

# MCB/Neuro 8o - Neurobiology of Behavior

Today's Topic:

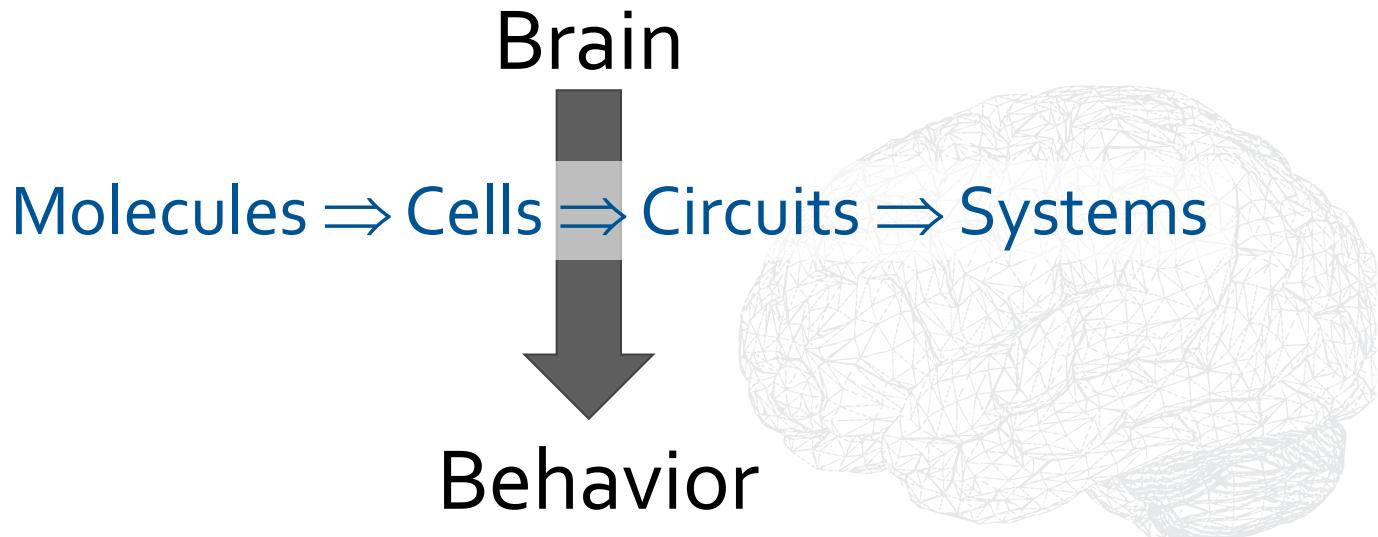
## *Circuits of the Nervous System*

Optional reading: Purves et al., *Neuroscience* 6<sup>th</sup> pages 10-16

Lecture notes, review questions, office hour times available at:

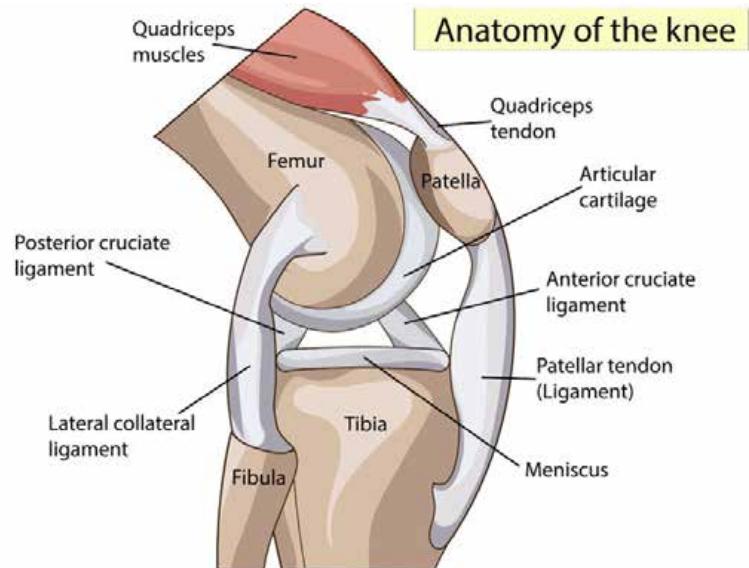
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# MCB/Neuro 80 – Neurobiology of Behavior

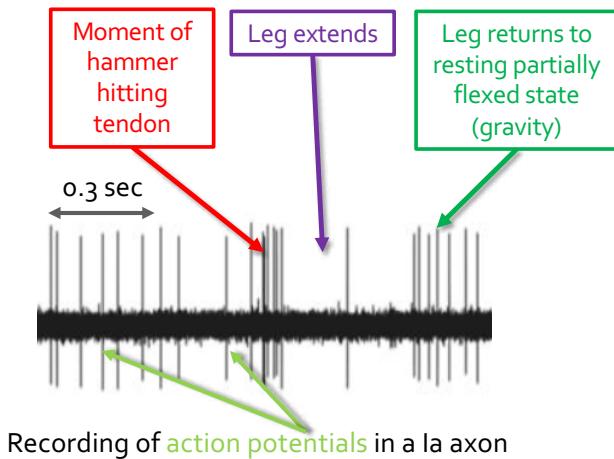


# Steps in myotatic reflex

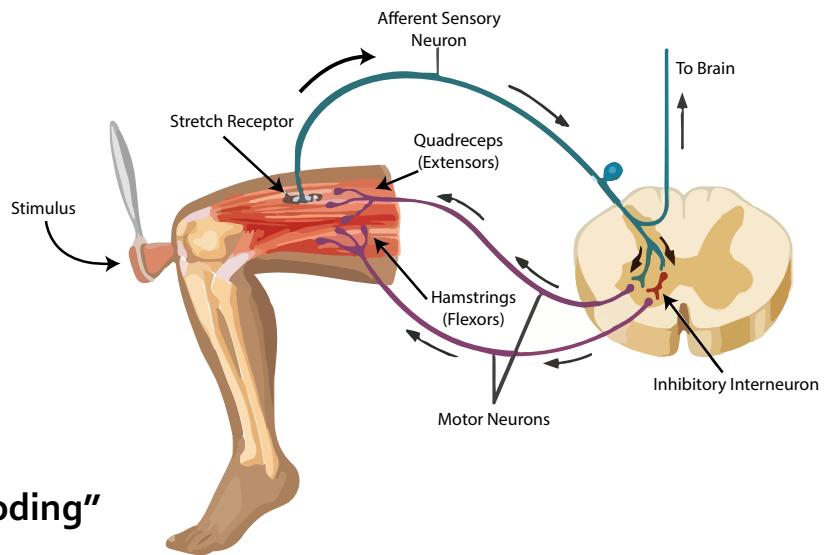
- **Stimulus:** Stretch quadriceps muscle by tapping patellar tendon
- **Transduction:** Convert stimulus (e.g. mechanical) into an electrical signal.
- **Encode:** converts sensory information (local receptor potential) into neuronal code (action potential)
- **Sensory-motor synapse** elicits an action potential (AP) in the motor neuron
- **Muscle fiber activation**
- **Inhibition** of antagonistic muscle.



# Action potentials recorded in the sensory neuron during myotatic reflex

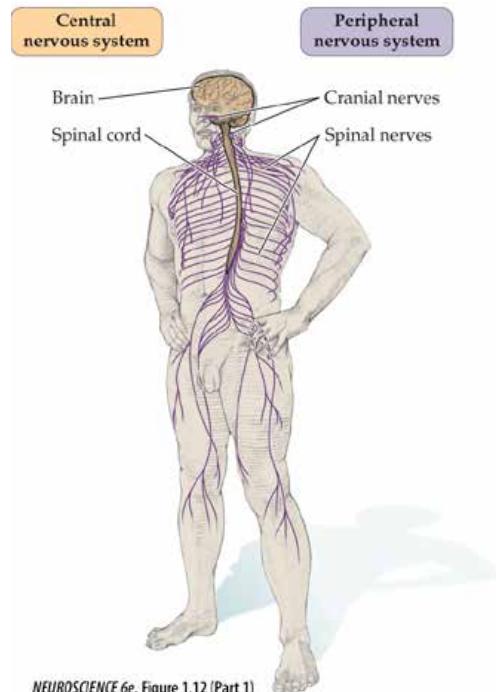


“Frequency coding”



# Organization within the nervous system

- Central nervous system (CNS)
  - Brain
  - Spinal cord
- Peripheral nervous system (PNS)
  - Sensory
  - Motor
    - Somatic (voluntary)
    - Autonomic (involuntary)
      - Sympathetic
      - Parasympathetic



**Activation of the SYMPATHETIC nervous system would result in all of  
the following EXCEPT**

Increased heart rate

Increased blood pressure

Increased gut peristalsis

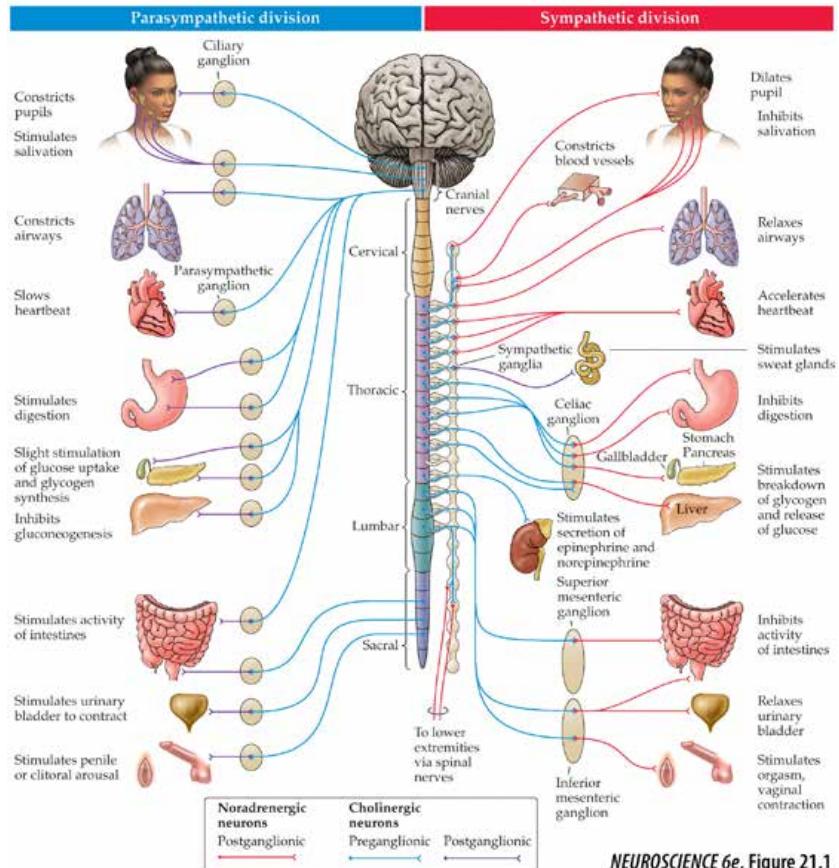


Increased respiratory capacity

None of the above -

# Sympathetic vs. parasympathetic

	Parasympathetic	Sympathetic
<u>Reaction</u>	<u>"Rest and digest"</u>	<u>"Flight or fight"</u>
Blood pressure	Lowers	Raises
Heart rate	Slows	Speeds up
Blood flow to muscle	Decrease	Increase
	Increase	Decrease
<u>Purpose</u>	Reduce energy expenditure, build up reserves	Selective energy expenditure for intense activity
<u>Neurotransmitter</u>	acetylcholine	norepinephrine
<u>Location of ganglia</u>	Near to target	Far from target
	Originates in cranial and sacral	Originates in lumbar and thoracic

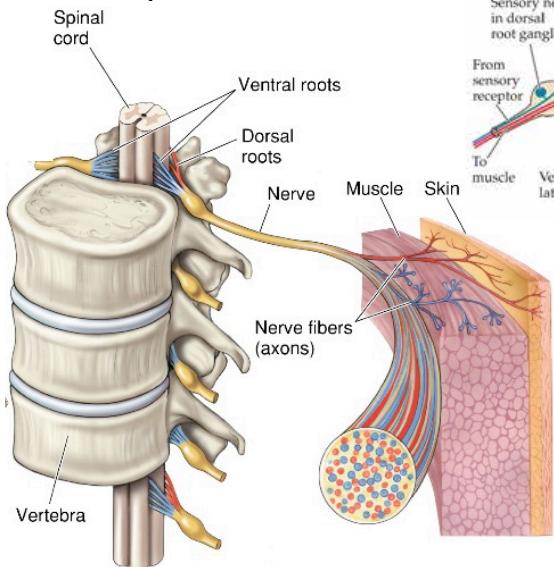


NEUROSCIENCE 6e, Figure 21.1

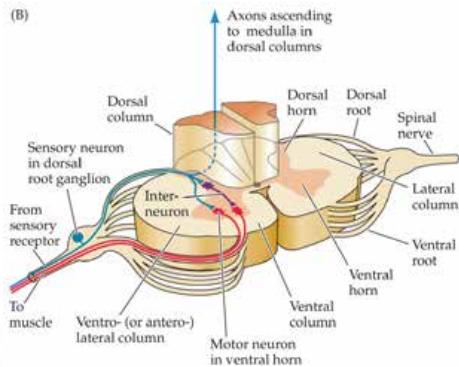
# The central nervous system

(from bottom to top)

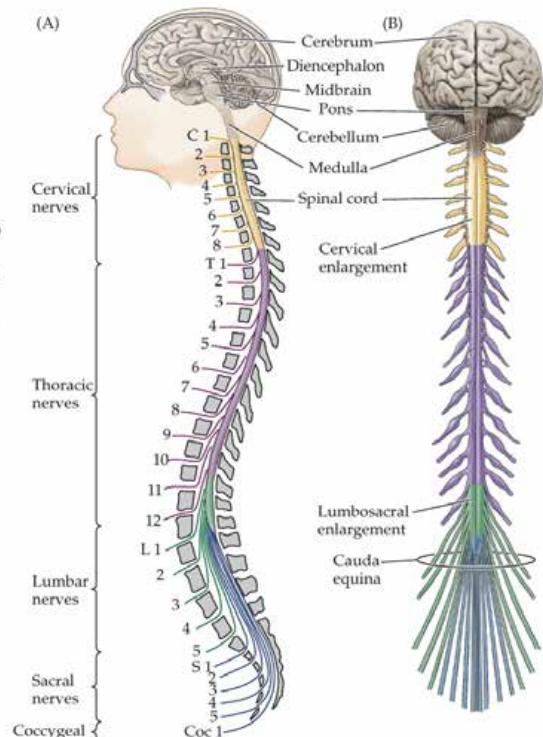
- Spinal cord



(B)



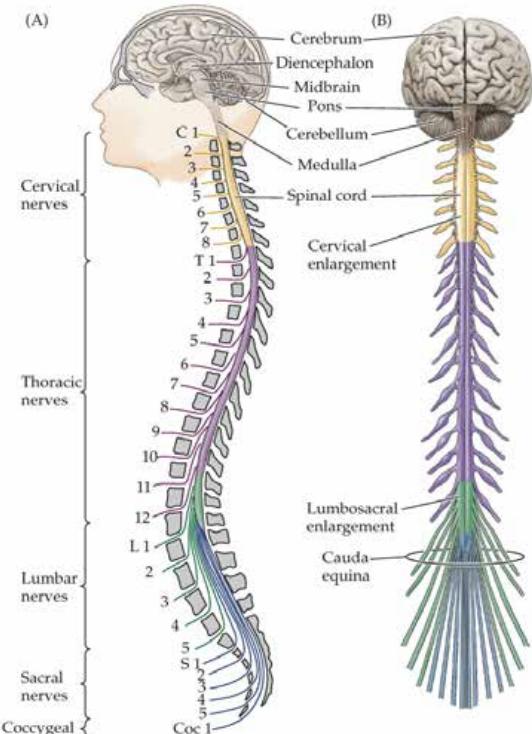
(A)

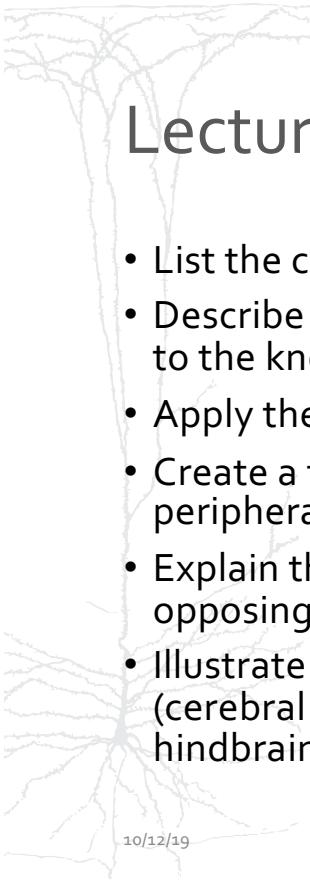


NEUROSCIENCE 6e, Figure A3

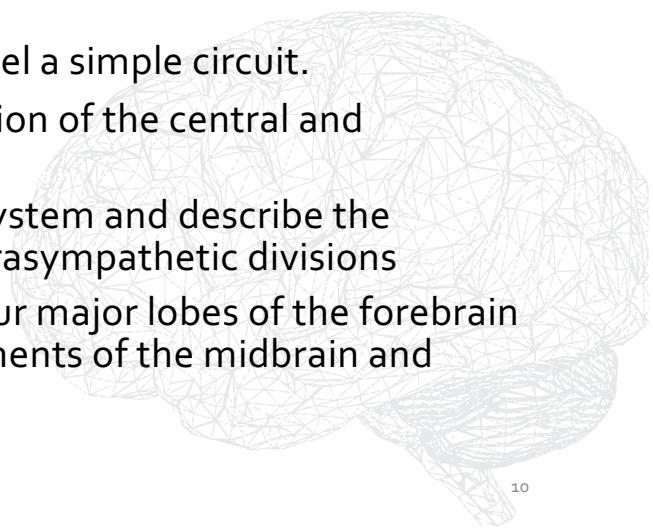
# The central nervous system

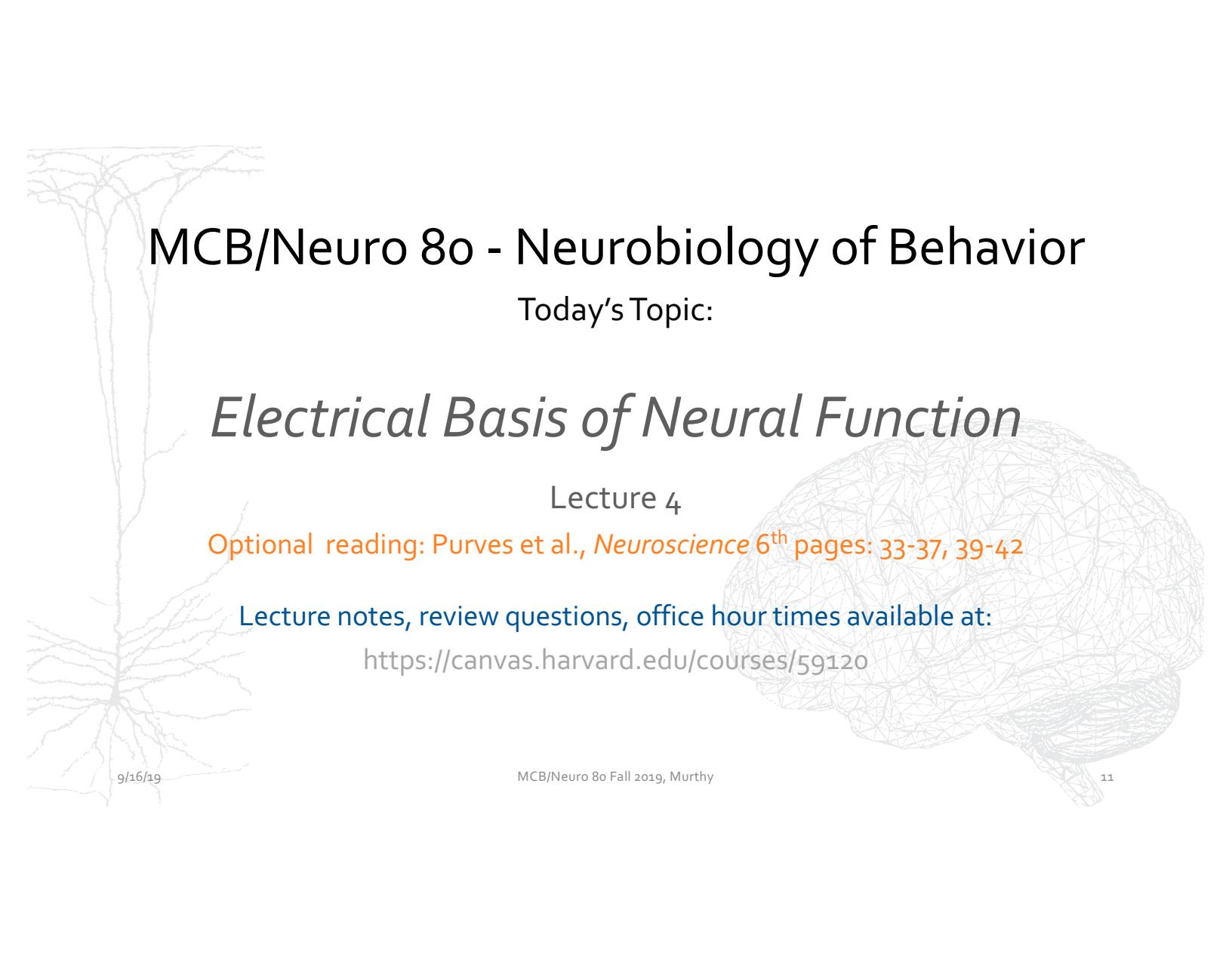
- Spinal cord
- Medulla and pons-(brainstem)- respiration, circulation, posture, "maintenance" and "vital" functions
- Midbrain - auditory and visual centers, esp. "unconscious" vision – eye movement and startle reflexes, motion sensitivity
- Cerebellum - muscle and reflex coordination
- Diencephalon
  - Thalamus - sensory and motor relays and gateways to the cortex
  - Hypothalamus – unconscious drives. Autonomic command center





# Lecture 3 – Learning Objectives

- List the components of behavior.
  - Describe the anatomical organization and electrical signaling that give rise to the knee jerk reflex circuit.
  - Apply the law of dynamic polarization to label a simple circuit.
  - Create a flowchart illustrating the organization of the central and peripheral branches of the nervous system
  - Explain the role of the autonomic nervous system and describe the opposing effects of the sympathetic and parasympathetic divisions
  - Illustrate the function and location of the four major lobes of the forebrain (cerebral cortex) as well as the main components of the midbrain and hindbrain
- 



# MCB/Neuro 8o - Neurobiology of Behavior

Today's Topic:

## *Electrical Basis of Neural Function*

Lecture 4

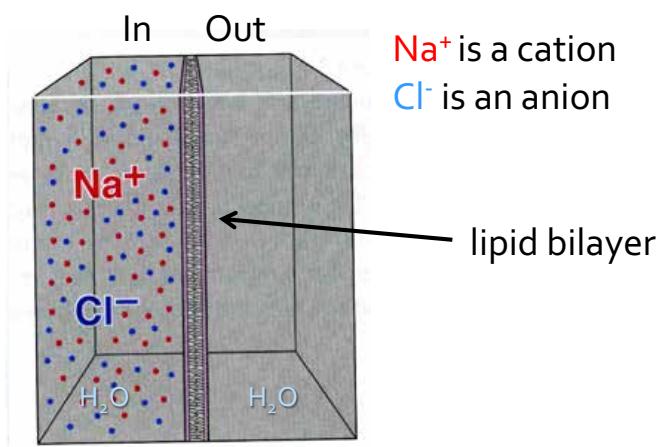
Optional reading: Purves et al., *Neuroscience* 6<sup>th</sup> pages: 33-37, 39-42

Lecture notes, review questions, office hour times available at:

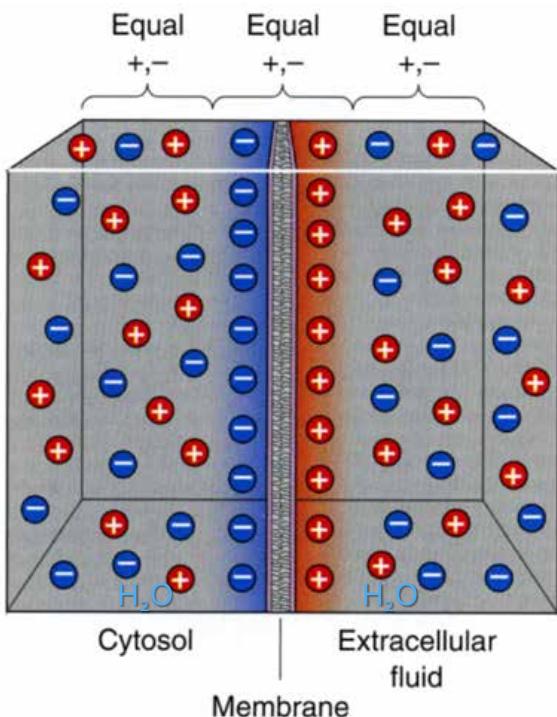
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# Diffusion of ions across lipid bilayer membrane

- What happens?:



# The electrical gradient is the membrane potential



- In neurons and glia, impermeant anions in the cytosol (mainly big negatively charged proteins) plus a large number of cation channels open "at rest" (mainly K<sup>+</sup> "leak" channels) lead to a potential difference across the membrane.
- Inside has net negative charge
- Outside has net positive charge
- Opposite charges attract so they line up on either side of the membrane which stores charge like an electrical **capacitor** 
- The bulk solution on both sides is electro-neutral
- To understand the exact value of the membrane potential we have to delve deeper...

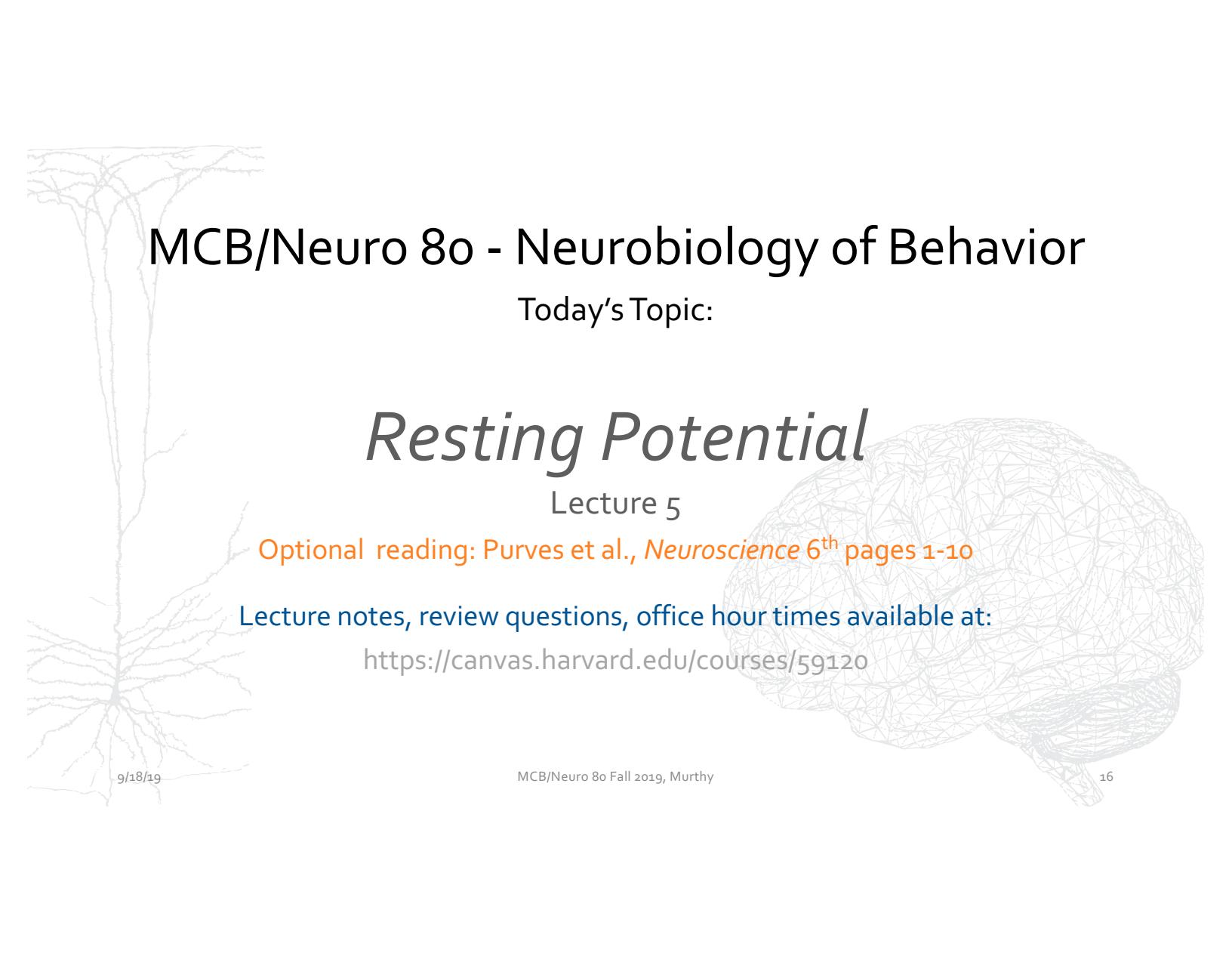
# How do we calculate this potential?

- In the case we just went through (only potassium channels present) the resting potential is reached when there is no longer any net flow of  $K^+$ . That is when the forces pulling  $K^+$  in and out are equal and the system has stabilized at equilibrium

“Equilibrium” for an ion is reached  
when  
its particular Concentration gradient  
and the  
cell’s Electrical gradient  
are  
*equal* and *opposite*

# Learning Objectives

1. Contrast ways electricity in the nervous system differs from electricity in wires.
2. What is a lipid bilayer composed of and how are these molecules arranged? Why, in the absence of channels, is it so impermeable to ions?
3. What are ion selective channels, and briefly describe what they do and what causes their selectivity?
4. If a membrane of a cell is permeable to all ions, is there a point when net ion flow across the membrane finally stops? Why or why not (in 2 sentences or less)?
5. Diagram how a cell membrane is like a capacitor.
6. How does ion selectivity in membrane channels give rise to a non-zero membrane potential?



# MCB/Neuro 8o - Neurobiology of Behavior

Today's Topic:

## *Resting Potential*

Lecture 5

Optional reading: Purves et al., *Neuroscience* 6<sup>th</sup> pages 1-10

Lecture notes, review questions, office hour times available at:

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## Which ion has the highest internal concentration?

K+



Na+

Cl-

Ca++

## Nernst potentials

$$E_{ion} = \frac{RT}{zF} \ln \frac{[C_{out}]}{[C_{in}]}$$

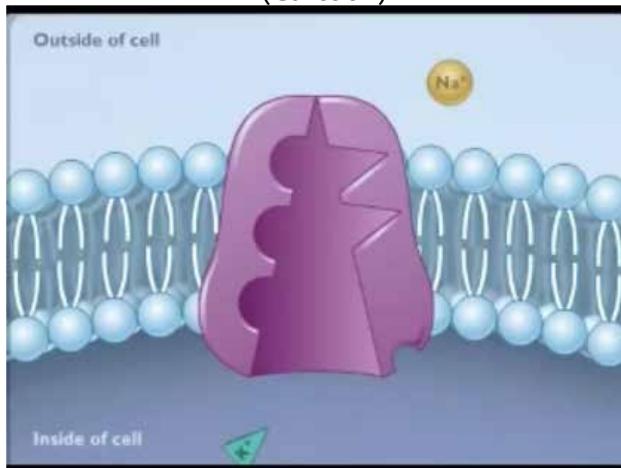
Outside Conc.	Inside Conc	Ratio Out:In	Eq. Potential (37°C)
$[K^+]_o = 5 \text{ mM}$	$[K^+]_i = 107 \text{ mM}$	1:20	-80 mV
$[Cl^-]_o = 150 \text{ mM}$	$[Cl^-]_i = 13 \text{ mM}$	11.5:1	-65 mV
$[Na^+]_o = 150 \text{ mM}$	$[Na^+]_i = 15 \text{ mM}$	10:1	60 mV
$[Ca^{2+}]_o = 2 \text{ mM}$	$[Ca^{2+}]_i = 0.0002 \text{ mM}$	10,000:1	120 mV

$$V_{\{\text{memb}\}} = \frac{RT}{F} \ln \frac{P_{K^+}[K_{out}^+] + P_{Na^+}[Na_{out}^+] + P_{Cl^-}[Cl_{in}^-]}{P_{K^+}[K_{in}^+] + P_{Na^+}[Na_{in}^+] + P_{Cl^-}[Cl_{out}^-]}$$

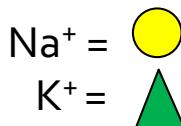
- If the permeability to Na<sup>+</sup> suddenly increased to many fold higher than the permeability to K<sup>+</sup>
- Then what happens to the membrane potential?
- Cell would move from -70 mV towards +60 mV (i.e., depolarize)
- That is what happens during an action potential- more on this next time
- If the permeability to Cl<sup>-</sup> increased, then what would happen?

# Sodium Potassium Pump

(Cartoon)



<https://www.youtube.com/watch?v=Gsxn49jVnhE>

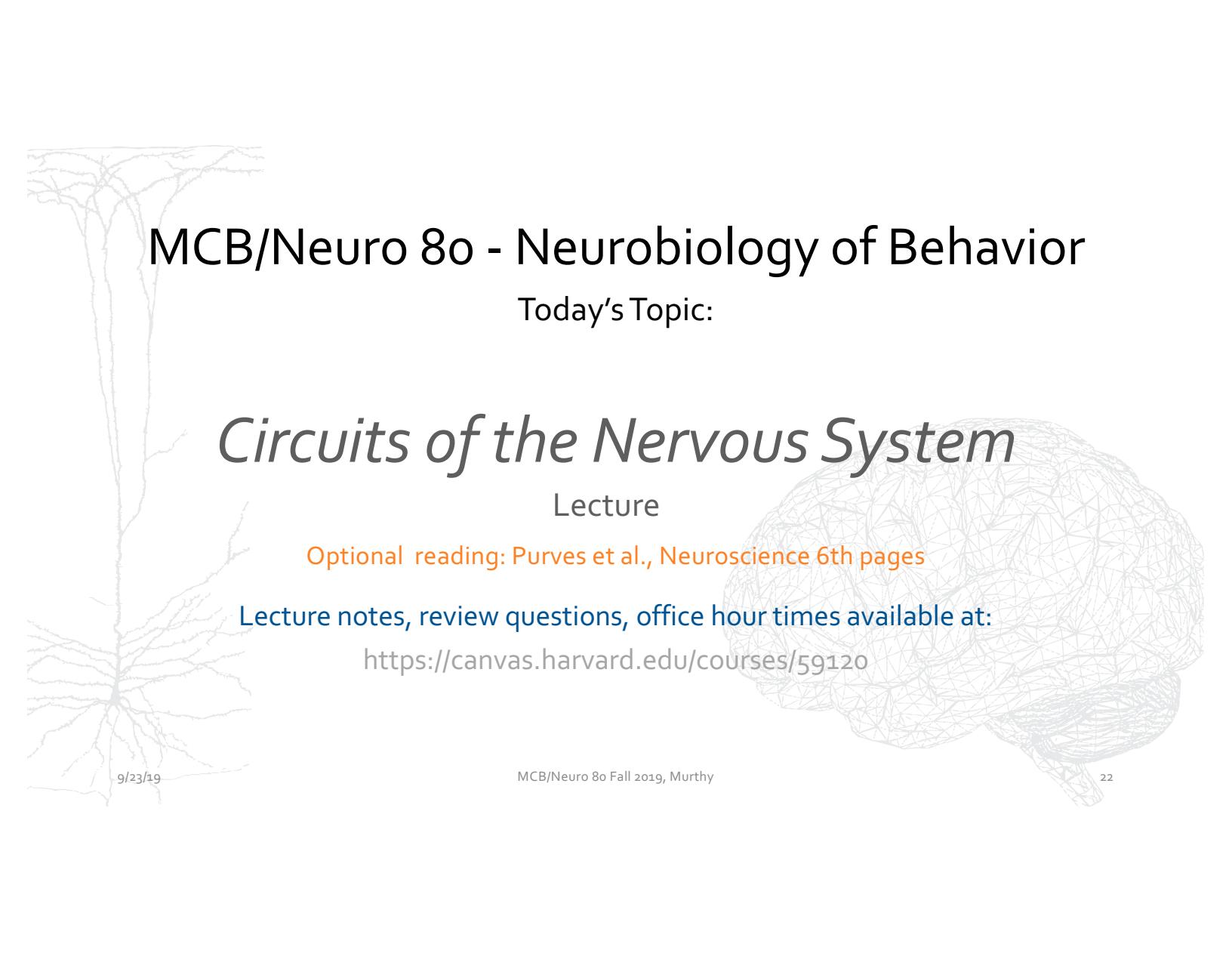


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- The pump is an ATPase.
- 70% of all energy consumption (ATP conversion to ADP) in brain is used to pump  $\text{Na}^+$  out and  $\text{K}^+$  back into neurons. This ATP is generated by glycolysis which is dependent on Oxygen.
- The pump is electrogenic : it sends 3 $\text{Na}^+$  out for 2 $\text{K}^+$  in. Thus it tends to make the inside more negative (10s of mVs) as well as maintain the concentration gradient.

# Learning Objectives

1. What two gradients are in balance when an ion is said to be at its equilibrium potential?
2. Draw a graph of neuron's cell membrane potential as a function of changing extracellular potassium concentration (and how it differs from the graph of a glial cell)
3. Recall the equilibrium potentials of potassium, sodium, and chloride and know which way each would flow in a resting neuron.
4. Be able to apply the Nernst and GHK equations and know when to use which equation.
5. Explain how the  $\text{Na}^+/\text{K}^+$  pump functions and why it is necessary.



# MCB/Neuro 8o - Neurobiology of Behavior

Today's Topic:

## *Circuits of the Nervous System*

Lecture

Optional reading: Purves et al., Neuroscience 6th pages

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# Ohm's law

- $V$  (voltage) =  $I$  (current) x  $R$  (resistance)
- 1 volt (V) = 1 amp (A) x 1 ohm (W)
- or  $I=V/R$
- $R=1/g$  ( $g$  is “conductance” and similar to permeability in GHK, thus  $I=gV$ )
- $V$  is the electrical “driving force” which is the difference between the membrane potential ( $V_{mem}$ ) and the ion’s equilibrium potential ( $E_{ion}$ )
- So, ionic current = the ion’s conductance x its driving force
  - $I_K = g_K * (V_{mem} - E_K)$
  - $I_{Na} = g_{Na} * (V_{mem} - E_{Na})$
  - $I_{Cl} = g_{Cl} * (V_{mem} - E_{Cl})$

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## What is the first step in an action potential?

voltage gated sodium channel inactivate

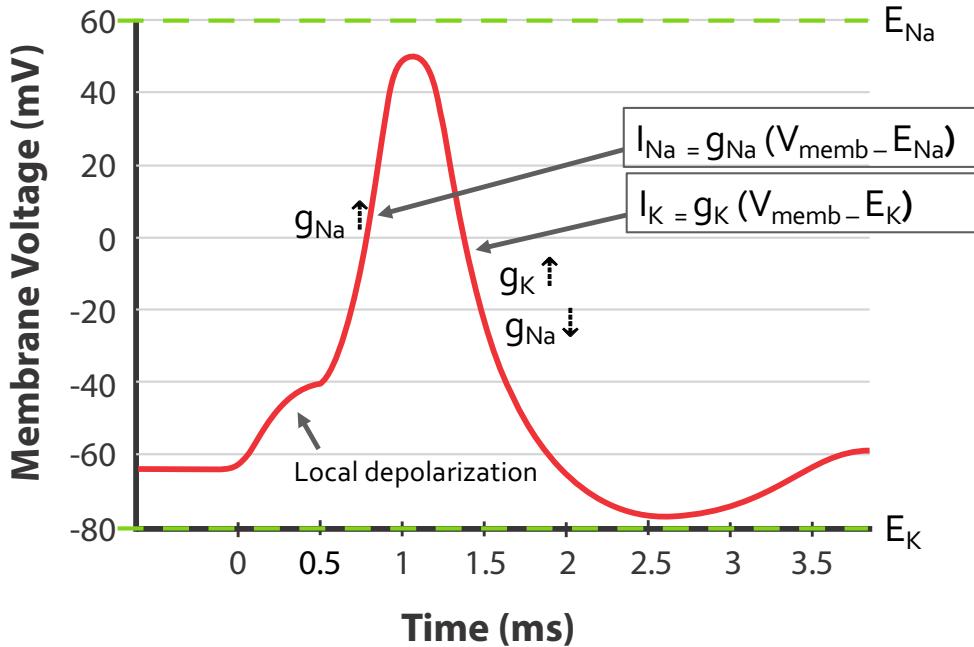
voltage gated sodium channels open

voltage gated potassium channels open

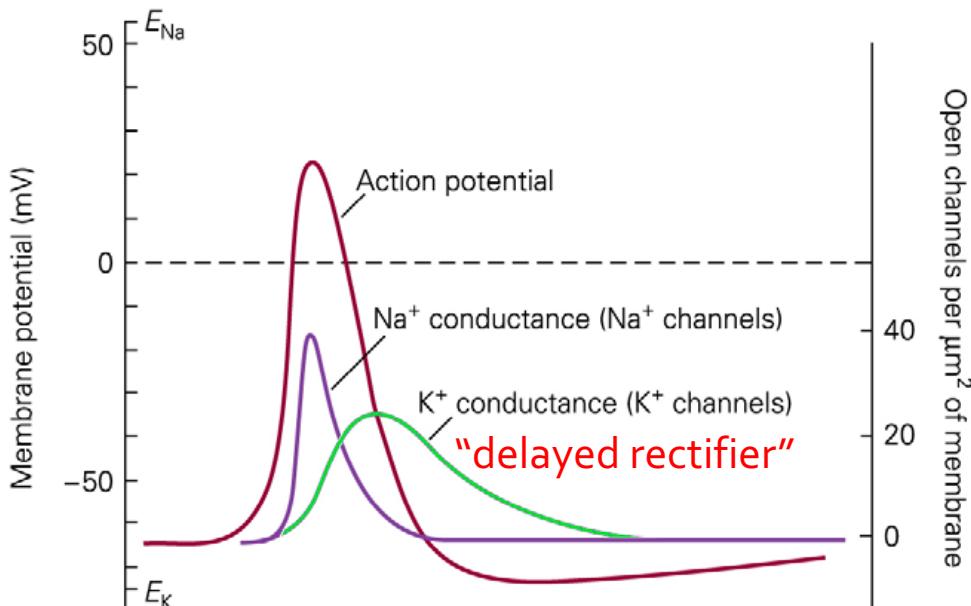
membrane is depolarized from resting potential

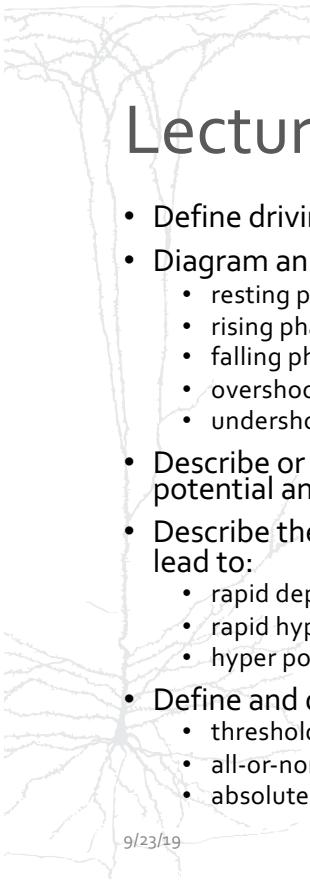


# Action potential



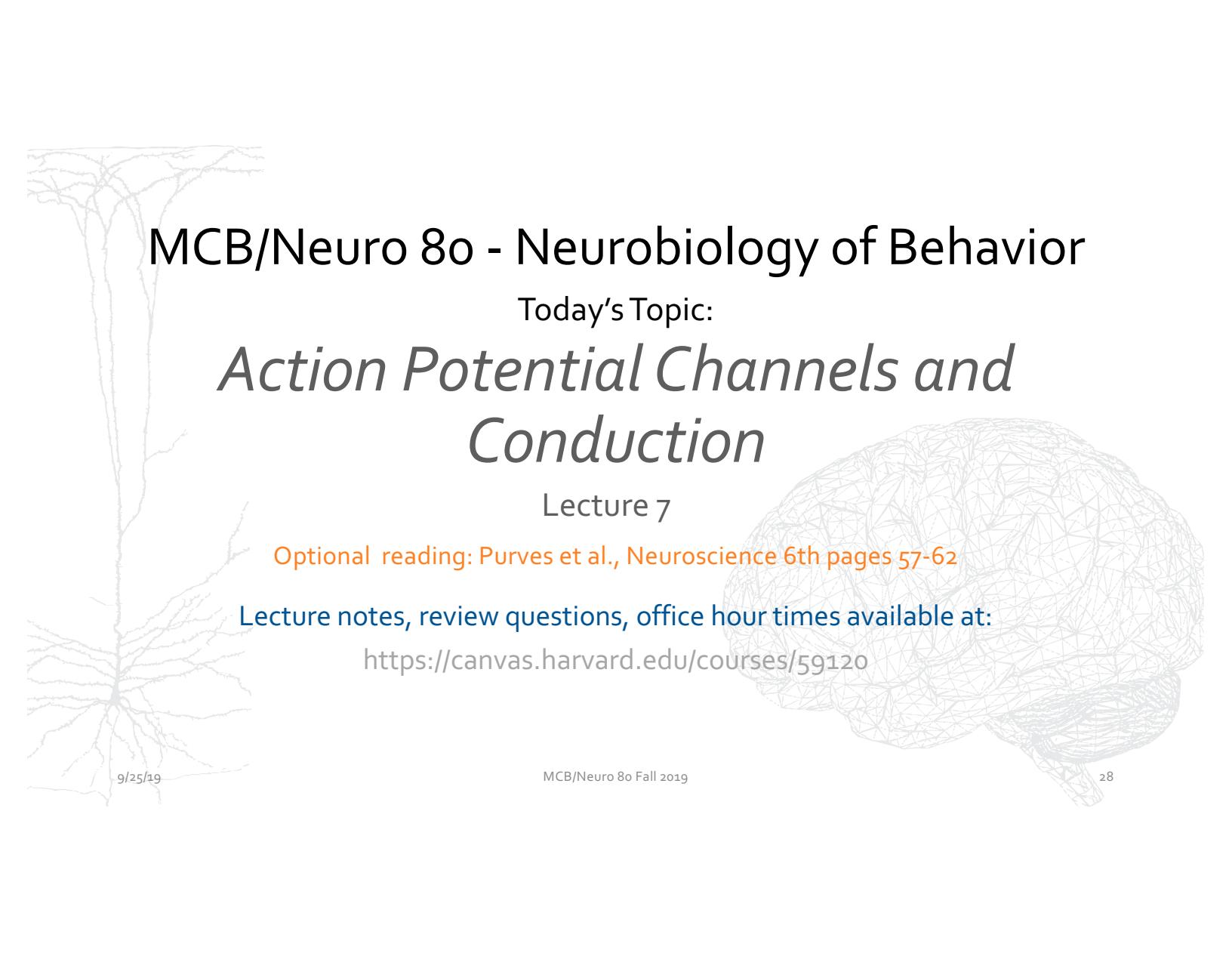
# Hodgkin and Huxley's model (via voltage clamp experiments)





# Lecture 6 – Learning Objectives

- Define driving force, conductance and current and know how they are related by Ohm's law.
- Diagram an action potential as a function of voltage over time and label the following stages:
  - resting potential
  - rising phase
  - falling phase
  - overshoot
  - undershoot
- Describe or illustrate how changes in  $\text{Na}^+$  and  $\text{K}^+$  conductances influence the membrane potential and lead to an action potential.
- Describe the ionic events (which channels are involved, direction and magnitude of ion flow) that lead to:
  - rapid depolarization of an action potential (rising phase)
  - rapid hyper polarization (falling phase)
  - hyper polarization (undershoot)
- Define and describe the biological mechanism for each of the following:
  - threshold
  - all-or-none property of action potentials
  - absolute refractory period



# MCB/Neuro 80 - Neurobiology of Behavior

Today's Topic:

## *Action Potential Channels and Conduction*

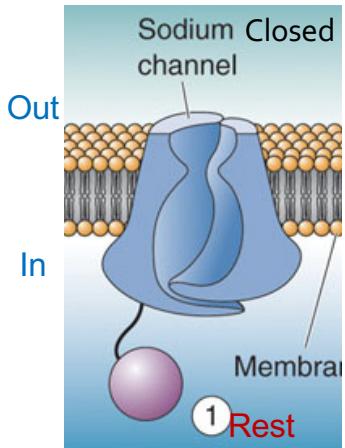
Lecture 7

Optional reading: Purves et al., Neuroscience 6th pages 57-62

Lecture notes, review questions, office hour times available at:

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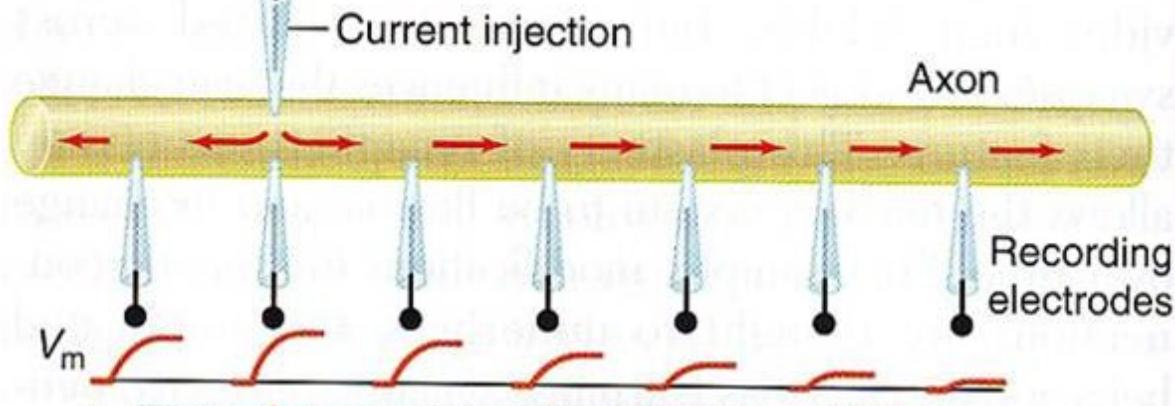
# : Na Channel Activation and Inactivation



- At  $V_{rest}$  channel is closed but not inactivated (1)
- Depolarization not only opens the channel (2),
- but with a delay inactivates it (3). ( $K^+$  channels are  $V$  sensitive but don't inactivate-they close when  $V_{membrane}$  returns to negative values)
- Repolarization to  $V_{rest}$  de-inactivates the channel but it is closed (4)
- **Time until de-inactivation occurs sets the absolute refractory period**

Site of  $I_{Na^+}$   
during rising  
phase of action  
potential

The distance over which the local sodium entry affects  $V_m$  is related to the axon's cable properties—this is the physics of local potentials



Traces show  $V_{memb}/time$   
measured simultaneously at  
many progressively more  
distant sites along an axon

Peak  
Of AP

Therefore, conduction velocity be changed by modifying cable properties

Decreased Axial Resistance

**Large Axon Caliber**

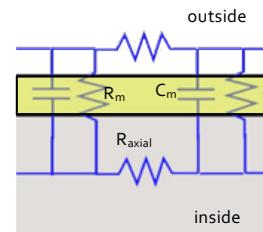
V

Increased  
Axial  
Resistance

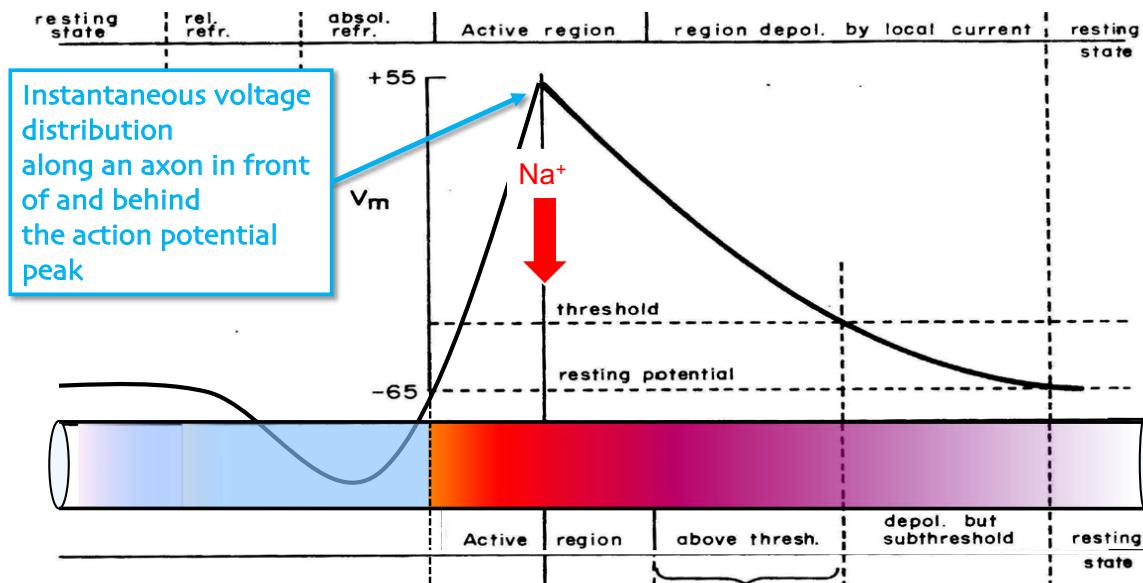
Threshold

**Small Caliber**

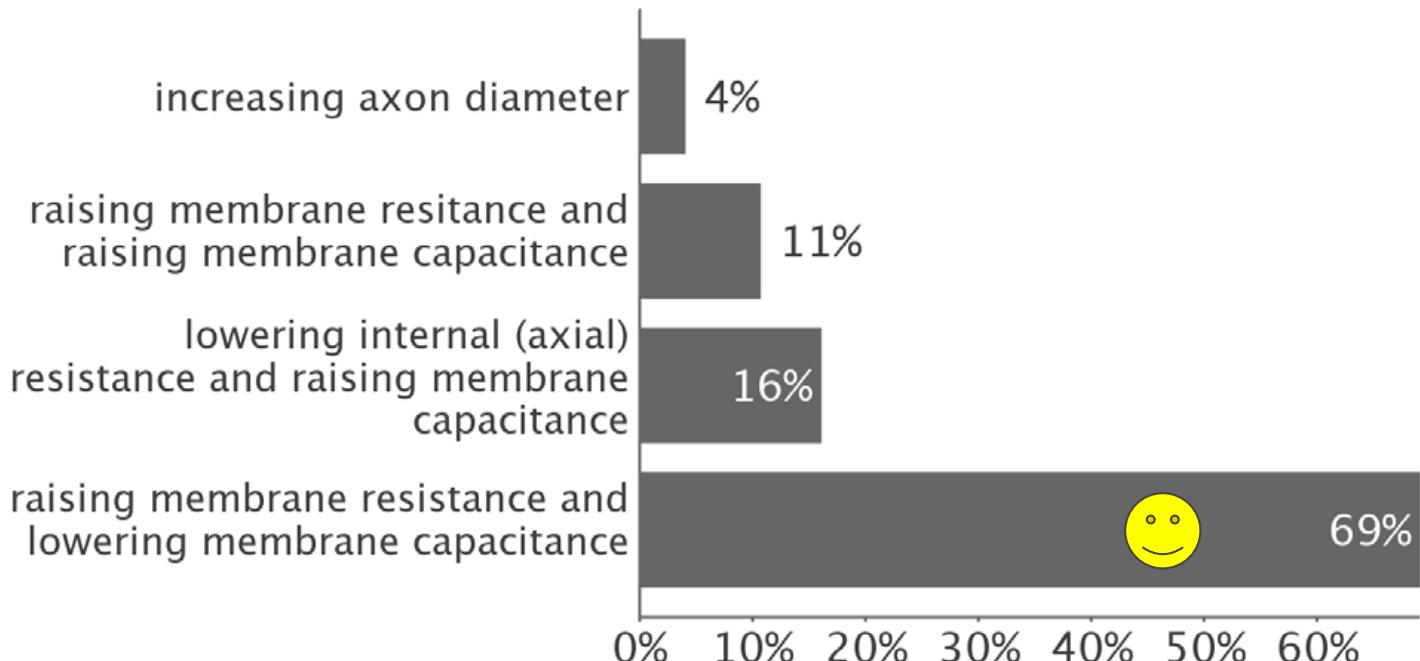
Length (mm)



# Action potential conduction

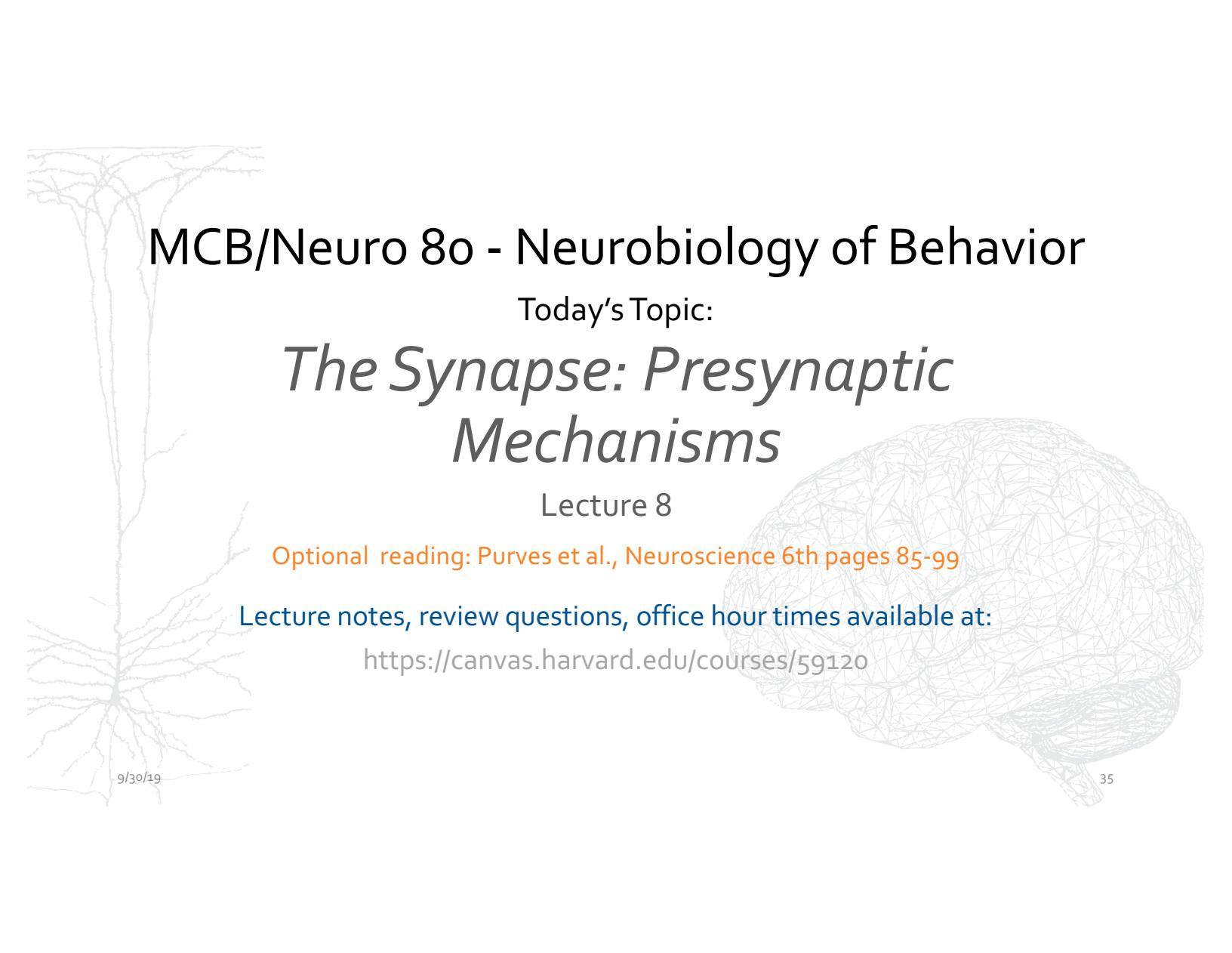


## Myelin speeds action potential conduction by



# Learning Objectives

1. Define and describe the biological mechanism for each of the following:
  - threshold
  - all-or-none property of action potentials
  - absolute refractory period
2. Basic properties of ion channels (activation, inactivation, open, close)
3. Know how an action potential alters the membrane potential along an axon (voltage vs distance)
4. Explain the ways in which an axon's passive properties (membrane resistance, membrane capacitance, and internal resistance) alter a voltage change with distance from the site where an action potential is peaking.
5. How and why does axon caliber affect conduction velocity?
6. How does myelin affect cable properties and conduction velocity? Why are nodes of Ranvier necessary?



# MCB/Neuro 8o - Neurobiology of Behavior

Today's Topic:

## *The Synapse: Presynaptic Mechanisms*

Lecture 8

Optional reading: Purves et al., Neuroscience 6th pages 85-99

Lecture notes, review questions, office hour times available at:

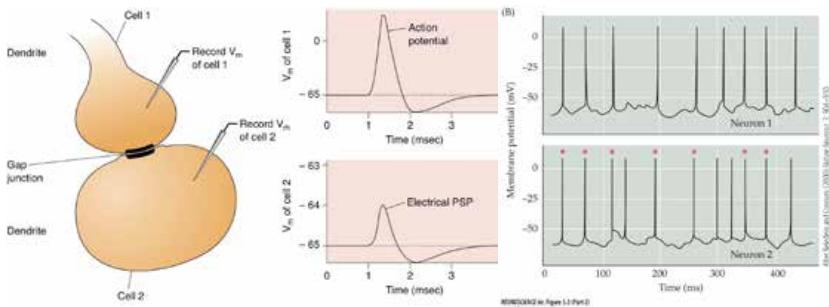
<https://canvas.harvard.edu/courses/59120>

# Advantages of electrical synapses

- Very fast (< 1ms), no channels to open
- Bi-directional current flow
  - From cell "A" to "B" and from "B" to "A"
  - Passes both depolarizing and hyperpolarizing current
- Energy efficient (don't need many molecules)
- Relatively fail-safe

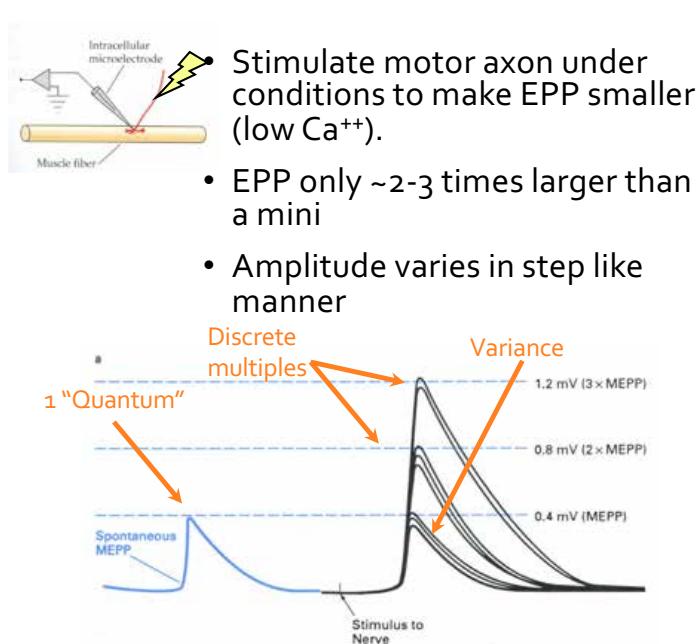
## • Disadvantages

- Difficult to modulate
- Can't change the "sign"
- Response is same size/duration or smaller (no gain)

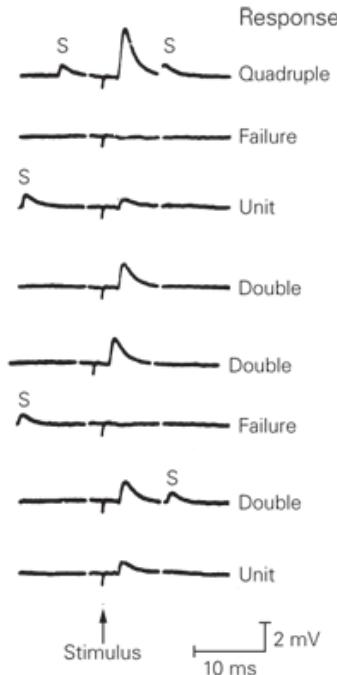


- Good for synchronizing neurons (rapid) and for circuits where timing is critical
  - Common in early development (neurons very synchronized)
  - Brainstem (cells synchronize breathing)
  - Thalamus (generate brain waves)
  - 'Escape reflex' in many organisms
  - Also common in glia

# Postsynaptic potentials built of multiple minis

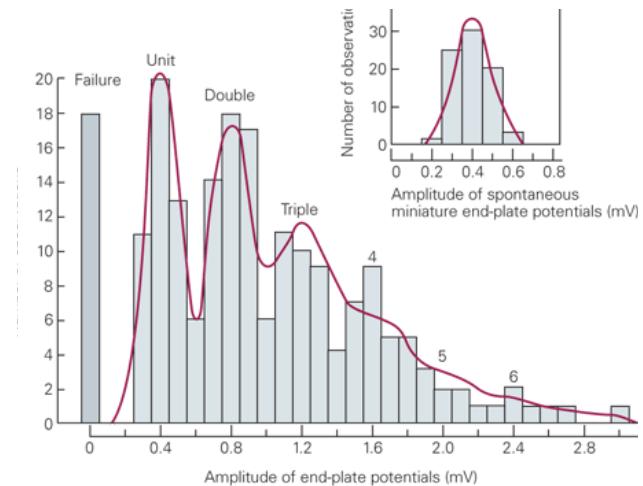
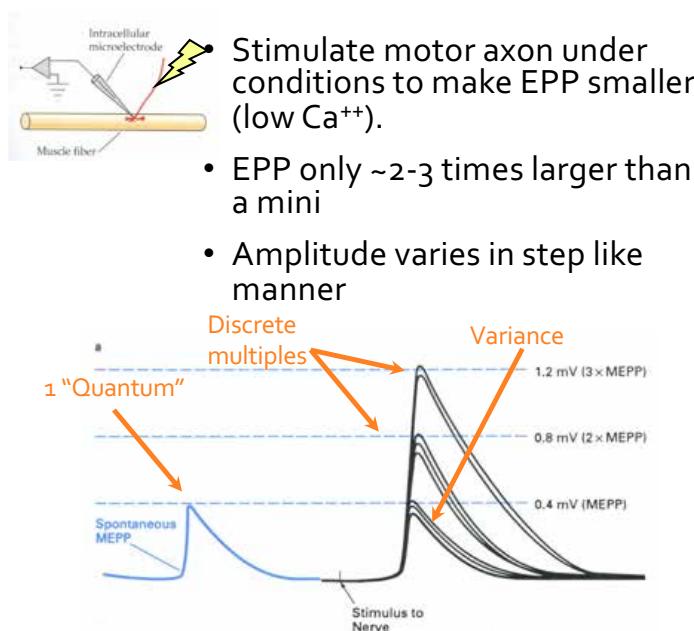


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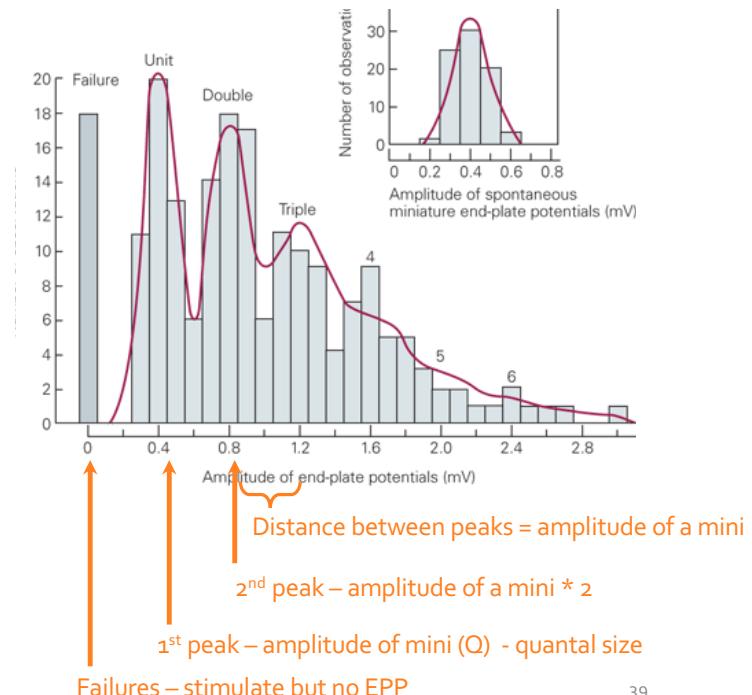
# Postsynaptic potentials built of multiple minis



Distribution matches a Poisson distribution (low probability discrete event)

# Postsynaptic potentials built of multiple minis

- Q (quantal size): Amplitude of the postsynaptic response to one vesicle (mini)
  - Tells you about how many postsynaptic receptors were activated by NT
- M (Quantal content/number) : average number of vesicles released by 1 presynaptic action potential
  - Tells you about properties in the presynaptic terminal
  - $M = \frac{\text{Mean EPP amplitude}}{\text{Mean mini amplitude}}$



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## What determines the size of a mini (quantal size)?

Number of vesicles released

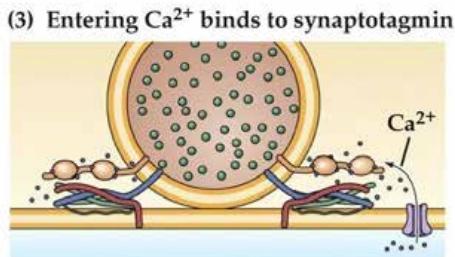
Number of post-synaptic receptors activated



Concentration of internal Ca<sup>++</sup>

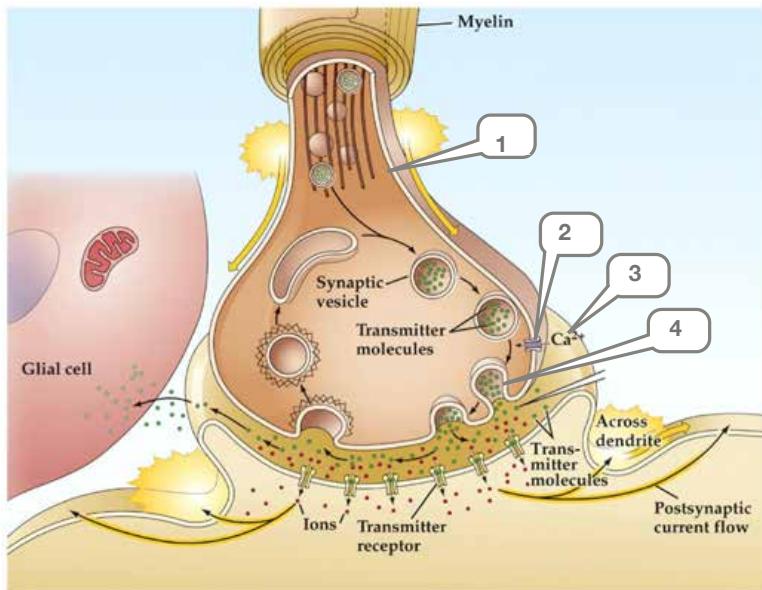
Number of presynaptic action potentials

# Vesicle fusion is catalyzed by SNARE proteins twisting together



- Proteins that bring membranes together:
  - Syntaxin and SNAP-25: found on presynaptic plasma membrane
  - Synaptobrevin: found on synaptic vesicles
  - Synaptotagmin: found on vesicles, acts as  $\text{Ca}^{++}$  sensor
- Syntaxin, SNAP-25, Synaptobrevin and ATP “Zipper” down into a tight, high energy complex (nanometers from fusion)
- Entering  $\text{Ca}^{++}$  binds to Synaptotagmin
- Confirmation change of Synaptotagmin causes vesicle fusion (very fast – 0.2 ms)

# Steps in synaptic transmission – presynaptic release

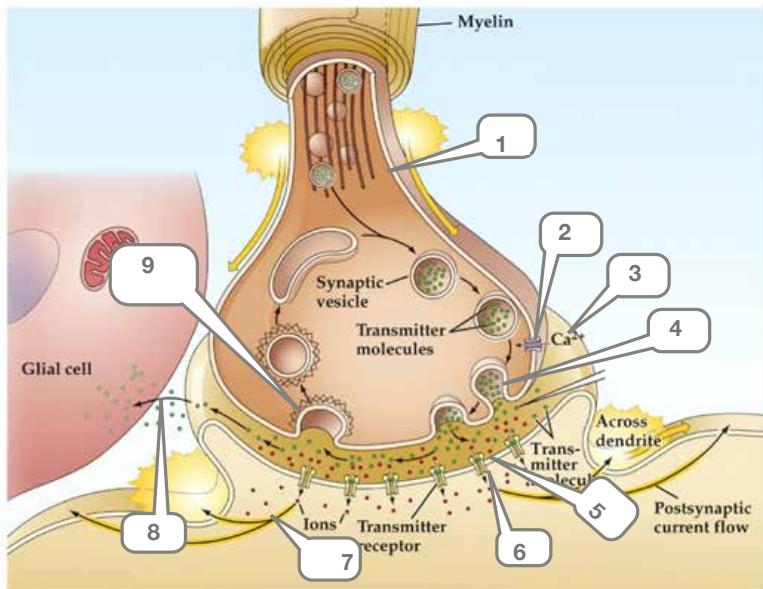


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1. Action potential conducted along axon and into presynaptic nerve terminal
2. The ensuing depolarization opens voltage-gated calcium channels
3.  $I_{\text{Ca}} = g_{\text{Ca}} (V_m - E_{\text{Ca}})$  so  $\text{Ca}$  flows in even at peak pf depolarization ( $E_{\text{Ca}} = 120\text{mV}$ )
4. Intracellular  $\text{Ca}^{++}$  triggers vesicle fusion and neurotransmitter release

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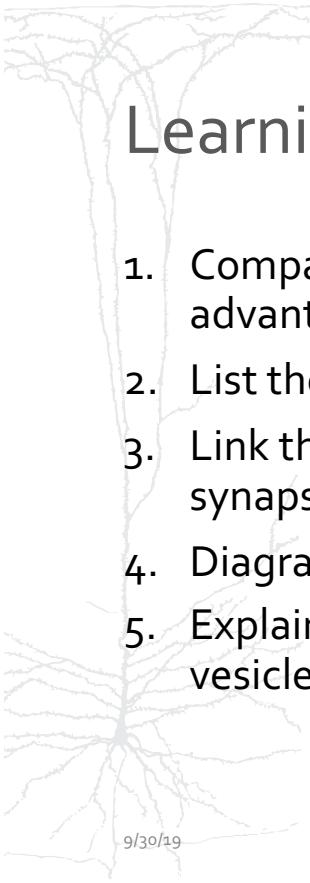
# Steps in synaptic transmission



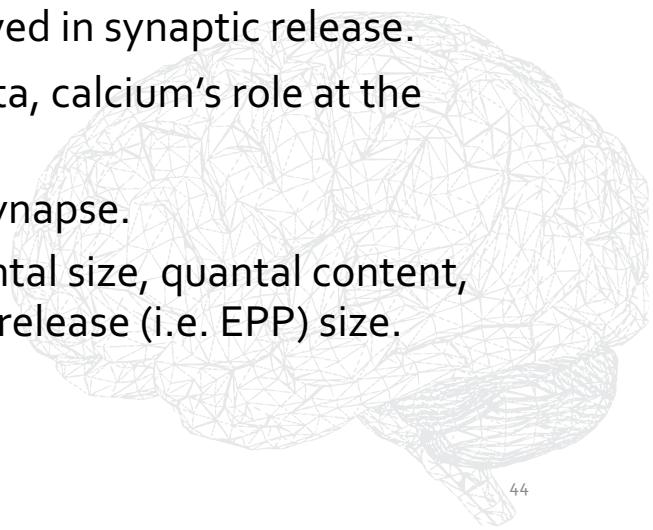
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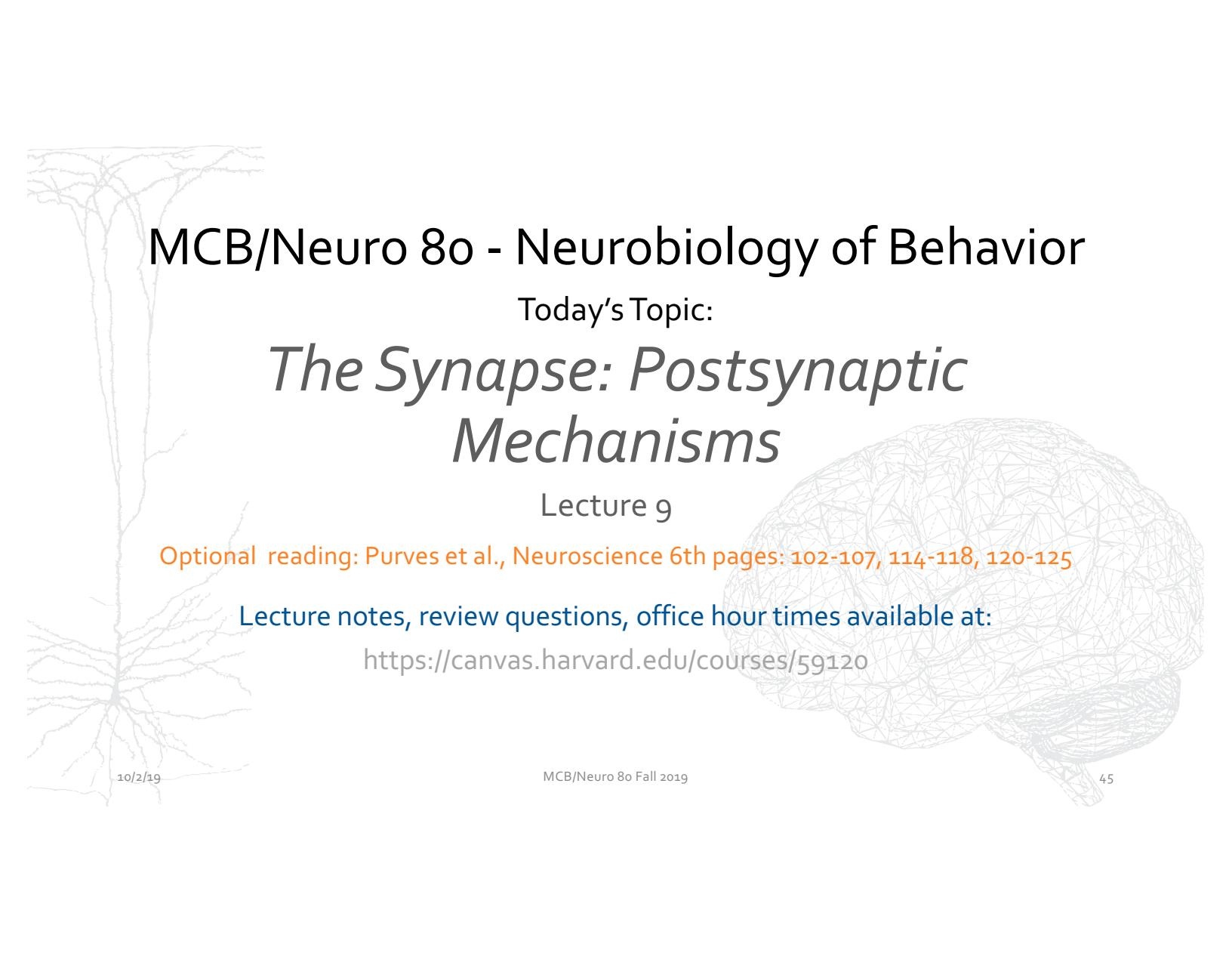
5. Transmitter binds to receptors in postsynaptic membrane
6. Opening of postsynaptic inotropic channels (or other changes - metabotropic)
7. Postsynaptic current causes changes in potential, altering the excitability of the postsynaptic cell.
8. Removal of neurotransmitter by glial uptake, diffusion, reuptake or enzymatic degradation
9. Retrieval of vesicular membrane from plasma membrane

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# Learning objectives for Lecture 8

1. Compare chemical and electrical synapses including any advantages or disadvantages.
  2. List the steps and key machinery involved in synaptic release.
  3. Link the synaptic terms: vesicles, quanta, calcium's role at the synapse, and the SNARE complex.
  4. Diagram and label a typical chemical synapse.
  5. Explain the relationships between quantal size, quantal content, vesicles, and evoked neurotransmitter release (i.e. EPP) size.
- 



# MCB/Neuro 80 - Neurobiology of Behavior

Today's Topic:

## *The Synapse: Postsynaptic Mechanisms*

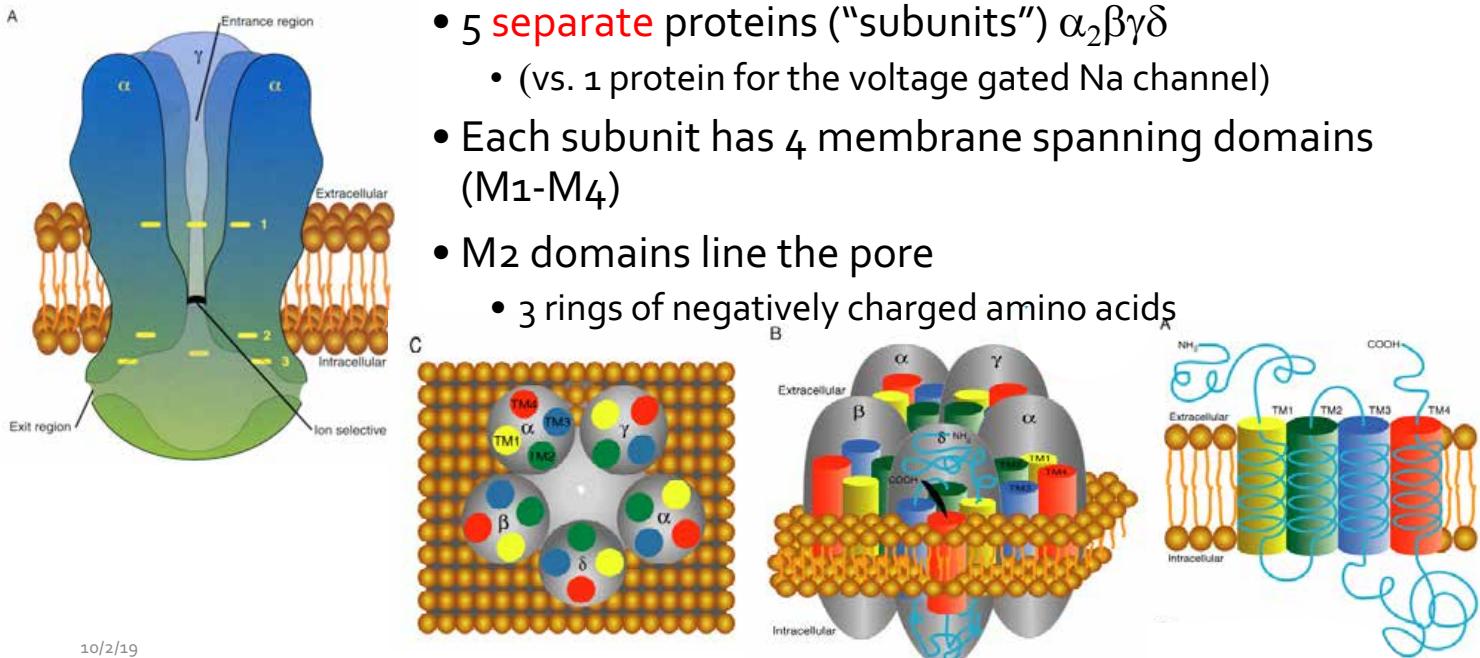
Lecture 9

Optional reading: Purves et al., Neuroscience 6th pages: 102-107, 114-118, 120-125

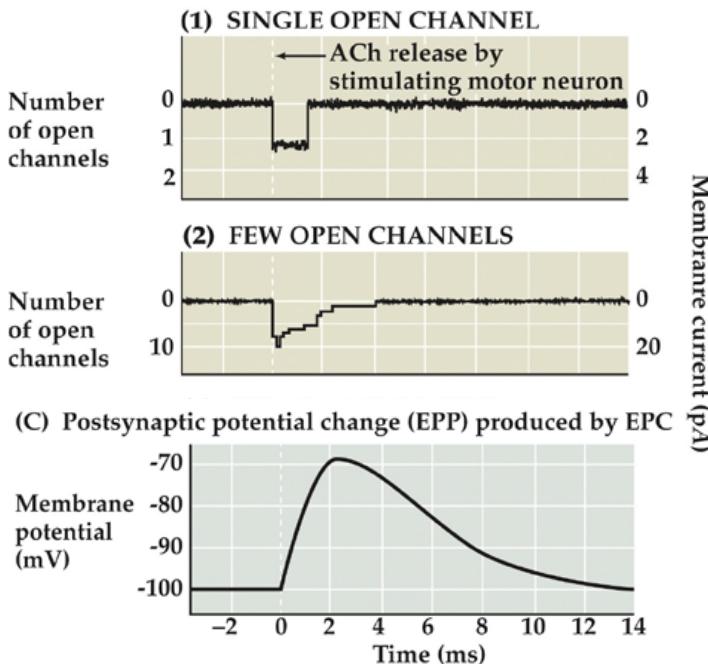
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<https://canvas.harvard.edu/courses/59120>

# ACh receptor structure – a ligand gated ion channel

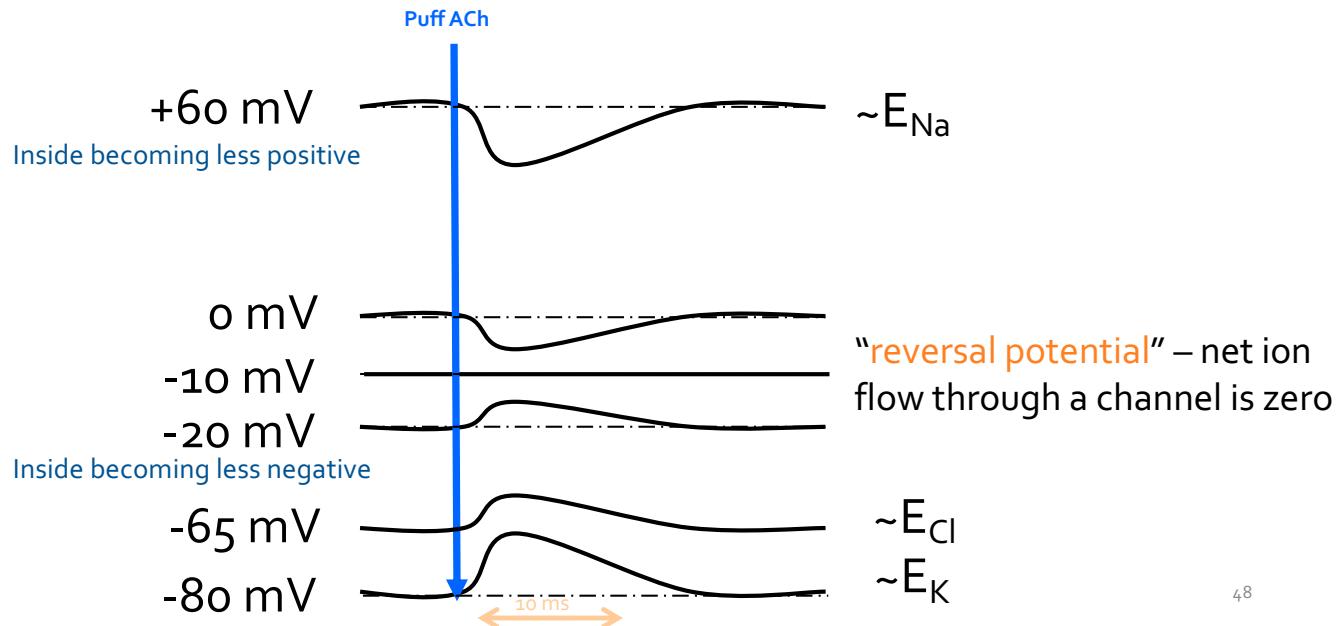


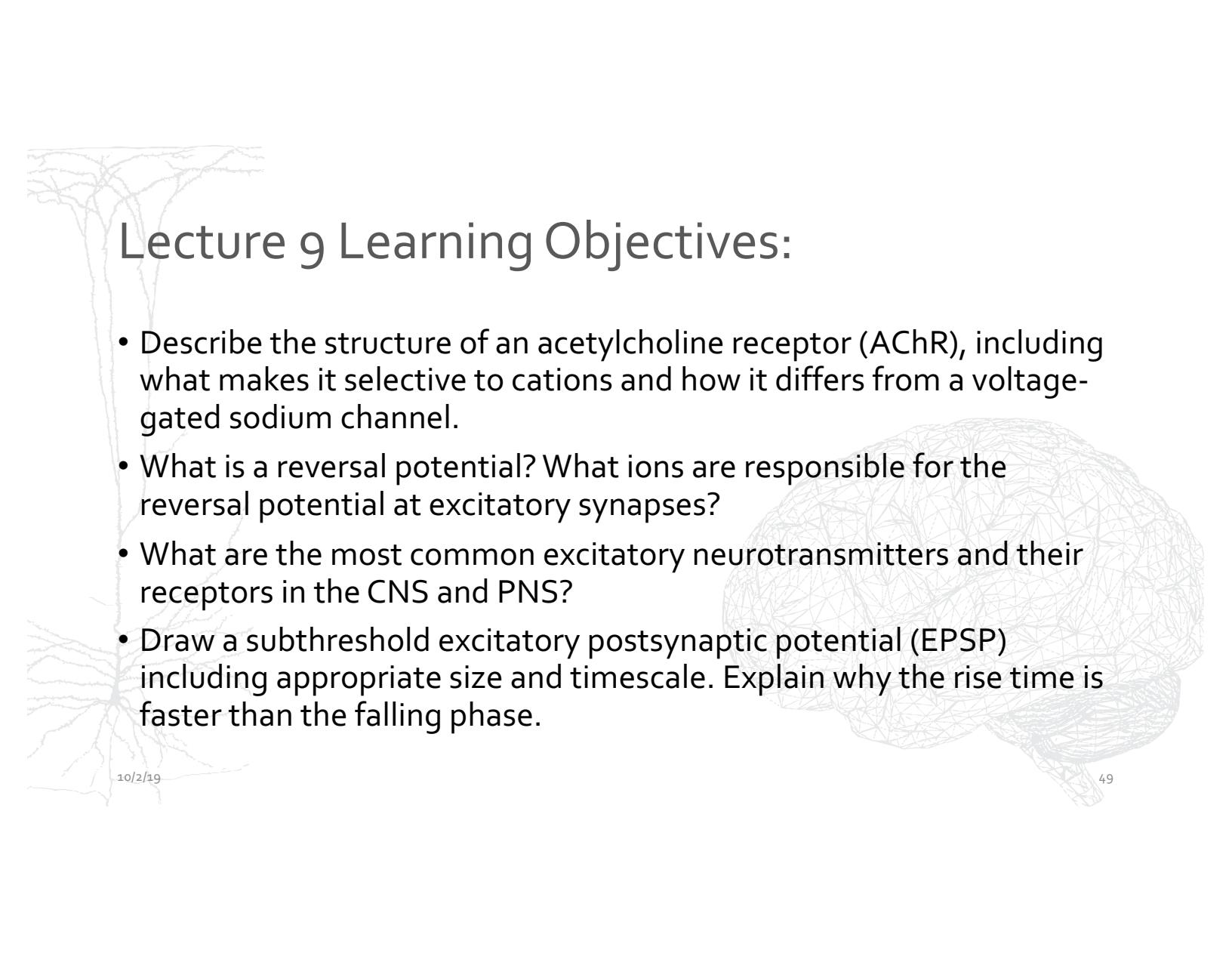
# The postsynaptic potential is due to the sum of the currents through many channels



- All channels open at nearly the same time but close randomly
- Channel current sum together to produce the total membrane current
- Current flow through AChR channels
  - Remember downward deflection (negative; inward) is depolarizing
- Change in membrane potential in the muscle (EPP)
  - Upward deflection (positive voltage) is depolarizing
- Rising phase ligand gated ion channels **open**
- Falling phase ligand gated ion channels **closed** - K<sup>+</sup> through leak channels (always open) repolarize the membrane

What ions go through the channel? By changing the membrane potential by current injection we can get an idea





# Lecture 9 Learning Objectives:

- Describe the structure of an acetylcholine receptor (AChR), including what makes it selective to cations and how it differs from a voltage-gated sodium channel.
- What is a reversal potential? What ions are responsible for the reversal potential at excitatory synapses?
- What are the most common excitatory neurotransmitters and their receptors in the CNS and PNS?
- Draw a subthreshold excitatory postsynaptic potential (EPSP) including appropriate size and timescale. Explain why the rise time is faster than the falling phase.



# MCB/Neuro 8o - Neurobiology of Behavior

Today's Topic:

## *Synapses: Inhibition and Integration*

Lecture 10

Optional reading: Purves et al., Neuroscience 6th pages:

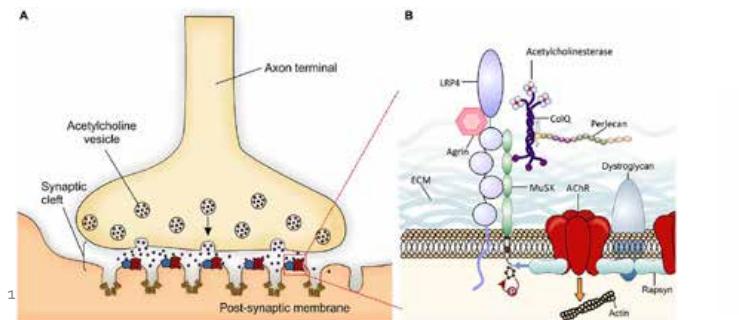
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# Excitatory ligand-gated ion channels

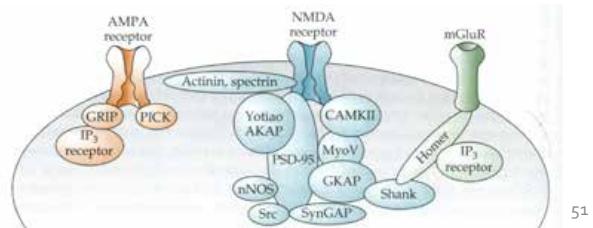
## Neuromuscular junction (NMJ)

- Acetylcholine (ACh) [ $M = 50+$ ]
- Very high quantal content
- nicotinic Acetylcholine Receptor (nAChR)
  - $g_{Na} = g_K$
  - desensitizes



## Central nervous system (brain)

- Glutamate
- Lower quantal content [ $M = 1-10$ ]
- AMPA
  - $g_{Na} = g_K$
  - desensitizes
- NMDA
  - $g_{Na}, g_K$  and  $g_{Ca}$
  - Ligand-gated and voltage-gated
  - does not desensitize



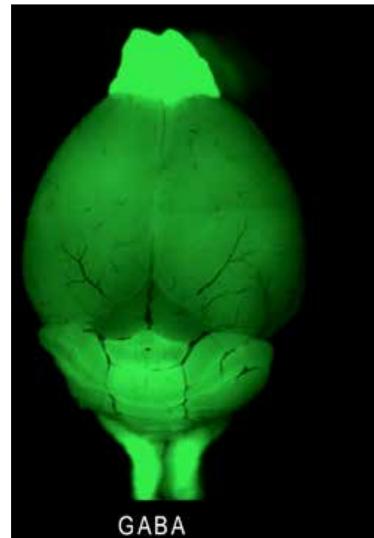
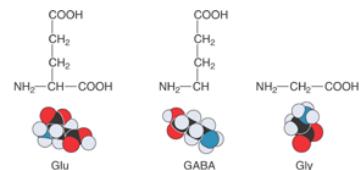
# Two NTs for Ionotropic Inhibition

## 1. GABA - (short for $\gamma$ -aminobutyric acid)

- **Everywhere** (Cortex, midbrain, etc)
- Most important inhibitory NT in Brain
- Ionotropic receptor: GABA "A" receptor

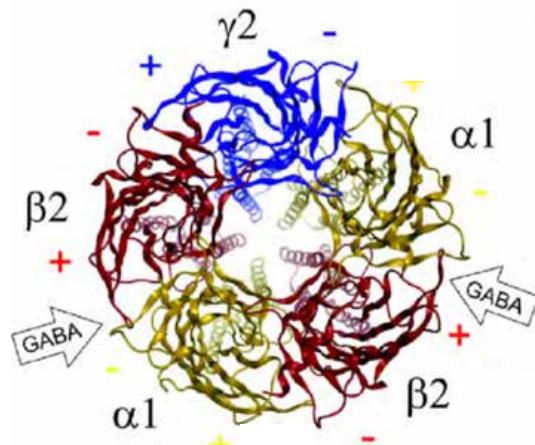
## 2. Glycine – an amino acid

- **Spinal cord, brainstem** (evolutionarily older)
- Also in the retina (50:50 with GABA)
- Low levels in other areas
- Ionotropic receptor: GlycineR



## Ionotropic GABA and glycine receptors: ligand-gated chloride channels

- Analogous to AChR (same gene family), similar in structure except:
  - affinity for different neurotransmitters
  - the channel pore (lined by the M2 membrane spanning domains -) is lined by positively charged amino acids, as opposed to negative charges in the AChR.
- These ligand-gated ion channels are anionic. When neurotransmitter binds,  $g_{Cl}$  increases
- Effect is to keep  $V_m$  near  $E_{Cl}$  which is below threshold ( $E_{rev} = E_{Cl}$  for GABA/glycine receptors)
- This is in contrast to excitatory neurotransmitters that are trying to depolarize the cell to above threshold ( $E_{rev} = -10mV$ )



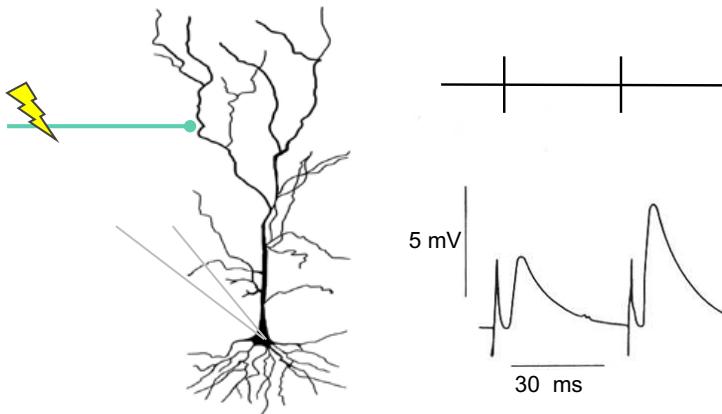
## To summarize...

1. **Distance matters:** The farther an excitatory synapse is from the initial segment (trigger zone) the less powerful it is.
2. **Things don't add up right:** Synaptic potentials of different axons sum in a *non-linear* way
3. **A little bit of  $g_{Cl^-}$  goes a long way:** IPSPs interposed between EPSPs and the initial segment block the EPSPs from reaching threshold
4. **Piggy-back**  : Temporal Summation
5. **No Piggy-back**  : Inhibition changes shape of EPSP preventing temporal summation

## Temporal summation and facilitation are the same phenomena



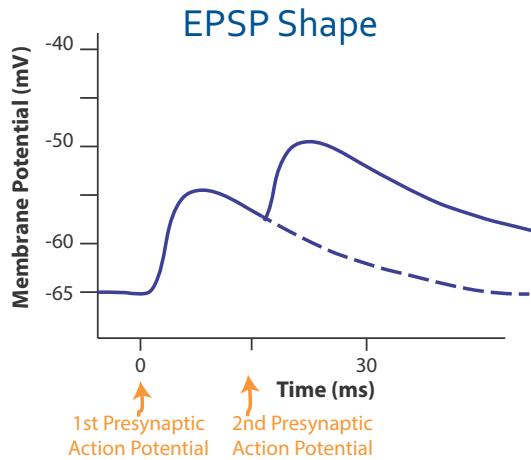
# Facilitation - Second of two closely timed EPSPs bigger than the first, **PRESYNAPTIC MECHANISM**



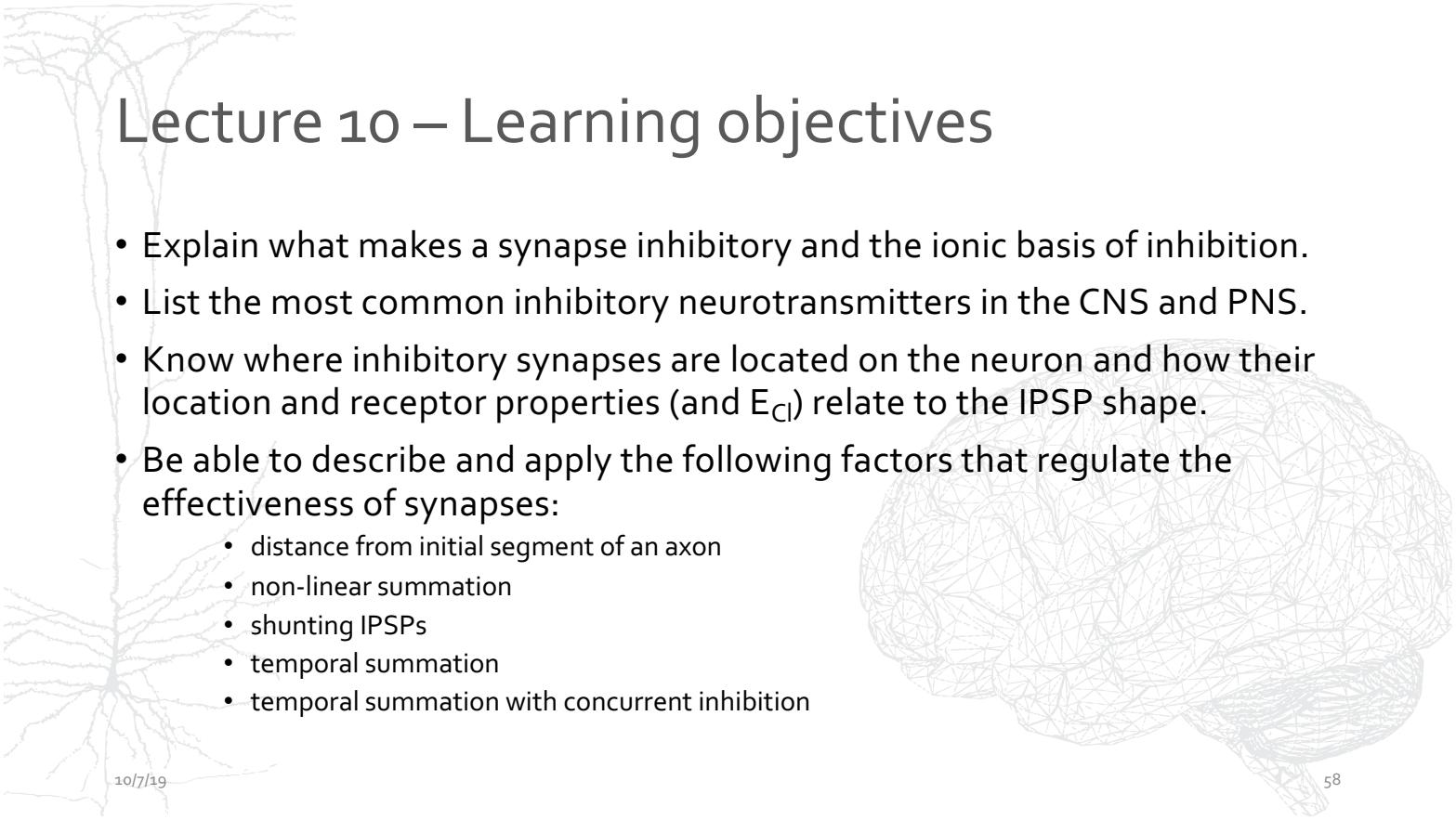
- "Residual calcium" hypothesis:  $\text{Ca}^{++}$  enters to trigger transmitter release, then is removed.
- When second stimulus is soon after the first, "new"  $\text{Ca}^{++}$  enters before the initial pulse is fully removed.
- Why does a little bit make a big difference?  $m$  (quantal content) proportional to  $[\text{Ca}^{++}]^4$ . ( $20\% \text{ Ca}^{++} \uparrow$  leads to  $100\% \uparrow$  release.)

- Stimulate very quickly (25 Hz)

# Temporal Summation allows one EPSP to “piggy back” on another - POSTSYNAPTIC

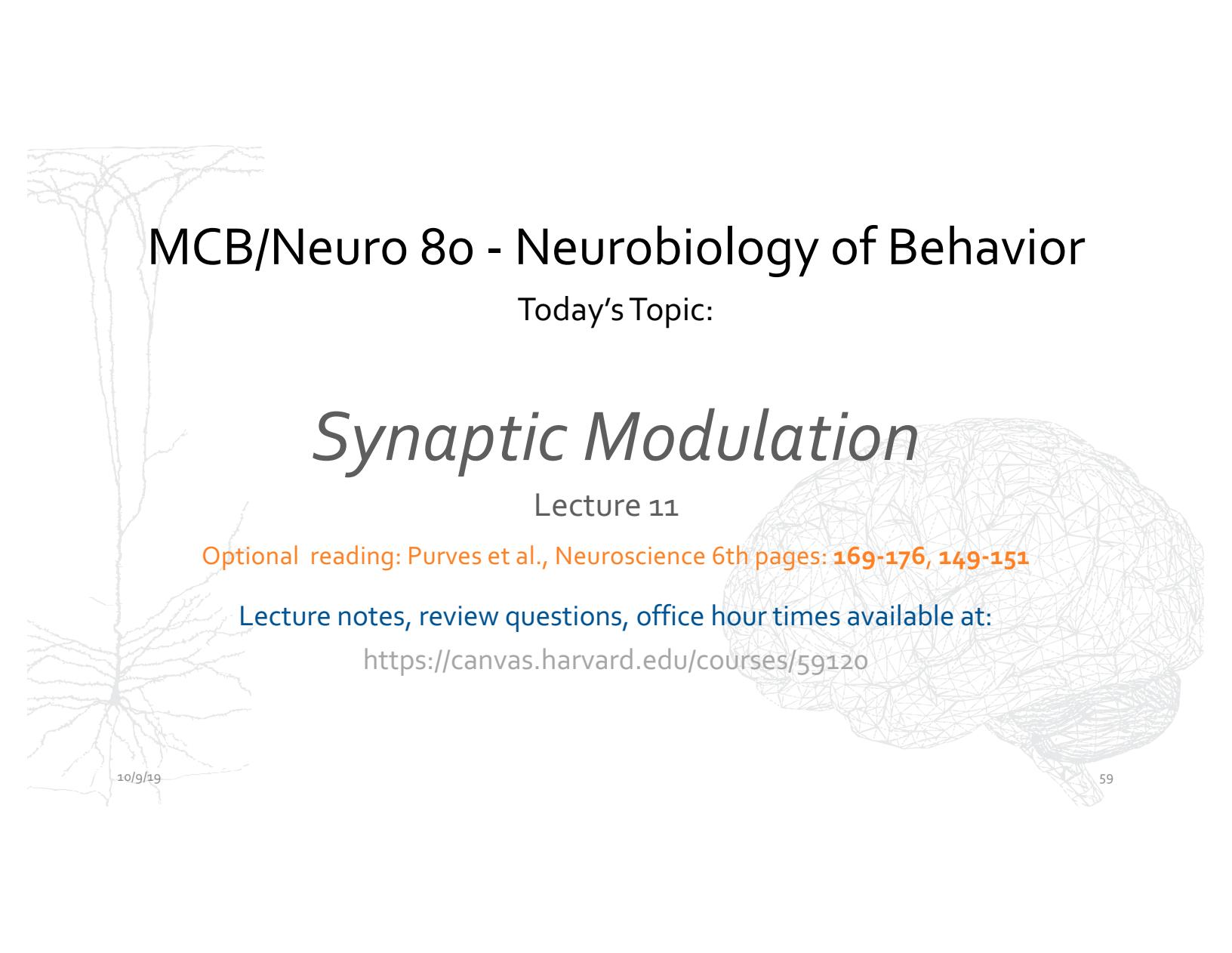


- EPSP shape has a fast rise and slow fall
- During the rise, LGICs are open so  $R_{mem}$  is low and charge passes through quickly.
- During the fall, LGICs are closed, so  $R_{mem}$  is higher and it takes longer time to remove the added positive charge
- When a presynaptic terminal is activated at high frequency the postsynaptic amplitude sums because each EPSP sits on the falling phase of the previous potential



# Lecture 10 – Learning objectives

- Explain what makes a synapse inhibitory and the ionic basis of inhibition.
- List the most common inhibitory neurotransmitters in the CNS and PNS.
- Know where inhibitory synapses are located on the neuron and how their location and receptor properties (and  $E_{Cl}$ ) relate to the IPSP shape.
- Be able to describe and apply the following factors that regulate the effectiveness of synapses:
  - distance from initial segment of an axon
  - non-linear summation
  - shunting IPSPs
  - temporal summation
  - temporal summation with concurrent inhibition



# MCB/Neuro 8o - Neurobiology of Behavior

Today's Topic:

## *Synaptic Modulation*

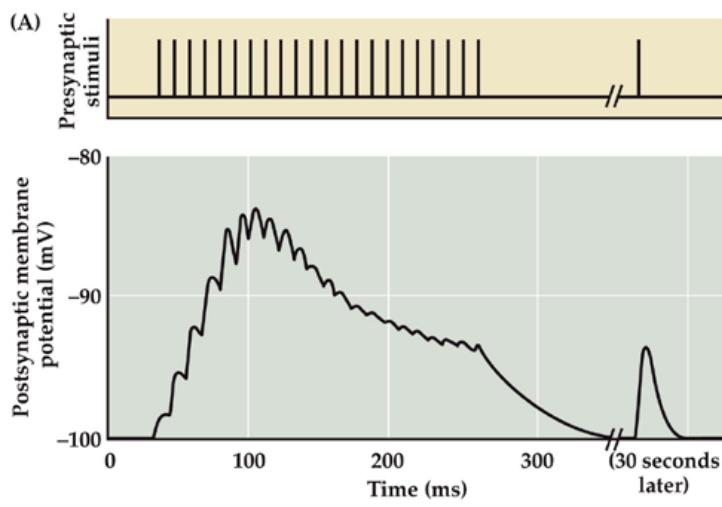
Lecture 11

Optional reading: Purves et al., Neuroscience 6th pages: **169-176, 149-151**

Lecture notes, review questions, office hour times available at:

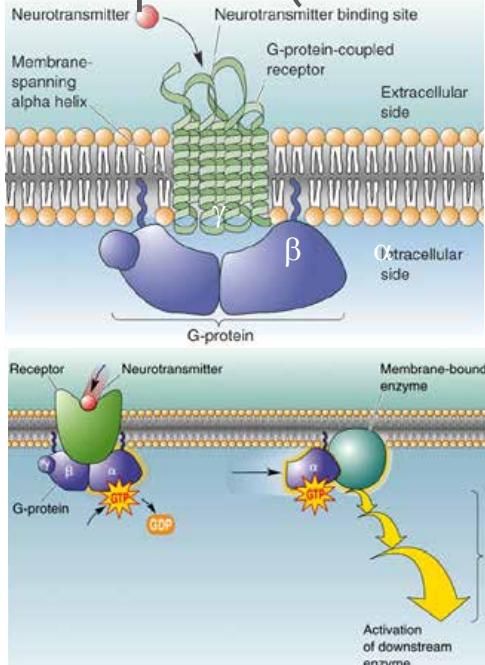
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# Presynaptic changes are rapid, usually short-lived



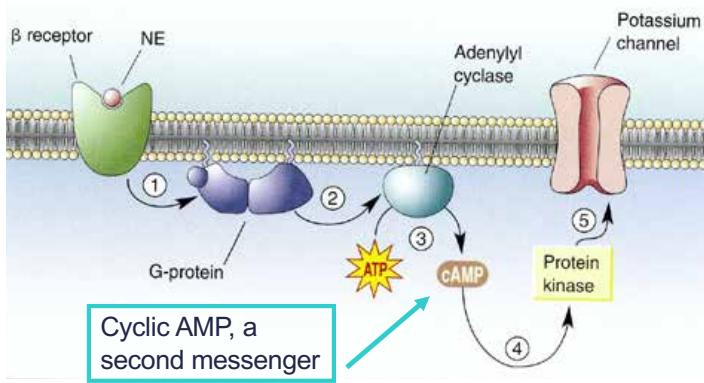
- Changes in the presynaptic release (not impacting receptors) are usually rapid and short-lived
- Each cell can have different short term responses – depends on vesicle pools, channels, etc.
- Can combine facilitation and depression for complex responses

# Metabotropic receptors are G protein-coupled receptors (GPCRs)



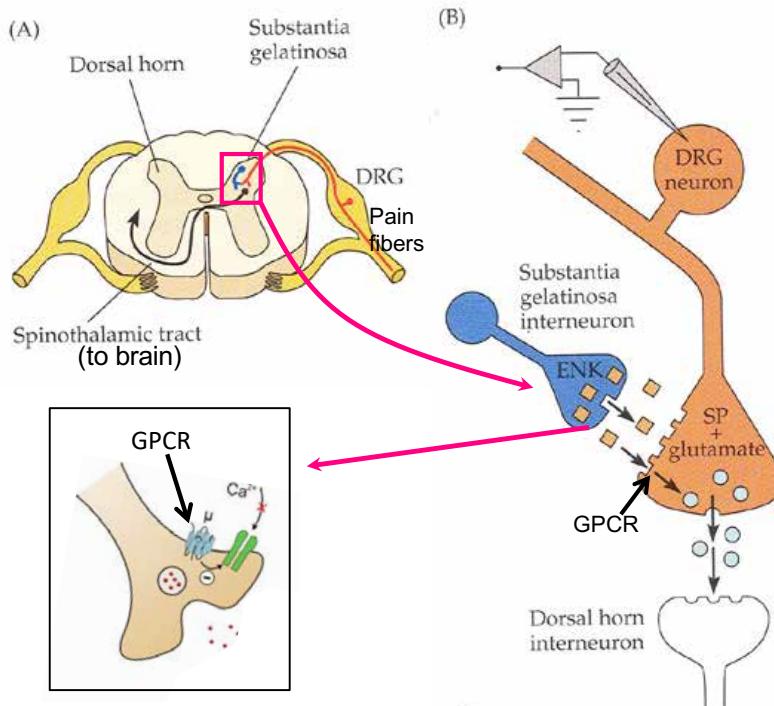
- Huge family of genes (~2000)
- Diverse group of receptors - small neurotransmitters, catecholamines, peptides, etc.
- Intracellular domain binds a set of three proteins -  $\alpha$ ,  $\beta$ , and  $\gamma$ - together called G proteins because they bind GTP
- Three steps in transmission
  1. Binding of the neurotransmitter to the extracellular receptor protein
  2. Activation of G-proteins
  3. Activation of effector systems

# Second messengers

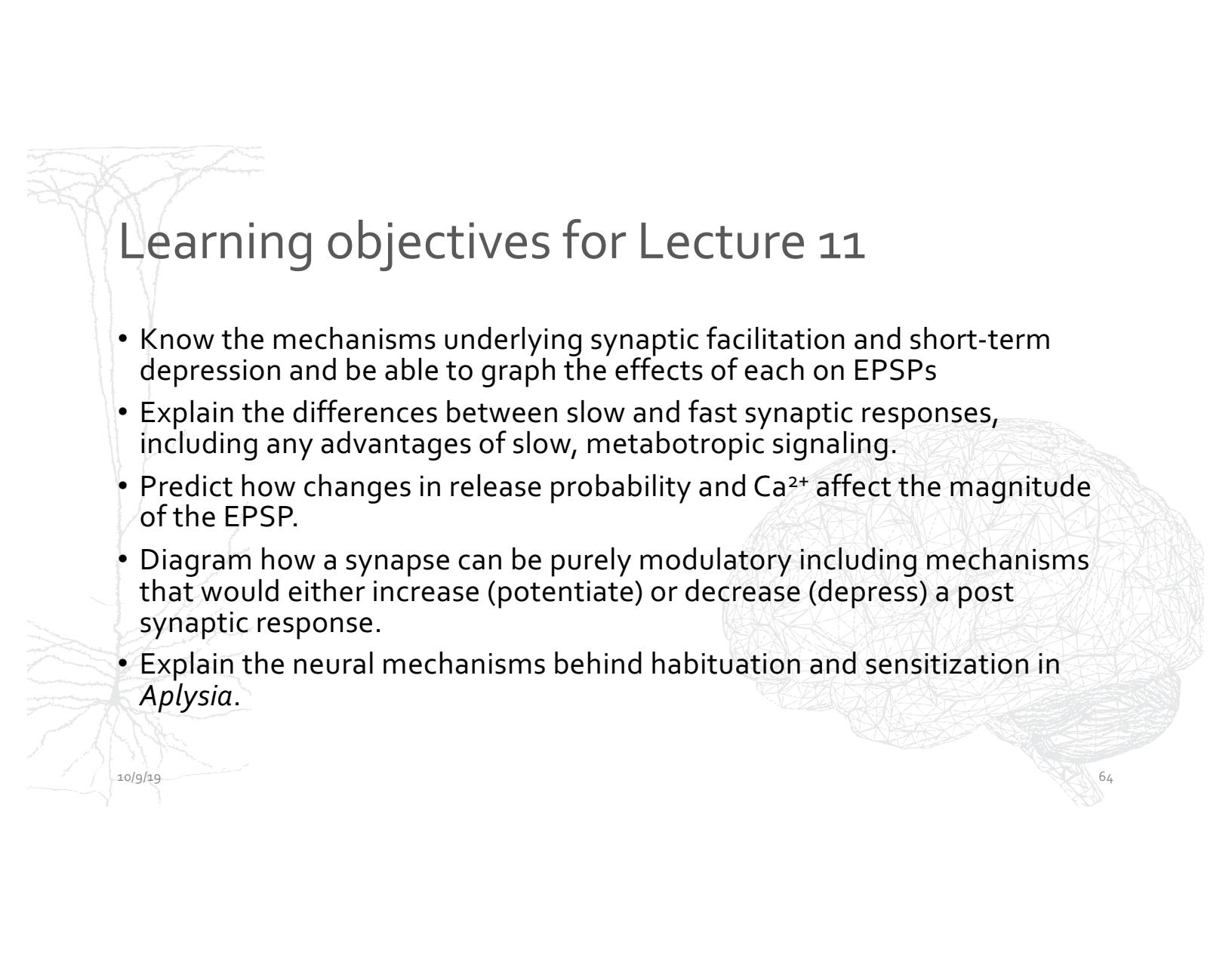


- Frequently, the activated proteins are enzymes, which generate small molecules that affect channels (or something else). These molecules are called "second messengers."
  - e.g., cyclic AMP (cAMP) is generated from ATP by adenylyl cyclase
  - cAMP activates protein kinase A (PKA), which can activate many proteins, including channels, receptors, etc.
- 3 general second messenger systems that interact with specific G-proteins
  - Increase cAMP ( $G_s$ )
  - Decreases cAMP ( $G_i/G_o$ )
  - Stimulates phospholipase C, DAG, IP<sub>3</sub> and PKC ( $G_q$ )

# Pain modulation by opioid receptors



- Dorsal root ganglion cells sense pain, interneuron releases enkephalin
- Enkephalin binds GPCR
- G-protein (Go) inhibits VG Ca channel
- Less neurotransmitter release when activated



# Learning objectives for Lecture 11

- Know the mechanisms underlying synaptic facilitation and short-term depression and be able to graph the effects of each on EPSPs
- Explain the differences between slow and fast synaptic responses, including any advantages of slow, metabotropic signaling.
- Predict how changes in release probability and  $\text{Ca}^{2+}$  affect the magnitude of the EPSP.
- Diagram how a synapse can be purely modulatory including mechanisms that would either increase (potentiate) or decrease (depress) a post synaptic response.
- Explain the neural mechanisms behind habituation and sensitization in *Aplysia*.