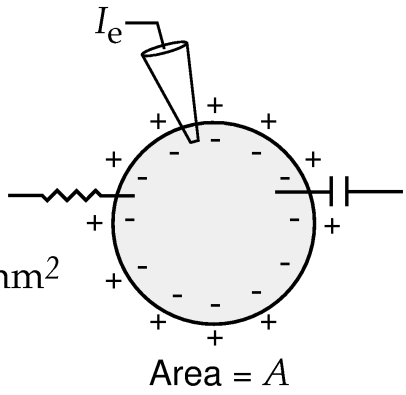
$$I_C = C\frac{dV_m(t)}{dt}$$

The capacitance and membrane resistance of a neuron considered as a single compartment with area A

$$\Delta V = I_e R_m$$

$$R_m = r_m / A$$

$$r_m \approx 1\ \mathrm{M\Omega\ mm^2}$$



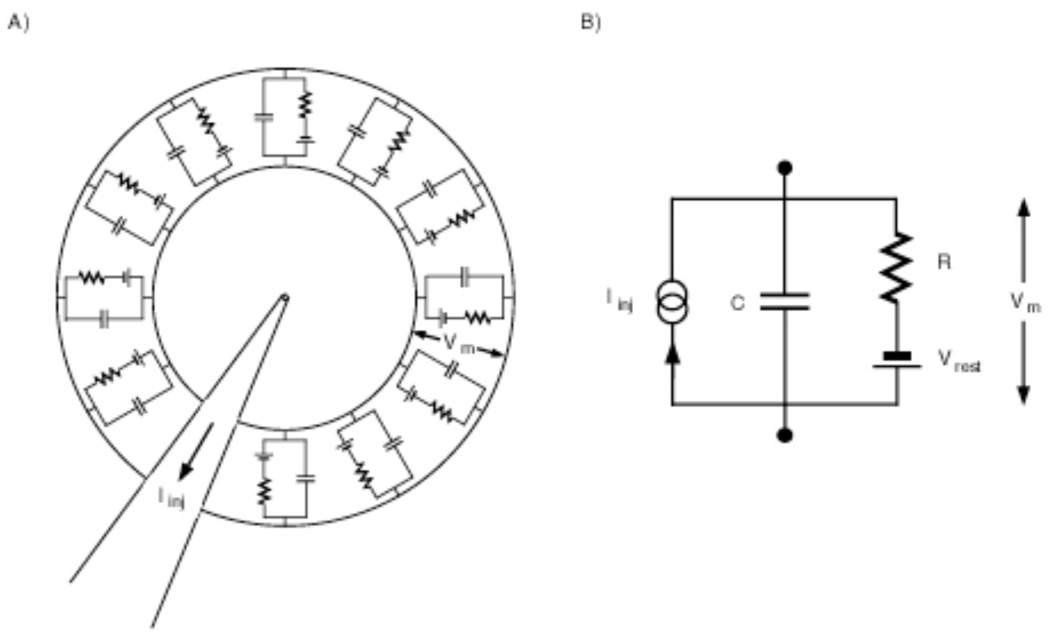
$$Q = C_m V$$

$$C_m = c_m A$$

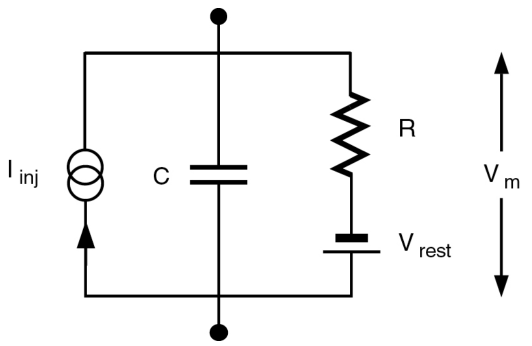
$$c_m \approx 10\ \mathrm{nF/mm^2}$$

The insulation of the membrane is modeled as a capacitance and the pores are described by a conductance.

RC-Circuit if we inject a current I



RC-Circuit



$$I_R = \frac{V_m - V_{rest}}{R}$$

Kirchhoffs law:

$$C\frac{dV_m(t)}{dt} + \frac{V_m(t) - V_{rest}}{R} = I_e(t)$$

Membrane Equation:

$$\tau\frac{dV_m(t)}{dt} = -V_m(t) + V_{rest} + RI_e(t)$$

$$\tau = RC$$

with units

$$\Omega F = \sec$$

Example: Inject current I_0 at t=0:

$$\tau\frac{dV_m(t)}{dt} = -V_m(t) + V_{rest} + RI_e(t)$$

$$V_m(t) = v_0 e^{\frac{-t}{\tau}} + v_1$$

Solution of the ODE

Equilibrium $(t \to \infty)$

$$v_1 = V_{rest} + RI_0$$

$$0 = -V_m + V_{rest} + RI_0(t)$$

$$V_m(t=0) = v_0 + v_1 = V_{rest}$$

$$V_m(t=0) = V_{rest}$$

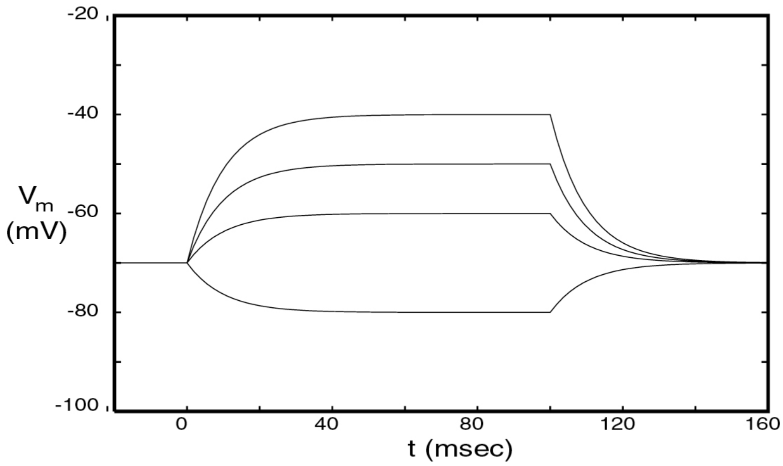
Def.: $V_\infty = RI_0$

$$V_m(t) = V_\infty(1 - e^{\frac{-t}{\tau}}) + V_{rest}$$

Example: Inject current I_0:

Synaptic input into RC-Circuit:

$$V_m(t) = V_\infty(1 - e^{\frac{-t}{\tau}}) + V_{rest} \qquad V_m(t) = V_\infty e^{\frac{-(t - t_{off})}{\tau}} + V_{rest}$$



Appendix: Model neurons

Numerical integration

Analytic solution of the ODE

Solution of an ordinary differential equation

$$\frac{dr_i}{dt} = \frac{I - r_i}{\tau}$$

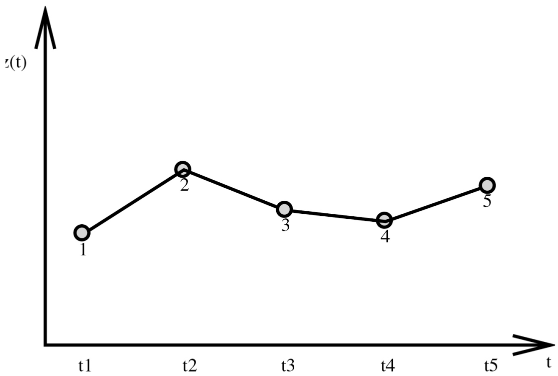
Separate the variables

$$\int \frac{dr_i}{I - r_i} = \int \frac{dt}{\tau} \qquad (-1)\cdot \ln\left|I - r_i\right| = \frac{t}{\tau} - \ln\left|k\right| \qquad I - r_i = ke^{-\frac{t}{\tau}}$$

$$r_i = I - ke^{-\frac{t}{\tau}}$$

The constant k is determined from the boundary conditions

Numeric solution of the ODE



$$r(t_1) = m(t_1 - t_0) + r(t_0)$$

Or more general using the stepsize h:

$$r(t + h) = mh + r(t)$$

$$\frac{dr}{dt} = m = \frac{r(t+h) - r(t)}{h}$$

The Euler-integration method approximates the unknown function *r*(t) piecewise by lines, by computing the slope *m* of the function in each interval. It then estimates the next value from the previous and the slope.
The Euler method is simple, but allows only for small stepsizes to be sufficiently exact.

Rule of the thump for h: $h = \frac{\tau_{\min}}{10}$

Example

$$\tau \frac{d}{dt} r_i = -r_i + I$$

$$\tau \frac{r_i(t+h) - r_i(t)}{h} = -r_i + I$$

$$r_i(t+h) = \frac{h}{\tau}\left(-r_i(t) + I\right) + r_i(t)$$