Introduction to Neural Computation

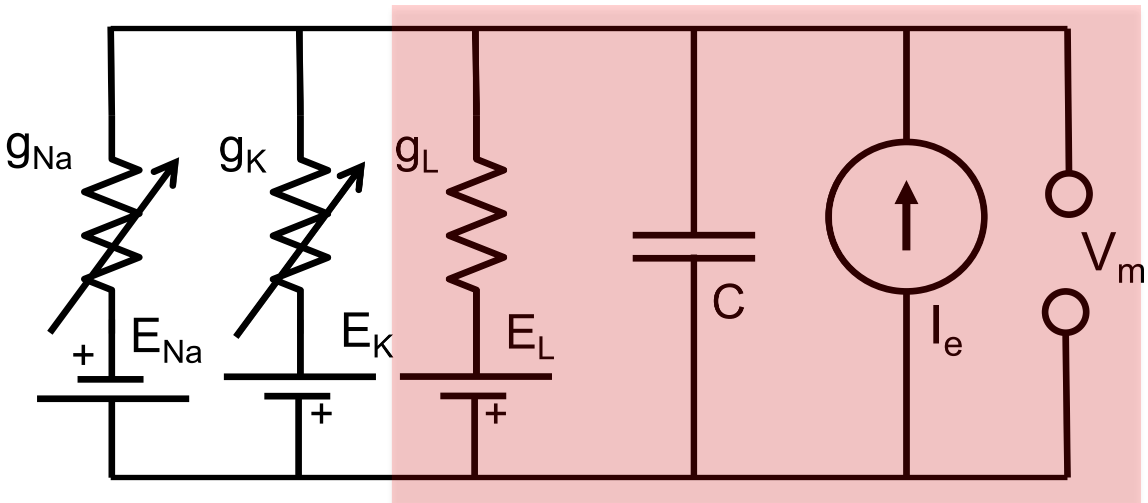
Michale Fee

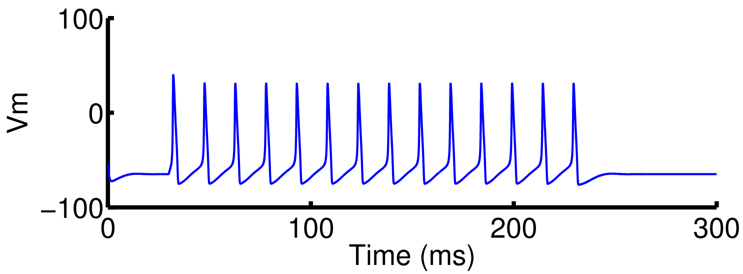
MIT BCS 9.40 — 2017

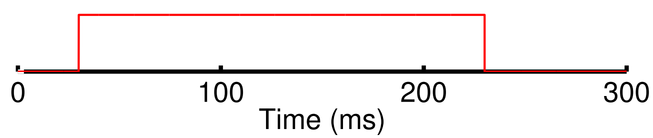
Lecture 2 – RC Neuron Model

A mathematical model of a neuron

- Equivalent circuit model





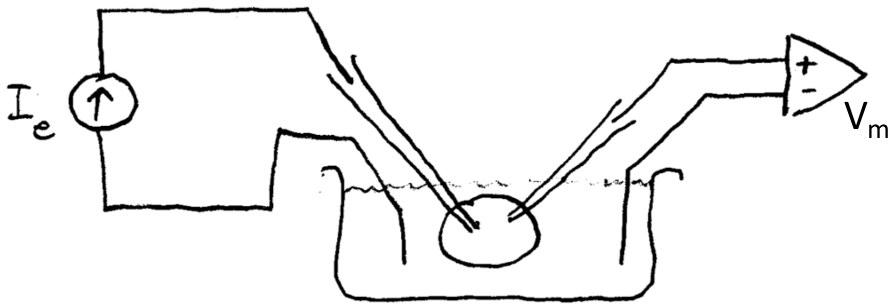


Alan Hodgkin
Andrew Huxley, 1952

Learning objectives for Lecture 2

- To understand how neurons respond to injected currents
- To understand how membrane capacitance and resistance allows neurons to integrate or smooth their inputs over time (RC model)
- To understand how to derive the differential equations for the RC model
- To be able to sketch the response of an RC neuron to different current inputs
- To understand where the ‘batteries’ of a neuron come from

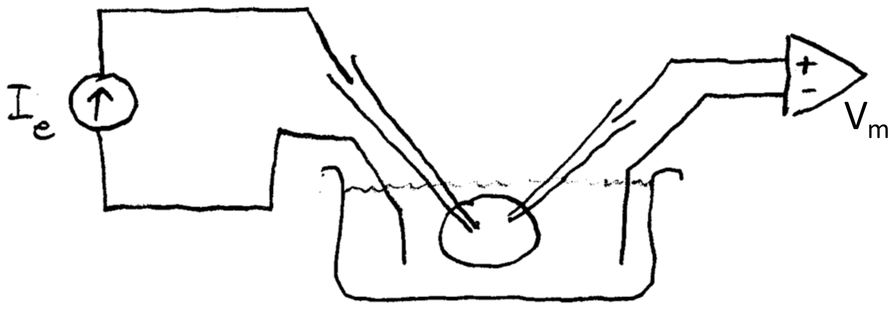
Why understand how neurons respond to injected current?

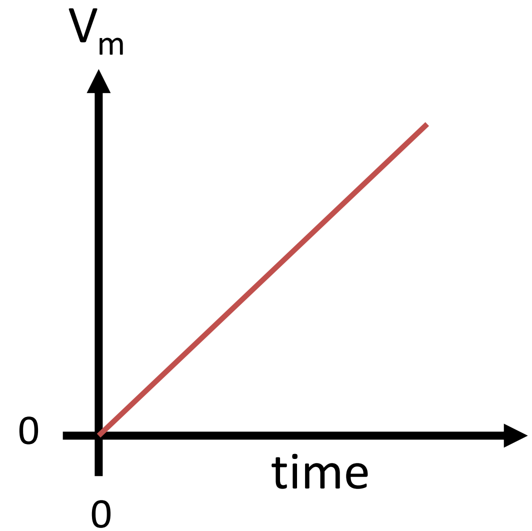


- First, because nearly every aspect of computation and signaling in a neuron is controlled by voltage. This control is almost entirely mediated by the voltage sensitivity of ion channels.

- In the brain, neurons have current injected into them:
  - Through synapses from other neurons
  - Or as a result of sensory stimuli

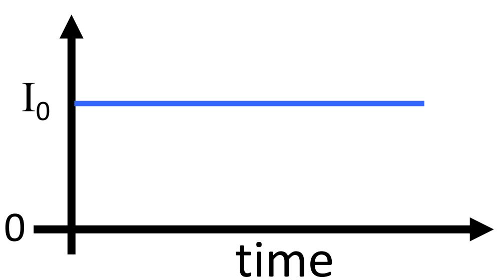
Why understand how neurons respond to injected current?



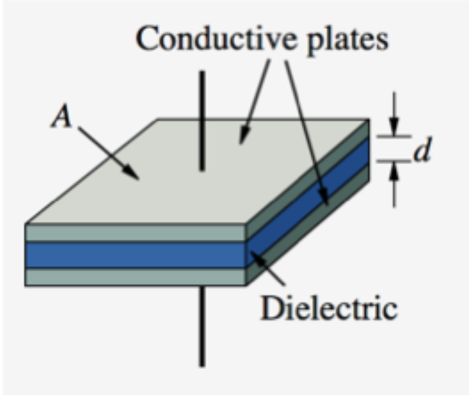


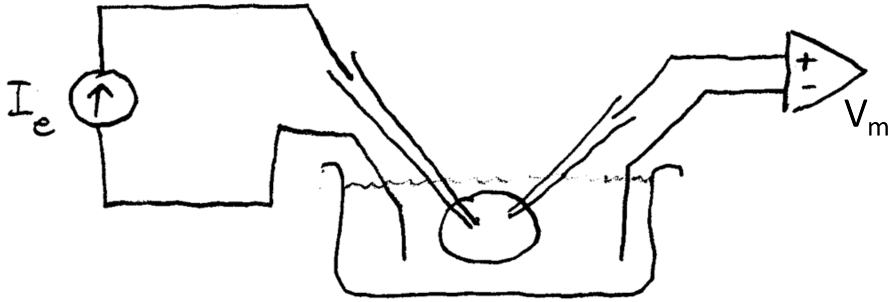
Neurons can perform analog numerical integration over time

$$\text{Voltage}(t) = \int_0^t \text{Current}(t)\, d\tau$$



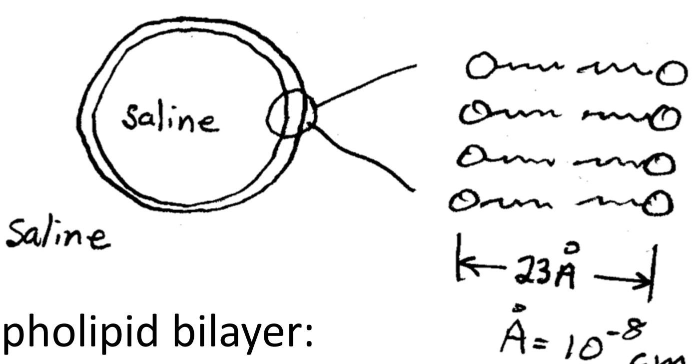
A neuron is a capacitor





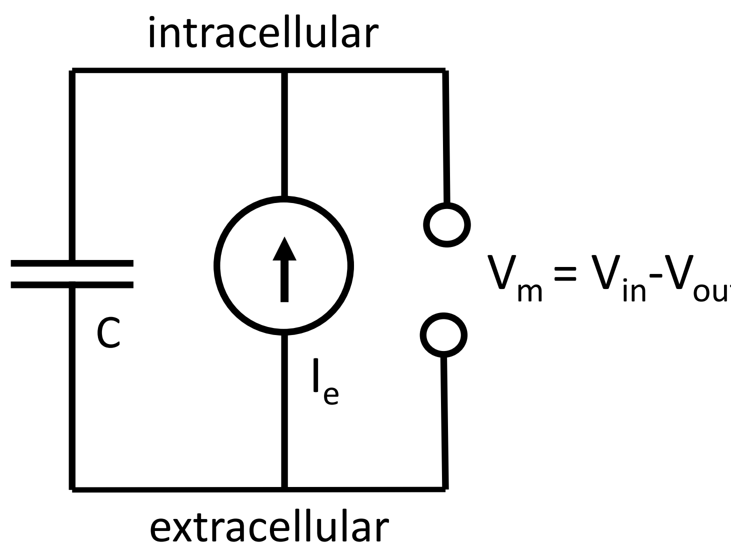
Why is this a capacitor?

A capacitor is two conductors separated by an insulator



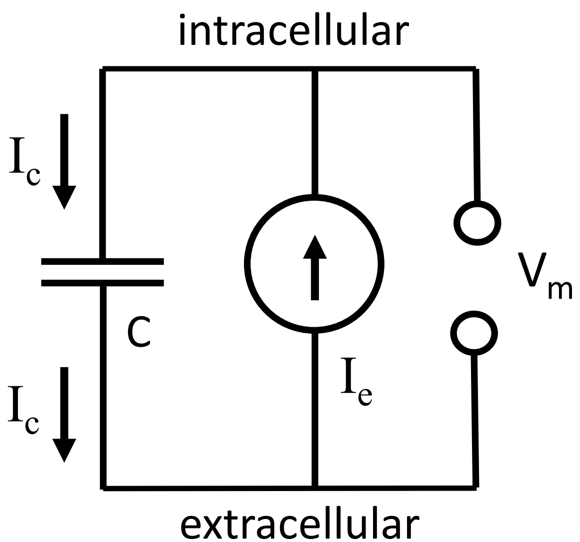
Phospholipid bilayer:
—polar head
—non-polar tail

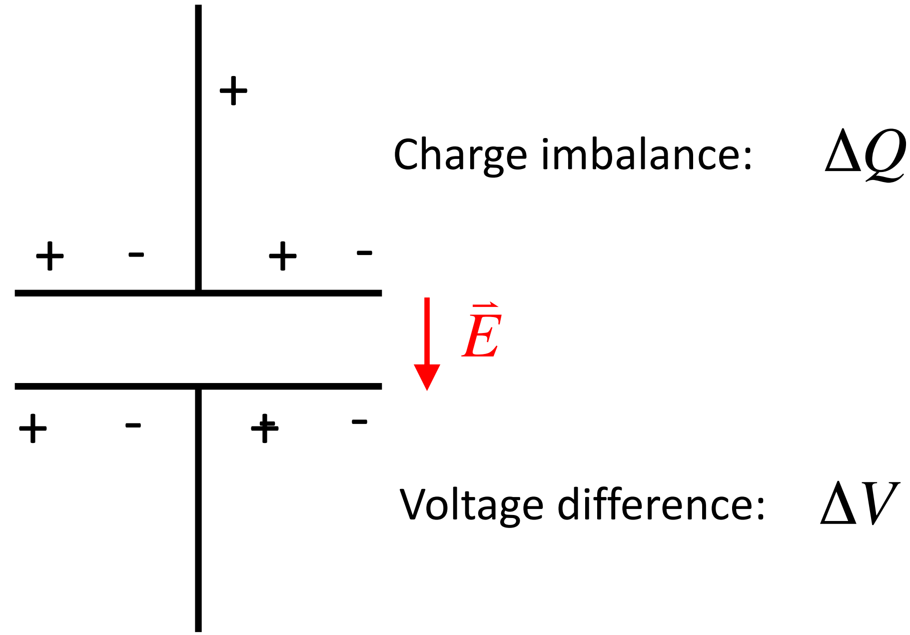
Equivalent circuit



What happens when we inject current into our neuron?

A neuron is a capacitor





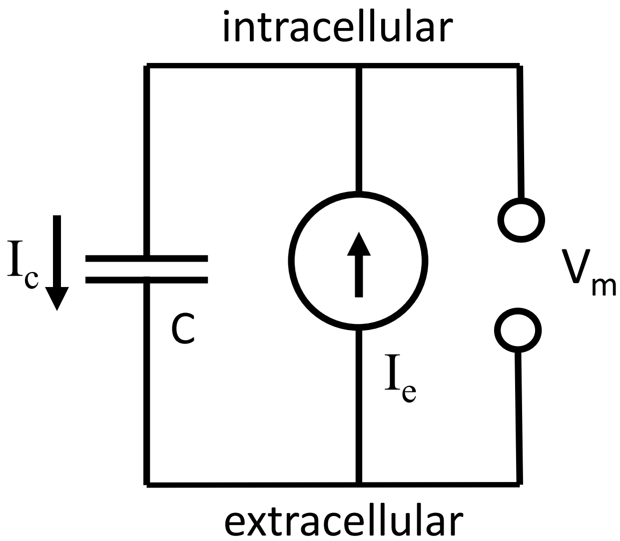
As positive charges build up on the inside of the membrane, they repel positive charges away from the outside of the membrane…

This looks like a current flowing through the capacitor!

$$\Delta Q = C \cdot \Delta V$$

Q: charge (Coulombs, C = 6 x 10^{18} charges)
C: capacitance (Farads, F)
V: voltage difference across capacitor (Volts, V)

A neuron is a capacitor



$$\Delta Q = C \cdot \Delta V$$

Definition of capacitive current

$$I_c(t) = \frac{dQ}{dt} = C\frac{dV_m}{dt}$$

But, Kirchoff's current law tells us that the sum of all currents into a node is zero

$$-I_c + I_e = 0$$

Thus, we can write the differential equation that describes the change in voltage of our neural capacitor with injected current

$$I_e(t) = C\frac{dV_m}{dt}$$

I_e has units of Amperes, which is Coulombs per second

capacitor
Response of a ~~neuron~~ to injected current

$$I_e(t) = C\frac{dV_m}{dt}$$

We can integrate this differential equation over time, starting with initial voltage V_0 at time zero.

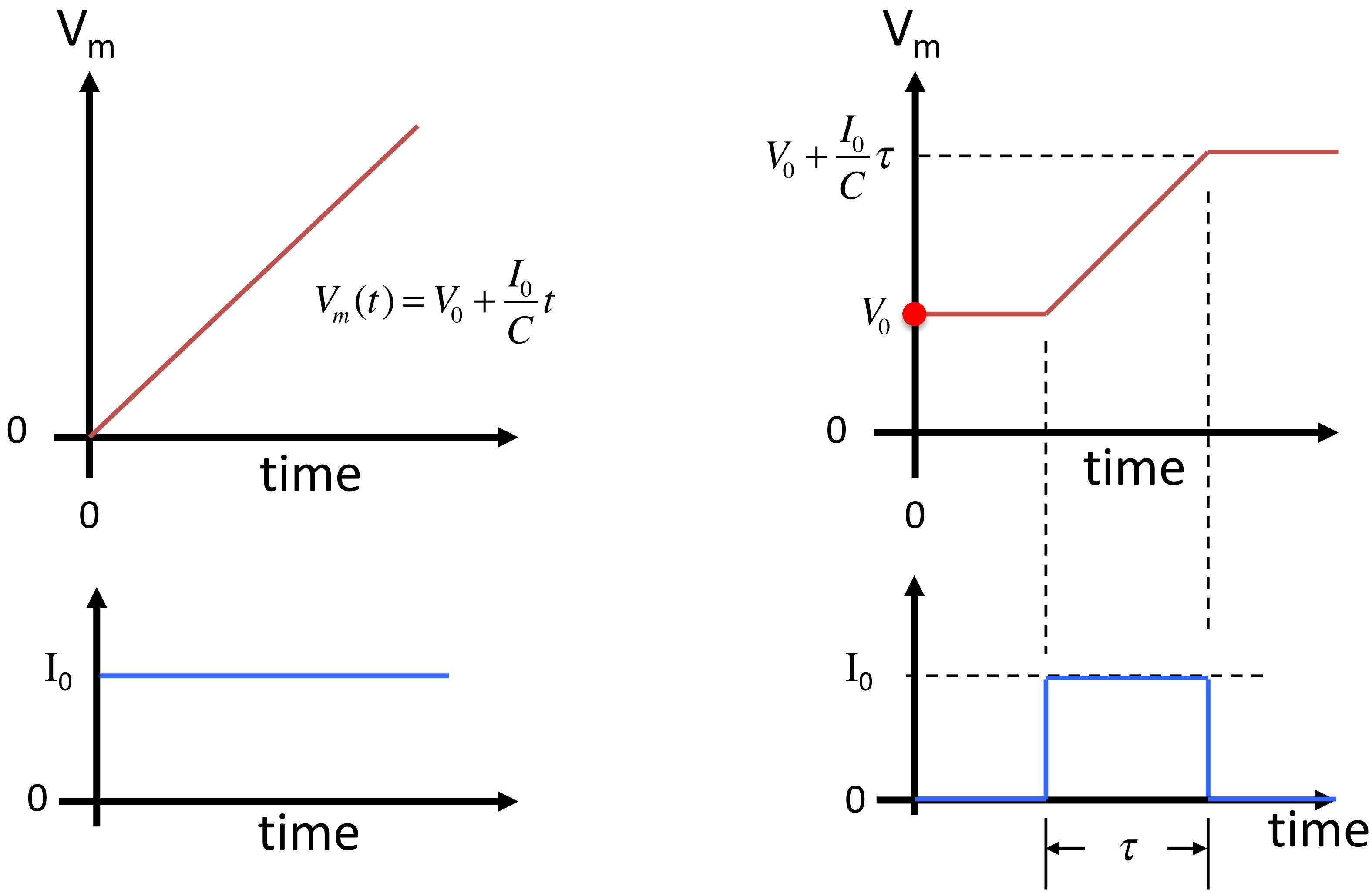
$$V_m(t) = V_0 + \frac{1}{C}\underbrace{\int_0^t I_e(\tau)d\tau} \qquad \int_0^t I_e(\tau)d\tau \ = \ \Delta Q$$

Think about the integral as adding up all the current from time 0 to time t

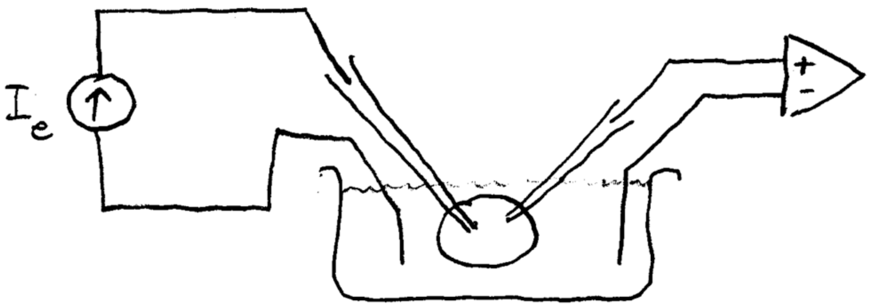
Thus, the total change in voltage is just given by

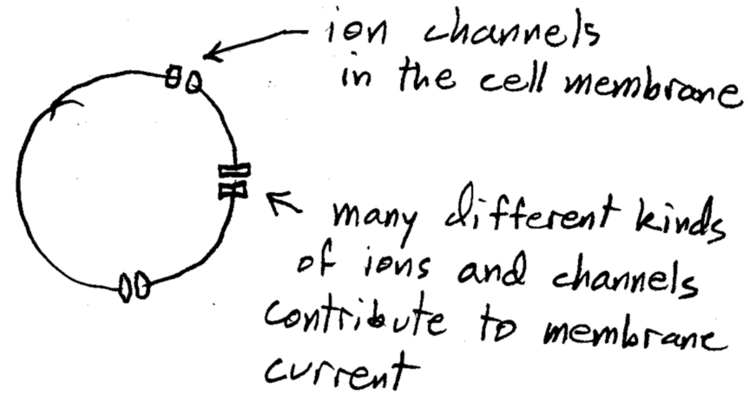
$$\Delta V = \frac{1}{C}\Delta Q$$

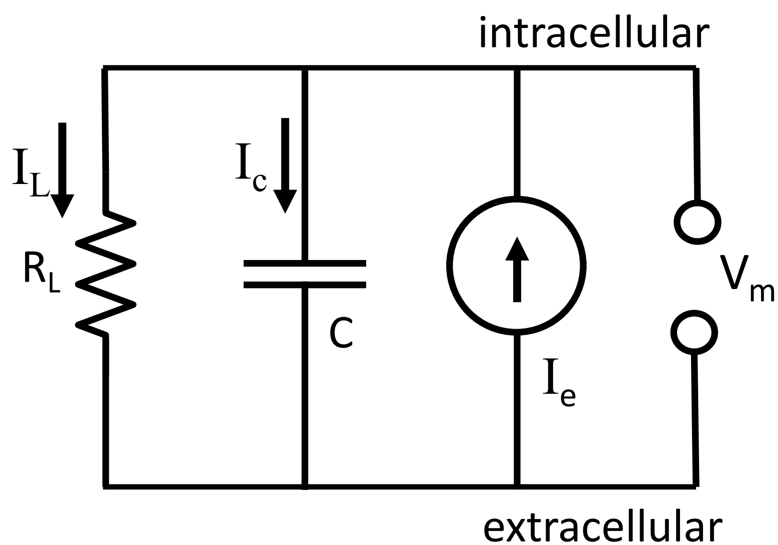
Some examples



A neuron is a leaky capacitor





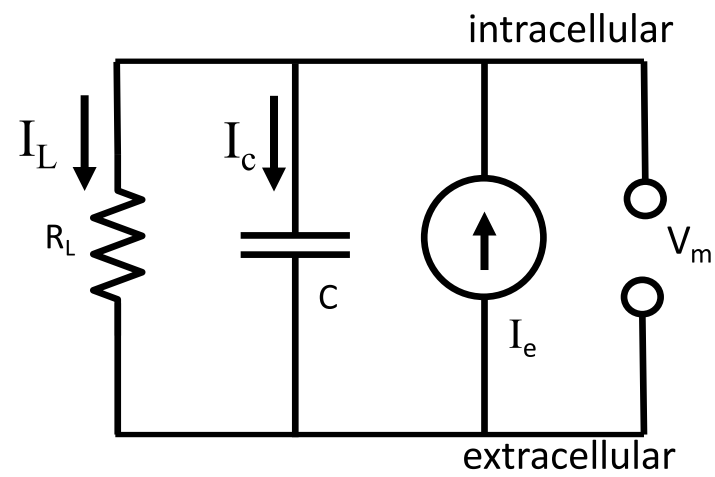


I_c = membrane capacitive current

I_L = membrane ionic current

Our equation for our model becomes:

$$I_L + I_c = I_e$$



$$I_L \quad + \quad C\frac{dV}{dt} \quad = \quad I_e$$

electrode current

membrane capacitive current

membrane ionic current

outward current
'+' leaving the cell $\Rightarrow$ positive

inward current
'+' entering the cell $\Rightarrow$ negative

Simple case: a leak

- We are going to begin by considering the simplest case of a membrane current – a simple leak (like a hole in the membrane)

- In this case, the current through the ion channel can be modeled using Ohm's Law

$$I_L = \frac{V_m}{R_L}$$

Plugging this into our equation above, we get

$$I_L + I_c = I_e$$

$$\frac{V_m}{R_L} + C\frac{dV_m}{dt} = I_e$$

Multiplying by R_L, we get:

$$V_m + R_L C\frac{dV_m}{dt} = R_L I_e$$

$$V_m + R_L C \frac{dV_m}{dt} = R_L I_e$$

What is the steady-state solution to this equation?

Set $dV_m / dt = 0$

We find that:

$$V_m \quad \Rightarrow \quad V_\infty = R_L I_e$$

Thus, we can rewrite our equation as follows

$$V_m + \tau \frac{dV_m}{dt} = V_\infty \qquad \text{where} \quad \tau = R_L C$$

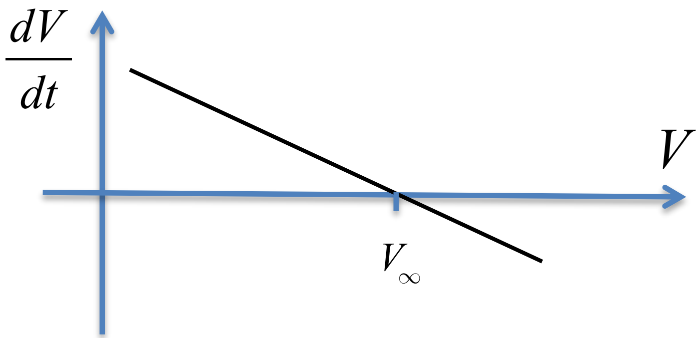
An aside about first-order linear differential equations

We can rewrite our equation in the following form:

$$\frac{dV}{dt} = -\frac{1}{\tau}\left(V - V_\infty\right)$$

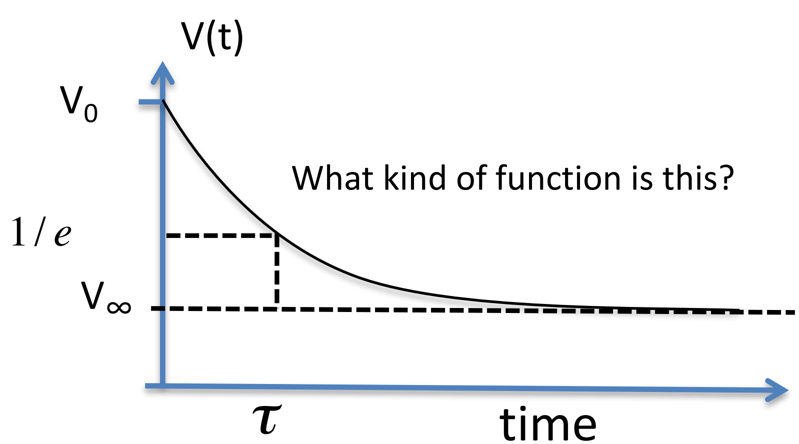
We see that the derivative is

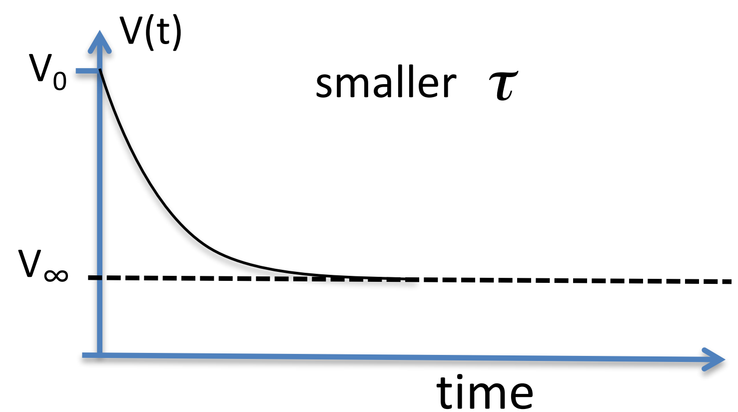
- negative if $V > V_\infty$
- positive if $V < V_\infty$



Thus, the voltage always approaches the value V_∞

And it approaches at a rate proportional to how far V is from V_∞





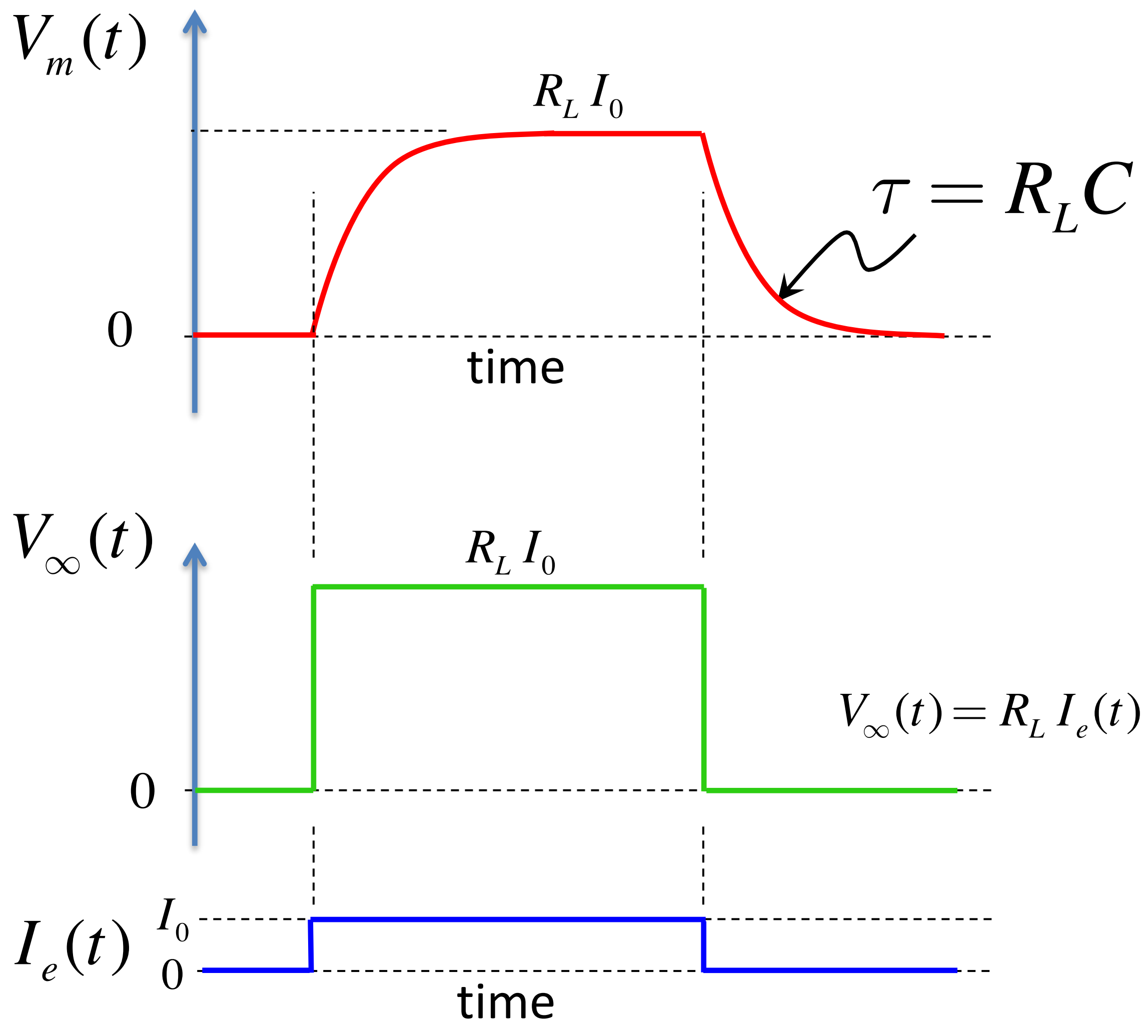
Thus, under the condition that I_e is constant (and thus V_∞) is constant:

$$V(t) - V_\infty = (V_0 - V_\infty)e^{-t/\tau}$$

While this solution applies only in the case of constant V_∞, it can be very useful

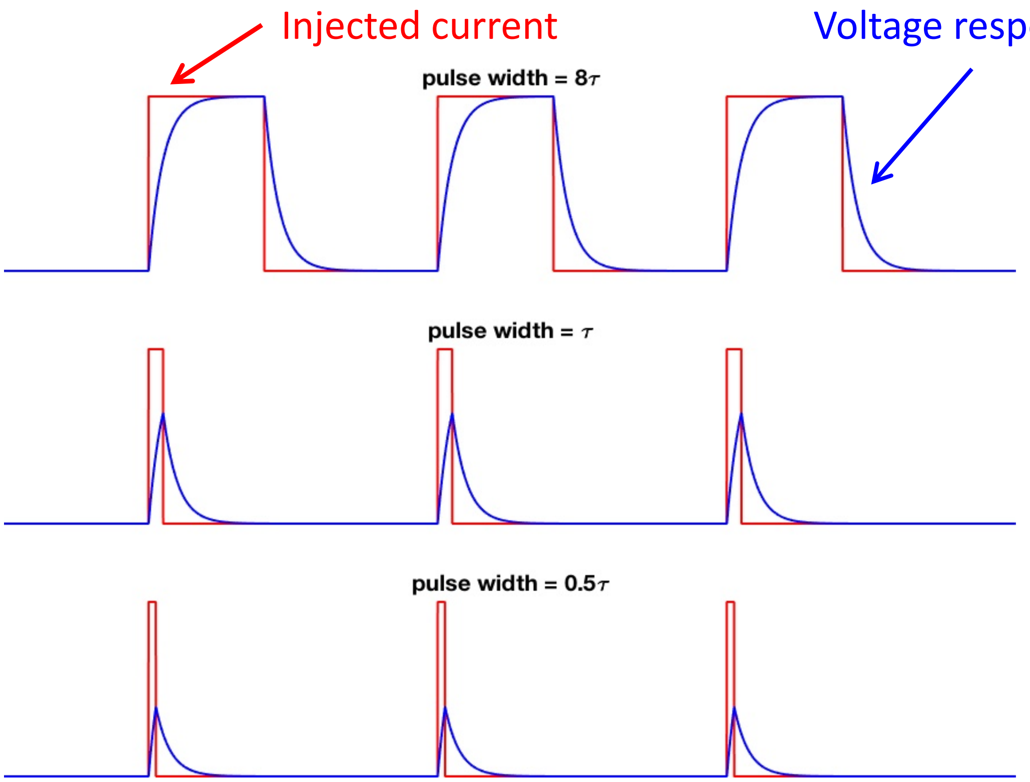
Response to current injection

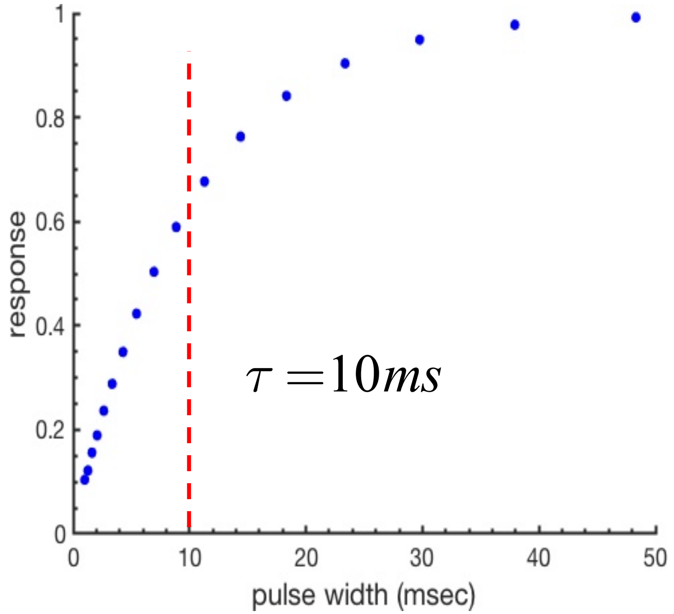
Let's see what happens when we inject current into our model neuron with a leak conductance.



An RC neuron acts like a filter

Responding well to inputs slower than τ, but not to inputs faster than τ





The first-order linear differential equation is fundamental to understanding many processes in physics, chemistry, biology and neural computation

$$V + \tau \frac{dV}{dt} = V_\infty$$

$$V(t) = V_\infty + (V_0 - V_\infty) e^{-t/\tau}$$

Even more complex systems involve differential equations that are not (much) more difficult to understand and solve.

Origin of 10 millisecond time scale

$$R \approx 10^8\,\Omega = 100\,M\Omega$$

$$C \approx 10^{-10}\,F$$

$$\tau = RC \sim 10\,ms$$

A closer look at membrane resistance

We have described the relation between voltage and current using Ohms Law ($V=I_L R_L$)

$$I_L = R_L^{-1} V$$

We can rewrite Ohm's Law in terms of a quantity called 'conductance.'

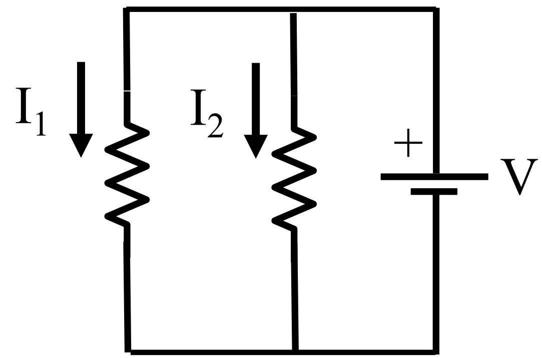
$$G_L = R_L^{-1}$$

$$I_L = G_L V$$

R_L has units of Ohms (Ω)

G_L has units of Ohms^{-1} or Siemens (S)

Conductances in parallel add



$$I_{tot} = I_1 + I_2$$

$$I_{tot} = G_1 V + G_2 V$$

$$I_{tot} = (G_1 + G_2) V$$

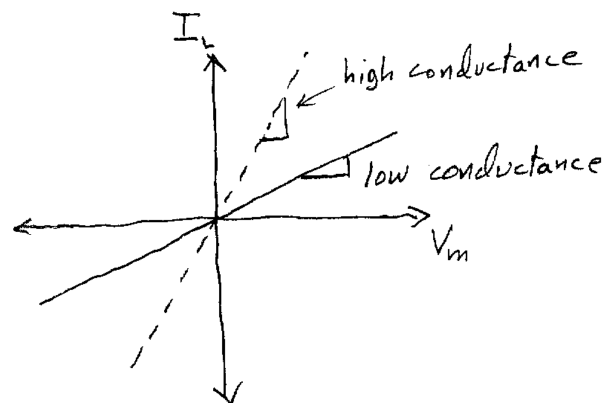
$$G_{tot} = G_1 + G_2$$

Twice the area, twice the holes, twice the conductance, twice the current at a given voltage

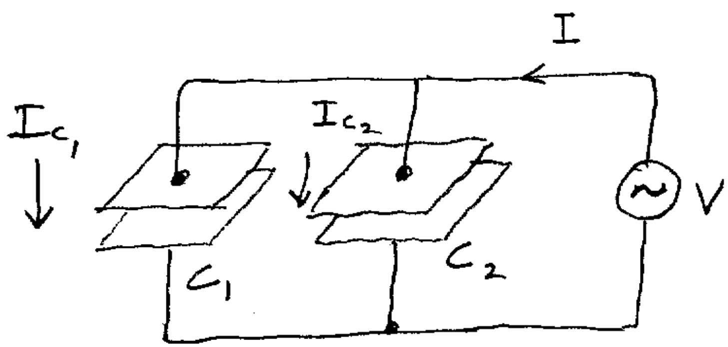
$$I_L = G_L V_m$$
$$= A\, g_L V_m$$

Specific leak conductance (mS/mm^2)

Membrane area (mm^2)



A closer look at membrane capacitance



$$I_{Ctot} = I_{C1} + I_{C2}$$

$$I_{Ctot} = C_1 \frac{dV}{dt} + C_2 \frac{dV}{dt}$$

$$I_{Ctot} = (C_1 + C_2) \frac{dV}{dt}$$

$$C_{tot} = C_1 + C_2$$

Capacitances in parallel add!

Thus, the capacitance of a cell depends linearly on surface area

$$C = c_m A \qquad A = 4\pi r^2$$

membrane area

specific capacitance (10 nF/mm^2)

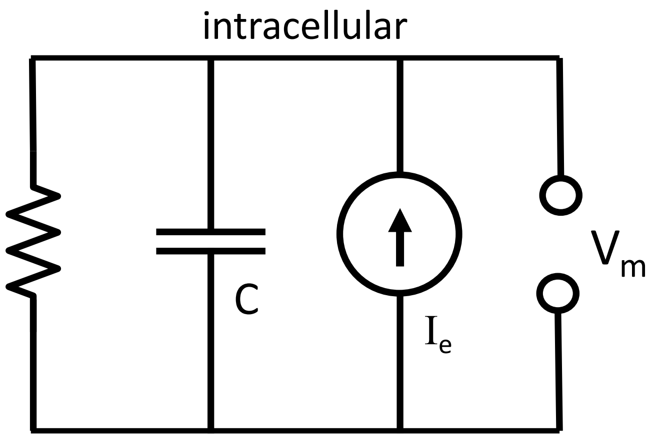
Membrane time constant

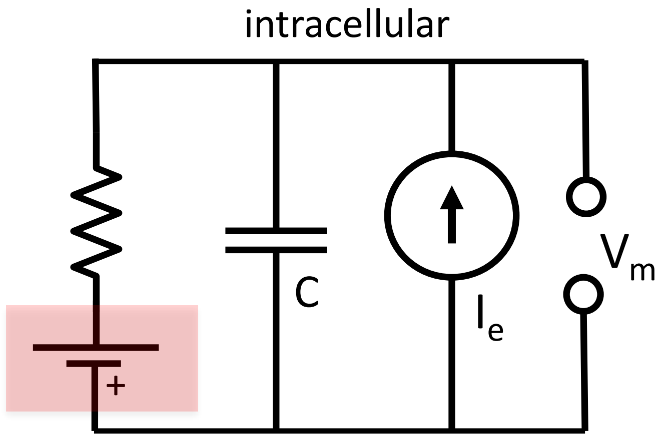
Neuron time constant:

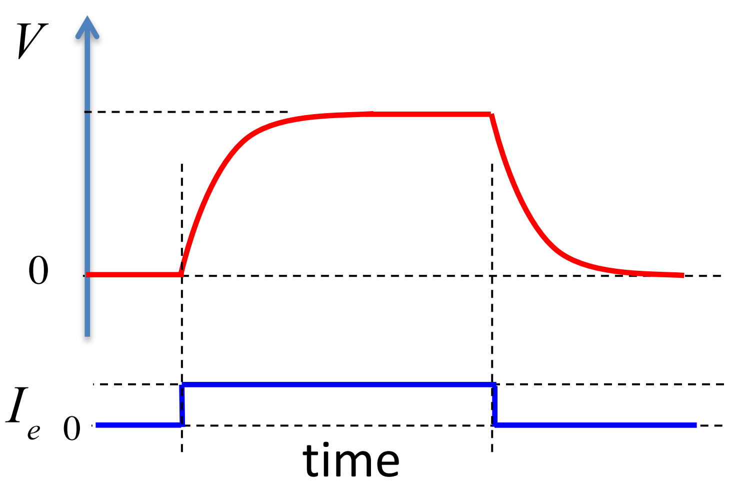
$$\tau_m = R_L C$$
$$= \frac{C}{G_L} = \frac{c_m A}{g_L A} = \frac{c_m}{g_L}$$

Thus, the time constant of a neuron is a property of the membrane, not dependent on cell geometry (size, shape, etc!).

Let’s add a battery to our neuron!

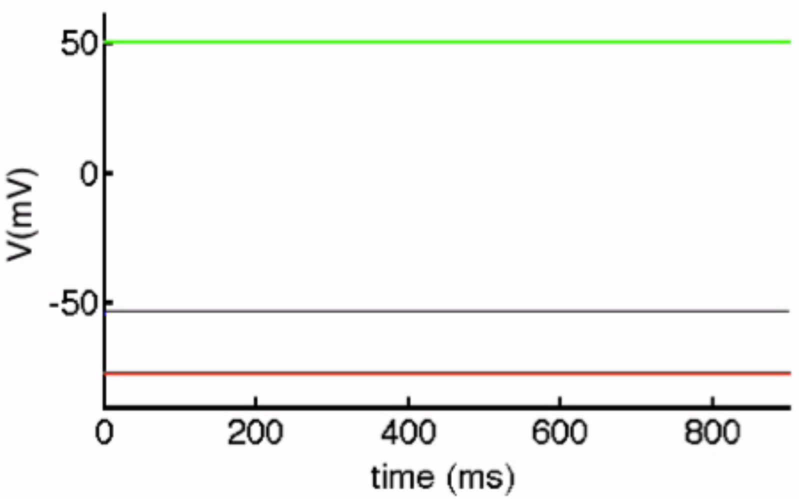


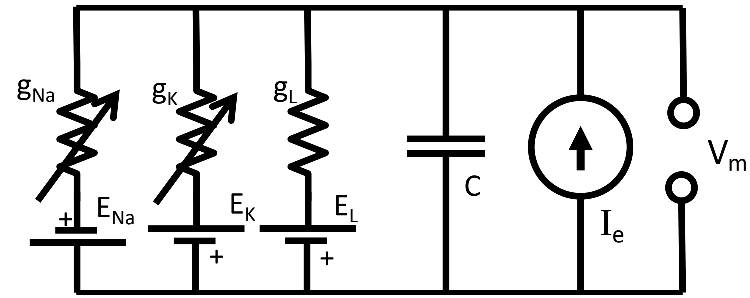




Outline of HH model

Voltage and time-dependent ion channels are the 'knobs' that control membrane potential.



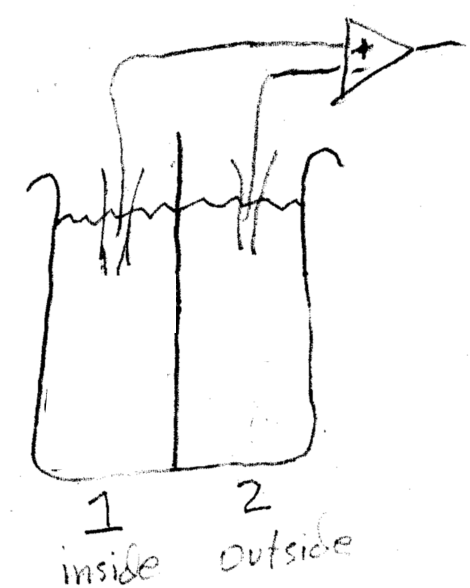


- Some ion channels push the membrane potential positive.
- Other ion channels push the membrane potential negative.
- Together these channels give the neural machinery flexible control of voltage!

Where do the batteries of a neuron come from?

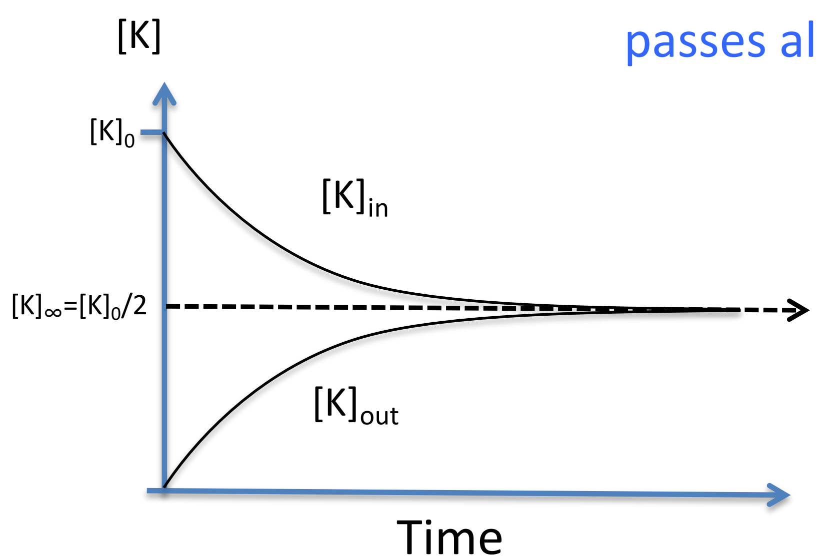
1) Ion concentration gradients

2) Ion-selective permeability of ion channels

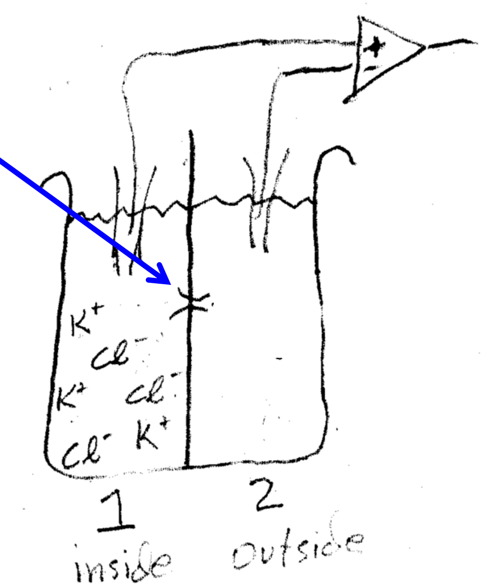


Neurons have batteries

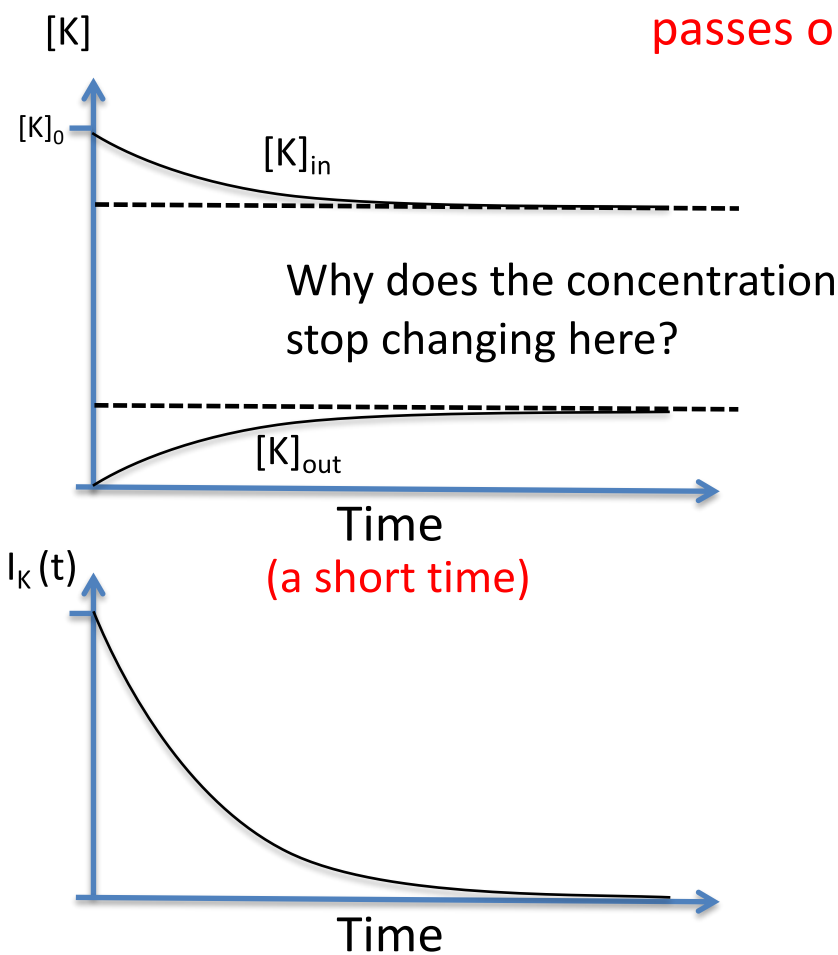
'Non-selective' pore
passes all ions



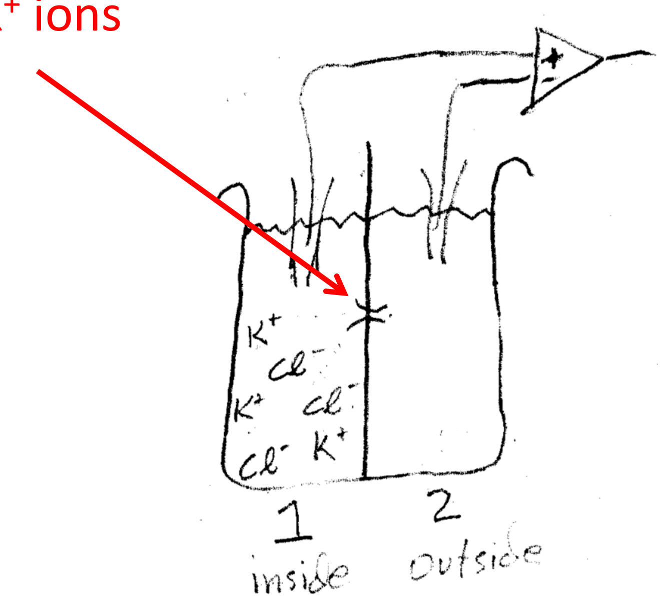
(a long time)



Neurons have batteries



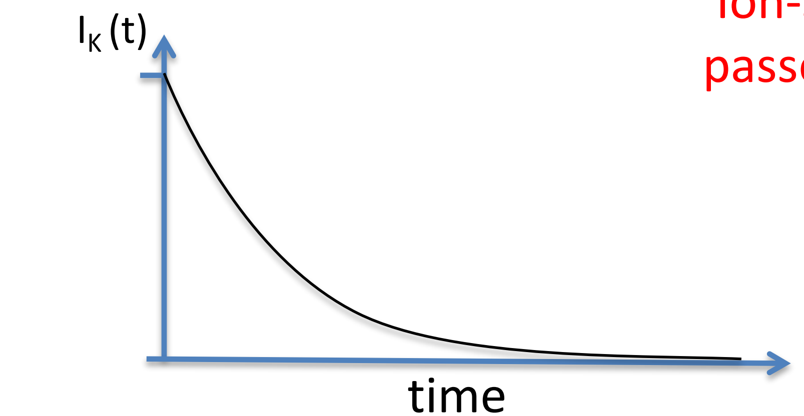
'Ion-selective' pore passes only K^+ ions

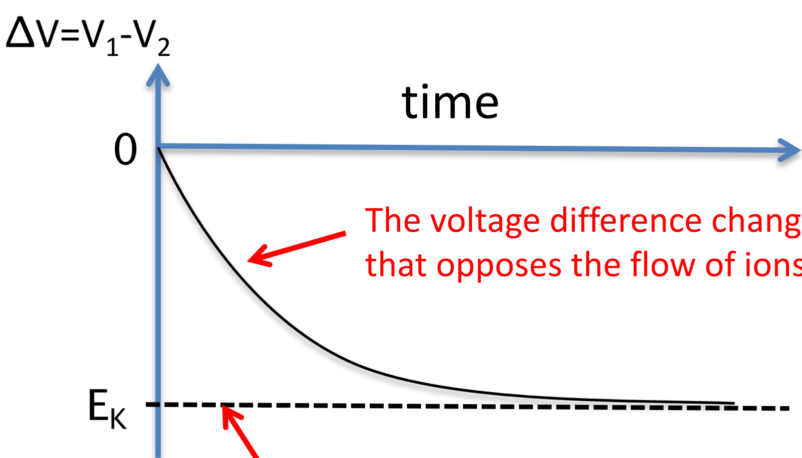


Why do the ions stop flowing from side 1 to side 2?

Neurons have batteries

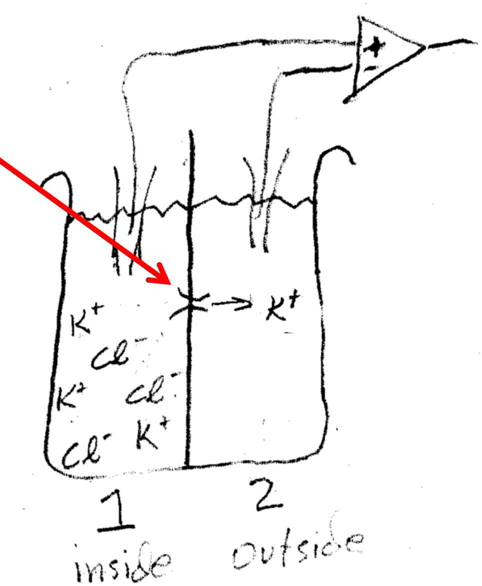
‘Ion-selective’ pore passes only K^+ ions





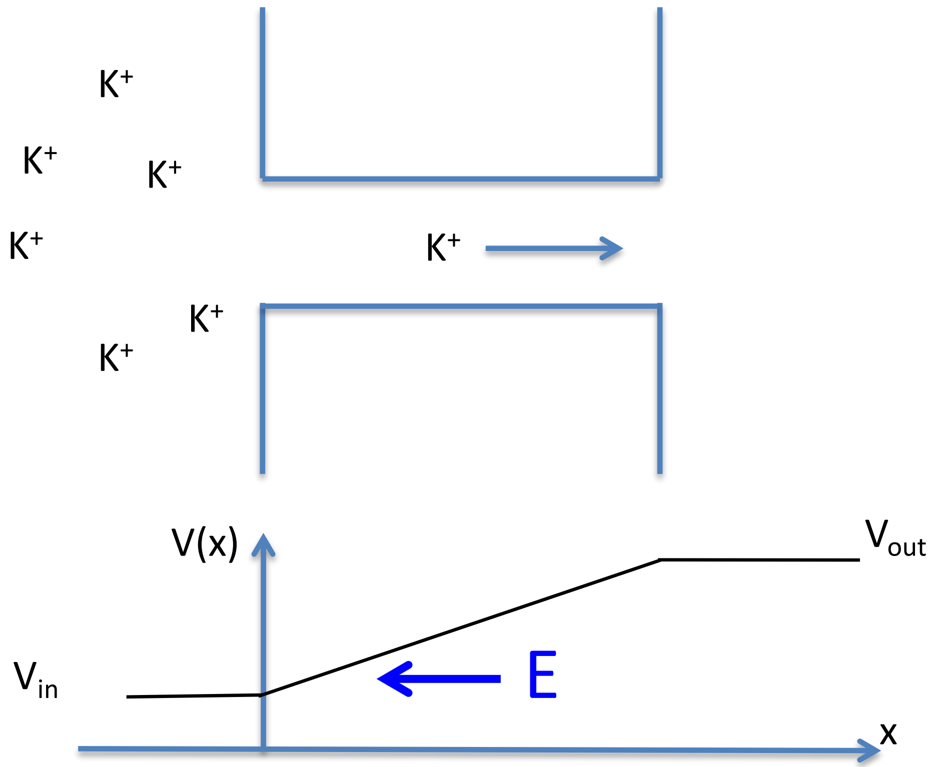
The voltage difference changes in a direction that opposes the flow of ions.

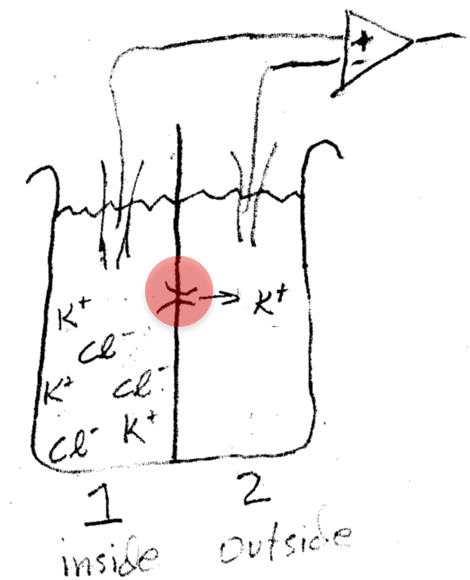
It reaches an ‘equilibrium potential’ at a value that gives zero net flow of ionic current.



This voltage difference is a battery for our model neuron!!

Neurons have batteries





There will be some electric field strength such that the 'drift' will exactly balance the diffusion produced by the concentration gradient…

Nernst Potential

Neurons have batteries

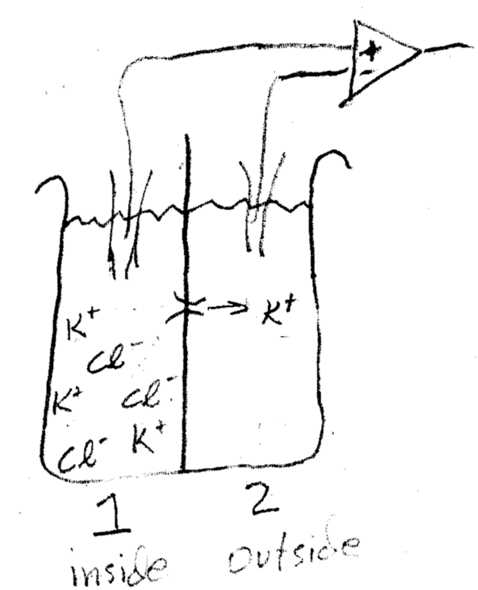
- Where do the 'batteries' of a neuron come from?

  1) Ion concentration gradients

  2) Ion-selective pores (channels)

- How big is the battery (how many volts?)

  This is determined by a balance between diffusion down a concentration gradient balanced by 'drift' in the opposing electric field.



Electrodiffusion and the Nernst Potential

One can use Ohm's law and Fick's first law to derive the Nernst potential

— At this voltage, the drift current in the electric field exactly balances current due to diffusion

$$I_{Tot} = I_{Drift} + I_{Diffusion} = 0$$

Ohm's Law

$$I_{Drift} = \frac{Aq^2\varphi(x)D}{kT}\frac{\Delta V}{L}$$

Fick's First Law

$$I_{Diffusion} = -AqD\frac{\partial\varphi}{\partial x}$$

$$\Delta V = \frac{kT}{q}\ln\left(\frac{\varphi_{out}}{\varphi_{in}}\right)$$ at equilibrium

Derive Nernst potential using the Boltzmann equation

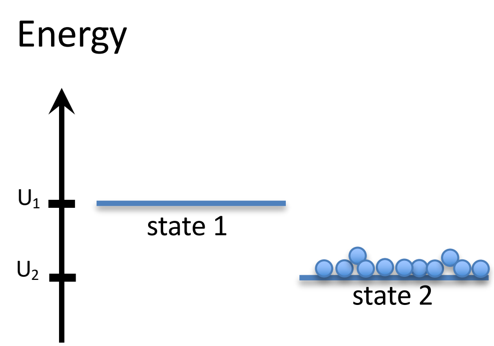
The Boltzmann equation describes the ratio of probabilities of a particle being in any two states, at thermal equilibrium:

$$\frac{P_{state1}}{P_{state2}} = e^{-\left(\frac{U_1 - U_2}{kT}\right)}$$

$k =$ Boltzmann constant (J/K)

$T =$ temperature (K) = 273 + T_C

$kT =$ thermal energy (J)



$kT = 0$

$$\frac{P_{state1}}{P_{state2}} = 0$$

Derive Nernst potential using the Boltzmann equation

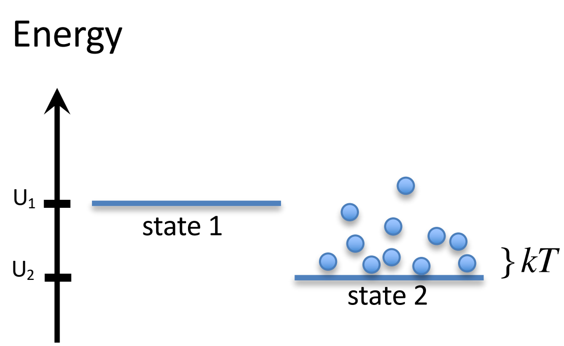
The Boltzmann equation describes the ratio of probabilities of a particle being in any two states, at thermal equilibrium:

$$\frac{P_{state\,1}}{P_{state\,2}} = e^{-\left(\frac{U_1 - U_2}{kT}\right)}$$

$k =$ Boltzmann constant (J/K)

$T =$ temperature (K)

$kT =$ thermal energy (J)



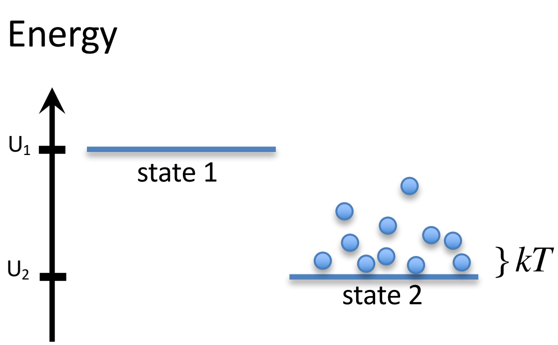
$kT > 0$

$$\frac{P_{state\,1}}{P_{state\,2}} > 0$$

Derive Nernst potential using the Boltzmann equation

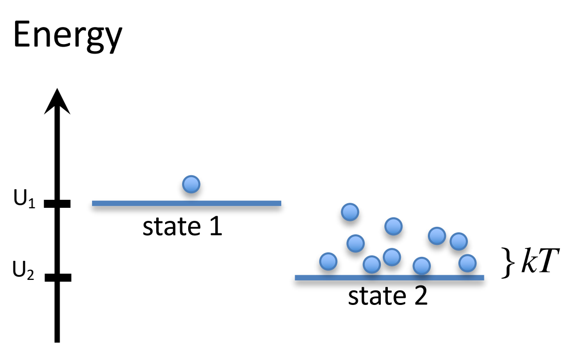
The Boltzmann equation describes the ratio of probabilities of a particle being in any two states, at thermal equilibrium:

$$\frac{P_{state1}}{P_{state2}} = e^{-\left(\frac{U_1 - U_2}{kT}\right)}$$



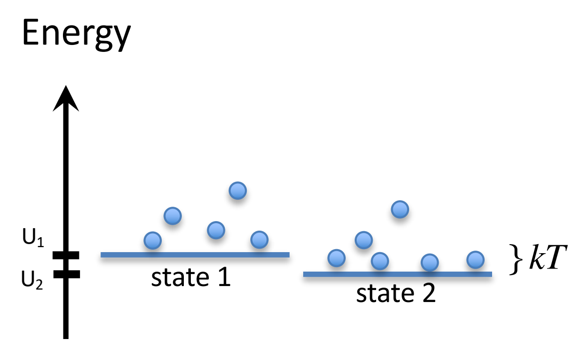
$\Delta U >> kT$

$$\frac{P_{state1}}{P_{state2}} \approx 0$$



$\Delta U = 2kT$

$$\frac{P_{state1}}{P_{state2}} = e^{-2}$$



$\Delta U < kT$

$$\frac{P_{state1}}{P_{state2}} \approx 1.0$$

Nernst Potential

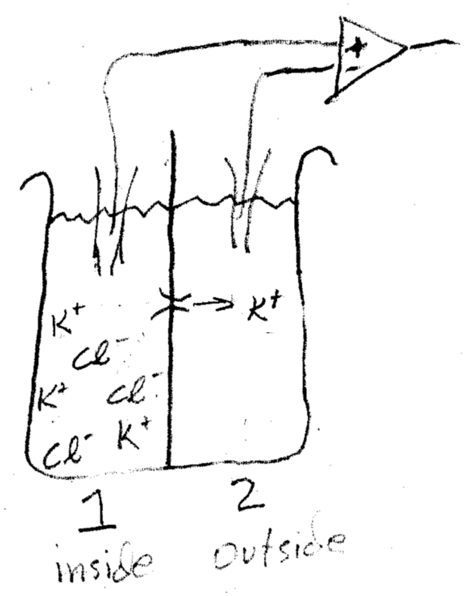
We can compute the equilibrium potential using the Boltzmann equation:

$$\frac{P_{in}}{P_{out}} = e^{-\frac{U_{in}-U_{out}}{kT}} = e^{-\frac{q(V_{in}-V_{out})}{kT}}$$

$U = qV =$ electrical potential (J)

$q =$ charge of ion

$q =$ 1.6x10^{-19}C for monovalent ion



Nernst Potential

We can compute the equilibrium potential using the Boltzmann equation:

$$\frac{P_{in}}{P_{out}} = e^{-\frac{U_{in}-U_{out}}{kT}} = e^{-\frac{q(V_{in}-V_{out})}{kT}}$$

$U = qV =$ electrical potential (J)

$q =$ charge of ion

$q = 1.6\text{x}10^{-19}\text{C}$ for monovalent ion

$$V_{in} - V_{out} = -\frac{kT}{q}\ln\left(\frac{P_{in}}{P_{out}}\right)$$

$$\frac{kT}{q} = 25mV \text{ for monovalent ion}$$

$$\Delta V = V_{in} - V_{out} = 25mV\ \ln\left(\frac{P_{out}}{P_{in}}\right)$$

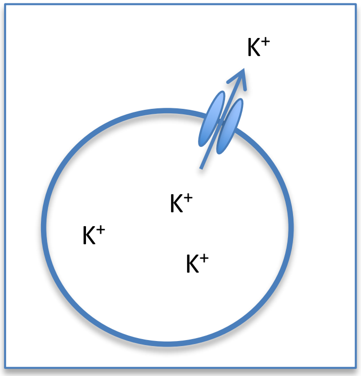
$$\Delta V = 25mV\ln\left(\frac{[K]_{out}}{[K]_{in}}\right) = E_K$$

Don't get confused by this notation. E_K is the equilibrium potential (voltage) for the K ion.
'E' here does not refer to an electric field.

The Nernst potential for potassium

Intracellular and extracellular concentrations of ionic species, and the Nernst potential

Ion	Cytoplasm (mM)	Extracellular (mM)	Nernst (mV)
K^+	400	20	-75

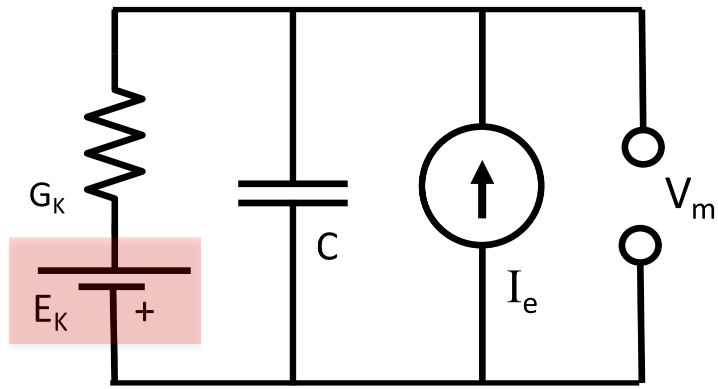


$$E_k = \frac{kT}{q} \ln\left(\frac{20}{400}\right)$$

$\frac{kT}{q}$ = 25mV at 300K (room temp) for monovalent ion

$$E_K = 25mV(-3.00) = -75mV$$

How to implement an ion specific conductance as a battery in our model neuron



Learning objectives for Lecture 2

- To understand how membrane capacitance and resistance allows neurons to integrate or smooth their inputs over time (RC model)
- To understand how to derive the differential equations for the RC model
- To be able to sketch the response of an RC neuron to different current inputs
- To understand where the 'batteries' of a neuron come from.

Extra notes on how to derive the Nernst potential using the equations for electrodiffusion

Electrodiffusion and the Nernst Potential

In the last lecture, we found that the relation between drift velocity and force for an ion in an electric field is:

$$\vec{F} = \frac{kT}{D}\vec{v}_d$$

where $f = {}^{kT}\!/_{D}$ is just the coefficient of friction given by the Einstein-Smoluchovski relation.

$\vec{F} = q\vec{E}$ = electric force on ion due to electric field E

q = total ion charge in Coulombs

$\vec{E}$ = electric field (V/m)

k =Boltzmann constant (J/K)

T =temperature (K)

kT =thermal energy (J)

D =diffusion constant (m^2/s)

Electrodiffusion and the Nernst Potential

Thus, we can write the drift velocity as:

$$v_d = \frac{qD}{kT}E$$

$\frac{qD}{kT}$ is the ion mobility, which describes how fast an ion will move in an electric field - (m/s)/(V/m)

We can find the total current density (amperes per unit area) as

$$\frac{I}{A} = q\,N_A c\,v_d$$

$N_A c$ = ion density (ions/m^3)

c = molar ion concentration (mol/m^3)

N_A = Avagadro's number (ions/mol)

Substituting v_d from above, we get that:

$$\frac{I}{A} = \frac{q^2 N_A D}{kT} cE$$

Electrodiffusion and the Nernst Potential

Next we use the fact the the electric field is the spatial derivative of the electrical potential (voltage)

$$\vec{E} = -\vec{\nabla} V, \qquad E_x = \frac{\partial V}{\partial x}$$

We can find the total current density (amperes per unit area) due to the electric field:

$$\frac{I}{A} = -\frac{q^2 N_A D}{kT} c \frac{\partial V}{\partial x}$$

Electrodiffusion and the Nernst Potential

Put it all together and we get

$$\left[\frac{I}{A}\right]_{Tot} = -qN_A D\left[\frac{q}{kT}c\frac{\partial V}{\partial x} + \frac{\partial c}{\partial x}\right]$$

This has units of current per unit area (Amperes/m^2)

We know that at equilibrium, the total current is zero. Thus,

$$\frac{q}{kT}c\frac{\partial V}{\partial x} + \frac{\partial c}{\partial x} = 0$$

q = charge of a single ion
c = molar concentration (mol/m^3)
N_A = Avagadro's number

A good reference for this derivation is Hille's chapter on 'Elementary Properties of Ions in Solution' (p. 261-269 of the second edition)

Electrodiffusion and the Nernst Potential

Divide through by c and q/kT and we get

$$\frac{\partial V}{\partial x} + \left(\frac{kT}{q}\right)\frac{1}{c}\frac{\partial c}{\partial x} = 0$$

Use the fact that $\frac{\partial \ln c(x)}{\partial x} = \frac{1}{c(x)}\frac{\partial c(x)}{\partial x}$

$$\frac{\partial V}{\partial x} + \left(\frac{kT}{q}\right)\frac{\partial \ln c(x)}{\partial x} = 0$$

Electrodiffusion and the Nernst Potential

Now we can integrate both terms

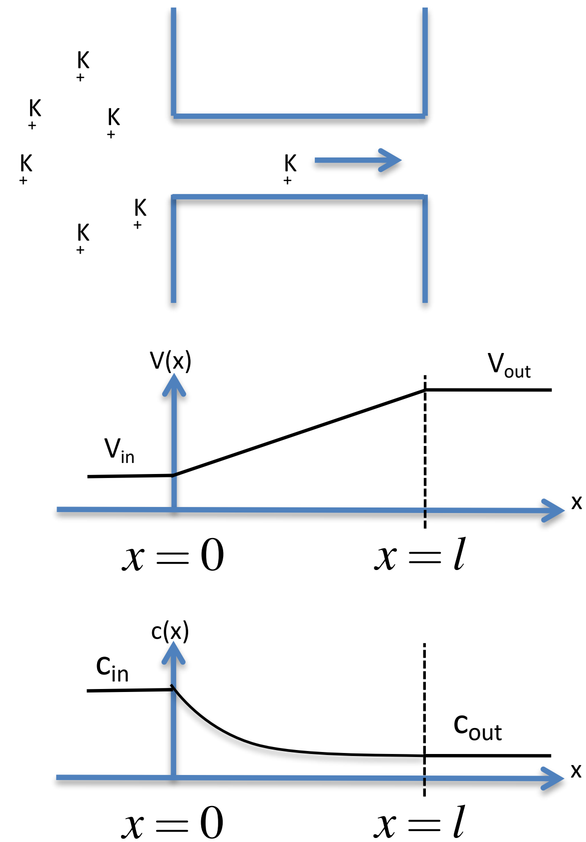
$$V(x)\Big|_{x=0}^{x=l} + \left(\frac{kT}{q}\right)\ln c(x)\Big|_{x=0}^{x=l} = 0$$

$$V_{out} - V_{in} = -\left(\frac{kT}{q}\right)\left[\ln c_{out} - \ln c_{in}\right]$$

$$\Delta V = \frac{kT}{q}\ln\left(\frac{c_{out}}{c_{in}}\right), \text{ where } \Delta V = V_{in} - V_{out}$$

at equilibrium

Don’t get confused by this notation. E_K is the equilibrium potential (voltage) for the K ion. ‘E’ here does not refer to an electric field.



$$c(x) = c_{in} e^{-\frac{x}{l}\ln\left(\frac{c_{out}}{c_{in}}\right)}$$