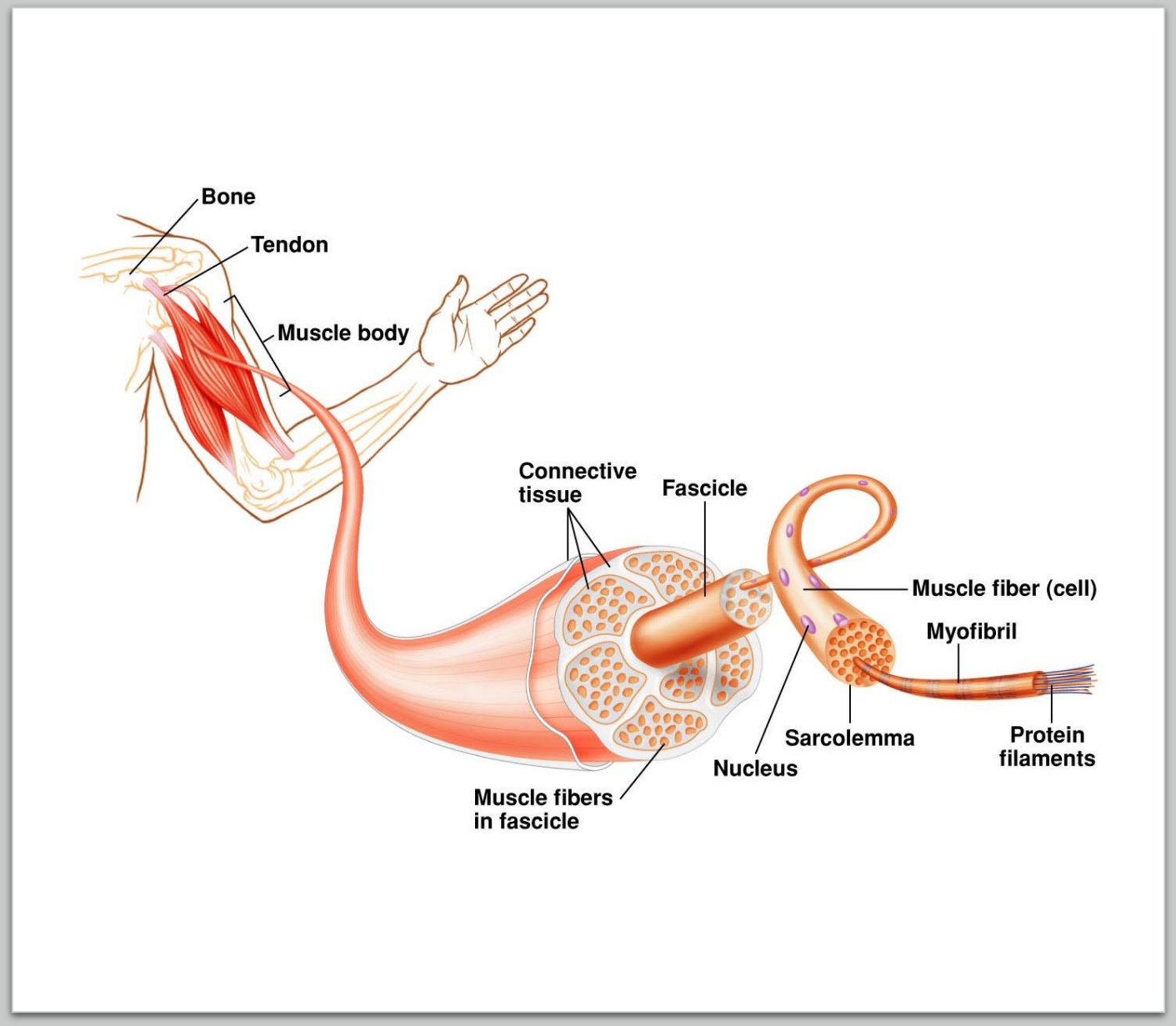
Excitation contraction coupling

DR. Arwa Rawashdeh

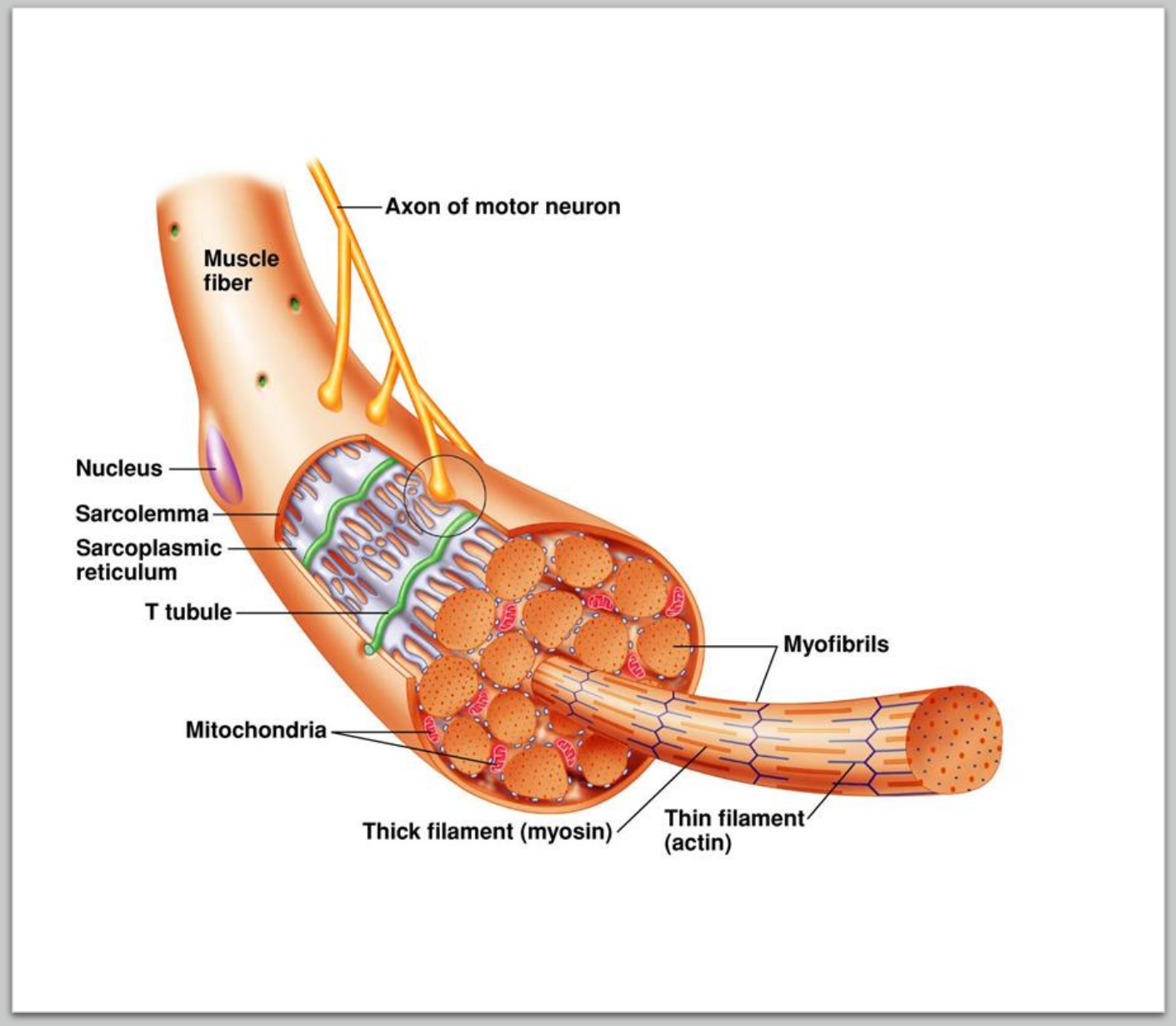
Skeletal Muscle Structure

Muscle = group of fascicles



Muscle fiber components

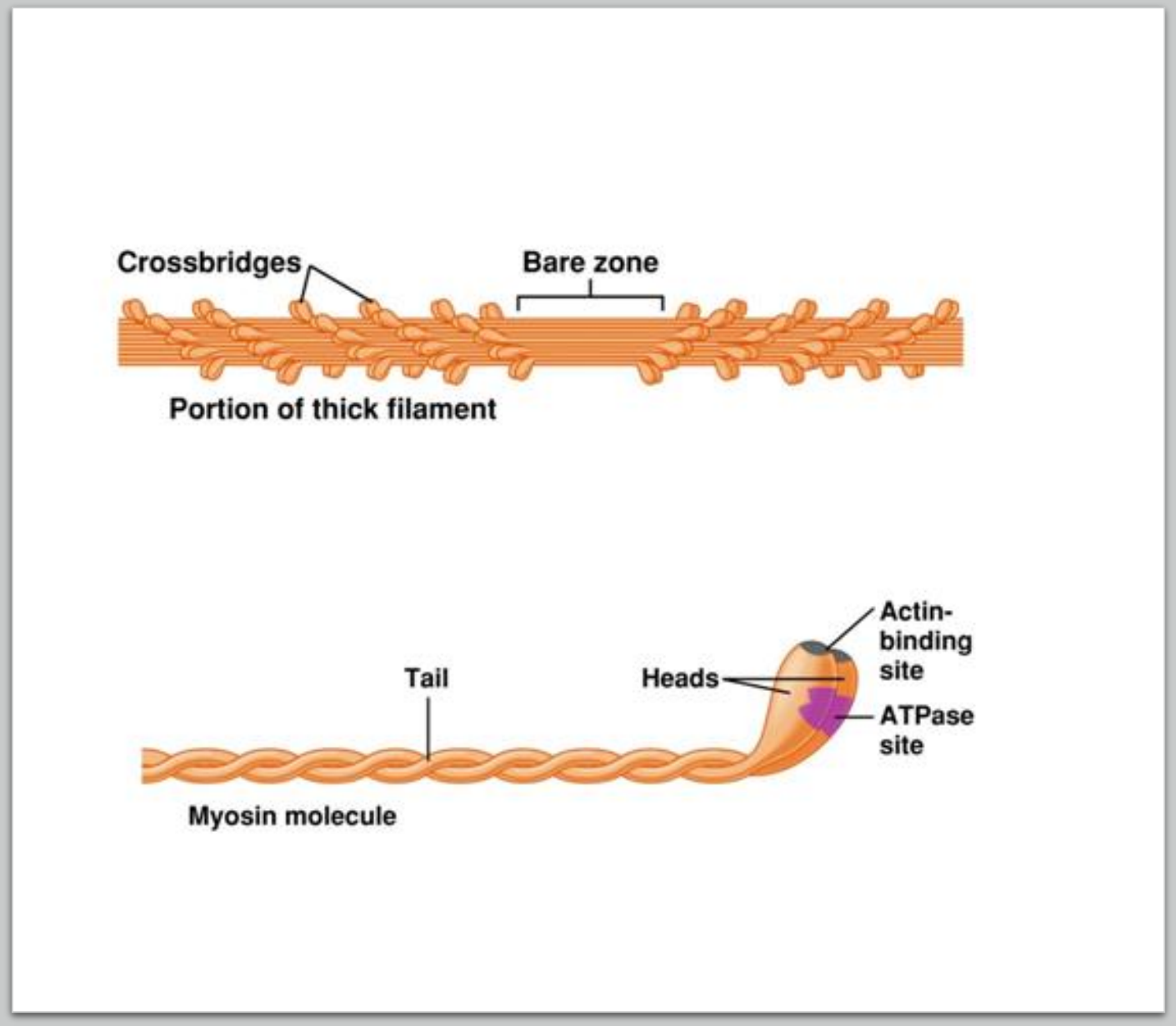
- Sarcolemma: muscle cell membrane
- Sarcoplasma: muscle cell cytoplasm
- Motor end plate: contact surface with axon terminal
- T tubule: cell membrane extension into the sarcoplasm (to reach the myofibrils)
- Cisternae: areas of the endoplasmic reticulum dedicated to Ca++ storage (located on each side of the T-tubules)
- Myofibrils: organized into sarcomeres



Muscle contraction: Cell events

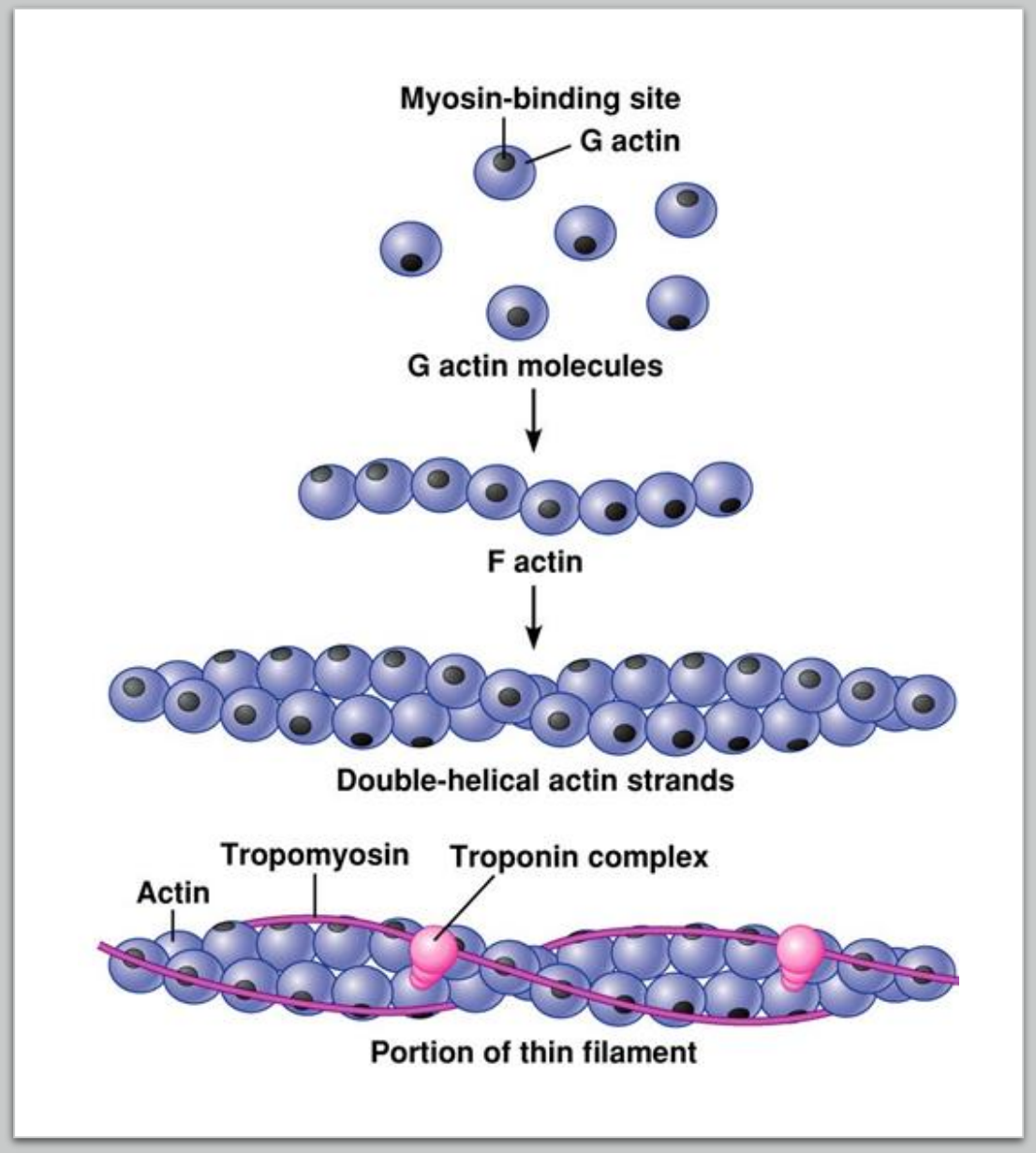
Myosin structure

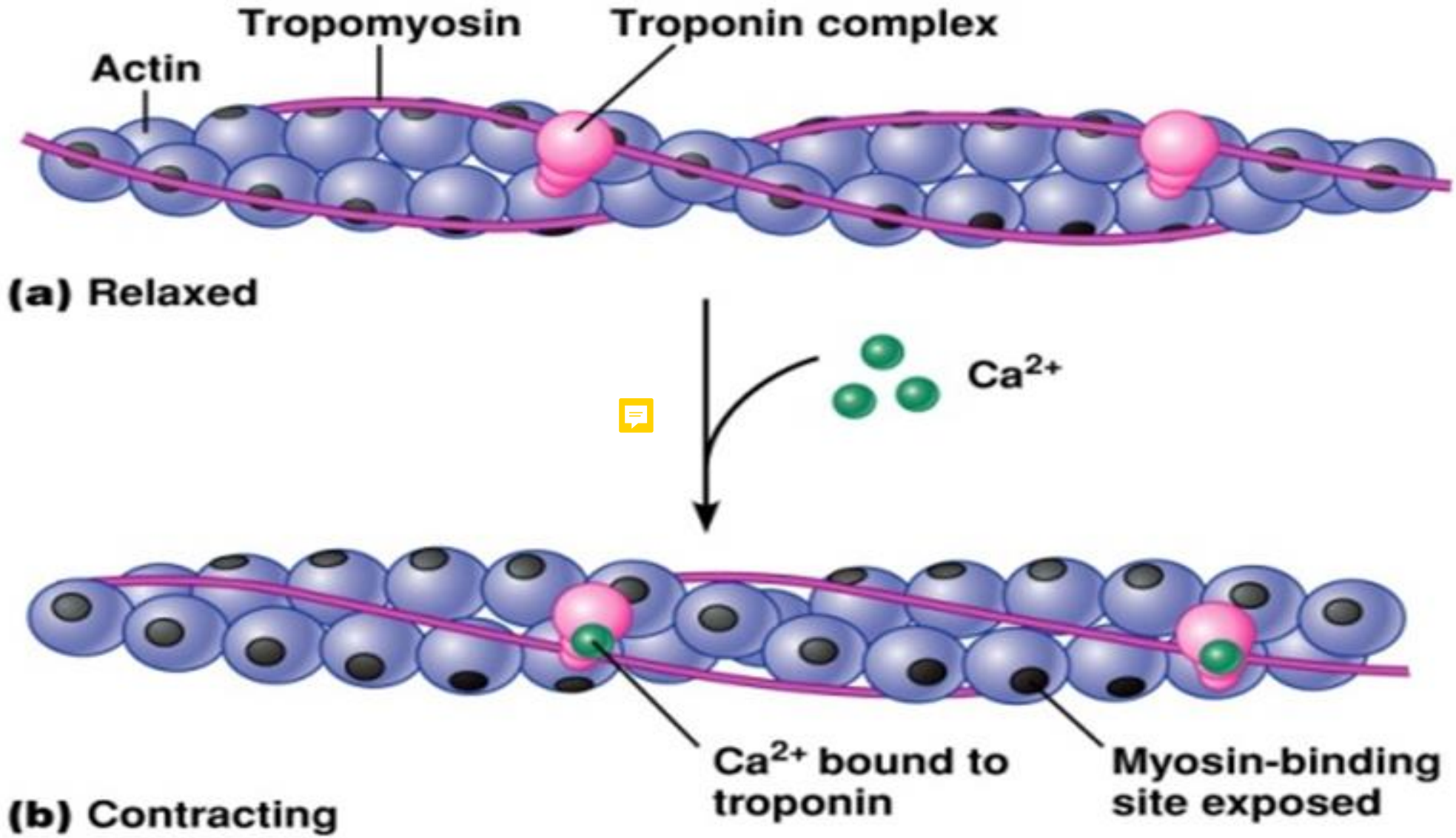
- Many myosin molecules per filament, golf club shape
- Long tail topped by a thickening: the head → forms crossbridges with the thin filament
- Presence of the enzyme, ATPase in the head → release energy for contraction

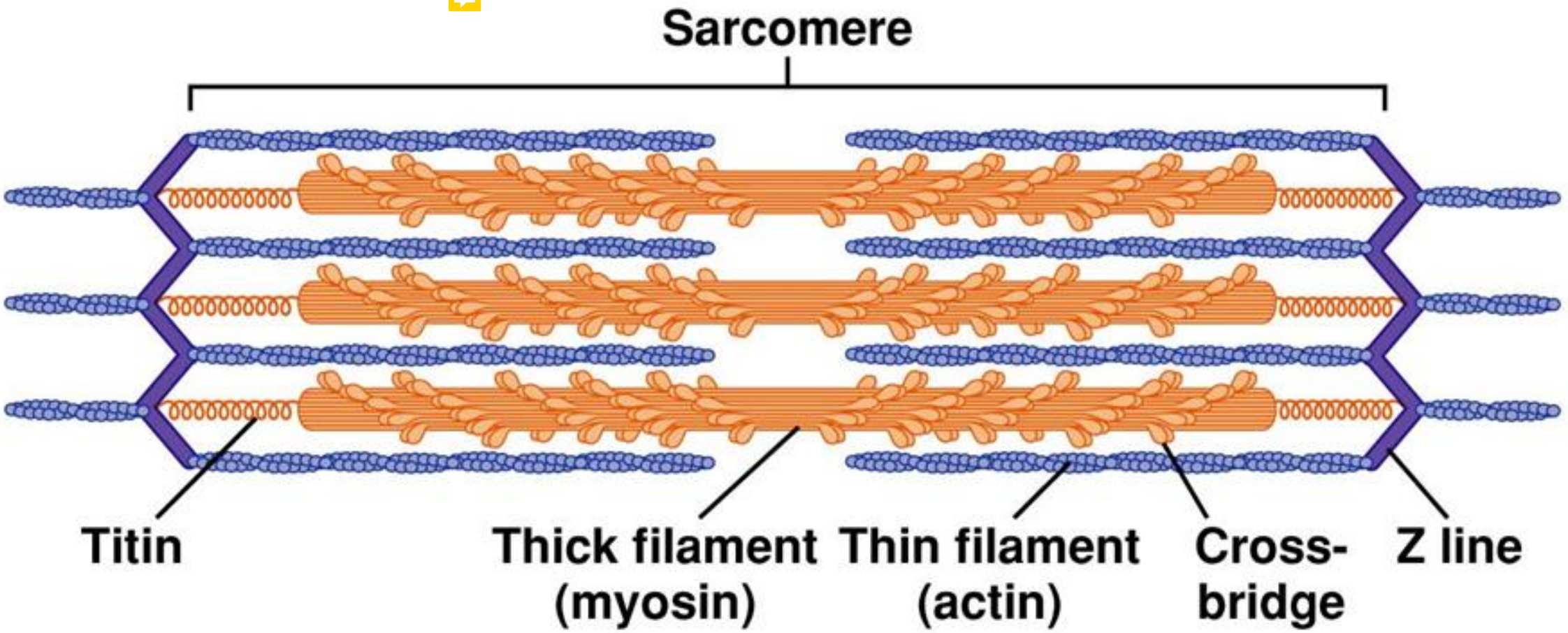


Actin structure

- Formed by 3 different proteins:
- globular (G) actins: bind to myosin heads
- tropomyosin: long, fibrous molecule, extending over actin, and preventing interaction between actin and myosin
- troponin: binds reversibly to calcium and able to move tropomyosin away from the actin active site

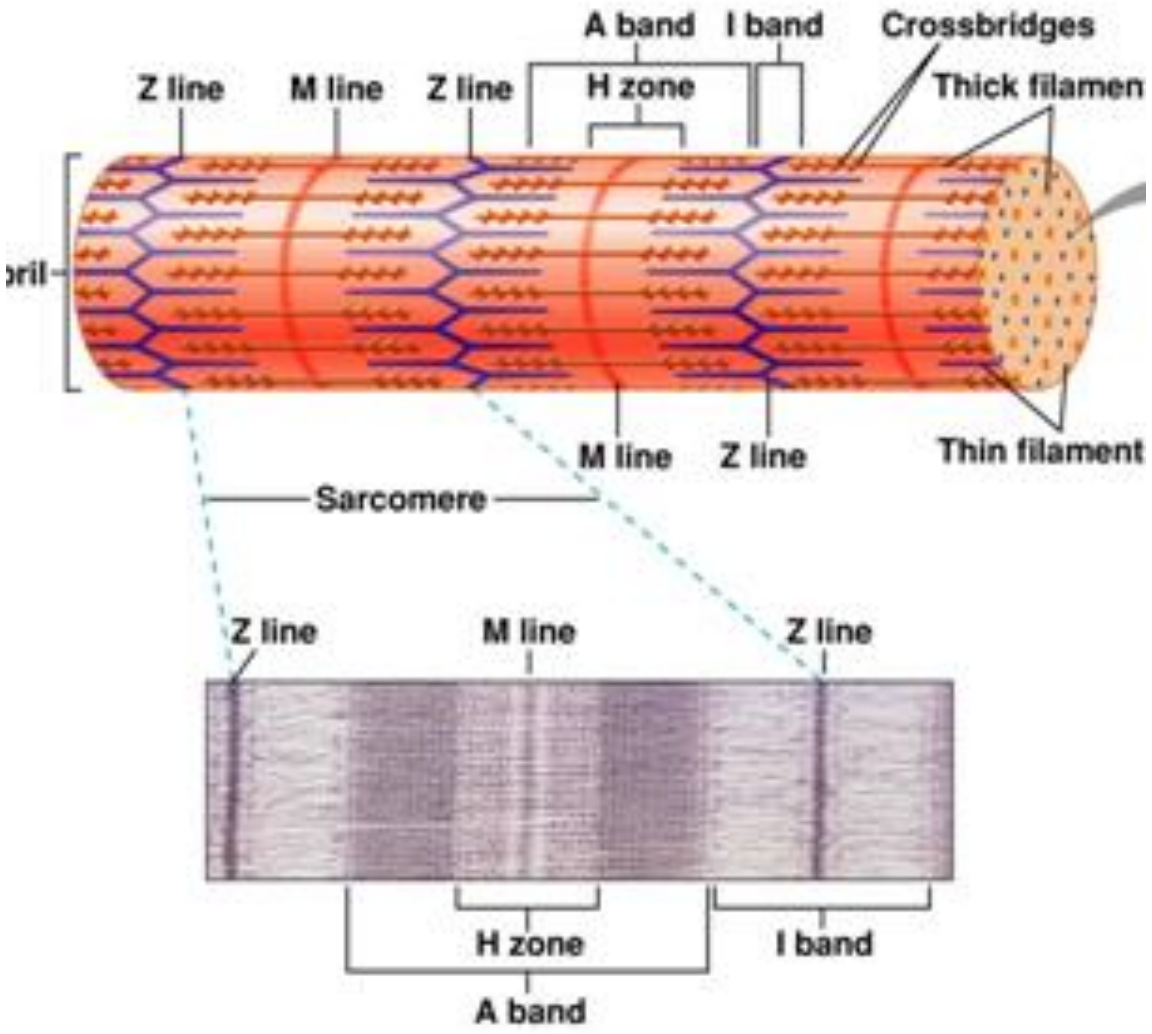


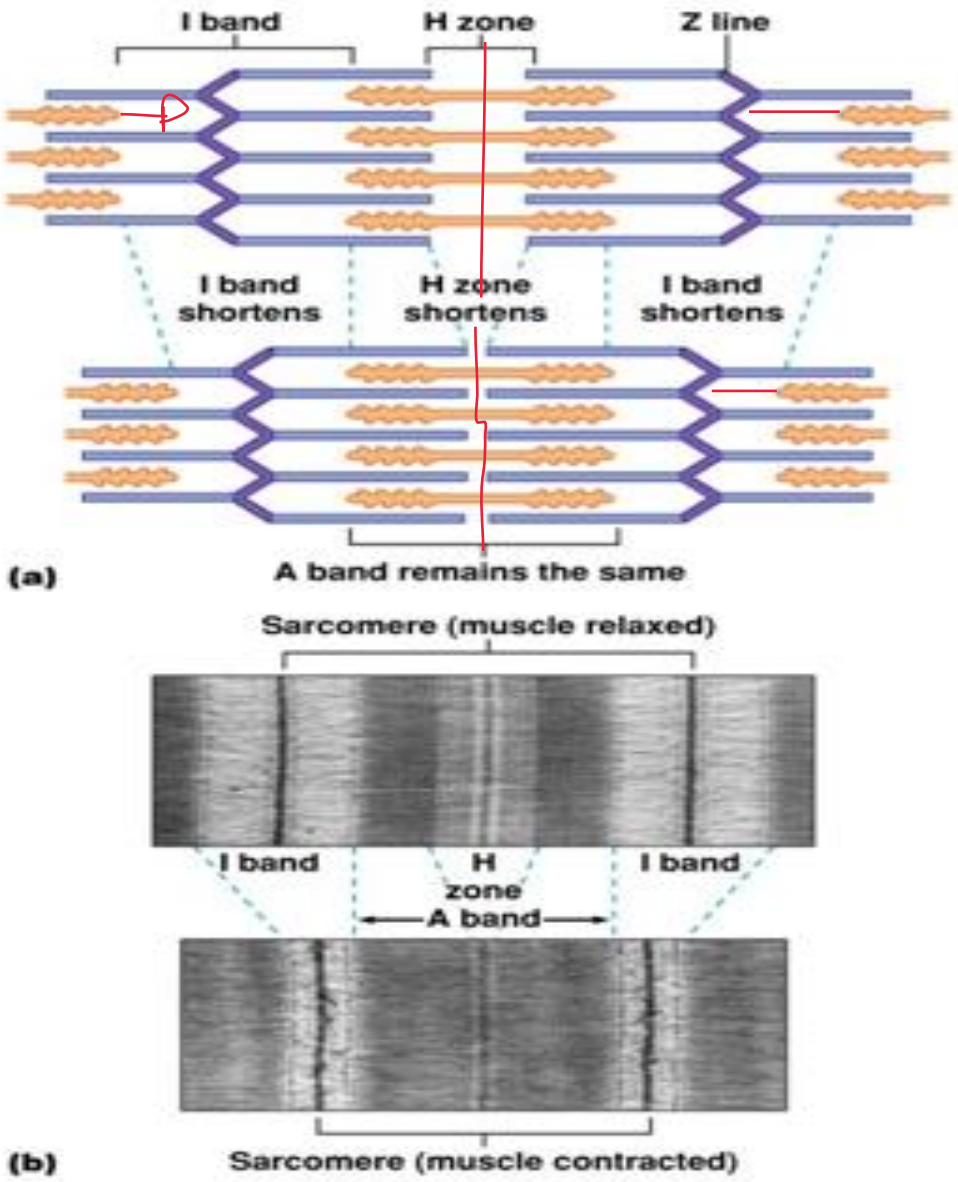

Tropomyosin
Troponin complex
Actin
(a) Relaxed
Ca^{2+}
Ca^{2+} bound to troponin
Myosin-binding site exposed
(b) Contracting

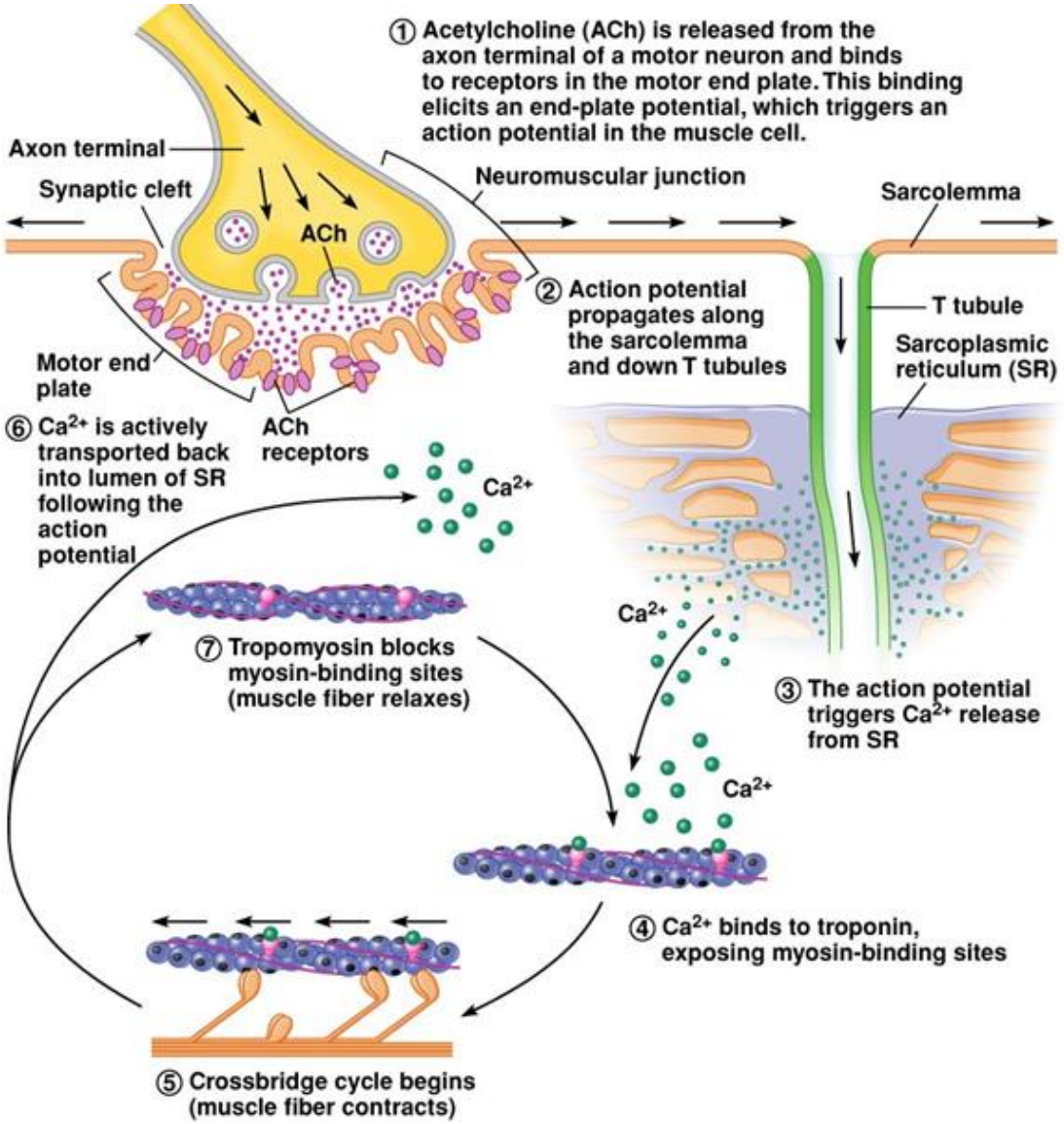

Sarcomere
Titin
Thick filament (myosin)
Thin filament (actin)
Cross-bridge
Z line

The sarcomere

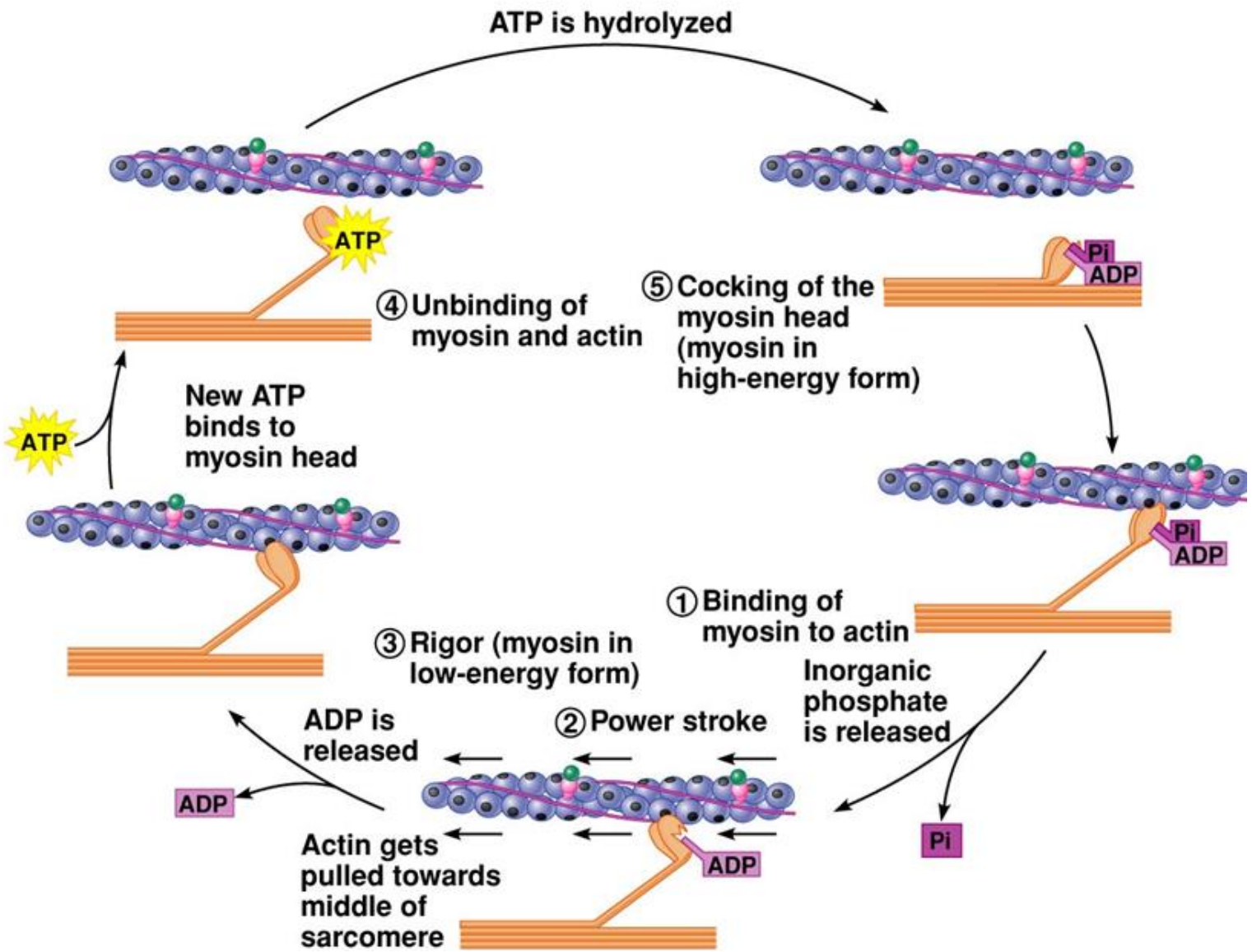
- The myofibrils are organized into a repetitive pattern, the sarcomere
- Myosin: thick filament
- Actin: thin filament
- Bands formed by pattern: A and I and H bands
- Z line: area of attachment of the actin fibers
- M line: Myosin fiber centers




I band
H zone
Z line
I band shortens
H zone shortens
I band shortens
A band remains the same
(a)
Sarcomere (muscle relaxed)
I band
H zone
I band
A band
Sarcomere (muscle contracted)
(b)



The mechanism of force generation in muscle

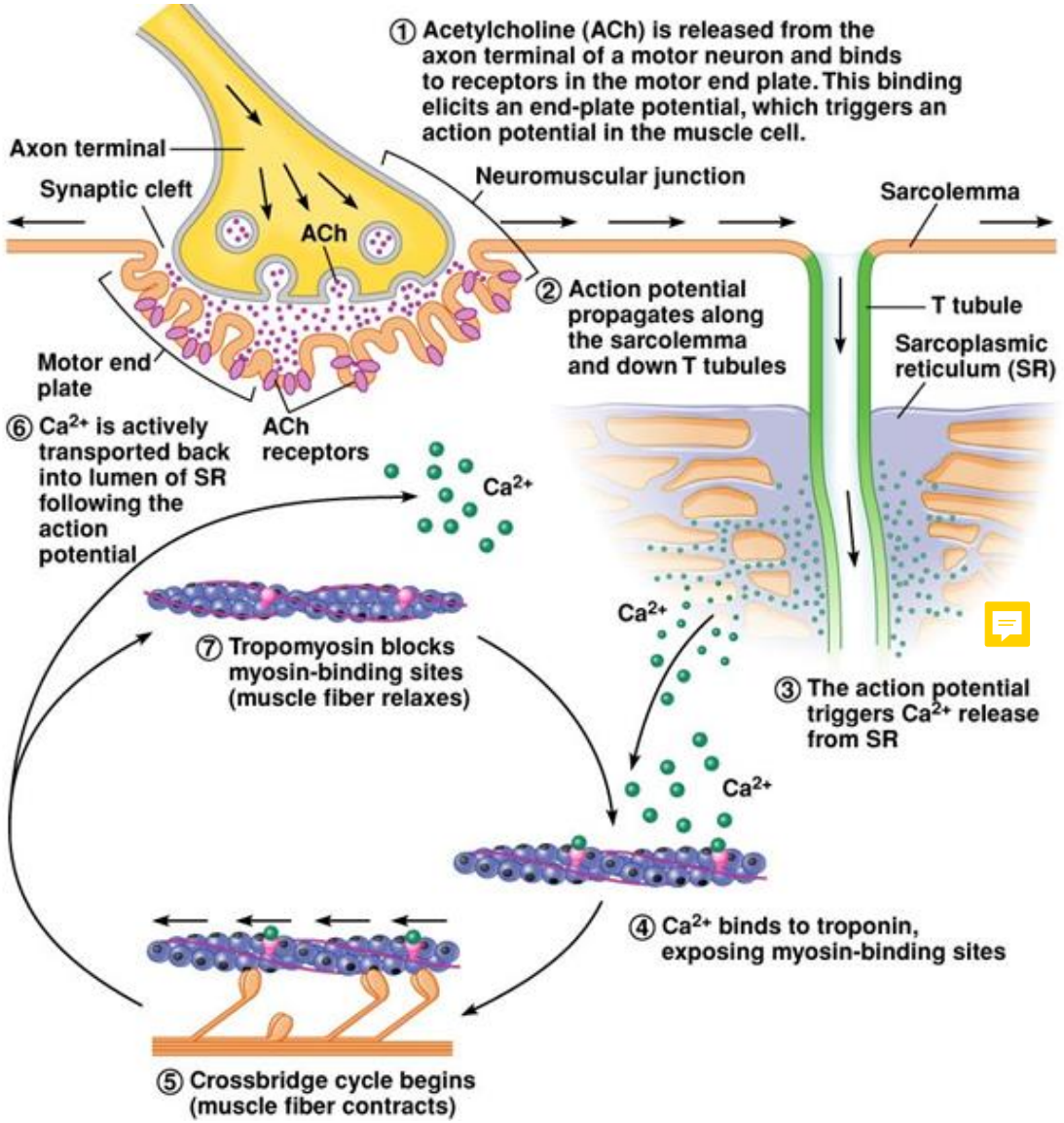

ATP is hydrolyzed
ATP
④ Unbinding of myosin and actin
⑤ Cocking of the myosin head (myosin in high-energy form)
Pi
ADP
New ATP binds to myosin head
ATP
Pi
ADP
① Binding of myosin to actin
③ Rigor (myosin in low-energy form)
Inorganic phosphate is released
ADP is released
② Power stroke
ADP
Pi
Actin gets pulled towards middle of sarcomere
ADP

Mechanics of muscle contraction

DR. ARWA RAWASHDEH

Objectives

- Define the microscopic skeletal muscle contraction



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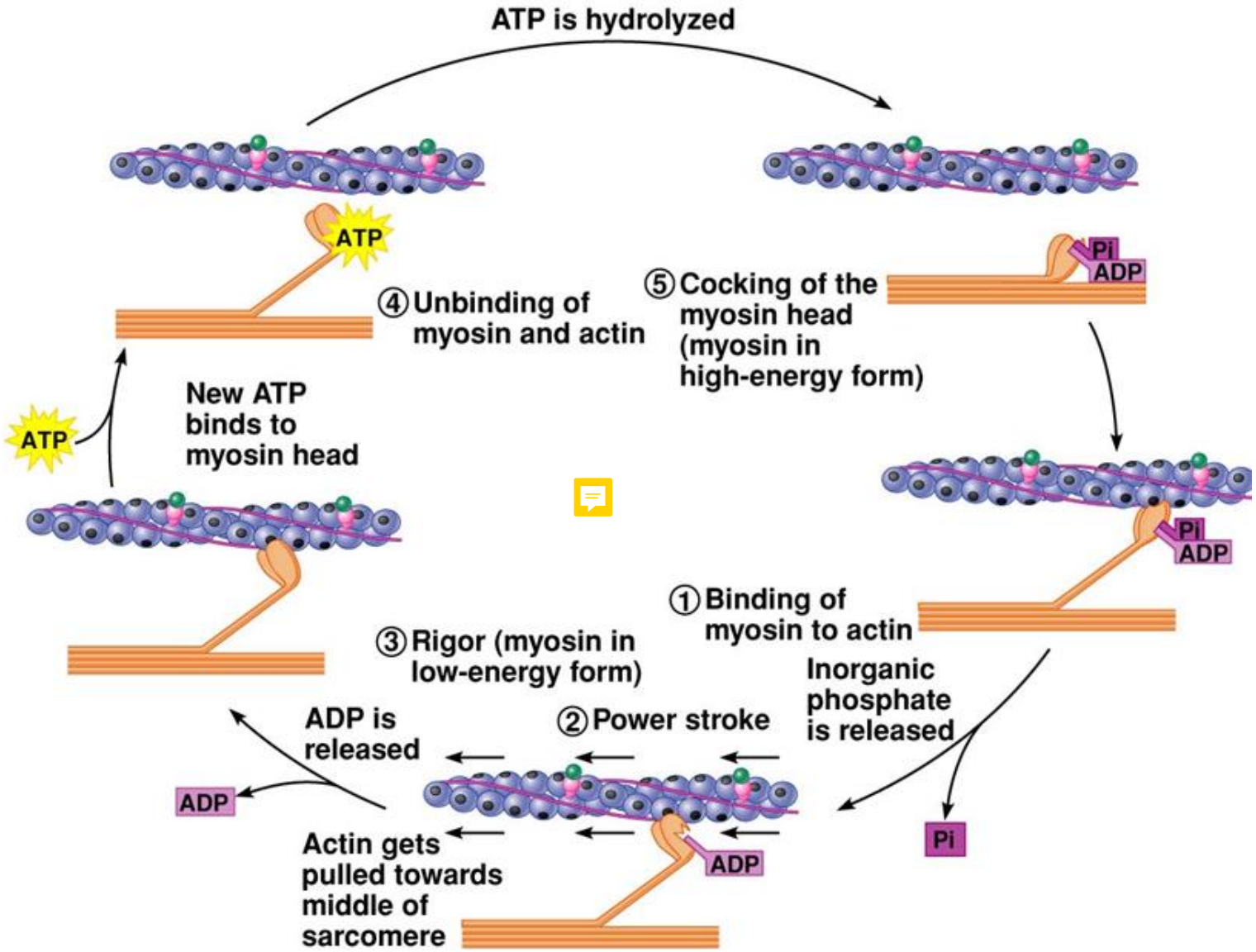
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Pi
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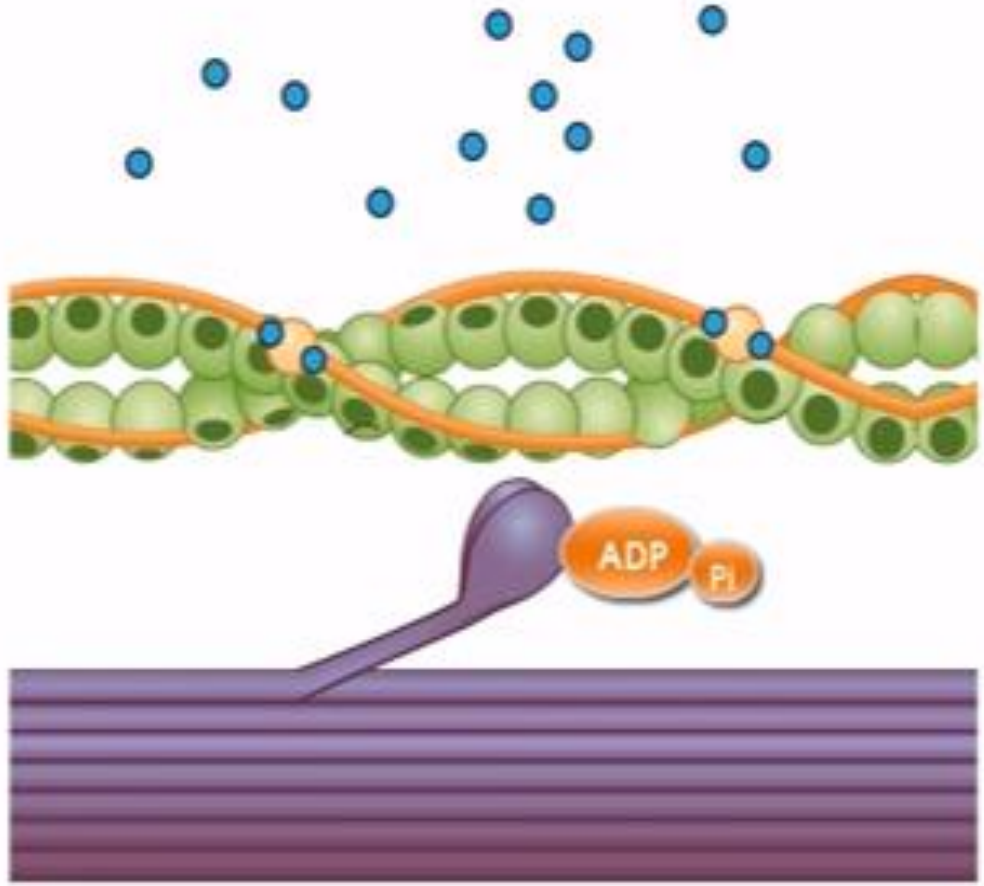


"Cocked Position"

1. Calcium binds

2. Cross bridge

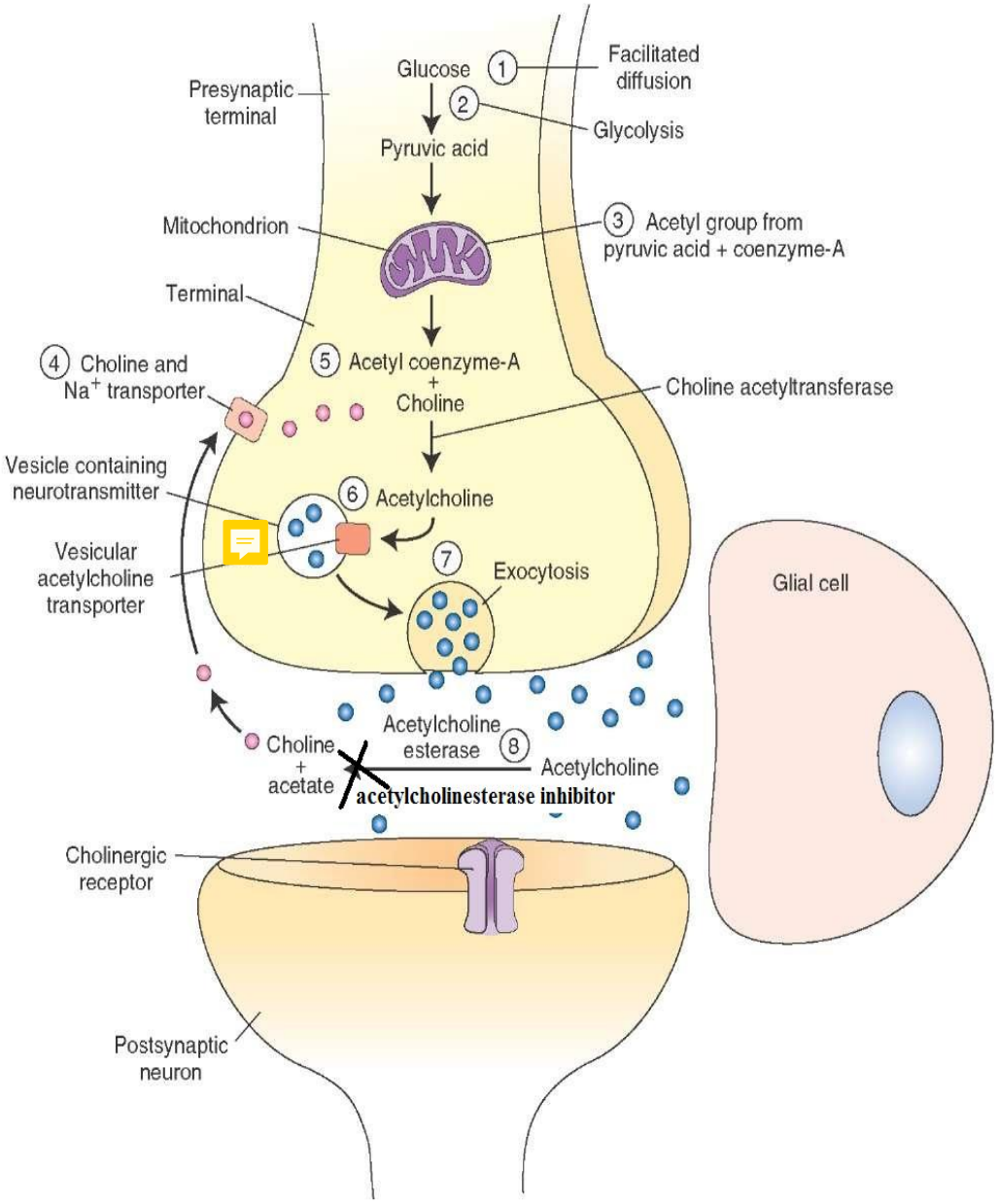
3. Power Stroke

4. ATP binding

5. ATP hydrolysis

Spastic Paralysis

- Ingestion of insecticides Killer
- Nerve gas poison (Sarin)

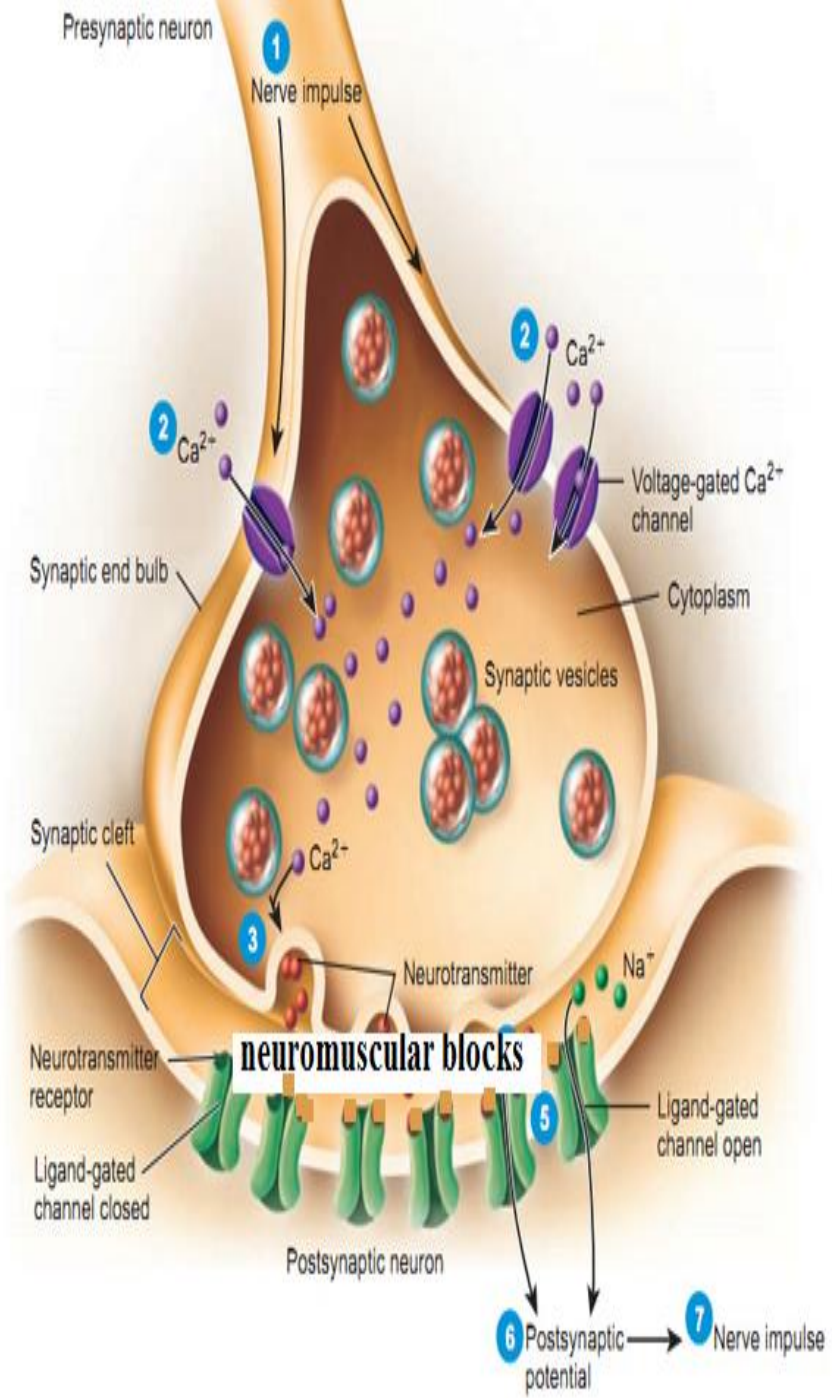


Flaccid Paralysis

- Topical anaesthetic shot into this muscle; neuromuscular blocker
- Relaxation of diaphragm during anaesthesia; neuromuscular blocker
- Snake Bites (COBRA) ; neuromuscular blocker
- Myasthenia gravis

is a relatively rare autoimmune disorder in which antibodies form against nicotinic acetylcholine (ACh) postsynaptic

- Botulinum disease; prevent Ach release



Summation and tetanization Comparison of smooth and skeletal contraction

Dr. Arwa Rawashdeh

Objectives

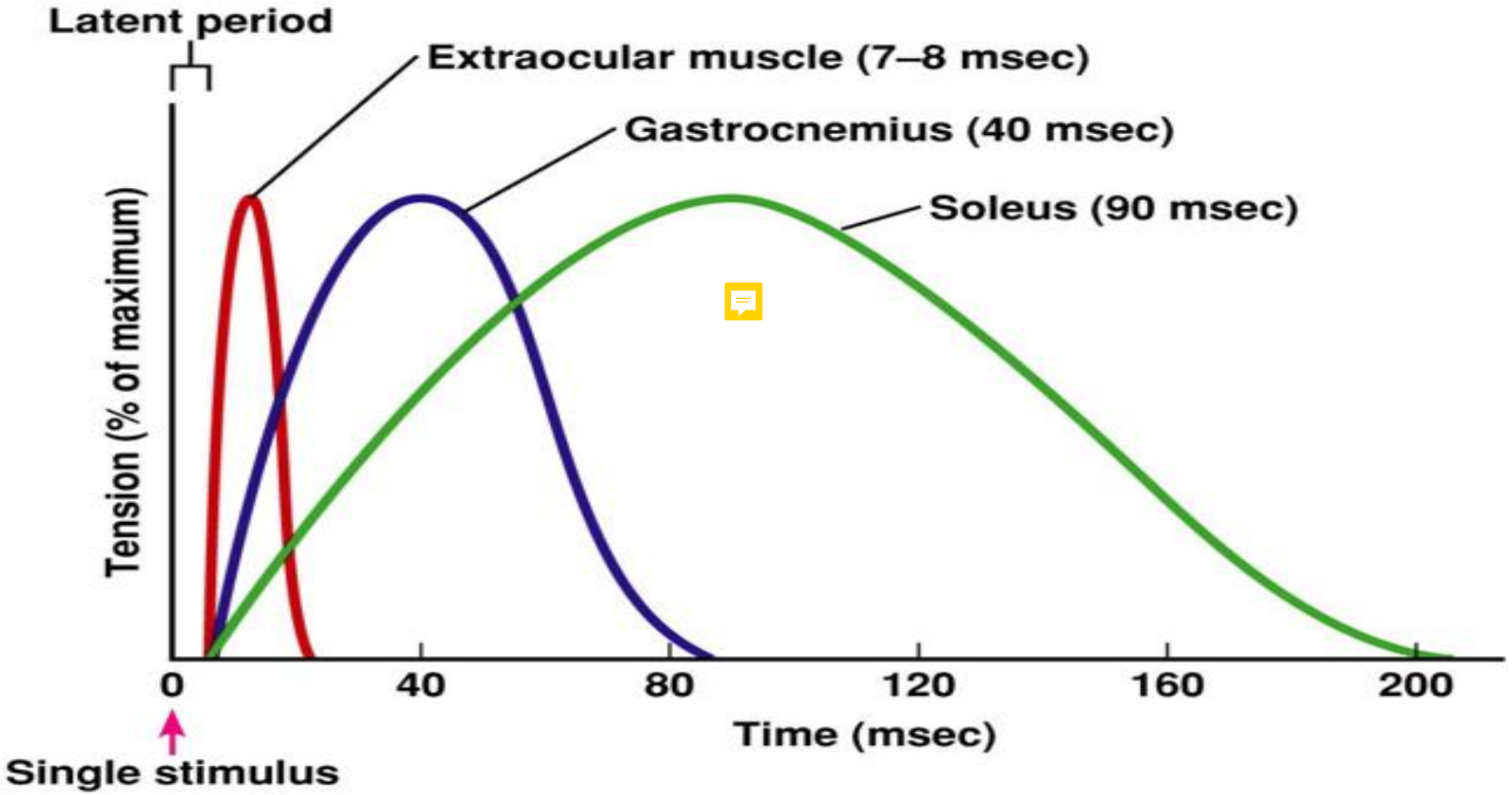
- Types of skeletal muscle
- Summation and tetanus
- Fatigue
- Comparison between skeletal and smooth muscle contraction

Properties of Skeletal Muscle Fiber Types

	Slow oxidative (red)	Fast oxidative (red)	Fast glycolytic (white)
Oxidative capacity	High	High	Low
Glycolytic capacity	Low	Intermediate	High
Speed of contraction	Slow	Intermediate	Fast
Myosin ATPase activity	Low	Intermediate	High
Mitochondrial density	High	High	Low
Capillary density	High	High	Low
Myoglobin content	High	High	Low
Resistance to fatigue	High	Intermediate	Low
Fiber diameter	Small	Intermediate	Large
Motor unit size	Small	Intermediate	Large
Force-generating capacity	Low	Intermediate	High

Types of muscle fibers

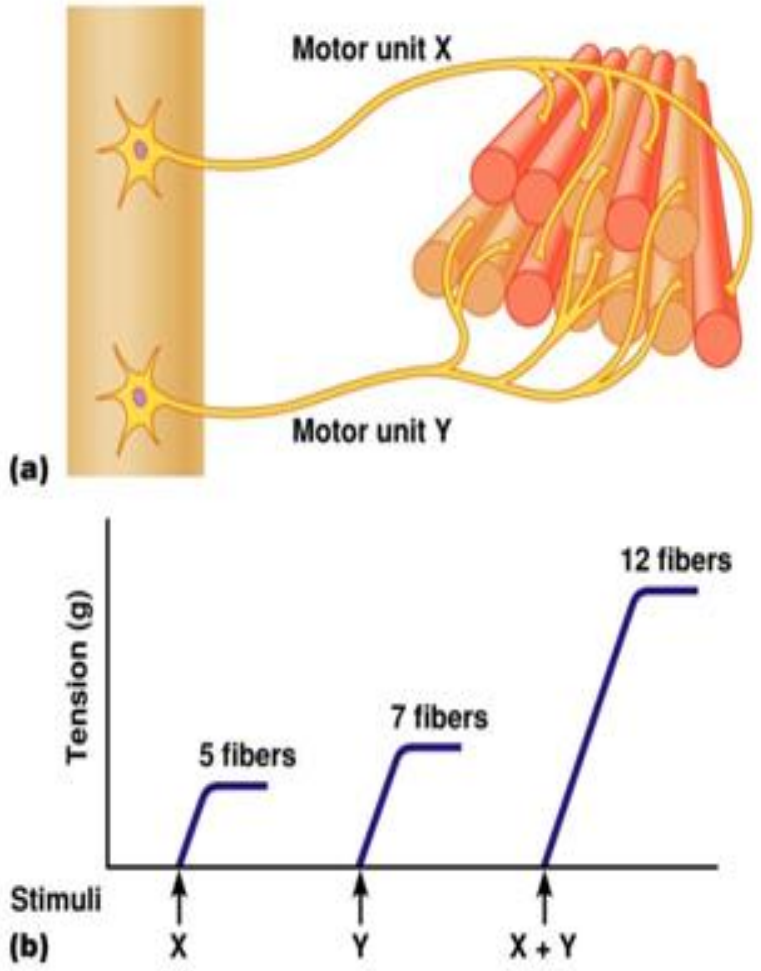
- Various muscles contract at different speed → composed of different types of muscle fibers



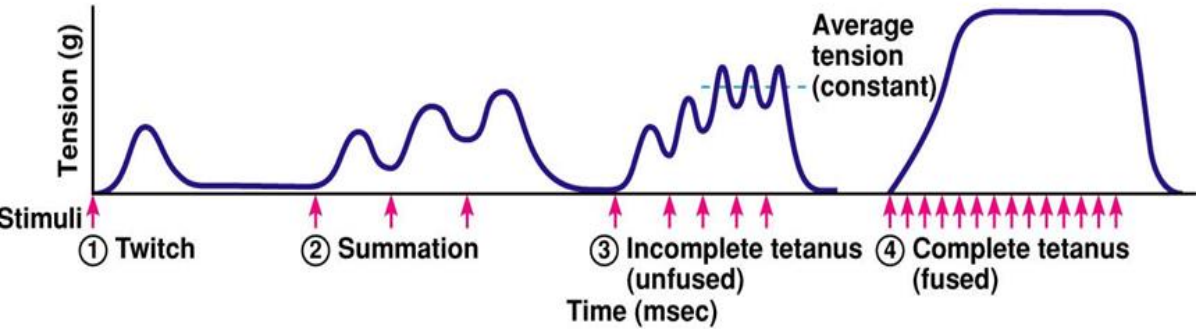
Recruitment

Henneman's size principle states that under load, motor units are recruited from smallest to largest. In practice, this means that slow-twitch, low-force, fatigue-resistant muscle fibers are activated before fast-twitch, high-force, less fatigue-resistant muscle fibers.

This has two very important physiological benefits. First, it minimizes the amount of fatigue an organism experiences by using fatigue-resistant muscle fibers first and only using fatigable fibers when high forces are needed. Secondly, the relative change in force produced by additional recruitment remains relatively constant.



Summation and tetanus

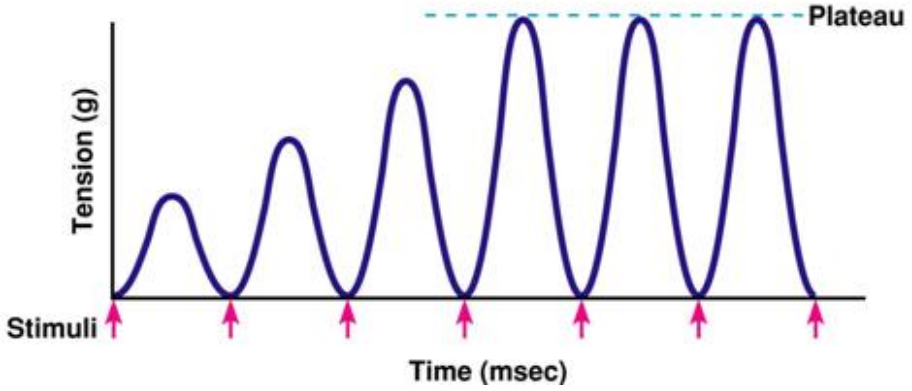


- Summation: Rapid sequence of stimuli→ muscle twitches fuse into each other, each subsequent one being stronger that its precedent

- Tetanus: very rapid sequence of stimuli: no relaxation

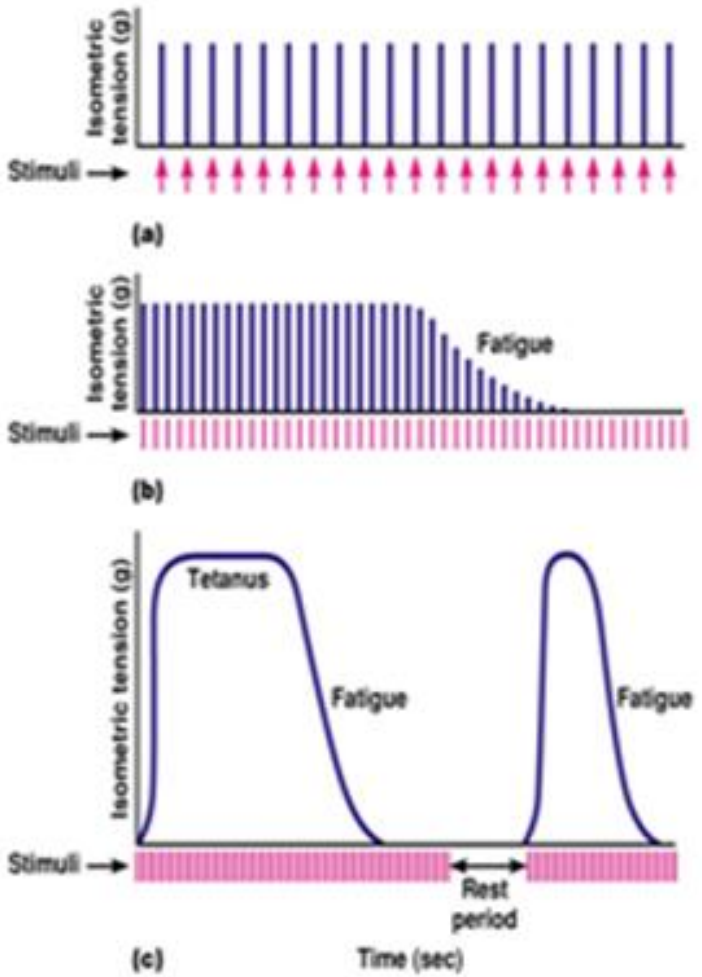
Effect of consecutive stimuli: Treppe

Treppe (warm-up): gradual increase in contraction intensity during sequential stimulation



Muscle fatigue

- Muscle fatigue: a decline in the ability of the muscle to sustain the strength of contraction

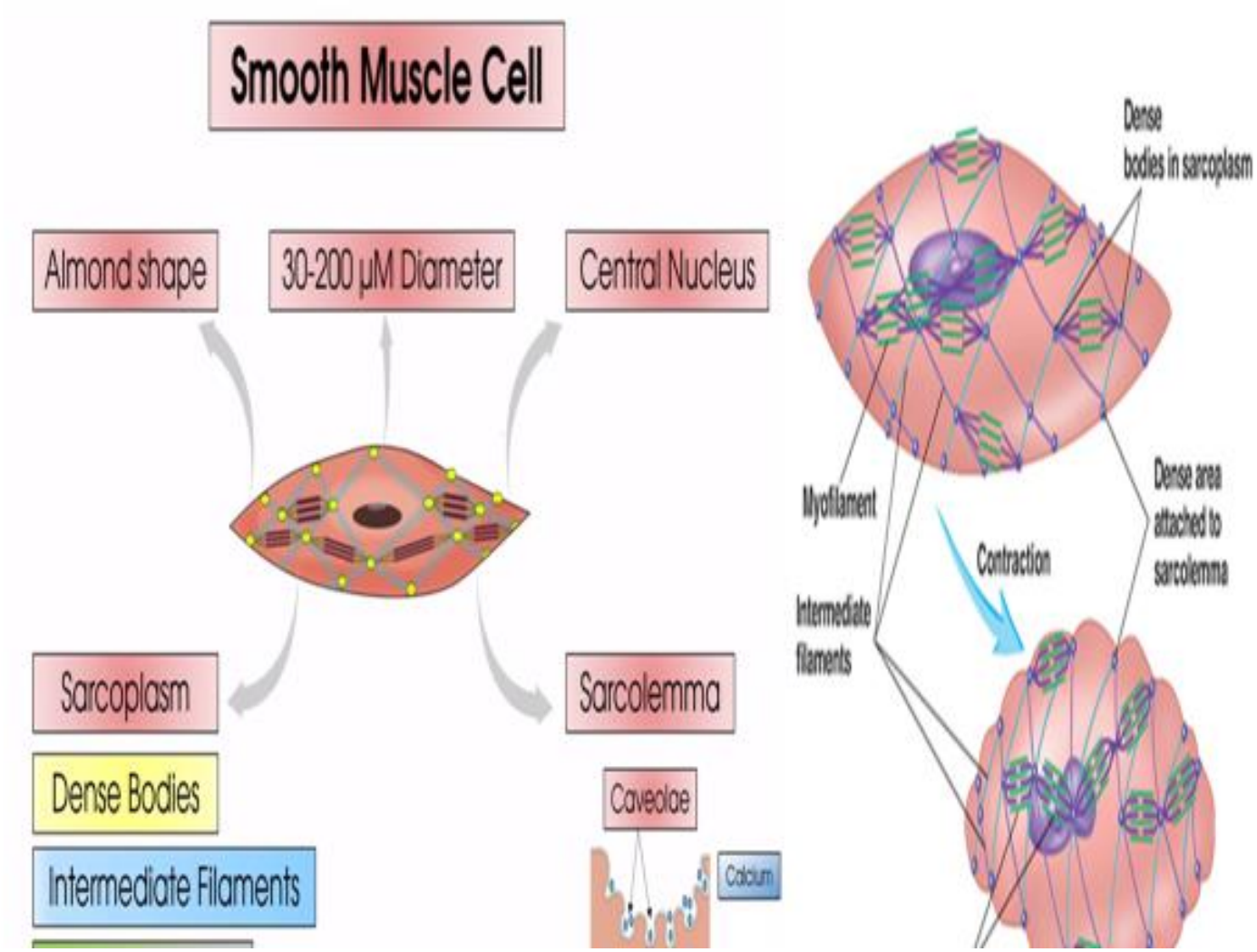


- Causes:

- Rapid build-up of lactic acid
- Decrease in oxygen supply
- Decrease in energy supply (glucose, glycogen, fatty-acids)
- Decreased neurotransmitter at the synapse

Structure of Smooth Muscle

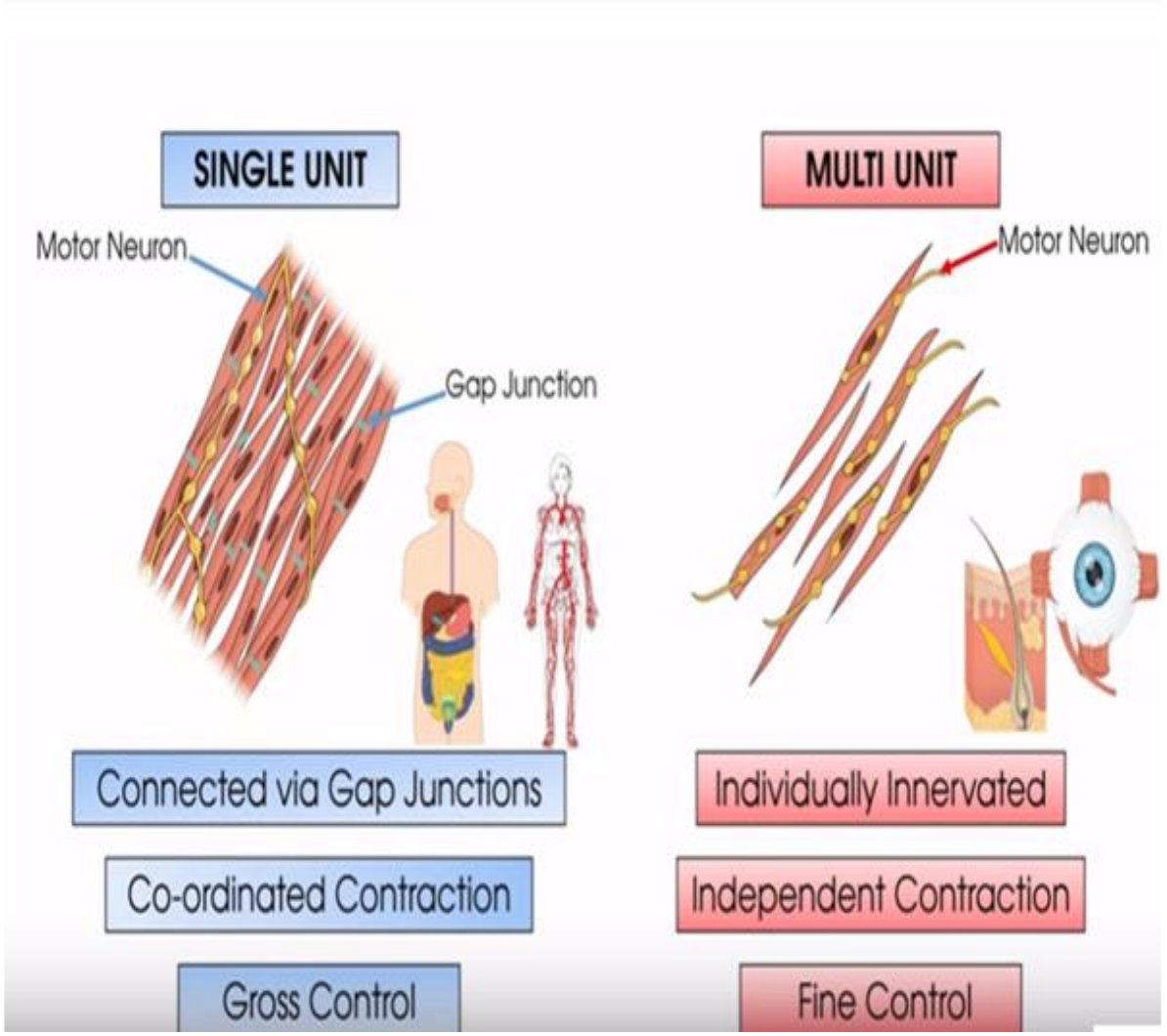
- Fibers smaller than those in skeletal muscle
- Spindle-shaped; single, central nucleus
- More actin than myosin
- No sarcomeres
  - Not arranged as symmetrically as in skeletal muscle, thus NO striations.
- Caveolae: indentations in sarcolemma;
  - May act like T tubules
- Dense bodies instead of Z disks
  - Have noncontractile intermediate filaments



Types of smooth muscle

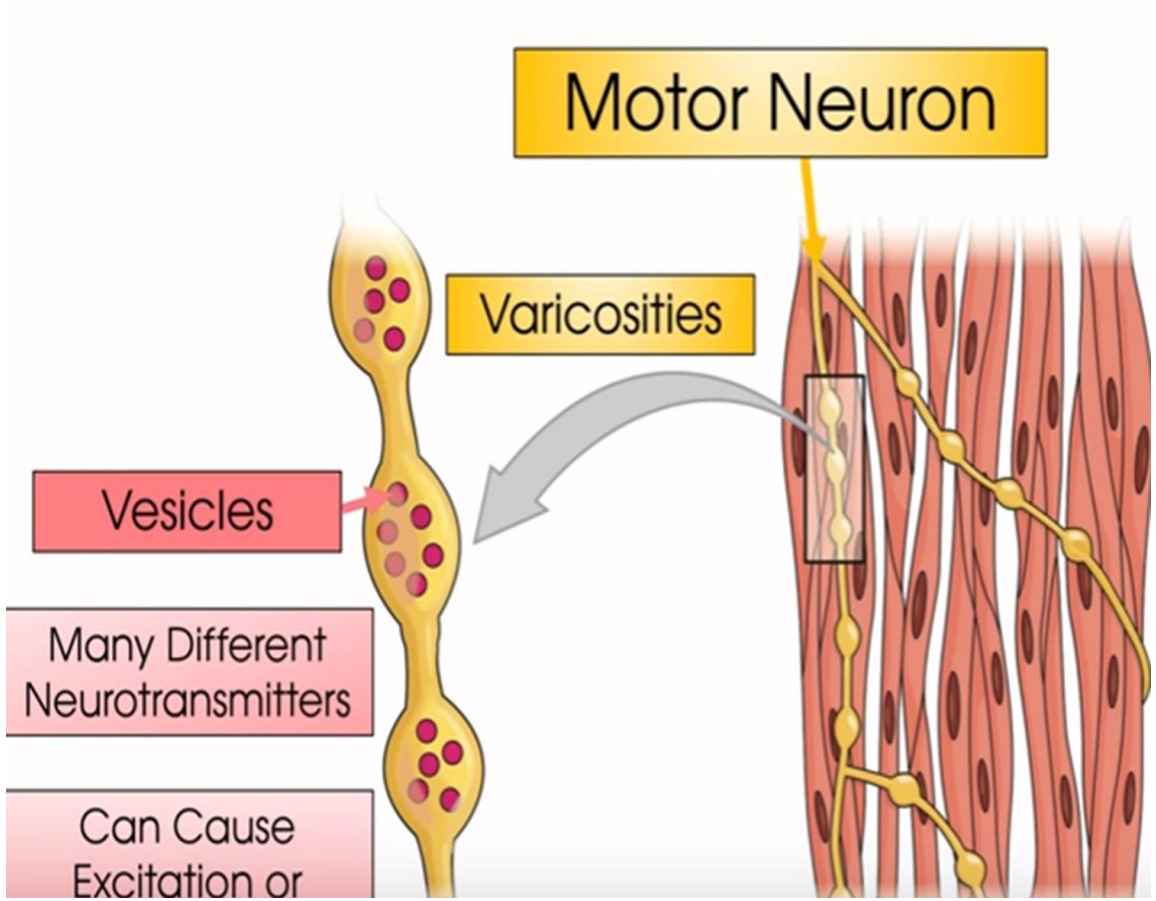
- **Multi-Unit Smooth Muscle.** This type of smooth muscle is composed of discrete, separate smooth muscle fibers.. Some examples of multi-unit smooth muscle are the ciliary muscle of the eye, the iris muscle of the eye, and the piloerector muscles that cause erection of the hairs when stimulated by the sympathetic nervous system.

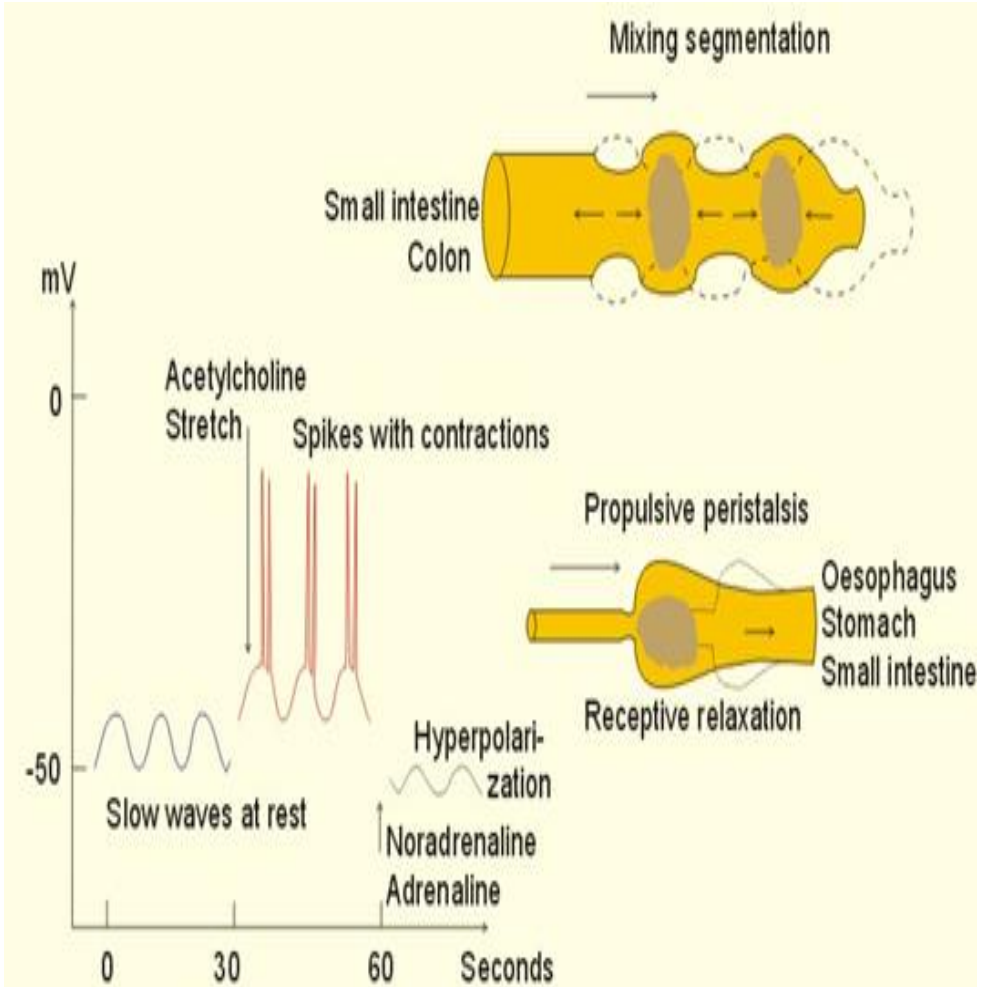
- **Unitary Smooth Muscle.** The term “unitary” is confusing because it does not mean the muscle fibers. Instead, it means a mass of hundreds to thousands of smooth muscle fibers that contract together as a single unit. the cell membranes are joined by many *gap junctions* through which ions can flow freely from one muscle cell.



Varicosities

Axons of neurons in the Autonomic nervous system do not form the highly organized NMJs with smooth muscle, as seen between motor neurons and skeletal muscle fibers. Instead, there is a series of neurotransmitter-filled bulges called varicosities as an axon courses through smooth muscle, loosely forming motor units . A varicosity releases neurotransmitters into the synaptic cleft.

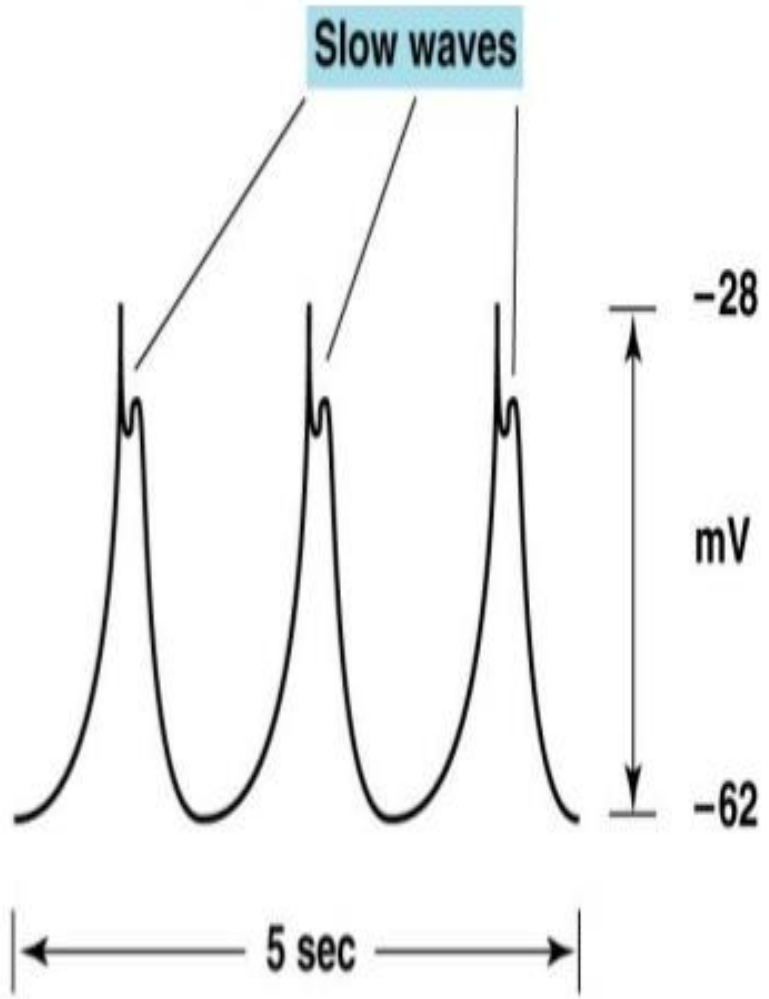




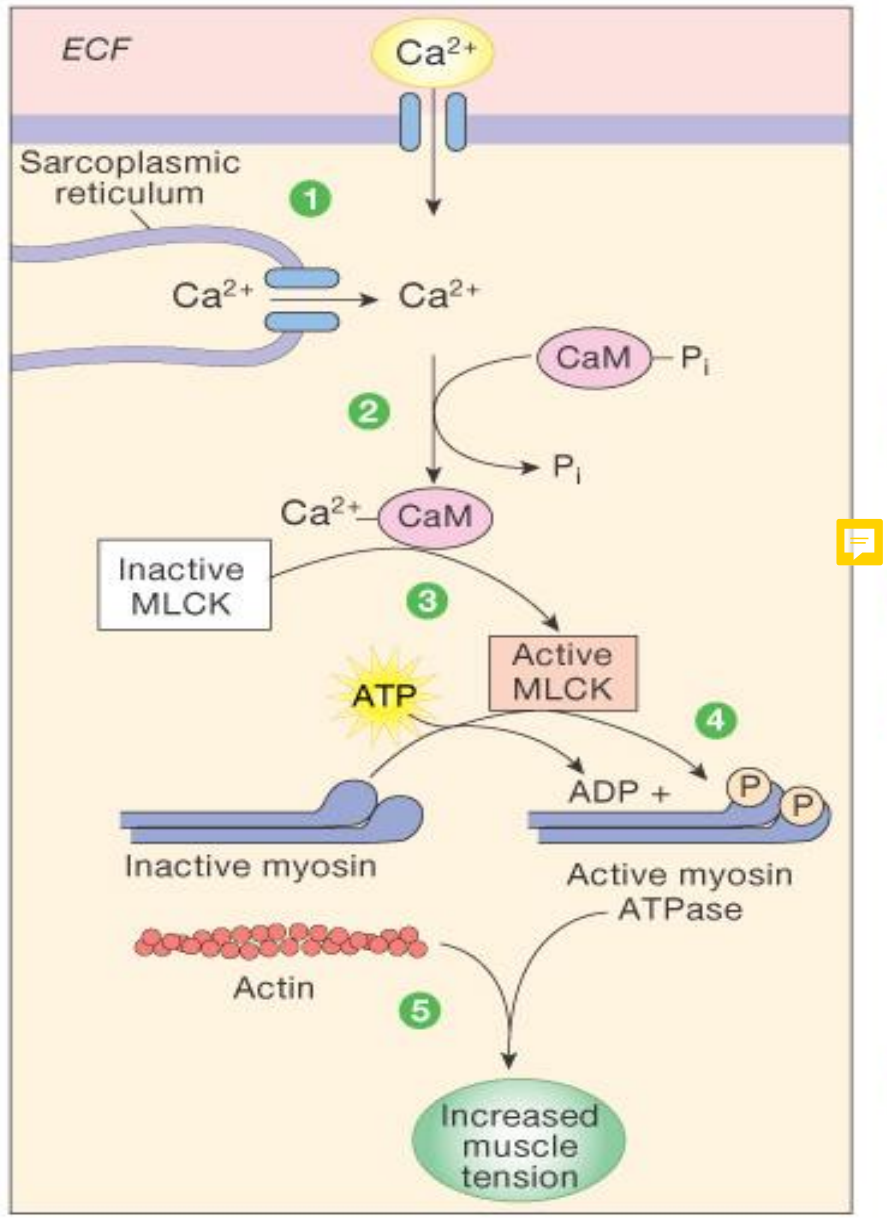
Occur automatically in response to endogenous pacemaker activity.

Rhythm of contractions is paced by graded depolarizations called slow waves.

- Slow waves produced by interstitial cells of Cajal.
- Slow waves spread from 1 smooth muscle cell to another through nexuses.

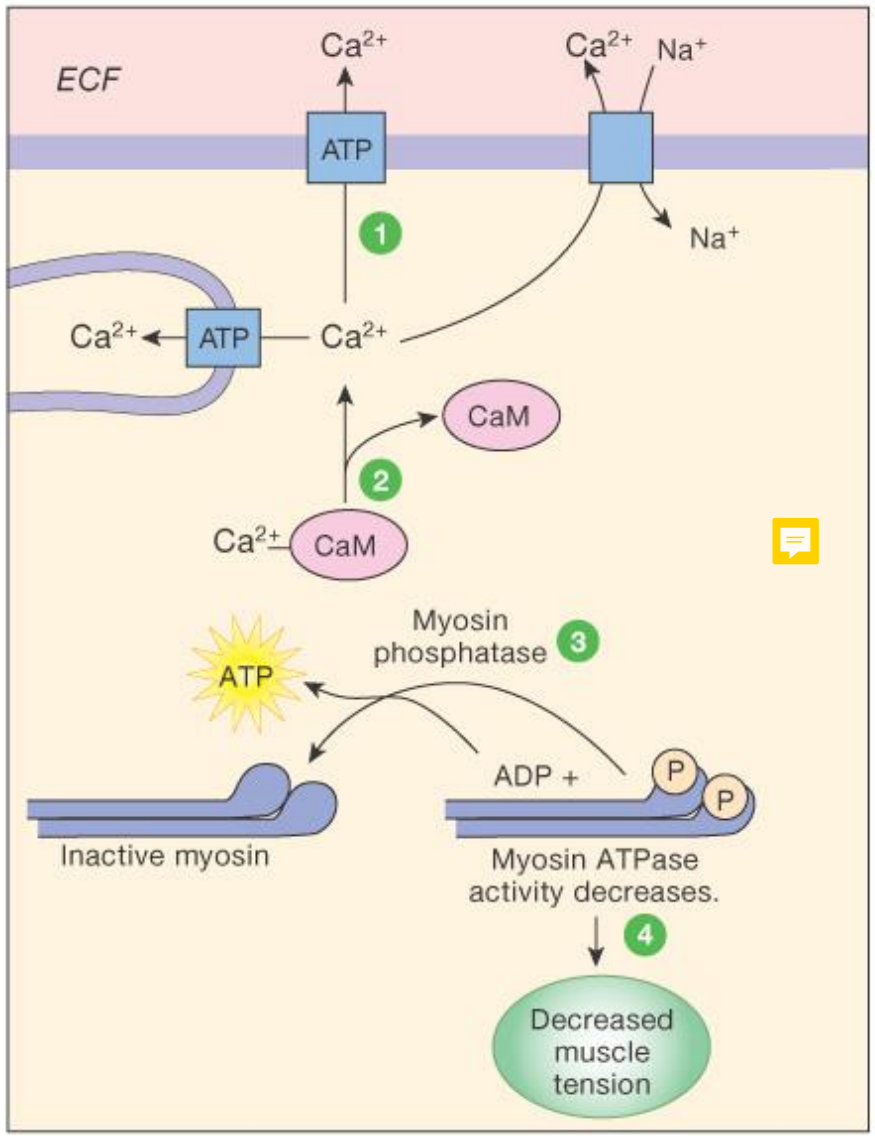


Smooth muscle contraction: mechanism



1. Intracellular Ca^{2+} concentrations increase when Ca^{2+} enters cell and is released from sarcoplasmic reticulum.
2. Ca^{2+} binds to calmodulin (CaM).
3. Ca^{2+}–calmodulin activates myosin light chain kinase (MLCK).
4. MLCK phosphorylates light chains in myosin heads and increases myosin ATPase activity.
5. Active myosin crossbridges slide along actin and create muscle tension.

Smooth muscle relaxation: mechanism



1. Free Ca^{2+} in cytosol decreases when Ca^{2+} is pumped out of the cell or back into the sarcoplasmic reticulum.

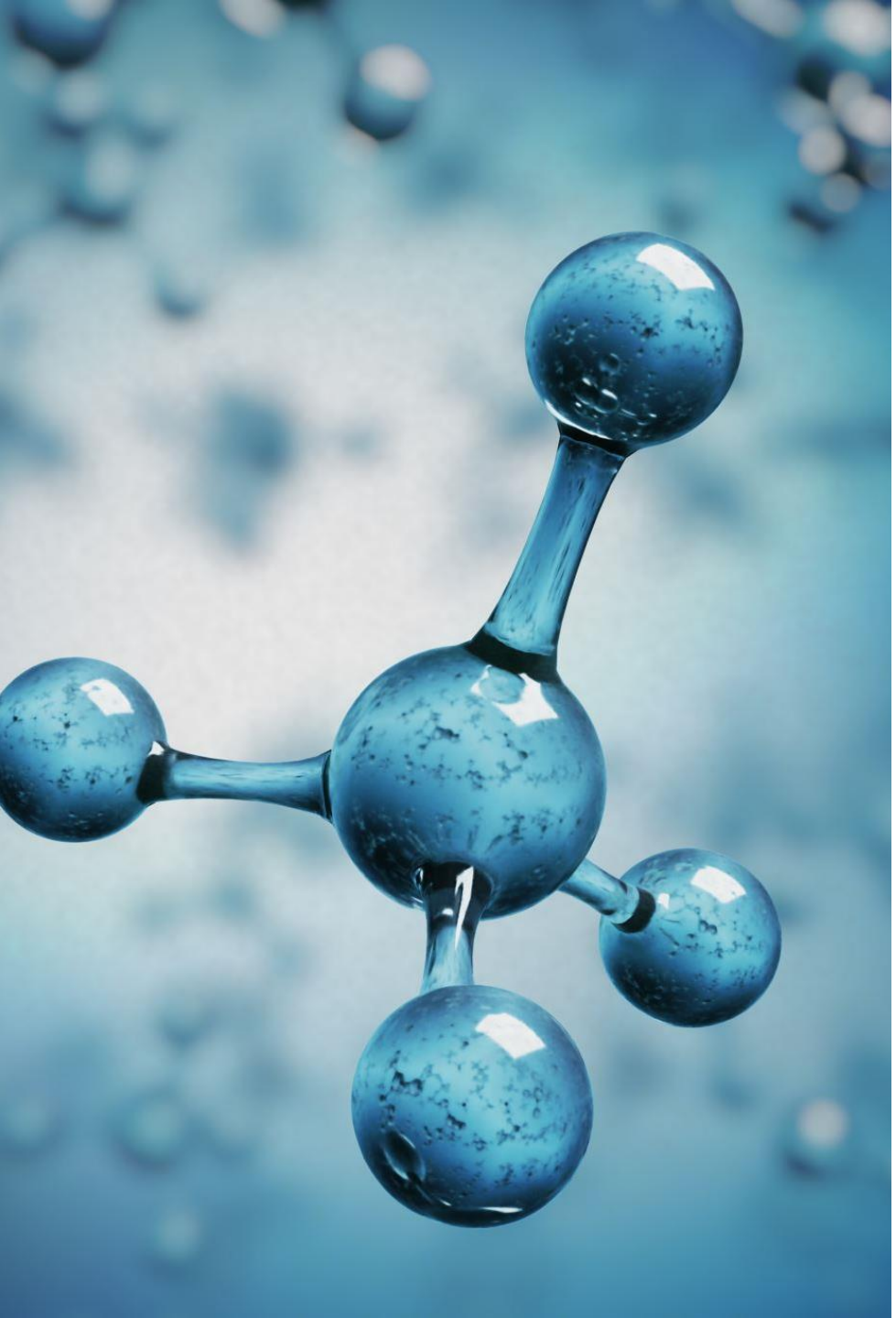
2. Ca^{2+} unbinds from calmodulin (CaM).

3. Myosin phosphatase removes phosphate from myosin, which decreases myosin ATPase activity.

4. Less myosin ATPase results in decreased muscle tension.

General Organization of autonomic nervous system and control of visceral function

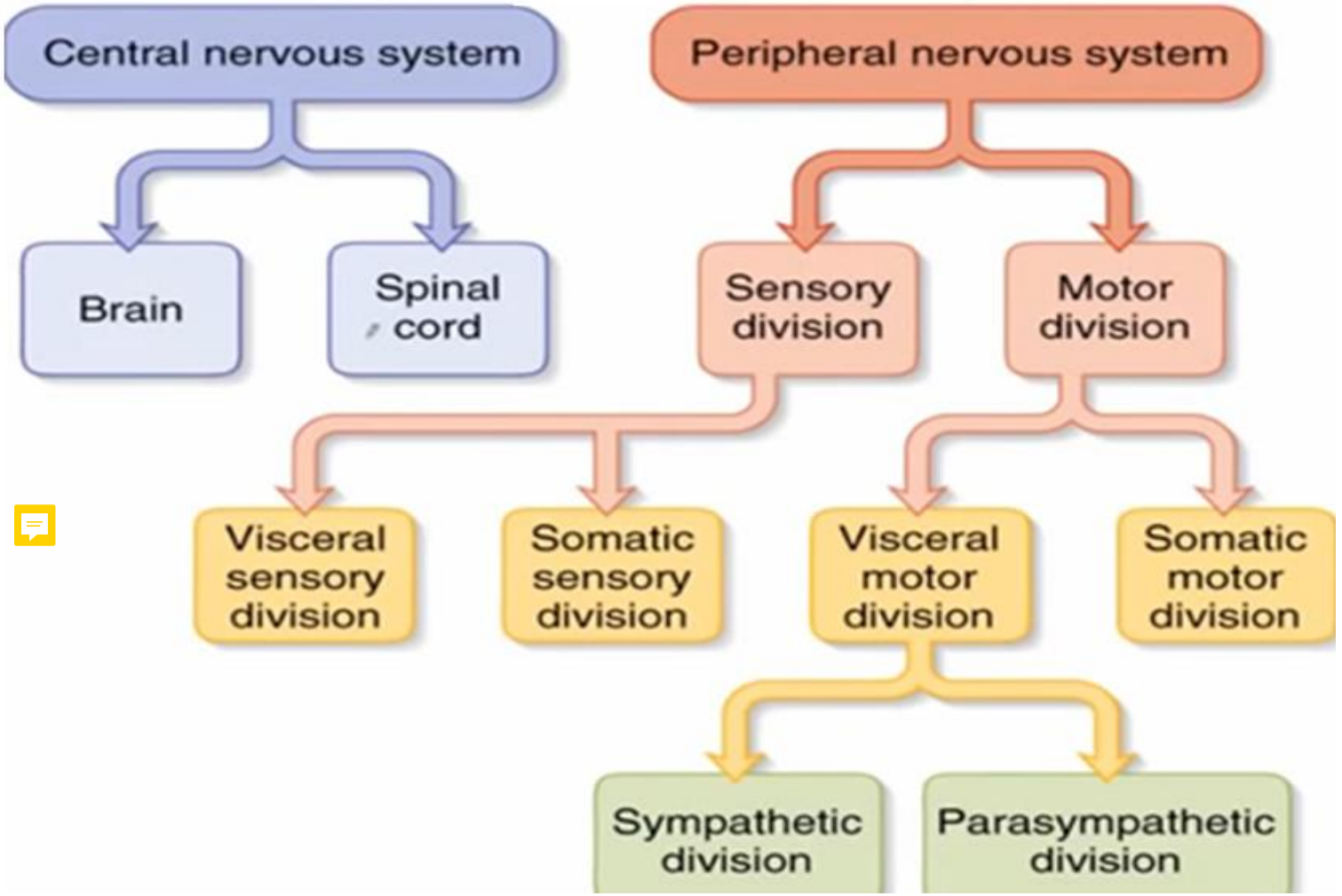
Dr. Arwa Rawashdeh



Objectives

- **Introduction and general organization of ANS**
- **Chemical transmission of autonomic junctions cholinergic and adrenergic transmission**
- **Types of cholinergic and adrenergic receptors**

General Organization of autonomic nervous system (ANS)



Somatic and ANS system

The two system differ in

- Effectors
- Efferent pathways (and their neurotransmitters)
- Target organ responses to neurotransmitters

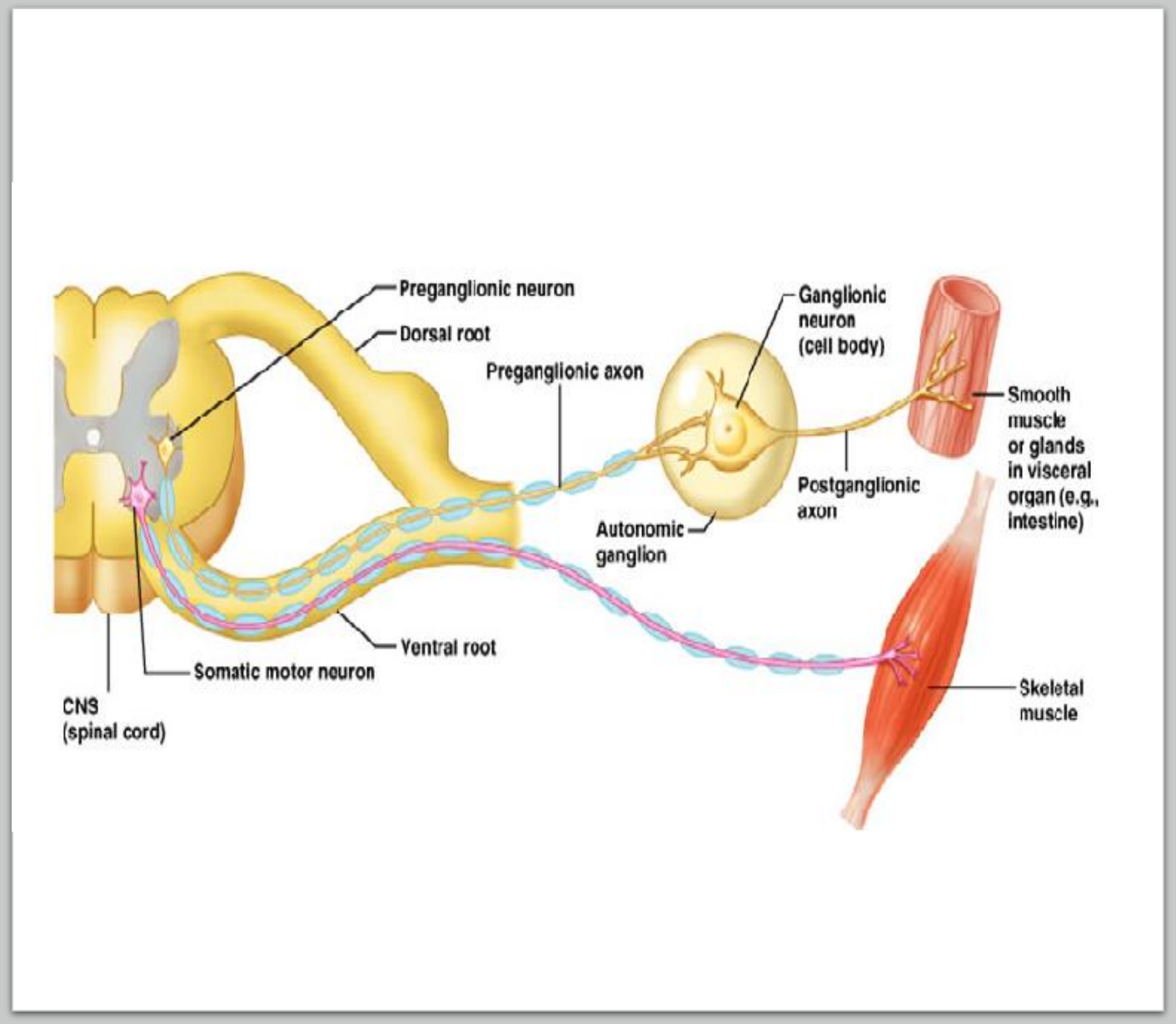
- Effectors

Skeletal muscle

- Somatic nervous system

ANS

- Cardiac
- Smooth muscle
- Glands



Neurotransmitter effects

- Somatic nervous system
  - All somatic motor neurons release acetylcholine (ACh)
  - Effects are always stimulatory
- ANS
  - Preganglionic fibers release ACh
  - Postganglionic fibers release norepinephrine or ACh at effectors
  - Effect is either stimulatory or inhibitory, depending on type of receptors

Efferent pathway

- Somatic nervous system
  - A, thick, heavily myelinated somatic motor fiber makes up each pathway from the CNS to the muscle
- ANS pathway is a two-neuron chain
  1. Preganglionic neuron (in CNS) has a thin, lightly myelinated preganglionic axon
  2. Ganglionic neuron in autonomic ganglion has an unmyelinated postganglionic axon that extends to the effector organ

Division and anatomy of ANS

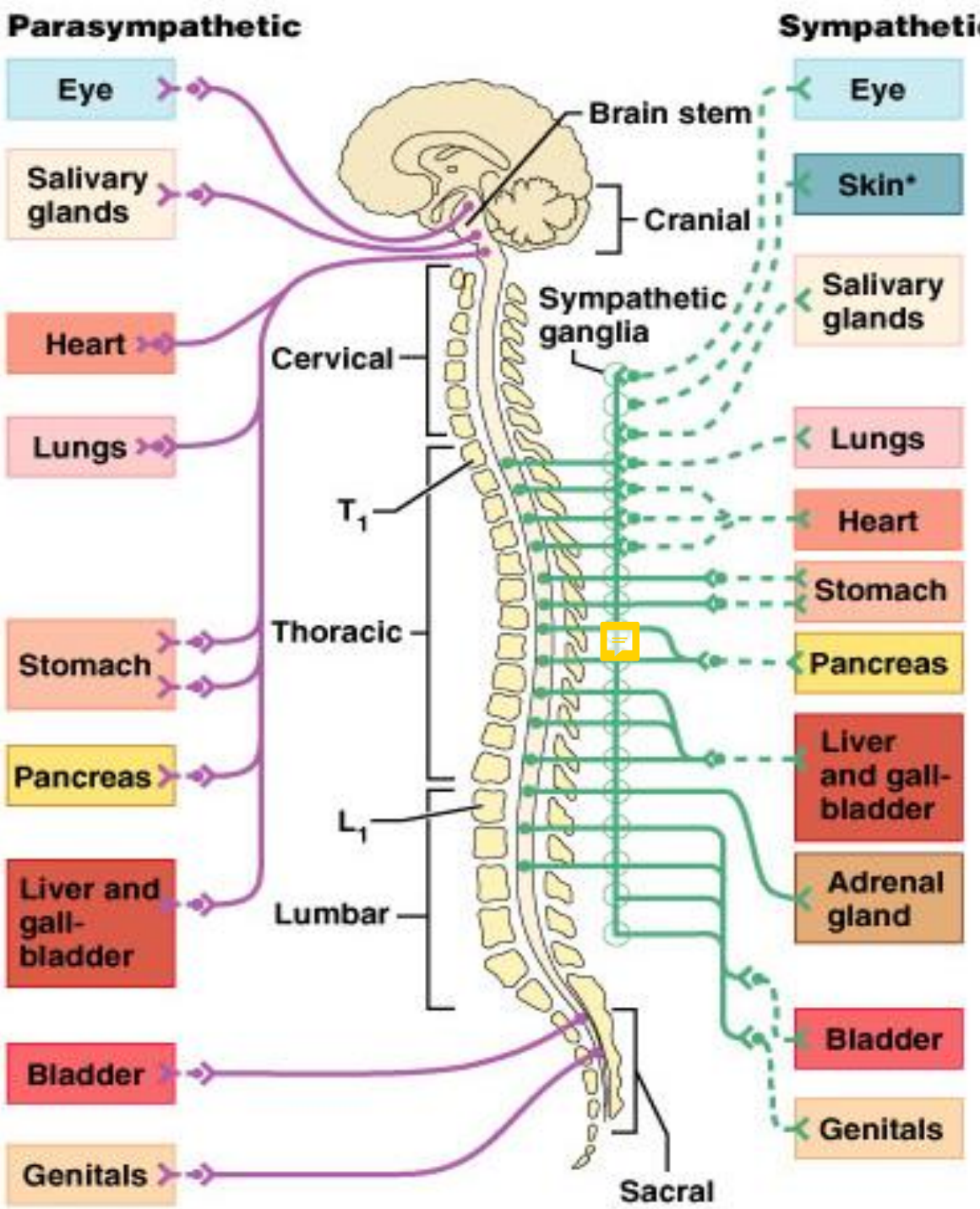
1. Sympathetic division
2. Parasympathetic division

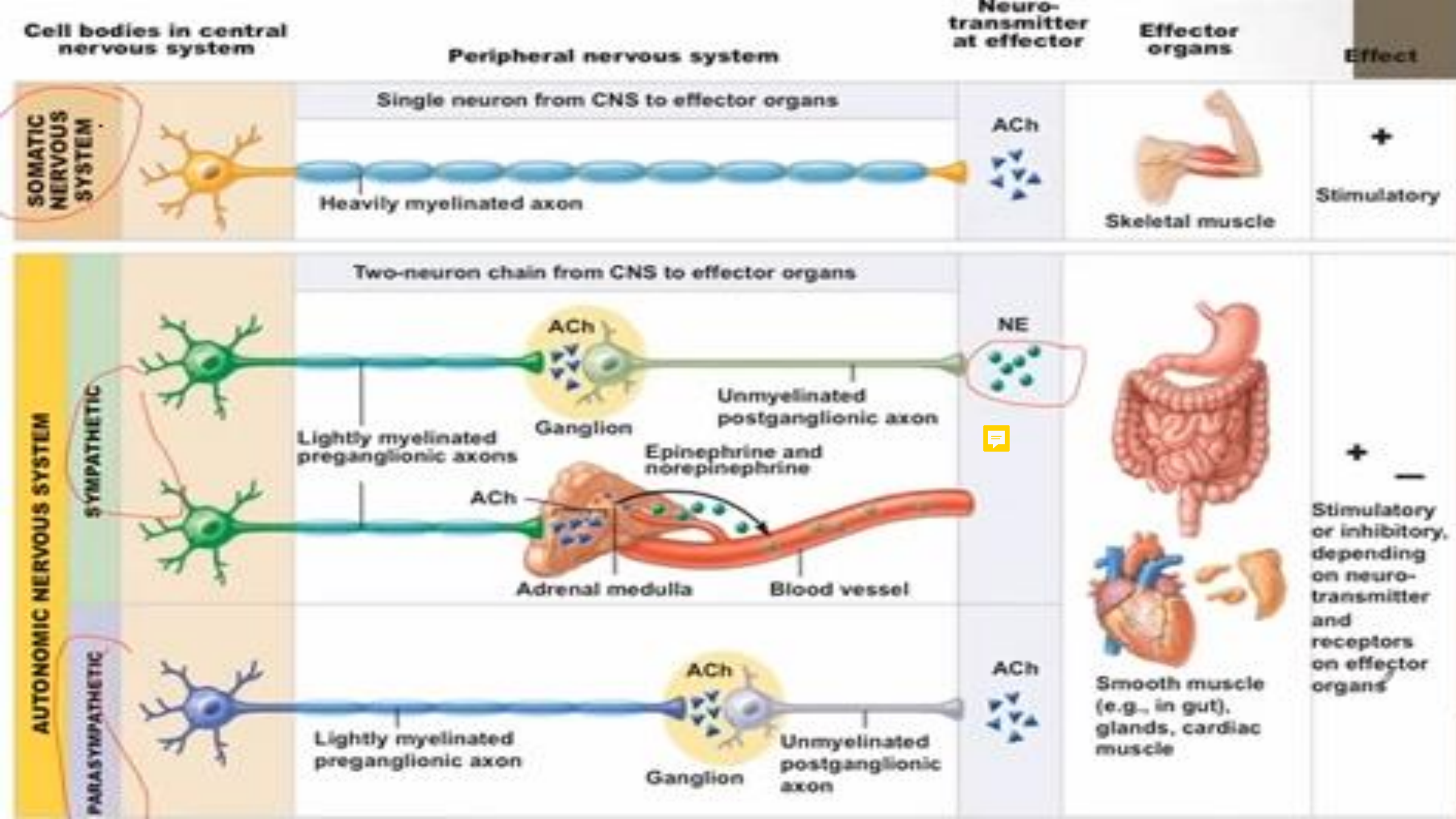
- Dual innervation
  - Almost all visceral organs are served by both divisions, but they cause opposite effects

Division	Origin of Fibers	Length of Fibers	Location of Ganglia
Sympathetic	Thoracolumbar region of the spinal cord	Short preganglionic and long postganglionic	Close to spinal cord
Parasympathetic	Brain and sacral spinal cord (craniosacral)	Long preganglionic and short postganglionic	In visceral effector organs

craniosacral

thoracolumbar




Cell bodies in central nervous system
Peripheral nervous system
Neuro-transmitter at effector
Effector organs
Effect
SOMATIC NERVOUS SYSTEM
Single neuron from CNS to effector organs
Heavily myelinated axon
ACh
Skeletal muscle
+
Stimulatory
AUTONOMIC NERVOUS SYSTEM
SYMPATHETIC
Two-neuron chain from CNS to effector organs
ACh
Ganglion
NE
Unmyelinated postganglionic axon
Lightly myelinated preganglionic axons
Epinephrine and norepinephrine
ACh
Adrenal medulla
Blood vessel
+
—
Stimulatory or inhibitory, depending on neuro-transmitter and receptors on effector organs
PARASYMPATHETIC
Lightly myelinated preganglionic axon
ACh
Ganglion
Unmyelinated postganglionic axon
ACh
Smooth muscle (e.g., in gut), glands, cardiac muscle

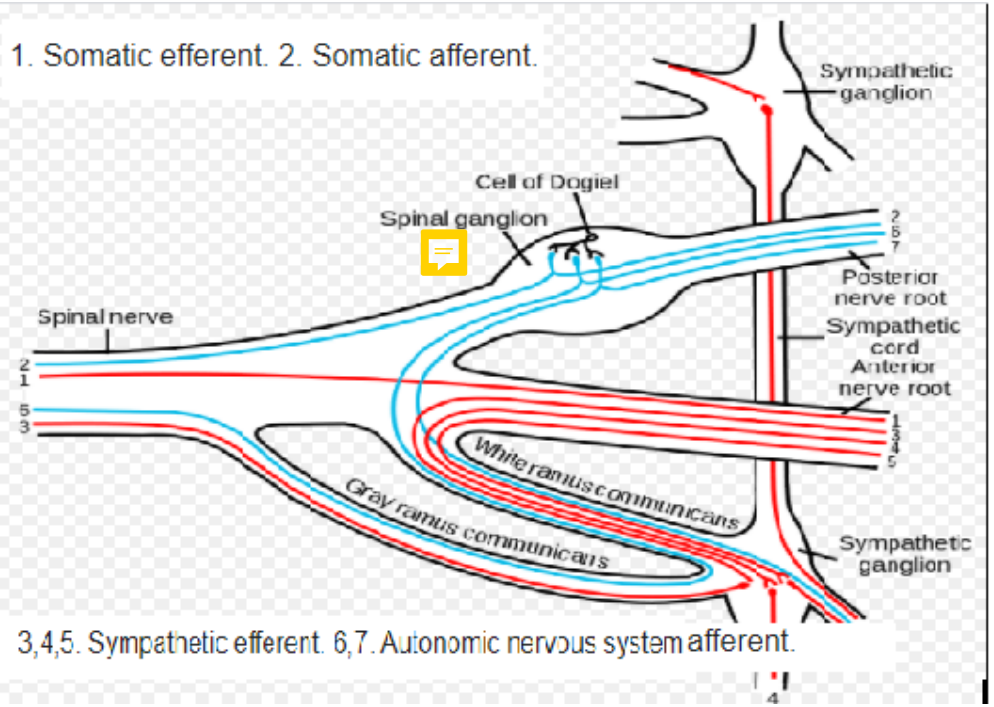
Location of sympathetic trunk

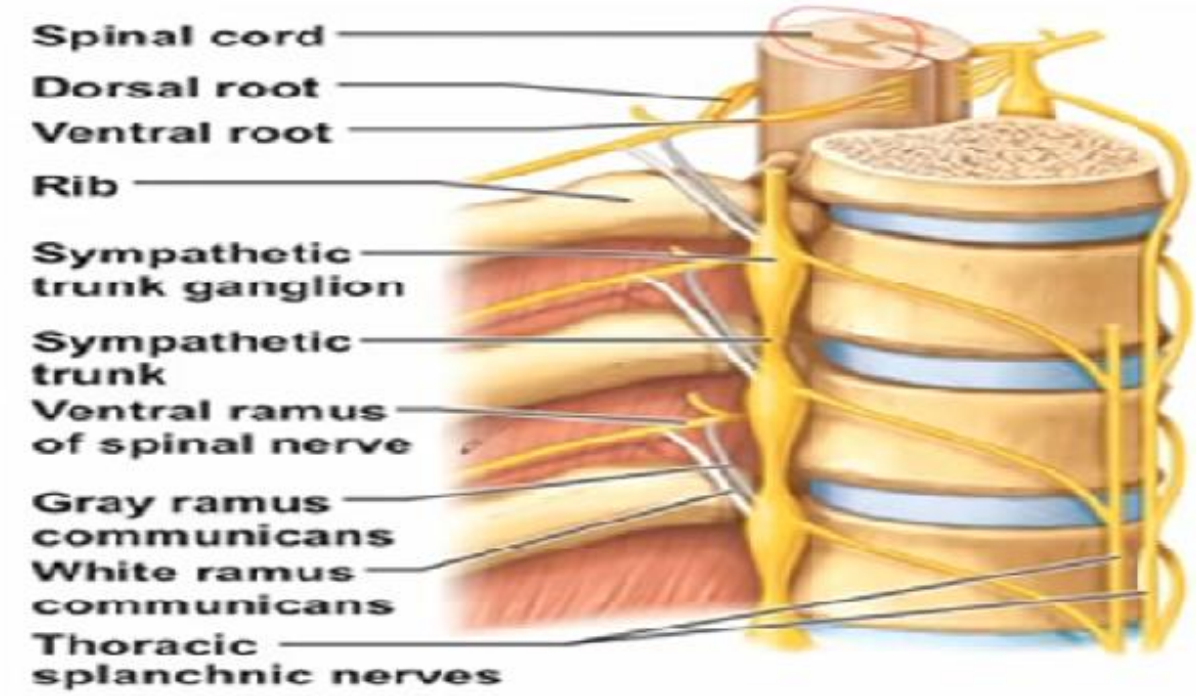
- Preganglionic neurons are in spinal cord segments $T_1 - L_2$
- Sympathetic neurons produce the lateral horns of the spinal cord
- Preganglionic fibers pass through the white rami communicantes and enter sympathetic trunk (paravertebral) ganglia

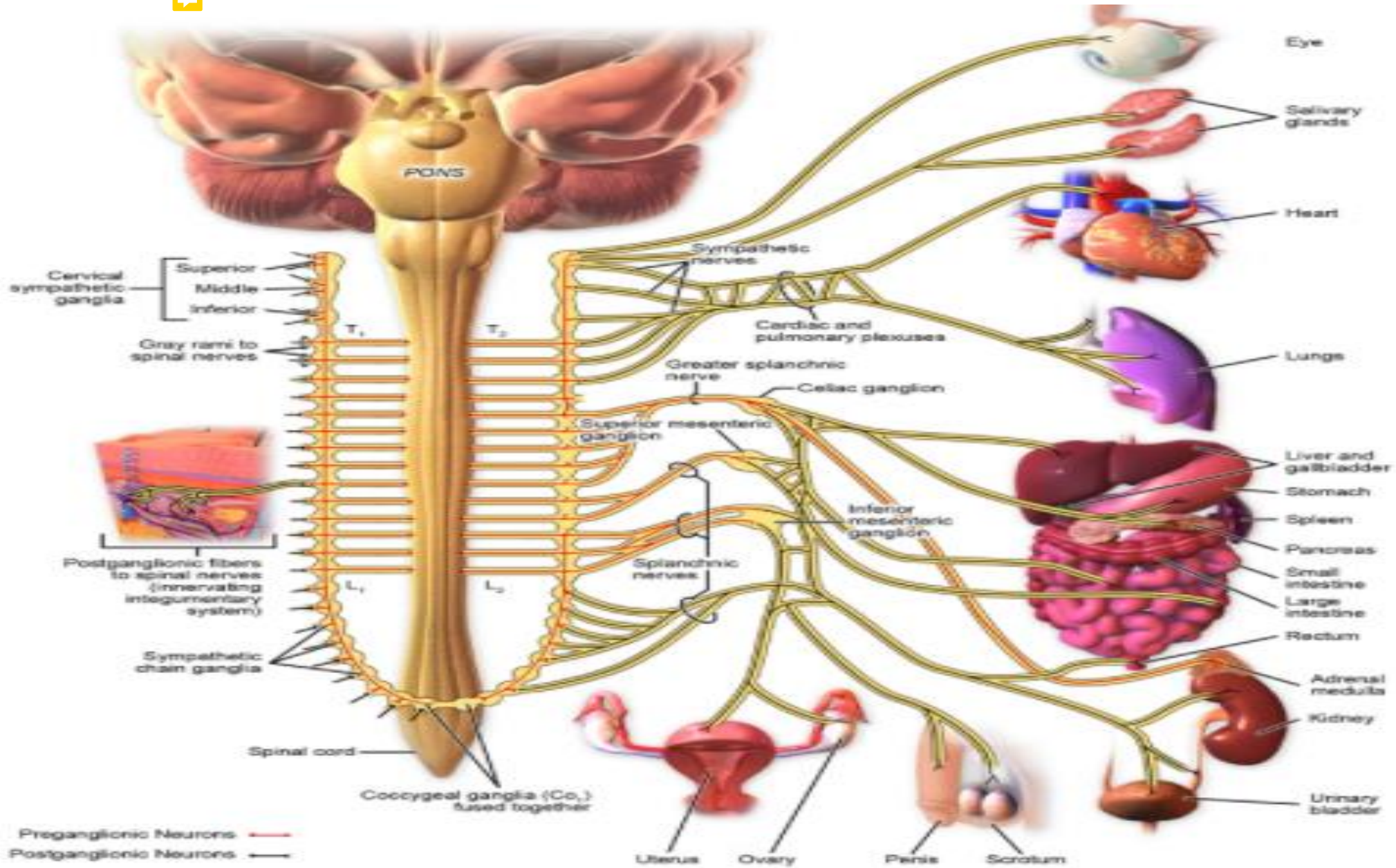
Upon entering a sympathetic trunk ganglion a preganglionic fiber may do one of the following:

1. Synapse with a ganglionic neuron within the same ganglion
2. Ascend or descend the sympathetic trunk to synapse in another trunk ganglion
3. Pass through the trunk ganglion and emerge without synapsing

Location of sympathetic trunk





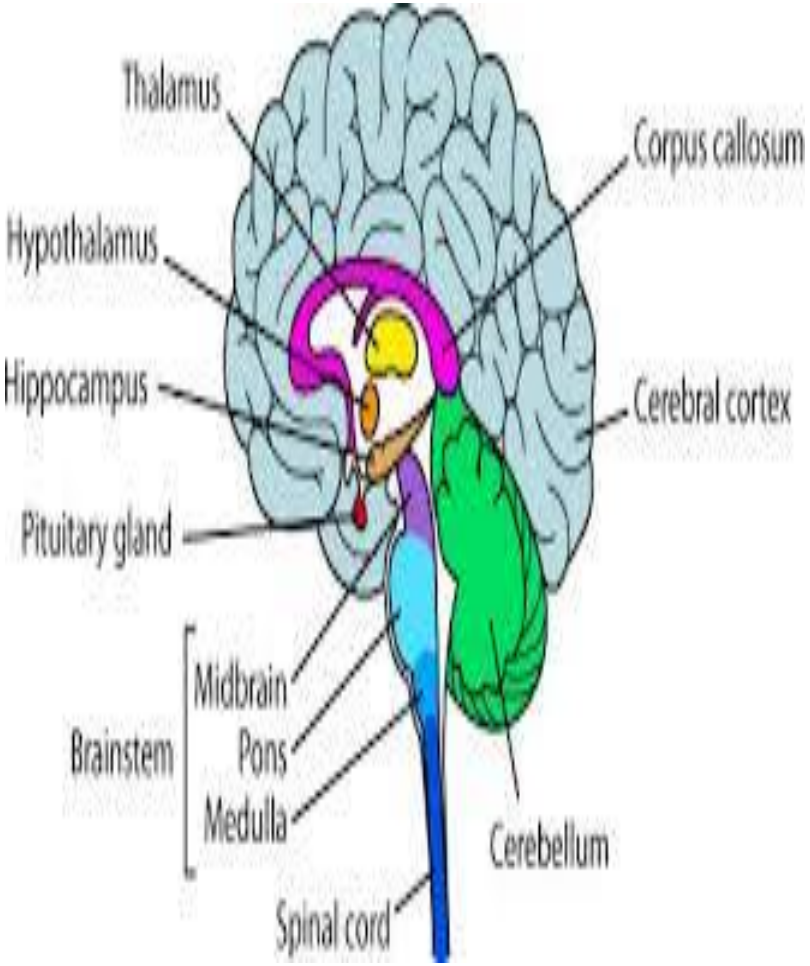

PONS
Cervical sympathetic ganglia
Superior
Middle
Inferior
Gray rami to spinal nerves
T1
T2
L1
L2
Postganglionic fibers to spinal nerves (innervating integumentary system)
Sympathetic chain ganglia
Spinal cord
Coccygeal ganglia (Co1) fused together
Sympathetic nerves
Cardiac and pulmonary plexuses
Greater splanchnic nerve
Celiac ganglion
Superior mesenteric ganglion
Inferior mesenteric ganglion
Splanchnic nerves
Eye
Salivary glands
Heart
Lungs
Liver and gallbladder
Stomach
Spleen
Pancreas
Small intestine
Large intestine
Rectum
Adrenal medulla
Kidney
Urinary bladder
Uterus
Ovary
Penis
Scrotum
Preganglionic Neurons
Postganglionic Neurons

Control of ANS functioning

- Hypothalamus—main integrative center of ANS activity
- Subconscious cerebral input via limbic lobe connections influences hypothalamic function
- Other controls come from the cerebral cortex, the reticular formation, and the spinal cord

Role of sympathetic division

- Mobilizes the body during activity; is the "fight-or-flight" system
- Promotes adjustments during exercise, or when threatened
  - Blood flow is shunted to skeletal muscles and heart
  - Bronchioles dilate
  - Liver releases glucose



Parasympathetic nervous system and division outflow

- Also called the **craniosacral** system because all its preganglionic neurons are in the brain stem or sacral levels of the spinal cord
  - Cranial nerves III,VII, IX and X
  - In lateral horn of gray matter from S2-S4
- Only innervate internal organs (not skin)
- **Acetylcholine** is neurotransmitter at end organ as well as at preganglionic synapse: “cholinergic”

	Cranial Nerve	Ganglia (Terminal Ganglia)	Effector Organ(s)
Cranial Outflow	Oculomotor (III)	Ciliary	Eye
	Facial (VII)	Pterygopalatine Submandibular	Salivary, nasal, and lacrimal glands
	Glossopharyngeal (IX)	Otic	Parotid salivary glands
	Vagus (X)	Within the walls of target organs	Heart, lungs, and most visceral organs
Sacral Outflow	S_2-S_4	Within the walls of target organs	Large intestine, urinary bladder, ureters, and reproductive organs

Role of Parasympathatic division “rest & digest”

- Promotes maintenance activities and conserves body energy
- Its activity is illustrated in a person who relaxes, reading, after a meal
  - Blood pressure, heart rate, and respiratory rates are low
  - Gastrointestinal tract activity is high
  - Pupils are constricted and lenses are accommodated for close vision

BODY TISSUE/ORGAN	SYMPATHETIC RESPONSE*	PARASYMPATHETIC RESPONSE*
Eye 	Dilates pupils	Constricts pupils
Lungs 	Dilates bronchioles	Constricts bronchioles and increases secretions
Heart 	Increases heart rate	Decreases heart rate
Blood vessels 	Constricts blood vessels	Dilates blood vessels
Gastrointestinal 	Relaxes smooth muscles of gastrointestinal tract	Increases peristalsis
Bladder 	Relaxes bladder muscle	Constricts bladder
Uterus 	Relaxes uterine muscle	
Salivary gland 		Increases salivation

Neurotransmitters

Cholinergic fibers release the neurotransmitter ACh

- All ANS preganglionic axons
- All parasympathetic postganglionic axons

Adrenergic fibers release the neurotransmitter NE

- Most sympathetic postganglionic axons
- Exceptions: sympathetic postganglionic fibers secrete ACh at sweat glands and some blood vessels in skeletal muscles

Overview of sensory neuron function

Dr. Arwa rawashdeh

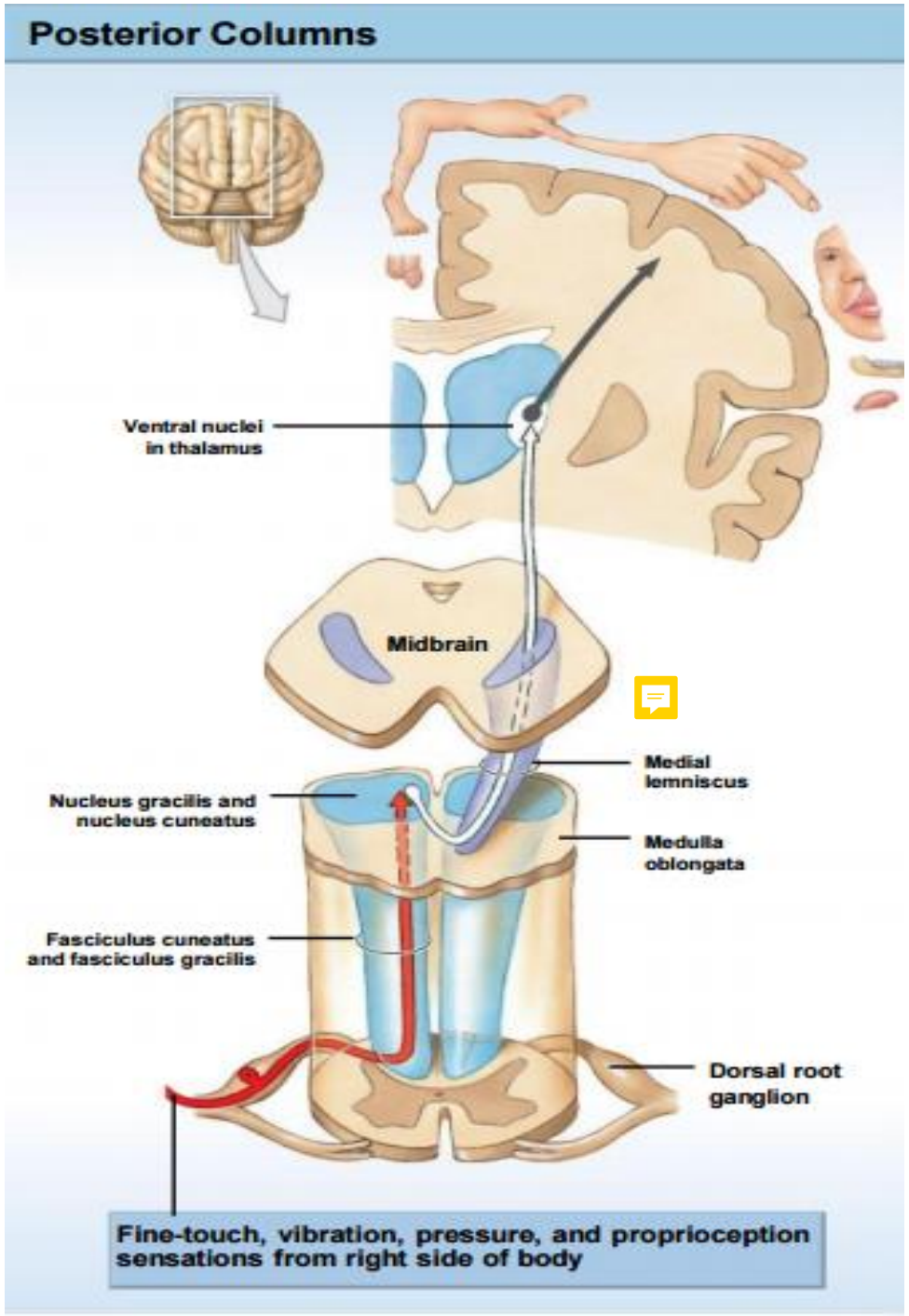
Sensory and Motor Tracts

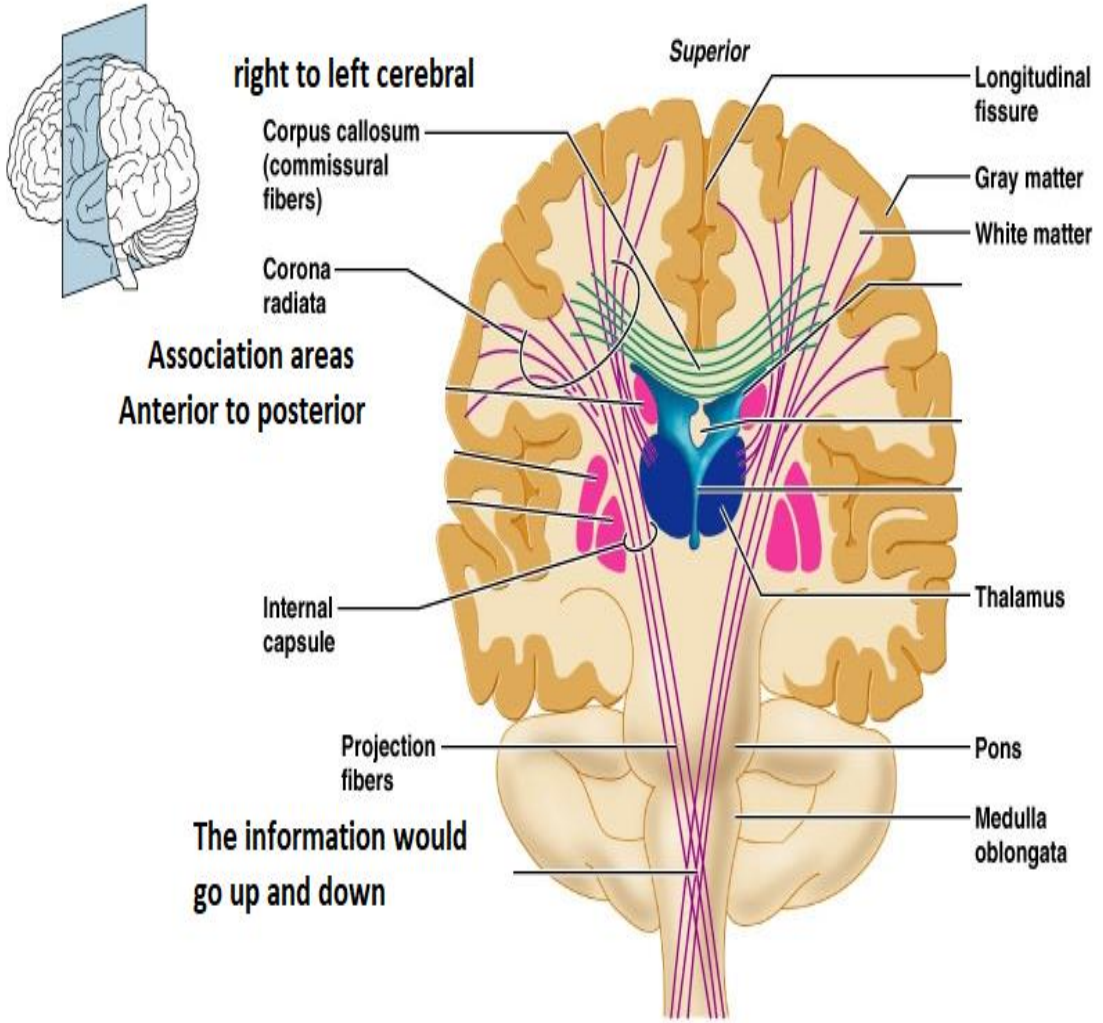
- Millions of sensory neurons are delivering information to the CNS all the time
- Millions of motor neurons are causing the body to respond in a variety of ways
- Sensory and motor neurons travel by different tracts within the spinal cord

- Communication to and from the brain involves **tracts**
- **Ascending tracts** are sensory
  - Deliver information to the brain
- **Descending tracts** are motor
  - Deliver information to the periphery
- Naming the tracts
  - If the tract name begins with “spino” (as in **spino**cerebellar), the tract is a **sensory tract** delivering information from the spinal cord to the cerebellum (in this case)
  - If the tract name ends with “spinal” (as in vestibulo**spinal**), the tract is a **motor tract** that delivers information from the vestibular apparatus (in this case) to the spinal cord

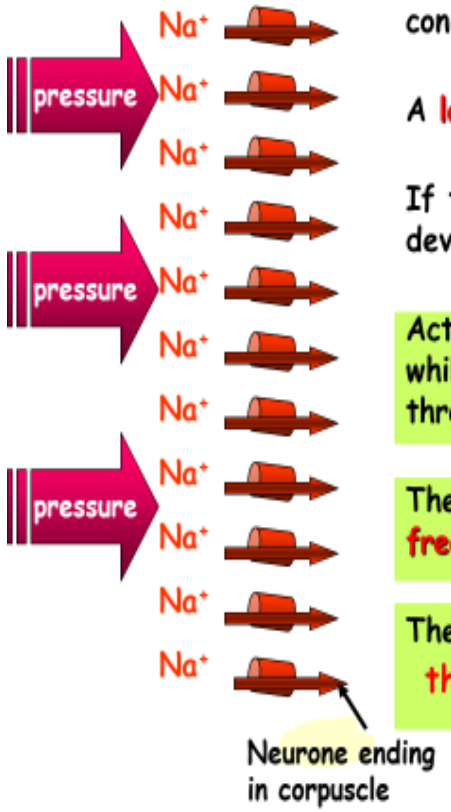
Sensory Tracts

- There are three major sensory tracts
  - The **posterior column tract**
  - The **spinothalamic tract**
  - The **spinocerebellar tract**
- The three major sensory tracts involve chains of neurons
  - **First-order neuron**
    - Delivers sensations to the CNS
    - The cell body is in the dorsal or cranial root ganglion
  - **Second-order neuron**
    - An interneuron with the cell body in the spinal cord or brain
  - **Third-order neuron**
    - Transmits information from the thalamus to the cerebral cortex


Posterior Columns
Ventral nuclei in thalamus
Midbrain
Medial lemniscus
Nucleus gracilis and nucleus cuneatus
Medulla oblongata
Fasciculus cuneatus and fasciculus gracilis
Dorsal root ganglion
Fine-touch, vibration, pressure, and proprioception sensations from right side of body


right to left cerebral
Superior
Corpus callosum (commissural fibers)
Longitudinal fissure
Gray matter
White matter
Corona radiata
Association areas
Anterior to posterior
Internal capsule
Thalamus
Projection fibers
Pons
Medulla oblongata
The information would go up and down

The greater the pressure the more sodium channels open



More sodium ions diffuse in down the concentration gradient

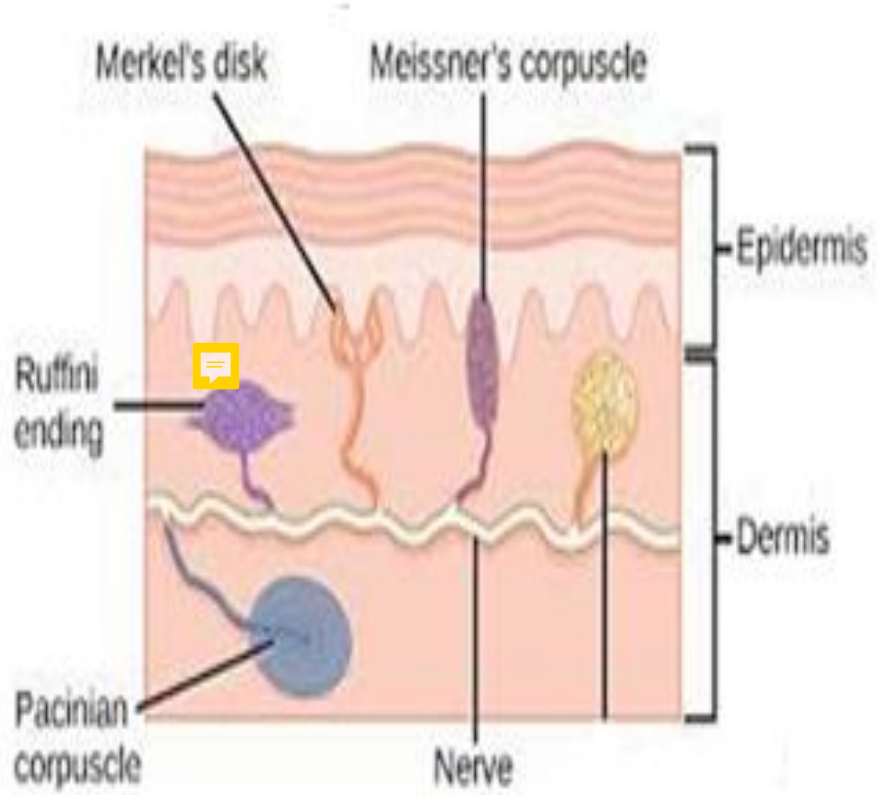
A larger generator potential is created

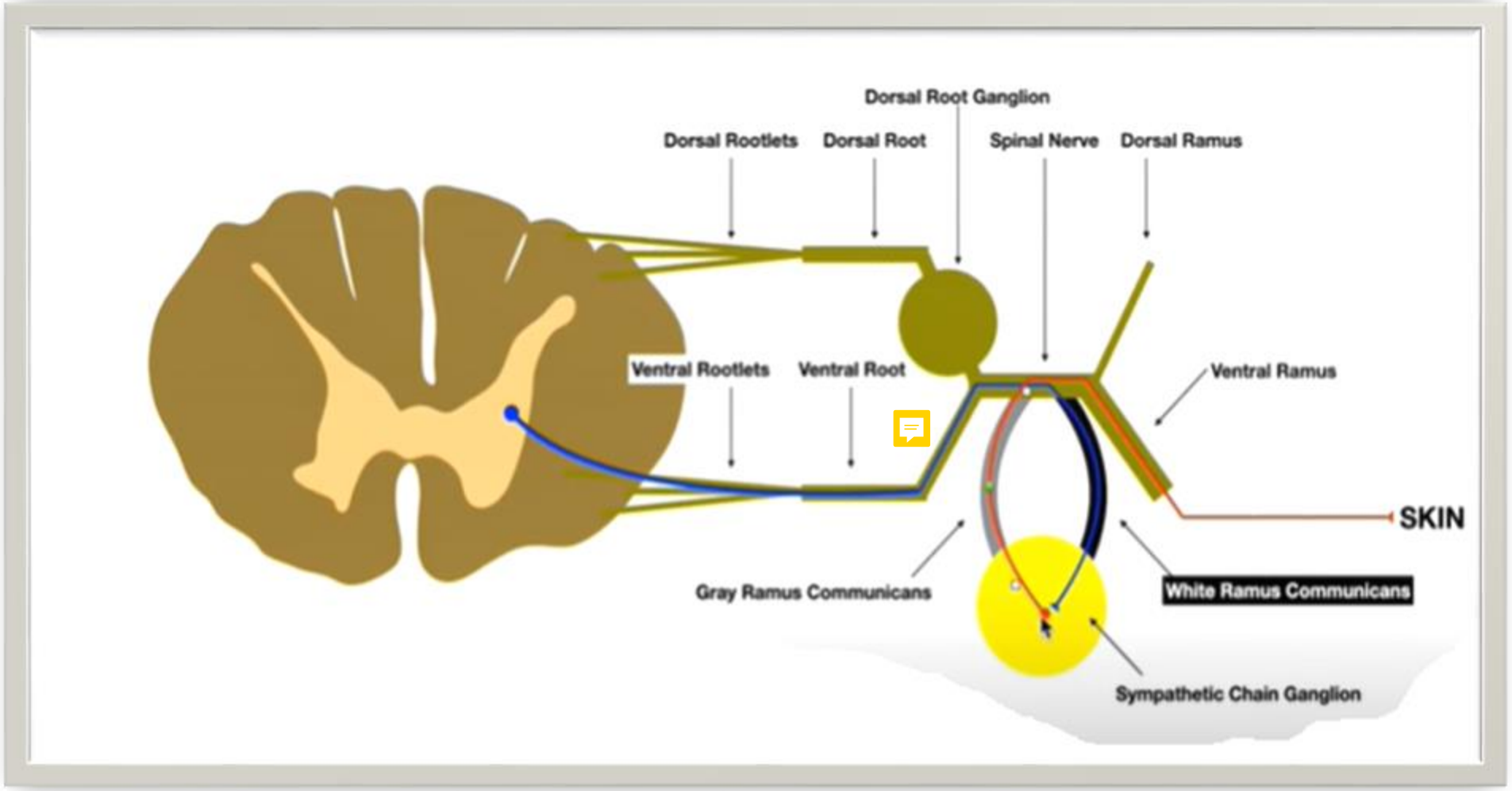
If the threshold is reached an action potential develops

Action potentials will continue to be developed while the generator potential is at or above the threshold

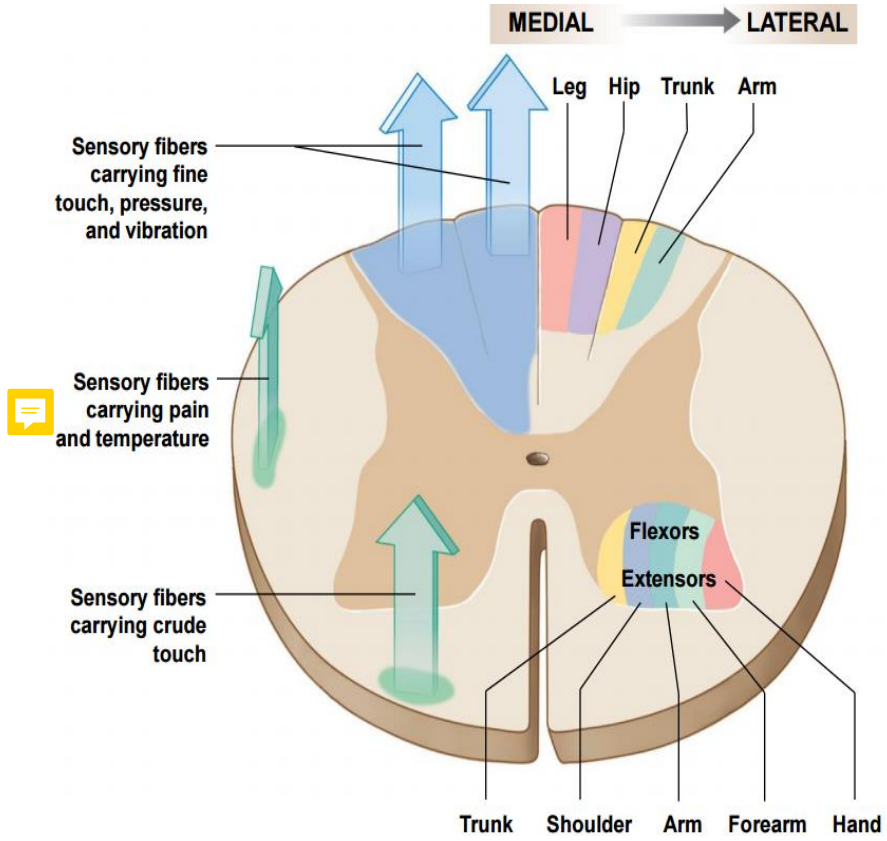
The greater the pressure the greater the frequency of nerve impulses along the neurone

The maximum frequency is limited by the refractory period




Dorsal Root Ganglion
Dorsal Rootlets
Dorsal Root
Spinal Nerve
Dorsal Ramus
Ventral Rootlets
Ventral Root
Ventral Ramus
SKIN
Gray Ramus Communicans
White Ramus Communicans
Sympathetic Chain Ganglion

- Neurons in the sensory tracts are arranged according to three anatomical principles
  - **Sensory modality**
    - Fine touch sensations are carried in one sensory tract
  - **Somatotopic**
    - Ascending tracts are arranged according to the site of origin
  - **Medial-lateral rule**
    - Sensory neurons that enter a low level of the spinal cord are more medial within the spinal cord
    - Sensory neurons that enter at a higher level of the spinal cord are more lateral within the spinal cord



CEREBRUM/CEREBRAL HEMISPHERES

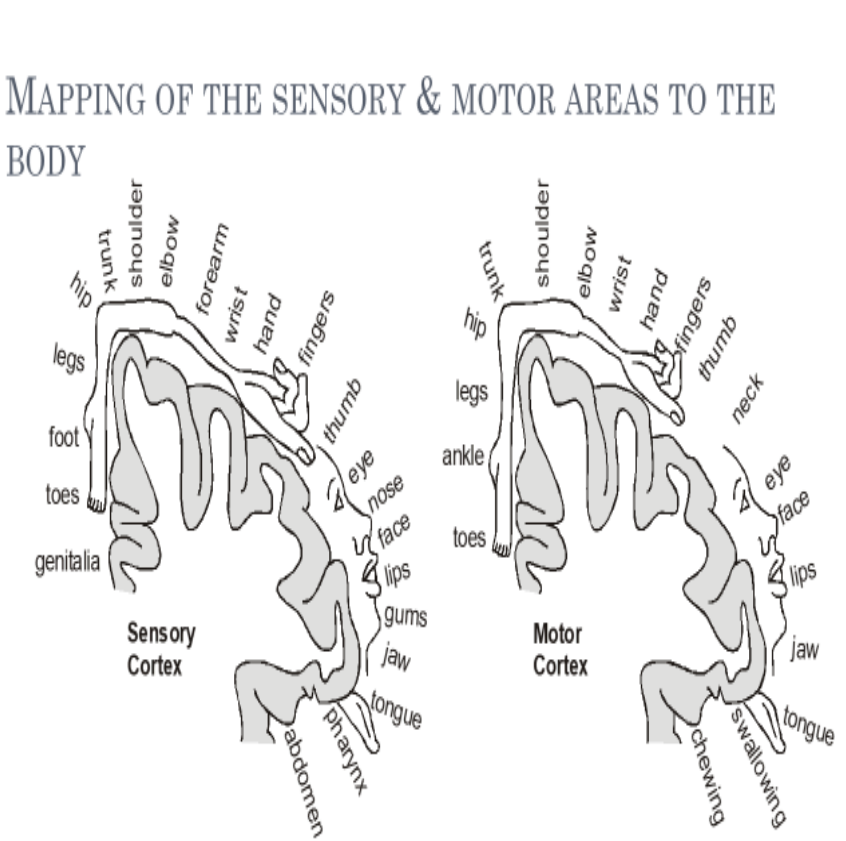
Sensory areas of the cerebral hemispheres receive impulses from sense organs and transmit them to the association areas

The association areas of the cerebral hemispheres receive impulses - interpret them in the light of similar past experiences and transmit impulses to motor areas

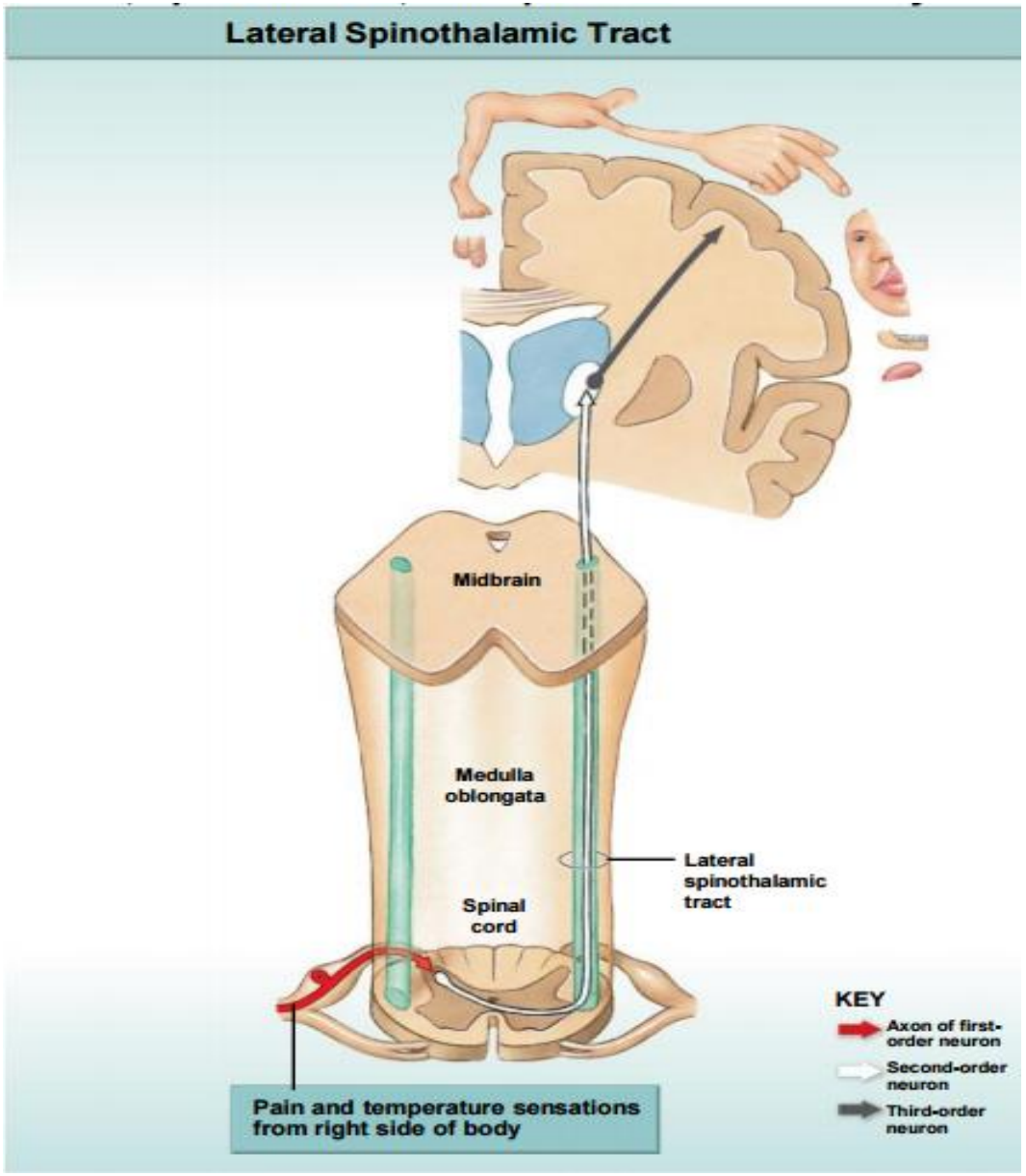
The motor areas transmit impulses to the effectors

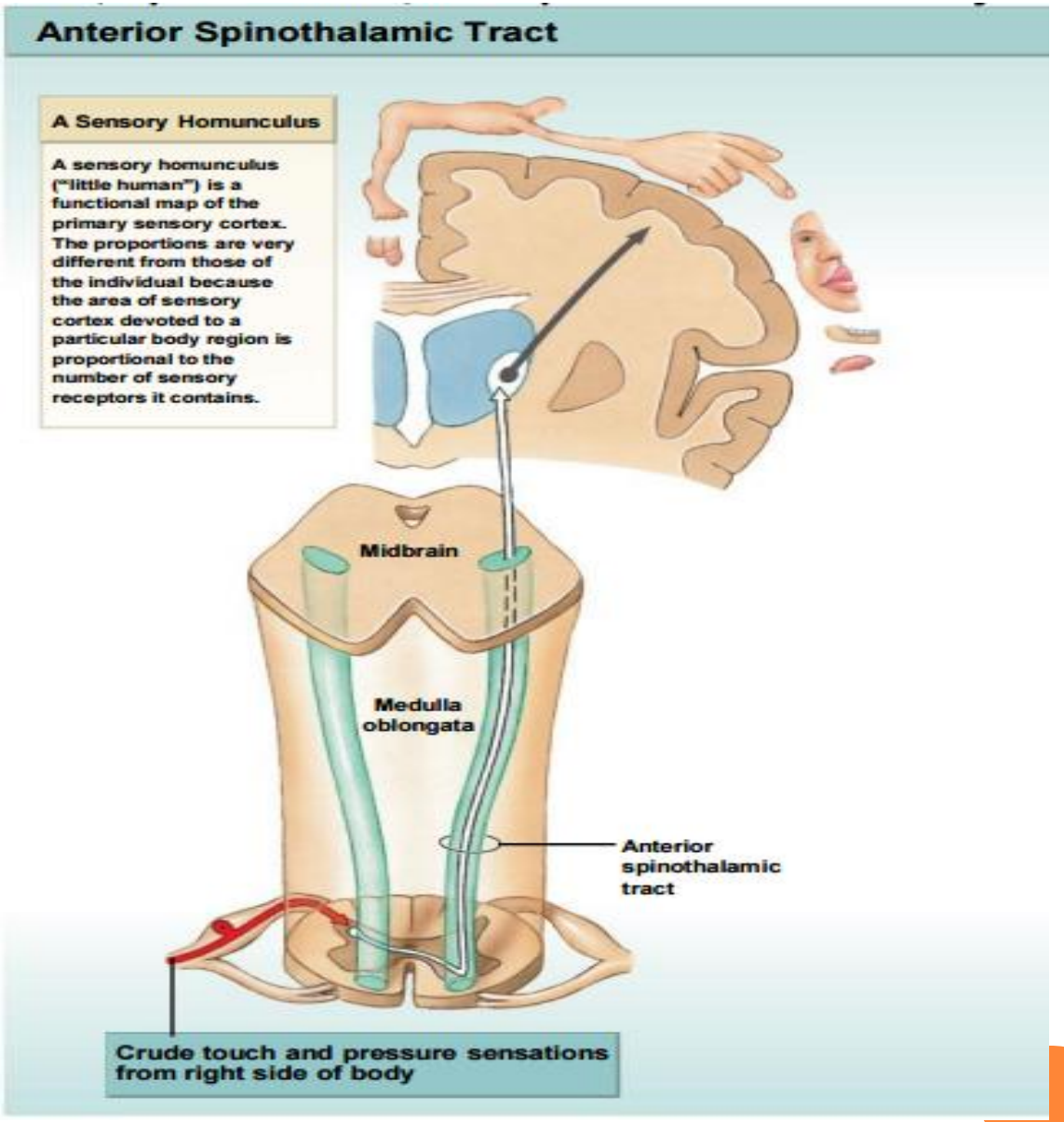
The size of the sensory and motor areas is related to the number of receptors in that area

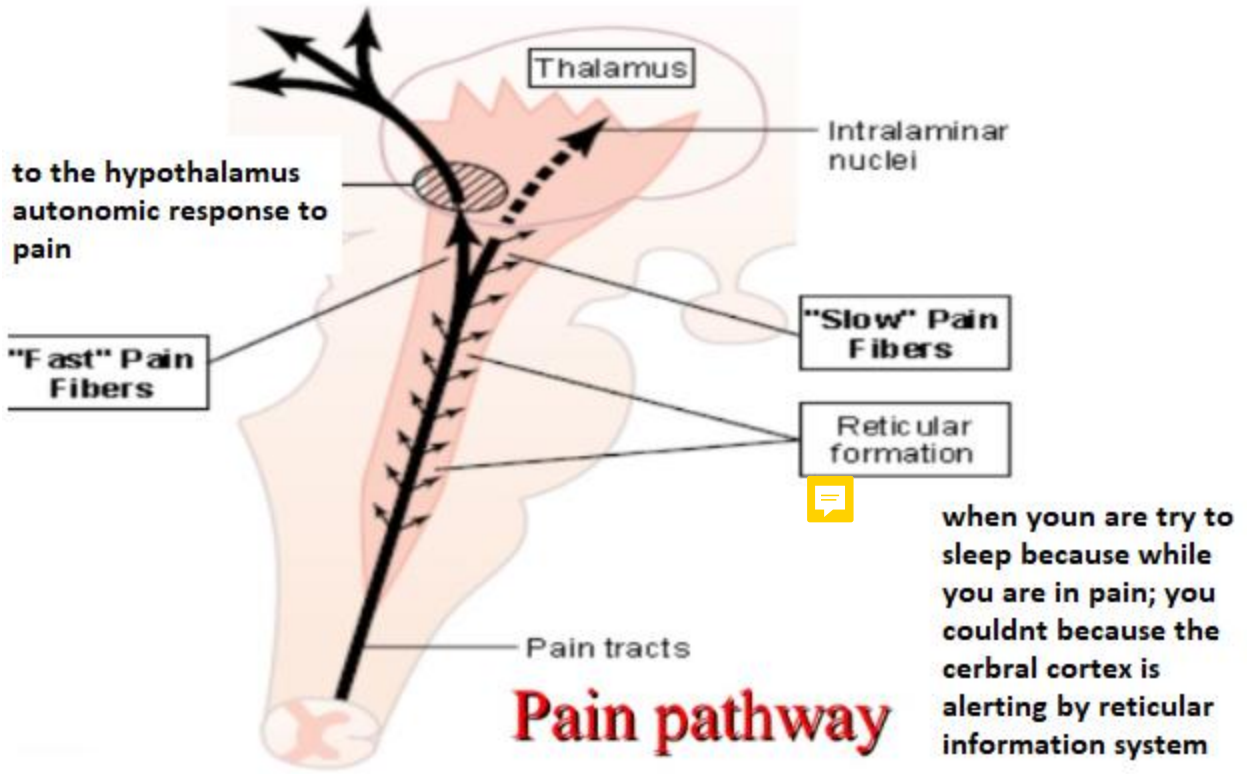
The left and right cerebral hemispheres control the opposite sides of the body



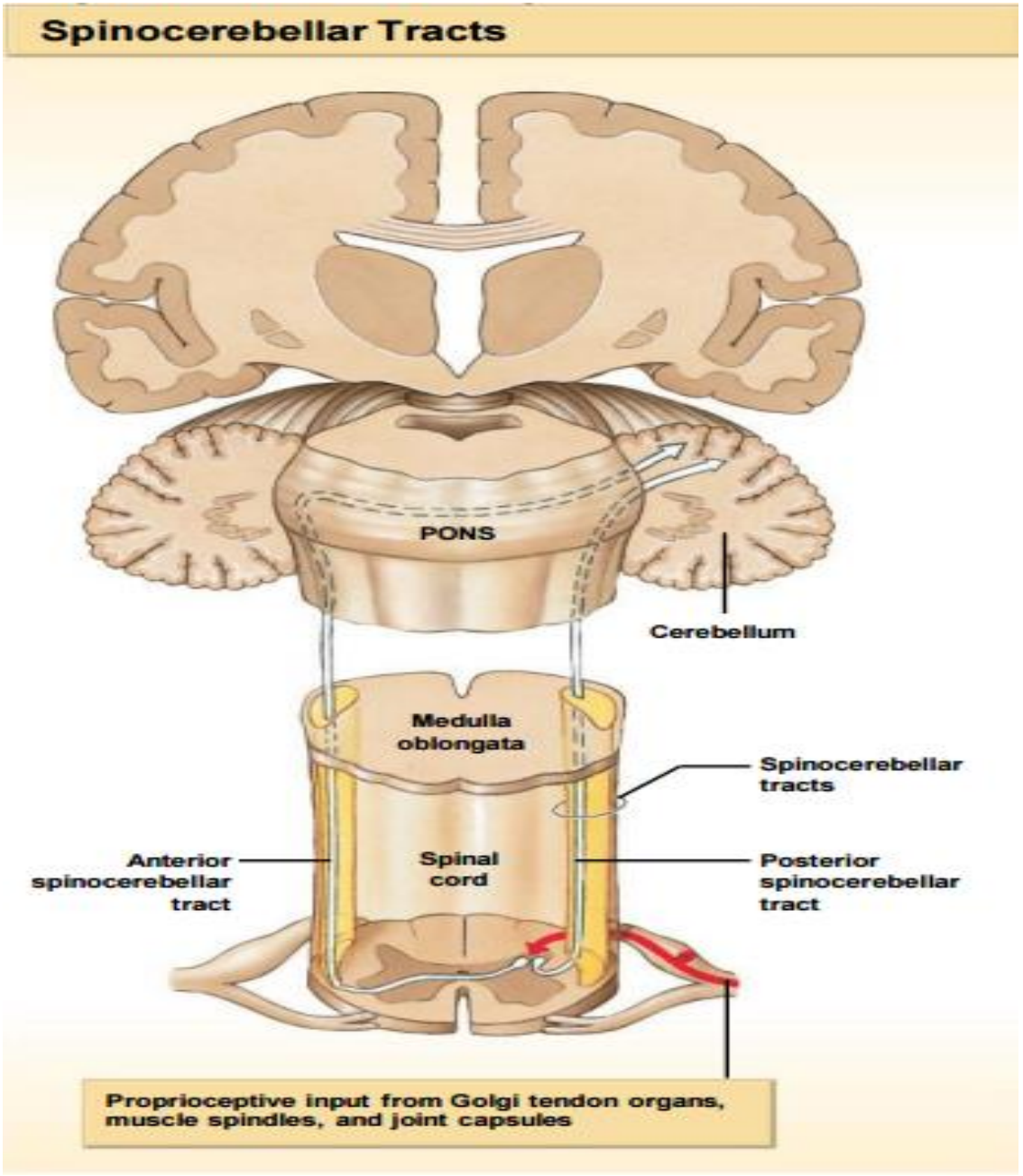
		Location of Neuron Cell Bodies				
Tract	Sensations	First-Order	Second-Order	Third-Order	Final Destination	Site of Crossover
POSTERIOR COLUMNS						
Fasciculus gracilis	Proprioception, fine touch, pressure, and vibration from levels inferior to T_6	Dorsal root ganglia of lower body; axons enter CNS in dorsal roots and ascend within fasciculus gracilis	Nucleus gracilis of medulla oblongata: axons cross over before entering medial lemniscus	Ventral posterolateral nucleus of thalamus	Primary sensory cortex on side opposite stimulus	Axons of second-order neurons, before joining medial lemniscus
Fasciculus cuneatus	Proprioception, fine touch, pressure, and vibration from levels at or superior to T_6	Dorsal root ganglia of upper body; axons enter CNS in dorsal roots and ascend within fasciculus cuneatus	Nucleus cuneatus of medulla oblongata: axons cross over before entering medial lemniscus	Ventral posterolateral nucleus of thalamus	As above	As above


Lateral Spinothalamic Tract
Midbrain
Medulla oblongata
Spinal cord
Lateral spinothalamic tract
Pain and temperature sensations from right side of body
KEY
Axon of first-order neuron
Second-order neuron
Third-order neuron


Anterior Spinothalamic Tract
A Sensory Homunculus
A sensory homunculus ("little human") is a functional map of the primary sensory cortex. The proportions are very different from those of the individual because the area of sensory cortex devoted to a particular body region is proportional to the number of sensory receptors it contains.
Midbrain
Medulla oblongata
Anterior spinothalamic tract
Crude touch and pressure sensations from right side of body



when youn are try to sleep because while you are in pain; you couldnt because the cerbral cortex is alerting by reticular information system


Spinocerebellar Tracts
PONS
Cerebellum
Medulla oblongata
Spinocerebellar tracts
Anterior spinocerebellar tract
Spinal cord
Posterior spinocerebellar tract
Proprioceptive input from Golgi tendon organs, muscle spindles, and joint capsules

Tract	Sensations	Location of Neuron Cell Bodies: First-Order	Second-Order	Third-Order	Final Destination	Site of Crossover
SPINOTHALAMIC TRACT						
Lateral spinothalamic tracts	Pain and temperature sensations	Dorsal root ganglia; axons enter CNS in dorsal roots and enter posterior gray horn	In posterior gray horn: axons enter lateral spinothalamic tract	Ventral posterolateral nucleus of thalamus	Primary sensory cortex on side opposite stimulus	Axons of second-order neurons, at level of entry
Anterior spinothalamic tracts	Crude touch and pressure sensations	As above	In posterior gray horn: axons enter anterior spinothalamic tract on opposite side	As above	As above	As above
SPINOCEREBELLAR TRACTS						
Posterior spinocerebellar tracts	Proprioception	Dorsal root ganglia; axons enter CNS in dorsal roots	In posterior gray horn: axons		Cerebellar cortex on side of stimulus	None
Anterior spinocerebellar tracts	Proprioception	As above	as above		Axons of most second-order neurons cross before entering tract and then cross again within cerebellum	

Types of sensory neuron

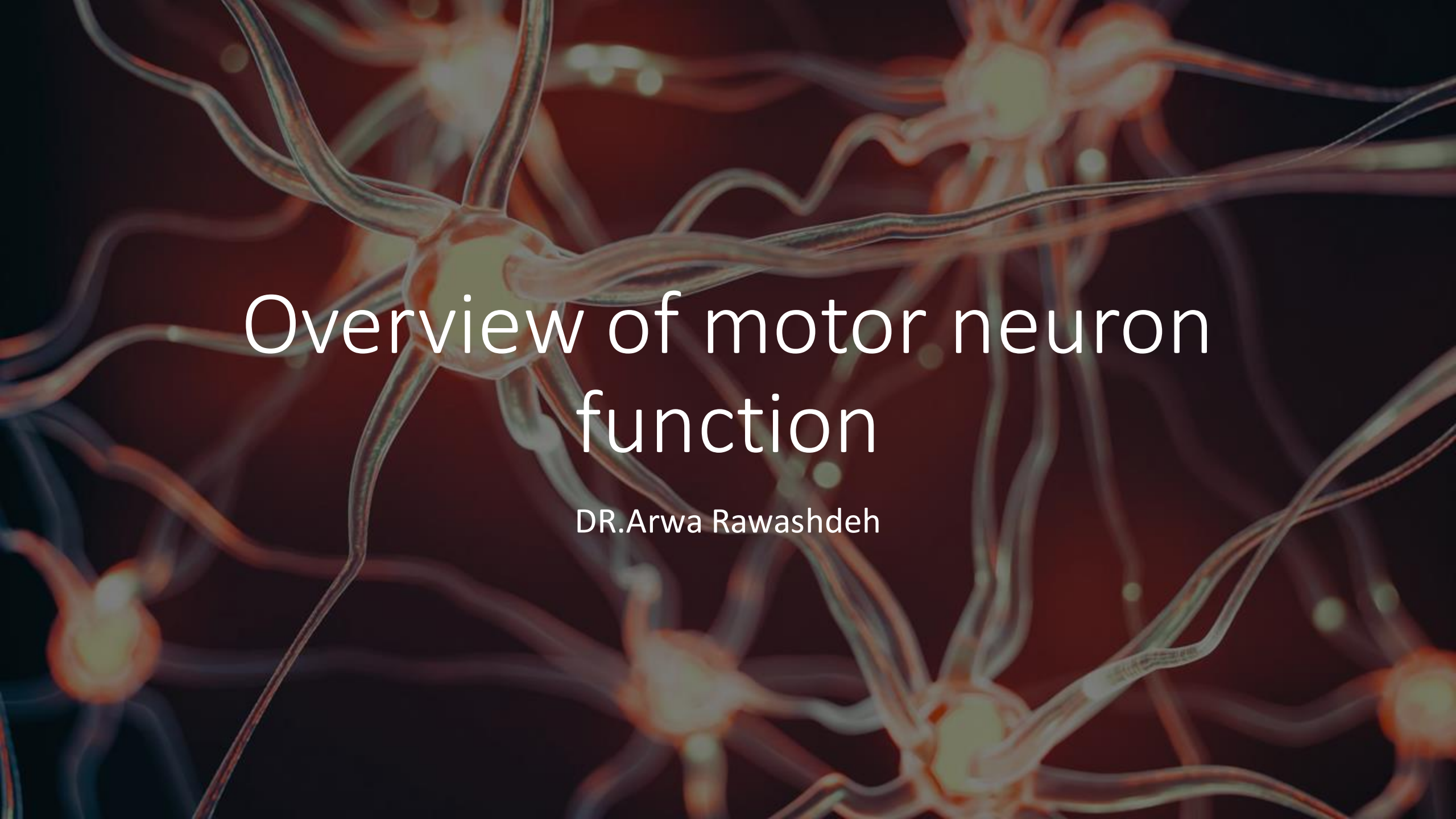
SENSORY NEURONS FIBER TYPES

Fiber Type	Alternate Name	Myelinated	Receptors	Sensory Modality	Fiber Tract
A-α	Ia Ib	yes	Muscle Spindle Golgi Tendon Organ	Proprioception	Posterior Columns
A-β	II	yes	Meissner Corpuscle Merkel Disk Ruffini Corpuscle Pacinian Corpuscle	distinctive touch fine and crude touch stretching deep pressure and vibration	Posterior Columns
A-δ	III	yes	Hair Follicle Receptor Free Nerve Ending	Touch Fast pain Temperature cold	ALSTS
C	IV	no	Free Nerve Ending	slow Pain Temperature Hot	ALSTS

mechanical stimulation

chemical stimulation

H+, K+, bradykinin, histamine



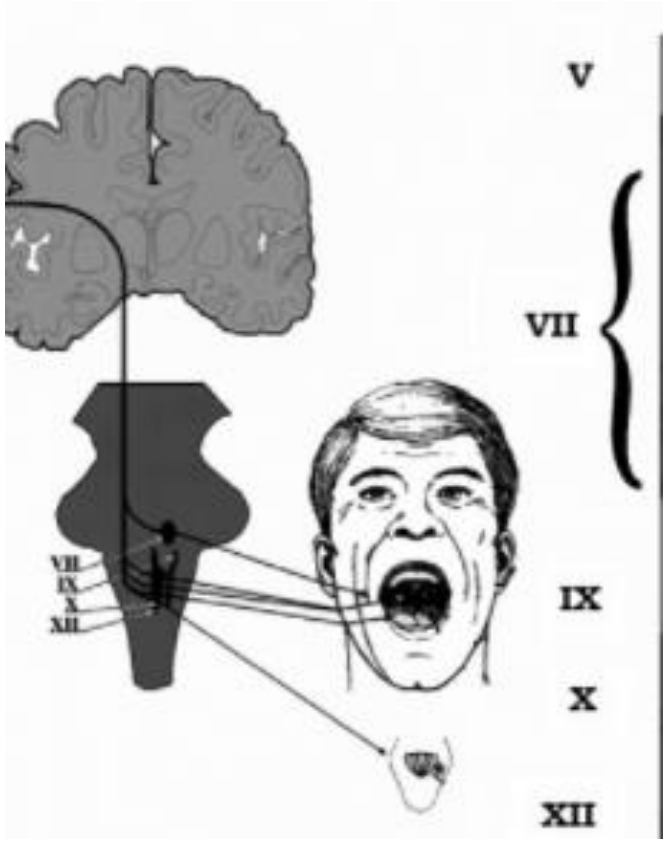
Overview of motor neuron function

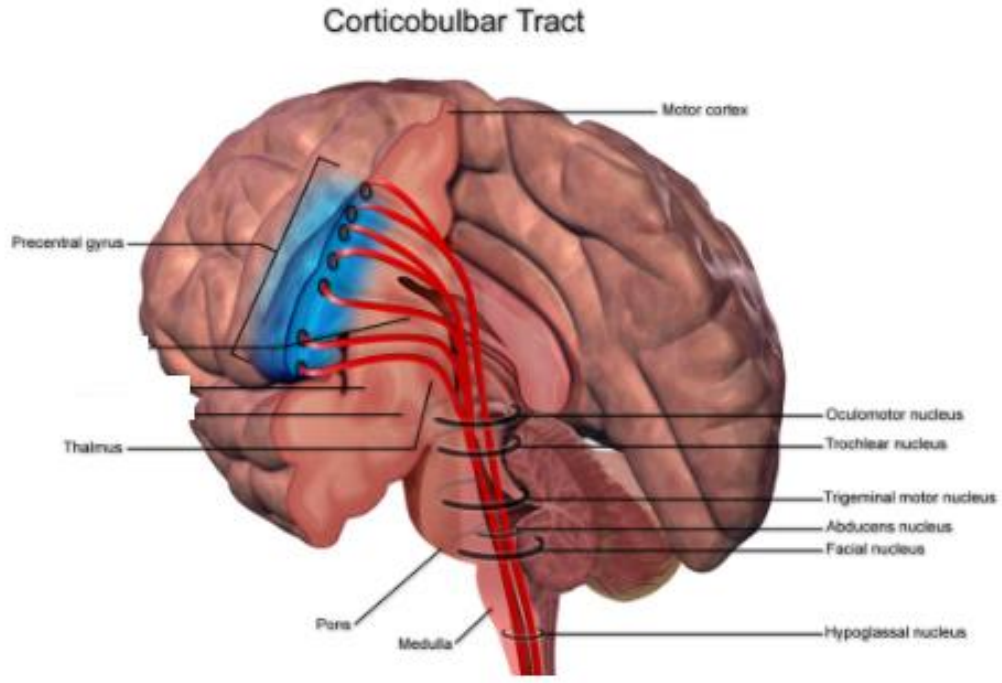
DR.Arwa Rawashdeh

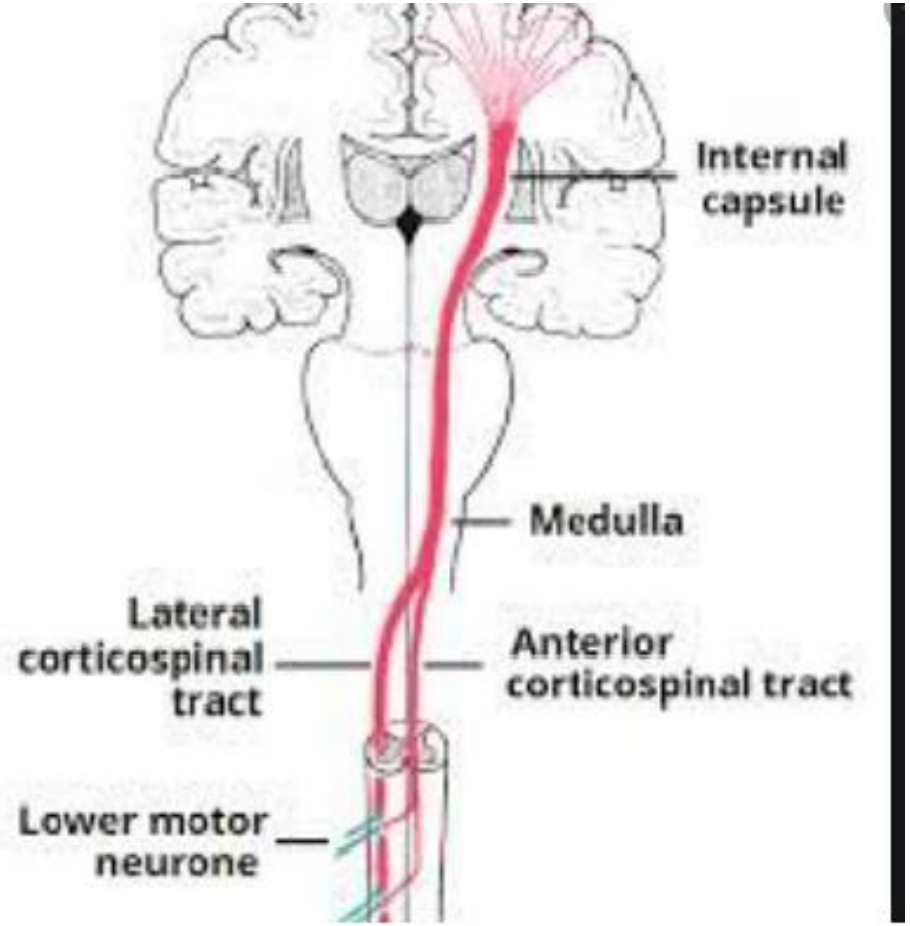
Upper (UMN)and lower motor neuron tracts (LMN)

UMN	Corticospinal	Corticobulbar
LMN	Anterior gray horn in the spinal cord	Cranial nerve nuclei

Corticobulbar Tract





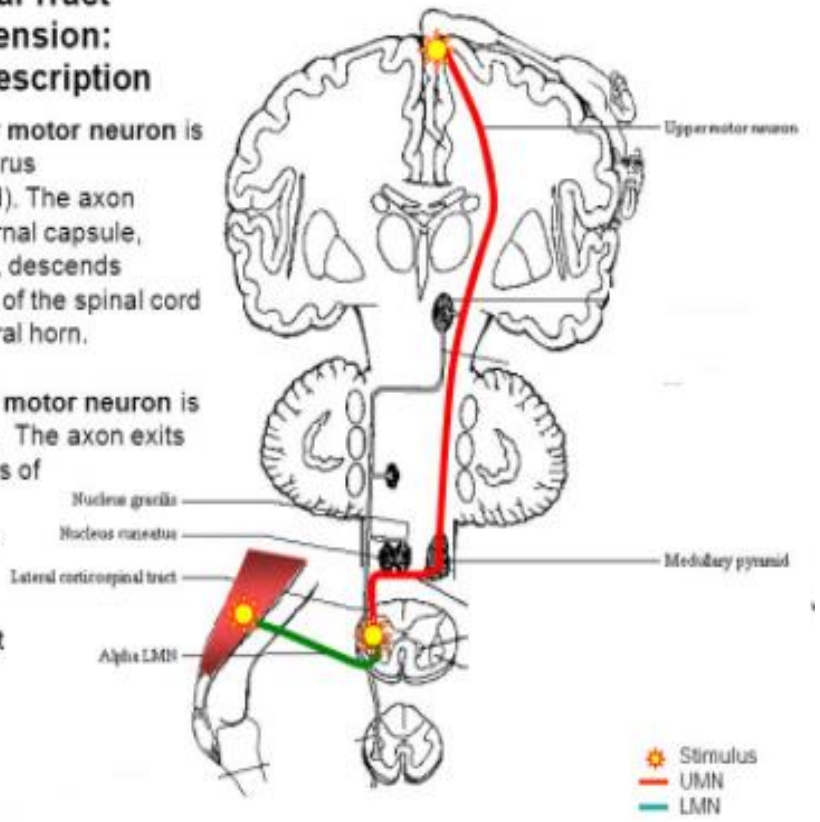


Corticospinal Tract
Voluntary Knee Extension: Neuroanatomical Description

The cell body of the **upper motor neuron** is located in he precentral gyrus (somatotopically organized). The axon descends through the internal capsule, decussates in the medulla, descends through the lateral column of the spinal cord and terminates in the ventral horn.

The cell body of the **lower motor neuron** is located in the ventral horn. The axon exits the CNS via ventral rootlets of spinal nerves and innervates skeletal muscle via a peripheral nerve.

Skeletal muscles contract to produce the force to extend the knee.



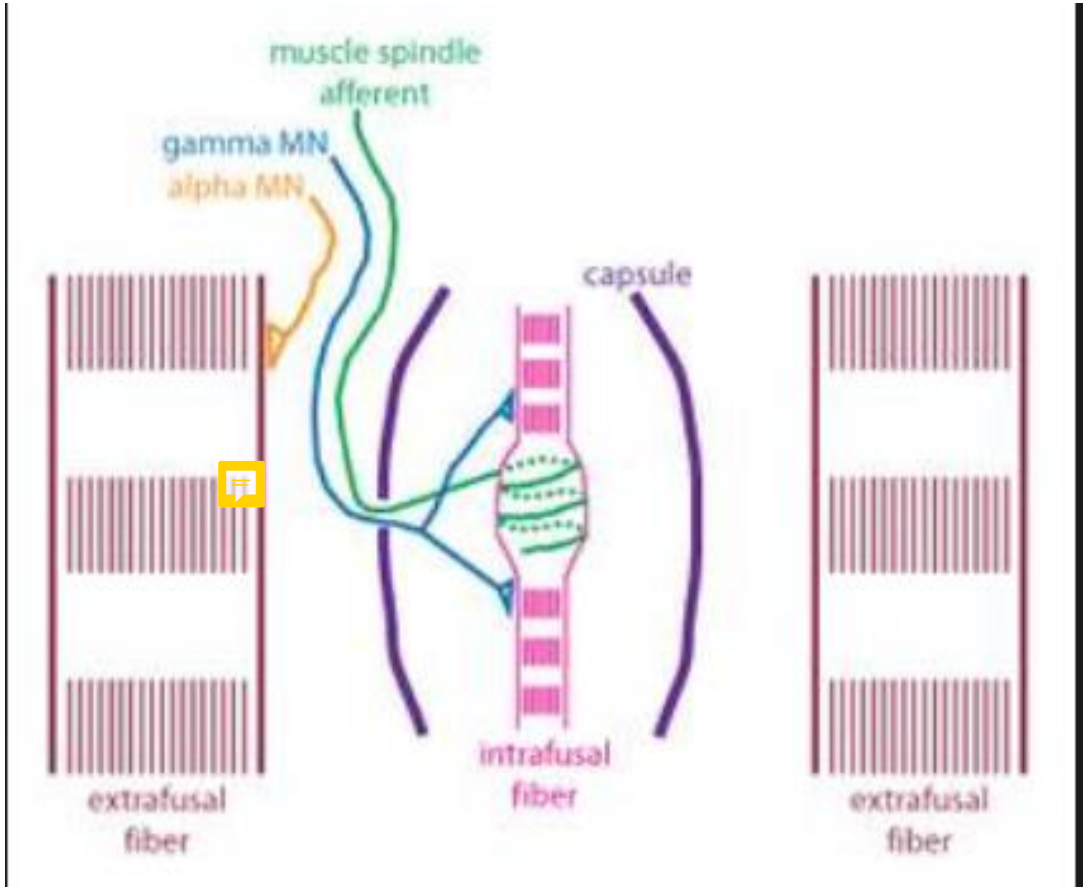
Corticospinal tract

CLASSIFICATION OF LMN

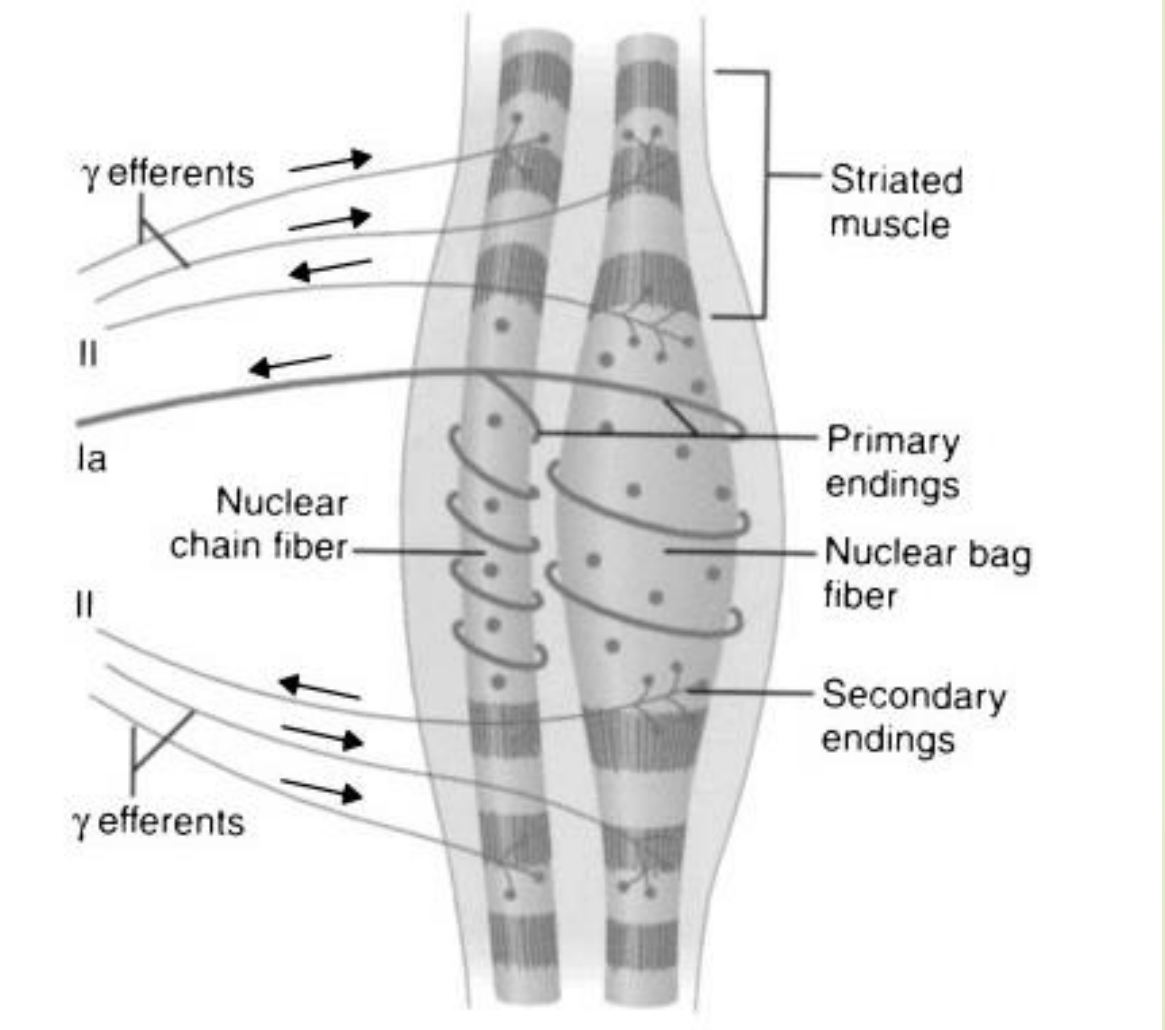
Lower motor neurons are classified based on the type of muscle fiber they innervate:

•Alpha motor neurons (α-MNs) innervate extrafusal muscle fibers, the most numerous type of muscle fiber and the one involved in muscle contraction.

•Gamma motor neurons (γ-MNs) innervate intrafusal muscle fibers, which together with sensory afferents compose muscle spindles. These are part of the system for sensing body position (proprioception)



The stretch reflex (myotatic reflex)



WHAT ARE LOWER MOTOR NEURON

All voluntary movement depend upon excitation of lower motor neuron by upper motor neuron

These are the only neurons that innervate the skeletal muscle fibers, they function as the final common pathway, the final link between the CNS and skeletal muscles

WHERE THEY COME FROM

- Motor Neuron in spinal cord **in the anterior gray horn**

- Motor component of cranial nerve nuclei in brain stem (Those in cranial nerves innervate the skeletal muscles associated with the movements of the eyes, tongue, chewing, swallowing, vocalizing.)

Upper motor lesion

1. Stroke (occurs when the blood supply to part of your brain is interrupted or reduced)
2. Demyelination the axons of nerve fibers (multiple sclerosis and B12 deficiency)
3. Amyotrophic lateral sclerosis (ALS) is a neurodegenerative neuromuscular disease that results in the progressive loss of motor neurons that control voluntary muscles

Lower motor neuron lesion

1. Polio virus damage the anterior gray horn
2. Spinal muscular atrophy (genetic disease that damage the anterior gray horn)
3. Neuropathy (damage to the nerve because of herniated disc or diabetes
4. Botulinum toxin (inhibit the Ach release)
5. Amyotrophic lateral sclerosis (ALS)

Corticobulbar tract lesion

BULBAR PALSY

is a similar disorder as psedobulbar palsy but is caused by lower motor neuron lesions

It consists of **LMN signs** in regions innervated by the **facial (VII), glossopharyngeal (IX), Vagus (X) and hypoglossal (XII**

PSEUDOBULBAR PALSY

results from an upper motor neuron lesion to the corticobulbar pathways

It results from **bilateral lesion of UMN's** of the muscles of the tongue (XII), face (VII), speech and swallowing (IX,X)

Corticospinal tract lesions

MASS

UMN

- Disuse atrophy
- Decrease the mass of skeletal muscle (15-20%) Damage to UPPER motor neuron

LMN

- Decrease Ach release (nicotinic and muscarinic receptors)

Nicotinic for muscle contraction

Muscarinic for cell signaling pathway and stimulate transcription factors and lead to the synthesis of muscle proteins and decrease in protein synthesis leads to proteolysis

- Denervation atrophy
- Decrease in muscle mass (70-80%)

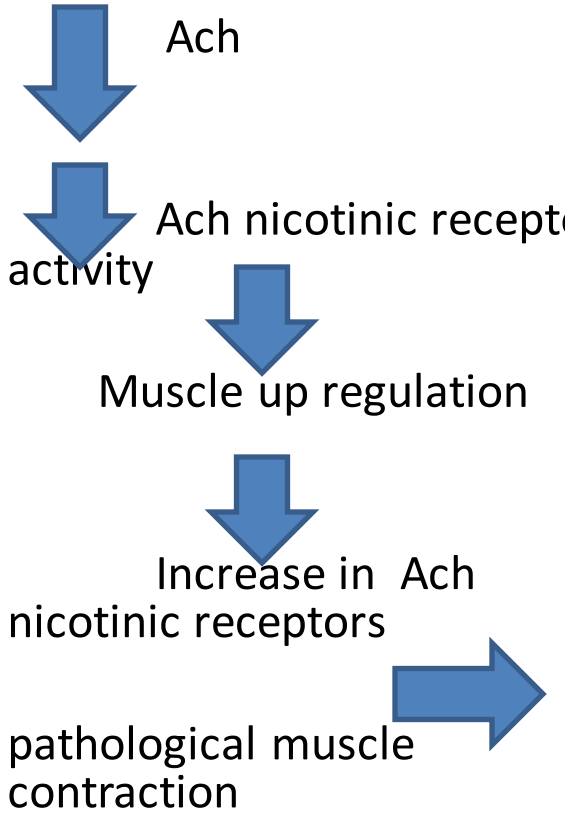
Fasciculations

Only in lower motor neuron lesions

Involuntary pathological muscle contraction

Increase the sensitivity of ligand channels (even the tapping could stimulate the channels)

Fibrillation (Expressed on EMG)



Tone , deep tendon reflex and reflex

LMN
Flaccid paralysis

action potential the LMN
(Extrafusal and intrafusal)

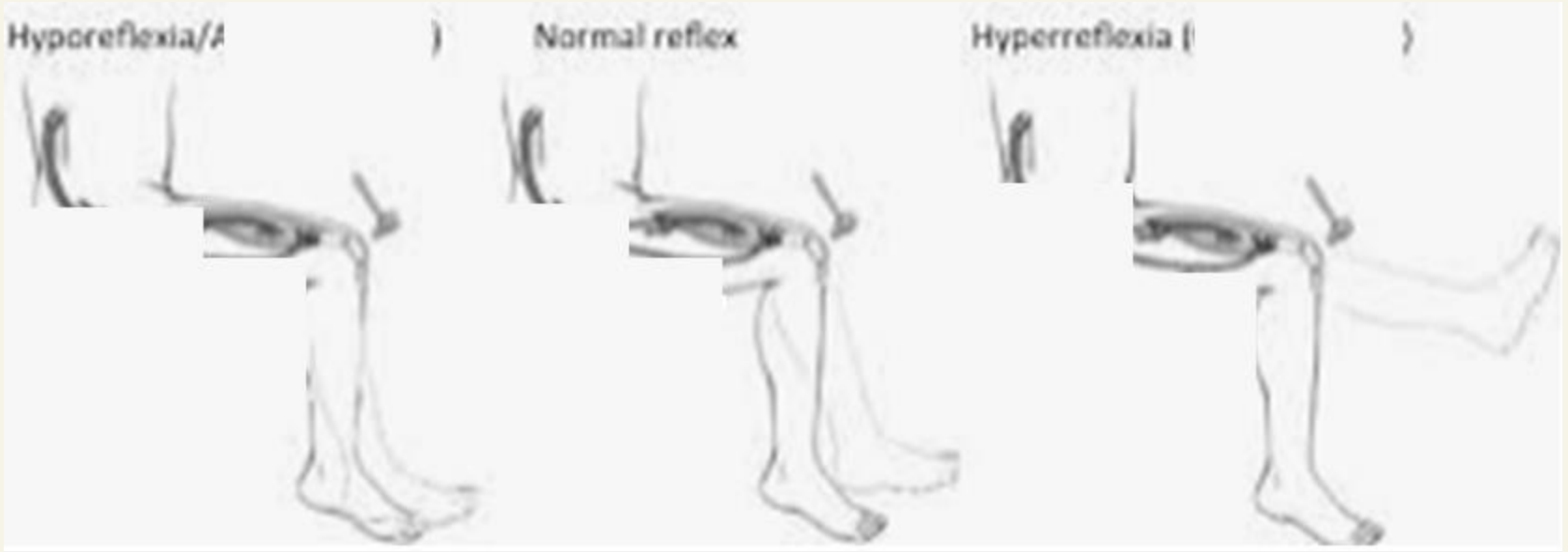
Hypotonia (alpha)
Hypo- reflexia (Gamma)
Decrease the activity of muscle spindle

UMN
Spastic paralysis

action potential at the level of medullary nucleus

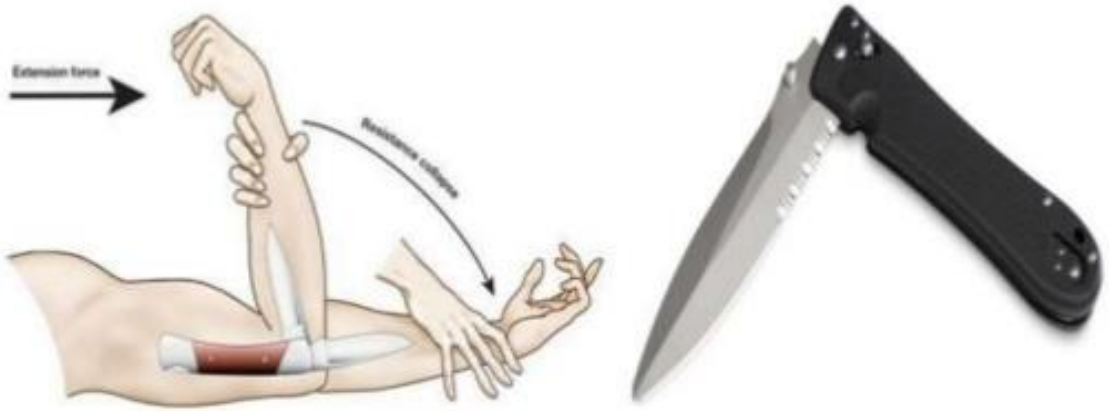
action potential the LMN (Extrafusal and intrafusal)

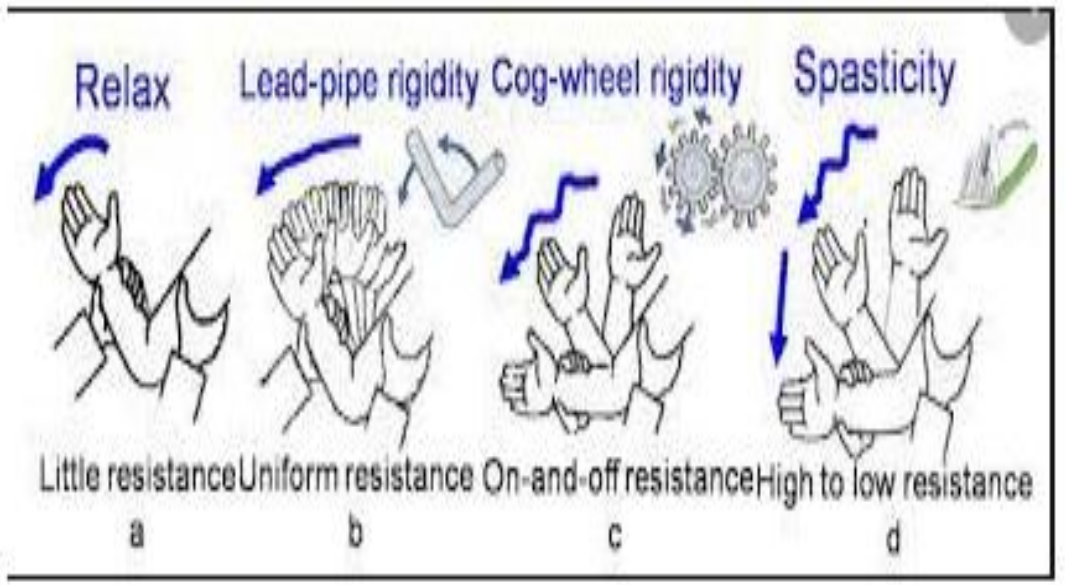
hypertonia (alpha)
hyper- reflexia(Gamma)


Hyporeflexia/A
)
Normal reflex
Hyperreflexia (
)

Difference between spasticity and rigidity

CLASP KNIFE REFLEX





Spasticity and rigidity are 2 types of hypertonic states elicited when examining the tone of limbs. It is important to differentiate between them to arrive at a correct diagnosis.

Spasticity:

Seen in pyramidal tract lesions

Classically termed 'Clasp knife spasticity' – more tone during the initial part of movement – as in opening a pocket knife

Rigidity:

like parkinsonism

Cog wheel rigidity – Tremor superimposed on hypertonia – resulting in intermittent increase in tone during the movement – felt as jerks

Lead pipe rigidity – Uniform increase in tone

Overview of cardiovascular system

DR. Arwa Rawashdeh

objectives

Overview of structure and function of the heart

Intrinsic cardiac conduction system

Conduction or electrophysiology pathway

The heart

Positioned between two bony structures – sternum and vertebrae

The heart is in the middle of the thorax, with the apex facing toward the left and inferiorly, at the level of the 5th intercostal space. The base of the heart is the posterior part of the heart.

Function of the heart

Primary (main) function:

1.Acts as a muscular pump:

in order to maintain adequate level of blood flow throughout CVS by pumping blood under pressure into vascular system.

2.Responsible for the mass movement of fluid in body.

Secondary functions:

1. Transportation:

Delivers O_2 to tissues, & brings back CO_2 to lungs

Carries absorbed digestion products to liver & tissues

Carries metabolic wastes to kidneys to be excreted

Distribution of body fluids

2. Regulation:

Hormonal: carries hormones to target tissues to produce their effects.

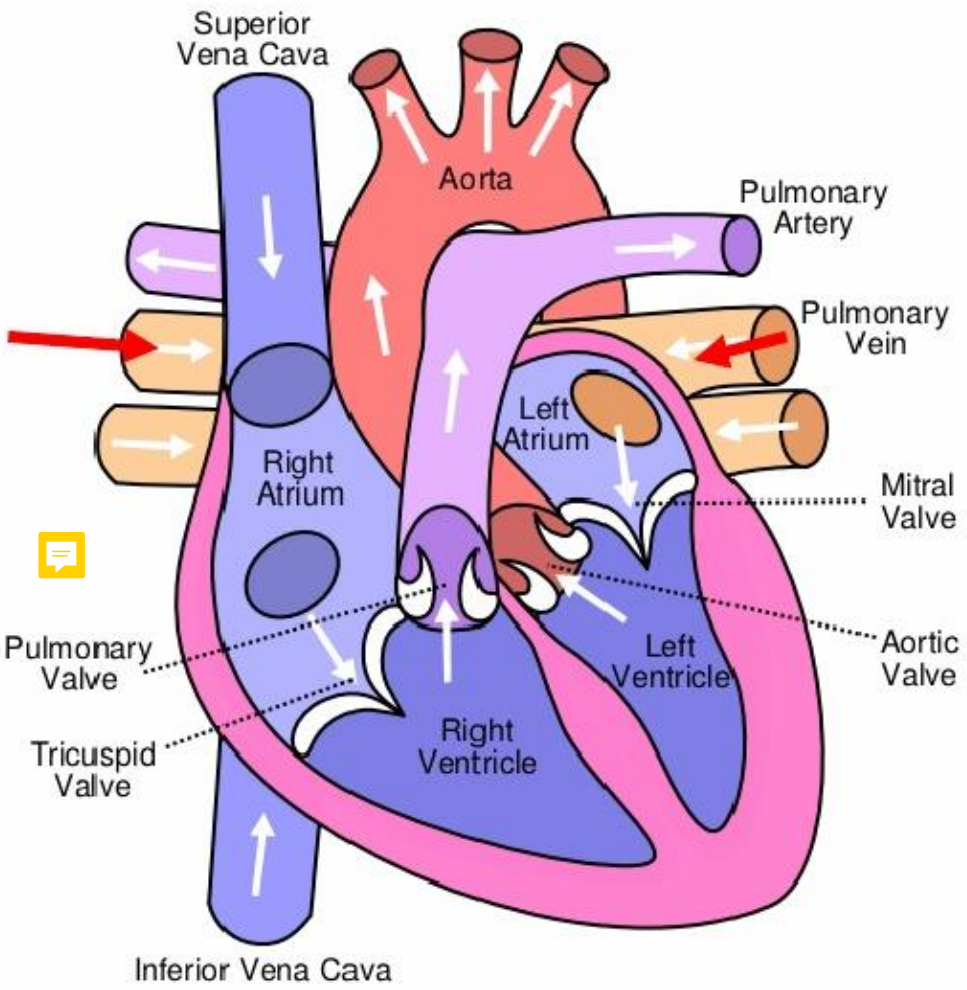
Immune: carries antibodies, leukocytes (WBCs), cytokines, & complement to aid body defense mechanism against pathogens.

Protection: carries platelets, & clotting factors to aid protection of the body in blood clotting mechanism.

Temperature: helps in regulation of body temperature, by diverting blood to warm the body.

Oxygenated blood from the right lung returns to the heart through the right pulmonary vein.
Oxygenated blood from the left lung returns to the heart through the left pulmonary vein.

THE PULMONARY VEINS ARE THE ONLY VEINS THAT CARRY OXYGENATED BLOOD.



Valves

Two semilunar valves :

- One way valves.
- At origin of pulmonary artery & aorta.
- Pulmonary (Rt) & Aortic (Lt).
- Open during ventricular contraction.

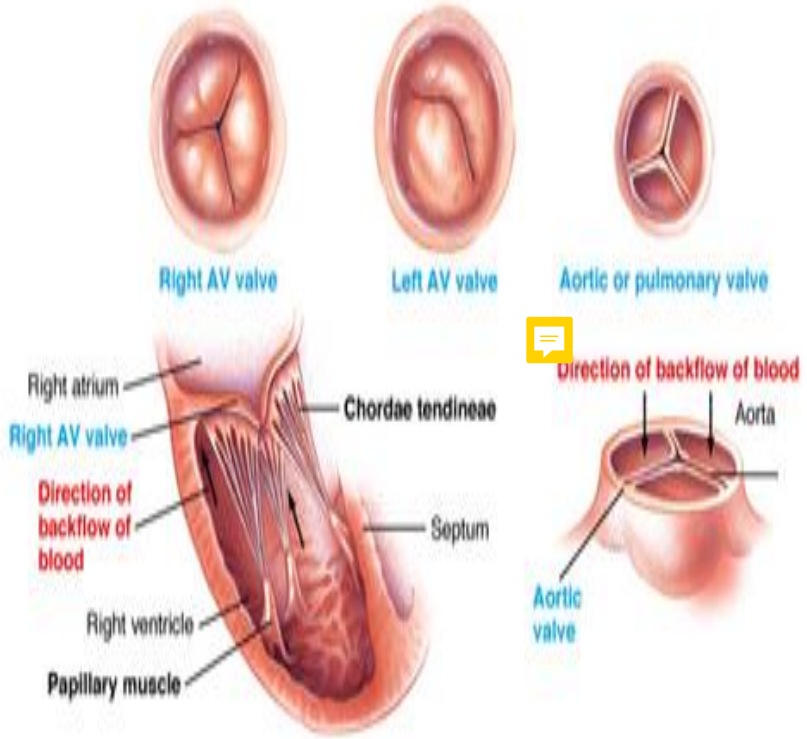
Two atrioventricular (AV) valves:

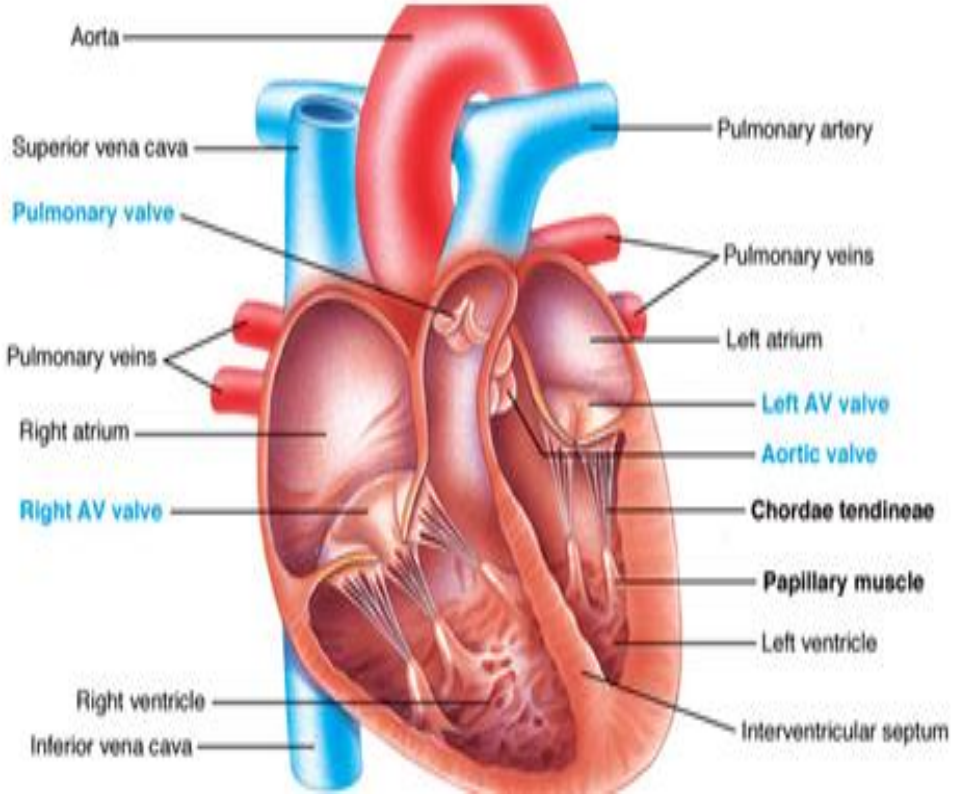
- One way valves.
- allow blood to flow from atria into ventricles.
- Tricuspid (Rt) & Mitral (Lt).

No valves between atria and veins

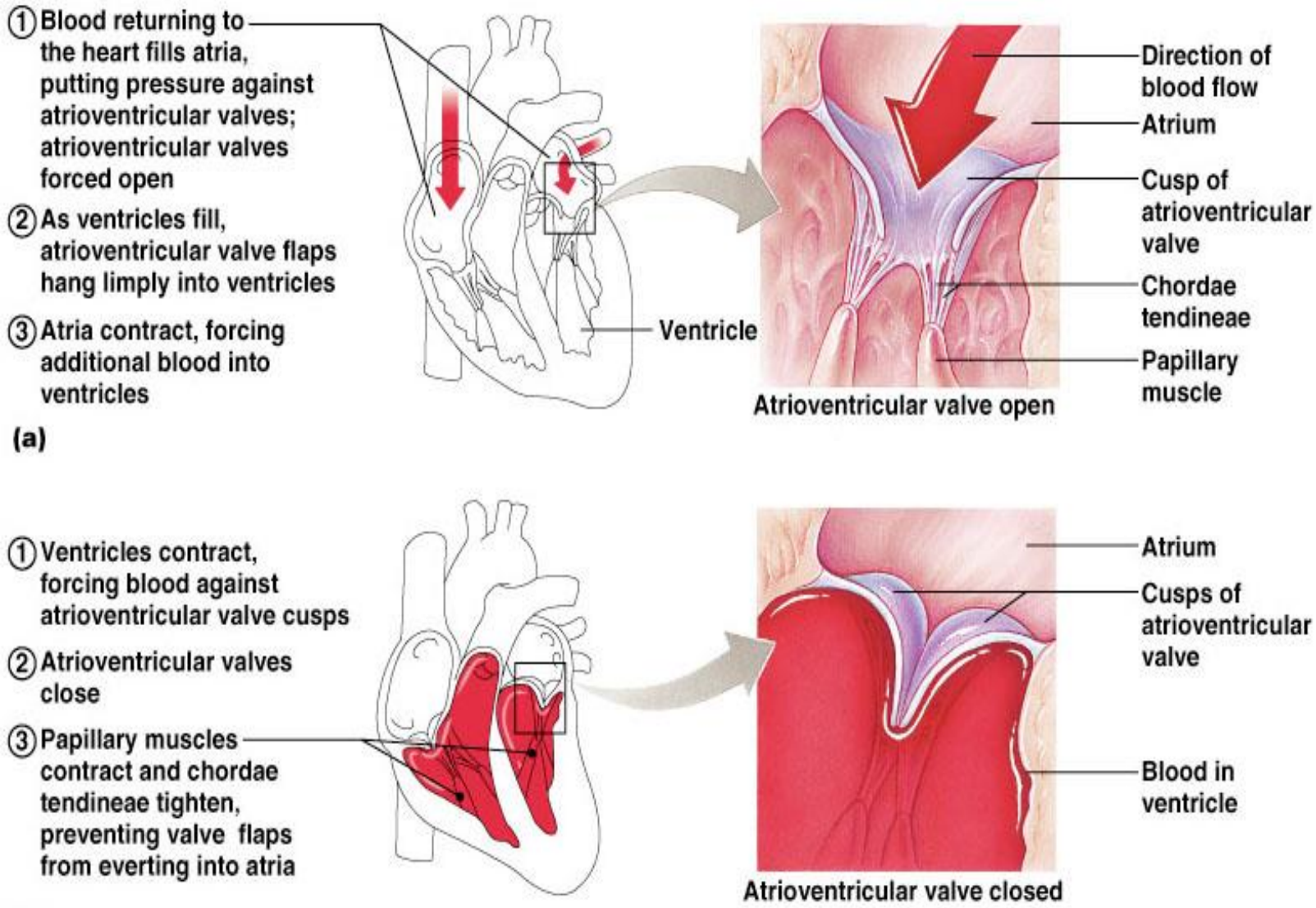
- Atrial pressures usually are not much higher than venous pressures sites

- where venae cava enter atria are partially compressed during atrial contraction

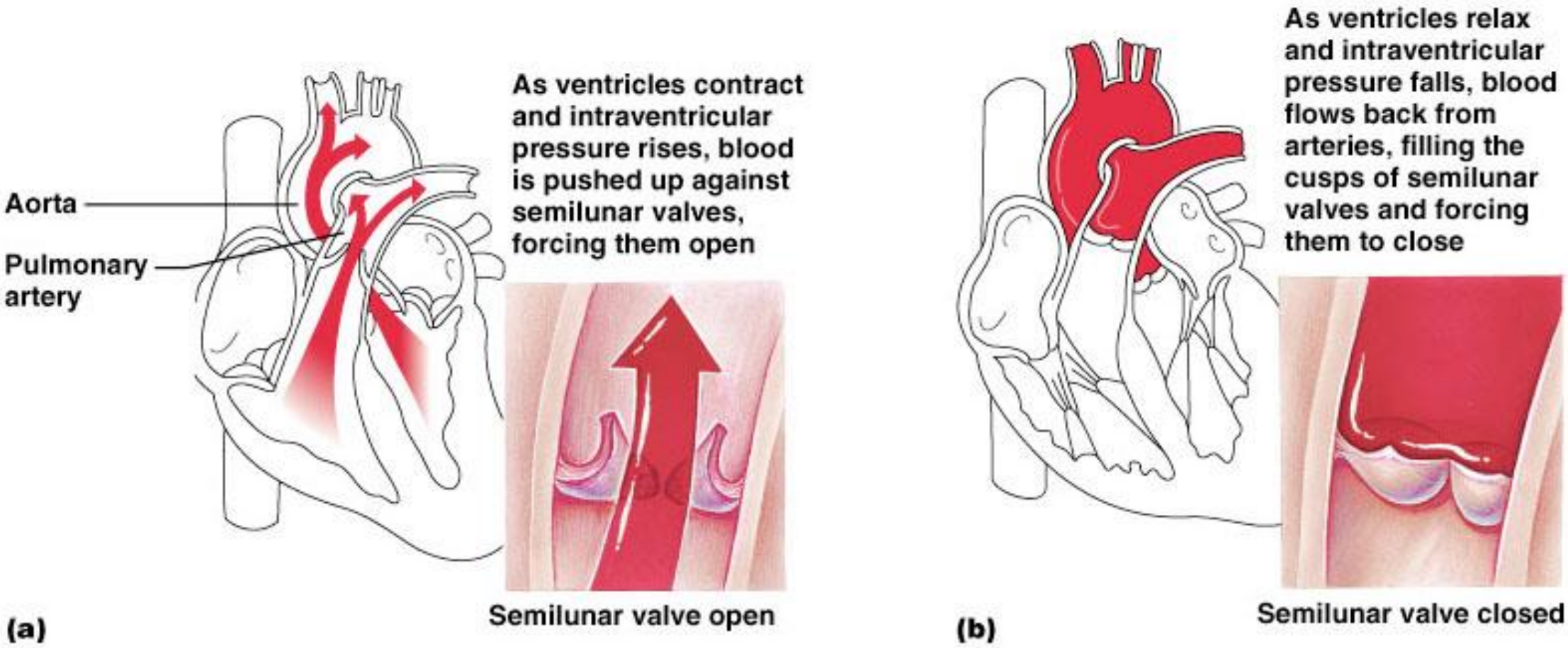

Right AV valve
Left AV valve
Aortic or pulmonary valve
Right atrium
Right AV valve
Direction of backflow of blood
Right ventricle
Papillary muscle
Chordae tendineae
Septum
Direction of backflow of blood
Aorta
Aortic valve


Aorta
Superior vena cava
Pulmonary valve
Pulmonary veins
Right atrium
Right AV valve
Right ventricle
Inferior vena cava
Pulmonary artery
Pulmonary veins
Left atrium
Left AV valve
Aortic valve
Chordae tendineae
Papillary muscle
Left ventricle
Interventricular septum

Atrioventricular valve function



Semilunar valve function



Intrinsic cardiac conduction system

- Electrophysiology of the heart is so special it had the ability to intrinsically depolarize itself it doesn’t really depend upon the nervous system

- The heart exhibits was called automaticity (the heart has its intrinsic ability on its own to spontaneously depolarize itself and then trigger action potentials to send it out to all other parts of the heart)

Types of heart cells

Two different types of myocardium ; nodal cells

- Nodal cells are non contractile cells these are the ones that generates automaticity set a rhythm or the base (SA, AV, AV Bundle(His), Bundle branches (left and right), Purkinje fibers)
- Contractile cells(actin and myosin, troponin and tropomyosin, sarcoplasmic reticulum) those ones that force and pushing the blood out of the heart

Conduction system or Electrophysiology system

SA node

Crescent shape structure ;Superior component of the right atrium just beneath the large vessel here called superior vena cava;

Sets the pace at around 60 to about 80 beats per minute (normal heart beat) on its own without any extrinsic innervation and this is called sinus rhythm

Bachman's bundle

The electrical potential conducted from the right atrium by SA node to the left atrium through Bachman's bundle

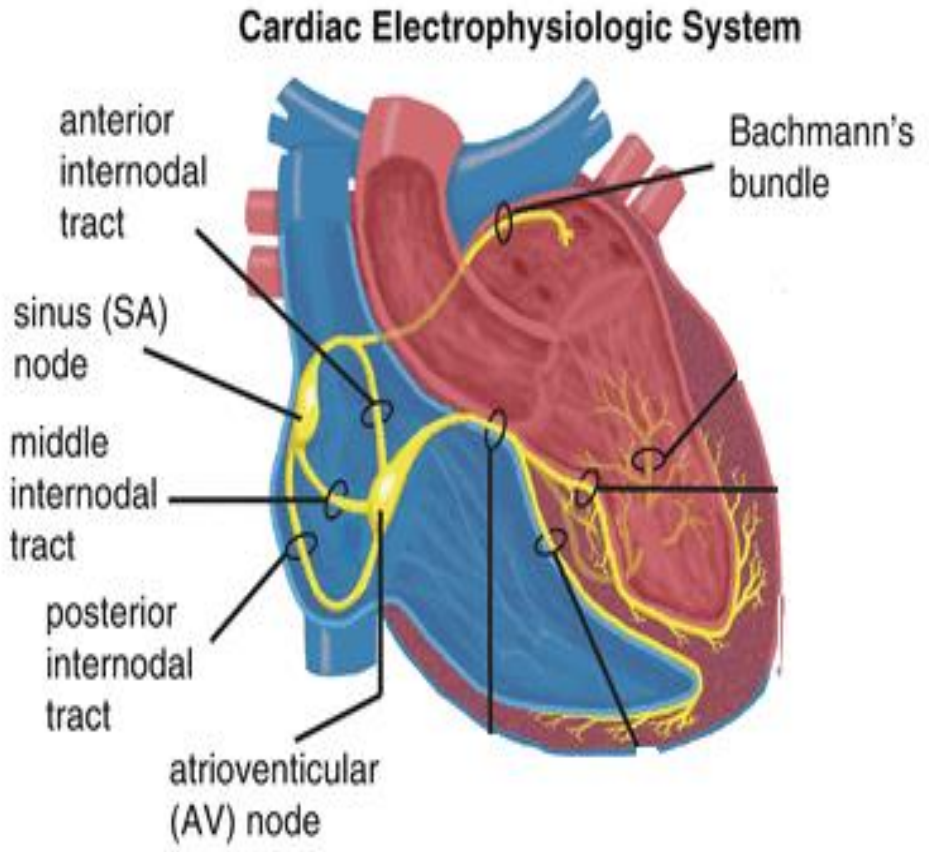
Internodal pathway

This will supply all the other parts of the right atrium but eventually all this internodal pathways converge on this second important structure to the AV node

AV node

Runs from the actual right atrium to the interventricular septum so it is acting as a connection, the gateway between the atria and the ventricles because what happened is some potentials of Bachman's bundle can make their way over here to the AV node also

So all the action potentials that are coming from the SA node that are being spread out to the internodal pathway or the Bachman's bundle are converging to the AV node



Overview of Physiology of cardiac muscle and overview of arterial blood pressure

DR. Arwa Rawashdeh

Conduction system or Electrophysiology system

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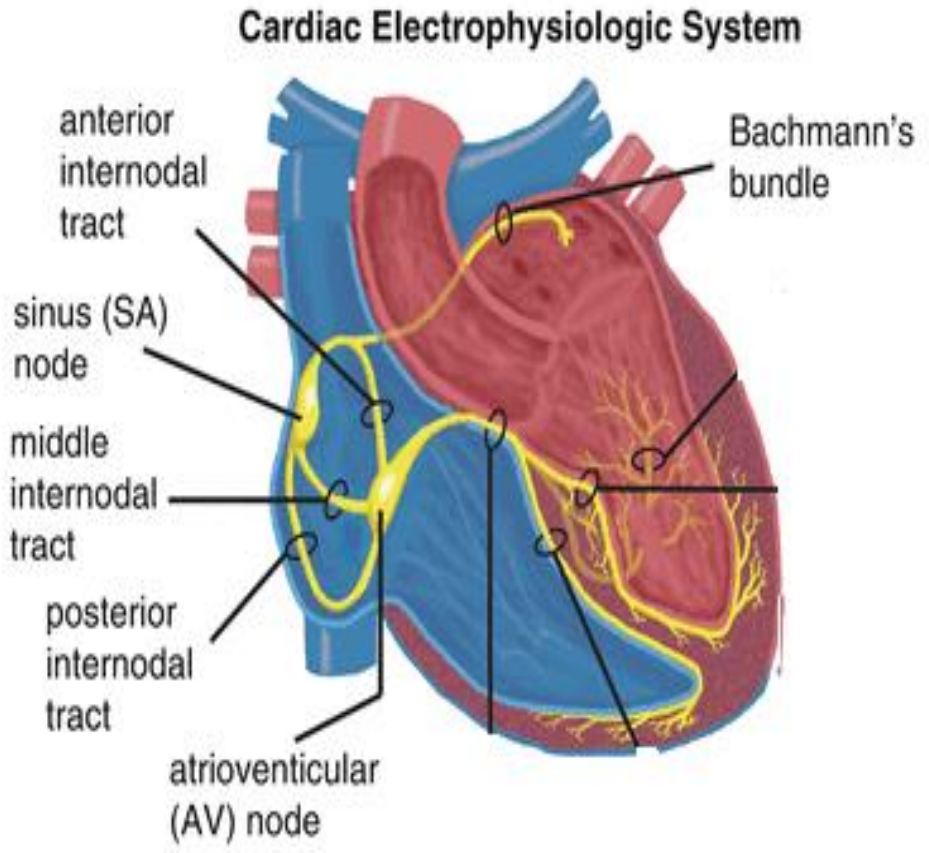


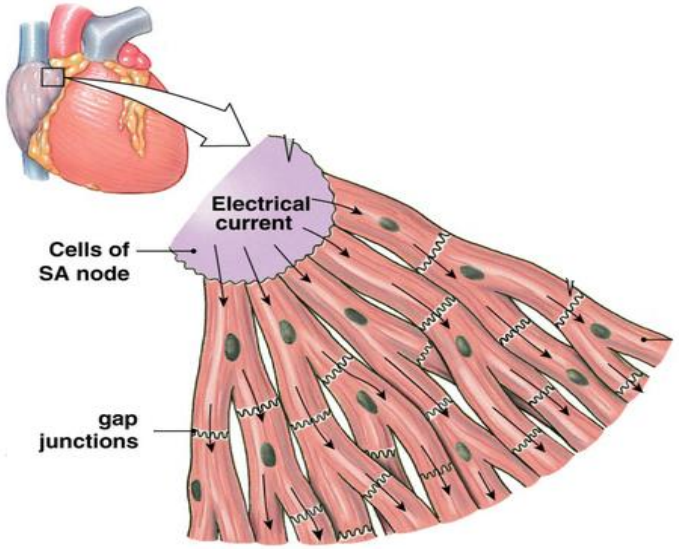
Conduction pathway

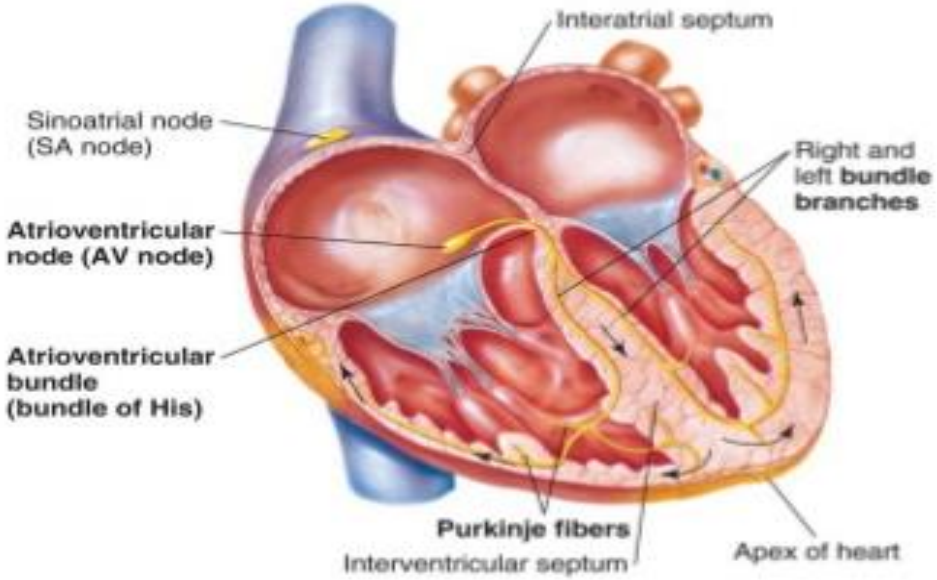
- Once the AV node receives the signals it is going to take a bit of time about 0.1 second which is a little bit longer than how much it takes for them to move all the way from SA node to AV node
- The significant of this that is want to give a time for the atrium to contract before the ventricles contract so they have enough time to push the blood into ventricles

But why it takes 0.1 seconds ? Two microscopic reasons for this:

1. These nodes are riddled with a ton of gap junctions which are just basically channels that allow for ions to pass from cell to cell however the AV node which consists of a bundle of those nodal cells it has lot fewer gap junction than these other nodal cells so a lot less gap junction
2. Smaller diameter so the actual fibers are actually a lot smaller in diameter ; the larger the diameter of the structure the faster the velocity of the conduction is going to move

- From AV node it is going to move to bundle of his
- Bundle of his to two bundle of branches(right bundle branch and left bundle branch)
- From there to purkinje fibers





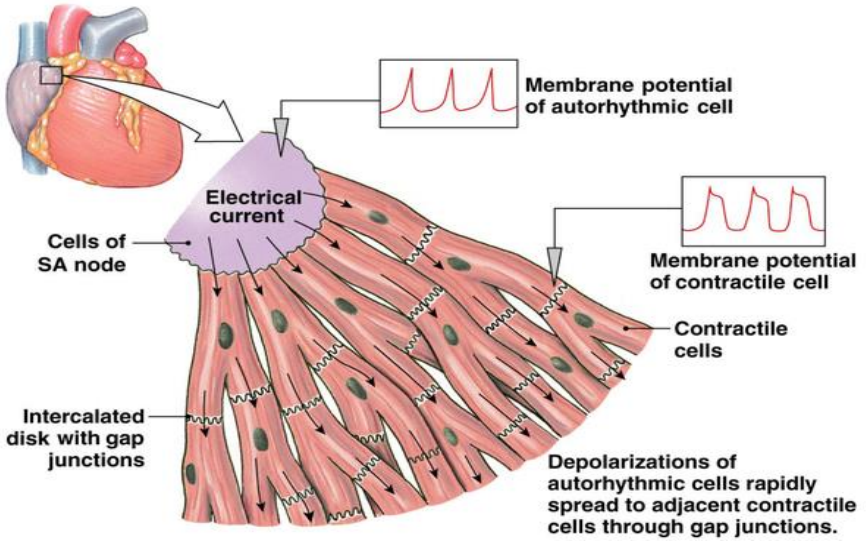
Microscopic structure of gap junctions and desmosomes

When accumulating a lot and a lot of cells inside the nodal cells , the cations that are being loaded inside the cell is going to move to contractile cells through the gap junction that connects nodal cell with contractile one

Then from to cell to cell to cell ……

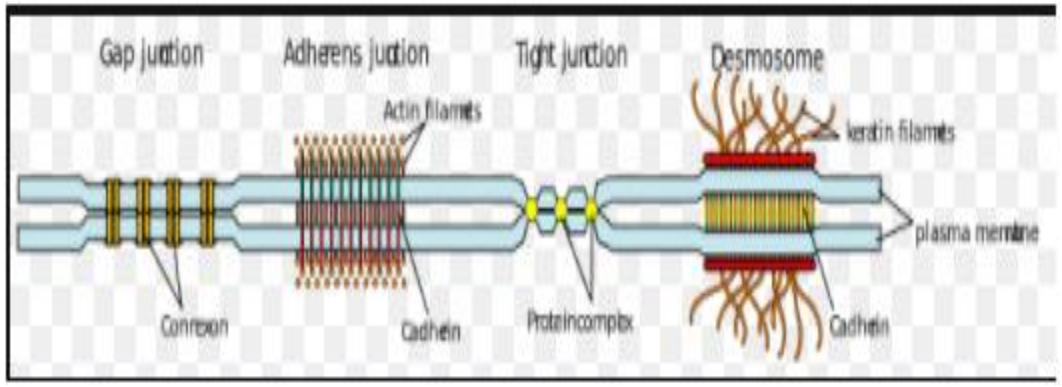
The gap junction is made from specific protein called **connexons**

To keep the cells tight together when the cells contracting and preventing stretching of the gap junction , we have a special structure called **desmosomes**



Desmosomes gets up a bunch of different protein;

- protein connects cell to cell for the cell-to-cell communication called **cadherins**
- and anther protein made up of different bunch of protein called **desmoplakin**
- and anther chemical protein,
- anther protein consisting of protein filaments **keratin**

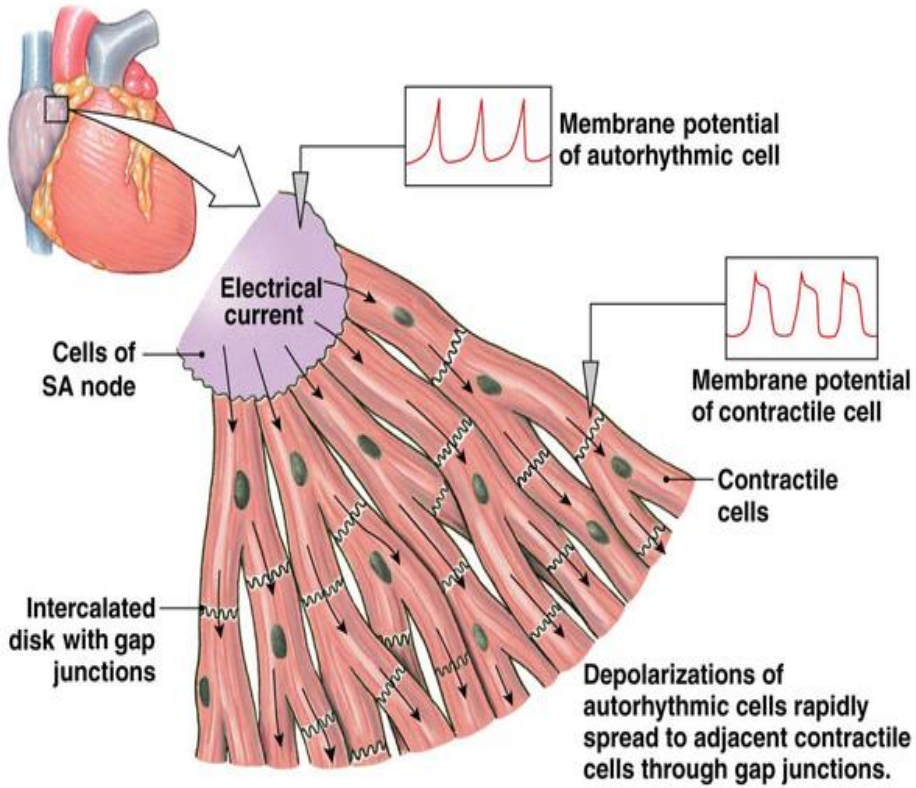


Intercalated disks

- Desmosomes is basically acting like adhesion molecules from cell to cell and keeping the cells very tightly connecting and that's really really important

- This lead us to concept whenever we have two cells communicating to each other and I have a combination of desmosomes and gap junctions they called together **intercalated disks**

- **Intercalated disks are basically a bunch of gap junctions and desmosomes connecting the actual cardiac cells together**



Arterial blood pressure

Overview of Vascular system component

Overview of Physics of Blood pressure

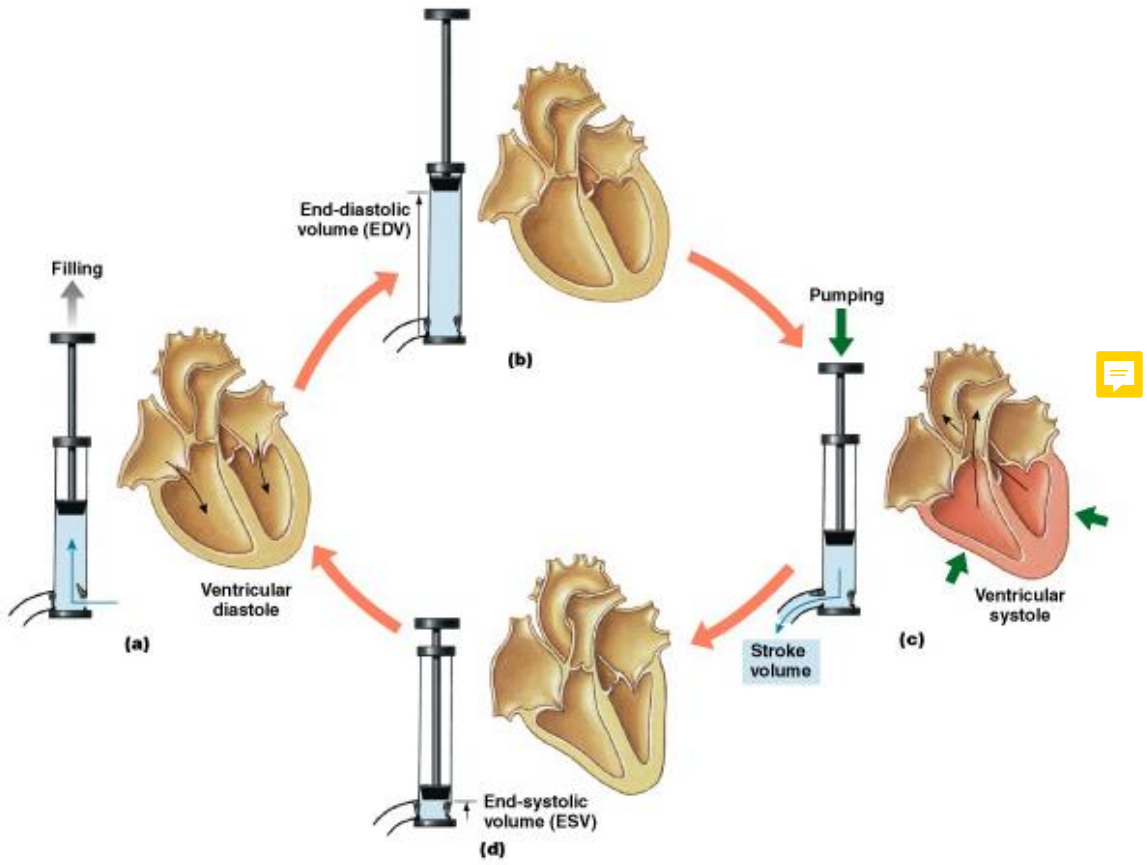
Resistance and capacitance

Overview of Stroke volume and starling law of the heart

Cardiac Cycle

- The two atria contract at the same time, then they relax while the two ventricles simultaneously contract.
- The contraction phase of the ventricle chambers is called systole.
- The relaxation phase is called diastole.

Stroke Volume(SV)



Frank – Starling Principle

- End diastolic volume: volume: The amount of blood that remains in the ventricle just before ventricular early systole is the EDV
- End systolic volume: The amount of blood that remains in the ventricle at the end of ventricular systole is the ESV

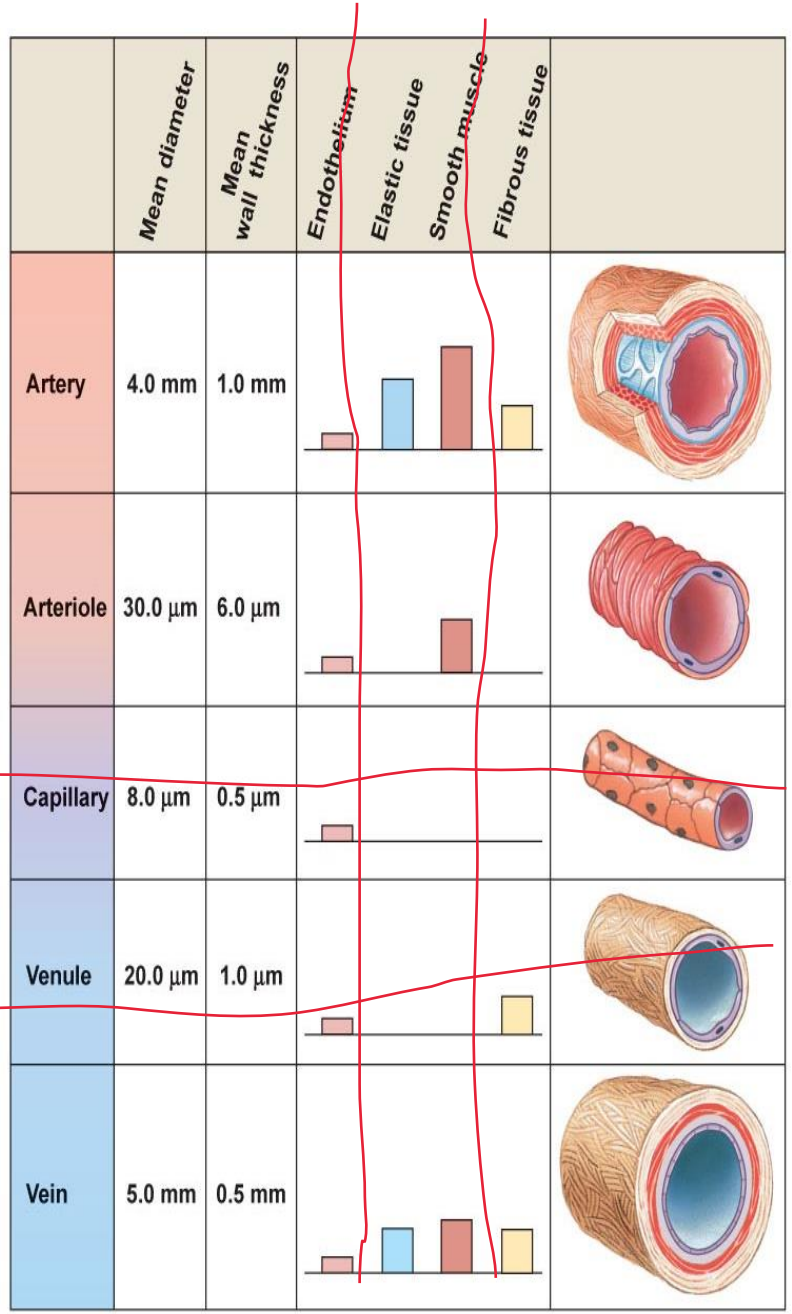
$$SV = EDV - ESV$$

Frank – Starling Principle

- The Frank–Starling law of the heart (also known as Starling's law and the Frank–Starling mechanism) represents the relationship between stroke volume and end diastolic pressure
- This principle illustrates the relationship between cardiac output and left ventricular end diastolic volume
- The law states that the stroke volume of the heart increases in response to an increase in the volume of blood in the ventricles, before contraction (the end diastolic volume), when all other factors remain constant.
- As a larger volume of blood flows into the ventricle, the blood stretches the cardiac muscle fibers, leading to an increase in the force of contraction.
- The Frank-Starling mechanism allows the cardiac output to be synchronized with the venous return, arterial blood supply
- The physiological importance of the mechanism lies mainly in maintaining left and right ventricular output equality
- If this mechanism did not exist and the right and left cardiac outputs were not equivalent, blood would accumulate in the pulmonary circulation (were the right ventricle producing more output than the left) or the systemic circulation (were the left ventricle producing more output than the right).

Blood Vascular walls

- All blood vessels are lined with a thin layer of endothelium, a type of epithelium which is supported by a basement membrane
  - called the tunica intima (or tunica interna)
  - only layer of capillary walls
- The walls of most arteries and veins have layers of smooth muscle and/or elastic connective tissue called the tunica media and fibrous connective tissue called the tunica externa, surrounding the endothelium
  - the thickness of the tunica media and externa vary in different vessels depending on their function or the amount of internal (blood) pressure that they encounter
- Most blood vessels contain vascular smooth muscle arranged in circular layers which is partially contracted at all times creating a condition known as muscle tone
- Additional contraction of the smooth muscle results in vasoconstriction which narrows the diameter of the vessel lumen
- Relaxation of the smooth muscle results in vasodilation which widens the diameter of the vessel lumen
- Neurotransmitters, hormones and paracrine signals influence vascular smooth muscle tone which in turn will affect blood pressure and blood flow throughout the cardiovascular system



Blood pressure

❖Blood pressure =cardiac output X total peripheral resistance

- $\boldsymbol{BP = CO\ X\ TPR}$

First, we want to decide what CO and TPR is , then we get to the right meaning of BP

❖Cardiac output (Flow)= Heart rate X Stroke volume

$\boldsymbol{CO\ (F) = HR\ X\ SV}$

ml/min= Beat/min X ml/ Beat

Cardia out put

- **HR**
- PSNS -
- SNS +
- Hormones (EPI, NE) +
- IONS: Ca++, Na+ , K+ dependents on their level increase or decrease

SV

+ Preload ; Increase the blood volume returns increase diastolic volume

+ Contractility ; SNS (EPI,NE+), Hormones (glucagon,T3 and T4), IONS like Ca++

- Afterload; Hypertension, Atherosclerotic plaques , TPR

Adrenergic Receptors

- Located throughout the body
- Are receptors for the sympathetic neurotransmitters
- Alpha-adrenergic receptors: respond to NE
- Beta-adrenergic receptors: respond to EPI

What do the receptors do?

Activation of **α receptors** leads to smooth muscle contraction

Activation of **β2 receptors** leads to smooth muscle relaxation

Activation of **β1 receptors** leads to smooth muscle contraction (especially in heart)

Clinical Utility of drugs which affect the adrenergic nervous system:

a. **Agonists** of the **β_2 receptors** are used in the treatment of asthma (relaxation of the smooth muscles of the bronchi)

b. **Antagonists** of the **β_1 receptors** are used in the treatment of hypertension and angina (slow heart and reduce force of contraction)

c. **Antagonists** of the **α_1 receptors** are known to cause lowering of the blood pressure (relaxation of smooth muscle and dilation of the blood vessels)

Cardiac output and perfusion blood pressure

DR. Arwa Rawashdeh

Cardiac output

CONTINUED CARDIA OUTPUT

- Anther formula relate to CO

1 ml= 1 Cm3

Flow = Cm3/min

- Anther formula relate to flow

Velocity (Cm2/min)= Flow (cm3/min)

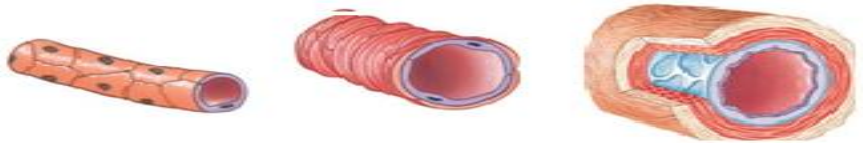
Cross sectional area (Cm2)

V= F/A

- How to relate this to cardiac output

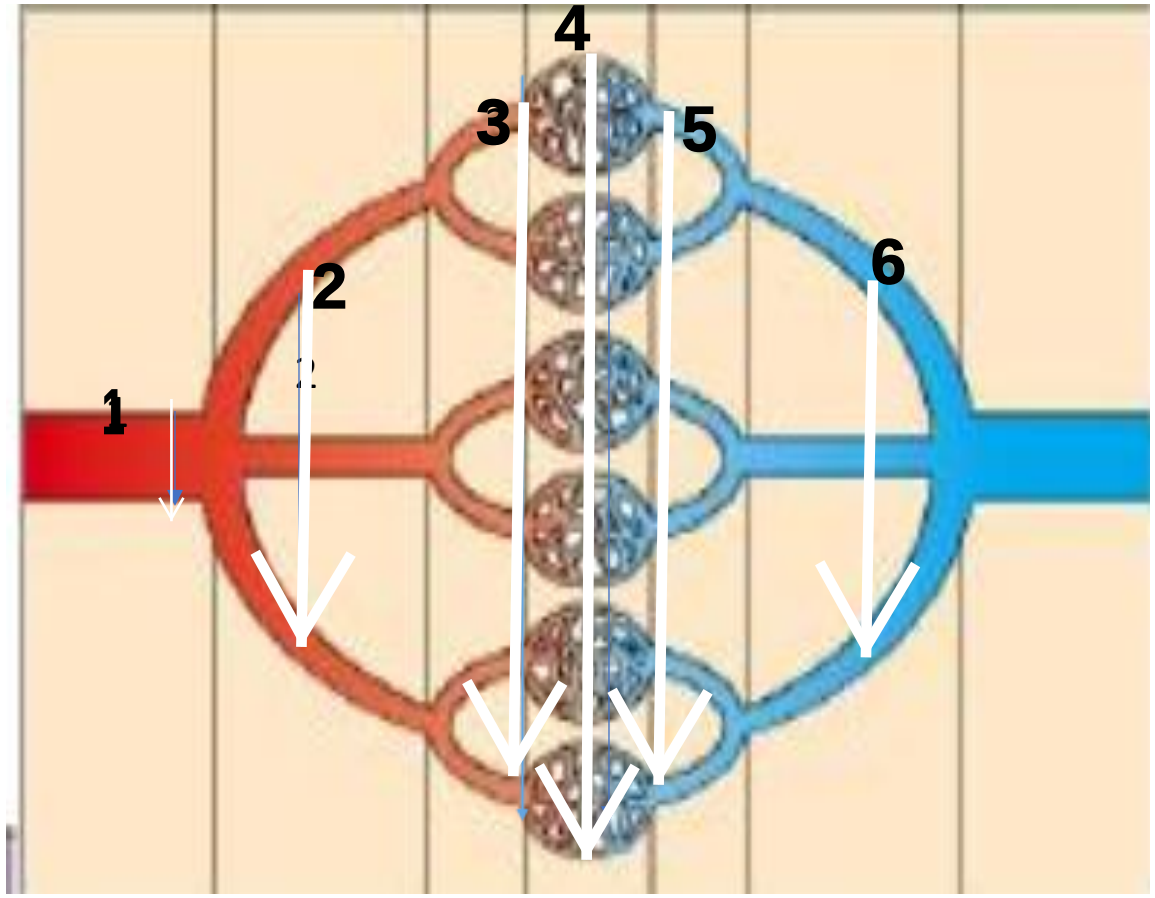
- Increase Flow (CO) Increase V
- Cross sectional area; measured in units of bier square because the blood vessels are cylinder in shape

A (πr^2); Increase A Decrease V



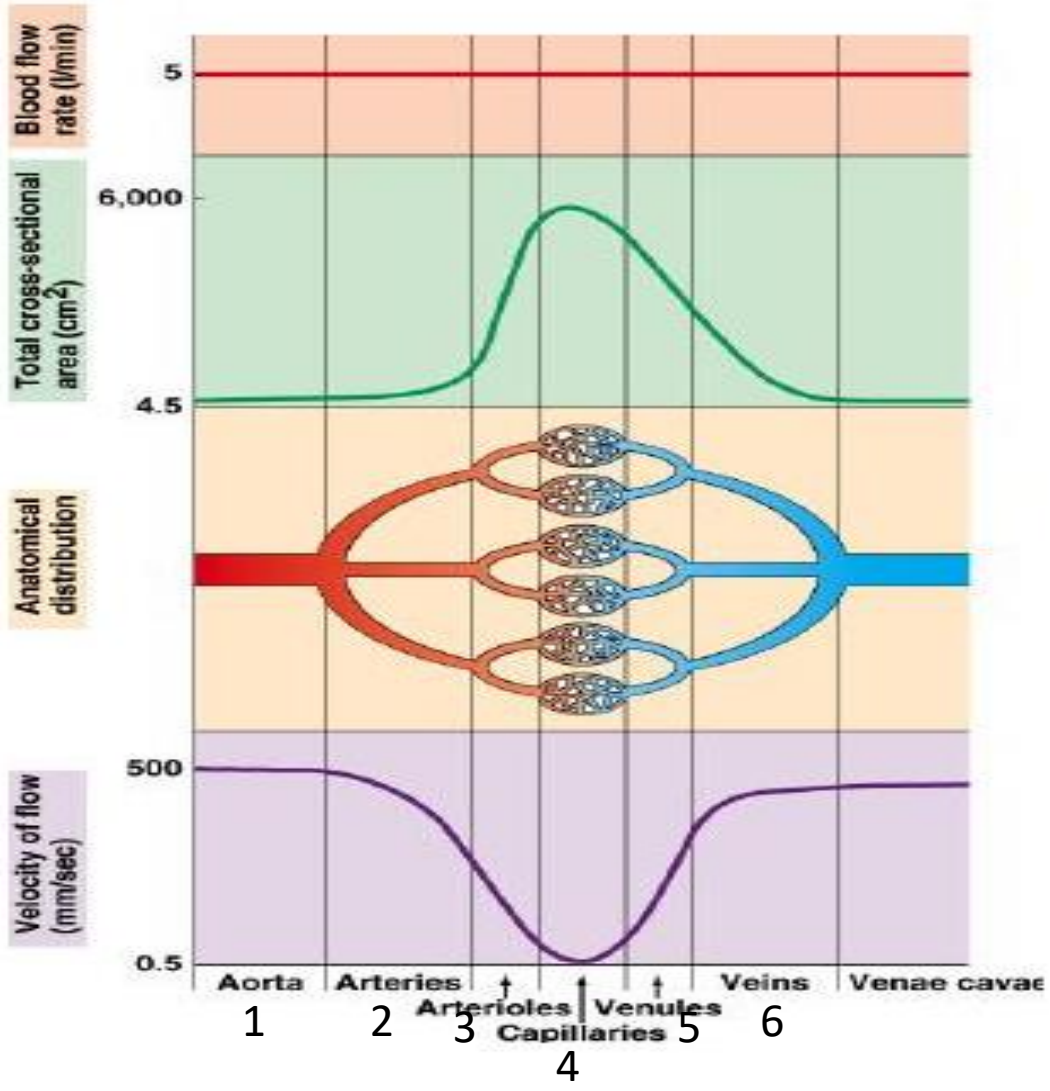
Cross –sectional area and velocity

- *This big one here is aorta (1) then the aorta splits it gives off arteries (2) then arterial branches (3) and then capillary branches ten to hundred per capillary bed (4) and after drain from the capillary bed then they go to what called venules (5) and from the venules they come eventually into the veins (6) and again to vena cava system*
- *compare the cross sectional are the capillary and cross-sectional area aorta and velocity*
- *As you increase the cross-sectional area the velocity decrease*
- *The velocity is the slowest in the capillaries and faster in the aorta*



Velocity and cross-sectional area

- The cross-sectional area for the aorta is going to be very very small as you start to move toward arterioles to capillaries it is going to start rising
- As you get towards the venules it starts decreasing again and comes back down
- Once you hit the arterioles that's when the actual specifically the cross-sectional area increases



Resistance

Resistance

- *How to relate TPR to blood pressure*
- $F = \Delta P / R$ Ohm's Law
- $CO = \Delta P / TPR$
- $R = 8nl/\pi r4$ $Poiseuille's\ law$
- $n\ \alpha\ R$
- $n =\ viscosity$

Polycythemia (high Hct)$\alpha\ n$*; a lot of friction between the layers, because whenever blood is flowing it flows in layers when there is a lot of friction rubbing up against between those layers because increase in viscosity and slow the flow down*

Anemia $\frac{1}{\alpha} n$

$L\ \alpha\ R$

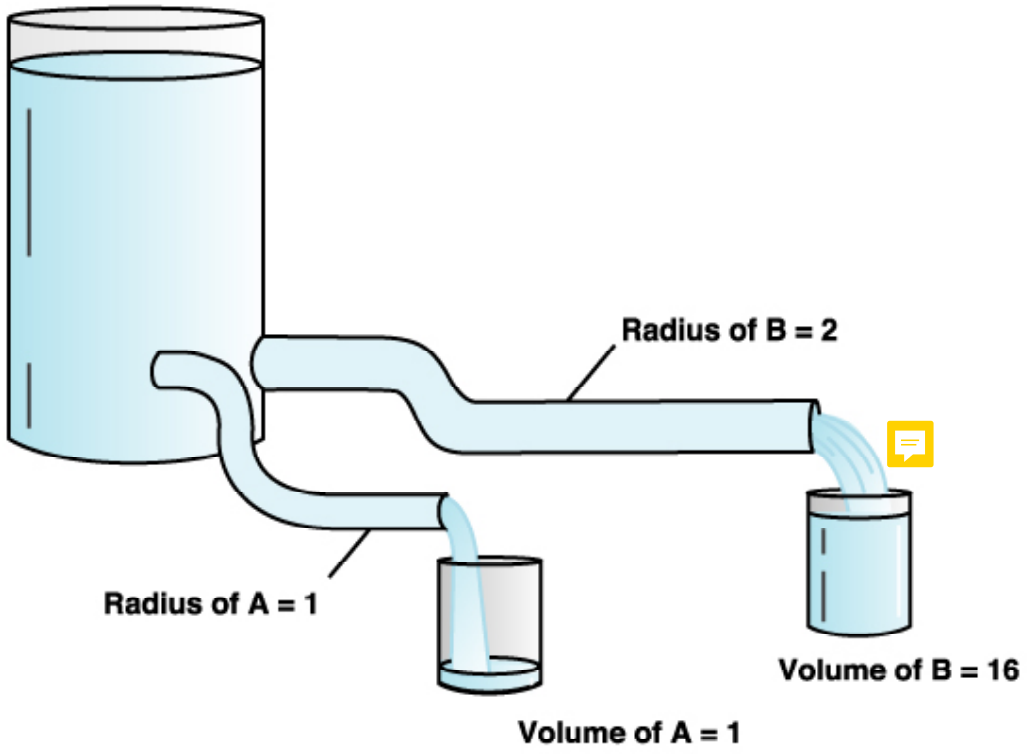
Increase in Weight and height increases in L

$r = 1/\alpha\ R$ the most important factor that affecting the R because it is raised to power 4

Vasodilation increase in r

Vasoconstriction decrease in r

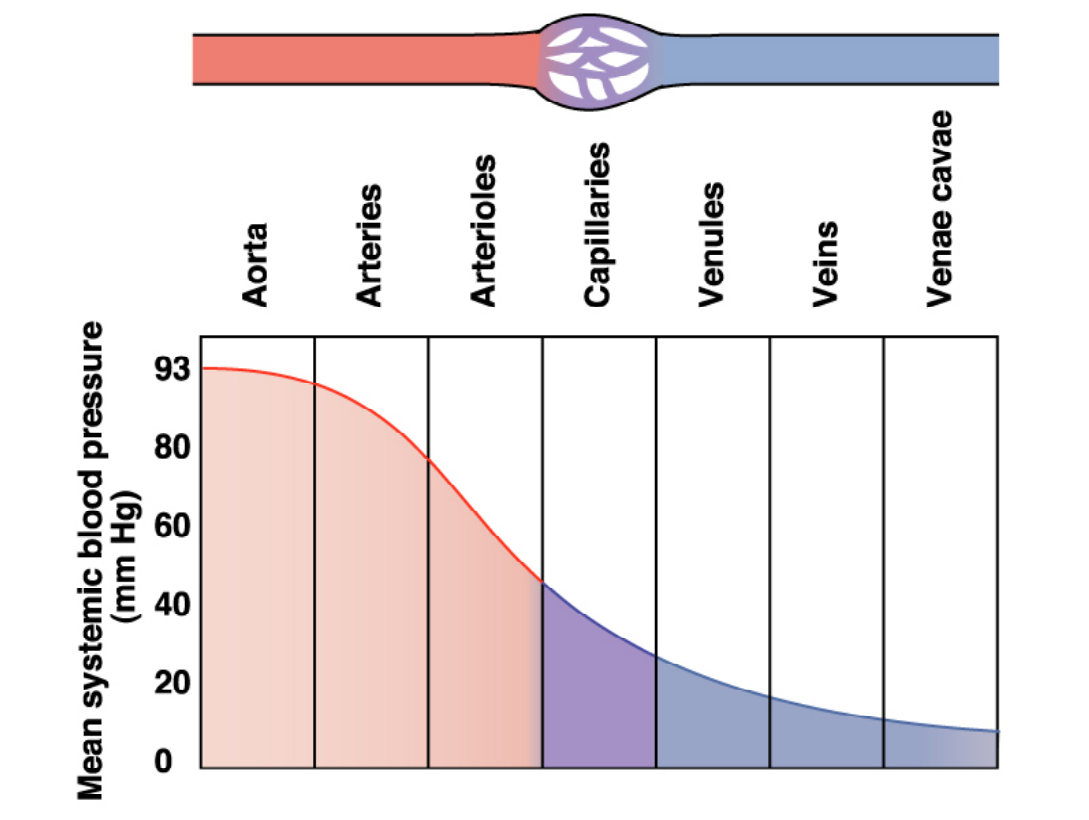
Effect of radius on resistance and blood flow

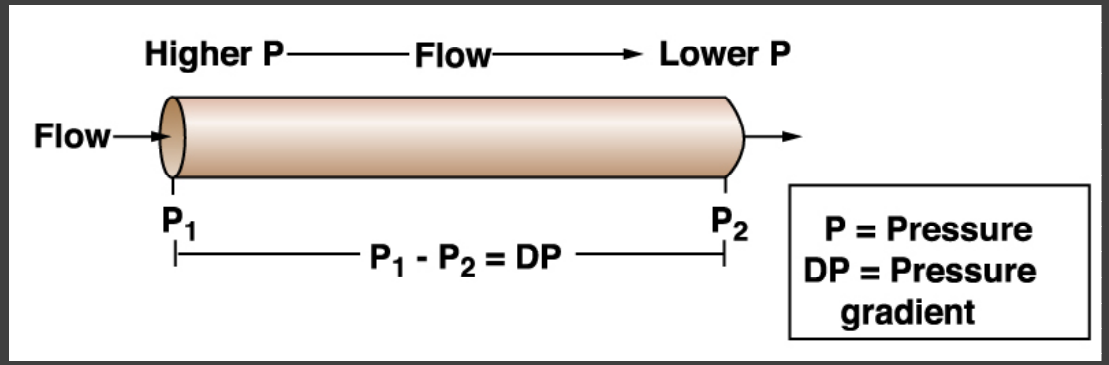


Resistance ~ $\frac{1}{\text{radius}^4}$	
Tube A	Tube B
R ~ $\frac{1}{1^4}$	R ~ $\frac{1}{2^4}$
R ~ 1	R ~ $\frac{1}{16}$

Flow ~ $\frac{1}{\text{resistance}}$	
Tube A	Tube B
Flow ~ $\frac{1}{1}$	Flow ~ $\frac{1}{\frac{1}{16}}$
Flow ~ 1	Flow ~ 16

Perfusion blood pressure





- Blood flows down a pressure gradient
- The absolute value of the pressure is not important to flow, but the difference in pressure (DP or gradient) is important to determining flow.

Perfusion pressure

- **Perfusion pressure (Δp) = Mean arterial pressure (MAP) – the central venous pressure(CVP)**
- *The central venous pressure (CVP) determines the right atrial pressure (RAP)*
- *The volume of blood pumped toward heart is your central venous pressure and the venous pressure affect your right atrium pressure and it is about 3-8mmHg; it is small we don't even consider it often*
- *So what we say that the*
- *(**Δp**) = Mean arterial pressure (MAP) what does that mean???*

Systolic pressure

- *When ever the heart contracting it pumping the blood outside the heart ; the force at which we are trying to push the blood out of the heart and into the actual major arteries is the systolic pressure (left ventricles to aorta) and on average it is a bout 120mmHg*
- *When ever the blood comes into the aorta it stretches the wall of the aorta so the wall of the aorta is going to be stretched now this is not that is stretching the walls is the systolic pressure but what happens is eventually; the actual aorta is very elastic and wants to recoil and squeeze the blood downwards or upwards to the head and the neck*

Diastolic blood pressure

- *Whenever the aorta is coming back to it is natural size the point when is relaxing and going back to its normal size original size ; this is called the diastolic blood pressure and on average it is about 80mmHg*

“Conductance” of blood in a vessel and
Its relation to resistance

Conductance (C_L) is a measure of the blood flow through a vessel for a given pressure difference. .

$$C = \frac{\Delta V}{\Delta P}$$

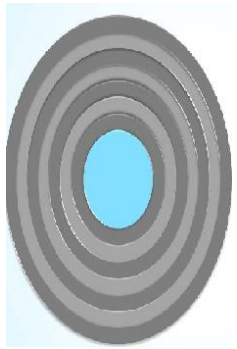
This is generally expressed in terms of milliliters per second per millimeter of mercury pressure, but it can also be expressed in terms of liters per second per millimeter of mercury or in any other units of blood flow and pressure.

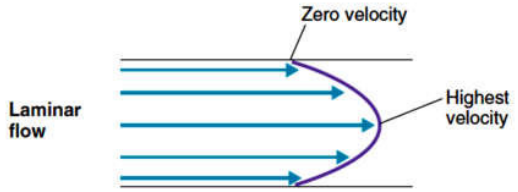
It is evident that conductance is the exact reciprocal of resistance in accord with the following equation:

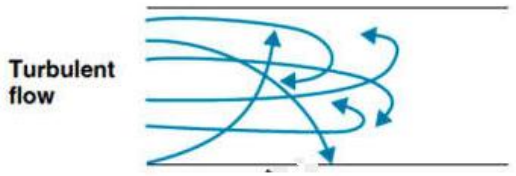
Conductance= 1/Resistance

The vascular compliance is proportional to the vascular distensibility and vascular volume of any given segment of the circulation. The compliance of a systemic vein is 24 times that of its corresponding artery because it is about 8 times as distensible, and it has a volume about 3 times as great.

Blood flow and Laplace's law







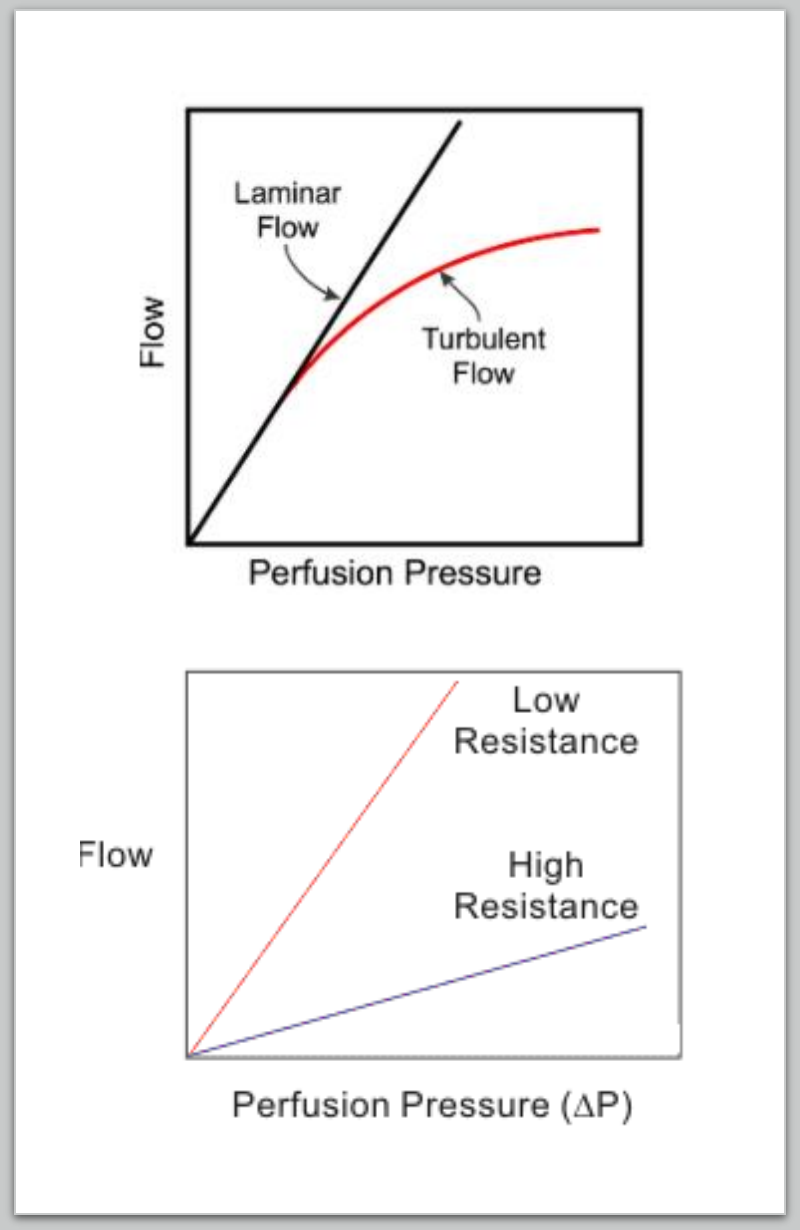
Blood flow

Laminar flow : normal blood flow in the blood vessels (physiological)

- *As you go toward the edges the velocity the blood is going to be slower and the velocity in the middle is highest*
- *So imagine you are looking to blood vessels as a circle, and you are looking at the flow from the back you are going to notice that is flow is very concentric and this type of flow is silent*

Turbulent flow : pathological and physiological one

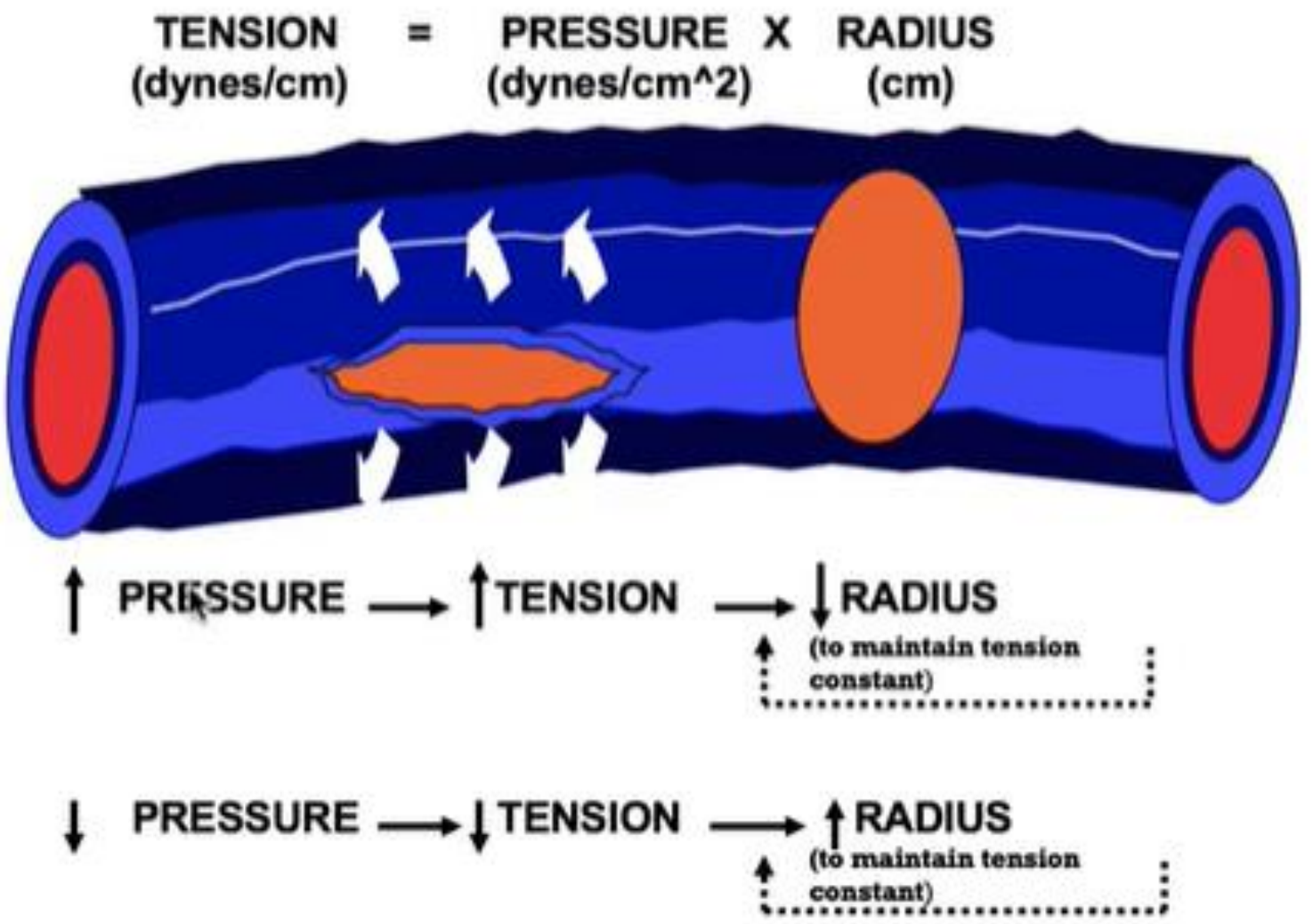
- *Inside our heart you have a valves mitral valve and aortic valve whenever blood is being pumped upward right it can hit mitral valve as it hits mitral valve it can develop turbulent flow*
- *Imagine a blood vessels and plaques inside ; as the normal flow gets to the occlusion it start developing a turbulence and that gives a lot of heat and changes the action of perfusion pressure and produce what called brutes and can be heard at carotid artery so if you take a stethoscope and put it over carotid artery you can hear it as actual sounds that caused by turbulent flow. It also can produce murmurs*



If you look at the graph here ; as you increase the pressure the flow is increasing in laminar or turbulent flow, but you get to the point where the flow veers off and the flow start decreasing as the perfusion pressure start increasing

If there is a turbulent flow it decreases the actual flow the volume of blood that circulating through an area of blood vessel per a minute and increase the perfusion pressure and the resistance is going to be very high

Implication of Laplace's law

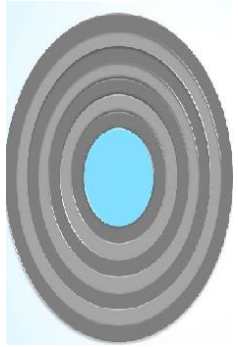


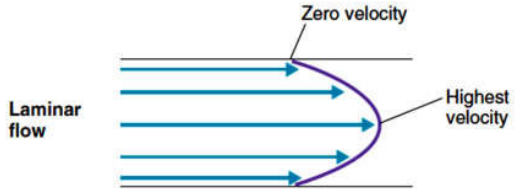
Cardiac cycle and heart sounds

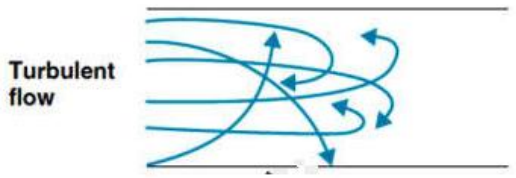
Arwa Rawashdeh

Blood flow and Laplace's law

Blood flow







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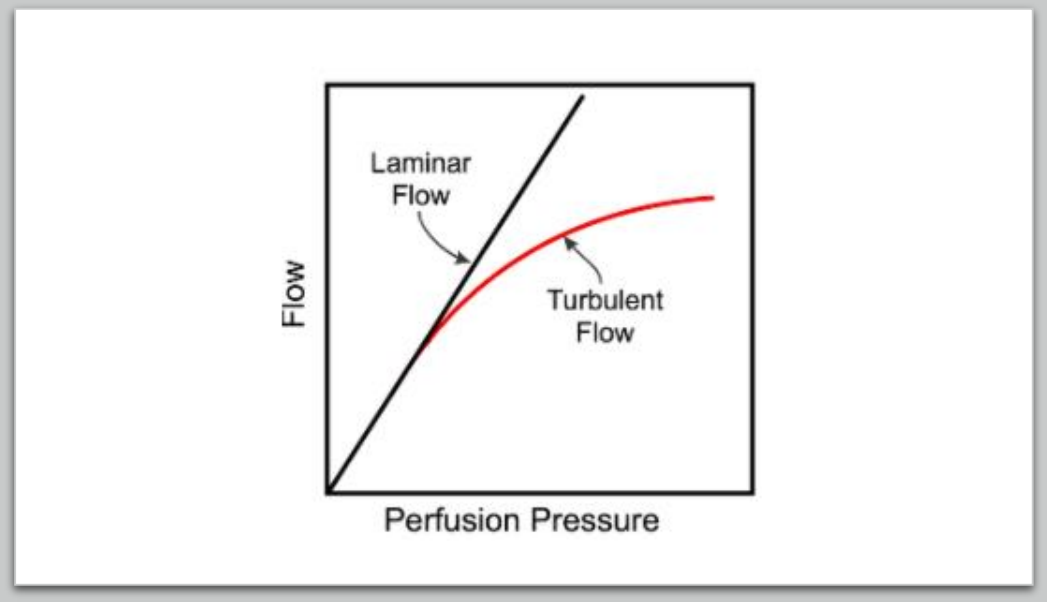

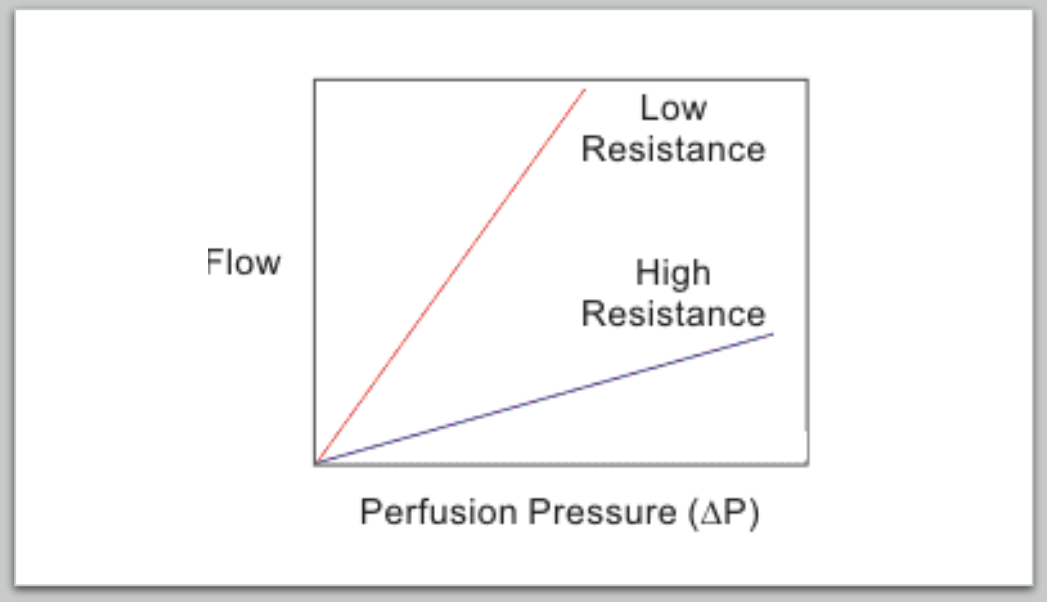

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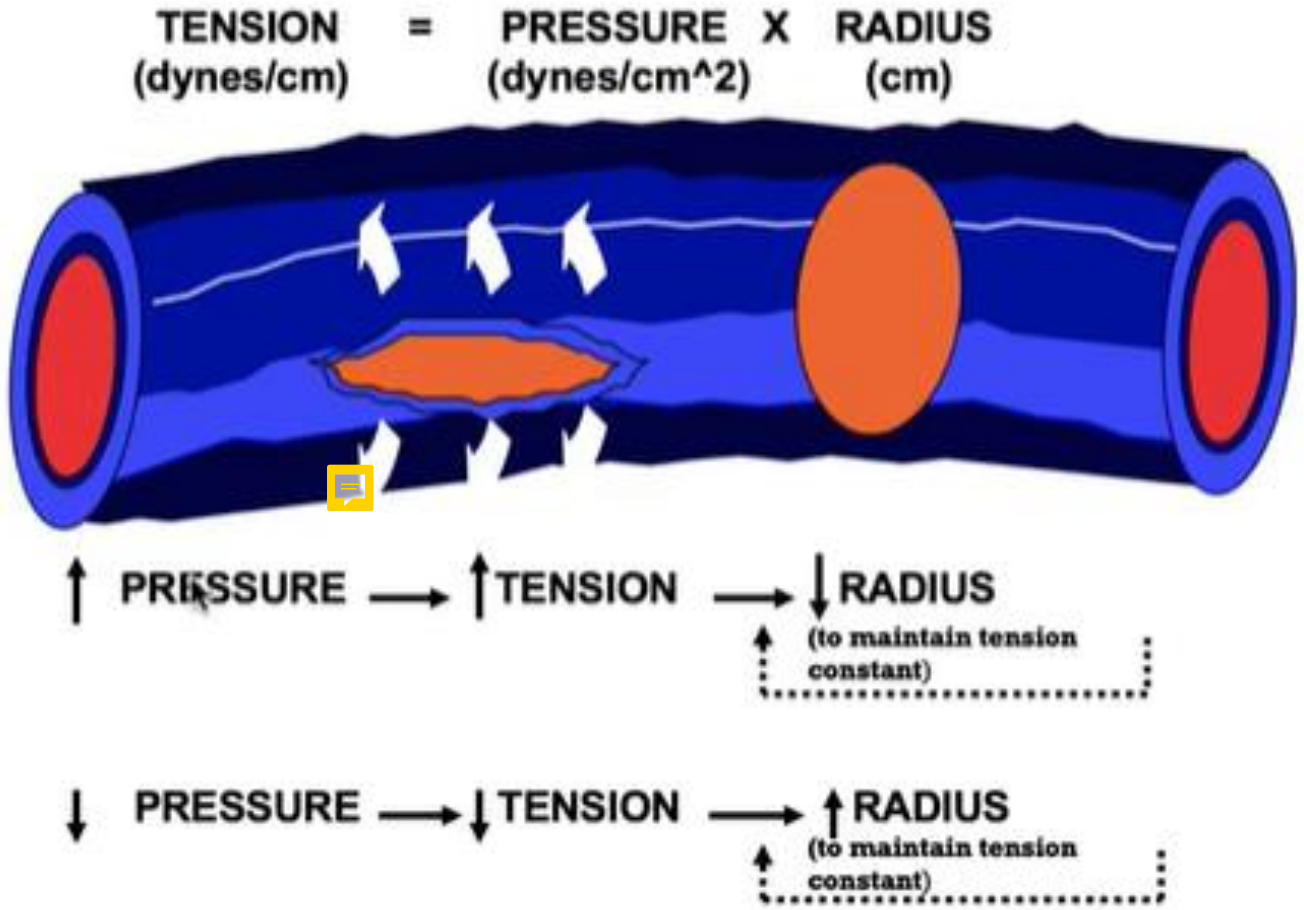
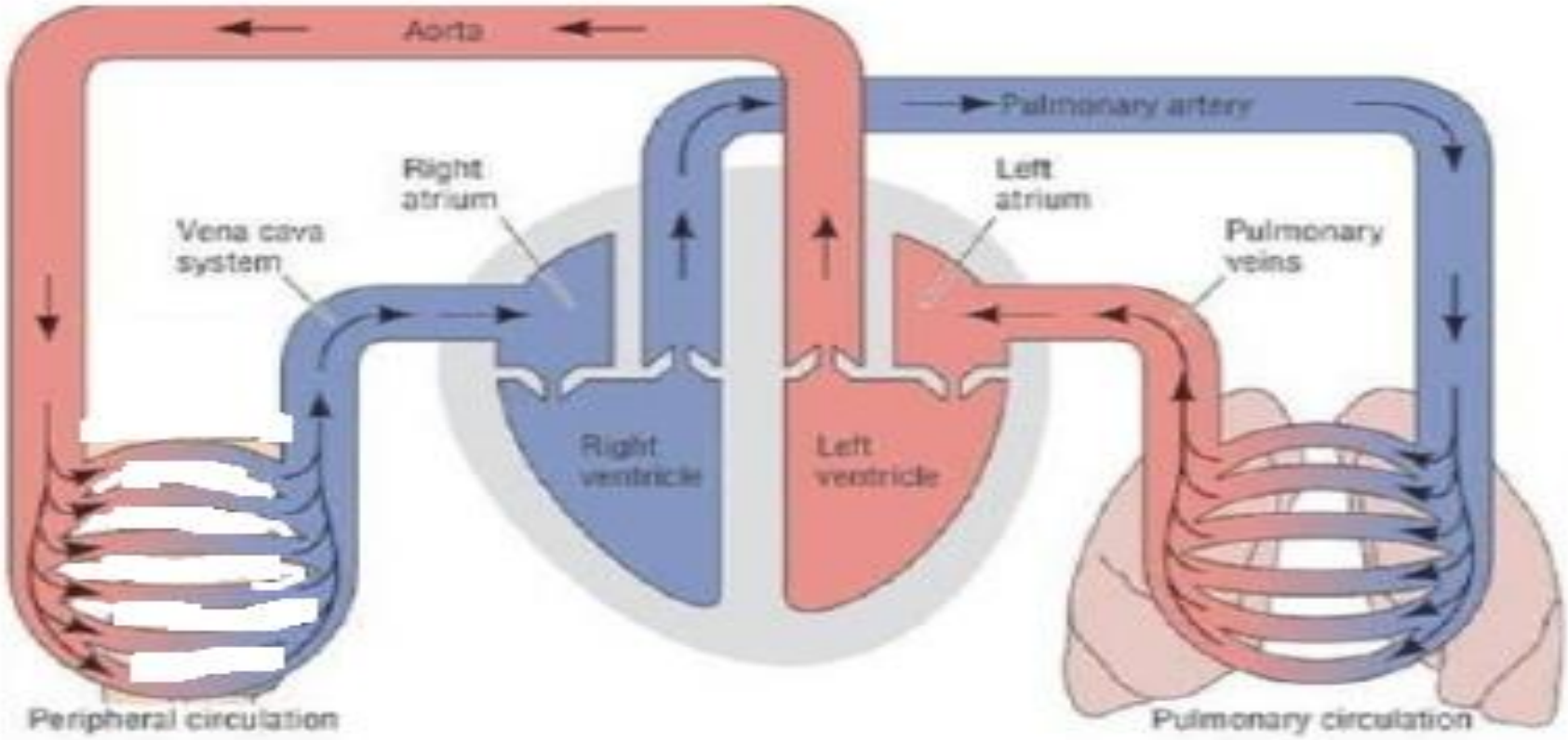


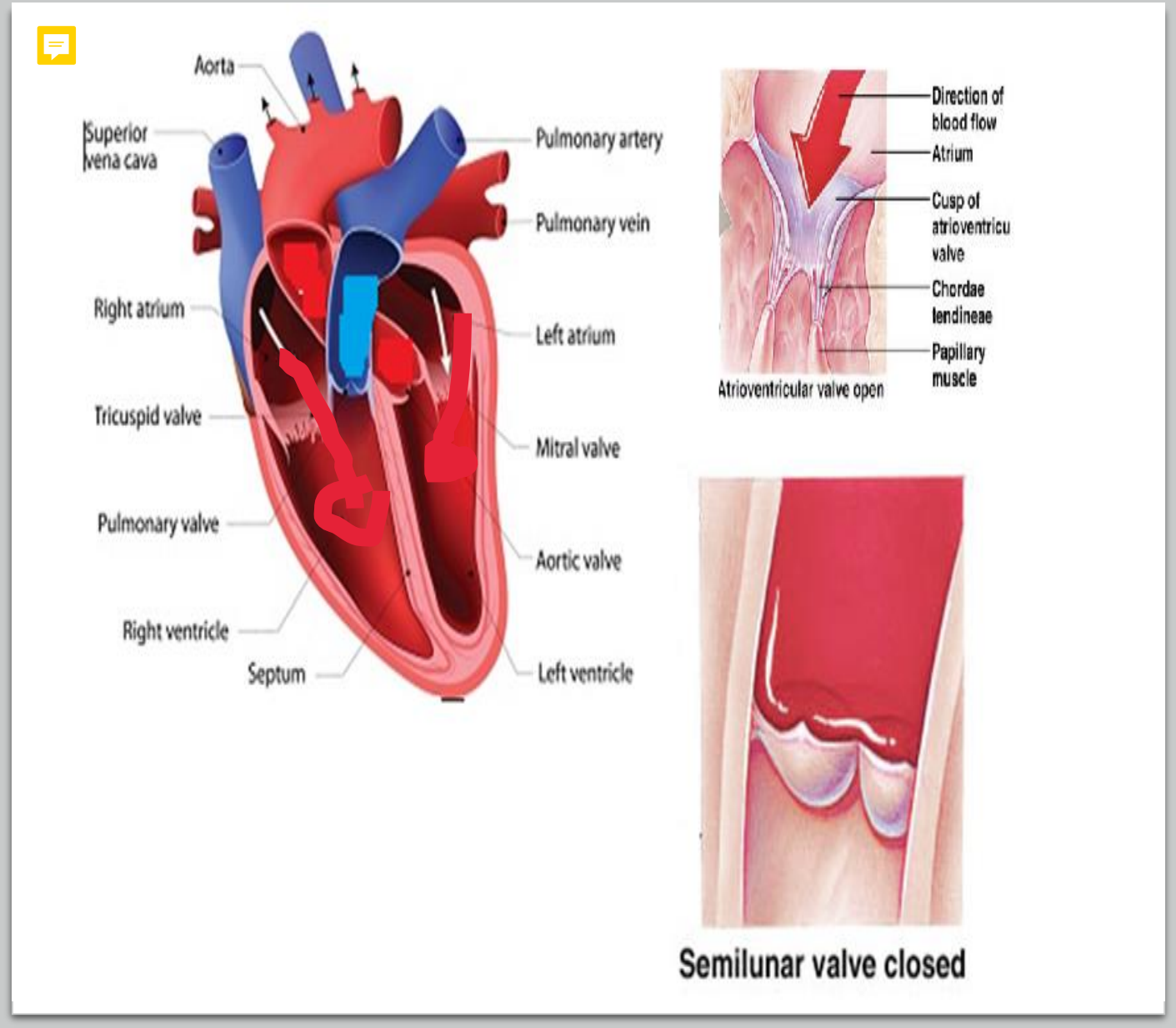
Cardiac cycle

Cardiac Cycle



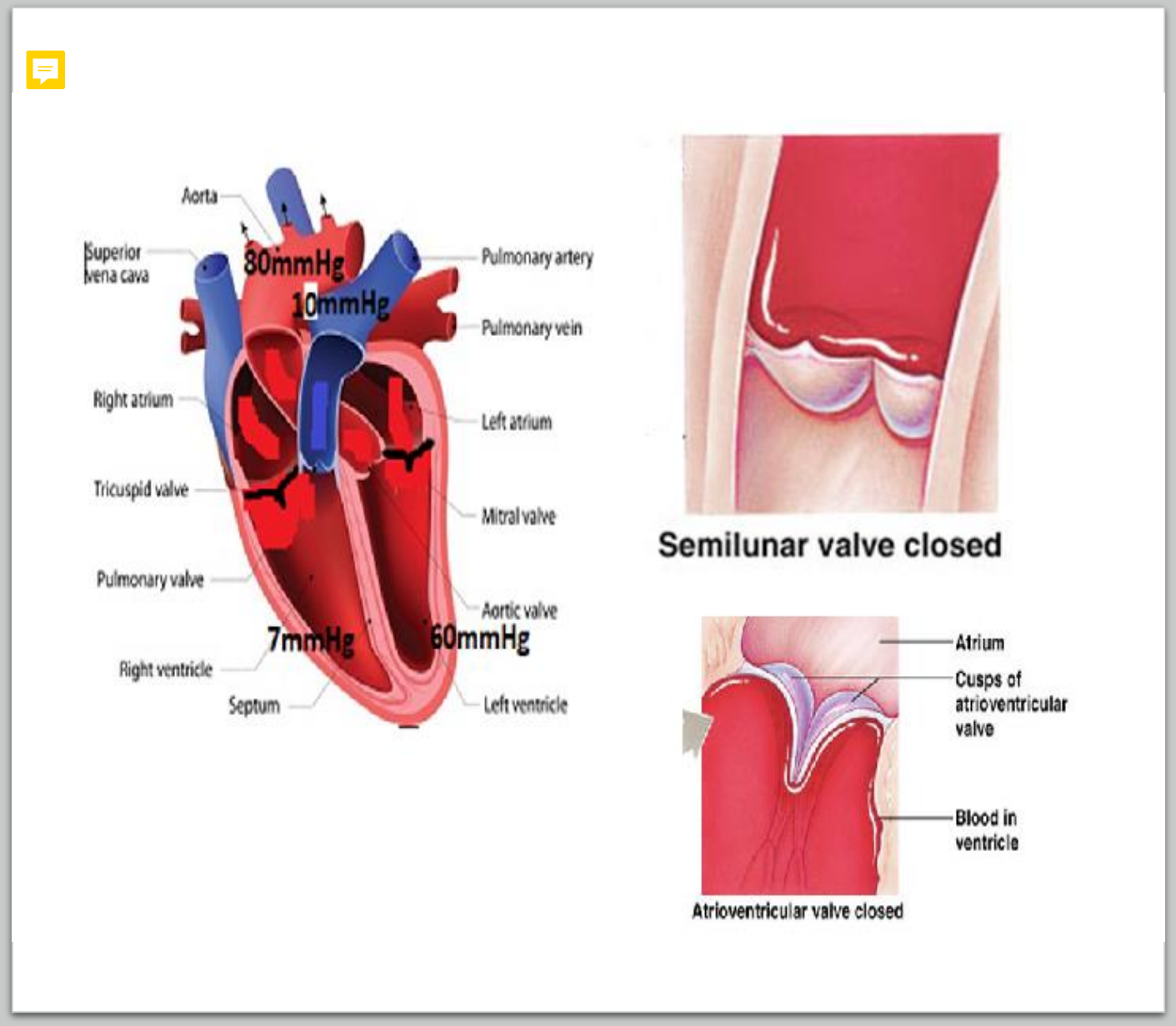
Mid to Late ventricular diastole

- Atrial pressure > ventricular pressure
- Arterial pressure > ventricular pressure
- AV valves Open
- SLV valves closed



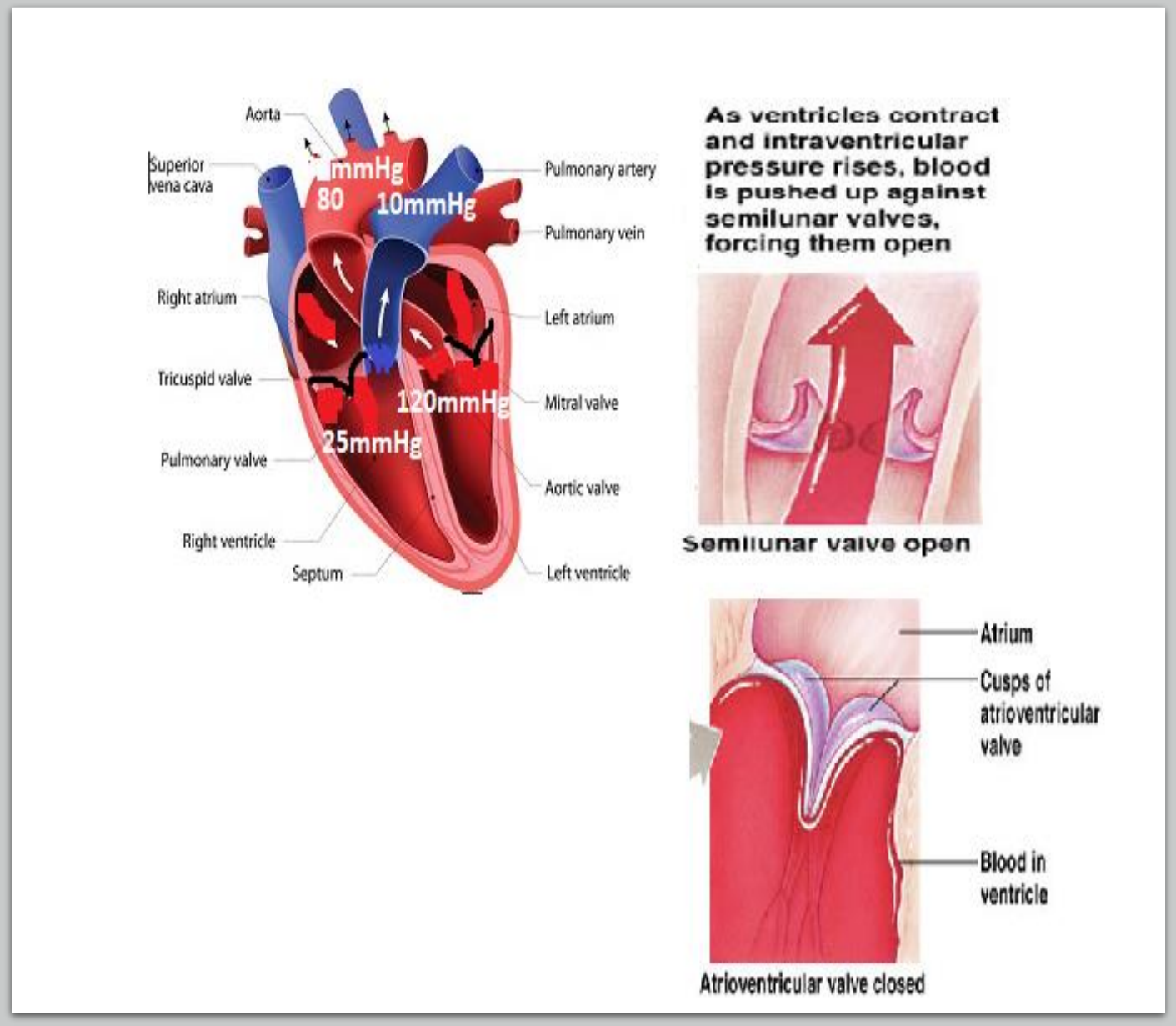
Isovolumetric contraction

- Atrial pressure < ventricular pressure
- Arterial pressure > ventricular pressure
- AV valves closed Lub sound “S1”
- SLV valves closed



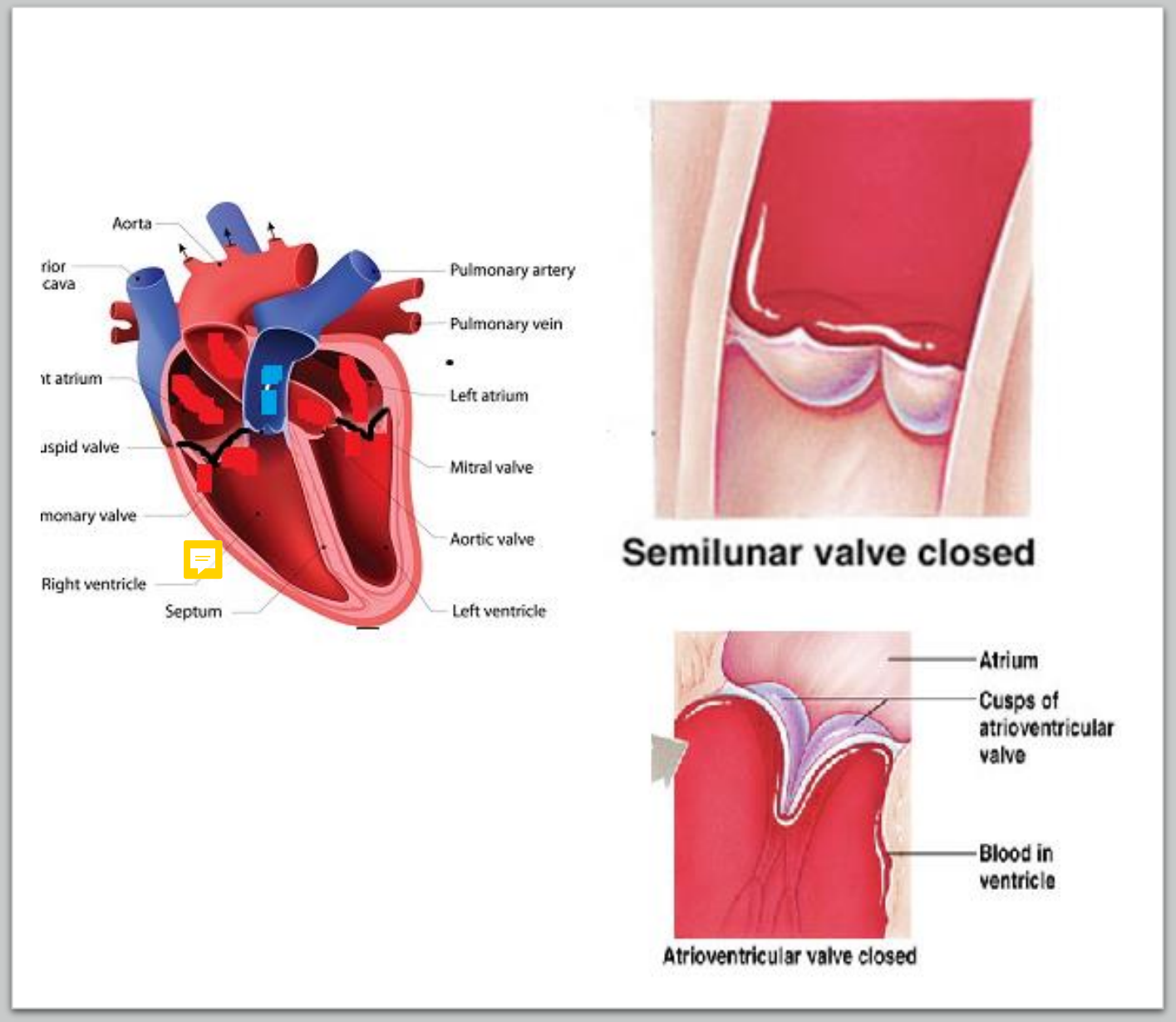
Mid to late ventricular systole or ventricular ejection

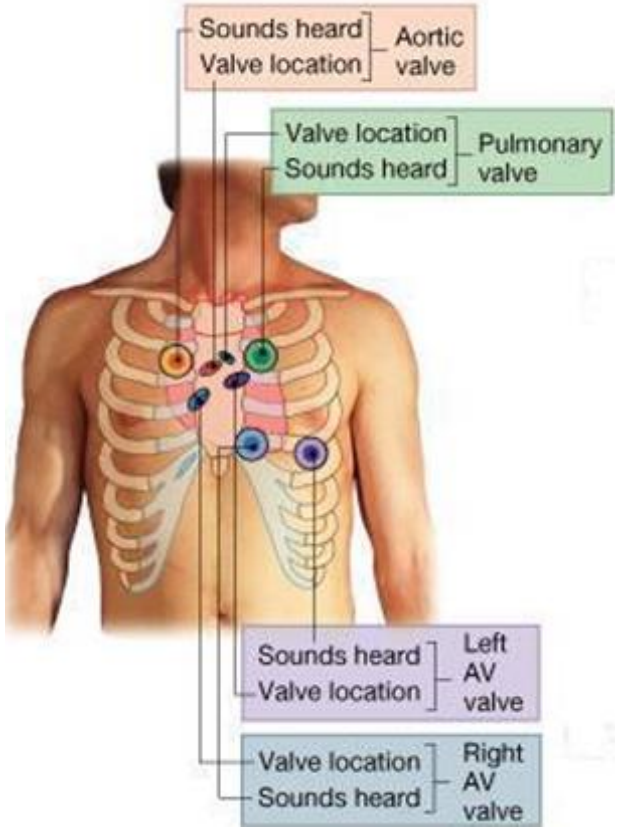
- Atrial pressure < ventricular pressure
- Arterial pressure < ventricular pressure
- AV valves closed
- SLV valves open

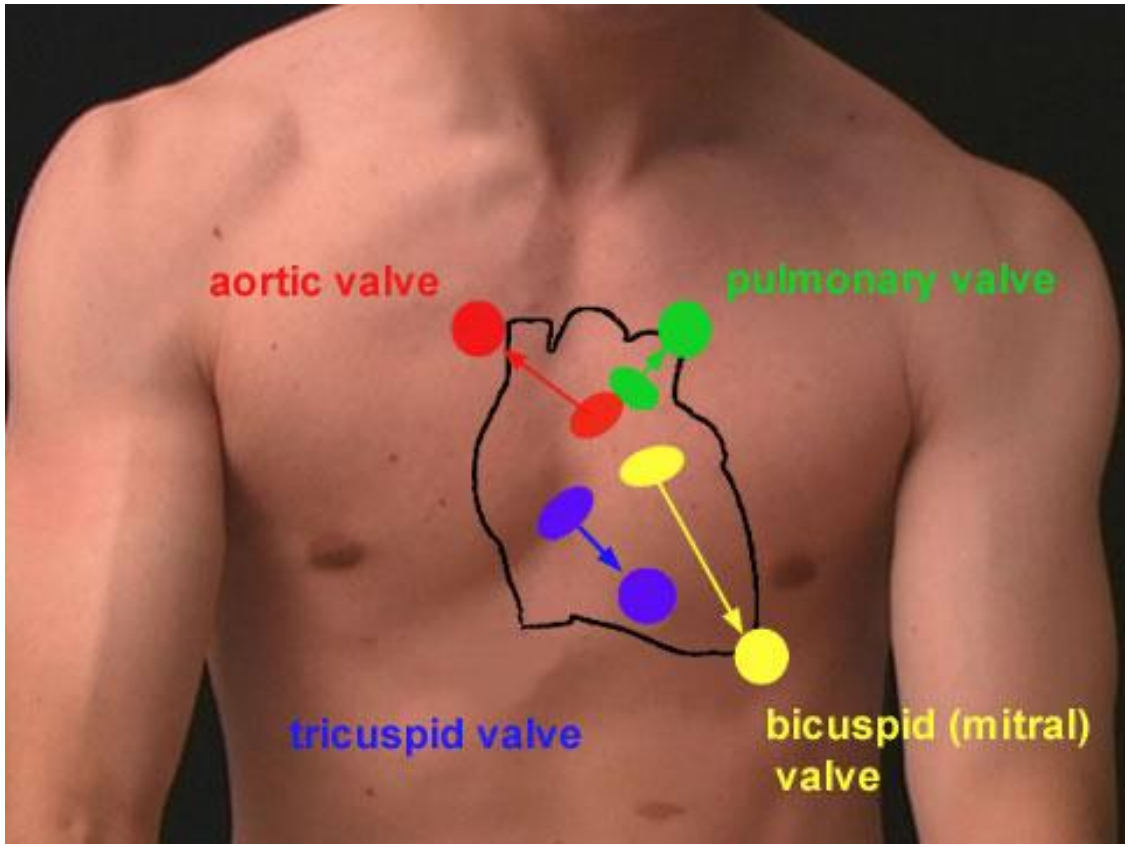


Isovolumetric relaxation

- Atrial pressure < ventricular pressure
- Arterial pressure > ventricular pressure
- AV valves closed
- SLV valves closed “Dub”sound







Positioning of stethoscope

FIRST HEART SOUND (S1)

- First component due to turbulent rushing of blood towards A-V valves
- 2nd component occurs due to the closure of the A-V valves
- The mitral component heard at the apex beat area [left 5th intercostal space at midclavicular line]
- The tricuspid component is best heard in the 4th intercostal space at the left sternal border

SECOND HEART SOUND (S2)

- This sound is produced by the vibration associated with the closure of the semilunar valves (aortic and pulmonary) at the end of ventricular systole.

- This sound is sharp and loud and described as “DUB.”
- Two subcomponents
- Pulmonary component heard at the level of 2nd left intercostal space.
- Aortic component is heard at the level of the 2nd right interscostal space near the right border of the sternum.

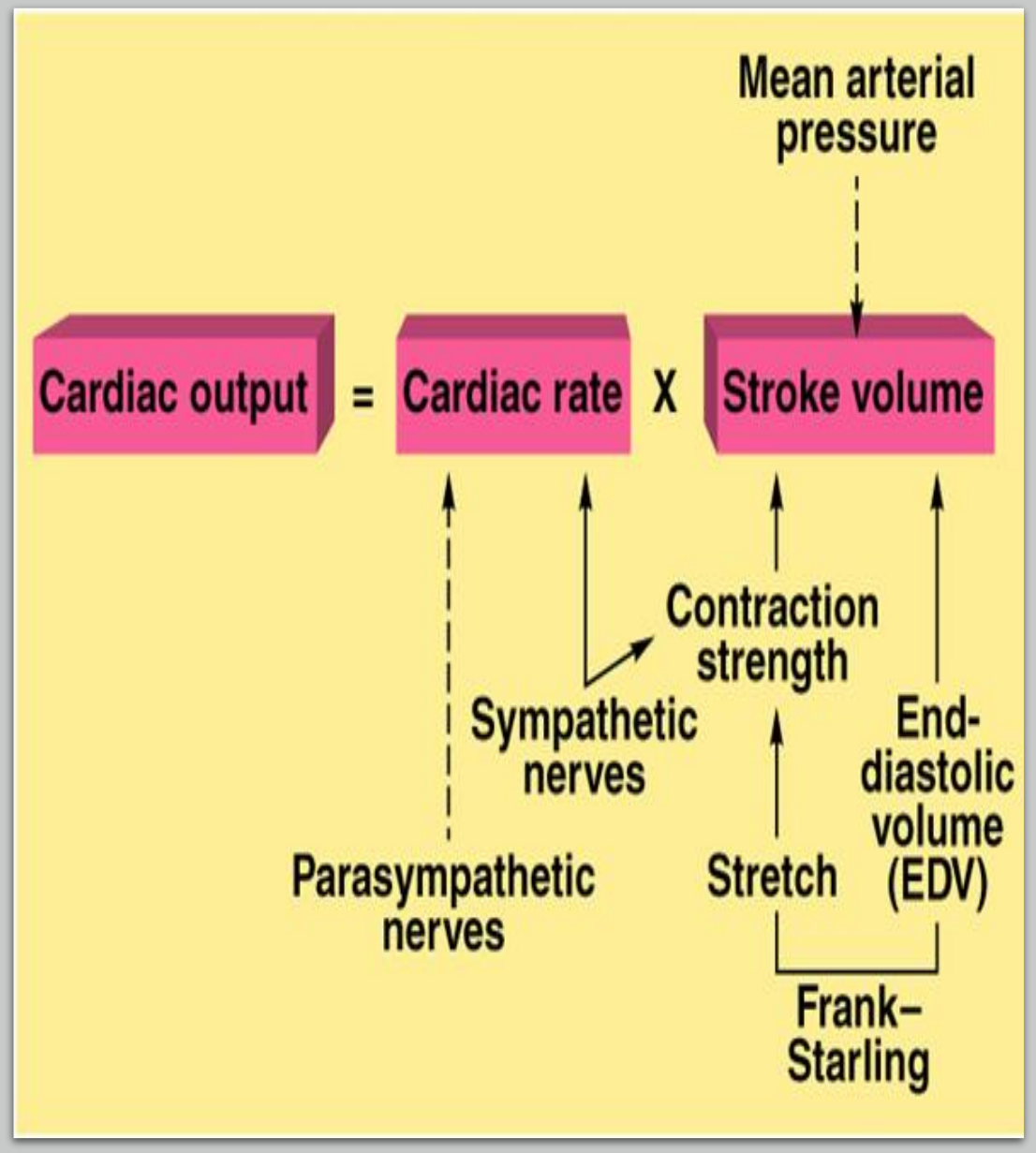
Regulation of cardiac output

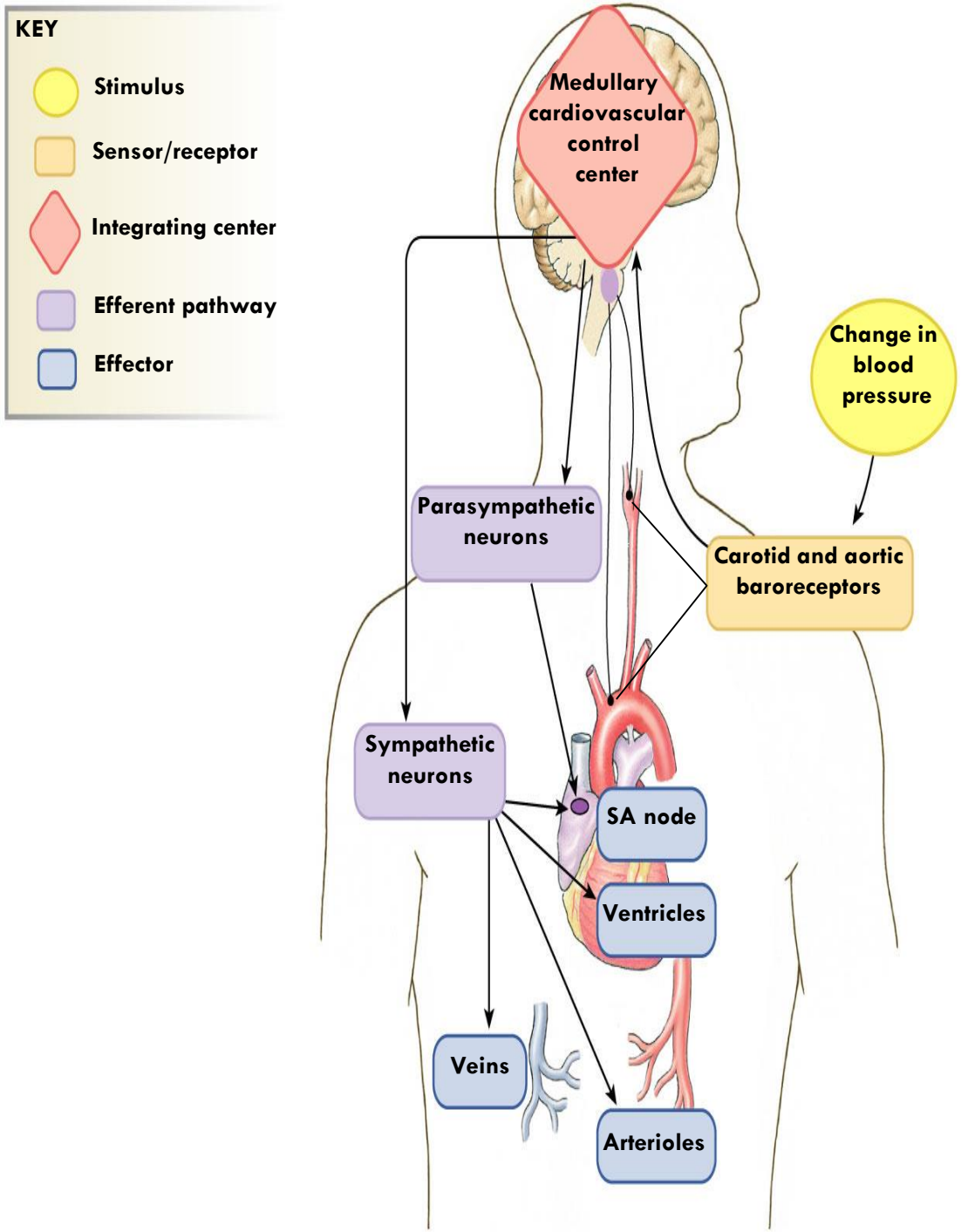
Dr. Arwa Rawashdeh

Regulation of cardiac output (implication of frank- starling law)

- Nervous system modifies the cardiac rate

- Pacemakers trigger the action potential
- Positive inotropes (increase the contractility)
- Negative inotropes (decrease the cardiac contractility)



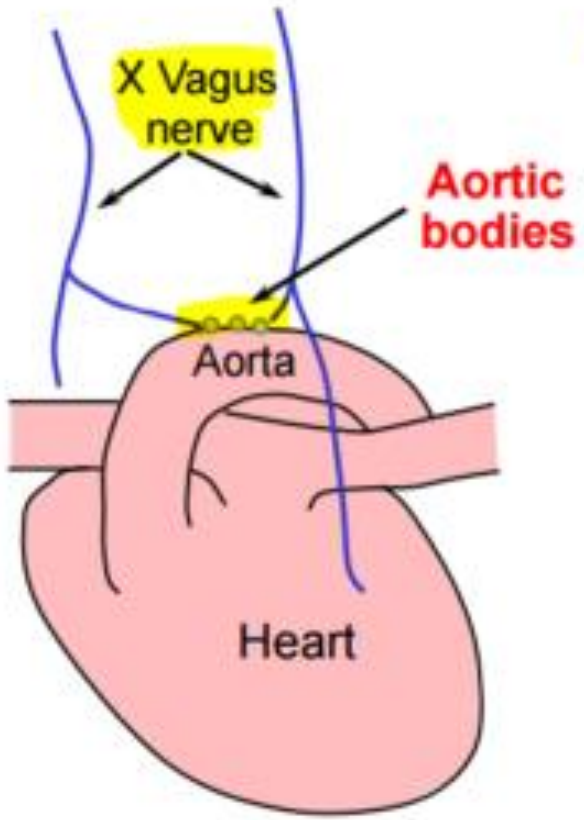


Peripheral chemoreceptors (**carotid and aortic bodies**) and **central chemoreceptors** (medullary neurons) primarily function to regulate respiratory activity.

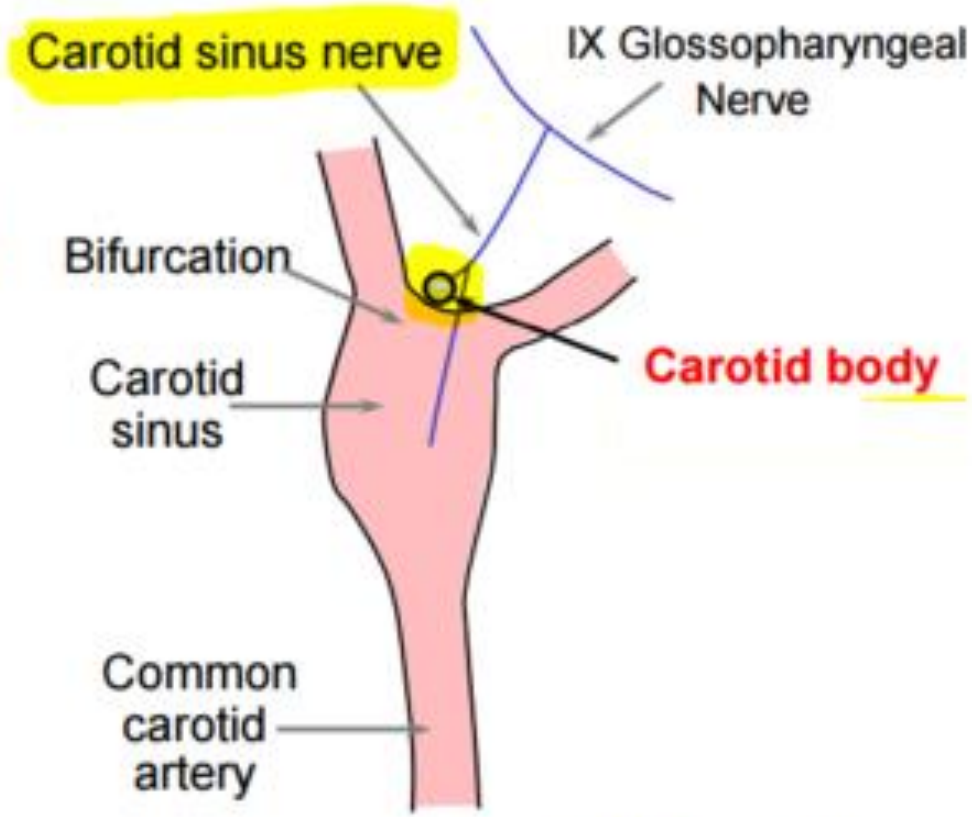
This is an important mechanism for maintaining arterial blood PO_2, PCO_2, and pH within appropriate physiological ranges. For example, a fall in arterial PO_2 (hypoxemia) or an increase in arterial PCO_2 (hypercapnia) leads to an increase in the rate and depth of respiration through activation of the chemoreceptor reflex.

Chemoreceptor activity, however, also affects cardiovascular function either directly (by interacting with medullary vasomotor centers) or indirectly (via altered pulmonary stretch receptor activity). Impaired gas exchange in the lungs, which can be caused by hypoventilation, decreases arterial PO_2 and pH, and increases arterial PCO_2. These changes stimulate chemoreceptor activity leading to enhanced sympathetic outflow to the heart and vasculature via activation of the rostral ventrolateral medulla.

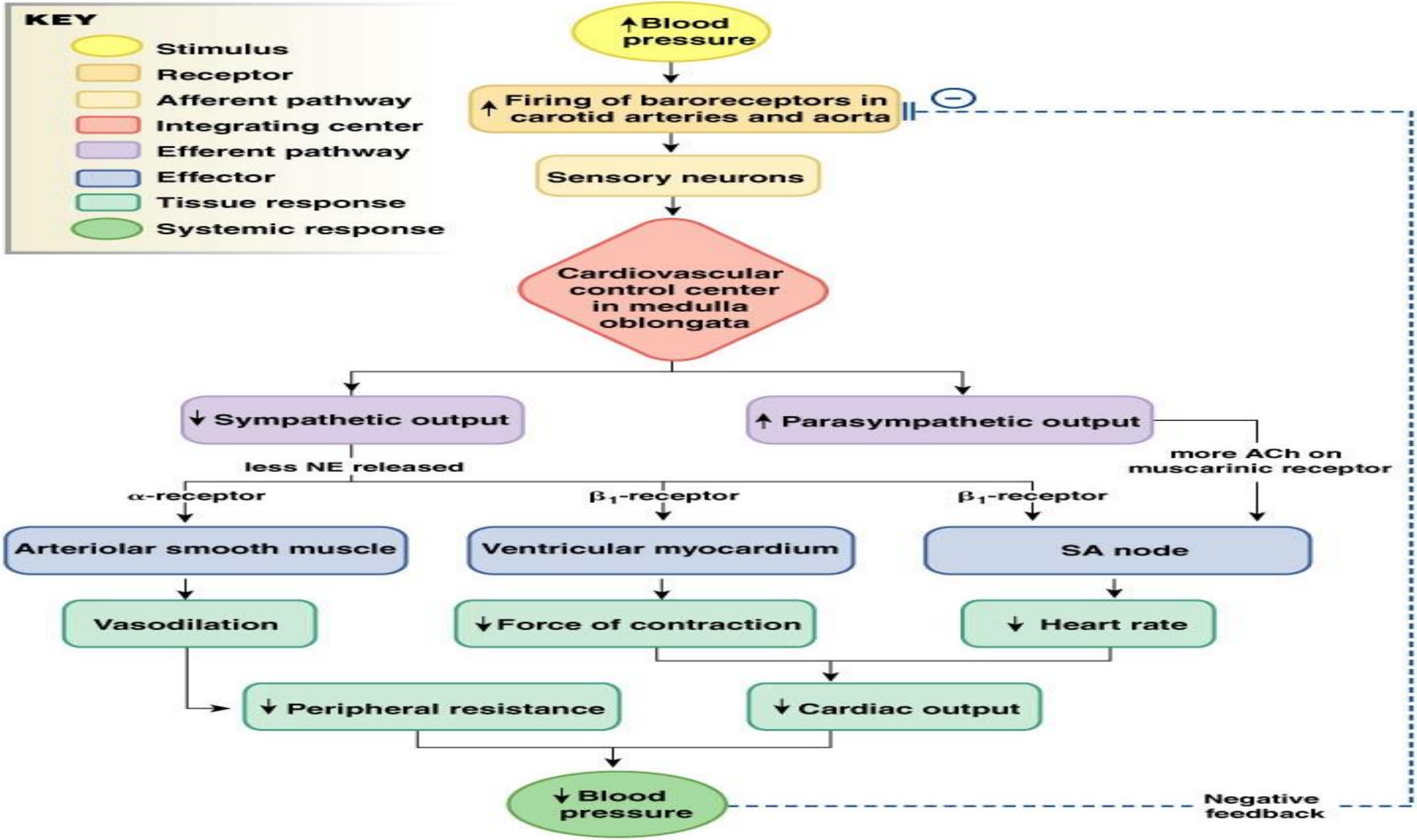
Cerebral ischemia activates central chemoreceptors in a manner that produces simultaneous activation of sympathetic and vagal nerves to the cardiovascular system.

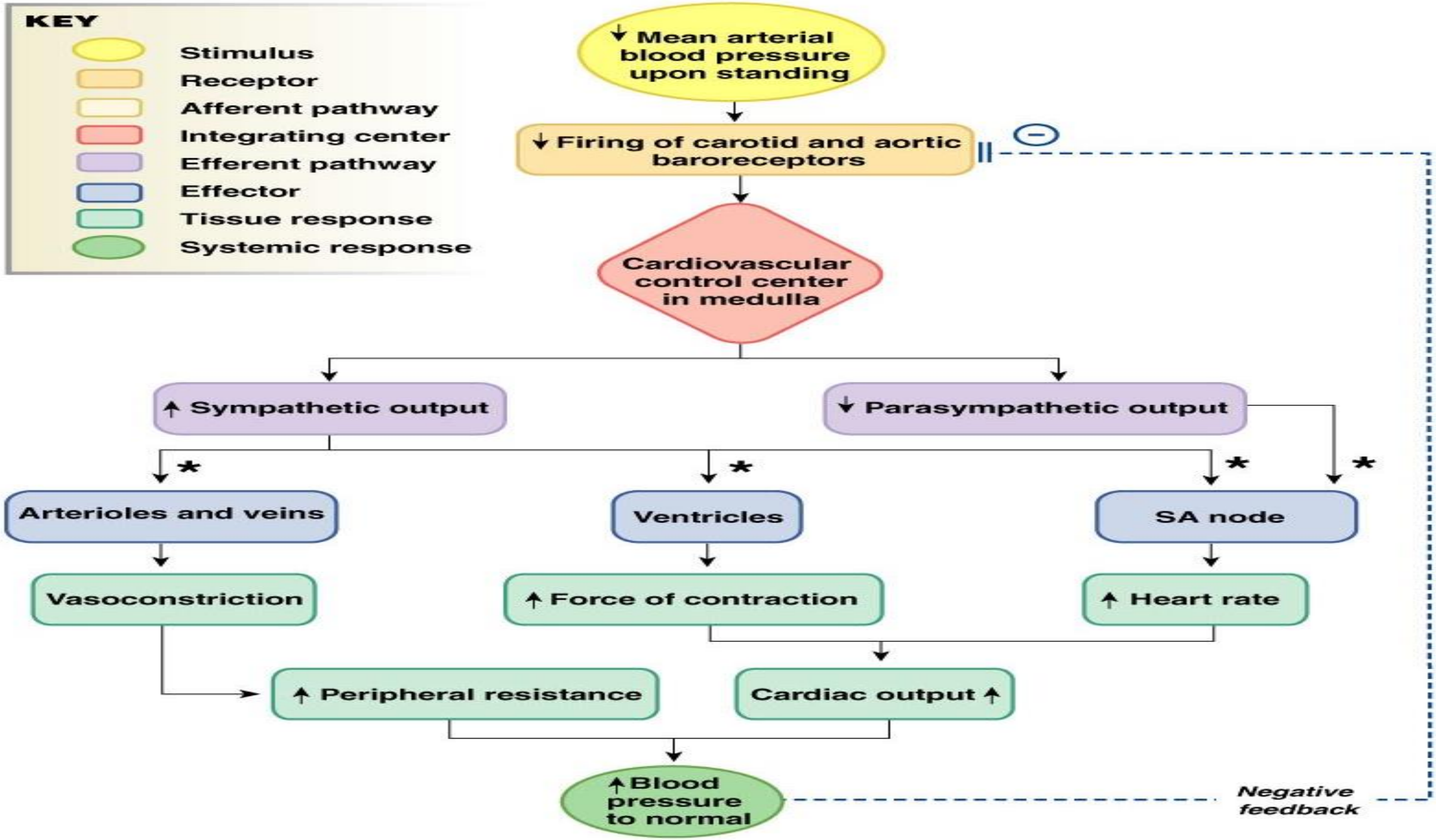


Aortic bodies present on upper part of the aortic arch and innervated by the vagus



Carotid body present at the top of the bifurcation of the common carotid artery, innervated by the carotid sinus nerve. Most important in humans


KEY
Stimulus
Receptor
Afferent pathway
Integrating center
Efferent pathway
Effector
Tissue response
Systemic response
↑Blood pressure
↑ Firing of baroreceptors in carotid arteries and aorta
Sensory neurons
Cardiovascular control center in medulla oblongata
↓ Sympathetic output
↑ Parasympathetic output
less NE released
more ACh on muscarinic receptor
α-receptor
β1-receptor
β1-receptor
Arteriolar smooth muscle
Ventricular myocardium
SA node
Vasodilation
↓Force of contraction
↓ Heart rate
↓ Peripheral resistance
↓ Cardiac output
↓Blood pressure
Negative feedback


KEY
Stimulus
Receptor
Afferent pathway
Integrating center
Efferent pathway
Effector
Tissue response
Systemic response
↓ Mean arterial blood pressure upon standing
↓ Firing of carotid and aortic baroreceptors
Cardiovascular control center in medulla
↑ Sympathetic output
↓ Parasympathetic output
Arterioles and veins
Ventricles
SA node
Vasoconstriction
↑ Force of contraction
↑ Heart rate
↑ Peripheral resistance
Cardiac output ↑
↑ Blood pressure to normal
Negative feedback

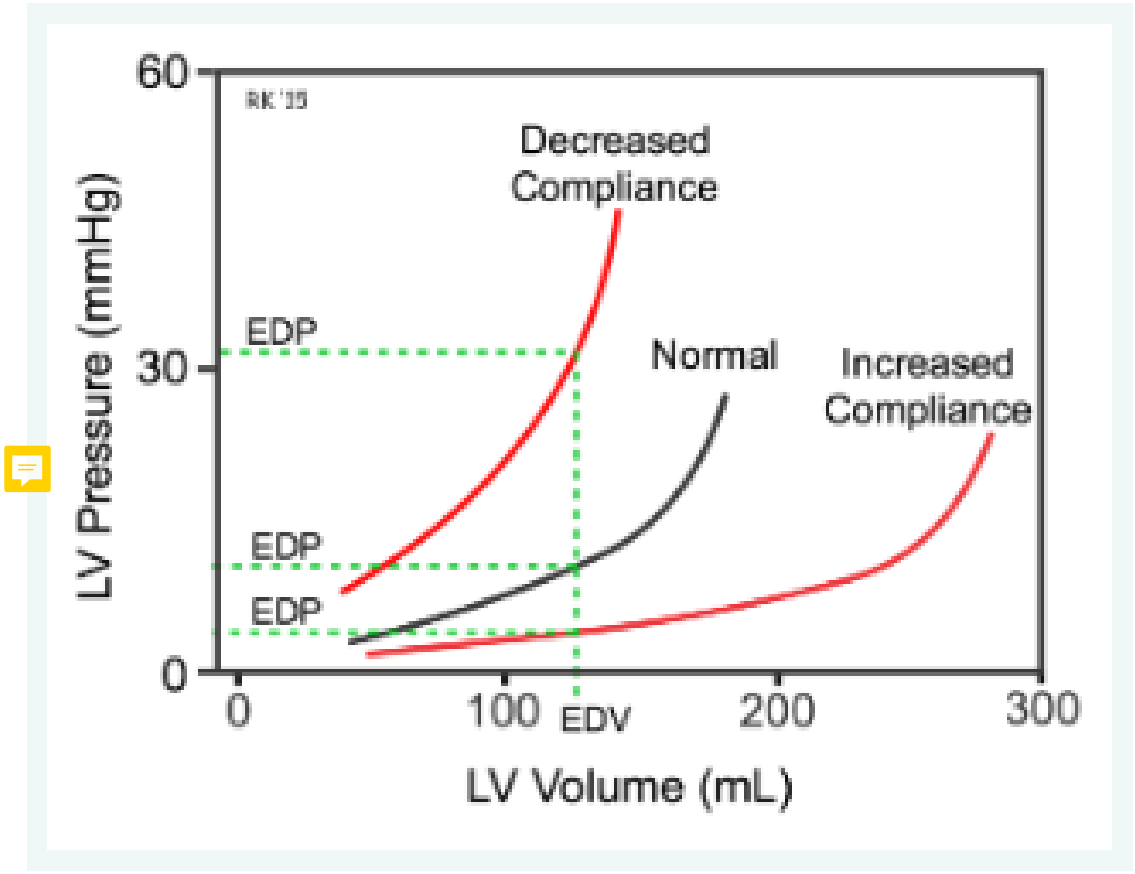
Ventricular Compliance

- As the ventricle fills with blood, the pressure and volume that result from filling are determined by the compliance of the ventricle. Normally, compliance curves are plotted as the change in volume (ΔV) over the change in pressure (ΔP). Therefore, the slope of the relationship is the reciprocal of the compliance, which is sometimes referred to as ventricular "stiffness."

- As the ventricle fills with blood and its volume increases, the pressure within the ventricular chamber passively increases (see the Normal filling curve in the figure). The relationship is not linear, particularly at higher volumes, because the compliance of the ventricular wall decreases ("stiffness" increases) the more the ventricular wall is stretched. This occurs in most biological tissues.

- in ventricular hypertrophy the ventricular compliance is decreased (i.e., the ventricle is "stiffer") because the thickness of the ventricular wall increases; therefore, ventricular end-diastolic pressure (EDP) is higher at any given end-diastolic volume (EDV)

- In a disease state such as dilated cardiomyopathy, the ventricle becomes very dilated without appreciable thickening of the wall. This dilated ventricle will have increased compliance as shown in the figure; therefore, although the EDV may be very high, the EDP may not be greatly elevated.

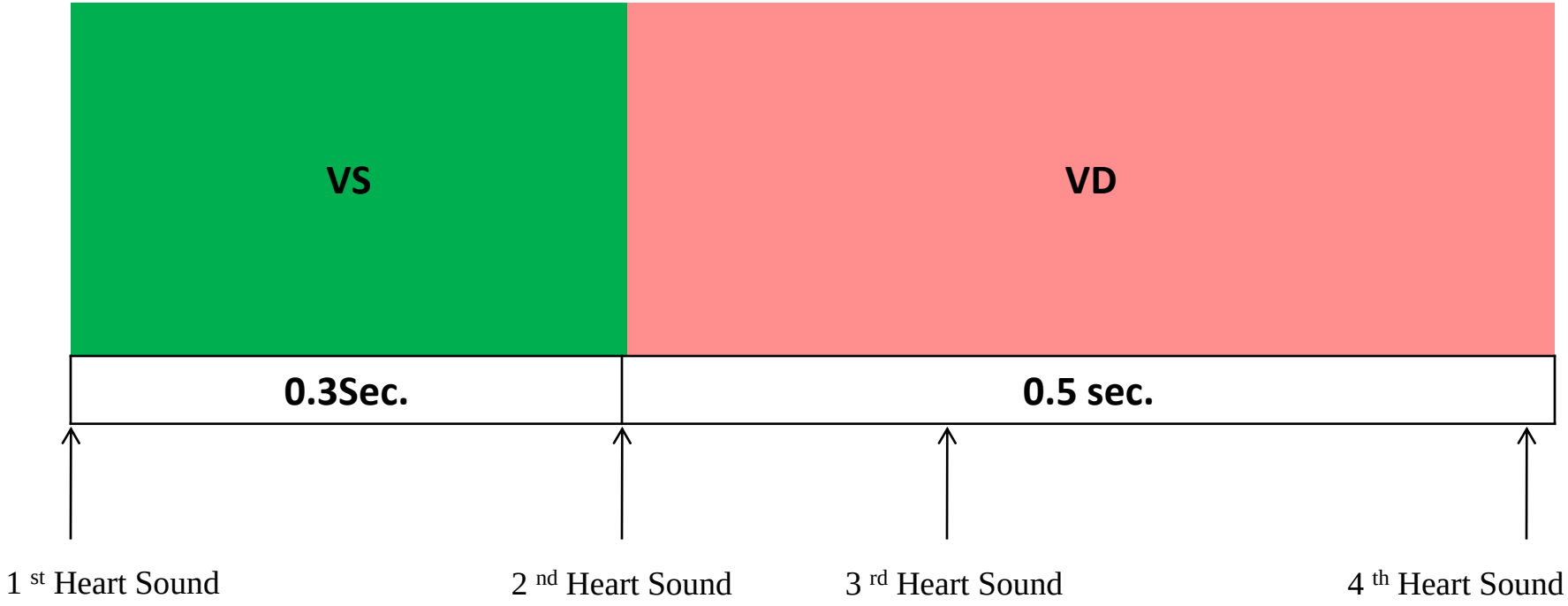


SUMMARY OF HEART SOUND

Heart Sound	Occurs during:	Associated with:
S1	Isovolumetric contraction	Closure of mitral and tricuspid valves
S2	Isovolumetric relaxation	Closure of aortic and pulmonic valves
S3	Early ventricular filling	Normal in children; in adults, associated with ventricular dilation (e.g., ventricular systolic failure)
S4	Atrial contraction	Associated with stiff, low compliant ventricle (e.g., ventricular hypertrophy

HEART SOUNDS: ASSOCIATION WITH CARDIAC CYCLE

At a normal heart rate, one cardiac cycle last for *0.8 seconds*!



Cardiac Cycle = “events of one complete heartbeat”

AS – Atrial Systole; AD – Atrial Diastole ; VS – Ventricular systole; VD – Ventricular diastole

Isometric contraction (length-tension relationship)

- The Frank-Starling mechanism occurs as the result of the length-tension relationship observed in striated muscle, including skeletal muscles and cardiac muscle.

- As a muscle fiber is stretched, active tension is created by altering the overlap of thick and thin filaments. The greatest isometric active tension is developed when a muscle is at its optimal length.

- In most relaxed skeletal muscle fibers, passive elastic properties maintain the muscle fibers length near optimal, as determined usually by the fixed distance between the attachment points of tendons to the bones at either end of the muscle.

- In contrast, the relaxed sarcomere length of cardiac muscle cells, in a resting ventricle, is lower than the optimal length for contraction. There is no bone to fix sarcomere length in the heart (of any animal) so sarcomere length is very variable and depends directly upon blood filling and thereby expanding the heart chambers.

Isometric/isotonic contractions

- Cardiac hypertrophy is an adaptive process which occurs as a result of increased stress endured by the heart

- Concentric hypertrophy is associated with increased left ventricular wall thickness; An increase in pressure, common in hypertension or resistance training (increase your muscle size).

- Eccentric hypertrophy is characterized by dilatation of the left ventricular chamber; An increase in volume, common endurance training (increase your breathing and heart rate) .

- Examples of activities that involve isotonic contractions include walking, running or lifting a light object.

- concentric and eccentric. In a concentric contraction, the muscle shortens when its tension is greater than the force opposing it, such as your biceps does when perform an arm curl. In an eccentric contraction, the force is greater than the muscle tension, causing the muscle to elongate; this happens when going downstairs or sitting down in a chair, as the effects of gravity add to the opposing force.

- “Isometric” means “same length,” the muscle does not shorten, and its tension never exceeds the opposing force. Examples of isometric exercises include holding a weight in place above the ground or pushing against a stationary object. While the entire muscle does not change length during an isometric contraction, the individual muscle fibers will shorten. isometric exercises can help to strengthen a muscle.