Neuronal Models - part I

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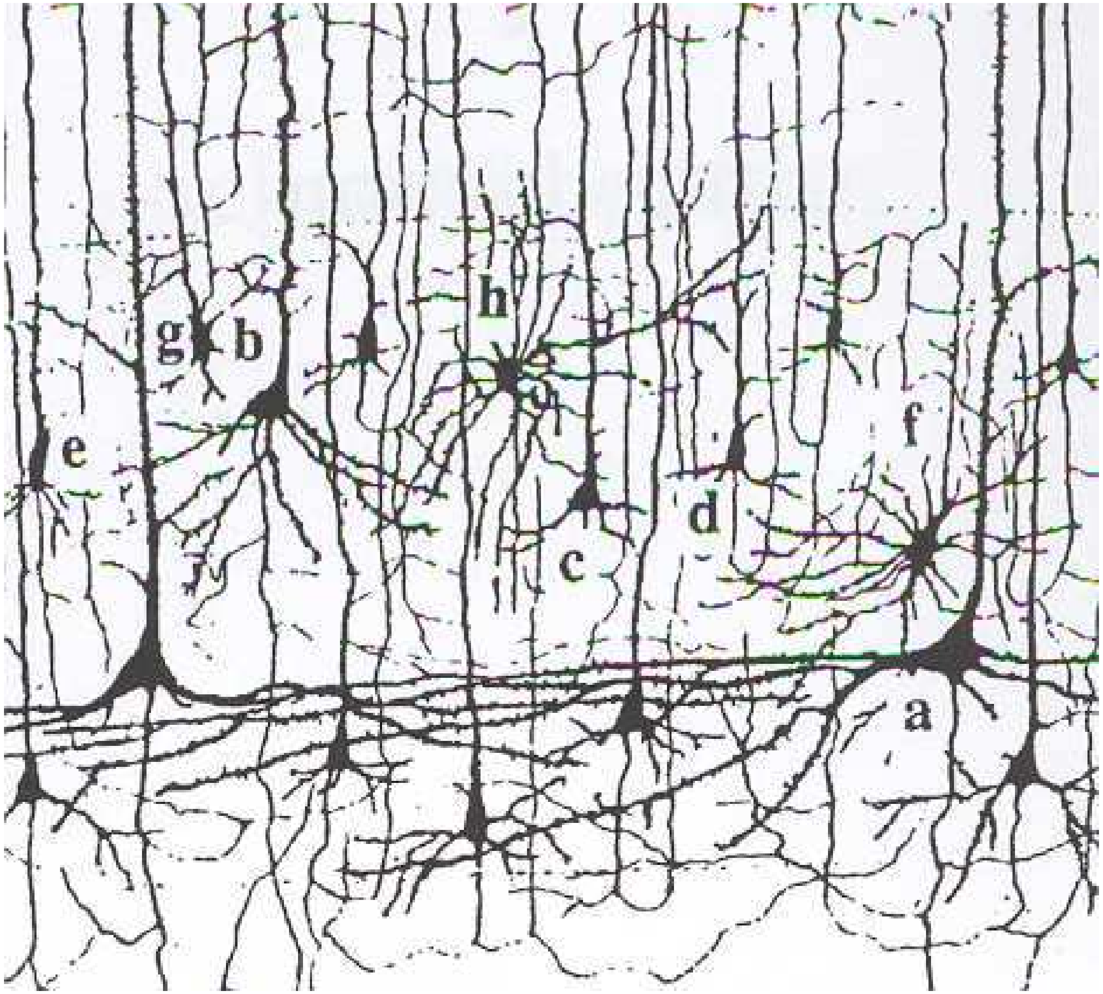
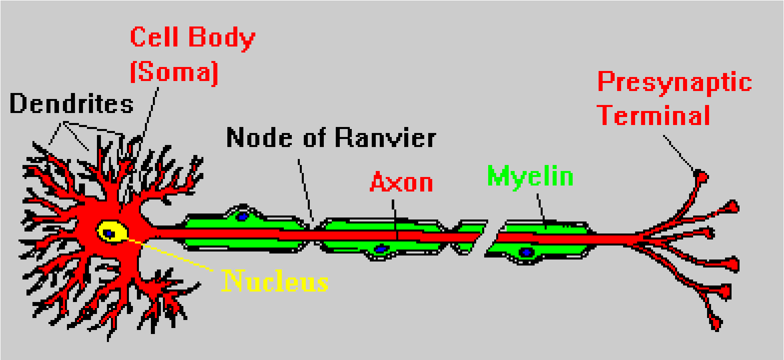
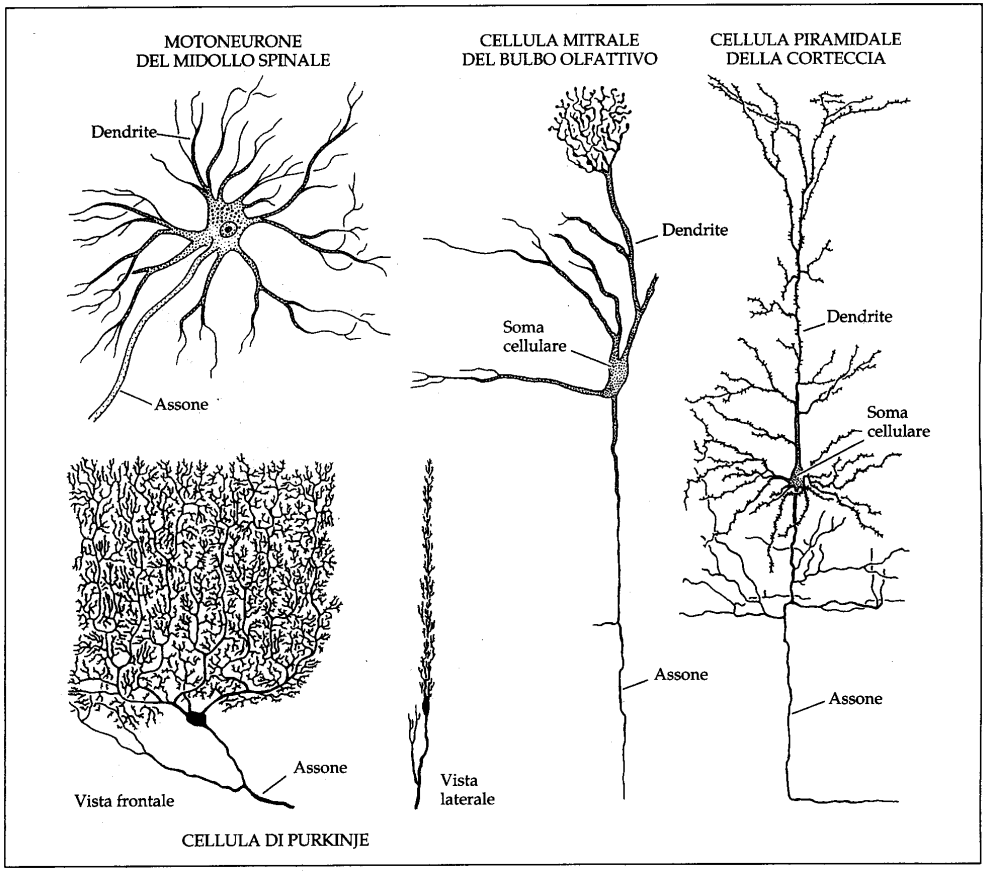
Neurons



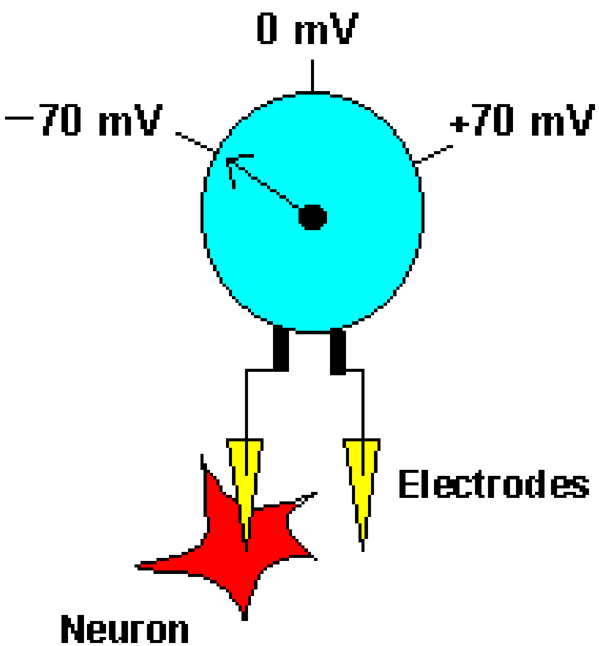
- human brain $\rightarrow 10^{11}$ neurons, density in the cortex: $10^5/\mathrm{mm}^3$

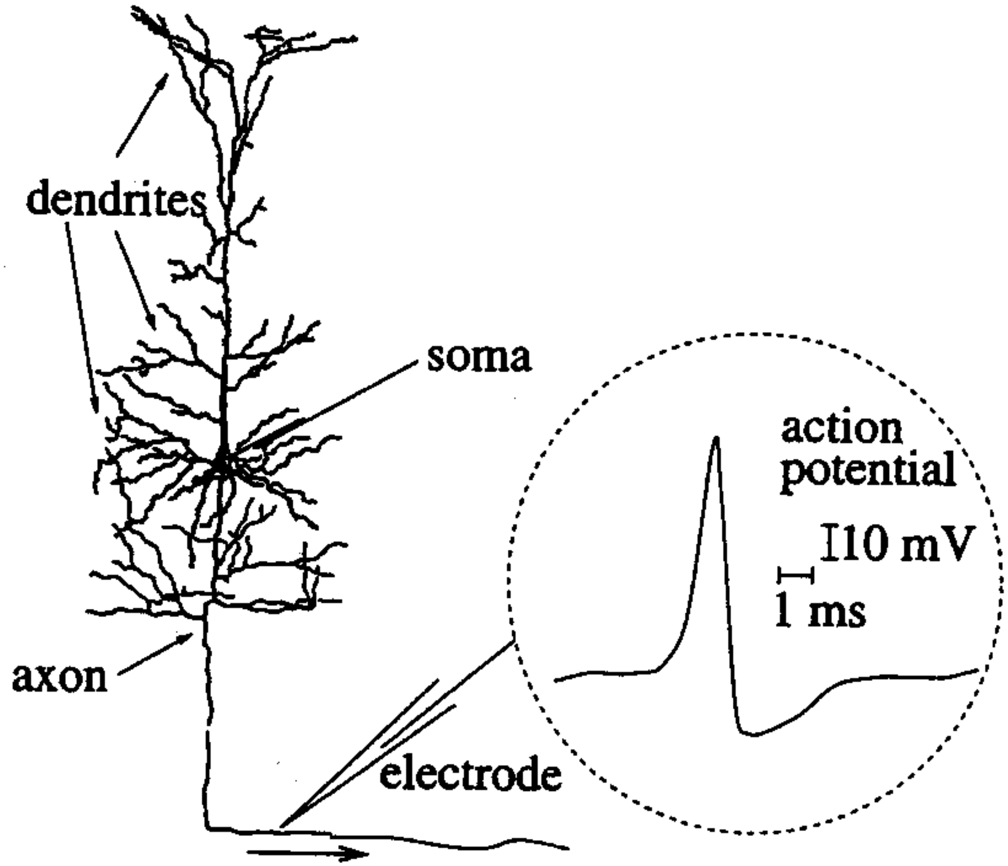
Morphology


Cell Body
(Soma)
Dendrites
Node of Ranvier
Presynaptic
Terminal
Axon
Myelin
Nucleus


MOTONEURONE
DEL MIDOLLO SPINALE
CELLULA MITRALE
DEL BULBO OLFATTIVO
CELLULA PIRAMIDALE
DELLA CORTECCIA
Dendrite
Assone
Dendrite
Soma
cellulare
Assone
Dendrite
Soma
cellulare
Assone
Assone
Vista frontale
Vista
laterale
CELLULA DI PURKINJE

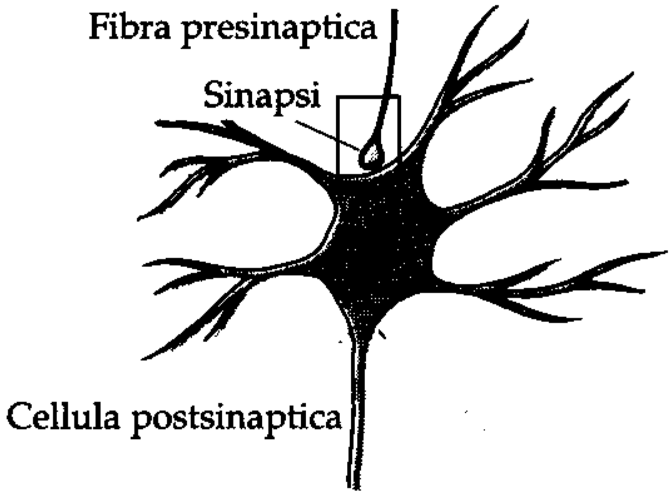
Neuronal Signals - Action Potential





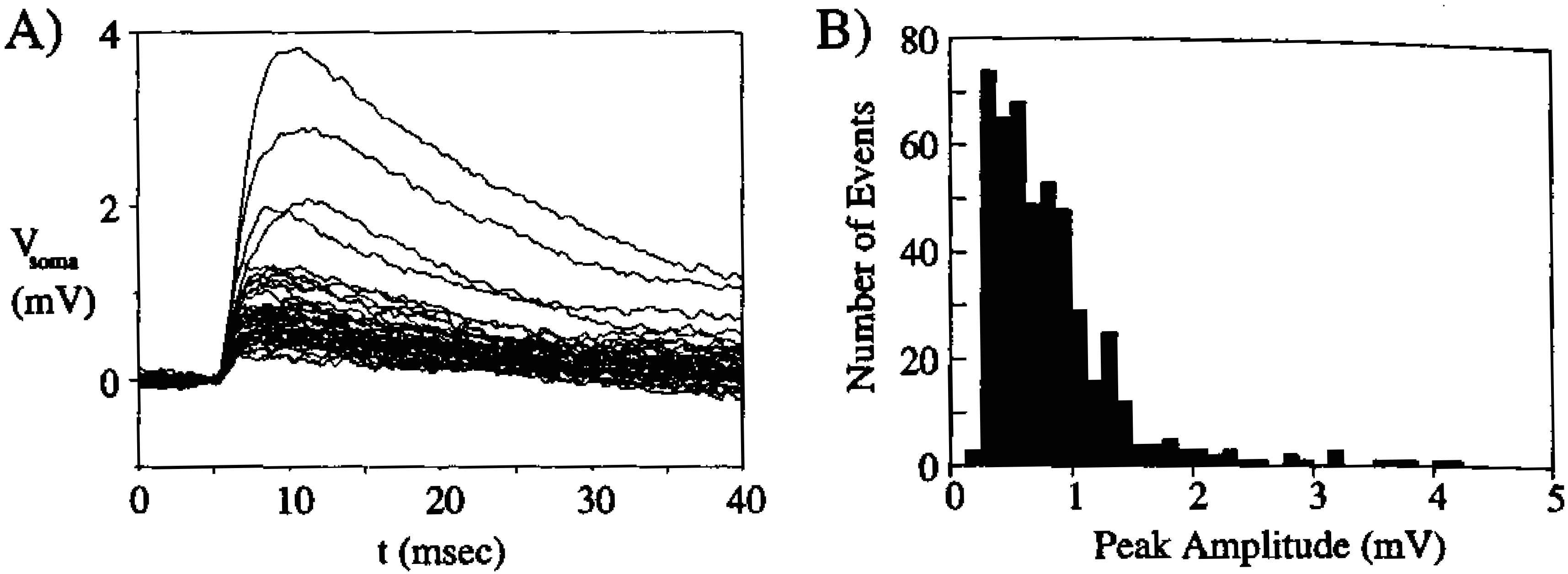
- membrane potential
- no stimuli → rest potential
- The action potential is the elementary unit of the neuronal transmission → depolarization, hyperpolarization

Synapses



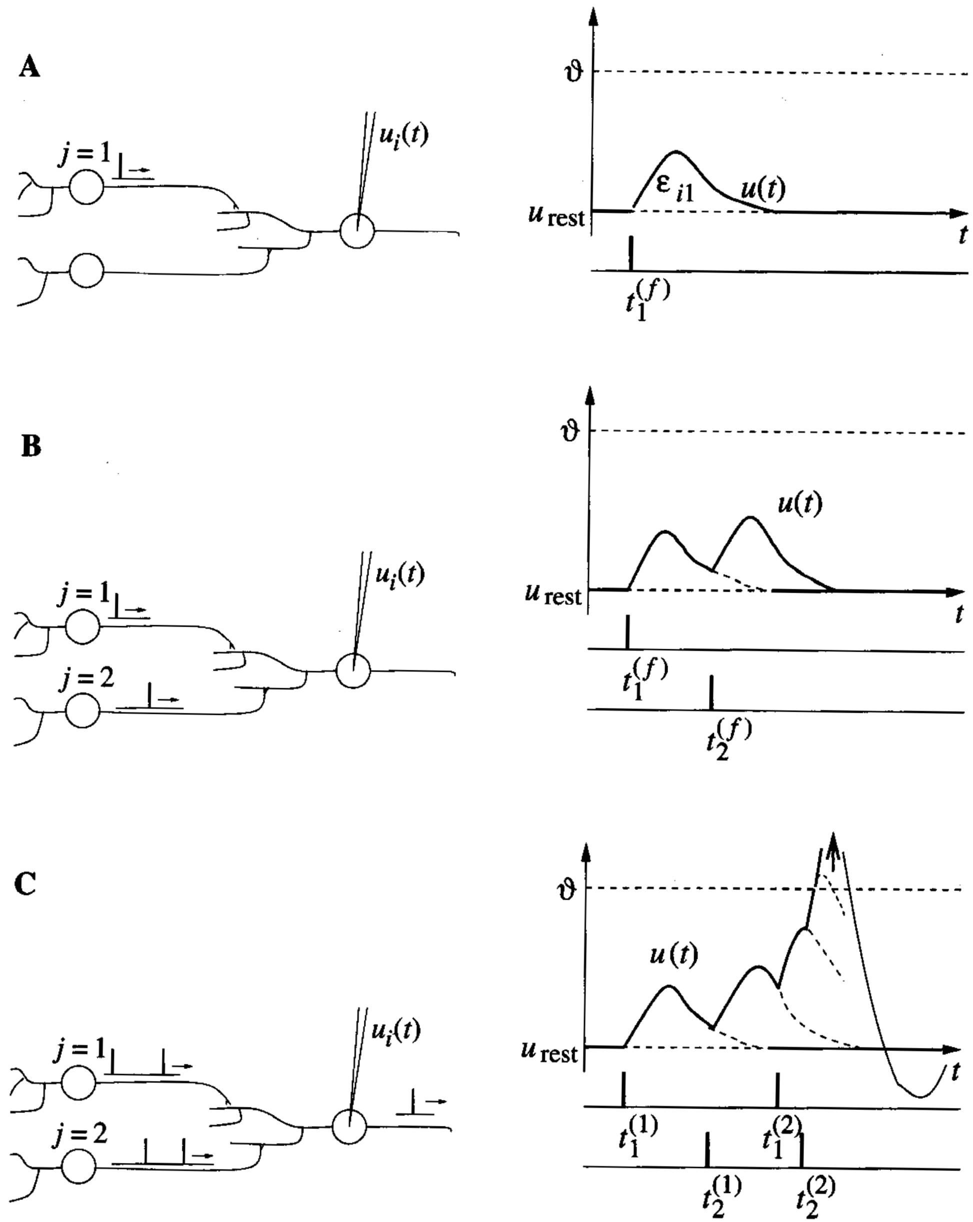
- chemical synapses $\rightarrow$ neurotransmitters (glutamate, GABA)
- electrical synapses (gap junctions)

Post synaptic potentials

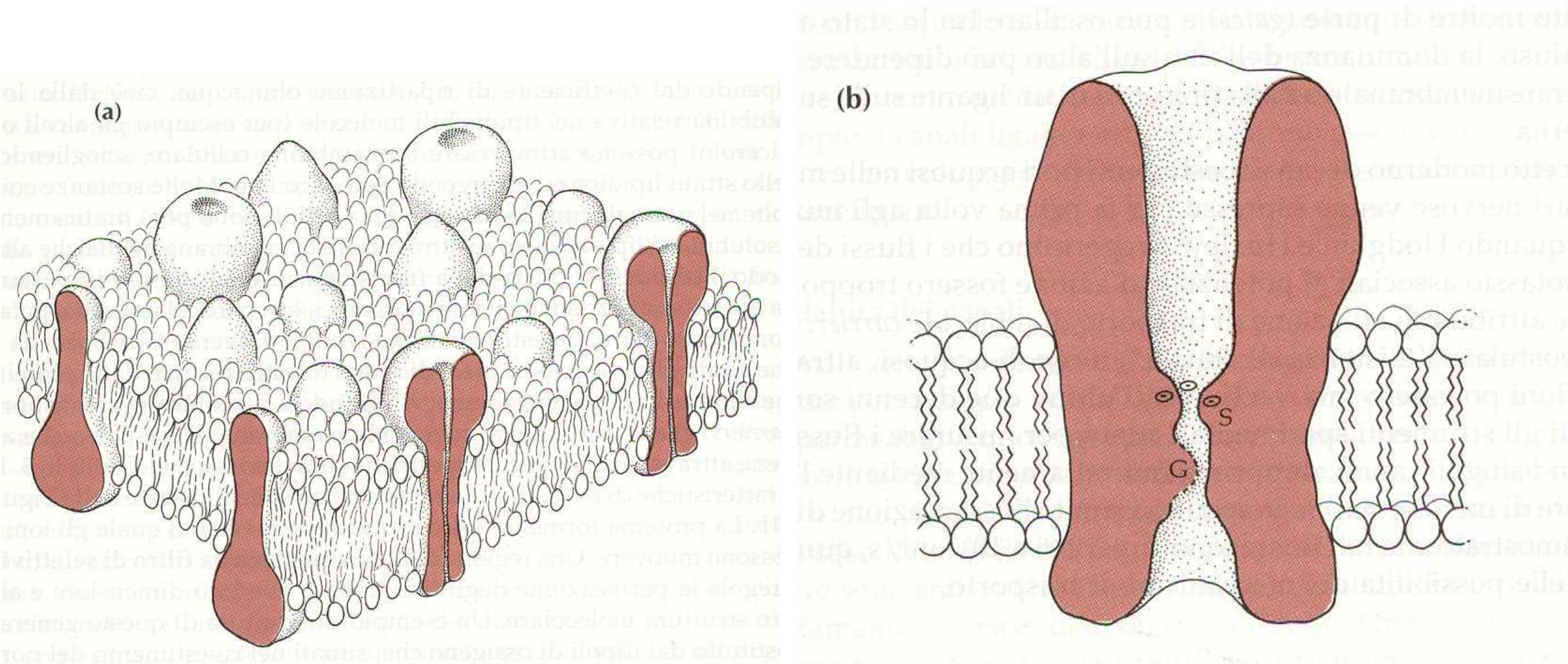


- postsynaptic potential $\rightarrow$ excitatory (PPSE)/inhibitory (PPSI)
- excitatory synapse/inhibitory synapse
- number of synapses in the cortex $\rightarrow 10^4$ (85% excitatory, 15% inhibitory) BUT ONLY $5-10\%$ ARE ACTIVE!

Neuronal dynamics - firing threshold



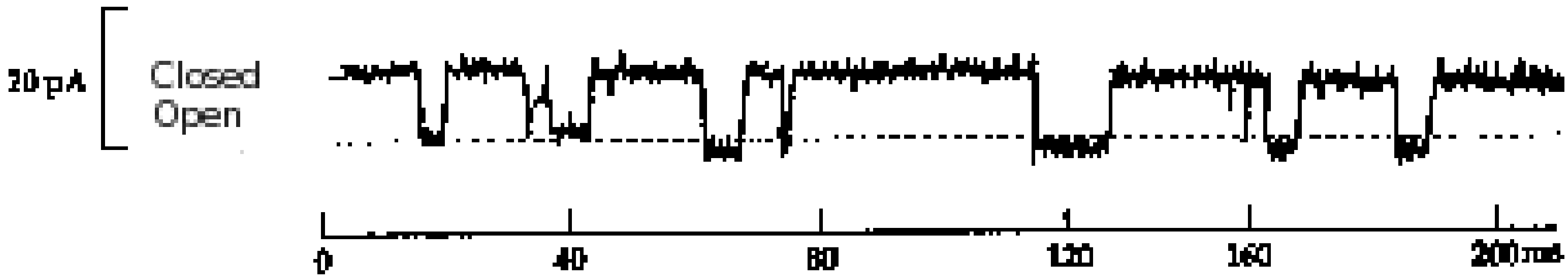
Neuronal membrane - Ionic channels



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/(cm^2·s)) and $\Delta[C]$ difference of ion concentration (mol/cm^3)

- conductance of the membrane $\rightarrow$ electric current transportation

Ionic current - 2

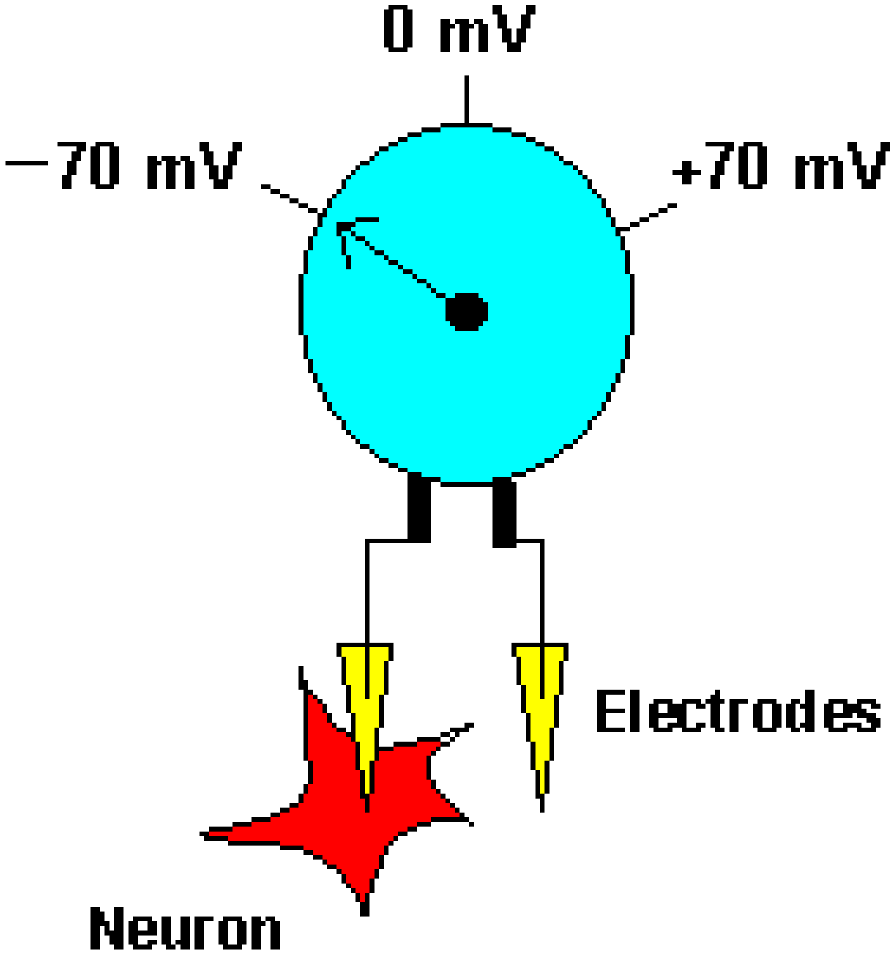
The current flowing through ion channel depends on:

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

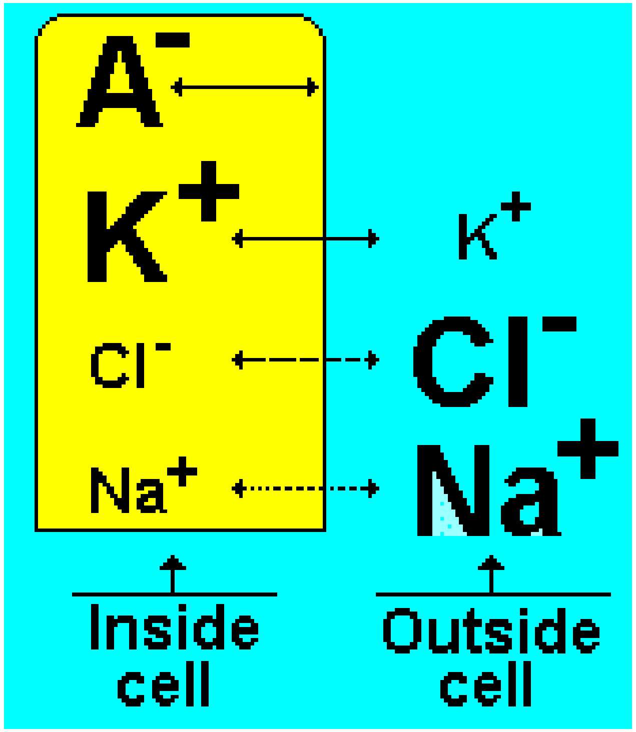
$$J_{diff} = -D\frac{d[C]}{dx}$$

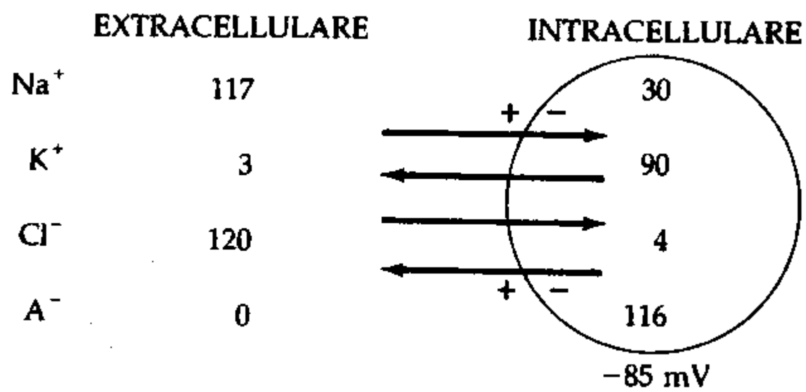
  where J_{diff} (number of ions/cm^2/s) is the flux due to the diffusion, D (cm^2/s) is the diffusion coefficient and $[C]$ (number of ions/cm^3) is the ion concentration
- voltage applied to the membrane

Origin of the rest potential



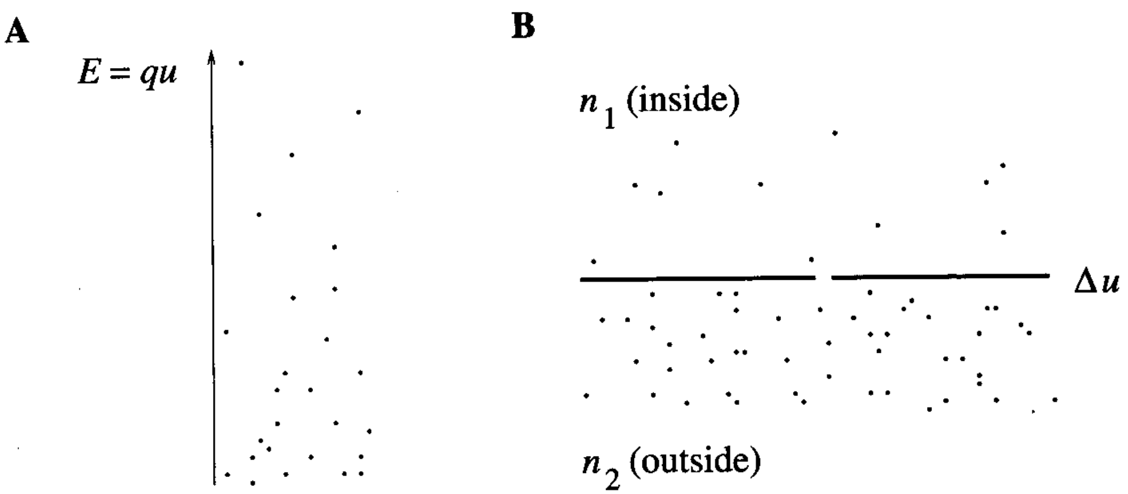
A simplified cell model





- 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^+

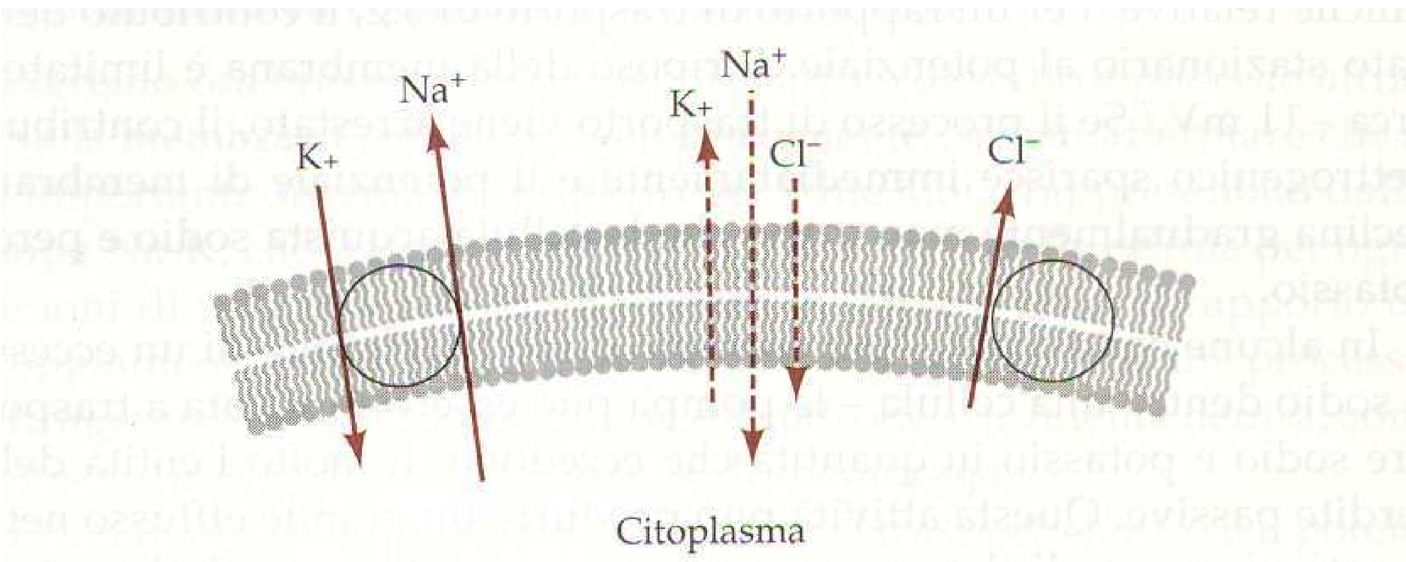
Nernst Equation - 2

- 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^+ $\rightarrow$ depolarization of the membrane (above the equilibrium potential of K^+) $\rightarrow$ K^+ flows out
- ionic pumps are necessary to restore the dynamical equilibrium (constant concentrations inside and outside) $\rightarrow$ 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.

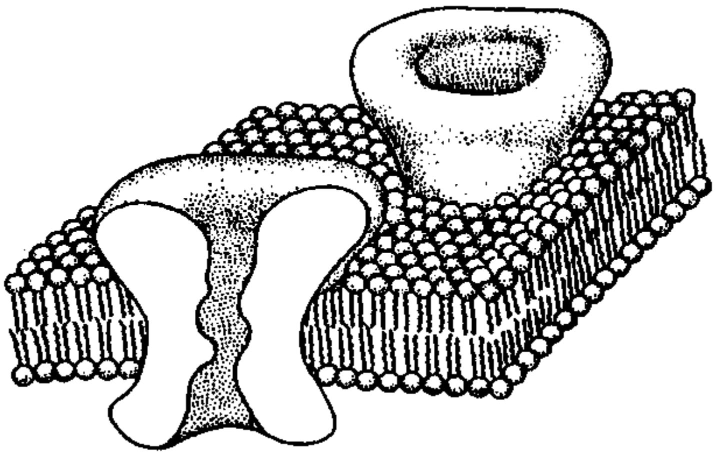
- neglecting the effect of Cl$^-$ ($p_k : p_{Na} : p_{Cl} = 1 : 0.04 : 0.1$)

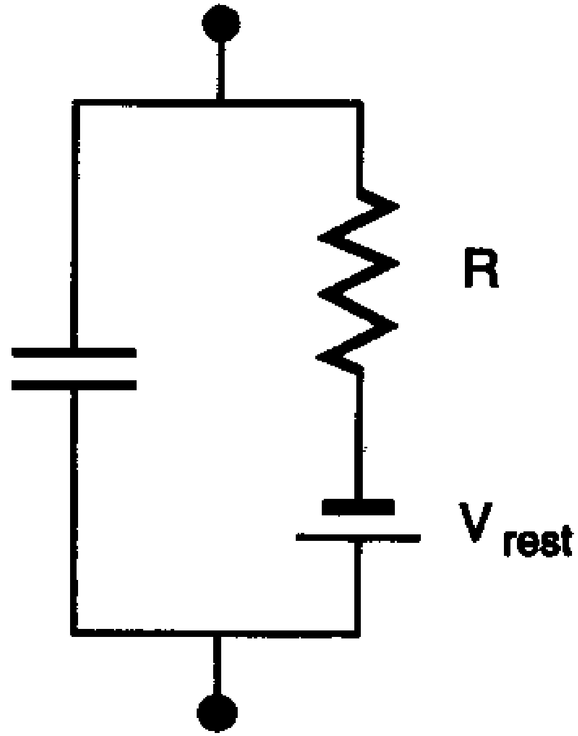
$$V_{rest} = \frac{k_B T}{q} \ln \frac{[K^+]_e + b[Na^+]_e}{[K^+]_i + b[Na^+]_i} \simeq -67mV \qquad b = p_{Na}/p_k \simeq 0.04;$$

- including the effect of ionic pumps

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

Membrane - passive electric properties





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