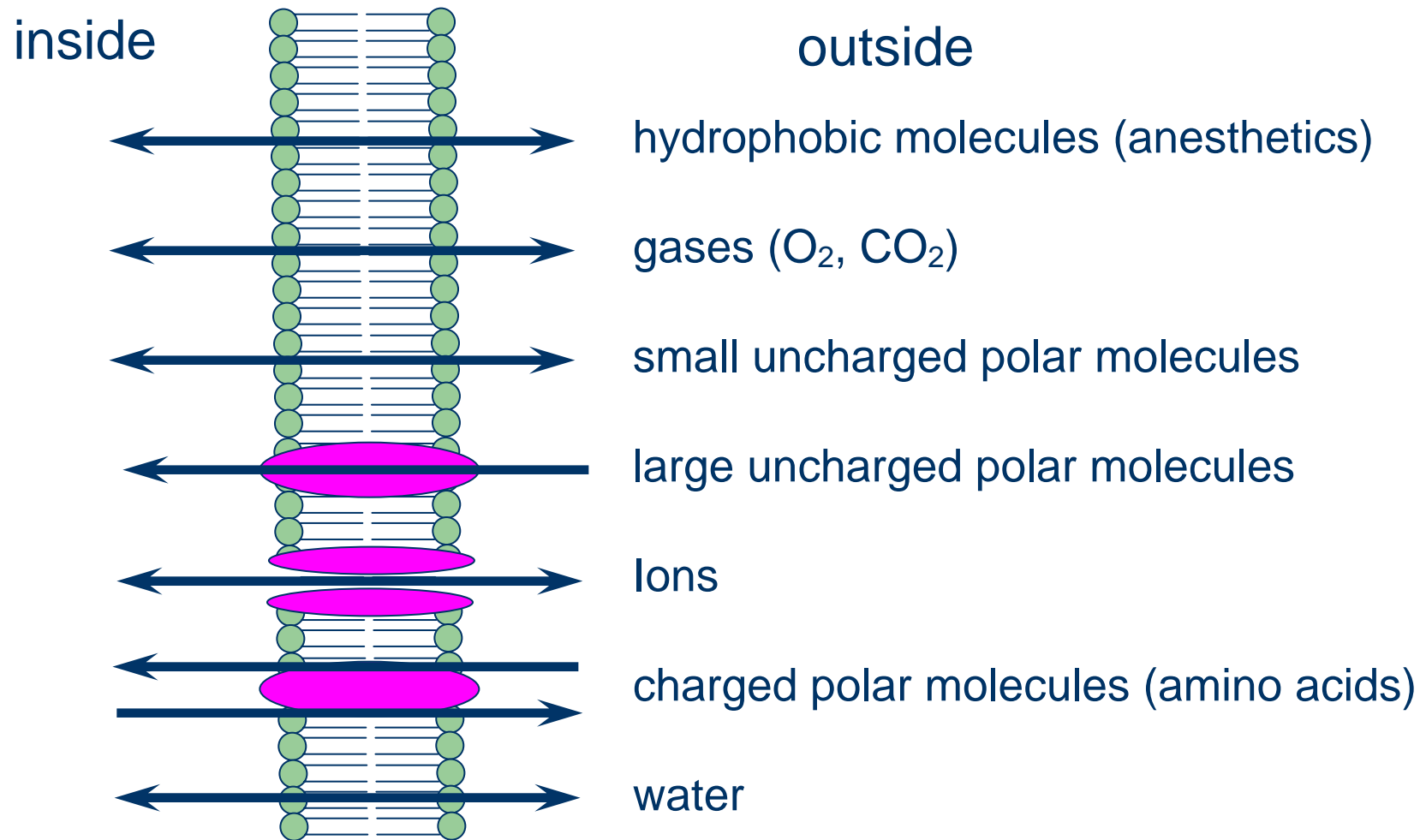


# Membrane Potential

Jim Huettner

# The Lipid Bilayer is a Selective Barrier



# 3

## Review of Electricity

Charge	Q		Coulombs	C
Current	I	Coulombs / sec	Amps	A
Voltage	V	Joules / Coulomb	Volts	V
Conductance	G		Siemens	S
Resistance	R		Ohms	$\Omega$

$$G = 1 / R \quad R = 1 / G$$

4

# Ohm's Law

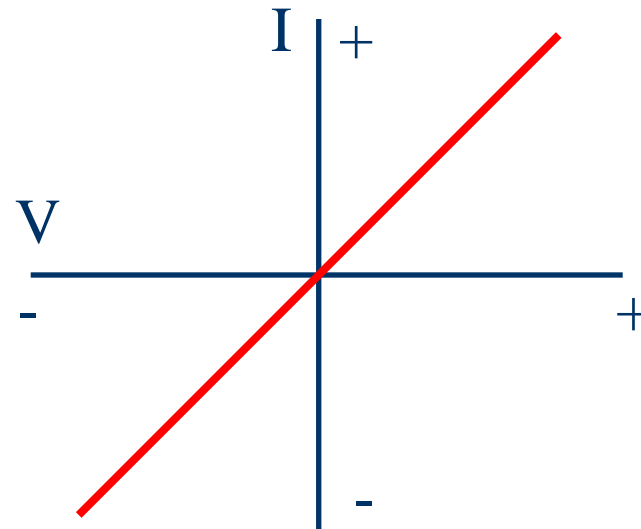
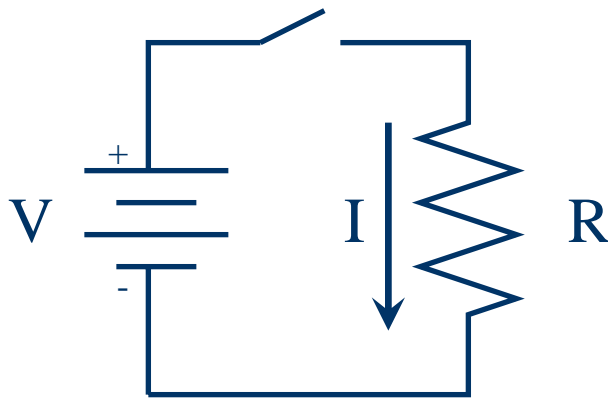
$$V = I * R = I / G$$

$$I = V / R = V * G$$

$R \propto \text{length}$



$R \propto 1/\text{area}$



# 5

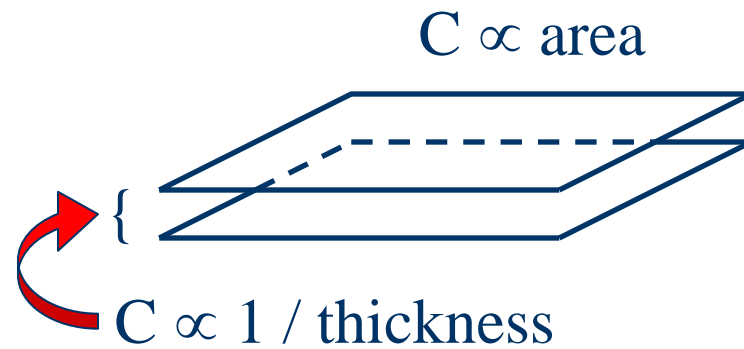
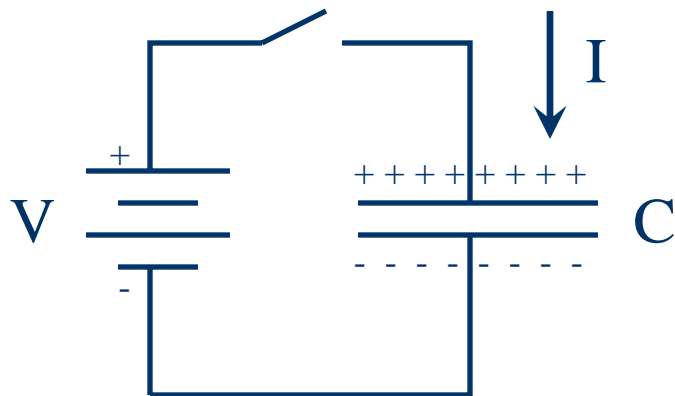
## Capacitance

Capacitance    C    Coulombs / Volt    Farads    F

$$C = Q / V$$

$$Q = C * V$$

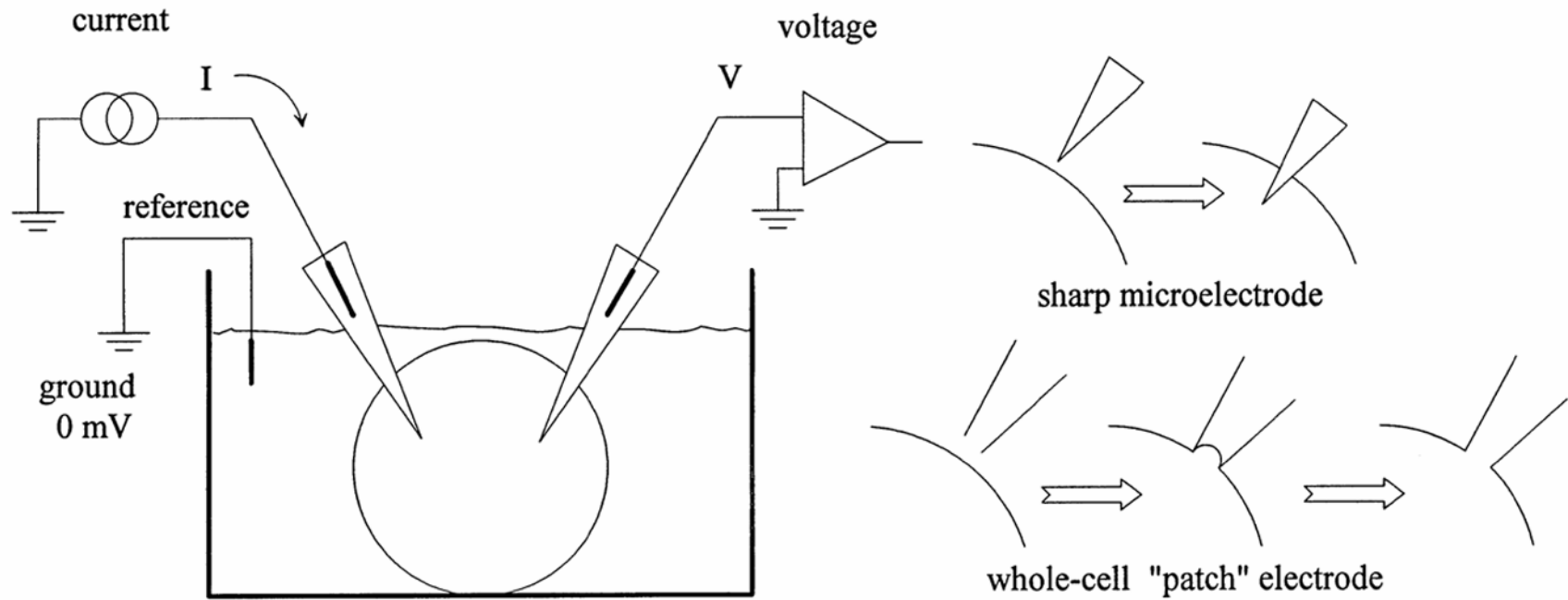
$$I = dQ / dt = C * dV / dt$$



For biological membranes:  
Specific Capacitance =  $1 \mu\text{F} / \text{cm}^2$

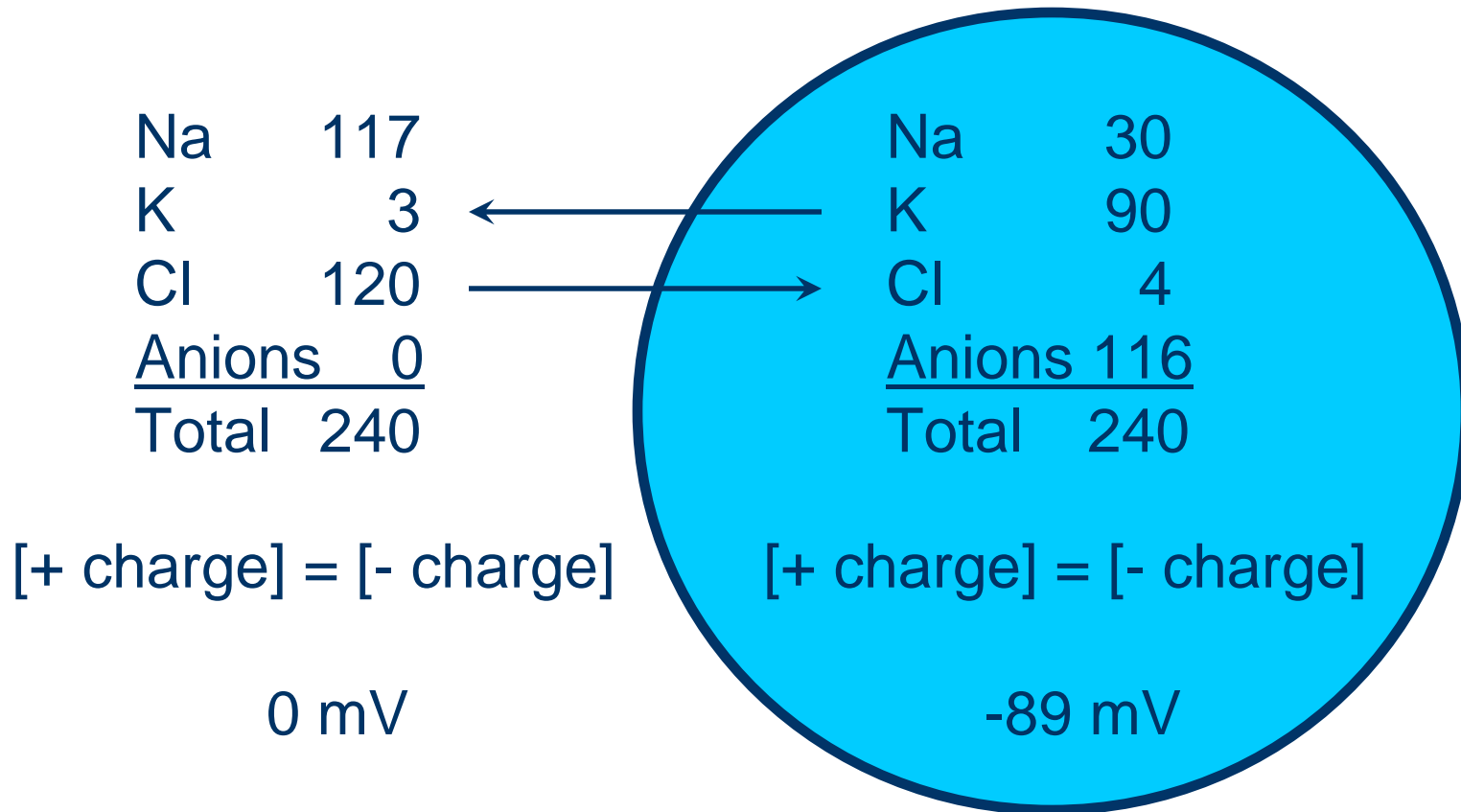
# 6

## Recording Membrane Potential



7

## Ion Concentrations

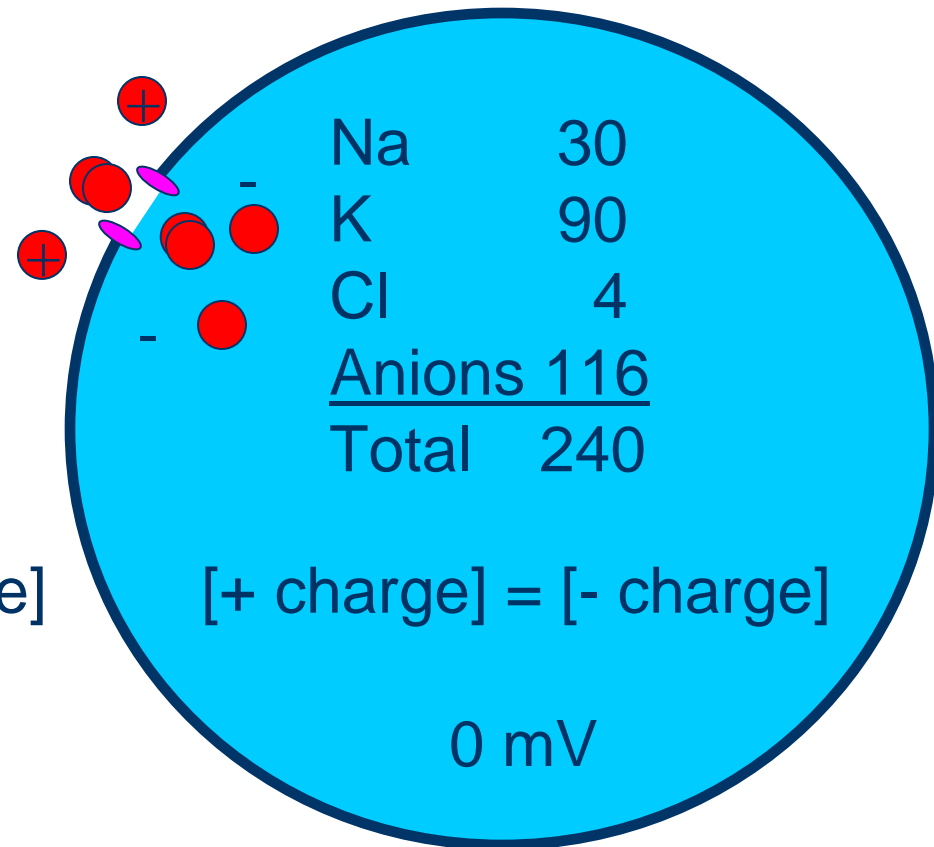


## Movement of Individual K<sup>+</sup> ions

Na	117
K	3
Cl	120
<u>Anions</u>	<u>0</u>
Total	240

[+ charge] = [- charge]

0 mV



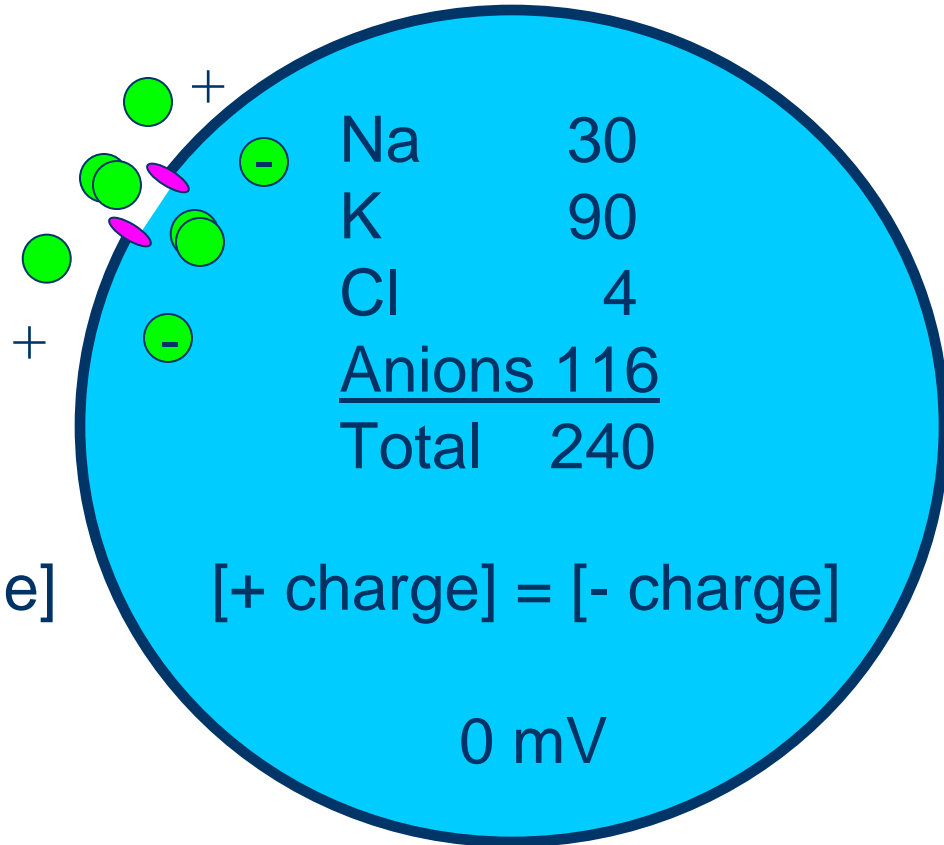
9

## Movement of Individual Cl<sup>-</sup> ions

Na	117
K	3
Cl	120
<u>Anions</u>	<u>0</u>
Total	240

[+ charge] = [- charge]

0 mV



## Sample Problem

- How many ions must cross the membrane of a spherical cell 50  $\mu\text{m}$  in diameter ( $r = 25 \mu\text{m}$ ) to create a membrane potential of  $-89 \text{ mV}$ ?

$$Q \text{ (Coulombs)} = C \text{ (Farads)} * V \text{ (Volts)}$$

$$\text{Specific Capacitance} = 1.0 \mu\text{Farad} / \text{cm}^2$$

$$\text{Surface area} = 4 \pi r^2$$

$$\text{Faraday's Constant} = 9.648 \times 10^4 \text{ Coulombs} / \text{mole}$$

$$\text{Avogadro's \#} = 6.022 \times 10^{23} \text{ ions} / \text{mole}$$

## Calculations

$$\text{Area} = 4 \pi r^2$$

1

$$= 4 \pi (25 \times 10^{-4} \text{ cm})^2$$

$$= 7.85 \times 10^{-5} \text{ cm}^2$$

$$= 78.5 \times 10^{-6} \mu\text{Farads}$$

$$= 78.5 \times 10^{-12} \text{ Farads}$$

$$Q = C * V$$

2

$$= 78.5 \times 10^{-12} \text{ Farads} * 0.089 \text{ Volts}$$

$$= 7 \times 10^{-12} \text{ Coulombs}$$

---


$$\Rightarrow 7 \times 10^{-12} \text{ Coulombs} / 9.65 \times 10^4 \text{ Coulombs per mole}$$

3

$$= 7.3 \times 10^{-17} \text{ moles of ions must cross the membrane}$$

$$= 0.073 \text{ femptomoles or } \sim 44 \times 10^6 \text{ ions}$$

## The Nernst Equation

Calculates the membrane potential at which an ion will be in electrochemical equilibrium.

At this potential: total energy inside = total energy outside

Electrical Energy Term:  $z * F * V$

Chemical Energy Term:  $R * T * \ln [\text{Ion}]$

Z is the charge, 1 for Na<sup>+</sup> and K<sup>+</sup>, 2 for Ca<sup>2+</sup> and Mg<sup>2+</sup>, -1 for Cl<sup>-</sup>

F is Faraday's Constant =  $9.648 \times 10^4$  Coulombs / mole

R is the gas constant = 8.315 Joules / °Kelvin \* mole

T is the temperature in °Kelvin

## Nernst Equation Derivation

$$zF * V_{in} + RT * \ln [K^+]_{in} = zF * V_{out} + RT * \ln [K^+]_{out}$$

$$zF (V_{in} - V_{out}) = RT (\ln [K^+]_{out} - \ln [K^+]_{in})$$

$$E_K = V_{in} - V_{out} = (RT / zF) \ln ([K^+]_{out} / [K^+]_{in})$$

$$E_K = 2.303 (RT / F) * \log_{10} ([K^+]_{out} / [K^+]_{in})$$

In General:

$$E_{ion} = (60 \text{ mV} / z) * \log ([ion]_{out} / [ion]_{in}) \quad @ \quad 30^\circ$$

## Nernst Potential Calculations

- First K and Cl

$$E_K = 60 \text{ mV} \log (3 / 90) = 60 * -1.477 = -89 \text{ mV}$$

$$E_{Cl} = (60 \text{ mV} / -1) \log (120 / 4) = -60 * 1.477 = -89 \text{ mV}$$

Both Cl and K are at electrochemical equilibrium at -89 mV

- Now for Sodium

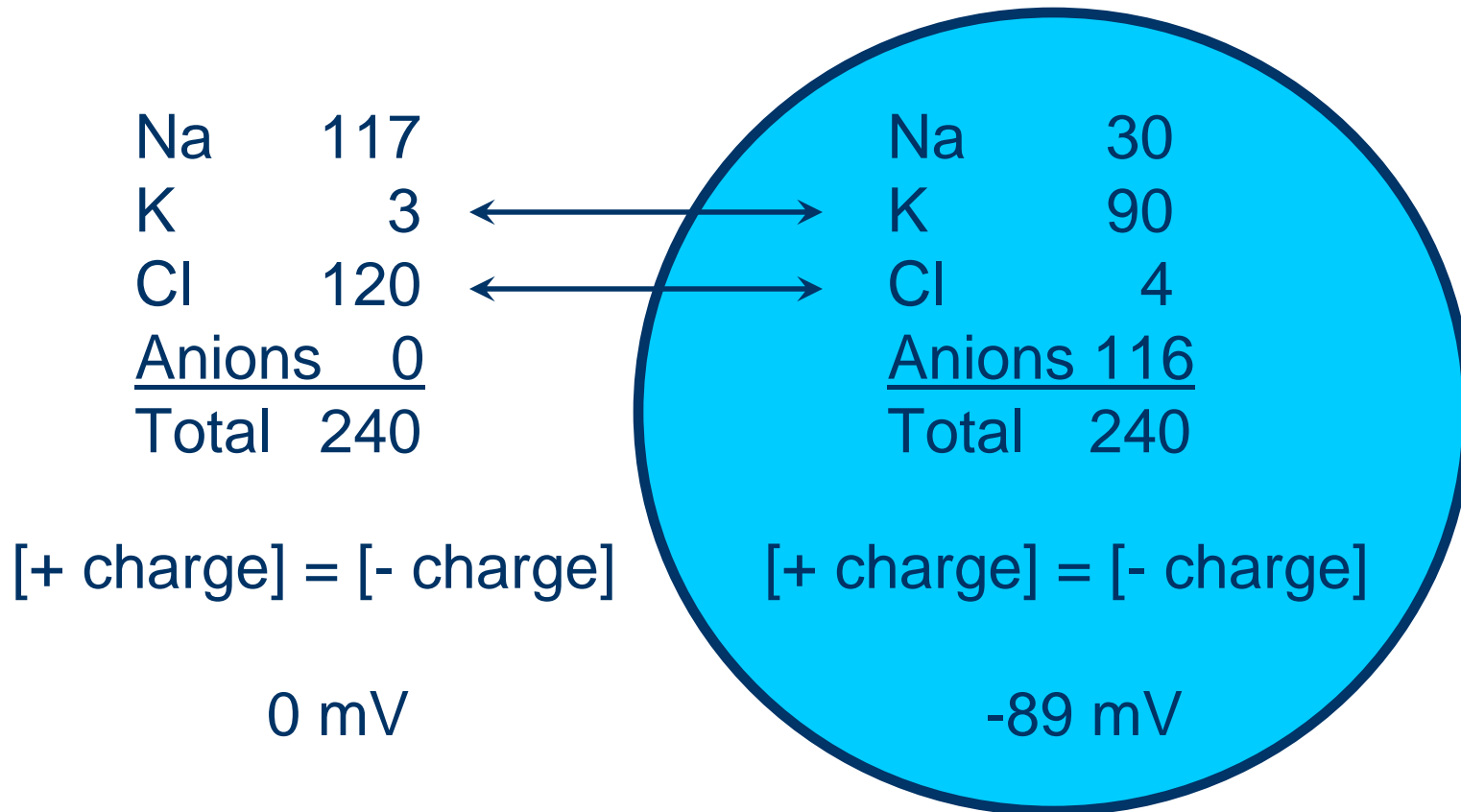
$$E_{Na} = 60 \text{ mV} \log (117 / 30) = 60 * 0.591 = +36 \text{ mV}$$

When  $V_m = -89 \text{ mV}$ , both the concentration gradient and electrical gradient for Na are from outside to inside

## At Electrochemical Equilibrium:

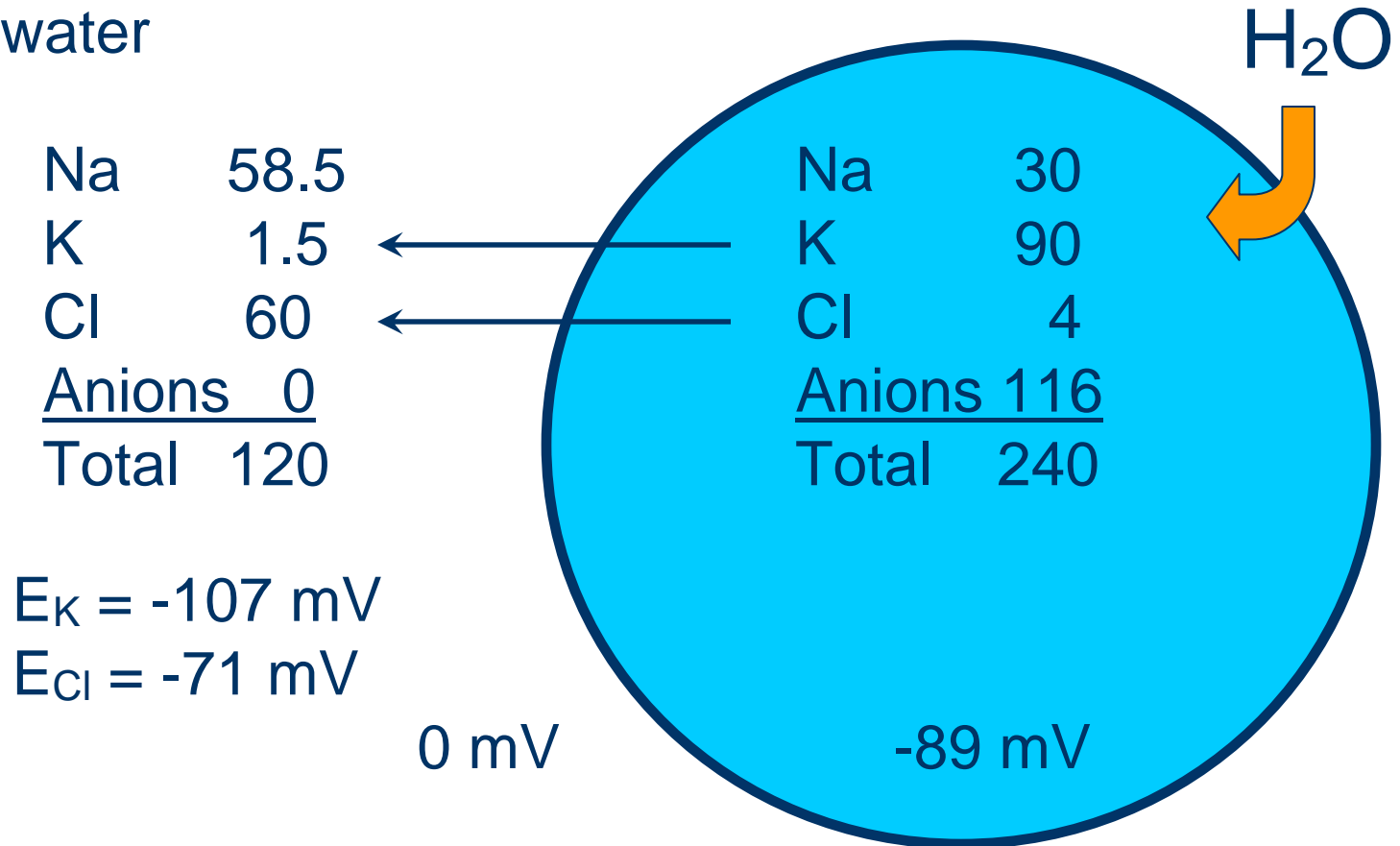
- The concentration gradient for the ion is exactly balanced by the electrical gradient
- There is no net flux of the ion
- There is no requirement for any sort of energy-driven pump to maintain the concentration gradient

## Ion Concentrations



# Environmental Changes: Dilution

Add water



## Environmental Changes: $\uparrow K^+$ or $\downarrow Cl^-$

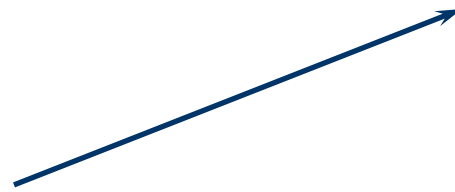
Starting Conditions

	Out	In
Na	117	30
K	3	90
Cl	120	4
Anions	0	116

$$E_K = E_{Cl} = -89 \text{ mV}$$

Relative Volume = 1

$\uparrow K^+$

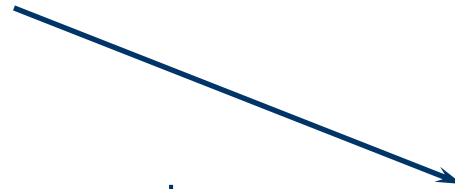


Na	114	29
K	6	91
Cl	120	7.9
Anions	0	112.1

$$E_K = E_{Cl} = -71 \text{ mV}$$

Relative Volume = 1.034

$\downarrow Cl^-$



Na	117	30.5
K	6	89.5
Cl	60	2.1
Anions	60	117.9

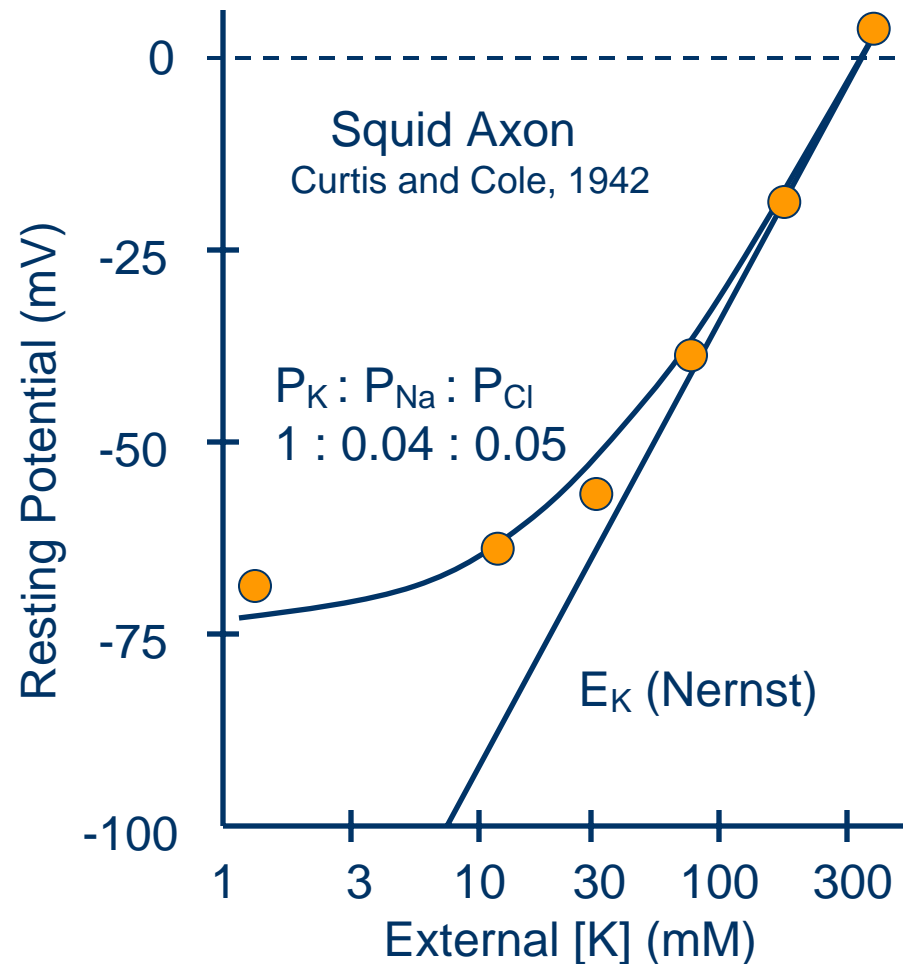
$$E_K = E_{Cl} = -88 \text{ mV}$$

Relative Volume = 0.984

# Deviation from the Nernst Equation

Resting membrane potentials in real cells deviate from the Nernst equation, particularly at low external potassium concentrations.

The Goldman, Hodgkin, Katz equation provides a better description of membrane potential as a function of potassium concentration in cells.



# The Goldman Hodgkin Katz Equation

$$V_m = 60\text{mV} * \log \left( \frac{P_K * [K]_{\text{out}} + P_{\text{Na}} * [\text{Na}]_{\text{out}} + P_{\text{Cl}} * [\text{Cl}]_{\text{in}}}{P_K * [K]_{\text{in}} + P_{\text{Na}} * [\text{Na}]_{\text{in}} + P_{\text{Cl}} * [\text{Cl}]_{\text{out}}} \right)$$

- Resting  $V_m$  depends on the concentration gradients and on the relative permeabilities to Na, K and Cl. The Nernst Potential for an ion does not depend on membrane permeability to that ion.
- The GHK equation describes a steady-state condition, not electrochemical equilibrium.
- There is net flux of individual ions, but no net charge movement.
- The cell must supply energy to maintain its ionic gradients.

## GHK Equation: Sample Calculation

Suppose  $P_K : P_{Na} : P_{Cl} = 1 : 0.1 : 1$

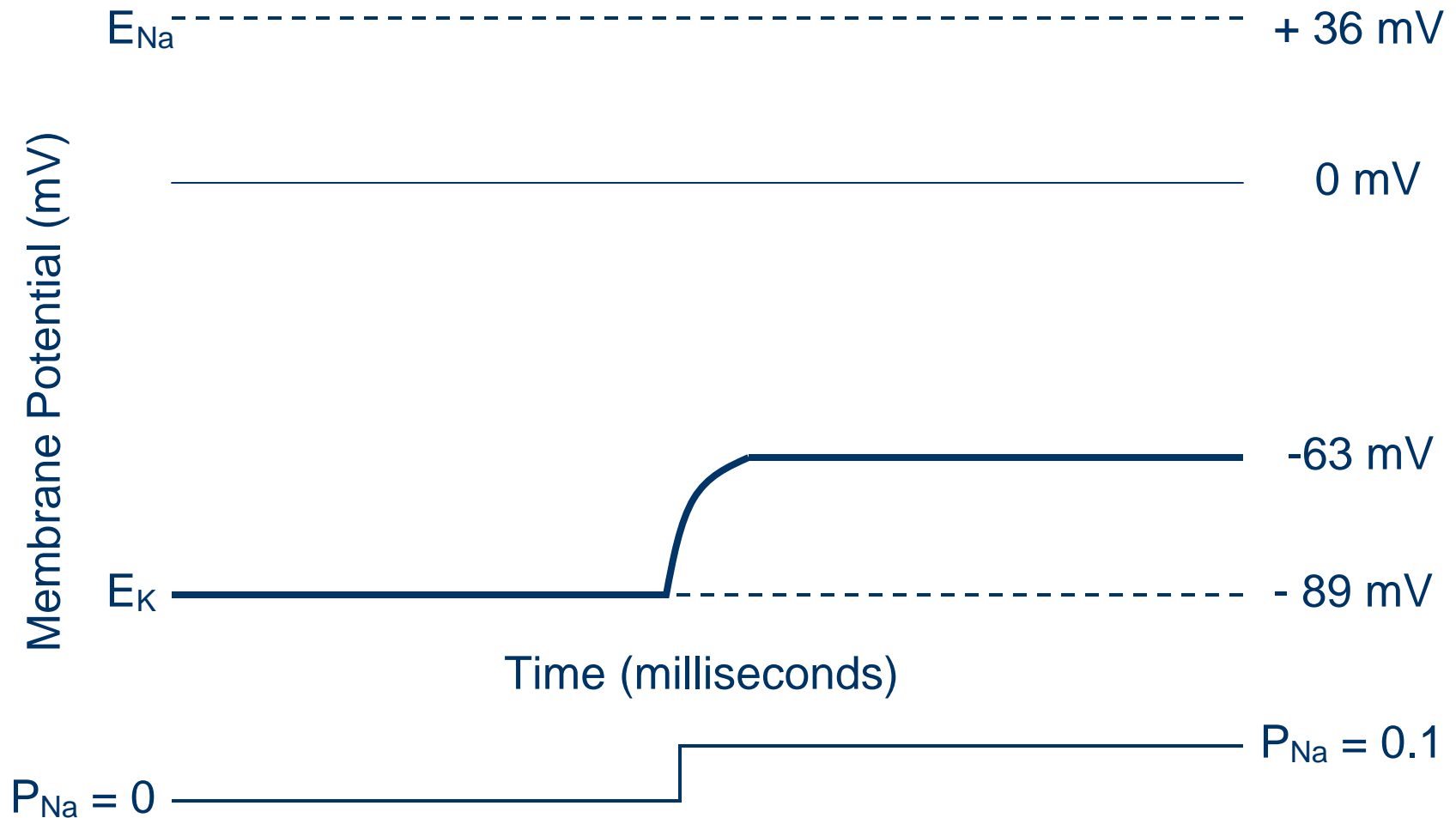
$$V_m = 60\text{mV} * \log\left(\frac{3 + 11.7 + 4}{90 + 3 + 120}\right)$$

$$= 60 \text{ mV} * \log (18.7 / 213)$$

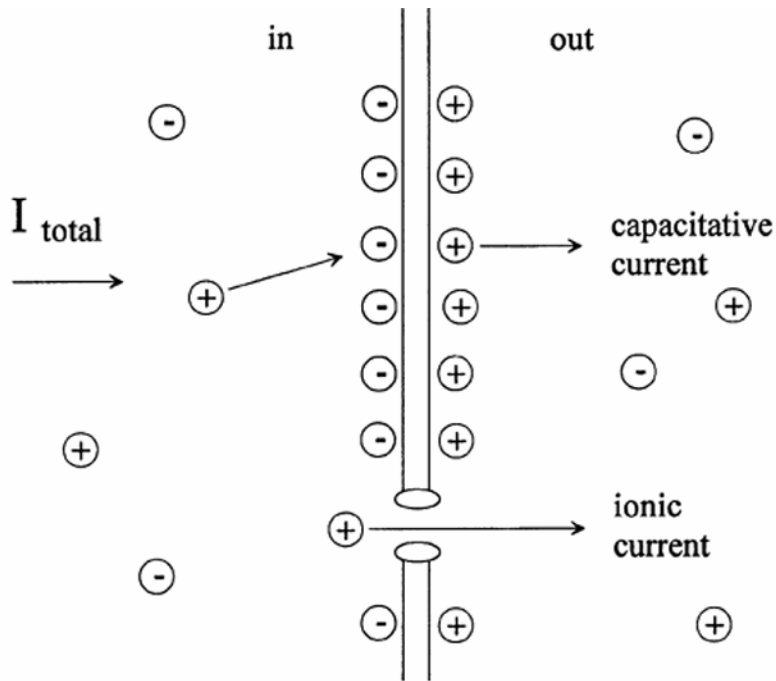
$$= 60 \text{ mV} * -1.06$$

$$= -63 \text{ mV}$$

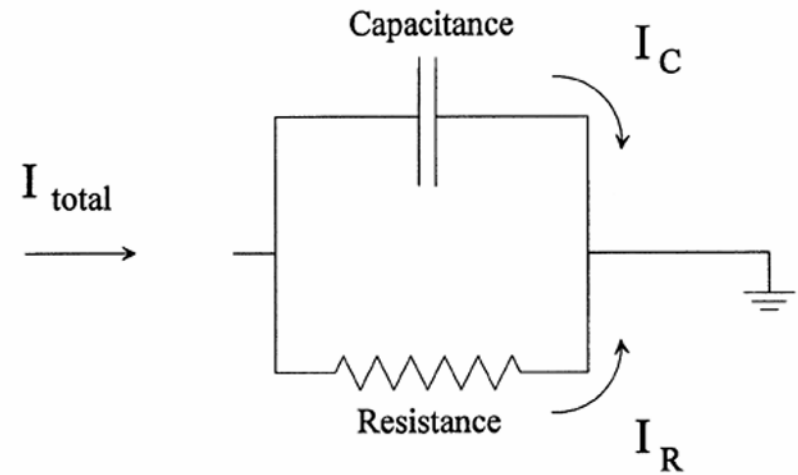
## Membrane Potential as a Function of Time



# Changing Membrane Potential



Physical Model



Electrical Model

## A simple model cell

A membrane sphere with conducting pores. The sphere contains, and is bathed in saline. The equivalent circuit is a capacitor and resistor in parallel. Inject a square pulse of current with a microelectrode, some of it will charge the capacitance and some will go through the resistance of the conducting pores.

$$I_{\text{Tot}} = I_R + I_C \quad \text{where} \quad I_R = V_m / R \quad \text{and} \quad I_C = C * dV_m / dt$$

$$\Rightarrow dV_m / dt = (I_{\text{Tot}} / C) - (V_m / (R * C))$$

The solution of this equation is:  $V_m = I_{\text{Tot}} * R * (1 - \exp(-t / \tau))$   
 where  $\tau = R * C$  is the membrane time constant

At equilibrium, when  $t \gg \tau$   $V_m = I_{\text{Tot}} * R$

Where  $R = 1 / \Sigma G_{\text{pores}}$  is called the Input Resistance

When  $t = \tau$  then  $(1 - \exp(-t / \tau))$  becomes  $(1 - \exp(-1)) = 0.632$

## Sample Calculation

A spherical cell, 100  $\mu\text{m}$  in diameter, that has 200 open channels, each with a conductance of 10 pS.

Surface area of a sphere is  $A = 4 * \pi * r^2$

$$\text{Area} = 4 * 3.1416 * (50 * 10^{-4} \text{ cm})^2 = 3.1 * 10^{-4} \text{ cm}^2$$

$$C = 3.1 * 10^{-4} \mu\text{Farads}$$

$$G_{\text{Tot}} = 200 * 10 \text{ pS} \text{ so } R_{\text{in}} = 1 / G_{\text{Tot}} = 5 * 10^8 \Omega \text{ and}$$

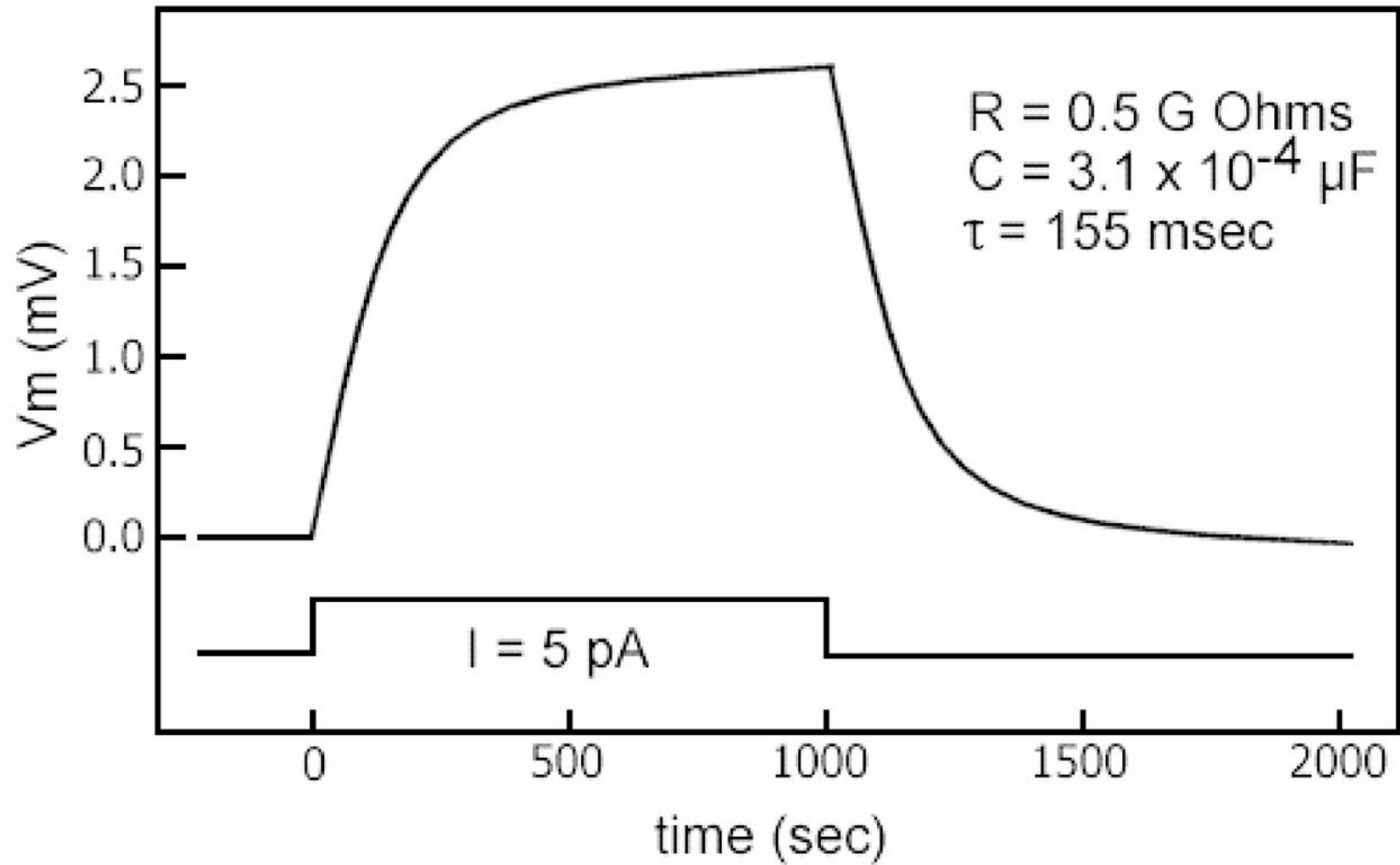
$$\tau = R_{\text{in}} * C = 155 \text{ msec}$$

A square pulse of current, 5 pA for 1 second will produce a change in membrane potential that will reach a steady state value of

$$V = I * R = 5 * 10^{-12} \text{ A} * 5 * 10^8 \Omega = 2.5 \text{ mV}$$

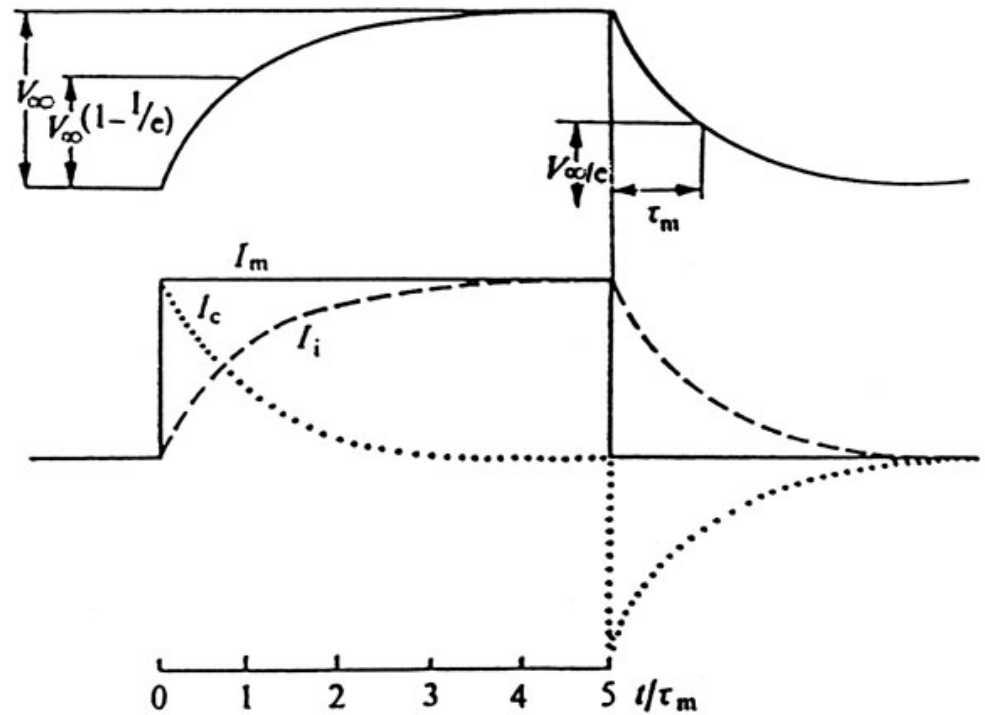
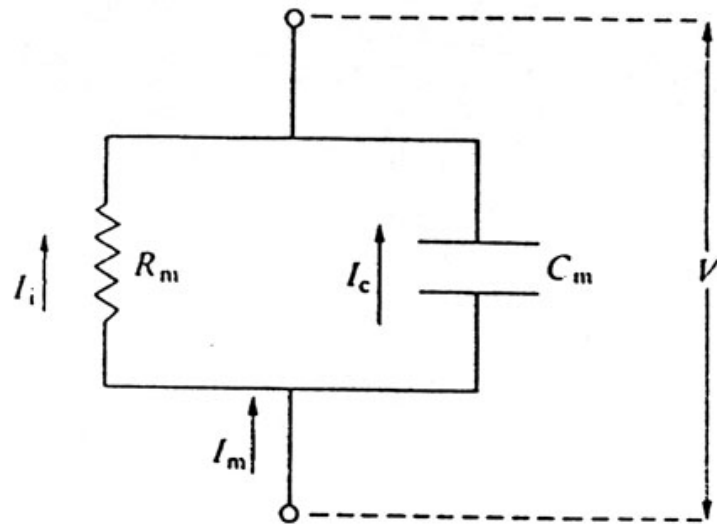
26

## Plot of Potential versus Time



27

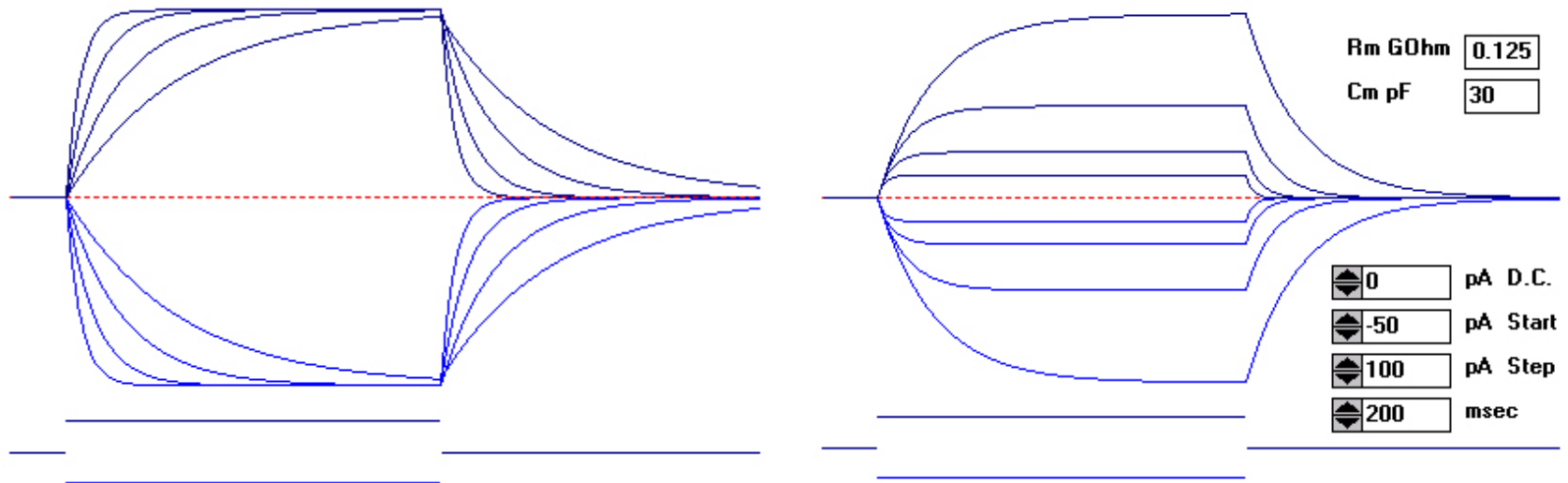
# Ionic and capacitative current



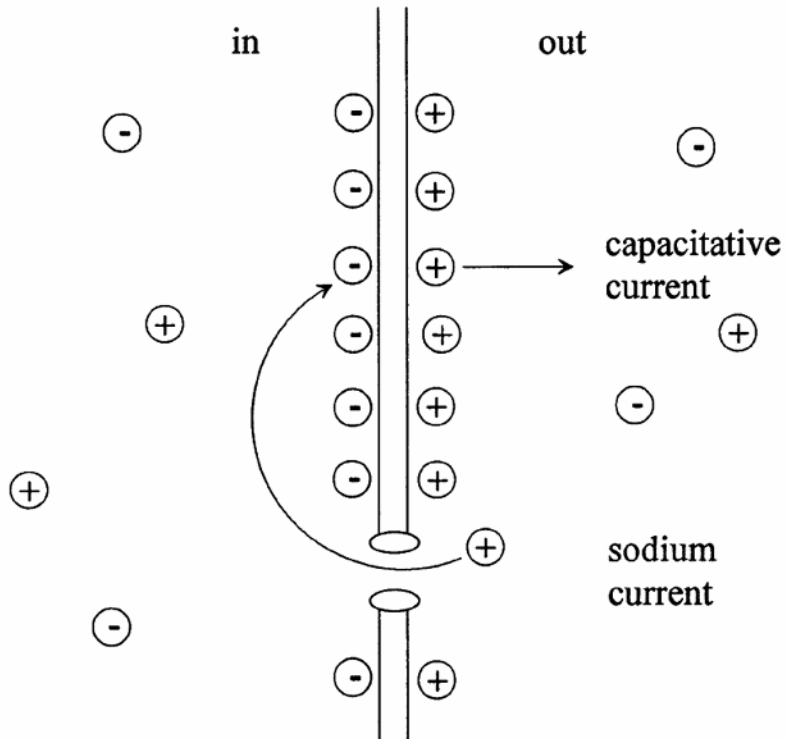
# changing C versus changing R

R=1; C=7.5, 15, 30, 60

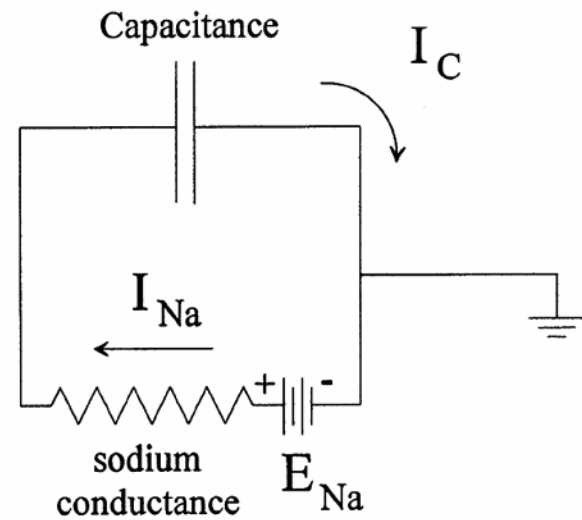
C=30; R = 0.125, 0.25, 0.5, 1



# Equivalent Circuit for Sodium Entry



Physical Model



Electrical Model

## Competing Batteries Model

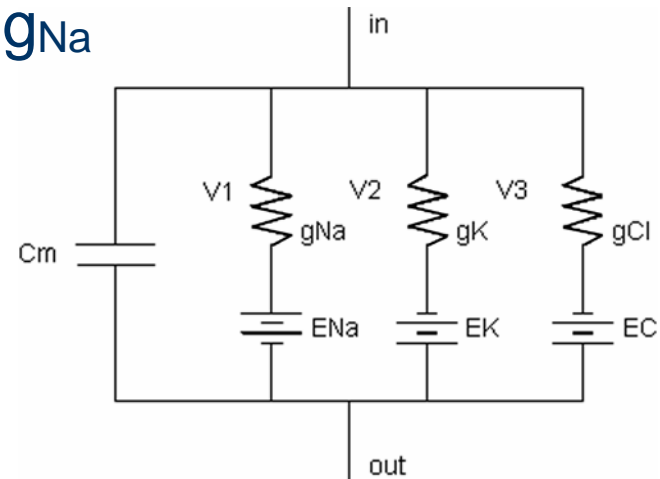
Ohm's Law:  $V = I * R$ , so  $I_{Na} = V_1 * g_{Na}$

$$I_K = V_2 * g_K \quad I_{Cl} = V_3 * g_{Cl}$$

At rest there is no net current

$$I_{Na} + I_K + I_{Cl} = 0$$

$$\Rightarrow V_1 * g_{Na} + V_2 * g_K + V_3 * g_{Cl} = 0$$



$$V_m \text{ or } V_{rest} = V_1 + E_{Na} = V_2 + E_K = V_3 + E_{Cl}$$

$$\Rightarrow V_1 = V_m - E_{Na} \quad \text{and} \quad V_2 = V_m - E_K \quad \text{and} \quad V_3 = V_m - E_{Cl}$$

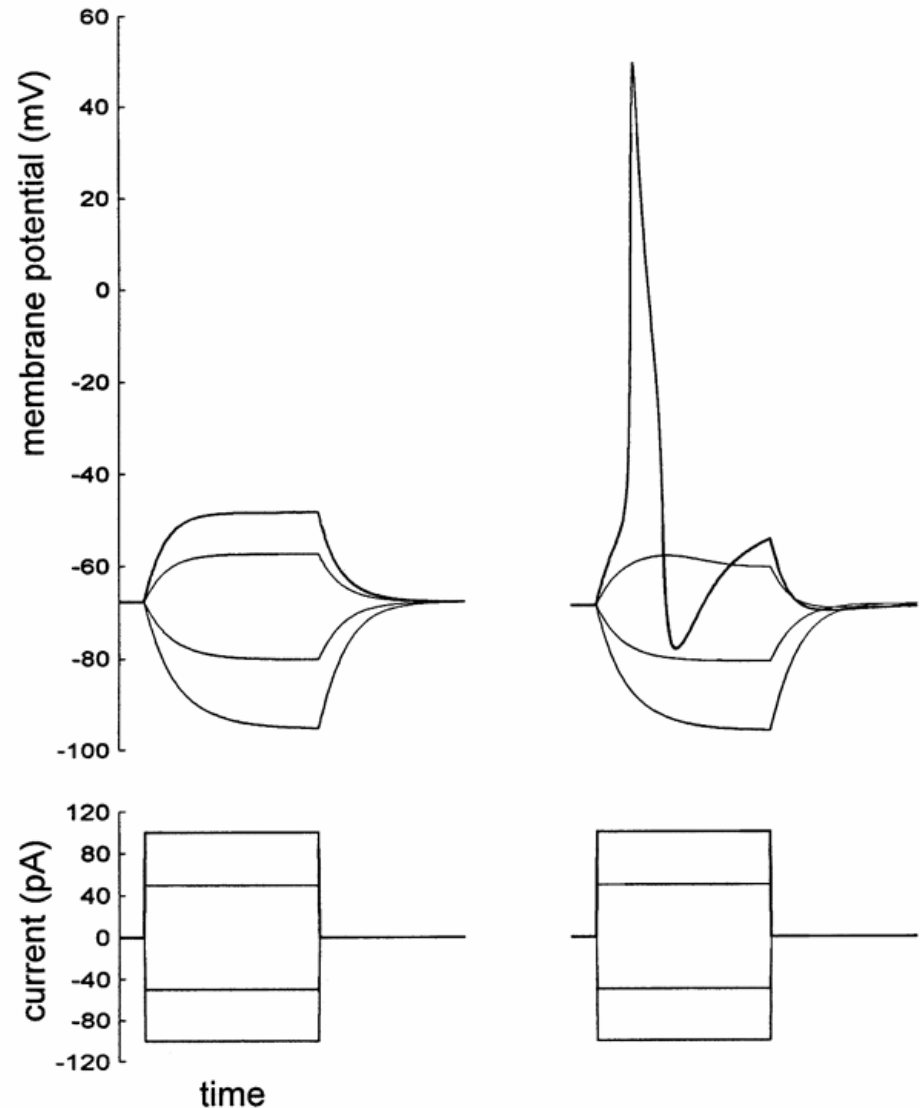
$$\Rightarrow 0 = (V_m - E_{Na}) * g_{Na} + (V_m - E_K) * g_K + (V_m - E_{Cl}) * g_{Cl}$$

$$V_m = \frac{g_{Na}E_{Na} + g_K E_K + g_{Cl}E_{Cl}}{g_{Na} + g_K + g_{Cl}}$$

$$I_{ion} = g_{ion} * (V_m - E_{ion})$$

## Passive v.s. Active

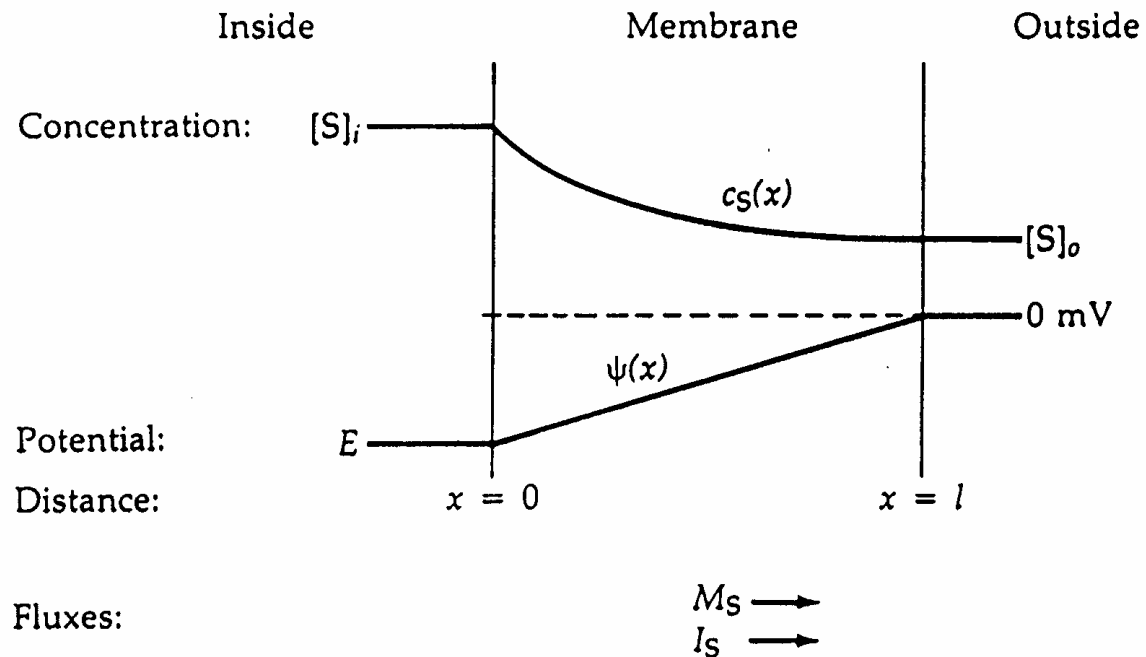
- All cells exhibit passive changes in membrane potential when stimulated
- Only excitable cells fire action potentials
- Excitability depends on specialized channels



# GHK constant field theory

Nernst-Plank electrodiffusion equation

$$I = -z F D \left( \frac{dc}{dx} + \frac{F z c}{R T} \frac{d\psi}{dx} \right)$$

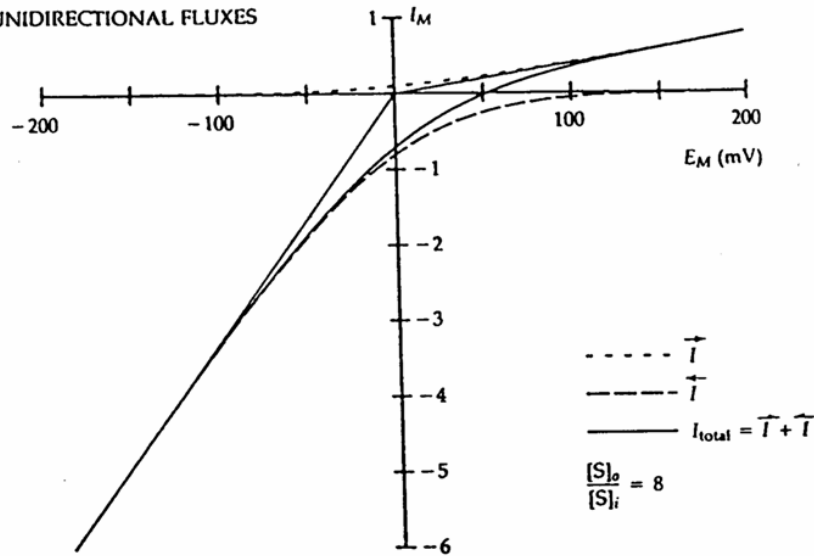


## 2 ELECTRODIFFUSION IN A MEMBRANE

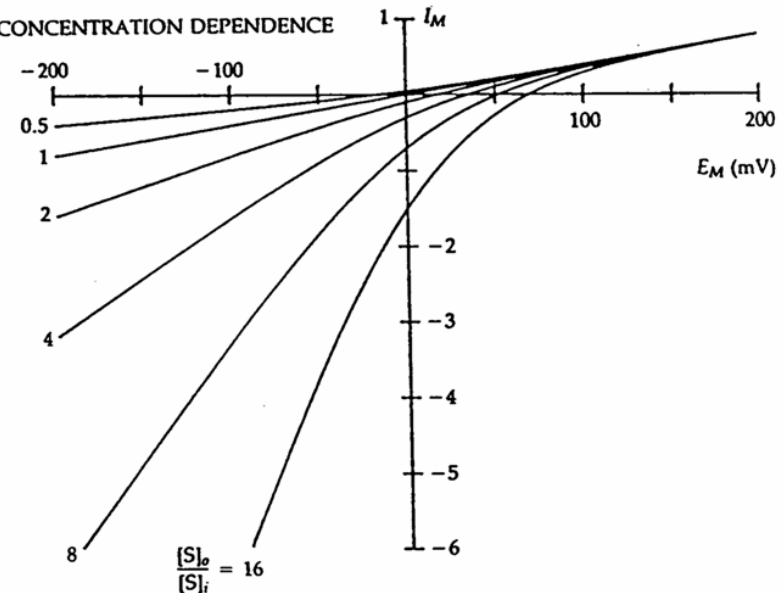
The flow of ion S across a hypothetical membrane is associated with a chemical flux  $M_S$  and an electric current  $I_S$ . The ionic concentration profile in the membrane is  $c_S(x)$  and the electrical potential profile is  $\psi_S(x)$ .

# GHK constant field equation

(A) UNIDIRECTIONAL FLUXES



(B) CONCENTRATION DEPENDENCE

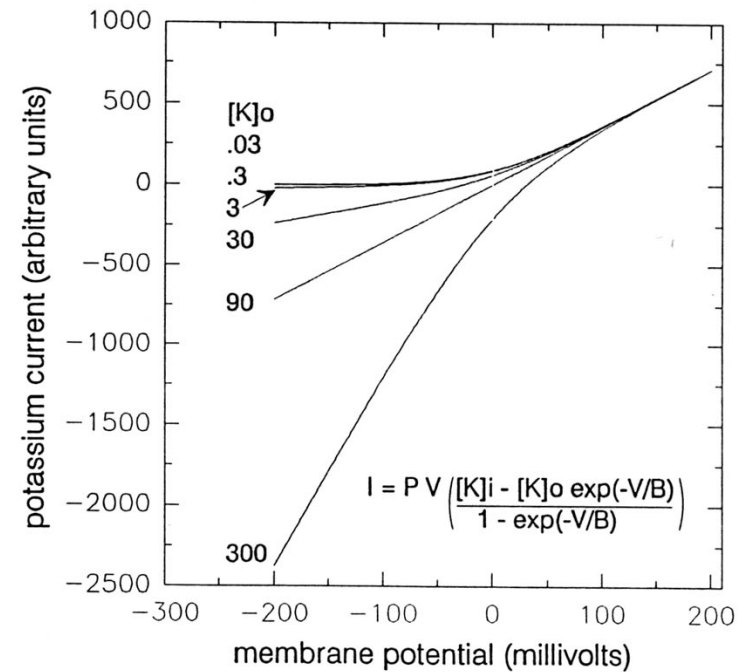
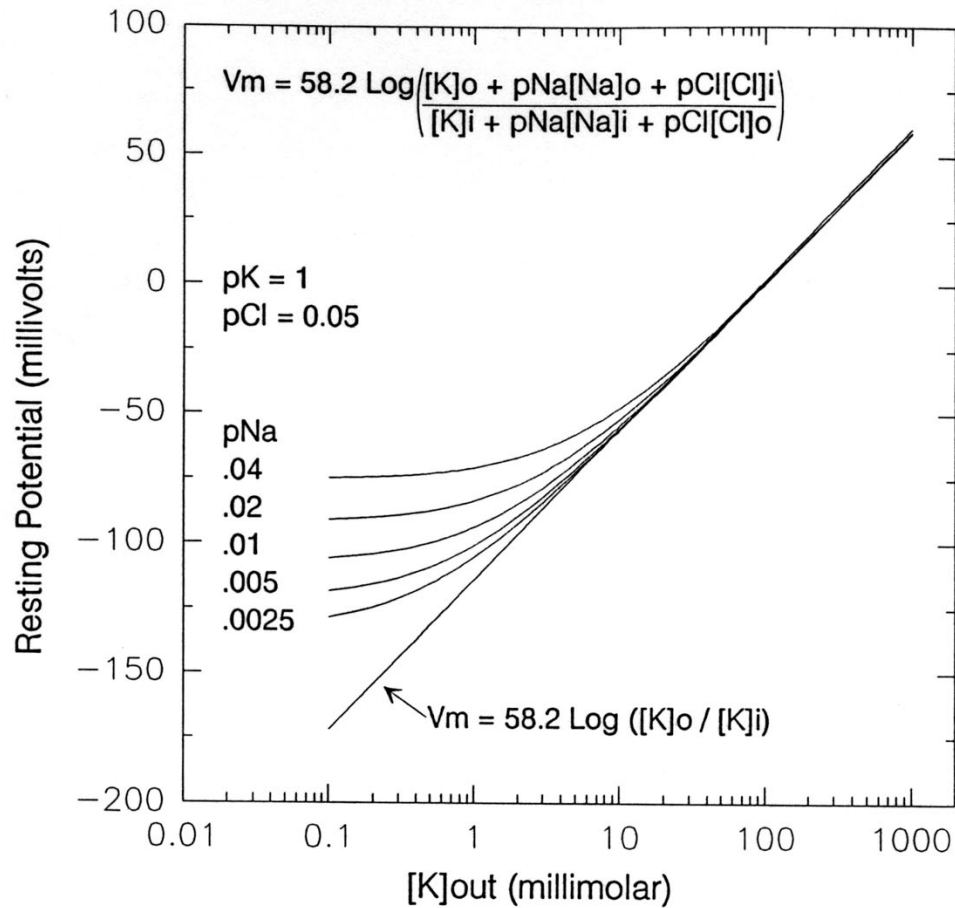


## 2 CURRENT-VOLTAGE CURVES OF GHK THEORY

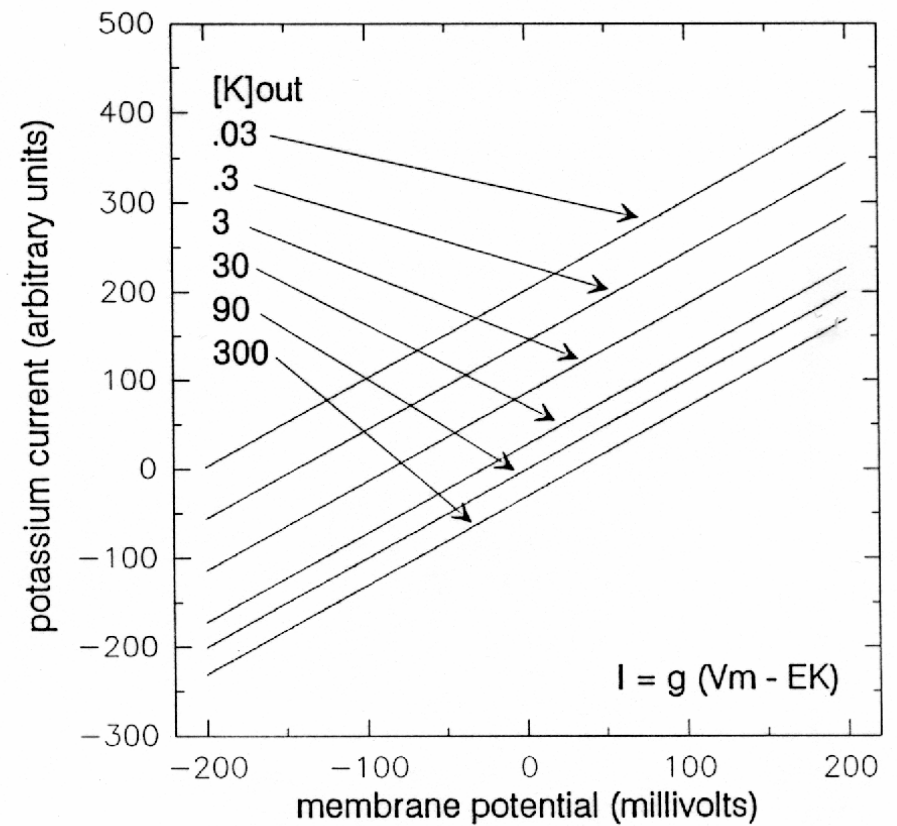
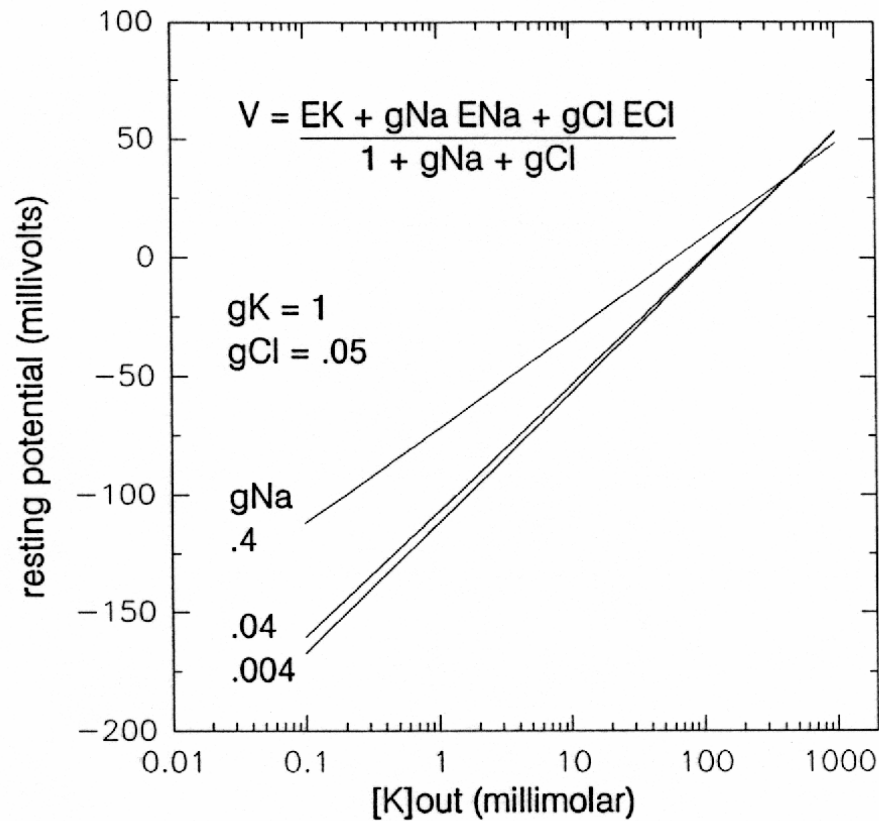
Theoretical  $I$ - $E$  relations for a homogeneous membrane obeying the Goldman (1943) and Hodgkin and Katz (1949) current equation for a single permeant, univalent cation. (A) Eightfold rectification with an eightfold concentration gradient, showing how asymptotes extrapolate to the origin and showing the underlying unidirectional efflux and influx making up the total current. (B) Change of curvature and of reversal potential as the external concentration is varied from 0.5 to 16 while the internal concentration is kept constant at 1. (Current and concentration in arbitrary units.)

$$\text{Current} = \frac{P z^2 E F^2 ([S]_i - [S]_o \exp(-z F E / R T))}{R T (1 - \exp(-z F E / R T))}$$

# GHK Equations



# Linear Competing Batteries



## Summary:

- I. Cell membranes form an insulating barrier that acts like a parallel plate capacitor ( $1 \mu\text{F} / \text{cm}^2$ )
- II. Only a small number of ions must cross the membrane to create a significant voltage difference  
 $\Rightarrow$  bulk neutrality of internal and external solution
- III. Cells need channels to regulate their volume
- IV. Permeable ions move toward electrochemical equilibrium
  - $E_{\text{ion}} = (60 \text{ mV} / z) * \log ([\text{Ion}]_{\text{out}} / [\text{Ion}]_{\text{in}}) @ 30^\circ\text{C}$
  - Electrochemical equilibrium does not depend on permeability, only on the concentration gradient

## Summary (continued):

- v. The Goldman, Hodgkin, Katz equation gives the steady-state membrane potential when Na, K and Cl are permeable

$$V_m = 60\text{mV} * \log \left( \frac{P_K * [K]_{\text{out}} + P_{\text{Na}} * [Na]_{\text{out}} + P_{\text{Cl}} * [Cl]_{\text{in}}}{P_K * [K]_{\text{in}} + P_{\text{Na}} * [Na]_{\text{in}} + P_{\text{Cl}} * [Cl]_{\text{out}}} \right)$$

- In this case,  $V_m$  does depend on the relative permeability to each ion and there is steady flux of Na and K  
  
⇒ The cell must supply energy to maintain its ionic gradients