511-2018-09-14-neurophysiology

Rick Gilmore

Today's Topics

- **Quiz 1**
- Why brains?
- The resting potential

Why brains?

Sterling & Laughlin, 2015

- Tiny, single-celled bacterium
- Feeds on glucose
- Chemo ("taste") receptors on surface membrane
- Flagellum for movement
- Food concentration regulates duration of "move" phase
- ~4 ms for chemical signal to diffuse from anterior/posterior

- 300K larger than E. Coli
- Propulsion through coordinated beating of cilia
- Diffusion from head to tail ~40 s!
- Use electrical signaling instead
    - Na^+ channel opens (e.g., when stretched)
    - Voltage-gated Ca^{++} channels open, Ca^{++} enters, triggers cilia
    - Signal across cell within ms

- ~10x larger than paramecium
- 302 neurons + 56 glial cells (out of 959)
- Swim, forage, mate

Neural communication

- Electrical
    - Fast(er)
    - Within neurons
- Chemical
    - Diffusion slow(er)
    - Within & between neurons

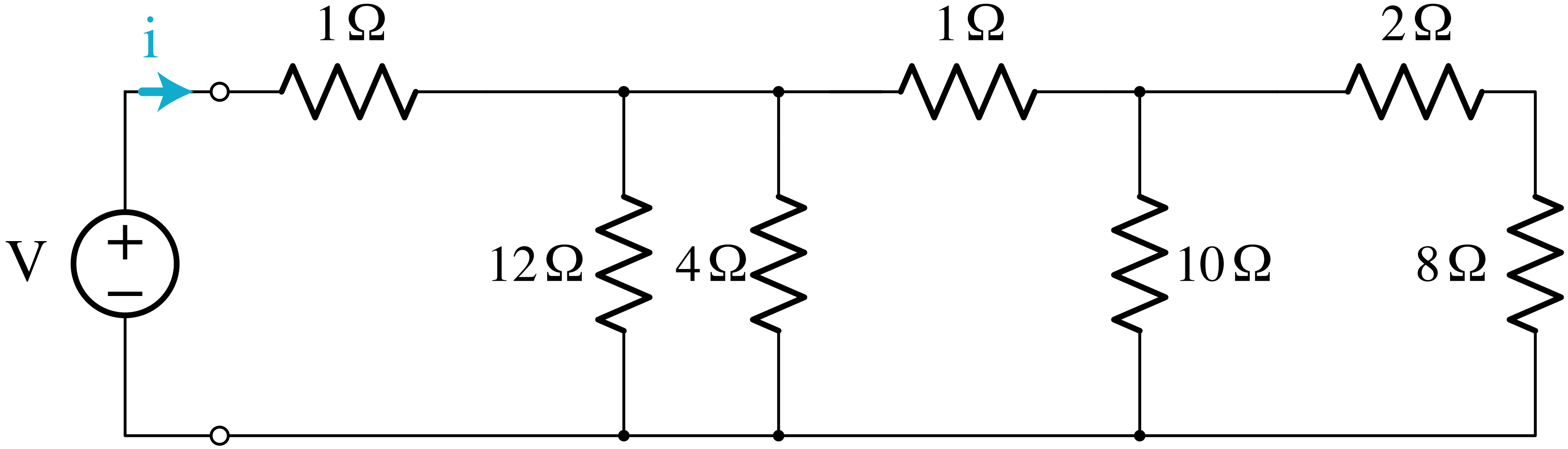
How are messages generated?

- Electrical potential (== voltage)
  - Think of potential energy
  - Voltage ~ pressure
  - Energy that will be released if something changes

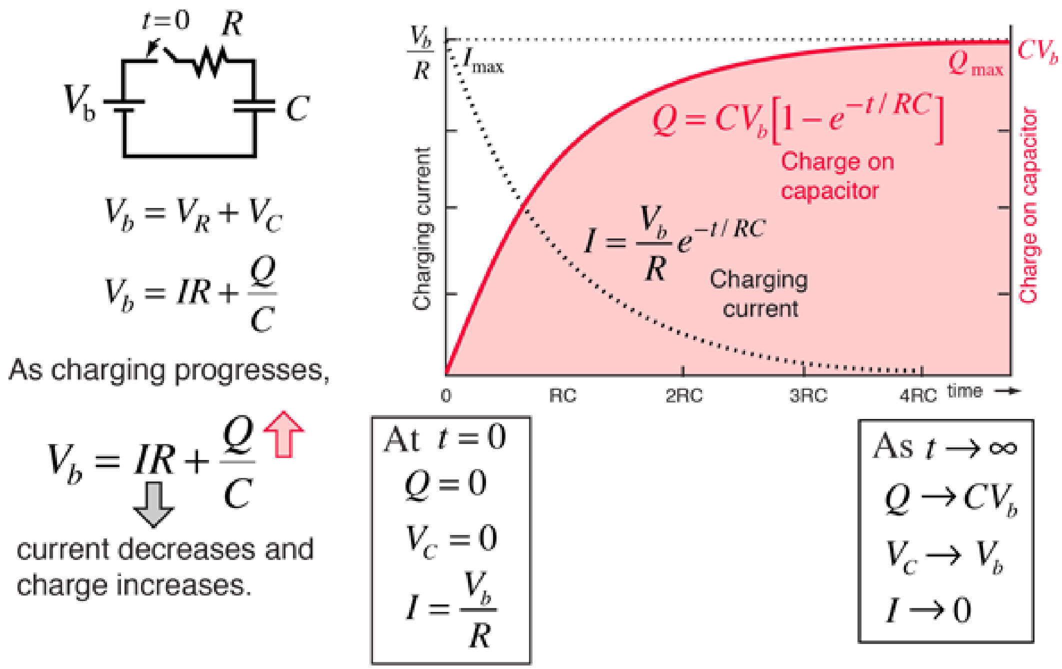
Neurons as electrical devices

$$E = IR$$

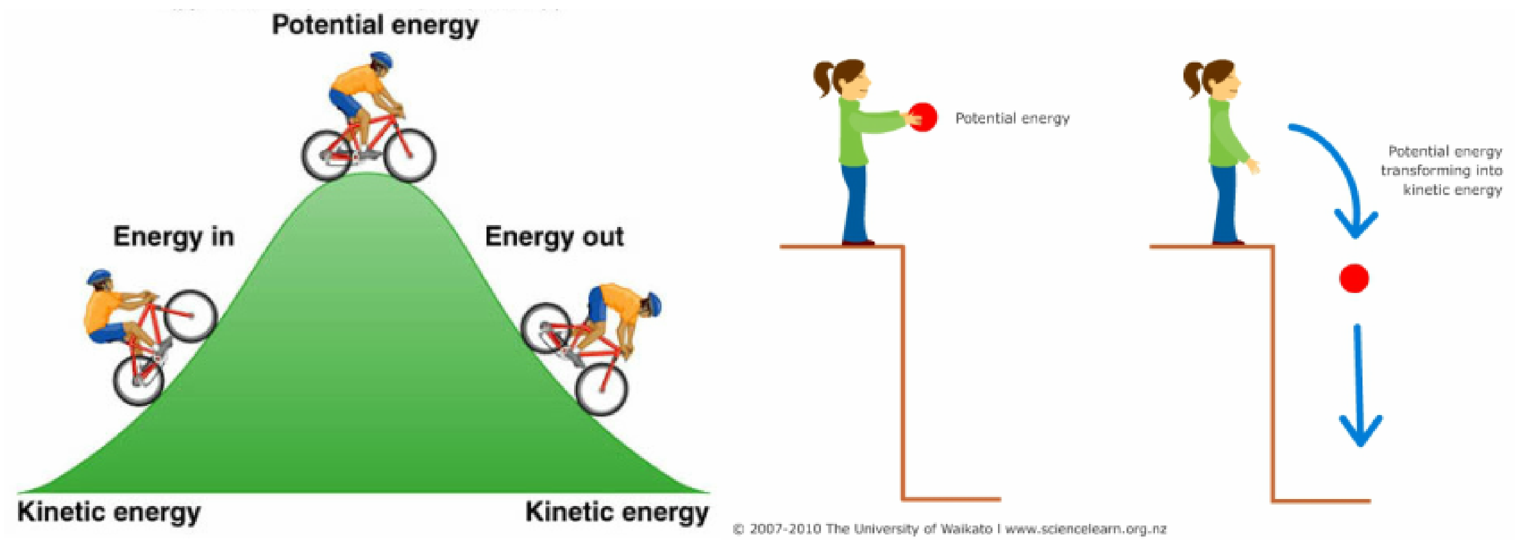
- Current flow (I) across membrane
- Membrane varies in permeability (R) to ion flow



- Membrane stores (& releases) charge like



Potential energy



http://physics20project.weebly.com/uploads/1/6/4/8/16484122/1358825569.png

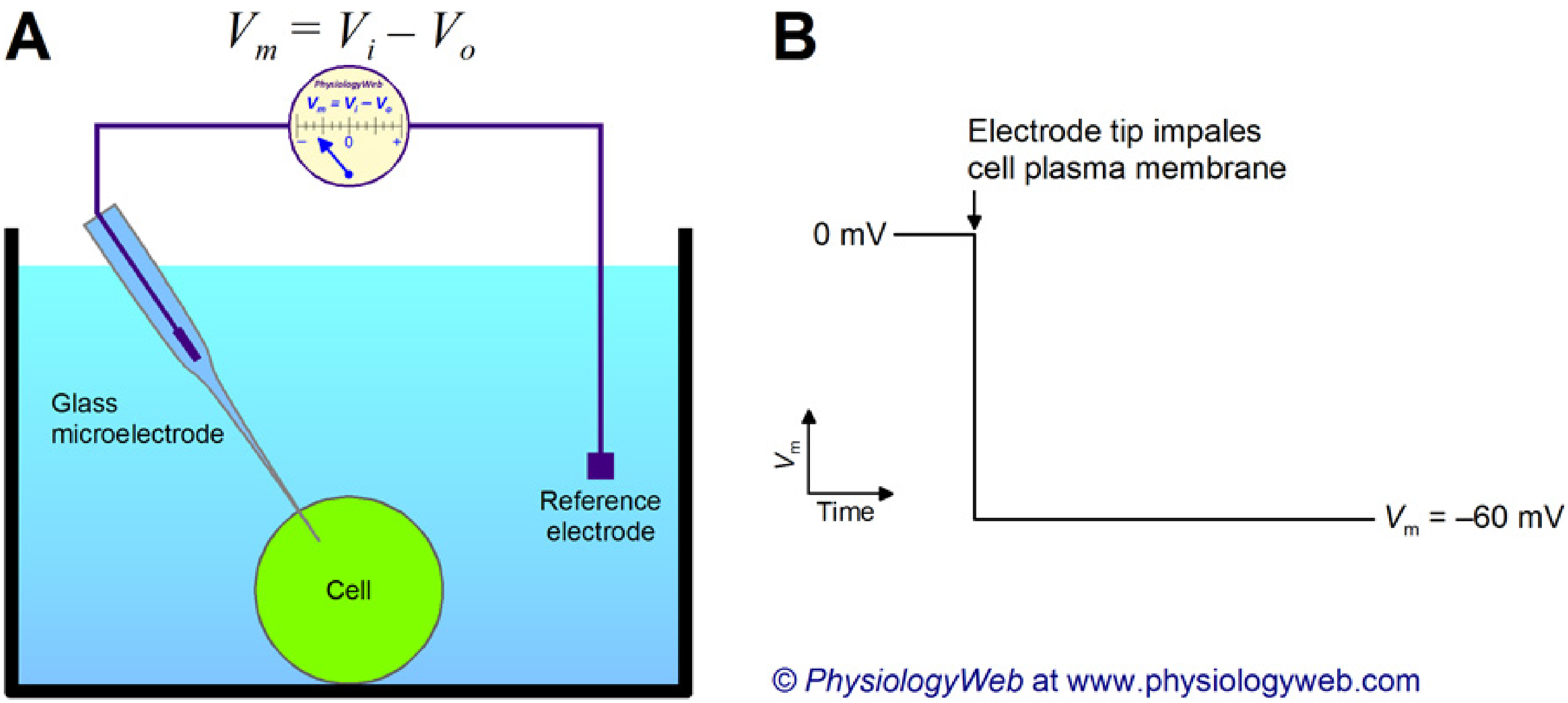
Types of neural electrical potentials

- Resting potential
- Action potential

Resting potential

- Measurement
  - Electrode on inside
  - Electrode on outside (reference)
  - Inside - Outside = potential

Resting potential



http://www.physiologyweb.com/lecture_notes/resting_membrane_potential/figs/measuring_the_membrane_pot

Resting potential

- Neuron (and other cells) have
  - Inside is -60-70 mV, with respect to outside
  - About 1/20th typical AAA battery
- Like charges repel, opposites attract, so
  - Positively charged particles pulled in
  - Negatively charged particles pushed out

Where does the resting potential come from?

- Ions
- Ion channels
- Separation between charges
- A balance of forces

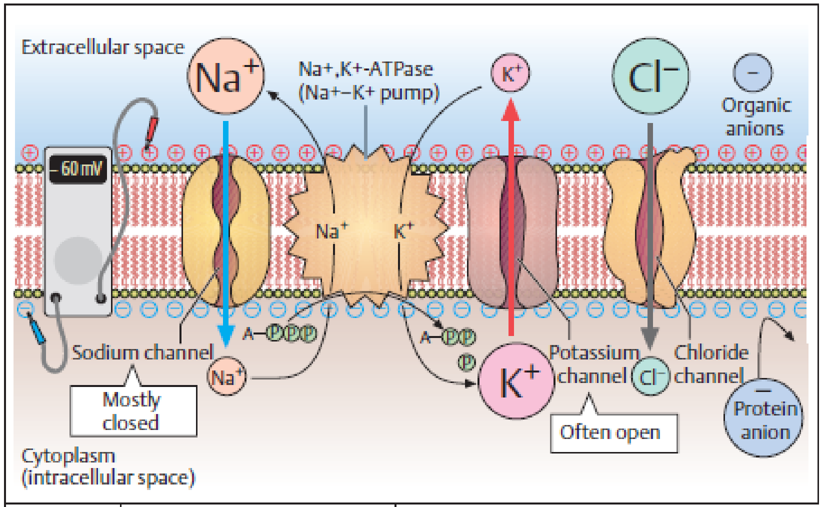
We are the champIONs, my friend

- Potassium, K^+
- Sodium, Na^+
- Chloride, Cl^-
- Calcium, Ca^{++}
- Organic anions, A^-

Party On

- Annie (A^-) was having a party.
  - Used to date Nate (Na^+), but now sees Karl (K^+)
- Hired bouncers called
  - "The Channels"
  - Let Karl and friends in or out, keep Nate out
- Annie's friends (A^-) and Karl's (K^+) mostly inside
- Nate and friends (Na^+) mostly outside
- Claude (Cl^-) tagging along

Party On

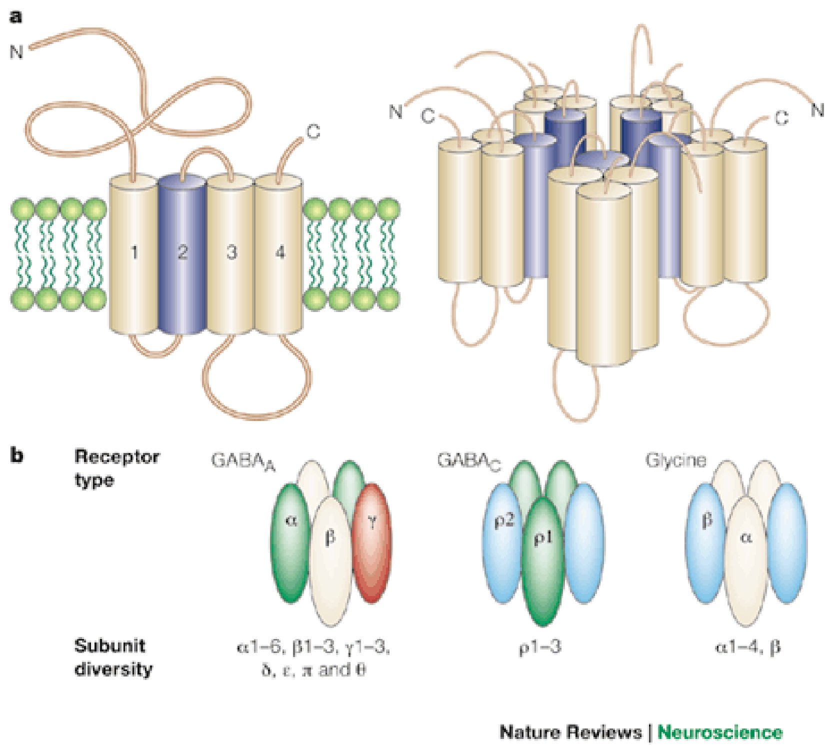


Ion	Concentration Cytoplasm (mM)	Extracellular space (mM)
K^+	139	4
Na^+	12	145
Cl^-	4	116
Organic anions	138	134

Fig. 1.13 **Membrane potential of a cell.** (After Koolman and Röhm)

Ion channels

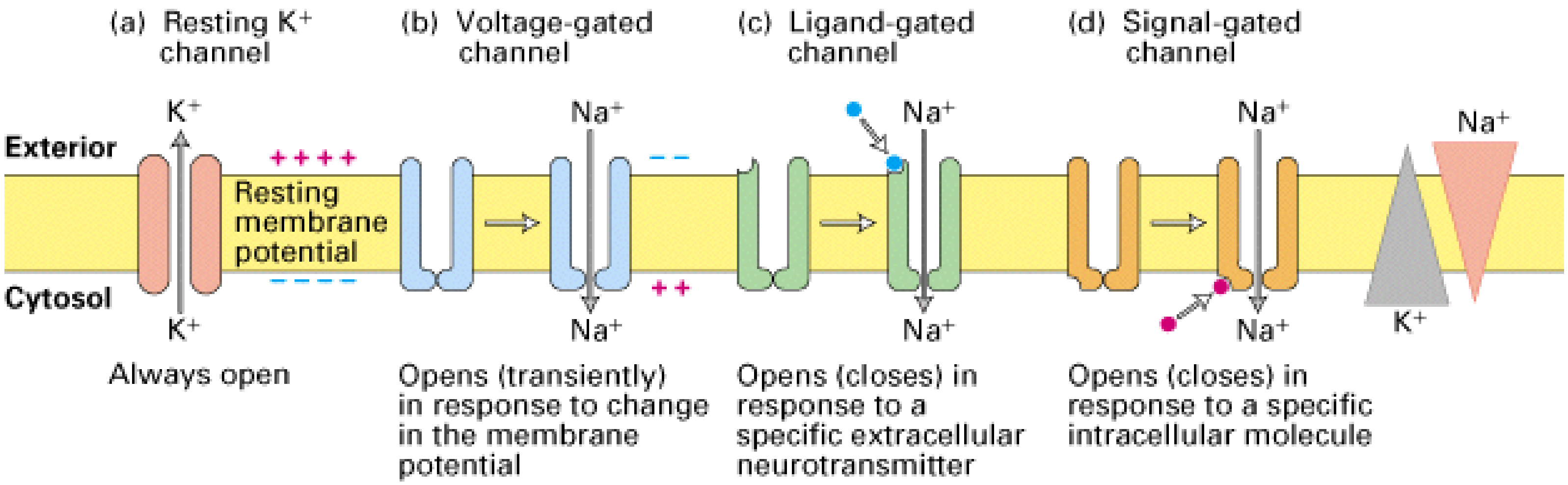
- Macromolecules that form openings in membrane
- Different types of subunits


a
N
C
1
2
3
4
N
C
C
N
b
Receptor type
GABA$_A$
α
β
γ
GABA$_C$
ρ2
ρ1
Glycine
β
α
Subunit diversity
α1–6, β1–3, γ1–3, δ, ε, π and θ
ρ1–3
α1–4, β
Nature Reviews | Neuroscience

Ion channels

- Selective
- Vary in permeability
- Types
    - Passive/leak
    - Voltage-gated
    - Ligand-gated (chemically-gated)
    - Transporters

Ion channels

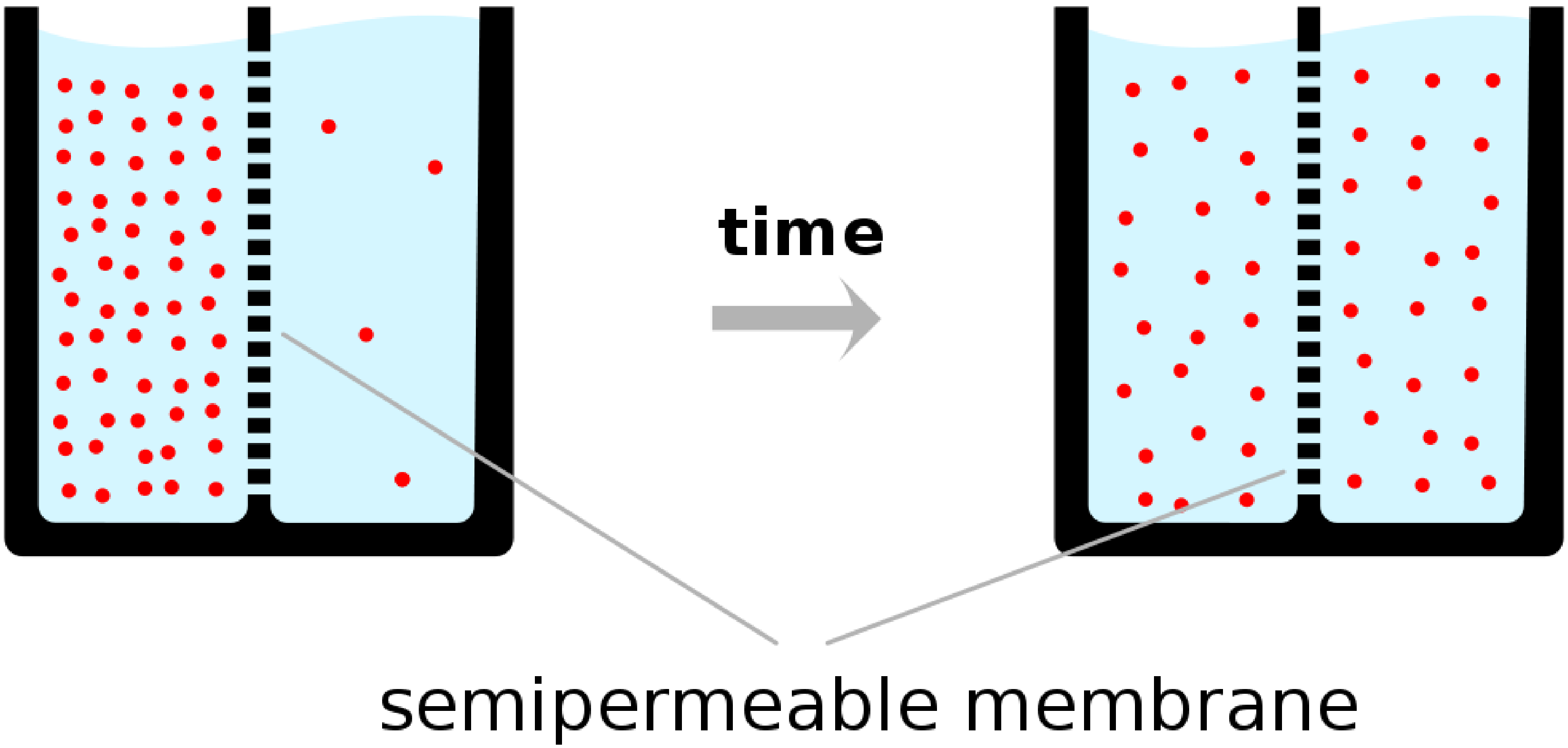


http://www.zoology.ubc.ca/~gardner/F21-08.GIF

Neuron at rest permeable to K^+

- Passive K^+ channels open
- K^+ flows out
- K^+ outflow creates charge separation from A-
- Charge separation creates voltage
- Voltage prevents K^+ concentration from equalizing b/w inside and out

Force of diffusion



https://upload.wikimedia.org/wikipedia/commons/thumb/7/72/Diffusion.en.svg/1000px-Diffusion.en.svg.png

https://upload.wikimedia.org/wikipedia/commons/1/12/Bubble_bath.jpg

Neuron at rest

- Force of diffusion
  - K^+ moves from high concentration (~140 mM inside) to low (~4 mM outside)
  - Movement of charged particles == current

Neuron at rest

- Electrostatic pressure
  - Voltage build-up stops K^+ outflow
  - Voltage called "reversal potential"
  - K^+ positive, so reversal potential negative (w/ respect to outside)
  - Reversal potential close to resting potential

Equilibrium potential and Nernst equation

$$V_{\mathrm{K}} = \frac{RT}{(+1)F} \ln \frac{[\mathrm{K}^+]_o}{[\mathrm{K}^+]_i}$$

http://www.physiologyweb.com/lecture_notes/resting_membrane_potential/figs/nernst_equation_v_k.gif

Building on intuition

http://www.daily-player.com/images/articles/finger-in-the-dyke.jpg

Back to neurons

- Na^+ also has reversal potential
- Membrane at rest has low Na^+ permeability
- Concentrated outside neuron (~145 mM) vs. inside (~12 mM)
- Some Na^+ flows
- Equilibrium potential is positive (with respect to outside)

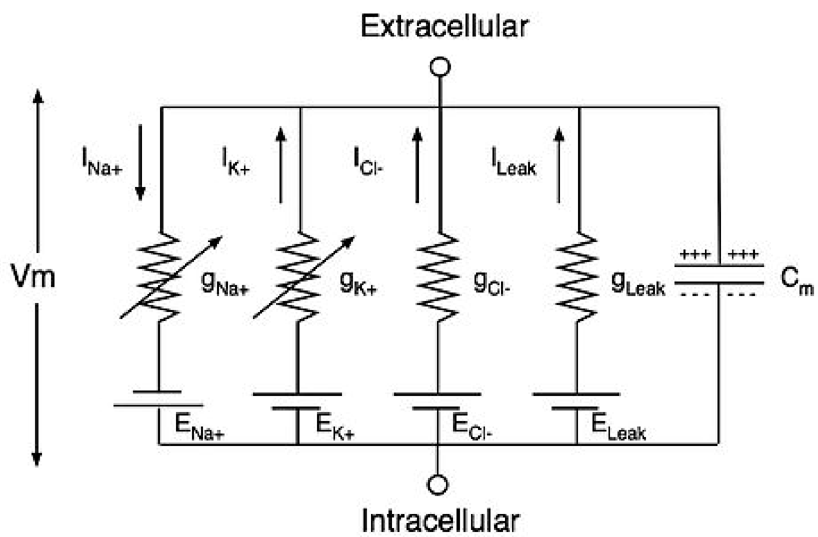
Resting potential

- Net effects of ion flow across membrane
- Goldman-Hodgkin-Katz equation

$$V_{\mathrm{m}} = \frac{RT}{F} \ln\left(\frac{p_{\mathrm{K}}[\mathrm{K}^+]_{\mathrm{o}} + p_{\mathrm{Na}}[\mathrm{Na}^+]_{\mathrm{o}} + p_{\mathrm{Cl}}[\mathrm{Cl}^-]_{\mathrm{i}}}{p_{\mathrm{K}}[\mathrm{K}^+]_{\mathrm{i}} + p_{\mathrm{Na}}[\mathrm{Na}^+]_{\mathrm{i}} + p_{\mathrm{Cl}}[\mathrm{Cl}^-]_{\mathrm{o}}} \right)$$

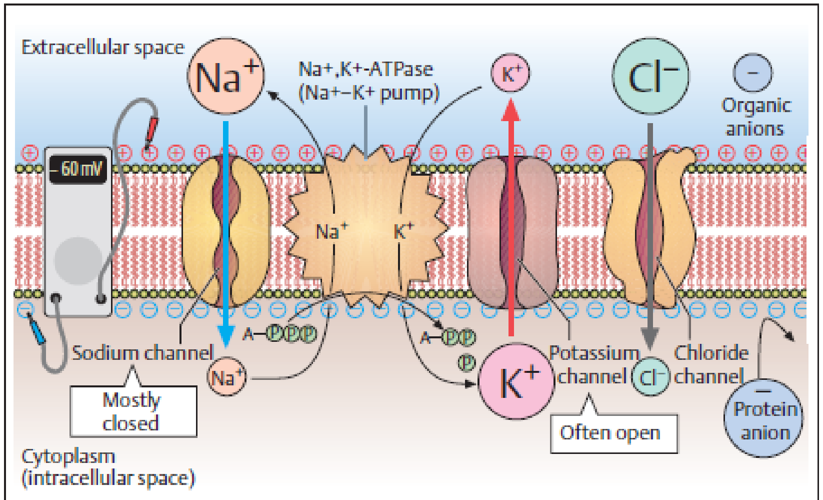
http://www.physiologyweb.com/calculators/figs/ghk_equation.gif

Electrical circuit model



https://upload.wikimedia.org/wikipedia/commons/thumb/3/33/MembraneCircuit.jpg/500px-MembraneCircuit.jpg

Resting potential



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Summary of forces

Ion	Concentration gradient	Electrostatic force
K^+	Inside >> Outside, outward	- (pulls K^+ in)
Na^+	Outside >> Inside, inward	- (pulls Na^+ in)

Driving force and equilibrium potential

- "Driving Force" on a given ion depends on its equilibrium potential.
- Driving force larger if membrane potential far from equilibrium potential for ion.
-
    - Voltage that keeps current (inside/outside) concentrations the same
    - Voltage membrane potential will approach if **only** that ion flows

Equilibrium potentials calculated under typical conditions

Ion	[inside]	[outside]	Voltage
K^+	~150 mM	~4 mM	~ -90 mV
Na^+	~10 mM	~140 mM	~ +55-60 mV
$Cl-$	~10 mM	~110 mM	- 65-80 mV

$$V_{\mathrm{K}} = \frac{RT}{(+1)F} \ln \frac{[\mathrm{K}^+]_o}{[\mathrm{K}^+]_i}$$

Video summary of resting potential

Next time…

- See also https://en.wikipedia.org/wiki/Membrane_potential
- Or, what could make Annie's party go haywire?

References