Electrochemical Gradients

Ion Gradients

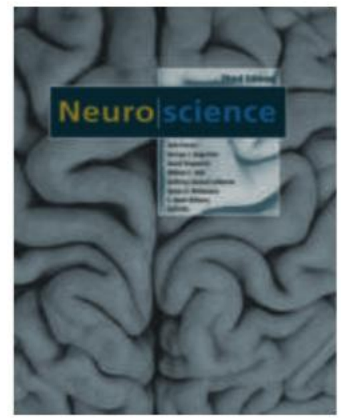
Cell Membranes

Ion Channels

Topics I	Topics II
Introduction	Synaptic Transmission
Electrochemical Gradients	Electrophysiology Techniques
Passive Membrane Properties	Basic Circuits (Spinal Cord)
Action Potential I	Sensory Systems Overview
Voltage-Gated Ion Channels	Synaptic Plasticity
Ligand-Gated Ion Channels	Recapitulation

Study Material

- NEUROSCIENCE Third Edition
  - – Dale Purves
- Chapter 2 pages 34-43



THE COVER
Dorsal view of the human brain.
(Courtesy of S. Mark Williams.)

NEUROSCIENCE: Third Edition

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Aims for this Lecture

- Know the values of the main ion concentration gradients.
- Understand the interaction between diffusion gradients and electrical fields.
- Know and understand the Nernst equation.
- Understand the effect of multiple permeabilities (Goldman equation).
- Know the typical resting membrane potential.

Recapitulation L1

- Diffusion is fast over short distances (organelles to small cells), but very slow over long distances (many cells to organs).
- Multicellular organisms need to communicate and need to do so quickly and efficiently.
- Electrical signals across cell membranes are the main signals in nervous systems.

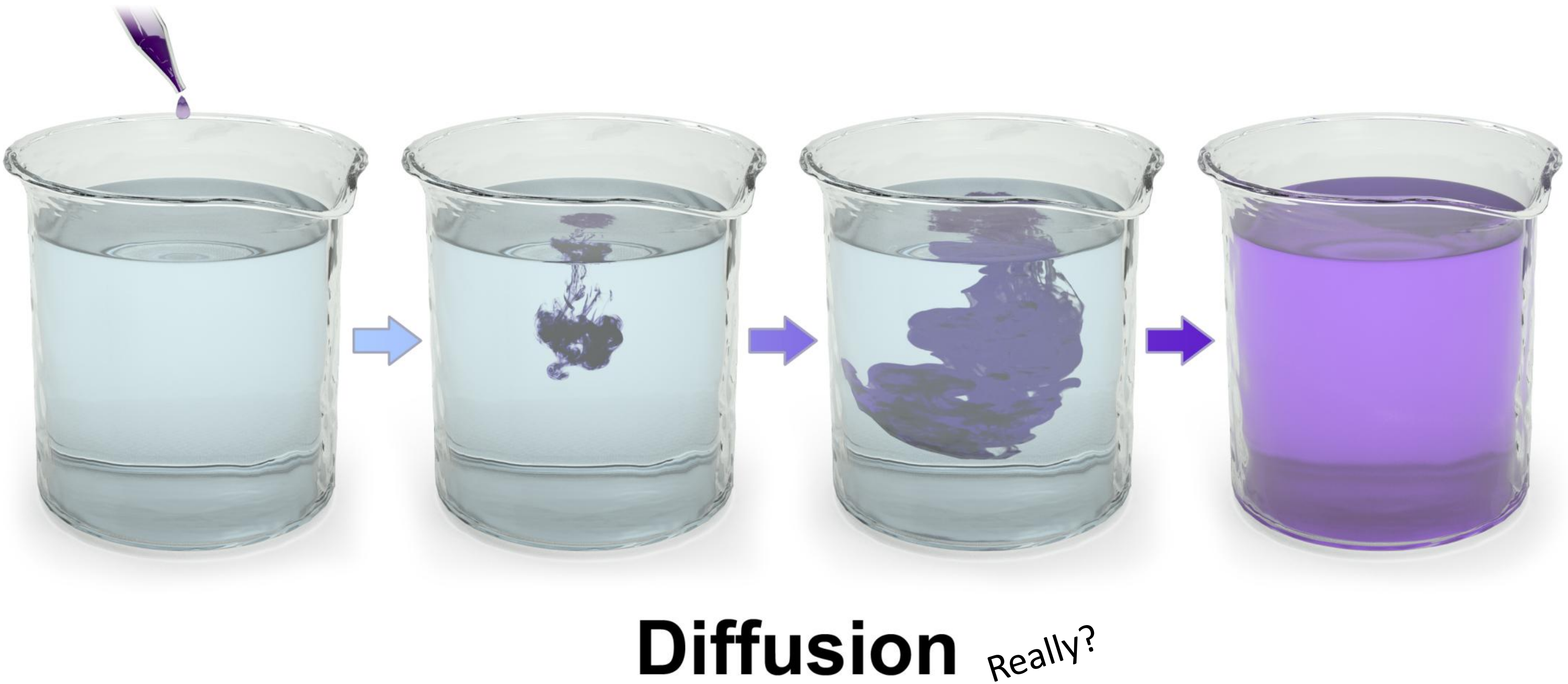
Biophysical Basis

All the phenomena that we will be talking about in the next two hours are manifestations of ion flux across membranes.

Which brings us to the central question…

… why did the ion cross the membrane?

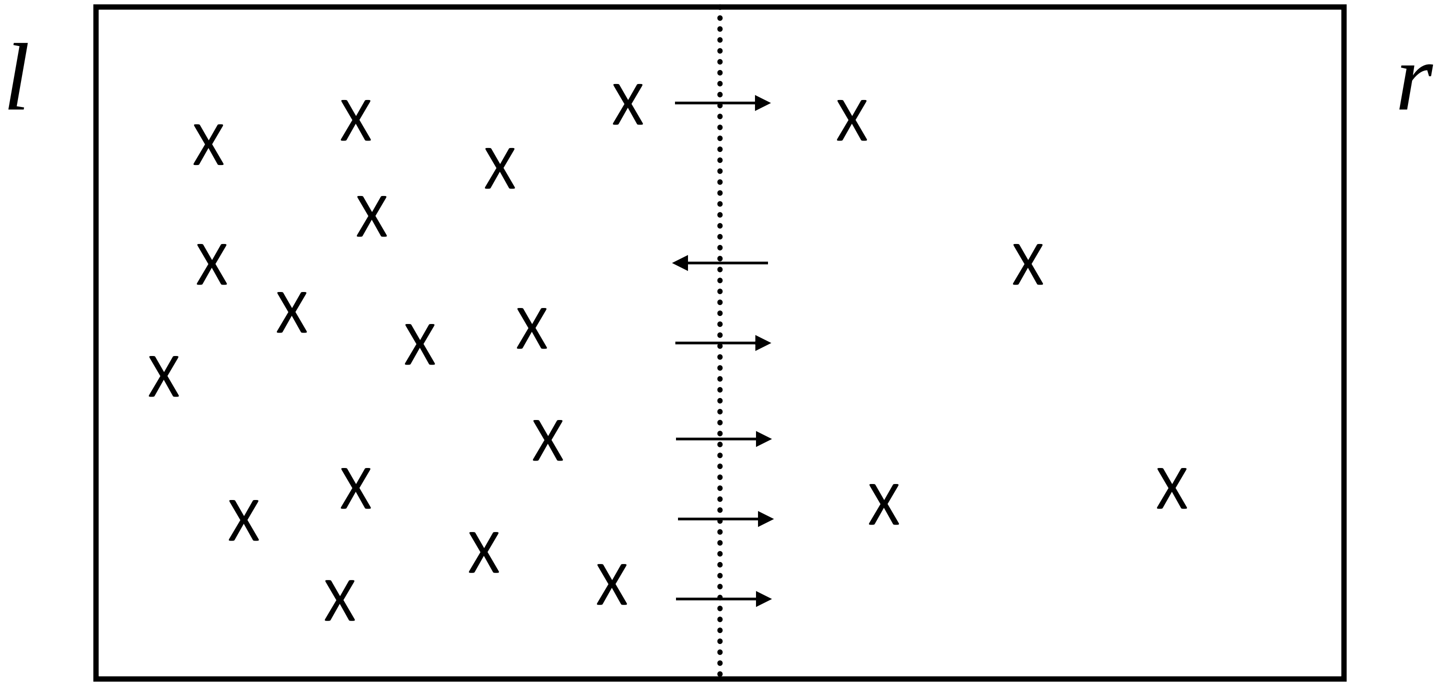
Diffusion and Movement



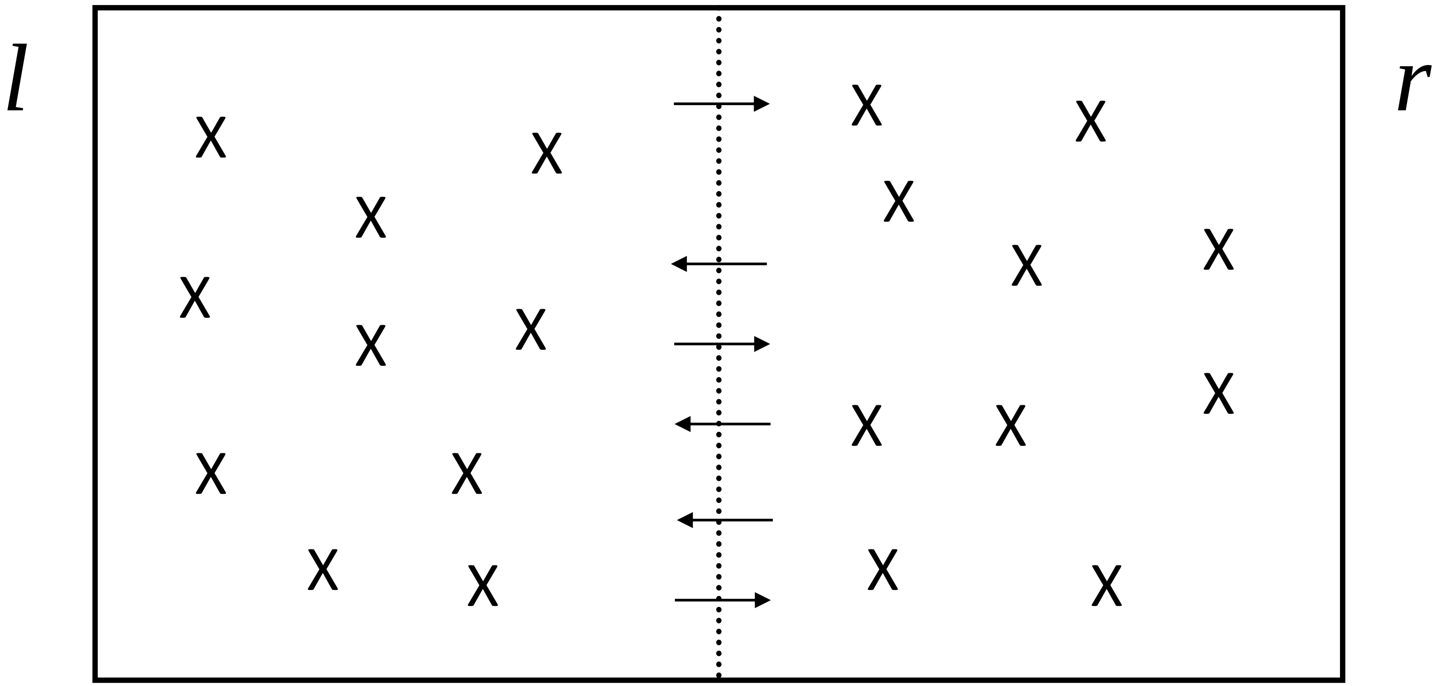
Really?

Wikimedia: Diffusion

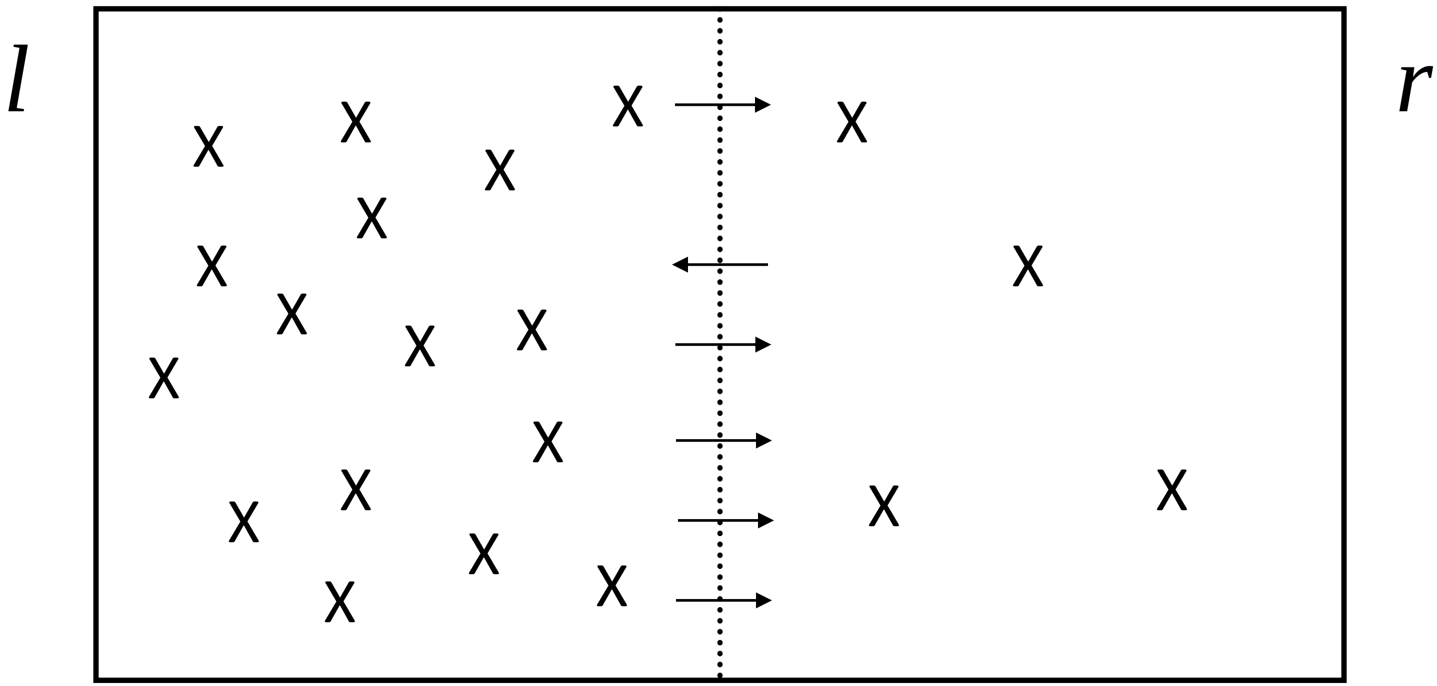
Diffusion



Diffusion



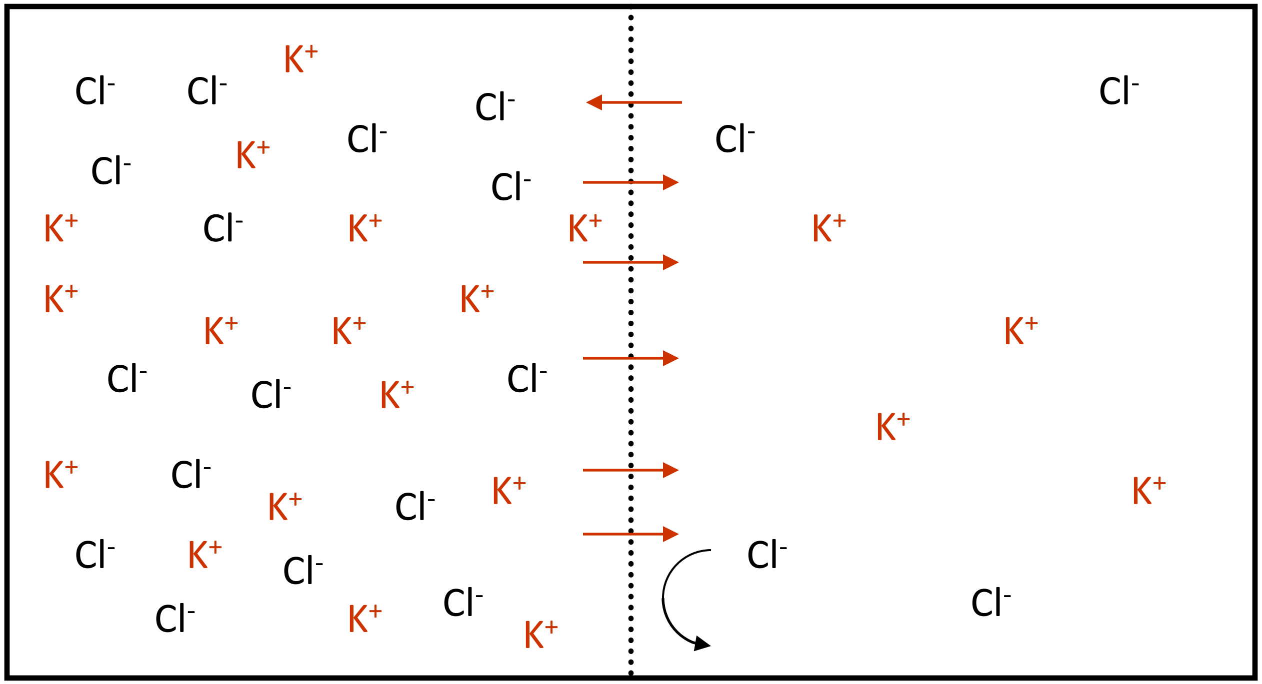
Chemical Potential



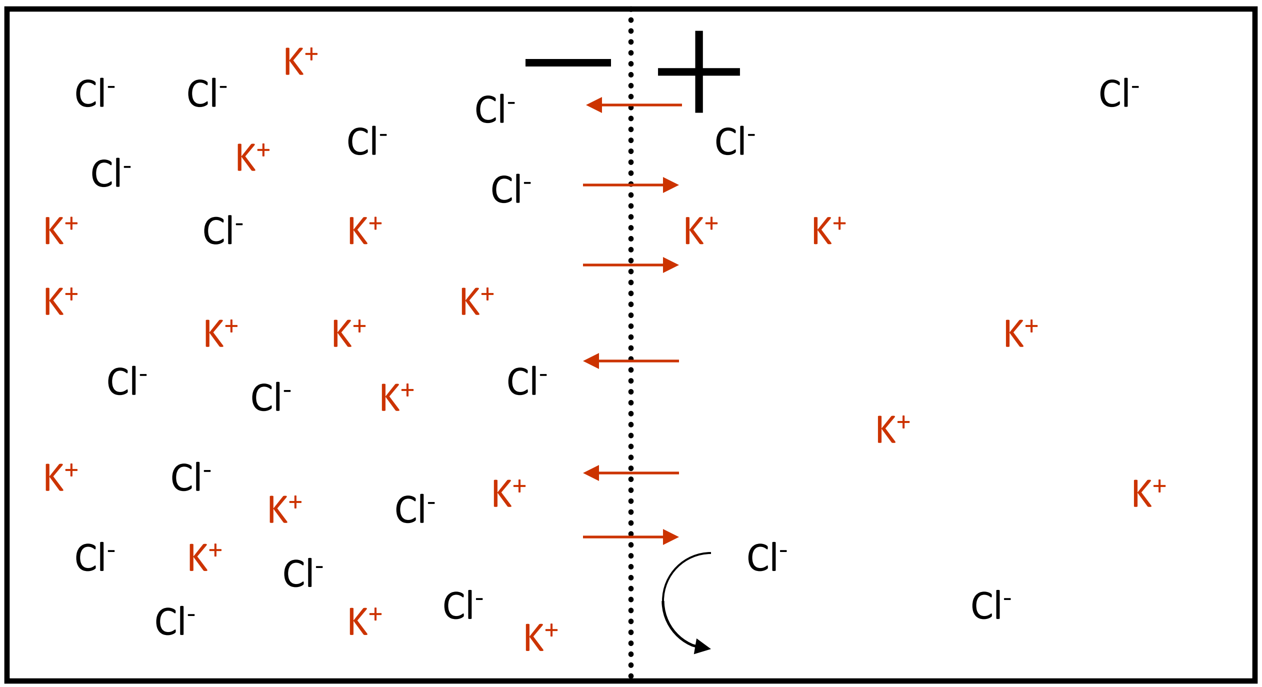
$$\Delta\mu = RT \ln \frac{[X]_r}{[X]_l}$$

Constant pressure and temperature

Electrical Potential



Electrical Potential



Equilibrium

Electrical Field

$$nzF(E_i - E_o)$$

Chemical Energy

$$nRT \ln \frac{[K^+]_o}{[K^+]_i}$$

n	Amount (Mol)
z	Valence (+1 for K)
F	Faraday‘s constant (charge of one Mole of Ions)
E	Potential
R	Gas constant
T	Temperature (absolute K)
[ ]	Concentration in the respective compartment

Nernst Equation

$$zF(E_i - E_o) = RT \ln \frac{[K^+]_o}{[K^+]_i}$$

$$E_i = \frac{RT}{zF} \ln \frac{[K^+]_o}{[K^+]_i}$$

Nernst Equation
Describes equilibrium
No **net** flux

Specific Equilibrium Potentials

$$E_i = \frac{RT}{zF} \ln \frac{[K^+]_o}{[K^+]_i}$$

$$E_i = 61(mV) \log \frac{[K^+]_o}{[K^+]_i}$$

	Intracellular	Extracellular	E
Potassium Ions	155 mM	4 mM	-98 mV
Sodium Ions	12 mM	145 mM	+67mV

Mixed Potentials

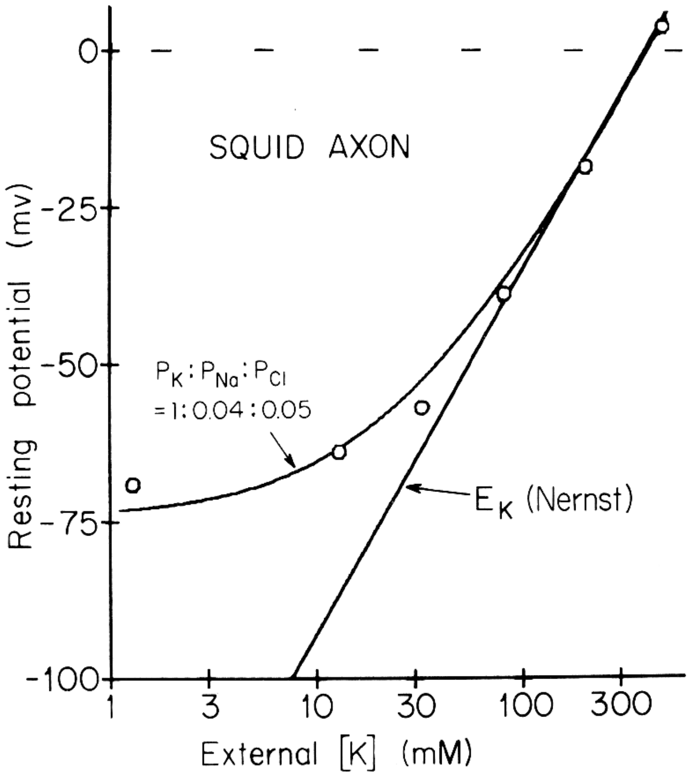


Figure 1–8 Dependence of resting membrane potential on the external K^+ ion concentration in a squid giant axon. The sum of $[Na^+]_o$ and $[K^+]_o$ were kept constant as $[K^+]_o$ was varied. The line labeled E_K shows the expected Nernst potential for K^+ ions, and the curved line is a solution of the Goldman-Hodgkin-Katz voltage equation (Equation 10), assuming that P_K:P_{Na}:P_{Cl} of the axon membrane is 1.0:0.04:0.05. (Data after Curtis and Cole. *J. Cell Comp. Physiol.* 19:135–144, 1942.)

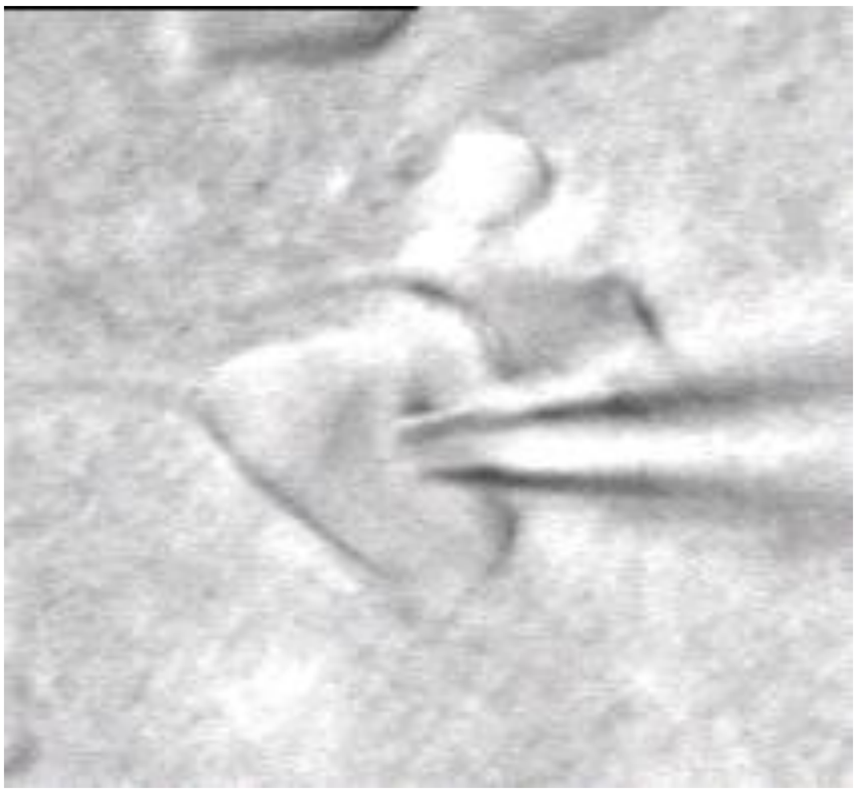
Goldmann, Hodkin, Katz

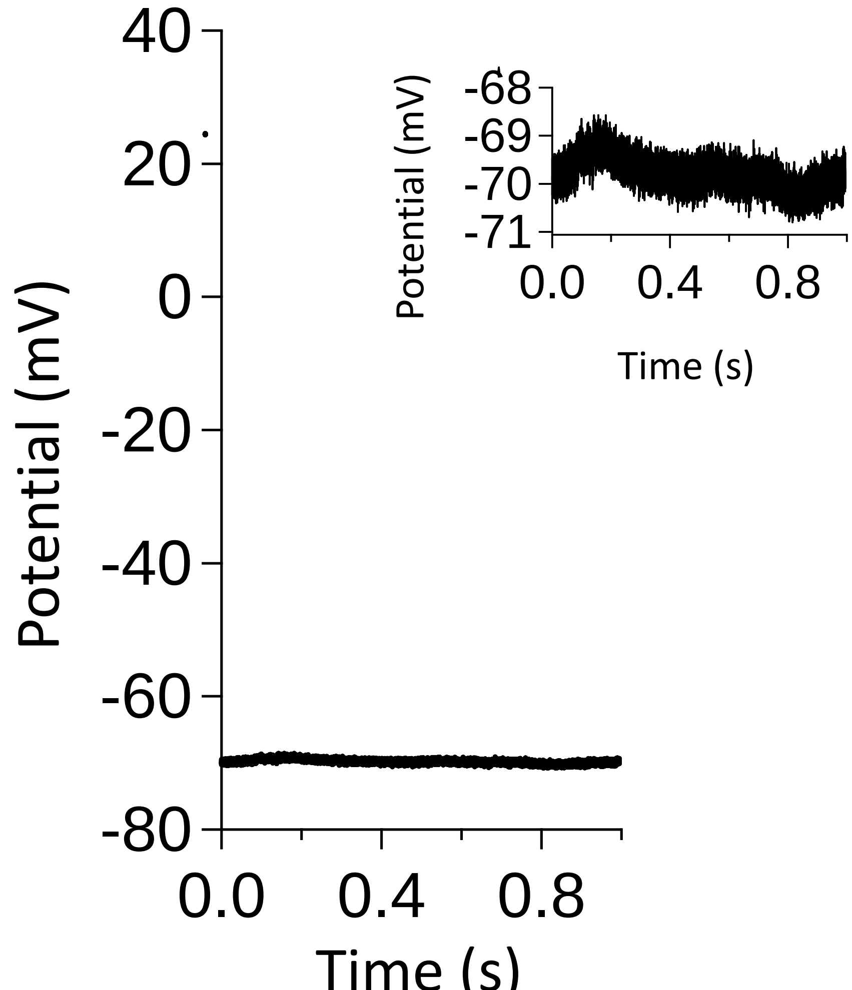
$$E_i = \frac{RT}{F}\ln\left(\frac{P_K[K^+]_o + P_{Na}[Na^+]_o}{P_K[K^+]_i + P_{Na}[Na^+]_i}\right)$$

Table 1–4 Free Ionic Concentrations and Equilibrium Potentials for Mammalian Skeletal Muscle

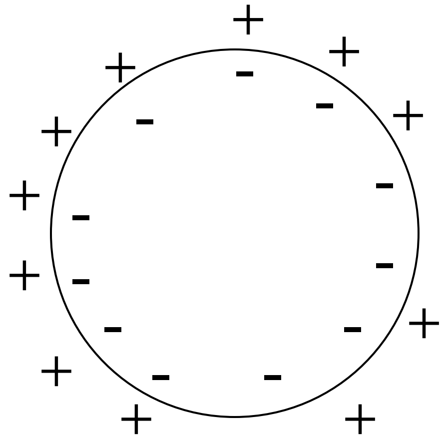
Ion	Extracellular Concentration (mM)	Intracellular Concentration (mM)	$\frac{[\text{Ion}]_o}{[\text{Ion}]_i}$	Equilibrium Potential[a] (mV)
Na^+	145	12	12	+67
K^+	4	155	0.026	−98
Ca^{2+}	1.5	$<10^{-7}$ M	>15,000	>+128
Cl^-	123	4.2[b]	30[b]	−90[b]

Resting Membrane Potential





A simple calculation..



Spherical cell 25 µm radius

$$A = 4\pi r^2 = 7.85\times10^{-5}cm^2$$
$$V = \frac{4}{3}\pi r^3 = 6.5\times10^{-8}cm^3$$

Avogadro‘s number 6.0221 10^23
Elementary charge 1.6022 10^-19 C

Specific capacitance **1 µF/cm²**

Number of ions, needed to charge this capacitor to 100 mV

$$= 4.9\times10^{7}$$

Total number of ions in a saline solution of 300 mM

$$= 1.2\times10^{13}$$

Fraction of ions needing to cross the membrane

$$\frac{4.9\times10^{7}}{1.2\times10^{13}} = 3.9\times10^{-6} = 0.00039\%$$

Electrostatic Force

- 2 individuals (weighing 72 kg – made up of water for simplicity's sake).
- At a distance of 10 m from each other
- Of all their charged particles (protons electrons..) they decide to exchange 0.5% such that person 1 is positively and person 2 negatively charged.
- What force do these two persons exert on each other.

Result

Coulomb’s law

$$F = \frac{1}{4\pi\varepsilon_0}\frac{Q_1 Q_2}{r^2}$$

$$\varepsilon_0 = 8.85 \cdot 10^{-11} \frac{A^2 s^2}{Nm^2}$$

$$r = 10m$$

$$Q_1 = Q_2 = 7.7 \cdot 10^8 C$$

Force = 5.35*10^{25} N

As a comparison:
The gravitational attraction between moon and earth is around 1.98*10^{20} N

If the two individuals were as far apart from each other as earth and moon, the force would amount to about 3.6*10^{10} N

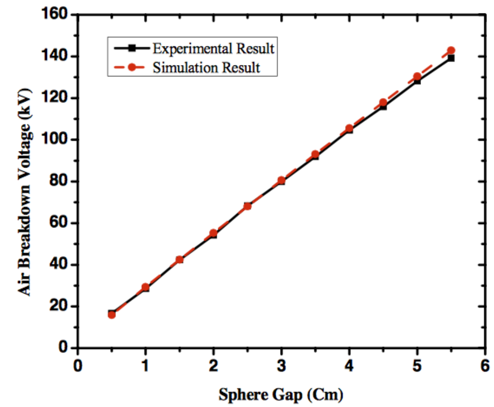
Voltage?

Subrata Karmakar | J. Electrical Systems 8-2 (2012): 209-217

Regular paper

An Experimental Study of Air Breakdown Voltage and its Effects on Solid Insulation

Journal of Electrical Systems



How does 70 mV over 8 nm compare to the breakdown voltage in air?

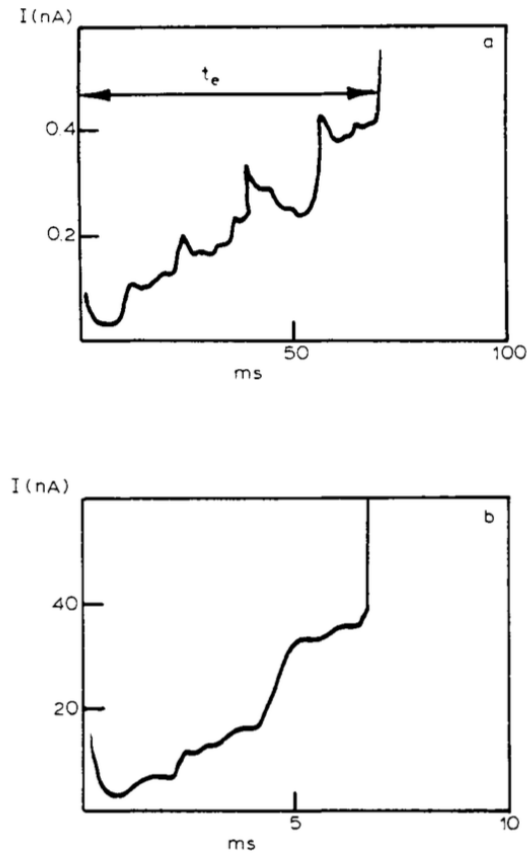


Fig. 1. The breakdown current at the stepwise voltage application. (a) The erythrocyte membrane, $\boldsymbol{U} = 300$ mV. (b) The planar bilayer of the oxidized cholesterol membrane, $\boldsymbol{U} = 200$ mV. The drastic current jump in both the cases corresponds to the irreversible membrane rupture. t_1 is the membrane lifetime.

Equivalent to 87.5 kV per cm!

360 *Biochimica et Biophysica Acta* 902 (1987) 360–373 Elsevier

BBA 73656

The electrical breakdown of cell and lipid membranes: the similarity of phenomenologies

L.V. Chernomordik, S.I. Sukharev, S.V. Popov, V.F. Pastushenko, A.V. Sokirko, I.G. Abidor and Y.A. Chizmadzhev

Institute of Electrochemistry, USSR Academy of Sciences, Leninsky prospect 31, 117071 Moscow (U.S.S.R.)

Breakdown Voltages

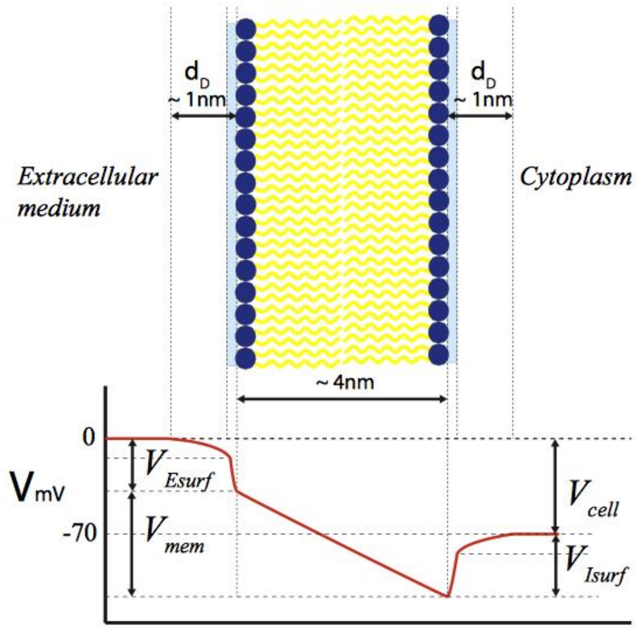
Substance	Dielectric Strength (MV/m)
Helium (relative to nitrogen)[3]	0.15
Air [4]	3.0
Alumina[3]	13.4
Window glass[3]	9.8 - 13.8
Silicone oil, mineral oil[3][5]	10 - 15
Benzene[3]	163
Polystyrene[3]	19.7
Polyethylene[6]	19 - 160
Neoprene rubber[3]	15.7 - 26.7
Distilled water[3]	65 - 70
High vacuum (field emission limited)[7]	20 - 40 (depends on electrode shape)
Fused silica[8]	25–40 at 20 °C
Waxed paper[9]	40 - 60
PTFE (Teflon, extruded)[3]	19.7
PTFE (Teflon, insulating film)[3][10]	60 - 173
Mica[3]	118
Diamond[11]	2000
PZT	10–25[12][13]
Vacuum	10^{12}

Wikipedia

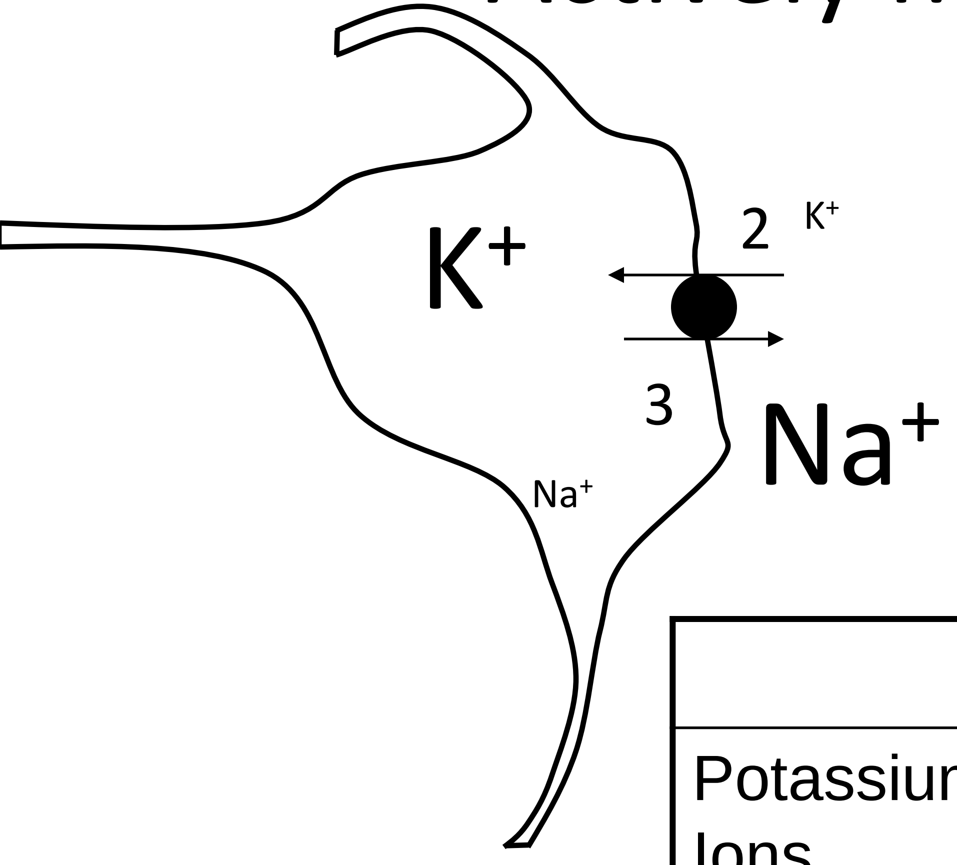
Imaging Voltage in Neurons

Darcy S. Peterka,[1,*] Hiroto Takahashi,[1] and Rafael Yuste[1]
[1]HHMI, Department of Biological Sciences, Columbia University, New York, New York 10027, USA
*Correspondence: dp2403@columbia.edu
DOI 10.1016/j.neuron.2010.12.010

membrane, even briefly reversing its polarity. In fact, the membrane potential changes are sizable (100 mV), and given that they occur across a very narrow section of dielectric material, the plasma membrane (only a few nanometers wide), these changes are associated with an enormous electric field (10^7–10^8V/m), which can be modulated at kHz frequencies by neurons.



Actively Maintained



	Intracellular	Extracellular
Potassium Ions	155 mM	4 mM
Sodium Ions	12 mM	145 mM

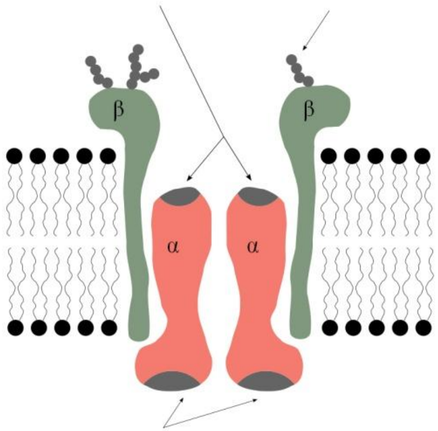
Na/K ATPase

Review

Mechanistic studies of sodium pump

Larry D. Faller

Archives of Biochemistry and Biophysics 476 (2008) 12–21



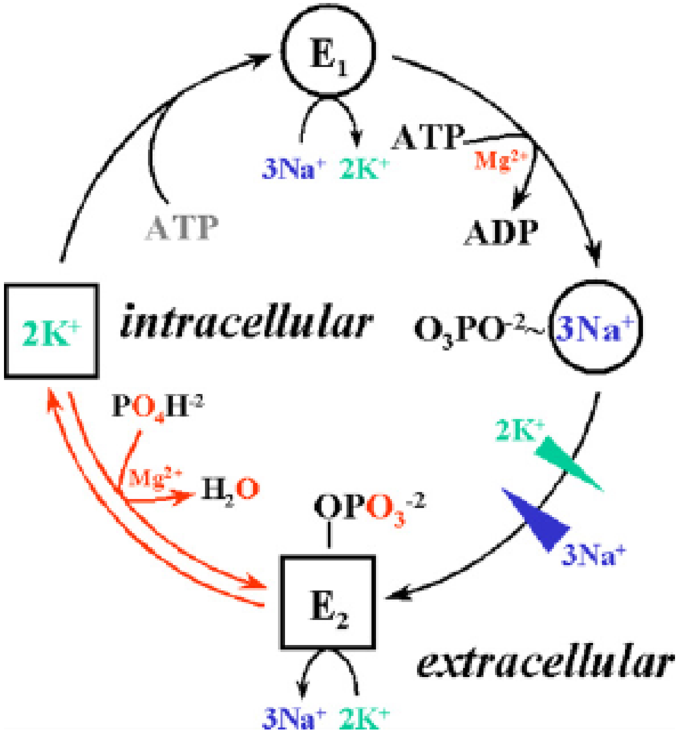


Fig. 1. Reaction cycle. The minimal steps in the catalysis-transport cycle of sodium pump are shown schematically. Black arrows indicate the normal, clockwise direction of the reaction sequence. Oxygen isotope (red) exchange may occur in the reversible step colored red. The cycle represents the sidedness, as well as repetition, of the reactions. For example, the 3 Na^+ (blue) that displace 2 K^+ (green) intracellularly are subsequently displaced by 2 K^+ extracellularly, generating the inward Na^+ (larger) and outward K^+ (smaller) gradients indicated by wedge shapes. A circle and a square symbolize the limiting protein conformations (E_1 and E_2, respectively) with enclosed ions indicating occlusion. Different colors denote ATP acting as an effector (gray) or substrate (black).

First description

The influence of some cations on an adenosine triphosphatase from peripheral nerves.
SKOU JC.
Biochim Biophys Acta. 1957 Feb;23(2):394-401.

The Simulators

- Please use the instructions file to unzip and install the simulation environments.
- For the moment focus on the diffusion simulator and the Goldmann simulator.

- Email me questions or even better ask them in class.