Neurophysiology
part one

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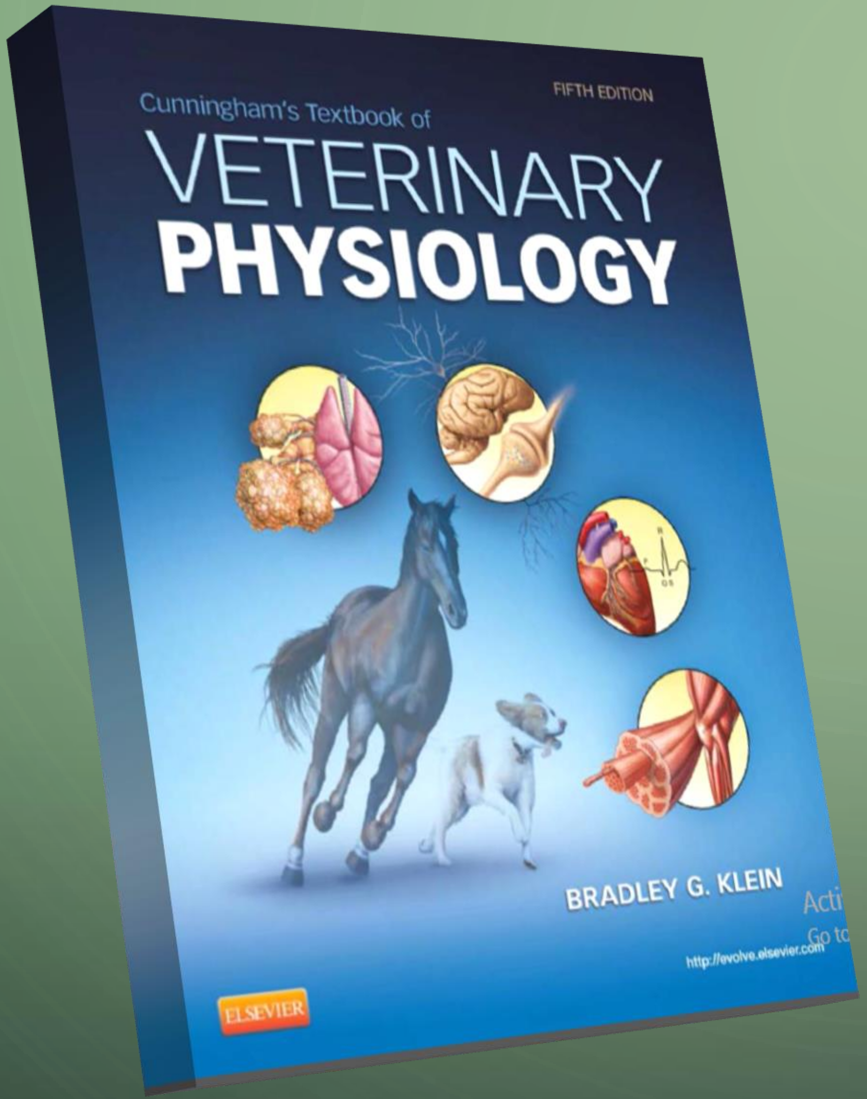

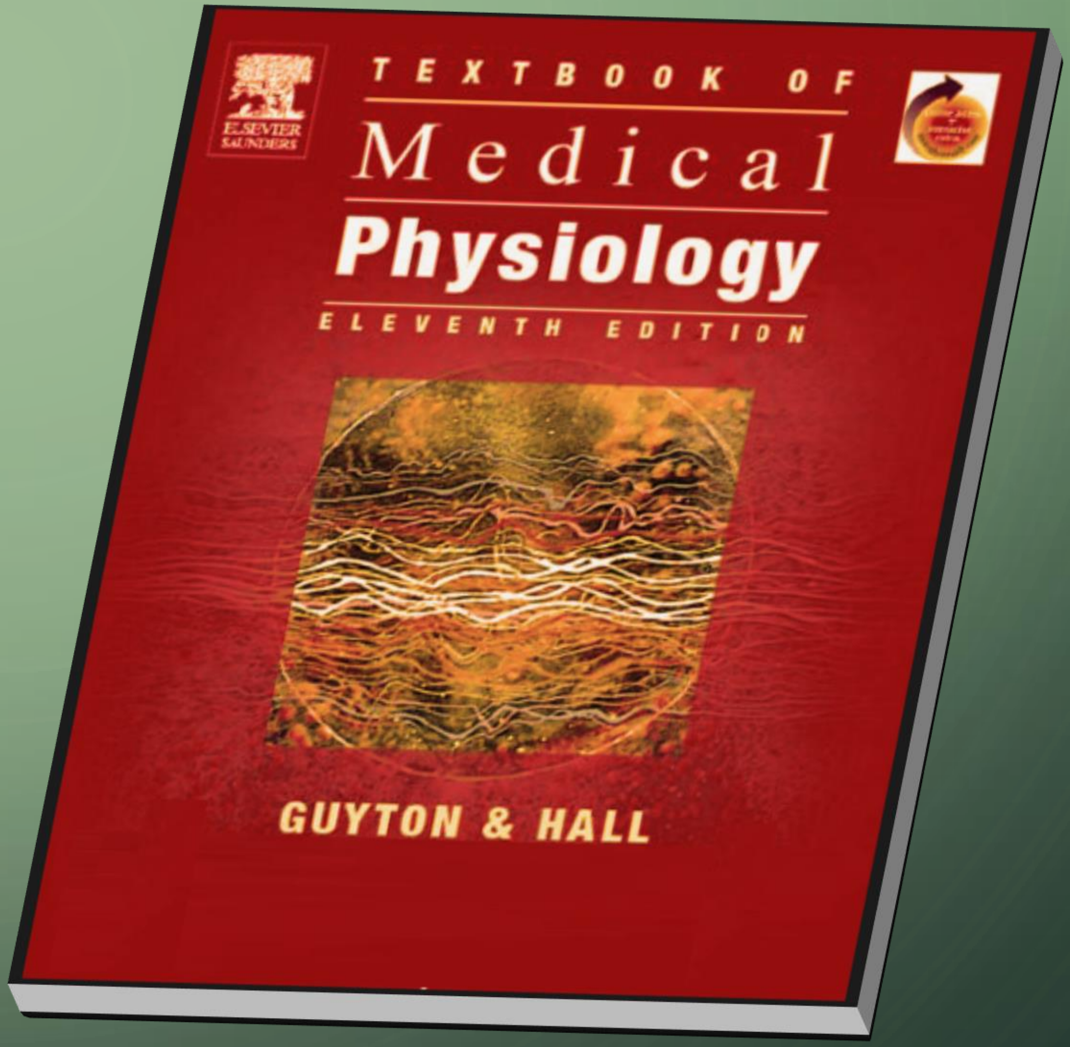

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Introduction

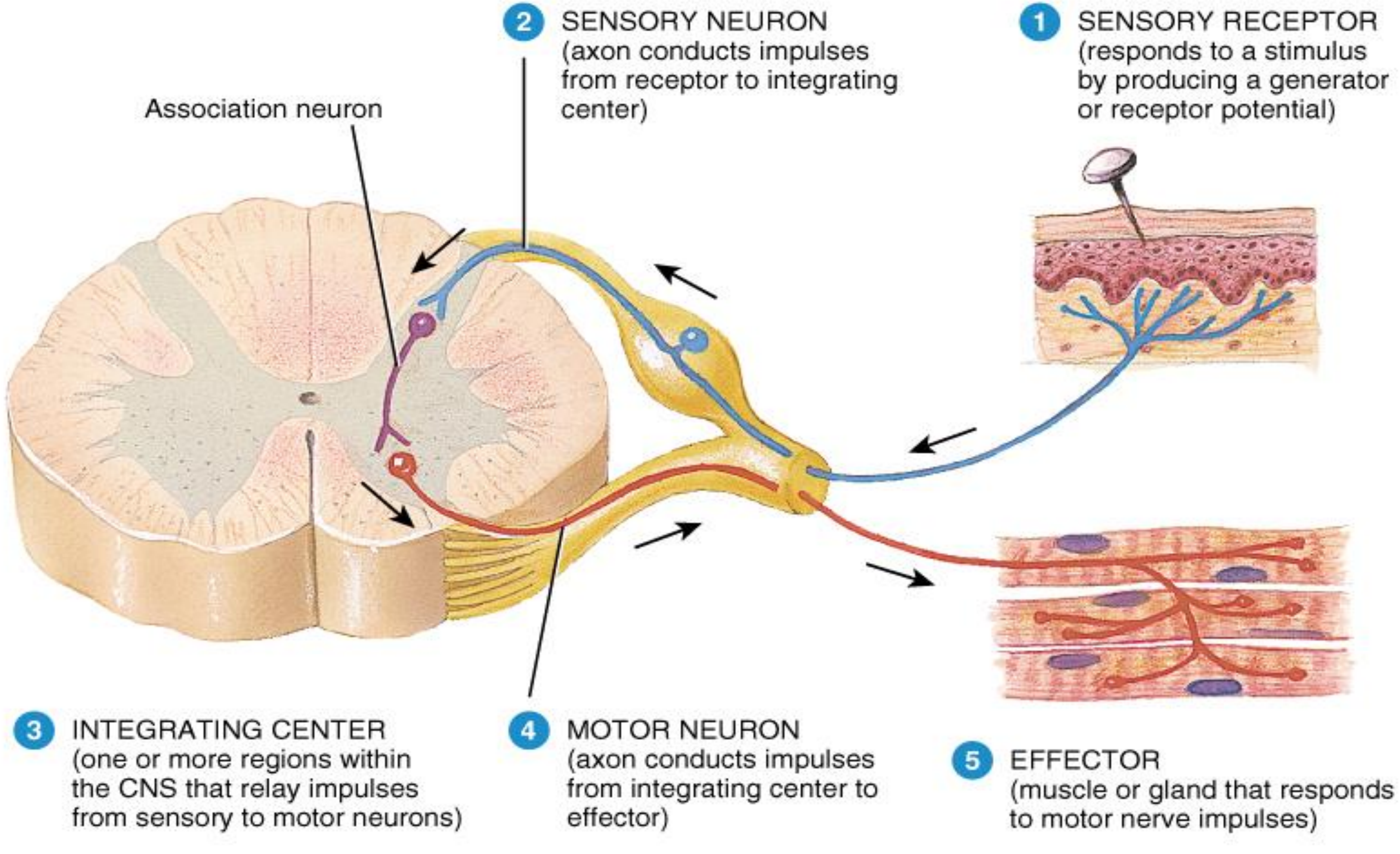
- The nervous system is a highly complex multicellular system which is one of the major coordinating systems of the body.
- Clarifying many of the concepts that concern the nervous system is important for understanding other systems of the body.
- Functions of the Nervous System:
  - communication system of the body.
  - Controls body functions and actions.
  - Maintains physiological homeostasis.

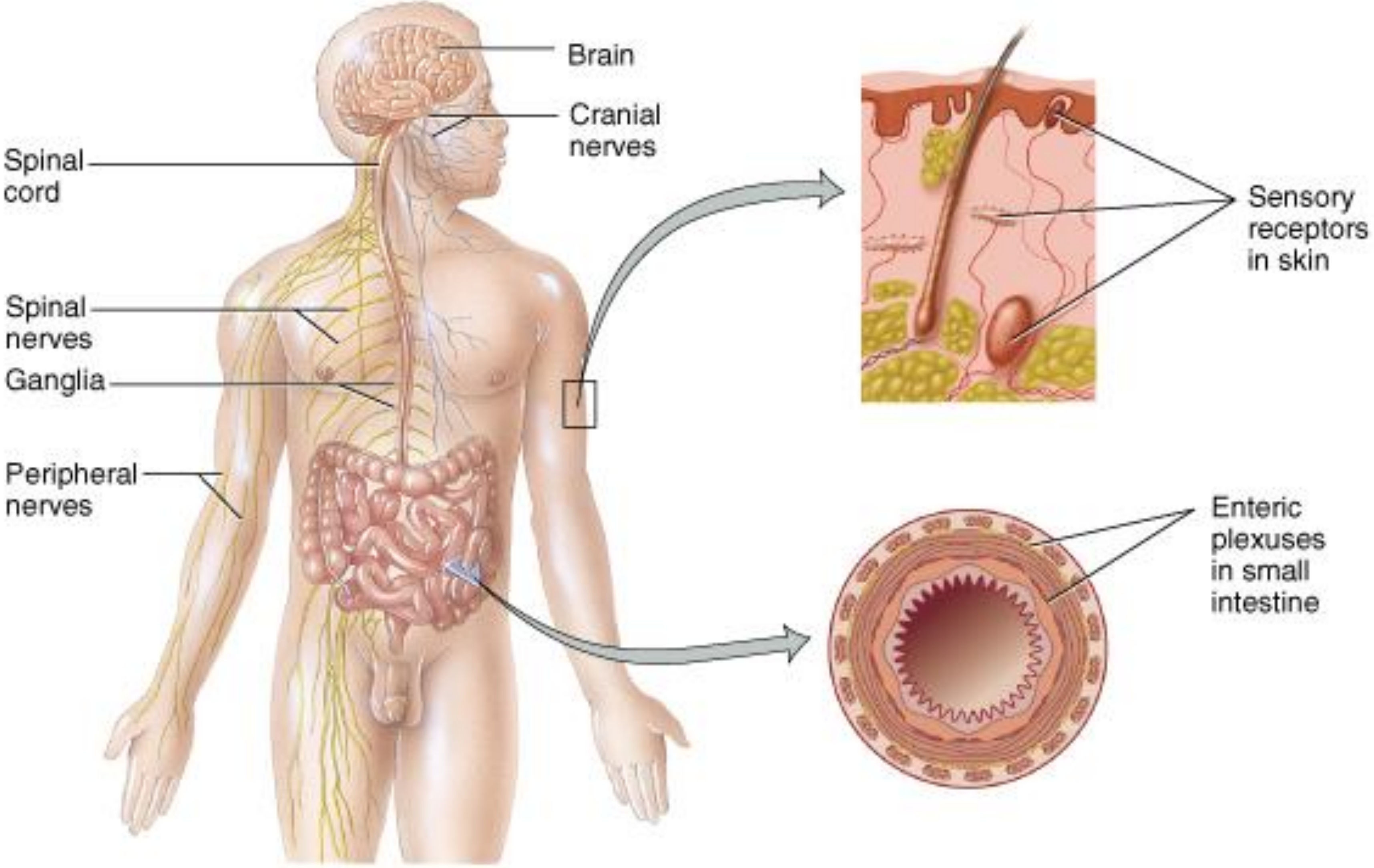
Functions of the Nervous System

- **Sensory Functions:** Sensory receptors detect both internal and external stimuli.
  - Functional unit: Sensory or Afferent Neurons

- **Integrative Functions:** CNS integrates sensory input and makes decisions regarding appropriate responses
  - Functional Unit: Interneurons or Association Neurons of the Brain and Spinal cord

- **Motor Functions:** Response to integration decisions.
  - Functional Unit: Motor or Efferent Neurons


2 SENSORY NEURON
(axon conducts impulses from receptor to integrating center)
1 SENSORY RECEPTOR
(responds to a stimulus by producing a generator or receptor potential)
Association neuron
3 INTEGRATING CENTER
(one or more regions within the CNS that relay impulses from sensory to motor neurons)
4 MOTOR NEURON
(axon conducts impulses from integrating center to effector)
5 EFFECTOR
(muscle or gland that responds to motor nerve impulses)


Brain
Cranial nerves
Spinal cord
Spinal nerves
Ganglia
Peripheral nerves
Sensory receptors in skin
Enteric plexuses in small intestine

Organization of the Nervous System

Central nervous system (CNS)

- Brain
- Spinal cord

Peripheral nervous system (PNS)

Efferent (motor)

- Somatic—to skeletal muscle
- Visceral—to cardiac muscle
  - —to smooth muscle
  - —to exocrine glands

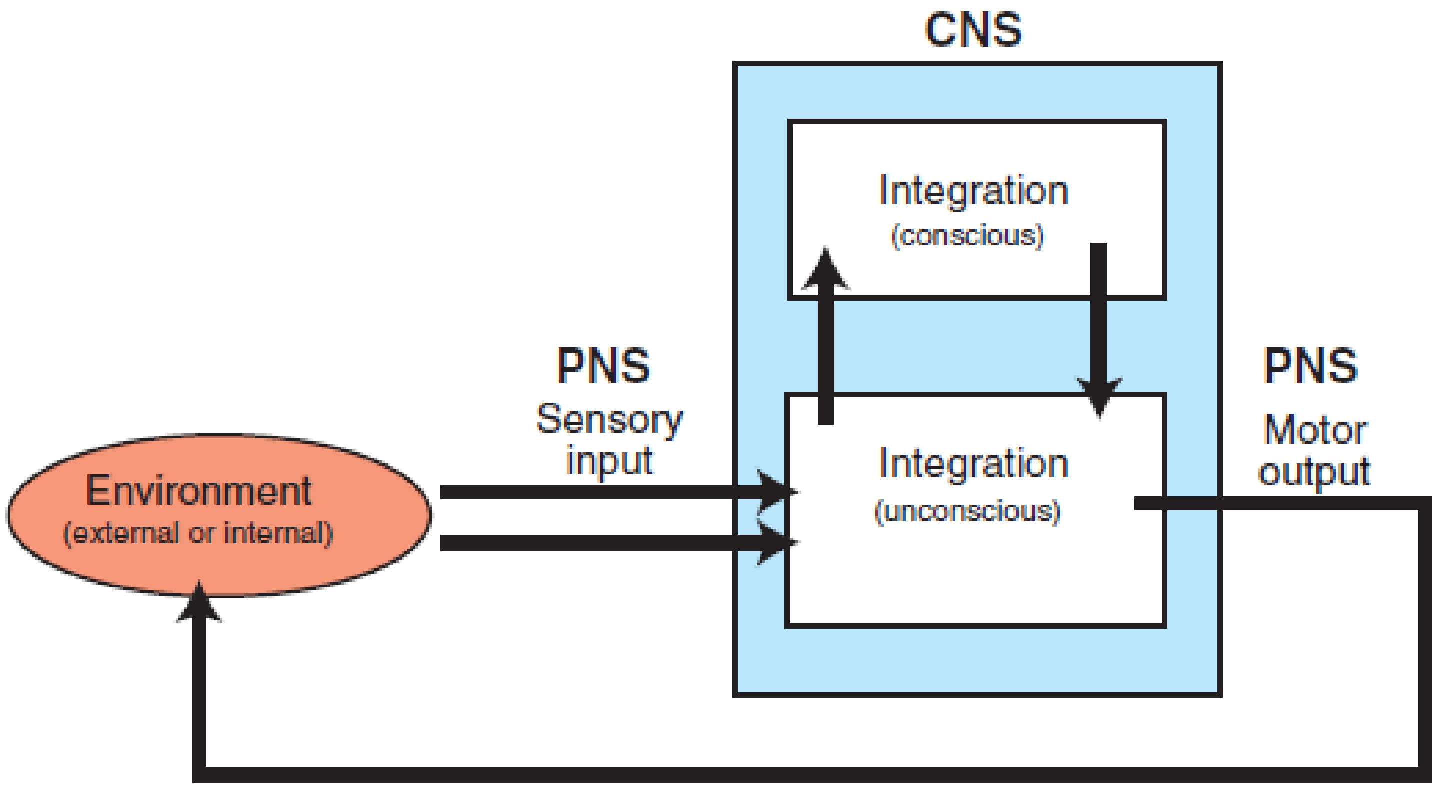
Afferent (sensory)

- Somatic—from skin
  - —from retina
  - —from membranous labyrinth
- Visceral—from thoracic and abdominal organs
  - —from olfactory epithelium
  - —from taste buds

Components of the Nervous System

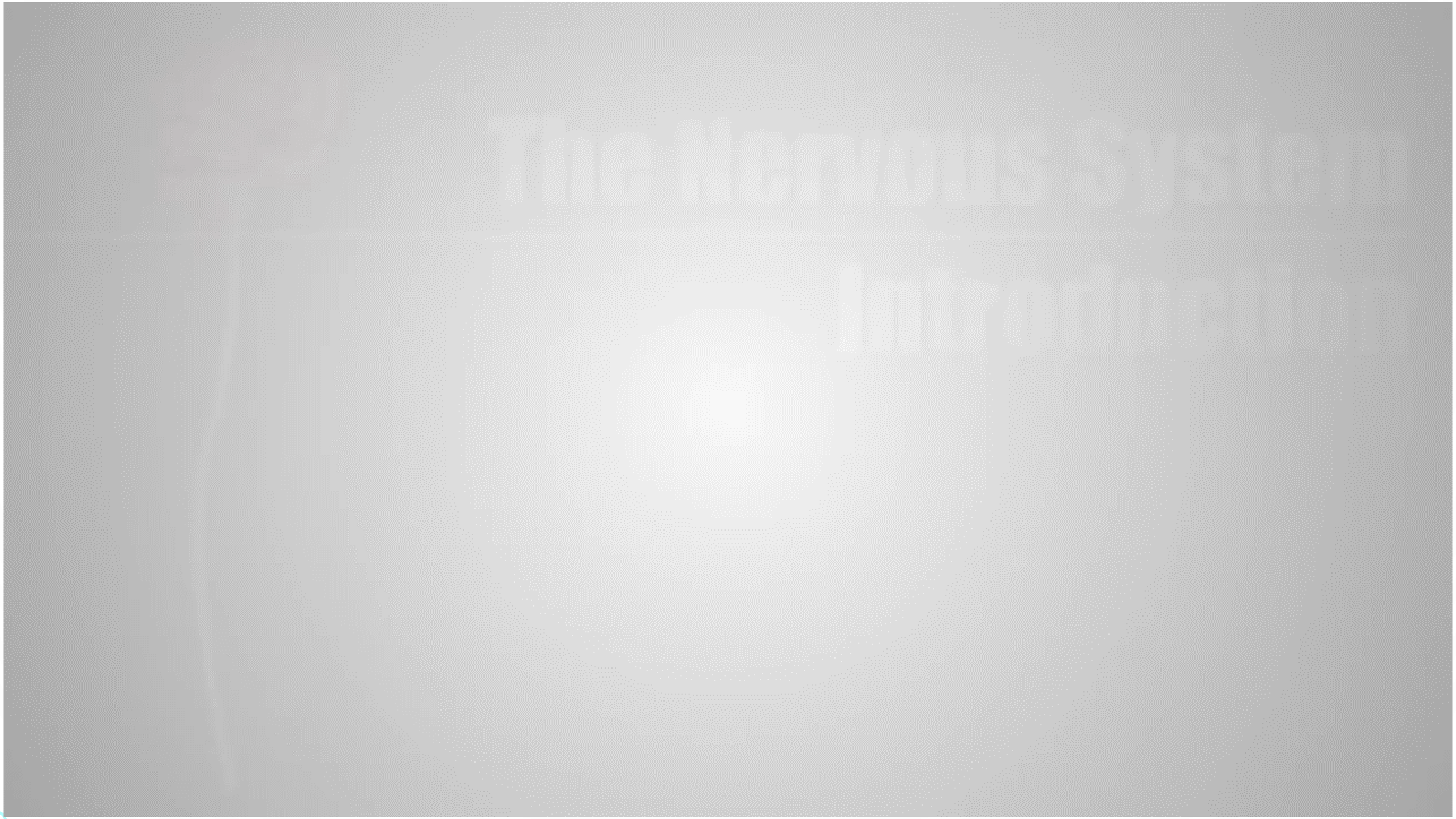
- Central Nervous System
  - Brain
  - Spinal Cord
- Peripheral Nervous System
  - Sensory and Motor Nerves
  - Cranial Nerves
  - Spinal Nerves
- Autonomic
  - Sympathetic
  - Parasympathetic

General Functions of the Nervous System

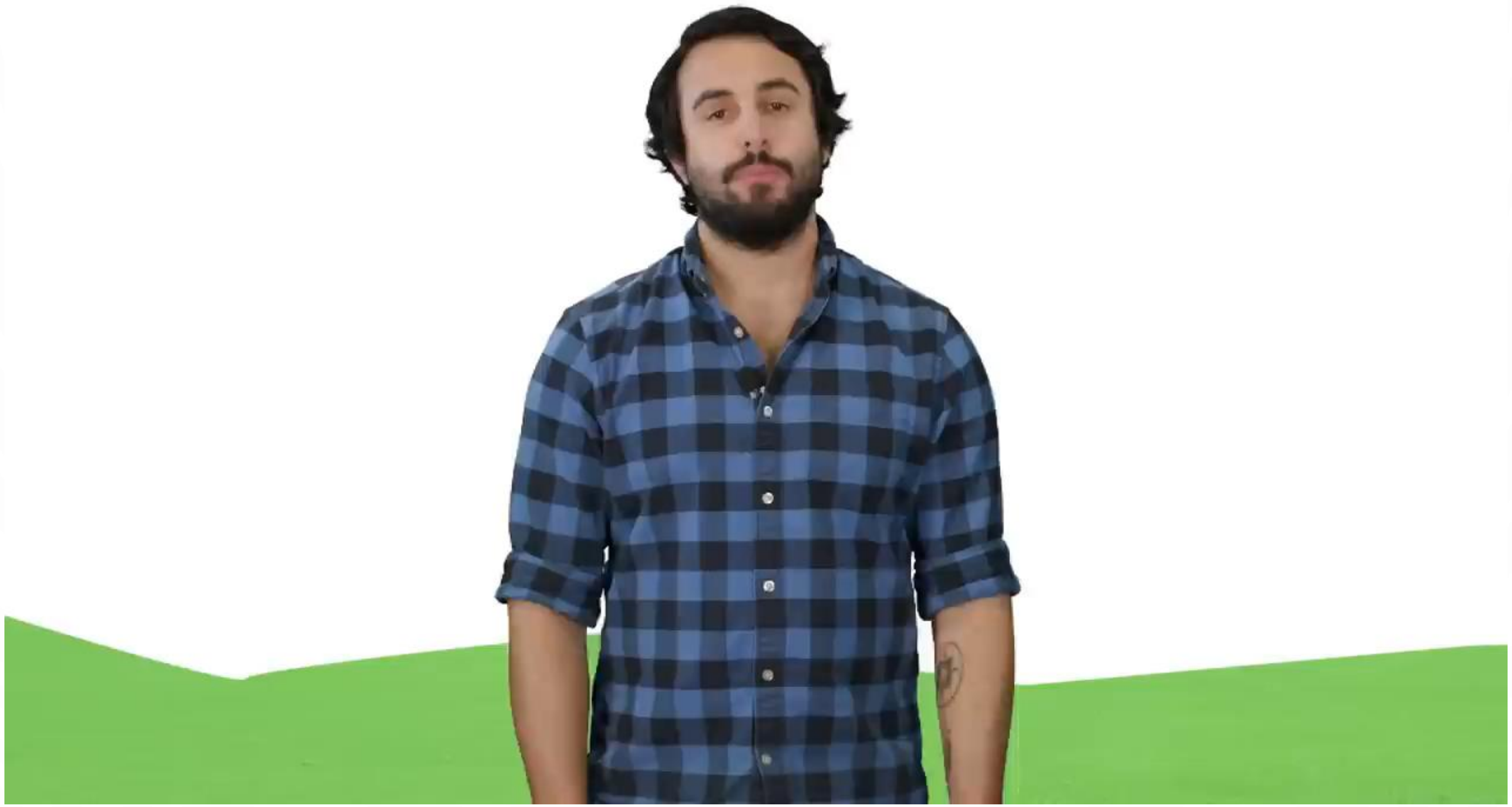


The Nervous System

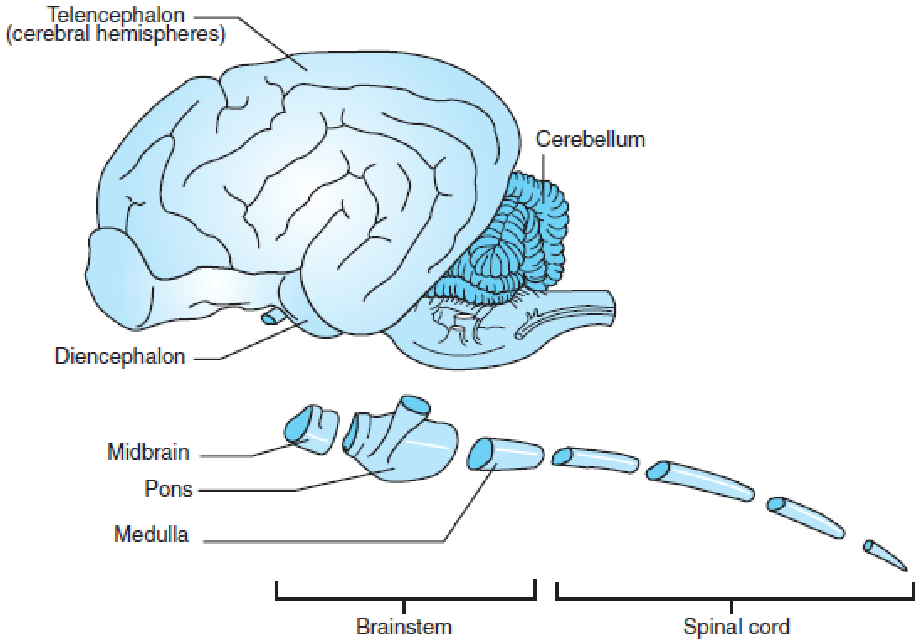
- Central Nervous System (CNS)
  - Brain
  - Spinal Cord
- Peripheral Nervous System (PNS)
  - Motor Neurons
    - Somatic Nervous System
      - voluntary movements via skeletal muscles
    - Autonomic Nervous System
      - organs, smooth muscles
      - Sympathetic
        - “Fight-or-Flight” responses
      - Parasympathetic
        - maintenance
  - Sensory Neurons



The CNS: Brain and Spinal Cord



Anatomical regions of CNS

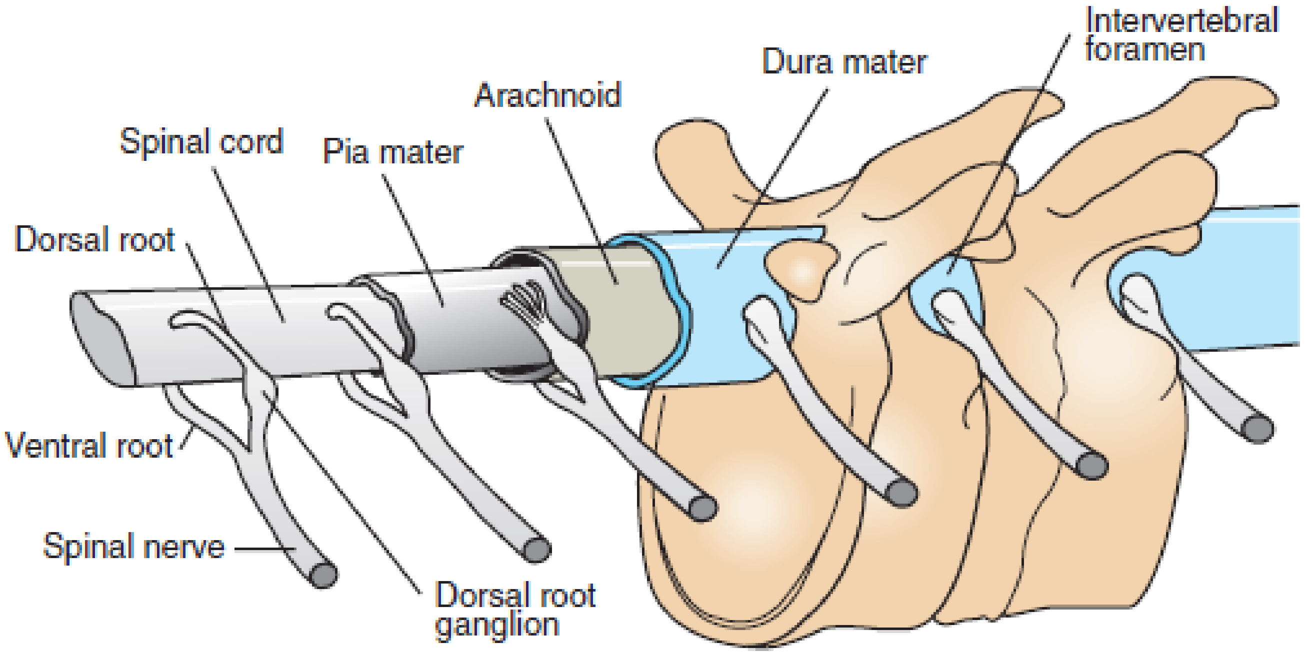


- Spinal cord
- Brain stem
  - Medulla
  - Pons
  - Mid brain
- Diencephalon
- Telencephalon

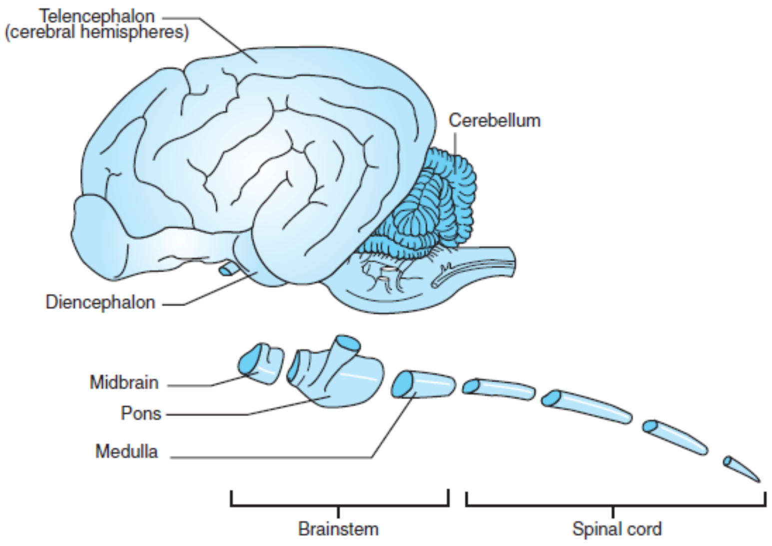
The spinal cord

- The most caudal region
- Sensory nerves enter from dorsal roots
- Motor nerves exit from ventral roots
- Contains
  - cell bodies and dendrites of motor neurons
  - Vertical tracts of sensory n. to the brain and motor n. from the brain
- The isolated spinal cord can control simple reflexes,
- such as muscle stretch reflexes and limb withdrawal from painful stimuli.

The spinal cord

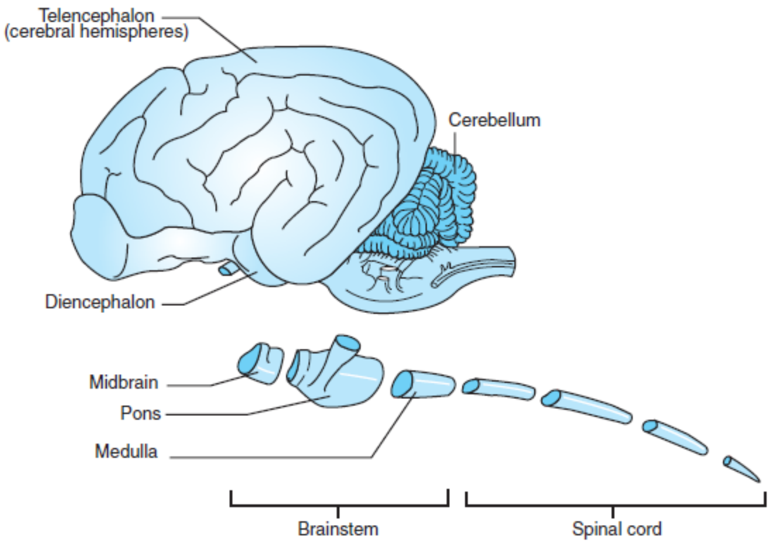


Brain Stem



- Medulla
  - Lies rostral to the spinal cord
  - The cell bodies of medullary neurons aggregates in sensory or motor nuclei, called: *cranial nerve nuclei.*
  - play a critical role in life support functions:
    - Respiratory
    - Cardiovascular
    - Feeding (taste, tongue movement, swallowing, digestion)

Brain Stem



- The pons
  - Rostral to the medulla
  - contains the cell bodies of large numbers of neurons in a two-neuron chain that relays information from the cerebral cortex to the cerebellum.
  - Receives sensory inf. from face, motor control of chewing.
  - The cerebellum is not a part of the brainstem
  - The cerebellum is important for smooth, accurate, coordinated movement and for motor learning.

Brain stem

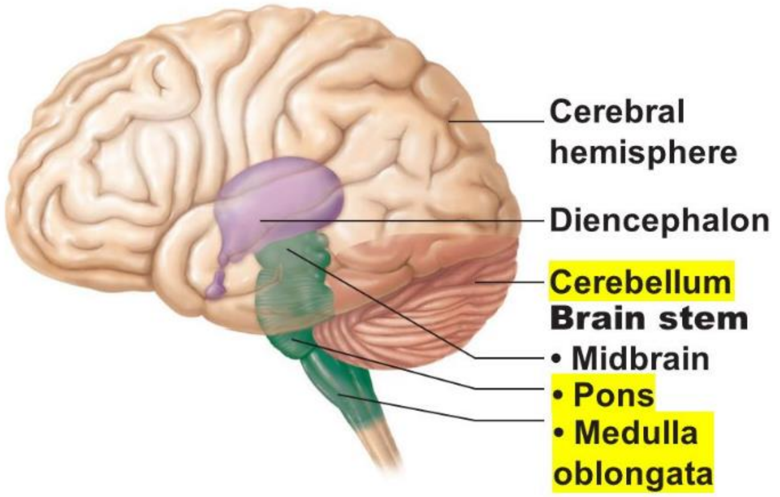


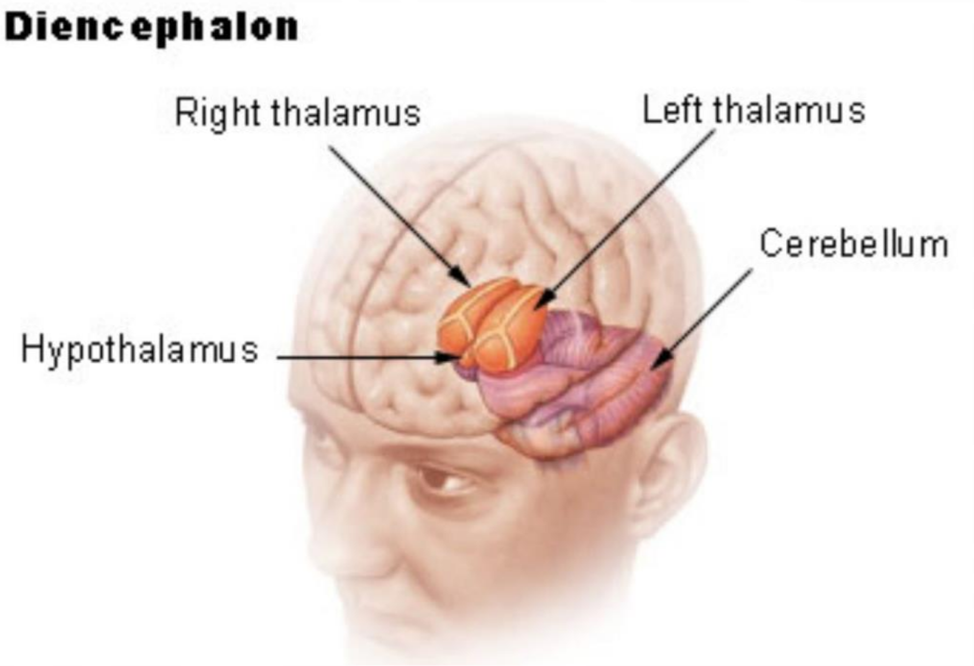
Figure 12.3d

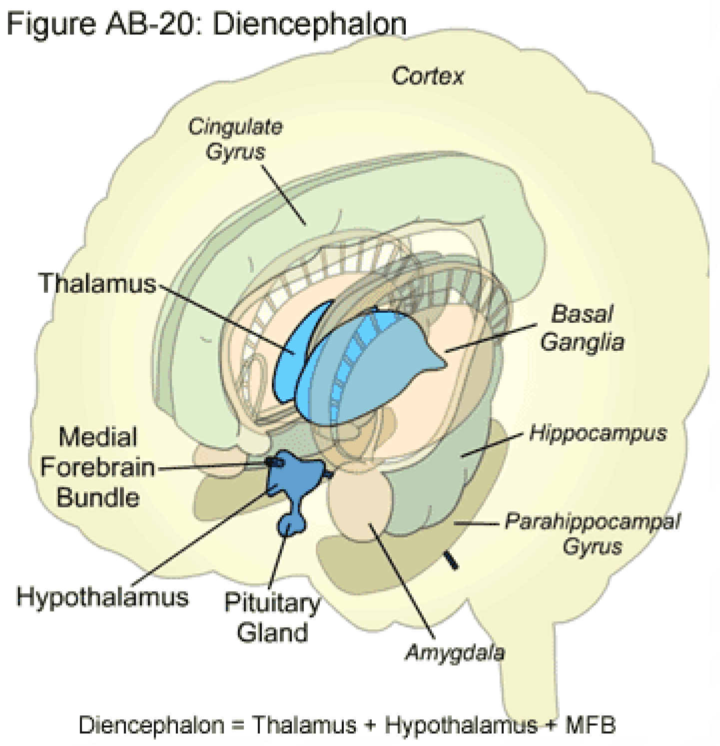
- Mid brain (Mesencephalon)
  - Rostral to the pons
  - processing and relaying visual and auditory information
  - Directly controls eye movement
  - Reticula formation:
  - A netlike complex of many small clusters of cell bodies (nuclei),
  - modulating consciousness and arousal, pain perception, and spinal reflexes, as well as in movement

Diencephalon

- contains the thalamus and the hypothalamus
- The *thalamus* is a relay station of information being passed to the cerebral cortex from sensory systems and other brain regions
- The *hypothalamus* regulates the autonomic nervous system, controls hormone secretion of the pituitary gland, and plays a major role in physiological and behavioral aspects of homeostasis (e.g., maintenance of temperature and blood pressure; feeding).

Diencephalon



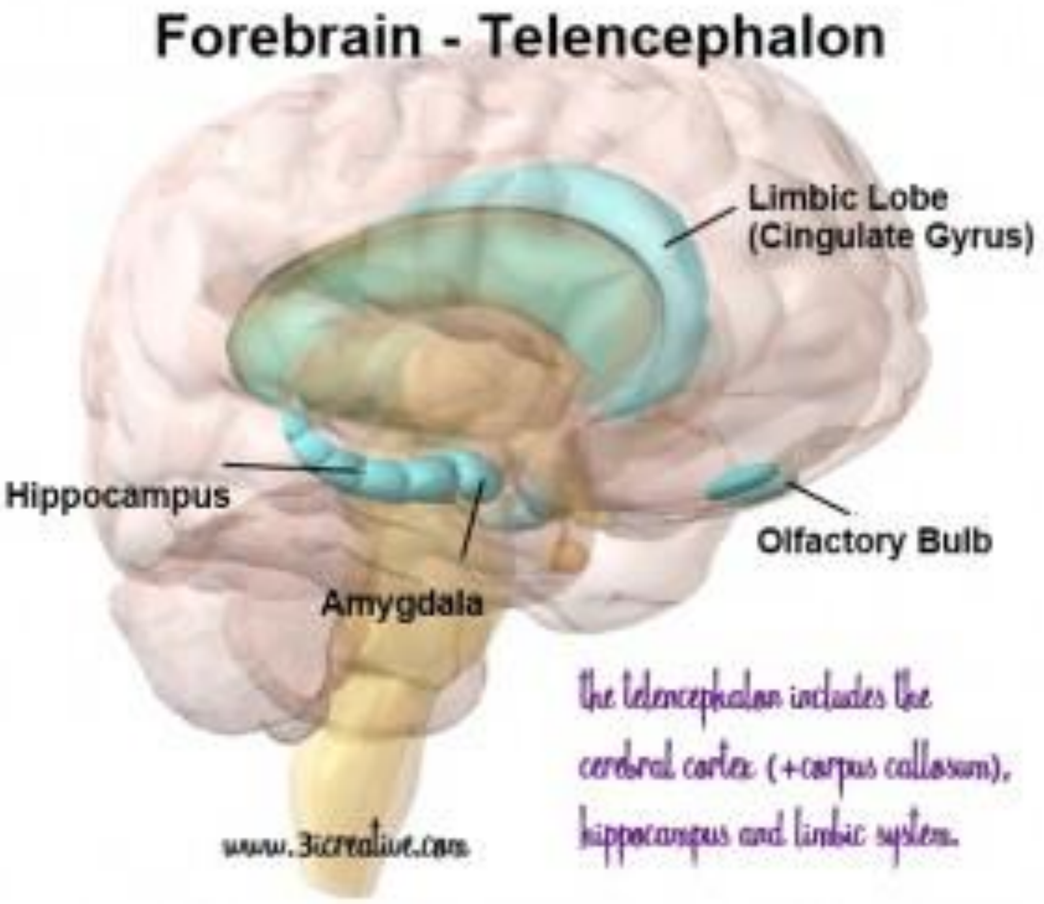


Telencephalon

- made up of the cerebral cortex and a small
- number of prominent subcortical structures, such as the basal ganglia and hippocampus

- The *cerebral cortex* mediates the most complex forms of sensory *integration* and conscious sensory perception.
- The *basal ganglia* are a collection of nuclei that modulate the motor functions of cerebral cortex
- the *hippocampus* plays an important role in memory and spatial learning.

Telencephalon



Central Nervous System (CNS)

- The entire CNS is surrounded by three protective layers called meninges:
- The innermost layer, lying next to the CNS, is the pia mater, which is a single layer of fibroblast cells joined to the outer surface of the brain and spinal cord.
- The middle layer, the arachnoid, so named because of its spiderweb appearance, is a thin layer of fibroblast cells that traps cerebrospinal fluid between it and the pia mater (in the subarachnoid space).
- The outermost meningeal layer, the dura mater, is a much thicker layer of fibroblast cells that protects the CNS. Within the brain cavity of the skull, the dura mater is often fused with the inner surface of the bone.

Cerebrospinal fluid (CSF)

- Cerebrospinal fluid (CSF) is a clear, colorless fluid found within the subarachnoid space, the central canal of the spinal cord, and the ventricular system of the brain
- CSF is produced primarily in the ventricles of the brain, flows down a pressure gradient from the ventricles to the subarachnoid space, where it bathes the surface of the CNS, and from the subarachnoid space eventually passes into the venous system.
- It can also serve as an important diagnostic tool to indicate CNS infection, inflammation, or tumor activity. CSF also serves as a shock absorber for the CNS during abrupt body movement.

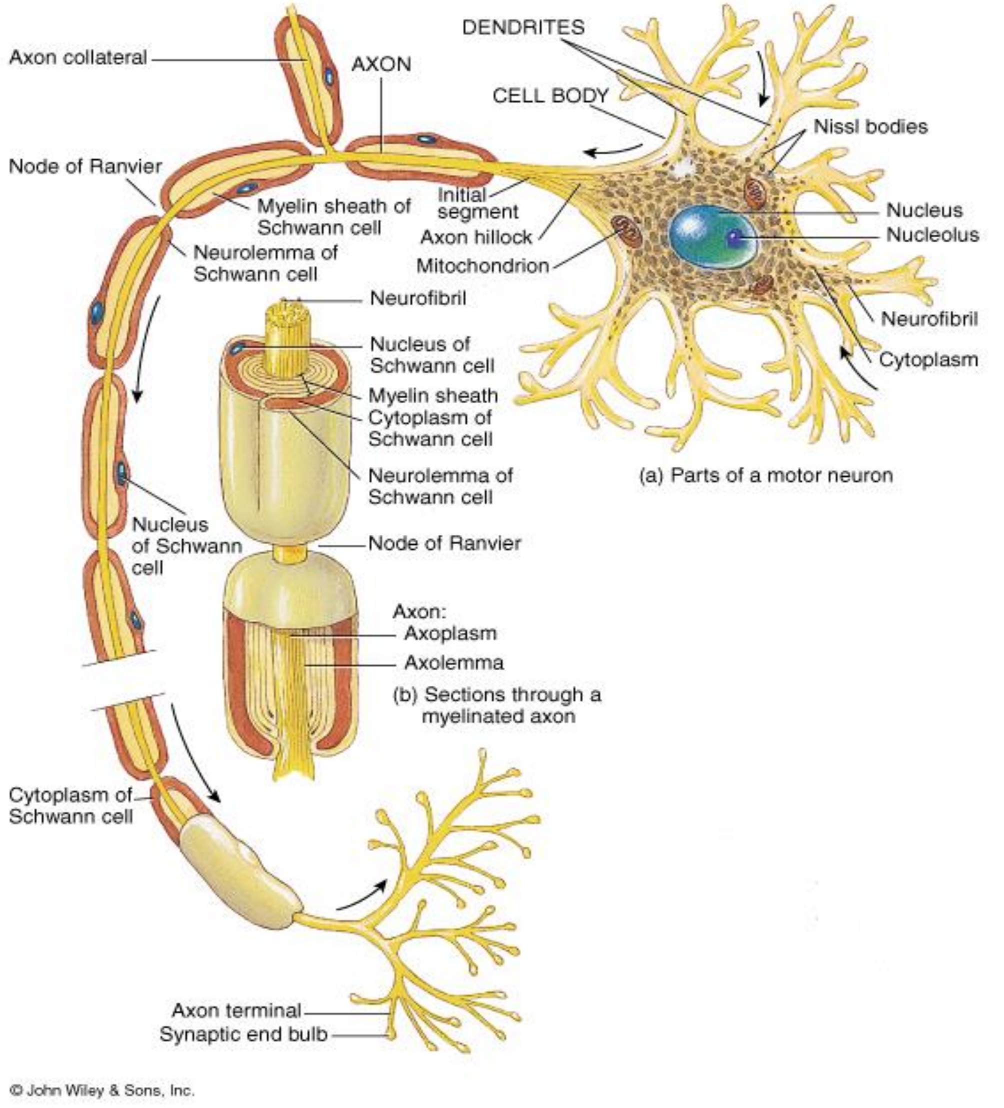
Peripheral Nervous System (PNS)

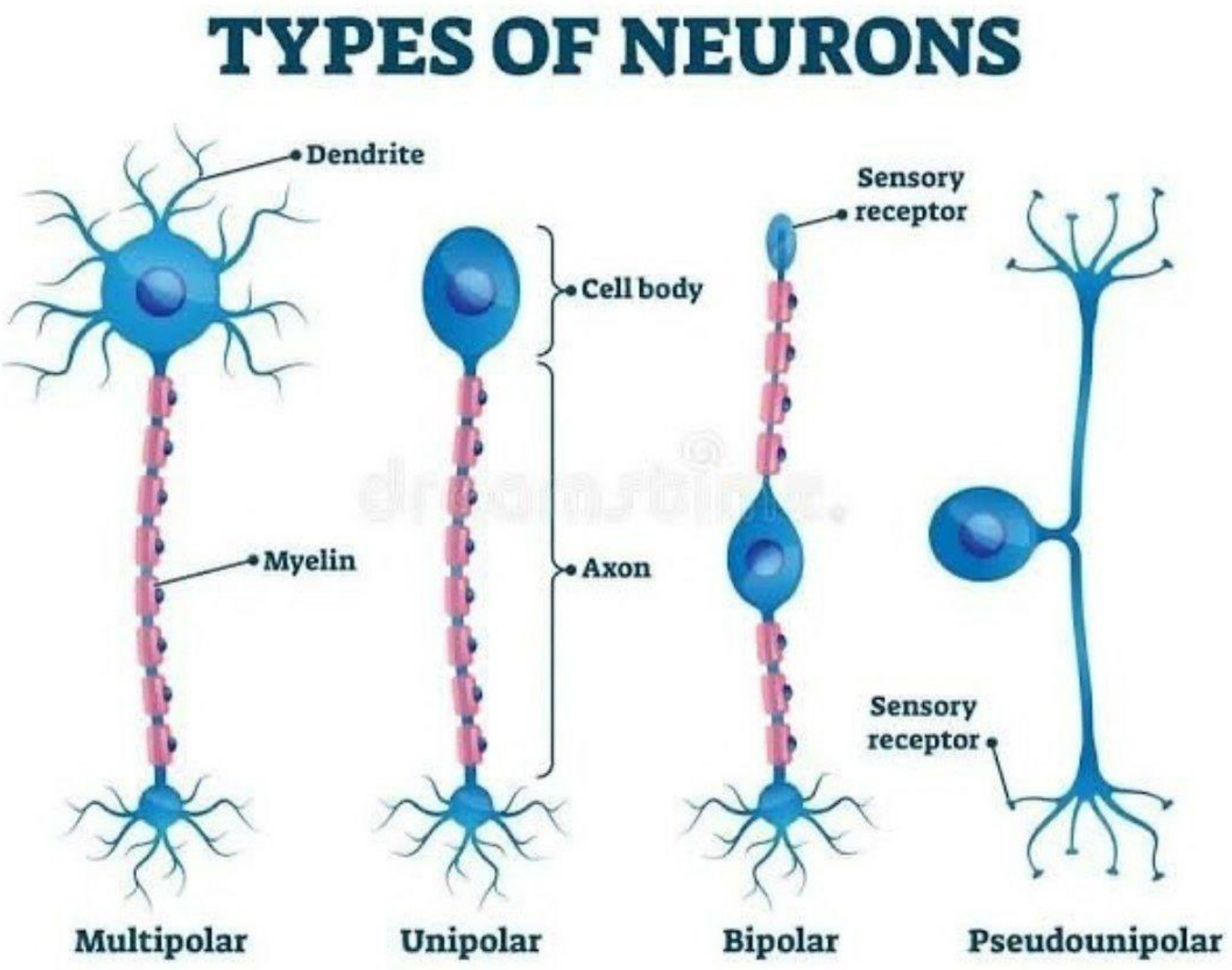
The Neuron

- Dendrites: Carry nerve impulses toward cell body. Receive stimuli from synapses or sensory receptors.

- Cell Body: Contains nucleus and nissl bodies, a form of rough endoplasmic reticulum.

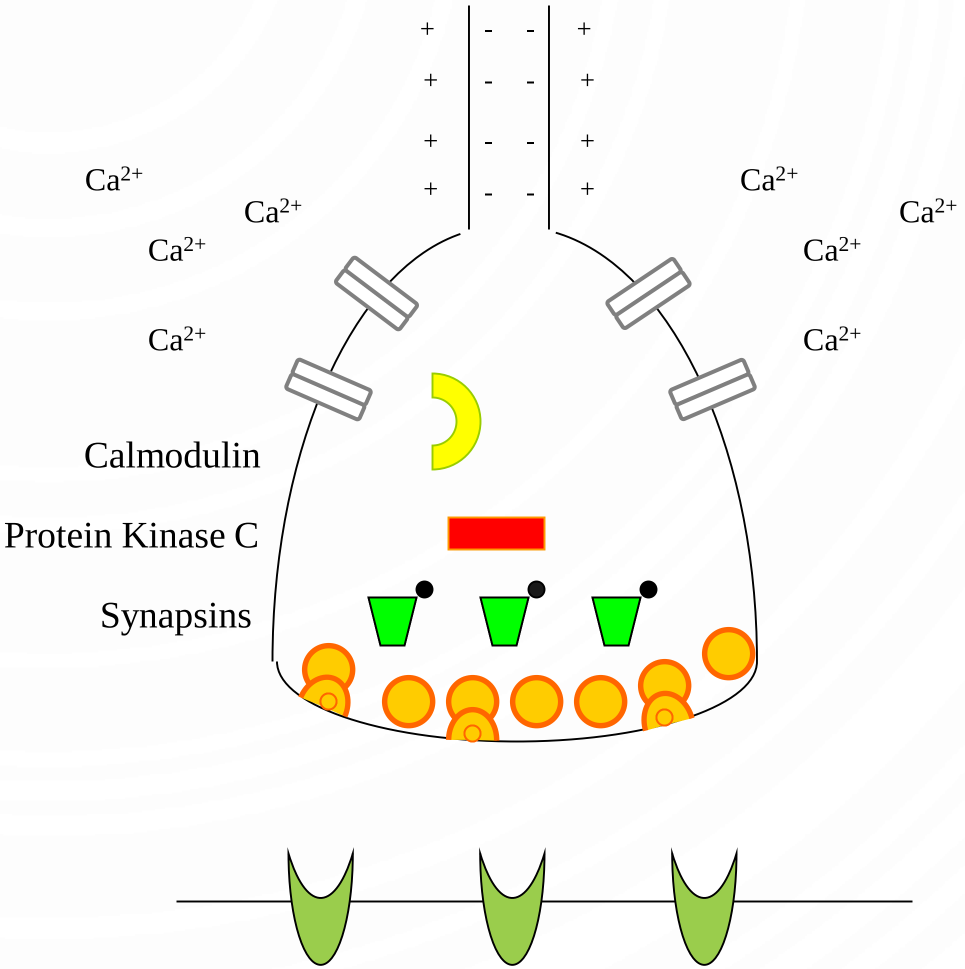
- Axon: Carry nerve Impulses away from the cell bodies. Axons interact with muscle, glands, or other neurons.




TYPES OF NEURONS
Dendrite
Cell body
Sensory
receptor
Myelin
Axon
Sensory
receptor
Multipolar
Unipolar
Bipolar
Pseudounipolar

Chemical Synapses

- Many voltage-gated Ca^{2+} channels in the terminal button
  - AP in knob opens Ca^{2+} channels
  - Ca^{2+} rushes in.
- Ca^{2+} induced exocytosis of synaptic vesicles
- Transmitter diffuses across synaptic cleft and binds to receptors on subsynaptic membrane



The Synapse

Neurotransmitters

- Neurotransmitter responsible for the primary postsynaptic effect at the neuromuscular junction, a variety of neurotransmitters, in addition to acetylcholine, can be used to produce the principal postsynaptic effect at neuron-to-neuron synapses.

Amino Acids
Glutamate
Glycine
γ-Aminobutyric acid (GABA)

Amines
Acetylcholine
Serotonin
Histamine

Catecholamines
Dopamine
Norepinephrine
Epinephrine

Peptides*
Substance P
Vasopressin
Somatostatin

Opioids
Leu-enkephalin
Met-enkephalin
β-Endorphin

Purines
Adenosine
Adenosine triphosphate (ATP)

Atypical (Nontraditional)
Gases
Nitric oxide
Carbon monoxide

Endogenous Cannabinoids (Endocannabinoids)
Anandamide
2-Arachidonylglycerol

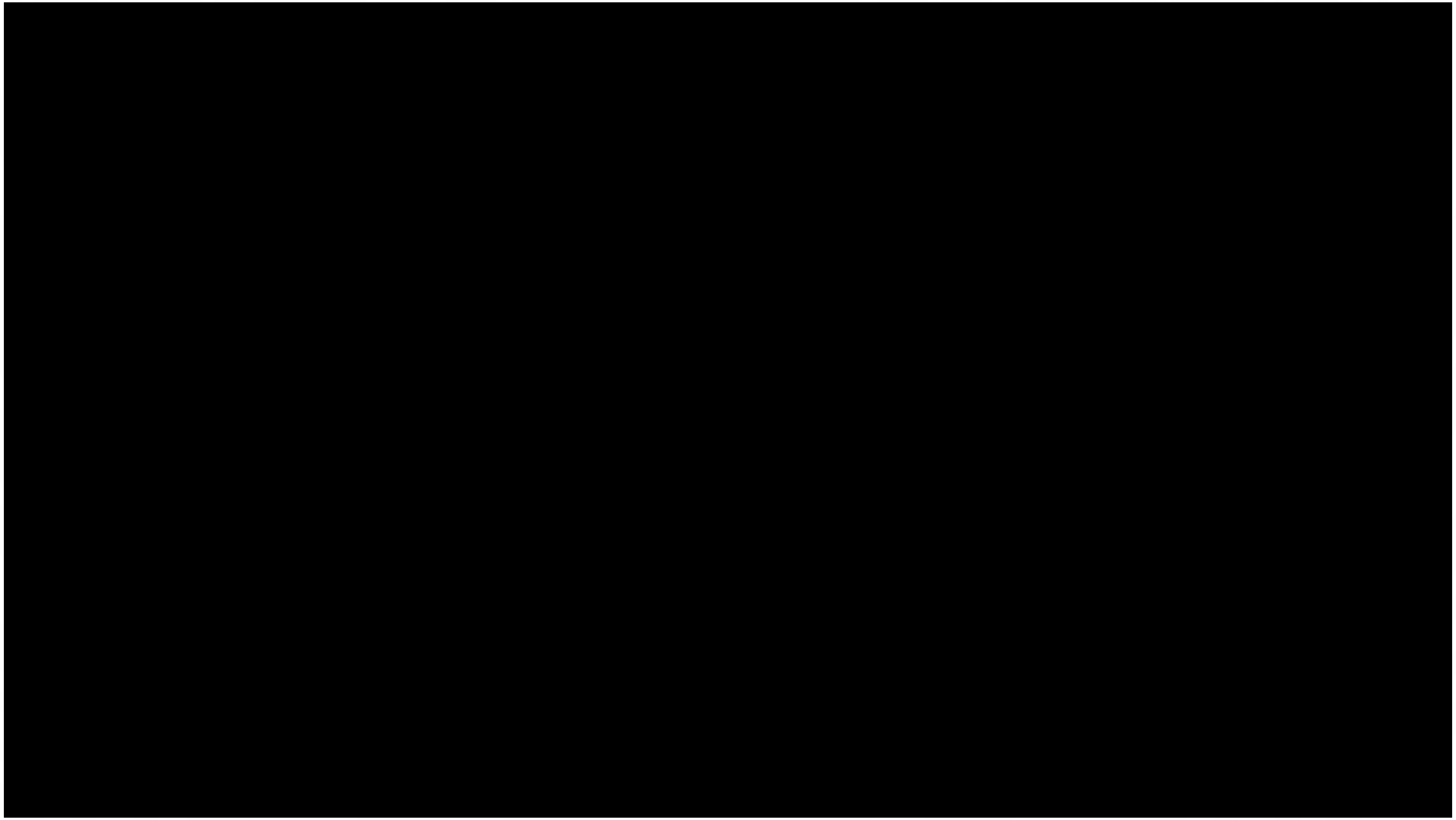
Types of Neurotransmitters

Ionotropic and Metabotropic Receptors

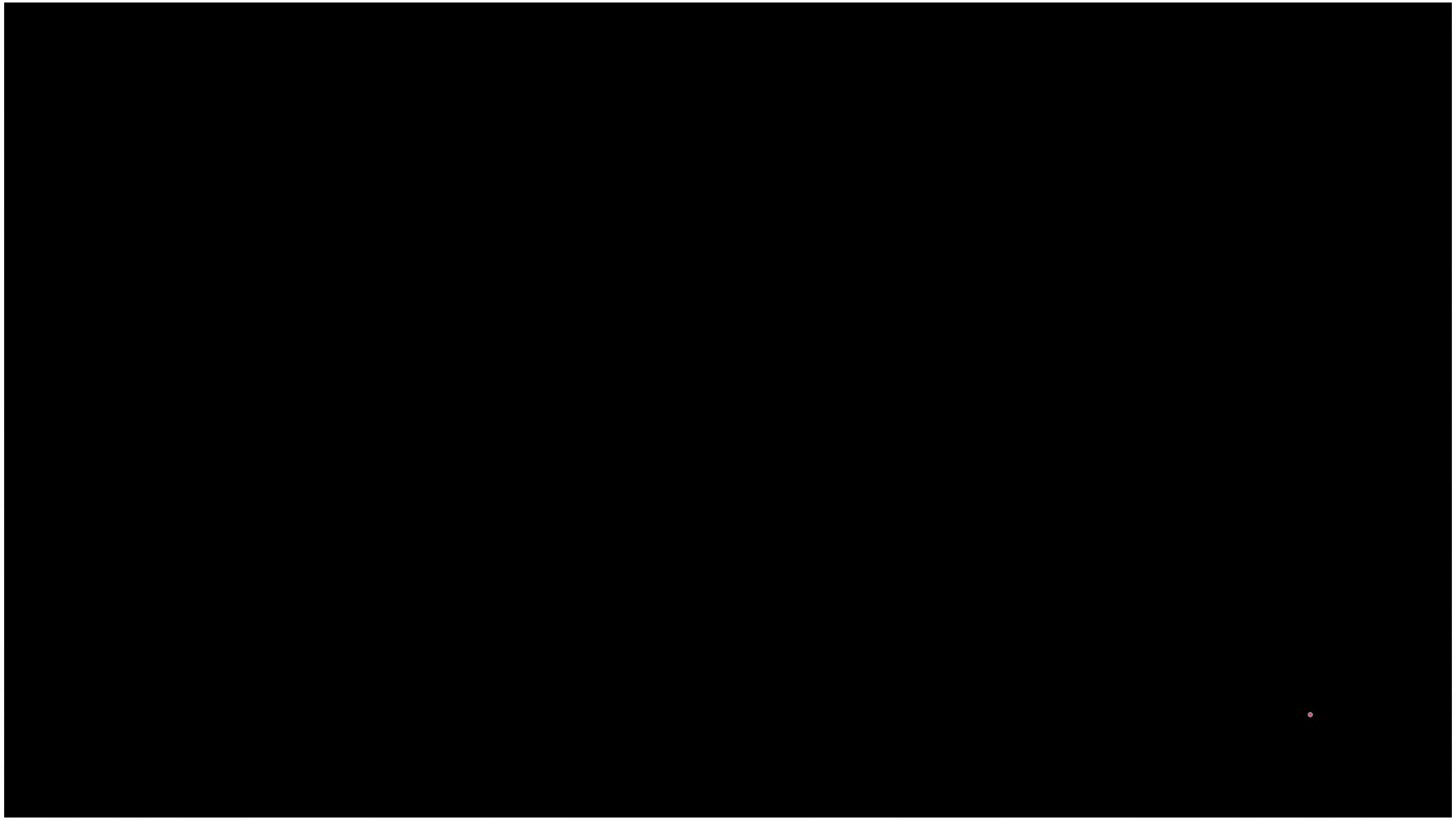
Ionotropic and Metabotropic Receptors

Neurotransmitters and Receptors

Action of neurotransmitters



Neurotransmitters overview

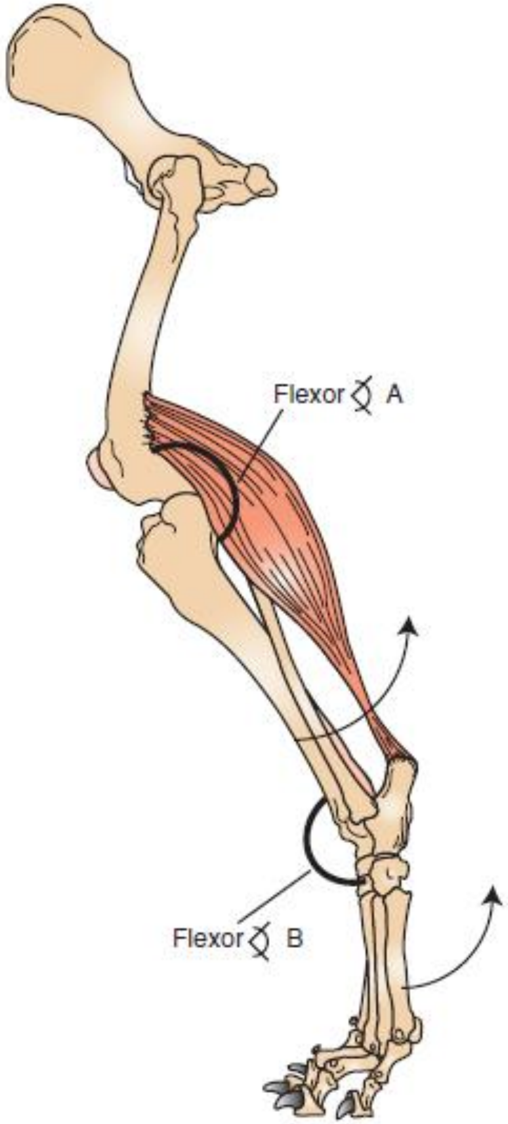


Neurotransmitters overview

Neurotransmitter	Abbreviation	Behaviors or Diseases Related to These Neurotransmitter
Acetylcholine	ACh	Learning and memory; Alzheimer's disease' muscle movement in the peripheral nervous system
Dopamine	DA	Reward circuits; Motor circuits involved in Parkinson's disease; Schizophrenia
Norepinephrine	NE	Arousal; Depression
Serotonin	5HT	Depression; Aggression; Schizophrenia
Glutamate	GLU	Learning; Major excitatory neurotransmitter in the brain
GABA	GABA	Anxiety disorders; Epilepsy; Major inhibitory neurotransmitter in the brain
Endogenous Opiods	Endorphins, Enkephalins	Pain; Analgesia; Reward

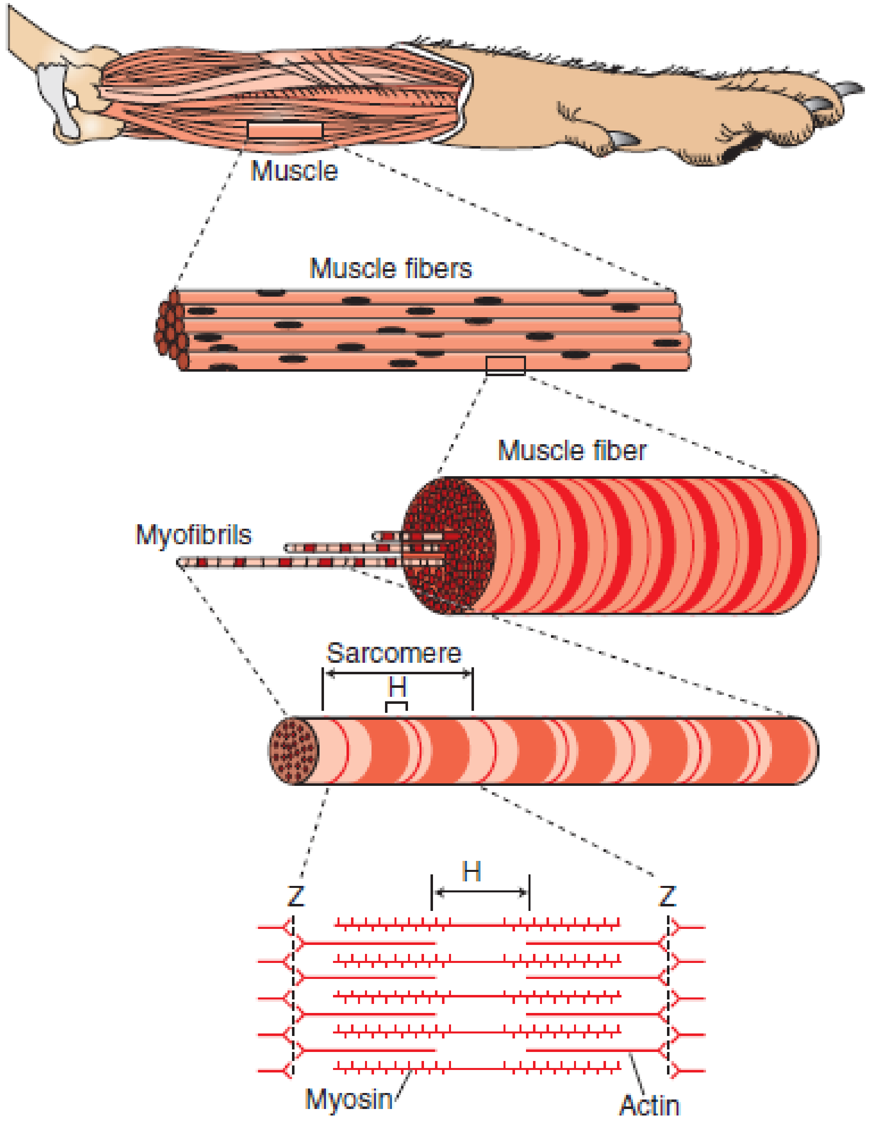
The Physiology of Muscle

- There are three types of muscles:
  - Skeletal
  - Cardiac
  - Smooth
- Body movement is the result of contraction (shortening) of a skeletal muscle attached across a movable joint.
- Contraction of the muscle will decrease the flexor angle at joint A (the stifle joint) and increase the flexor angle at joint B (the tarsal joint).
- This will produce the respective movements about the joints indicated by the arrows.



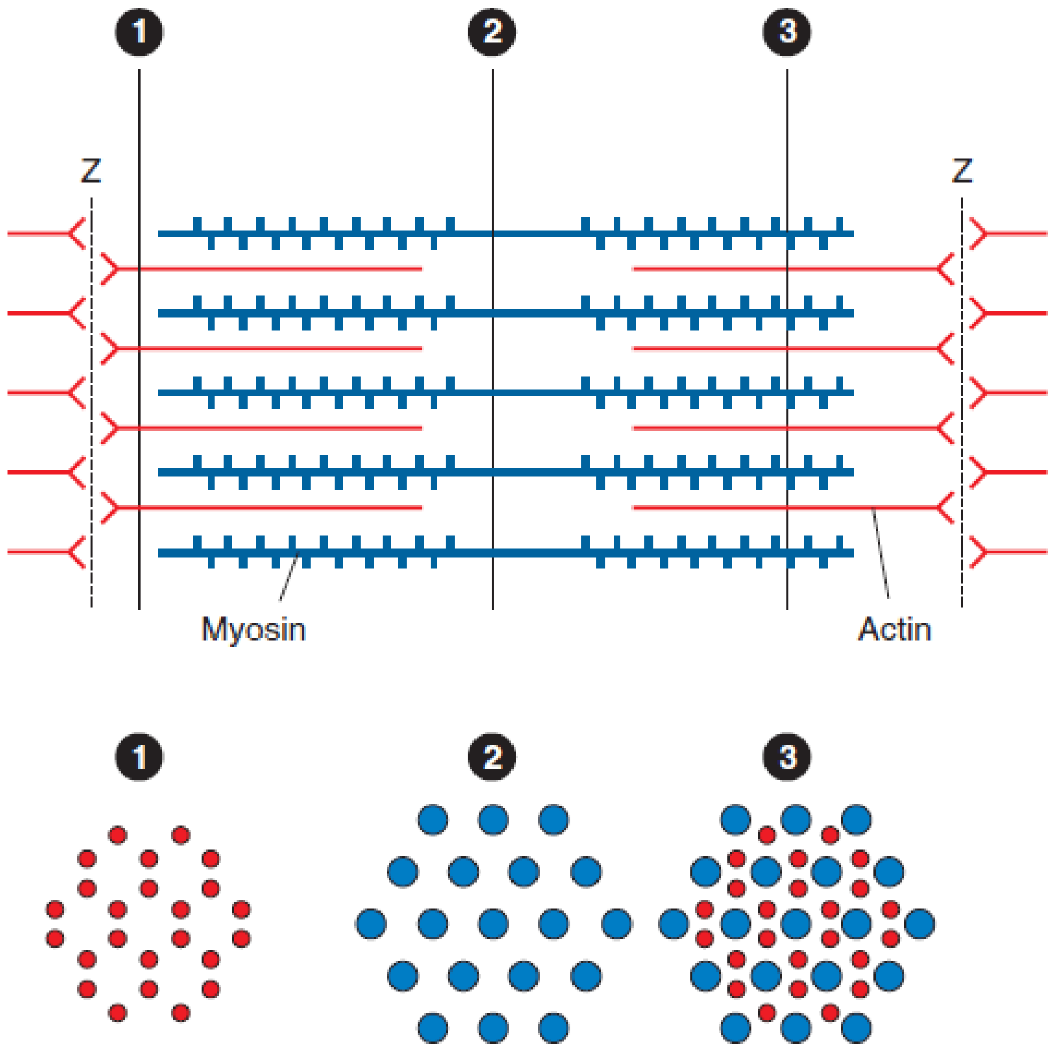
Skeletal muscle organization

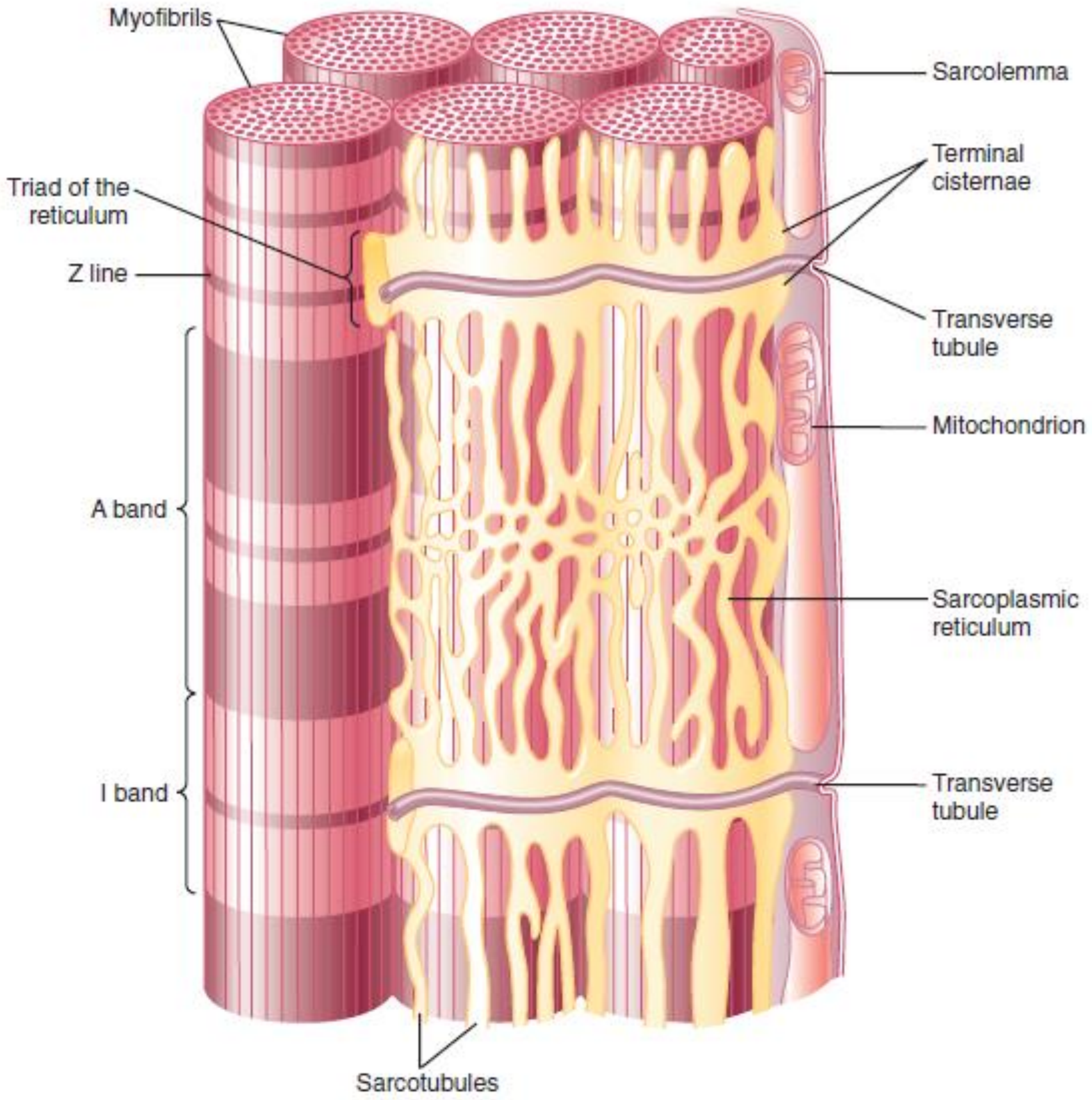
- Each muscle fiber contains several hundred to several thousand myofibrils arranged in parallel along its length, like a handful of spaghetti.
- Each myofibril is made up of a linear series of repeating sarcomeres, the basic contractile units of the muscle fiber, which can number in the tens of thousands.



Skeletal muscle organization

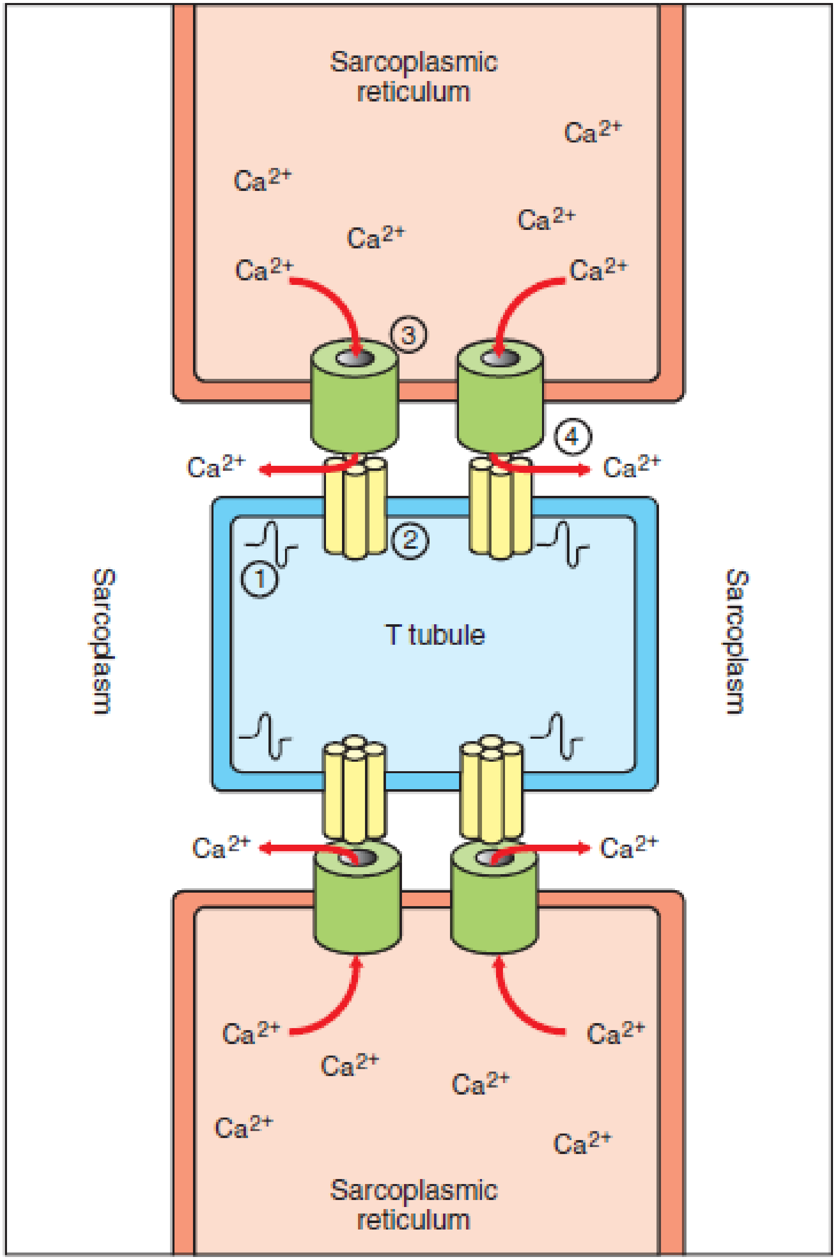
- Parallel arrangement of actin and myosin filaments in a sarcomere.
  - Top, The viewer is looking at one end of a sarcomere.
  - Bottom, The view of filament organization respectively seen by the observer at each of the three transverse sectioning points indicated in the top part of the figure.




Myofibrils
Sarcolemma
Terminal cisternae
Triad of the reticulum
Z line
Transverse tubule
Mitochondrion
A band
Sarcoplasmic reticulum
I band
Transverse tubule
Sarcotubules

Transvers tubules and sarcoplasmic reticulum

- 1, Propagation of action potential produces depolarization of the TT membrane.
- 2, Depolarization induces opening of voltage-gated Ca2+ channel aggregates in the TT membrane.
- 3, Opening of Ca2+ release channels on the SR membrane results from mechanical coupling with opening of voltage-gated Ca2+ channels on the TT.
- 4, Ca2+ is released from the SR into the sarcoplasm, where it can bathe the sarcomeres (not shown) to induce contraction.



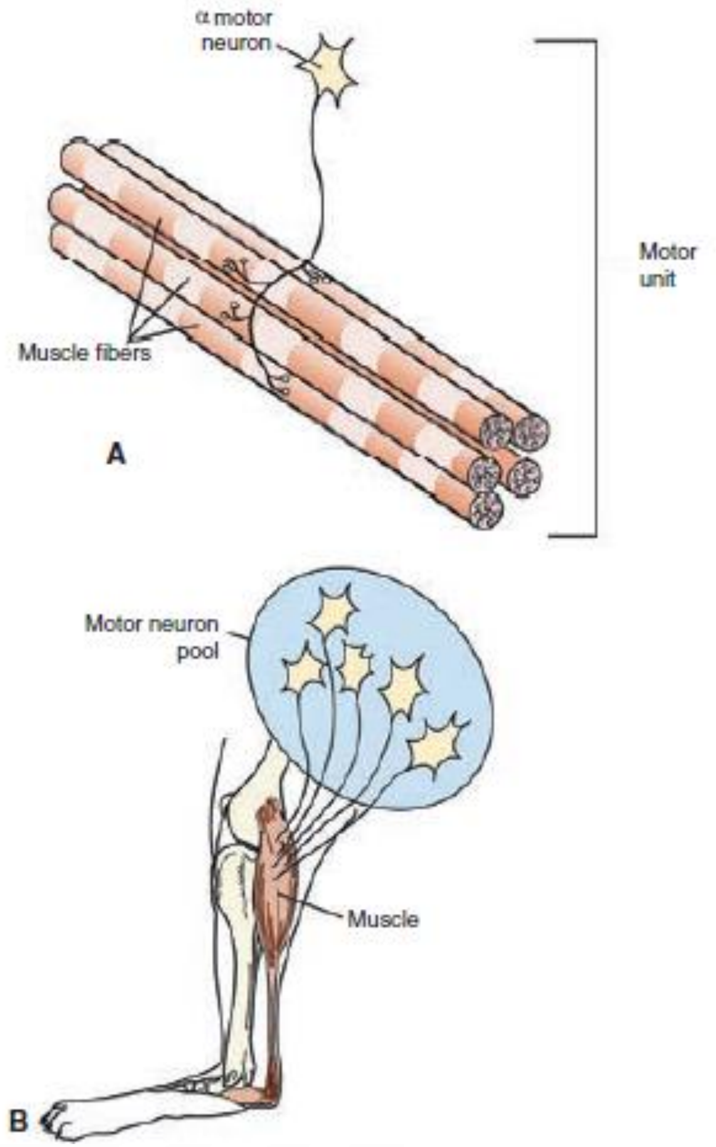
Muscle contraction

Muscle contraction cycle

The muscle contraction cycle describes the series of events that cause contraction of the sarcomere, the contractile unit of muscle fibers.

Innervation of skeletal muscle

- A, A motor unit is an α motor neuron and all the skeletal muscle fibers it innervates.
- B, Neuronal cell bodies of all the motor units from a single muscle form a cluster within the CNS called the motor neuron pool of that muscle.

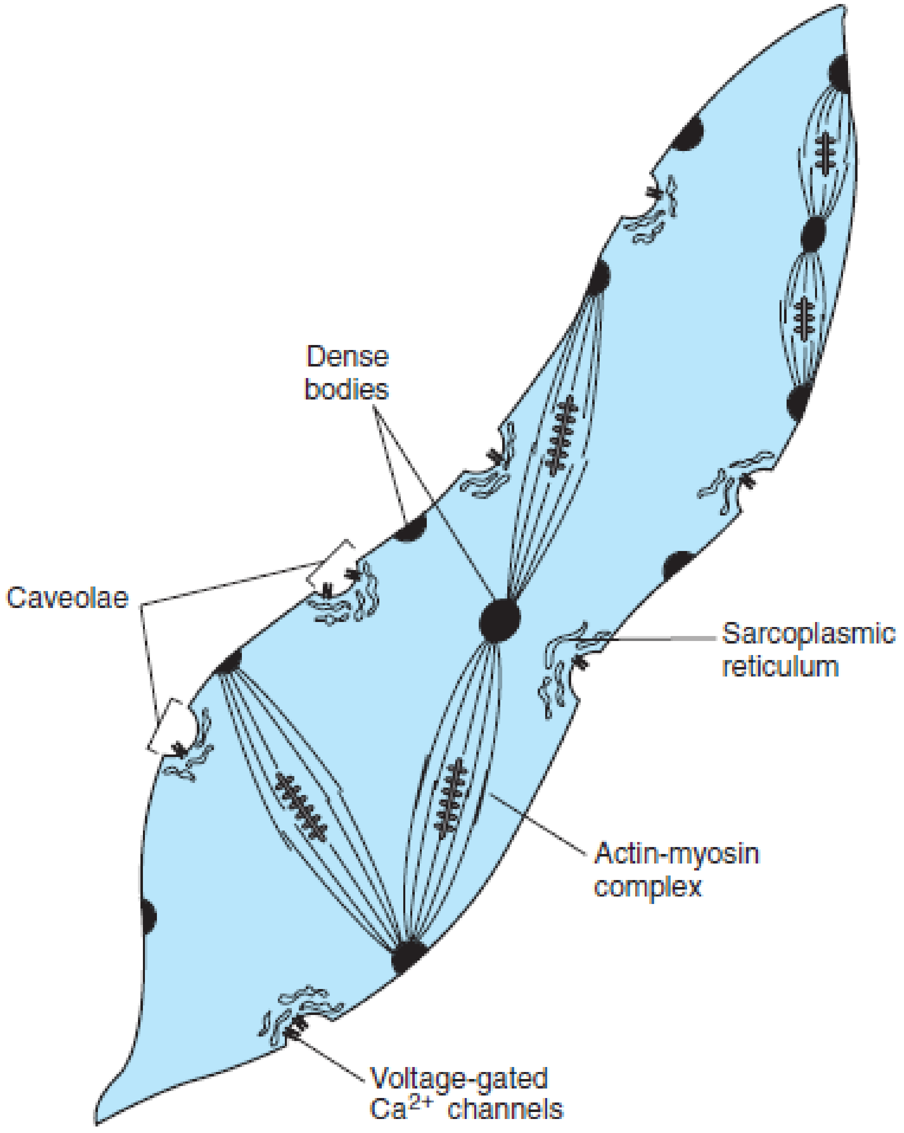


Innervation of skeletal muscle

- In motor units a relationship exists among the functional type of muscle fiber innervated, the number of muscle fibers innervated, and motor neuron size.
- Small motor units tend to be made up of a motor neuron with a small cell body and a narrow, slower-conducting axon that innervates a small number of slow-twitch fibers.
- Large motor units have a motor neuron with a large cell body and a faster-conducting, wide axon innervating a large number of fast-twitch fibers.
- Activation of a small motor unit produces a smaller, slower, less fatiguable increment of contractile force in the muscle compared with a larger motor unit.
- The neuronal cell bodies of all the motor units from a single muscle form a cluster within the central nervous system (CNS) called the motor neuron pool of that muscle.
- Within the motor neuron pool for a given muscle, there is a range of motor unit sizes. Muscles with a larger proportion of smaller motor units tend to be amenable to finer control of contractile force.

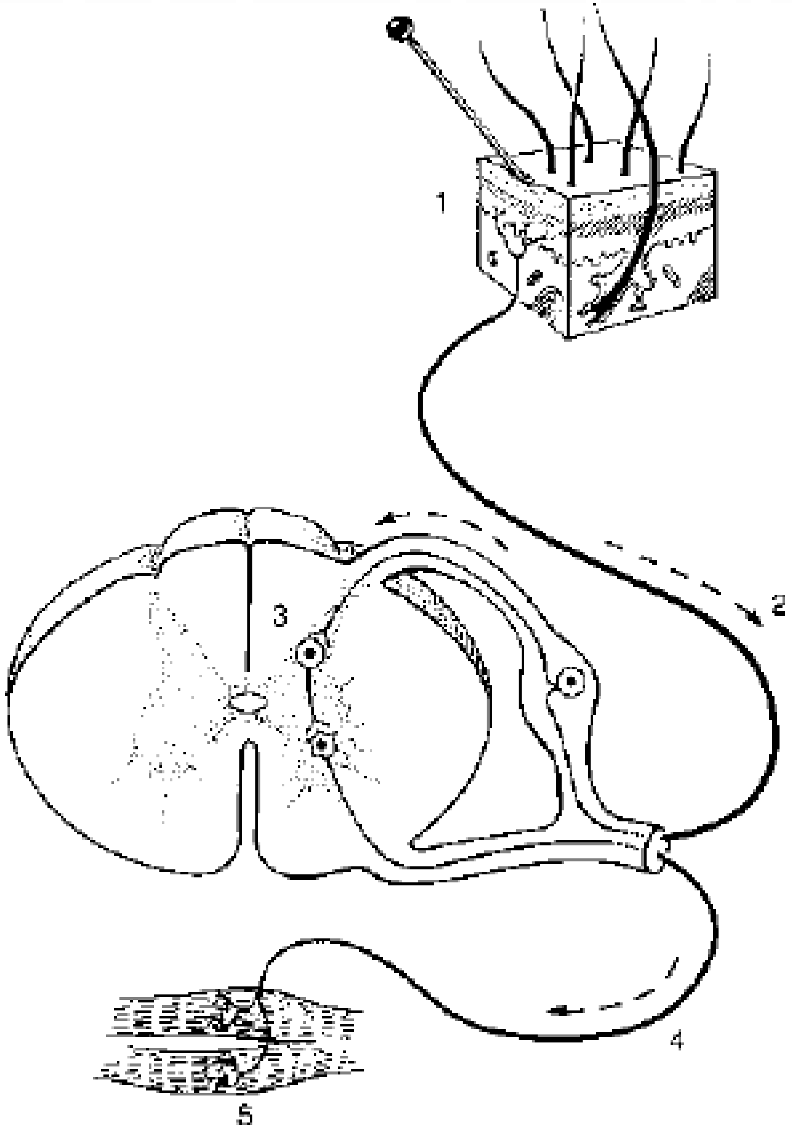
organization of a smooth muscle cell

- T tubules are absent, and the sarcoplasmic reticulum is poorly developed.
- Transmembrane diffusion of extracellular Ca2+, through voltage-gated Ca2+ channels in caveolae, plays an important role in initiating contraction.
- Actin and myosin are present, with actin anchored to dense bodies.
- Activating the actin-myosin complex can change the cell's shape.



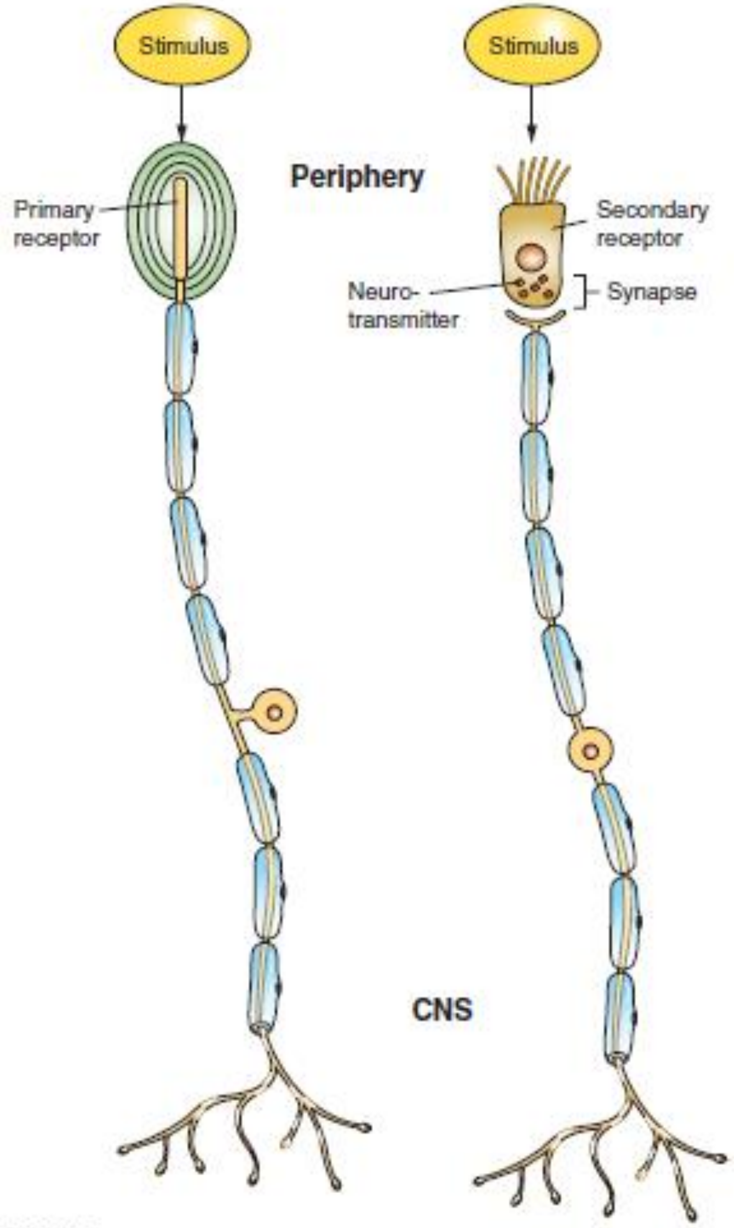
The Concept of a Reflex

- A Reflex Arc:
  - 1, a receptor
  - 2, a sensory neuron
  - 3, one or more synapses in the CNS
  - 4, a motor neuron
  - 5, a target organ, usually a muscle



Primary and secondary sensory receptors

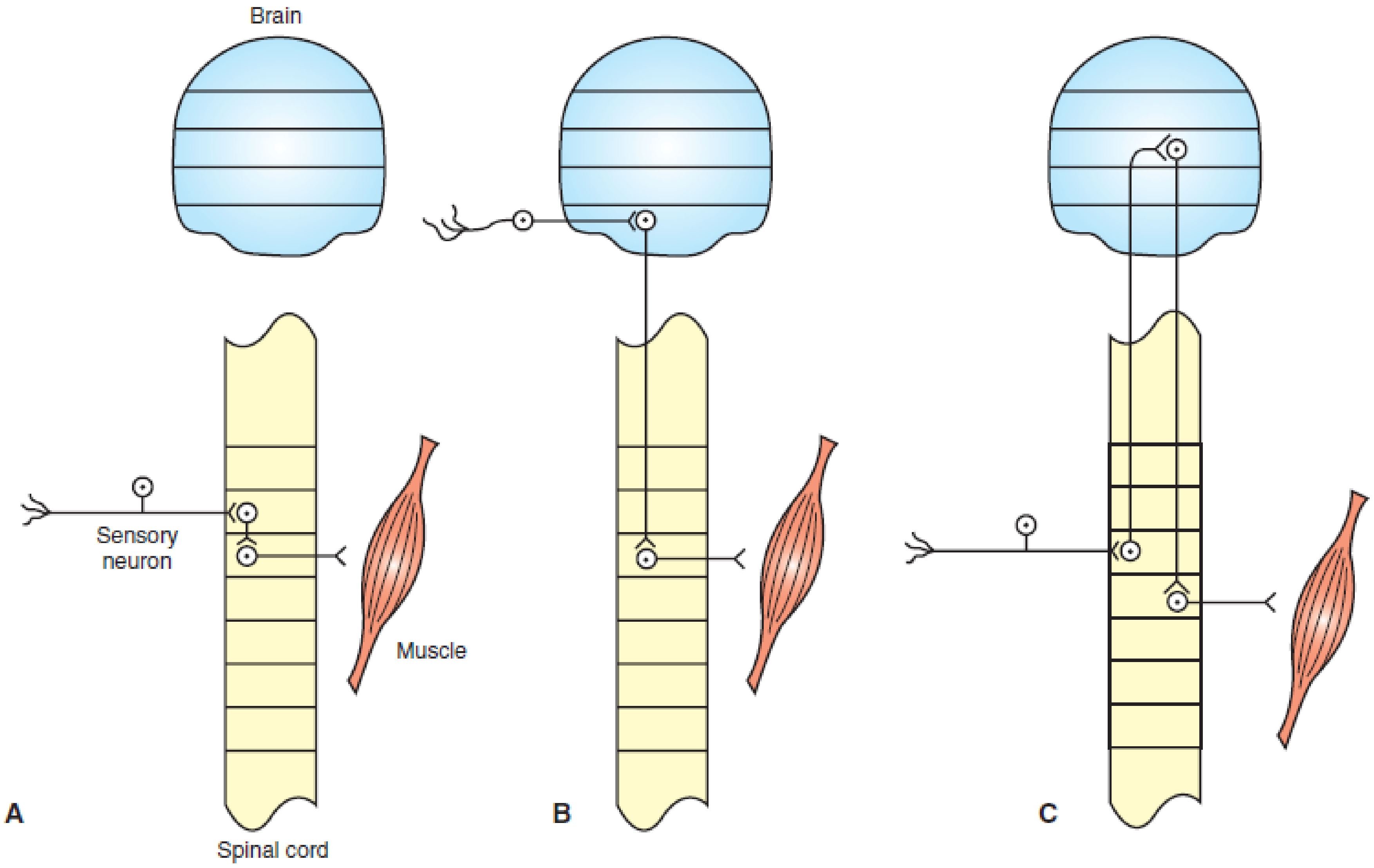
- A primary sensory receptor (left) is a neuron with a peripheral ending specialized for stimulus transduction. In this particular case, the encapsulated peripheral ending of the neuron transduces the stimulus.
- The secondary receptor (right) is a nonneural cell designed for stimulus transduction, which subsequently releases neurotransmitter onto an adjacent neuron.



Segmental and intersegmental reflexes

- A, In the segmental reflex the sensory neuron input, CNS circuitry, and motor neuron output traverse only a small number of rostrocaudal segments of the CNS. (The quadriceps stretch reflex (knee jerk reflex) and the pupillary light reflex)
- B, Intersegmental reflex arcs traverse several CNS segments. In some intersegmental reflexes the sensory neuron input and motor neuron output are separated by several segments.(vestibulospinal reflexes)
- C, The long-loop intersegmental reflex arc traverses several CNS segments, even though the sensory input and motor output are located in close rostrocaudal proximity.(proprioceptive positioning reaction)
- Horizontal lines delimit either spinal cord segments (e.g., L1, L2) or major brain divisions (e.g., medulla, pons).

Segmental and intersegmental reflexes



Clinical correlations

History :

- Worried owners call you about their 4-month- old Tennessee Walking Horse colt. He appeared normal this morning when they let him out to pasture with his mother, but later this afternoon, the mare and the foal did not come in to be fed. The owners went out to the pasture and found the mare with the foal, who would not get up. He was lying on his side and seemed unable to position himself sternal. When the owners tried to reposition him, the foal thrashed, trying to get away. You tell the owners not to move the foal and that you will be there soon.

Clinical correlations

- Clinical ExamInation :

The foal appears to be responsive but in great pain and unable to rise. ‘temperature, pulse, and respirations are all mildly increased. There appears to be a swelling along the cervical (neck) area in the region of Cl-C3.

The swelling is hard (bone) and has some fluid (inflammation)

as well. There is some crepitus in the area of the swelling (possible fracture site).

Clinical correlations

The foal displays no other areas of swelling or trauma. Neurological examination reveals normal cranial nerves. In the front limbs the biceps and triceps reflexes seem increased on both sides. Deep pain is present, and cutaneous sensation is increased bilaterally. In the hind limbs the femoral, sciatic, and tibial responses are increased.

Clinical correlations

- **Comment :**
- Although it is difficult to localize a fracture definitively, based on history and physical examination a fracture seems likely. The fracture appears to be in the region of Cl-C3. Radiographs would be ideal to make a definitive diagnosis. On neurological testing of the biceps, triceps, sciatic, femoral, and cranial tibial responses, all assess segmental reflex arcs. Because of a high cervical fracture, the descending motor tracts that supply both the thoracic and the pelvic limbs are affected.

Clinical correlations

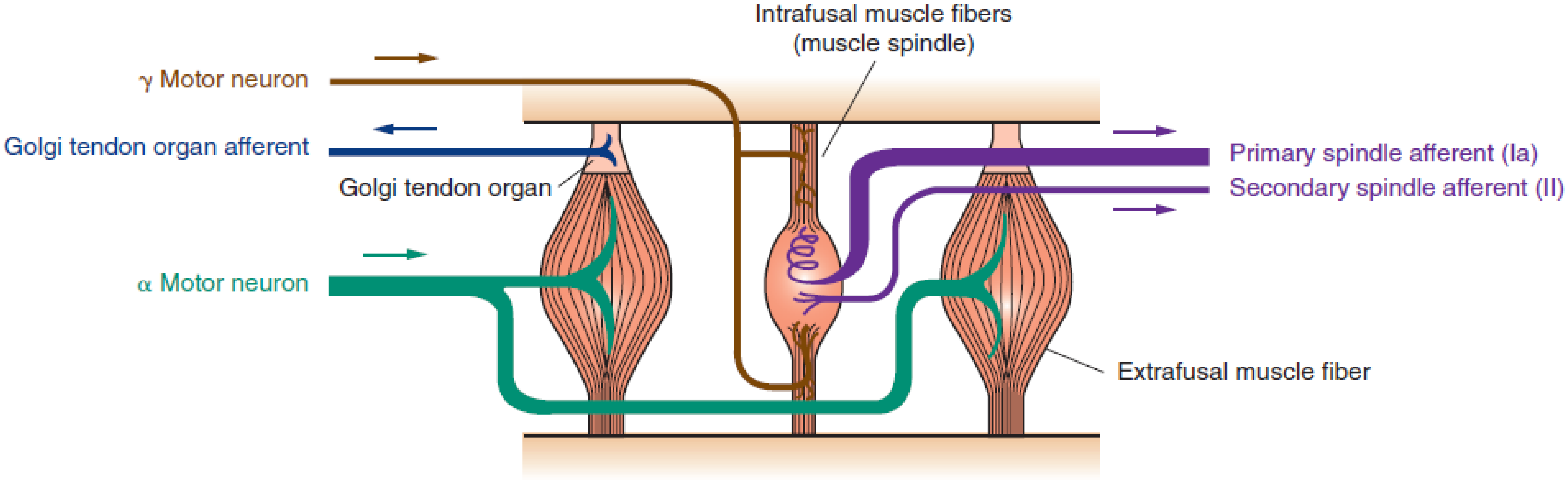
- **Treatment.**
- The prognosis for this foal is poor Based on the physical examination and clinical signs, a fracture is likely, and there is little hope for recovery. The complications associated with trying to manage a foal as the fracture heals are enormous. The fracture may not heal, and the foal could have severe residual neurological deficits. In most cases, these foals are euthanized fairly quickly because of the poor prognosis.

Skeletal Muscle Receptor Organs

- Movement is orchestrated by the central nervous system (CNS) through its control of the motor unit.
- To control body movement appropriately, the CNS must
  - (1) assess the effect of gravity on the many muscles of the body,
  - (2) determine the initial position of the body parts to be moved, and
  - (3) detect any discrepancy between the intended movement and the movement that actually occurs. When such discrepancies are detected, appropriate adjustments can be made.
- Two important receptor systems have evolved in the skeletal muscles of mammals to provide the CNS with the aforementioned information:
  - the muscle spindle
  - the Golgi tendon organ

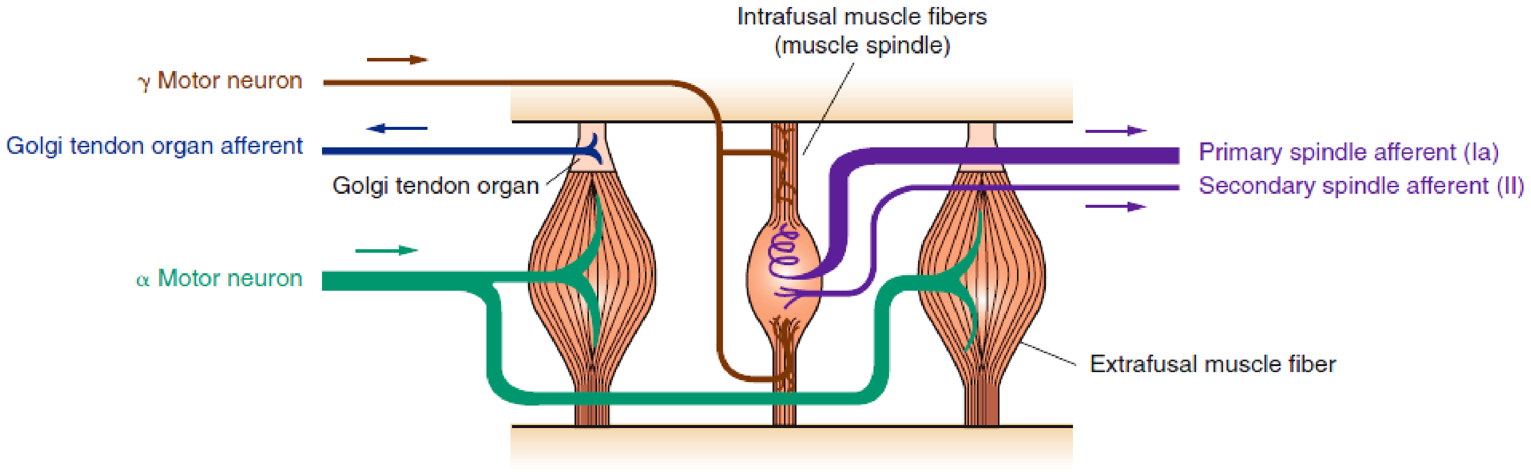
Skeletal Muscle Receptor Organs

- The muscle spindles, arranged in parallel to the contracting skeletal muscle fibers, provide information about muscle length
- The Golgi tendon organ, arranged in series with the contracting skeletal muscle fibers, detects muscle tension



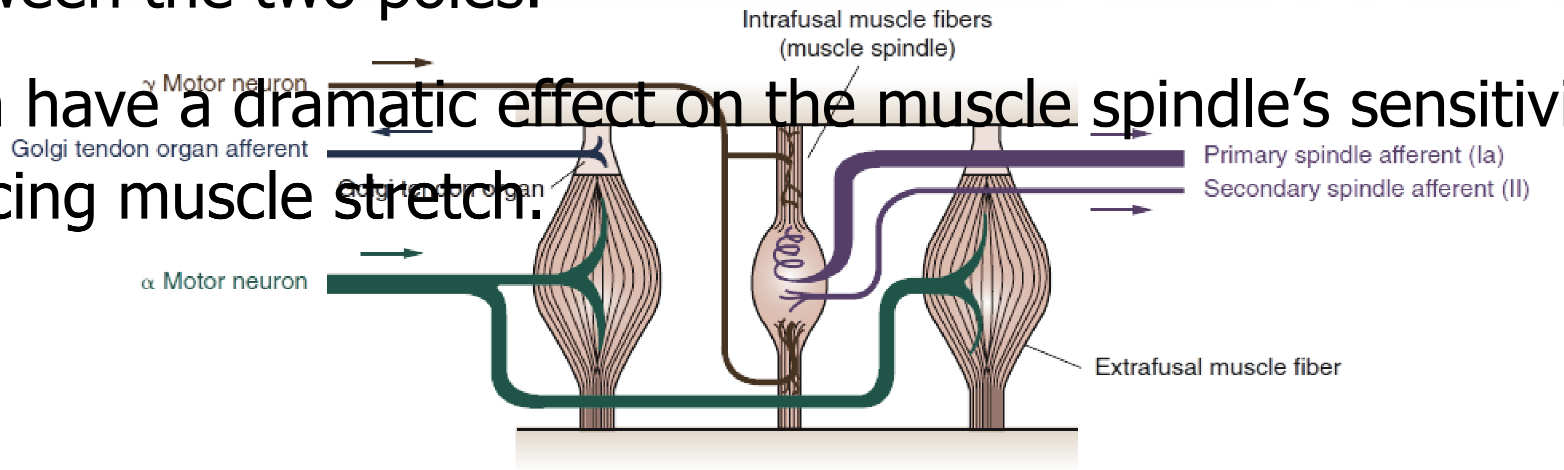
The Muscle Spindle

- The muscle spindle is an encapsulated group of about 3 to 12 small, slender, specialized skeletal muscle fibers
  - these muscle fibers are called intrafusal muscle fibers
  - the majority of muscle fibers in a muscle belly, located outside the capsule, are called extrafusal muscle fibers.
- If the muscle is stretched, lengthening the extrafusal muscle fibers, causes the intrafusal fibers of the muscle spindle also be stretched.



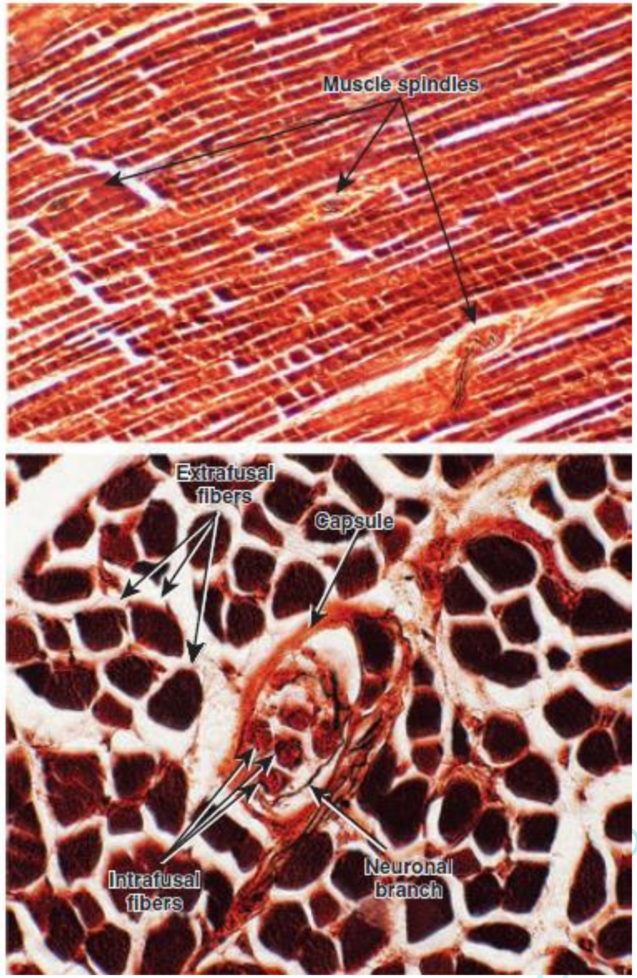
The Muscle Spindle

- Unlike extrafusal muscle fibers, the contractile elements of intrafusal muscle fibers are restricted to their polar ends, with none in their middle (equatorial) region. Therefore, their polar ends can contract, but their equatorial region cannot.
- Such contraction does not directly contribute to the shortening of the gross muscle, but it can tighten the region of the intrafusal fiber that lies between the two poles.
- This can have a dramatic effect on the muscle spindle's sensitivity for transducing muscle stretch.



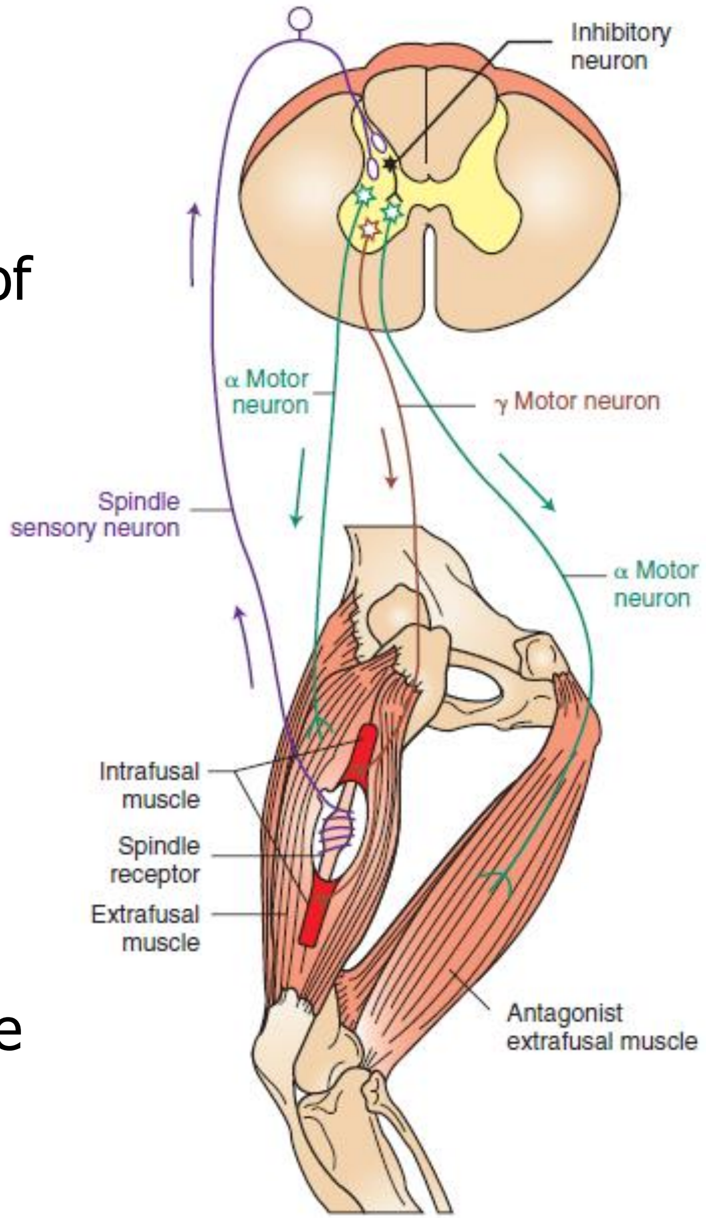
The Muscle Spindle

- The muscle spindle receptor is an encapsulated group of specialized (intrafusal) skeletal muscle fibers supplied with both motor and sensory innervation.
  - A, Longitudinal section through a skeletal muscle showing that the encapsulated muscle spindles are oriented parallel to the more numerous extrafusal fibers of the muscle. The ends of the muscle spindle are attached to the extracellular matrix of the extrafusal fibers.
  - B, Higher-magnification view of a transverse section through a muscle spindle. Intrafusal fibers can be seen within the spindle's tissue capsule. These fibers are fewer, shorter, and more slender than the surrounding extrafusal fibers. A portion of the spindle's innervation can also be seen



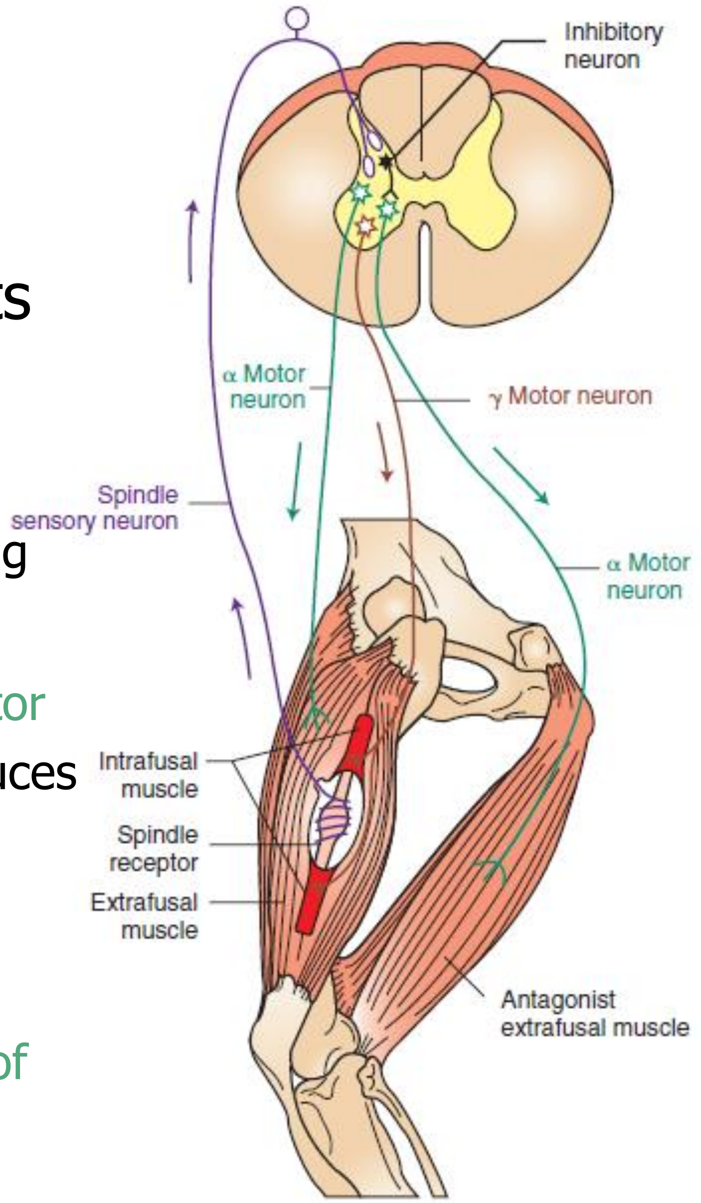
The Muscle Spindle

- Spindle sensory neurons arise from the equatorial region of the intrafusal muscle fibers and carry action potentials from the spindle to the CNS by way of the peripheral nerves.
- The contractile, polar regions of the intrafusal muscle fibers are innervated by motor neurons called gamma (γ) motor neurons.
- Extrafusal muscle fibers—the muscle fibers that cause the physical shortening of the muscle—are supplied by a different population of motor neurons (those that comprise the motor units) called alpha (ɑ) motor neurons.



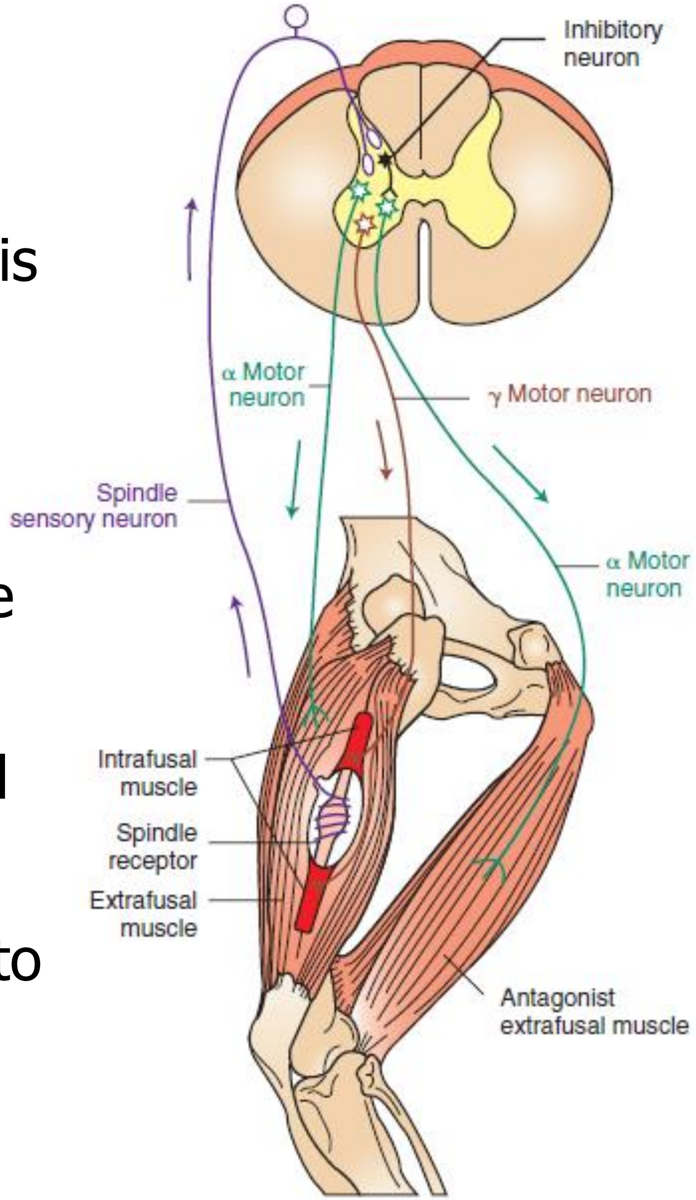
The Muscle Spindle

- stretching a given muscle can lead to a rapid, reflex contraction of that same muscle, bringing it back to its original length.
  - Stretching the muscle lengthens the intrafusal muscle fibers of the spindle, increasing the frequency of action potential discharge along the sensory output neurons of the spindle.
  - This leads to an increase in action potential frequency in the α motor neurons on which the spindle sensory neurons synapse. This produces contraction of the extrafusal fibers innervated by those α motor neurons, which results in contraction (shortening) of the muscle.
  - Contraction of the muscle results in a shortening of the muscle spindle's equatorial region. This eventually reduces the frequency of action potentials occurring on the spindle sensory neurons to the prestretch level, terminating the response. (The cycle is a classic negative-feedback system.)



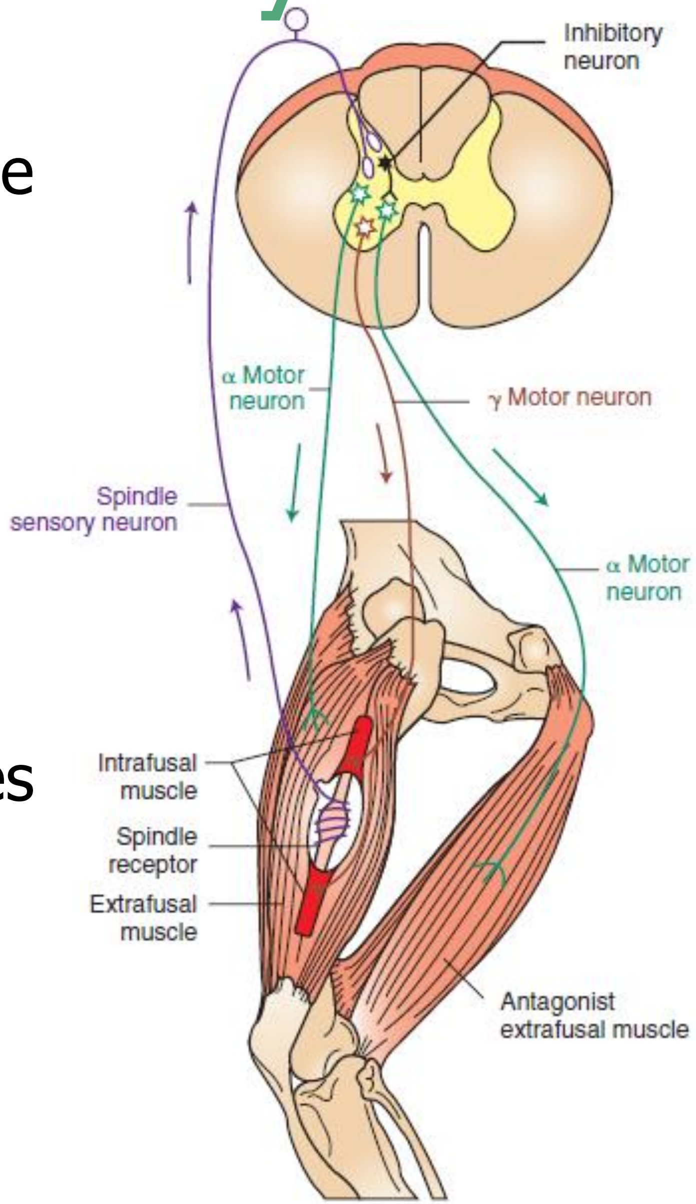
The Muscle Spindle Stretch Reflex

- The muscle spindle stretch reflex (illustrated here as the knee jerk reflex) begins when the spindle receptor organ is stretched.
- This causes action potentials on the receptor's sensory neurons, which in turn cause excitatory postsynaptic potentials (EPSP) on the α motor neurons returning to the extrafusal muscle fibers of that same muscle.
- Action potentials on the α motor neurons cause extrafusal muscle fibers to contract, and the knee extends ("jerks").
- Through an inhibitory interneuron, the α motor neurons to the antagonist muscles are simultaneously inhibited.



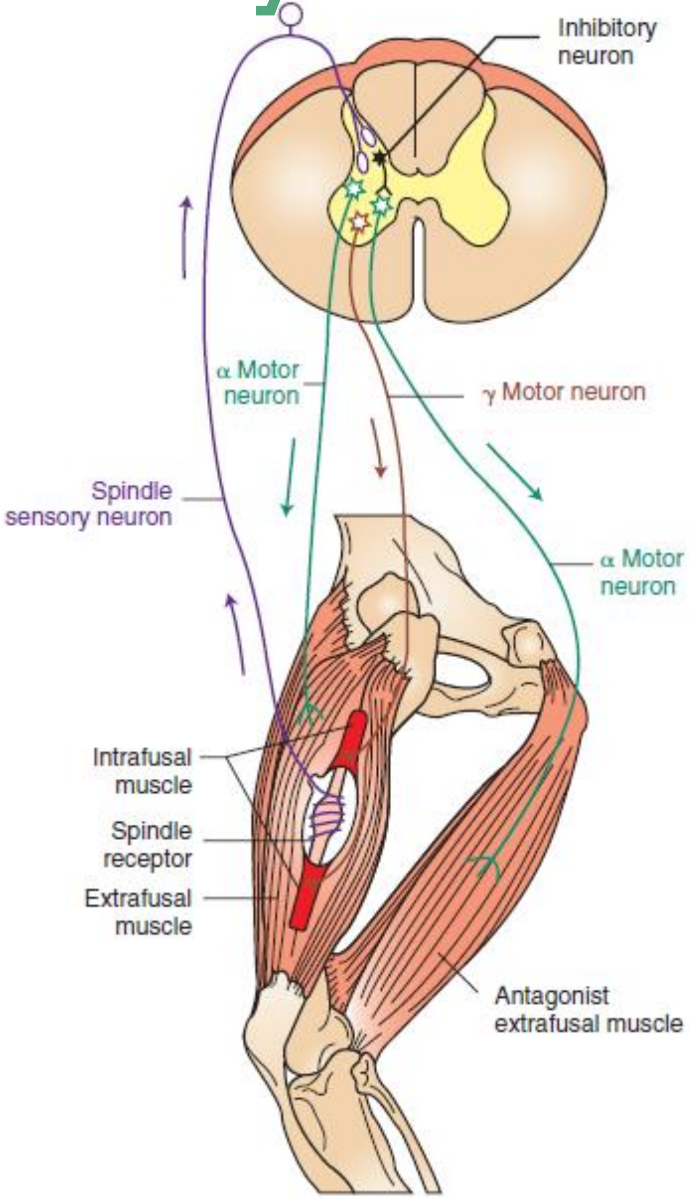
CNS control on spindle sensitivity

- The γ motor neurons innervate the intrafusal muscle fibers at their polar ends, the regions containing contractile protein.
- Action potentials on the γ motor neurons cause shortening of the polar regions of the intrafusal muscle fibers, stretching the equatorial portion
- This motor innervation of a receptor organ regulates the sensitivity of the muscle spindle.



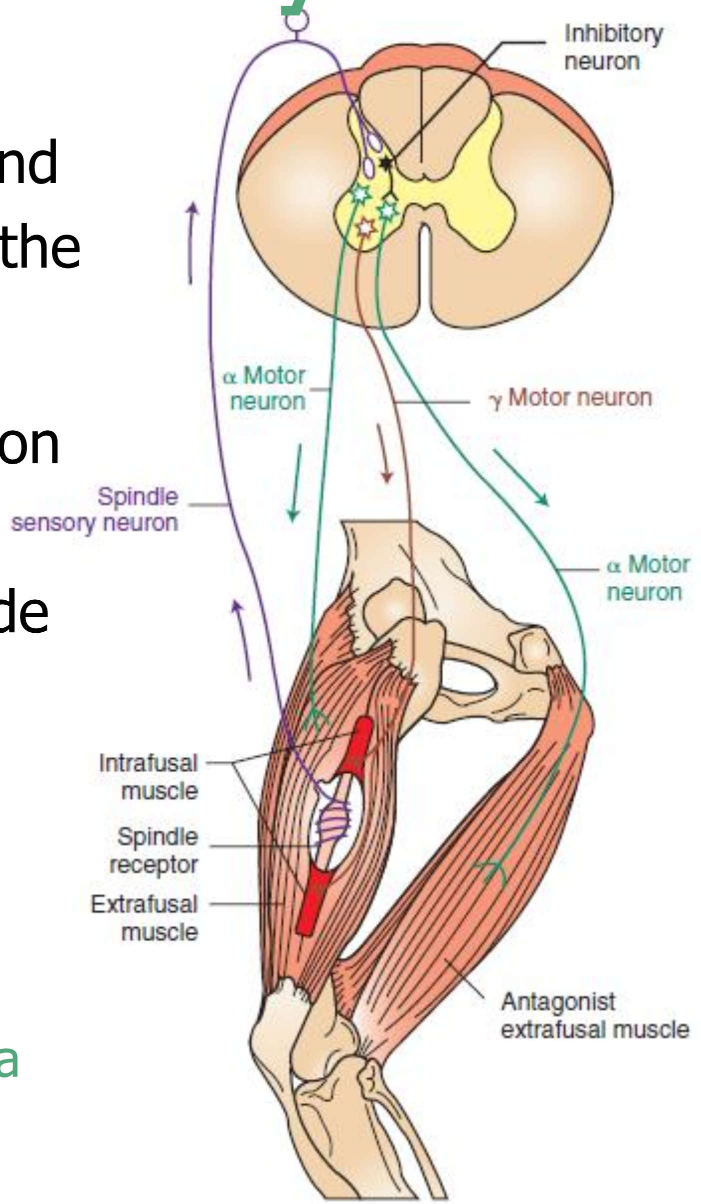
CNS control on spindle sensitivity

- Shortening of a gross muscle resulting from initiation of extrafusal muscle fiber contraction has the potential to slacken the intrafusal muscle fibers given their parallel relationship to the extrafusal fibers.
- This would severely limit the ability of the muscle spindle to transduce stretch.
- However, this does not normally occur because contraction of the polar regions of intrafusal fibers resulting from γ motor neuron activation is initiated concurrently with shortening of extrafusal fibers caused by ɑ motor neuron activation.



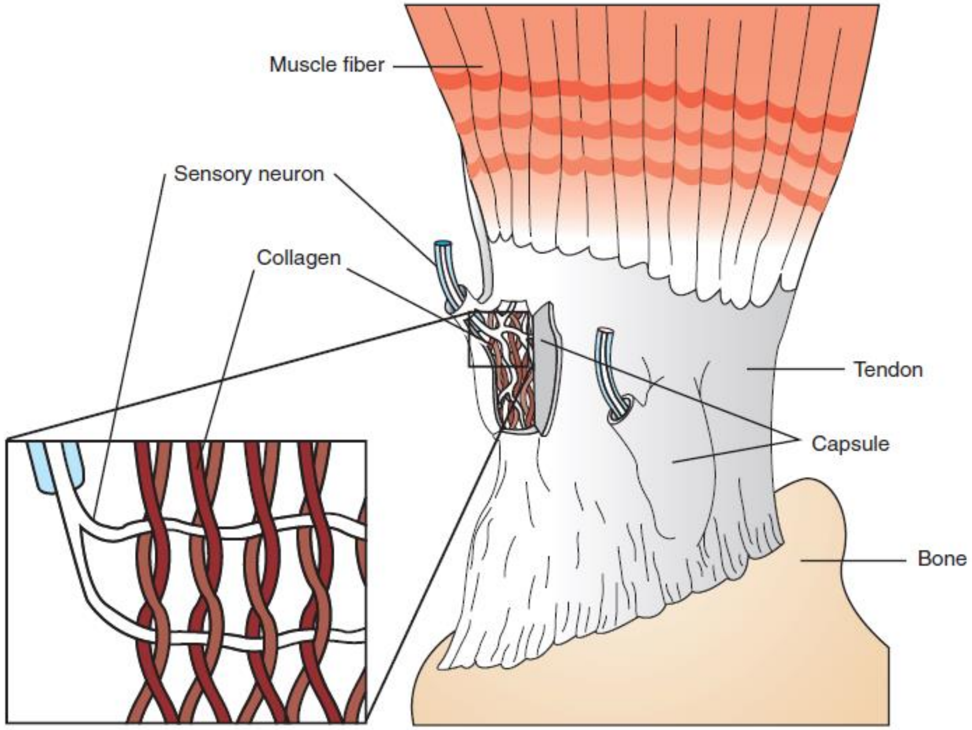
CNS control on spindle sensitivity

- This allows the spindle receptor organ to remain taut and sensitive to sudden stretches of the gross muscle over the entire range of its length.
- This γ motor neuron control mechanism can also function to differentially regulate the sensitivity of the muscle spindle, depending on the type of movement to be made (e.g., novel and unpredictable vs. stereotypical).
- There are actually two types of γ motor neurons;
  - one regulates the sensitivity of the muscle spindle to the dynamic phase of stretch (γD; gamma dynamic)
  - one regulates sensitivity to steady-state length (γS; gamma static).



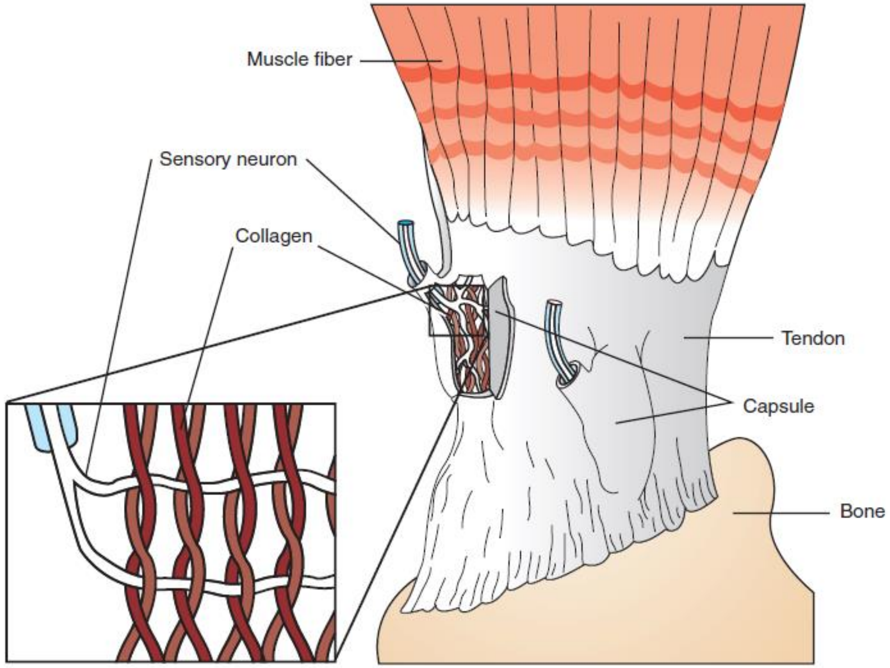
The Golgi Tendon Organ

- The Golgi tendon organ is located in the tendons of skeletal muscle, in series with the extrafusal fibers.
- It detects tension in the tendon, produced by muscle contraction, and sends information about this tension to the central nervous system.
- Sensory neuron branches of the organ are intertwined among braided collagen fibrils (inset), which fold up and pinch the neural branches when tension develops in the tendon.



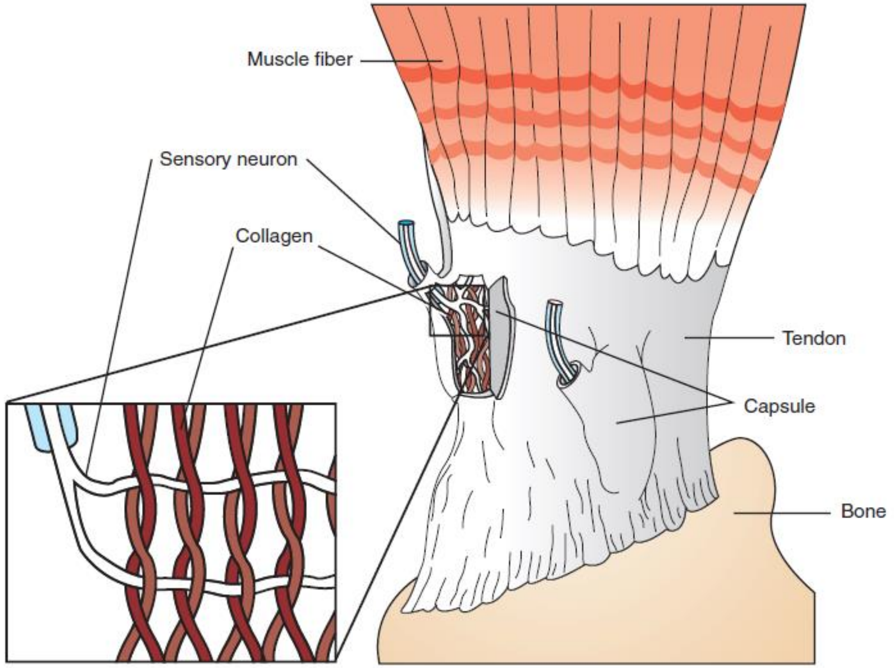
The Golgi Tendon Organ

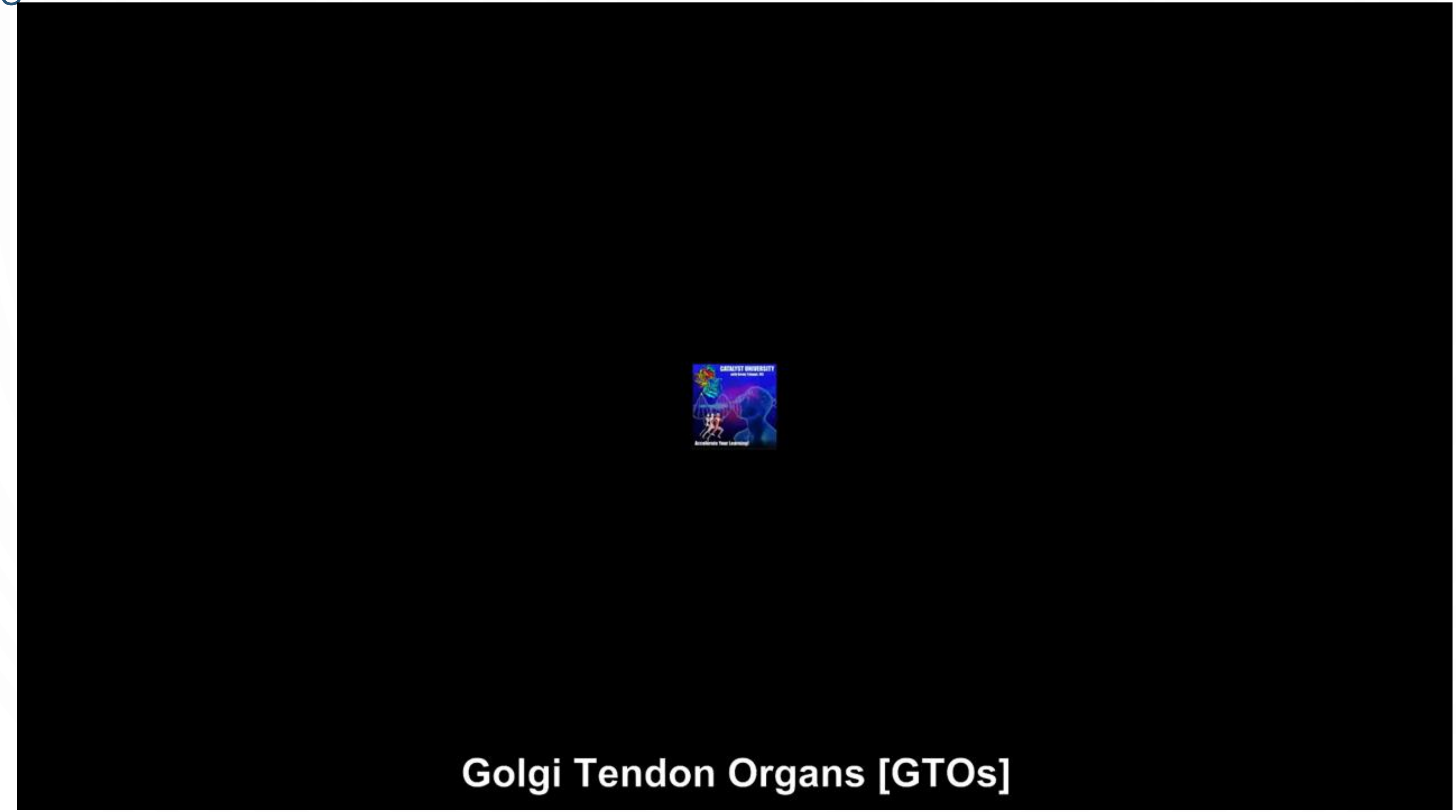
- This sensory neuron, as with those of the muscle spindle, carries action potentials to the CNS by way of peripheral nerve and dorsal root.
- The Golgi tendon organ has no motor innervation.
- Because the Golgi tendon organ is in series with a group of extrafusal fibers and the tendon, when the extrafusal fibers shorten during contraction, tension is applied to the tendon organ. This causes the braided collagen fibrils of the organ to tighten and squeeze the endings of the sensory neuron.
- Action potentials are therefore generated and sent to the CNS along the sensory neuron at a frequency proportional to the tension developed by the muscle.

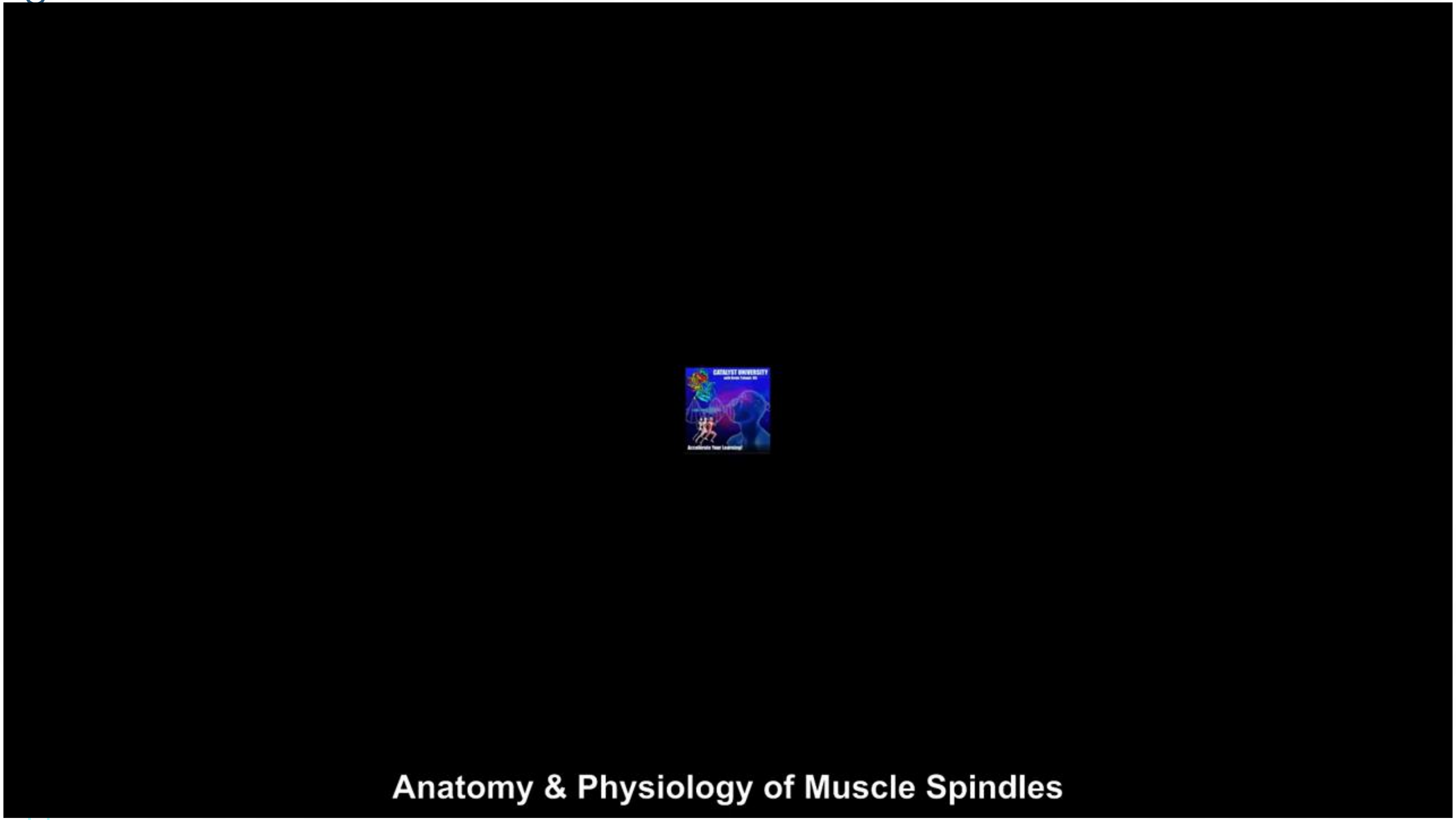


The Golgi Tendon Organ

- In contrast, the muscle spindle is arranged in parallel with the extrafusal muscle fibers, and when they contract, the spindle reduces its action potential frequency.
- When action potentials from spindle sensory neurons reach the CNS, they monosynaptically produce EPSPs in the α motor neurons returning to the same muscle.
- Action potentials along sensory neurons from Golgi tendon organs have the opposite effect: they activate inhibitory interneurons, polysynaptically producing IPSPs on α motor neurons to the same muscle. This leads to a reduced extrafusal muscle fiber contraction




Golgi Tendon Organs [GTOs]


Anatomy & Physiology of Muscle Spindles

Chapter 13

Integrative Physiology I: Control of Body Movement