Neuro 80 Lecture 3

September 11

Circuits of the Nervous System

MC quiz available today – Friday

BRAIN

Molecules → cells → circuits → systems

BEHAVIOR

Behavior

- the way in which an animal or person acts in response to a particular situation or stimulus
  - Stimulus: external or internal
  - Neuronal processing:
    - Electrical signals are the common lang.
    - Transmit and integrate signals
  - Response (motor)

Reflexes

- A reaction to a stimulus not requiring conscious awareness
- Patellar tendon reflex (myotatic or stretch reflex)

Patellar Tendon Reflex

- ~20ms versus voluntary reaction ~200 ms
- reflex latency is shorter in shorter people

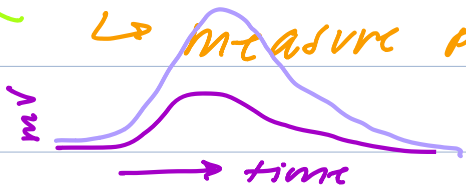
1. Stimulus: stretch quadriceps by tapping patellar tendon w/ rubber hammer
2. Transduction: convert stimulus (e.g. mechanical) into an electrical signal

GRADED POTENTIAL (analog signal)

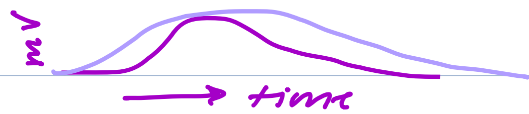
↳ muscle spindle inside muscle fiber sense stretching

↳ stretch causes + ions to flow into axon, creating a potential

↳ measure potentials as Δ in voltage



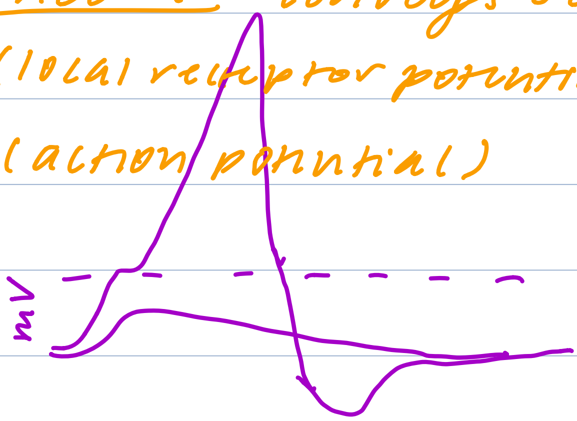
LARGER STIMULUS



LONGER STIMULUS

ACTION POTENTIAL (digital signal)

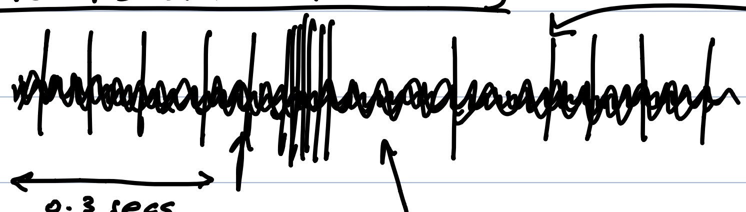
3. Encode: conveys sensory information (local receptor potential) into neuronal code (action potential)



action potentials are all or nothing

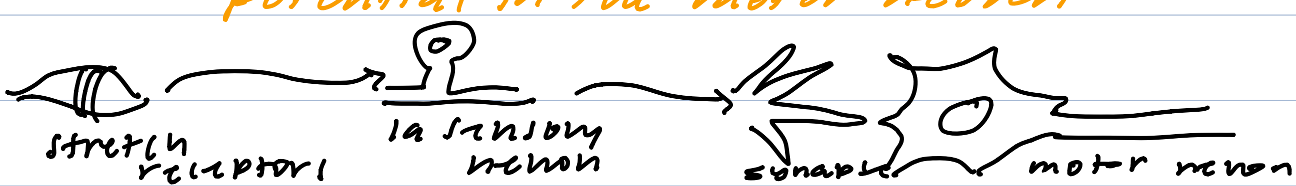
↳ stronger receptor potential, greater the frequency of action potentials (APs/second) → frequency encoding

Action Potential Recording



"frequency coding"

4. Sensory-motor synapse: elicits an action potential in the motor neuron



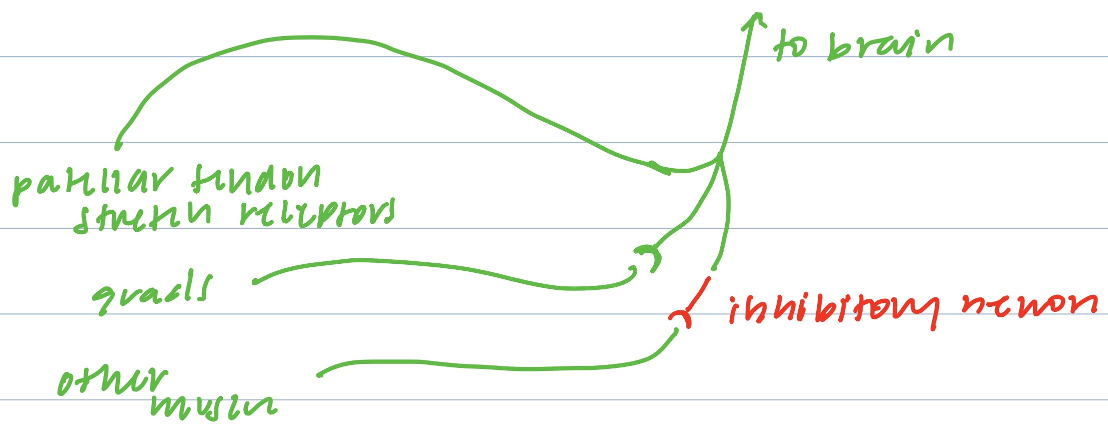
5. Muscle fiber activation:

↳ large synapse between motor neuron + muscle fiber (neuromuscular junction), causes muscle to contract

↳ more neurons = larger response

6. Inhibition of antagonistic muscles:

↳ inhibitory potentials move away from threshold, less likely to fire



Takeaways

- Δ in local (graded) potential can trigger propagated (all or none) electrical potential changes
- inhibition enhances computational repertoire

Gross Anatomy of the Nervous System

CNS vs PNS

brain + spinal cord

nerves (sensory and motor)

→ somatic (voluntary)

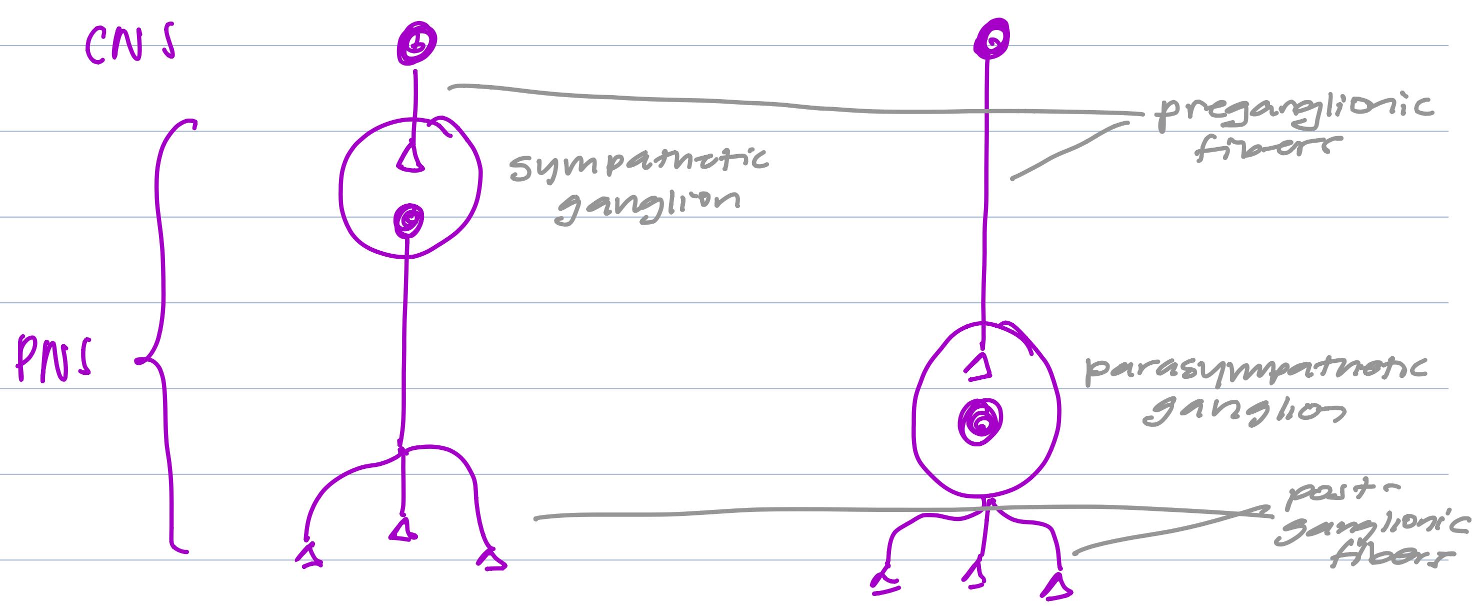
→ autonomic (involuntary)

→ sympathetic

→ parasymp

- Autonomic
  - controls internal milieu
  - continuously adjusted

	symp	parasymp
BP	↑	↓
HR	↑	↓
blood to muscle	↑	↓
digestive system	↓	↑
purpose	energy for intense activity	reduce energy, build reserves
location	next to spinal cord	near target organ
neurotrans	norepinephrine	acetyl choline
ganglia location	cranial / sacral	thoracic / lumbar



CNS

- white matter (axons) vs grey matter
- medulla and pons (brainstem, "maintenance / vital functions)

- midbrain - auditory/visual centers
- cerebellum - muscle/reflex coordination
- diencephalon -
  - thalamus: integration center
  - hypothalamus: unconscious drives, automatic command center
- cerebral cortex, folded rim of grey matter
  - "neocortex" w/ many layers
  - gyri: bumps
  - sulci: grooves
  - fissures: deep groves, organize regions
- sub-cortical
  - basal ganglia: movement
  - amygdala:
  - hippocampus: memory

- Phrenology: based on external skull shape
- Modern view: complex network of interconnected
  - histological mapping: • suggests functional distinctions
    Karl Broadman
  - functional mapping: • lesion studies (Paul Broca and speech problems)
    - direct brain stimulation
    - direct recording (micro electrodes)
    - fMRI (blood flow)

- cerebral cortex

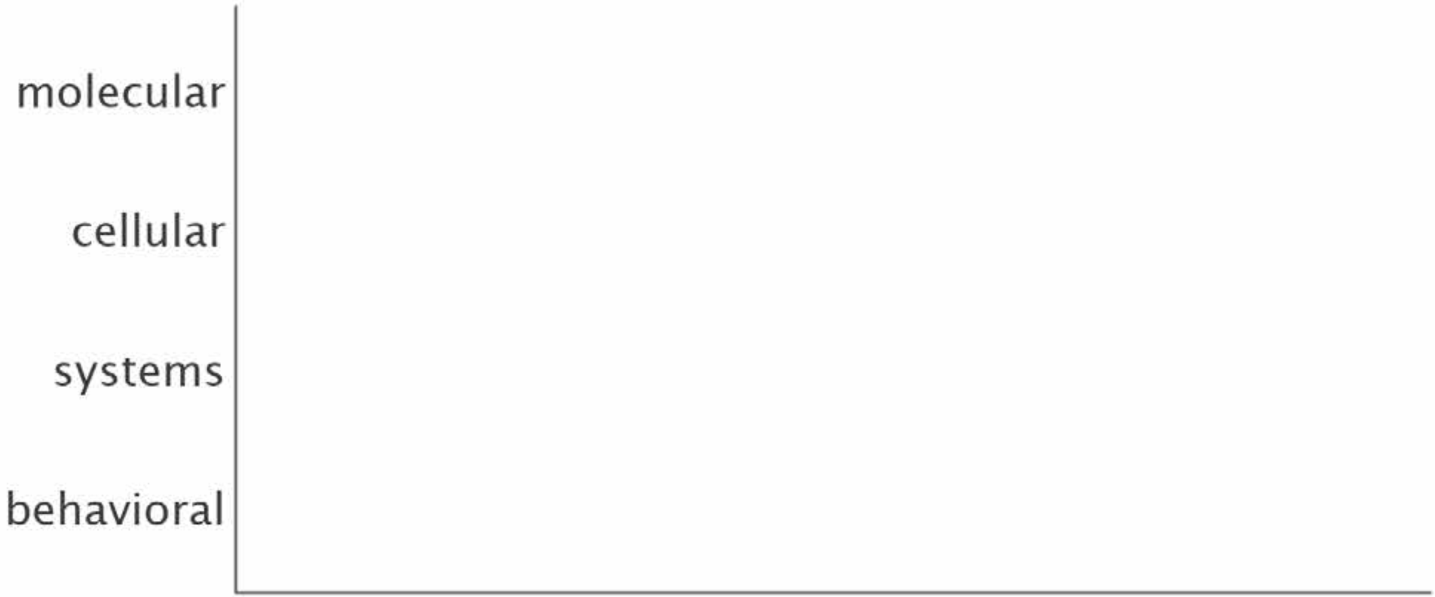
frontal : decision making (front of sulcus)

occipital : vision

temporal : hearing / language (under sylvian fissure)

parietal : sensation, integration

What level of neuroscience would you choose to study?



MCB/Neuro 80 - Neurobiology of Behavior

Today's Topic:

Circuits of the Nervous System

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

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

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

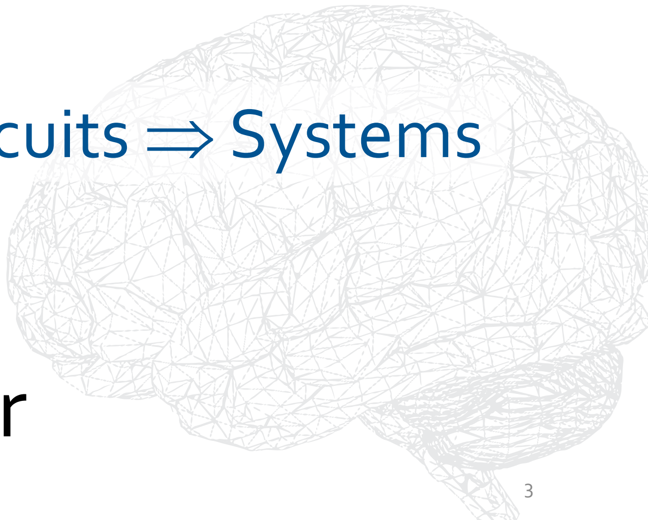
Sectioning is complete! You should have received an email yesterday. Email Katie if not

MCB/Neuro 80 – Neurobiology of Behavior

Brain

Molecules ⇒ Cells ⇒ Circuits ⇒ Systems

Behavior



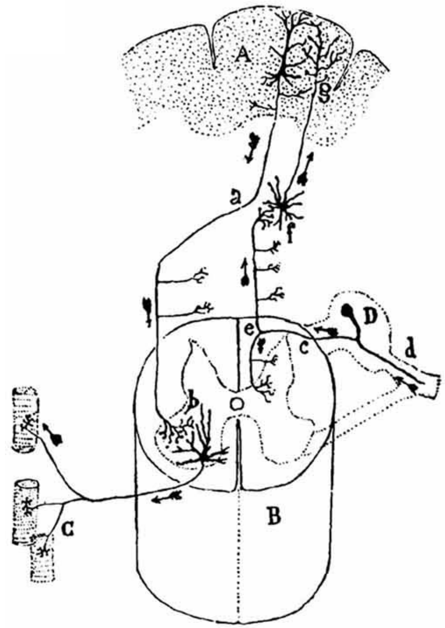
What is behavior?

Behavior: the way in which an animal or person acts in response to a particular situation or stimulus.

- Stimulus
  - Could be internal or external
- Neuronal processing
  - <u>Electrical signals</u> are the common language of the nervous system
  - Nervous system can transmit and <u>integrate</u> signals
- Response (motor)

Could Cajal's idea of directional connections between nerve cells underlie behavior?

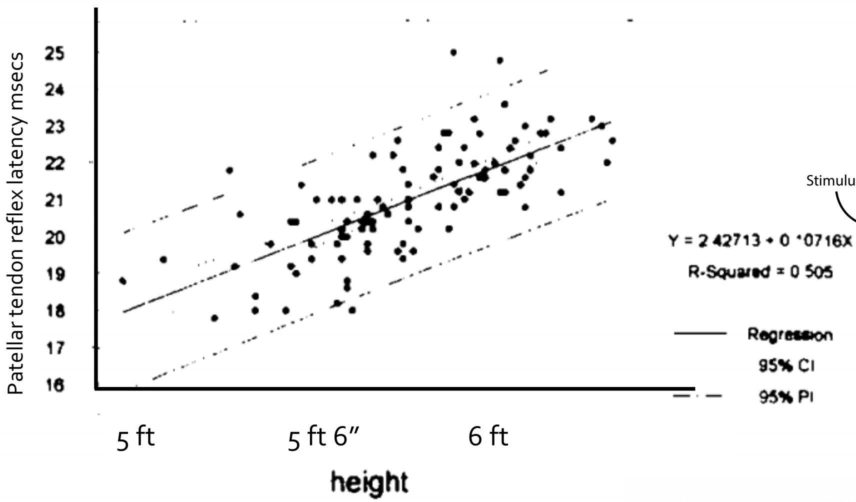
  - Sensory input might be structurally connected to motor output via neuronal connections

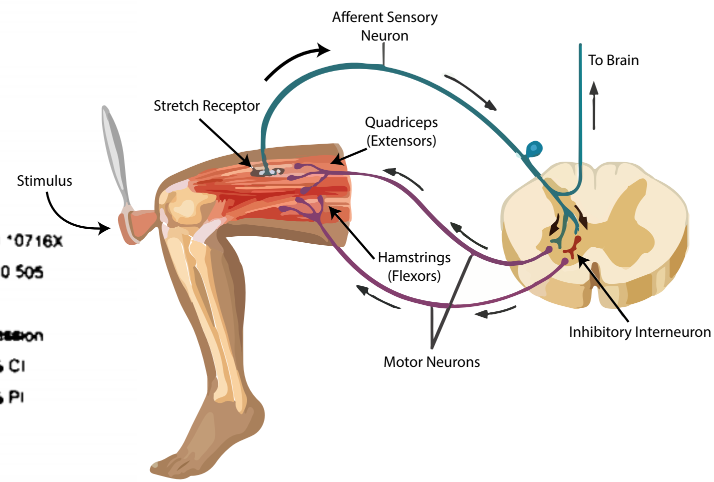


Simplest behaviors are….Reflexes

- What is a reflex?
  - a reaction in response to a stimulus not requiring conscious awareness .
- Examples?
- Let's try one the patellar tendon reflex or more generally called a myotatic or stretch reflex
- Let's step though this reflex to get an overview of how the nervous system functions.
- We will spend the next 30 min, discussing an event that takes <u>20 milliseconds</u> . - Again, this is an overview! We will be spending the next months on the details

The patellar tendon reflex has a very short latency between stimulus and reaction (~20 msecs). This is more than 10 times quicker than the consciously reaction time tested last week (>200 msecs)



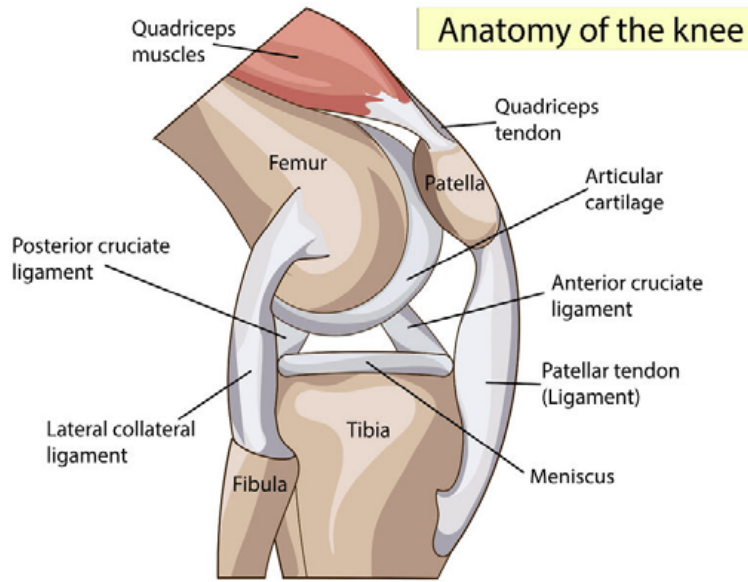


Clinical Neurology and Neurosurgery 99 (1997) 31–36

Reflex latency is also shorter in shorter people (why?).

Steps in myotatic reflex

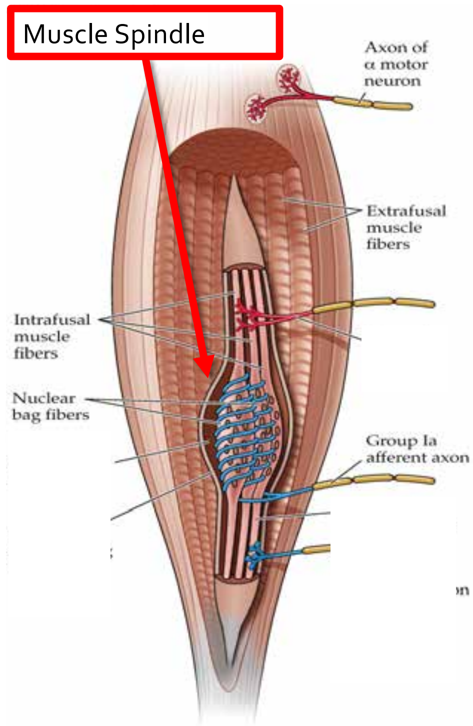
- Stimulus: stretch quadriceps muscle by tapping patellar tendon with rubber hammer.



https://www.jeffreybergmd.com

Steps in myotatic reflex

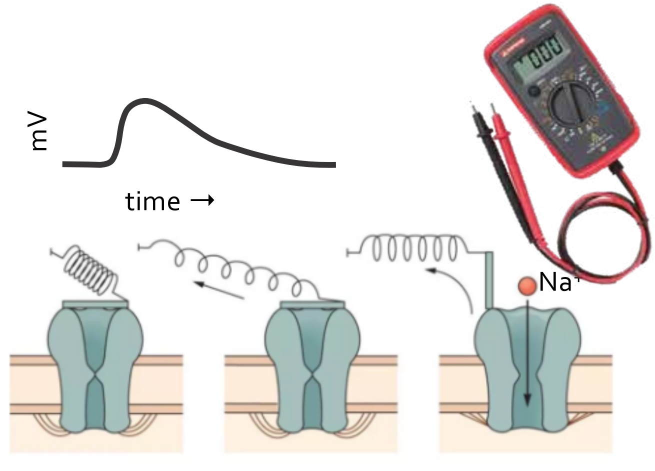
- Stimulus: Stretch quadriceps muscle by tapping patellar tendon
- Transduction: Convert stimulus (e.g. mechanical) into an electrical signal.
    - Sensory apparatus in muscle as a “spindle” that is innervated by sensory afferent Ia “one-A axon”
    - The stretch of the sensory ending causes positive ions to flow into the axon, making the inside of the axon less negative (**Receptor potential**)



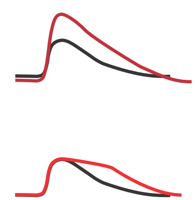
NEUROSCIENCE 6e, Figure 16.10 (Part 1)

Steps in myotatic reflex

- Stimulus: Stretch quadriceps muscle by tapping patellar tendon
- Transduction: Convert stimulus (e.g. mechanical) into an electrical signal.
  - Sensory apparatus in muscle as a "spindle" that is innervated by sensory afferent Ia "one-A axon"
  - The stretch of the sensory ending causes positive ions to flow into the axon, making the inside of the axon less negative (**Receptor potential**)
  - Measure these potentials as changes in voltage



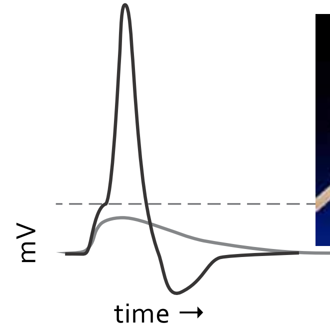
- Larger stimulus, larger receptor potential (more channels open)
- Longer stimulus, receptor potential longer in duration (channels stay open longer)

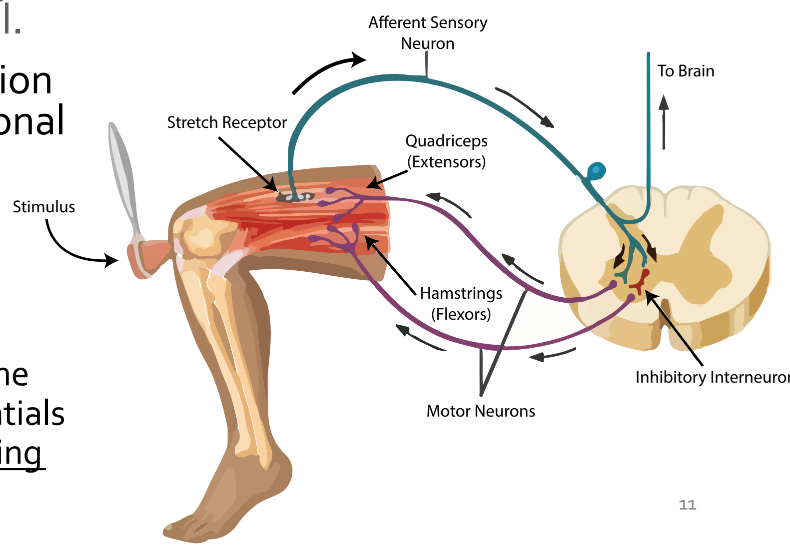


"Graded Potentials"

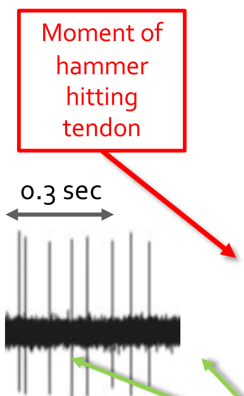
Steps in myotatic reflex

- 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)
  - If stretch is strong enough, the local potential reaches the threshold and triggers an action potential
  - Action potentials are “all or none”
  - The stronger the receptor potential the greater the frequency of action potentials (APs per second) → frequency encoding

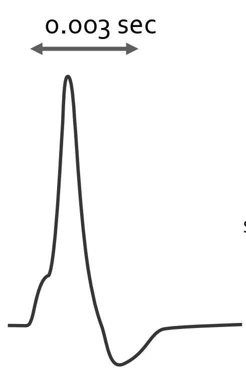


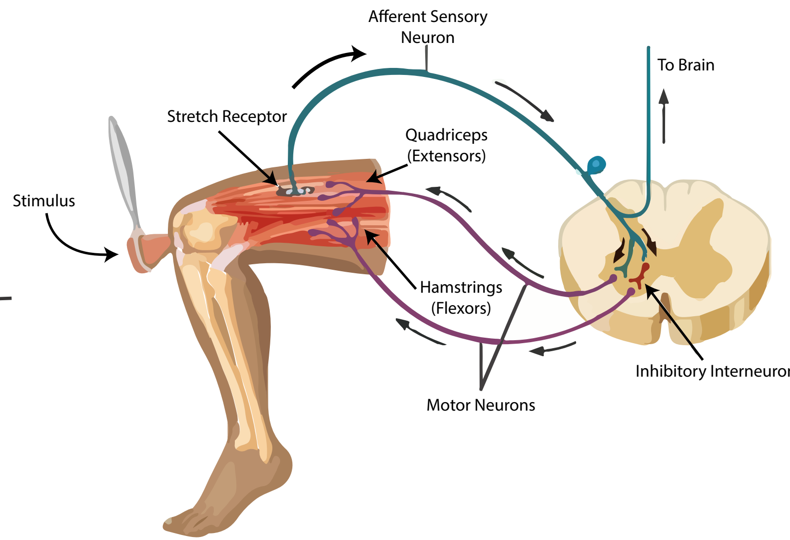


Action potentials recorded in the sensory neuron during myotatic reflex



Recording of action potentials in a Ia axon

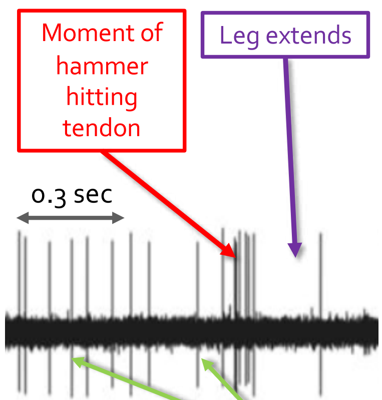




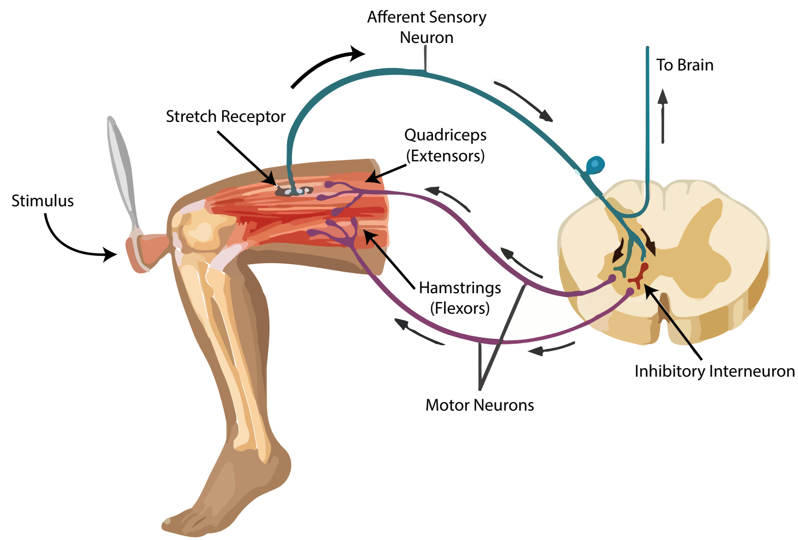
What happens to the Ia activity after the tap is completed?

- The activity level returns quickly to the baseline level of intermittent firing
- It increases in frequency until the foot is back to is resting position
- The activity stops abruptly as the foot extends
- The activity level remains high but does not increase or decrease until the foot returns to its resting position

Action potentials recorded in the sensory neuron during myotatic reflex



Recording of action potentials in a Ia axon



What happens next?

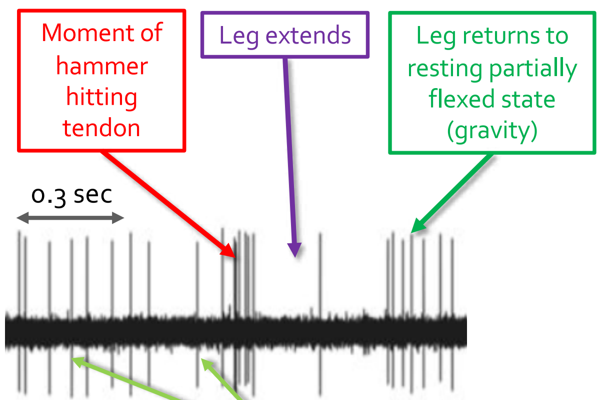
The activity level remains low at a new set point

The activity suddenly returns to its previous baseline value when the leg returns to its resting position

The activity level oscillates between high and low valaues

There is really no way of predicting what will happen next

Action potentials recorded in the sensory neuron during myotatic reflex



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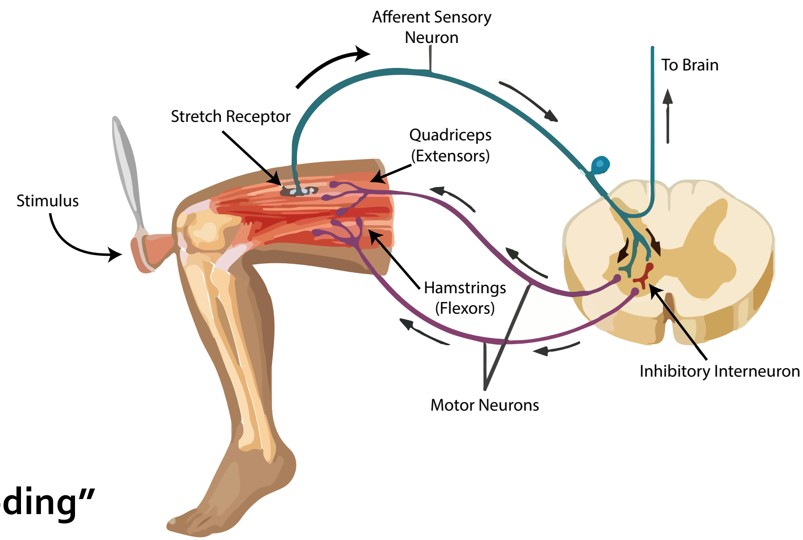
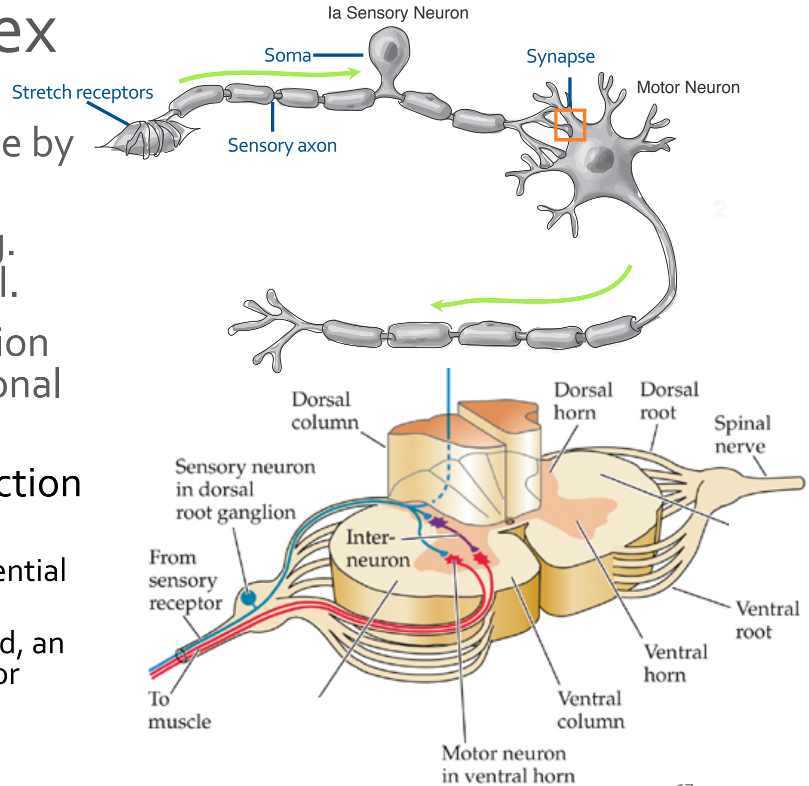


"Frequency coding"

Steps in myotatic reflex

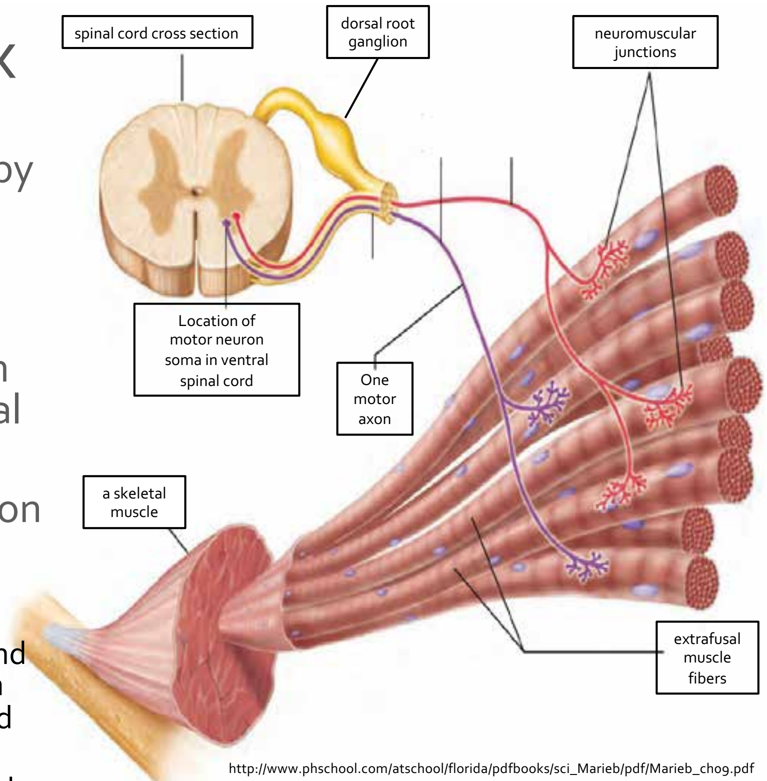
- Stimulus: Stretch quadriceps muscle by tapping patellar tendon
- Transduction: Convert stimulus (e.g. mechanical) into an electrical signal.
- Encode: converts sensory information (local receptor potential) into neuronal code (action potential)
- Sensory-motor synapse elicits an action potential (AP) in the motor neuron
  - The sensory neuron elicits a synaptic potential (graded potential) in the motor neuron
  - If the synaptic potential is above threshold, an action potential will travel down the motor neuron axon



NEUROSCIENCE 6e, Figure A6 (Part 2)

Steps in myotatic reflex

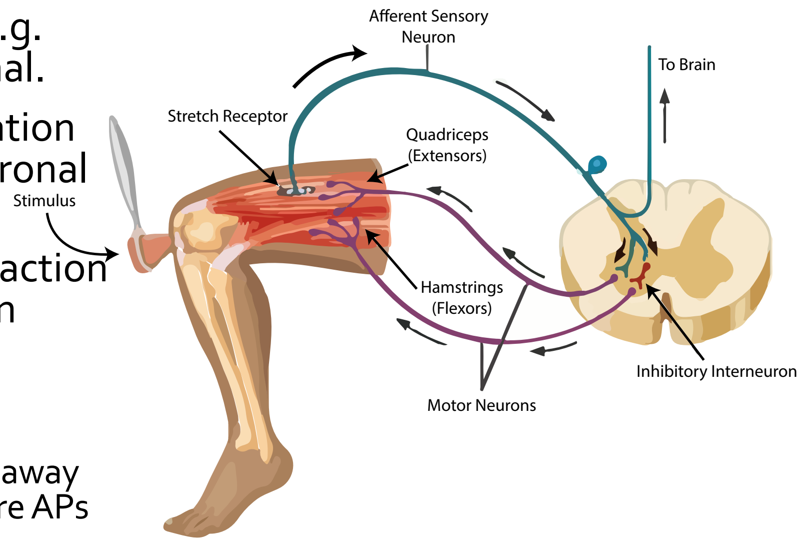
- Stimulus: Stretch quadriceps muscle by tapping patellar tendon
- Transduction: Convert stimulus (e.g. mechanical) into an electrical signal.
- Encode: converts sensory information (local receptor potential) into neuronal code (action potential)
- Sensory-motor synapse elicits an action potential (AP) in the motor neuron
- Muscle fiber activation
  - Large synapse between the motor neuron and muscle fiber (neuromuscular junction), when activated brings the muscle to threshold, and causes the muscle to contract
  - Strength of contraction is related to the number of motor neurons activated and frequency of APs



http://www.phschool.com/atschool/florida/pdfbooks/sci_Marieb/pdf/Marieb_ch09.pdf

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
  - Inhibitory synaptic potentials move away from threshold, thus less likely to fire APs



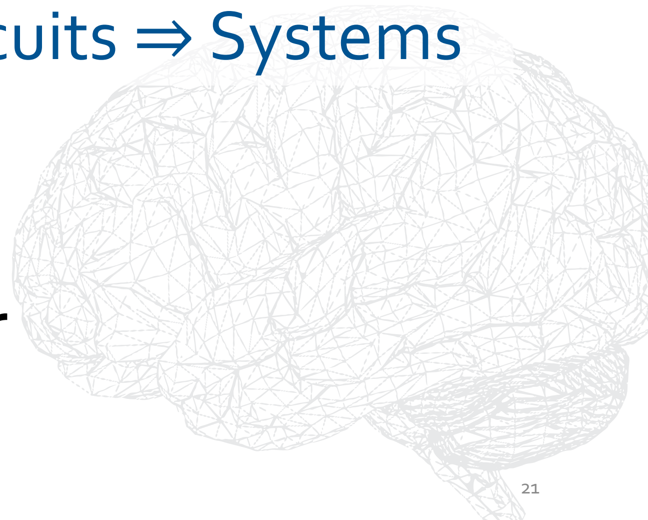
Principles of neural signaling

1. Transduction converts one type of stimulus to another (mechanical <-> electrical<-> chemical)
2. Electrical signals are the common language of the nervous system
3. Changes in local (graded) electrical potentials trigger propagated (all-or-none) electric potential changes
4. …at threshold
5. Inhibition enhances computational repertoire.
6. Specificity of neural connections give them meaning.

Brain

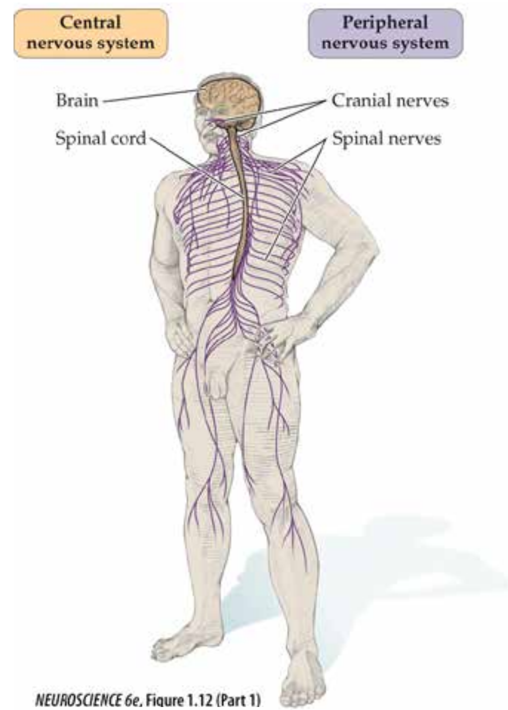
Molecules ⇒ Cells ⇒ Circuits ⇒ Systems

Behavior



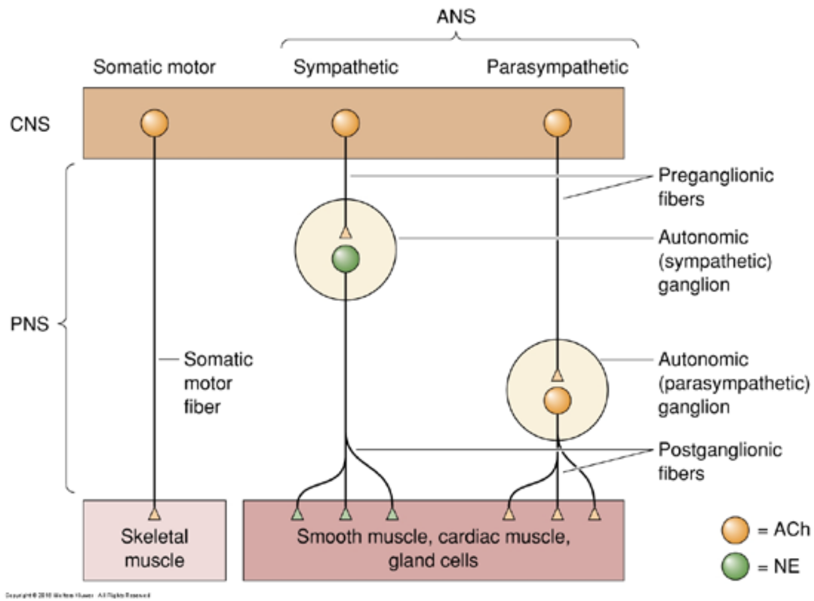
Organization within the nervous system

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



NEUROSCIENCE 6e, Figure 1.12 (Part 1)

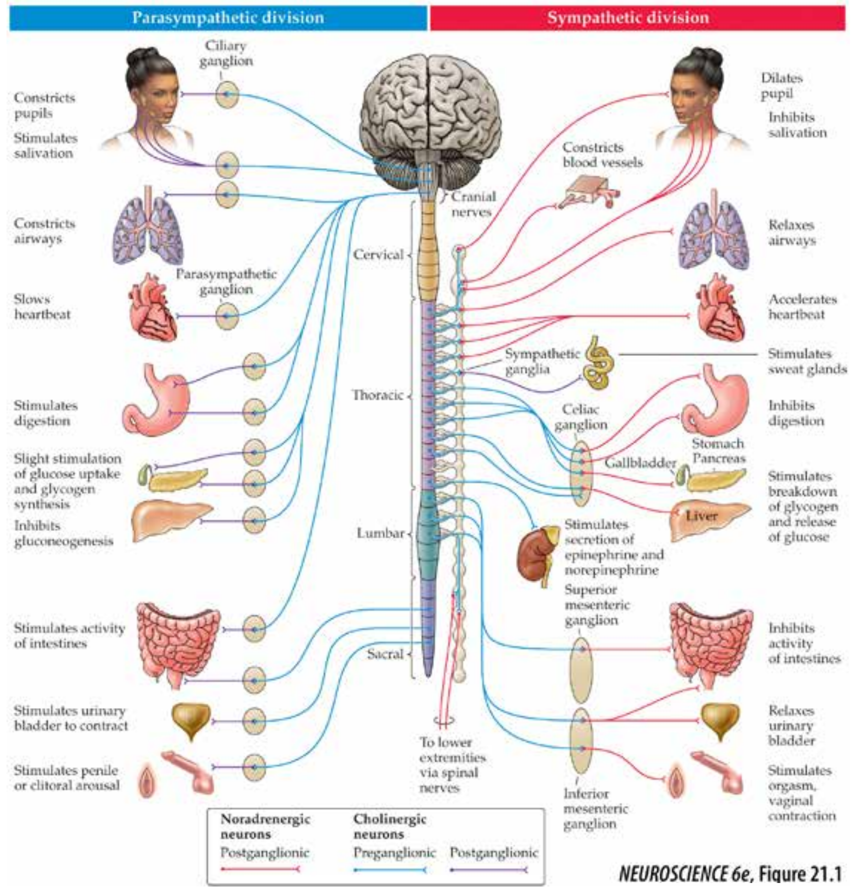
Autonomic Nervous System



- Controls internal milieu
- Examples:
  - peristalsis of stomach
  - heart rate
  - blood pressure
  - pupil diameter
  - salivation
  - etc.
- Continuous adjustments
- Unconscious
- Involuntary
- Automatic

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
Digestive activities	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 thoracic and lumbar



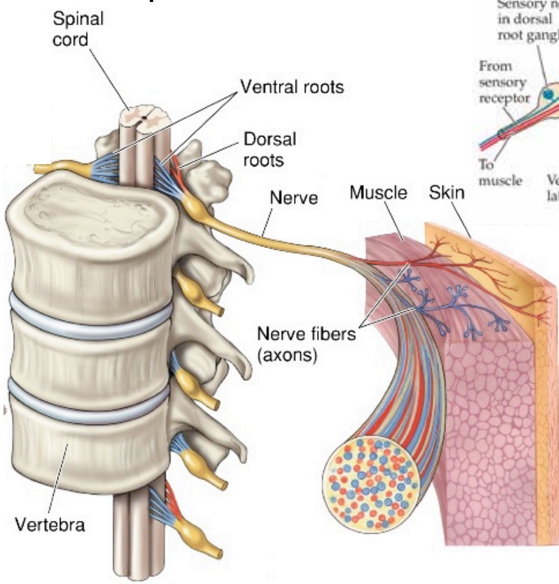
NEUROSCIENCE 6e, Figure 21.1

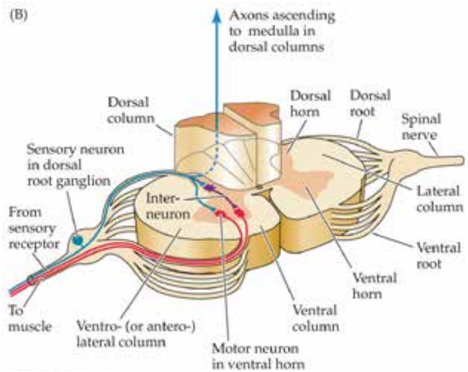
During activation of the parasympathetic nervous system, there is increased ___

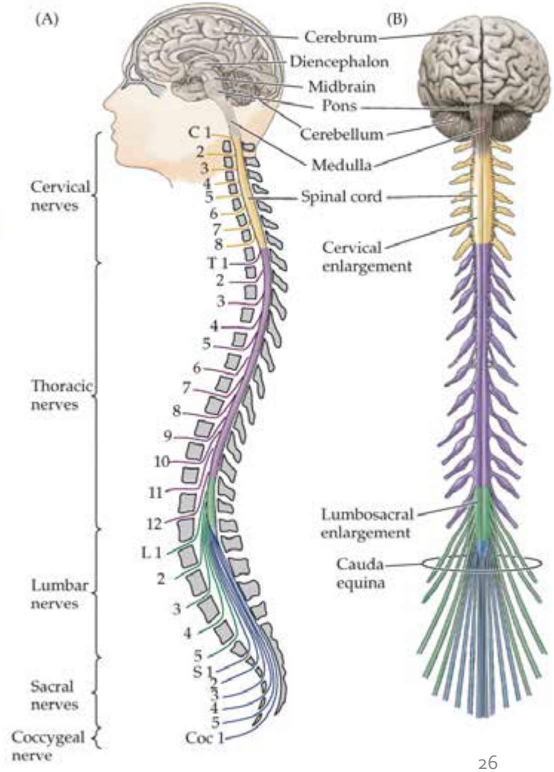
The central nervous system

(from bottom to top)

- Spinal cord



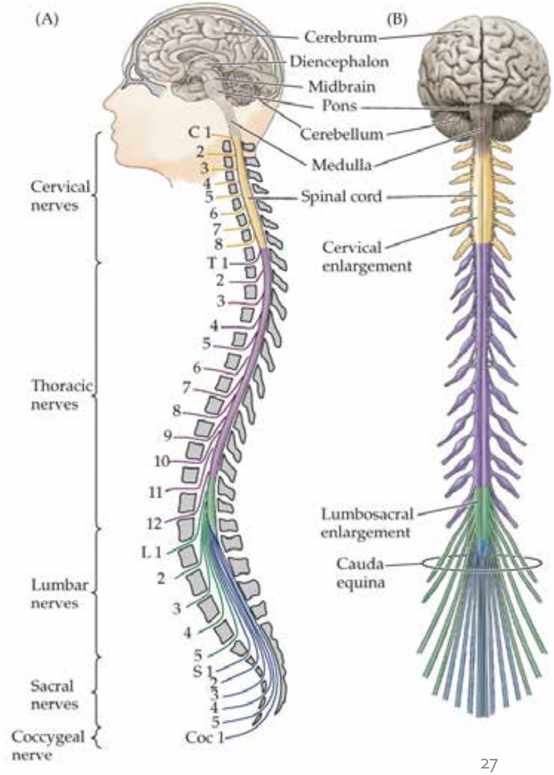




NEUROSCIENCE 6e, Figure A3

The central nervous system

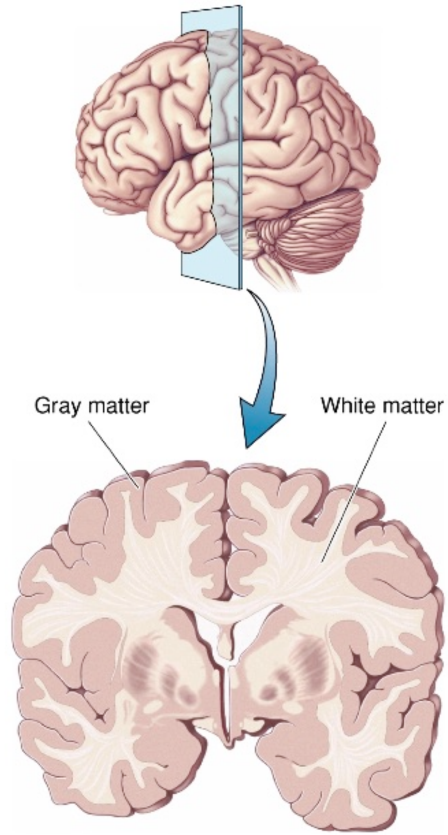
- Spinal cord
- Medulla and pons-(brainstem)- respiration, circulation, posture, “maintenance” and “vital” functions
- Midbrain - auditory and visual centers, esp. "unconscious" vision – eye movement and startle reflexes, motion sensitivity
- Cerebellum - muscle and reflex coordination
- Diencephalon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



NEUROSCIENCE 6e, Figure A3

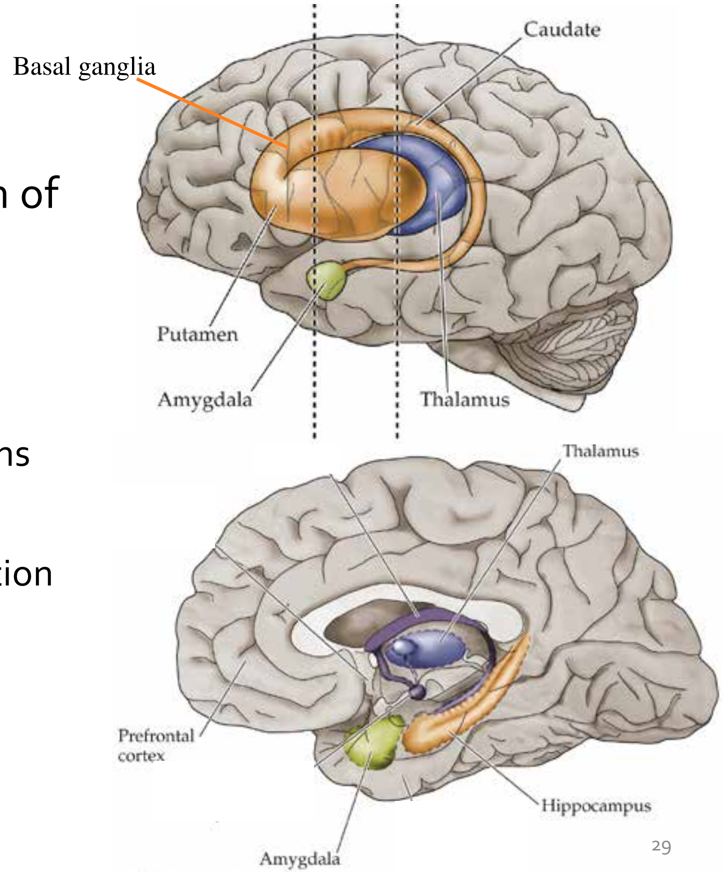
Cerebrum

- Cerebral cortex – outer, folded rim of gray matter
  - “Neocortex” organized into layers
  - Gyri – bumps/ridges
  - Sulci – small grooves/valleys
  - Fissures – deep groves, divide regions

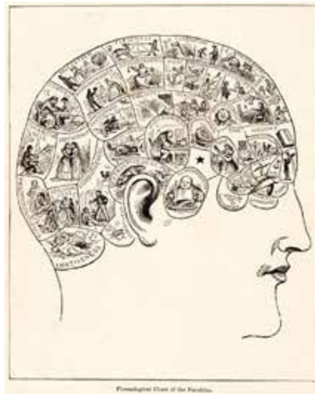
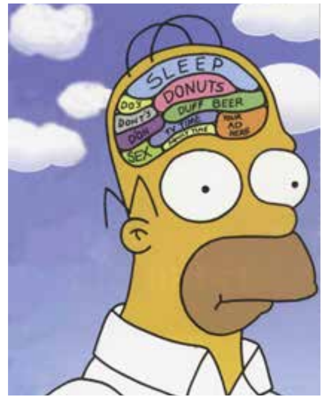


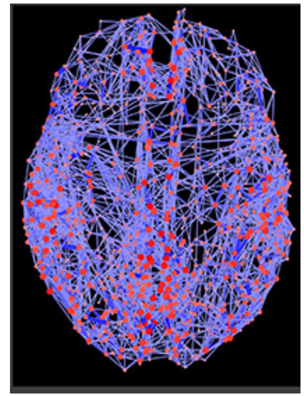
Cerebrum

- Cerebral cortex – outer, folded rim of gray matter
  - "Neocortex" organized into layers
  - Gyri – bumps/ridges
  - Sulci – small grooves/valleys
  - Fissures – deep groves, divide regions
- Subcortical regions
  - Basal ganglia – initiation and execution of movement
  - Amygdala – fear, emotion
  - Hippocampus – memory



Localization of brain function

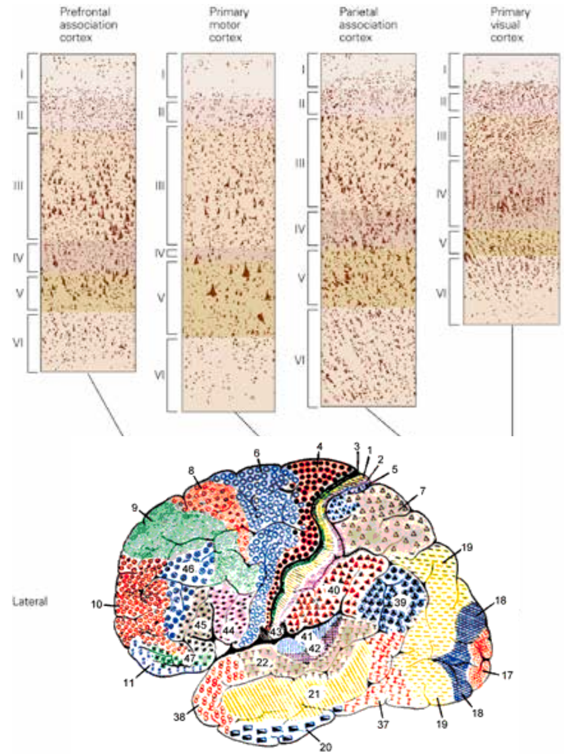






- Phrenology (early 1800's)
    - Mental abilities mapped to distinct brain regions based on external skull shape (and speculation!)
- Modern View – Complex network of interconnected modules
    - Brain regions act as modules for specialized processing
    - Local circuits perform computations within each area
    - Different regions have specialized functions but my be involved in numerous behaviors (multifunctional)
    - Systems are integrated with each other, so in the end none is completely distinct

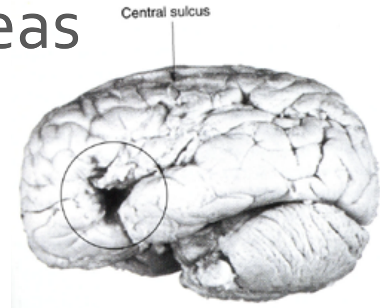
Determining function of brain areas

- Histological mapping
  - Karl Broadmann (1868-1912). Anatomical studies revealed differences in neuron shape, size and arrangement. Some sharp boundaries and differences among layers. Suggested <u>functional distinctions</u>

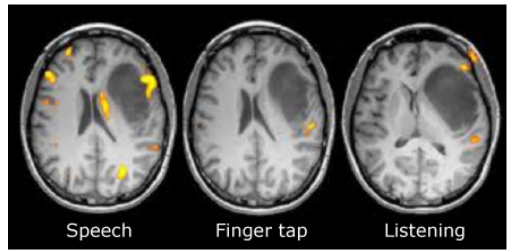


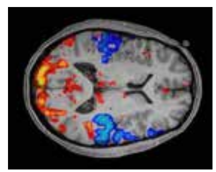
Determining function of brain areas

- Histological mapping
  - Karl Broadmann (1868-1912). Anatomical studies revealed differences in neuron shape, size and arrangement. Some sharp boundaries and differences among layers. Suggested <u>functional distinctions</u>
- Functional mapping
  - Lesion studies: what happens after damage
  - Direct brain stimulation
  - Direct recording (microelectrodes) – what stimulus do neurons respond to?
  - fMRI – measure blood flow in different brain regions during behavior



Paul Broca and Speech areas

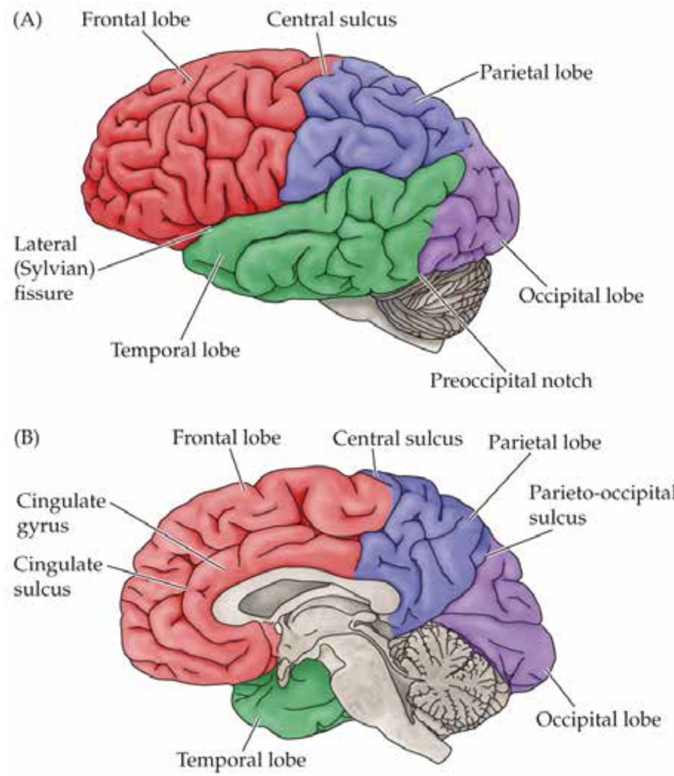




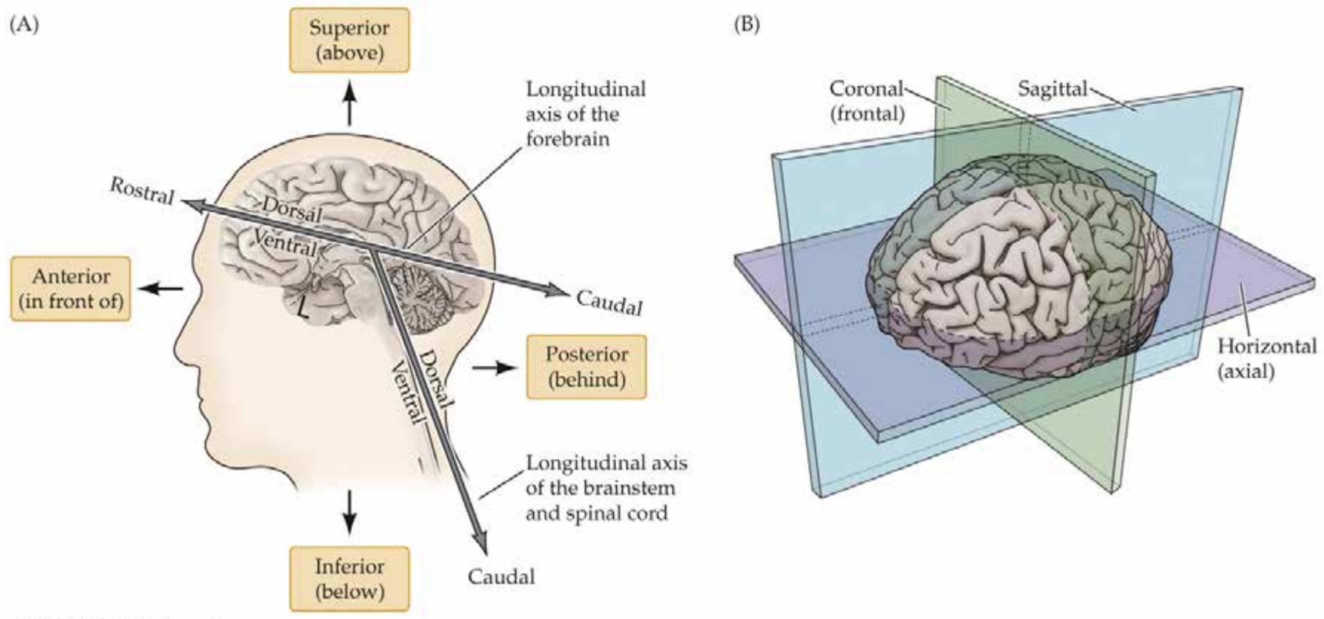
Activity is always relative – usually compared to "resting" control

Cerebral cortex

- Frontal lobe
  - executive function, decision making, personality, motor planning
- Parietal lobe
  - sensation (touch, temp, taste, pain) and integrating sensations
- Occipital lobe
  - Processing, integrating and interpreting visual information
- Temporal lobe
  - Hearing, language comprehension, memory formation and retrieval



Neuroanatomical terminology



***NEUROSCIENCE 6e*, Figure A1**

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

Lecture 3 - Circuits of the nervous system

Pre-class notes for September 11, 2019
Reading: *Neuroscience* by Purves et al. 6th edition, pages **10-16**

The nervous system is an amazingly complex, intricate, yet organized organ. The myriad cell types make billions of connections, but neurons do not function in isolation. They are organized into ensembles called n**euronal circuits**, which are synaptically connected neurons that carryout a specific function (e.g. reflex circuit, visual circuit). Neuronal circuits are the basic building blocks of behavior. A stimulus is sensed by neurons, this information is then transmitted and processed via electric signals through the nervous system which then causes a response (usually a motor response/movement).

A **reflex**, an automatic (unlearned, involuntary, and sometimes unconscious) response to a *stimulus*, is the simplest behavior. Reflexes are often mediated by relatively simple neuronal circuits, yet they demonstrate virtually all of foundational principles of neurobiology. As an overview and introduction to neural signaling, we will go through a circuit, introducing terms and concepts, the details of which will be explored in later lectures.

Stimulus - an extrinsic or intrinsic signal that causes a response. In sensory systems, the nature of the stimulus is specific to the sensory modality and the type of sensory receptors activated.

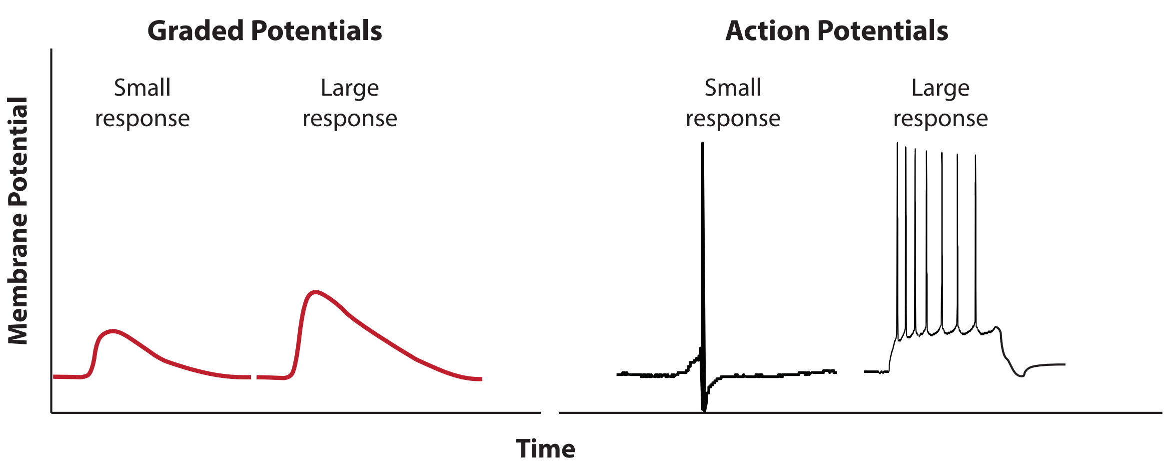
Electrical signal - the nervous system uses electrical signals, that is transient changes in the electrical potential difference across neuronal membranes (*membrane potential*), to propagate information. Details of electrical signals will be covered in lectures 4-10.

Graded potential - an electric signal that changes the membrane potential in a continuous manner (oppose to unitary, or "all or none" manner) typically in a small region of a neuron. Graded potentials can differ in size, shape, or duration, depending on the stimulus and response properties of the responding neuron. Graded potentials are commonly found at sensory receptors and synapses.

Receptor potential - a graded potential in the dendrites of a sensory neuron in response to a stimulus. A larger stimulus will create a larger potential. If the *threshold* to fire an action potential is met, an action potential will be initiated in the sensory neuron.

Action potential - an actively propagated impulse that conveys information across long distances. Action potentials are considered unitary or "all or none" such that the size and duration of each action potential remains constant. Details will be covered in later lectures.

Frequency coding - since action potentials are unitary in size and duration, the strength of the signal is determined by the frequency of the action potentials. A stronger signal increases the frequency of action potentials (i.e. number of action potentials per second).



Signal transduction - converting one kind of signal or stimulus into another type (e.g. mechanical stimulus to electrical signal or electrical signal to chemical signal).

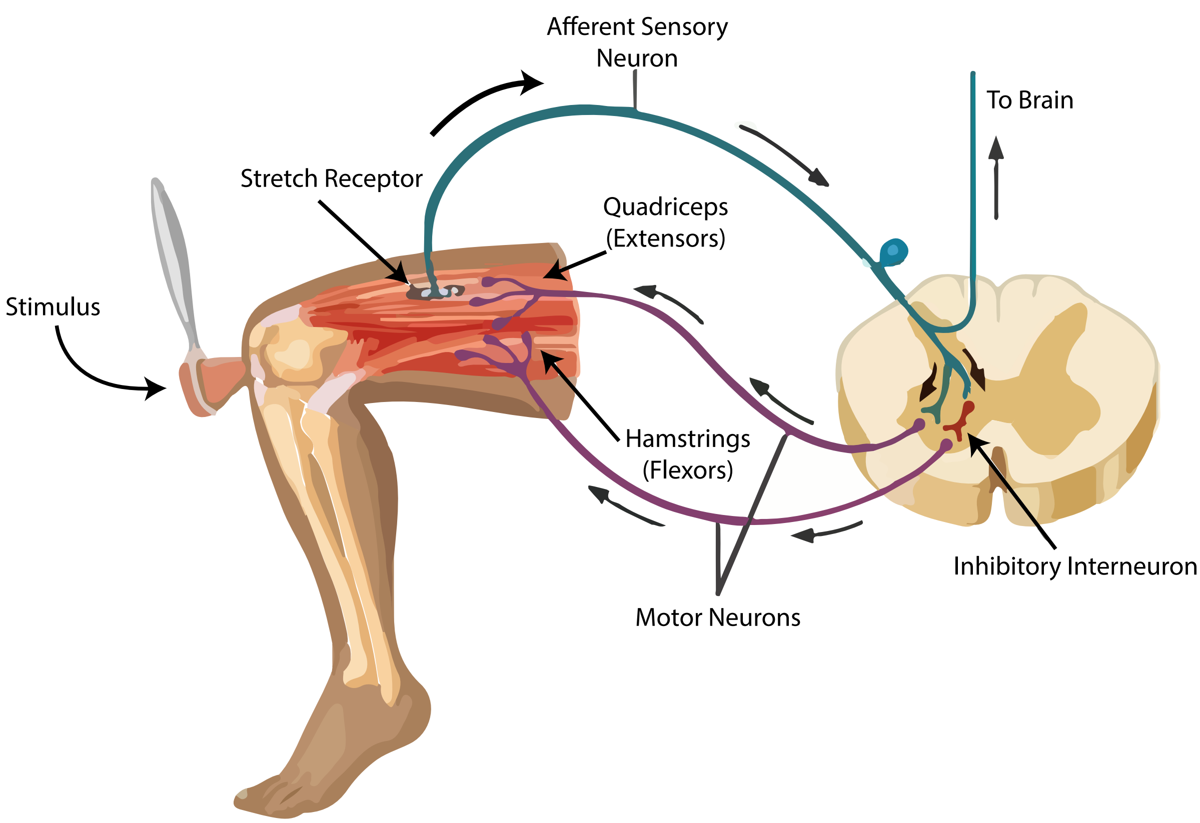
Excitatory neuron - a neuron, that when active and fires action potentials, increases the probability that the neurons it connects to via synapses will also fire an action potential.

Inhibitory (often an interneuron) - a neuron, that when active, that is fires action potentials, decreases the probability that the neurons it connects to via synapses will fire an action potential. Many inhibitory neurons do not send their axons very far, making local connections and are referred to as interneurons.

Sensory neuron - type of *afferent* neuron (a cell that carries sensory information *toward* the brain from the periphery).

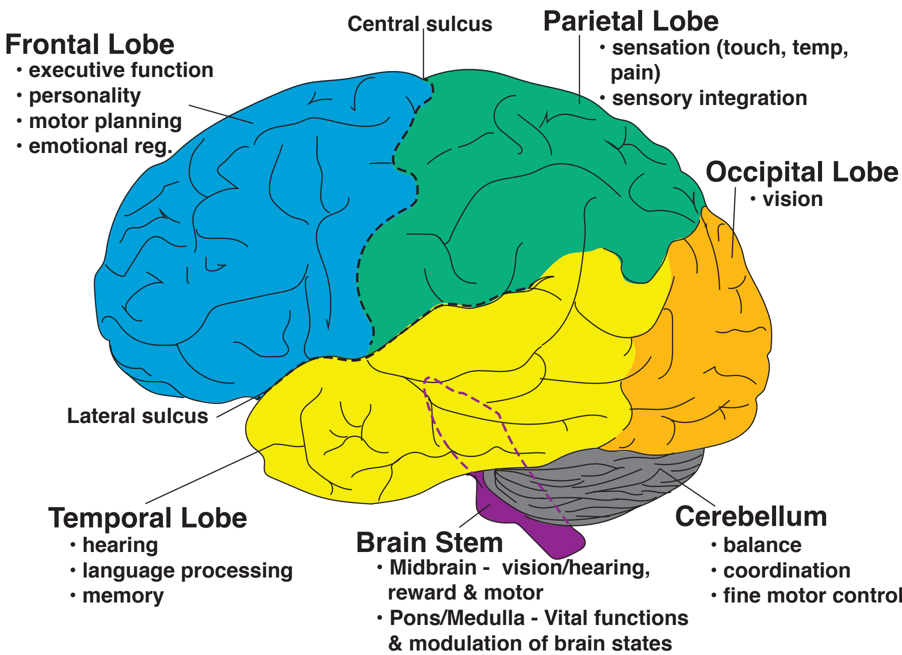
Motor neuron - type of *efferent* neuron (a cell that carries information *away* the brain to the periphery) that synapses onto skeletal muscle fibers.

Myotatic stretch reflex - also known as the knee-jerk response. Stimulating the stretch receptors in the quadriceps muscle initiates a receptor potential which then triggers an action potential in the sensory neuron. The action potential travels up the axon to the spinal cord where the sensory neuron makes a synapse with a motor neuron, causing an action potential in a quadriceps motor neuron axon. The action potential in the motor neuron travels down the leg to the synapse onto a muscle fiber and triggers a muscle contraction and behavioral response (leg extension). In addition to synapsing onto a quadriceps motor neurons, the sensory neuron also makes a synapse onto an inhibitory interneuron. This inhibition prevents the opposing muscle group (hamstrings) from contracting, allowing the leg to extend.



Neurons and neural circuits that process similar types of information make up neural systems. This is a very brief summary of the divisions of the nervous system, you can find more information in the lectures and section materials. The nervous system as a whole can be divided into the **central nervous system (CNS)**, which consists of the brain and spinal cord and the **peripheral nervous system (PNS)**, which consists of the cells outside of the CNS.

The brain is protected by the skull and surrounded by three layers of membranes or **meninges** that cushion and protect the brain. The brain is composed of two bilaterally symmetric hemispheres that are connected by tracts of axons (*white matter*). The **cerebrum** (or *telencephalon)* includes the **cerebral cortex**, the highly folded outer layer of cell bodies (*gray matter*) which is subdivided into lobes, and some subcortical regions: the **basal ganglia** (movement initiation), the **amygdala** (fear and emotions) and **hippocampus** (memory).



Beneath the cerebrum, is the **diencephalon**, which is further divided into the **thalamus** and **hypothalamus**. The thalamus relays (and processes) sensory information and sets conscious brain states (including sleep and attention). The hypothalamus regulates the brain and body by controlling hormonal release into the blood stream for wide ranging effects. The **cerebellum** is posterior and caudal to the cerebrum and is critical to fine motor control and motor learning. The brain stem is a evolutionarily old part of the nervous system and controls our vital

The PNS largely consists of nerves (bundles of axons) and ganglia (clusters of neuronal cell bodies) that lie outside of the brain and spinal cord and can be divided into the **sensory** and **motor** parts. The sensory components of the PNS send information about the internal and external environment to the CNS. They have their cell bodies in ganglia just outside of the spinal cord and enter via the *dorsal roots*. The motor component of the carries signals from the CNS to either skeletal muscles (via the **somatic motor system**) or smooth muscles, cardiac muscles, or glands (via the **autonomic motor system**). The autonomic nervous system helps control our normal body functions and is further divided into the **sympathetic** (arousing) and **parasympathetic** (calming) systems. These systems are in opposition and the sympathetic "*fight or flight"* system is activated when scared, while the parasympathetic *"rest and digest"* is activated when you are relaxed.

Learning Objectives: (By the <u>end</u> of Lecture 3 you should be able answer the following)

1. List the components of behavior.
2. Describe the anatomical organization and electrical signaling that give rise to the knee jerk reflex circuit.
3. Apply the law of dynamic polarization to label a simple circuit.
4. Create a flowchart or concept map illustrating the organization of the central and peripheral branches of the nervous system
5. Explain the role of the autonomic nervous system and describe the opposing effects of the sympathetic and parasympathetic divisions
6. Know the major functions the location of: the four major lobes of the forebrain (cerebral cortex), the diencephalon, brainstem, cerebellum, and spinal cord.