The Membrane Voltage

Neurons are excitable cells

Computational Neuroscience

University of Bristol

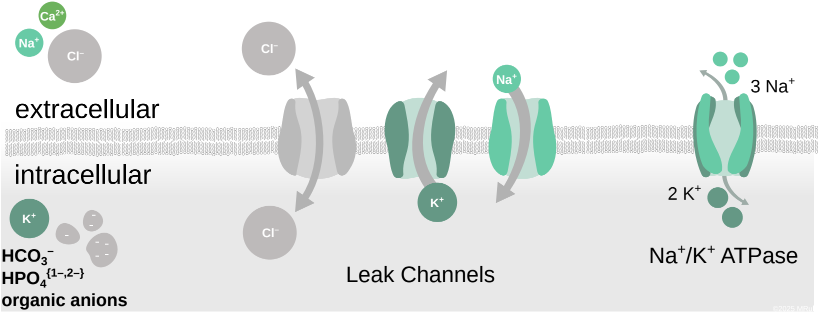
M Rule

Learning outcomes:

- Leak channels, $\mathrm{Na^+/K^+}$ATPase
- Nernst potential
- Effective circuit for passive membrane
- Detail the role of $\mathrm{Na^+, K^+, Cl^-}$ ions in the membrane voltage.

Neurons are excitable

- They maintain a voltage difference across their cell membrane
- Charged ions with differing intracellular/extracelluar concentrations → chemical "batteries"
  - Effective voltage depends on ion's charge & concentration difference
  - Powers voltage dynamics for computation & communication
  - Active pumps set and maintain concentration differences



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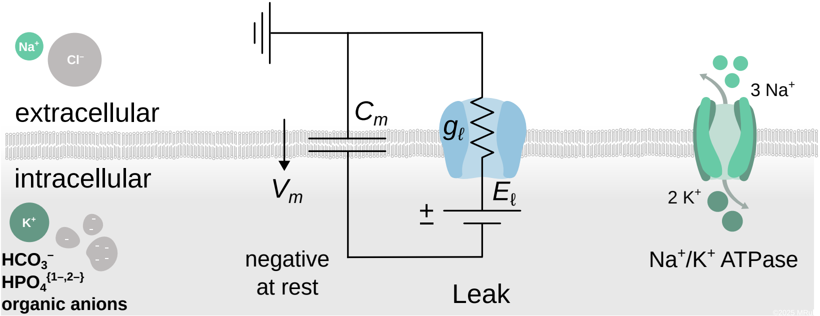

$Na^{+}Cl^{-}$
uK^{+}

draw a picture of the balance of energy (voltage) and entropy (diffusion) fluxes

Consider: ion C with charge z, concentrations $[C]_{\text{out}}$, $[C]_{\text{in}}$.

Moving ion inside:

- Δ**Energy** zFV — Electrical work
- Δ**Entropy** $R \ln\left(\frac{[C]_{\text{out}}}{[C]_{\text{in}}}\right)$ — Chemical work

Balance?

$$\begin{aligned}
\Delta\text{Energy} &= T \cdot \Delta\text{Entropy} \\
zFV &\propto RT \ln\left(\frac{[C]_{\text{out}}}{[C]_{\text{in}}}\right) \\
&\vdots \\
V &= \frac{T}{z}\frac{R}{F} \ln\left(\frac{[C]_{\text{out}}}{[C]_{\text{in}}}\right) \\
&= \frac{1}{z} E_0 \ln\left(\frac{[C]_{\text{out}}}{[C]_{\text{in}}}\right)
\end{aligned}$$

$\frac{R}{F} = \frac{\text{Gas constant}}{\text{Faraday constant}}$

Nernst potential

If we have time we can derive more details for intuituion

Often use $T = 310.15$ K (37°C), such that $E_0 := TR/F \approx 26.7$ mV

- T: Temperature (Kelvin, assume ∼310.15°K, i.e. 37°C + 273.15)
- R: Ideal gas constant $\approx 8.3145\,\mathrm{J\,K^{-1}\,mol^{-1}}$
- F: Faraday's constant $\approx 96{,}485\,\mathrm{C\,mol^{-1}}$

Example: Chloride reversal potential in mature pyramidal neuron

$z = -1$: Ion charge

$E_0 \approx 26.7$

$[\mathrm{Cl}^-]_{\mathrm{out}}$: 110 mM

$[\mathrm{Cl}^-]_{\mathrm{in}}$: 7 mM

E_{Cl^-}: Cl$^-$ reversal potential (voltage)

$$E_{\mathrm{Cl}^-} = \frac{1}{z} E_0 \ln\left(\frac{[\mathrm{Cl}^-]_{\mathrm{out}}}{[\mathrm{Cl}^-]_{\mathrm{in}}}\right) = (-26.7\,\mathrm{mV}) \ln\left(\frac{110\,\mathrm{mM}}{7\,\mathrm{mM}}\right) \approx 73.5\,\mathrm{mV}$$

GABA$_\mathrm{A}$ receptor passes Cl$^-$, typically uses $E_{\mathrm{GABA_A}} \sim 70$ mV

Reversal potentials often written as either E or V

Goldman–Hodgkin–Katz (GHK) voltage equation

In practice, multiple leak channels set resting voltage, and channels may be permiable to multiple ions; To calculate reversal potentials with multipl ionic fluxes you need to use the *Goldman–Hodgkin–Katz (GHK) voltage equation*.

$$E_m = E_0 \ln\left(\frac{P_{\mathrm{Na}}[\mathrm{Na}^+]_{\mathrm{out}} + P_{\mathrm{K}}[\mathrm{K}^+]_{\mathrm{out}} + P_{\mathrm{Cl}}[\mathrm{Cl}^-]_{\mathrm{in}}}{P_{\mathrm{Na}}[\mathrm{Na}^+]_{\mathrm{in}} + P_{\mathrm{K}}[\mathrm{K}^+]_{\mathrm{in}} + P_{\mathrm{Cl}}[\mathrm{Cl}^-]_{\mathrm{out}}}\right)$$

$$e^{E_m/E_0} = \text{ (permeability} \cdot \text{concentration) weighted average ...} \quad = \frac{\sum_i w_i e^{z_i(E_i/E_0)}}{\sum_i w_i}$$

$$w_i = P_i \cdot \begin{cases} [\,i\,]_{\mathrm{in}} & \text{if } z_i \text{ positive} \\ [\,i\,]_{\mathrm{out}} & \text{if } z_i \text{ negative} \end{cases}$$

Some of the voltage and ligand (i.e. neurotransmitter) gated channels we will cover are also permiable to multiple ions (at least in part), and require a similar treatment. But, each ion channel can be reduced to an *effective* reversal potential and conductance.

P: permeability, m/s

valences not ±1? solve balance of fluxes page left blank for notes

Modelling Scales

... Quantum Chemistry, Molecular dynamics

Molecules
Gillespie, Master Equation

Concentrations
Mass-Action Kinetics

Conductance Models
Hodgkin–Huxley

Spiking Models
Leaky Integrate and Fire

Rate Neurons
Neural Mass/Field Models

Poisson Neurons
Generalized Linear Models

Binary Neurons
McCulloch–Pitts, Hopfield, Perceptron

Cognitive Neuroscience, Psychology ...

Physiological, Quantitative

Biological Realism, Data needed to identify parameters

Computational Efficiency, Mathematical Tractability

Phenomenological, Qualitative

end

appendix

Jargon

depolarize v_m increases

repolarize v_m decreases towards resting potential

hyperpolarize v_m is driven below resting potential

Sign conventions

Let $v_m = v_{\text{interior}} - v_{\text{exterior}}$ denote a neuron's membrane voltage

A positive current applied to a neuron makes v_m _____?

- ***Engineer:*** increase
- ***Electrophysiologst:*** decrease!

Compromise:

- **inward current** makes v_m more positive
- **outward current** makes the membrane voltage more negative

remind them that inward flux of negative, e.g. Cl^-, ions makes a outward current

Nernst: Intuitive

Consider ion C^z and two equal, small volumes in the exterior/interior of the cell with extracellular/intracellular concentrations $[C]_{\text{out}}$ and $[C]_{\text{in}}$, respectively. Let $N = [C]_{\text{out}} + [C]_{\text{in}}$ be the total number of ions, and define $p = [C]_{\text{in}}/N$, the portion $p \in [0, 1]$ inside the cell.

The Nernst potential describes a relationship between p and membrane voltage V that minimizes free energy.

$$F = \text{energy} - T \cdot \text{entropy} \tag{1}$$

We will consider a voltage clamp experiment, which fixes V and allows p to relax to equilibrium. To minimize free energy in p, differentiate F and set to zero $\frac{\mathrm{d}}{\mathrm{d}p}F(p) = 0$, yielding the relation:

$$\frac{\mathrm{d}}{\mathrm{d}p}\text{energy} = T\frac{\mathrm{d}}{\mathrm{d}p}\text{entropy}. \tag{2}$$

Nernst: Intuitive

Entropy: Diffusion wants to equalize interior and exterior concentrations. The entropy is how many questions we need to ask to know whether a given ion is inside or outside the cell. We use entropy of a Bernoulli distribution for a coin-toss with $\Pr(\text{success} \sim \text{inside}) = p$:

$$\frac{\mathrm{d}}{\mathrm{d}p}\text{entropy} \propto \frac{\mathrm{d}}{\mathrm{d}p}\left\{-p\ln(p) - (1-p)\ln(1-p)\right\} = \ln\left(\frac{1-p}{p}\right). \tag{3}$$

Energy: The energy used to move p ions with charge z into a cell with electric potential difference V is

$$\frac{\mathrm{d}}{\mathrm{d}p}\text{energy} \propto \frac{\mathrm{d}}{\mathrm{d}p}\left\{zVp\right\} = zV. \tag{4}$$

Equating (3) and (4) per (2) gives the Nernst equation:

$$V = \frac{T}{z}\alpha\ln\left(\frac{1-p}{p}\right), \tag{5}$$

This V is the reversal potential for a given ion concentration $[C]_{\text{out}}/[C]_{\text{in}} = (1-p)/p$.

To recover physical units, use $\alpha = \frac{\text{Ideal gas constant}}{\text{Faraday's constant}} = \frac{R}{F}$.

end