PSYCH 260

Cellular neuroscience

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2021-09-20 15:24:24

How to play EyeWire (03:56)

http://eyewire.org

Announcements

- No class this Thursday, 9/16
- Exam 1 next Thursday, 9/23
  - 40 questions
- Complete 1 “component/section” in EyeWire, earn 5 extra credit points.
  - Take screen shot, email to Megan
  - Due before Friday, 10/1

Today's Topics

- Cells of the nervous system
  - *Glia*
  - *Neurons*
- How do these cells communicate?

Cells of the nervous system

We are human

- ~ 37 trillion (10^9) (Roy & Conroy, 2018) cells
- 10-100 trillion non-human cells

How many neurons and glia?

- Old “lore”: ~100 billion neurons
- New estimate (Azevedo et al., 2009)
  - ~86 +/- 8 billion neurons
  - ~85 +/- 9 billion glia
- 100-500 trillion synapses, 1 billion/mm^3

Could you count to 170 billion?

- How many years to count to 170 billion?
- 60 s/min x 60 min/hr x 24 hrs/day x 365 days/ yr = 31,536,000 s/yr
- 1.7e11/31,536,000 = 5,390 years

Mass, Neurons, Non-Neurons

The Journal of Comparative Neurology

536 F.A.C. AZEVEDO ET AL.

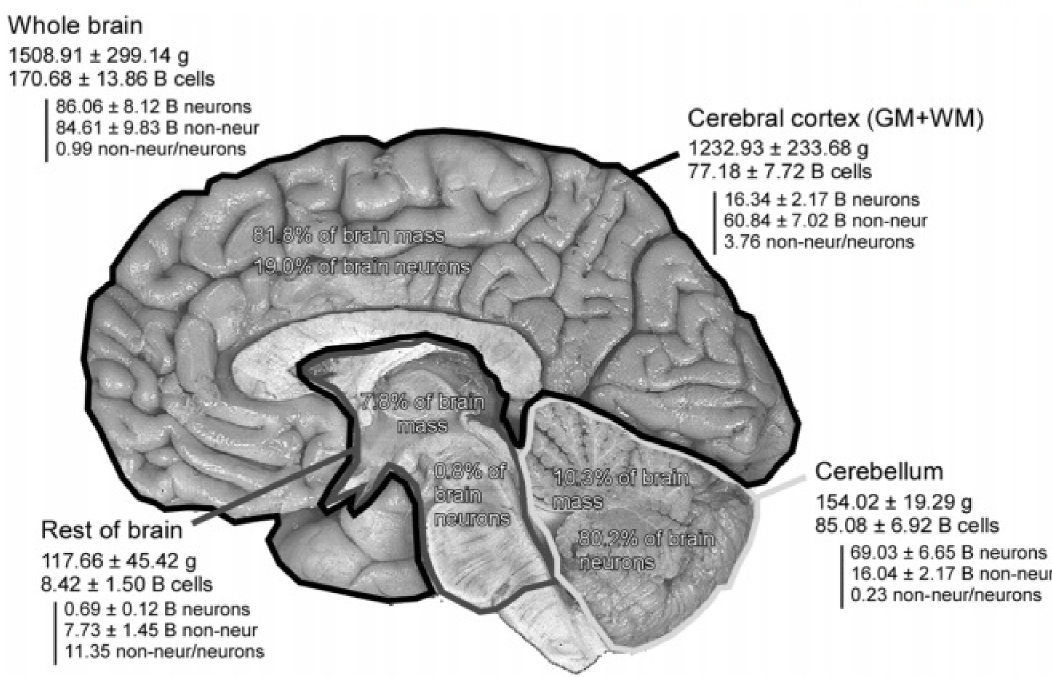
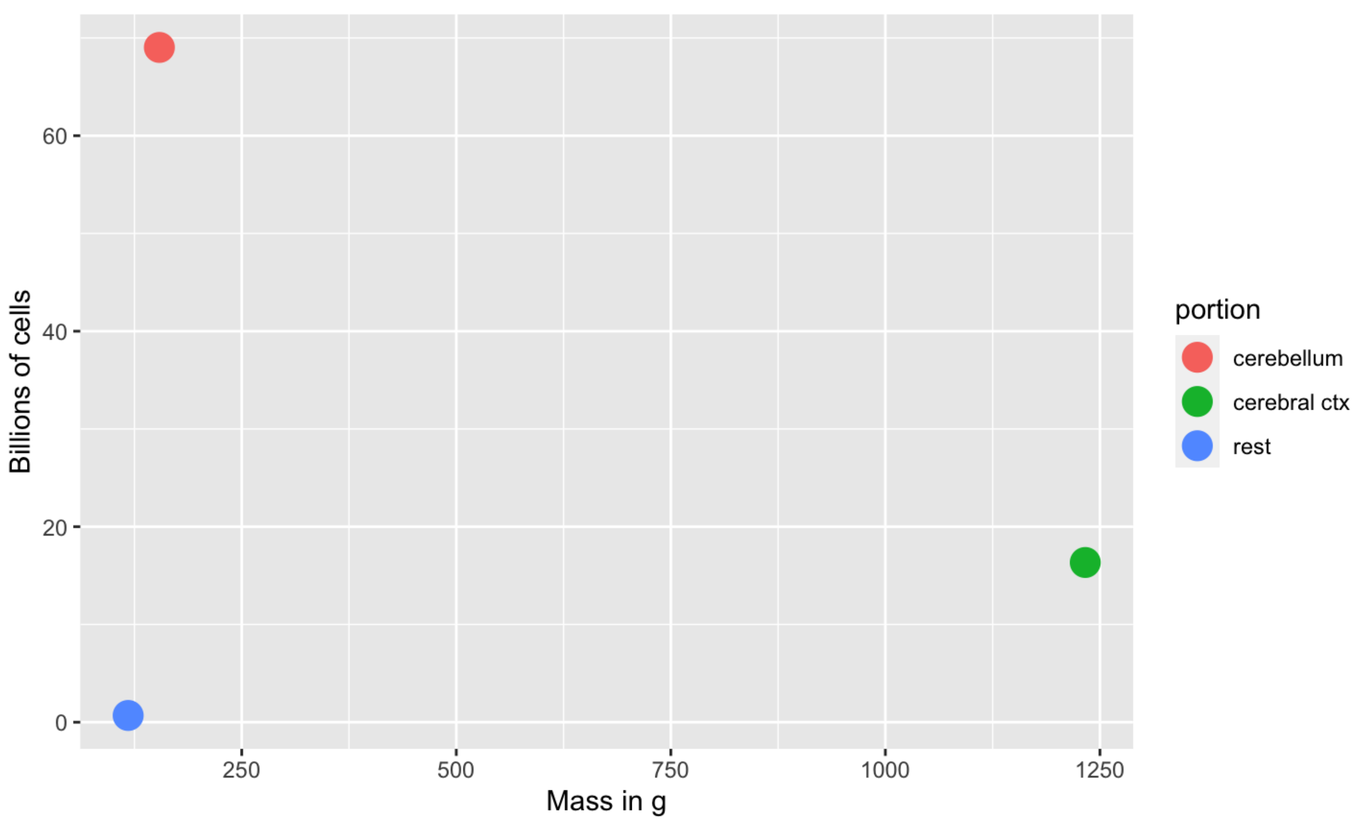


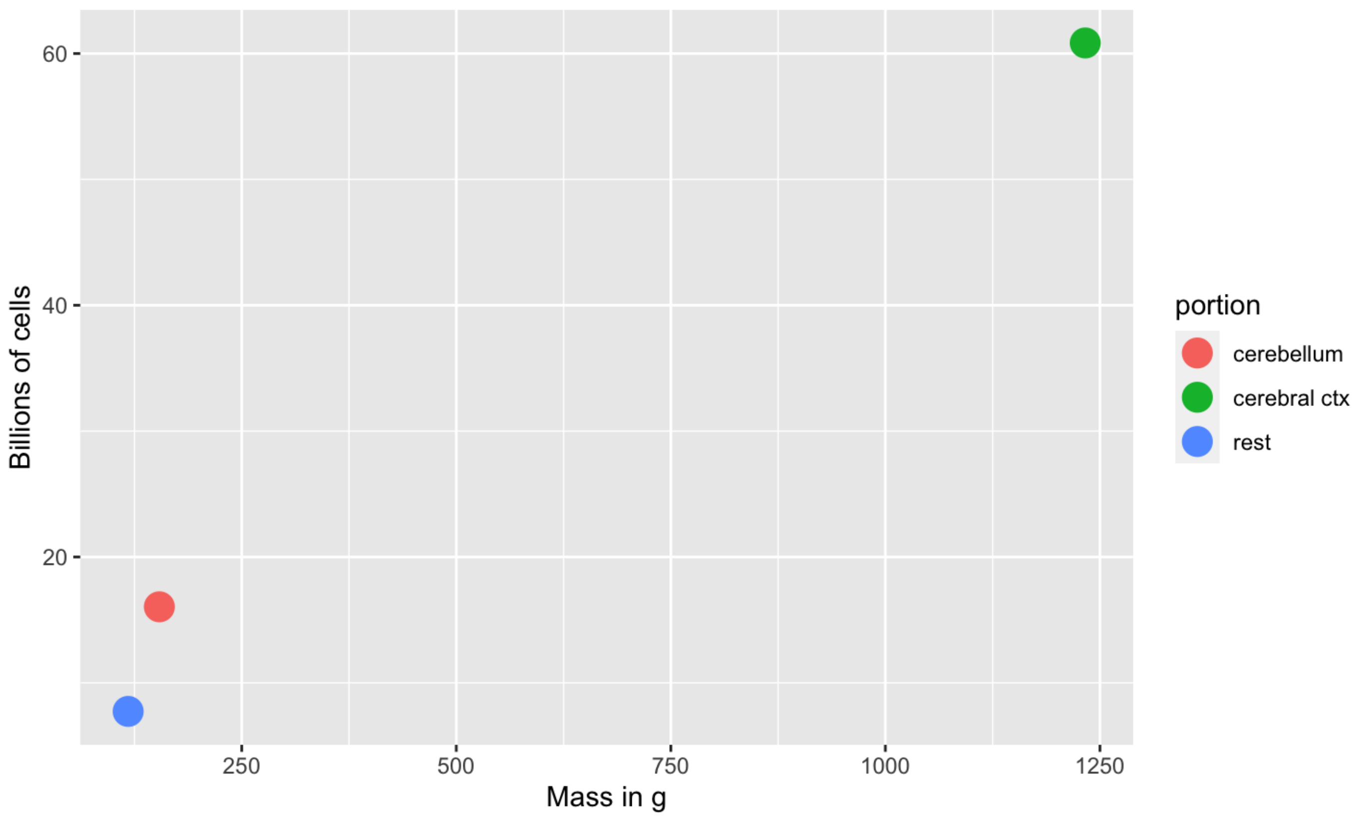
Figure 2.
Absolute mass, numbers of neurons, and numbers of nonneuronal cells in the entire adult human brain. Values are mean ± SD and refer to the two hemispheres together. B, billion.

(Azevedo et al., 2009)

Neurons by brain mass



Non-neuronal cells by brain mass

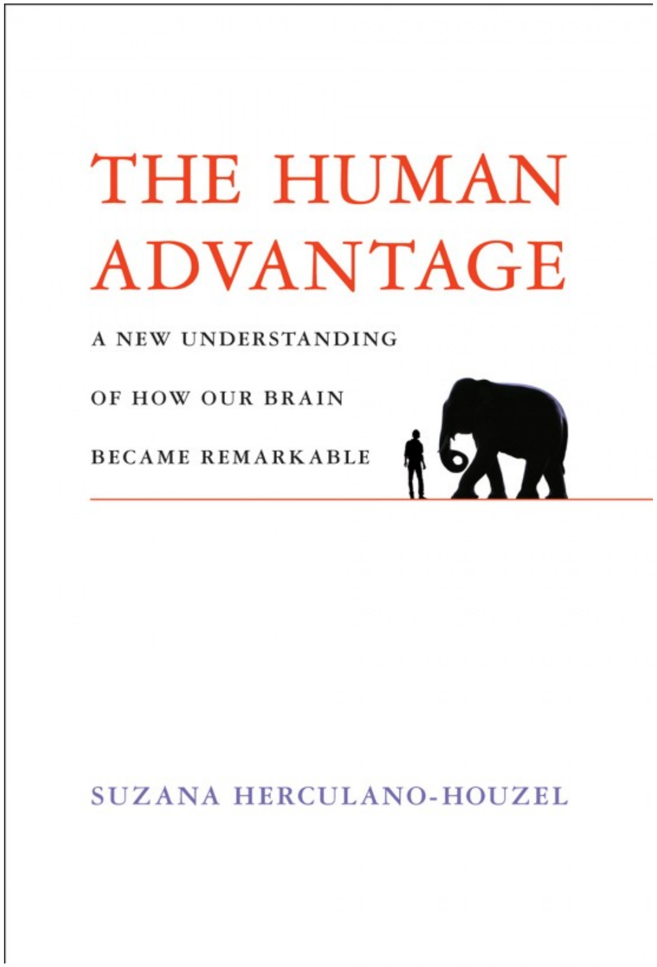


How many neurons and glia?

“These findings challenge the common view that humans stand out from other primates in their brain composition and indicate that, with regard to numbers of neuronal and nonneuronal cells, the human brain is an isometrically scaled-up primate brain.”

[(Azevedo et al., 2009)]

The Human Advantage



Glia (neuroglia)

- “Glia” means glue
- Functions
  - Structural support
  - Metabolic support
  - Brain development
  - Neural plasticity?

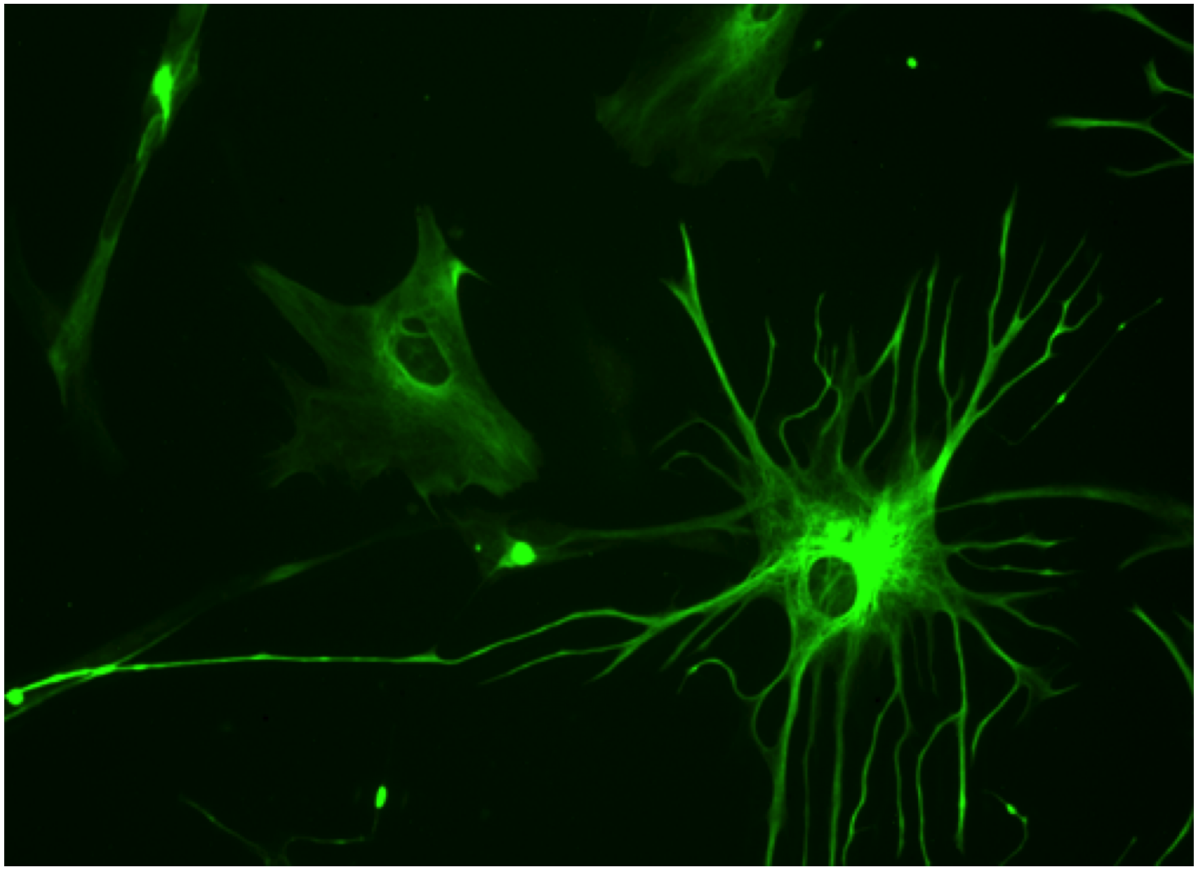
Astrocytes

- “Star-shaped”
- Physical and metabolic support
    - Blood/brain barrier
    - Regulate concentration of key ions (Ca^{++}/K^{+}) for neural communication
    - Regulate concentration of key neurotransmitters (e.g., glutamate)

Astrocytes

- Shape brain development, synaptic plasticity
- Regulate local blood flow
- Regulate/influence communication between neurons, (Bazargani & Attwell, 2016)
- Disruption linked to cognitive impairment, disease (Chung, Welsh, Barres, & Stevens, 2015)

Astrocytes



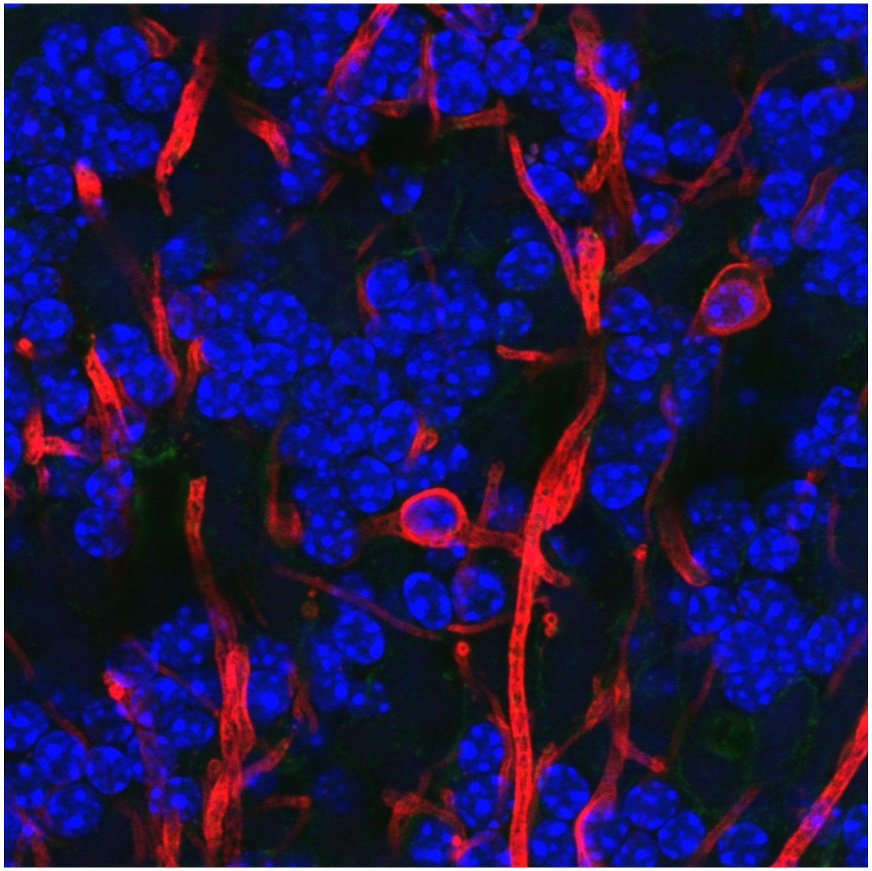
Myelinating cells

- Produce myelin or myelin sheath
  - White, fatty substance
  - Surrounds many neurons
  - The “white” in white matter
- Provide electrical/chemical insulation
- Make neuronal messages faster, less susceptible to noise

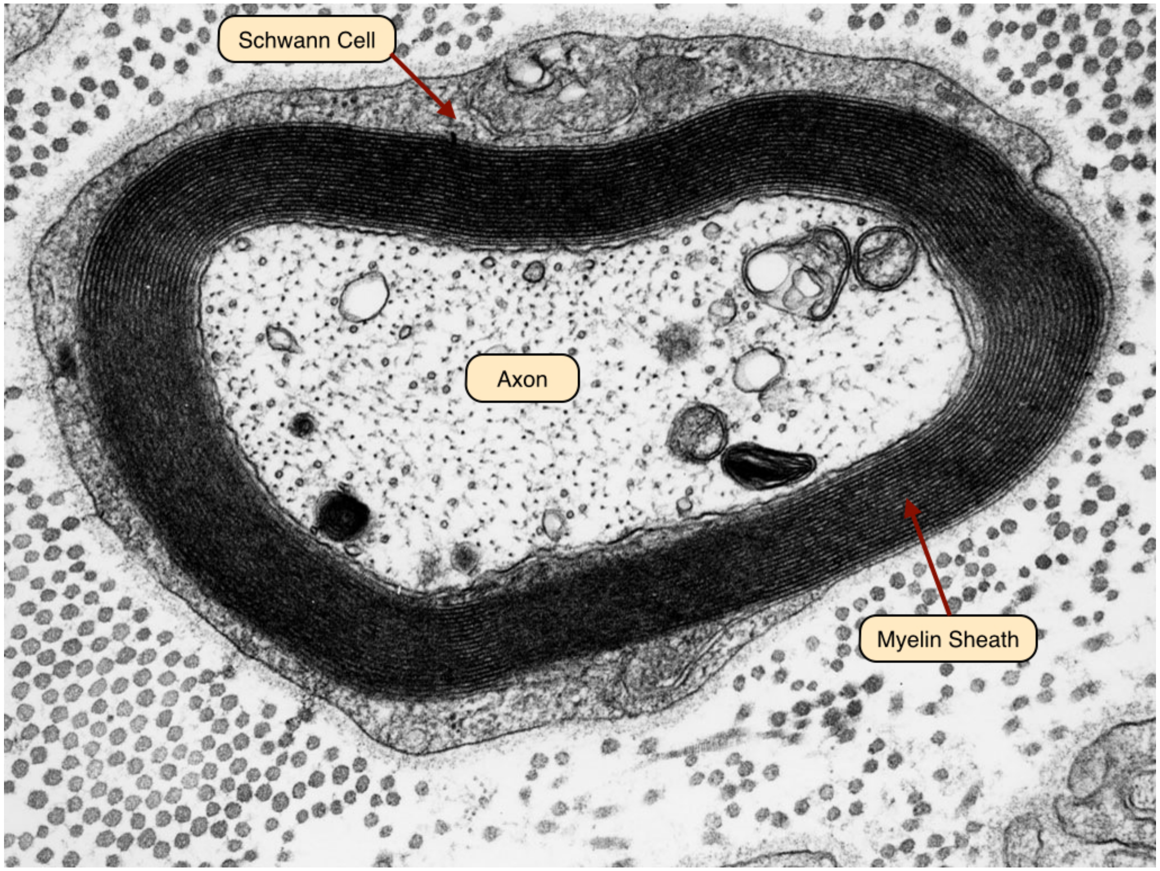
Types of myelin-producing cells

- Oligodendrocytes
  - In brain and spinal cord (CNS)
  - 1:many neurons
- Schwann cells
  - In PNS
  - 1:1 neuron
  - Facilitate neuro-regeneration

Oligodendrocytes



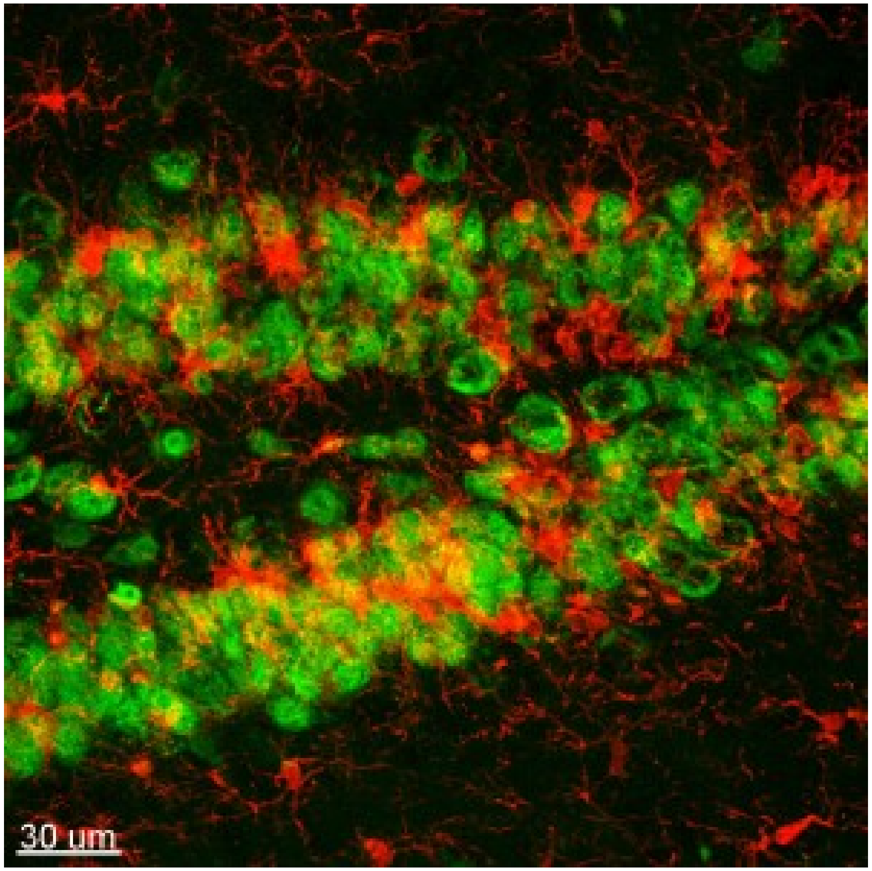
Schwann Cells



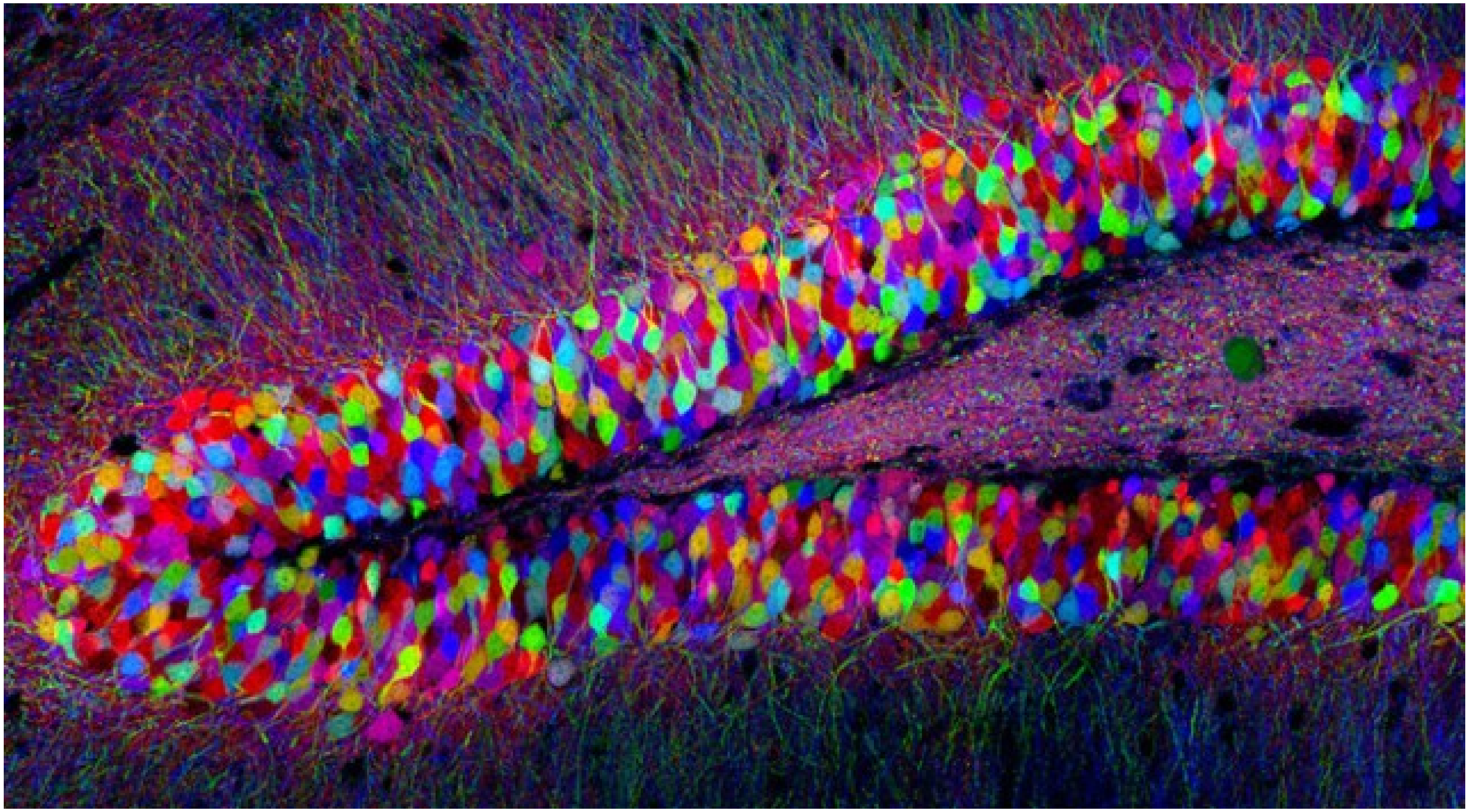
Microglia

- Phagocytosis
- Clean-up damaged, dead tissue
- Prune synapses in normal development and disease
- Disruptions in microglia pruning -> impaired functional brain connectivity and social behavior, (Zhan et al., 2014)

Microglia



Neurons



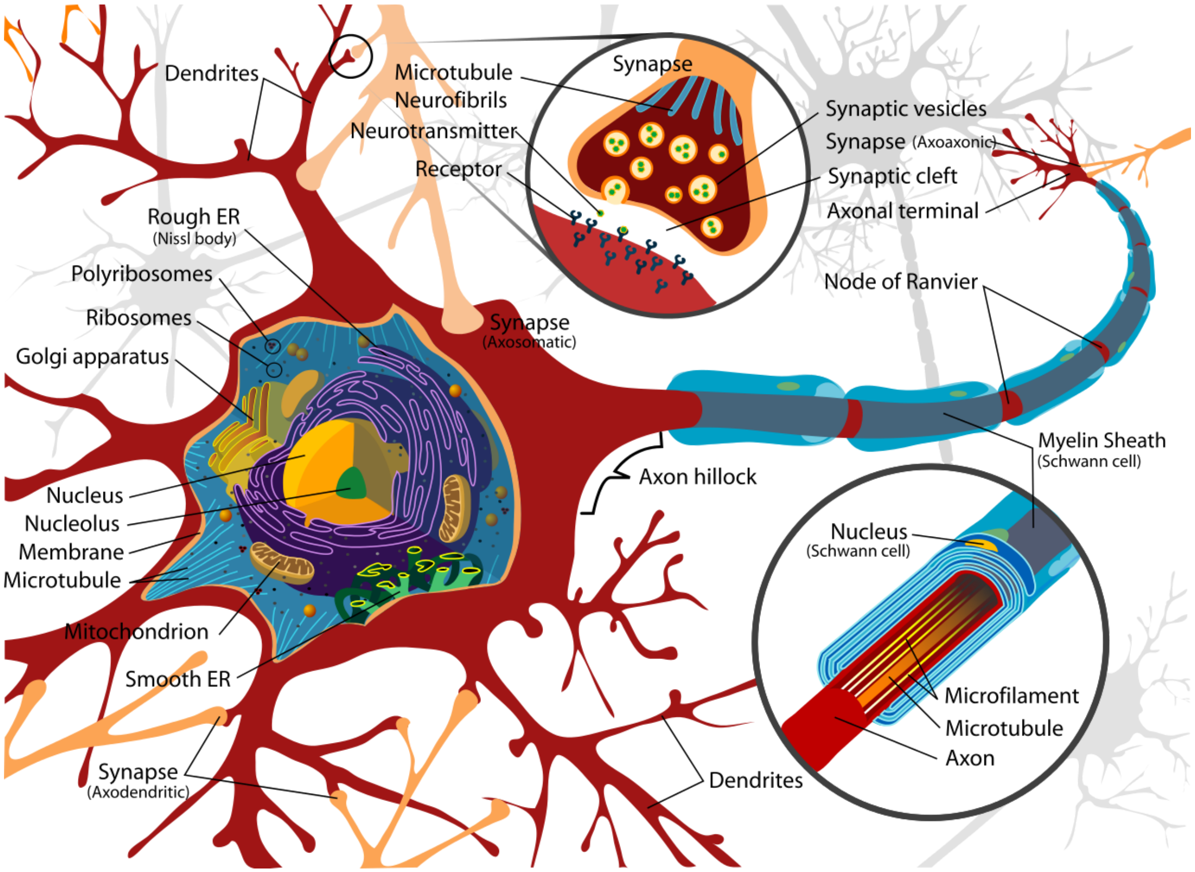
Fun facts about neurons

- Specialized for electrical & chemical communication
- Post-mitotic – don't divide
- Most born early in life, (Bhardwaj et al., 2006)
- Among longest-lived cells in body, may scale with organism lifespan (Magrassi, Leto, & Rossi, 2013)
- Can extend over long distances

Macrostructure of neurons

- Dendrites
- Soma (cell body)
- Axons
- Terminal buttons (boutons)

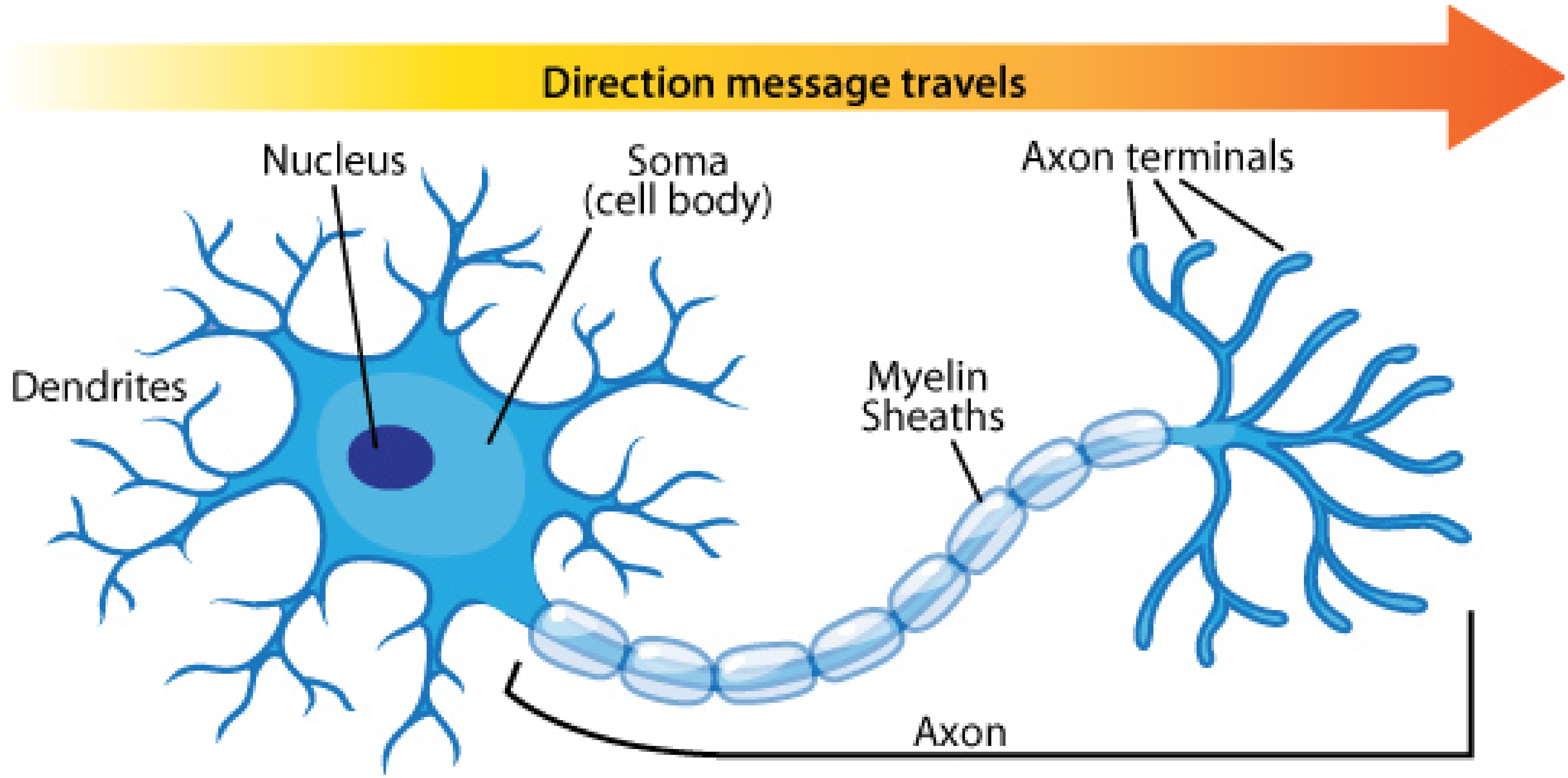
Structure of neurons



Dendrites

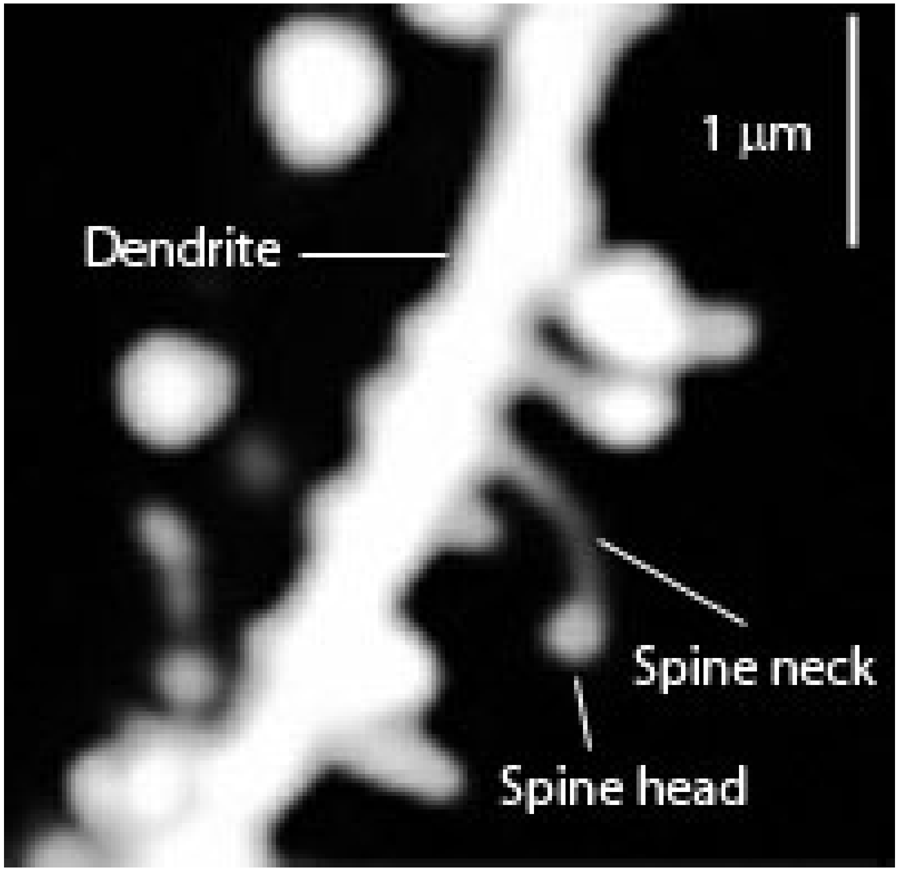
- Branch-like “extrusions” from cell body
- Majority of input to neuron
- Cluster close to cell body/soma
- Usually receive info
- Passive (do not regenerate electrical signal) vs. active (regenerate signal)
- Spines

Dendrites



Direction message travels
Nucleus
Soma
(cell body)
Axon terminals
Dendrites
Myelin
Sheaths
Axon

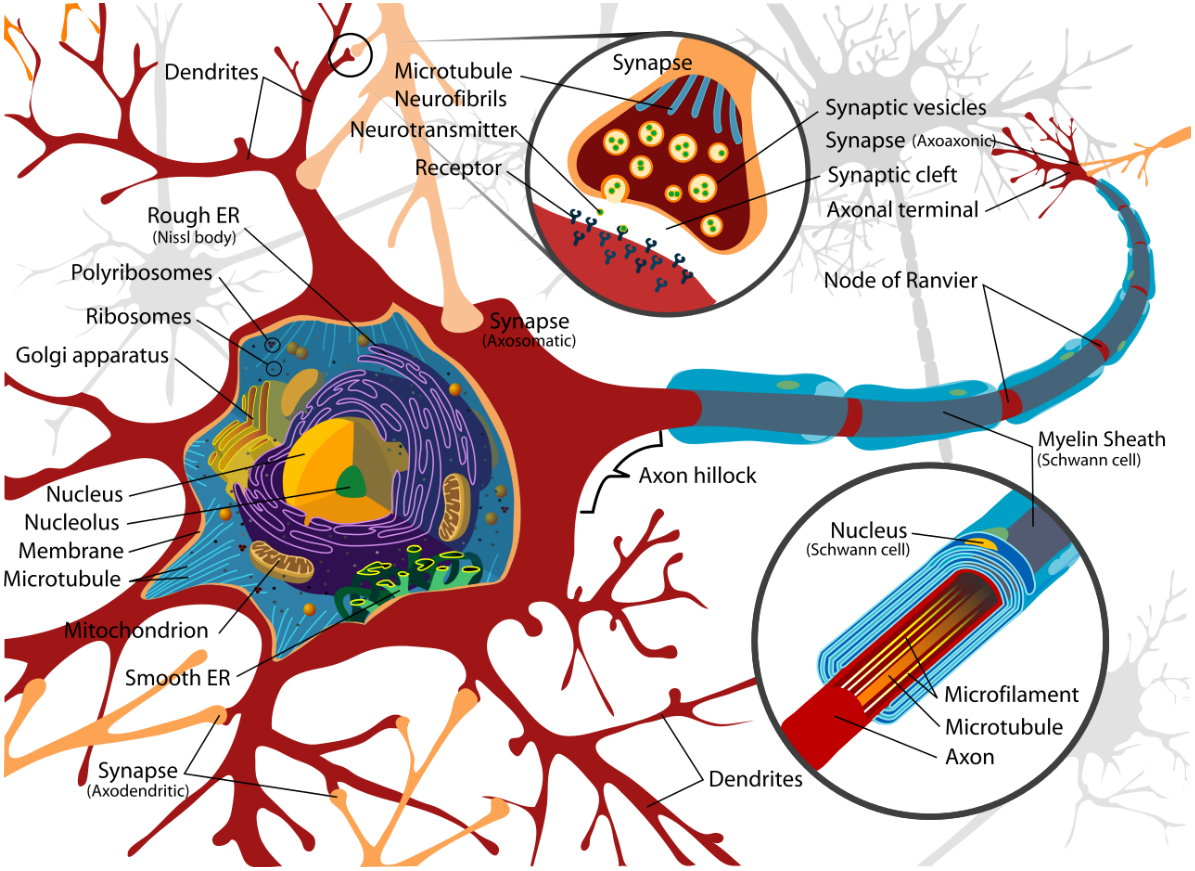
Dendritic Spines



Soma (cell body)

- Varied shapes
- Nucleus
  - Chromosomes
- Organelles
  - Mitochonrdria
  - Smooth and Rough Endoplasmic reticulum (ER)

Soma



Dendrites
Microtubule
Neurofibrils
Neurotransmitter
Receptor
Synapse
Synaptic vesicles
Synapse (Axoaxonic)
Synaptic cleft
Axonal terminal
Rough ER
(Nissl body)
Polyribosomes
Ribosomes
Golgi apparatus
Synapse
(Axosomatic)
Node of Ranvier
Myelin Sheath
(Schwann cell)
Axon hillock
Nucleus
Nucleolus
Membrane
Microtubule
Mitochondrion
Smooth ER
Nucleus
(Schwann cell)
Microfilament
Microtubule
Axon
Synapse
(Axodendritic)
Dendrites

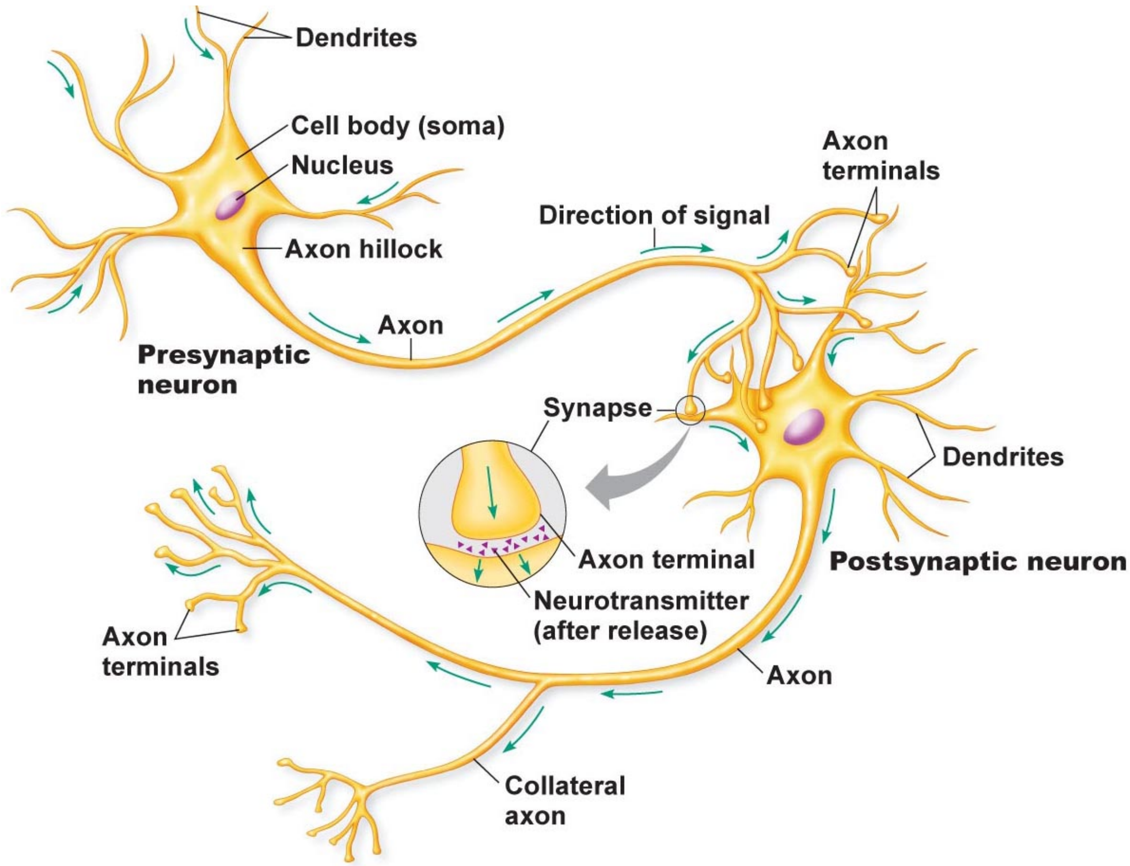
Axons

- Another branch-like “extrusion” from soma
- Extend farther than dendrites
- Usually transmit info

Axons

- Parts
  - **Initial segment** (closest to soma, unmyelinated)
  - **Nodes of Ranvier** (unmyelinated segments along axon)
  - Terminals, axon terminals, terminal buttons, synaptic terminals, synaptic boutons

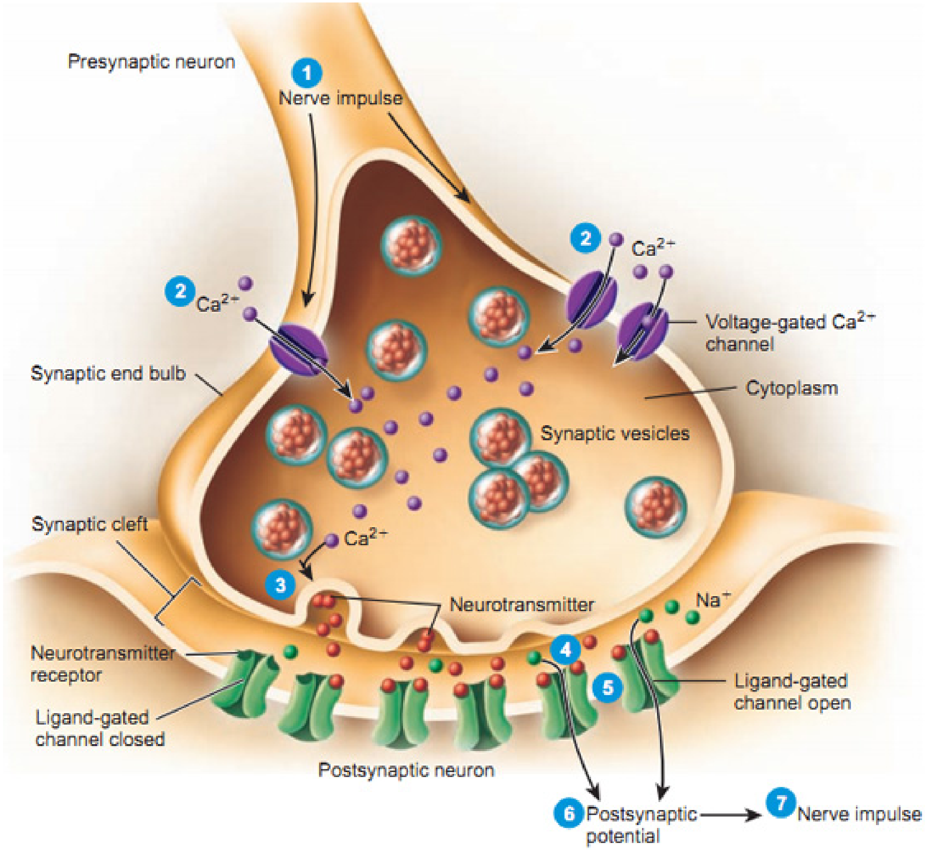
Axons


Dendrites
Cell body (soma)
Nucleus
Axon hillock
Axon
Presynaptic neuron
Direction of signal
Axon terminals
Synapse
Axon terminal
Neurotransmitter (after release)
Dendrites
Postsynaptic neuron
Axon terminals
Axon
Collateral axon

Synaptic bouton (terminal button)

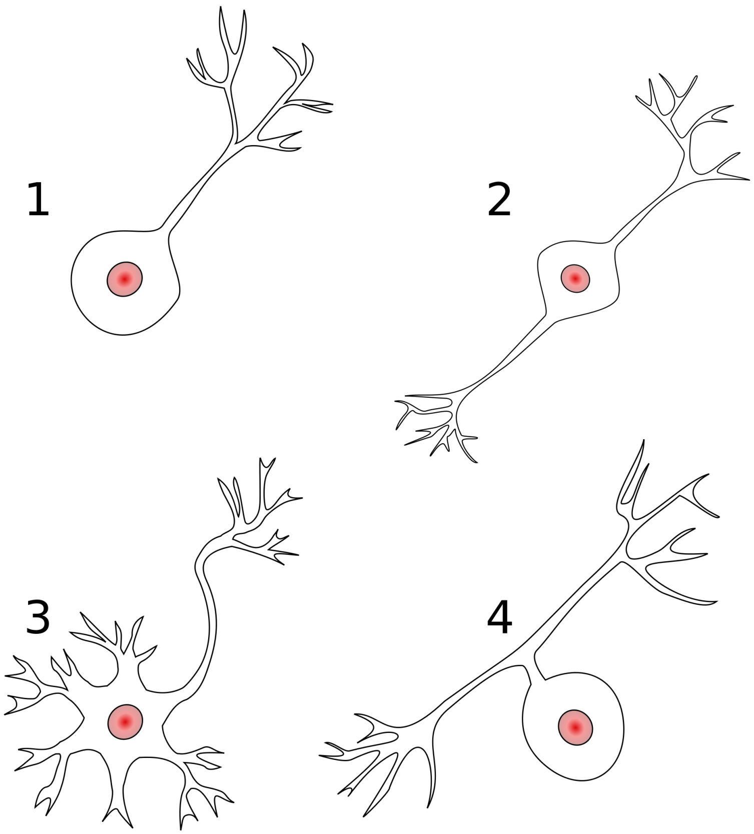
- Synapse (~5-10K per neuron)
- Presynaptic membrane (sending cell) and postsynaptic (receiving cell) membrane
- Synaptic cleft – space between cells
- Synaptic vesicles
  - Pouches of neurotransmitters
- Autoreceptors (detect NTs); transporters (transport NTs across membrane)

Synaptic bouton (terminal button)



Classifying neurons

- Functional role
  - Input (sensory), output (motor/secretory), interneurons
- Anatomy
  - Unipolar
  - Bipolar
  - Multipolar



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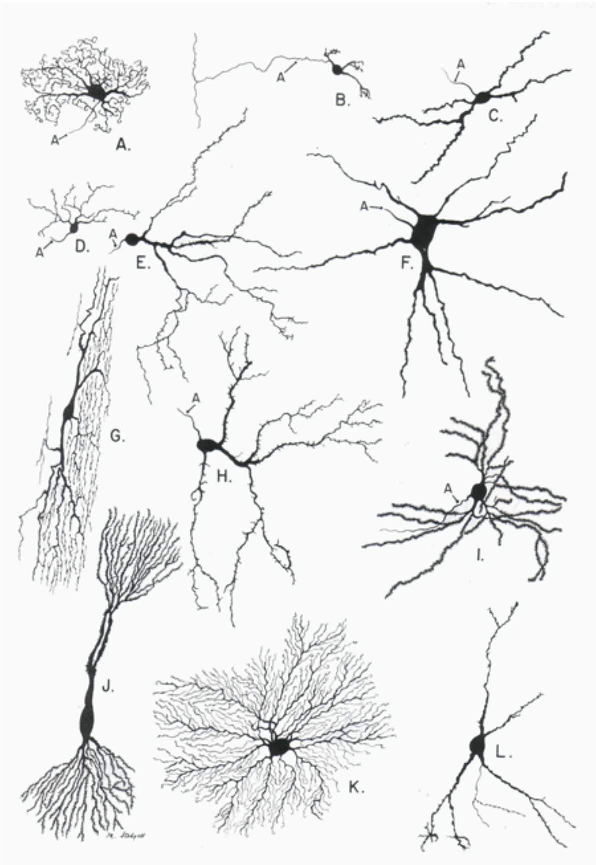
Neurons_uni_bi_multi_pseudouni.svg.pngg

Classifying neurons

- By specific anatomy
    - Pyramidal cells
    - Stellate cells
    - Purkinje cells
    - Granule cells

Neurons by type



How neurons communicate

Neural communication

- Electrical
  - Fast(er)
  - Metabolically costly
  - Within neurons

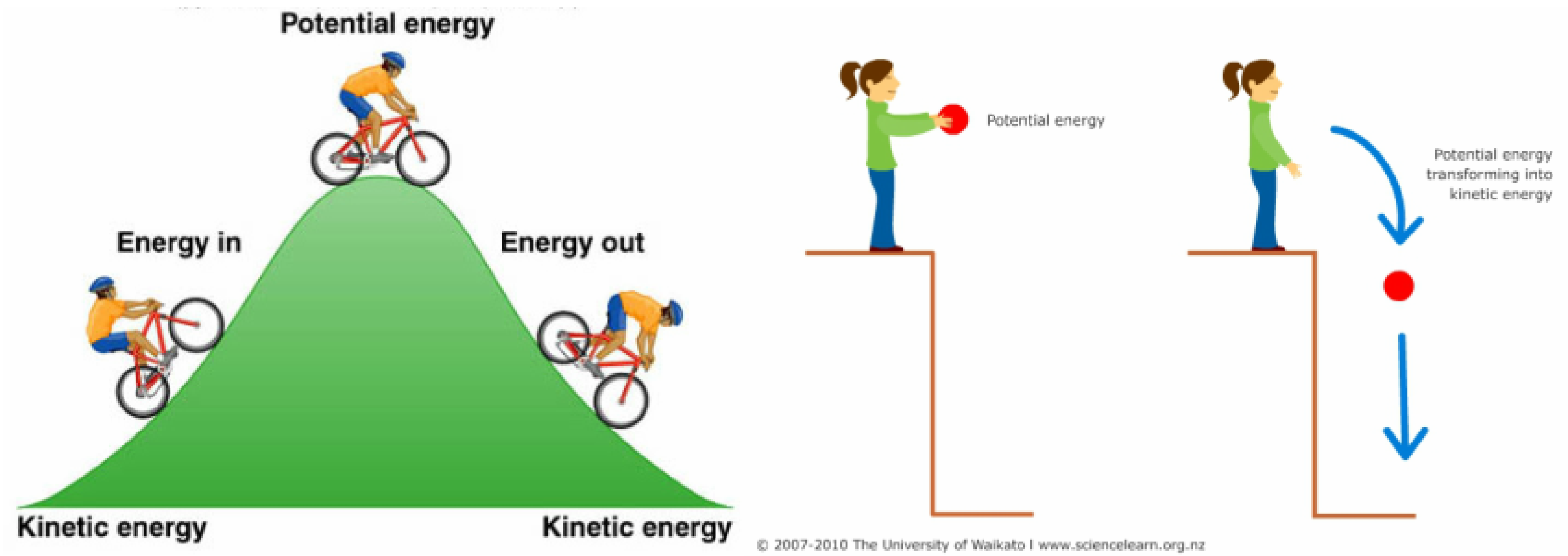
Neural communication

- Chemical
  - Slow(er)
  - Metabolically cheap
  - Between neurons, & brain <-> body (via hormones)

How are messages generated?

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

Potential energy



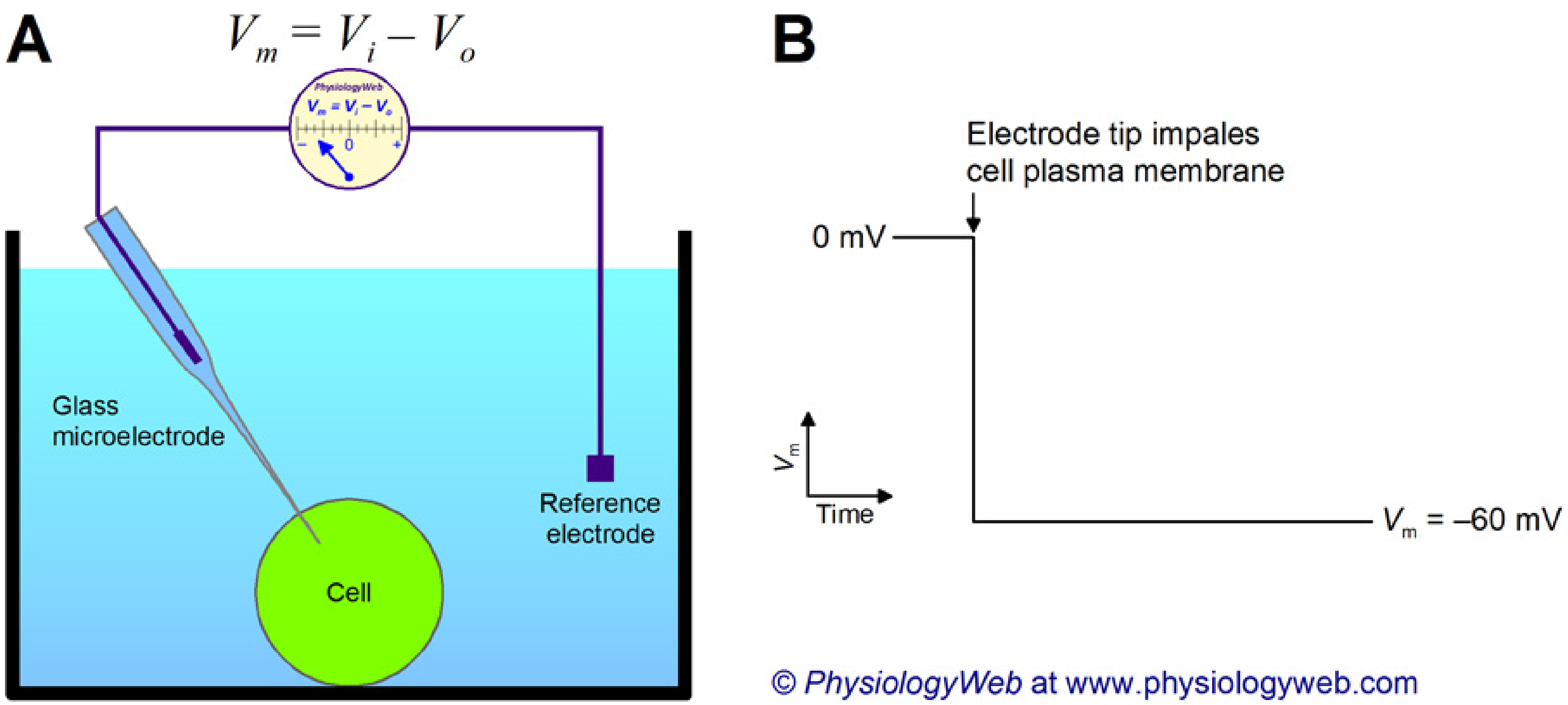
Types of neural electrical potentials

- Resting potential
- Action potential

Resting potential

- How to measure
  - Electrode on inside
  - Electrode on outside
  - Inside - Outside = potential

Resting potential



Resting potential

- Neuron (and other cells) have *potential energy*
  - Inside neuron 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^-
- Organic anions, A^-

Resting potential arises from

- A balance of forces
  - Force of diffusion
  - Electrostatic force
- Forces cause ion flows across membrane
- Ion channels allow ion flow

Ion channels

- Openings in neural membrane
- Selective
- Vary in permeability

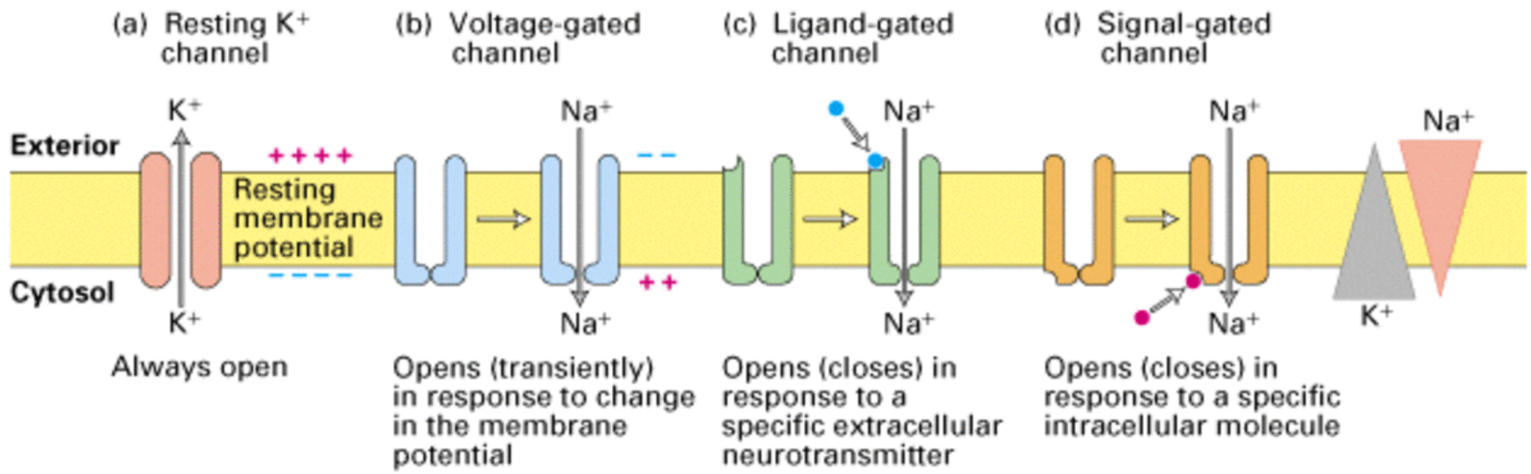
Ion channel Types

- *Passive/leak*
  - Always open
- *Voltage-gated*
  - Open/close at certain voltages

Ion channel Types

- *Ligand-gated* (chemically-gated)
    - Open/close in presence of special chemicals (ligands)
- Transporters/pumps
    - Move (transport/pump) ions using metabolic energy

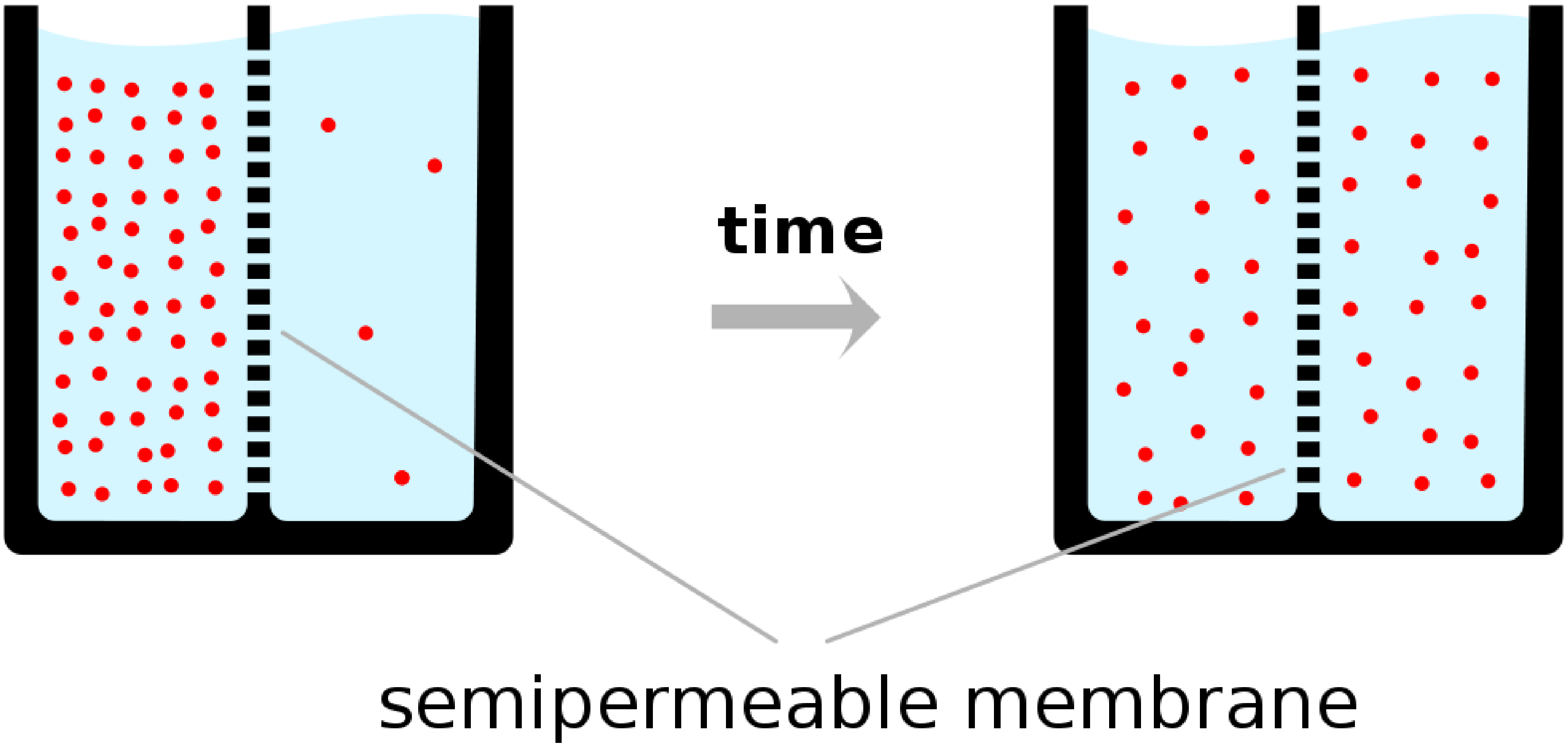
Ion channels



Neuron at rest permeable to K+

- Passive K+ channels open
- [K+] concentration inside >> outside
  - Transporter pumps K+ in
- And then, K+ flows out
  - Force of diffusion

Force of diffusion

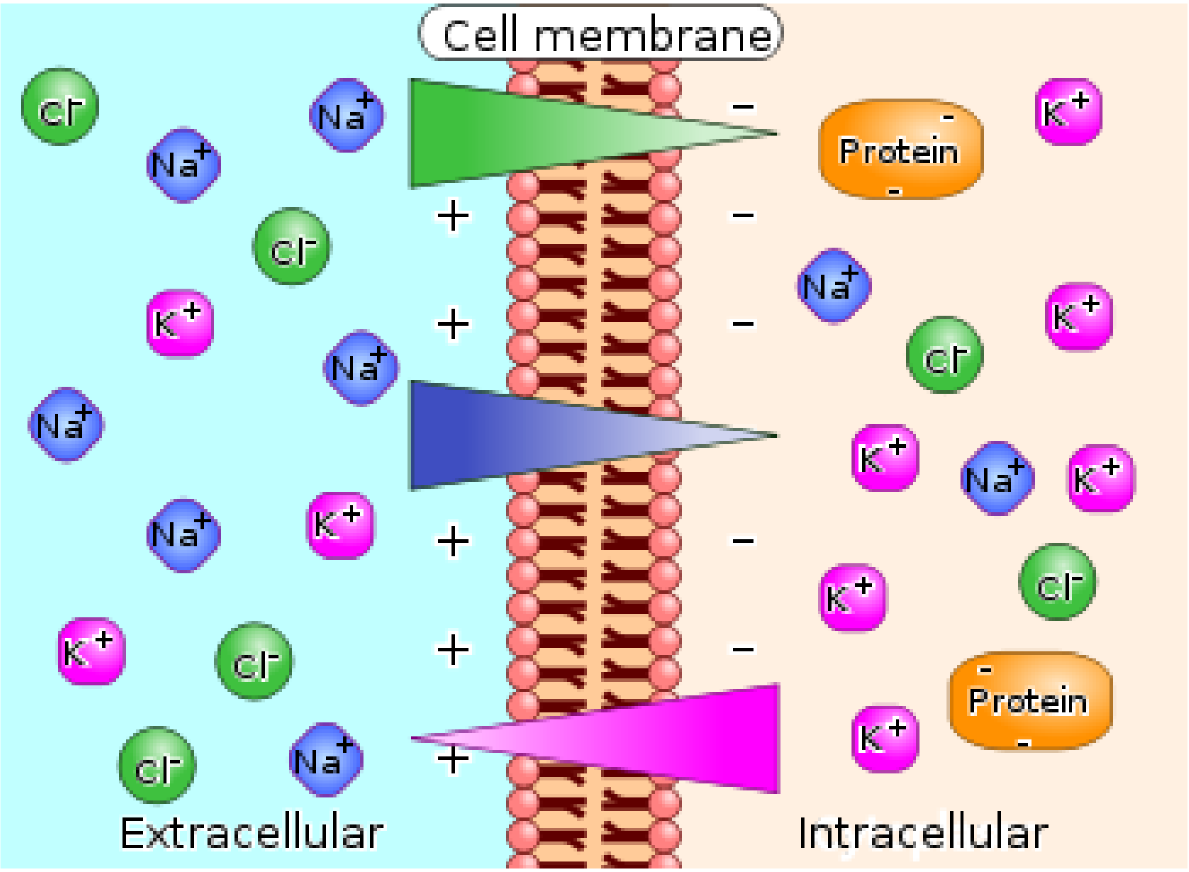


Force of diffusion

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+ || A-
- Charge separation creates a voltage
- Outside +/inside -
- Voltage build-up stops outflow of K+ (before inside/outside concentrations are ==)

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**
  - Positive K+ accumulate along outside
  - Negative A- accumulate along inside
  - K+ || A- along membrane creates battery-like voltage
  - Voltage build-up stops K+ outflow

Electrostatic force

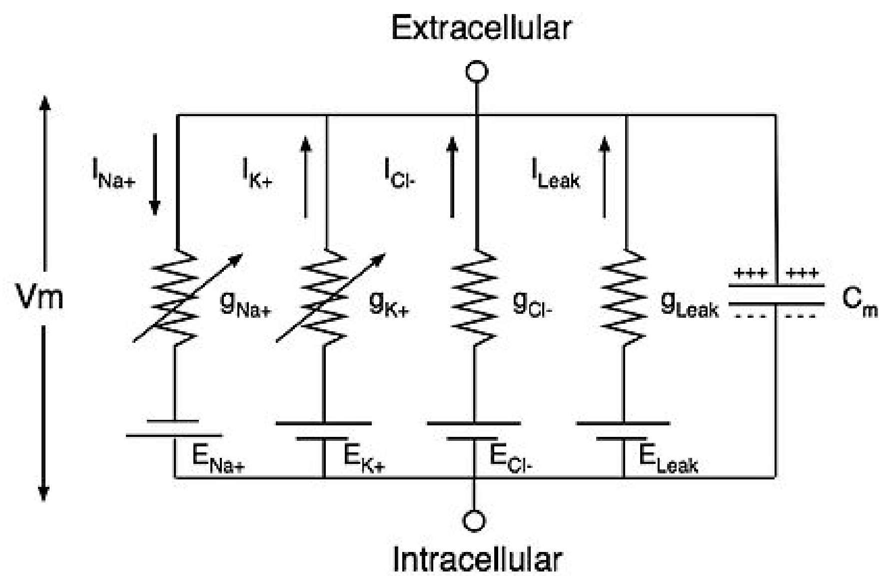
- Specific voltage called *equilibrium potential* for K+
- K+ positive, so equilibrium potential negative (w/ respect to outside)
- Equilibrium potential close to neuron resting potential

Equilibrium potentials calculated under typical conditions

Ion	[inside]	[outside]	Voltage
K+	~150 mM	~4 mM	~ -90 mV

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

Electrical circuit model



Resting potential ≠ K+ equilibrium potential

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

Next time

- More on neural communication
- What are the other ions doing?

References

Azevedo, F. A., Carvalho, L. R., Grinberg, L. T., Farfel, J. M., Ferretti, R. E., Leite, R. E., … others. (2009). Equal numbers of neuronal and nonneuronal cells make the human brain an isometrically scaled-up primate brain. *Journal of Comparative Neurology*, *513*(5), 532–541.

Bazargani, N., & Attwell, D. (2016). Astrocyte calcium signaling: The third wave. *Nature Neuroscience*, *19*(2), 182–189. https://doi.org/10.1038/nn.4201

Bhardwaj, R. D., Curtis, M. A., Spalding, K. L., Buchholz, B. A., Fink, D., Björk-Eriksson, T., … Frisén, J. (2006). Neocortical neurogenesis in humans is restricted to development. *Proceedings of the National Academy of Sciences*, *103*(33), 12564–12568. https://doi.org/10.1073/pnas.0605177103

Chung, W.-S., Welsh, C. A., Barres, B. A., & Stevens, B. (2015). Do glia drive synaptic and cognitive impairment in disease? *Nature Neuroscience*, *18*(11), 1539–1545. https://doi.org/10.1038/nn.4142

Magrassi, L., Leto, K., & Rossi, F. (2013). Lifespan of neurons is uncoupled from organismal lifespan. *Proceedings of the National Academy of Sciences*, *110*(11), 4374–4379. https://doi.org/10.1073/pnas.1217505110

Roy, A. L., & Conroy, R. S. (2018). Toward mapping the human body at a cellular resolution. *Molecular Biology of the Cell*, *29*(15), 1779–1785. https://doi.org/10.1091/mbc.E18-04-0260

Zhan, Y., Paolicelli, R. C., Sforazzini, F., Weinhard, L., Bolasco, G., Pagani, F., … Gross, C. T. (2014). Deficient neuron-microglia signaling results in impaired functional brain connectivity and social behavior. *Nature Neuroscience*, *17*(3), 400–406. https://doi.org/10.1038/nn.3641