Introduction to Neural Computation

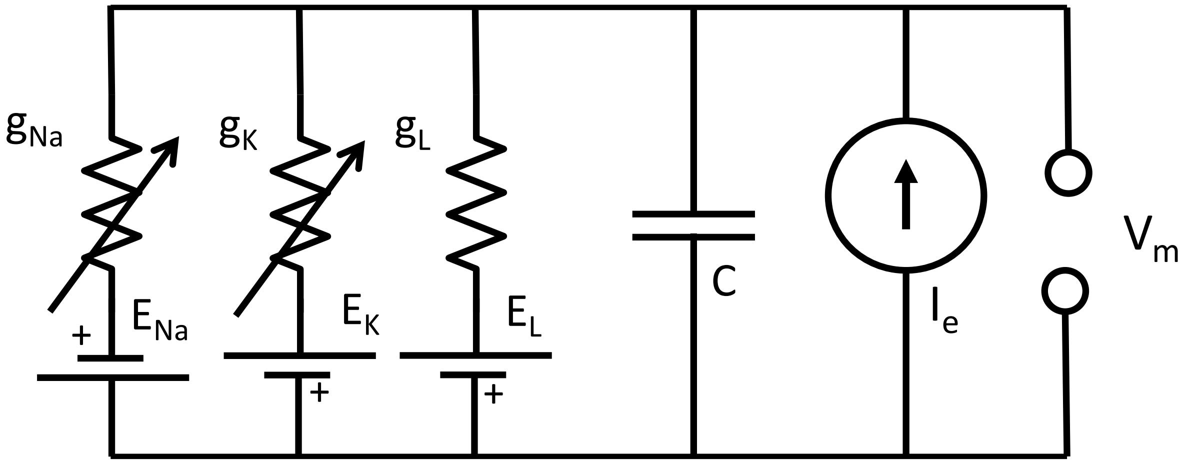
Michale Fee

MIT BCS 9.40 — 2018

Lecture 1 – Ionic Currents

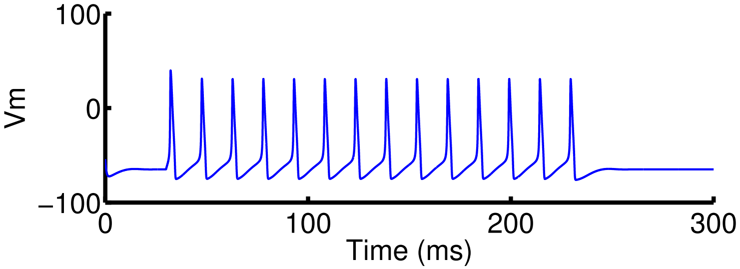
A mathematical model of a neuron

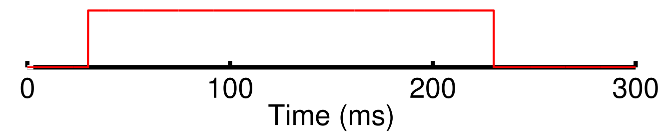
- Equivalent circuit model



- A conceptual model based on simple components from electrical circuits

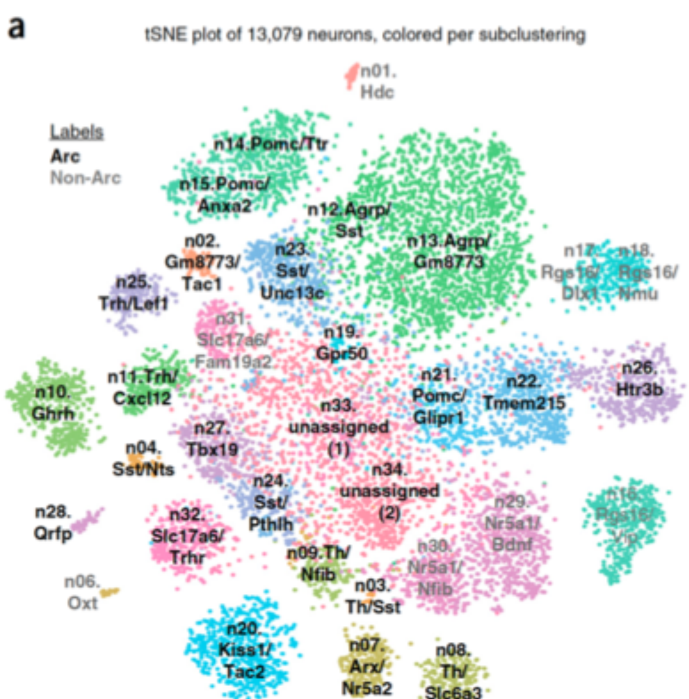
- A mathematical model that we can use to calculate properties of neurons

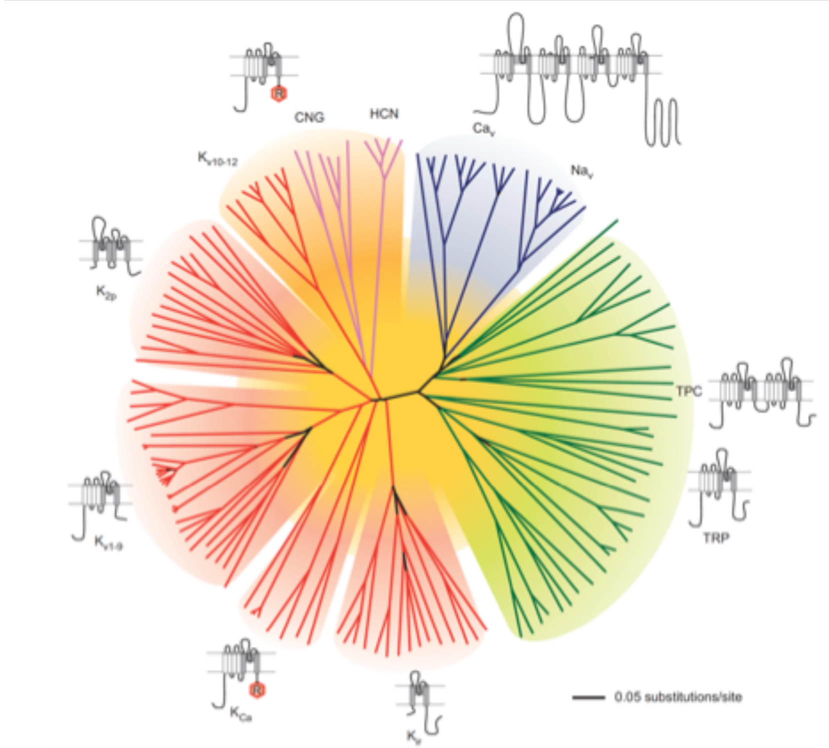




Why build a model of a neuron?

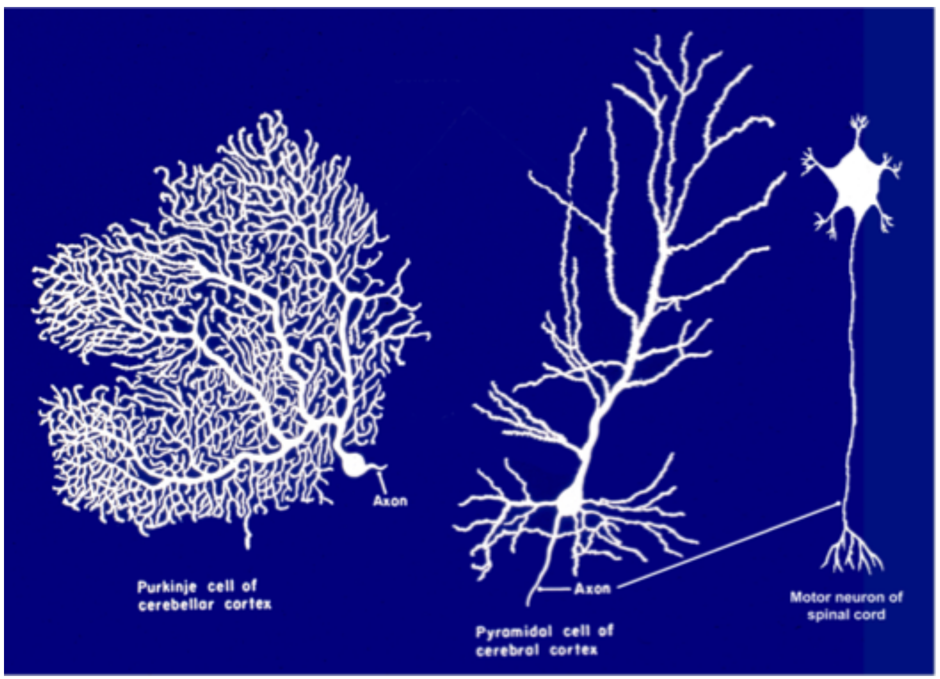
- Neurons are very complex.
- Different neuron types are defined by the genes that are expressed and their complement of ion channels
- Ion channels have dynamics at different timescales, voltage ranges, inactivation

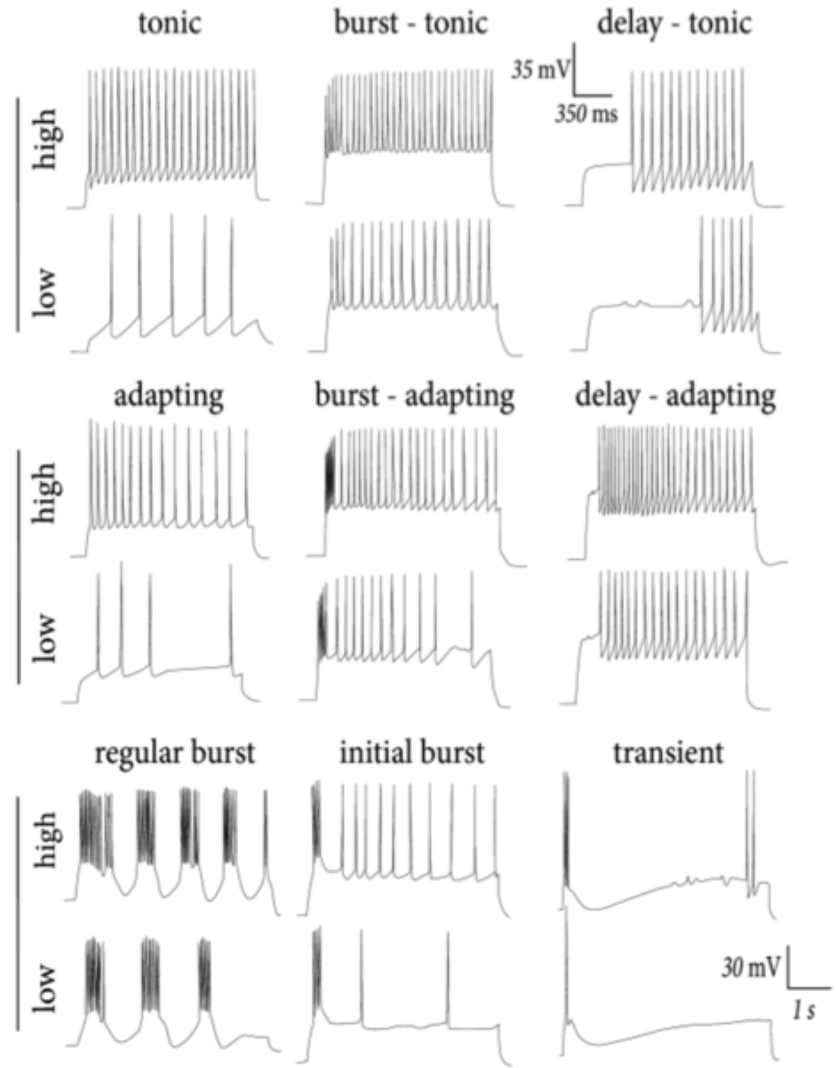




Neurons are extremely complex

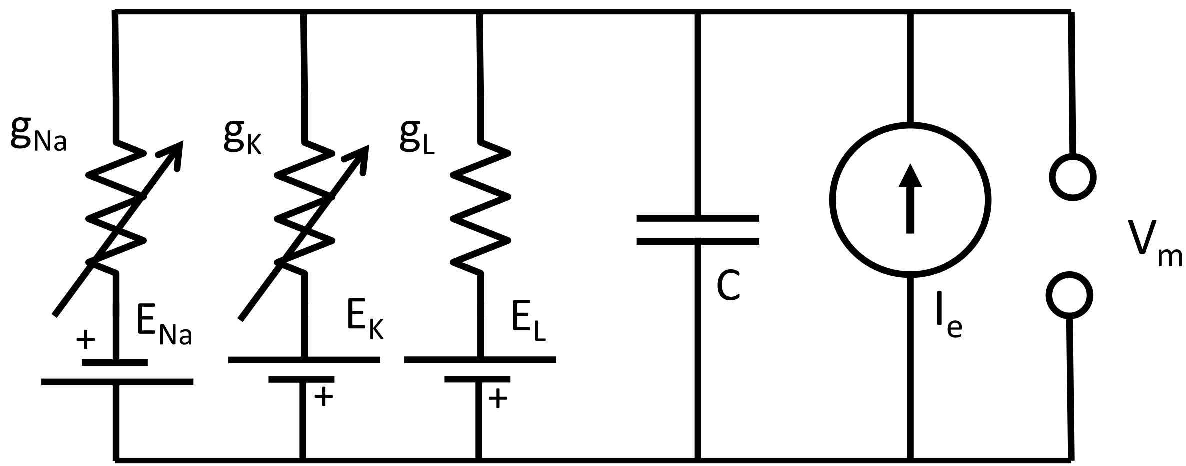
- Ion channel and morphological diversity lead to diversity of firing patterns
- It's hard to guess how morphology and ion channels lead to firing patterns
- … and how firing patterns control circuit behavior





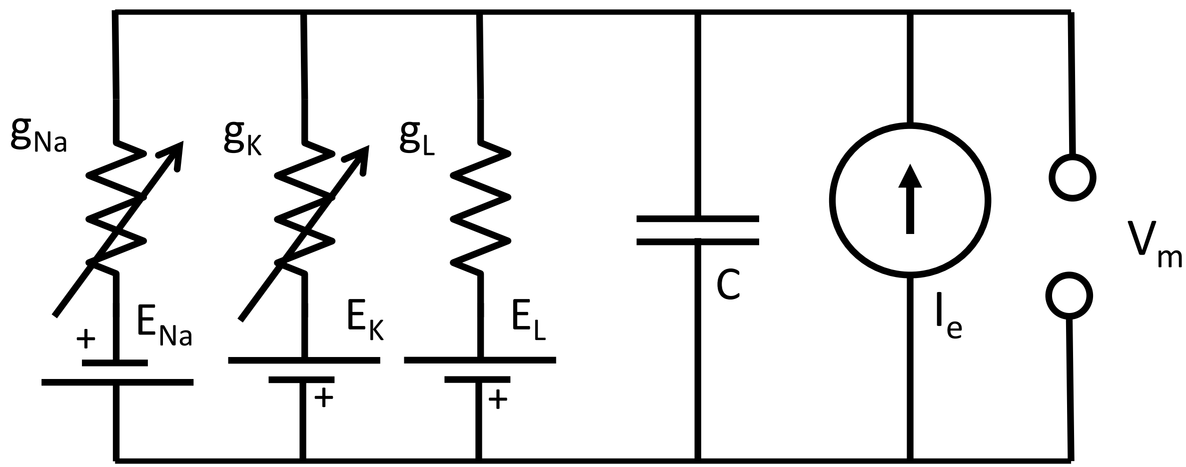
A mathematical model of a neuron

- Equivalent circuit model



- Different parts of this circuit do different interesting things
  – Power supplies
  – Integrator of past inputs
  – Temporal filter to smooth inputs in time
  – Spike generator
  – Oscillator

Ionic currents

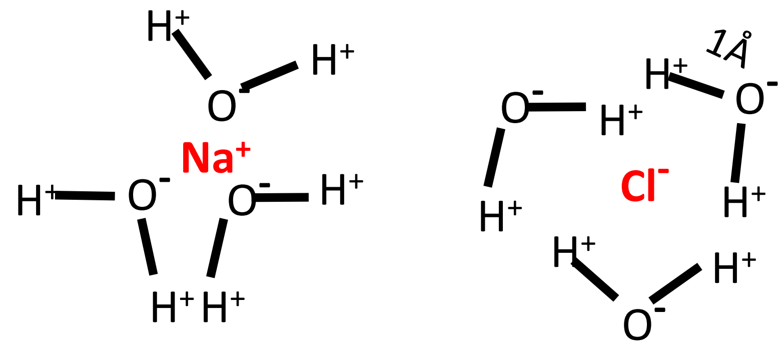


What are the wires of the brain?

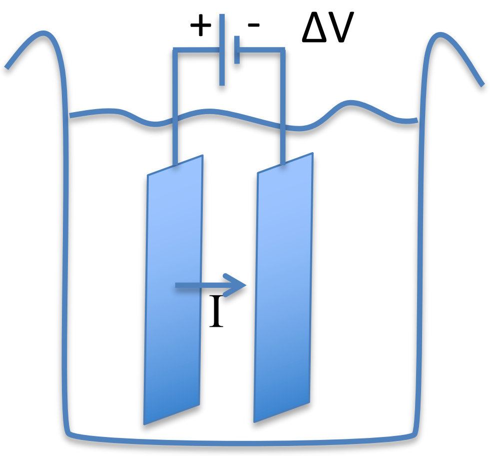
In the brain (in neurons), current flow results from the movement of ions in aqueous solution (water).

Basic electrochemistry

- Water is a polar solvent
- Intracellular and extracellular space is filled with salt solution (~100mM)
  - 6x10^{19} ions per cm^{3} (25Å spacing)



- Currents flow through a salt solution by two key mechanisms:
  - Diffusion
  - Drift in an electric field



Learning objectives for Lecture 1

- To understand how the timescale of diffusion relates to length scales

- To understand how concentration gradients lead to currents (Fick’s First Law)

- To understand how charge drift in an electric field leads to currents (Ohm’s Law and resistivity)

Thermal energy

- Every degree of freedom comes to thermal equilibrium with an energy proportional to temperature (Kelvin, K)

- The proportionality constant is the Boltzmann constant (k)

  $kT = 4x10^{-21}\ Joules$ at 300K)

- Kinetic energy : $\left\langle \frac{1}{2} m v_x^2 \right\rangle = \frac{1}{2} kT$ $\left\langle v_x^2 \right\rangle = \frac{kT}{m}$

- The mass of a sodium ion is 3.8×10^{-26} kg

$$\left\langle v_x^2 \right\rangle = 10^5 \mathrm{m}^2 / \mathrm{s}^2 \quad \Rightarrow \quad \bar{v}_x = 3.2 \times 10^2 \mathrm{m/s}$$

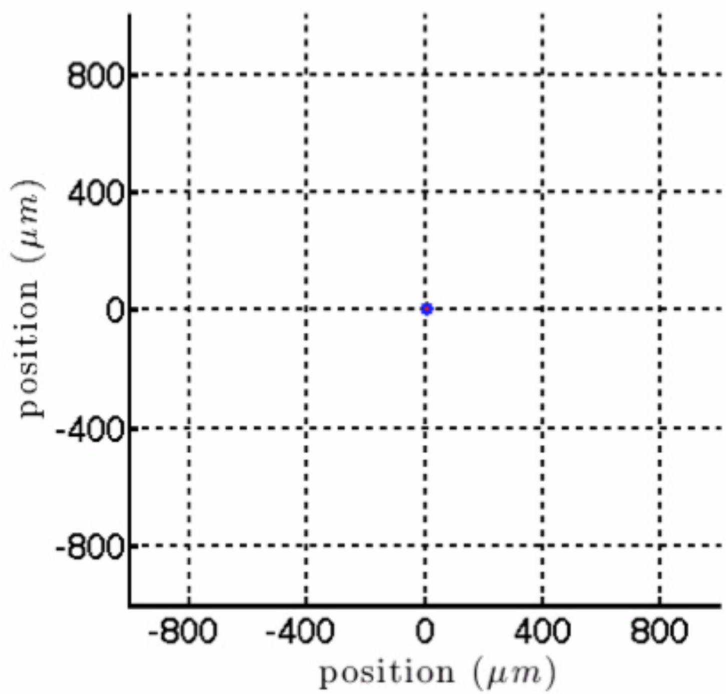
This would cross this 10m classroom in 3/10 second!

Here we follow 'Random Walks in Biology'
Howard C. Berg, Princeton Univ Press 1993

What is diffusion?

- A particle in solution undergoes collisions with water molecules very often (~10^{13} times per second!) that constantly change its direction of motion.

Collisions produce a 'random walk' in space



Spatial and temporal scales

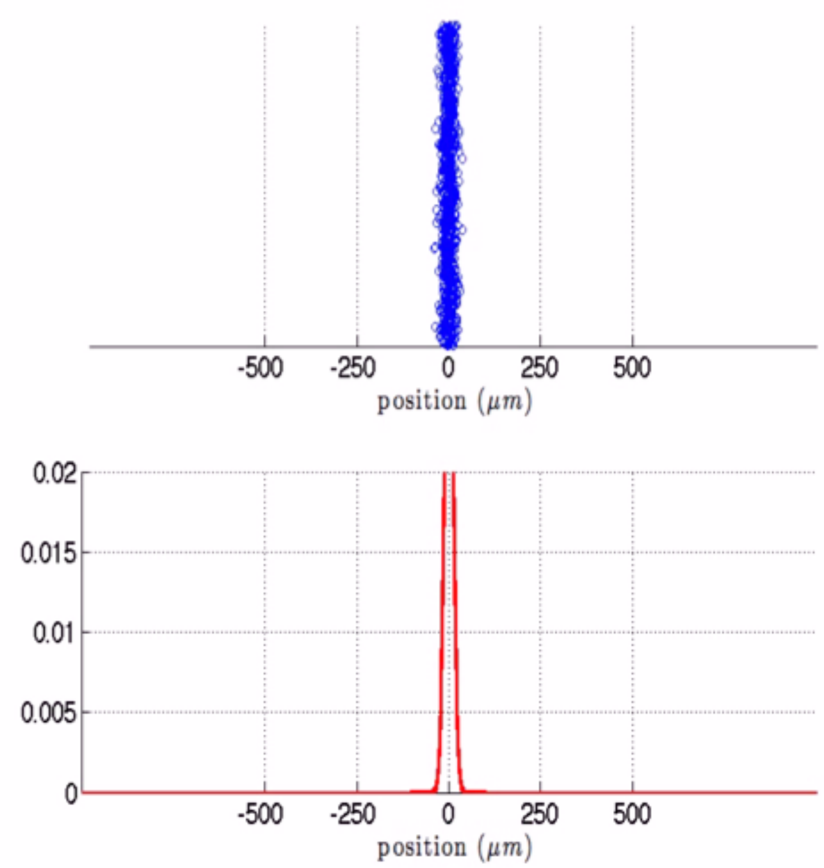
Diffusion is fast at short length scales and slow at long length scales.

- To diffuse across a cell body (10um) it takes an ion 50ms
- To diffuse down a dendrite (1mm) it takes about 10min
- How long does it take an ion to diffuse down a motor neuron axon (1m)?

10 years!

Distribution of particles resulting from diffusion in 1-D

- On average particles stay clustered around initial position
- Particles spread out around initial position
- We can compute analytically properties of this distribution!



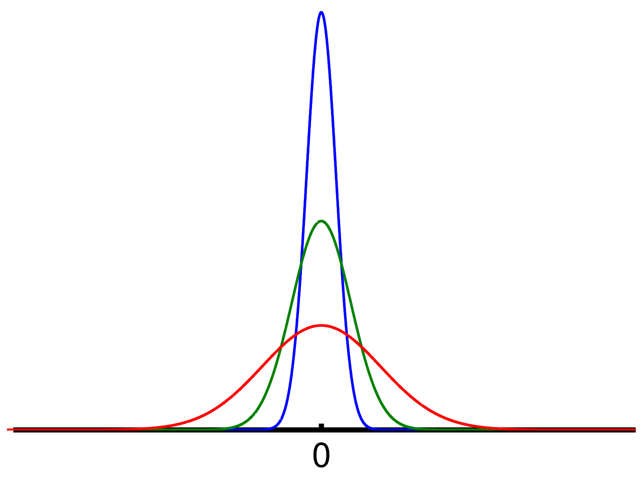
- An ensemble of particles diffusing from a point acquires a Gaussian distribution

- This arises from a binomial distribution for large number of time-steps (The probability of the particle moving exactly k steps to the right in n steps will be:

$$P(k;n,p)=\binom{n}{k}p^k(1-p)^{n-k}$$

$$\lim_{np\to\infty} P(k;n,p)=\frac{1}{\sqrt{4\pi Dt}}e^{-x^2/4Dt}$$

Gaussian Distribution



Random walk in one dimension

- We can mathematically analyze the properties of an ensemble of particles undergoing a random walk

- Consider a particle moving left or right at a fixed velocity v_x for a time τ before a collision.

- Imagine that each collision randomly resets the direction

- Thus, on every time-step,
  - half the particles step right by a distance $\delta = +v_x \tau$
  - and half the particles step to the left by a distance δ

Random Walk in 1-D

- Assume that we have N particles that start at position x=0 at time t=0
- $x_i(n)$ = the position of the i^{th} particle on time-step n: $n = t / \tau$
- Assume the movement of each particle is independent
- Thus, we can write the position of each particle at time-step n as a function of the position at previous time-step

$$x_i(n) = x_i(n-1) \pm \delta$$

- Use this to compute how the distribution evolves in time!

Average displacement is zero

- What is the average position of our ensemble?

$$\langle x_i(n)\rangle_i = \frac{1}{N}\sum_i x_i(n)$$

$$x_i(n) = x_i(n-1) \pm \delta$$

$$= \frac{1}{N}\sum_i \left[x_i(n-1) \pm \delta\right]$$

$$= \frac{1}{N}\sum_i \left[x_i(n-1)\right] \; + \; \cancelto{0}{\frac{1}{N}\sum_i (\pm\delta)}$$

$$\boxed{\langle x_i(n)\rangle_i = \langle x_i(n-1)\rangle_i}$$

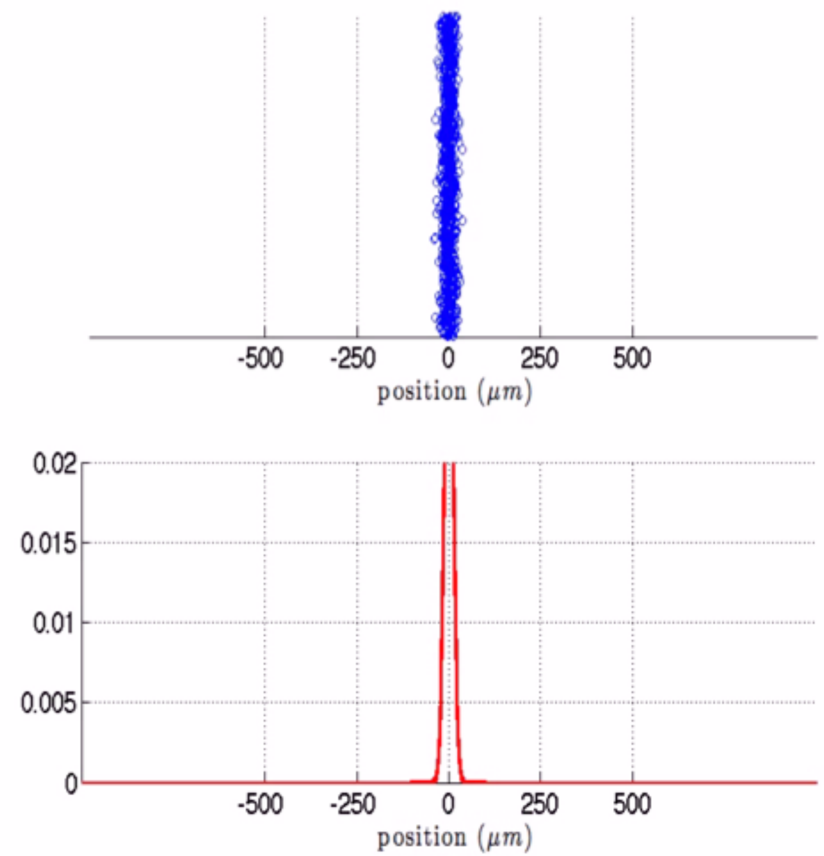
Here we follow ‘Random Walks in Biology’ Howard C. Berg, Princeton Univ Press 1993

Distribution of particles resulting from diffusion in 1-D

- On average particles stay clustered around initial position

- Particles spread out around initial position

- We can compute analytically properties of this distribution!



How far does a particle travel due to diffusion?

- We want to compute an average 'absolute value' distance from origin… Root mean square distance

$$\langle |x(n)| \rangle \qquad \rightarrow \sqrt{\langle x^2(n) \rangle}$$

$$x_i(n) = x_i(n-1) \;\pm\; \delta$$

$$x_i^2(n) = (x_i\,(n-1) \;\pm\; \delta)^2$$

$$= x_i^2(n-1) \;\pm\; 2\delta x_i(n-1) \;+\; \delta^2$$

Compute variance

$$\langle x^2(n) \rangle = \tfrac{1}{N} \sum_i x_i^2(n)$$

$$\langle x^2(n) \rangle = \langle x^2(n-1) \rangle \;+\; \cancelto{0}{\langle \pm 2\delta x_i(n-1) \rangle} \;+\; \langle \delta^2 \rangle$$

$$\langle x^2(n) \rangle = \langle x^2(n-1) \rangle \;+\; \delta^2$$

How far does a particle travel due to diffusion?

$$\left\langle x^2(n)\right\rangle = \left\langle x^2(n-1)\right\rangle + \ \delta^2$$

- Note that at each time-step, the variance grows by δ^2

$$\left\langle x^2(0)\right\rangle = 0 \ \ , \ \ \left\langle x^2(1)\right\rangle = \delta^2 \ , \ \left\langle x^2(2)\right\rangle = 2\delta^2 \ \ , \ldots \ \ \left\langle x^2(n)\right\rangle = n\delta^2$$

$$\left\langle x_i^{\,2}(t)\right\rangle = \frac{\delta^2 t}{\tau}, \qquad n = t/\tau$$

$$\left\langle x_i^{\,2}\right\rangle = 2Dt, \quad D = \delta^2/2\tau \quad \text{(Diffusion coefficient)}$$

$$\sqrt{\left\langle x^2\right\rangle} = \sqrt{2Dt}$$

Spatial and temporal scales

$$L = \sqrt{2Dt} \qquad L^2 = 2Dt \qquad t = L^2 / 2D$$

Diffusion is fast at short length scales and slow at long length scales.
Typical diffusion constants for small molecules and ions are ~10^{-5} cm^2/s

- L = 10µm = 10^{-3} cm t = 10^{-6}(cm^2)/2x10^{-5}(cm^2/s) = 50 ms
- L = 1mm = 10^{-1} cm t = 10^{-2}(cm^2)/2x10^{-5}(cm^2/s) = 500 s
- L = 1000mm = 10^2 cm t = 10^4(cm^2)/2x10^{-5}(cm^2/s) =

500,000,000 seconds!!

Fick's first law

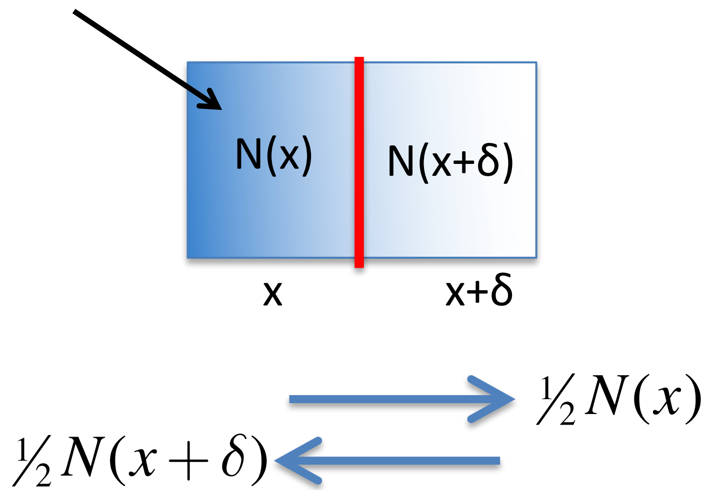
- Diffusion produces a net flow of particles from regions of high concentration to regions of lower concentration.

- The flux of particles is proportional to the concentration gradient.

$N(x)$ is the number of particles in the box at position x

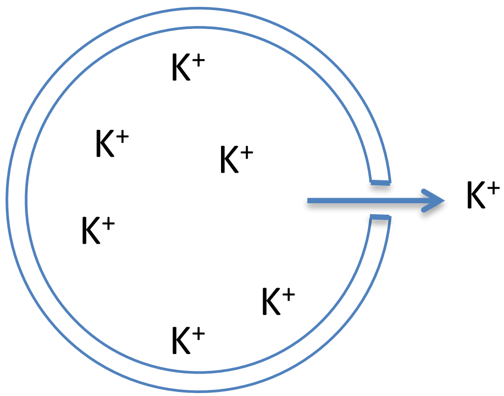
$$J_x = -D\,\frac{1}{\delta}[\varphi(x+\delta)-\varphi(x)]$$

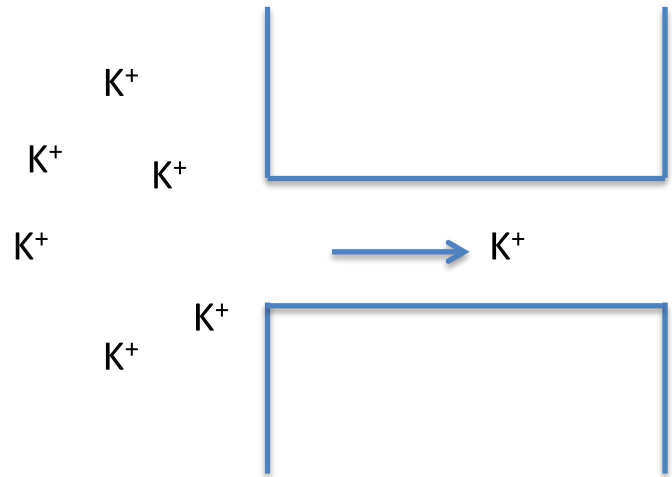
$$J_x = -D\frac{\partial\varphi}{\partial x}$$



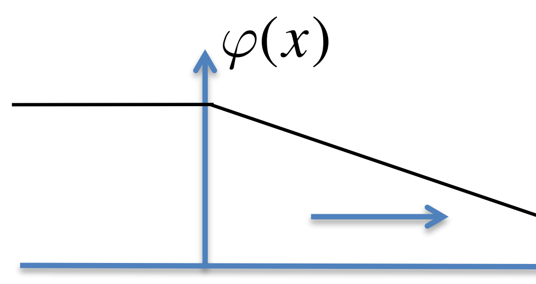
$\tfrac{1}{2}\left[N(x)-N(x+\delta)\right]$ is the net number of particles moving to the right in an interval of time τ

Diffusion produces a net flux of particles down a gradient





- Each particle diffuses independently and randomly!



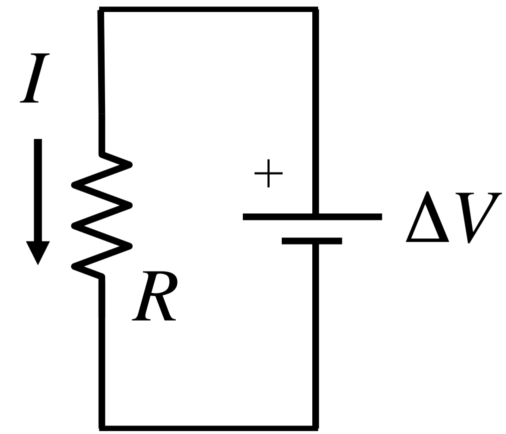
$$J_x = -D\frac{\partial \varphi}{\partial x}$$

- And yet concentration gradients produce currents!

- Eventually all concentration gradients go away…

Current flow in neurons obeys Ohm's Law

In a wire, current flow is proportional to voltage difference



Ohm's Law $$I = \frac{\Delta V}{R}$$

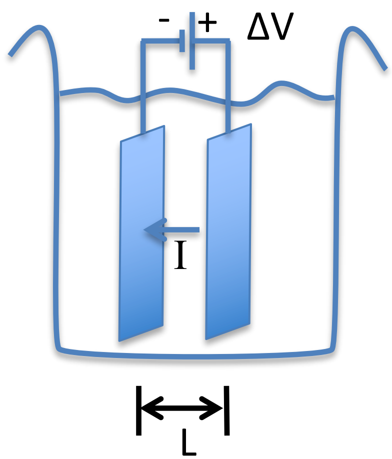
where

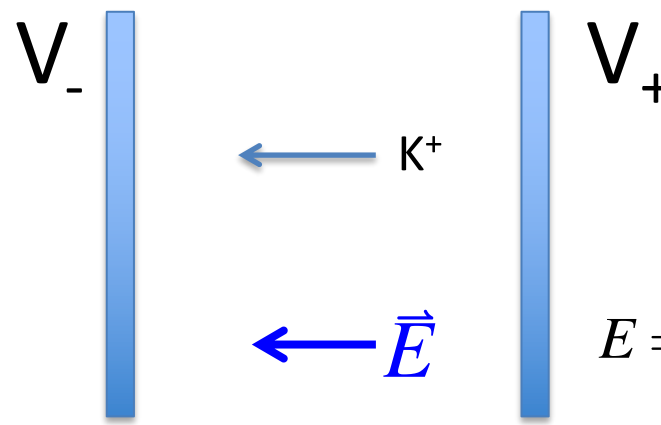
- I is current (Amperes, A)
- ΔV is voltage (Volts, V)
- R is resistance (Ohms, Ω)

Where does Ohm's Law come from?

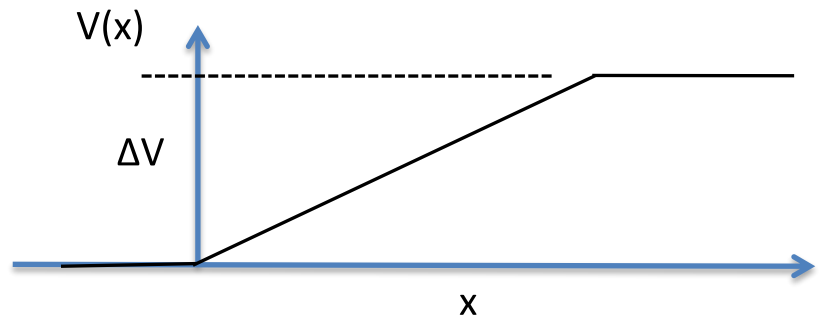
Consider a beaker filled with salt solution, two electrodes, and a battery that produces a voltage difference between the electrodes.

- The electric field produces a force which, in a solution, causes an ion to drift with a constant velocity — a current





$$E = \frac{\Delta V}{L}$$

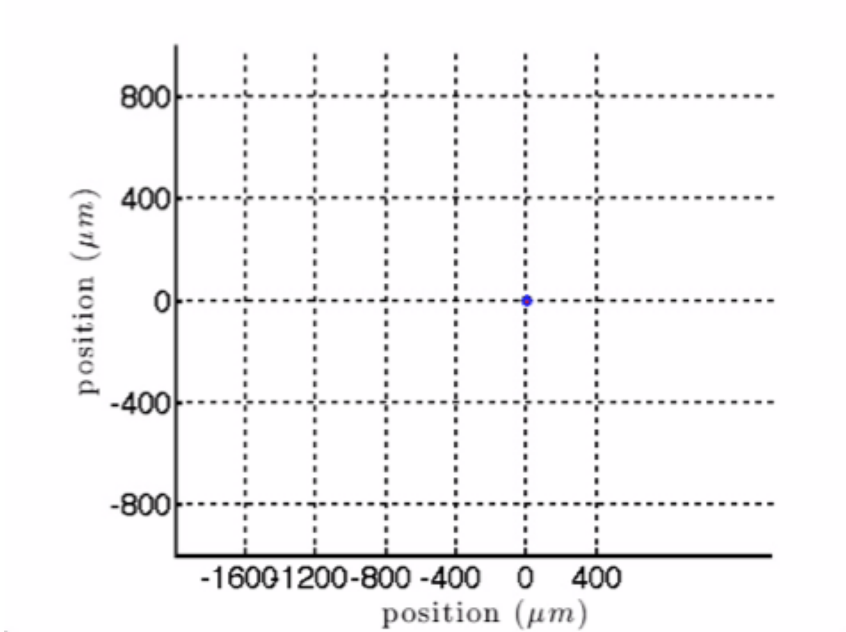


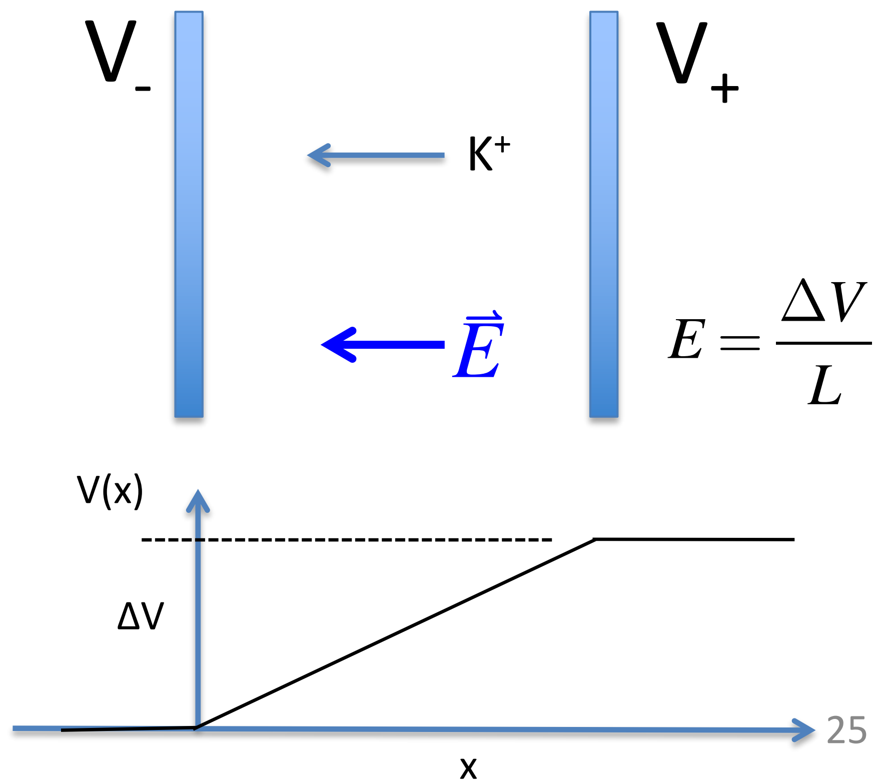
- Force: $\vec{F} = q\vec{E}$

Ion currents in an electric field

Currents are also caused by the drift of ions in the presence of an electric field.

- The electric field produces a force which, in a solution, causes an ion to drift with a constant velocity — a current





- Why constant velocity?

Ion currents in an electric field

Currents are also caused by the drift of ions in the presence of an electric field.

- Einstein realized that this is just a result of viscous drag (or friction)

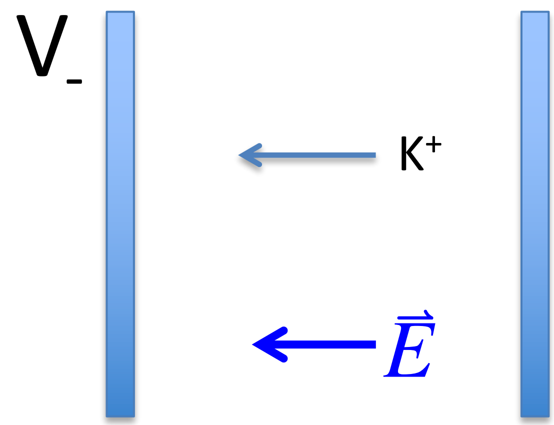
$$\vec{F} = f\,\vec{v}_d$$

- Einstein –Smoluchovski relation

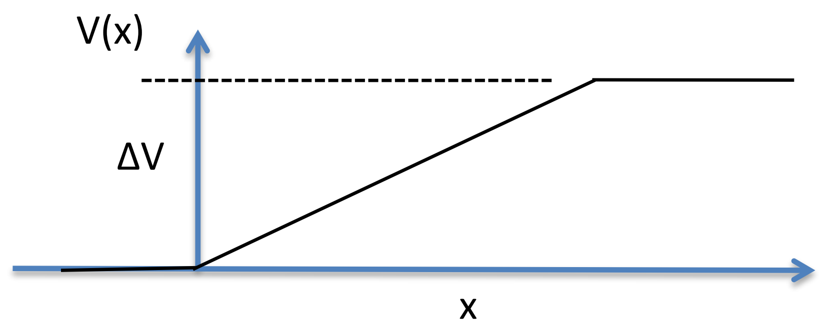
$$f = kT / D$$

- Drift velocity is given by

$$\vec{v}_d = \frac{D}{kT}\vec{F} = \frac{D}{kT}\left(q\vec{E}\right)$$



$$E = \frac{\Delta V}{L}$$



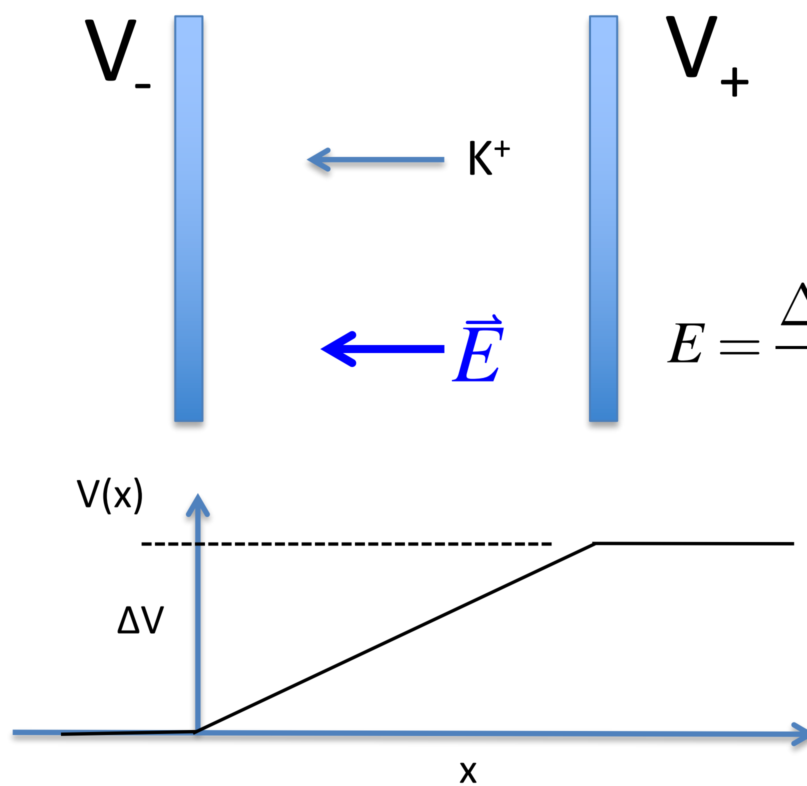
Ion currents in an electric field

Currents are also caused by the drift of ions in the presence of an electric field.

- The electric field produces a force which, in a solution, causes an ion to drift with a constant velocity — a current

$$I \propto v_d A$$

$$I \propto E A = \frac{\Delta V}{L} A$$



$$E = \frac{\Delta V}{L}$$

Ohm's Law in solution

In a solution, current flow per unit area is proportional to voltage gradients

$$I = \left(\frac{1}{\rho}\right)\frac{\Delta V}{L}A$$

ρ = resistivity ($\Omega \cdot$m)

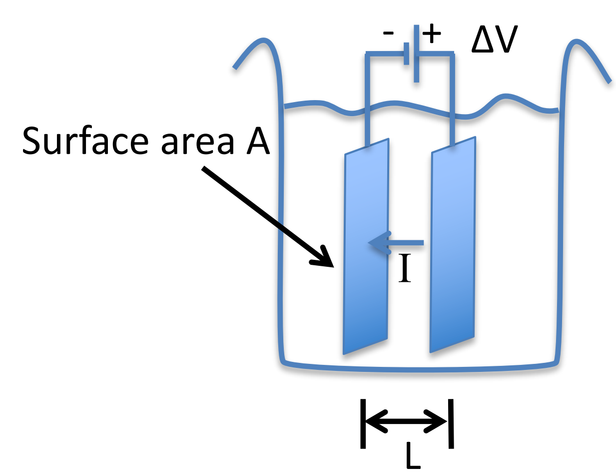
$$I = \frac{1}{R}\Delta V$$

- Let's make this look more like Ohm's Law

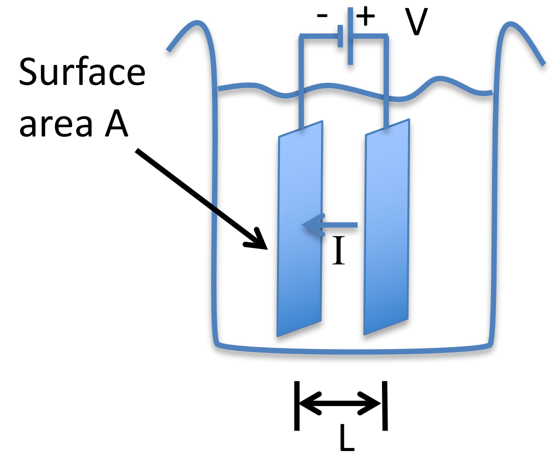
$$I = \left(\frac{A}{\rho L}\right)\Delta V$$

- Thus the resistance is given by:

$$R = \frac{\rho L}{A}$$



Resistivity of intra/extra cellular space



- Resistance of a volume of conductive medium is given by

$$R = \frac{\rho L}{A}$$

- ρ = 1.6 μΩ·cm for copper

- ρ = ~60 Ω·cm for mammalian saline – the brain has lousy conductors!

- The brain has many specializations to deal with lousy wires…

Learning objectives for Lecture 1

- To understand how the timescale of diffusion relates to length scales
  - Distance diffused grows as the square root of time

- To understand how concentration gradients lead to currents (Fick’s First Law)
  - Concentration differences lead to particle flux, proportional to gradient

- To understand how charge drift in an electric field leads to currents (Ohm’s Law and resistivity)

(Extra slide) Derivation of resistivity

Current density (Coulombs per second per unit area) is just drift velocity times the density of ions times the charge per ion.

$$\frac{I}{A} = q\varphi v_d$$

φ = ion density (ions per m^3)

$q = ze$ = ionic charge (Coulombs per ion)

= ion valence times 1.6x10^{-19} Coulombs

- Plugging in drift velocity from above, we get:

$$\frac{I}{A} = q\varphi \frac{D}{kT}(qE)$$

Derivation of resistivity

- Thus, the current density (coulombs per second per unit area is just proportional to the electric field:

$$\frac{I}{A} = \frac{q^2 \varphi D}{kT} E \qquad \frac{I}{A} = \left(\frac{1}{\rho}\right) E$$

- Solving for ρ we get:

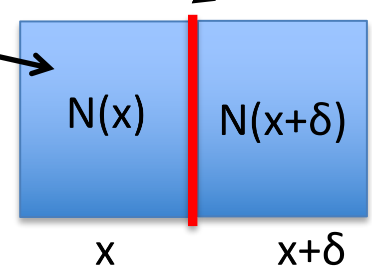
$$\rho = \frac{kT}{q^2 \varphi D}$$ = resistivity (Ω•m)

Extra slides on derivation of Fick's first law

We will now use a similar approach to derive a macroscopic description of diffusion – a differential equation that describes the the flux of particles from the spatial distribution of their concentration.

$N(x)$ is the number of particles in a box (of length δ) at position x

A is the area of the interface between the boxes



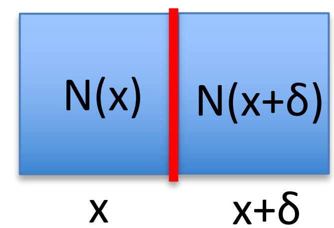
$$\tfrac{1}{2}N(x) \longrightarrow$$

$$\tfrac{1}{2}N(x+\delta) \longleftarrow$$

$\tfrac{1}{2}\left[N(x)-N(x+\delta)\right]$ is the net number of particles moving to the right in an interval of time τ

Extra slides on derivation of Fick's first law

We can calculate the flux in units of particles per second per area



$$J_x = -\frac{1}{A\tau}\frac{1}{2}[N(x+\delta) - N(x)]$$

multiply by δ^2 / δ^2

$$J_x = -\frac{\delta^2}{2\tau}\frac{1}{\delta}\left[\frac{N(x+\delta)}{A\delta} - \frac{N(x)}{A\delta}\right]$$

Particles per unit volume

Density - particles per unit volume

$$J_x = -D\,\frac{1}{\delta}[\varphi(x+\delta) - \varphi(x)]$$

$$J_x = -D\frac{\partial \varphi}{\partial x}$$

Note: To get density (ions/m^3) from molar concentration (mol/L), you have to multiply by N_Ax10^{-3}. (N_A is Avagadro's Number = 6.02x10^{23})