Neuroelectricity

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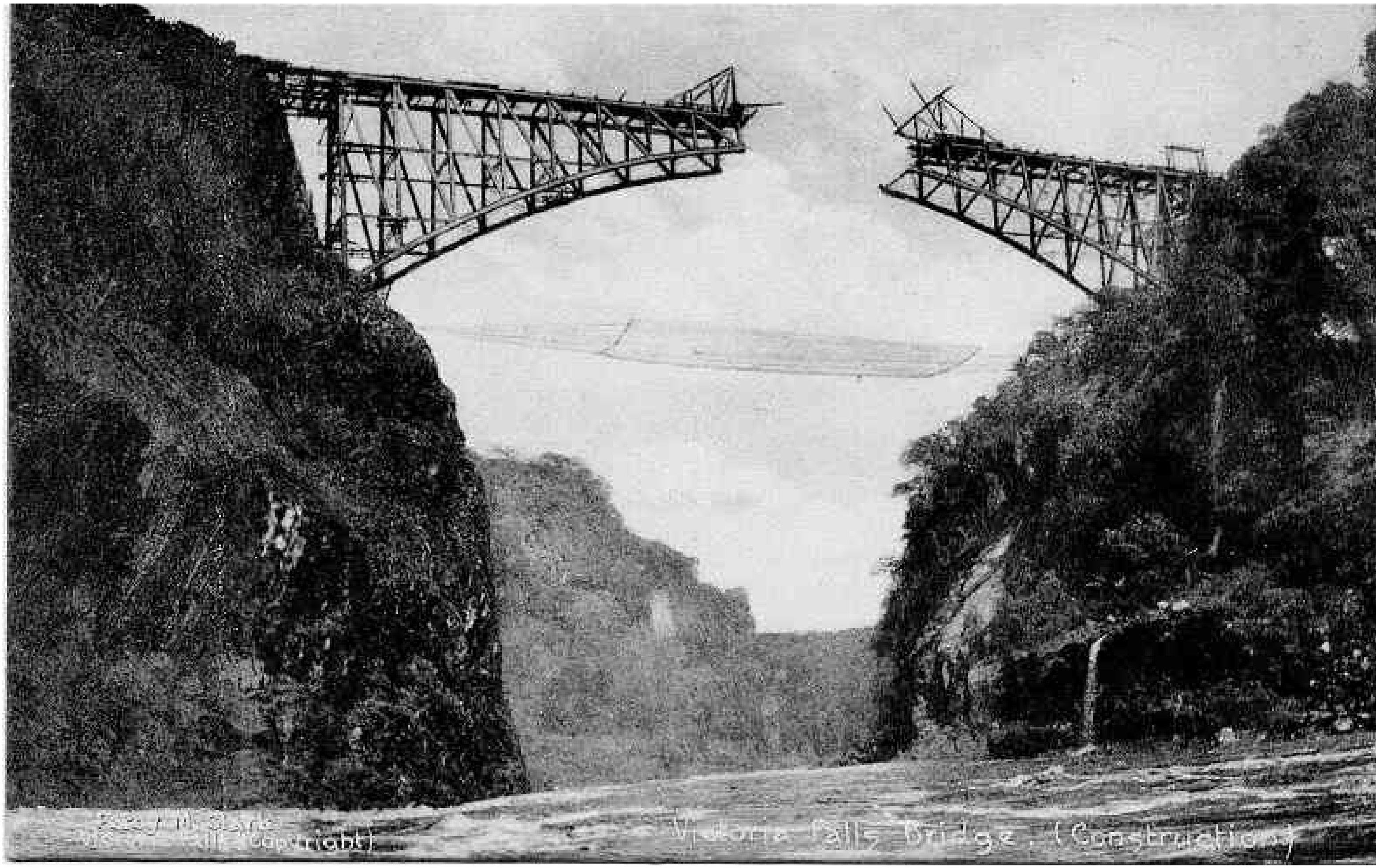
System Neuroscience



Bridging over scales: now in neuroelectricity

The aims

- Understand the generation of the electric field in the nervous system
- Learn mathematical techniques to analyze the electric signals
- Model the neuroelectric phenomena

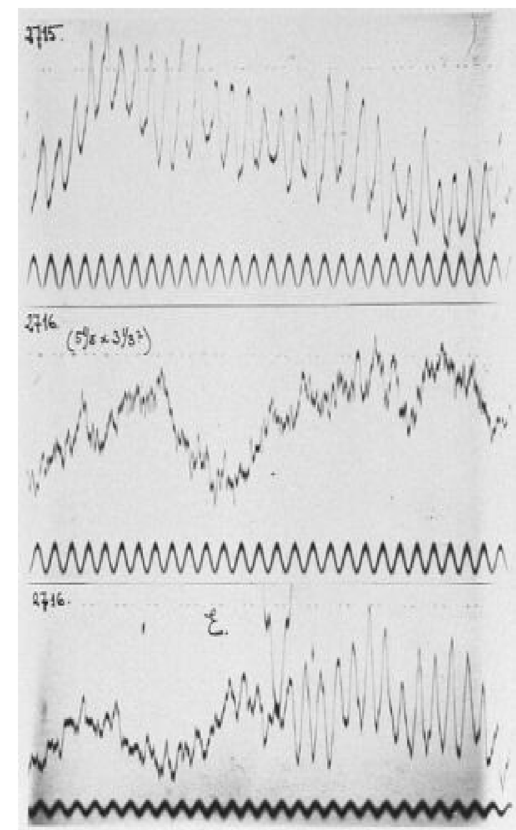
...on different scales.

Discovery of the electroencephalography (EEG) 1924

Hans Berger

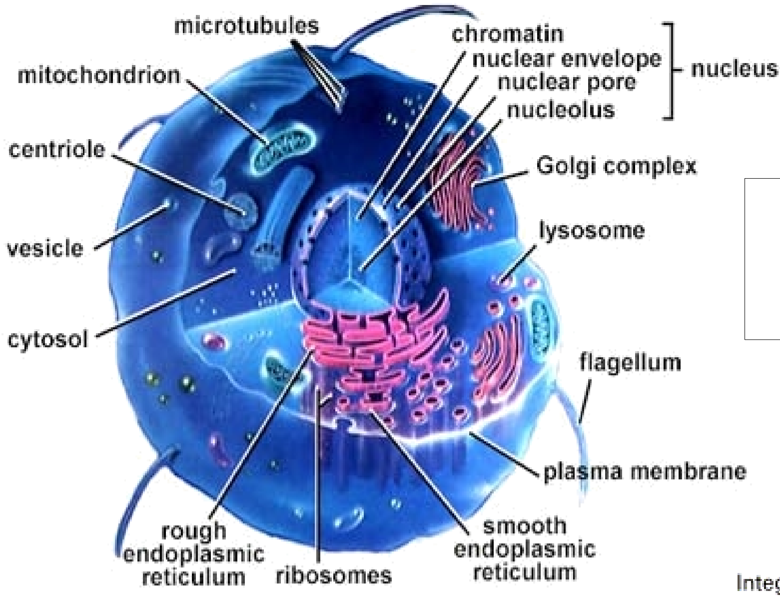
Actually, he was looking for telepathy

The first EEG record
The alpha rhythm
And the EEG features of epilepsy



The cell

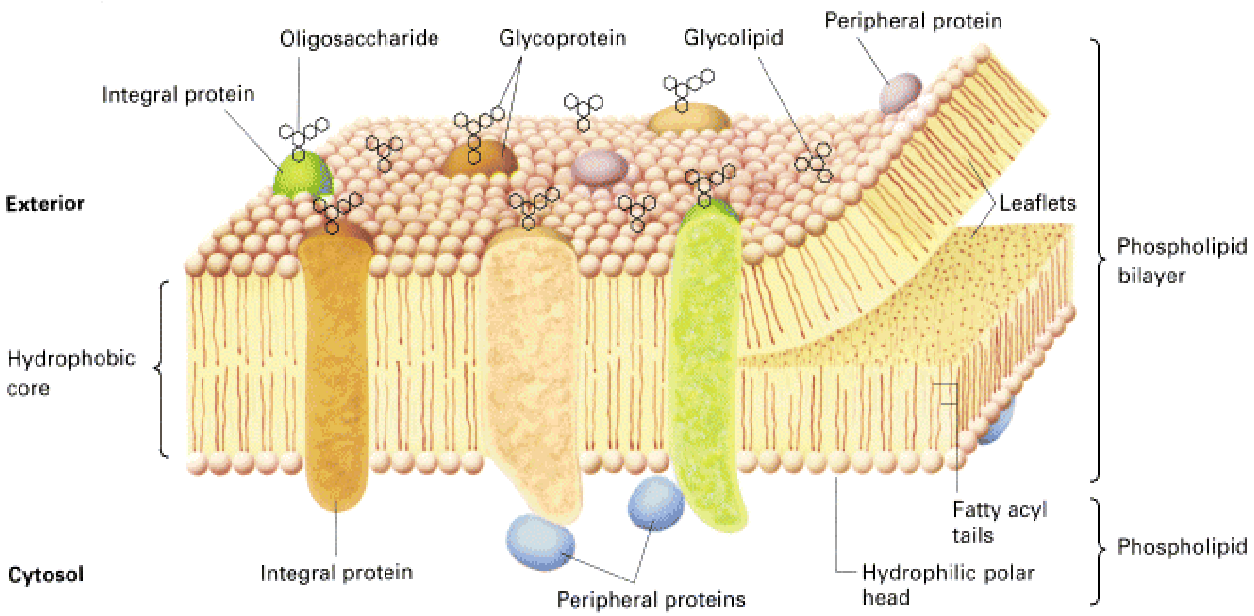
with electronmicroscope



nucleus
cytoplasm
membrane

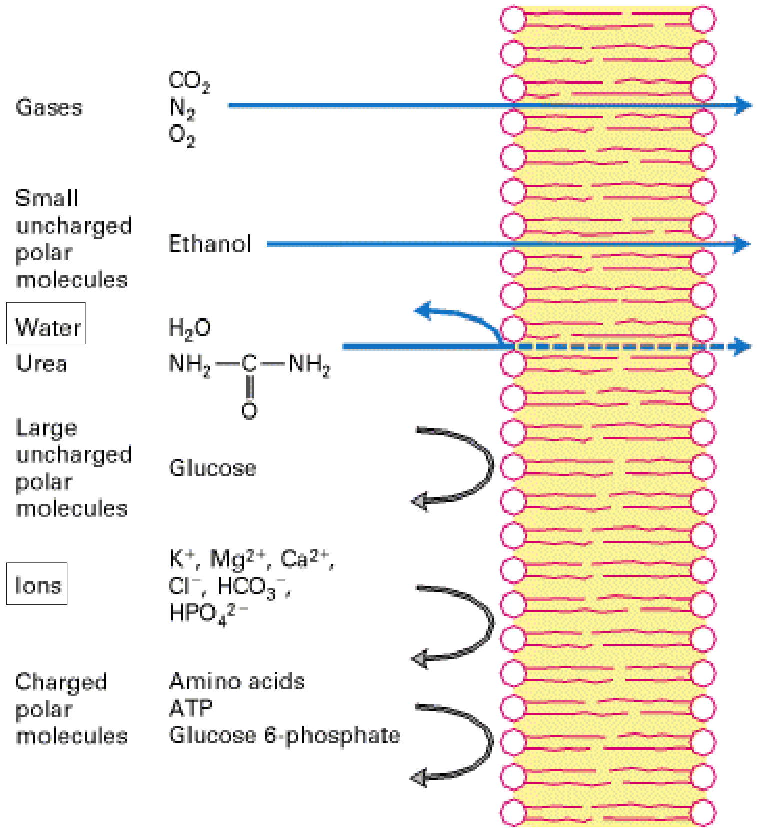
lipid bilayer
proteins
integral
peripheral

extracellular space (EC)
intracellular space (IC)

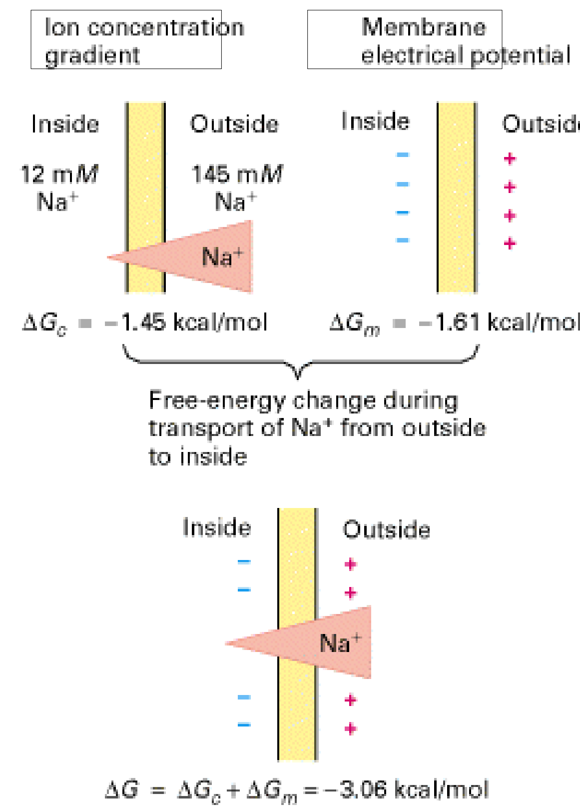


Trough the cell membrane

Different permeability, for different ions and molecules

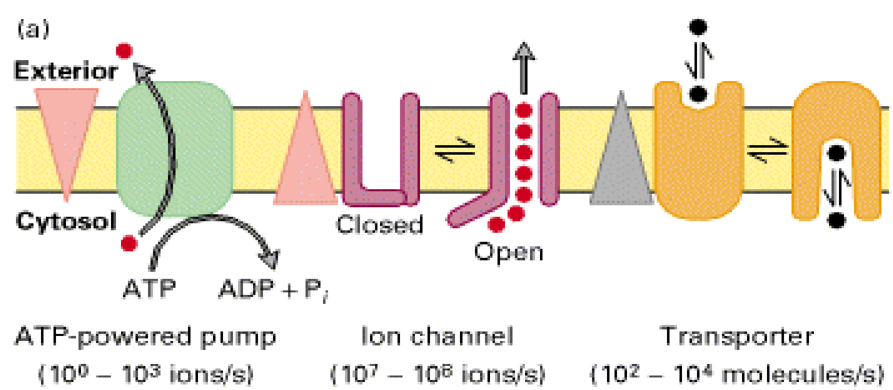


Forces of ion transport



Membrane transport, trough proteins

- pumps (+energy!)
- channels
- transporters

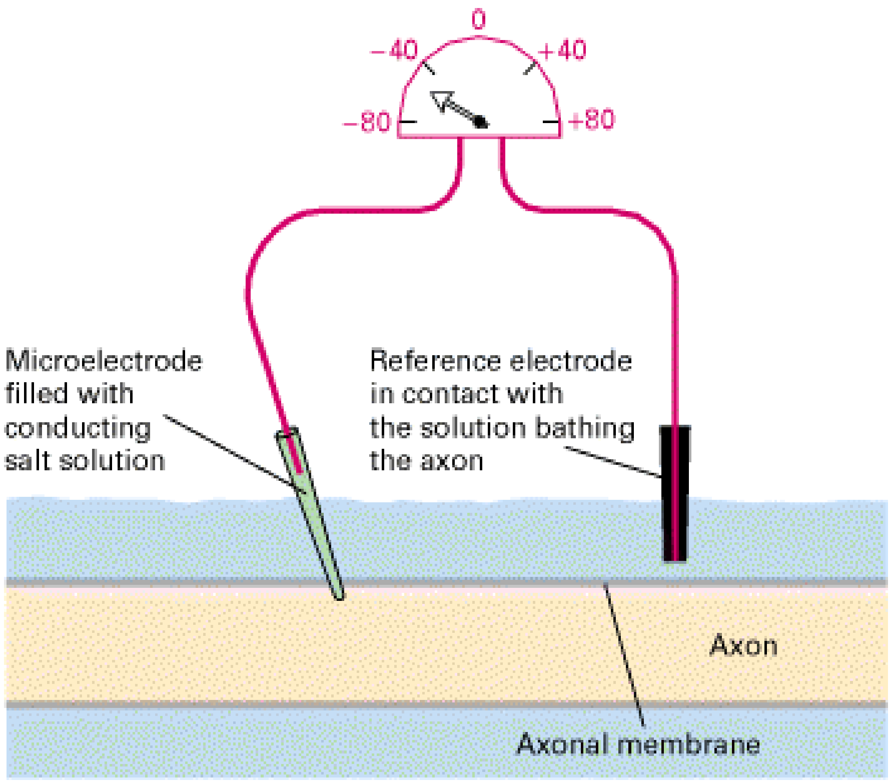


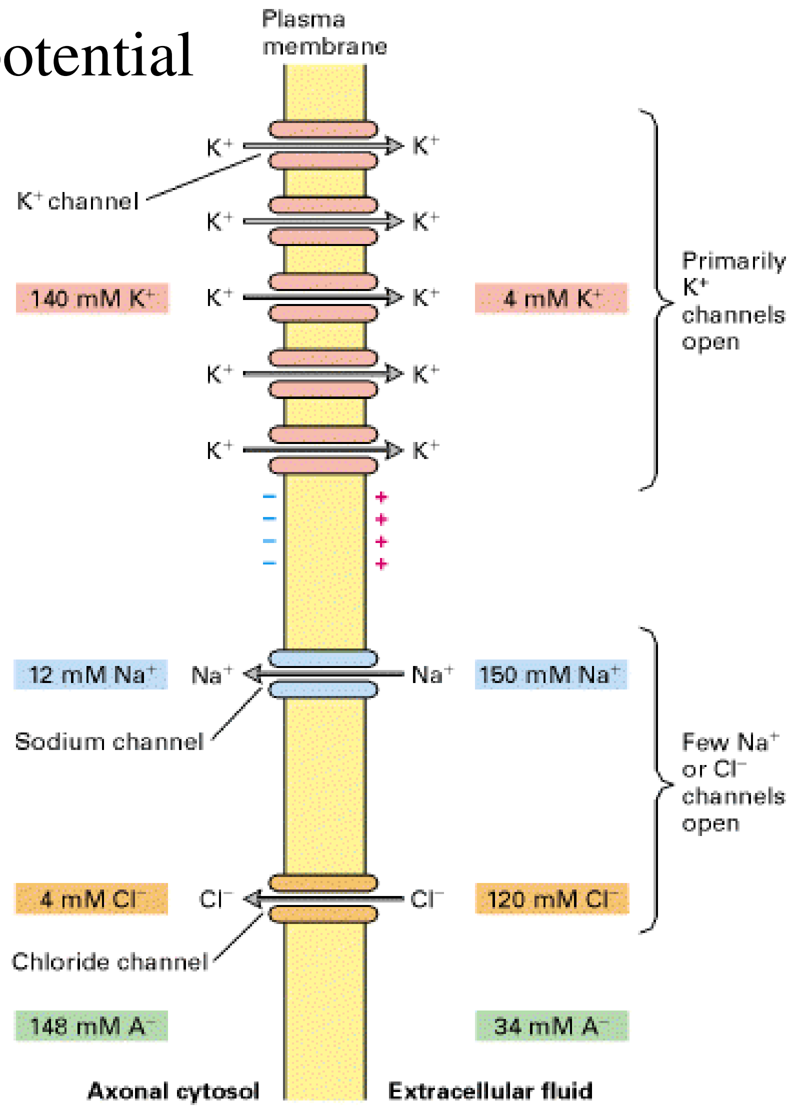
The electric neuron: resting potential

with electrode

The phenomenon:

Potential difference between the two side EC and IC of the membrane



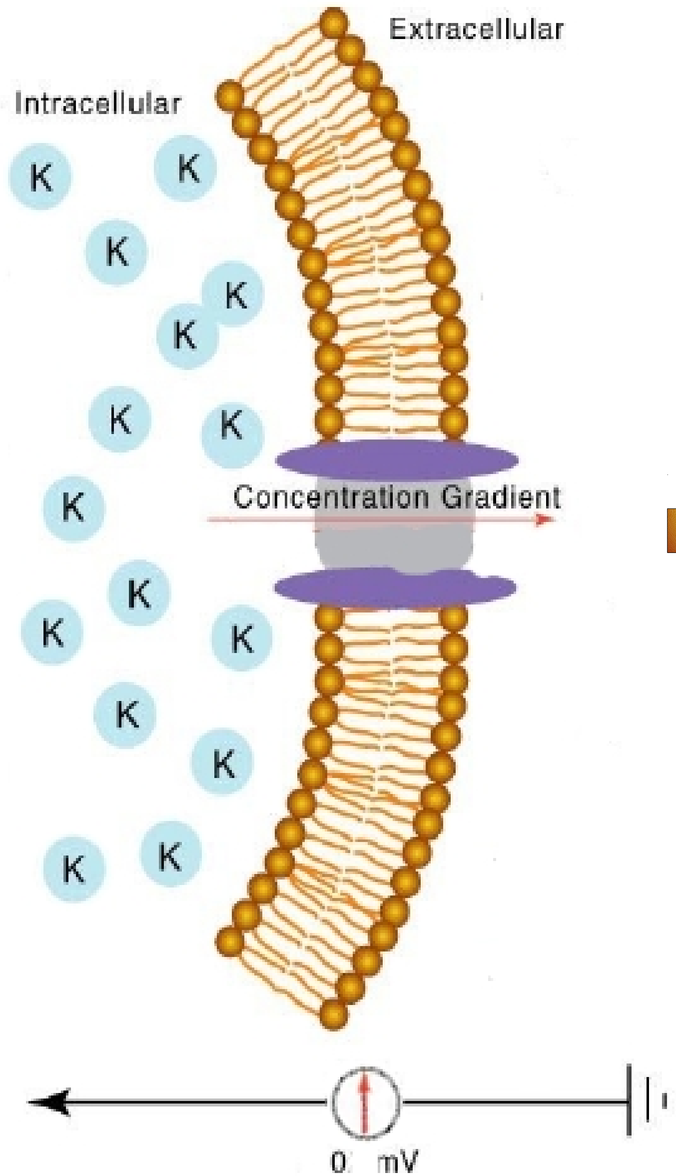


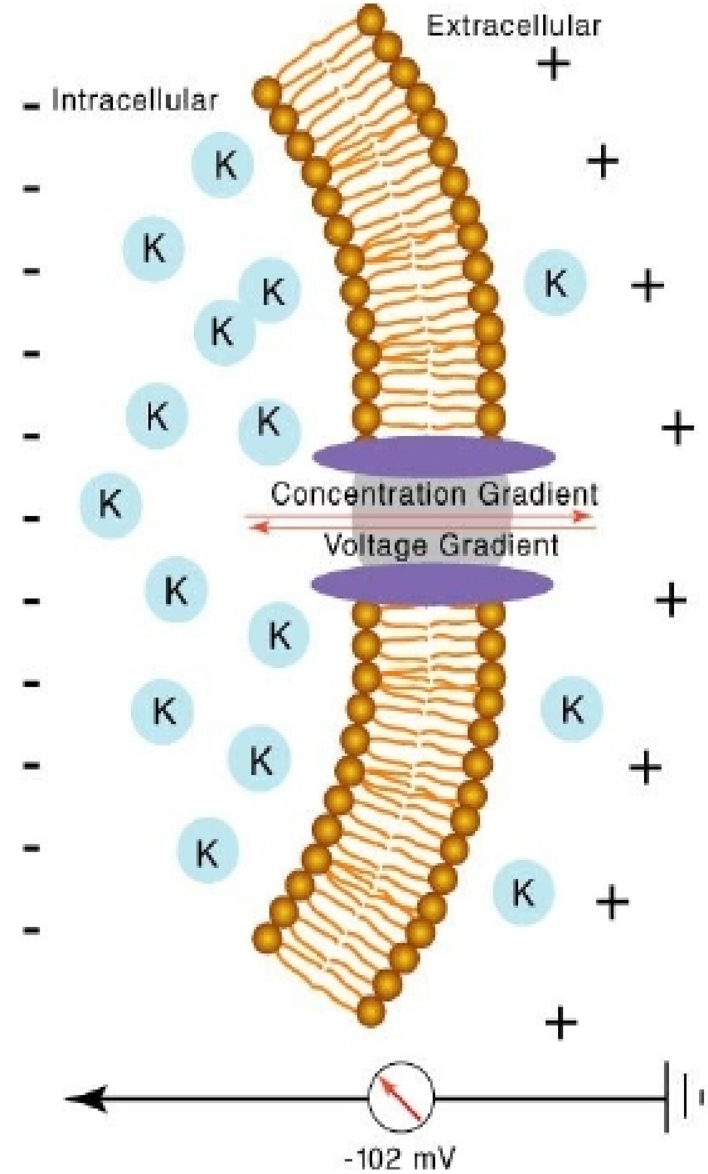
Reason:

on the two different sides of the membrane:

- different concentrations of ions on
- the two side of the membrane
- different permeability for different
- ions

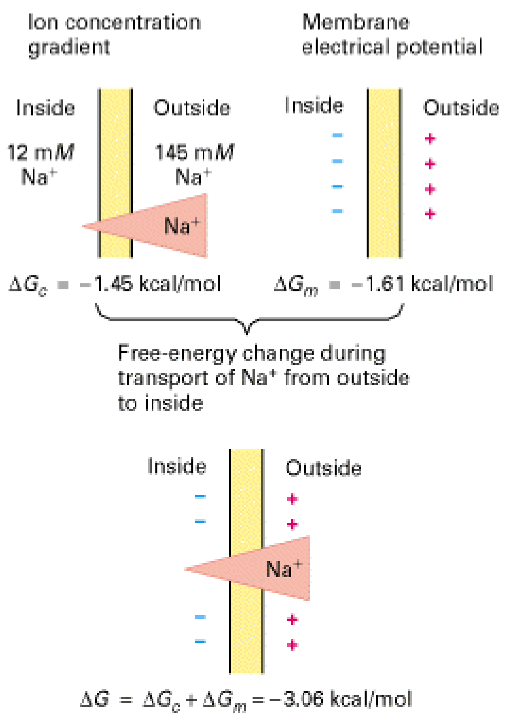
The generation of the resting potential





Larry R Squire and others: Fundamental Neuroscience *2nd Edition.*, *Academic Press*, 2002

Origin of the resting membrane potential



Nernst-Planck equation:
ionic flux (current) as a function of the electro-chemical potentials

Nernst-equation:
relationship between potential difference and ion concentration in equlibrium for one sort of ion

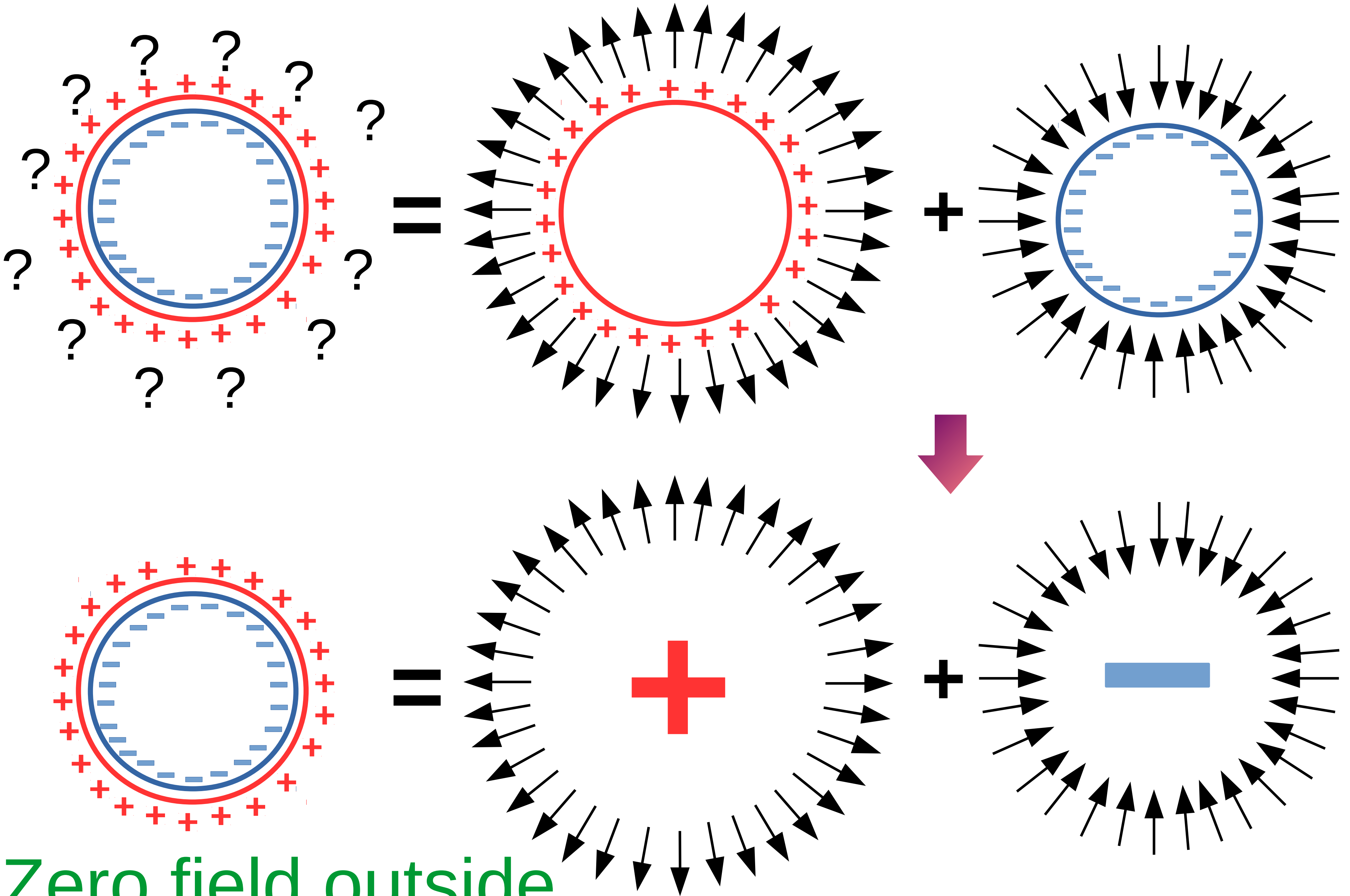
$$E = V_{IC} - V_{EC} = \frac{RT}{zF} \ln \frac{[C]_{EC}}{[C]_{IC}}$$

Goldman-Hodgkin-Katz-equation (GHK):
resting membrane potential as a function of the ion concentrations and permeabilities

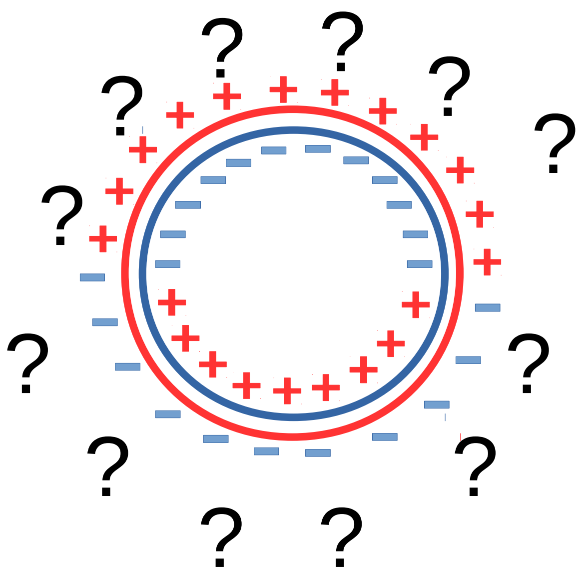
more, independently moveing ions
constant electric force intensity throug the membrane

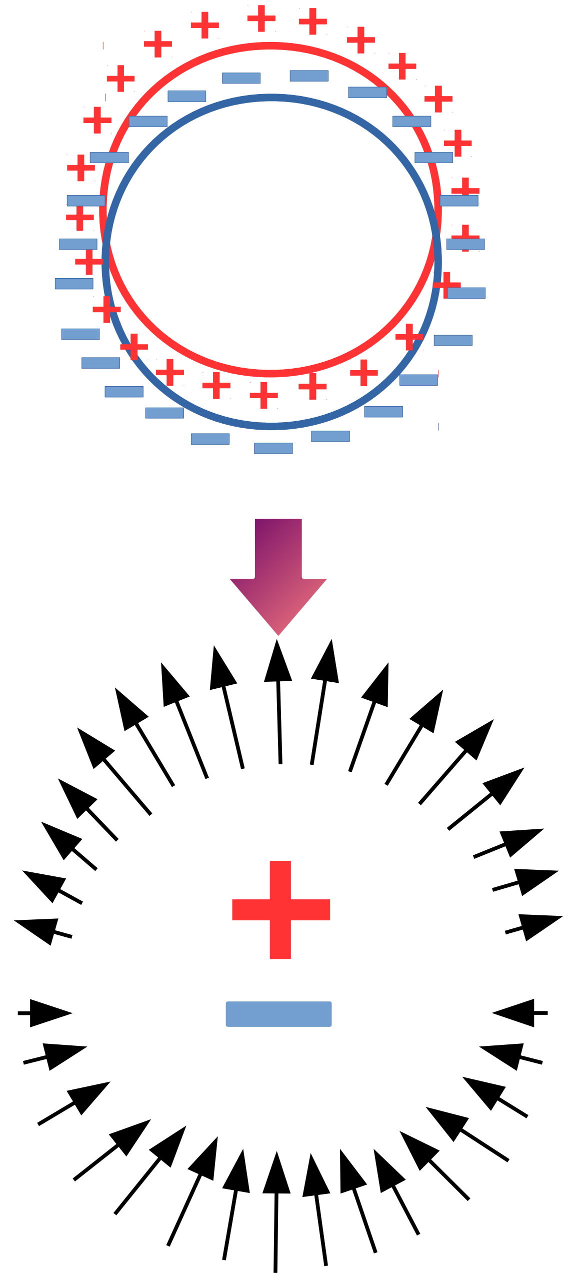
$$V_{rest} = \frac{RT}{F} \ln \frac{P_K [K^+]_{EC} + P_{Na} [Na^+]_{EC} + P_{Cl} [Cl^-]_{IC}}{P_K [K^+]_{IC} + P_{Na} [Na^+]_{IC} + P_{Cl} [Cl^-]_{EC}}$$

Extracellular electric field of a homogeneous spherical cell



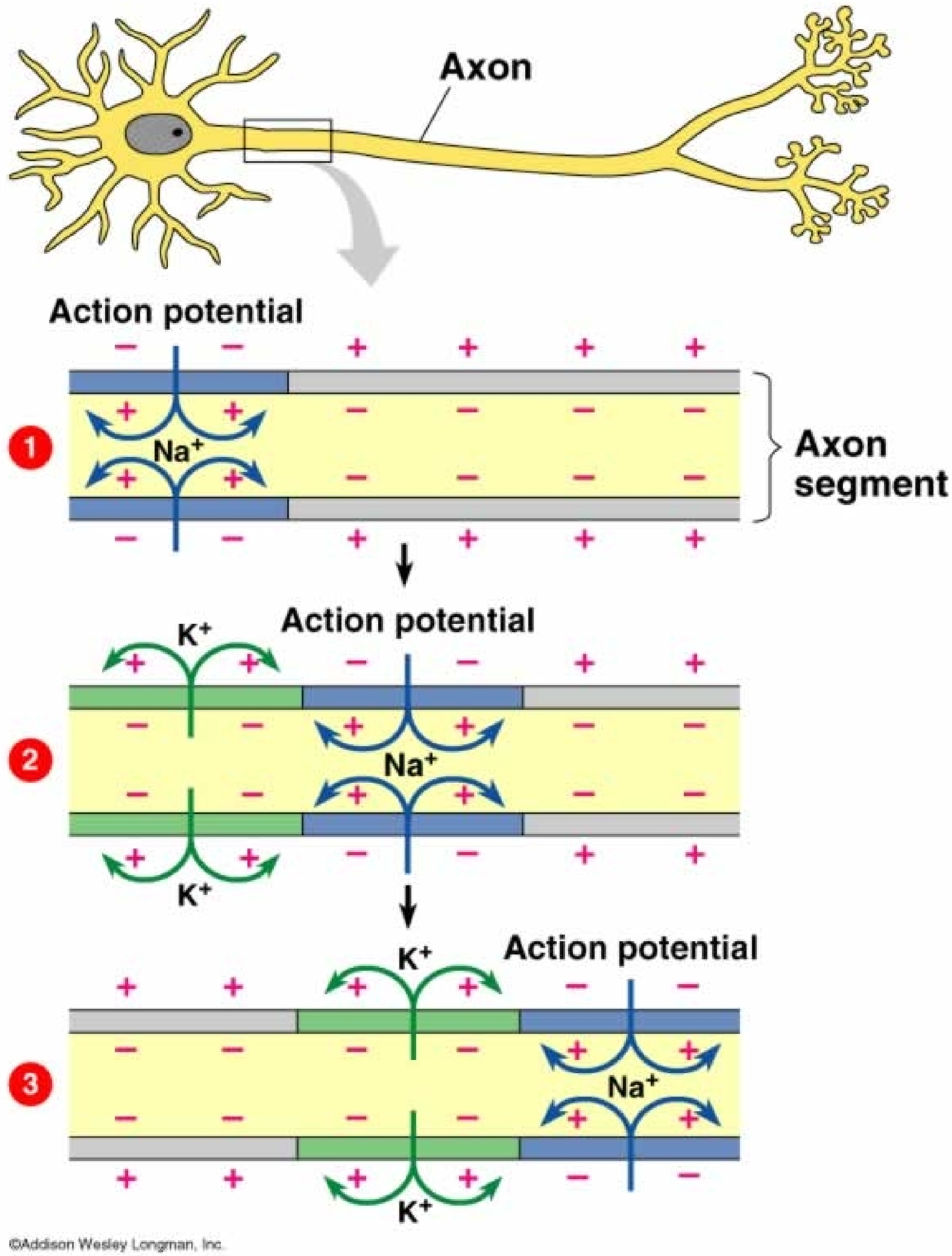
So, how could a cell has extracellular electric field ???

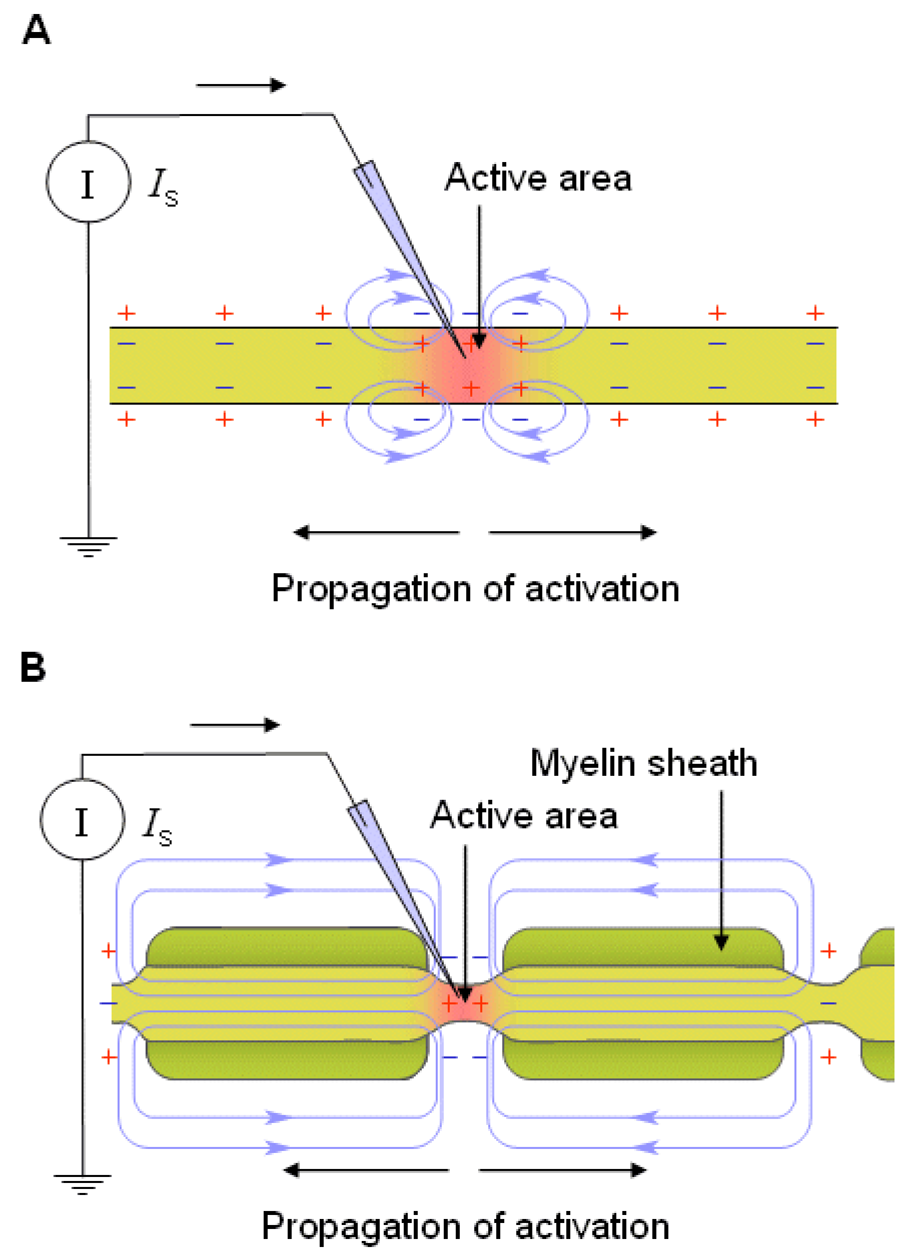




They can have dipole field!
If the membrane potential is non-homogeneous.

Propagation of the action potential



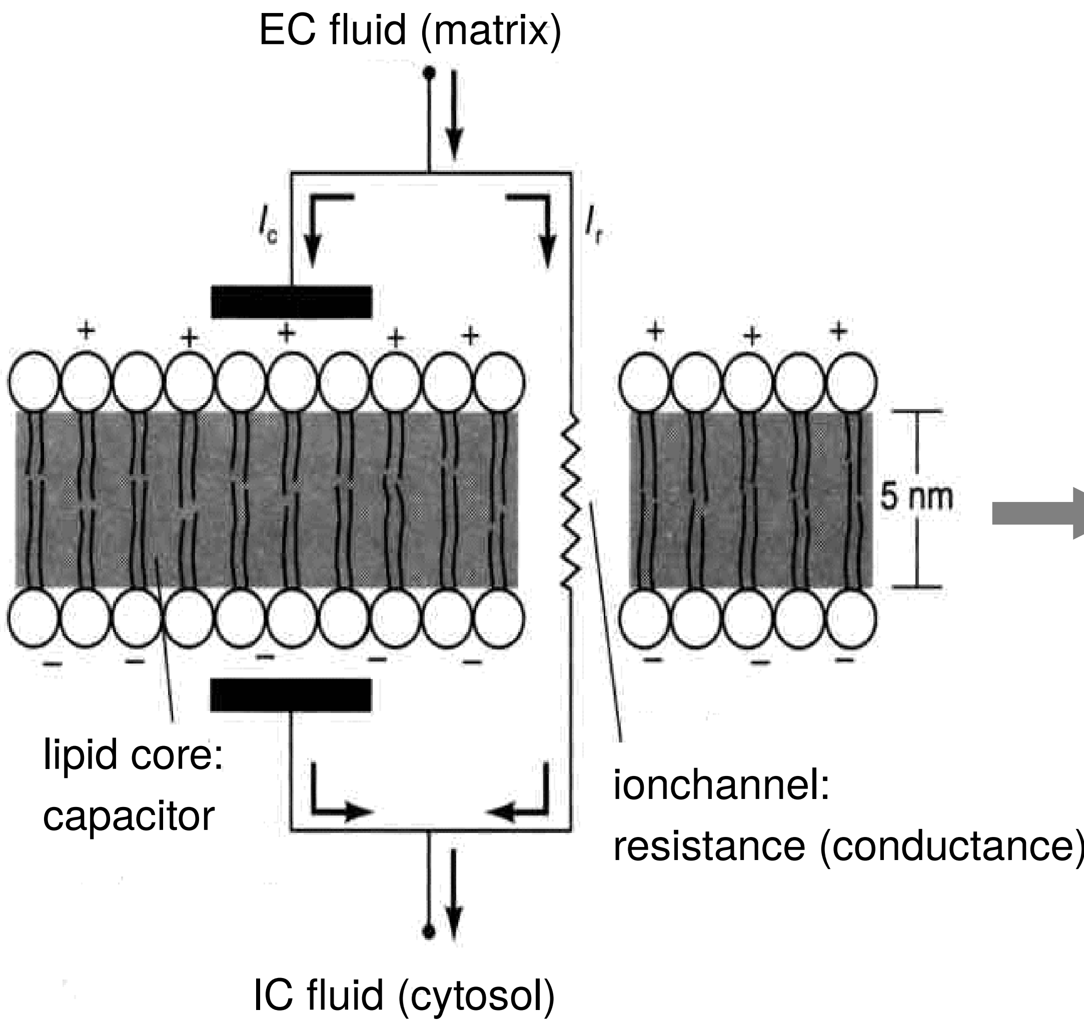


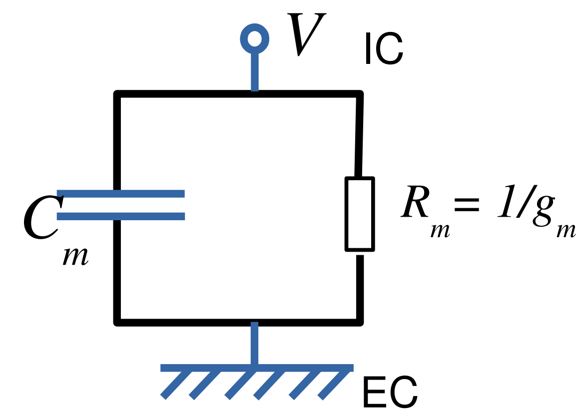
Computational Neuroscience

for quantitative description of the neural behavior

↳ **Mathematical**

Basics of the conductance-based models

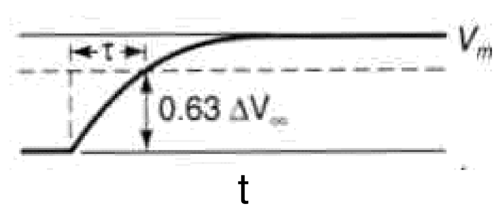




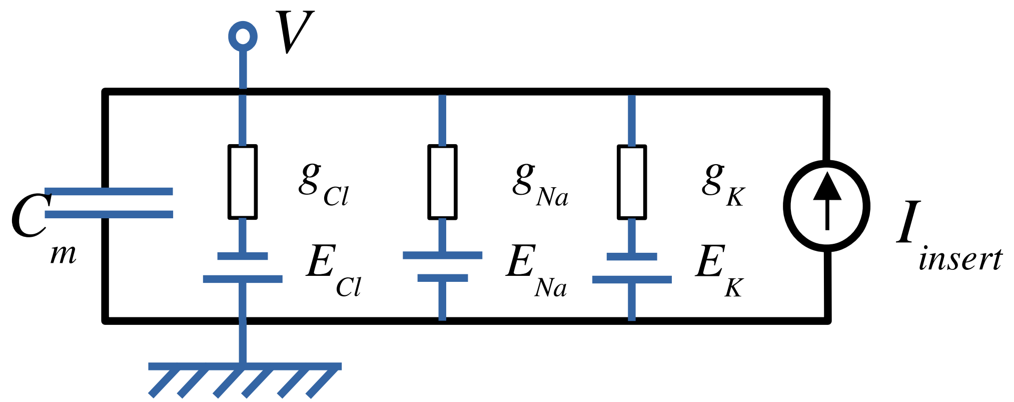
$$\underbrace{C_m \frac{dV(t)}{dt}}_{\text{capacitice current}} = \underbrace{-\frac{V(t)}{R_m}}_{} = \underbrace{-V(t)\, g_m}_{}$$

capacitice current

resistive or conductive current



Model with parallel conductances



Equation for current equlibrium:

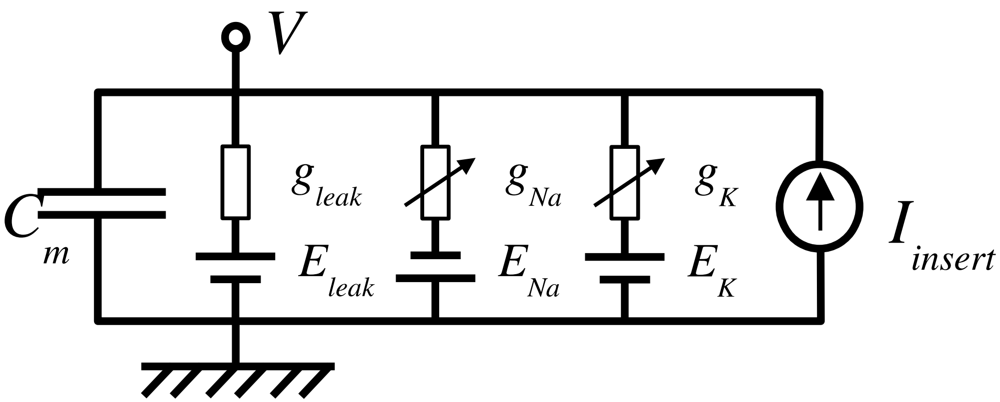
$$C_m \frac{dV(t)}{dt} = g_{Cl}\left(E_{Cl} - V(t)\right) + g_{Na}\left(E_{Na} - V(t)\right) + g_K\left(E_K - V(t)\right) + I_{insert}(t)$$

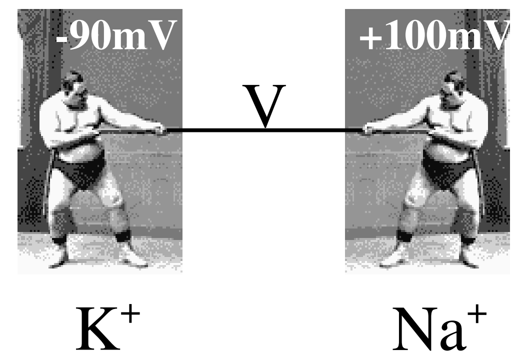
Nernst-potential

driving force

single ion current

The Hodgkin-Huxley model / 1





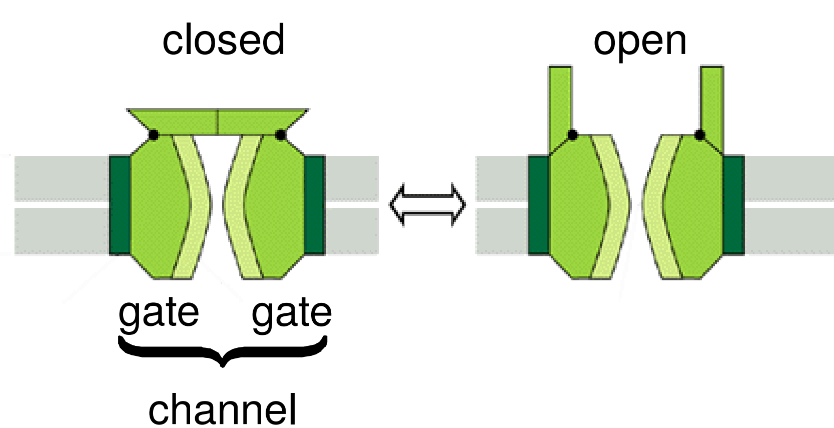
Equation for current equlibrium:

$$C_m \frac{dV(t)}{dt} = \underbrace{g_{leak}\left(E_{leak} - V(t)\right)}_{\text{Leak current (mainly } Cl^-\text{)}} + g_{Na}(t)\left(E_{Na} - V(t)\right) + g_K(t)\left(E_K - V(t)\right) + I_{insert}(t)$$

Equations for ionic currents:

$$g_{Na}(t) = \bar{g}_{Na} \cdot m^3(t) \cdot h(t)$$

$$g_K(t) = \bar{g}_K \cdot n^4(t)$$



The Hodgkin-Huxley model / 2

What is most important in the HH model: voltage dependent gating kinetics

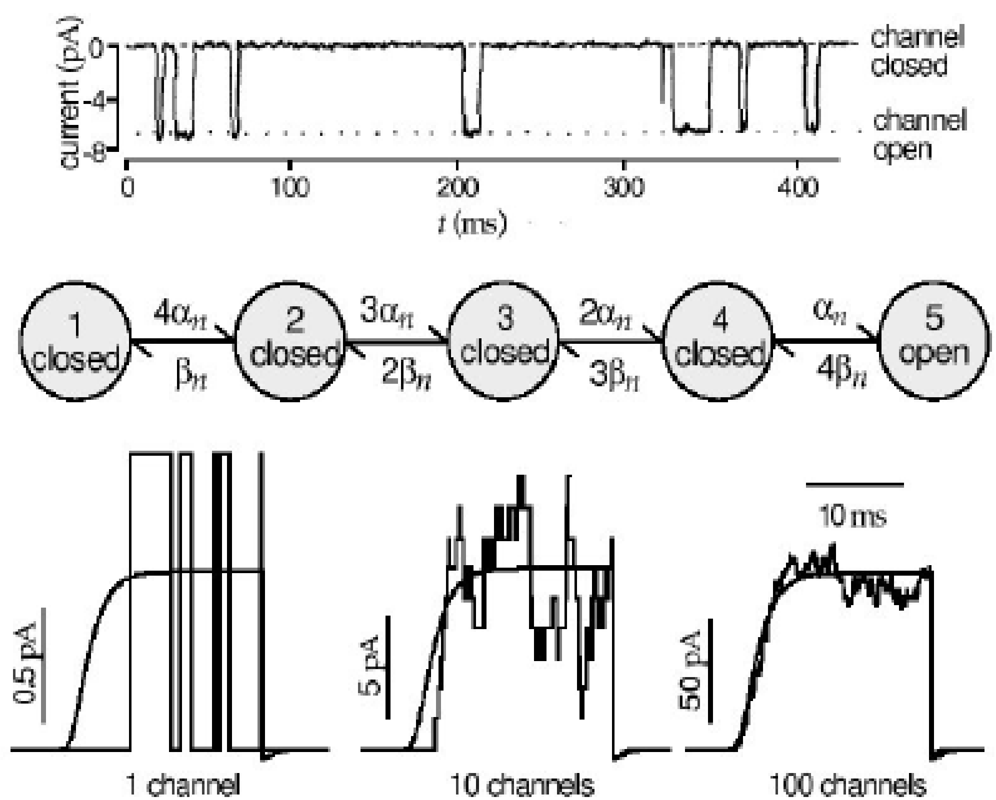
$$\text{closed} \underset{\beta_m}{\overset{\alpha_m}{\rightleftharpoons}} \text{open}$$

$$1\text{-}m \qquad\qquad m$$

$$\frac{dm(t)}{dt} = \alpha_m(V(t))(1-m(t)) - \beta_m(V(t))m(t) = \frac{m_\infty(V(t)) - m(t)}{\tau_m(V(t))}$$

$$m_\infty(V) = \frac{\alpha_m(V)}{\alpha_m(V) + \beta_m(V)}$$

$$\tau_m(V) = \frac{1}{\alpha_m(V) + \beta_m(V)}$$



P Dayan, LF Abbott: Theoretical Neuroscience, (MIT Press, Cambridge, 2001).

The Hodgkin-Huxley model / 3

What is most important in the HH model: voltage dependent gating kinetics

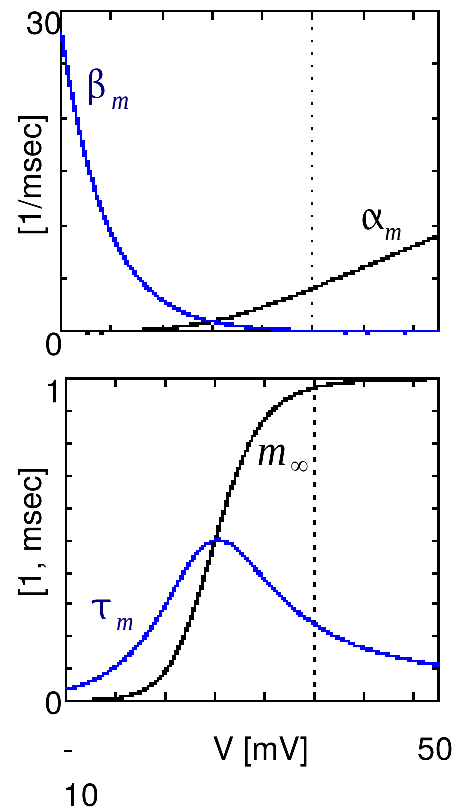
$$\text{closed} \underset{\beta_m}{\overset{\alpha_m}{\rightleftharpoons}} \text{open}$$

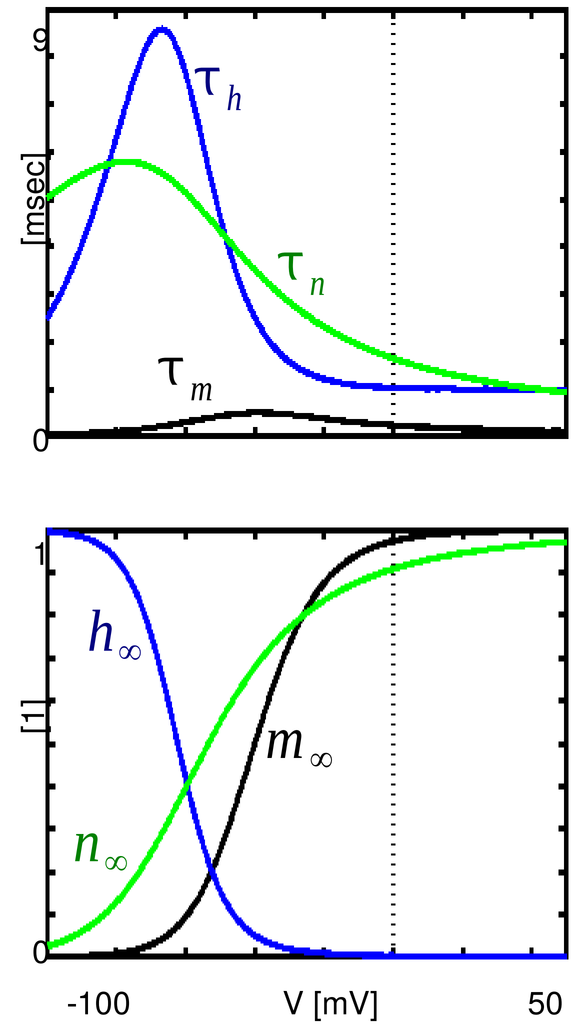
$$1\text{-}m \qquad\qquad m$$

$$\frac{dm(t)}{dt} = \alpha_m(V(t))(1-m(t)) - \beta_m(V(t))\,m(t) = \frac{m_\infty(V(t)) - m(t)}{\tau_m(V(t))}$$

$$m_\infty(V) = \frac{\alpha_m(V)}{\alpha_m(V)+\beta_m(V)}$$

$$\tau_m(V) = \frac{1}{\alpha_m(V)+\beta_m(V)}$$





The Hodgkin-Huxley model / 4

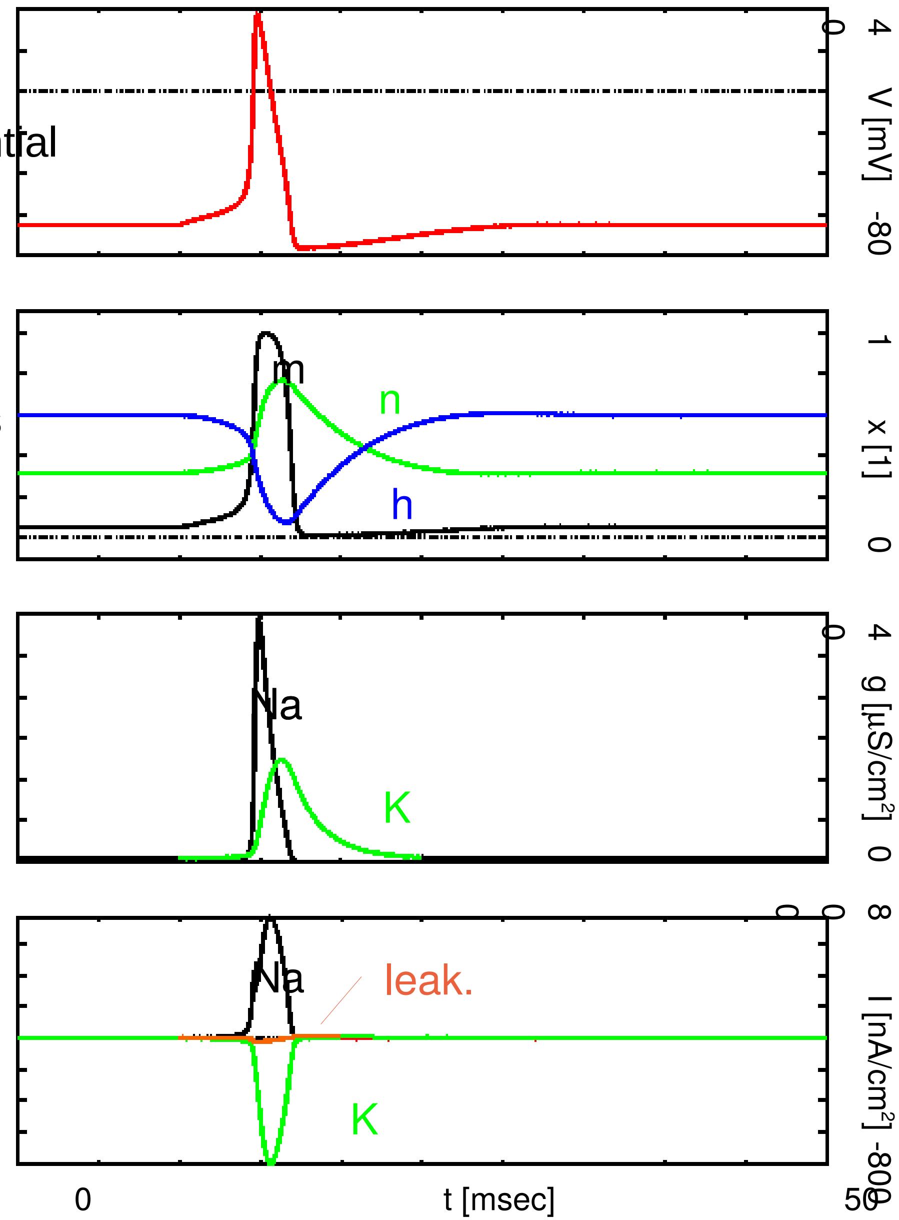
HH model in work:

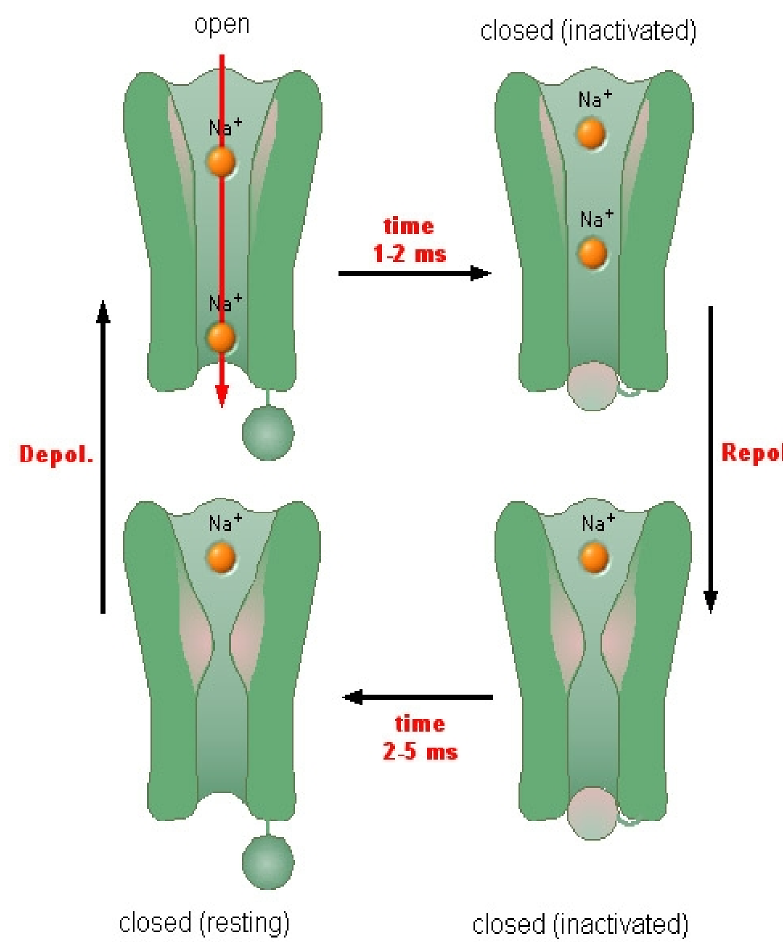
membranepotential

gating variables

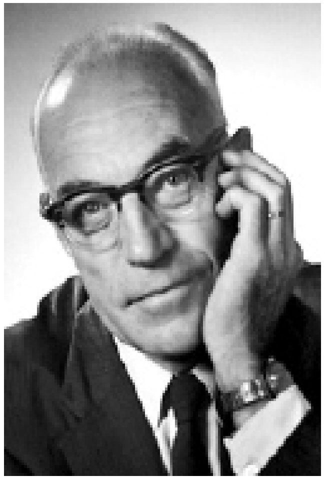
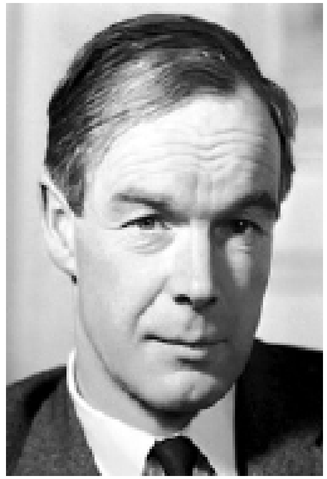
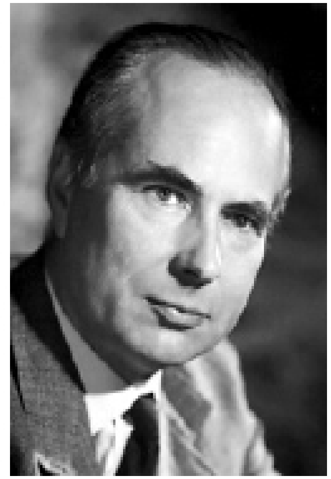
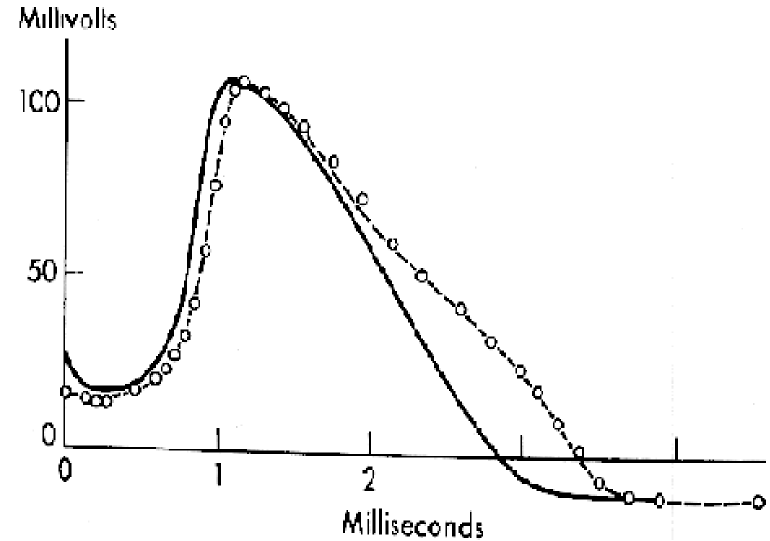
channel conductances

channel currents

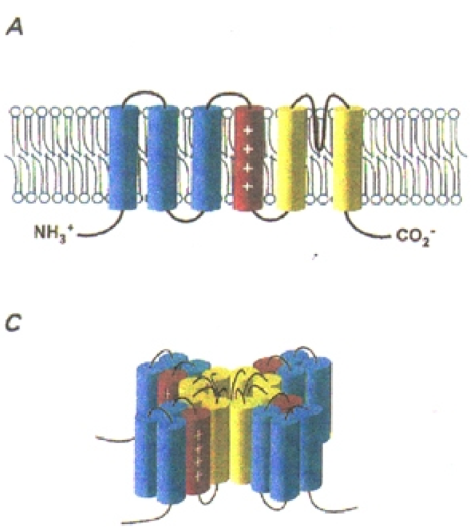


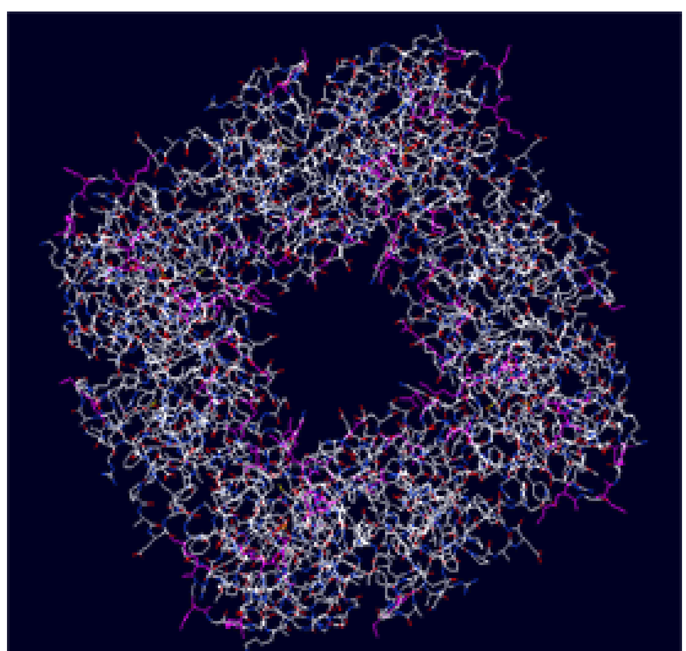
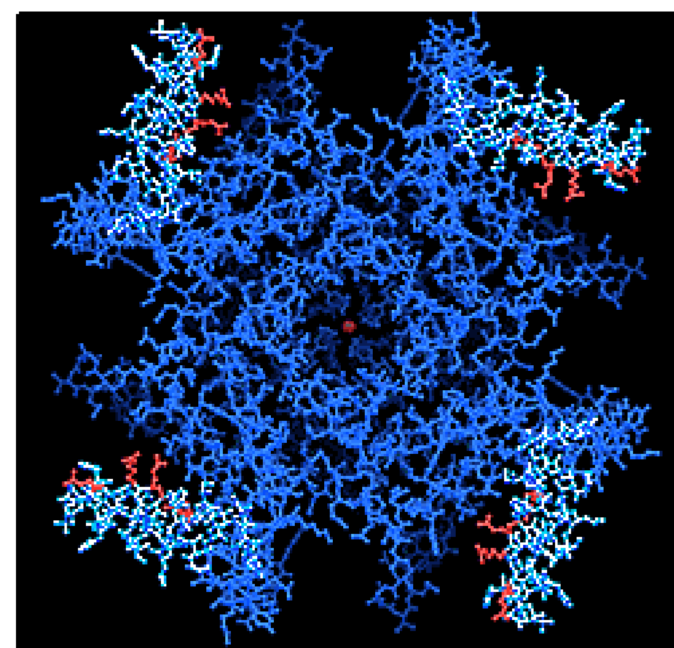


The Hodgkin-Huxley model / 5

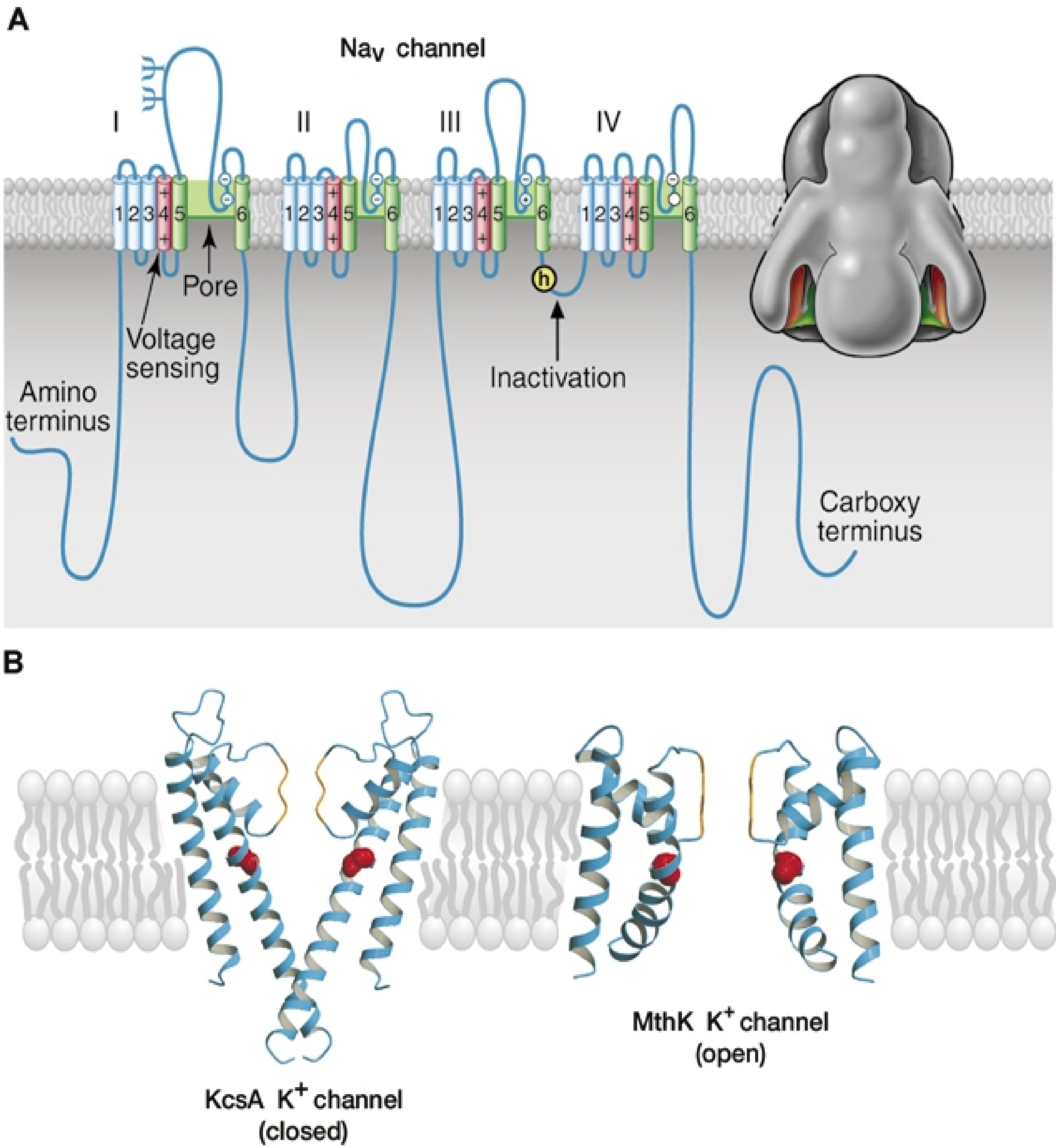





Sir John Carew Eccles, Alan Lloyd Hodgkin, Andrew Fielding Huxley: Awarded by Nobel-prize in medicine, 1963.



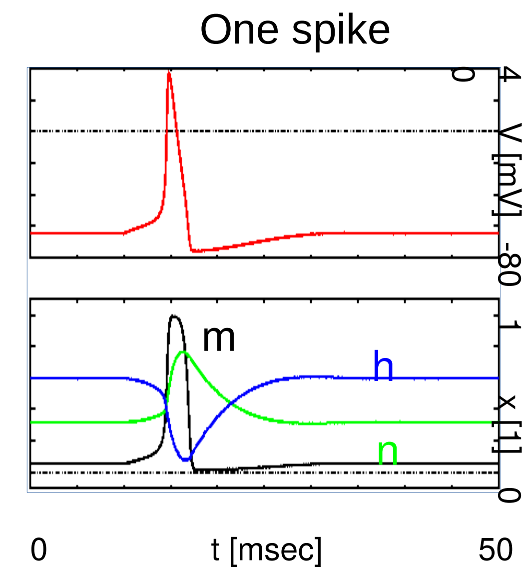
The Hodgkin-Huxley model / 6



The HH neuron model

$$C_m \frac{dV}{dt} = \bar{g}_{Na}\left(E_{Na} - V(t)\right) m^3(t) h(t) + \bar{g}_K\left(E_K - V(t)\right) n^4(t) +$$

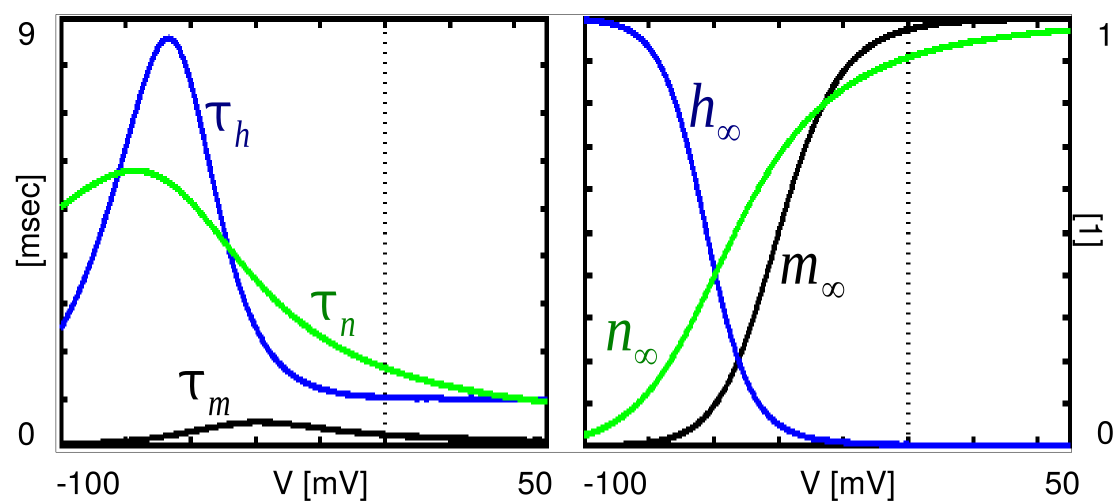
$$+ g_{leak}\left(E_{leak} - V(t)\right) + I_{external}(t)$$



$$\frac{dm}{dt} = \frac{m_\infty\left(V(t)\right) - m(t)}{\tau_m\left(V(t)\right)}$$

$$\frac{dh}{dt} = \frac{h_\infty\left(V(t)\right) - h(t)}{\tau_h\left(V(t)\right)}$$

$$\frac{dn}{dt} = \frac{n_\infty\left(V(t)\right) - n(t)}{\tau_n\left(V(t)\right)}$$



Over the HH-model

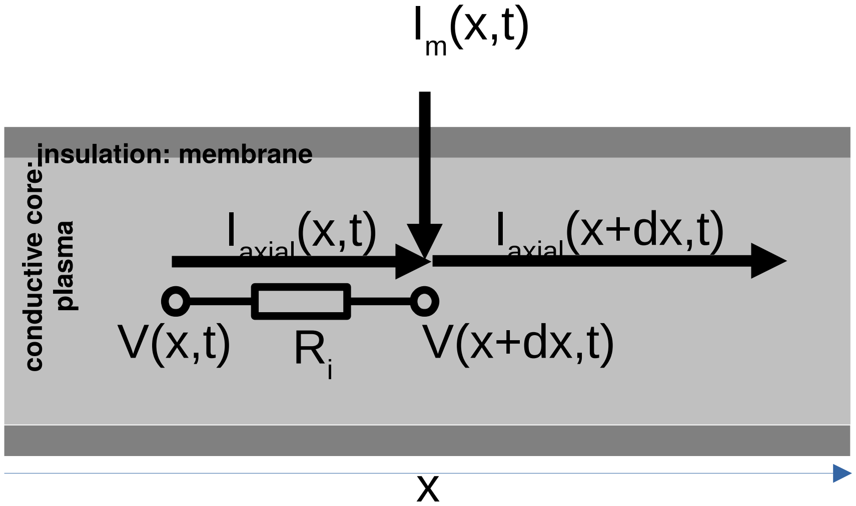
Different currents	**Function**
slow K^+	firing frequency adaptation
perzistent (non-inactivating) Na^+	burst
Ca^{2+}	burst
Ca^{2+}-(and V-) dependent K^+	burst, adaptation
H hyperpolarization activated	pacemaker

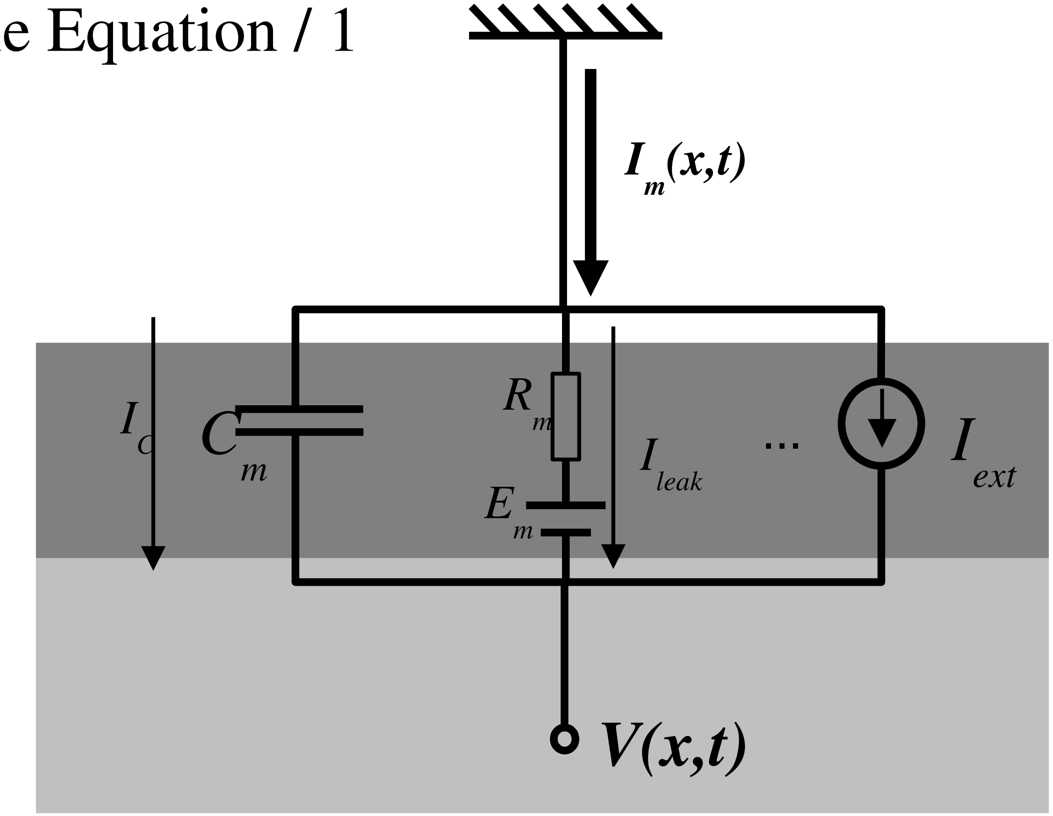
Voltage dependent currents $$I_X = g_X(t)(E_X - V(t)),\ \ g_X(t) = \bar{g}_X \prod_i p_X^{(i)}(t),\ \ \frac{dp_X^{(i)}}{dt} = \frac{p_{X\infty}^{(i)}(V(t)) - p(t)}{\tau_{p_X^{(i)}}(V(t))}$$

Ca^{2+} concentration $$\frac{d[Ca]_i}{dt} = \beta\ I_{Ca}(t) - \frac{[Ca]_i(t)}{\tau_{Ca}}$$

Ca^{2+}-dependent gate $$\frac{dp_X^{(i)}}{dt} = \frac{p_{X\infty}^{(i)}([Ca]_i(t)) - p(t)}{\tau_{p_X^{(i)}}([Ca]_i(t))}$$

The Cable Equation / 1





$$I_{axial}(x,t) = -\frac{1}{R_i}\frac{\partial V}{\partial x}$$

$$\frac{\partial I_{axial}}{\partial x} = I_m(x,t)$$

$$I_m(x,t) = I_C(x,t) + I_{leak}(x,t) + \ldots = -C_m\frac{\partial V}{\partial t} - \frac{V(x,t)}{R_m}$$

simplification: no voltage-dependent currents!

$$\frac{1}{R_i}\frac{\partial^2 V}{\partial x^2} - C_m\frac{\partial V}{\partial t} - \frac{V(x,t)}{R_m} = 0$$

$$\lambda^2\frac{\partial^2 V}{\partial x^2} - \tau\frac{\partial V}{\partial t} - V(x,t) = 0$$

x [cm], t [msec]

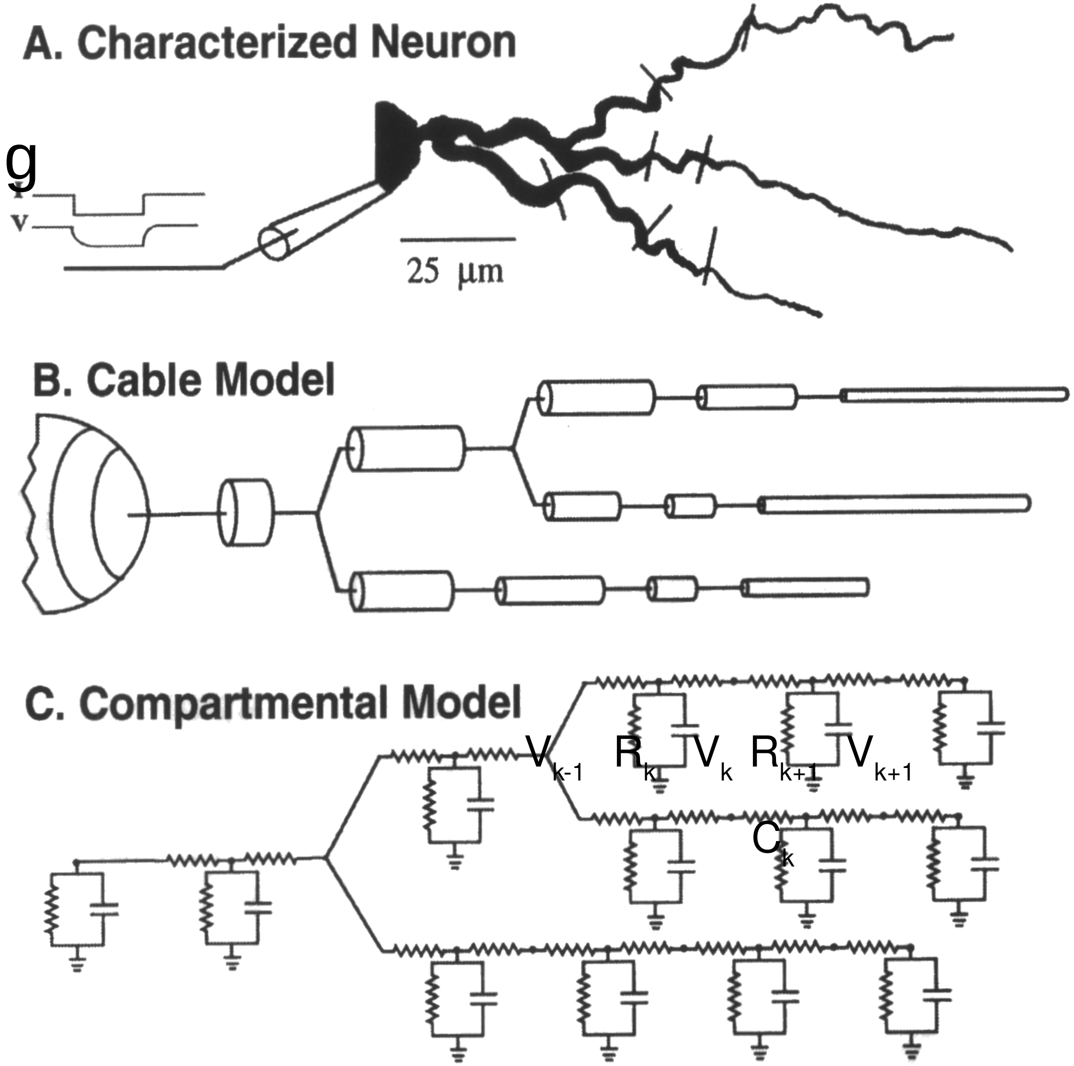
V [mV], I_{axial} [μA], I_m [μA/cm]

R_i [kΩ/cm], R_m [kΩcm], C_m [μF/cm]

$\lambda = \sqrt{R_m / R_i}\ [cm]$

$\tau = R_m C_m\ [msec]$

Multicompartmental modeling

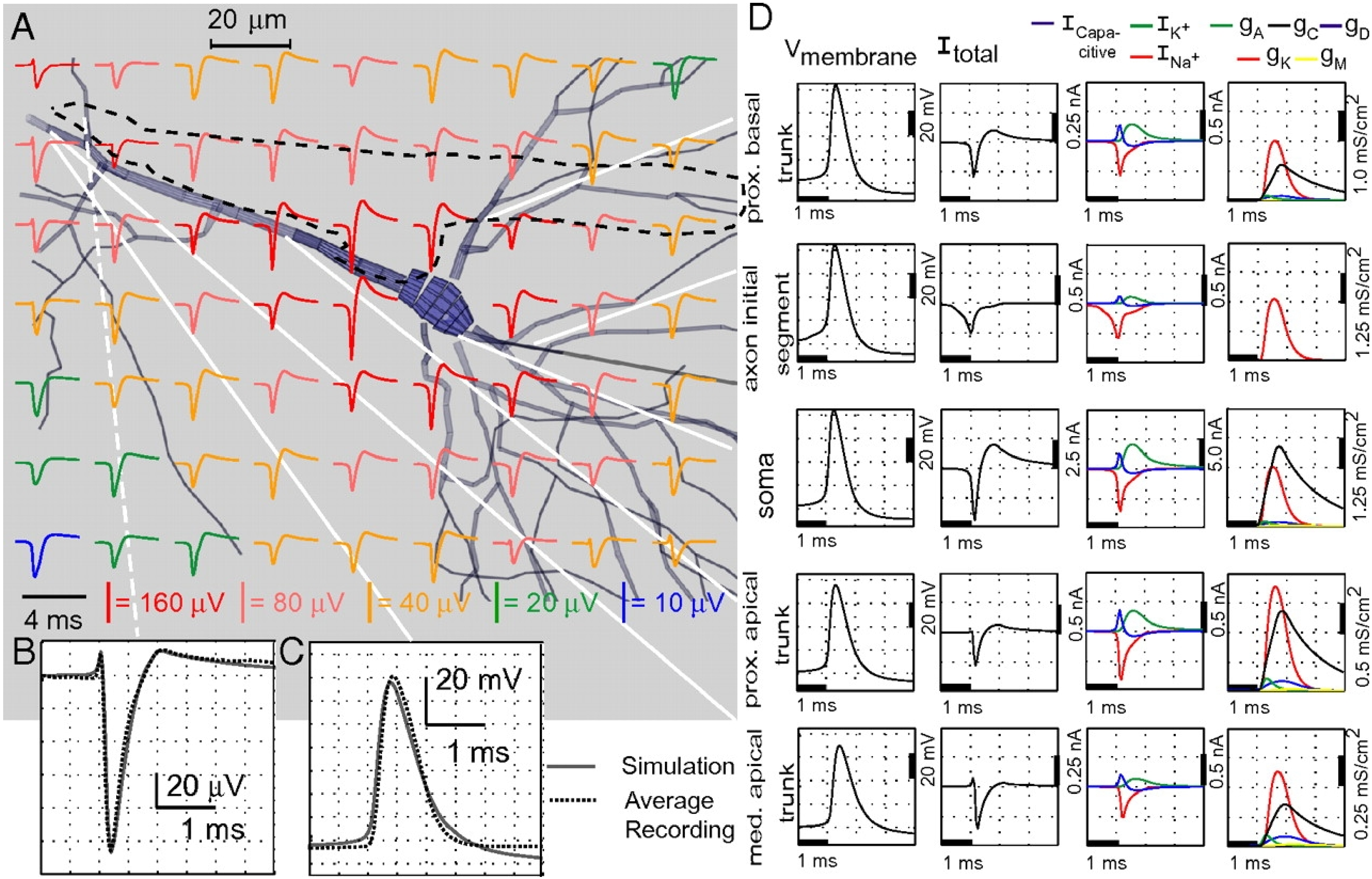


$$\frac{1}{R_i}\frac{\partial^2 V}{\partial x^2}-C_m\frac{\partial V}{\partial t}-\frac{V(x,t)}{R_m}=0$$

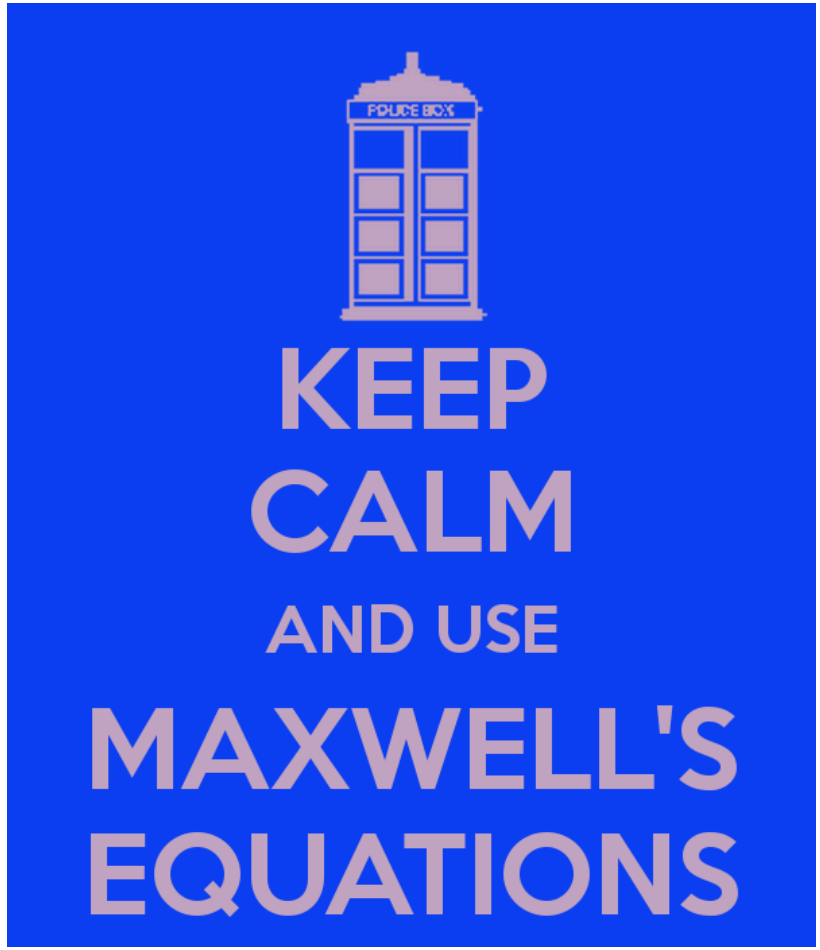
$$C_k\frac{dV_k}{dt}=\underbrace{I_k(t)}+\frac{V_{k-1}(t)-V_k(t)}{R_k}+\frac{V_{k+1}(t)-V_k(t)}{R_{k+1}}$$

all sorts of ionic currents (HH, etc)

Extracellular signature of the action potential



But how the extracellular potential of the neurons is generated?


POLICE BOX
KEEP
CALM
AND USE
MAXWELL'S
EQUATIONS

Oh, those popular Maxwell-equations… Exist in many forms!

Low frequencies: Only electrostatics will be applied

Name	Differential Form	Integral Form	
Gauss' Law	$\nabla \cdot \mathbf{E} = \frac{\rho}{\epsilon_0}$	$\int_S \mathbf{E} \cdot \hat{\mathbf{n}}\, dA = \frac{Q_{\text{enc}}}{\epsilon_0}$	(6.2)
Gauss' Law for Magnetism	$\nabla \cdot \mathbf{B} = 0$	$\int_S \mathbf{B} \cdot \hat{\mathbf{n}}\, dA = 0$	(6.3)
Faraday' Law	$\nabla \times \mathbf{E} = -\frac{\partial \mathbf{B}}{\partial t}$	$\oint_C \mathbf{E} \cdot d\mathbf{l} = -\frac{d}{dt} \int \mathbf{B} \cdot \hat{\mathbf{n}}\, dA$	(6.4)
Ampere-Maxwell Law	$\nabla \times \mathbf{B} = \mu_0 \mathbf{J} + \mu_0 \epsilon_0 \frac{\partial \mathbf{E}}{\partial t}$	$\oint_C \mathbf{B} \cdot d\mathbf{l} = \mu_0 (I + I_D)$	(6.5)

$$\nabla^2 V(r) = \frac{\partial^2 V(r)}{\partial x^2} + \frac{\partial^2 V(r)}{\partial y^2} + \frac{\partial^2 V(r)}{\partial z^2} = \frac{\rho(r)}{\epsilon_0}$$

The solution can be found by the linear sum of the fields of the point charges:

$$V_i = \frac{1}{4\pi\epsilon_0} \sum_{j=1}^{N} \frac{q_j}{|\boldsymbol{r}_i - \boldsymbol{r}_j|}$$

The Current Source Density (CSD)

$$\nabla^2 \Phi(r) = \frac{-I(r)}{\sigma}$$

In light electrolytic solution, the generation of the potential can be described by Poisson-equation

Continuity equation (charge conservation)

$$I(r) = -\nabla J(r)$$

Current Source Density

Low frequency approximation

$$E(r) = \nabla \Phi(r)$$

Ohm's law

$$J(r) = \sigma E(r)$$

Current density

Conductivity

The dipole approximation

$$V = kq\left[\frac{1}{r_+} - \frac{1}{r_-}\right] = kq\left[\frac{r_- - r_+}{r_+ r_-}\right]$$

For cases where r>>d, this can be approximated by

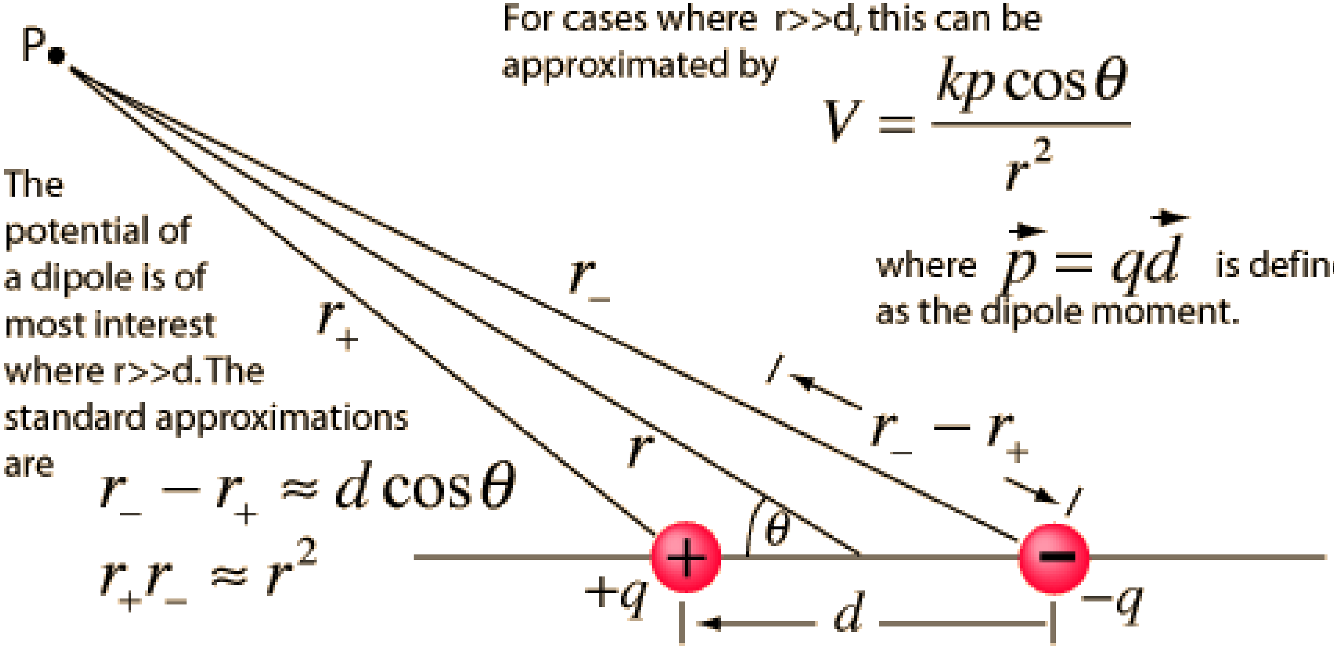
$$V = \frac{kp\cos\theta}{r^2}$$

where $\vec{p} = q\vec{d}$ is defined as the dipole moment.

The potential of a dipole is of most interest where r>>d. The standard approximations are

$$r_- - r_+ \approx d\cos\theta$$

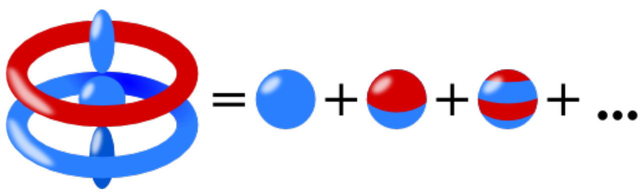
$$r_+ r_- \approx r^2$$

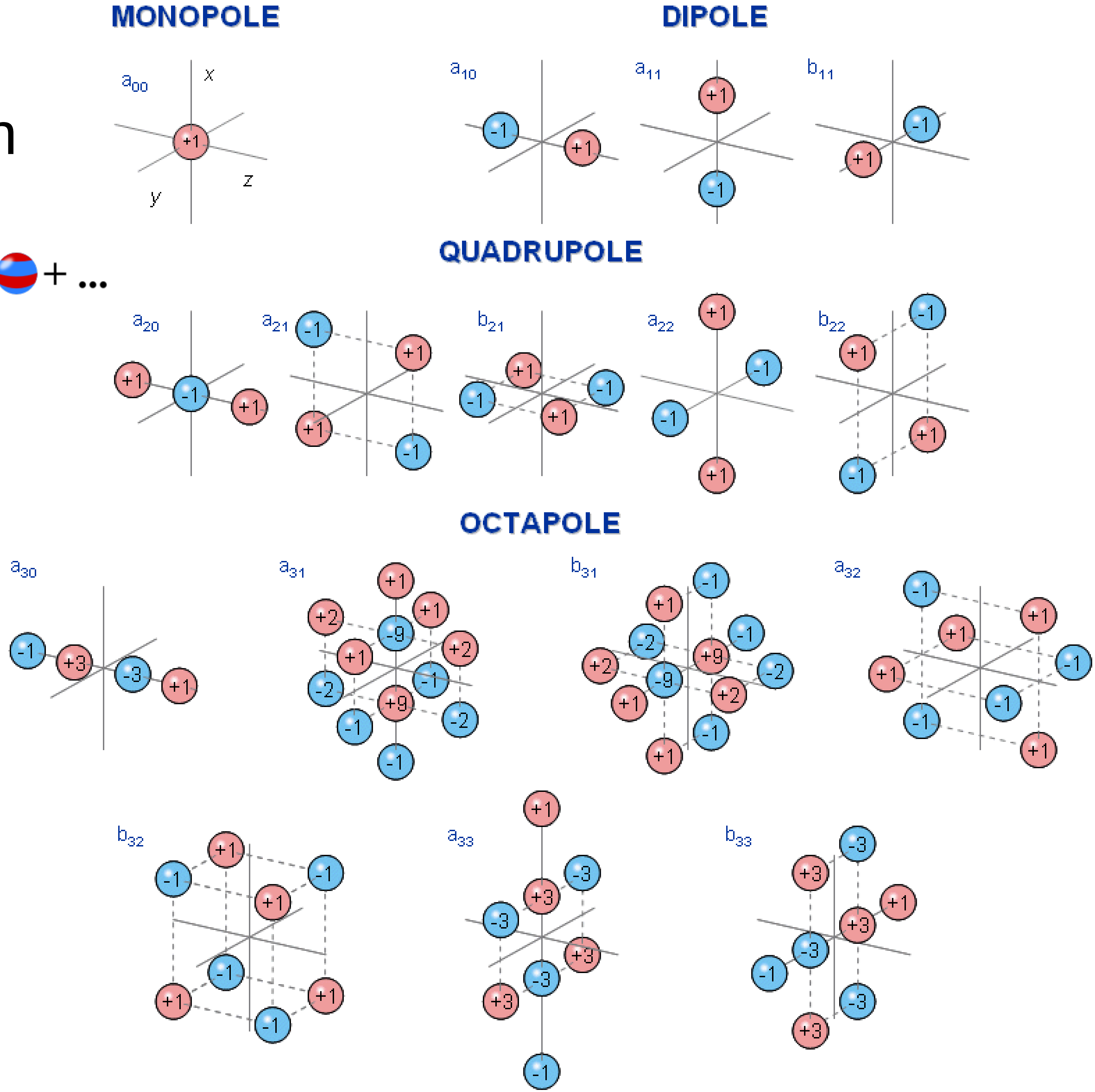


$$|\mathbf{r} - \mathbf{r}'| = |r^2 - 2\mathbf{r}\cdot\mathbf{r}' + r'^2|^{\frac{1}{2}} = r\left|1 - 2\frac{\hat{\mathbf{r}}\cdot\mathbf{r}'}{r} + \left(\frac{r'}{r}\right)^2\right|^{\frac{1}{2}}$$

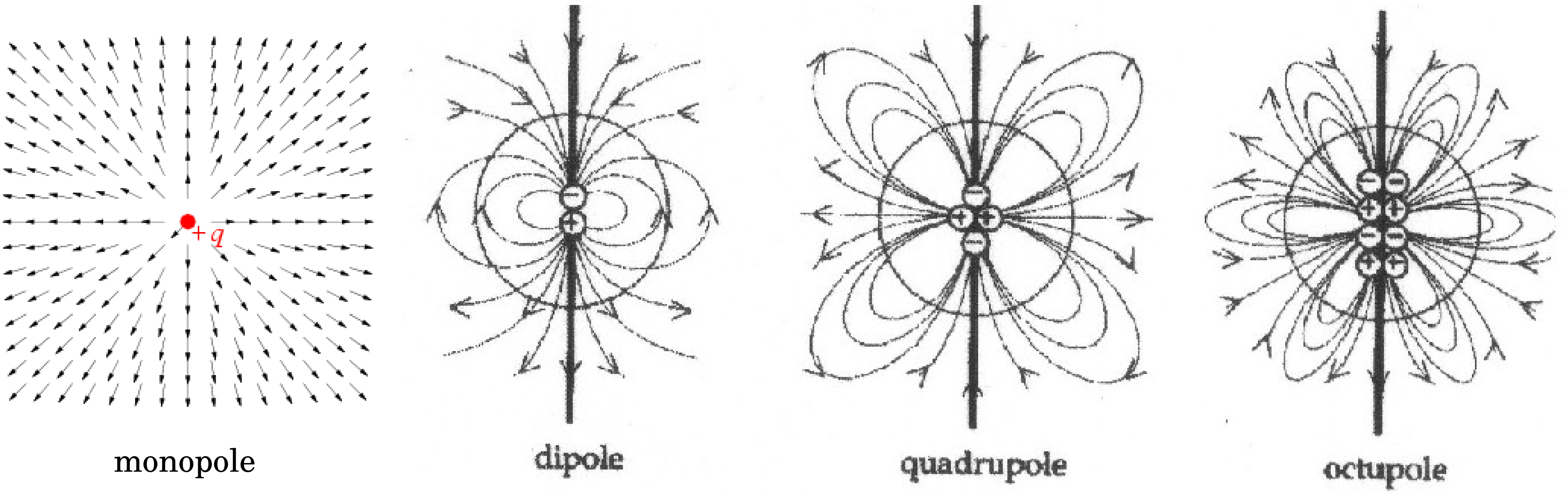
$$\frac{1}{|\mathbf{r} - \mathbf{r}'|} = \frac{1}{r}\frac{1}{\left|1 - 2\frac{\hat{\mathbf{r}}\cdot\mathbf{r}'}{r} + \left(\frac{r'}{r}\right)^2\right|^{\frac{1}{2}}}$$

Multipole expansion





The multipole expansion



$$V(R) = \frac{q_{\text{tot}}}{R} + \frac{1}{R^3} \sum_{\alpha=x,y,z} P_\alpha R_\alpha + \frac{1}{6R^5} \sum_{\alpha,\beta=x,y,z} Q_{\alpha\beta}(3R_\alpha R_\beta - \delta_{\alpha\beta} R^2) + \cdots$$

Higher exponent means faster spatial decay,
so on macroscopic scales the first non-vanishing term dominates!