PSYCH 260/BBH 203

Cellular neuroscience II

Rick O. Gilmore

2022-02-03 07:31:17

Prelude (4:20)

Prelude (2:33)

Announcements

- Exam 1 Thursday, 2/10
  - 40 questions
  - **No in-person/in-class meeting**
  - On Canvas, live at 3:05 PM; open until 10:00 PM

Today's Topics

- Electrical communication in neurons
- The action potential

How do neurons communicate?

Types of neural electrical potentials

- Resting potential
  - Voltage across neuronal membrane when cell is ‘at-rest’ (not firing)
- Action potential
  - Voltage across neuronal membrane when cell is active or firing

Where does the resting potential come from?

- Ions (charged particles)
- Ion channels
- Separation between charges
- A balance of forces

We are the champIONs, my friend

- Potassium, K^+
- Sodium, Na^+
- Chloride, Cl^-
- 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
- Claudia (Cl^-) tagging along

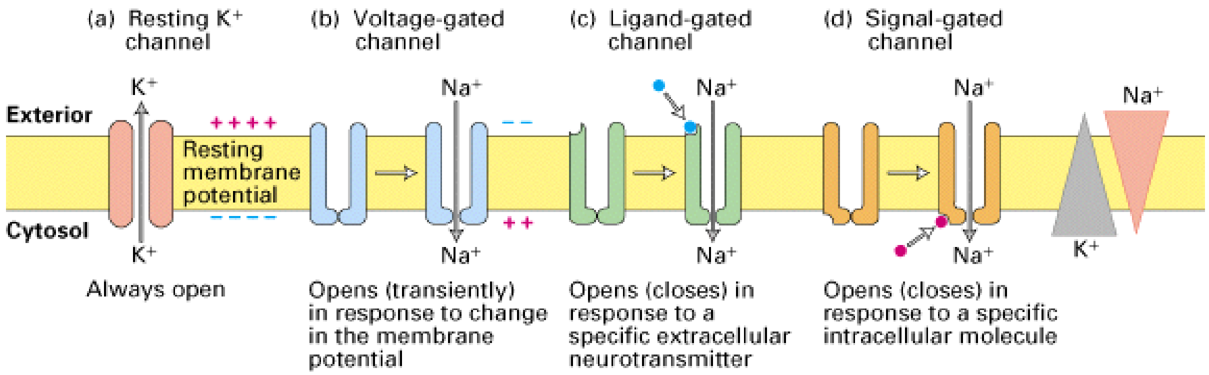
Resting potential arises from

- A balance of forces
    - *Force of diffusion*
    - *Electrostatic force*
- Forces cause ion flows across *membrane*
    - Force of diffusion consistent (over time)
    - Electrostatic force changes
- Ion channels allow ion flow

Ion channels

- Openings in neural membrane
- Selective for specific ions
- Vary in permeability (how readily ions flow)
- Types
  - *Passive/leak (always open)*
  - *Voltage-gated*
  - *Ligand-gated (chemically-gated)*
  - *Transporters/pumps*

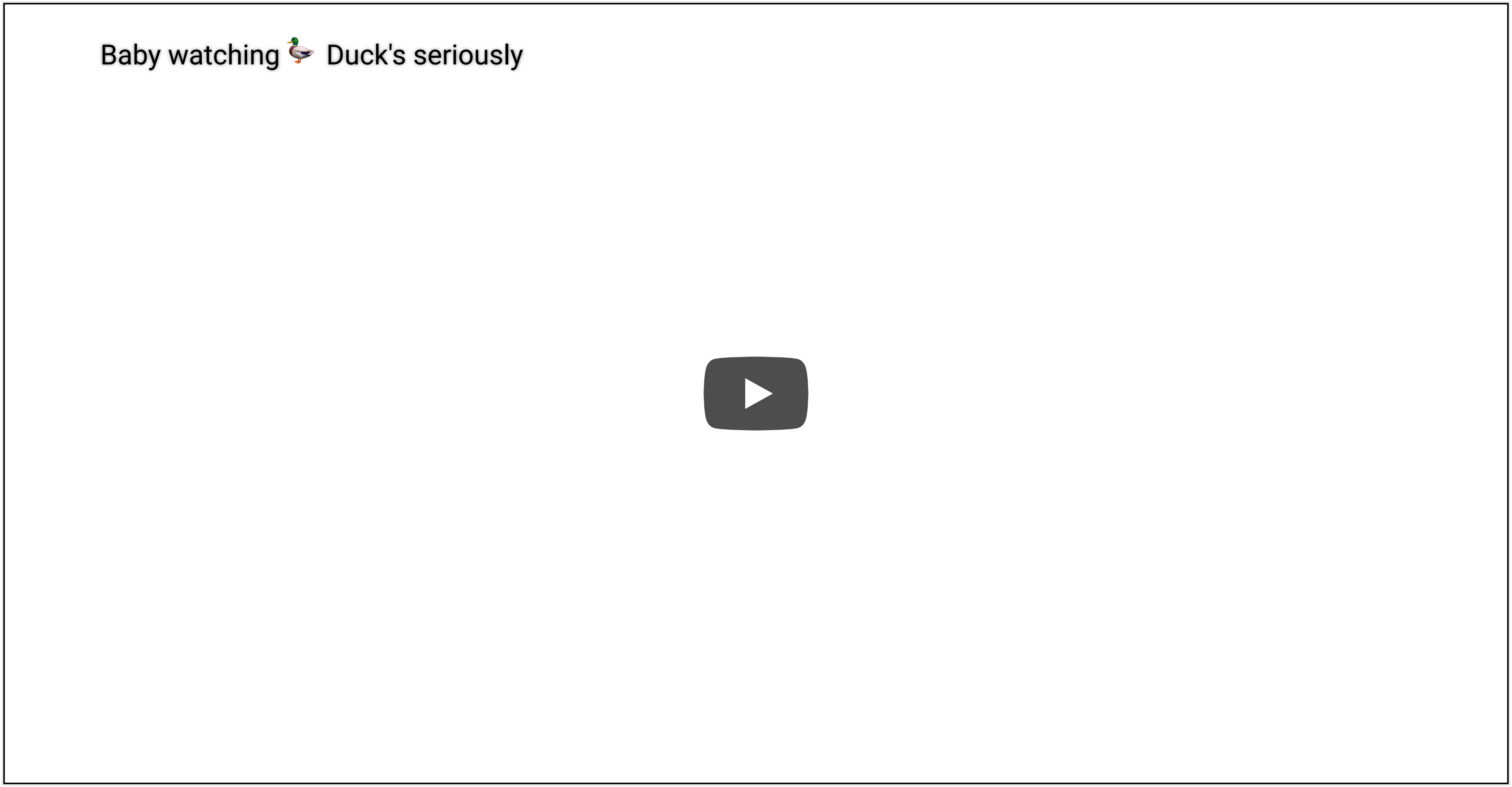
Ion channels



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

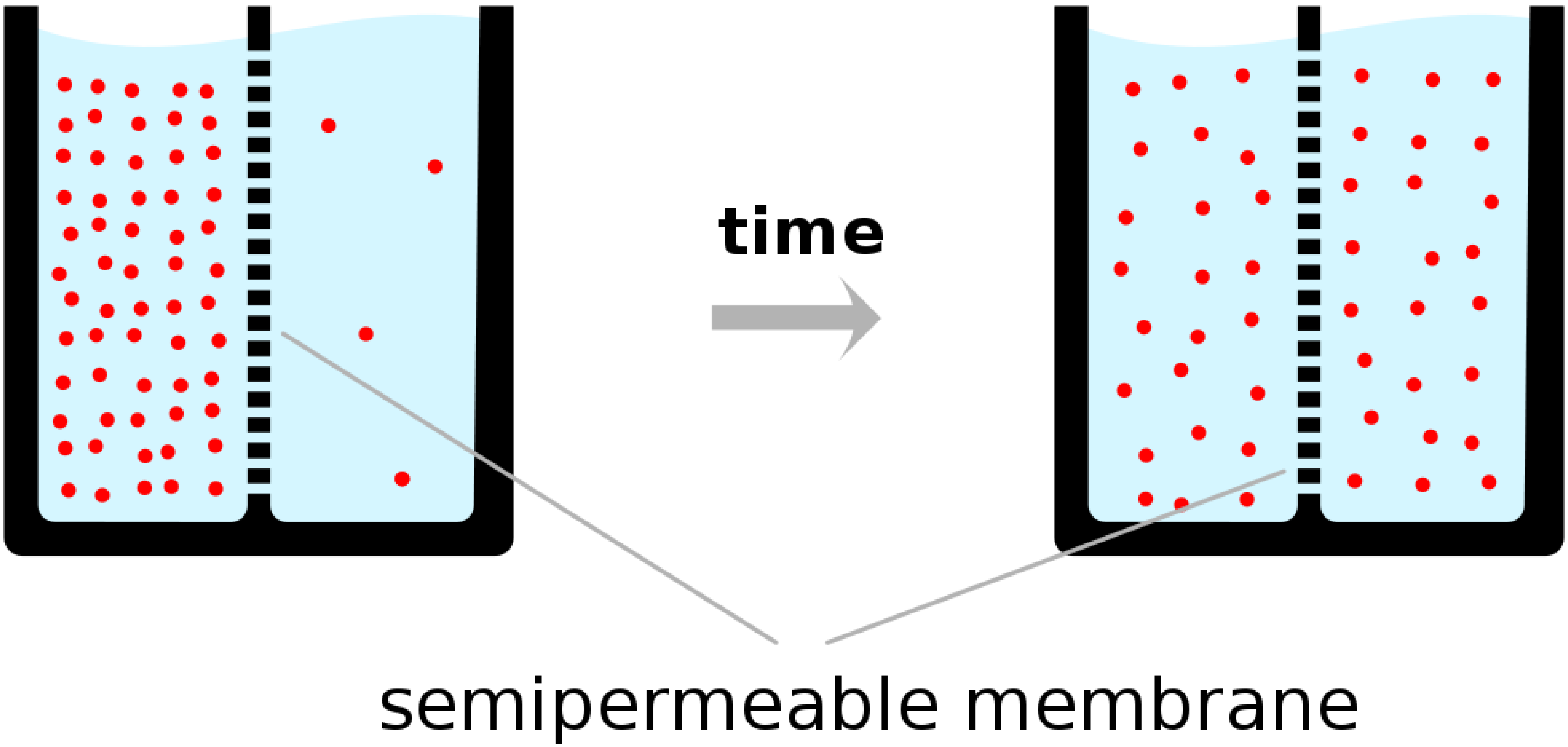
Neuron at rest permeable to K^+

- *Permeable*: Permits flow across/through
- Passive K^+ channels open
- $[K^+]$ concentration inside >> outside
- K^+ flows out
  - Neuron constantly brings K^+ in



https://www.youtube.com/watch?v=I_N82ZvLT-Q

Force of diffusion



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

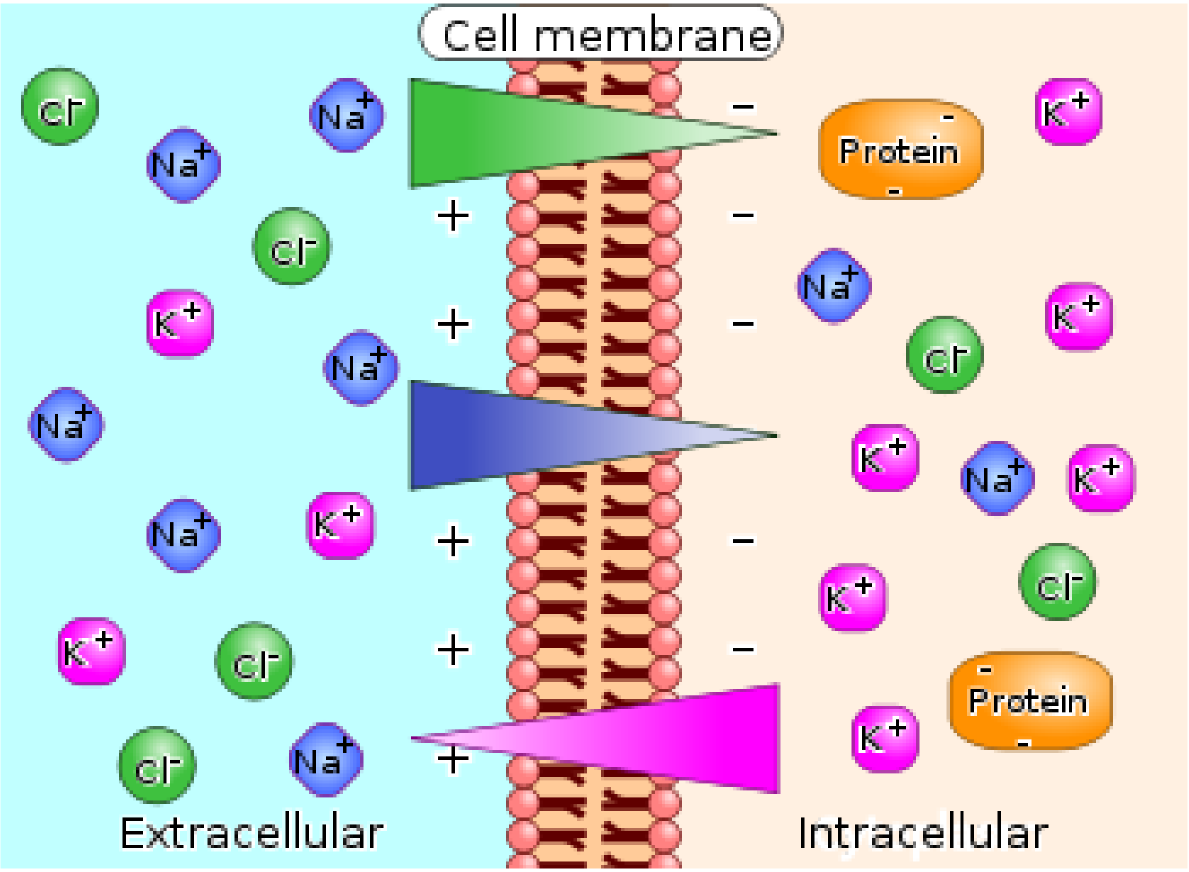
Force of diffusion

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

Neuron at rest permeable to K^+

- Organic anions (A^-) too large to move outside of cell
- A^- and K^+ largely in balance == no net internal charge
- K^+ outflow creates *charge separation*: K^+ (outside) <-> A^- (inside)
- Charge separation creates a voltage
- Outside +/inside -
- Voltage build-up stops outflow of K^+

The resting potential



Balance of forces in the neuron at rest

- **Force of diffusion**
    - K^+ moves from high concentration (inside) to low (outside)

Balance of forces in the neuron at rest

- **Electrostatic force**
  - Voltage build-up stops K^+ outflow
  - Specific voltage that stops flow == *equilibrium potential* for K^++
  - K^+ positive, so equilibrium potential negative (w/ respect to outside)
  - Equilibrium potential close to neuron's resting potential

Equilibrium potential and Nernst equation

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

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

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

http://www.physiologyweb.com/lecture_notes/resting_mem

Neuron resting potential ≠ K^+ equilibrium potential

- Resting potential not just due to K^+
- Other ions flow
- Resting potential == net effects of *all* ion flows across membrane

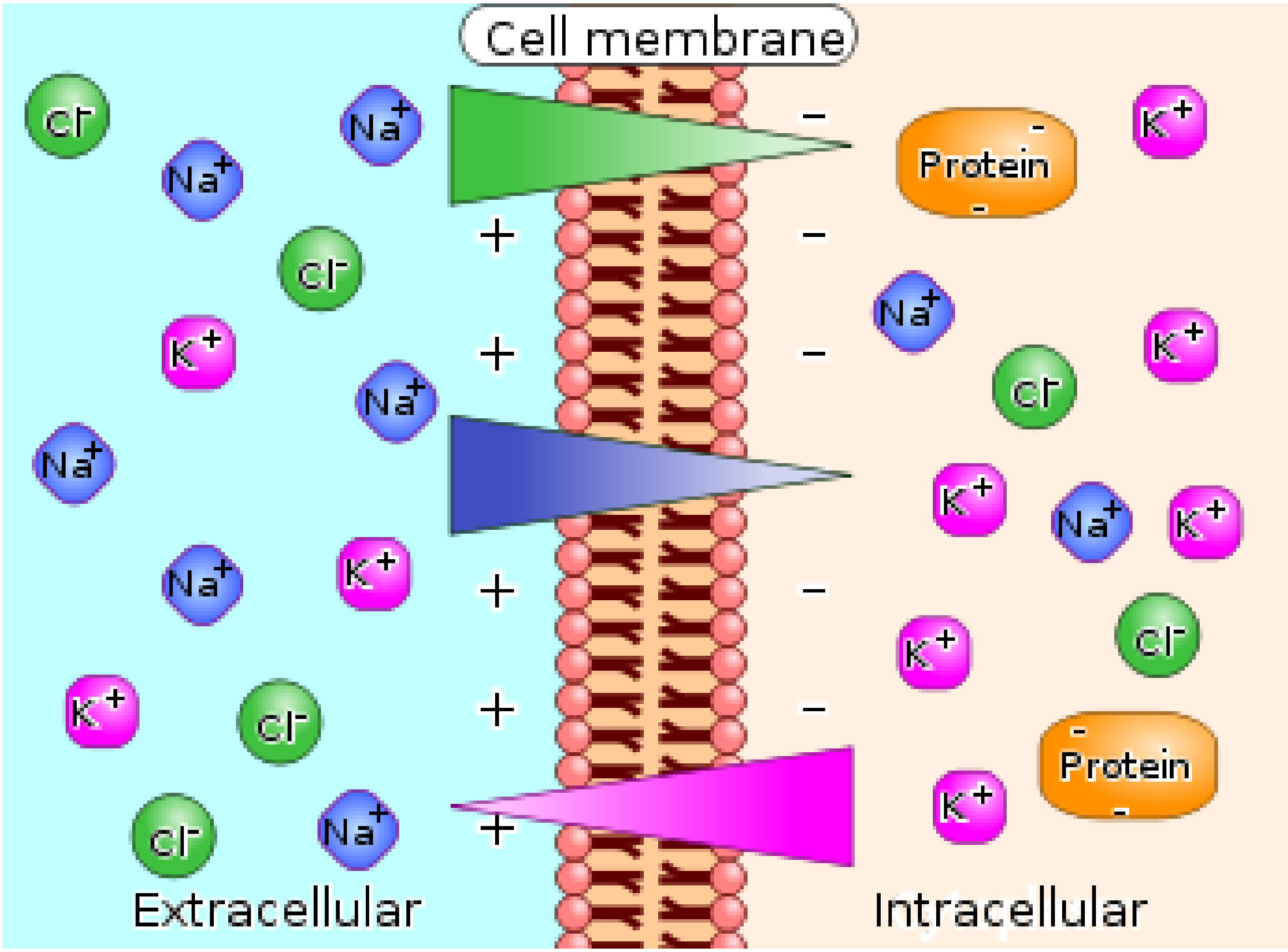
Goldman-Hodgkin-Katz equation

$$V_m = \frac{RT}{F} \ln\left(\frac{p_K[K^+]_o + p_{Na}[Na^+]_o + p_{Cl}[Cl^-]_i}{p_K[K^+]_i + p_{Na}[Na^+]_i + p_{Cl}[Cl^-]_o} \right)$$

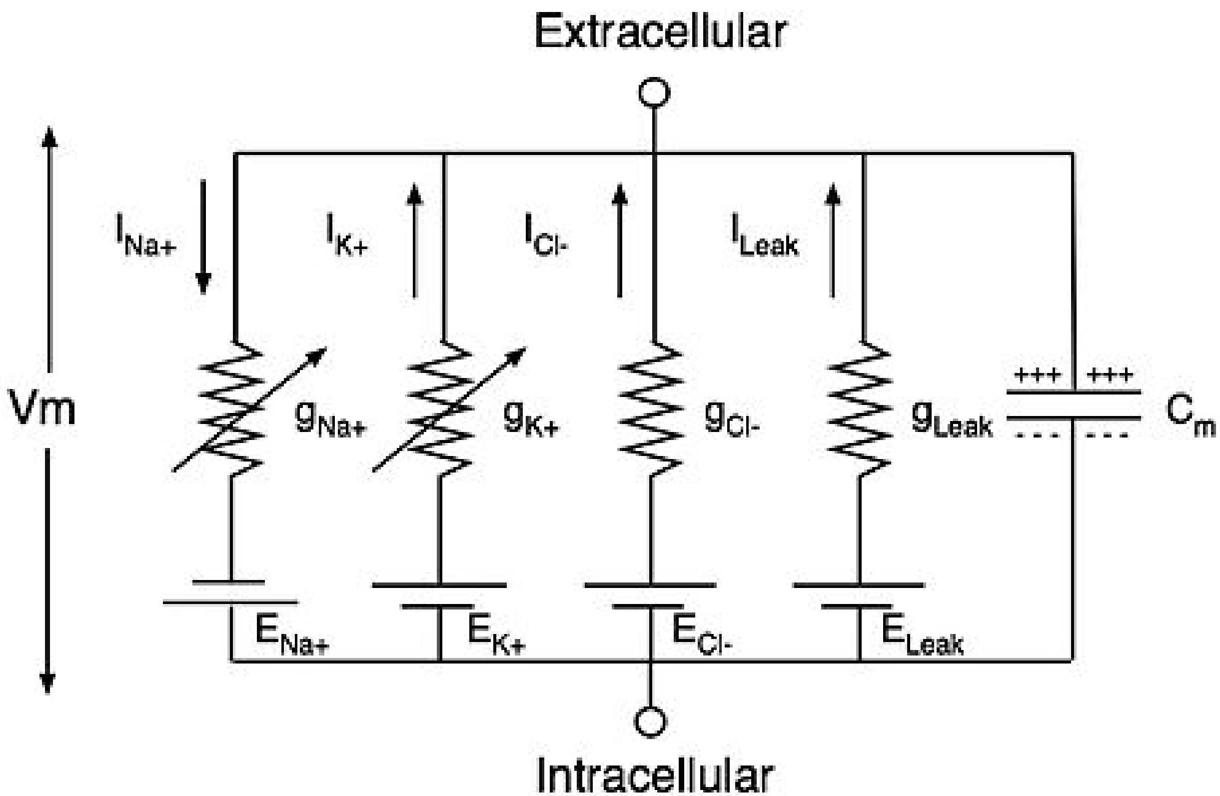
http://www.physiologyweb.com/calculators/figs/ghk_equation.gif

Na^+ role

- Na^+ concentrated **outside** neuron
- Membrane at rest not very permeable to Na^+
- Some, but not much Na^+ flows *in*
- Na^+ has equilibrium potential ~ + 60 mV
- Equilibrium potential is positive (with respect to outside)
- Would need positive interior to keep Na^+ from flowing in


Cell membrane
Cl⁻
Na⁺
K⁺
Protein
Extracellular
Intracellular

Electrical circuit model



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

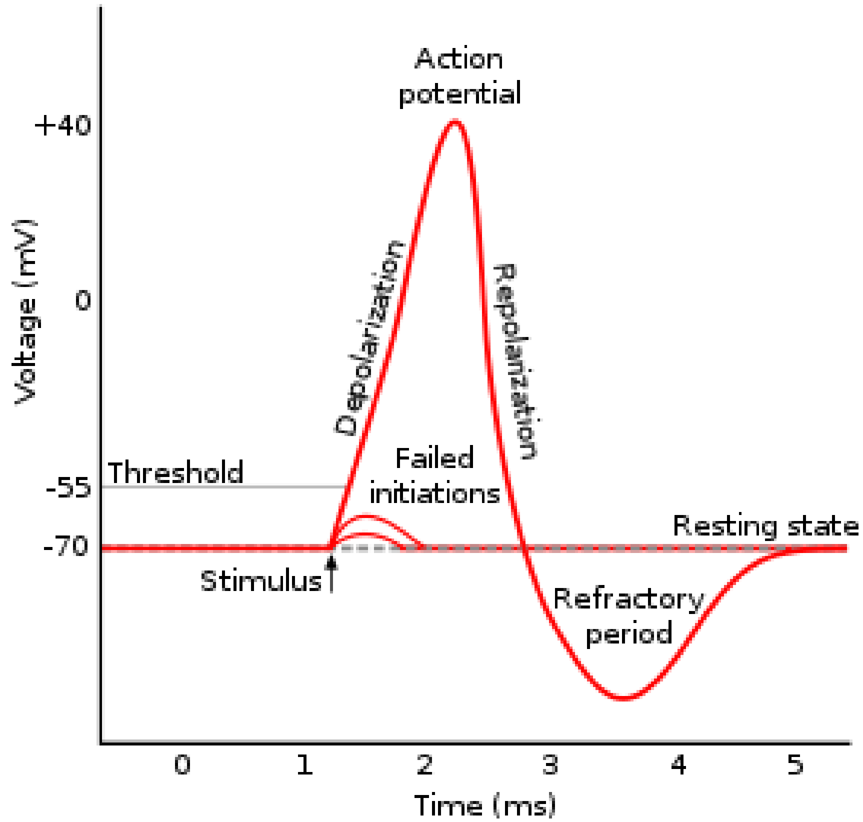
Summary of forces in neuron at rest

Ion	Concentration gradient	Electrostatic force	Permeability
K^+	Inside >> Outside	- (pulls K^+ **in**)	Higher
Na^+	Outside >> Inside	- (pulls Na^+ **in**)	Lower

What happens if something changes?

- Easier for Karl [K^+] to exit?
- Easier for Nate [Na^+] to enter?
- Some action!

Action potential



Phases of the action potential

- Threshold of excitation
- Increase (rising phase/depolarization)
- Peak
  - at positive voltage
- Decline (falling phase/repolarization)
- Return to resting potential (refractory period)

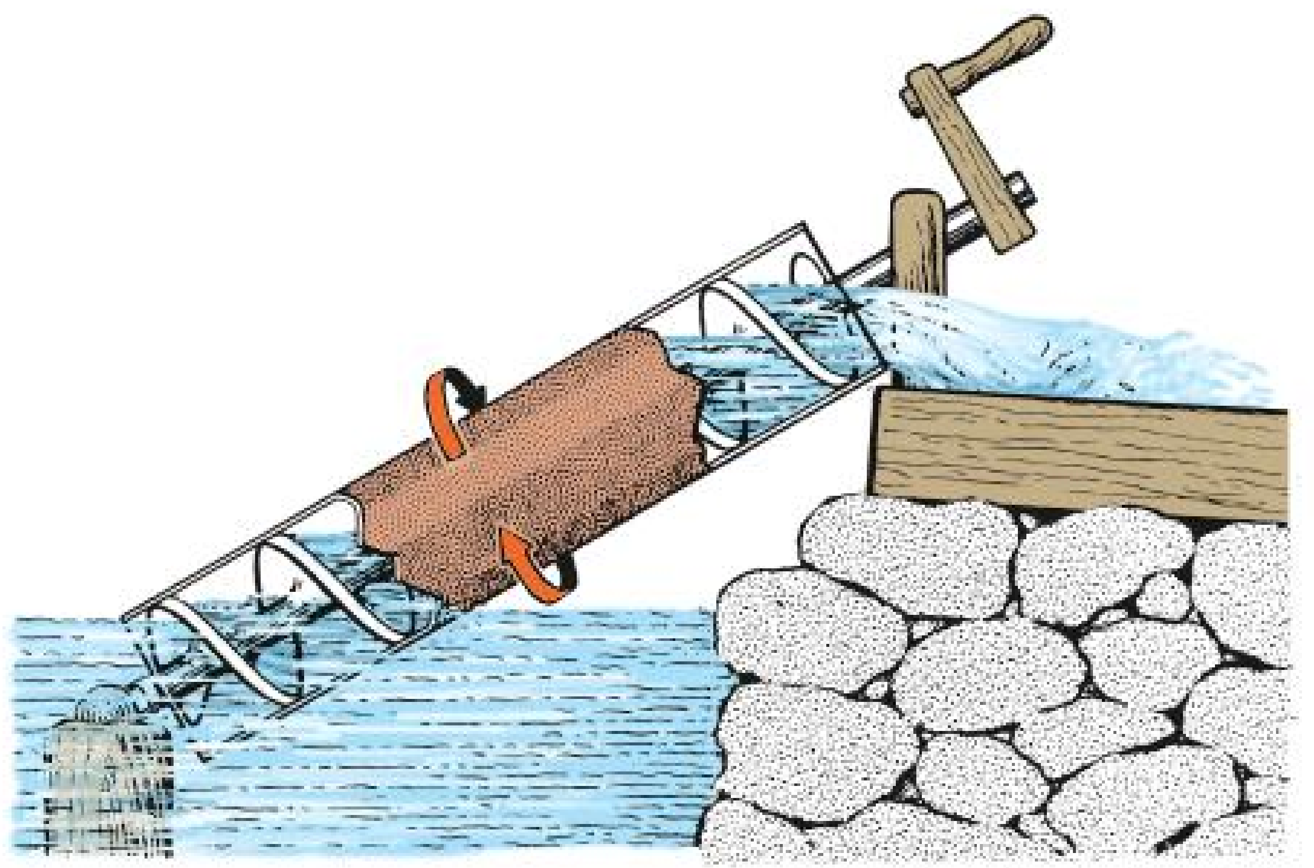
Action potential break-down

Phase	Neuron State
Rise to threshold	+ input makes membrane potential more +
Rising phase	Voltage-gated Na^+ channels open, Na^+ flows in
Peak	Voltage-gated Na^+ channels close and deactivate; voltage-gated K^+ channels open
Falling phase	K^+ flows out
Refractory period	Na^+/K^+ pump restores $[Na^+]$, $[K^+]$; voltage-gated K^+ channels close

What’s a Na^+/K^+ pump?

- Enzyme – Na^+/K^+ ATP-ase – embedded in neuron membrane
- Pumps Na^+ and K^+ *against* concentration gradients
- Na^+ out; K^+ in
- Uses adensosine triphosphate (ATP) form of chemical energy

Example in another domain



http://media-2.web.britannica.com/eb-media/75/103875-004-5F8D1D0E.jpg

Refractory periods

- *Absolute*
    - Cannot generate action potential (AP) no matter the size of the stimulus
    - Voltage-gated Na^+ channels inactivated, reactivate in time.

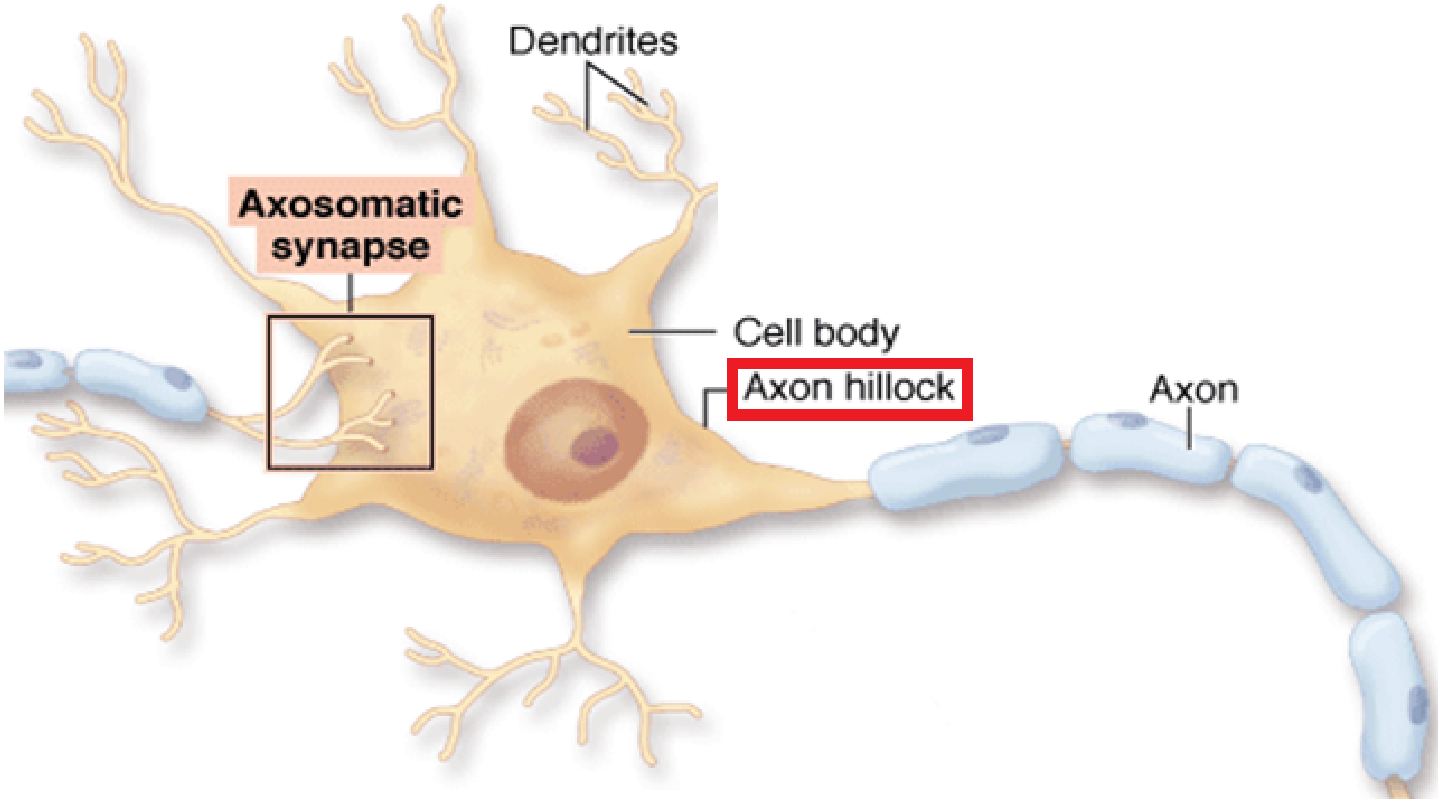
Refractory periods

- *Relative*
    - Can generate AP with larg(er) stimulus
    - Some voltage-gated K^+ channels still open
- Refractory periods put ‘spaces’ between APs

Generating APs

- *Axon hillock*
    - Portion of soma adjacent to axon
    - Integrates/sums input to soma
- *Axon initial segment*
    - Umyelinated portion of axon adjacent to soma
    - Voltage-gated Na^+ and K^+ channels exposed
    - If sum of input to soma > threshold, voltage-gated Na^+ channels open

Axon hillock, axon initial segment



Nodes of Ranvier

- *Regenerate* action potential
- Na^+ and K^+ channels exposed to extracellular environment
- Between Nodes of Ranvier, ions can’t move out, so move along
- Nodes of Ranvier -> Action potentials faster & reliable for a given diameter

Main points

- Resting potential maintained by balance of forces (diffusion, electrostatic)
- Action potential generated when balance is altered
  - $[Na^+]$ in: rising phase to + peak
  - $[K^+]$ out: falling phase

Next time

- More on the action potential
- Review for Exam 1

References