



Lecture 2: Neurons & Neurophysiology 1

PSYC 304



Announcements

HSP guest speakers

Do You Smoke Cigarettes?

You may be eligible to participate in a research study!

To check your eligibility:

Fill out the quick survey

SCAN ME



If eligible, you will be compensated
for your participation.

Participation will include:

- Questionnaires
- Computer tasks
- Viewing movie clips



THE UNIVERSITY
OF BRITISH COLUMBIA



Principal Investigator:
Dr. Schütz Christian G., MD, PhD, MPH
Psychiatry
H24-02776 v1.0 October 29, 2024

CAPU RISE:
Cannabis and Polysubstance Use:
Response Inhibition and Stress Exposure



Do you use cannabis?

You may be eligible to participate in a research study!

You will receive a paid honorarium and an image of your brain for your participation!

What does the study involve?

- Cannabis administration, MRI, questionnaires, & computer tasks
- 5 sessions and daily surveys (total time = 24 hours)

Who can participate?

You may be eligible to participate if you:

- Are 19-35 years old
- Have no major physical or mental health diagnoses
- Have used cannabis

Interested? Complete the screening survey using the QR code or at this link:
<https://rc.med.ubc.ca/redcap/surveys/?s=7MXHXL4ATA9WLKM>

If you would like to contact the research team directly:
Call 604-827-4287 or email brainlab.cannabis@ubc.ca

Principal Investigator: Christian Schütz, MD PhD MPH FRCPC

H20-03441 Version 8.0 2024/05/09



[https://rc.med.
ubc.ca/redcap/s
urveys/?s=LCP8
EK4447KTMC7](https://rc.med.ubc.ca/redcap/surveys/?s=LCP8EK4447KTMC7)

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[https://redcap.l
nk/8jec33jz](https://redcap.lnk/8jec33jz)



Analog review

Put your notes away and write down the important bits from last class



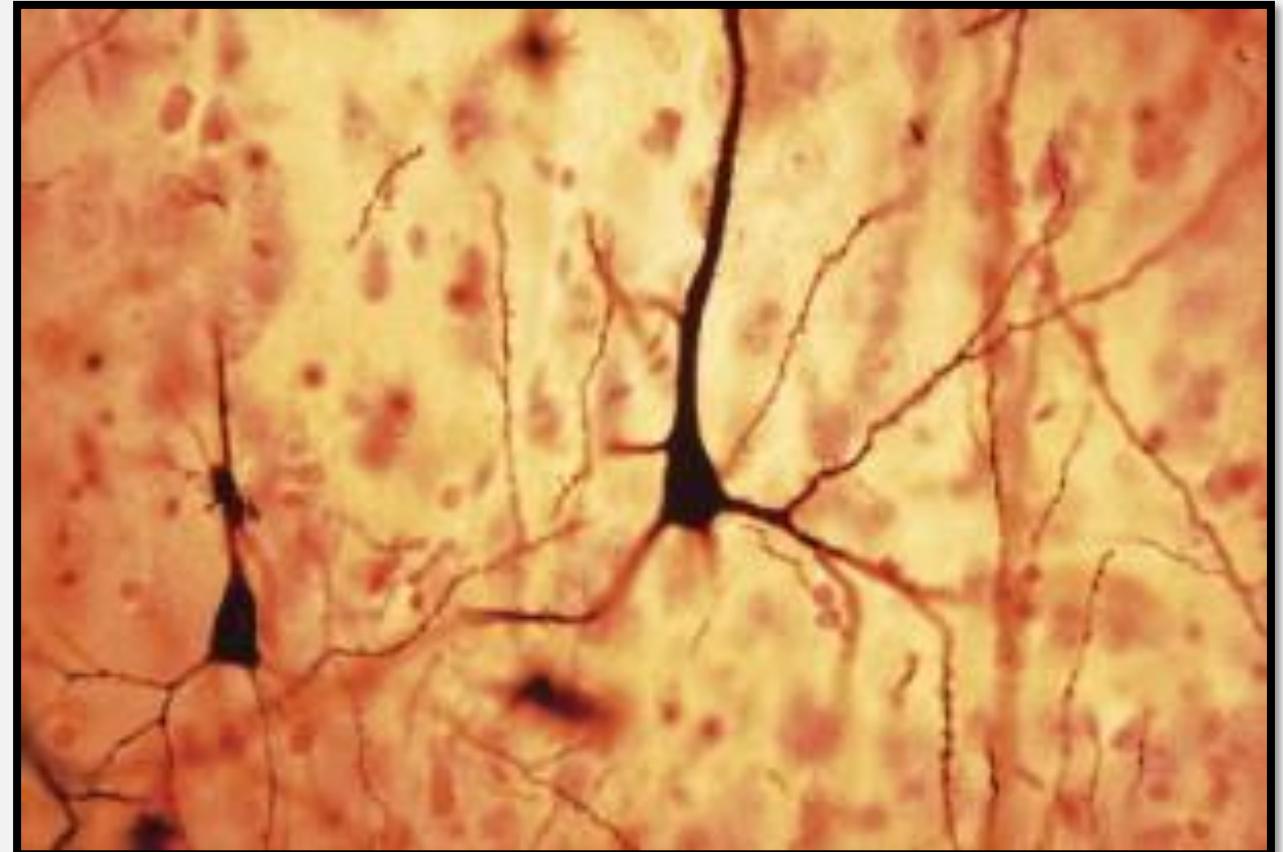
Lecture 2 ‘Seeing’ Neurons

PSYC 304

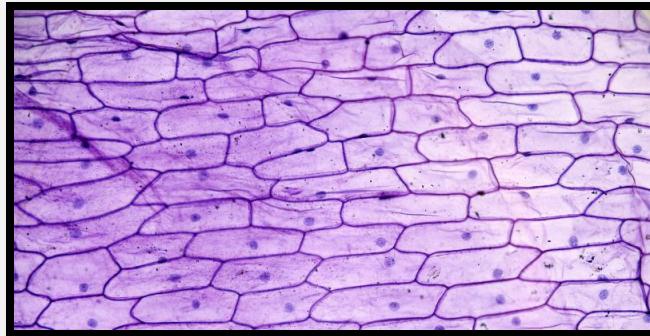
Neurons & Circuits: Learning outcomes

By the end of lecture, you will...

1. Appreciate that neurons and circuits are the foundational units of brain function.
2. Be able to label and differentiate between different types of neurons.
3. Be able to evaluate methods for identifying neurons as anatomical building blocks, including Golgi, dye injection, genetically-encoded fluorescent proteins, immunohistochemistry, electron microscopy and brain clearing
4. Understand research applications for different visualization techniques.



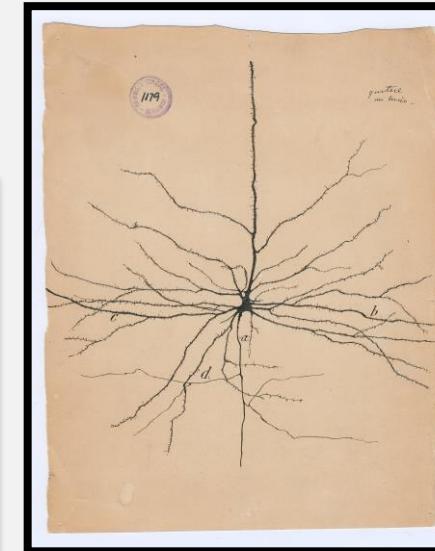
Neuron Doctrine



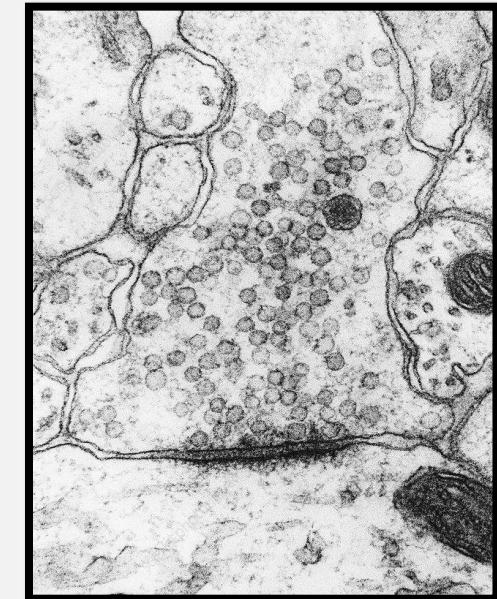
- Cell theory – 1830s
 - Theodor Schwann, Matthias Jakob Schleiden



- Reticular Theory
 - Camillo Golgi (1873) – Silver stain

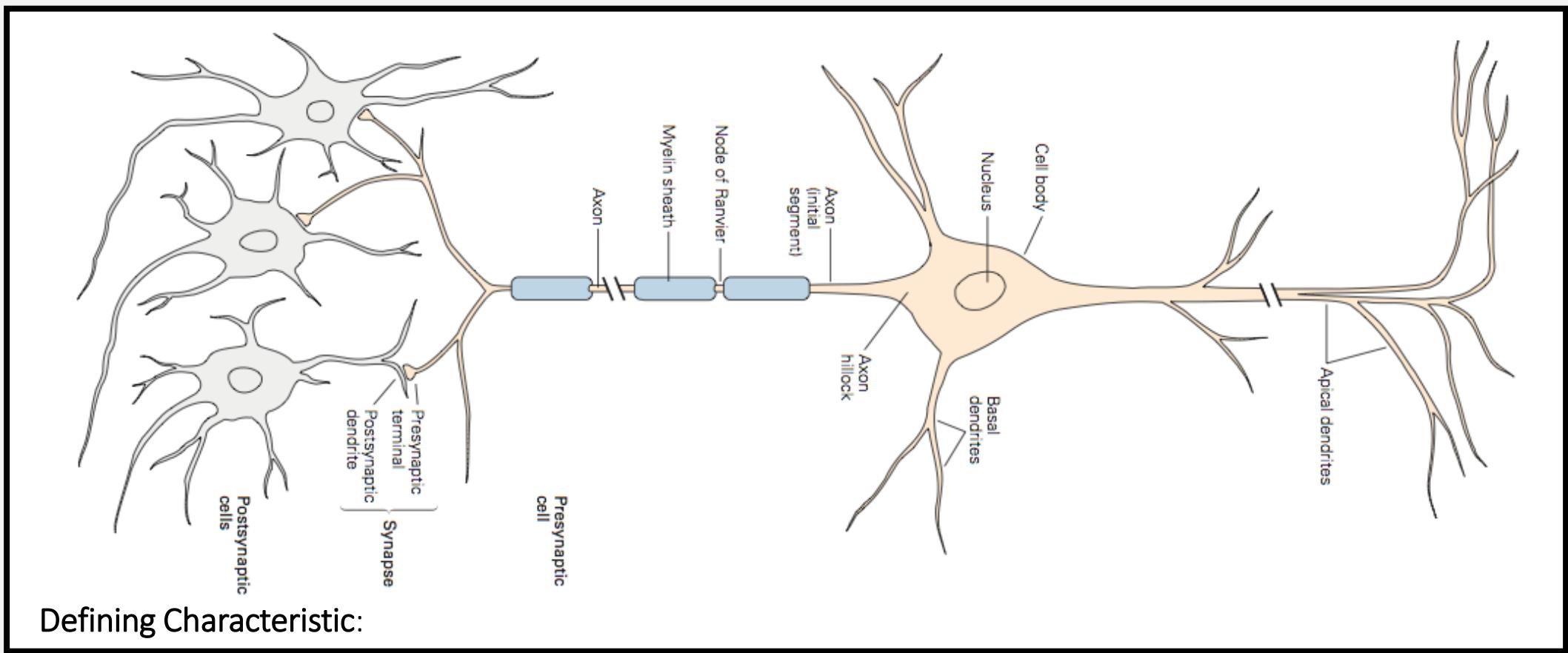


- Ramon Y Cajal (1889)



- Electron Microscopy (1950s)

A prototypical vertebrate neuron

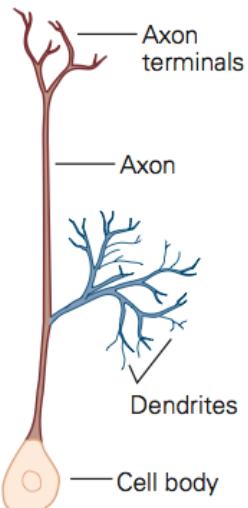


Kandel Fig 2-1

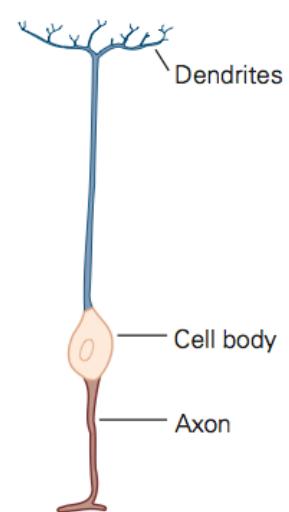
Many different types of neurons...

(what makes them different?)

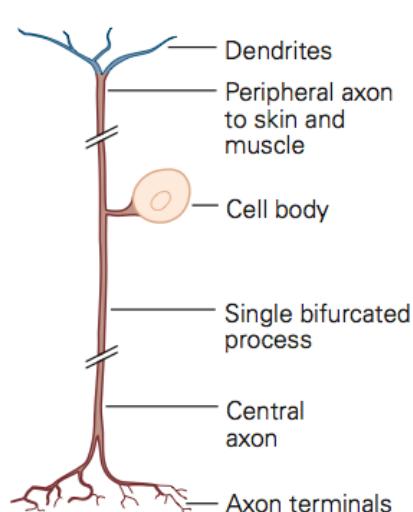
A Unipolar cell



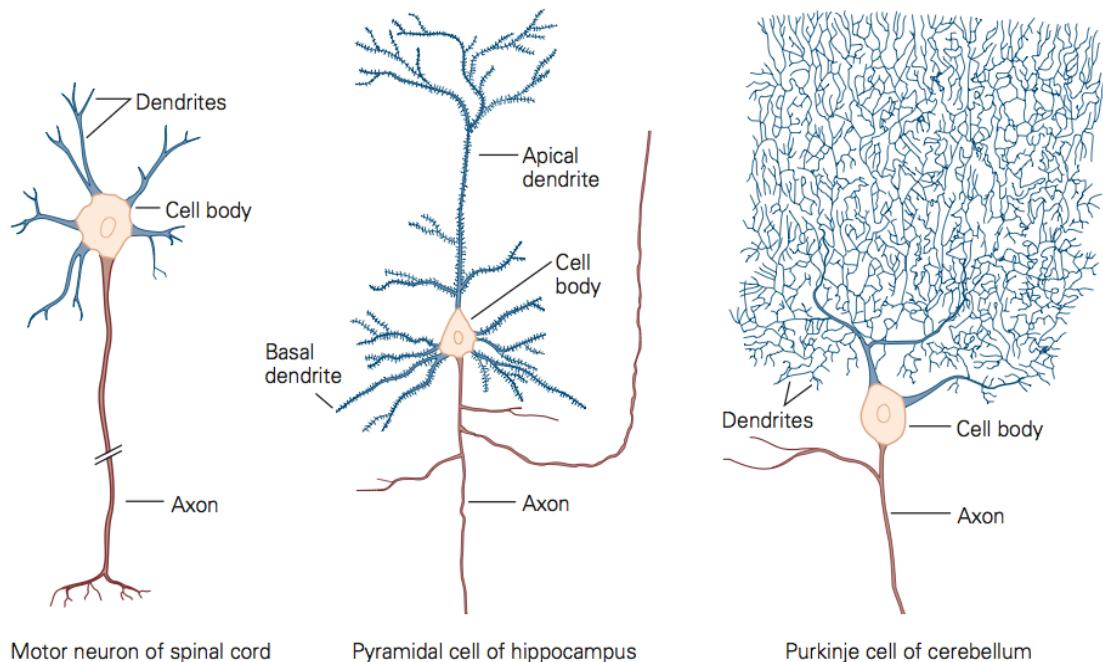
B Bipolar cell



C Pseudo-unipolar cell



D Three types of multipolar cells



Invertebrate neuron

Bipolar cell of retina

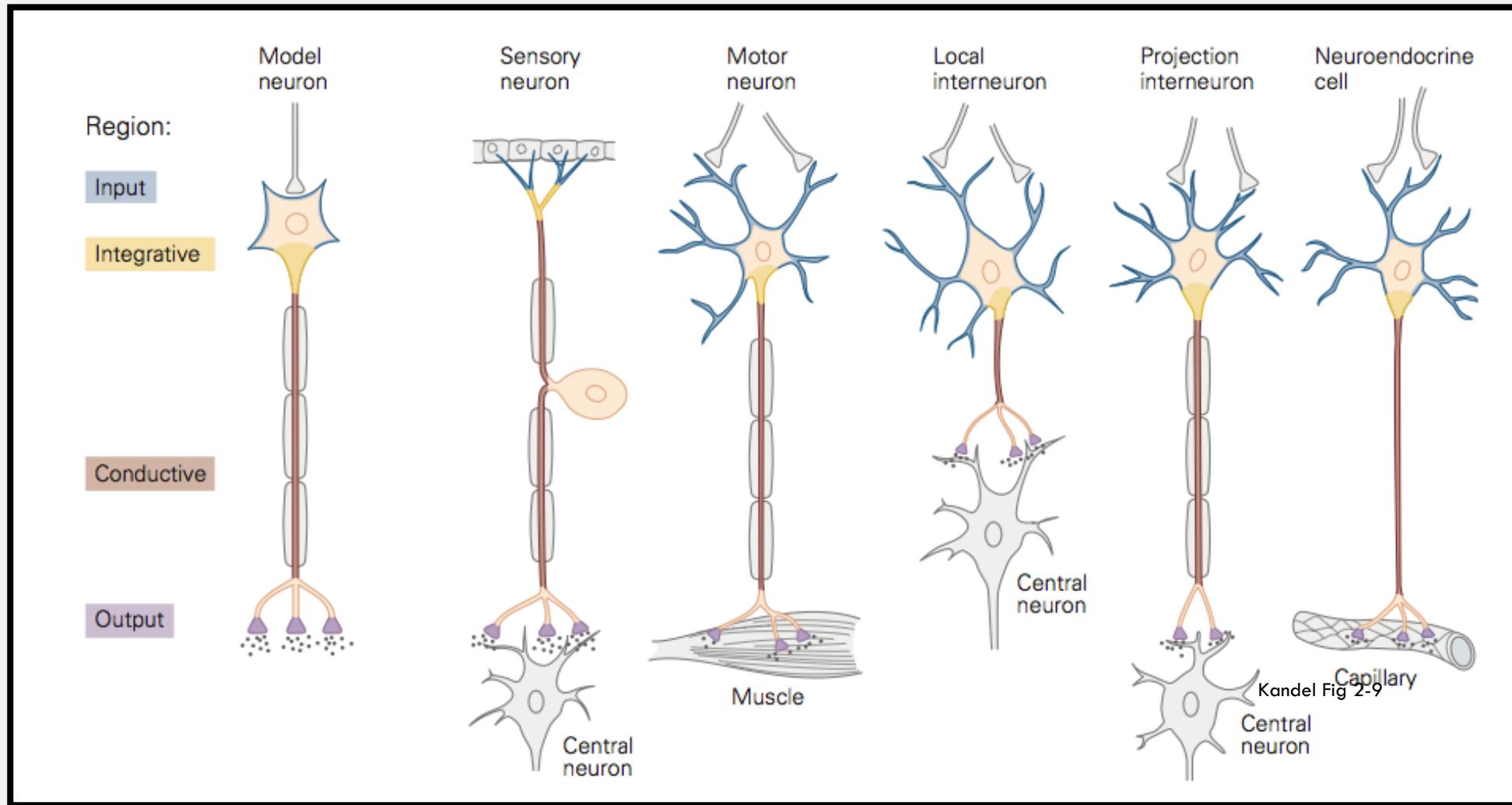
Ganglion cell of dorsal root

Motor neuron of spinal cord

Pyramidal cell of hippocampus

Purkinje cell of cerebellum

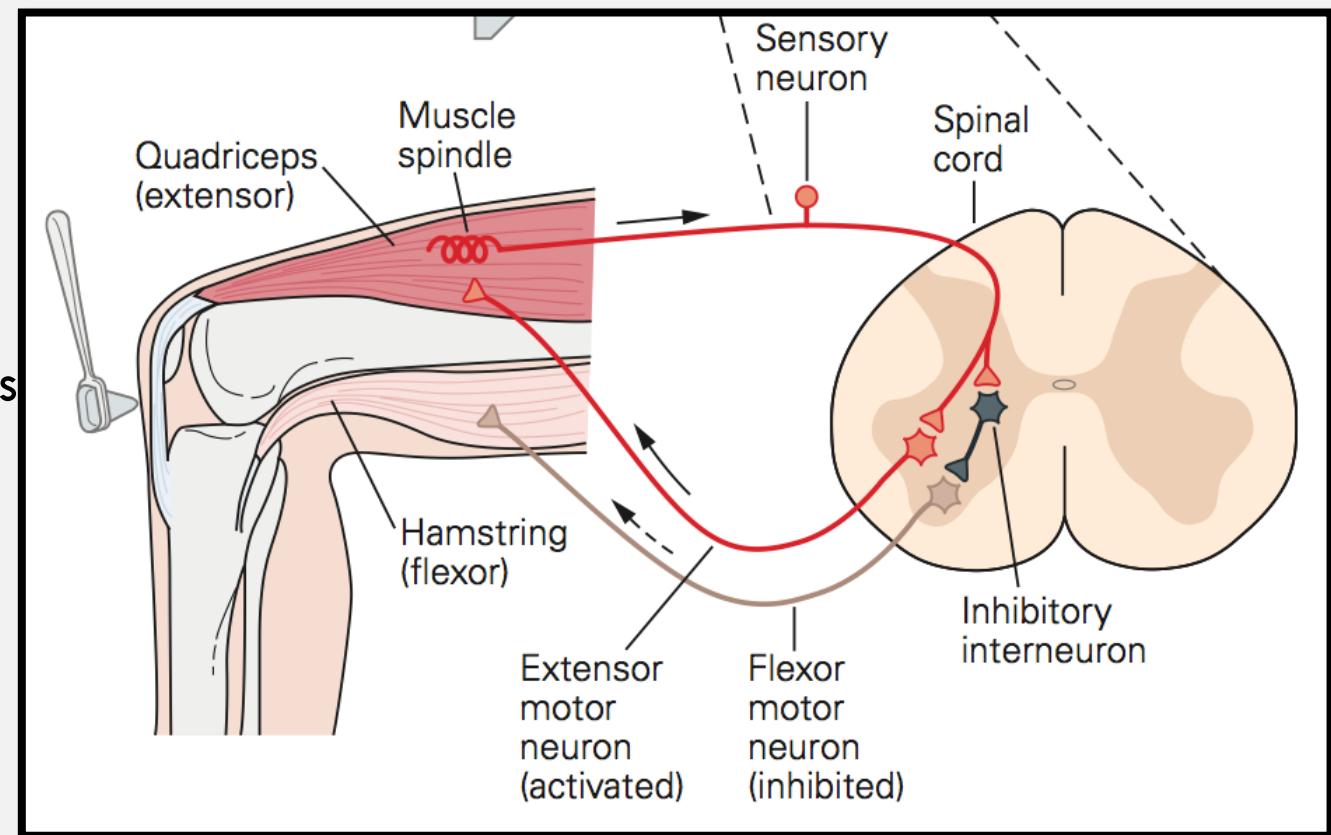
Similar functions



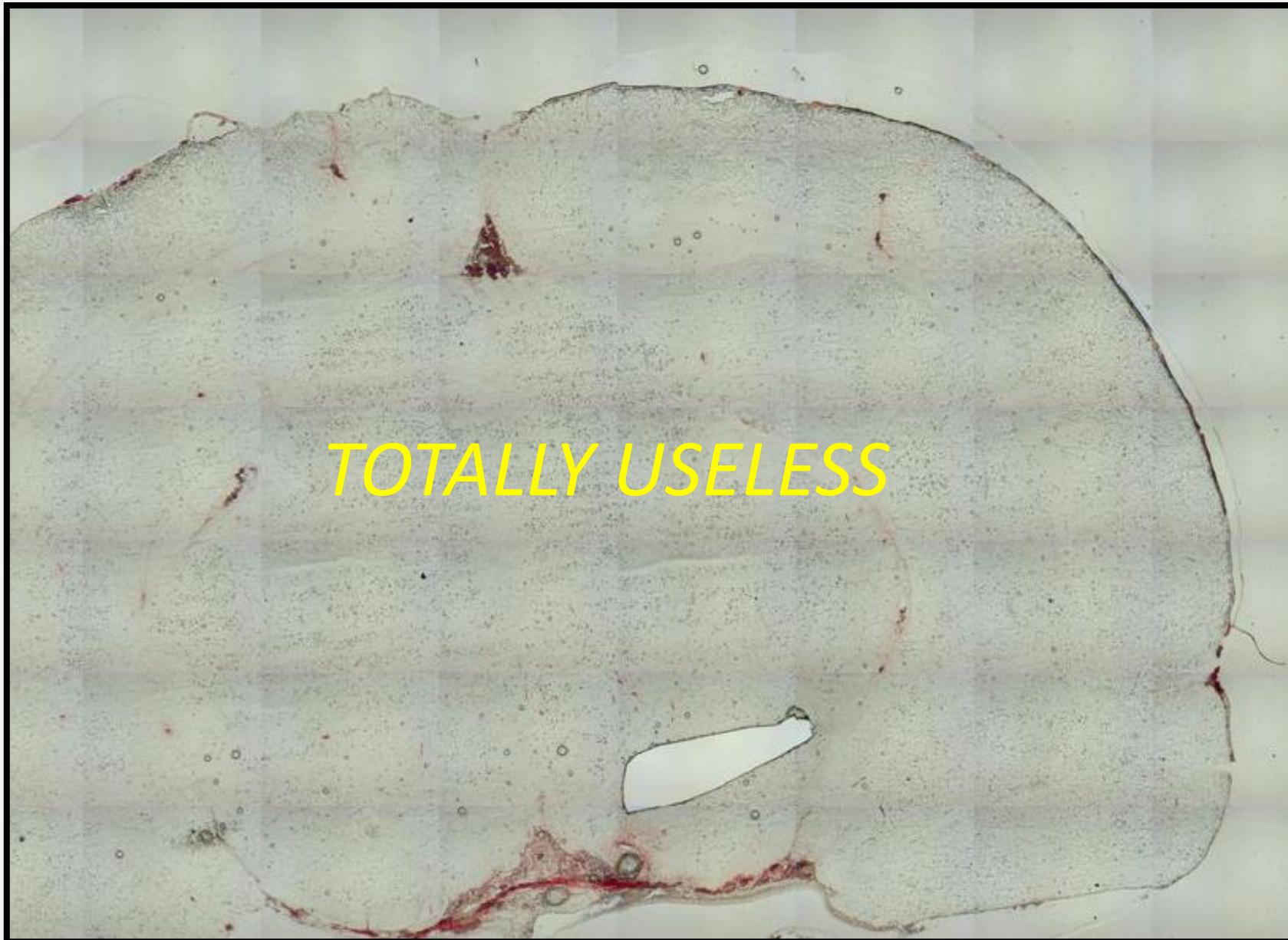
A surprisingly challenging problem:

Visualizing a neurons anatomy and connectivity in a circuit

- **Connectome** = the wiring/synaptic connectivity of all neurons
- Know connectome for a circuit - infer its function
- *What else can you do if you know the connectome?*

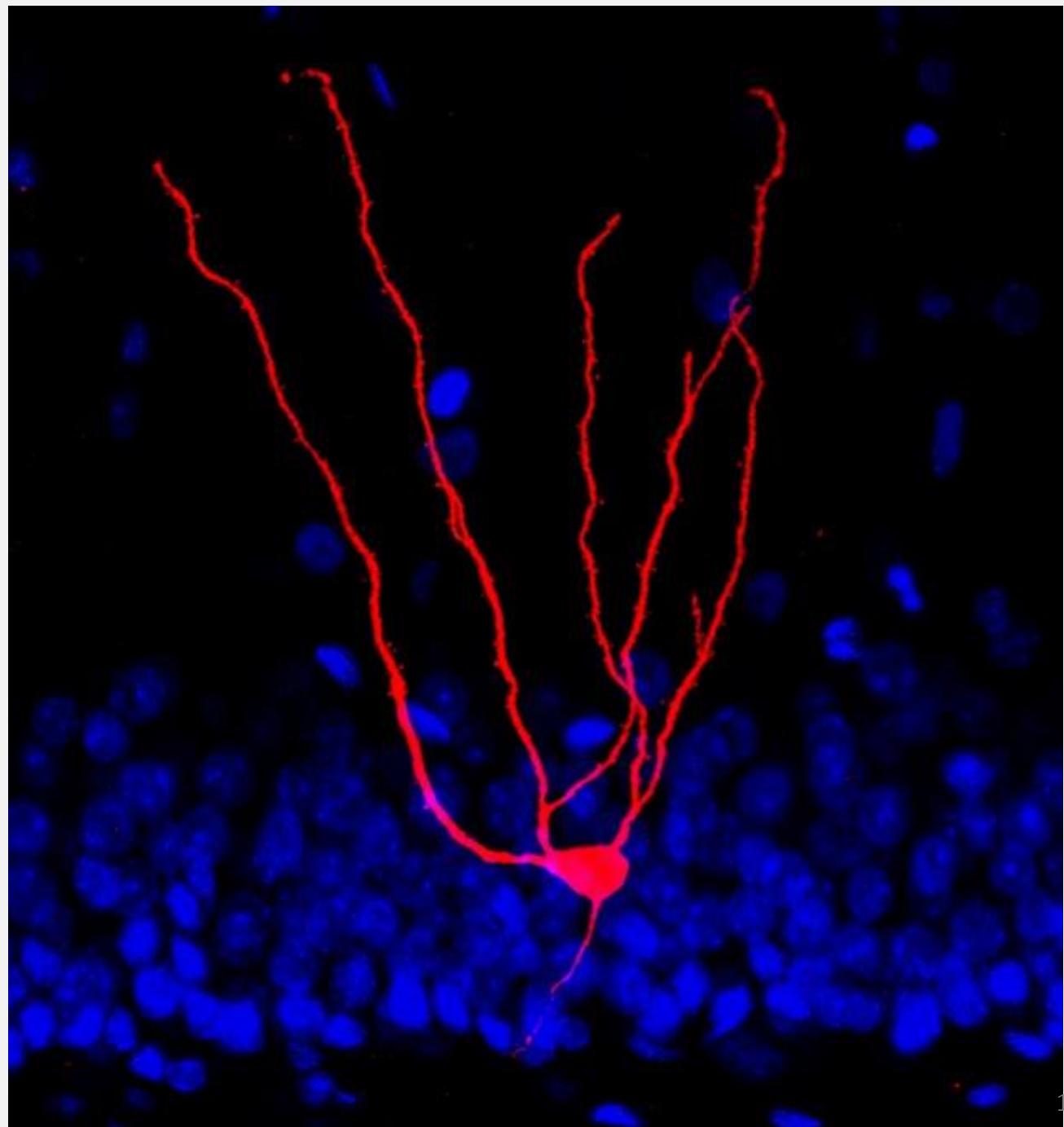


Mouse brain slice, unprocessed



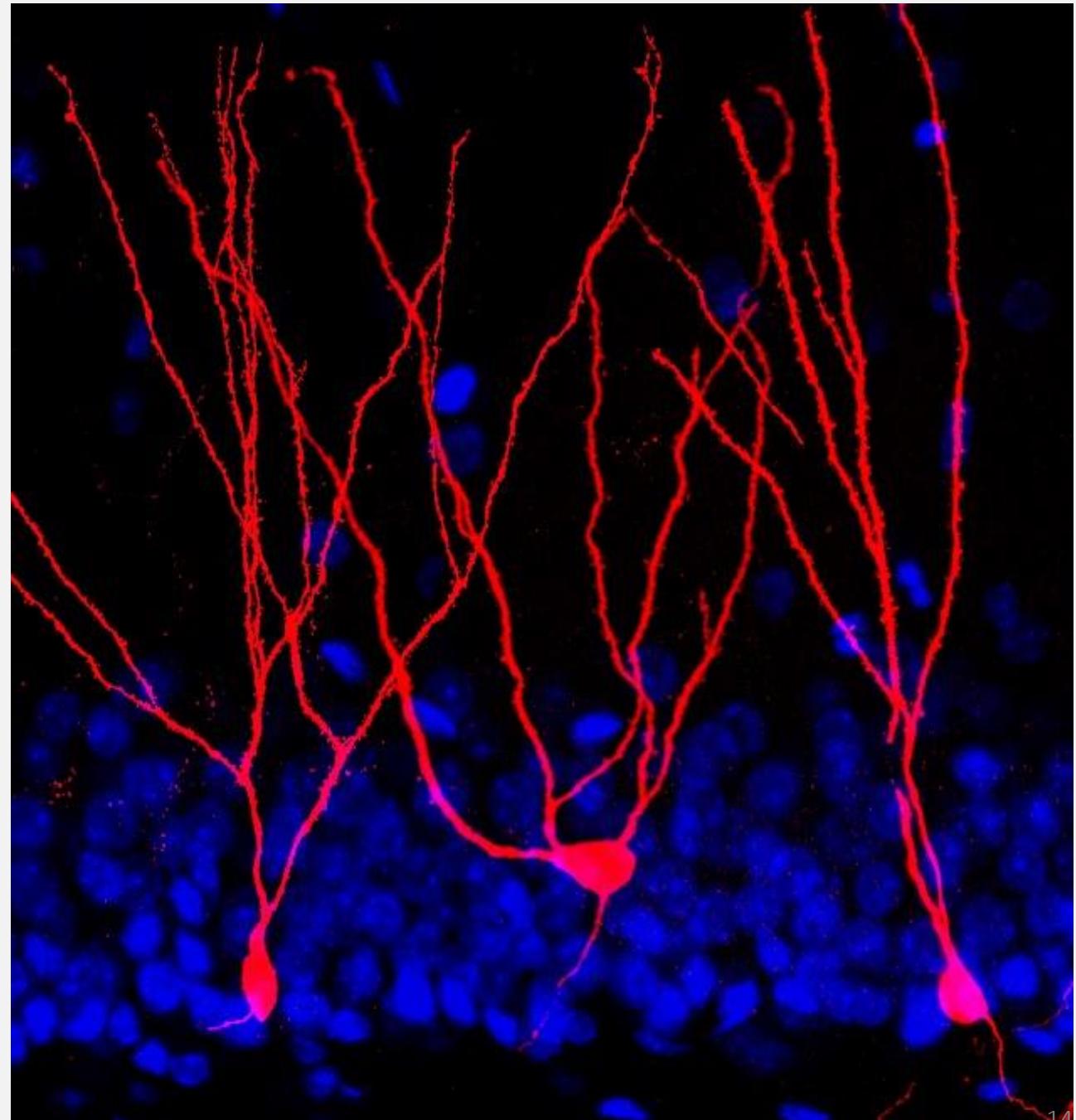
Visualizing Neurons

*Seeing only one neuron
makes it easy...*



Visualizing neurons

*Seeing only one neuron makes it easy...
But we want to picture circuits, so we stain
a few more*



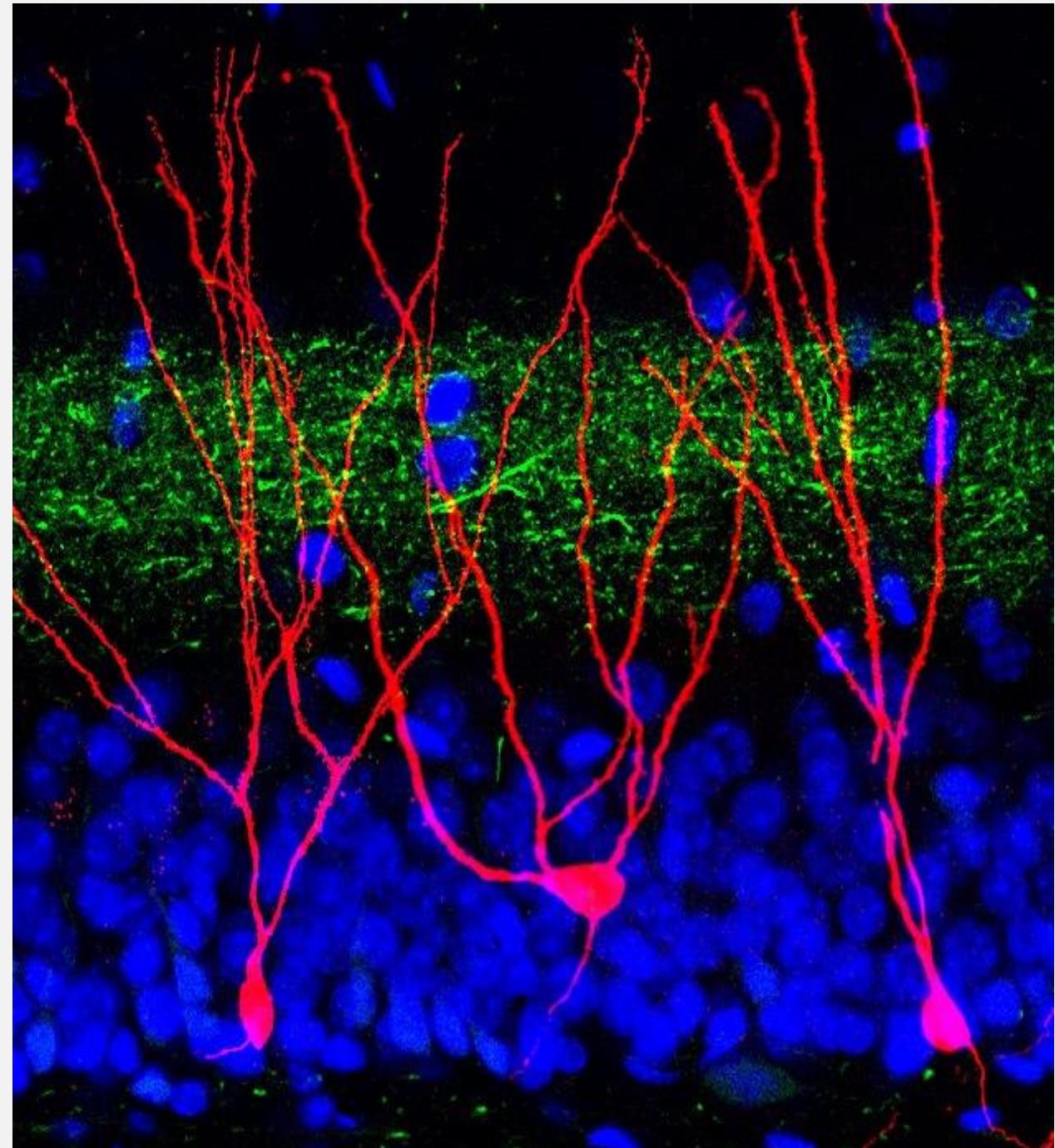
Visualizing neurons

Seeing only one neuron makes it easy...

But we want to picture circuits

Stain a few more

Stain a few other cell types



Visualizing neurons

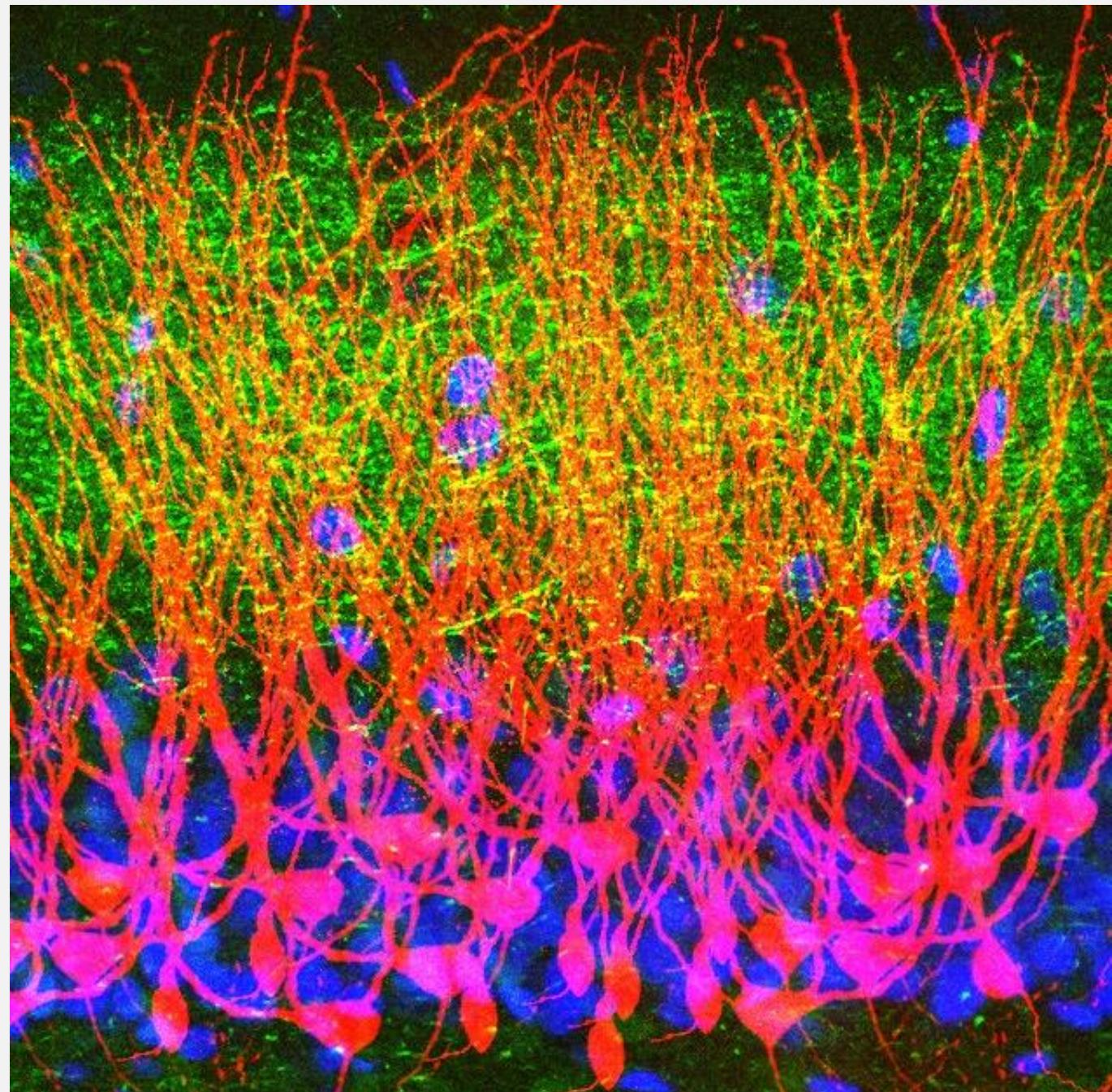
Seeing only one neuron makes it easy...

But we want to picture the circuits

Stain a few more

Stain a few other cell types

But now too many cells are labelled!



How do we visualize neurons?

Complementary approaches

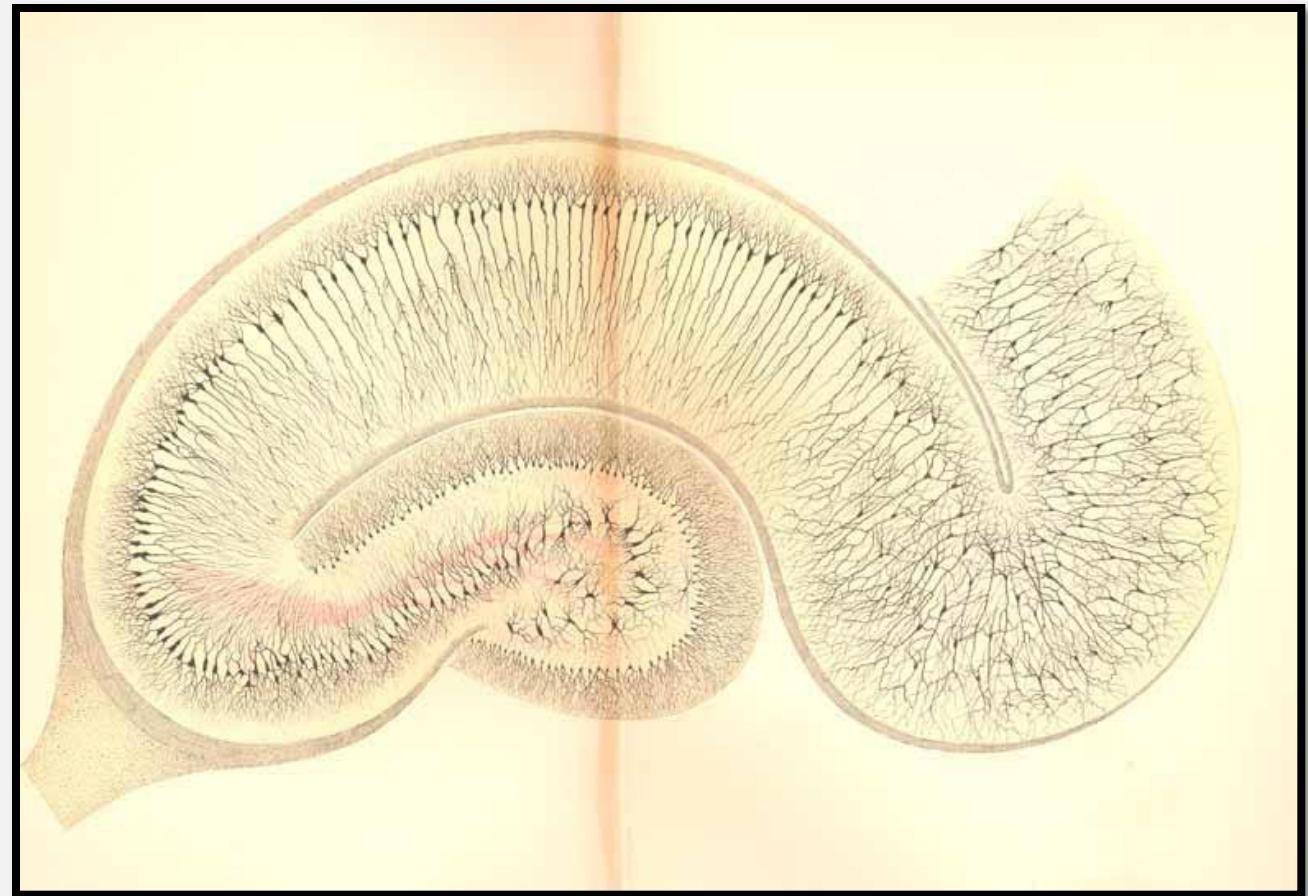
- dead tissue
- live tissue
- based on specific cell type or presence of specific molecules
- cheap vs expensive
- low vs high resolution
- easy vs hard
- fast vs slow

***Each has advantages and disadvantages (but whether an advantage or disadvantage depends on the experiment)

Methods for visualizing neurons

Method 1: The Golgi stain

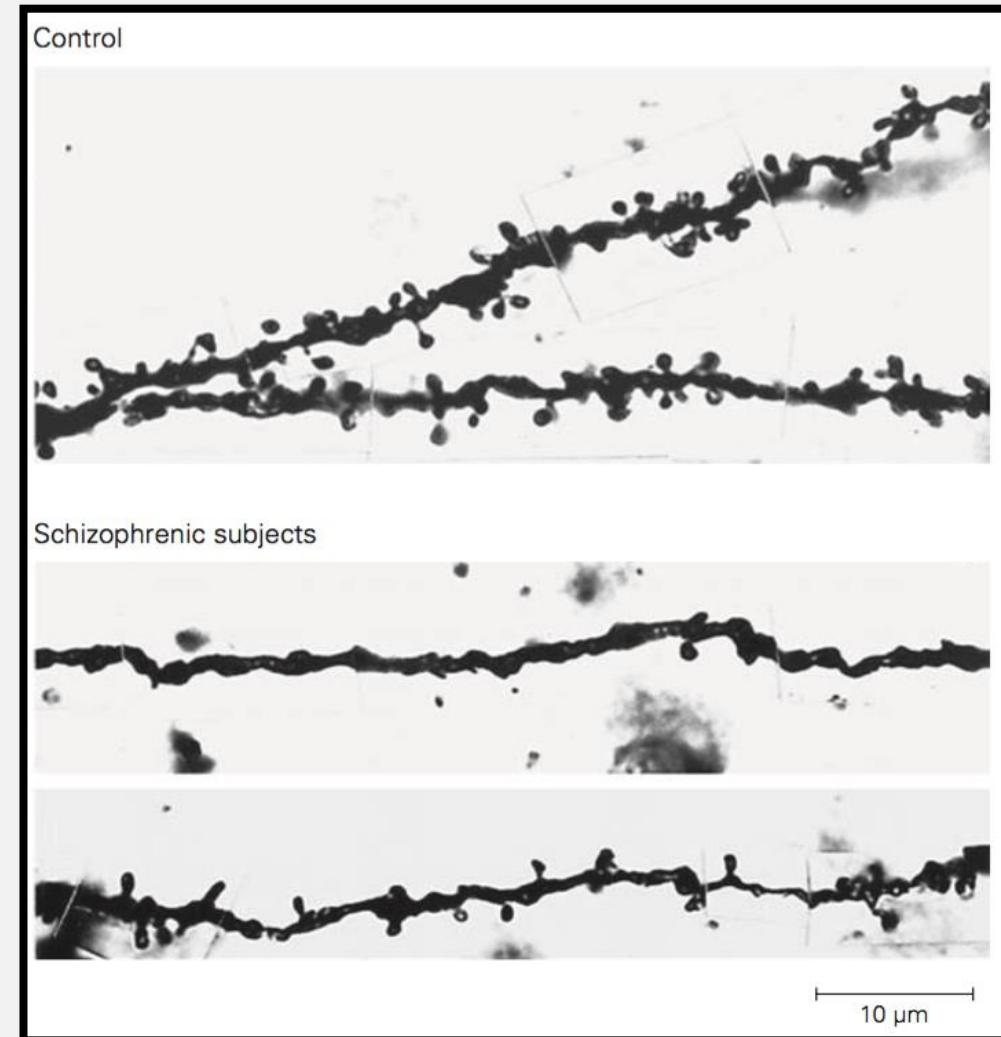
- chemical process that causes silver impregnation in neurons
- small % of neurons labelled
- unknown why some are labelled and not others
- can be used on dead tissue, including humans
- tried and true technique; relatively easy



Method 1: Golgi Stain

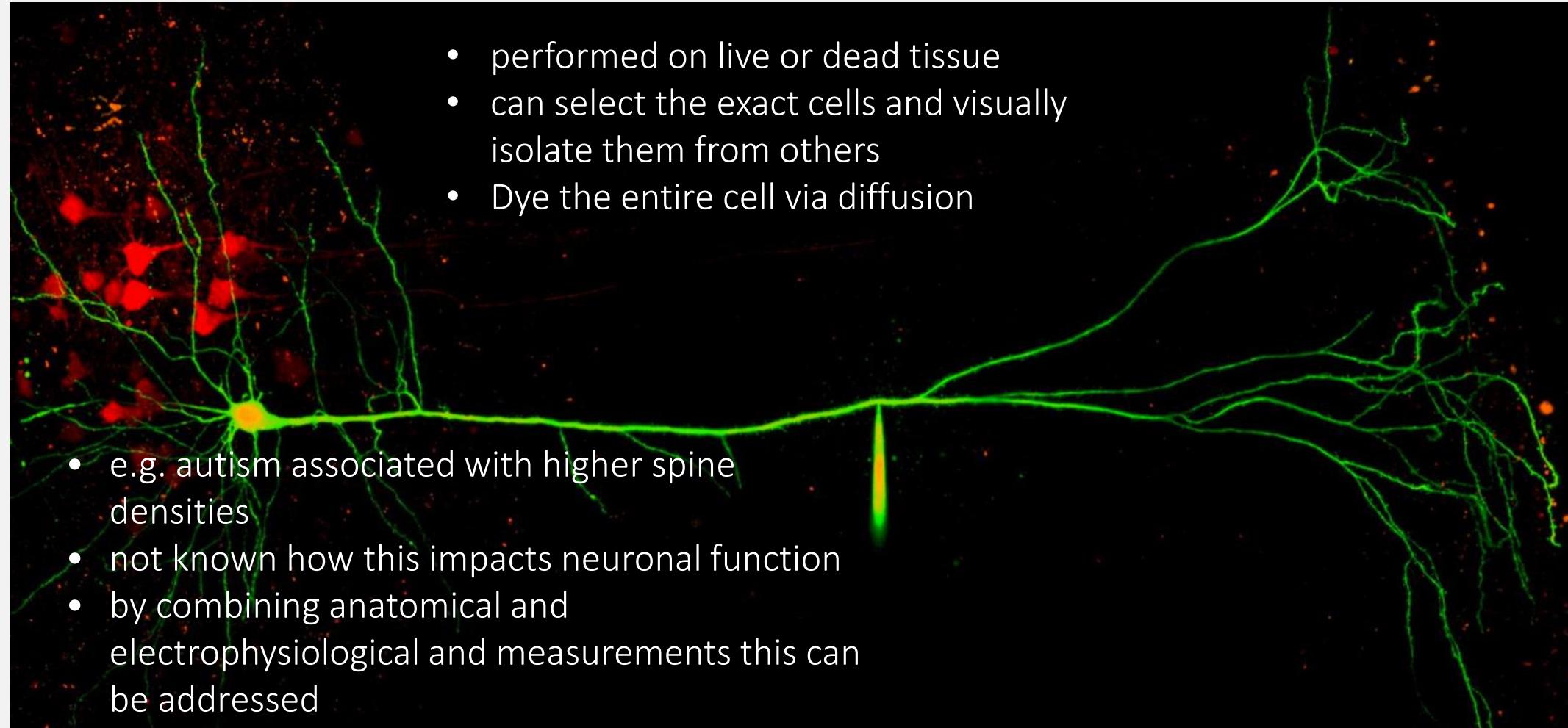
Golgi Stain in action

- The prefrontal cortex develops over the first decades of life
- synapses are pruned
- schizophrenia is a developmental disorder
- patients have fewer spines in prefrontal cortex



Kandel
Fig 62-4

Method 2: Dye filling neurons



- performed on live or dead tissue
 - can select the exact cells and visually isolate them from others
 - Dye the entire cell via diffusion
-
- e.g. autism associated with higher spine densities
 - not known how this impacts neuronal function
 - by combining anatomical and electrophysiological measurements this can be addressed

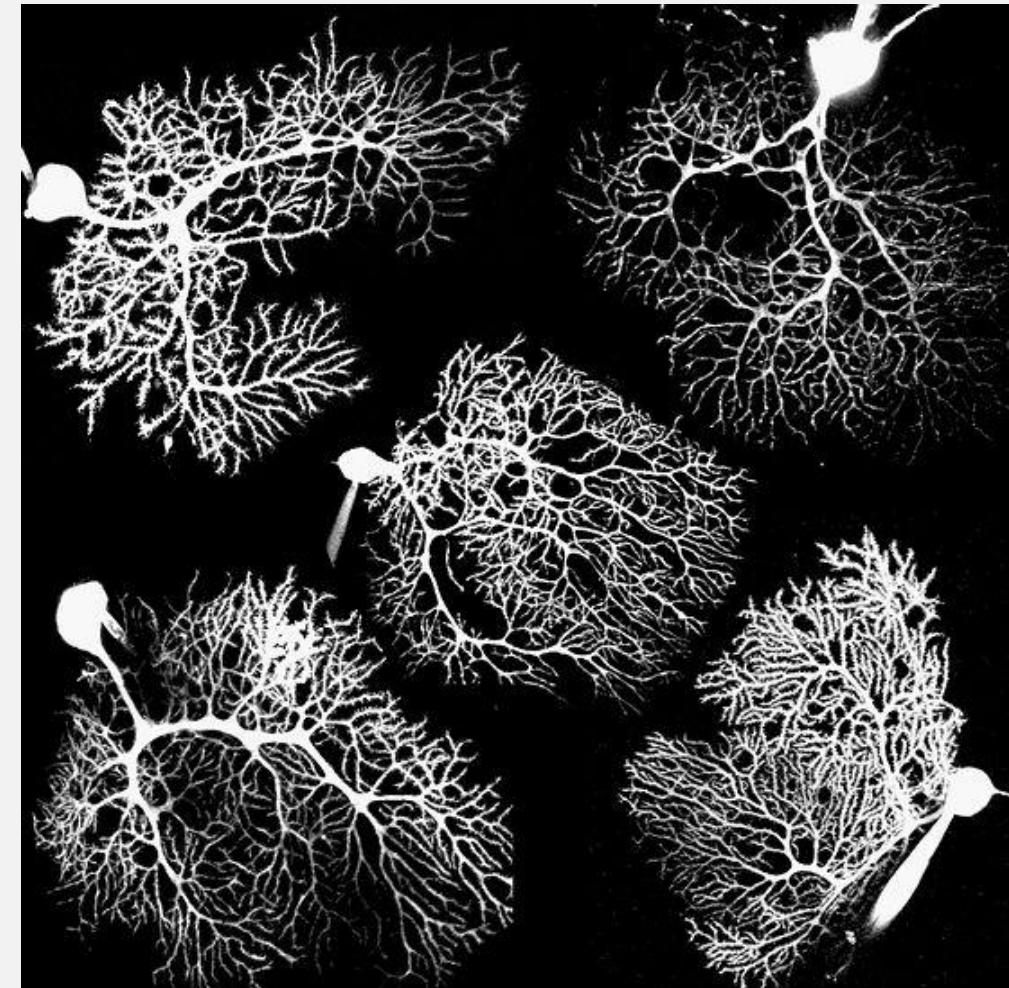


Interstellate

Method 2 – dye filling

Cerebellar Purkinje neurons

- What can we tell from the anatomy revealed?
- Can you spot the glass pipettes?

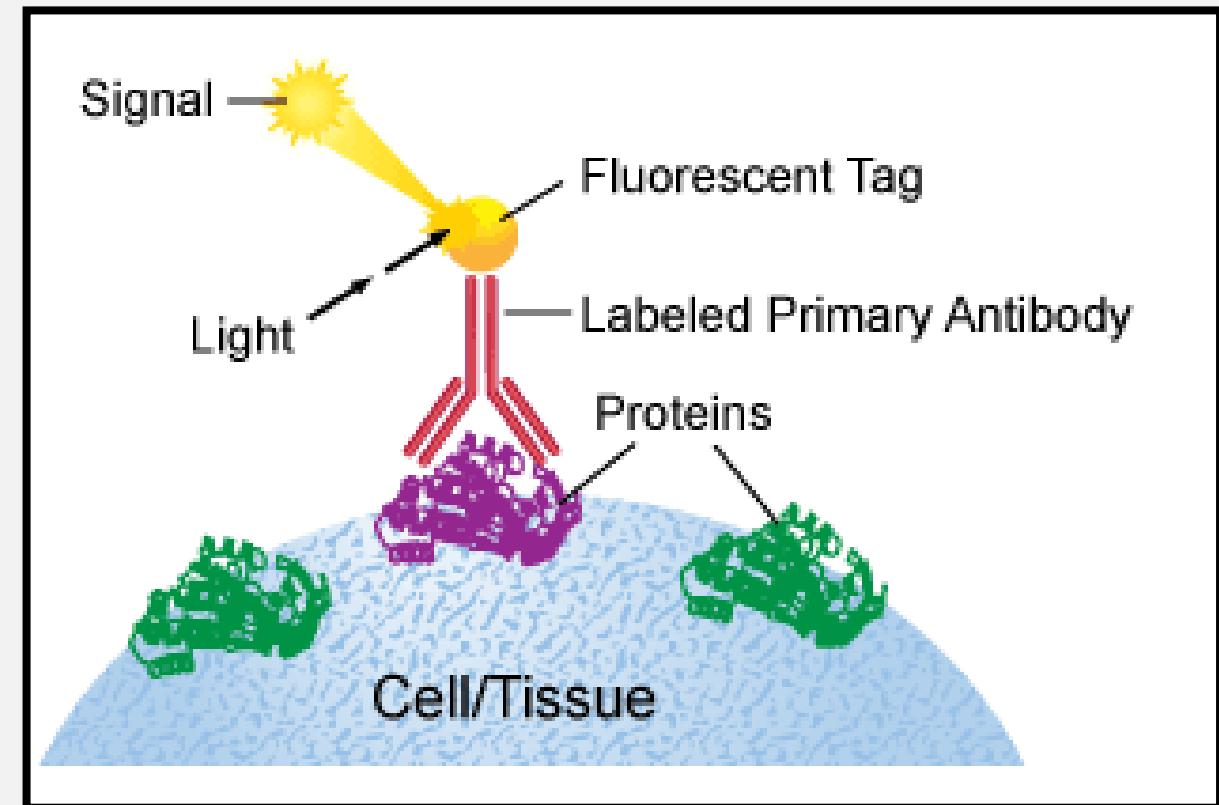




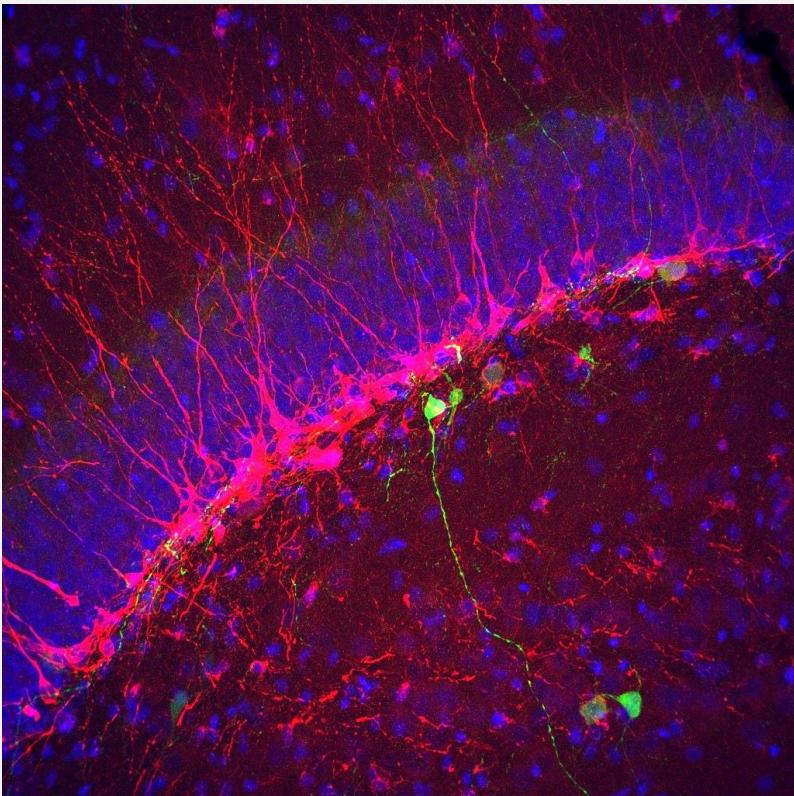
End of lecture 1

Method 3: Immunohistochemistry

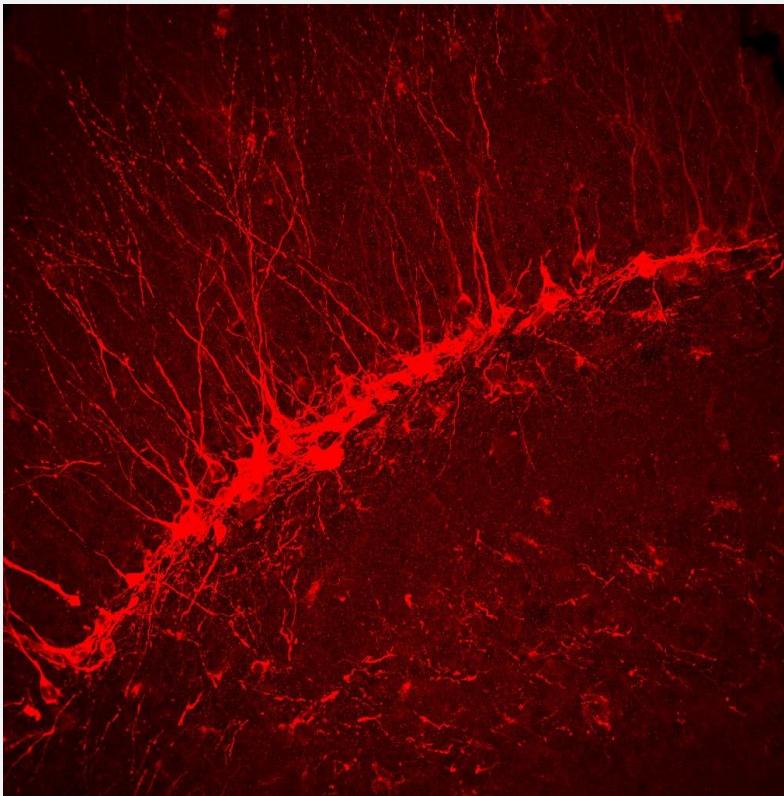
- Targets/identifies any specific protein (antigen) – biomarker localization
- can combine multiple antibodies to examine multiple cell types in same tissue, localization of different molecules within the same cell, etc.
- dead tissue, can be used on human tissue
- relatively cheap and feasible with standard technology
- has been used to show that one of the first pathological signs of Alzheimer's is a loss of synaptic proteins



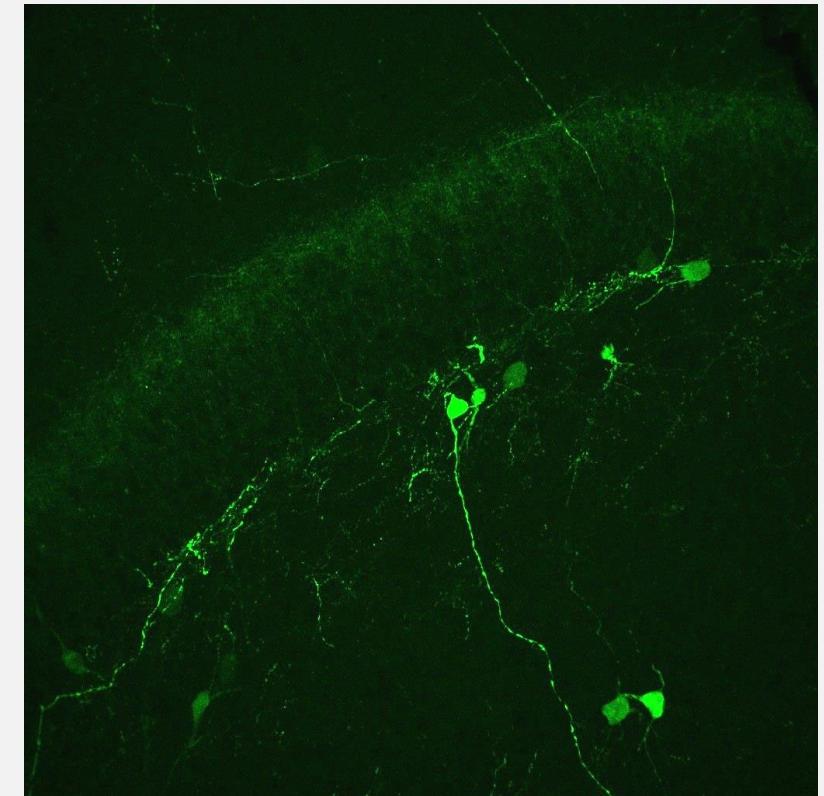
Immunohistochemistry example



DAPI (all cells)



Doublecortin (immature neurons)



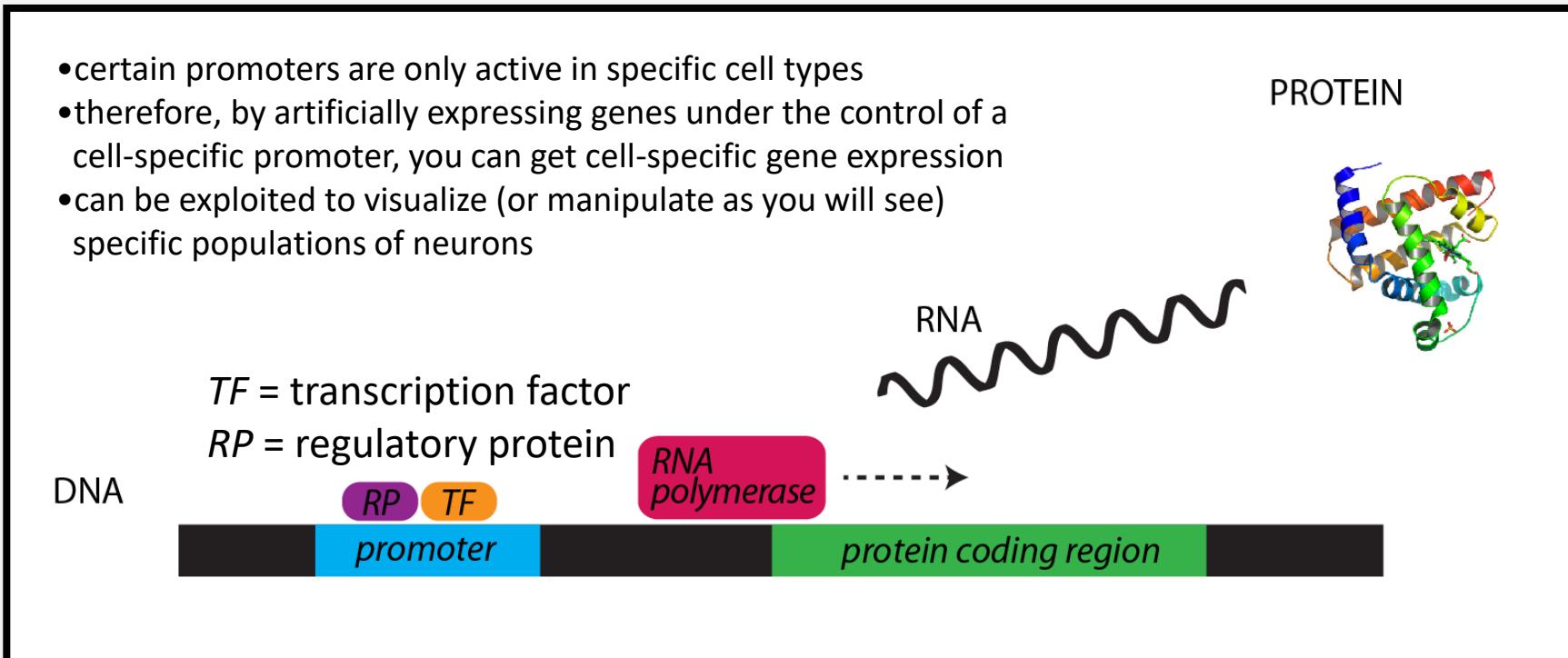
Calretinin (subtype of inhibitory interneuron)

Method 4: Genetically-encoded fluorescent proteins



Regulation of gene expression 101

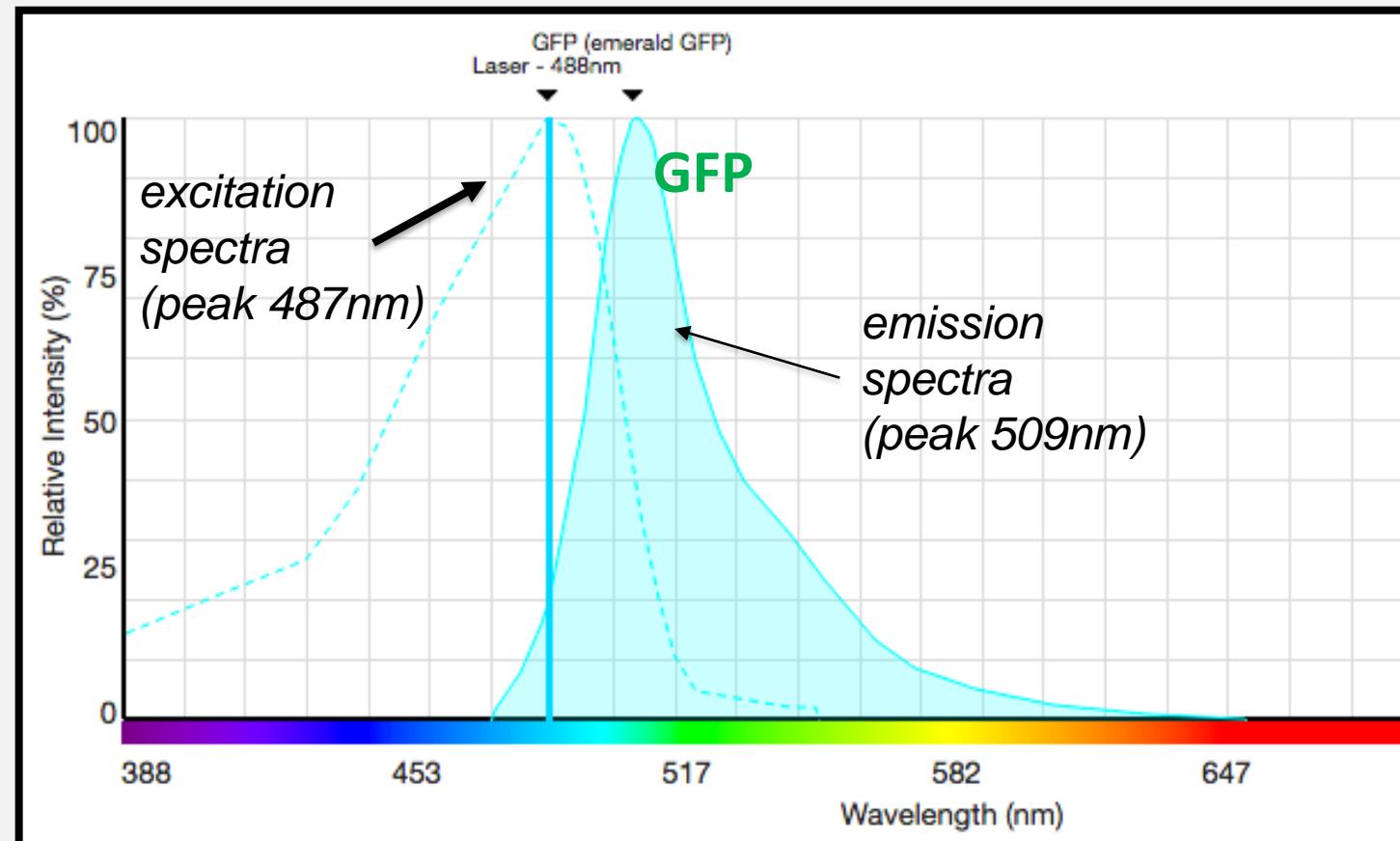
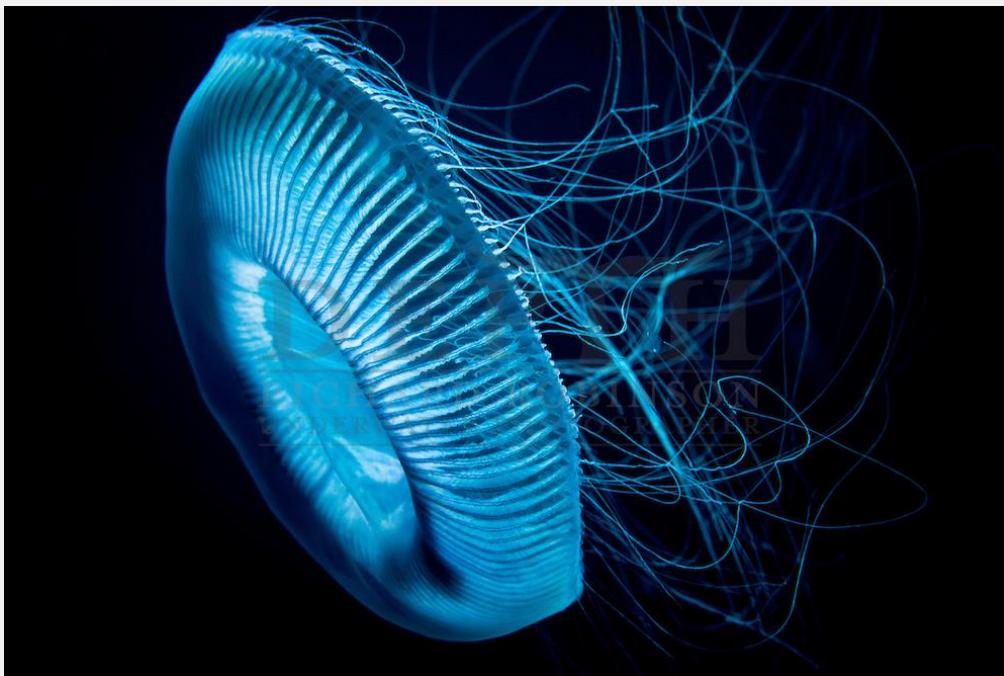
- All cells share the same DNA, but differential transcription causes different genes to be expressed in different cells → distinct neuron types, tissues, regions, etc.



Genetically-encoded fluorescent proteins

Green Fluorescent Protein (GFP)

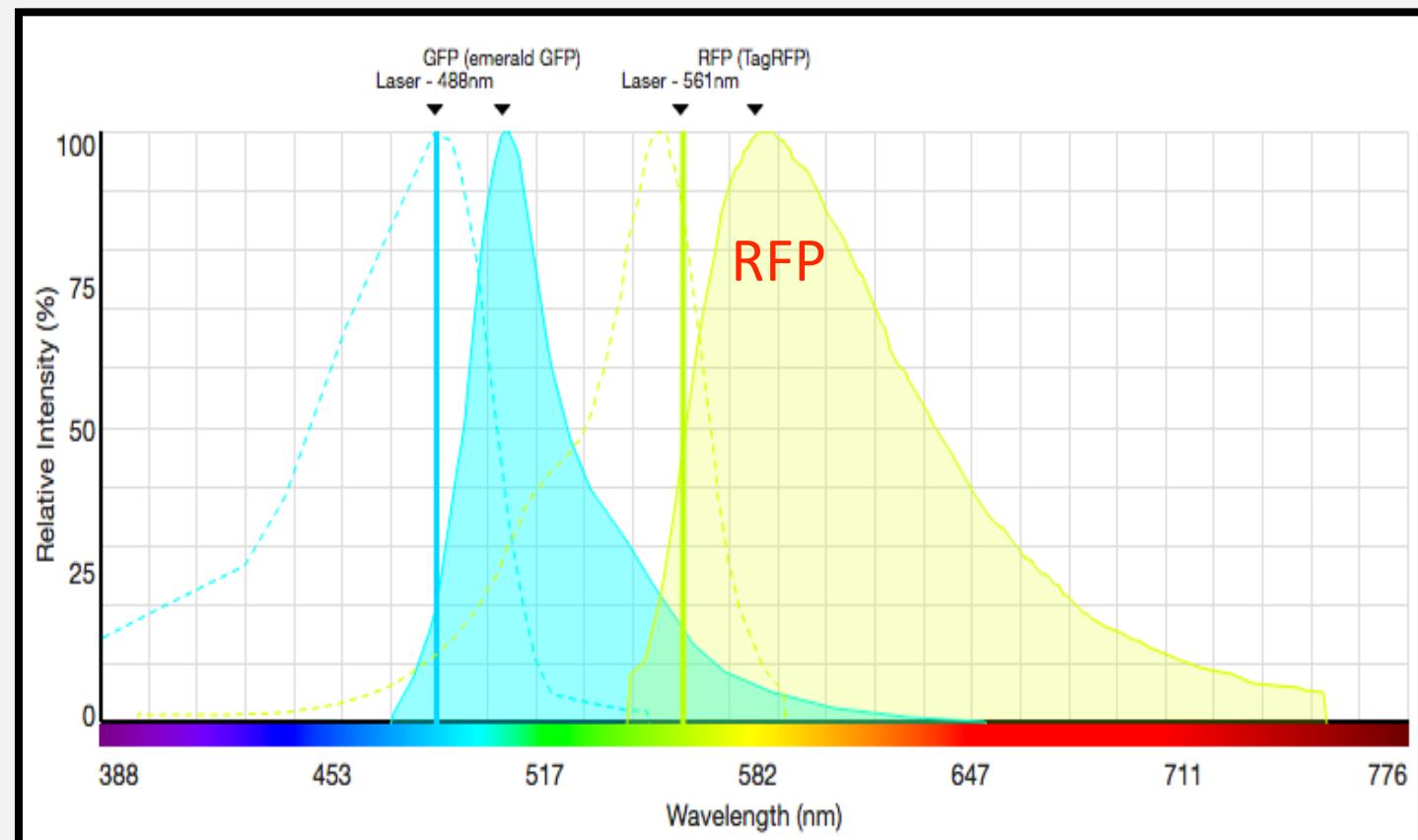
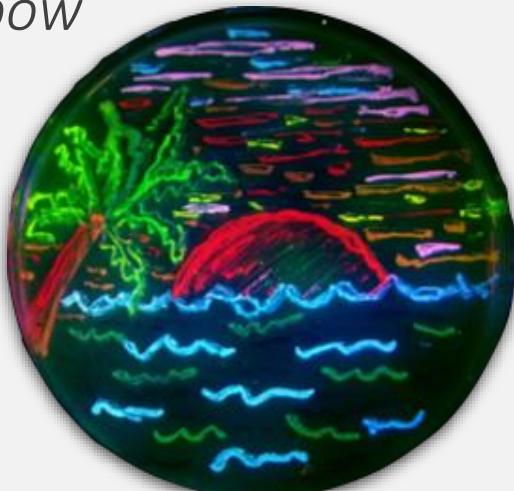
- Isolated from jellyfish



Genetically-encoded fluorescent proteins

Green Fluorescent Protein (GFP)

- Isolated from jellyfish
- Mutate GFP and FPs from other species to have all colours of the rainbow



Genetically-encoded fluorescent proteins

Details

- Critical choice – what promotor to use
- Create genetic construct – transgenic animal lines, viral transduction
- Costly set up, cheap and efficient once you have the transgenic animal or virus
- Can label genetically-identified cells, or label modified cells (did your DNA insertion work?)
- Challenges – variable gene expression



Choosing the right promotor

Example

- The CAG promoter is active (and therefore expresses GFP) in all cells
- Useful: did GFP+ cells from a donor animal survive when transplanted into a disease model?
- Can genotype these mice

Drawback?

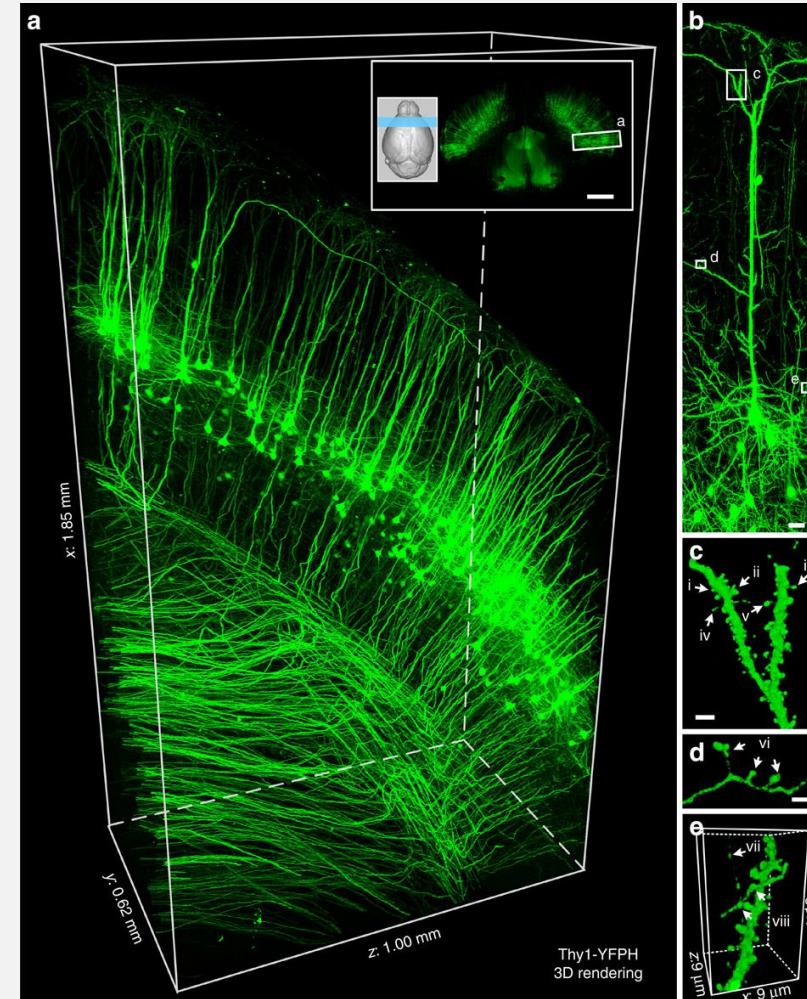


***CAG** = synthetic promoter composed of **Cytomegalovirus** enhancer + chicken **Actin** promoter region + splice acceptor of rabbit beta **Globulin** gene

Choosing the right promotor

Thy 1 promotor

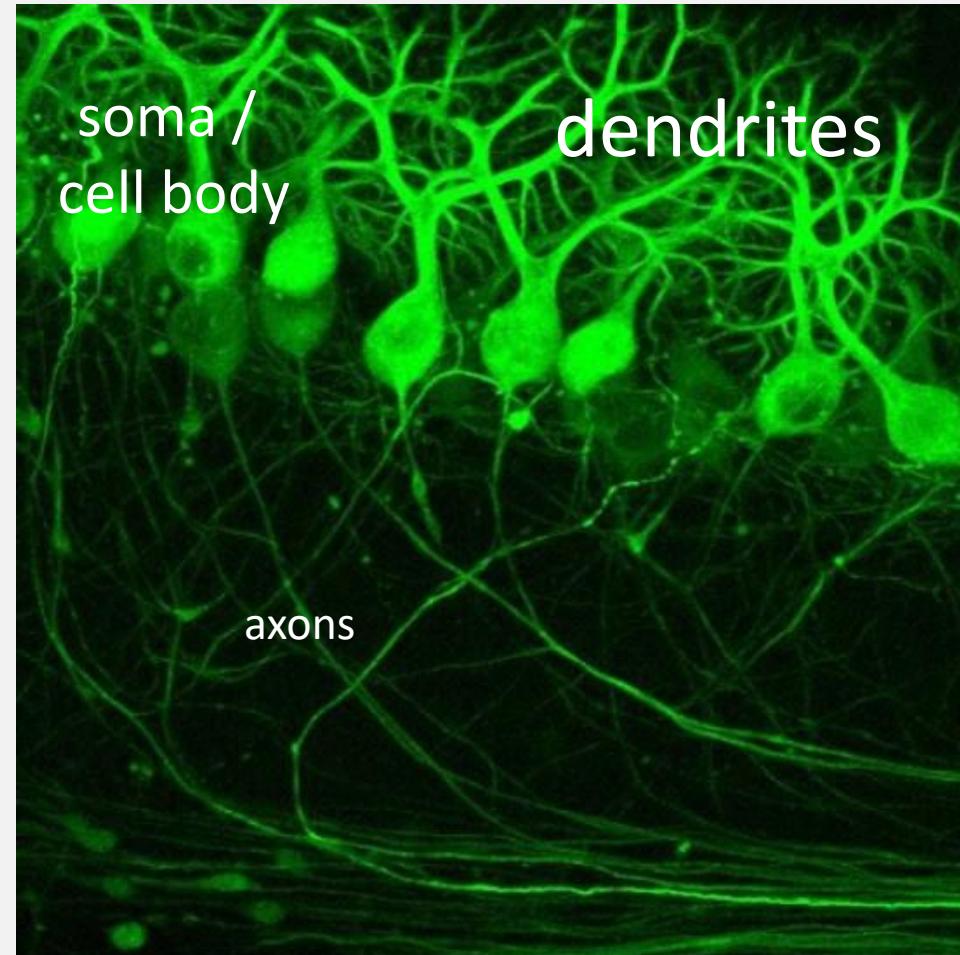
- Active in a fraction of all types of neurons
- Fancy Fluorescent Golgi
- Can do in-vivo imaging
 - Image over time
- No tissue treatment, chemicals



Promotor Choice

L7 promotor

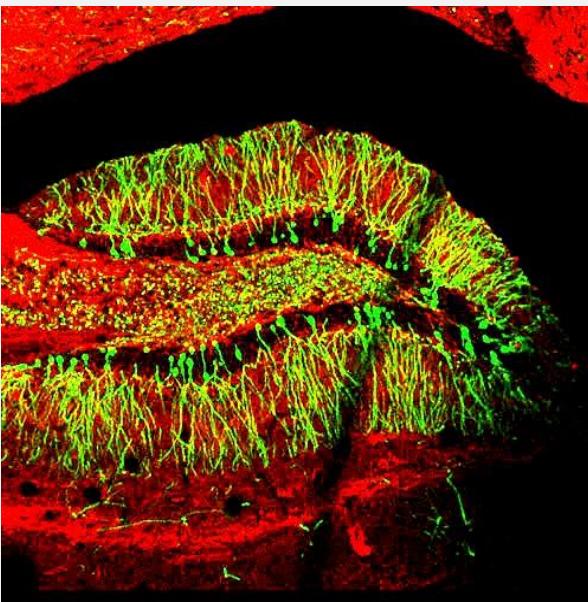
- Active (therefore produces GFP) only in cerebellar Purkinje neurons



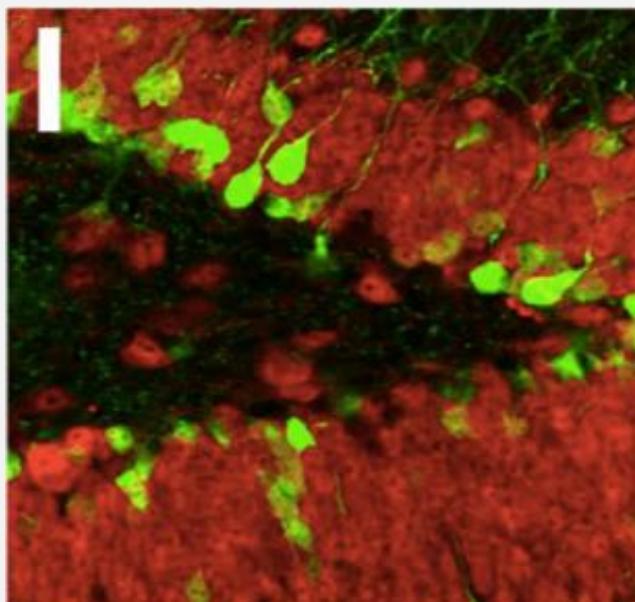
Wellcome Images

Promotor choice

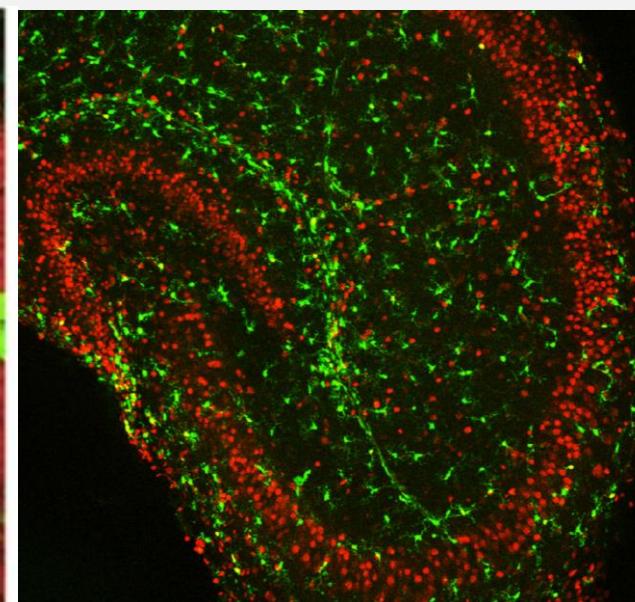
Different cells in the same brain region



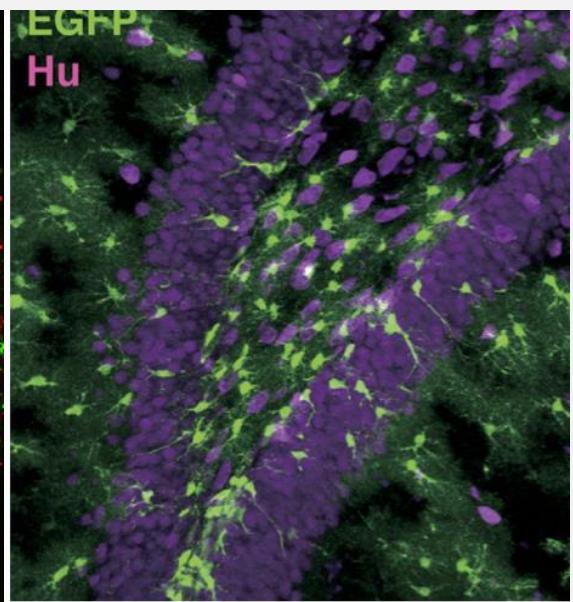
Thy1 promoter
• neurons



Doublecortin promoter
• immature neurons



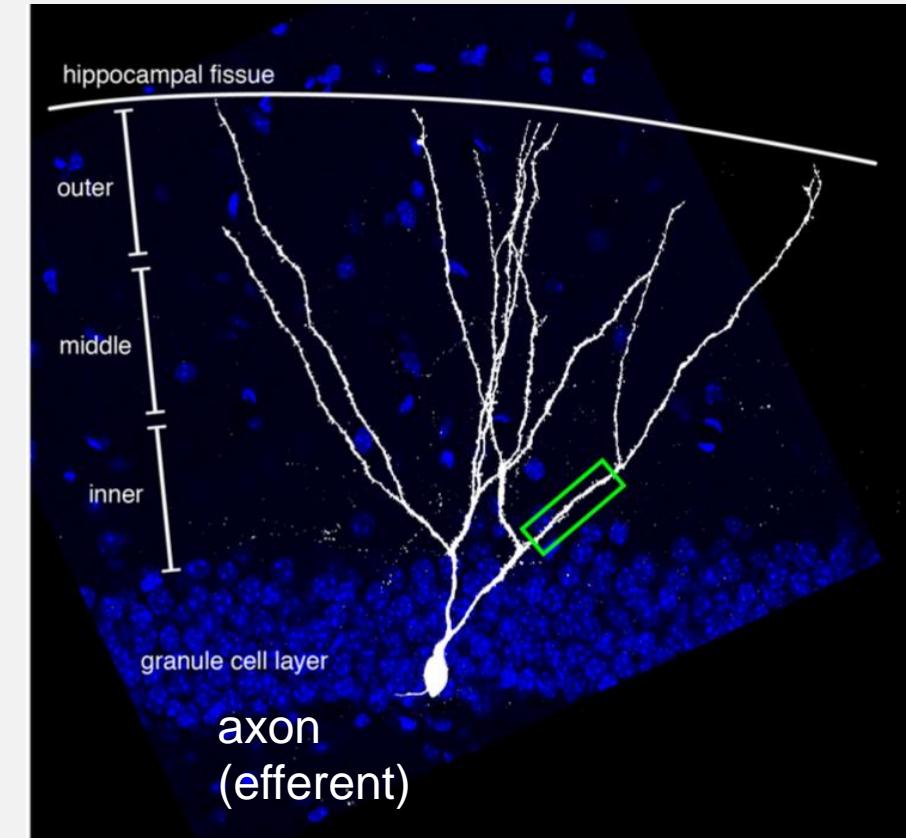
Iba1 promoter
• microglia



GFAP promoter
• astrocytes

Expressing FPs with viruses

- Inject engineered viral vectors into a specific brain region
- Does not require transgenic animals to obtain genetically modified cells
- Can target different cell types with different virus types
 - Neurons vs. glia
 - Dividing vs non-dividing
- Example: Retrovirus
- Requires surgery – can be invasive!

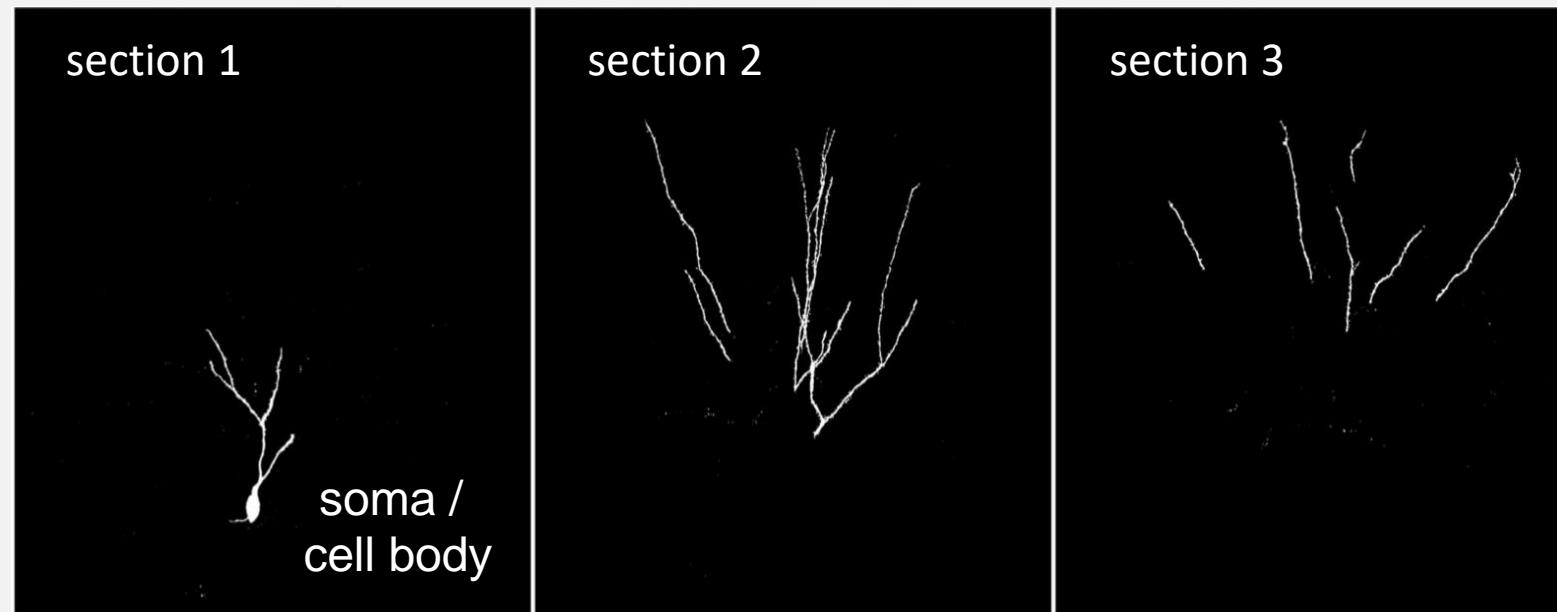


Adult-born neuron in the hippocampus,
labelled with a GFP-expressing retrovirus
(which only infects dividing cells)

Traditional visualization techniques

Disadvantages

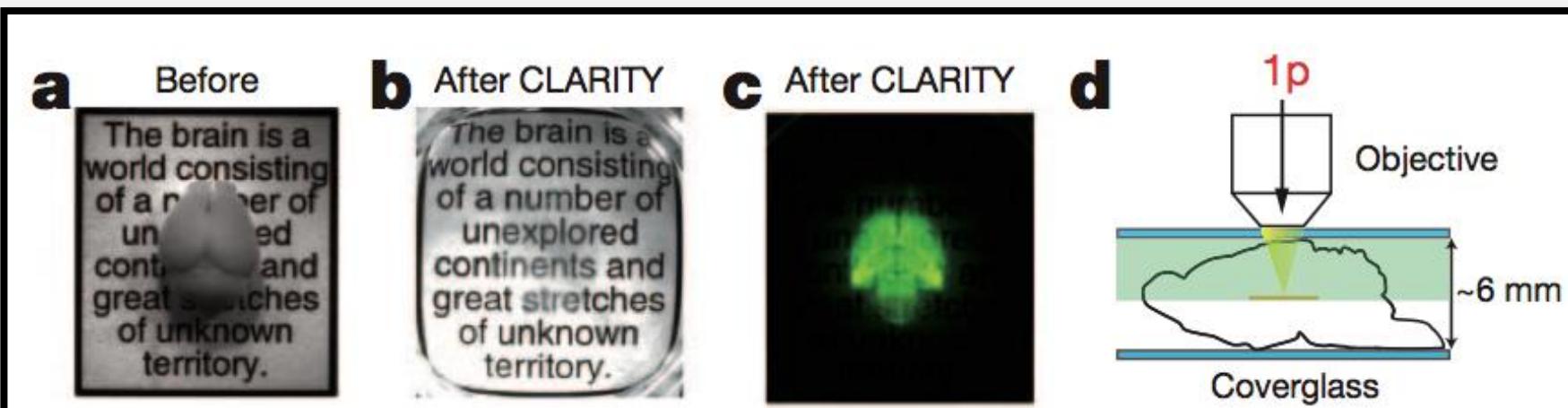
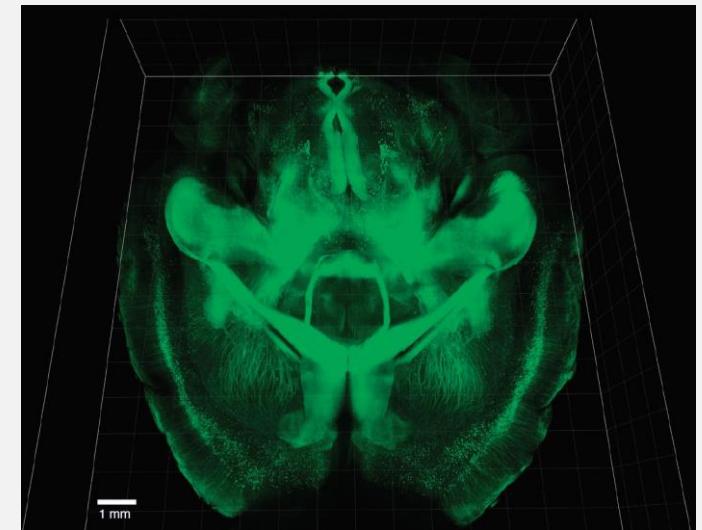
- Brain tissue must be cut to visualize neurons
- Anything that is translucent scatters light – thick brain tissue challenging



Clarity technique

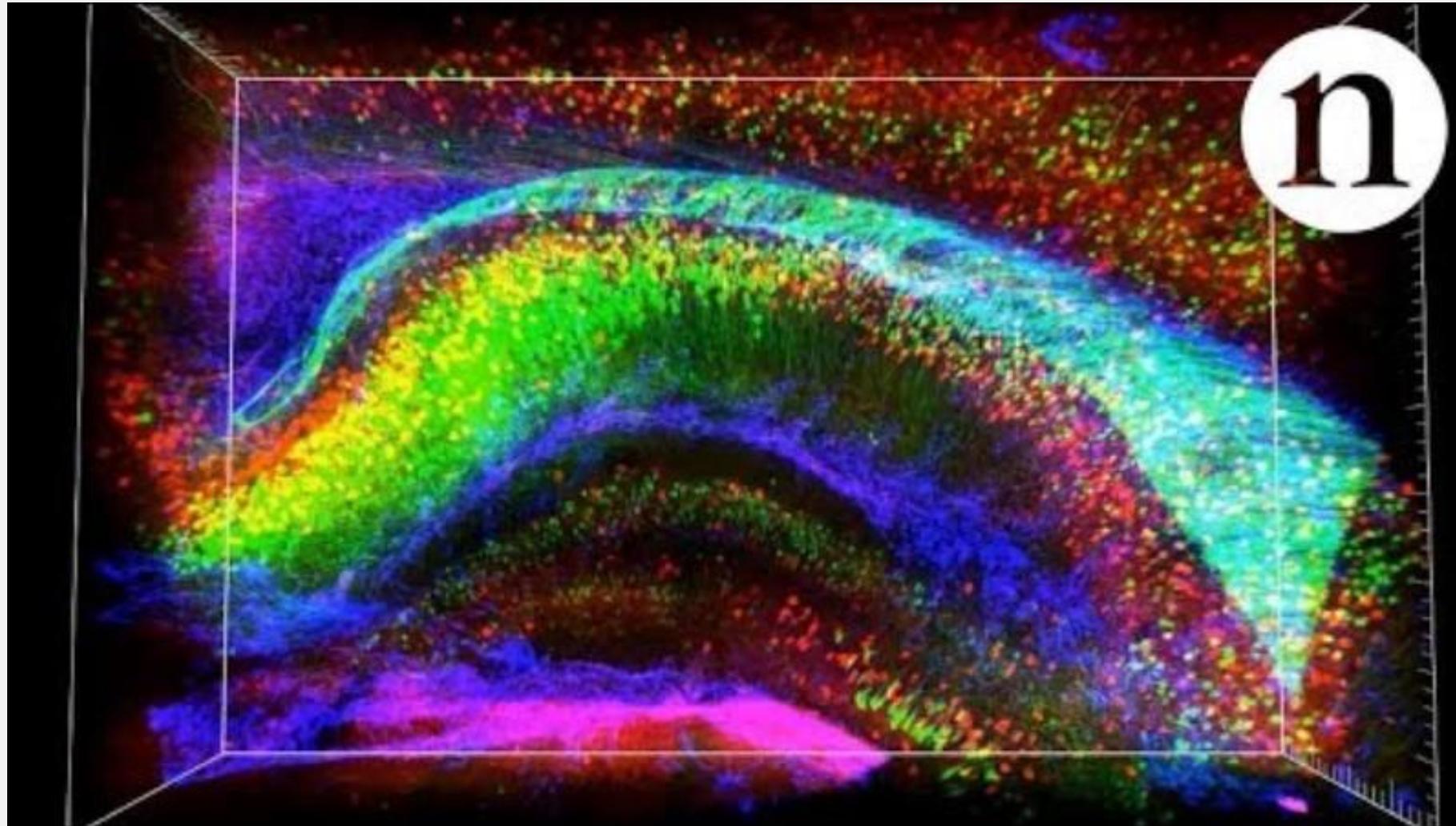
Brain clearing

- clear membranes/lipids/fats which scatter light
- Light can penetrate deeper, emitted light will be captured without scattering
 - Also allows the antibodies to penetrate
- Allows imaging of FPs in larger blocks of tissue
 - Can track axons over longer distances, identify networks, characterize coarse neuroanatomy



Chung, 2013, Nature (“CLARITY”)

Clarity



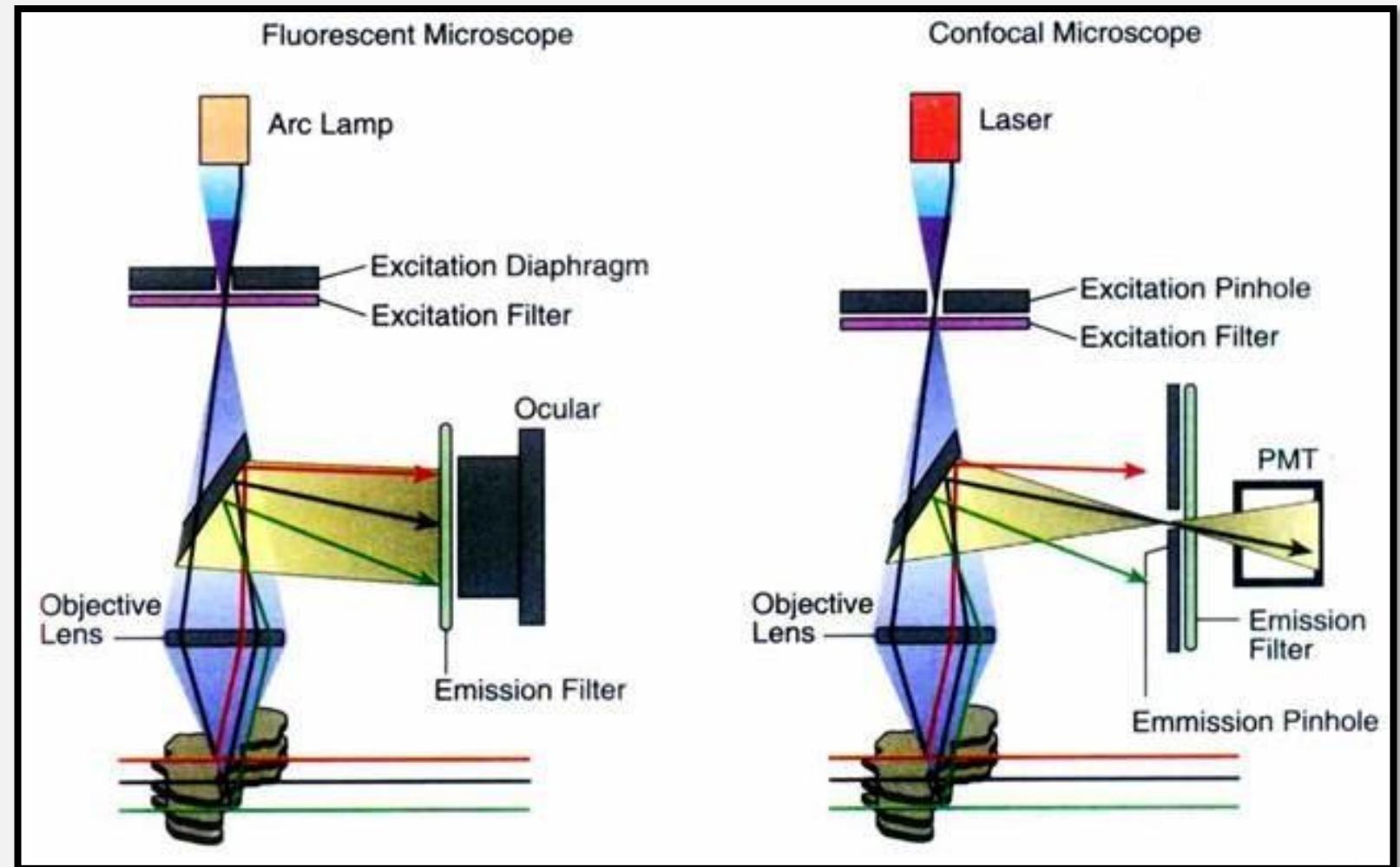
Visualizing FPs with Confocal Microscopy

Fluorescent microscope

- All light from tissue is reflected to the eye piece

Confocal Microscope

- Pinhole eliminates out-of-focus light, allowing visualization of a single focal plane
- Reconstruct images from different focal planes



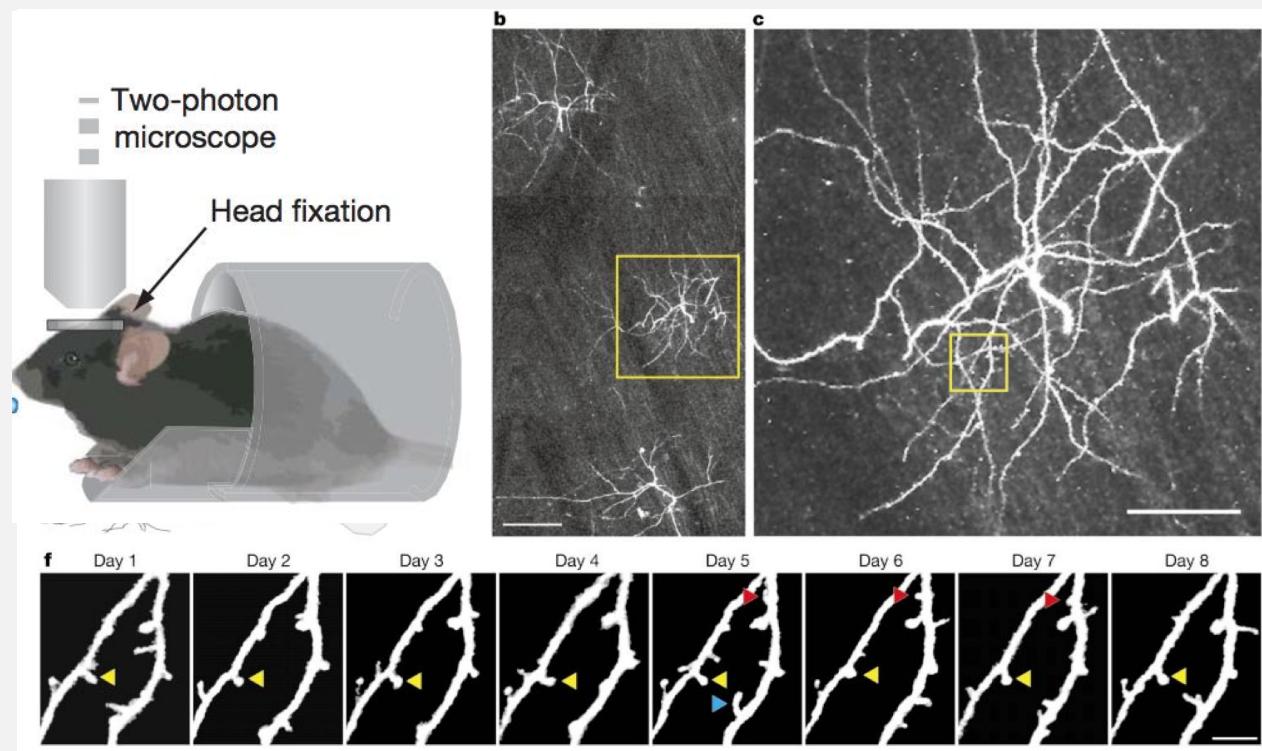
In vivo microscopy of GFP neurons

CLARITY

- Dead tissue
- Weakness: Neurons are not static
- Must image living tissue to see changes over time

2 photon microscopes

- Image deep into tissue through dura (100s μm)
- In yellow: stable mushroom spines
- In blue: spine gone within a day
- In red: slowly retracting spines

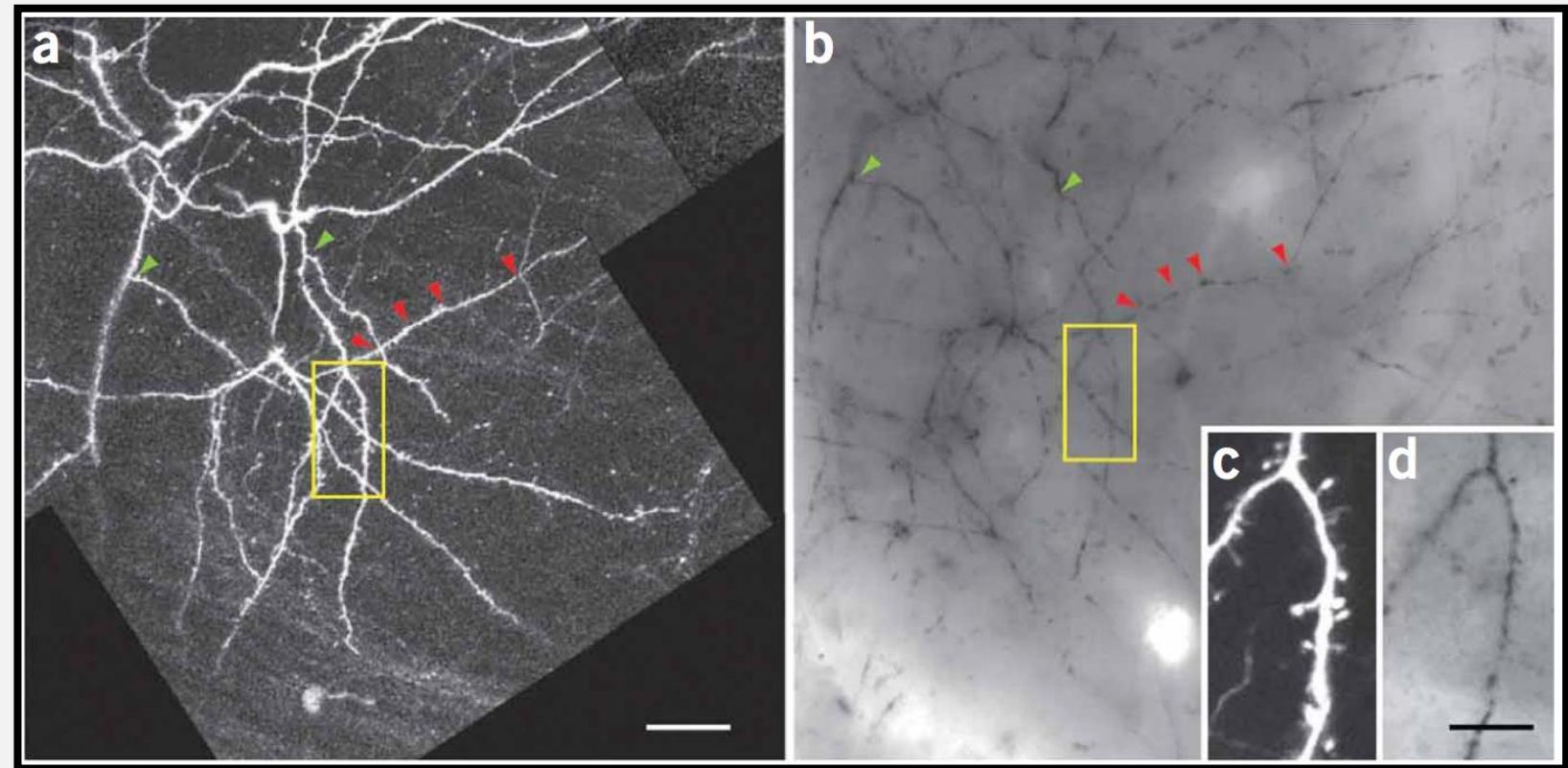


But, are these spines sites of functional synapses?

Method 5: Electron Microscopy

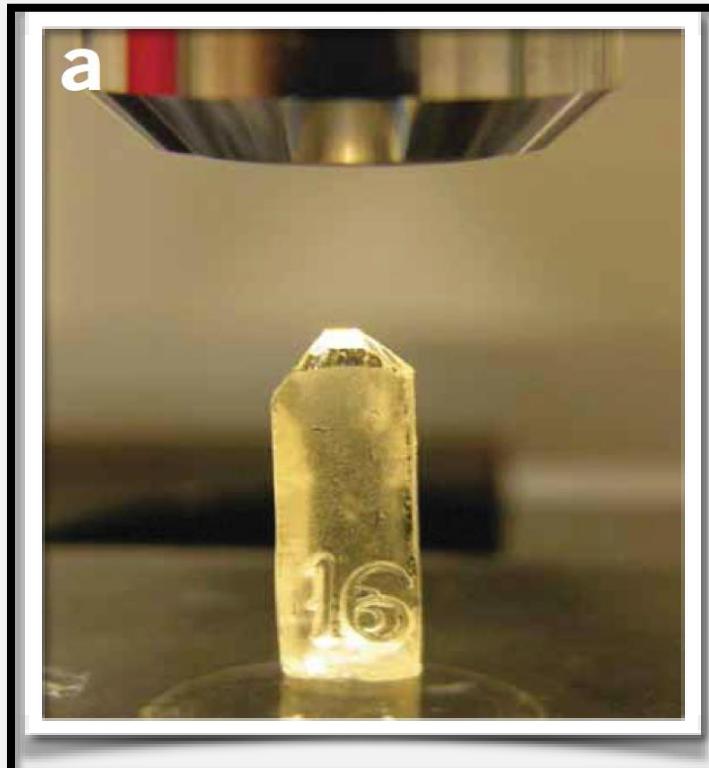
***Continuing from
previous GFP example***

- A) Fluorescent GFP
- B)
Immunohistochemical staining of GFP
 - Electron dense precipitate inside the GFP+ neurons

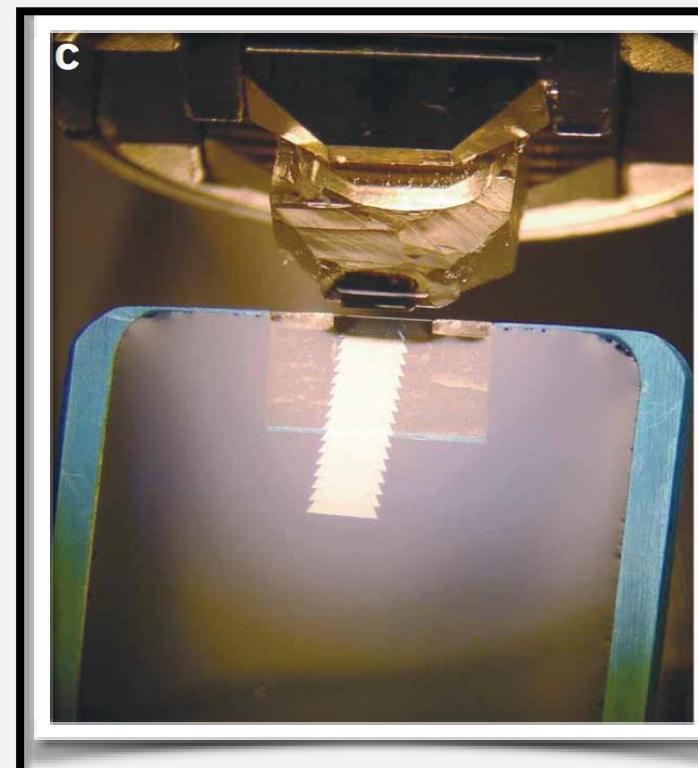


(EM can be combined with immunohistochemistry, FPs etc, or can use it on its own to examine detailed cellular anatomy with nm resolution)

Electron Microscopy



Tissue embedded in
a block of resin



Cut into 60 nanometer-
thick sections

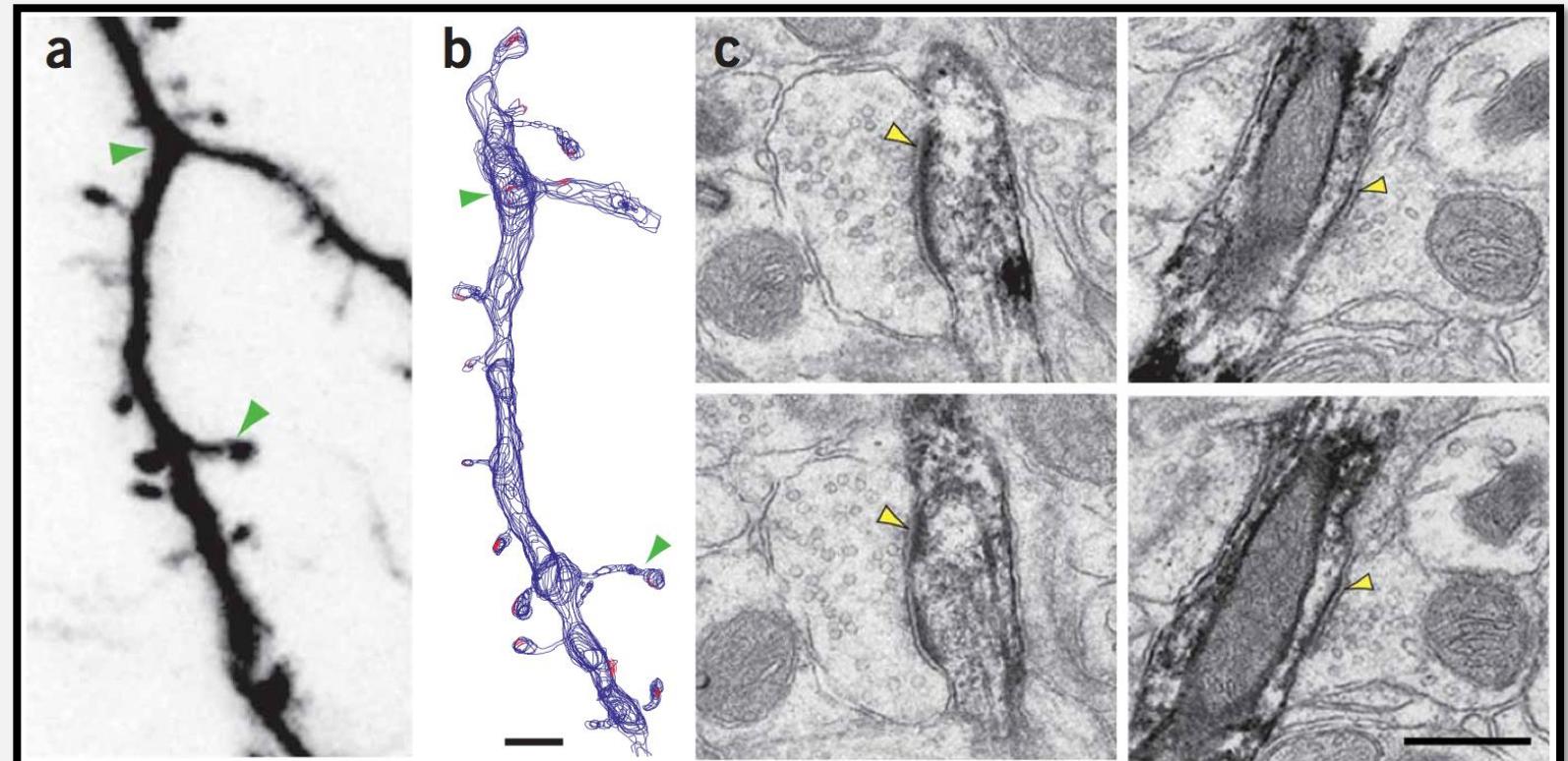


Imaged on electron
microscope

Electron Microscopy

Knott, 2009, Nature Protocols

- Best resolution
- Needs: an electron microscope (\$\$\$) and a technician (\$\$)
- Cons:
 - Time consuming
 - 12+ years to map connectivity of 302 neurons of the *C-elegans* NS
 - Often need to be done in a vacuum – molecules in air can scatter electrons
 - Stable environment



original GFP
(2-photon image)

reconstructed from
EM sections

images from individual EM sections,
showing bona fide synapses in spines
that were previously imaged ⁴² *in vivo*



BREAK



Neurophysiology 1

PSYC 304

Learning objectives

By the end of this lesson, you will...

1. Be able to describe how different ions contribute to the resting membrane potential of neurons and glial cells
2. Explain how the distribution of ions results in a negative charge inside neurons.
3. List the sequence of ion flows that underlies an important neuronal signal called an action potential.
4. Describe how specialized ion channels propagate the action potential from the start of an axon to the tips of its every branch.
5. Contrast the way the action potentials spread down myelinated versus unmyelinated axons.

Neurophysiology

- study of electrical and chemical processes in neurons.

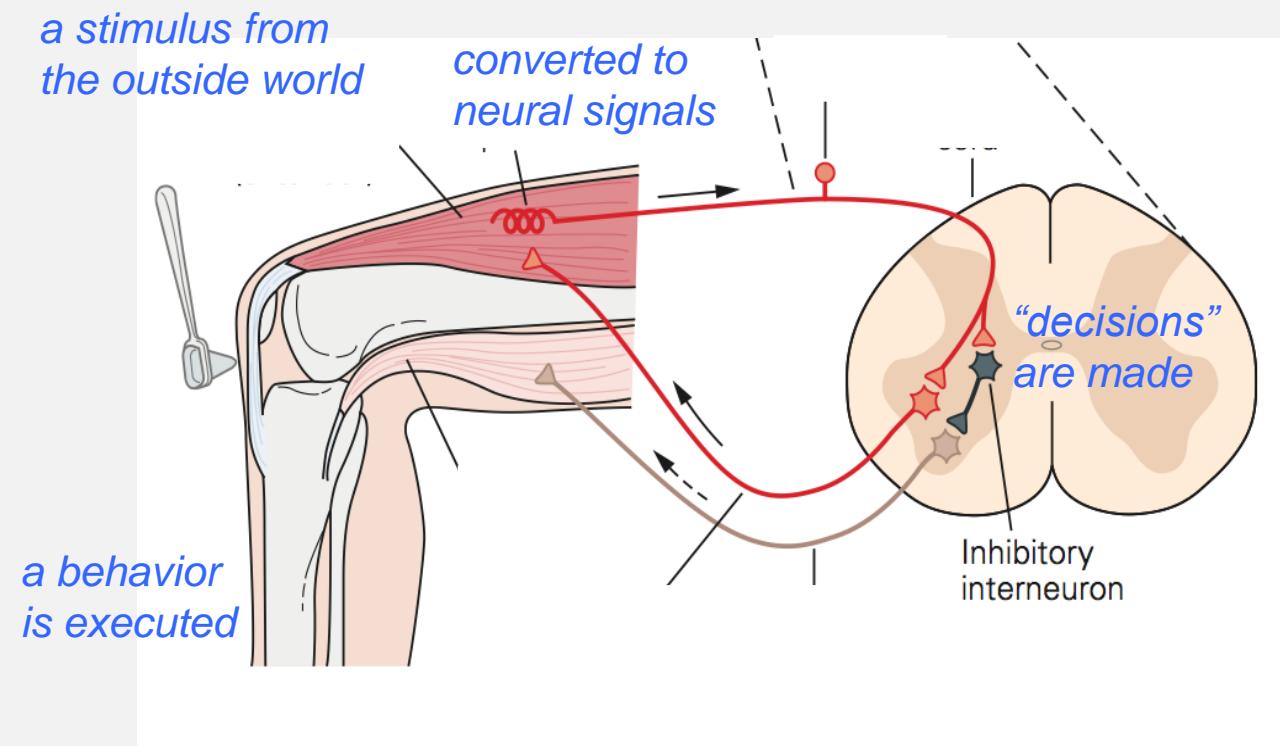
Electrochemical signaling

- Information flows *within* a neuron via electrical signals; information passes *between* neurons through chemical signals.

Two fundamental neuronal signals

Action potentials + synaptic transmission

- Dependant on electrical properties of neurons
- Determine how information is processed, and “decisions” are made



The Membrane Potential

Electrical Signals: Vocabulary

- All living cells have an electrical charge—more negative on the inside than on the outside.

Ions: Electrically charged molecules.

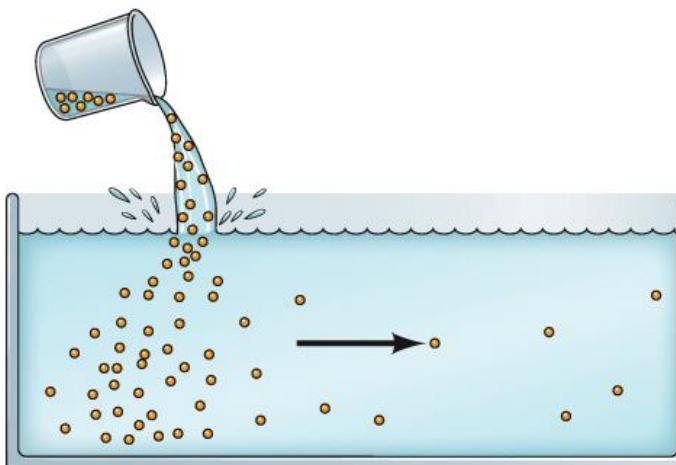
- **Anions** are negatively charged.
- **Cations** are positively charged.
- What are common ions involved in the electrical signaling of neurons?

Electrical Signals: Vocabulary

Diffusion: ions flow from areas of high concentration to low concentration

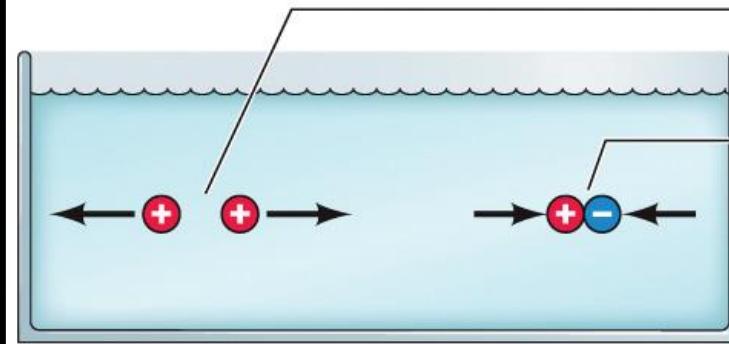
Electrostatic Pressure: like charges repel, opposite charges attract

(B) Diffusion



Particles move from areas of high concentration to areas of low concentration. That is, they move down their concentration gradient.

(A) Electrostatic forces



Like charges repel each other.

Opposite charges are attracted to each other.

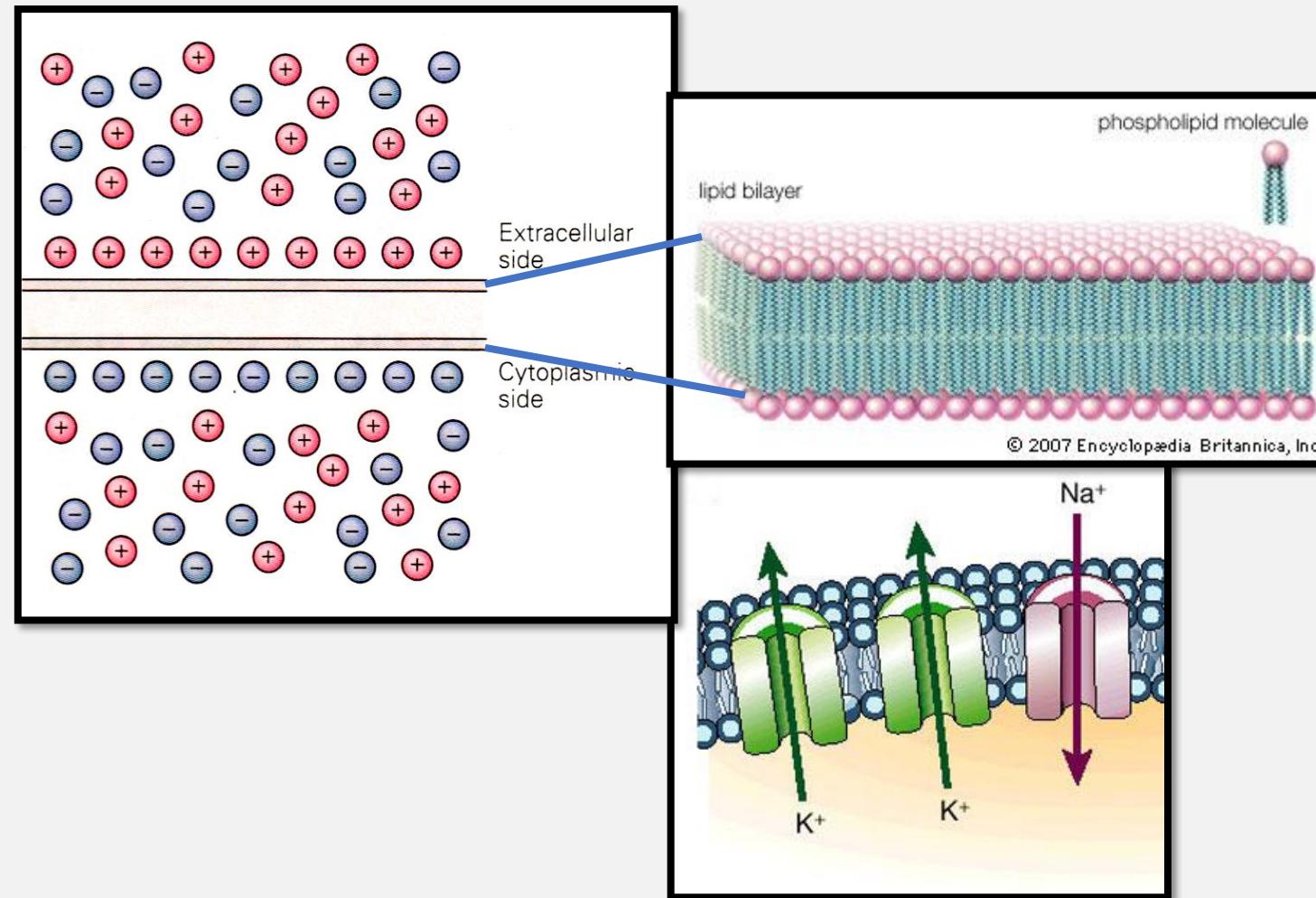
The membrane potential

Lipid Bilayer

- Separation of two conducting solutions
 - Cytoplasm & extracellular fluid
- Charged ions
 - Difference in the relative concentrations
 - Creates of a voltage difference

Membrane Potential

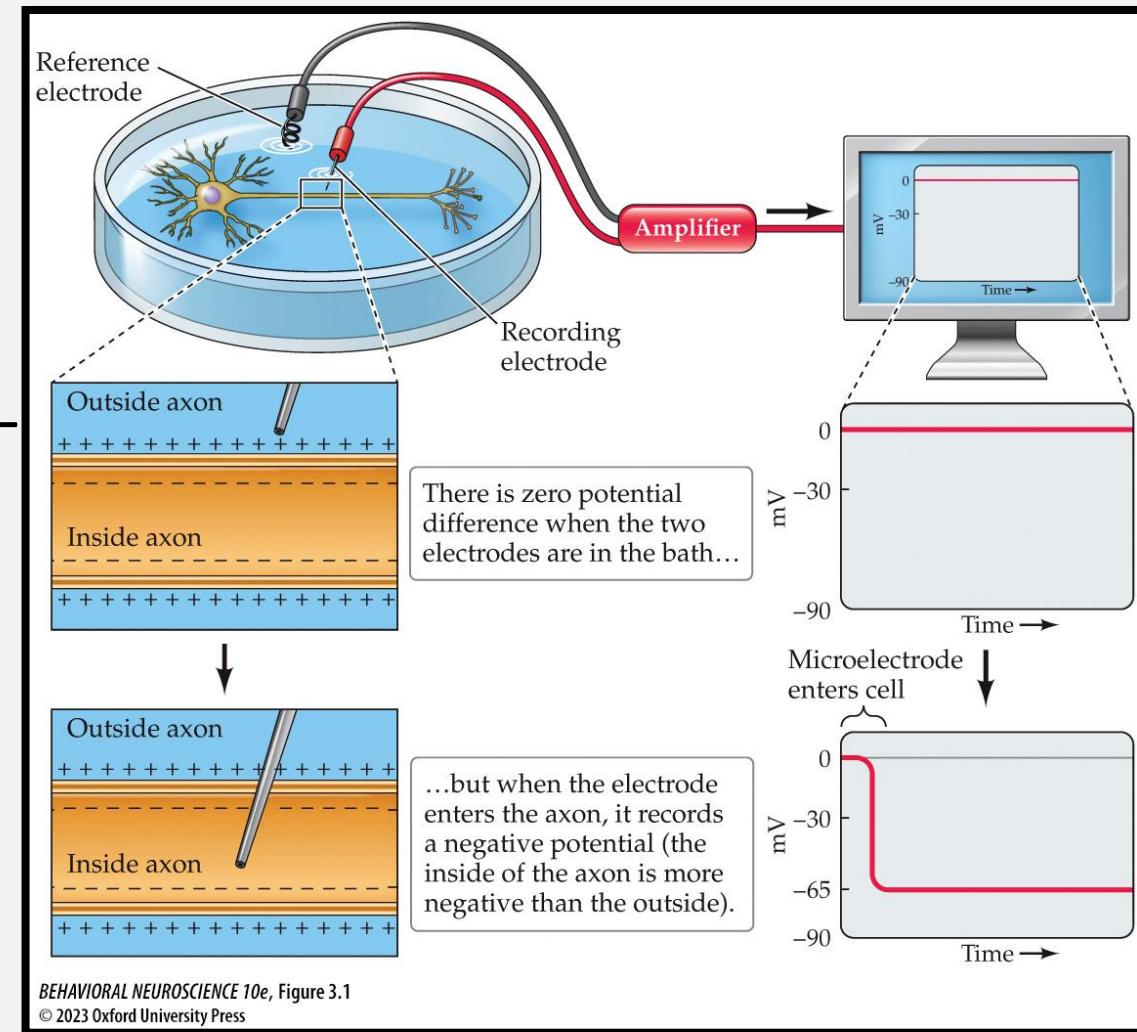
- Voltage difference across the membrane
- Flow of anion/cations = change in membrane potential
- Charged particles always travel through the path of least resistance



The membrane potential

Definition

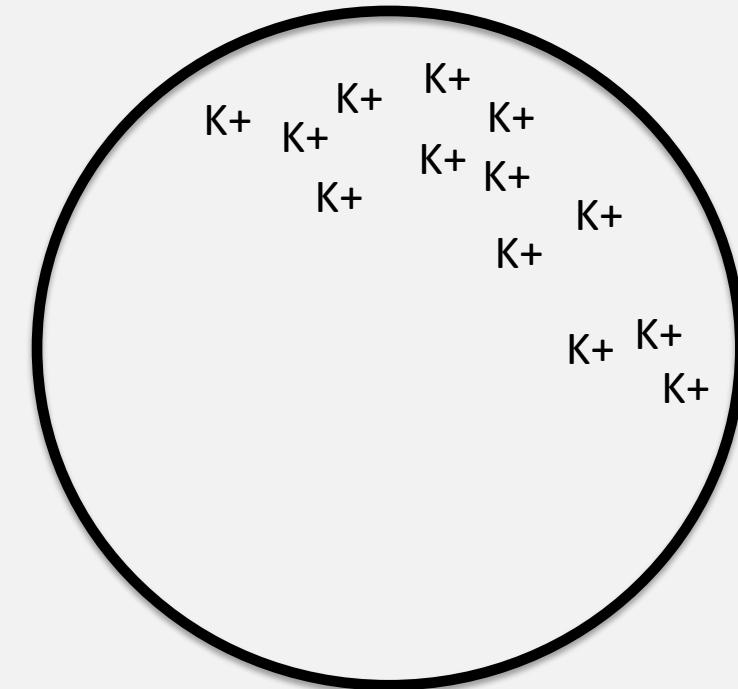
- $V_m = V_{in} - V_{out}$
- Measure with a voltmeter
 - Typically, a cell sits around -65 mV
 - Negative inside the cell
- Question: Why is V_m -65 mV



Resting membrane potential

Glial Cells

- $[K^+]$ inside = 400 mM
- $[K^+]$ outside= 20 mM
- Only permeable to K^+ at rest



Resting membrane potential

Glial Cells

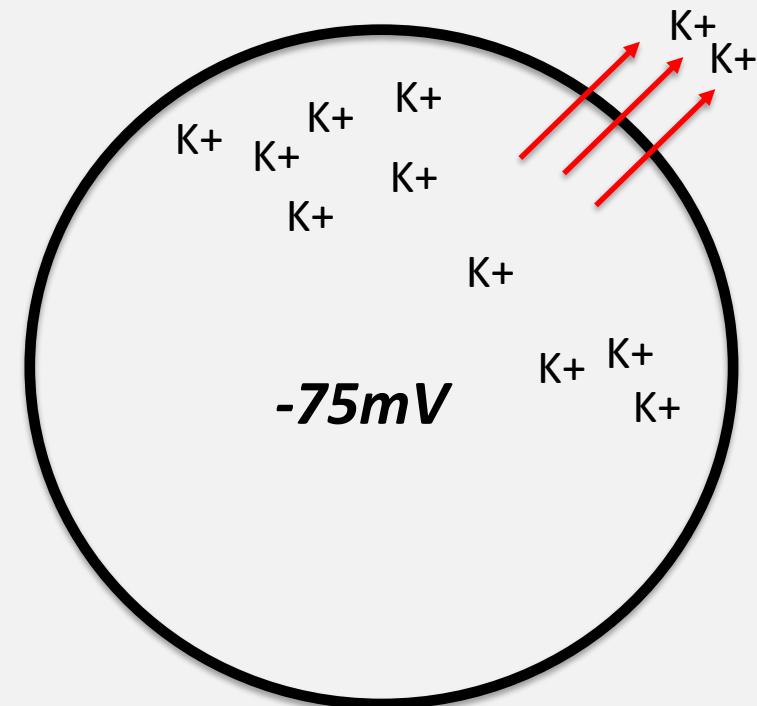
- Dictated by K+

Chemical/concentration gradient

- K+ diffuses out of cell
- Creates an *electrical gradient*

Equilibrium potential

- Chemical driving force = electrical driving force
- Conc forces K+ out, negative V_m pulls K+ in
- Result = -75 mV resting membrane potential



The Nernst Equation

Equilibrium potential

- Membrane potential when: chemical and electrical driving forces balance out

$$E_x = \frac{RT}{zF} \ln \frac{[X]_o}{[X]_i}$$

$$E_x = \frac{58 \text{ mV}}{z} \log \frac{[X]_o}{[X]_i}$$

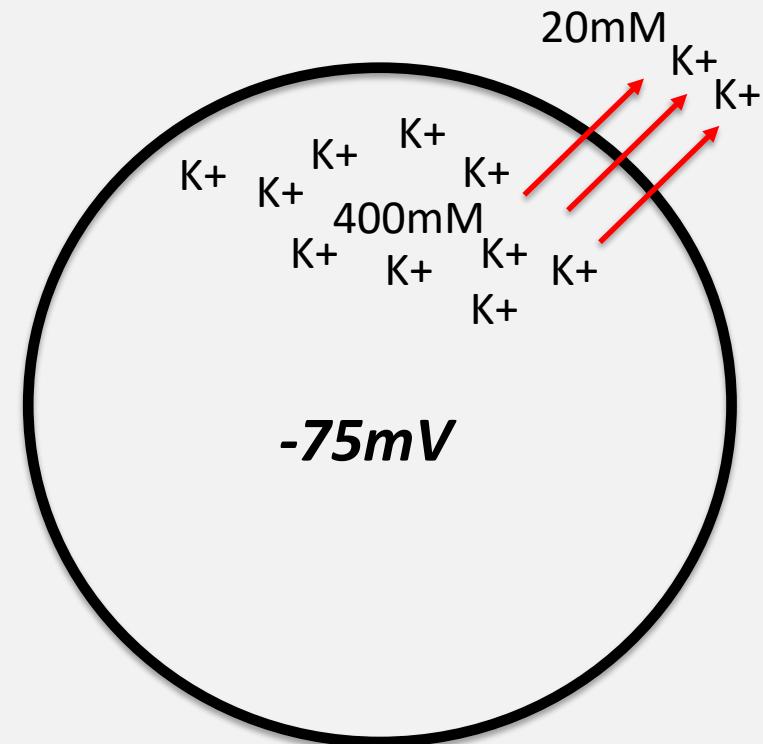
$$E_k = \frac{58 \text{ mV}}{1} \log \frac{[20]}{[400]} = -75 \text{ mV}$$

R, the gas constant—relates energy to temperature, for a mole of particles.

T, temp in Kelvin

F, Faraday constant—electric charge per mole of electrons

z, valence of ion



Note: I will NEVER ask you to use this equation to calculate anything on the exam, but you should know what the equation tells you

Resting membrane potential

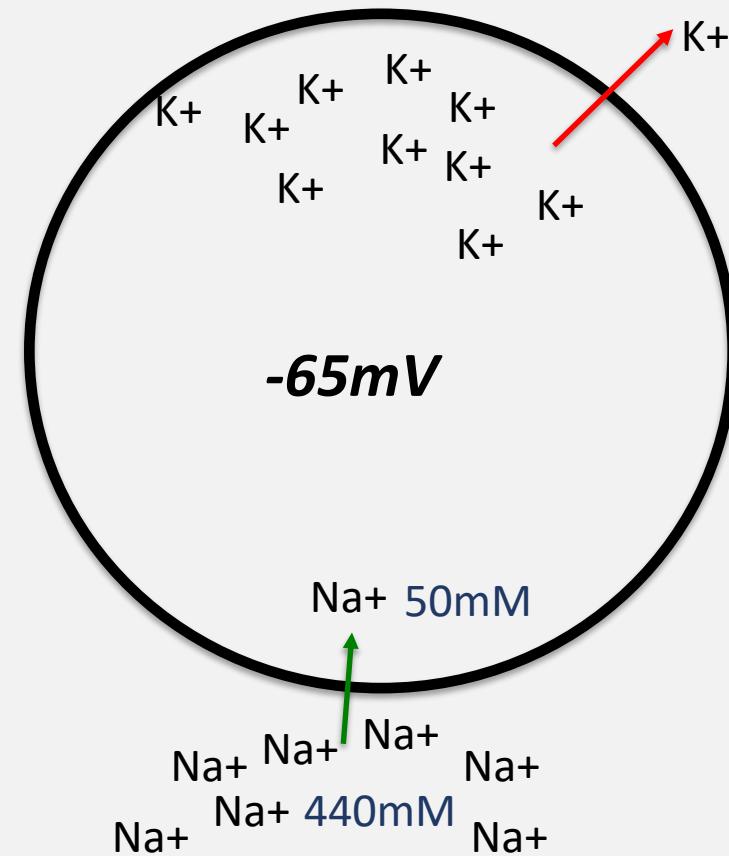
Neurons

- 3 major ions: K+, Na+, Cl-
- Also, slight permeability to **Na+** (Sodium ions)

Nernst for sodium

- Small Na+ conductance depolarizes the cell a little
 - V_m of -75mV to -65mV

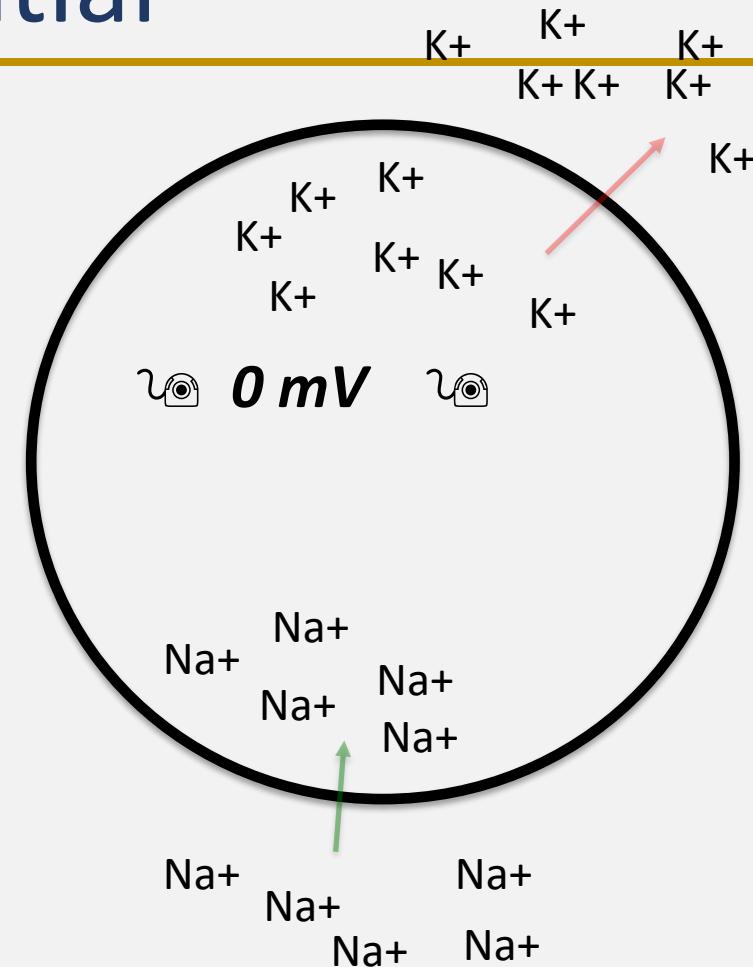
$$E_{\text{Na}} = \frac{RT}{F} \ln \frac{[\text{Na}]_o}{[\text{Na}]_i} = 58 \text{ mV} \log \frac{440}{50} = +55 \text{ mV}$$



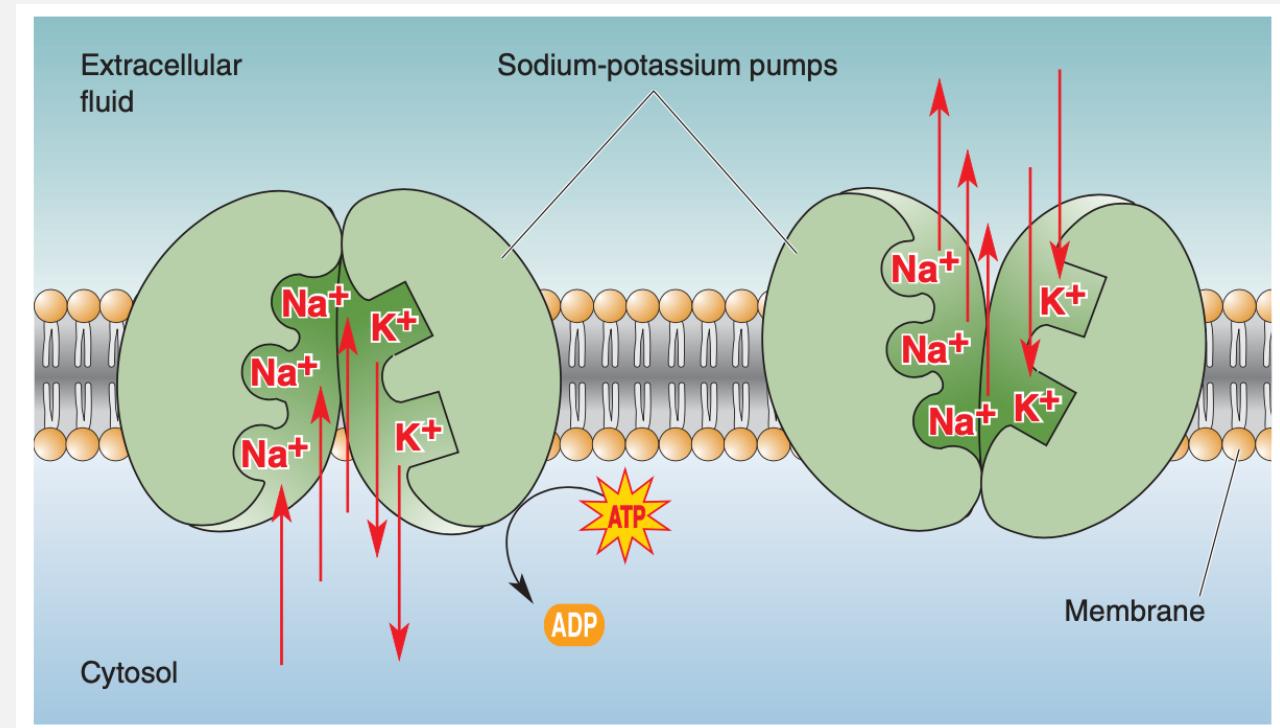
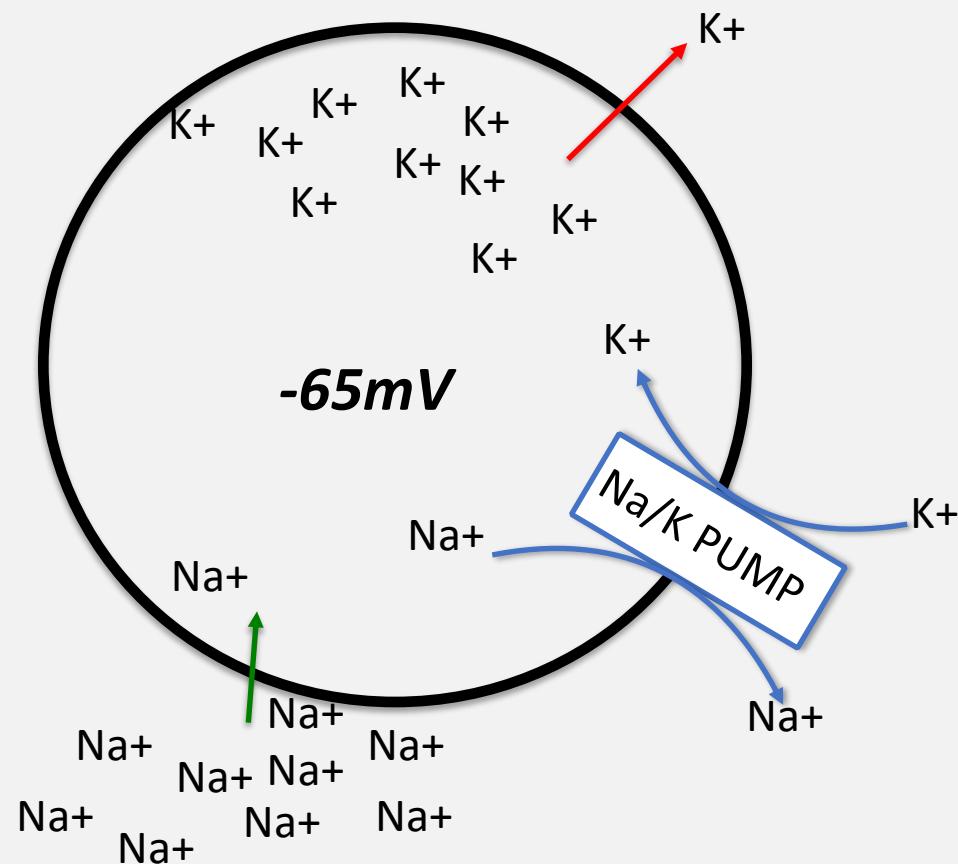
Resting membrane potential

Neurons

- Rundown of V_m



Na/K ATPase pump



Solution: Na/K pumps maintain the gradients, by pumping 3 Na^+ ions out and 2 K^+ ions in, against their electrochemical gradients

Resting membrane potential

Neurons

- Cl⁻ (chloride ions)
- [Cl⁻] in = 52mM
- [Cl⁻] out = 560mM

Concentration gradient

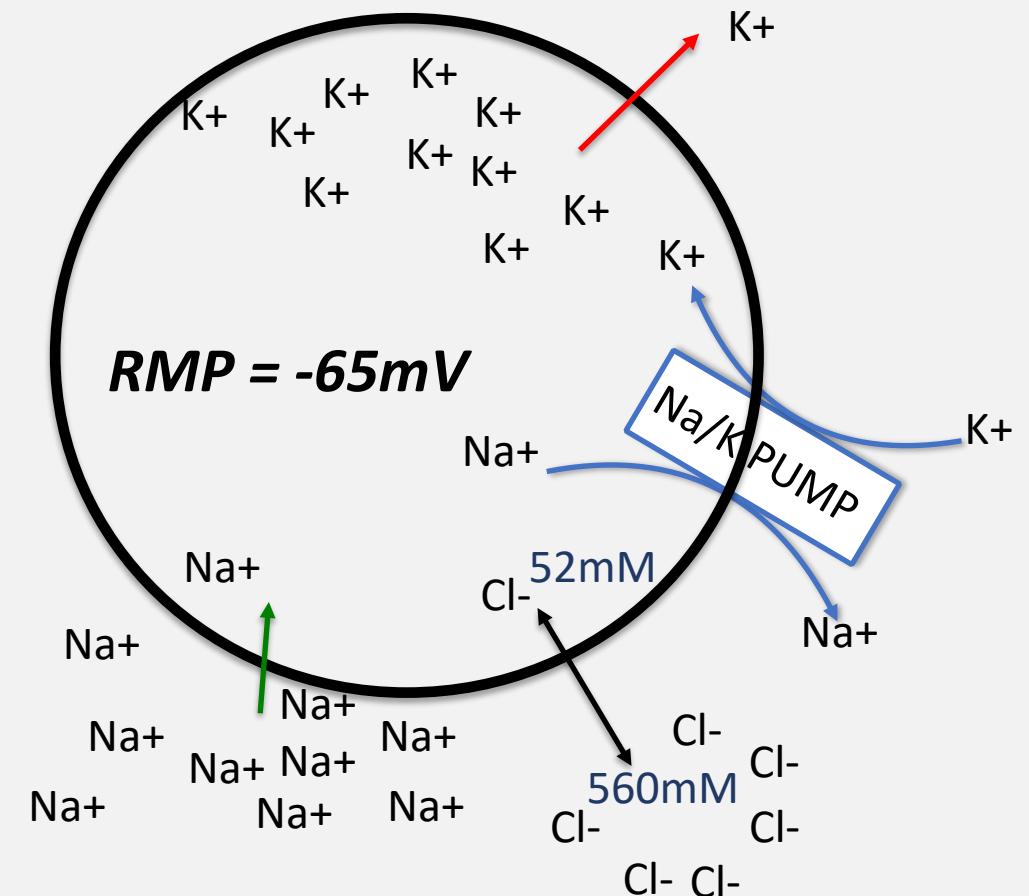
- Drives Cl⁻ in

Electrical gradient

- Pushes Cl⁻ out

Equilibrium potential

- -70 mV



Resting membrane potential of neurons

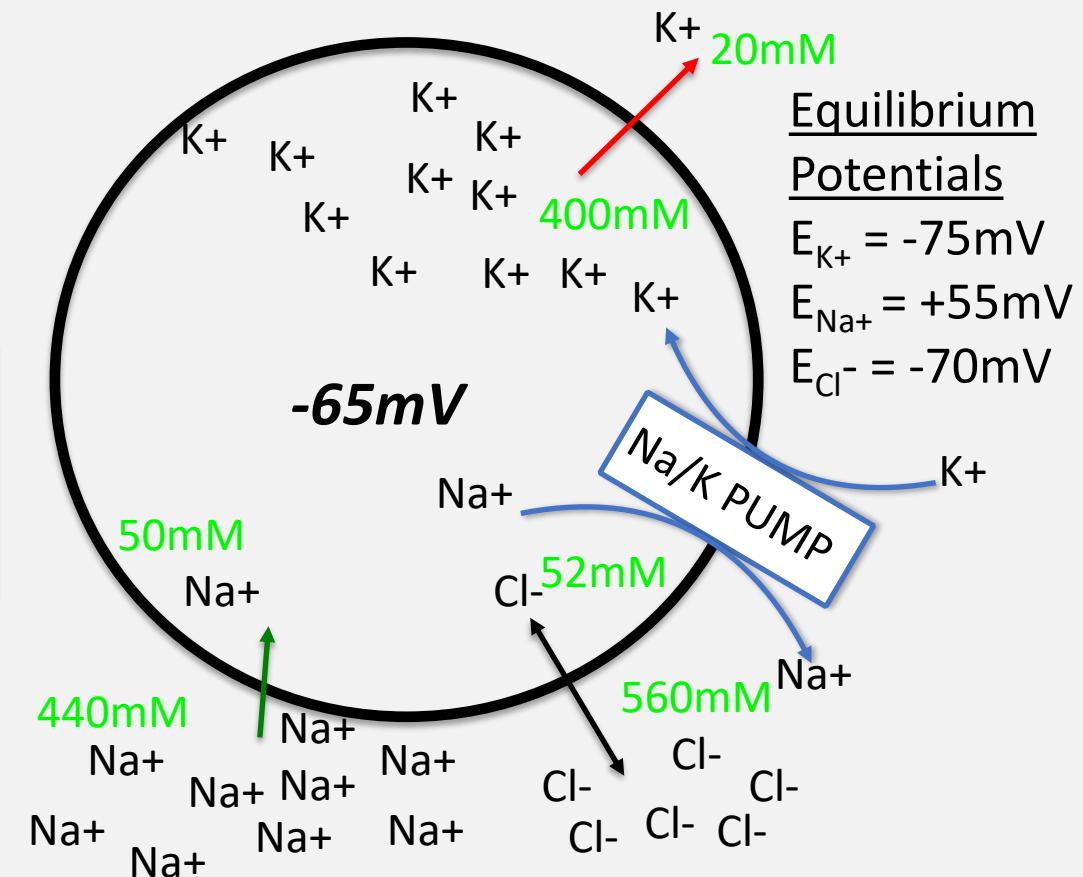
Dependent on Relative Permeabilities

- Na⁺, K⁺, Cl⁻

Goldman Equation

$$V_m = \frac{RT}{F} \ln \frac{P_K[K^+]_o + P_{Na}[Na^+]_o + P_{Cl}[Cl^-]_i}{P_K[K^+]_i + P_{Na}[Na^+]_i + P_{Cl}[Cl^-]_o}$$

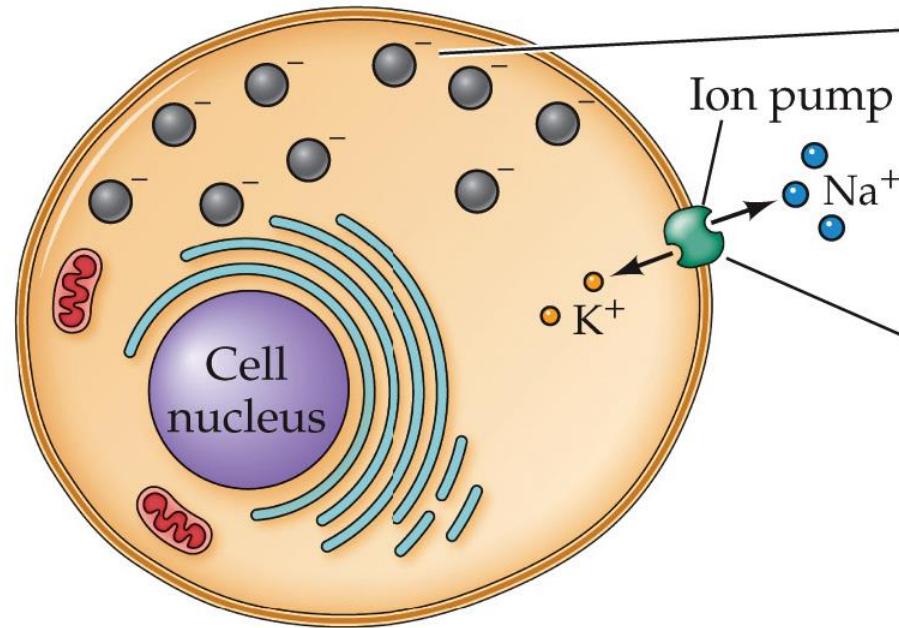
- where P = relative permeability
- at rest P_K:P_{Na}:P_{Cl} = 1.0 : 0.04 : 0.45



Resting membrane potential

Summary

(A) The sodium-potassium pump

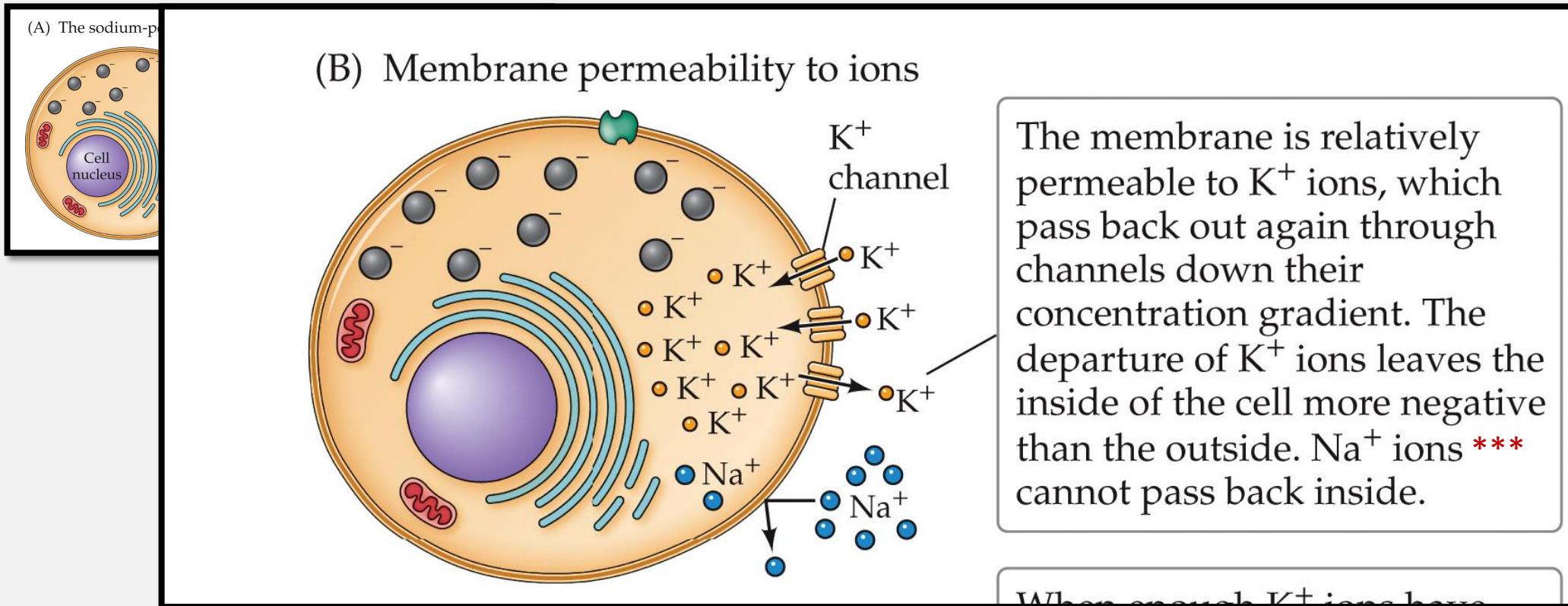


Cells contain many large, negatively charged molecules, such as proteins, that do not cross the membrane.

The sodium-potassium ($\text{Na}^+ \text{-K}^+$) pump continually pushes Na^+ ions out and pulls K^+ ions in. This ion pump requires considerable energy.

Resting membrane potential

Summary



*** Na^+ ions are only very slightly permeable compared to K^+ ions, and therefore, only have a minor impact on resting membrane potential

Resting membrane potential

Summary

(A) Cell

(B) Membrane

Cations like Na^+ push against the membrane's exterior, attracted to the negative interior. Likewise, anions coat the interior of the cell membrane, attracted to cations on the other side. Most of the cell's potential difference is due to these charges immediately surrounding the membrane.

(C) Equilibrium potential

When enough K^+ ions have departed to bring the membrane potential to -65 mV or so, the electrical attraction pulling K^+ in is exactly balanced by the concentration gradient pushing K^+ out. This is the K^+ equilibrium potential, approximately the cell's resting potential.

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Exercise:

Graphically represent chemical and electric driving forces for Na^+ and K^+ , at different membrane potentials

--use downward arrows of various sizes to indicate magnitude of inward current (ie positive charge flowing into the cell), upward arrows for outward current

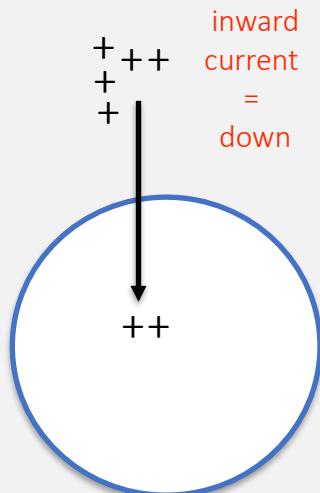
—hint: is the chemical driving force different depending on the membrane potential?

Na^+

$$\text{Chemical Driving Force} + \text{Electrical Driving Force} = \text{Net Driving Force}$$

75mV
55mV
35mV
10mV
-10mV
-30mV
-50mV

To help you remember that inward current is down, and outward current is up:



Exercise:

Graphically represent chemical and electric driving forces for Na^+ and K^+ , at different membrane potentials

--use downward arrows of various sizes to indicate magnitude of inward current (ie positive charge flowing into the cell), upward arrows for outward current

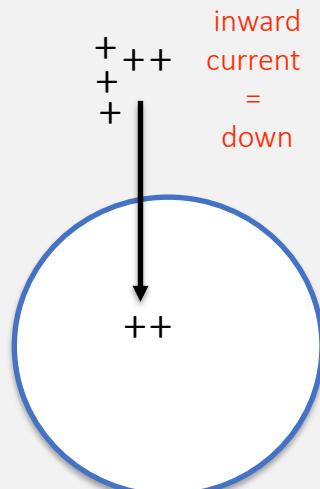
—hint: is the chemical driving force different depending on the membrane potential?

Na^+

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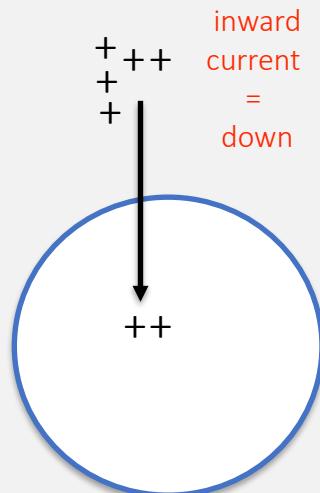
—hint: is the chemical driving force different depending on the membrane potential?

K^+

$$\text{Chemical Driving Force} + \text{Electrical Driving Force} = \text{Net Driving Force}$$

75mV
55mV
35mV
10mV
-10mV
-30mV
-50mV
-75mV

To help you remember that inward current is down, and outward current is up:



The Action Potential

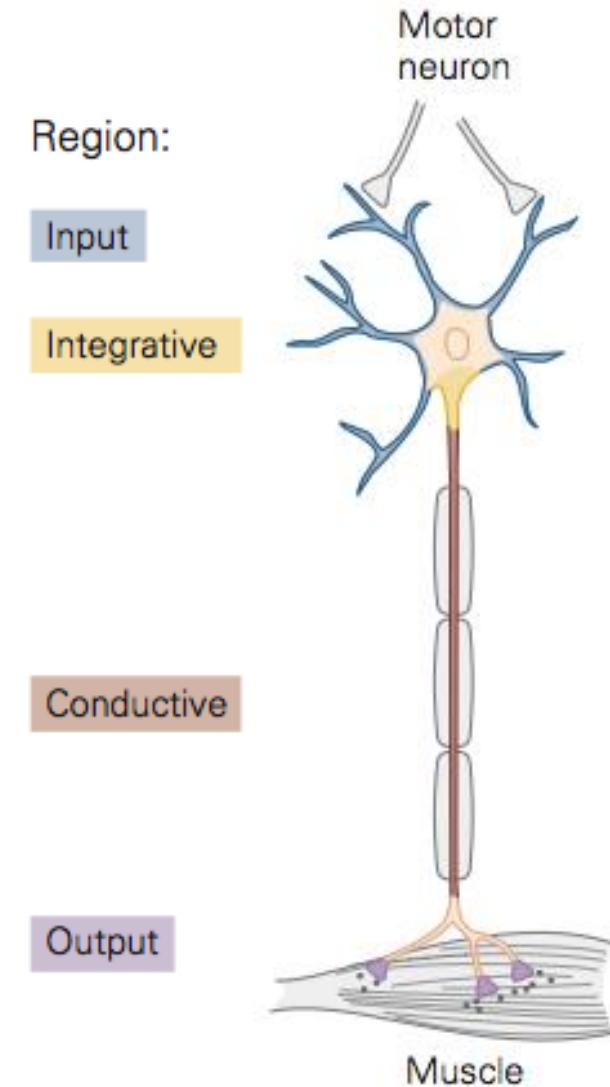
The Action Potential

The starting point of an electrical signal

- Hyperpolarized V_m
- Hyperpolarized meaning further from 0 mV membrane potential
- i.e. -65mV
- Can think of voltage as force that is going to push ions in or out of the cell
 - Like water pressure pushing water down a hose

What do we need?

- Regeneration of signal



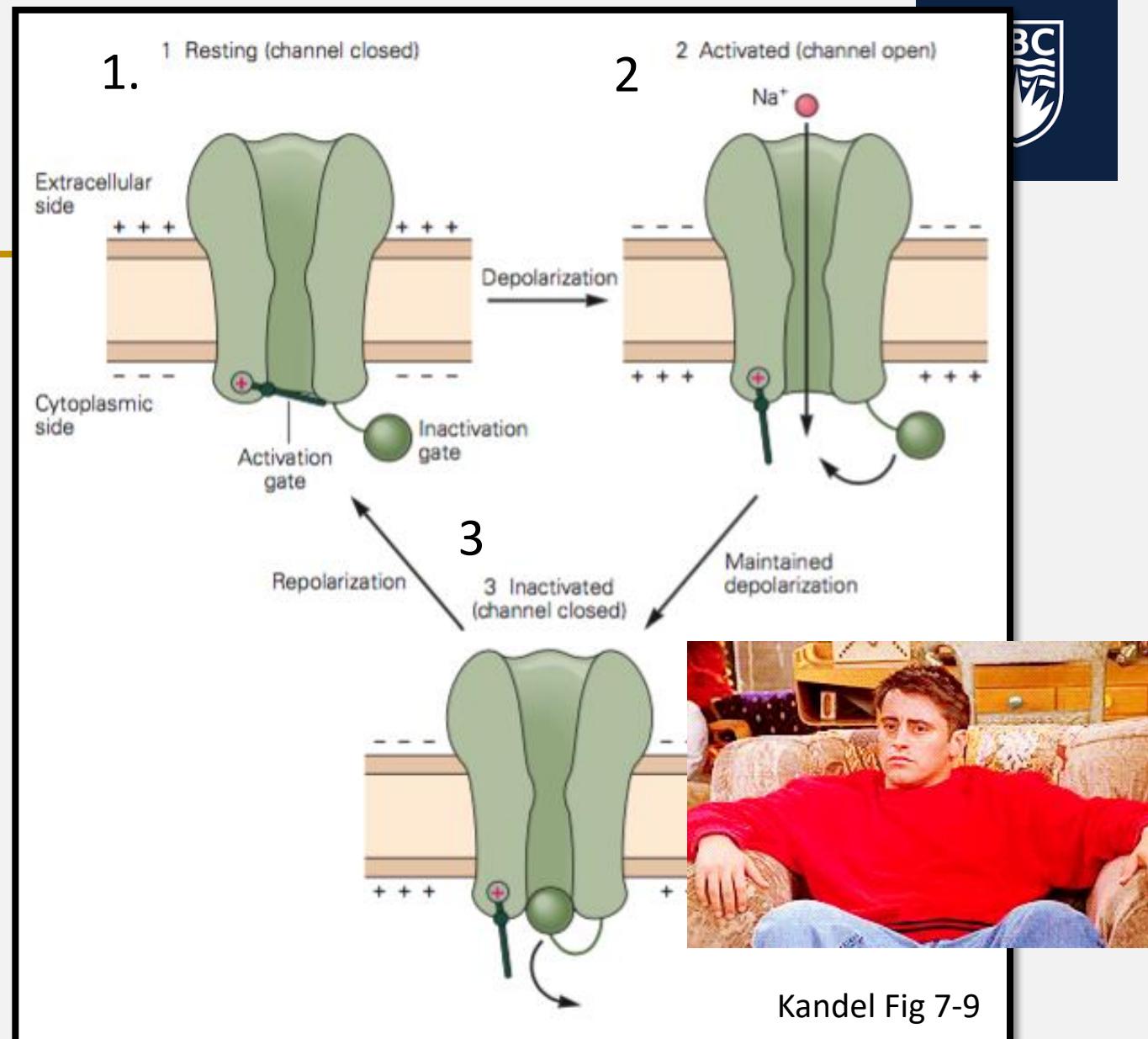
Voltage-gated ion channels

1. Resting

- VG channel closed
- Positively charged extracellular side
- Negatively charged cytoplasmic side

2. Activated

- Caused by potential change
- VG channel open
- Activation gate open
- Inactivation gate closing (but is a little slow)

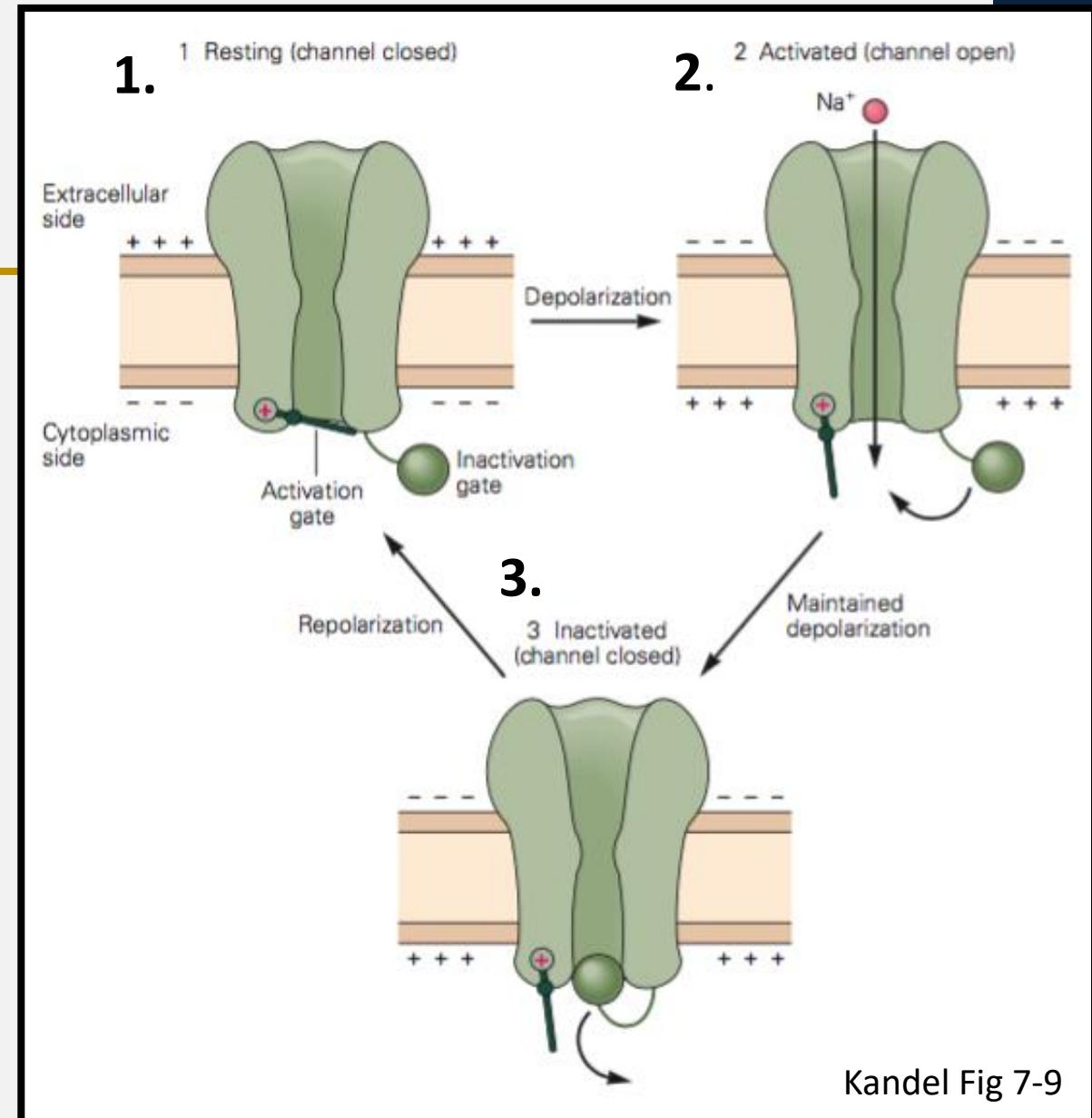


Voltage-gated ion channels



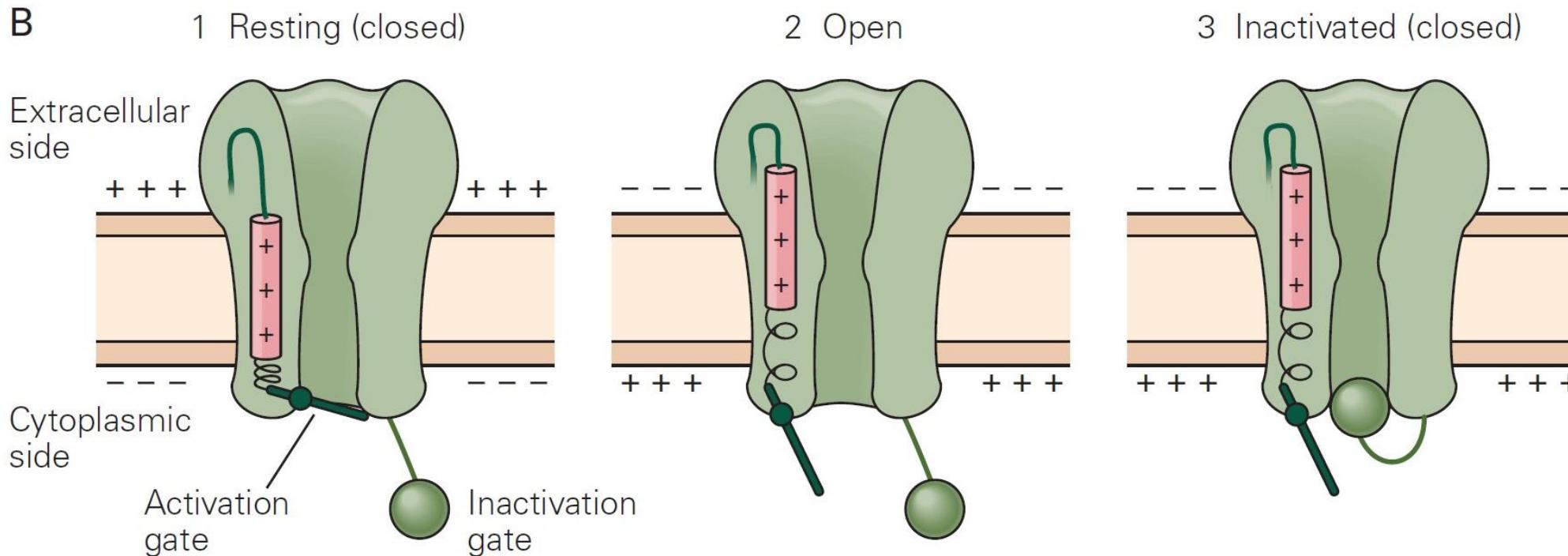
3. Inactivated

- Channel closed by the inactivation gate
- While inactivated the cell cannot fire another action potential – *Refractory period*



Kandel Fig 7-9

Voltage gated ion channels



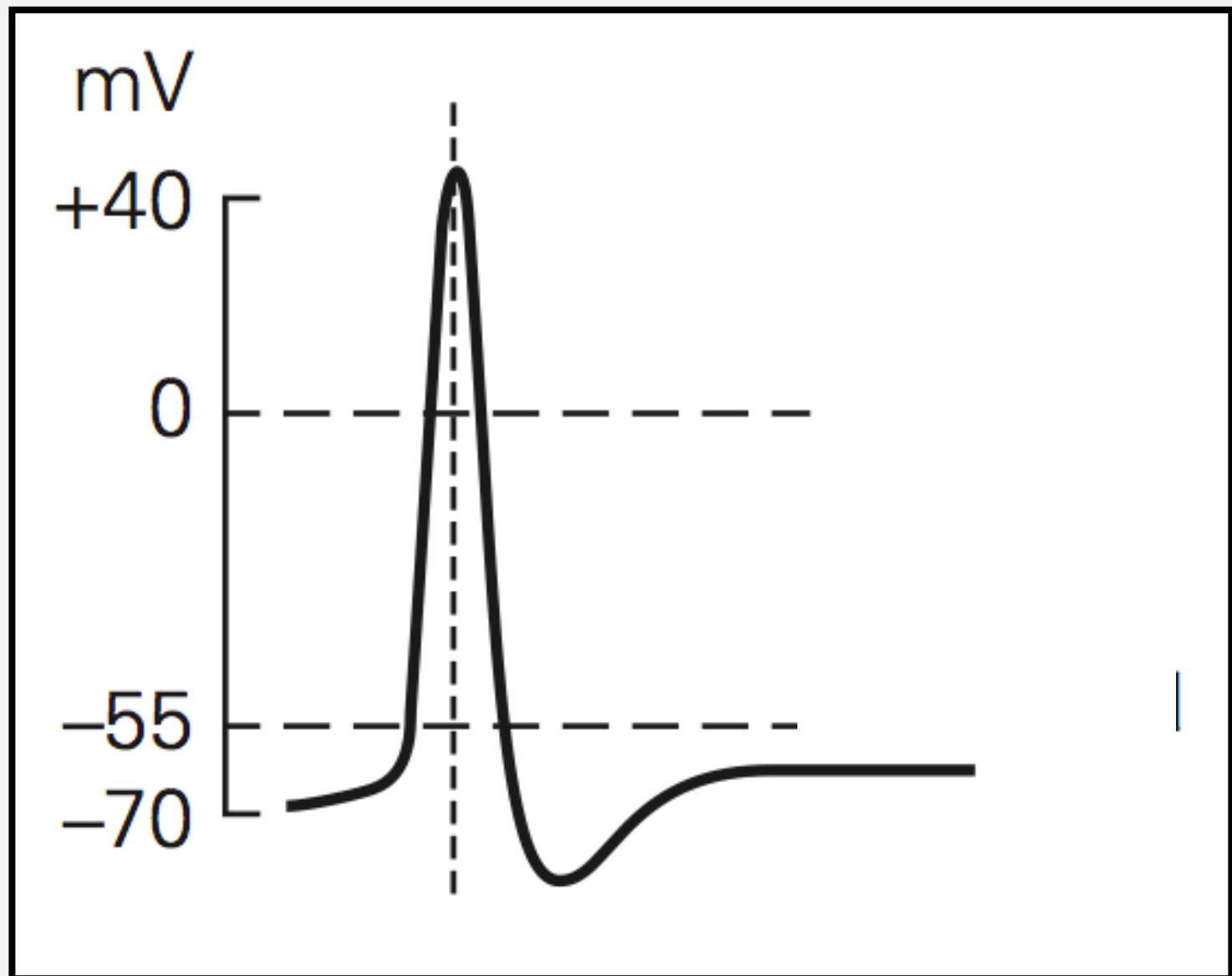
Exercise:

1) Please label when the typical neuron is: at resting membrane potential, and at threshold, is depolarized, and is hyperpolarized

2) **VG Na⁺ channels.**

Please indicate where on the plot the VG sodium channels are at rest, activated and inactivated

3) After Peaking at around +40 mV, the membrane potential plummets back down to past -70 mV. What is responsible for this shift? Label any important spots on the graph



$$V_m = \frac{RT}{F} \ln \frac{P_K[K^+]_o + P_{Na}[Na^+]_o + P_{Cl}[Cl^-]_i}{P_K[K^+]_i + P_{Na}[Na^+]_i + P_{Cl}[Cl^-]_o}$$



Remember: V_m at rest determined by:

$$P_K : P_{Na} : P_{Cl} = 1.0 : 0.04 : 0.45$$

But when Na^+ channels open:

$$P_K : P_{Na} : P_{Cl} = 1.0 : 20 : 0.45$$

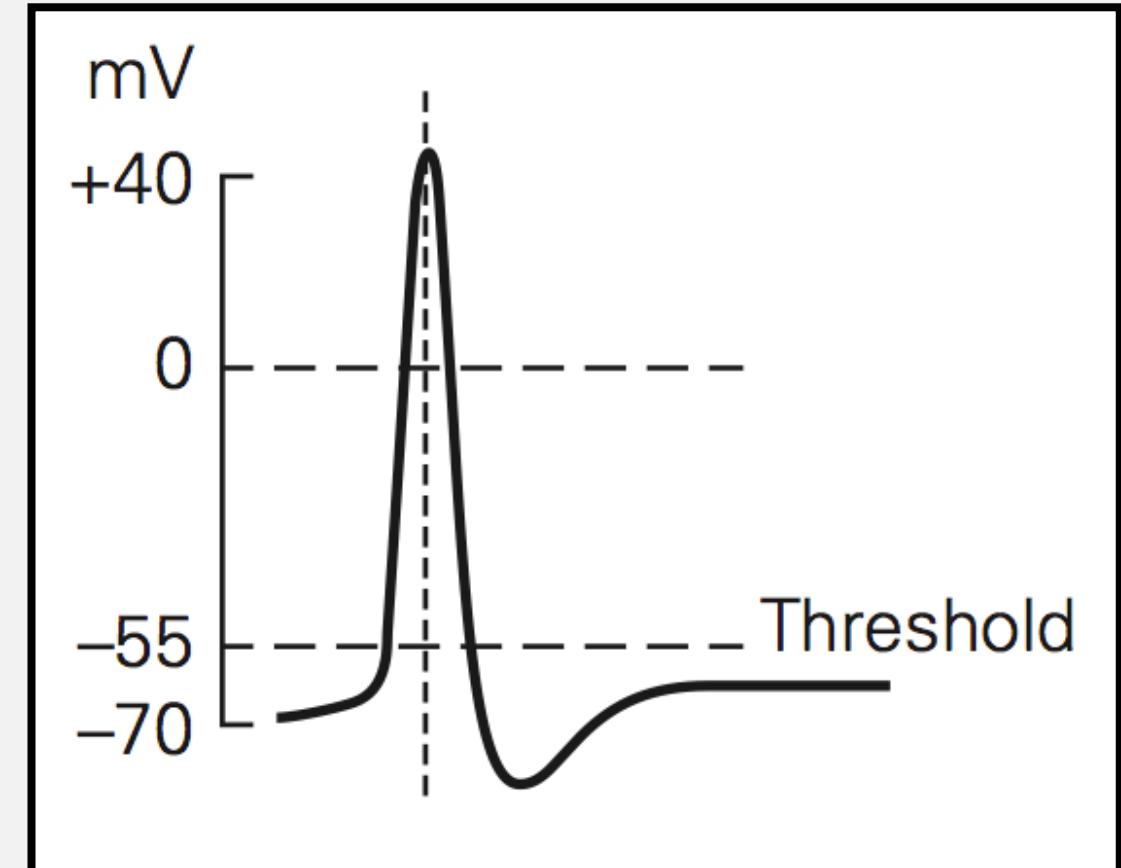
Action potentials

VG Na⁺ channels

- At rest: -70mV
- Activated: -55mV
- Inactivated: =+40 mV

VG K⁺ channels

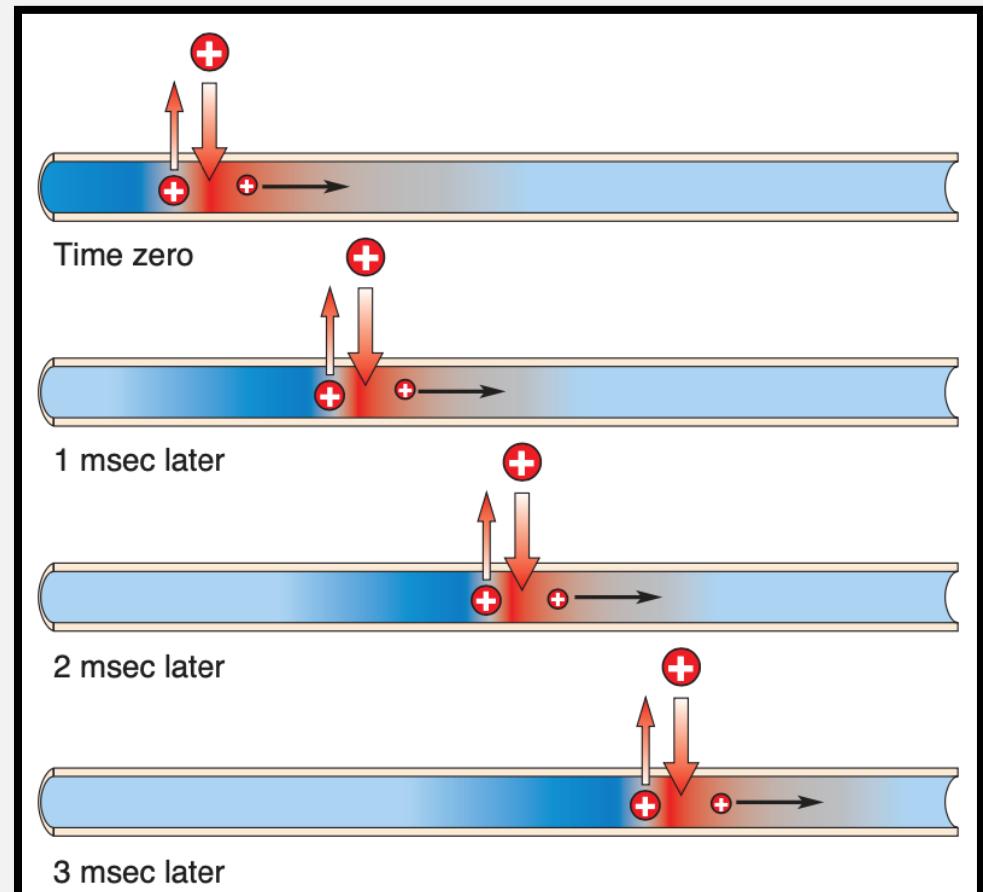
- The opening and closing of VG K⁺ channels rapidly brings the vicinity back to a hyperpolarized state
- Positive charge inside the cell and high [K⁺] forces K⁺ out
- Slow closing of VG K⁺ channels causes hyperpolarization



AP conduction down the Axon

One way train due to refractory period

- Current passively flows in both directions
- Only VG channels downstream are at rest and can open
- Local depolarization opens those VG Na⁺ channels
- Which opens adjacent VG Na⁺ channels
 - Etc. etc. etc.



Conducting an electrophysiological experiment

Hodgkin & Huxley model

- Needs
 - Healthy cells: (in vitro (culture/expression), ex vivo (an acute slice), in vivo (an alive animal)
 - Microscope, fine electrodes, noise reduction (grounding wires, faraday cages, vibration dampening)
 - Signal acquisition device: amplifier, digitizer, computer software

Consideration of Ohms Law

- V = Voltage (volts)
- I = Current (amperes)
- R = resistance (ohms)
- G = Conductance (Siemens)

$$G = 1/R$$

- Insulators – separate electrical conductors, are really good resistors

$$\Delta V = IR$$

Experimental set-up

Needs

Health cell(s)

Electrodes

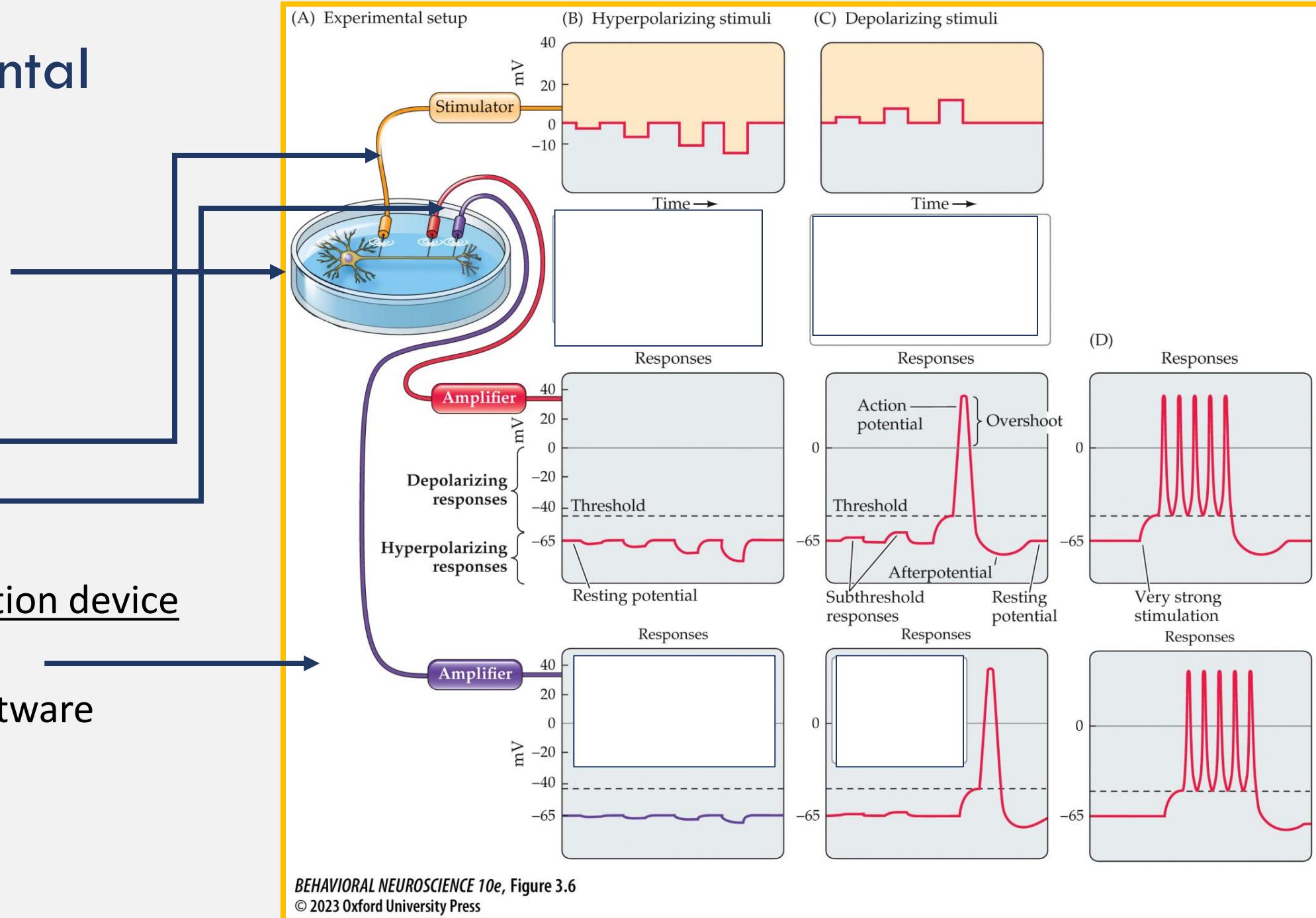
Stimulating

Recording

Signal acquisition device

Amplifiers

Computer software



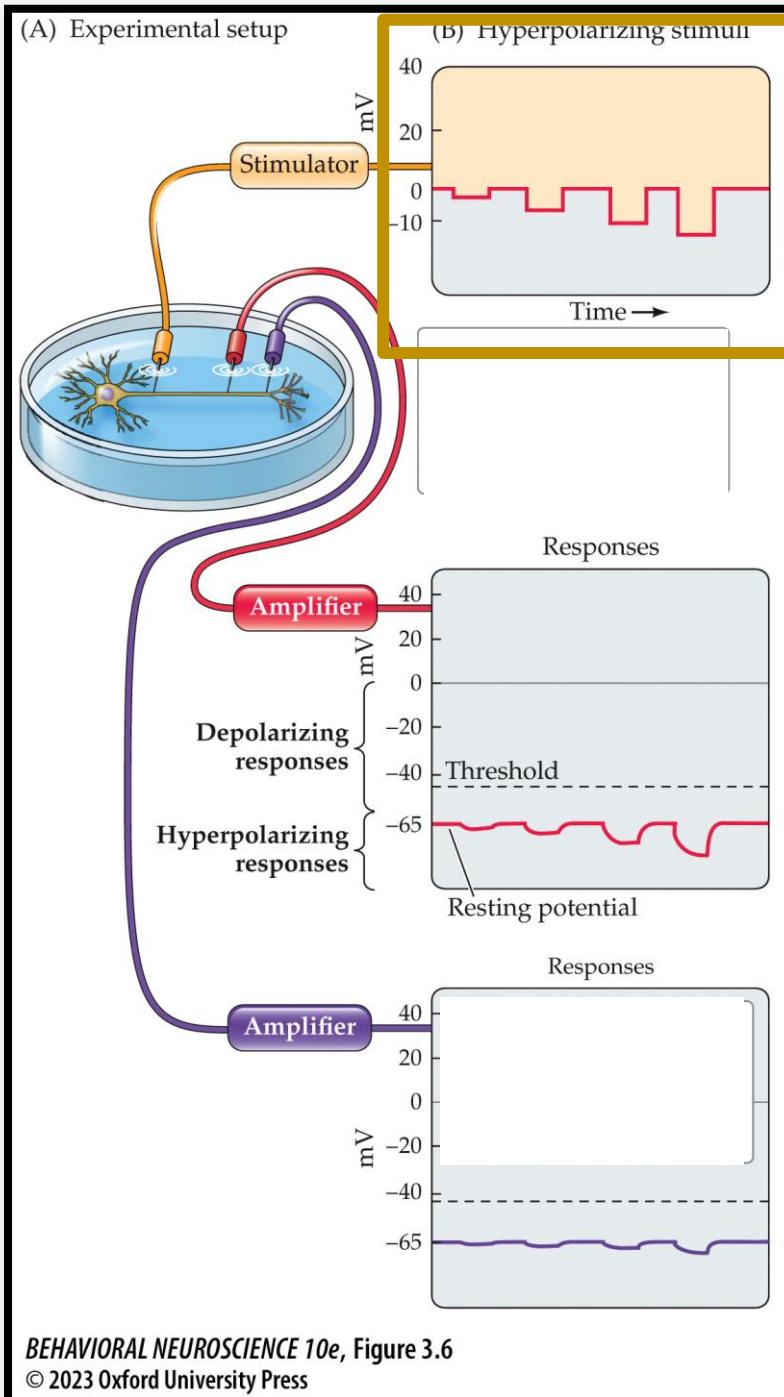
Hyperpolarizing Stimulus

Question:

What happens if we hyperpolarize the cell, i.e., make the membrane potential more negative?

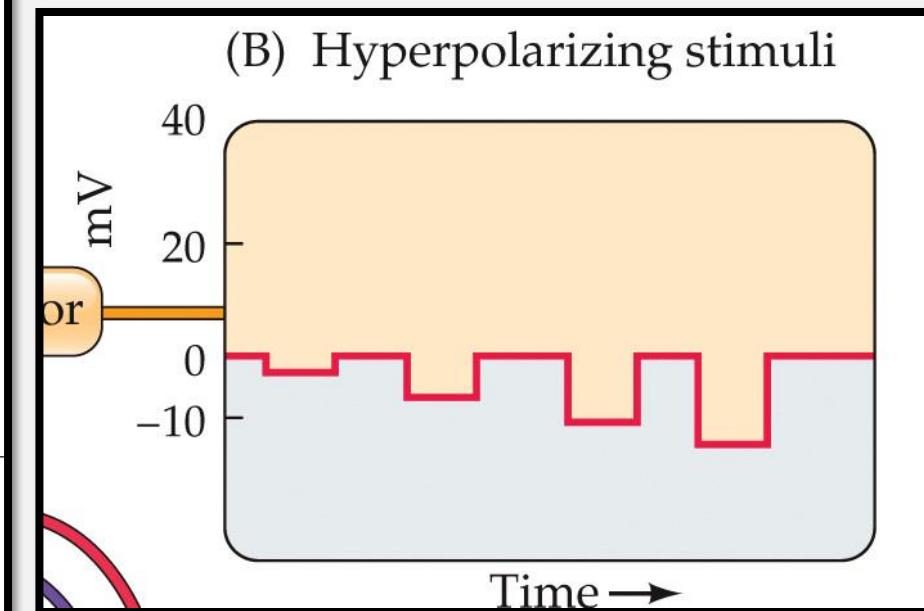
Step 1:

Provide hyperpolarizing stimuli of increasing strength over time



Step 1:

Provide hyperpolarizing stimuli of increasing strength over time



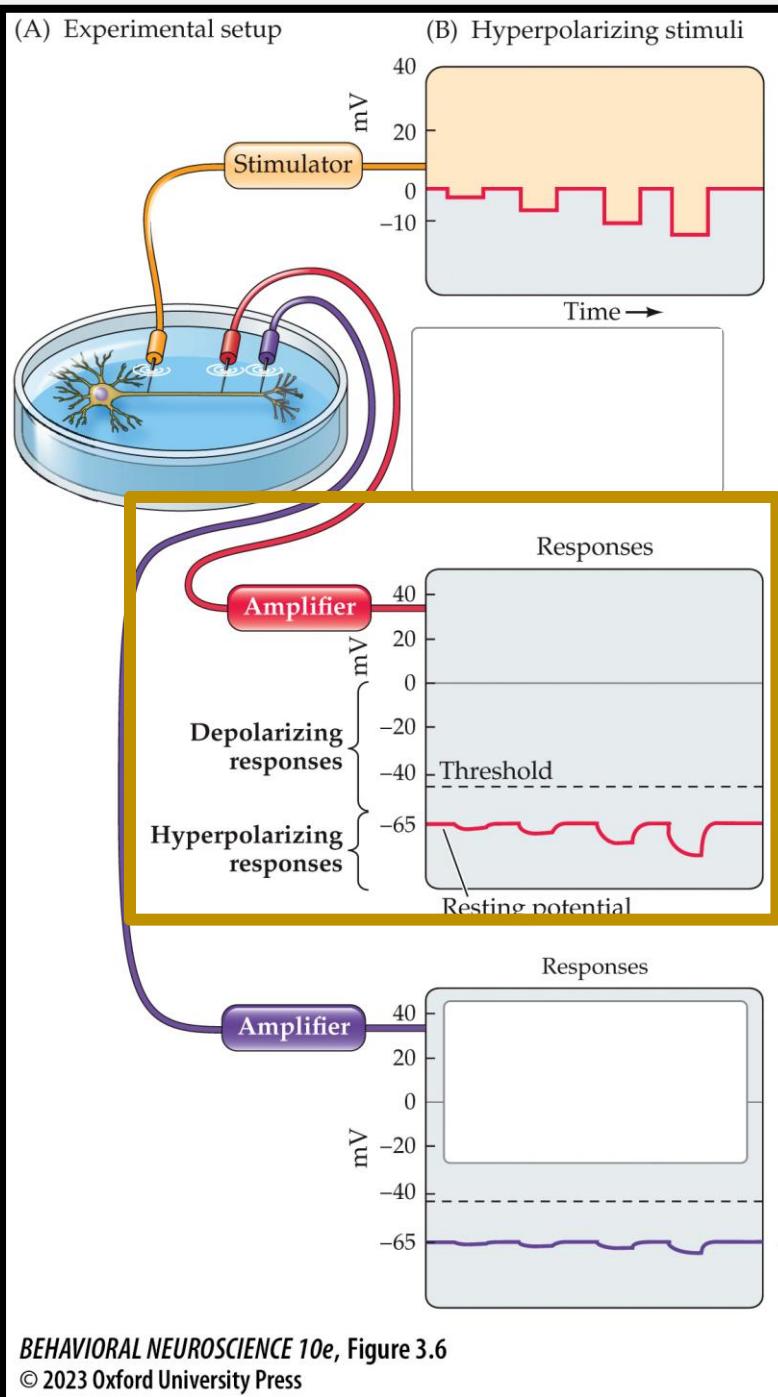
Hyperpolarizing Stimulus

Question:

What happens if we hyperpolarize the cell, i.e., make the membrane potential more negative?

Step 2:

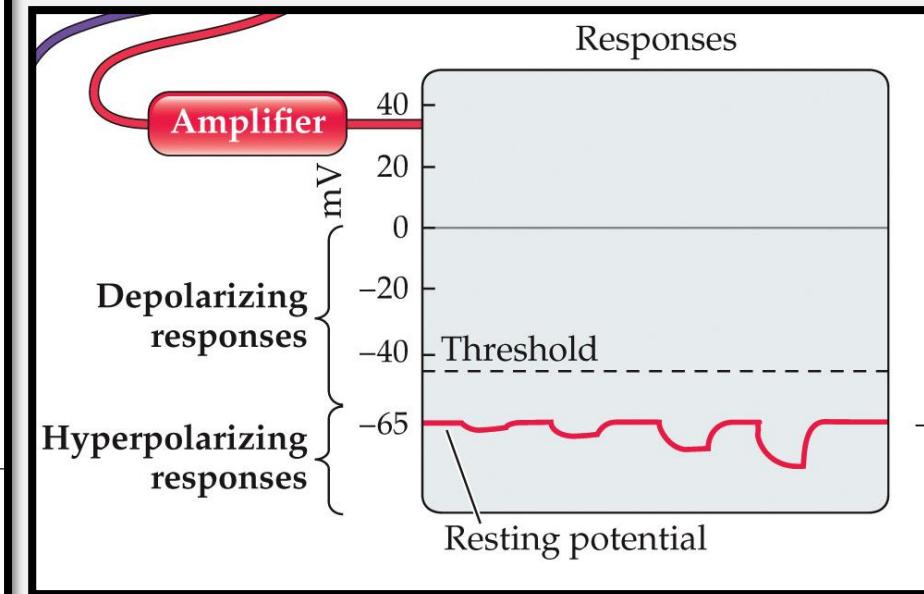
Observe response down the axon (what happens to the membrane potential?)



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Step 2:

Observe response down the axon (what happens to the membrane potential?)



Observation:

[Empty box for observation notes]

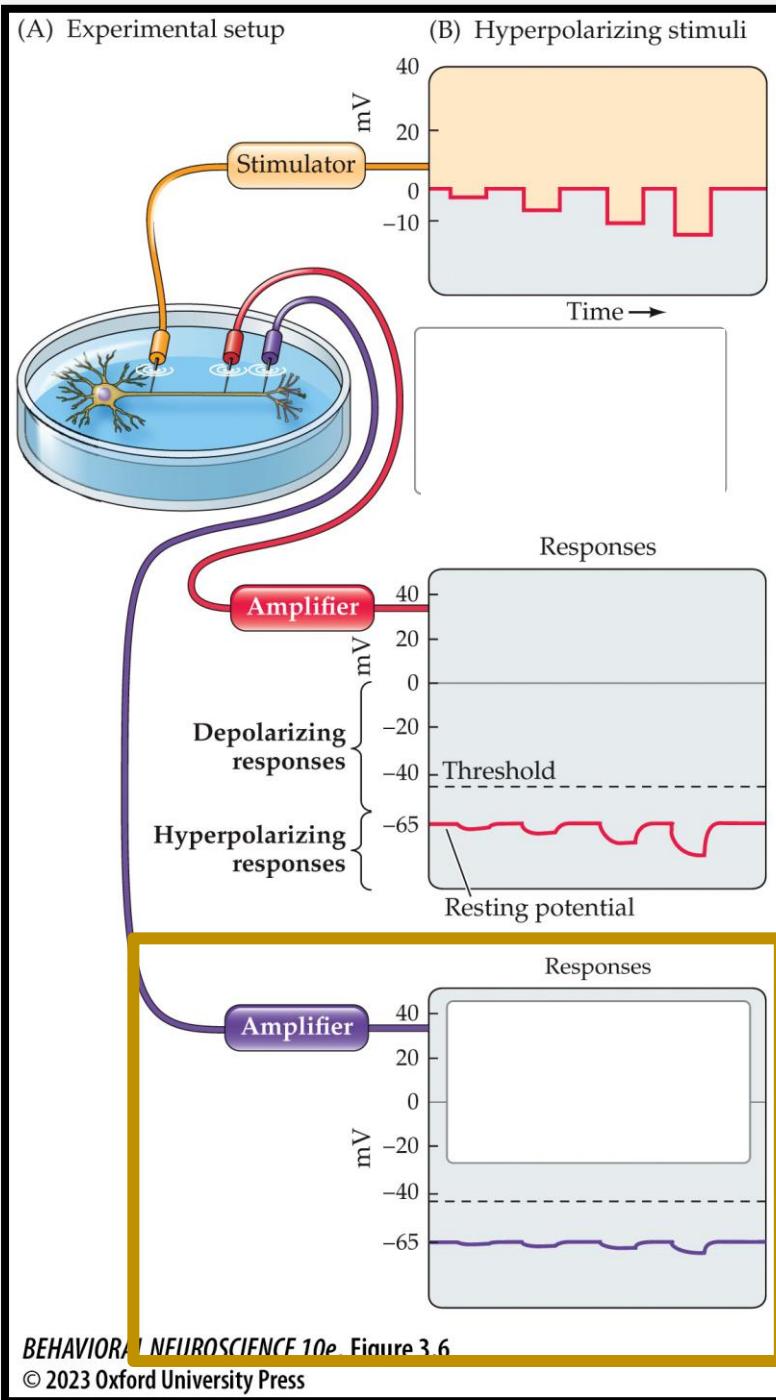
Hyperpolarizing Stimulus

Question:

What happens if we hyperpolarize the cell, i.e., make the membrane potential more negative?

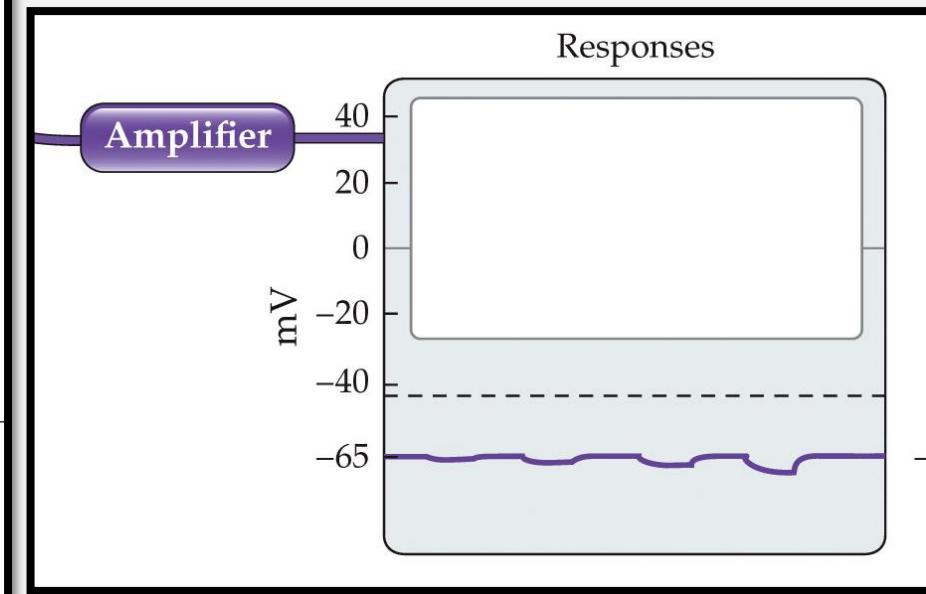
Step 3:

Observe response a bit further down the axon (what happens to the membrane potential?)



Step 3:

Observe response a bit further down the axon (what happens to the membrane potential?)



Observation

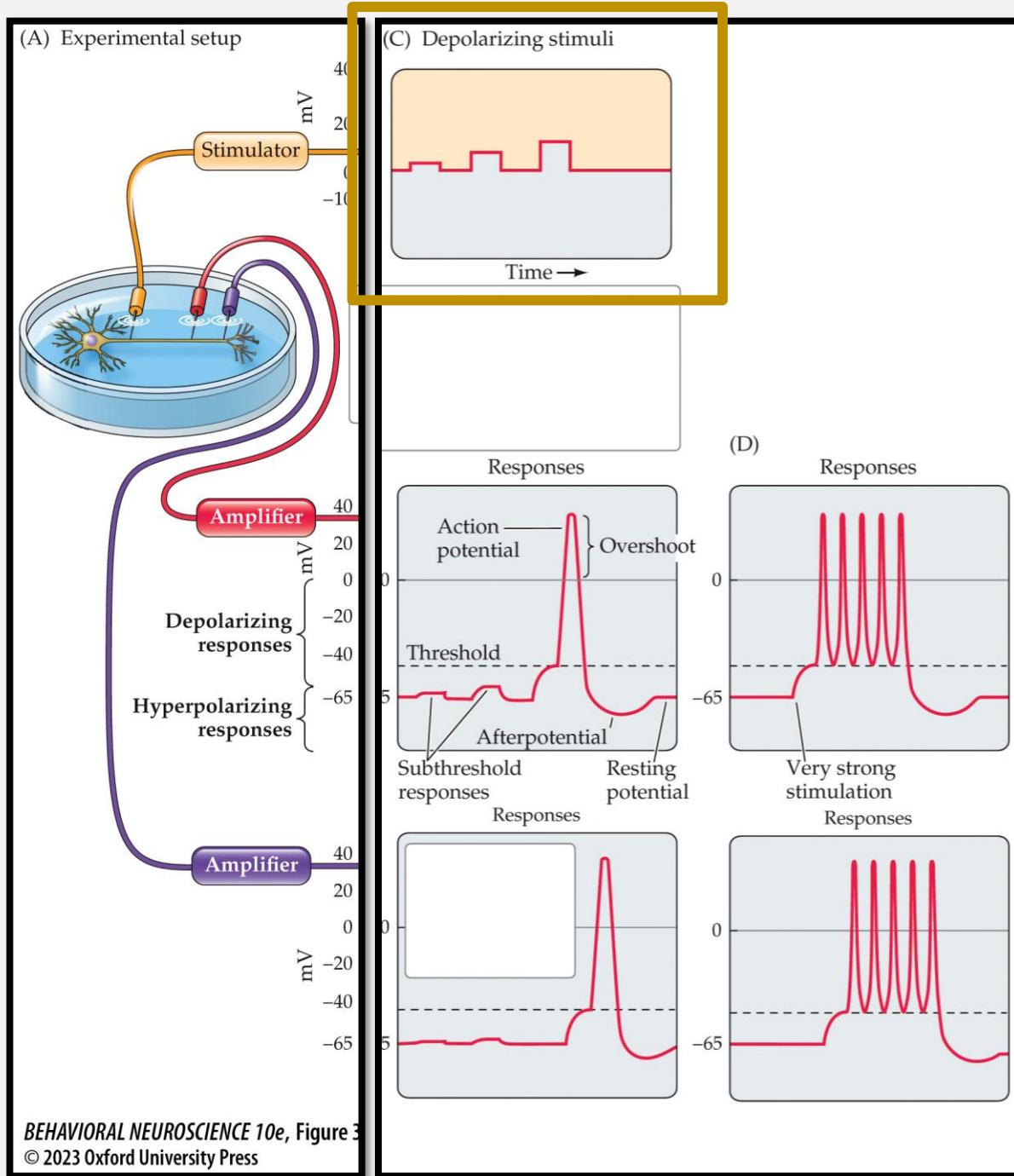
Depolarizing stimulus

Question:

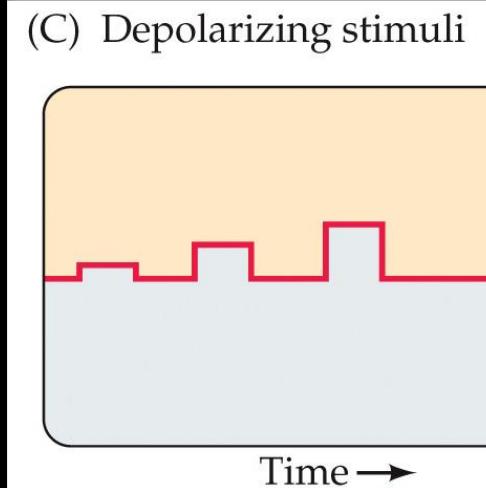
What happens if we depolarize the cell, i.e., decrease the membrane potential?

Step 1:

Provide depolarizing stimuli of increasing strength over time



Step 1:
Provide depolarizing stimuli of increasing strength over time



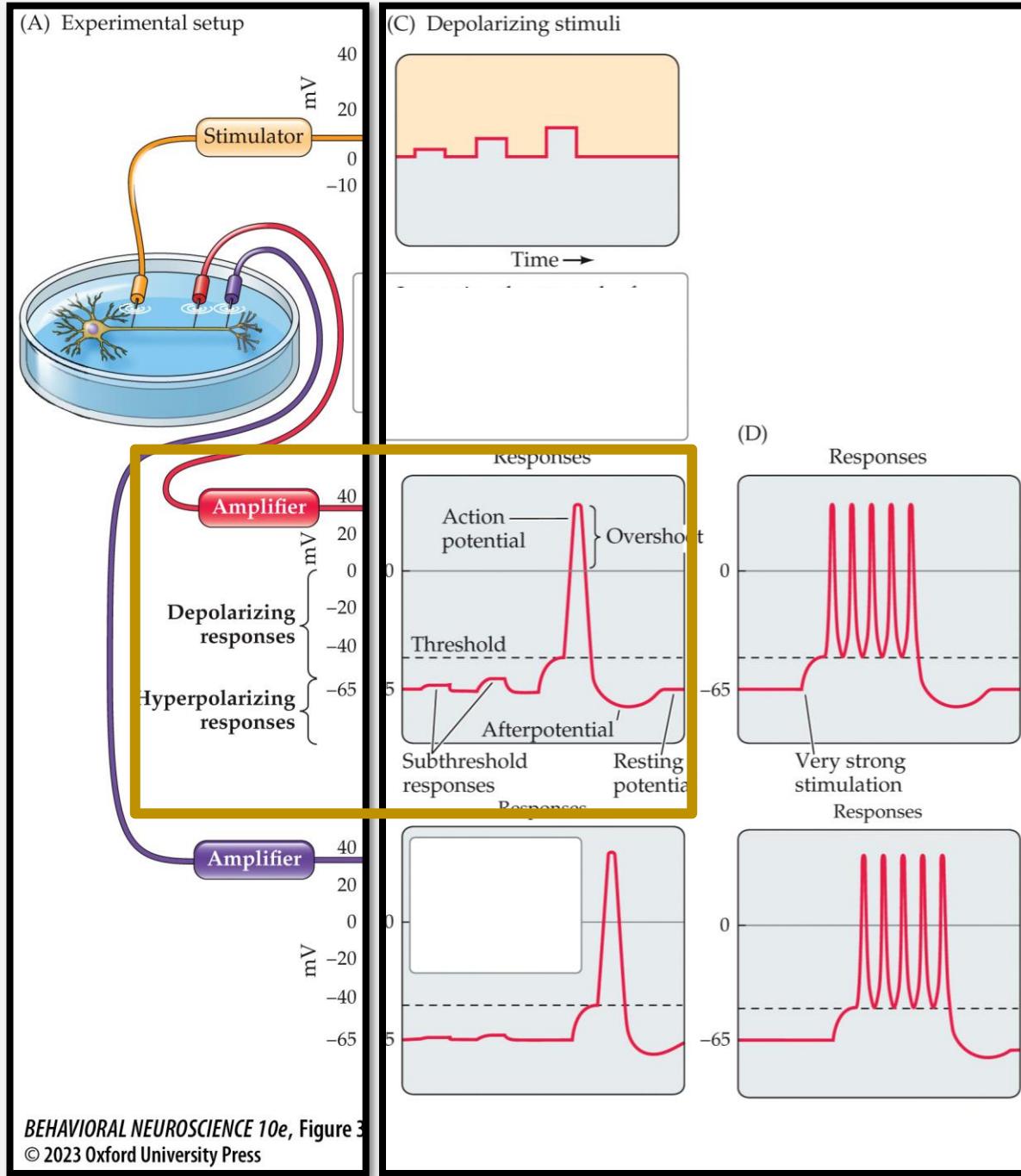
Depolarizing stimulus

Question:

What happens if we depolarize the cell, i.e., decrease the membrane potential?

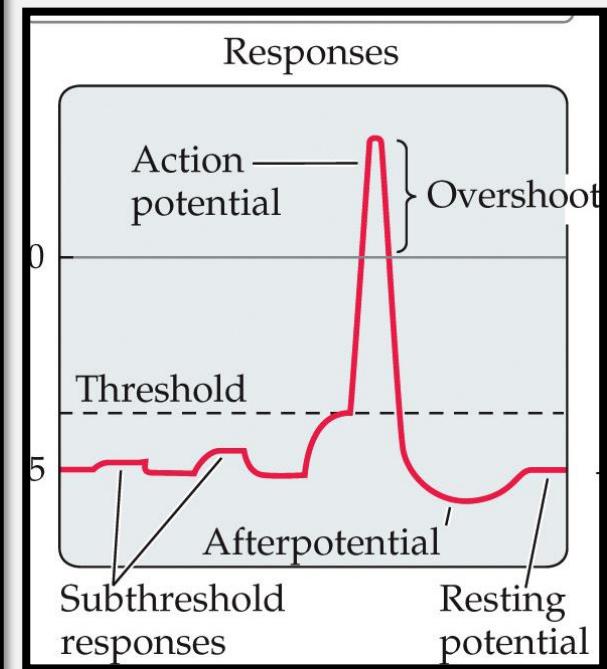
Step 2:

Observe adjacent aspect of axon for changes in membrane potential



Step 2:

Observe adjacent aspect of axon for changes in membrane potential



Observation

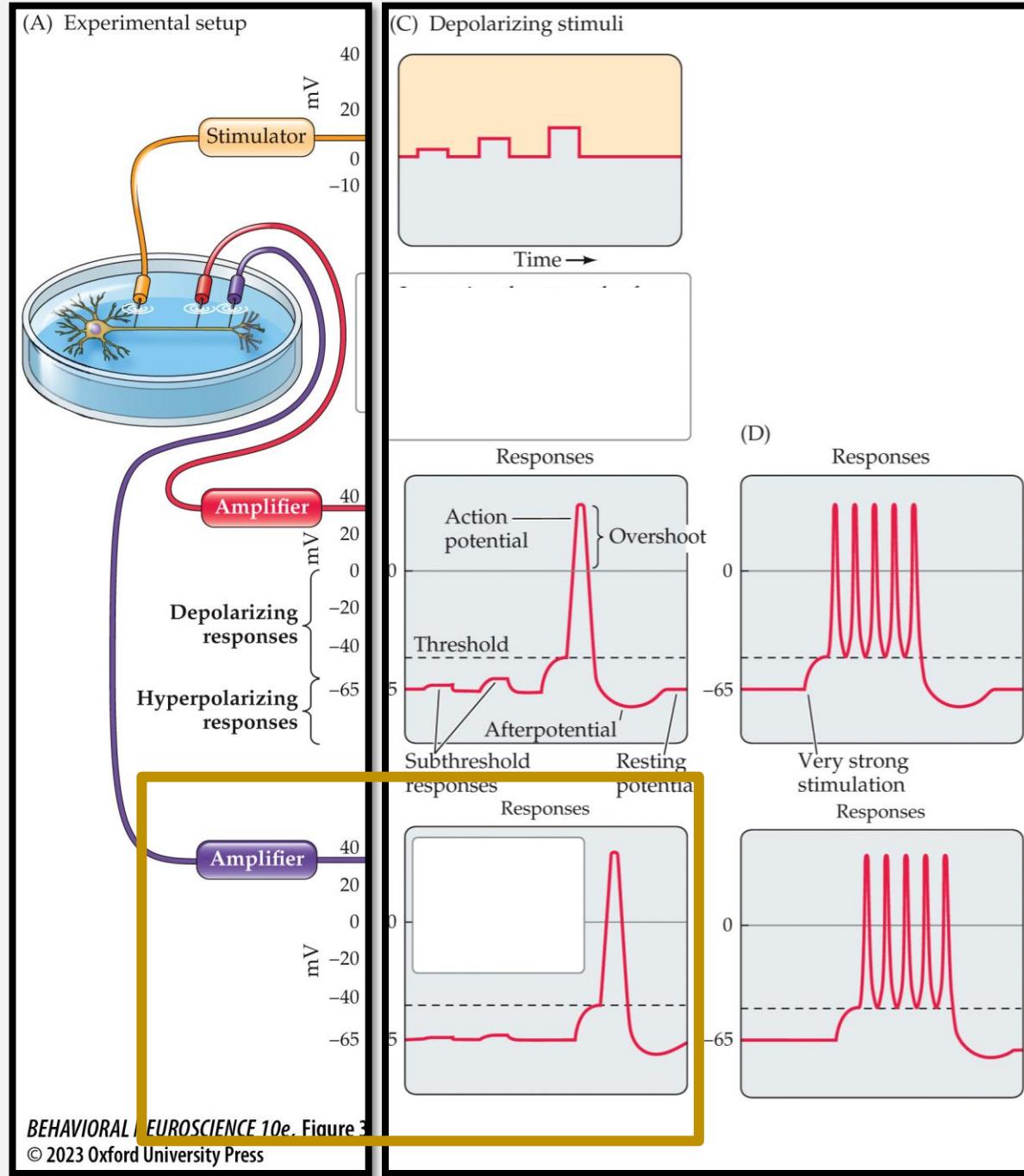
Depolarizing stimulus

Question:

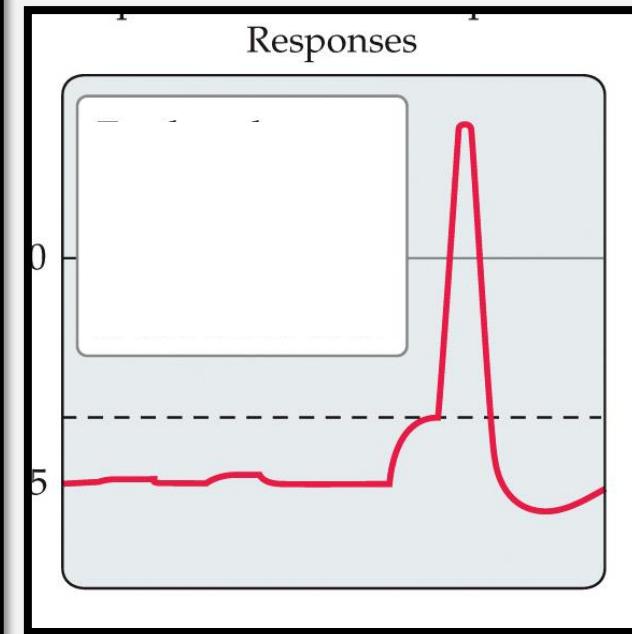
What happens if we depolarize the cell, i.e., decrease the membrane potential?

Step 3:

Observe 2nd adjacent aspect of axon for changes in membrane potential



Step 3:
Observe 2nd adjacent aspect of axon for changes in membrane potential



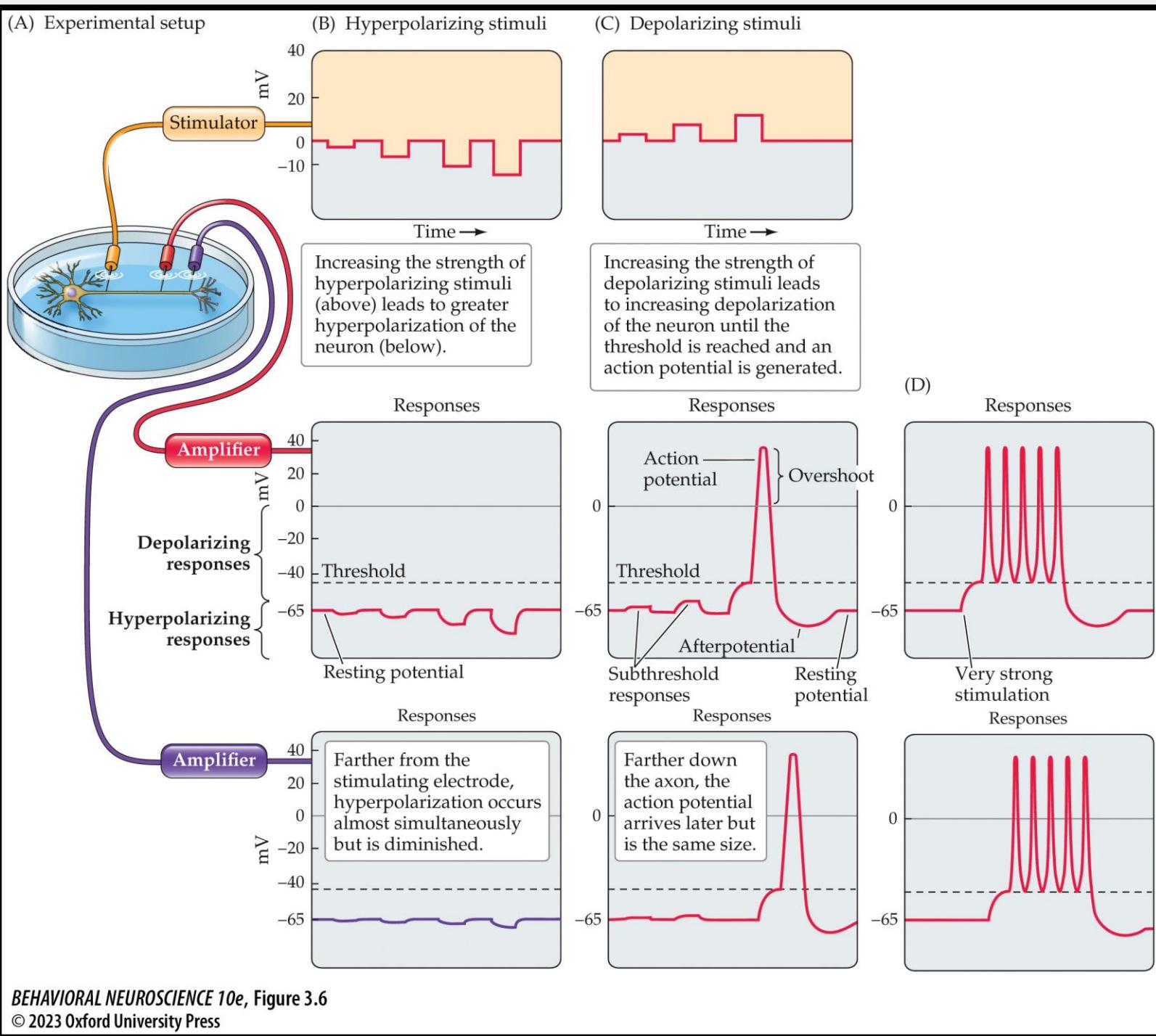
AP – Key Characteristics

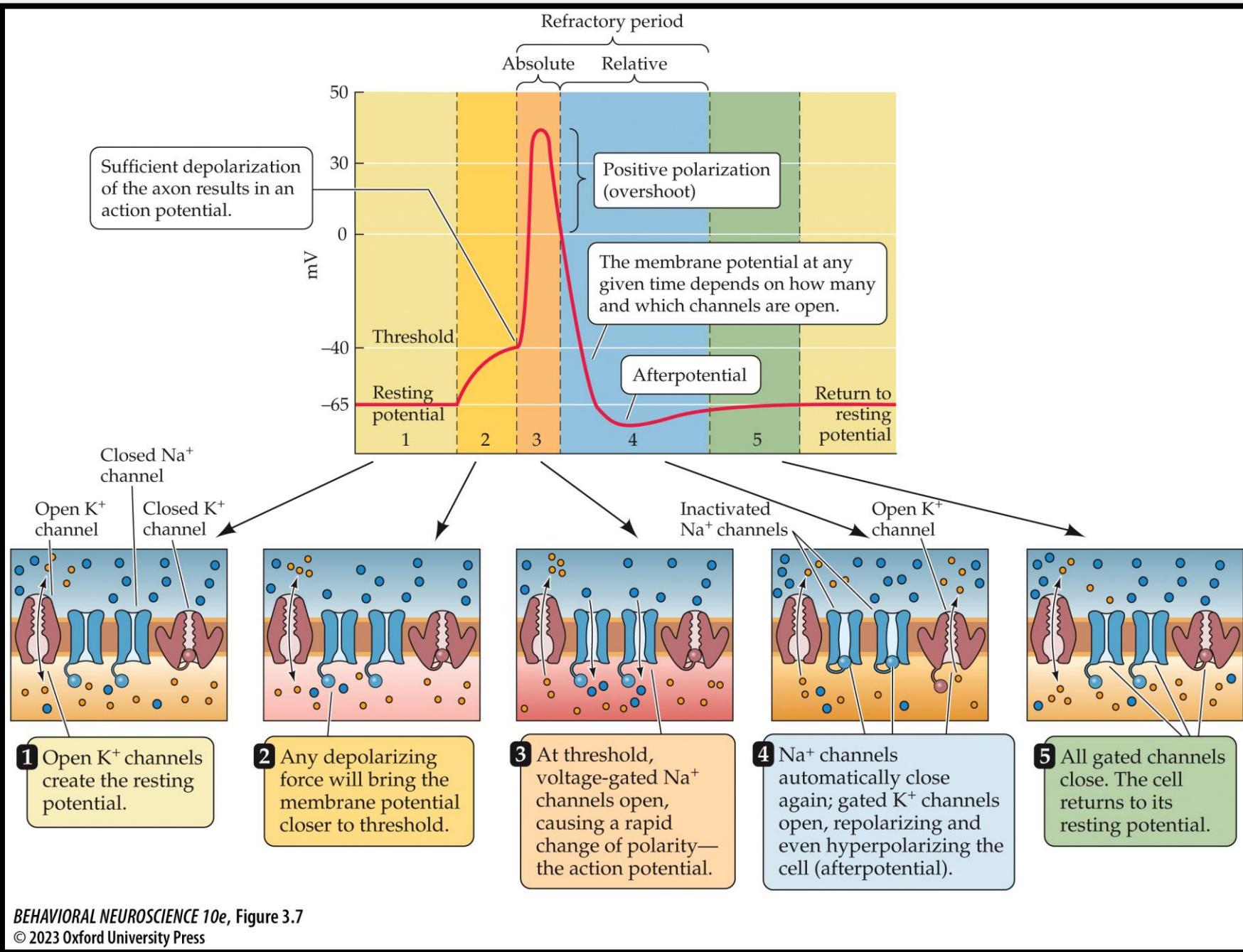
Summary

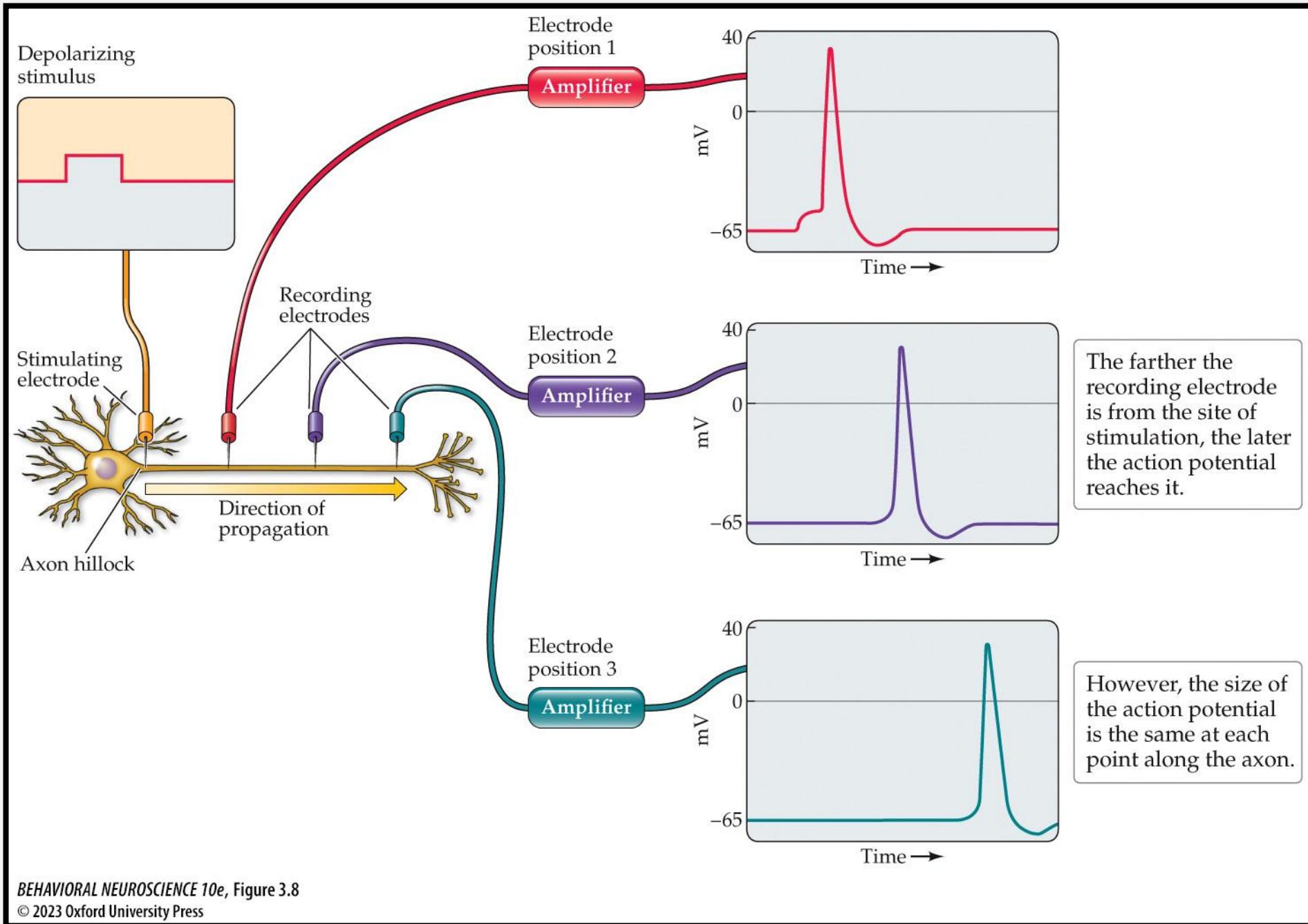
- Action potentials are produced by movement of Na^+ ions into the cell.
- At the peak of an action potential, the concentration gradient pushing Na^+ ions into the cell equals the positive charge driving them out.
- Membrane shifts briefly from a resting state to an active state and back (i.e., the membrane suddenly and briefly becomes permeable to Na^+ ions).

Steps

- Voltage-gated Na^+ channels open in response to depolarization, and Na^+ ions enter; more channels open and more Na^+ enters;
- Continues as membrane potential reaches the Na^+ equilibrium potential of +55 mV.
- As cell interior becomes more positive, voltage-gated K^+ channels open.
- K^+ moves out and the resting potential is restored.







AP – Key Characteristics

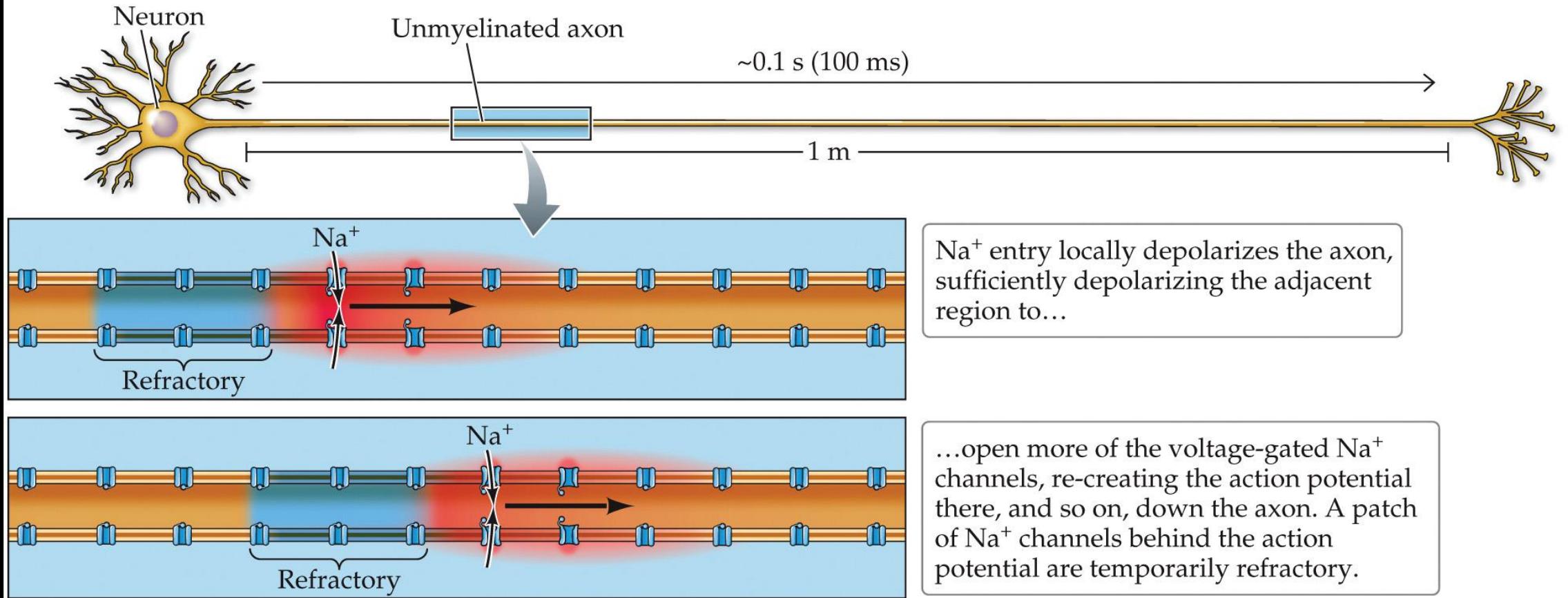
Summary

- Action potentials are regenerated along the axon—each adjacent section is depolarized and a new action potential occurs.
- Action potentials travel in one direction because of the refractory state of the membrane after a depolarization.
- Action potentials are an all or none process – when threshold is reached an action potential will occur at the same strength every time.

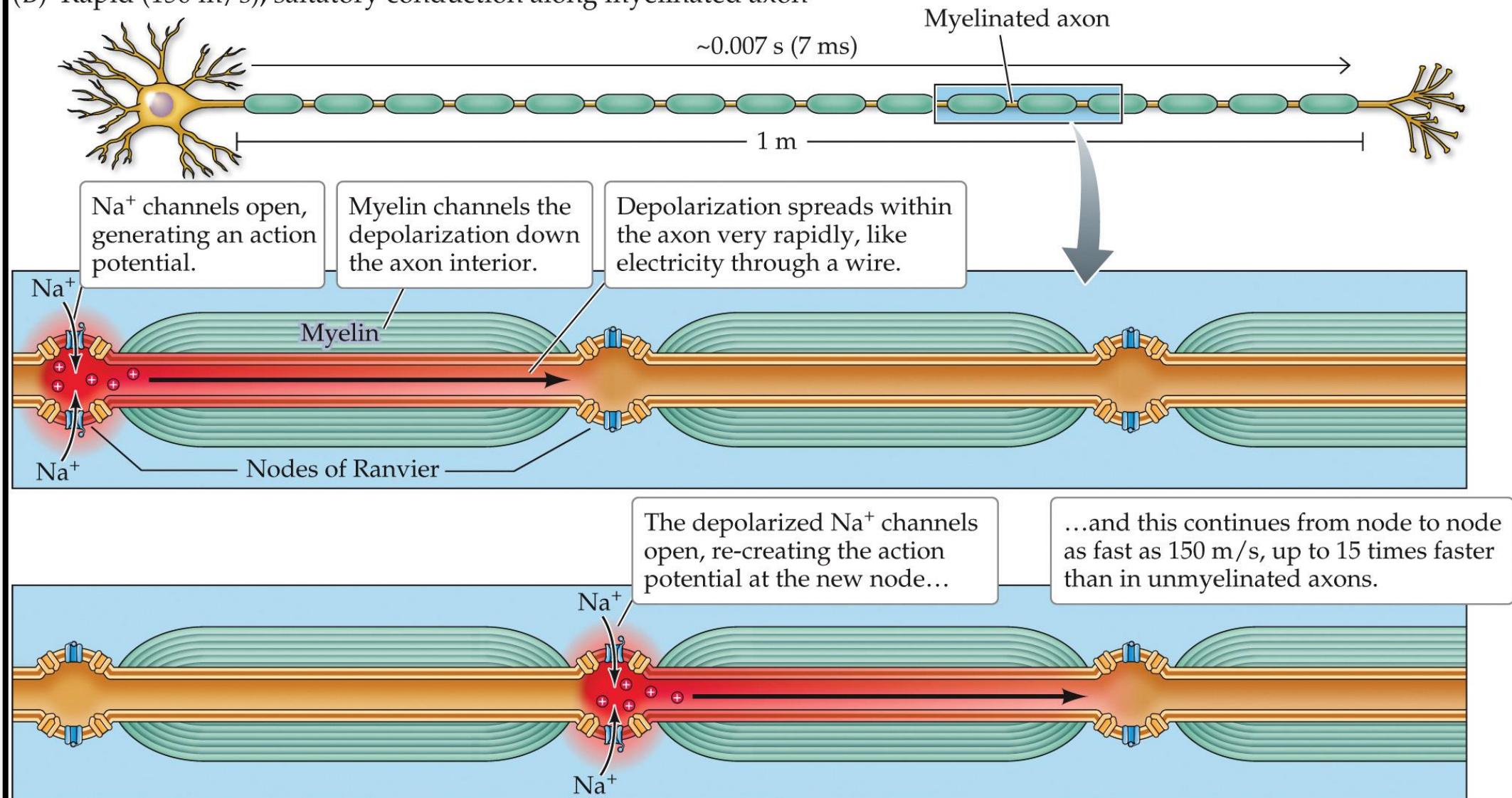
Conduction velocity

How can we increase the speed of propagation of action potentials?

(A) Slow (10 m/s) conduction of action potential along unmyelinated axon



(B) Rapid (150 m/s), saltatory conduction along myelinated axon



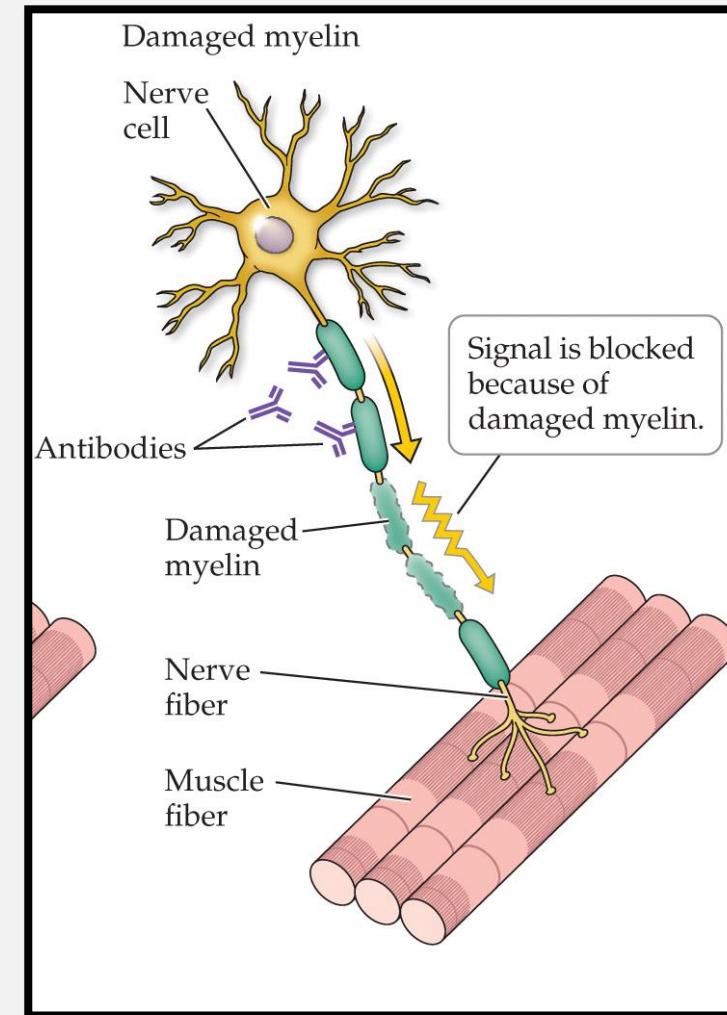
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Importance of myelin

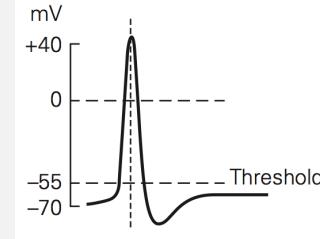
Multiple Sclerosis (MS)

- disorder that occurs when body's immune system produces antibodies that attack myelin, and thus conduction of action potentials.
- Wide variety of symptoms that affect sensory and/or motor systems, depending on which axons are attacked.

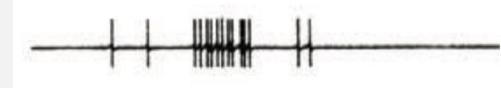


Methods for recording Action Potentials

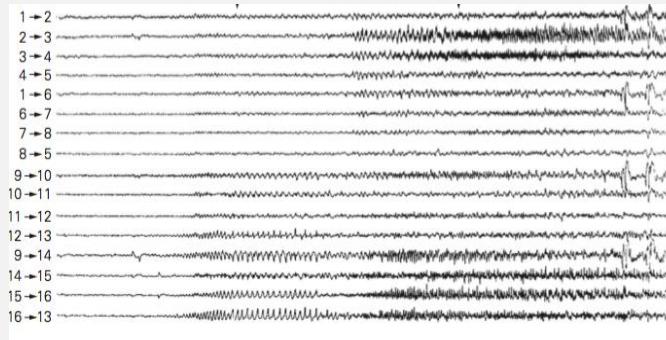
intracellular electrophysiology



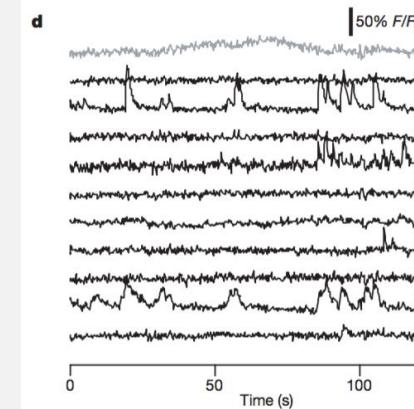
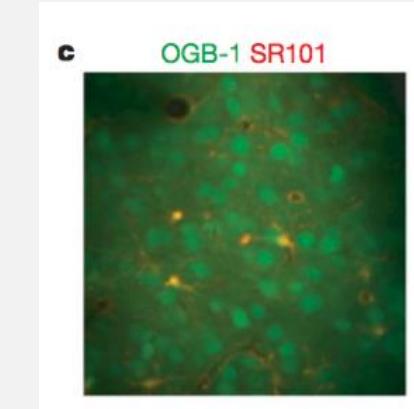
extracellular electrophysiology



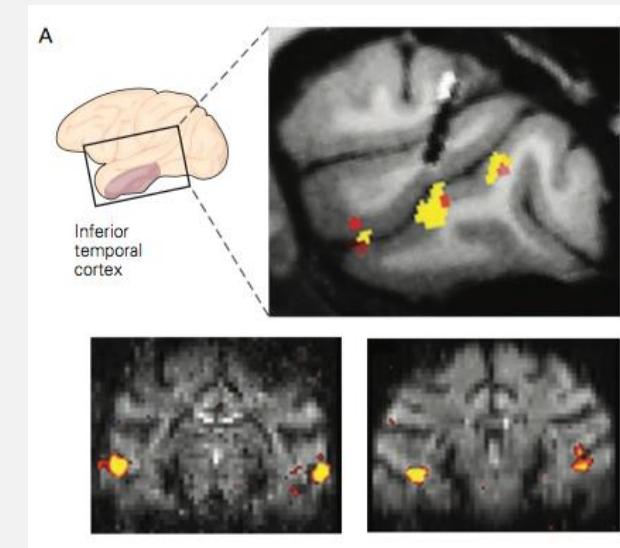
EEG



calcium imaging



functional imaging (eg fMRI)



increasingly indirect
reflections of APs