

Neuronal Models - part I

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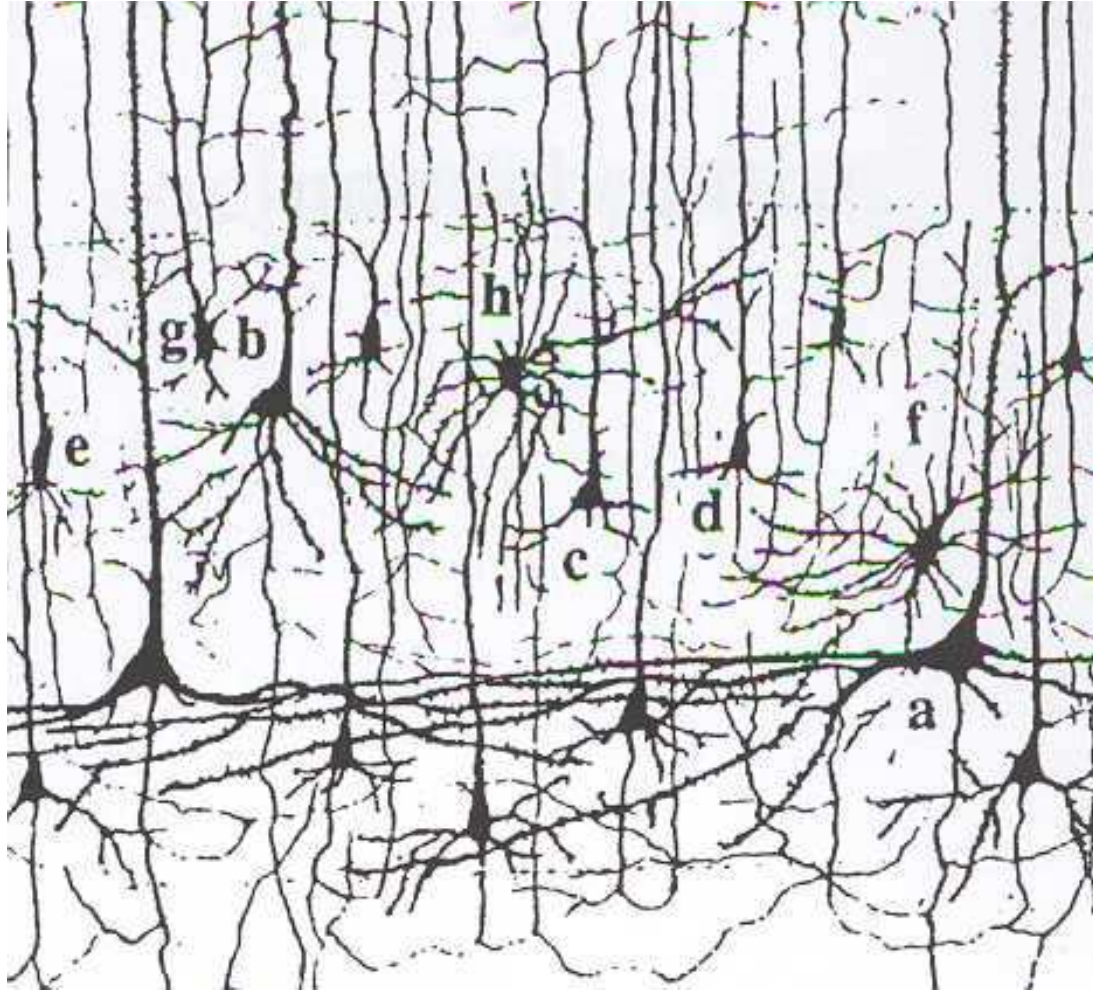
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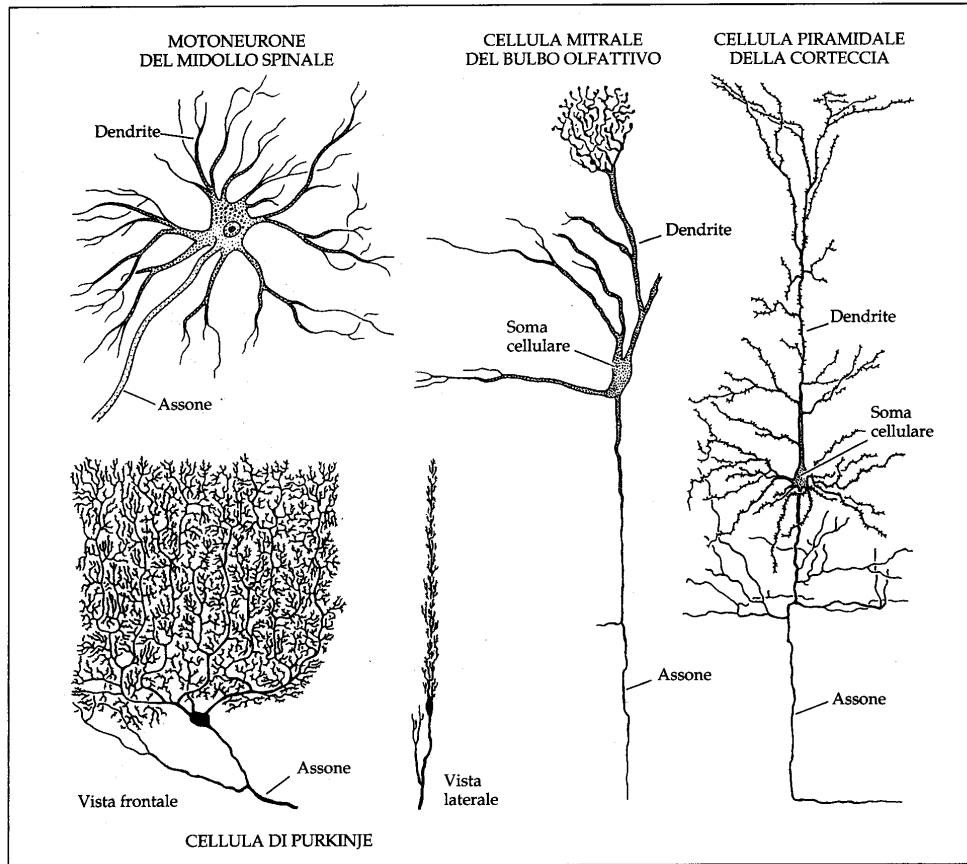
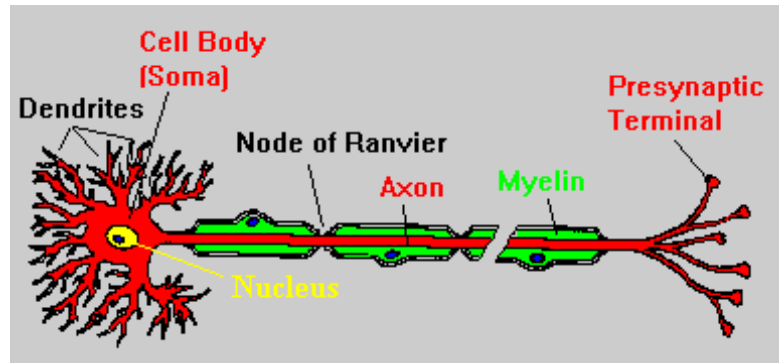
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Neurons

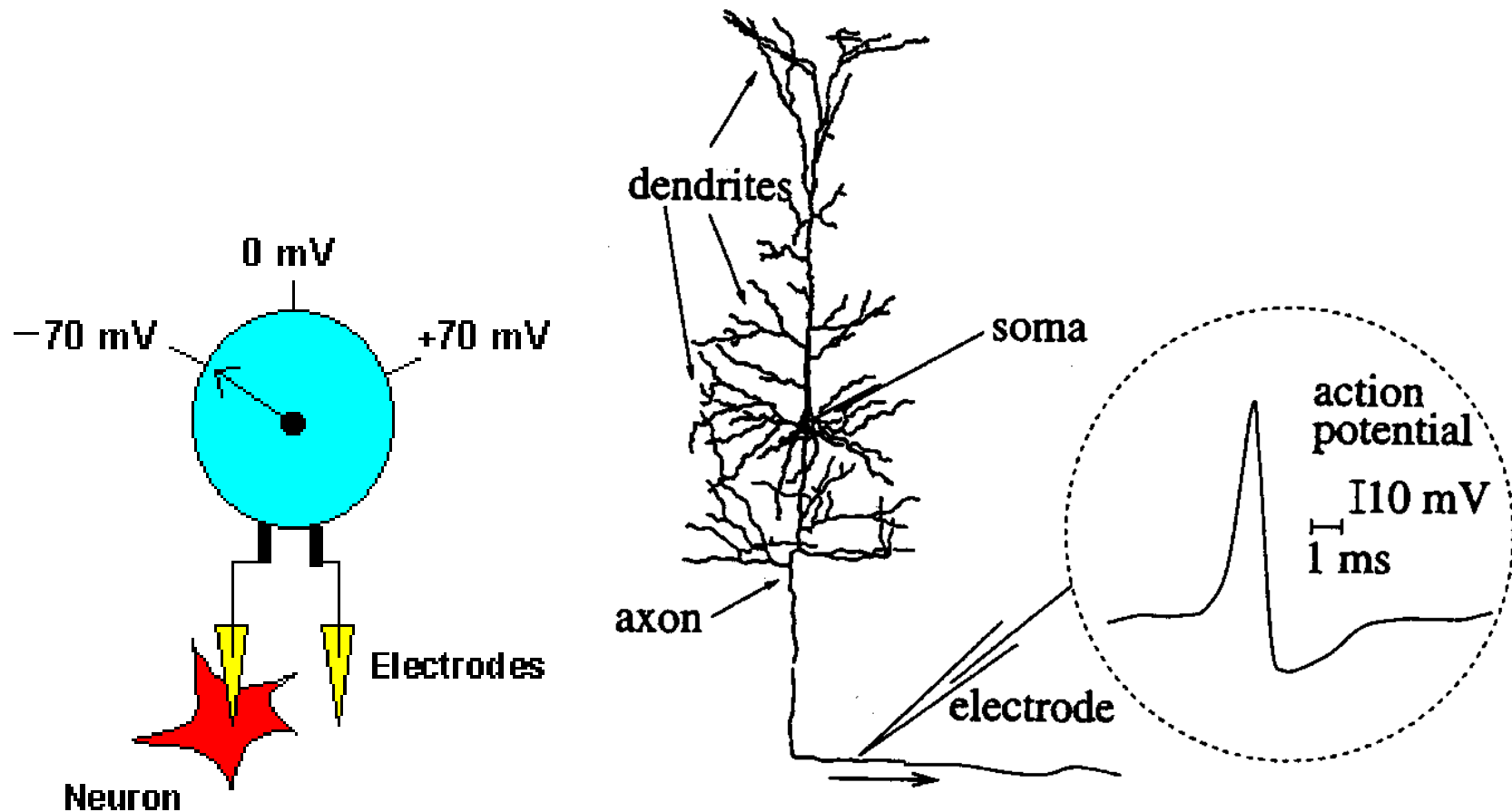


- human brain $\rightarrow 10^{11}$ neurons, density in the cortex: $10^5/\text{mm}^3$

Morphology

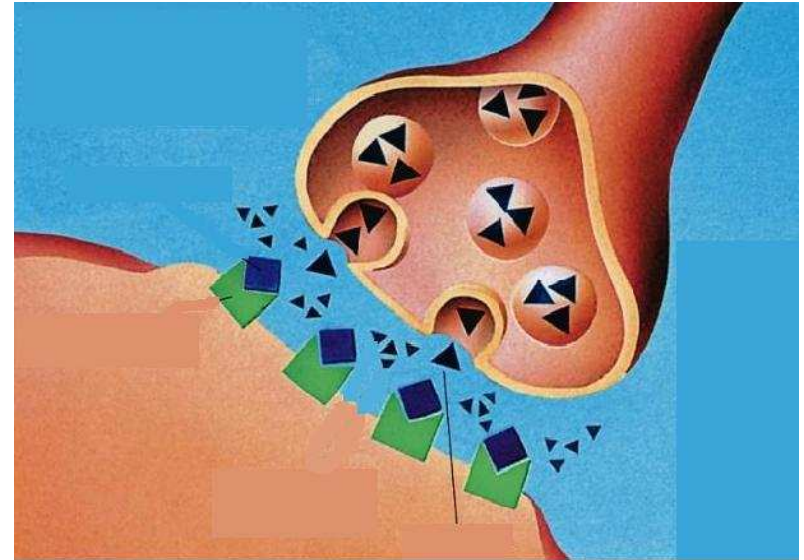
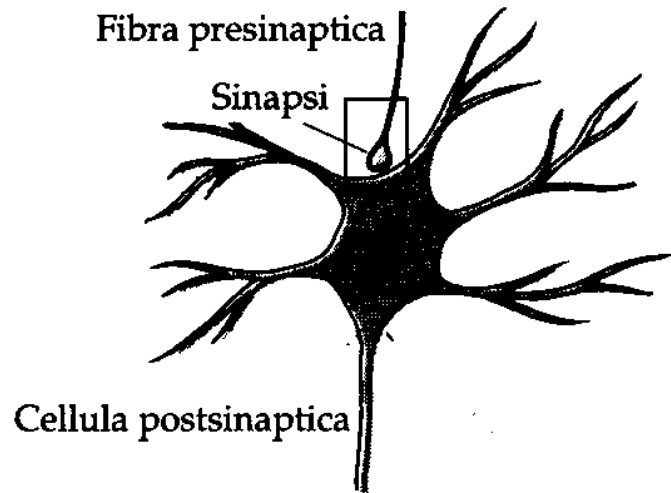


Neuronal Signals - Action Potential



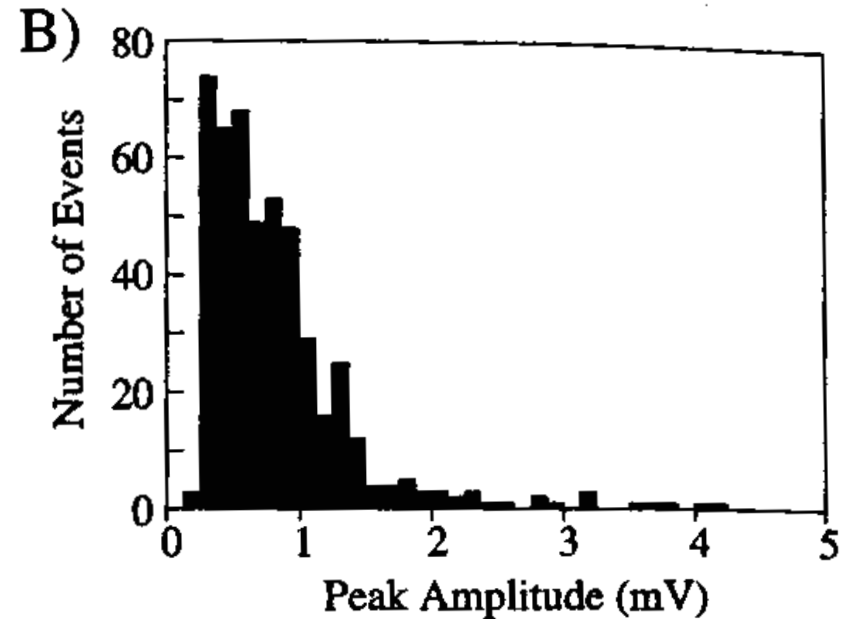
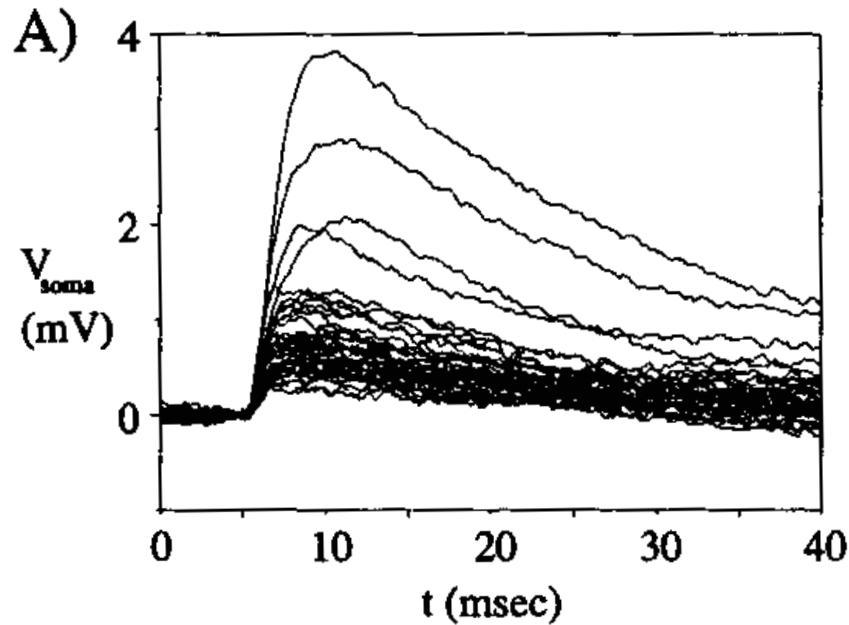
- membrane potential
- no stimuli → rest potential
- The **action potential** is the elementary unit of the neuronal transmission → depolarization, hyperpolarization

Synapses



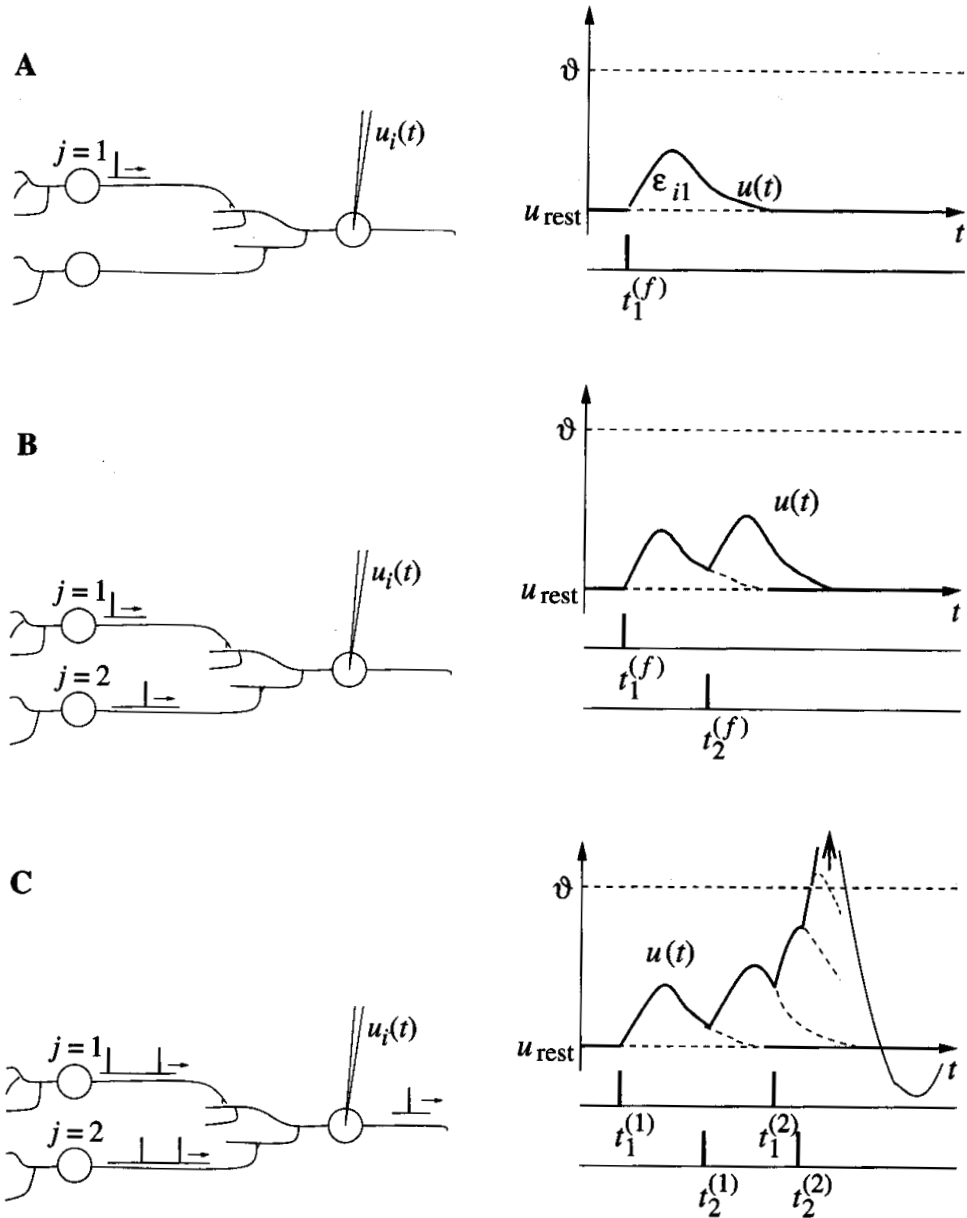
- chemical synapses → neurotransmitters (glutamate, GABA)
- electrical synapses (gap junctions)

Post synaptic potentials

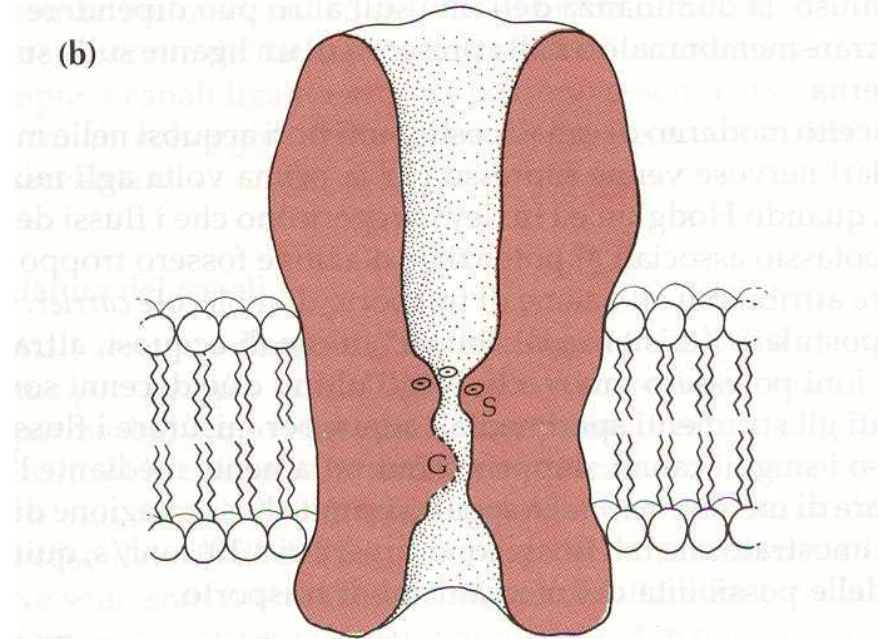
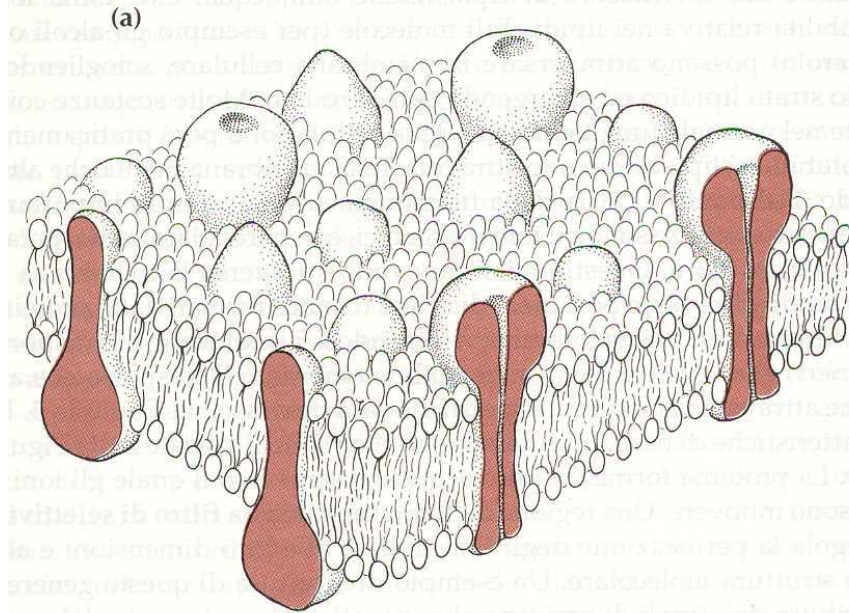


- postsynaptic potential → excitatory (PPSE)/inhibitory (PPSI)
- excitatory synapse/inhibitory synapse
- number of synapses in the cortex → 10^4 (85% excitatory, 15% inhibitory) BUT ONLY 5 – 10% ARE ACTIVE!

Neuronal dynamics - firing threshold



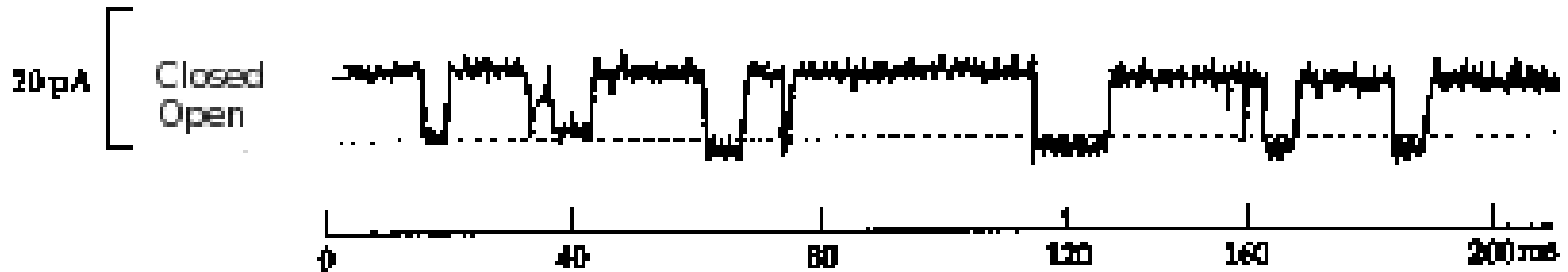
Neuronal membrane - Ionic channels



Structure of ionic channels:

- central pore
- filter of selectivity
- gates → stochastic oscillation between an **open** and a **closed** state

Ionic current - 1



- ion channel: **open=activated/closed=inactivated**
- **voltage-activated** channels
- **permeability**, p (cm/s), of the membrane to a specific ion:

$$J = -p\Delta[C]$$

J is the molar flux (mol/(cm²·s)) and $\Delta[C]$ difference of ion concentration (mol/cm³)

- **conductance** of the membrane → electric current transportation

Ionic current - 2

The current flowing through ion channel depends on:

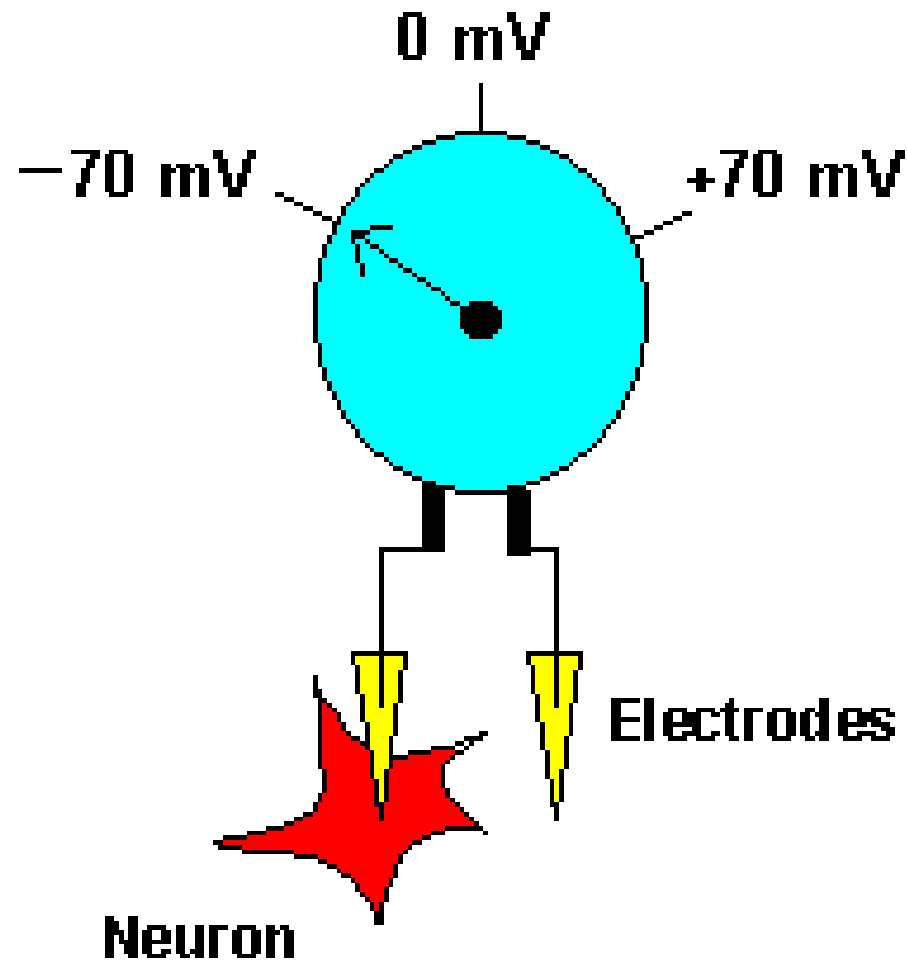
- conductance
- gradient of concentration → **Fick's law:**

$$J_{diff} = -D \frac{d[C]}{dx}$$

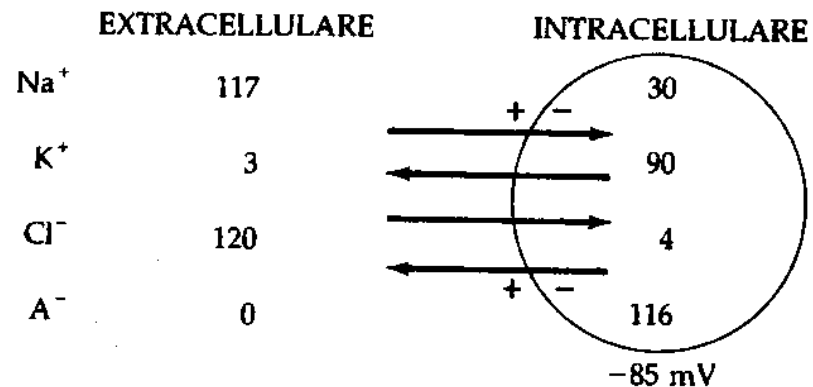
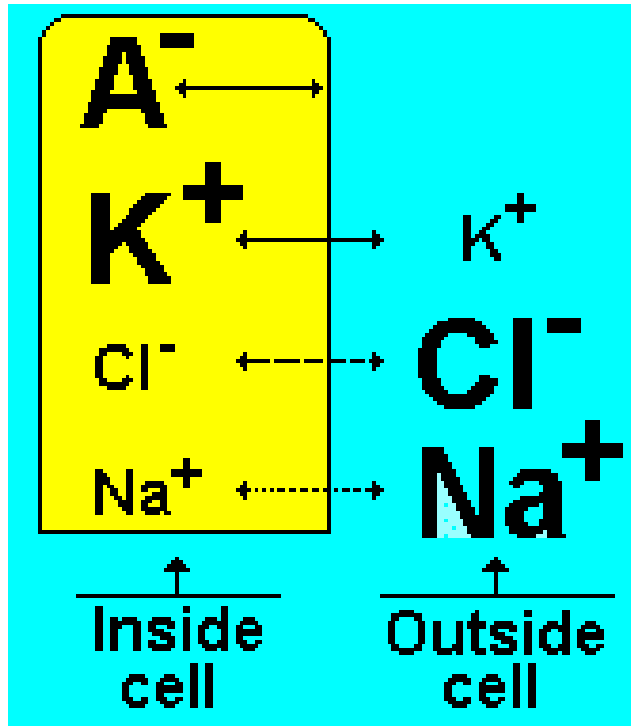
where J_{diff} (number of ions/cm²/s) is the flux due to the diffusion, D (cm²/s) is the diffusion coefficient and $[C]$ (number of ions/cm³) is the ion concentration

- voltage applied to the membrane

Origin of the rest potential

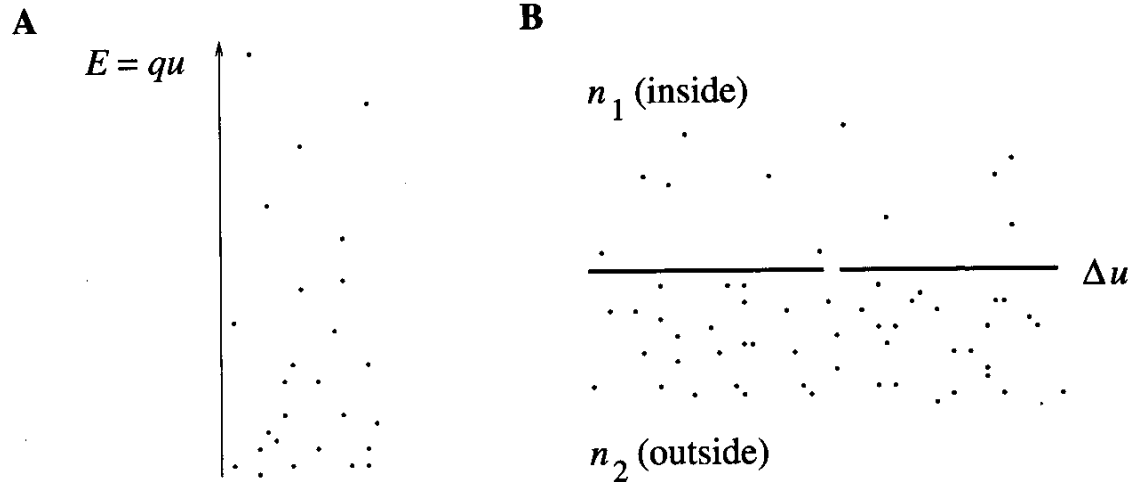


A simplified cell model



- simplified model → impermeability to Na^+
- key ingredient → gradient of concentration versus electric gradient
- when the cell is at rest gradient of concentration and electric gradient are equilibrated
- **equilibrium potential of a ion** → the value of the membrane potential giving no net flux

Nernst Equation - 1



Nernst equation links the equilibrium potential of an ion to the **external** and **internal** concentration ($[n]_2$ and $[n]_1$):

$$E_{ion} = \frac{k_B T}{q} \ln \frac{[n]_2}{[n]_1}$$

$k_B \simeq 1.38 \cdot 10^{-23} J/K$ Boltzmann constant; T is the temperature (in Kelvin) and q the charge of the ion (in Coulomb).

- $E_K \simeq -85mV \rightarrow$ in the simplified model the rest potential of the neuron is essentially dominated by the inner and outer concentration of K^+

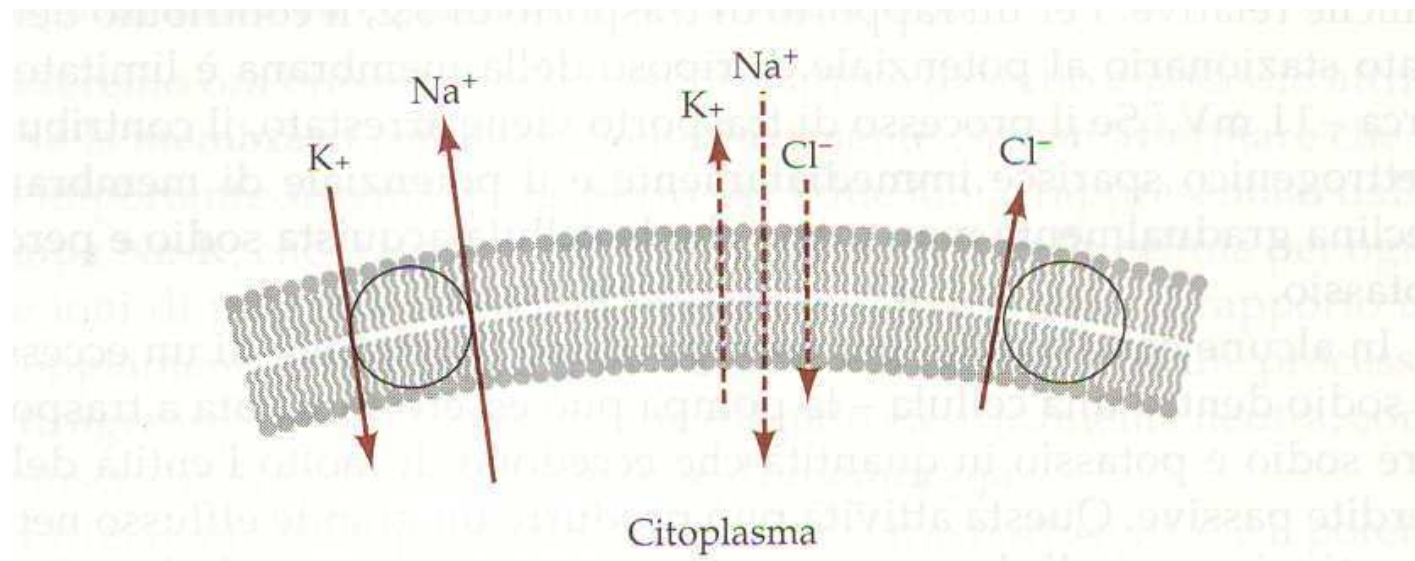
Nernst Equation - 2

- probability to find a molecule in a state with energy $U \rightarrow p(U) \propto \exp(-U/k_B T)$;
- ions with positive charge q in a static electric field $\rightarrow U(x) = qV(x)$, where $V(x)$ is the potential in x ;
- $p(U(x)) \propto [n(x)]$:

$$\frac{p(U(x_1))}{p(U(x_2))} = \frac{[n(x_1)]}{[n(x_2)]} = \exp(-q(V(x_1) - V(x_2))/k_B T)$$

- we get the Nernst equation if $\Delta V = (V(x_1) - V(x_2))$ is the voltage difference between inside and outside (i.e. the membrane potential by definition)

Sodium effect and ionic pumps



What happens if permeability to Na⁺ is considered?

- electric gradient/concentration gradient favor the inflow of Na⁺ → depolarization of the membrane (above the equilibrium potential of K⁺) → K⁺ flows out
- **ionic pumps** are necessary to restore the **dynamical equilibrium** (constant concentrations inside and outside) → Na:K pump (3 Na⁺ out/ 2 K⁺ in)

Ion permeability - G.H.K equation

- D.E. Goldman, A.L. Hodgkin e B. Katz :

$$V_{rest} = \frac{k_B T}{q} \ln \frac{p_k [K^+]_e + p_{Na} [Na^+]_e + p_{Cl} [Cl^-]_i}{p_k [K^+]_i + p_{Na} [Na^+]_i + p_{Cl} [Cl^-]_e};$$

where q is the ion electric charge; $[I]_j$ ($I = K^+, Na^+, Cl^-$) $j = i, e$ internal and external concentrations; p_k, p_{Na}, p_{Cl} permeabilities.

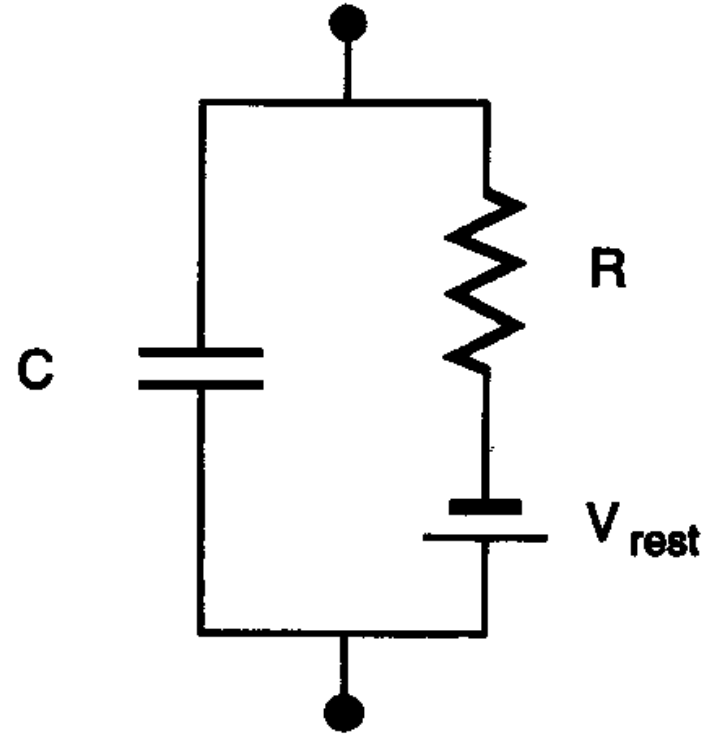
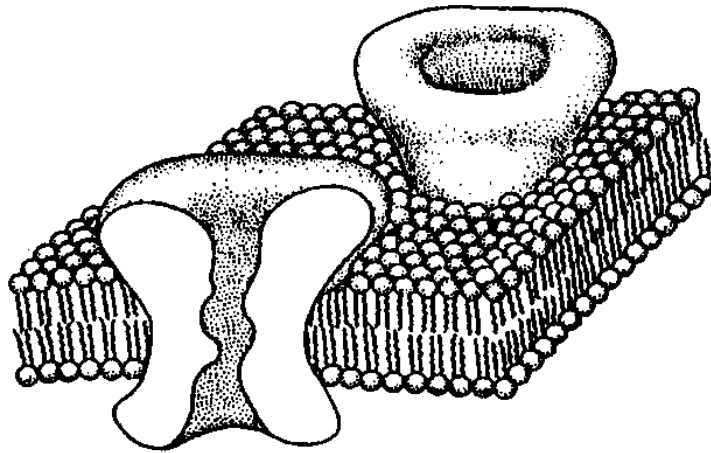
- neglecting the effect of Cl^- ($p_k : p_{Na} : p_{Cl} = 1 : 0.04 : 0.1$)

$$V_{rest} = \frac{k_B T}{q} \ln \frac{[K^+]_e + b [Na^+]_e}{[K^+]_i + b [Na^+]_i} \simeq -67mV \quad b = p_{Na}/p_k \simeq 0.04;$$

- including the effect of ionic pumps

$$V_{rest} = \frac{k_B T}{q} \ln \frac{r [K^+]_e + b [Na^+]_e}{r [K^+]_i + b [Na^+]_i} \simeq -73mV \quad r = 3/2 \text{ for pump Na : K}$$

Membrane - passive electric properties



- membrane divides two ionic solutions → capacitance ($C_m \simeq 1\mu F/cm^2$),
 $Q_m = 1\mu F/cm^2 \times 65mV \simeq 6.5 \times 10^{-8} C/cm^2 \rightarrow 4 \times 10^{11}$ monovalent ions/cm²
- ionic channels → resistance ($10^3 \Omega \cdot cm^2$)
- V_{rest} → voltage generator