THEORETICAL NEUROSCIENCE I

Lecture 2: Single compartment model

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Content

1 Equivalent circuits

The biophysical components of a neuron (i.e., cell membranes, intracellular plasma, channel proteins, etc) behave like electronic circuit components and are characterized by electrical *voltage*, *current*, *resistance*, *conductance*, *capacitance*, and so on.

We take advantage of this fact and describe neurons in terms of electronic *equivalent circuits.*

Axon lumen (Ohm's Law with resistance)

As a first example, consider an axon segment of length L and radius a. This segment presents an electrical resistance R_L to longitudinal currents:

$$R_L = \frac{r_L\, L}{\pi a^2} \qquad\qquad r_L \text{ } \textit{resistivity}$$

$$\text{for example} \quad L = 100\,\mu m \qquad a = 2\,\mu m \qquad r_L \approx 1\ k\Omega mm$$

$$R_L = \frac{1k\Omega\, mm\ \cdot\ 0.1\, mm}{\pi\ \cdot\ 0.002^2\, mm^2} \approx 8\, M\Omega$$

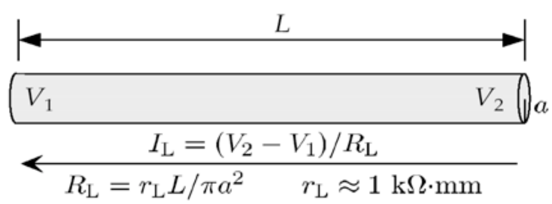

Figure 1: Ohm's law resistance. [1]

Ohm's Law:

Resistance is the ratio between voltage drop and current or, equivalently, voltage drop is the product of resistance and current:

$$R[Ohm] = \frac{V[Volt]}{I[Ampere]} \qquad \Leftrightarrow \qquad V[Volt] = R[Ohm]\, I[Ampere]$$

Causation works both ways! Voltage drops cause currents to flow. Flowing currents cause voltage drops.
For example, the voltage drop V_L required to drive a current $I_L = 1\,nA$ through this axon segment:

$$V_L = 8\,M\Omega \cdot 1\,nA = 8 \times 10^{+6}\,\Omega \,\cdot\, 1 \times 10^{-9}\,A = 8 \times 10^{-3}\,V = 8\,mV$$

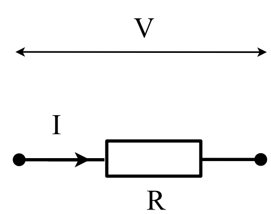

Figure 2: Circuit diagram with resistance R, voltage drop V, and current I.

Channel pore (Ohm's Law with conductance)
Consider a channel protein with a cylindrical pore of $L_C = 6\,nm$ length and crosssectional area of $A_C = 0.15\,nm^2$ and its *conductance* G_C (inverse of resistance):

$$G_C = \frac{1}{R_C} = \frac{A_C}{r_L\,L_C} \approx \frac{0.15\,nm^2}{1k\Omega\,mm\,\cdot\,6\,nm} \approx \frac{1}{40G\Omega} = 25pS$$

For conductance, **Ohm's Law** takes a slightly different form:

$$V[Volt] = \frac{I[Ampere]}{G[Siemens]} \qquad \Leftrightarrow \qquad I = G\,V \qquad\qquad S \equiv \frac{A}{V} = \Omega^{-1}$$

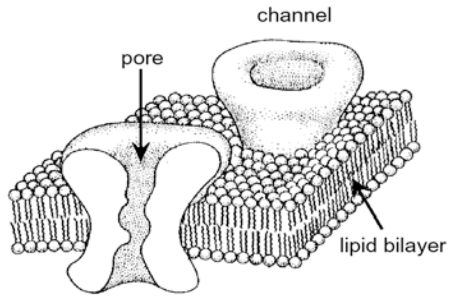

Figure 3: Channel pore [2]

Ion-specific conductance

Membranes with ion-specific channel proteins exhibit an ion-specific conductance. For the ion in question, the driving force is the difference between membrane potential and reversal potential. We modify Ohm's Law as follows:

$$I_X \;=\; G_X\,(V - E_X)$$

The conductance G_X needs to be calculated from the *resistivity* r_X (or *conductivity* g_X) and the cells surface area a:

$$G_X = g_X\,a = \frac{a}{r_X} = \frac{0.01\,mm^2}{1\,M\Omega mm^2} = 10\,nS$$

where we have used typical values for r_X and a.

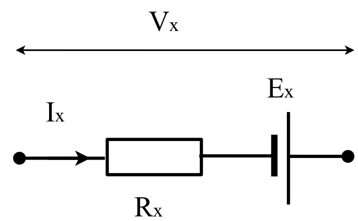

Figure 4: The 'equivalent circuit' of an ion-specific conductance is a resistance R_x (conductance) in series with a battery (reversal potential E_x).

Membrane capacitance

The membrane capacitance is governed by the *capacitor equation*:

$$Q[Coulomb] = C_m[Farad]\ V_m[Volt]$$

$$C_m[F] = c_m[F\,mm^{-2}]\ A[mm^2], \qquad c_m \approx 10\ nF/mm^2$$

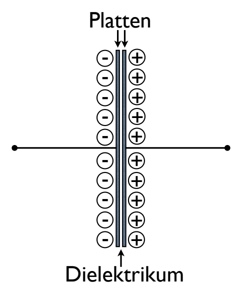

Figure 5: Membrane capacitance.

Time-derivative of capacitor equation

The charge Q changes only when a current I_m flows through the membrane:

$$\frac{dQ}{dt} = I_m \qquad 1A = \frac{1Coulomb}{1s}$$

Thus, the time derivative of the capacitor equation relates current *through* and voltage *across* a membrane:

$$I_m = \frac{dQ}{dt} = C_m \frac{dV_m}{dt}$$

Circuit diagram

In a capacitance, current and voltage are not proportional. Instead, current is proportional to the voltage change!

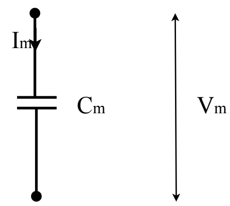

Figure 6: 'Equivalent circuit' of membrane capacitance C_m, with voltage V_m and current I_m.

2 Hydraulic analogues

Electrical quantity	Symbol	Physical unit	Hydraulic analogue
Voltage difference	V, U, v	Volt V, mV	pressure difference
Current flow	I, i	Ampère A, mA, μA	liquid flow
Resistance	R, r	Ohm Ω, $k\Omega$, $M\Omega$	constriction
Conductance	G, g	Siemens S, μS, pS	opening

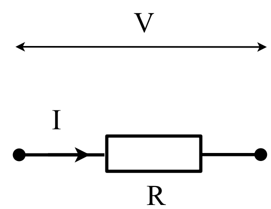

Figure 7: Circuit diagram with resistance R, voltage drop V, and current I.

Battery, voltage source

Electrical quantity	Symbol	Physical unit	Hydraulic analogue
Voltage difference	V, U, v	Volt V, mV	pressure pump
Current flow	I, i	Ampère A, mA, μA	liquid flow

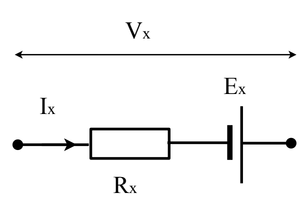

Figure 8: Circuit diagram with resistance R, voltage drop V, current I and battery E.

Capacitance

Electrical quantity	**Symbol**	**Physical unit**	**Hydraulic analogue**
Voltage change	$\frac{dV}{dt}$, $\frac{dv}{dt}$	$\frac{V}{s}$ or $\frac{mV}{ms}$	pressure change
Current flow	I, i	A, mA, μA	liquid flow
Capacitance	C, c	Farad F, μF, nF	elastic balloon

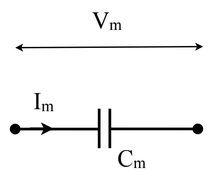

Figure 9: Circuit diagram v, i and c.

Hydraulic analogue of 'single-compartment model'

Voltage = pressure, current = flow

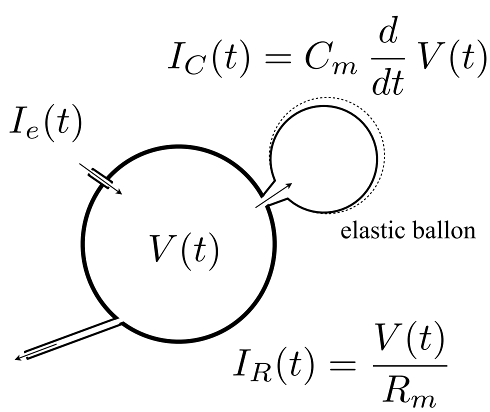

Figure 10: Single-compartment model. [3]

3 Single-compartment model

At the soma of a neuron, the membrane potential is relatively uniform across the entire surface. The soma is **"electrotonically compact"** and can be treated as a single **"compartment"**. Such a compartment is characterized by a single membrane potential, membrane capacity, and membrane resistance. Typical values are:

$$R_m \approx \frac{1\,M\Omega mm^2}{0.1 \text{ to } 0.01\,mm^2} = 10 \text{ to } 100\,M\Omega$$

$$C_m \approx 10\,nF/mm^2 \cdot \left(0.1 \text{ to } 0.01\,mm^2\right) = 0.1 \text{ to } 1\,nF$$

$$\tau_m = R_m\,C_m \approx 10\,ms \text{ to } 100\,ms.$$

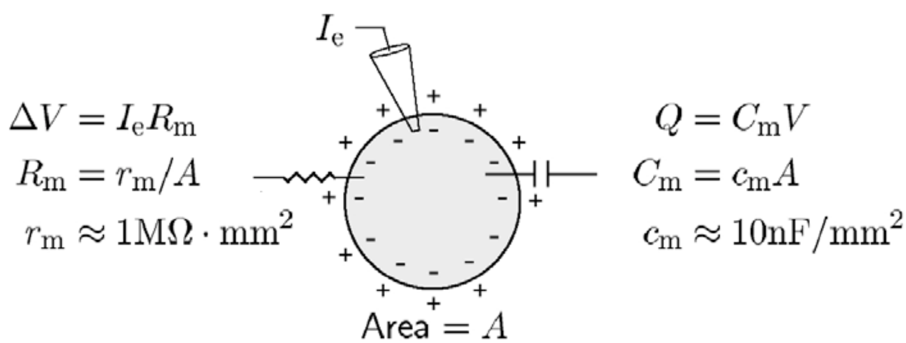

Figure 11: Single membrane potential. [4]

Basic equation

We now derive the basic equation of the single-compartment model. In addition to membrane resistance and capacitance, we consider an electrode, which has been inserted in the soma and which can serve two functions: it can deliver current and it can measure voltage. As always, we define the membrane current as an *outward* current. For an electrode current, the convention is different: it is defined as an *inward* current. Due to this convention, the inward electrode current (which may be zero) must equal the outward membrane currents:

$$I_e = I_R + I_C$$

Using Ohm's Law and the Capacitor Equation, we can express both components of the membrane current in terms of the membrane potential:

$$I_e = \frac{V_m}{R_m} + C_m \, \frac{dV_m}{dt}$$

$$I_R = \frac{V_m}{R_m} \qquad\qquad I_C = C_m \, \frac{dV_m}{dt}$$

This is the **basic equation** of the single-compartment model.

Alternative form

Often, this equation is written not in absolute but in 'specific' quantities (per unit membrane area). In this case, the equation reads

$$\frac{I_e}{A} = \frac{V_m}{r_m} + c_m \, \frac{dV_m}{dt}$$

Recall that we use capital letters (R_m, C_m) for absolute resistance and capacitance, but lower case letters (r_m, c_m) for resistivity and conductivity.

Equivalent circuit

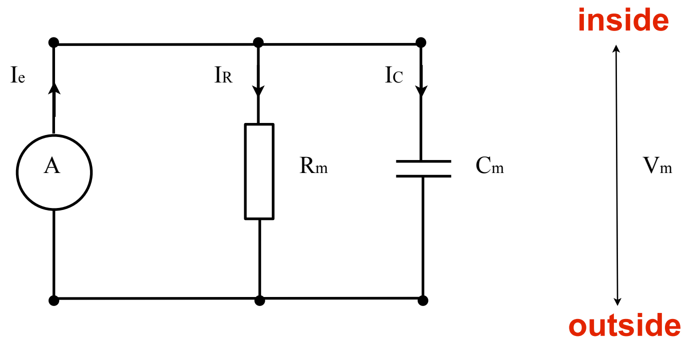

Figure 12: Parallel circuit diagram.

$$I_e = \frac{V_m}{R_m} + C_m \frac{dV_m}{dt}$$

Hydraulic analogue

Voltage = pressure, current = flow

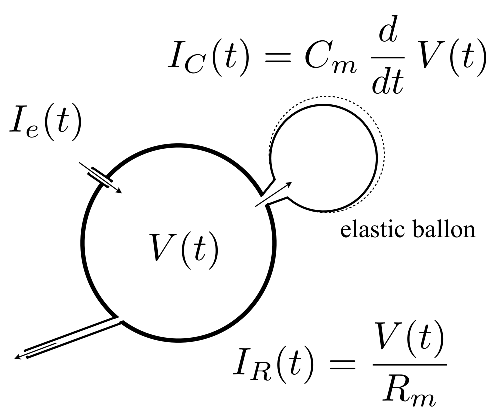

Figure 13: Single-compartment model. [3]

4 Solving for voltage

Given an arbitrary input current $I_e(t)$, we'd like to know:

- Membrane voltage $V_m(t)$ over time.
- Resistive current $I_R(t)$ over time.
- Capacitative current $I_C(t)$ over time.

Initially, we restrict ourselves to a constant input current $I_e(t) = I_0$. Later on, we shall generalize to time-varying inputs.

Time constant and equilibrium potential

To begin to understand the implications of our basic equation, we introduce the **membrane time-constant**

$$\tau_m = R_m \, C_m$$

and rearrange to isolate the voltage change:

$$\tau_m \frac{dV(t)}{dt} = -V(t) + R_m \, I_0$$

While I_0 remains constant, the potential will move towards a particular value, namely, $R_m \, I_0$. (As long as V is less than this value, dV is positive and V will increase. As long as V is larger than this value, dV is negative and V will decrease.)
Accordingly, we can consider $R_m \, I_e$ as an **equilibrium potential** V_∞ (dt. Grenzpotential).

$$0 = \tau_m \frac{dV(t)}{dt} = -V(t) + R_m \, I_e \qquad \Rightarrow \qquad V_\infty = R_m \, I_0$$

Our equation now reads

$$\tau_m \frac{dV(t)}{dt} = -V(t) + V_\infty$$

or

$$\frac{dV(t)}{dt} = -\frac{1}{\tau_m} \left[V(t) - V_\infty \right]$$

Exponential relaxation

The basic equation of our single-compartment model is a common linear differential equation (LDE), which describes an **exponential relaxation**. We speak of an exponential relaxation when a state variable x always returns ('relaxes') towards some equilibrium value and when the speed of this movement is proportional to the distance from the equilibrium value.

$$\frac{dV(t)}{dt} = -\frac{1}{\tau} \left[V(t) - V_\infty \right]$$

where V_∞ is the equilibrium value, and τ is the relaxation time.
Solution With $V(0) = V_0$, the solution is

$$V(t) = V_\infty + (V_0 - V_\infty) \exp\left(-\frac{t}{\tau}\right)$$

To check, differentiate the solution to obtain the left-hand side of the LDE:

$$LHS = \frac{dV(t)}{dt} = -\frac{1}{\tau} (V_0 - V_\infty) \exp\left(-\frac{t}{\tau}\right)$$

and substitute the solution $V(t)$ to obtain the right-hand side:

$$RHS = -\frac{1}{\tau} \left[V(t) - V_\infty \right] = -\frac{1}{\tau} (V_0 - V_\infty) \exp\left(-\frac{t}{\tau}\right)$$

$$\frac{dV(t)}{dt} = -\frac{1}{\tau}\left[V(t) - V_\infty\right] \qquad V(0) = V_0$$

$$V(t) = V_\infty + (V_0 - V_\infty)\exp\left(-\frac{t}{\tau}\right)$$

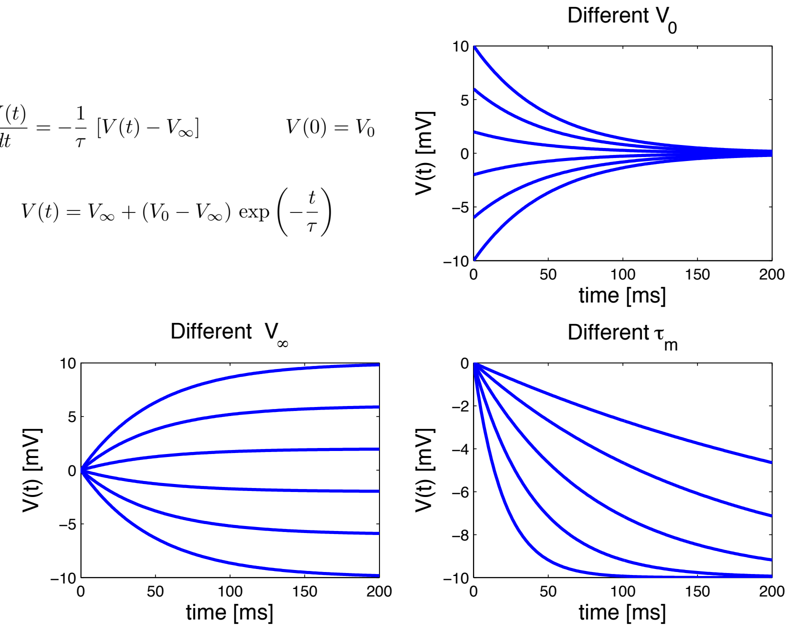

Figure 14: Find that both sides are identical. QED.

5 Solving for currents

Exact solution for a step-like input current:

$$\tau_m \frac{dV(t)}{dt} = -V(t) + V_\infty(t), \qquad\qquad V(0) = 0$$

$$\tau_m = R_m\, C_m \qquad\qquad V_\infty(t) = R_m\, I_e(t) = \begin{cases} R_m\, I_0 & t \geq 0 \\ 0 & t < 0 \end{cases}$$

The solution for the membrane potential is

$$V(t) = V_\infty - V_\infty \exp\left(-\frac{t}{\tau_m}\right)$$

Membrane currents

Given this solution, we can use Ohm's law and the capacitor equation

$$I_R = \frac{V(t)}{R_m} \qquad\qquad I_C = C_m \frac{dV(t)}{dt}$$

to compute the resistance current

$$I_R = \frac{V_\infty}{R_m} \left[1 - \exp\left(-\frac{t}{\tau_m}\right)\right] = I_0 \left[1 - \exp\left(-\frac{t}{\tau_m}\right)\right]$$

and the capacitance current

$$I_C = C_m \frac{-1}{\tau_m} \left[-V_\infty \exp\left(-\frac{t}{\tau_m}\right)\right] = I_0 \exp\left(-\frac{t}{\tau_m}\right)$$

Current division

Now we know how the additional current is divided between resistance and capacitance, and how this division changes over time:

$$V(t) = V_\infty \left[1 - \exp\left(-\frac{t}{\tau_m}\right)\right] \qquad I_R = I_e \left[1 - \exp\left(-\frac{t}{\tau_m}\right)\right] \qquad I_C = I$$

```
function SCM

    tau = 20;
    t = 0:1:100;
    Vinf = 100;
    Ie = 10;
    V = Vinf * (1 - exp(-t/tau));
    IR = Ie * (1 - exp(-t/tau));
    IC = Ie * exp(-t/tau);

    figure;
    subplot(1,3,1);
    plot(t,V,'LineWidth',2.0);
    xlabel('time t', 'FontSize', 24);
    ylabel('voltage V', 'FontSize', 24);
    axis 'square';

    subplot(1,3,2);
    plot(t,IR,'LineWidth',2.0);
    xlabel('time t', 'FontSize', 24);
    ylabel('current I_R', 'FontSize', 24);
    axis 'square';

    subplot(1,3,3);
    plot(t,IC,'LineWidth',2.0);
    xlabel('time t', 'FontSize', 24);
    ylabel('current I_C', 'FontSize', 24);
    axis 'square';

return;
```

Figure 15: Matlab script for plots

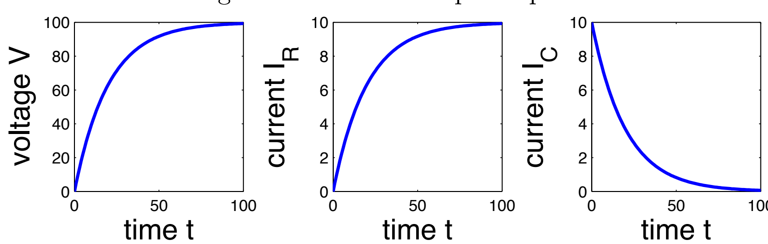

Figure 16: Plots time vs. voltage V, current I_R and current I_C

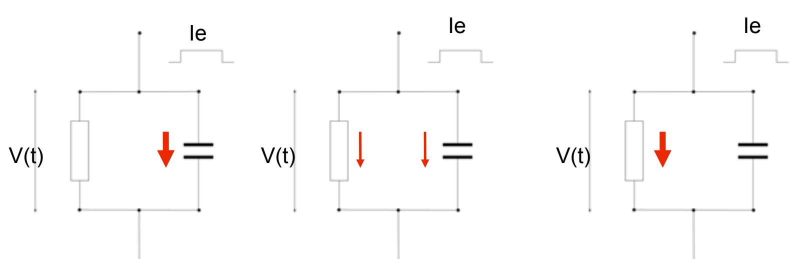

Figure 17: Equivalent electric diagrams for plots.

Hydraulic analogue, again

Voltage = pressure, current = flow

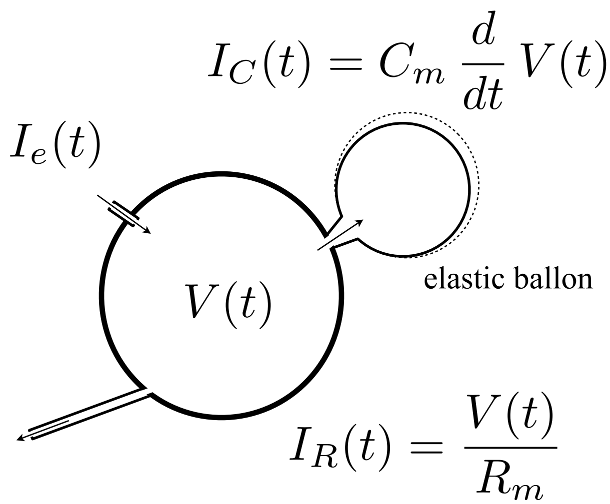

Figure 18: Single-compartment model. [3]

Some implications

With a time-varying electrode current $I_e(t)$ and equilibrium potential $V_\infty(t)$, we have

$$\tau_m \frac{dV(t)}{dt} = -V(t) + V_\infty(t),$$

$$\tau_m = R_m C_m, \qquad V_\infty(t) = R_m I_e(t)$$

$$I_R = V_m(t)/R_m, \qquad I_C = C_m \frac{dV_m(t)}{dt}$$

- Which quantities change *instantaneously* with a step change in the input current?
- Which quantities change *gradually* over time?
- How does the membrane potential behave?
- Where does the input current flow? Initially? After the membrane potential has equlibrated?
- How quickly does the membrane potential equlibrate?
- What are the effects of a step change in the membrane resistance?

6 Ion-specific currents (advanced)

So far, we have ignored the fact that membrane currents are carried by particular ions. We now make our single-compartment model more realistic by taking into account ion-specific conductances and reversal potentials. In our basic equation, we make explicit the membrane current *per unit area*, i_m:

$$c_m \frac{dV_m}{dt} = -i_m + \frac{I_e}{A}$$

In the past, we have calculated i_m from the membrane potential V_m and the total membrane resistance r_m.

$$i_m = \frac{V_m}{r_m}$$

Now we want to substitute a more detailed expression, which takes ion-specific conductances into account.

Single ion conductance

Total membrane current carried by ion X, with reversal potential E_X and conductivity g_X ($= \frac{1}{r_X}$).

$$c_m \frac{dV_m}{dt} = -i_m + \frac{I_e}{A} \qquad\qquad i_m = g_X(V_m - E_X)$$

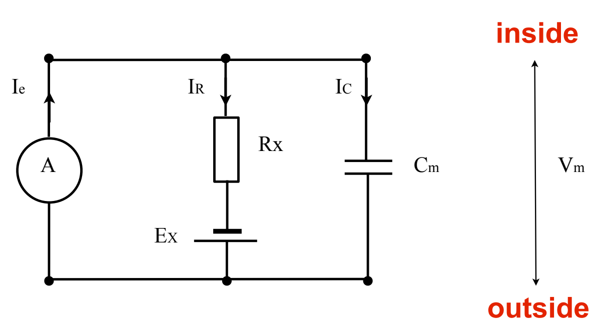

Figure 19: Electric diagram.

Multiple ion conductances

Total membrane current carried by several ions, say Na^+ and K^+, we need to take into account the reversal potential and specific conductivity of each ion:

$$c_m \frac{dV_m}{dt} = -i_m + \frac{I_e}{A} \qquad\qquad i_m = g_{Na}\left(V_m - E_{Na}\right) + g_K\left(V_m - E_K\right)$$

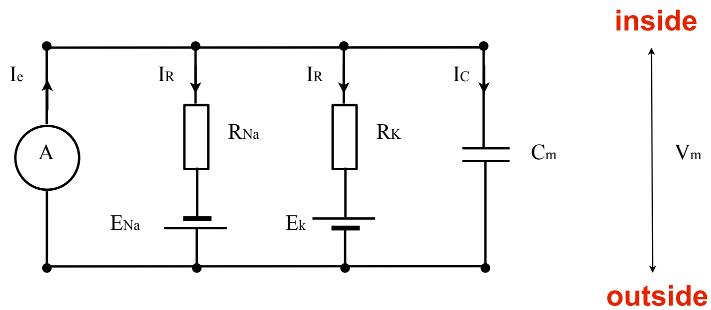

Figure 20: Electric diagram including Na and K as batteries.

Synaptic conductances

Total membrane current includes synaptic currents, also carried by particular ions. In contrast to 'normal' ionic conductances, synaptic conductances vary over time (depending on pre-synaptic activity):

$$i_m = g_{syn}(t)\left(V_m - E_{syn}\right) + g_{Na}\left(V_m - E_{Na}\right) + g_K\left(V_m - E_K\right)$$

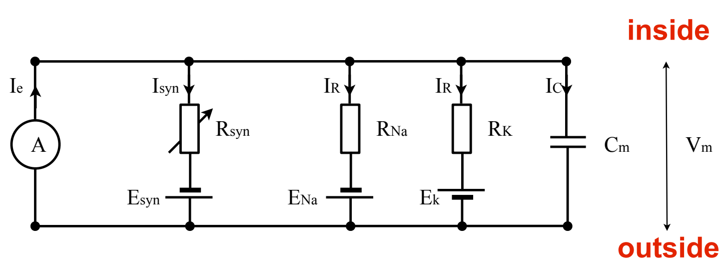

Figure 21: Electric diagram including the synaptic activity.

Generalization

The membrane current is the sum of all currents through the different types of ion channels, indexed by i. This includes leakage channels, voltage-gated channels, and synaptic channels (which are ligand-gated).

For ion-selective channels, the current vanishes when the membrane potential V equals the reversal potential E_i. For other values of V, the current increases or decreases linearly with $V - E_i$. Accordingly, $V - E_i$ can be considered the **driving force** for currents through conductance i.

We can now compute the membrane current per unit area i_m from the conductances g_i per unit area and the reversal potentials E_i:

$$c_m \frac{dV_m}{dt} = -i_m + \frac{I_e}{A} \qquad\qquad i_m = \sum_i g_i \, (V - E_i)$$

For example, a particular neuron might have channels for K^+, Na^+, Ca^{2+}, and Cl^-. In this case, we might write:

$$i_m \;=\; g_{K^+} \, (V - E_{K^+}) \;+\; g_{Na^+} \, (V - E_{Na^+}) \;+\; g_{Ca^{2+}} \, (V - E_{Ca^{2+}}) \;+$$

$$+ \; g_{Cl^+} \, (V - E_{Cl^+}) \;+\; g_L \, (V - E_L)$$

where g_L and E_L are the effective conductance and reversal potential of all remaining channels (including ion pumps), that are not explicitly included.

Channels with $E_i \approx V_{rest}$ are sometimes called **shunt** conductances (e.g., Cl^-).

Summary of 'Ion-specific conductances'

- Ion-specific conductances take reversal potential into account

- Total conductance is sum of individual conductances

- Total current is sum of individual currents

- Synaptic conductances are treated in the same way

7 Bibliography

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3. Dayan & Abbott (2001), Theoretical Neuroscience, MIT Press.

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