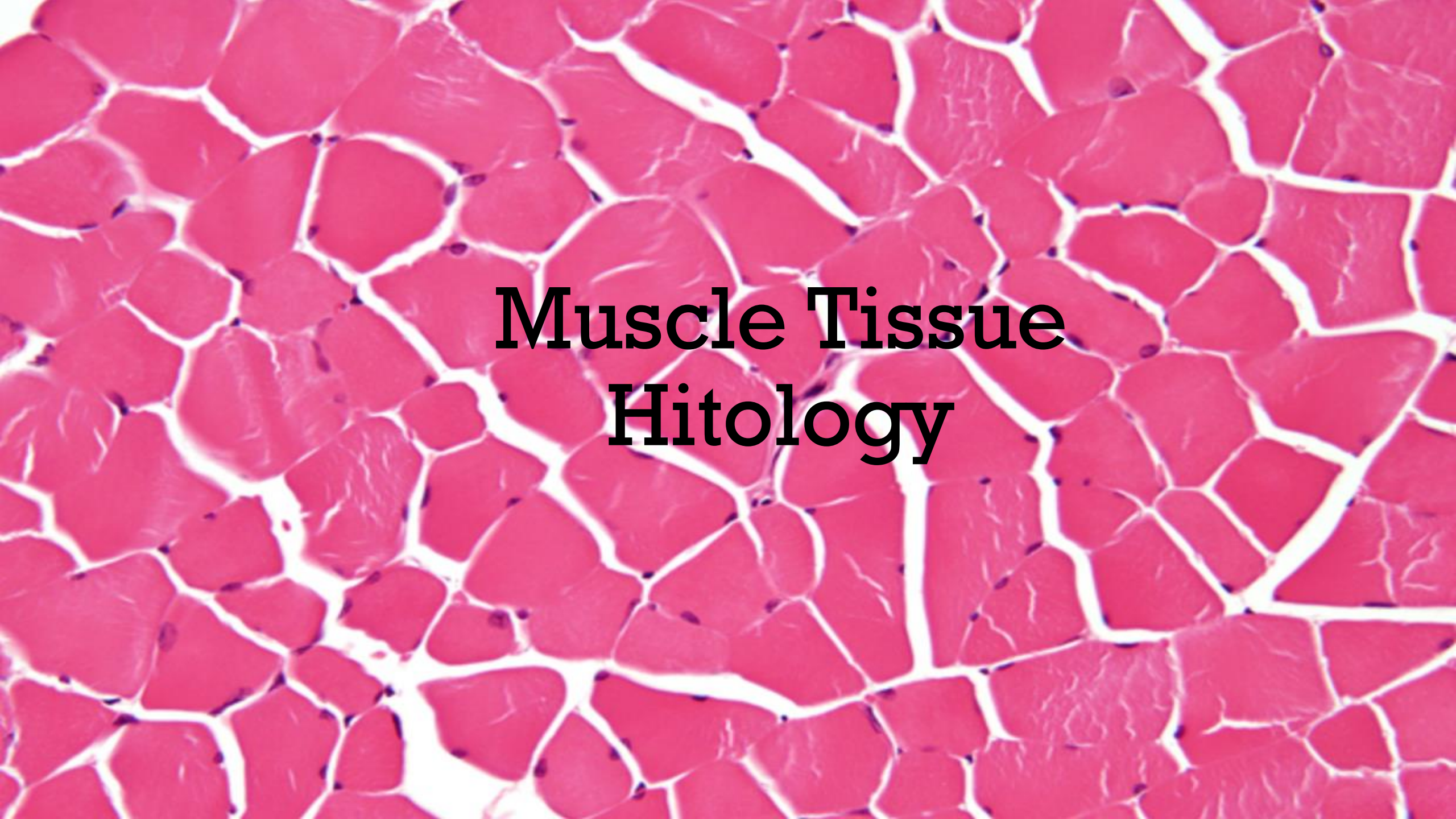
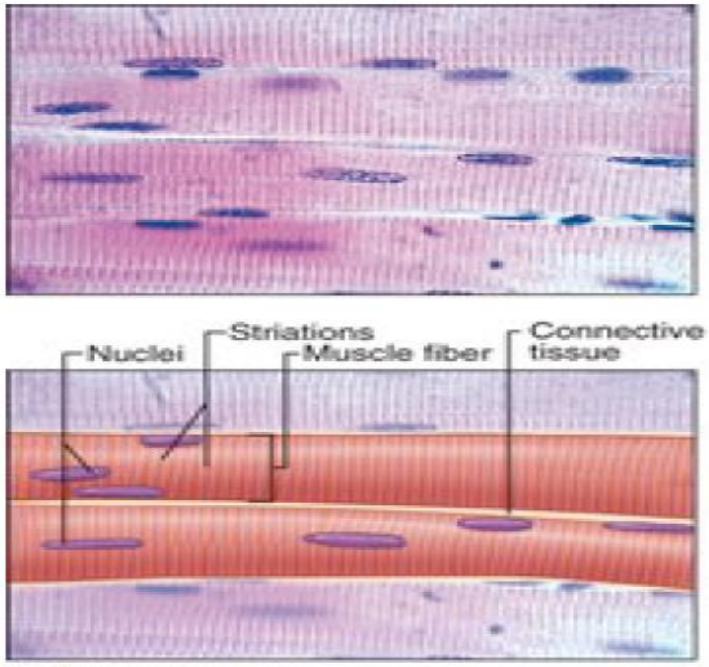


Muscle Tissue Hitology

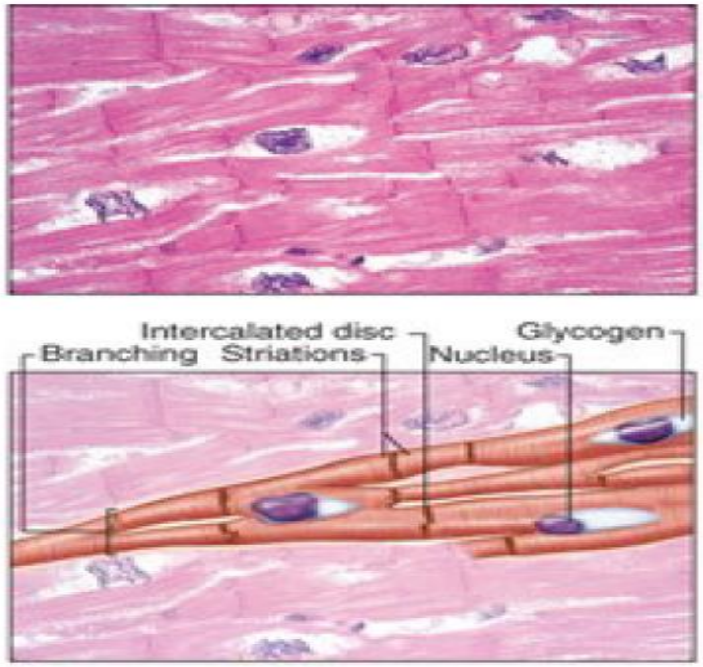
Type Of Muscles Tissue

Skeletal muscle



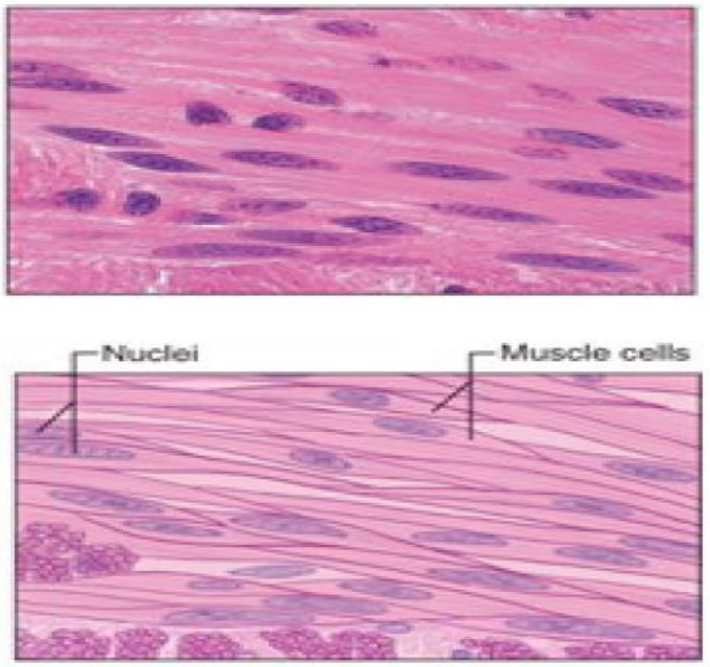
(a) Skeletal muscle

Cardiac muscles



(b) Cardiac muscle

Smooth muscles



(c) Smooth muscle

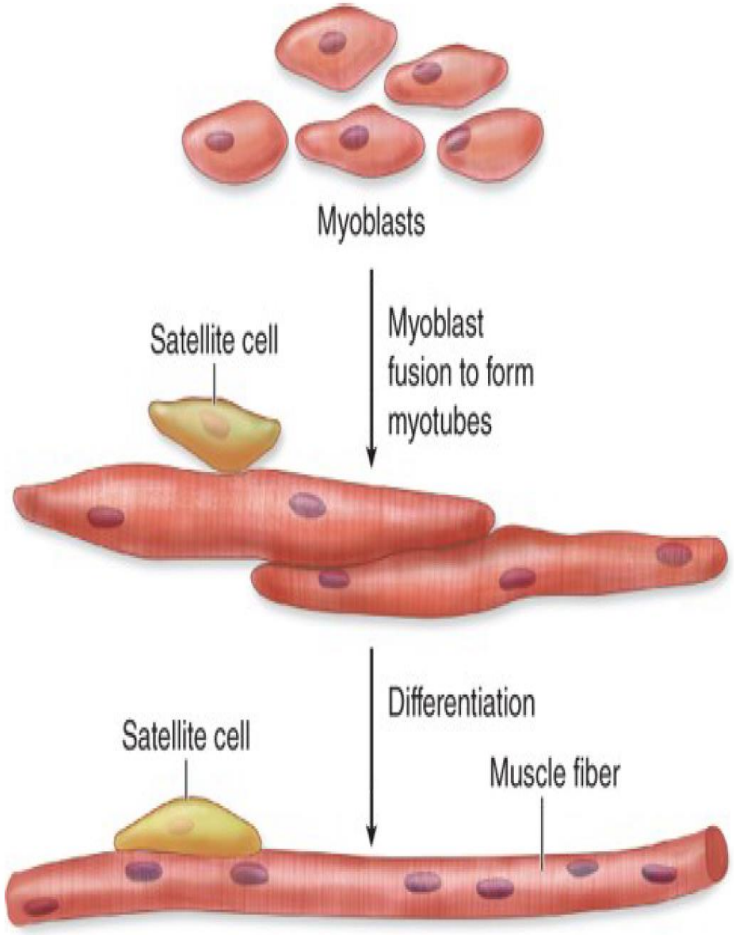
Types

- **Skeletal muscle**: bundles of very long, multinucleated cells with cross-striations. Their contraction is quick, forceful, and usually under voluntary control.
- **Cardiac muscle**: cross-striated and is composed of elongated (often branched) cells bound to one another at structures called intercalated discs (unique). Contraction is involuntary, vigorous, and rhythmic.
- **Smooth muscle**: consists of collections of fusiform cells that lack striations and have slow, involuntary contractions.

Skeletal Muscle development

Skeletal (or striated) muscle:

- Long, cylindrical multinucleated cells (10-100 µm diameter).
- Mesenchymal myoblasts--fuse--myotube--differentiate--striated muscle fibers.
- Satellite cells: A small population of reserve progenitor cells



Organization of skeletal muscle

- All three layers, plus the deep fascia (overlies the epimysium) are continuous with the connective tissue of a tendon at myotendinous junctions (join the muscle to bone, skin, or another muscle).

Muscle tissue are organized by connective tissue:

- **Epimysium**

External sheath of dense irregular connective tissue. Carries vessels, nerves, and lymphatics

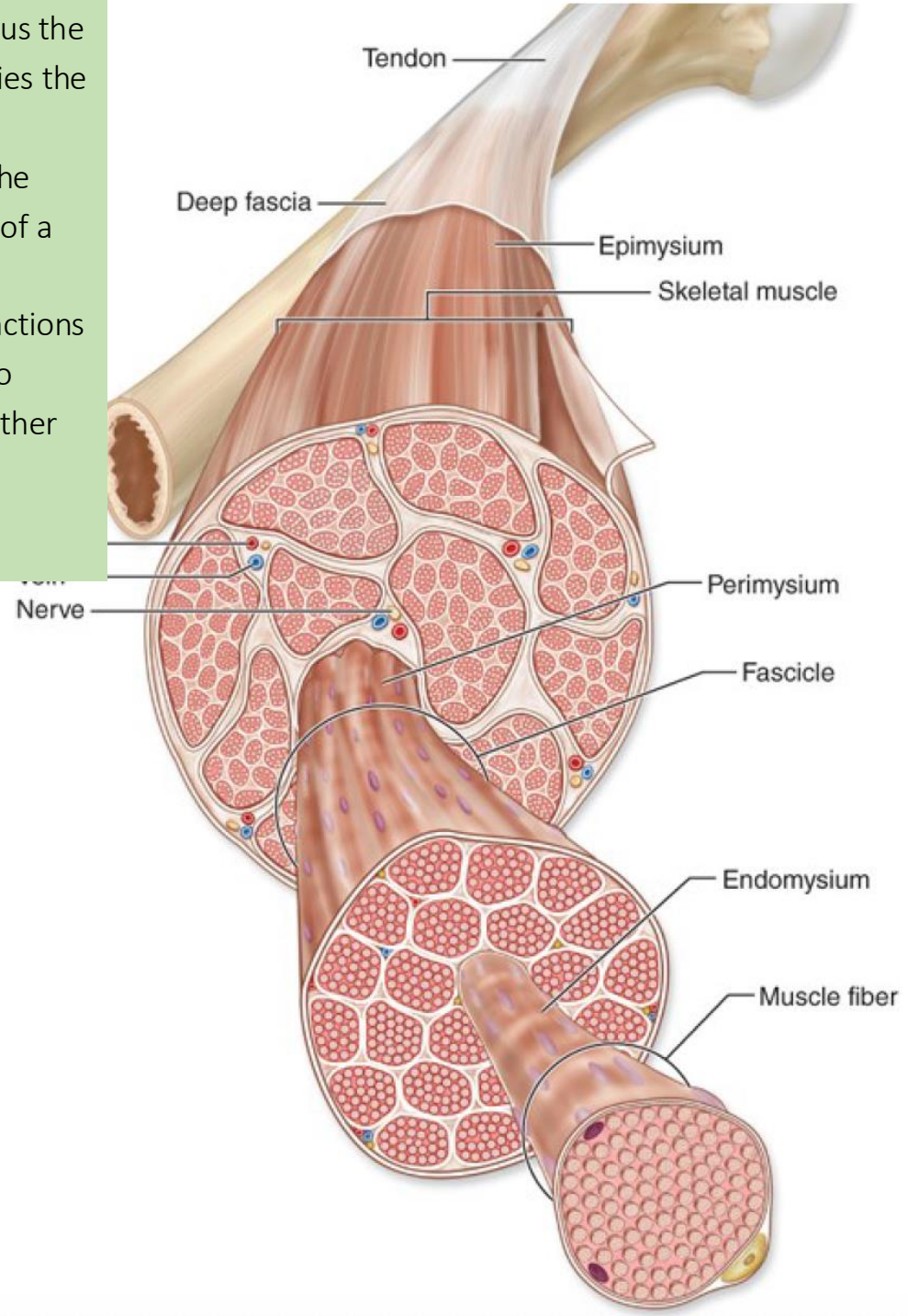
- **Perimysium**

Thin connective tissue layer that immediately surrounds each bundle of

muscle fibers (fascicle)

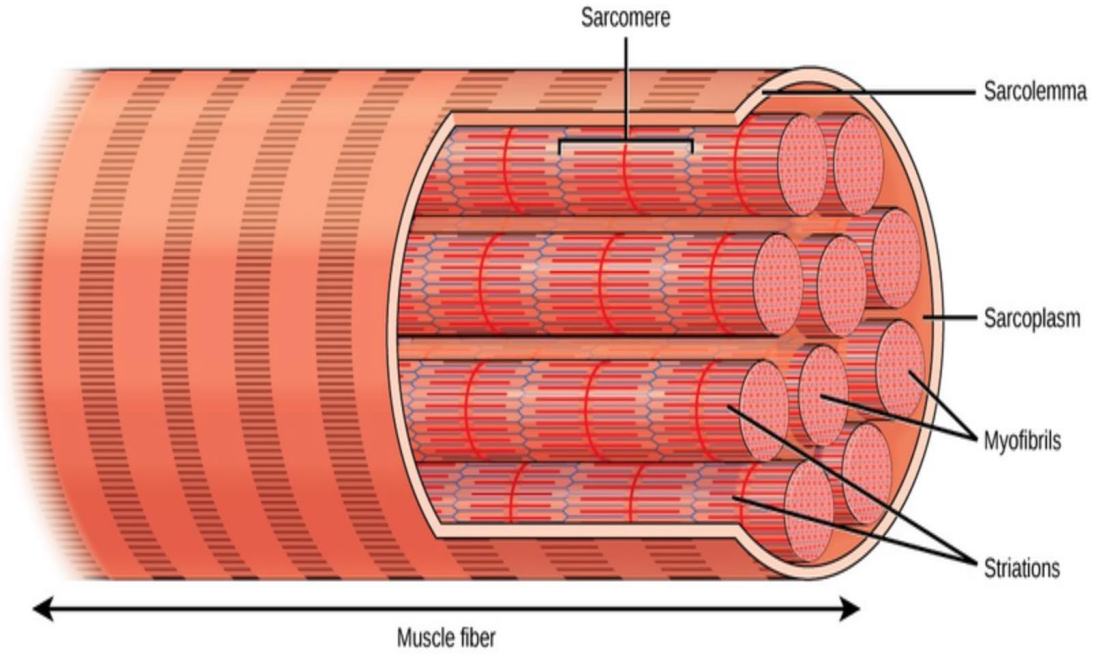
- **Endomysium**

Very thin and delicate layer of reticular fibers/scattered fibroblasts. fibers, capillaries form a rich network



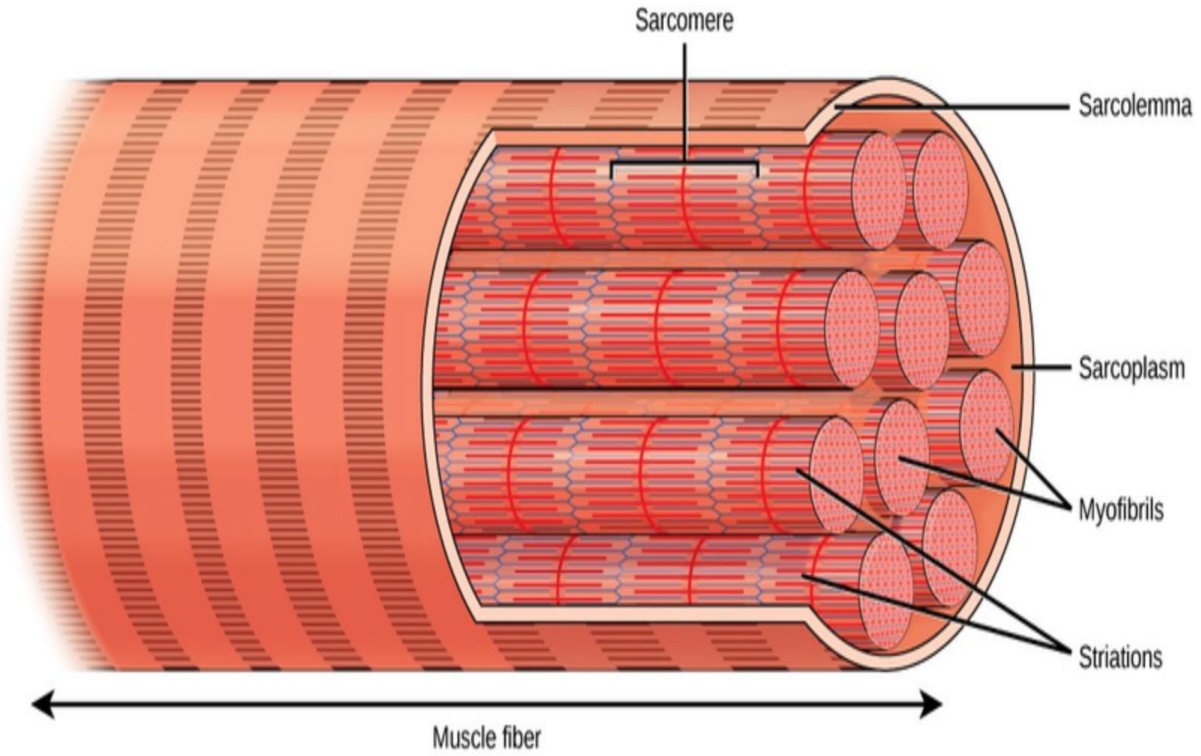
Organization Within Muscle Fibers

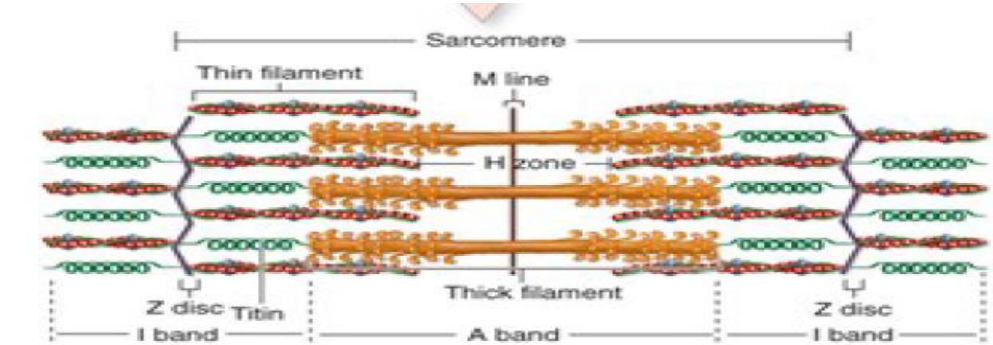
- Longitudinally, skeletal muscle fibers show striations of alternating light and dark bands
- Contains cylindrical filament bundles called myofibrils that run parallel to the long axis of the fiber
- Dark bands are called A bands ; the light bands are called I bands.
- The I band is bisected by a dark transverse line (Z disc).
- Sarcomere is the repetitive functional subunit of the contractile apparatus (extends between 2, Z discs), 2.5 um in resting muscle.

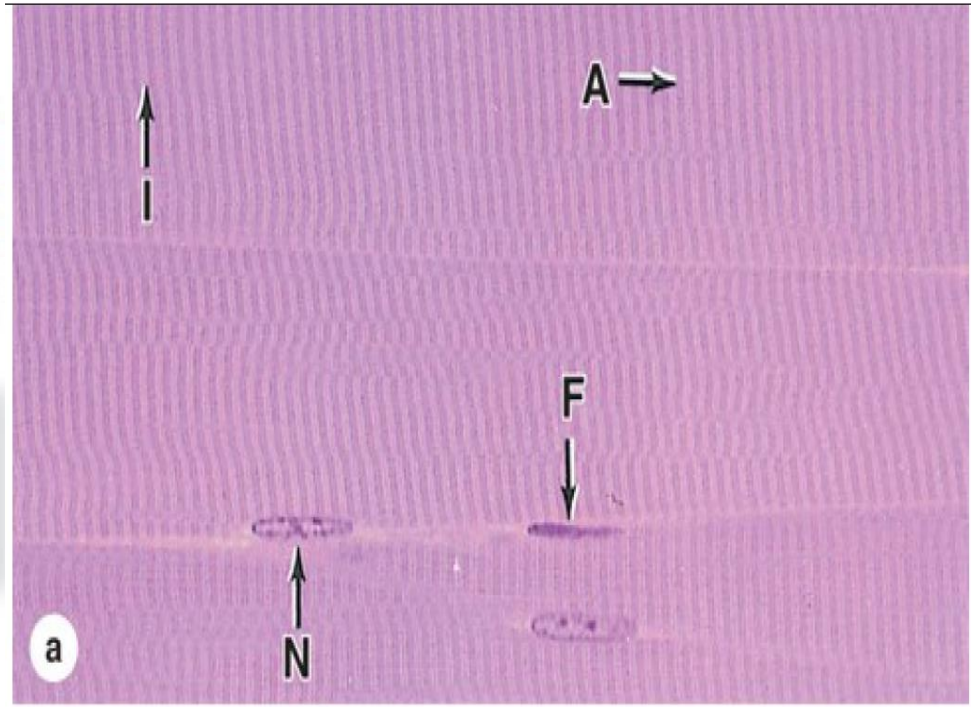


Skeletal Muscle Fiber

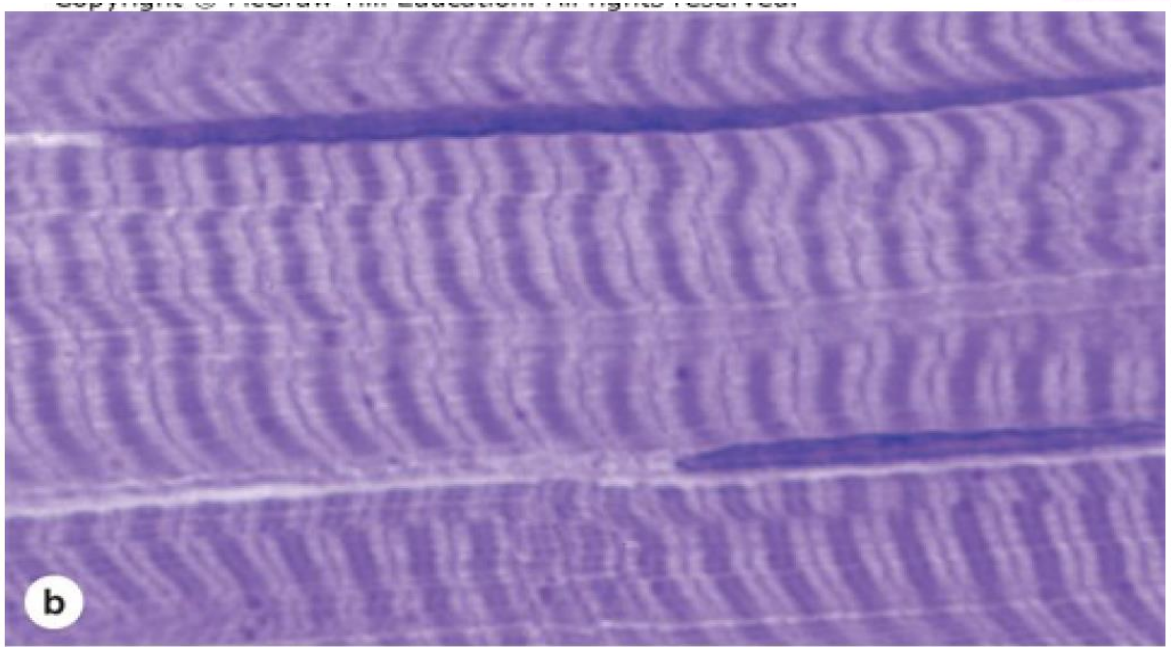
- Sarcomere the structure between two Z discs (each myofibril consist of a long series of sarcomeres)
- Sarcoplasm--- cytoplasm
- Sarcolemma---plasma membrane

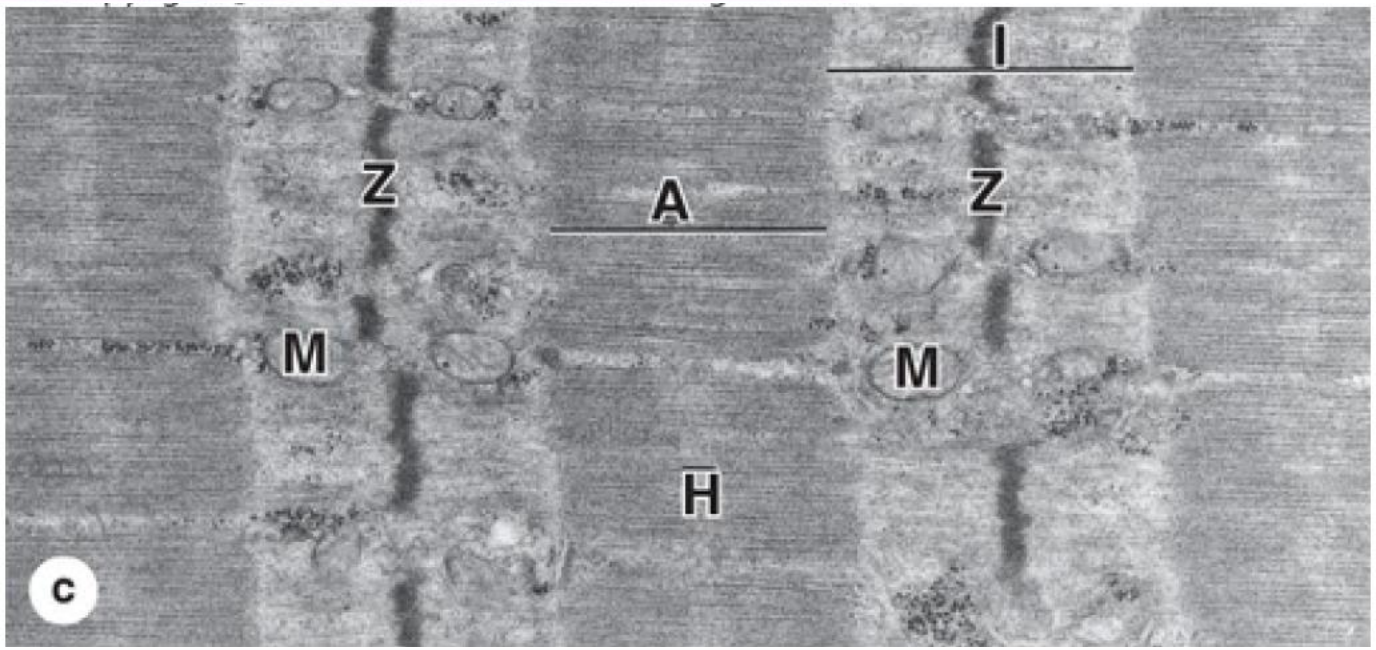






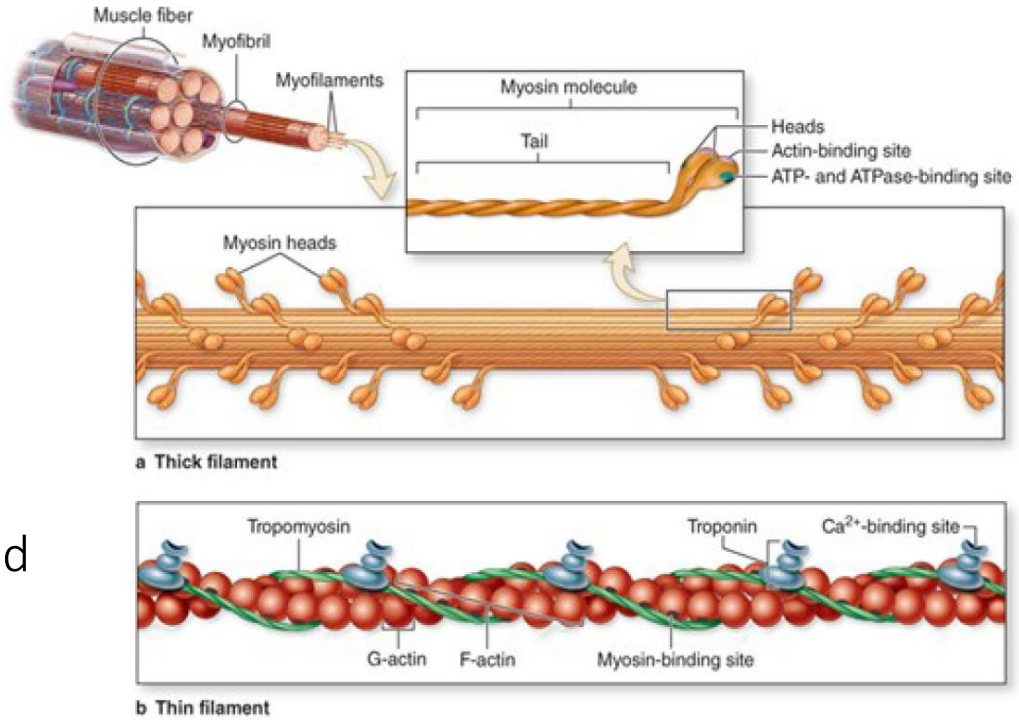
A: A Band
I: I Band
N: Nucleus of muscle fiber.
F: Nucleus of fibroblast
Z: Z disc
H: H zone
M: Mitochondria.





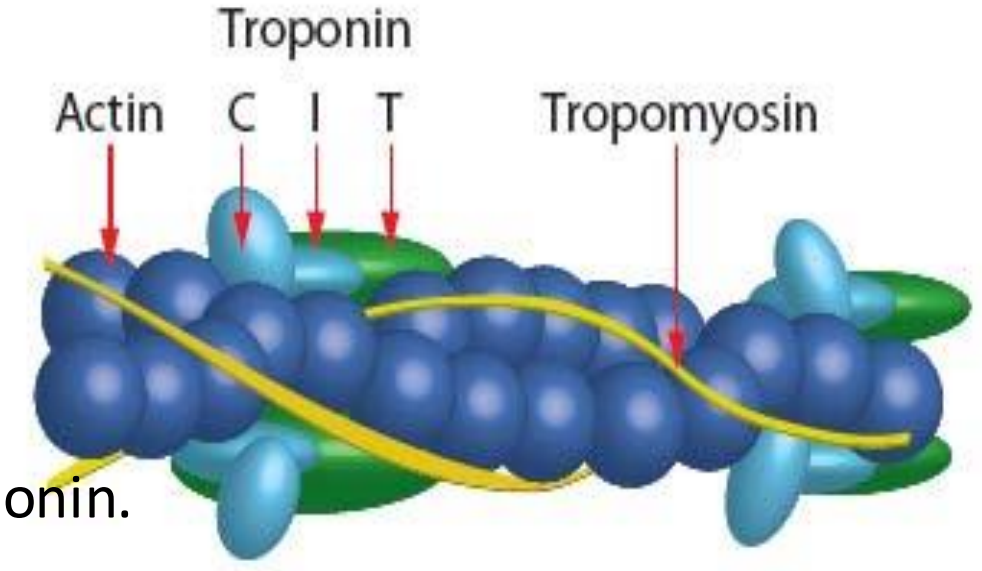
Myofilaments

- Composed of thick and thin filaments
- Thick: 200-500 myosins.
- Myosin is a large complex with two identical heavy chains and two pairs of light chains.
- Globular projections containing the four myosin light chains form a head at one end of each heavy chain.



- The myosin heads bind both actin, forming transient crossbridge between the thick and thin filaments, and ATP, catalyzing energy release (actomyosin ATPase activity).
- Several hundred myosin molecules are arranged within each thick filament with overlapping rodlike portions and the globular heads directed toward either end.

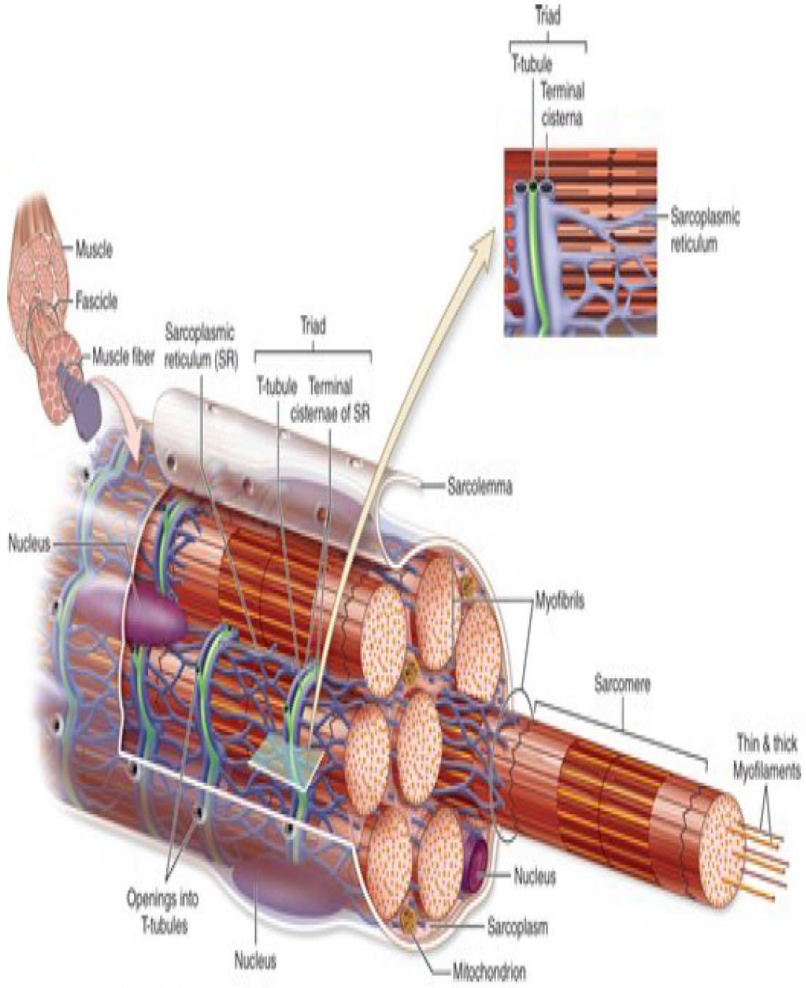
Myofilaments

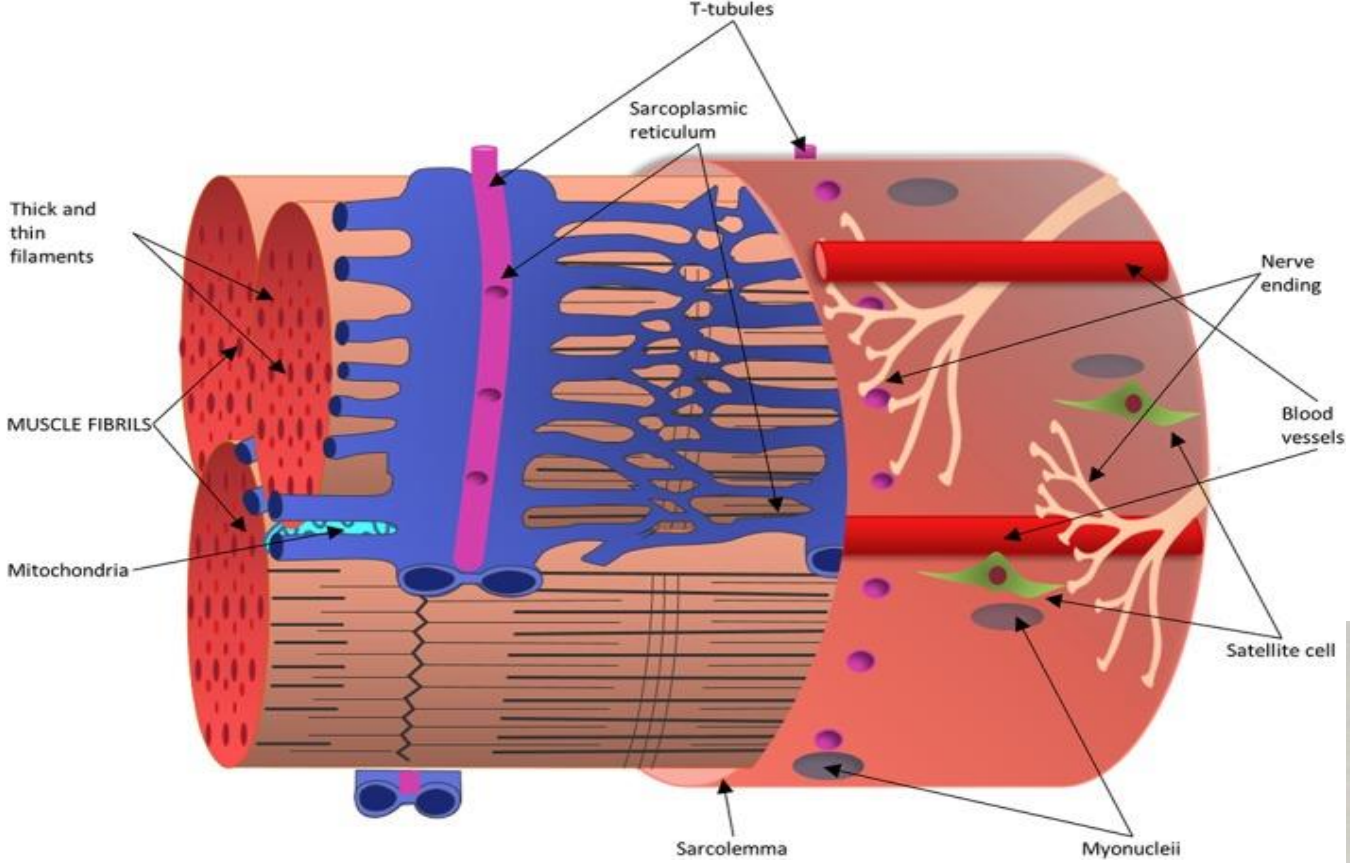


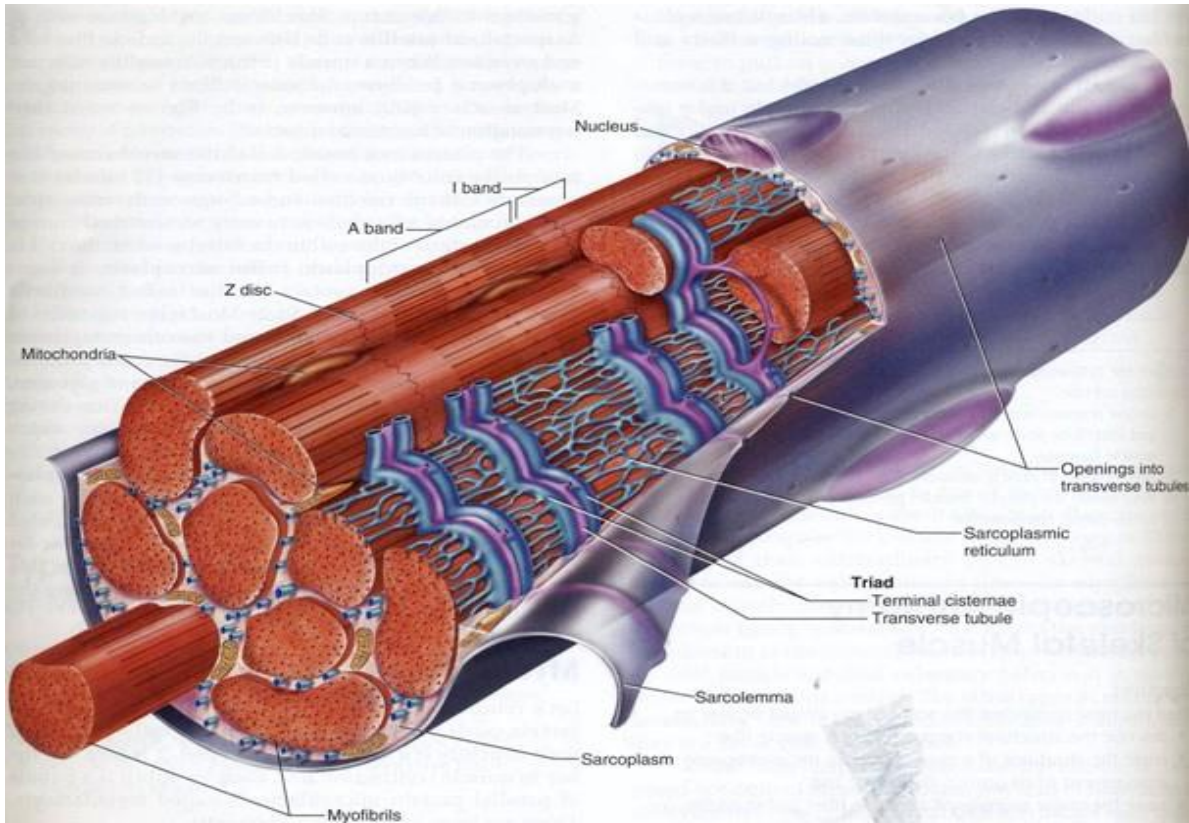
- Thin filaments: contains F-actin, tropomyosin, and troponin.
- The thin, helical actin filaments are each 1.0-µm long and 8-nm wide and run between the thick filaments.
- Each G-actin monomer contains a binding site for myosin
- Tropomyosin: long coil of two polypeptide chains located in the groove between the two twisted actin strands.
- Troponin: three subunits: TnT, which attaches to tropomyosin; TnC, which binds Ca2+; and TnI, which regulates the actin-myosin interaction.

Sarcoplasmic Reticulum & Transverse Tubule System

- The sarcoplasmic reticulum, contains pumps and other proteins for Ca^{2+} sequestration and surrounds the myofibrils.
- Calcium release from cisternae of the sarcoplasmic reticulum through voltage-gated Ca^{2+} channels is triggered by membrane depolarization produced by a motor nerve.
- The sarcolemma has deep invaginations called **T-tubules** that encircles each myofibril near I-A bands junction.
- Each of T-tubule becomes associated with two **terminal cisternae** of the sarcoplasmic reticulum…**TRIAD**

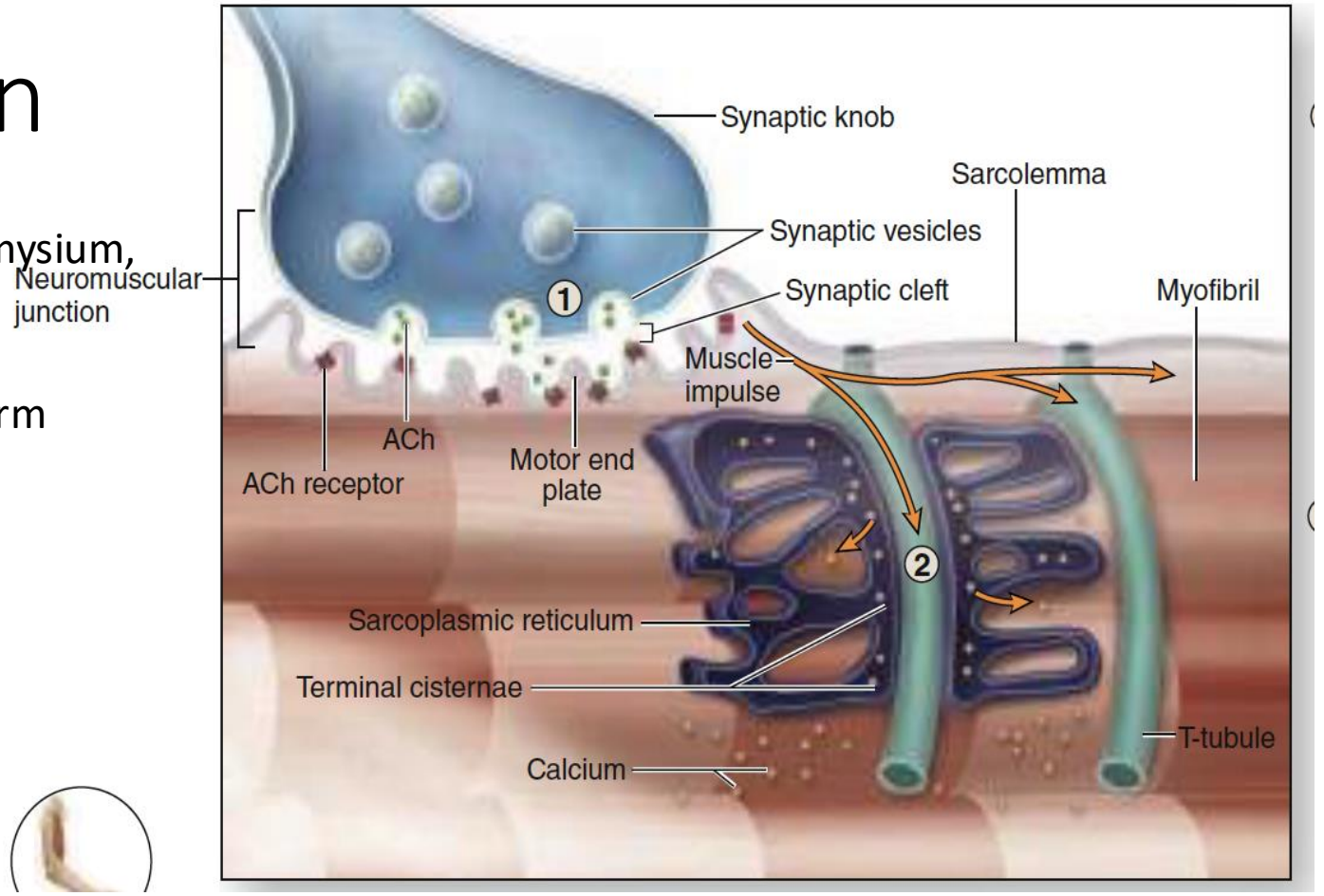



T-tubules
Sarcoplasmic reticulum
Thick and thin filaments
Nerve ending
MUSCLE FIBRILS
Blood vessels
Mitochondria
Satellite cell
Sarcolemma
Myonucleii


Nucleus
I band
A band
Z disc
Mitochondria
Openings into transverse tubules
Sarcoplasmic reticulum
Triad
Terminal cisternae
Transverse tubule
Sarcolemma
Sarcoplasm
Myofibrils

Innervation/contraction

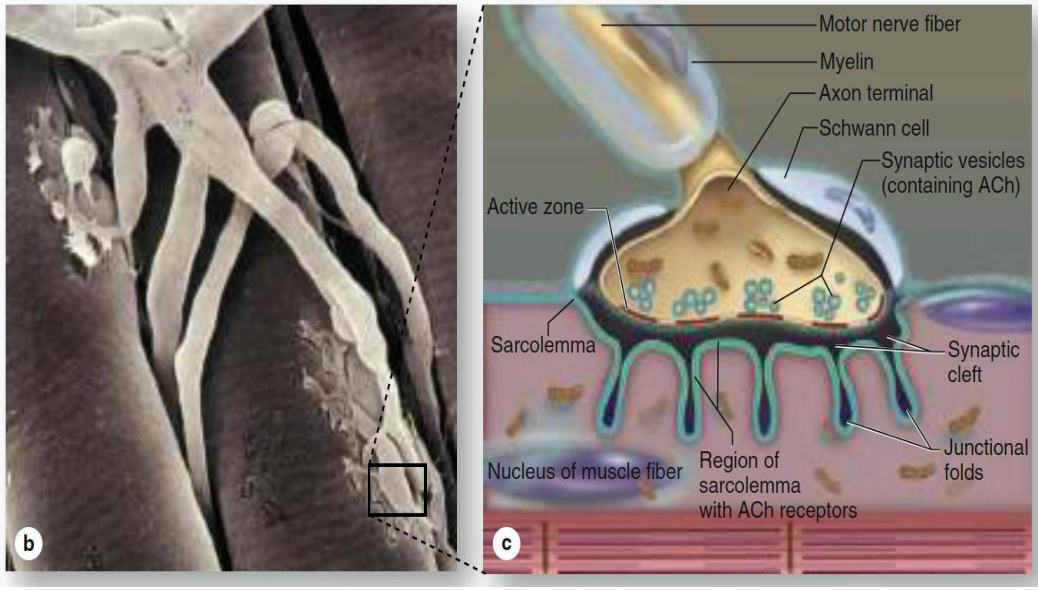
- Myelinated motor nerves branch out within the perimysium, where each nerve gives rise to several unmyelinated terminal twigs that pass through endomysium and form synapses with individual muscle fibers.
- Schwann cells enclose the small axon branches.
- Each axonal branch forms a dilated termination---- neuromuscular junctions, or motor end plates (MEP).



- The axon terminal contains mitochondria and numerous synaptic vesicles----neurotransmitter acetylcholine.
- Between the axon and the muscle is the synaptic cleft.
- Adjacent to the synaptic cleft---the sarcolemma---- deep junctional folds--- greater postsynaptic surface area and more acetylcholine receptors.

Innervation/contraction

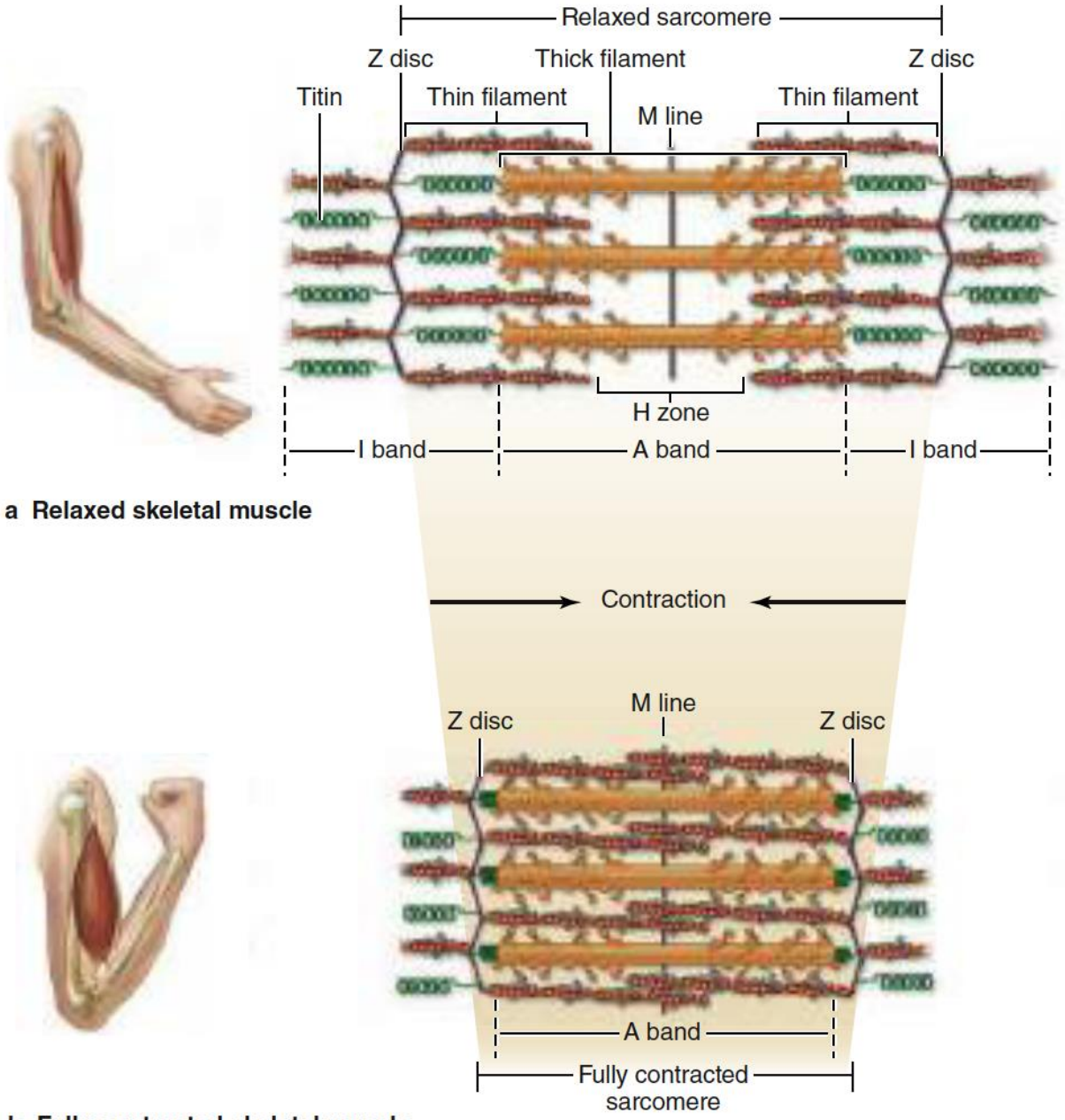
- Acetylcholine + receptor-----depolarizing the sarcolemma---muscle action potential.
- muscle action potential moves along the sarcolemma and along T-tubules.
- At triads the depolarization signal triggers the release of Ca^{2+} from terminal cisterns of the sarcoplasmic reticulum--- contraction cycle.
- An axon can form MEPs with one or many muscle fibers.
- Innervation of single muscle fibers by single motor neurons--- precise control of muscle activity--- extraocular muscles (**eye movements**).
- Larger muscles---motor axons branch profusely---innervate 100 or more muscle fibers (**motor unit**).

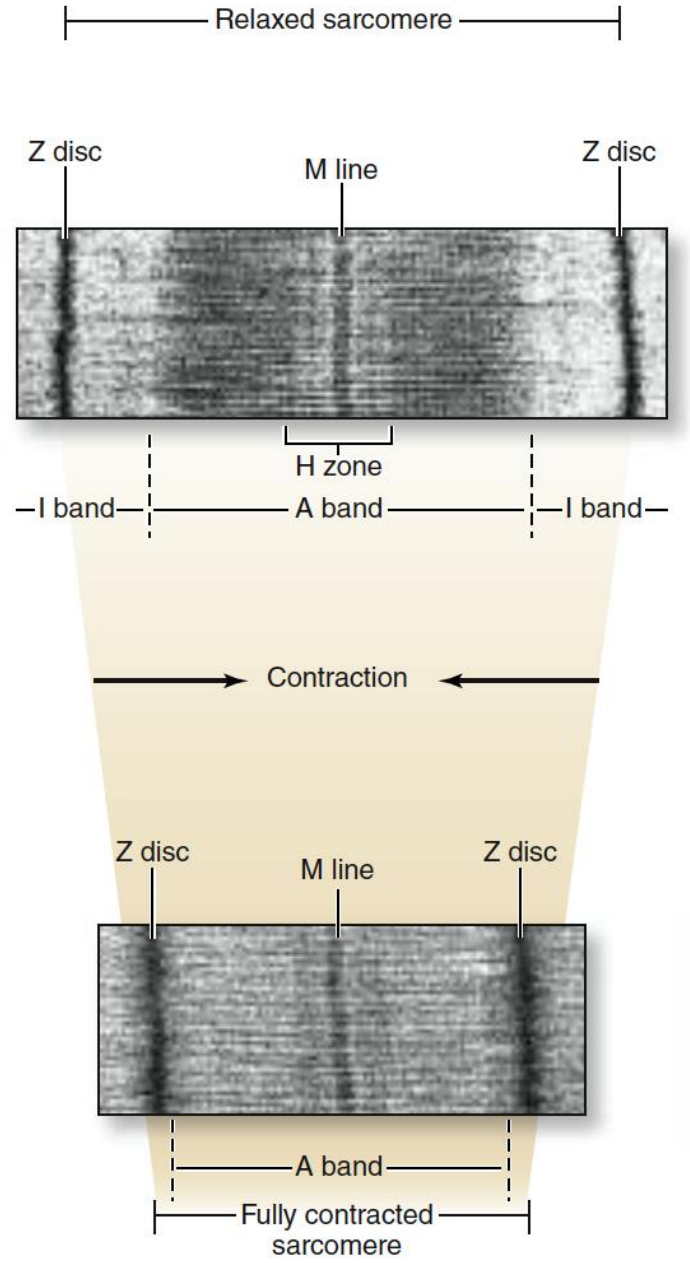


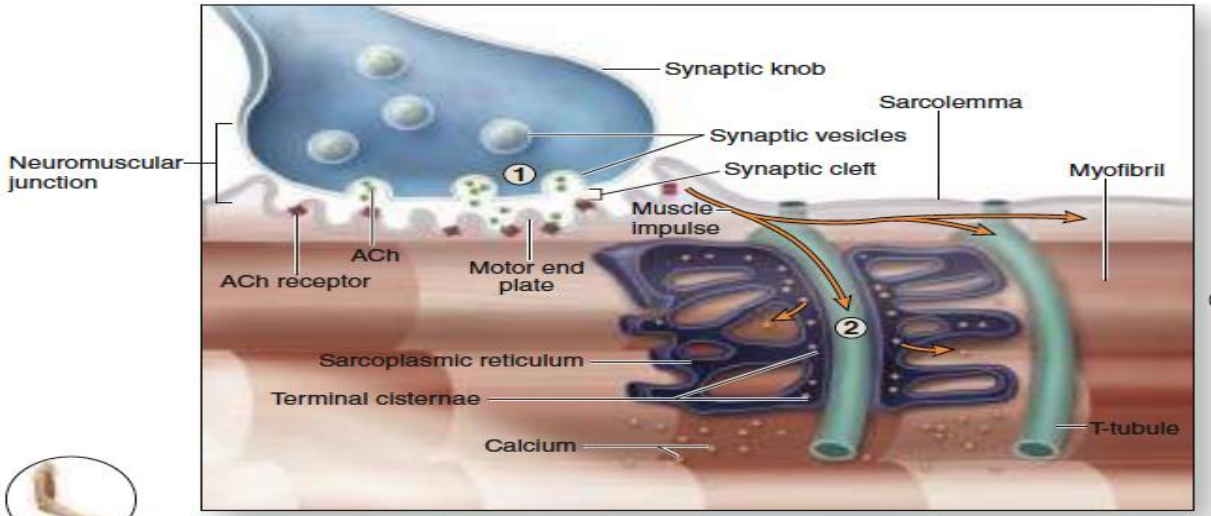
Innervation/contraction

- Striated muscle fibers do not show graded contraction---**all or none**.
- To vary the force of contraction--- fibers within a muscle fascicle do not all contract at the same time.
- large muscles with many motor units---firing of a single motor axon ------tension proportional to the number of muscle fibers it innervates.

Relaxation versus contraction

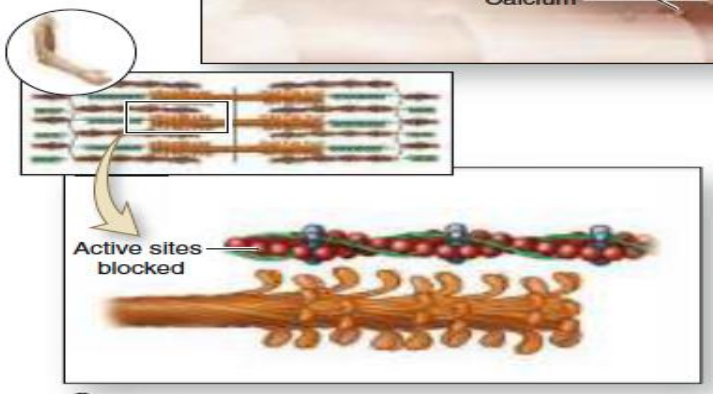




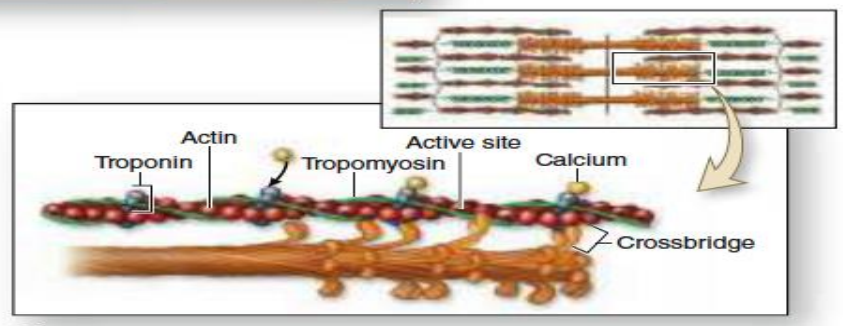


① A nerve impulse triggers release of ACh from the synaptic knob into the synaptic cleft. ACh binds to ACh receptors in the motor end plate of the neuromuscular junction, initiating a muscle impulse in the sarcolemma of the muscle fiber.

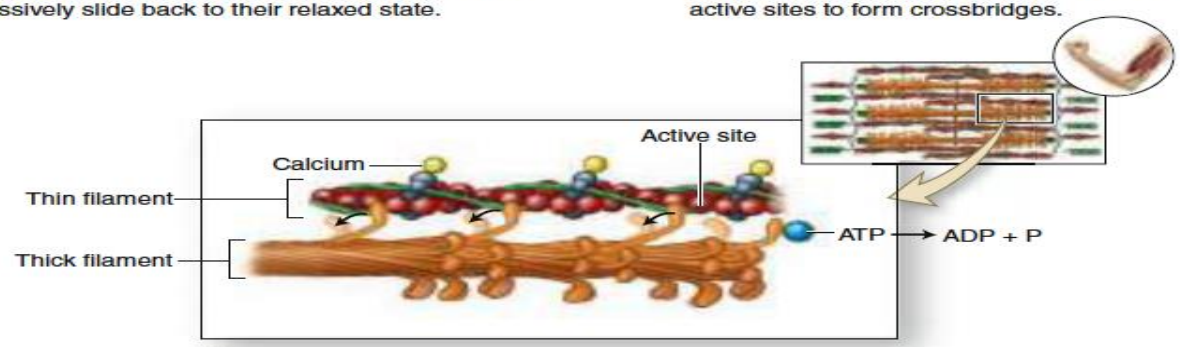
② As the muscle impulse spreads quickly from the sarcolemma along T tubules, calcium ions are released from terminal cisternae into the sarcoplasm.



⑤ When the impulse stops, calcium ions are actively transported into the sarcoplasmic reticulum, tropomyosin re-covers active sites, and filaments passively slide back to their relaxed state.



③ Calcium ions bind to troponin. Troponin changes shape, moving tropomyosin on the actin to expose active sites on actin molecules of thin filaments. Myosin heads of thick filaments attach to exposed active sites to form crossbridges.



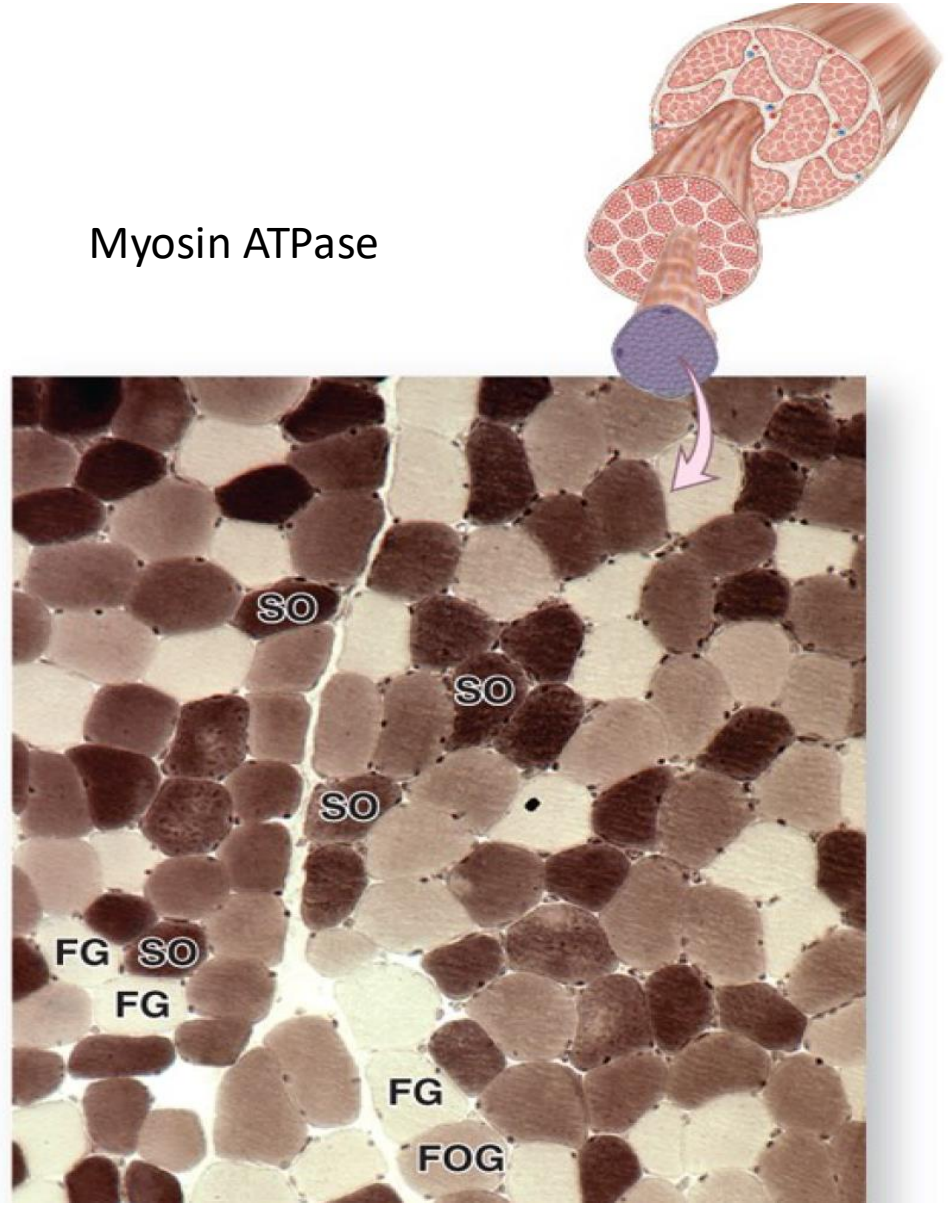
④ Myosin heads pivot, moving thin filaments toward the sarcomere center. ATP binds myosin heads and is broken down into ADP and P. Myosin heads detach from thin filaments and return to their prepivot position. The repeating cycle of *attach-pivot-detach-return* slides thick and thin filaments past one another. The sarcomere shortens and the muscle contracts. The cycle continues as long as calcium ions remain bound to troponin to keep active sites exposed.

Types of skeletal muscle fibe

Different types of fibers are based on:

1. Maximal rate of contraction (fast or slow fibers)---myosin isoforms.
2. Major pathway for ATP synthesis

   (oxidative phosphorylation or glycolysis).
3. Others: capillary density, # of mitochondria, content of glycogen and myoglobin (O_2 storage).



Slow oxidative

- Fibers are adapted for slow contractions over long periods without fatigue, many mitochondria, many surrounding capillaries, and much myoglobin, fresh tissue are dark or red in color.

Fast glycolytic:

- Fibers are specialized for rapid, shortterm contraction, few mitochondria or capillaries and depending largely on anaerobic metabolism of glucose derived from stored glycogen. Rapid contractions lead to rapid fatigue (lactic acid from glycolysis). appear white.

Fast oxidative-glycolytic

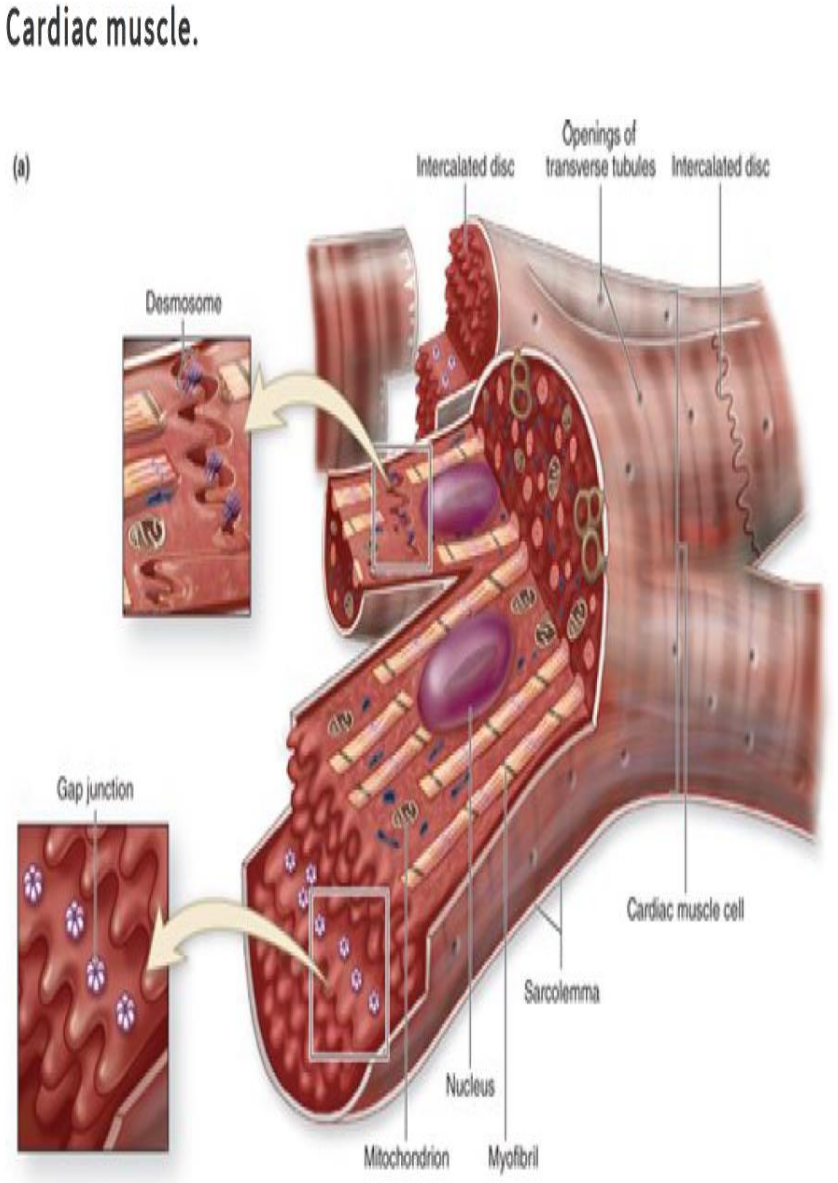
- Fibers have physiological and histological features intermediate between those of the other two types.

	Slow, Oxidative Fibers (Type I)	Fast, Oxidative-Glycolytic Fibers (Type IIa)	Fast, Glycolytic Fibers (Type IIb)
Mitochondria	Numerous	Numerous	Sparse
Capillaries	Numerous	Numerous	Sparse
Fiber diameter	Small	Intermediate	Large
Size of motor unit	Small	Intermediate	Large
Myoglobin content	High (red fibers)	High (red fibers)	Low (white fibers)
Glycogen content	Low	Intermediate	High
Major source of ATP	Oxidative phosphorylation	Oxidative phosphorylation	Anaerobic glycolysis
Glycolytic enzyme activity	Low	Intermediate	High
Rate of fatigue	Slow	Intermediate	Fast
Myosin-ATPase activity	Low	High	High
Speed of contraction	Slow	Fast	Fast
Typical major locations	Postural muscles of back	Major muscles of legs	Extraocular muscles

Myoglobin: globular sarcoplasmic protein similar to hemoglobin which contains iron atoms and allows for O_2 storage

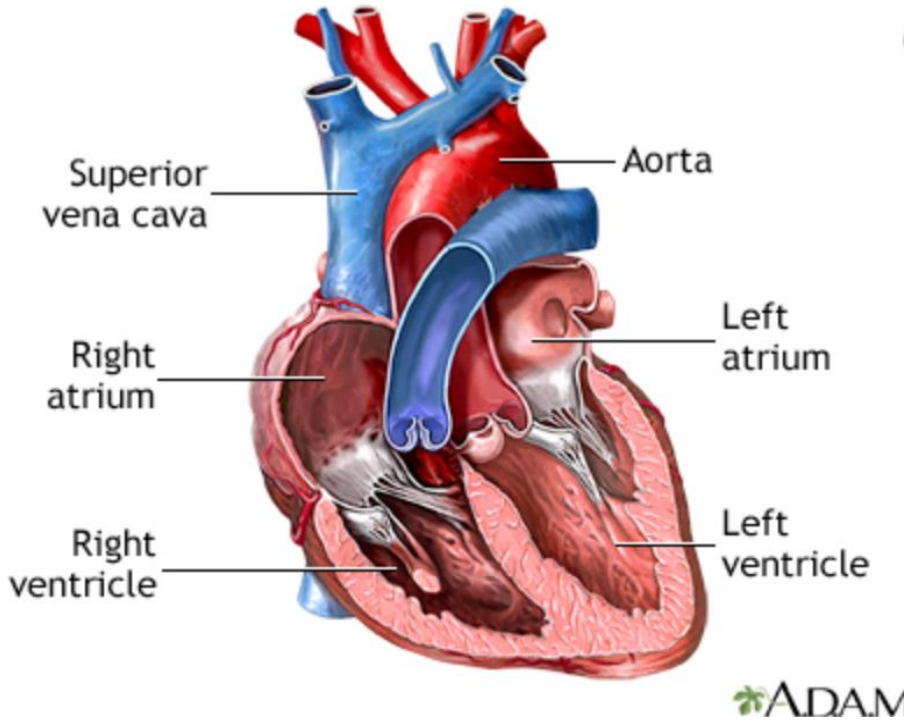
Cardiac Muscle

- Cells align into chain-like arrays.
- Form complex junctions between interdigitating processes
- Cells within one fiber often branch..
- Mature cardiac muscle cells are 15-30 µm in diameter and 85-120 µm long.
- Striated
- One centrally nucleus located.
- Each muscle cells is a surrounded by endomysium with a rich capillary network.
- A thicker perimysium separates bundles and layers of muscle fibers and in specific areas (larger masses of fibrous connective tissue: cardiac skeleton)



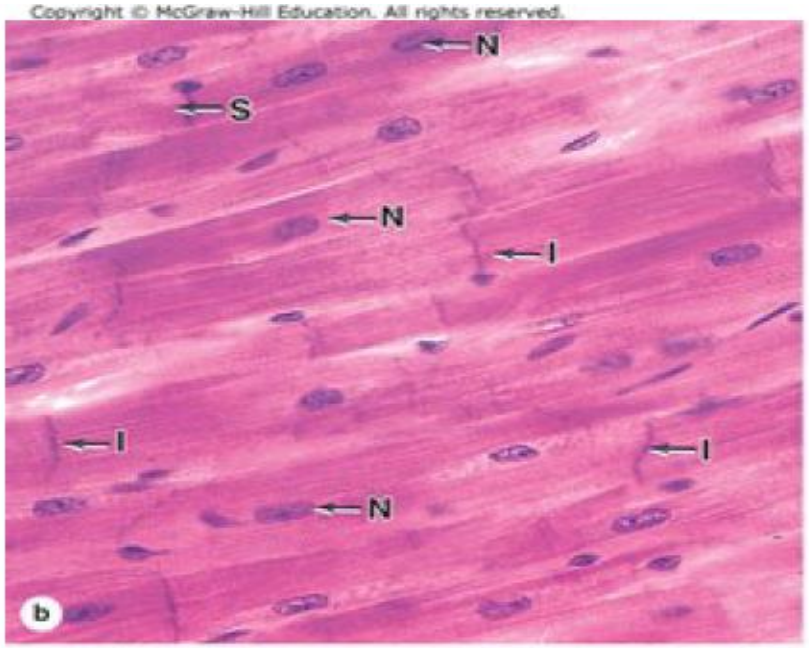
Cardiac Muscle

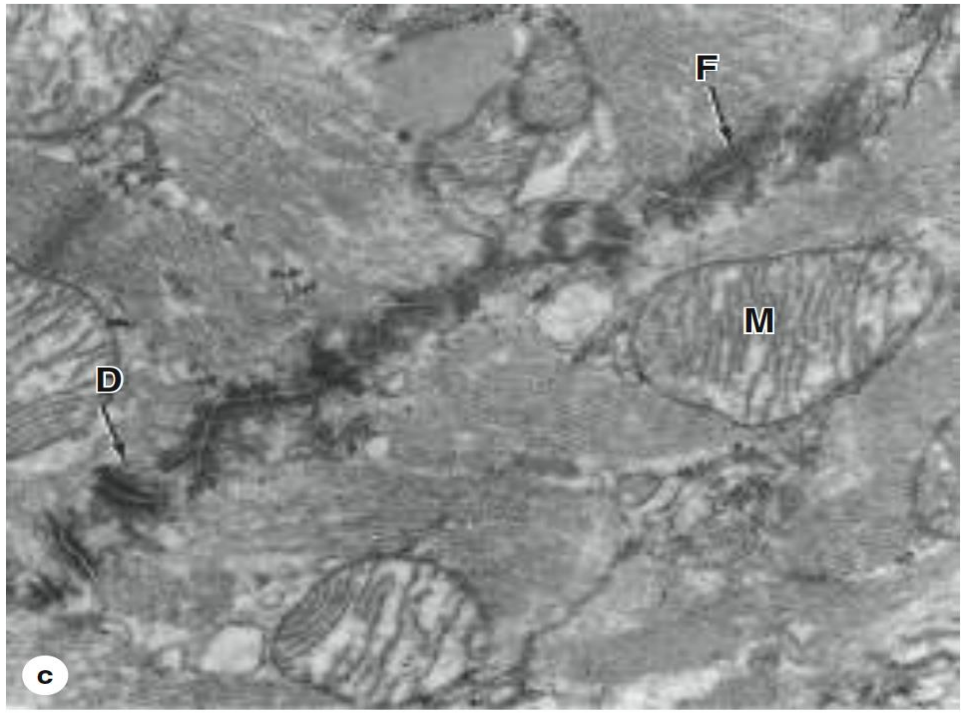
- Muscle of the heart ventricles is much thicker
- T-tubules in ventricular muscle fibers are well-developed.
- Sarcoplasmic reticulum is less well-organized.
- The junctions between its terminal cisterns and t-tubules involve only one structure of each type (**dyads**)
- Cardiac muscle fiber contraction is intrinsic and spontaneous
- Contraction initiated by nodes of unique myocardial fibers
- Contraction of individual myocardial fibers is all-or-none
- Rate of contraction is modified by autonomic innervation



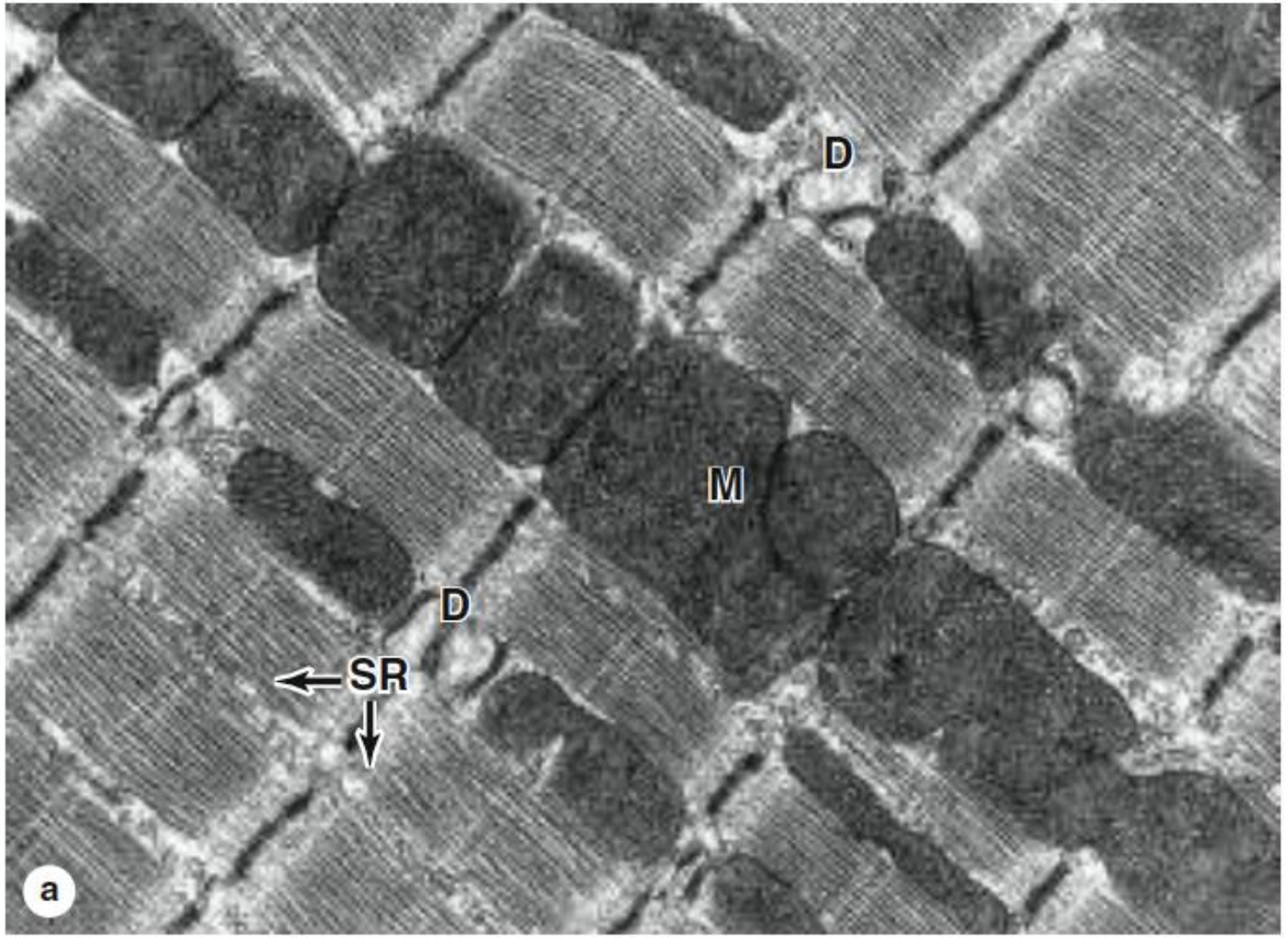
Cardiac muscle

- The fibers consist of separate cells joined at interdigitating regions called the intercalated discs.
- Intercalated discs: transverse lines that cross the fibers at irregular intervals where the myocardial cells join (junctional complexes).
- Transverse regions: many desmosomes and fascia adherens junctions--- strong intercellular adhesion.
- Longitudinally: run parallel to the myofibrils and are filled with gap junctions (ionic continuity between the cells).
- Central nuclei and myofibrils which are usually sparser and less well-organized



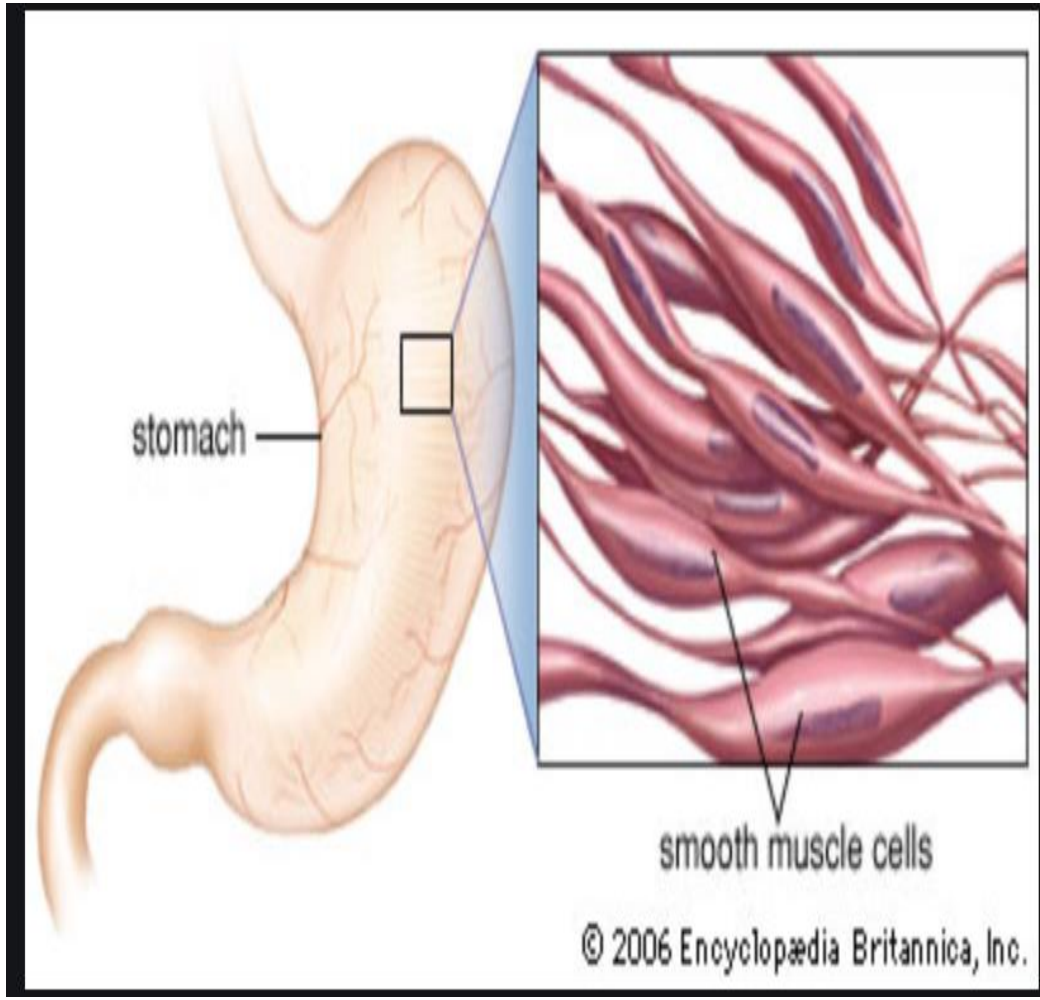


Where was this take from?

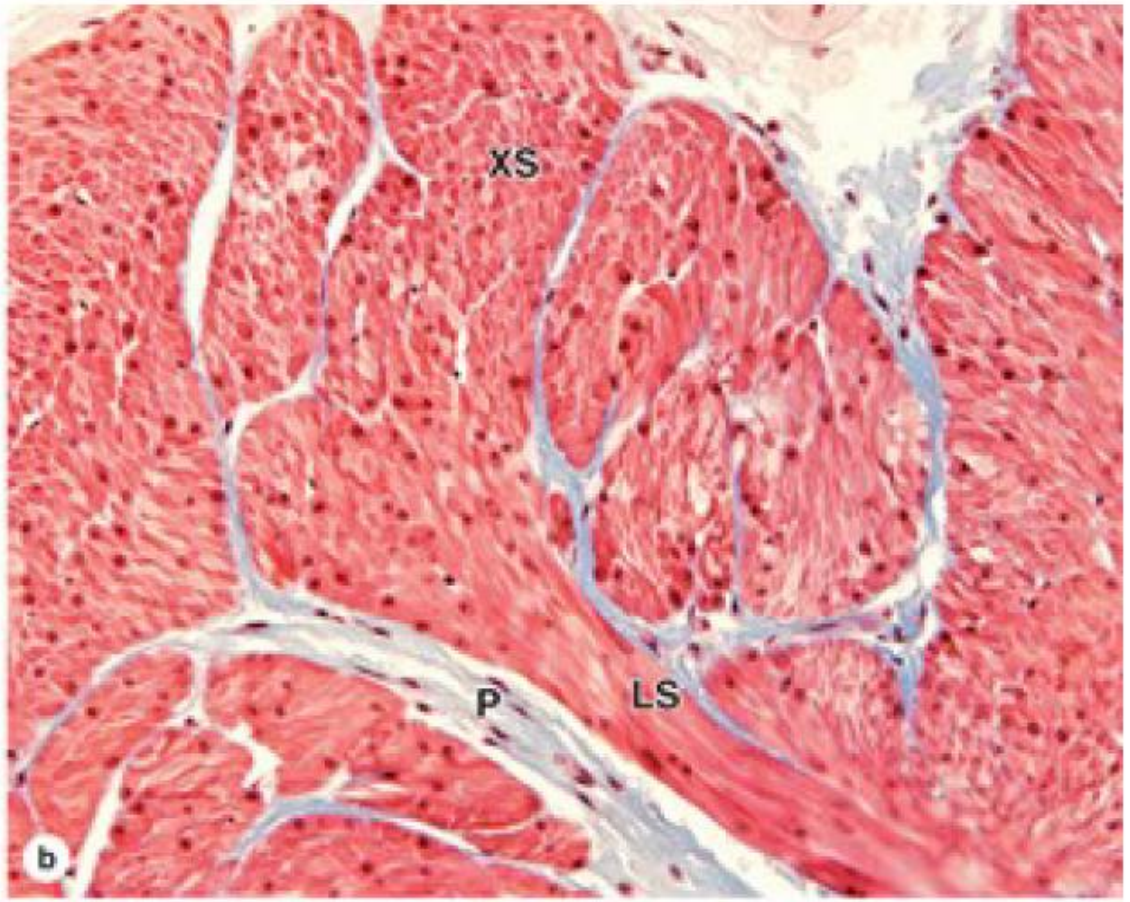


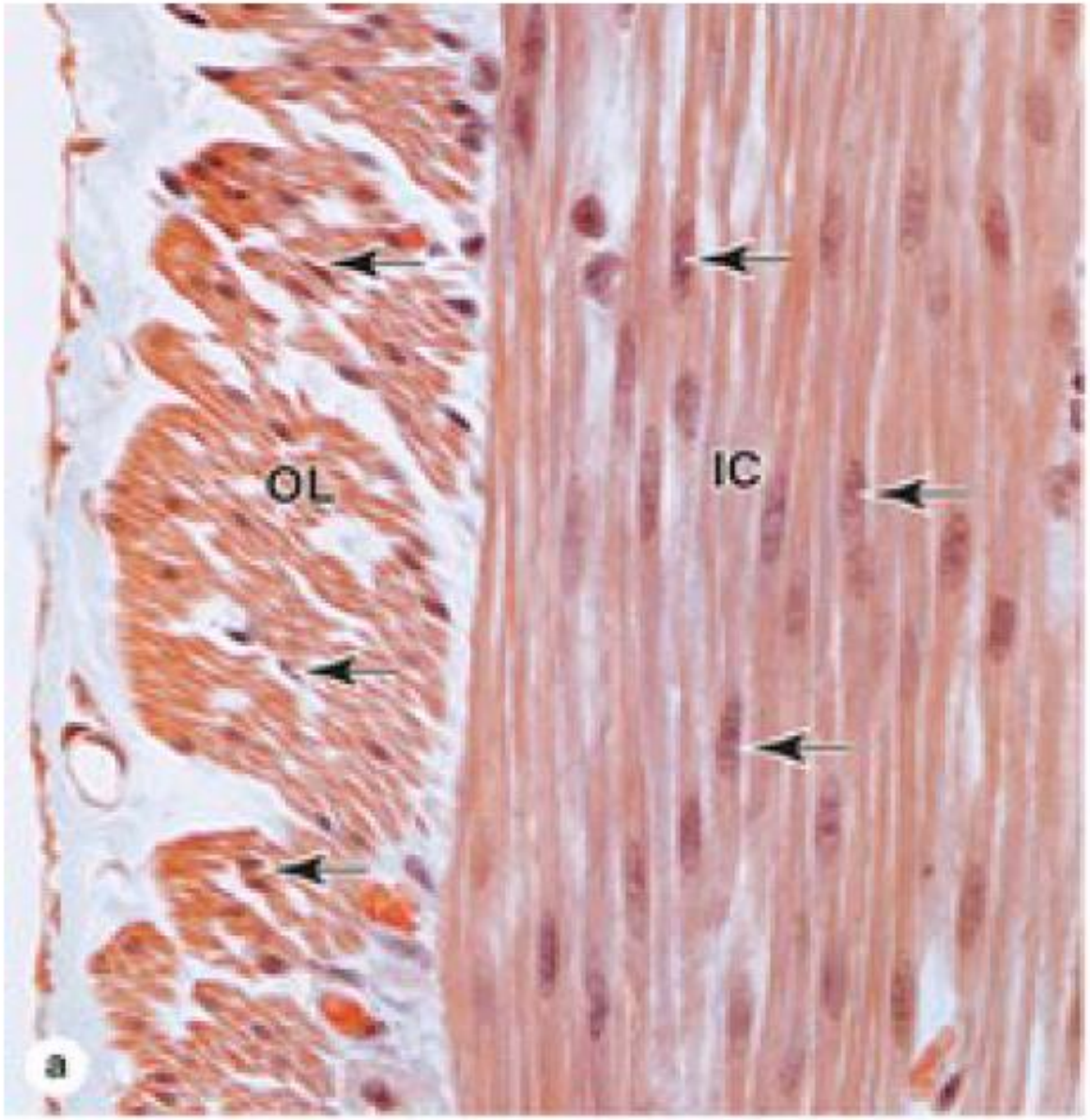
Smooth Muscle

- Slow and steady contraction.
- Under the control of autonomic nerves and various hormones.
- Present in blood vessels, digestive, respiratory, urinary, and reproductive tracts.
- Fibers of smooth muscle are elongated, tapering, and unstriated cells.
- Enclosed by an endomysium (a network of type I and type III).
- Length is 20 µm - 500 µm.



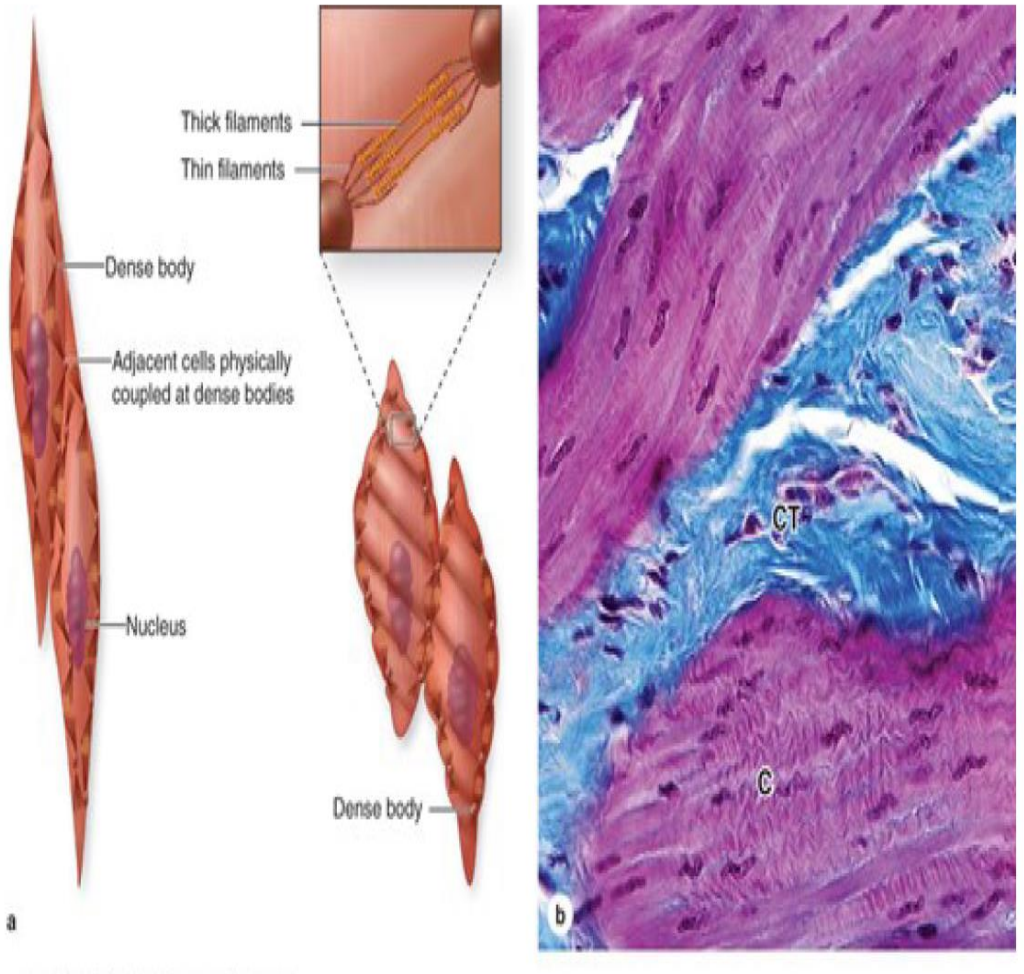
Smooth Muscles





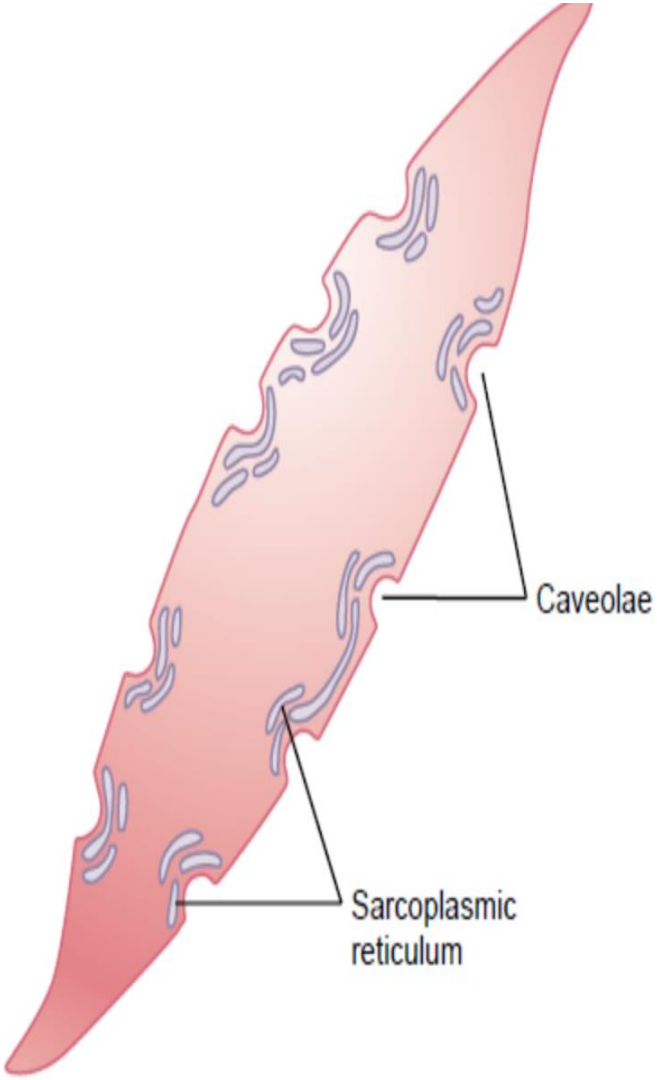
Characteristics and Contraction

- Dense bodies (similar to Z discs) is located in the cytoplasm and at the cell membrane
- Both thin filaments and intermediate (for adhesive junctions between cells).
- myosin filaments have a less regular arrangement and fewer crossbridges.
- Bundles of thin and thick myofilaments crisscross the sarcoplasm obliquely.
- Mitochondria, glycogen granules, and Golgi complexes located centrally near nucleus.



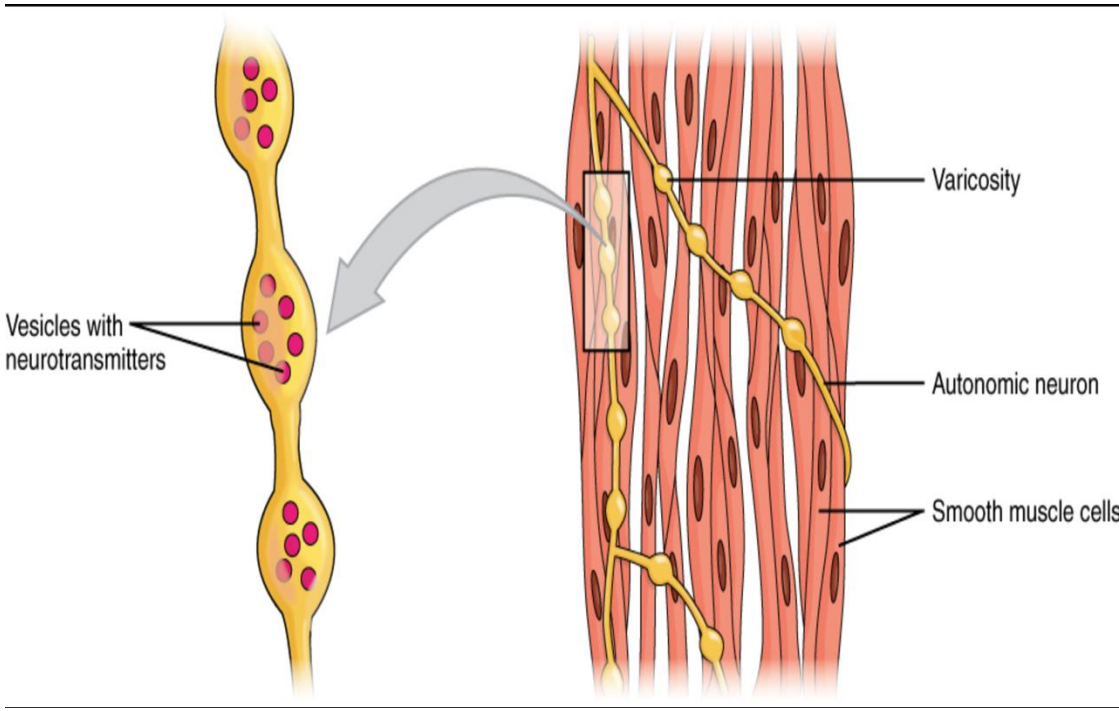
Characteristics and Contraction

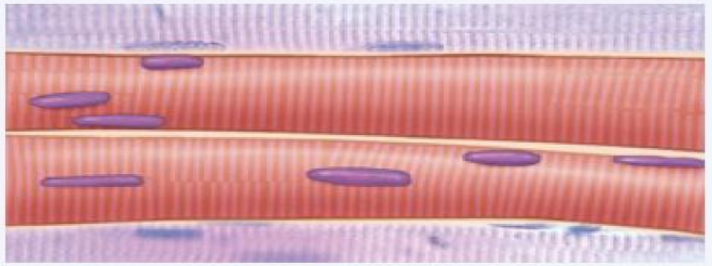
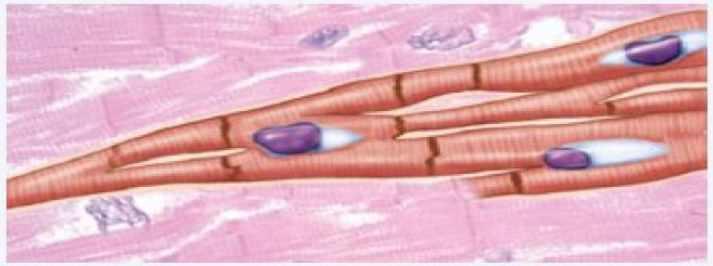
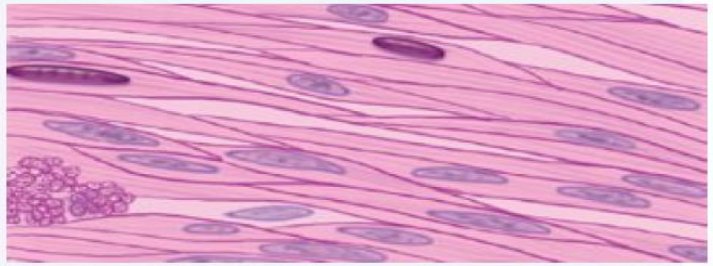
- Rudimentary sarcoplasmic reticulum
- Rich in gap junction.
- Caveolae are small plasmalemma invaginations which contain signaling components (ion channels).
- **NO** troponin and tropomyosin instead there are calmodulin and Ca^{2+} -sensitive myosin light-chain kinase (MLCK)



Smooth Muscle

- Lack well-defined neuromuscular junctions
- Axons of autonomic nerves have periodic swellings close to muscle fibers----synaptic vesicles----- acetylcholine or norepinephrine ---binds receptors in many muscle cells.
- Stimulation is propagated via gap junctions------ contract synchronously



	Skeletal Muscle	Cardiac Muscle	Smooth Muscle
			
Fibers	Single multinucleated cells	Aligned cells in branching arrangement	Single small, closely packed fusiform cells
Cell/fiber shape and size	Cylindrical, 10-100 µm diameter, many cm long	Cylindrical, 10-20 µm diameter, 50-100 µm long	Fusiform, diameter 0.2-10 µm, length 50-200 µm
Striations	Present	Present	Absent
Location of nuclei	Peripheral, adjacent to sarcolemma	Central	Central, at widest part of cell
T tubules	Center of triads at A-I junctions	In dyads at Z discs	Absent; caveolae may be functionally similar
Sarcoplasmic reticulum (SR)	Well-developed, with two terminal cisterns per sarcomere in triads with T tubule	Less well-developed, one small terminal cistern per sarcomere in dyad with T tubule	Irregular smooth ER without distinctive organization
Special structural features	Very well-organized sarcomeres, SR, and transverse tubule system	Intercalated discs joining cell, with many adherent and gap junctions	Gap junctions, caveolae, dense bodies
Control of contraction	Troponin C binds Ca^{2+}, moving tropomyosin and exposing actin for myosin binding	Similar to that of skeletal muscle	Actin-myosin binding occurs with myosin phosphorylation by MLCK triggered when calmodulin binds Ca^{2+}

Connective tissue organization	Endomysium, perimysium, and epimysium	Endomysium; subendocardial and subpericardial CT layers	Endomysium and less-organized CT sheaths
Major locations	Skeletal muscles, tongue, diaphragm, eyes, and upper esophagus	Heart	Blood vessels, digestive and respiratory tracts, uterus, bladder, and other organs
Key function	Voluntary movements	Automatic (involuntary) pumping of blood	Involuntary movements
Efferent innervation	Motor	Autonomic	Autonomic
Contractions	All-or-none, triggered at motor end plates	All-or-none, intrinsic (beginning at nodes of conducting fibers)	Partial, slow, often spontaneous, wavelike and rhythmic
Cell response to increased load	Hypertrophy (increase in fiber size)	Hypertrophy	Hypertrophy and hyperplasia (increase in cell/fiber number)
Capacity for regeneration	Limited, involving satellite cells mainly	Very poor	Good, involving mitotic activity of muscle cells

Regeneration Of Muscle Tissue

Skeletal muscle:

- The multinucleated cells cannot undergo mitosis
- Mesenchymal satellite cells lying inside the external lamina can participate in limited regeneration.

Cardiac muscle:

- lacks satellite cells
- Very little regenerative capacity beyond early childhood.
- Defects or damage replaced by proliferating fibroblasts and CT formation leading to myocardial scars.

Smooth muscle:

- Is capable of a more active regenerative response.
- Can undergo mitosis and replace the damaged tissue.

›› MEDICAL APPLICATION

The most common injury sustained by cardiac muscle is that due to **ischemia**, or tissue damage due to lack of oxygen when coronary arteries are occluded by heart disease. Lacking muscle satellite cells, adult mammalian cardiac muscle has little potential to regenerate after injury. However, certain fish and amphibians, as well as newborn mice, do form new muscle when the heart is partially removed, despite the lack of satellite cells. Research on the possibility of mammalian **heart muscle regeneration** builds on work with the animal models, focusing primarily on the potential of mesenchymal stem cells to form new, site-specific muscle.