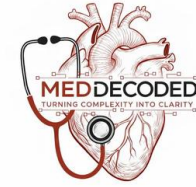


بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



الجراح



HISTOLOGY

FINAL | Lecture 9 + 10

وَلَقَدْ خَلَقْنَا الْإِنْسَانَ وَنَعَلَهُمَّا تَوْسُوسًا بِهِ نَفْسُهُ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ

Muscle Tissue

Written by : Yaman Khalil
Yamen Al-jarrah

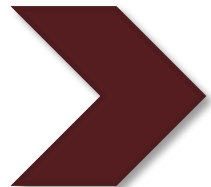


Reviewed by : Nezar Al-Sabatin

Color coding used in the modified:



Black: the original slides



Maroon: the doctor's explanation/words



Gray: additional information and explanation



Red: important information

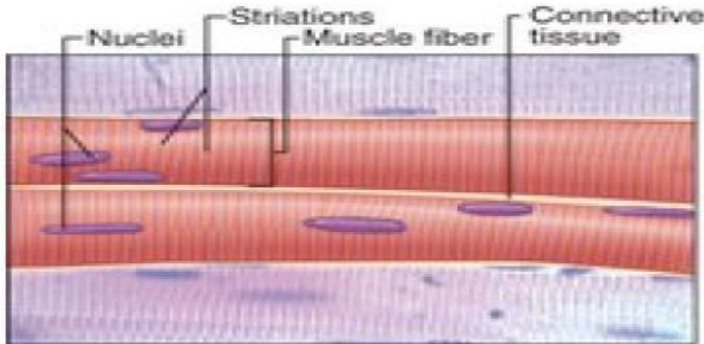
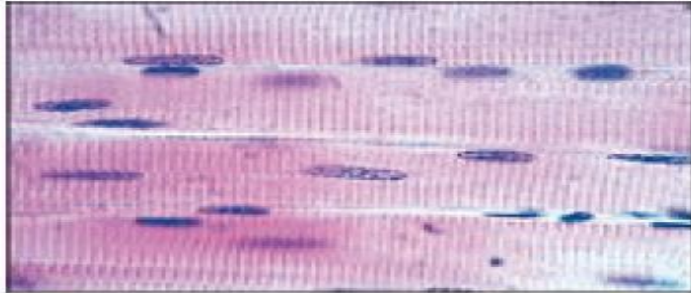
A microscopic image of skeletal muscle tissue, showing large, multinucleated, striated muscle fibers arranged in a regular, parallel pattern. The fibers are separated by connective tissue, and the nuclei are located at the periphery of the fibers. The overall appearance is that of a highly organized, contractile tissue.

Muscle Tissue Histology

Type Of Muscles Tissue

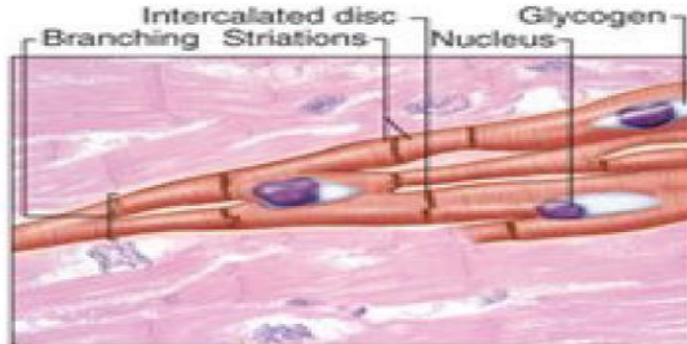
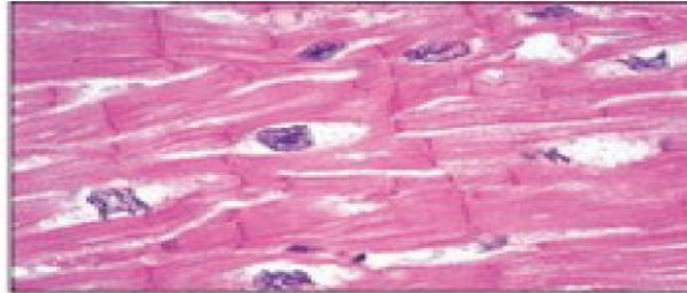
All the images are H&E stained

Skeletal muscle



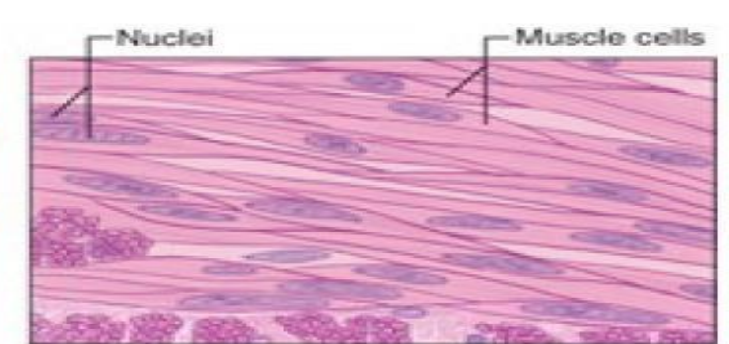
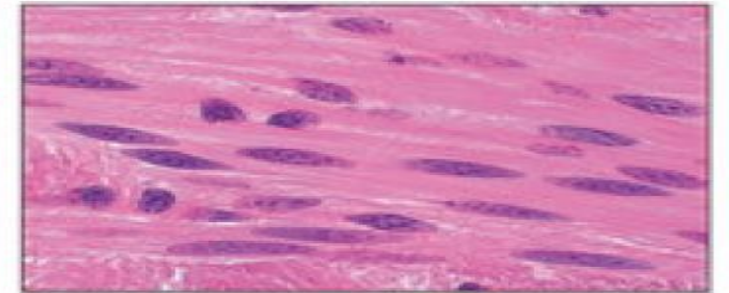
(a) Skeletal muscle

Cardiac muscles



(b) Cardiac muscle

Smooth muscles



(c) Smooth muscle

Source: Anthony L. Mescher: Junqueira's Basic Histology: Text and Atlas, 15th Edition. Copyright © McGraw-Hill Education. All rights reserved.

Longitudinal section, you won't see striations on cross-section samples.

Types

- **Skeletal muscle:** bundles of **very long, multinucleated** cells with **cross-striations**. Their contraction is **quick, forceful**, and usually under **voluntary** control.

The nuclei are peripheral.

Very unique, only found in the heart.

- **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**.

The nuclei are rounded, relaxed and centrally located. Cells are uninucleated (according to our textbook).

Found almost everywhere in the body. Responsible for involuntary functions in the body. It works with the ANS (autonomic nervous system).

- **Smooth muscle:** consists of collections of fusiform cells that **lack striations** and have **slow, involuntary** contractions.

Central nuclei, no branching of cells.

- Skeletal muscles aren't associated with the skeleton only, it also connects to cartilage and the connective tissue related to the skeletal system.
- An example of muscles that have a relation with connective tissue are muscles of facial expression; all of their muscle insertions are on connective tissue on the skin, that's why they can move the skin and make different facial expressions.
- Both skeletal muscles and cardiac muscles are cross-striated, but it's way more visible and evident in skeletal muscles.
- In skeletal muscle tissue pictures, the nuclei might look centered, but they're actually peripheral and they look that way because of the sectioning of the sample.

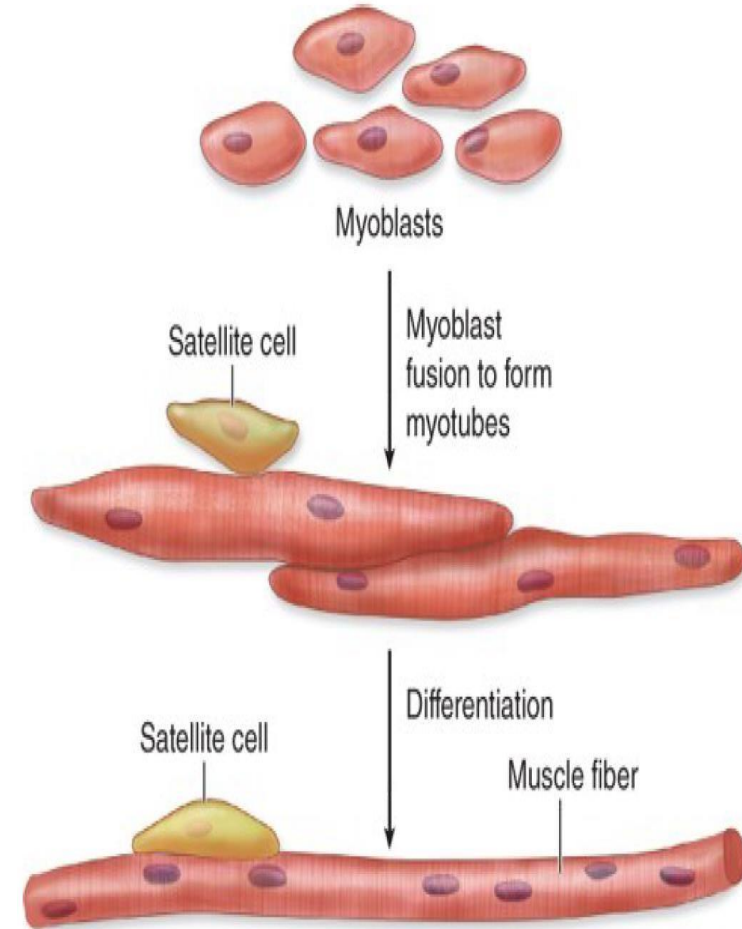
Skeletal Muscle development

Note: all muscle types originate from mesenchyme, the mesenchymal stem cells will differentiate into myoblasts. These myoblasts will fuse to form myotubes, and these myotubes will create longer muscles fibers later.

Skeletal (or striated) muscle:

- Long, cylindrical multinucleated cells (10-100 μm diameter). It's multinucleated because of the fused myoblasts to form the myotube.
- Mesenchymal myoblasts--fuse--myotube--differentiate--striated muscle fibers.
- Satellite cells: A small population of reserve progenitor cells

Some myoblasts do not differentiate and incorporate with the myotube, instead they retain their stemness and they're called satellite cells, these are found near the myotubes. Satellite cells could help when the muscles fibers are injured, these cells can differentiate and multiply to try and compensate for the lost muscle tissue.



Source: Anthony L. Mescher: Junqueira's Basic Histology: Text and Atlas, 15th Edition. Copyright © McGraw-Hill Education. All rights reserved.

Organization of skeletal muscle

Muscle tissue are organized by connective tissue:

- **Epimysium** Most external, thick and inelastic

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

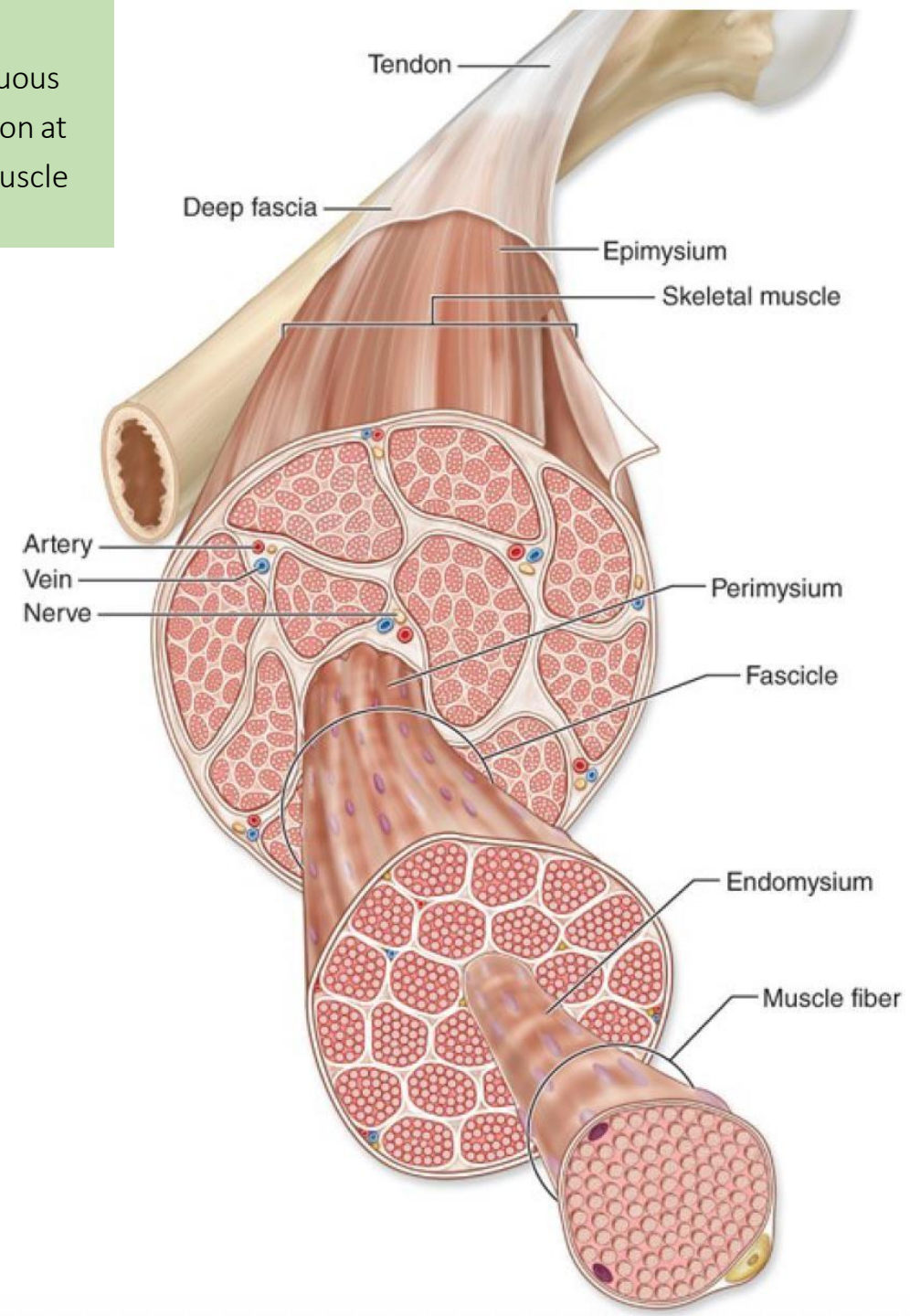
- **Perimysium** In the middle

Thin connective tissue layer that immediately surrounds each bundle of muscle fibers (fascicle)

- **Endomysium** Internal

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

- 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).



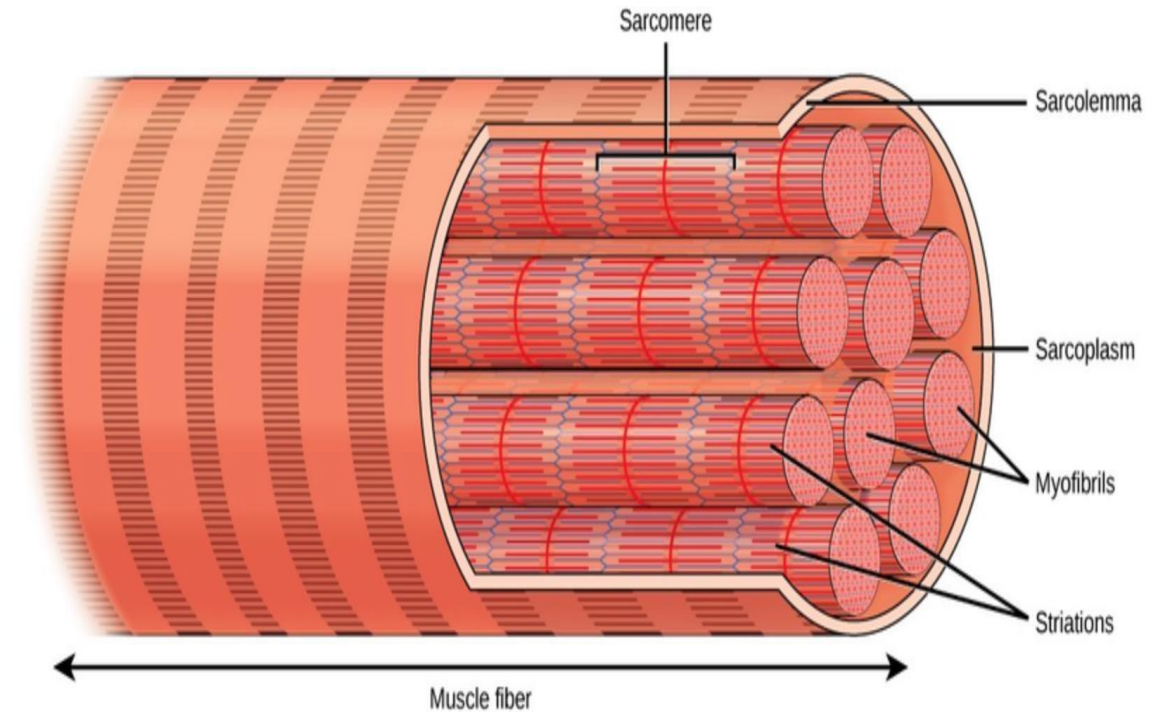
Organization of skeletal muscle

- The epimysium supports and aligns muscle fibers along the muscle's long axis. Major blood vessels and nerves pierce this connective tissue layer to reach the interior, where they supply and innervate the muscle fibers.
- The fascicles are made of several muscle fibers grouped together, they are surrounded and separated by the perimysium.
- Note: The Perimysium is quite thinner than the Epimysium.
- Each individual muscle fiber inside the fascicle is further surrounded and protected by the Endomysium.

Skeletal Muscle Fiber

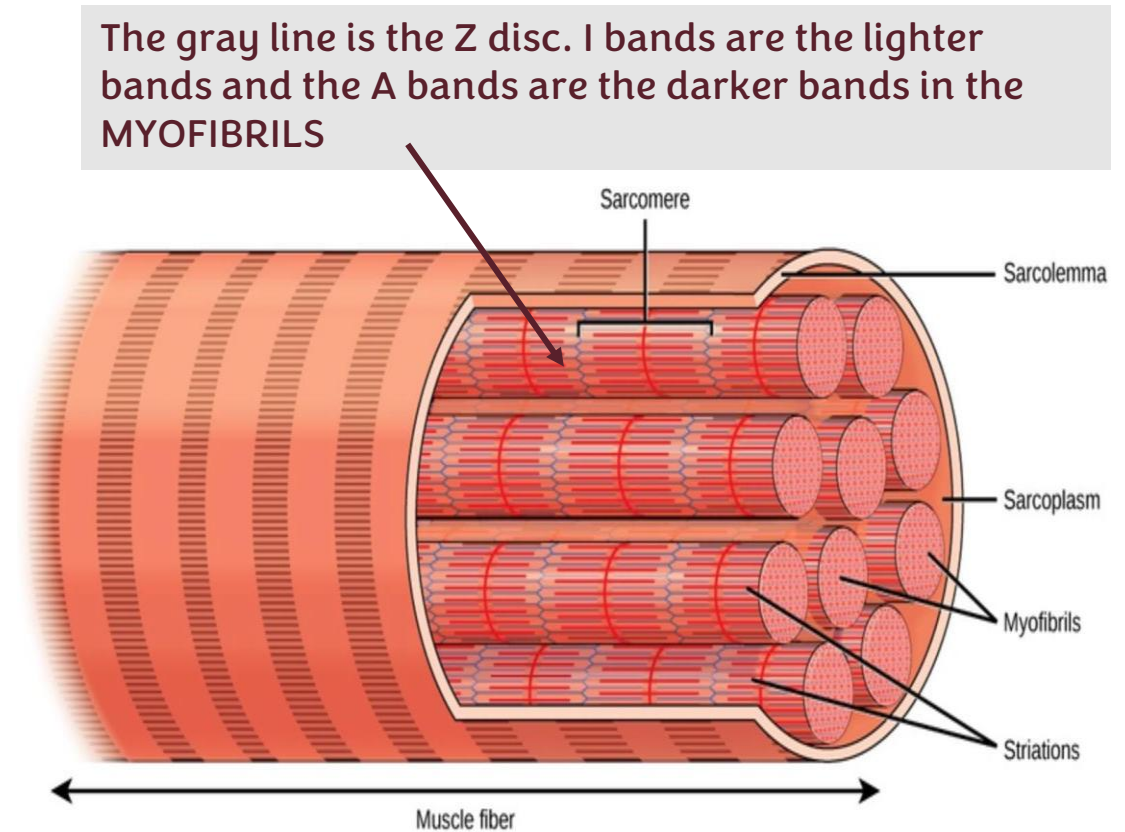
Skeletal muscles are cross-striated.

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



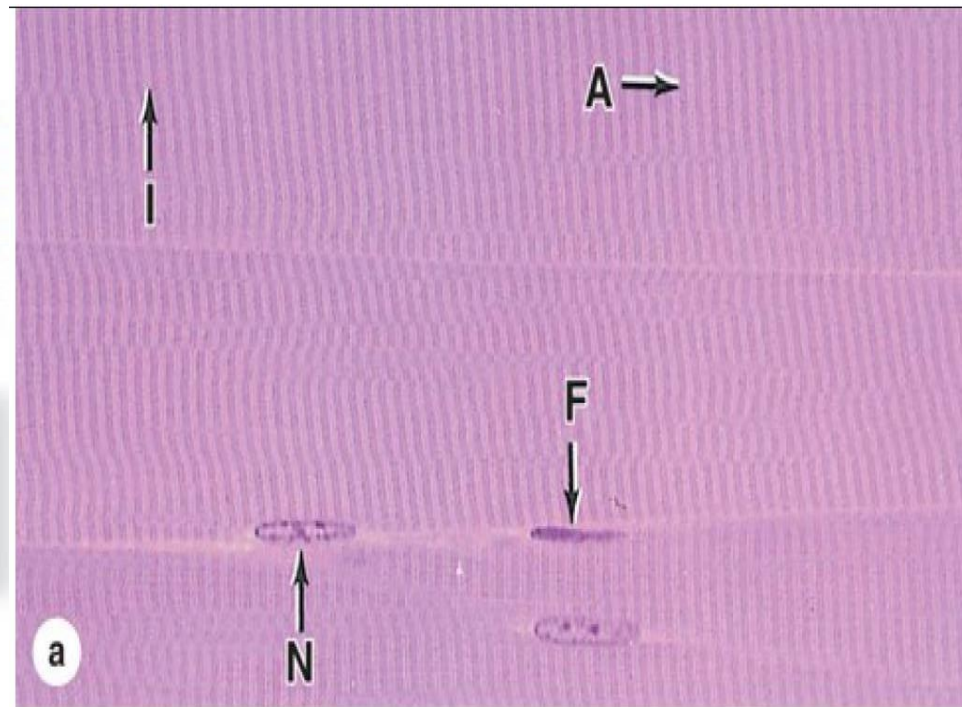
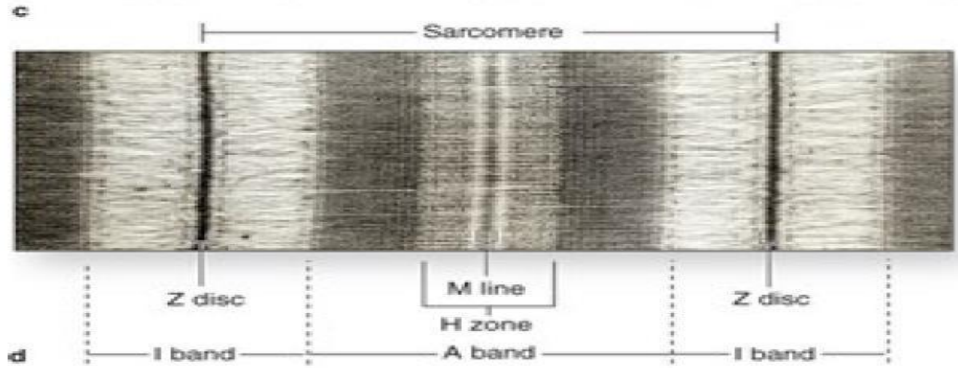
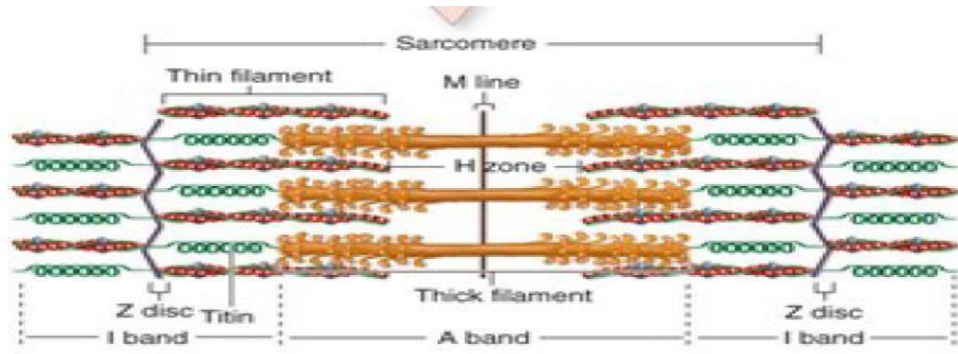
Organization Within Muscle Fibers

- 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.

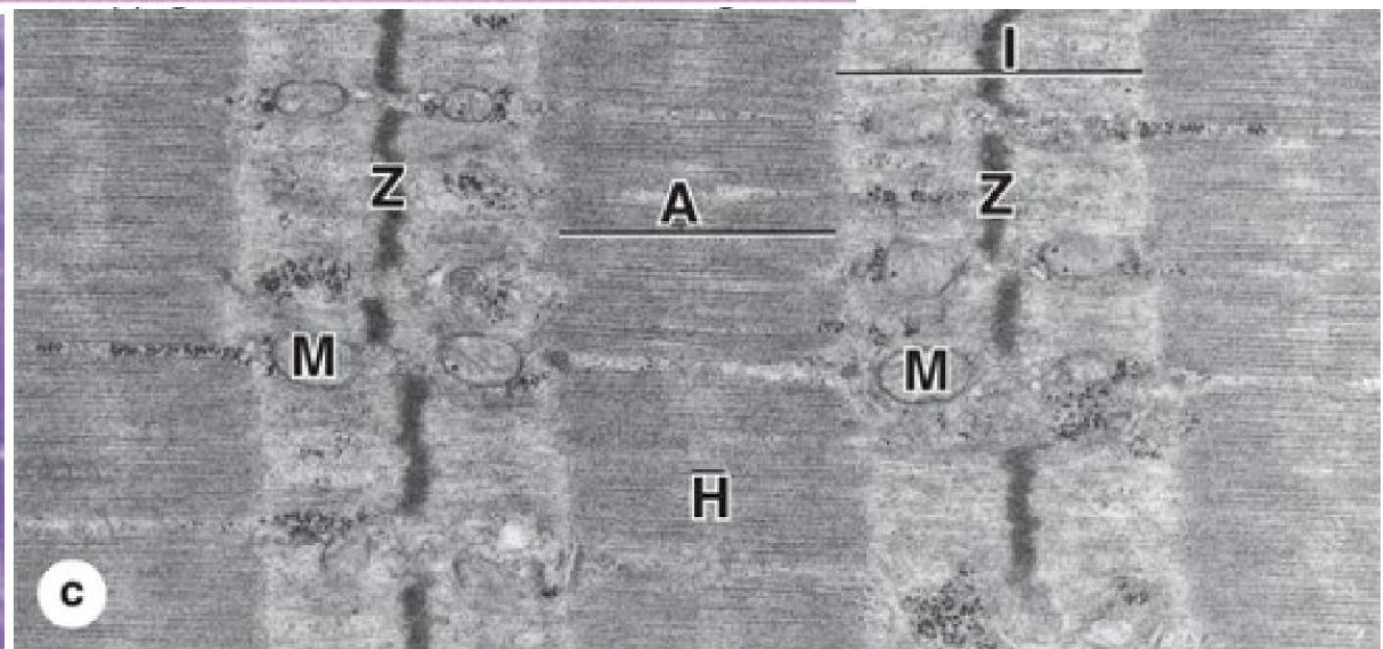
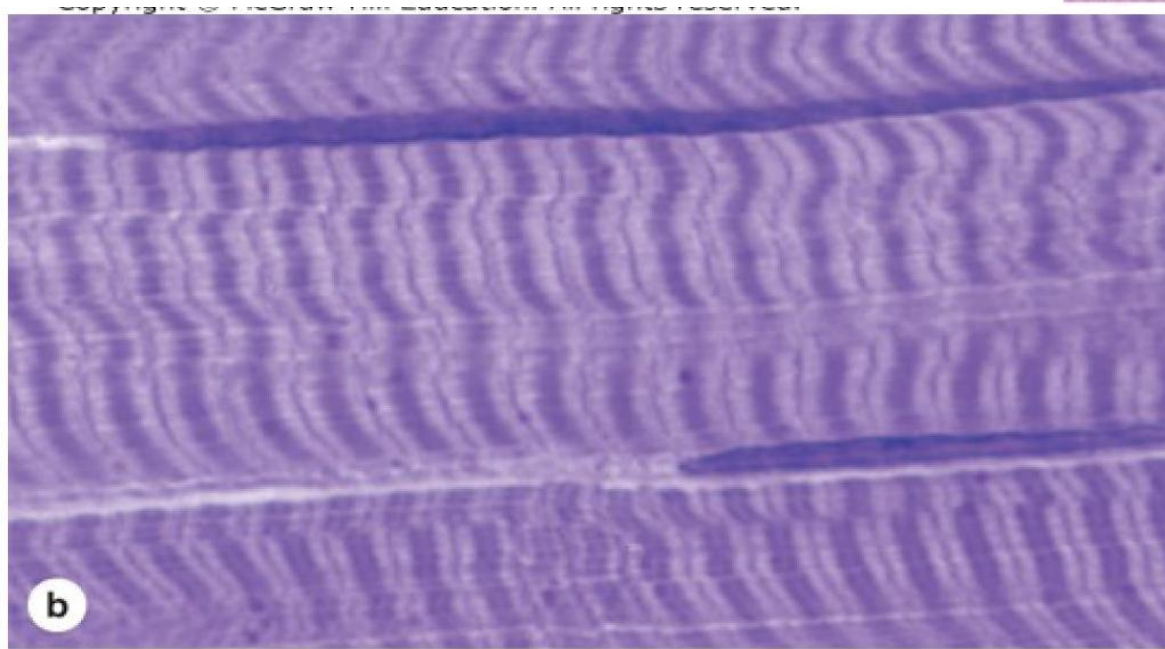


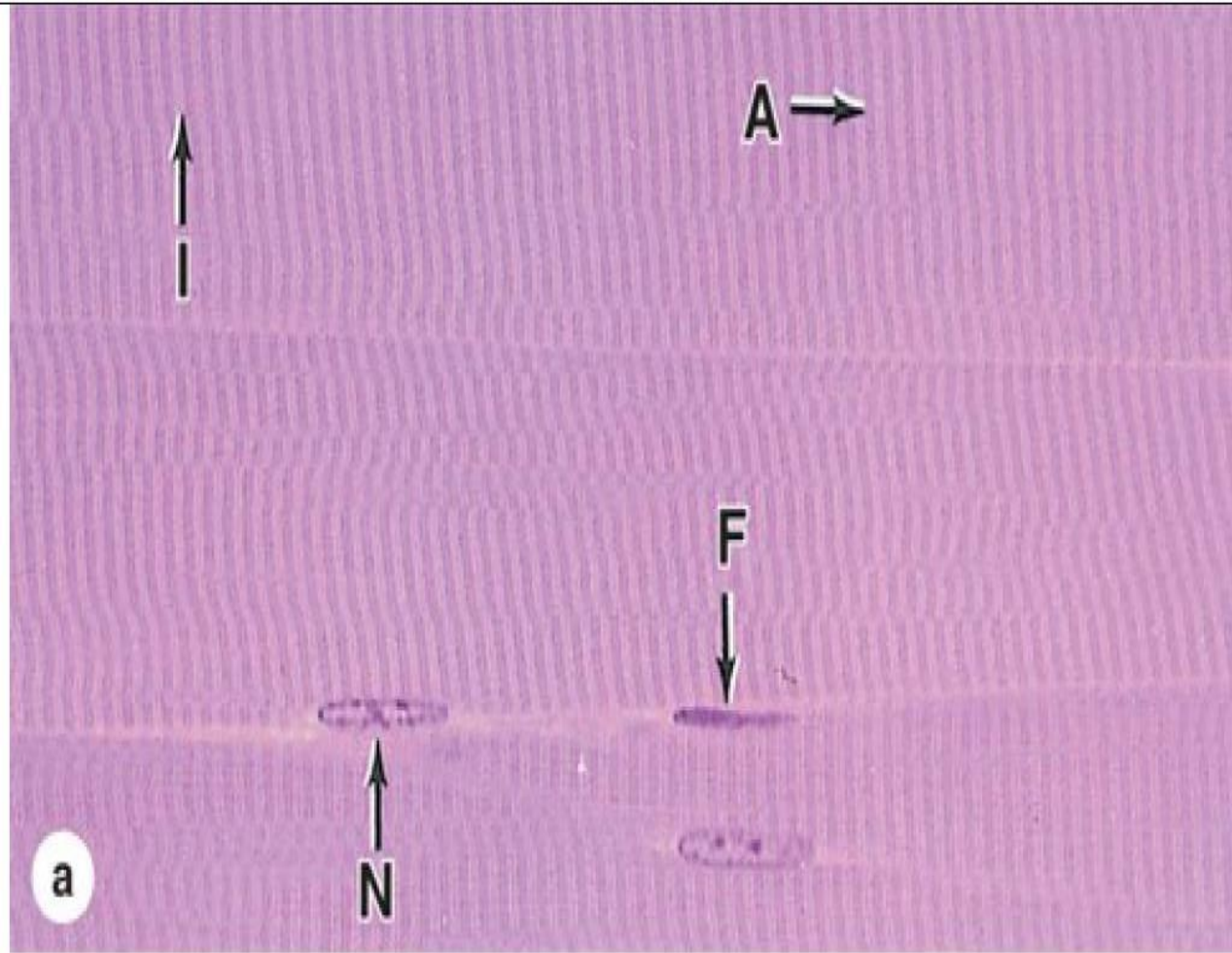
Organization Within Muscle fibers

- The sarcoplasm contains myofibrils, which are made of several elements, mainly the thin and thick filaments.
- The arrangement of myofibrils within the sarcoplasm is the reason of the cross-striation in muscle fibers.



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



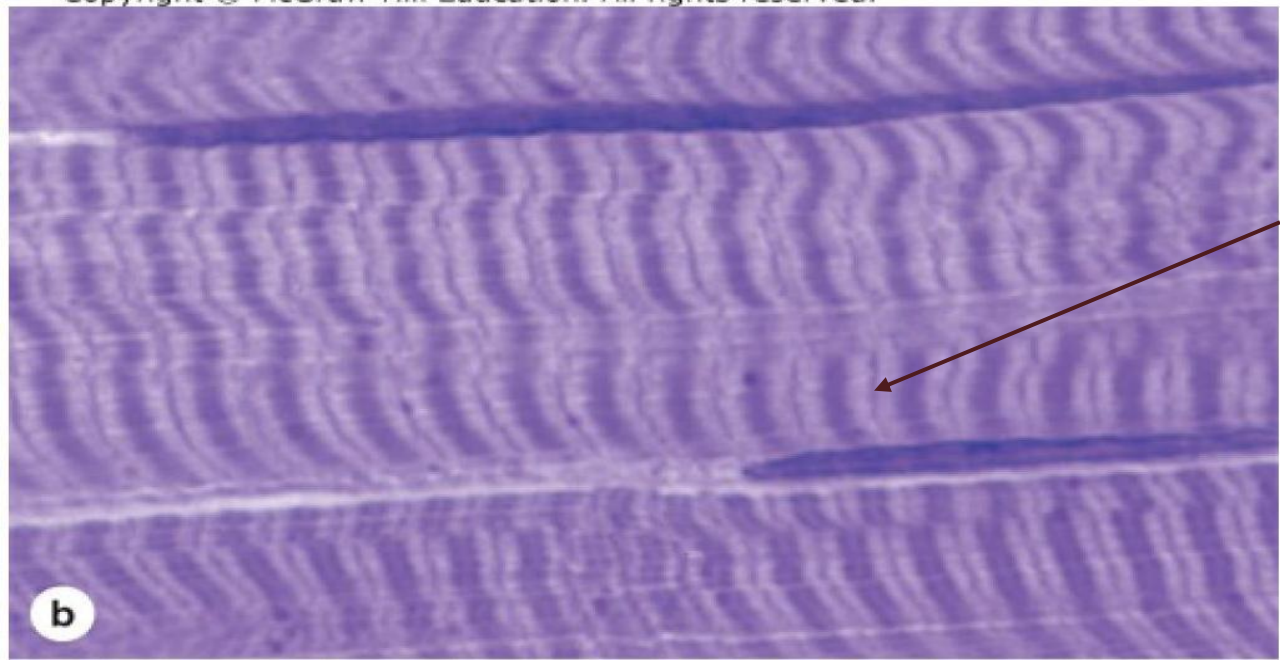


We have 2 different nuclei here, one of them is muscle fibers (N) and the other is the nuclei of fibroblasts (F). Fibroblasts are responsible of secreting the elements of the endomysium.

We can see three muscle fibers here (from up to down)

Stained with H&E || low magnification

This is a longitudinal section of the skeletal muscle , we know that because the cross striation is visible .



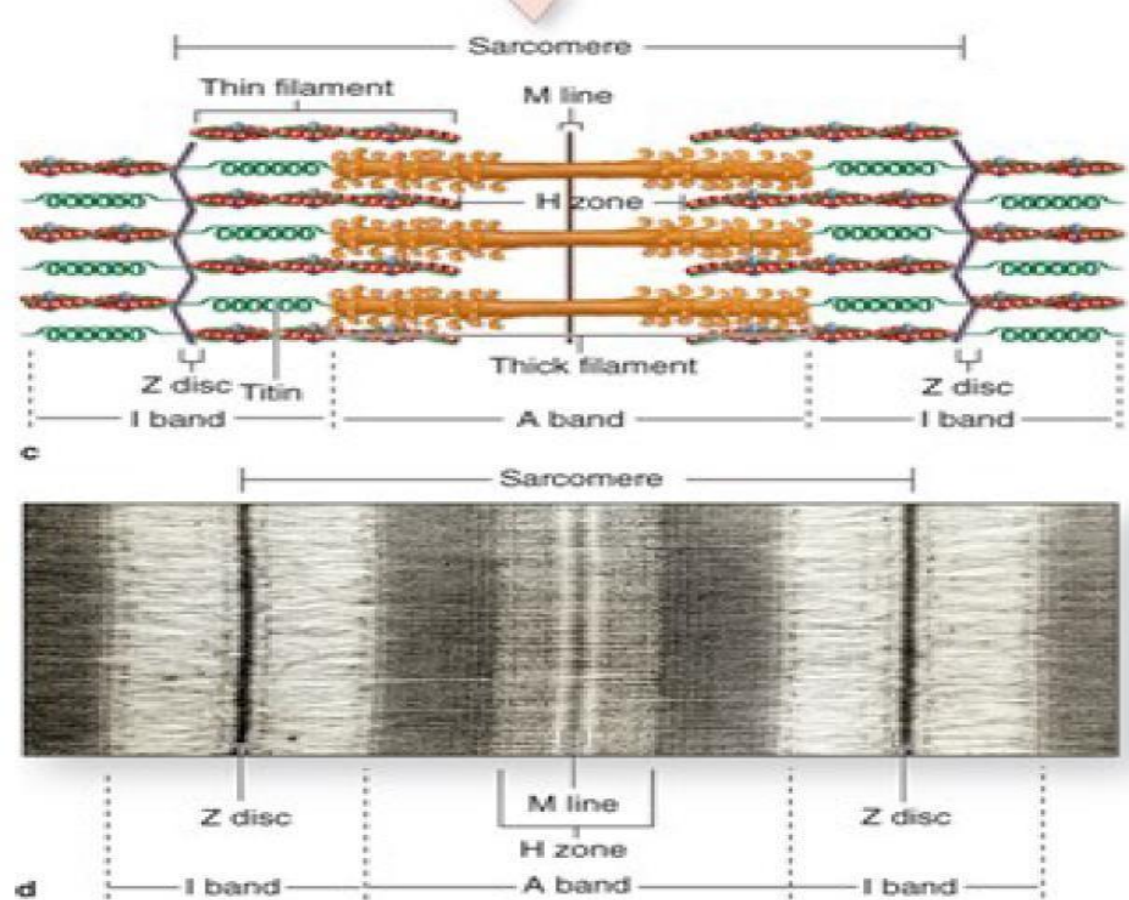
In the middle of the light band (I band) , you can spot a thin line which is the Z disc.

H&E stained || high magnification.

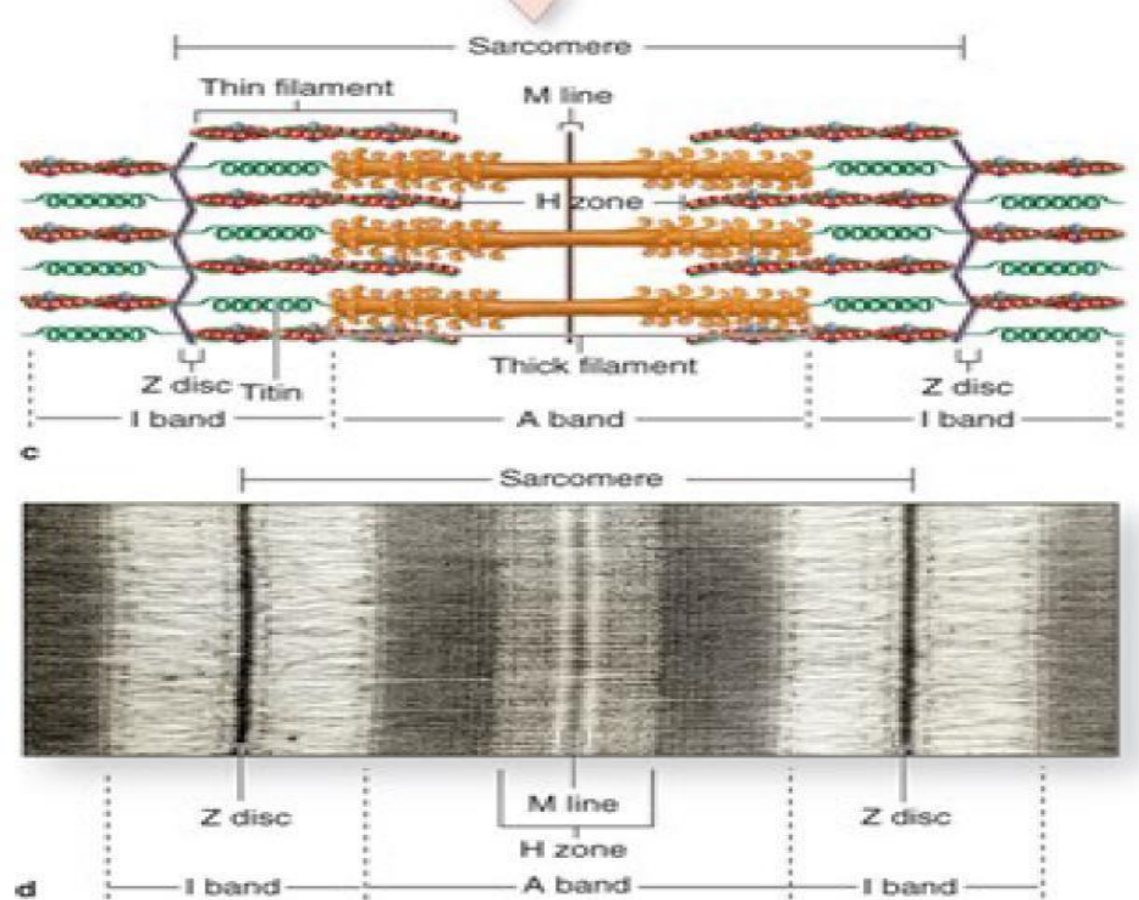
You can easily recognize the striation here!

This is a diagram of the sarcomere.

- The sarcomere extends between the 2 Z discs on the right and the left.
- The thin filaments are attached to the Z disc.
- The coiled structure (colored green in the diagram) is the Titin protein.
- The thick filaments are located in the middle of the sarcomere.
- The titin protein is attached to :
 - 1)The Z disc.
 - 2)The thick filament.



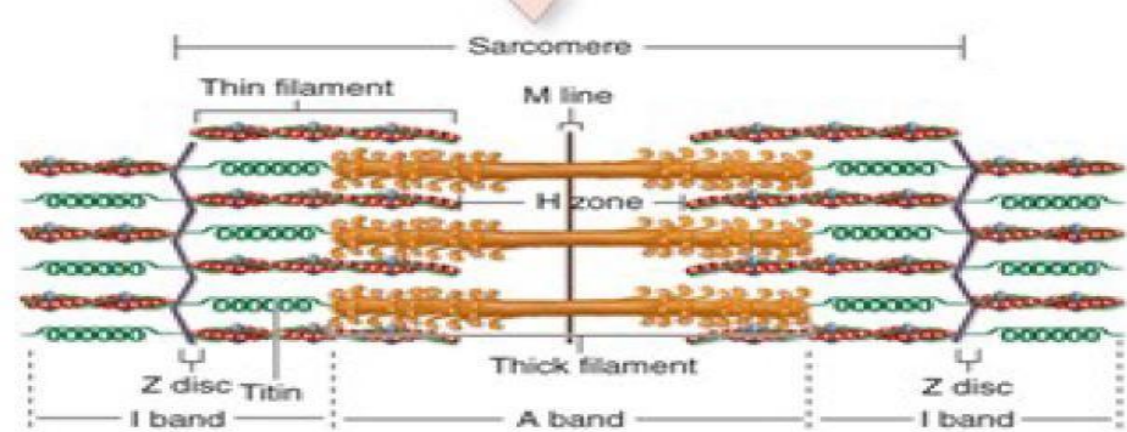
Note: Contraction of the muscles causes group contraction or shortening of sarcomeres and when the muscles relax, they will come back to normal.
Note (2): the thick filaments are **INDIRECTLY** attached to the Z disc (via Titin), while the thin filaments are **directly** attached to it.



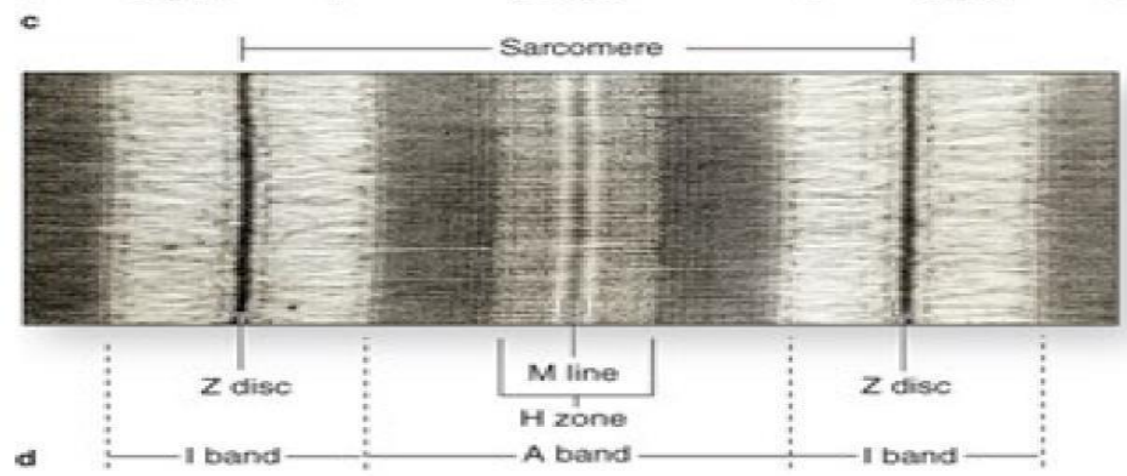
Note : The I band is the area occupied by the thin filaments, while the A band is the area occupied by the full length of the thick filaments, and a part of the thin filaments that is overlapping with the thick filaments.

Note (2): the Z disc bisects the I band.

- The thick filaments are in center of the sarcomere, while the thin filaments don't reach the center **DURING RELAXTION**. They **REACH** the center during contraction!!!
- The dark bands in the skeletal muscle fiber come from the thick filament, so the dark bands present where the thick filaments are.
- The (I band) is made of the thin filaments in addition to the titin protein (sometimes we may say thin filaments only for shortening).
- In the middle of the A band, there is an area only occupied by the thick filaments and it's called (H zone).
- The line bisecting the thick filaments is called the (M line). (a number of proteins are present in this location).

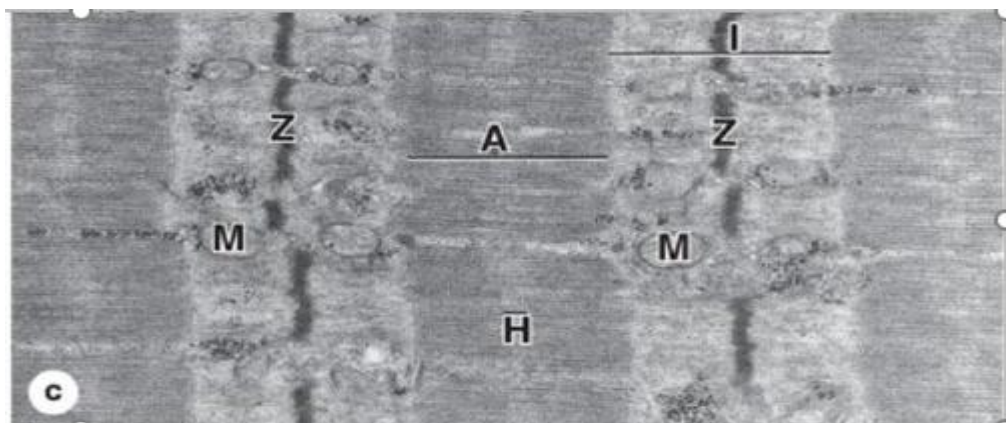


➤ The one full sarcomere is made of a full length A band, half an I band on the right and half an I band on the left.



In this TEM image, you can see a lighter area within the A band, which is the H zone. It appears like that because it only contains thick filaments without thin filaments. The remainder of the A band (excluding H zone) is darker because it contains both thick filaments and the overlapping thin filaments, while the I band is the lightest color because it only contains thin filaments.

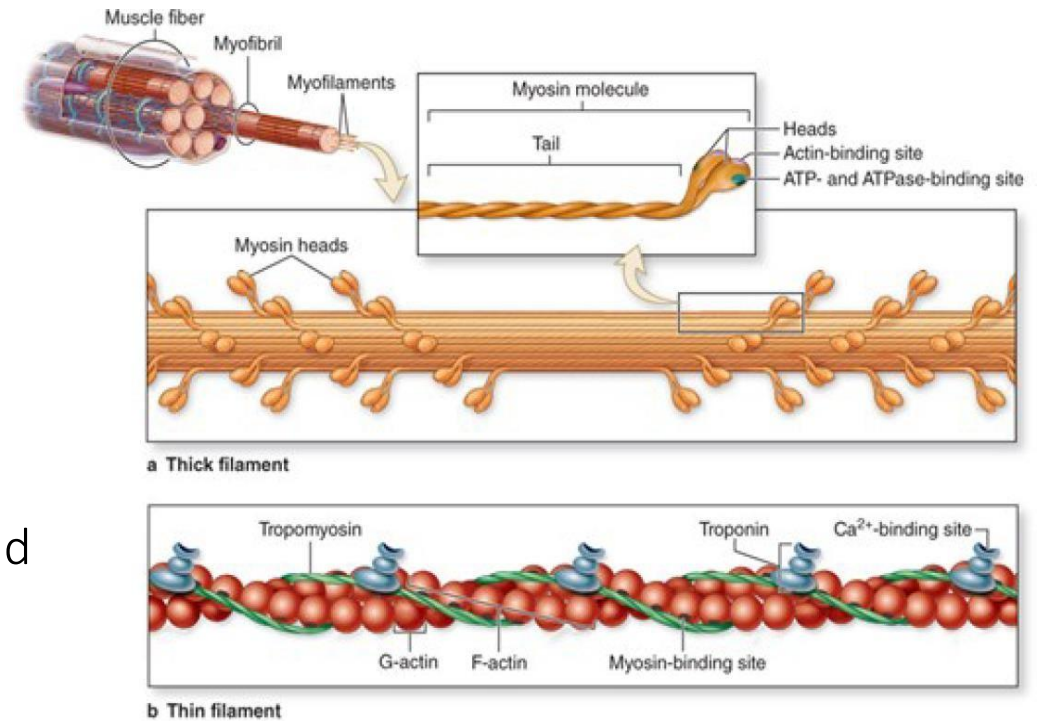
These images are taken from TEM.



In this image, we can see the mitochondria.

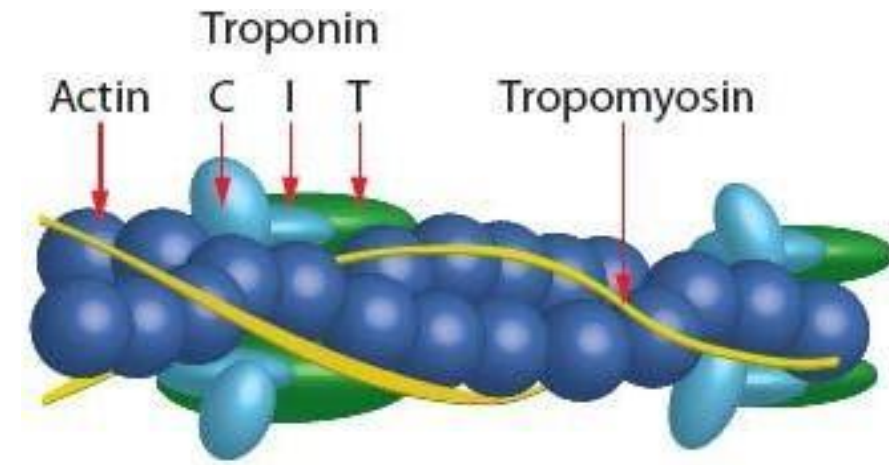
Myofilaments

- Composed of thick and thin filaments
- **Thick:** 200-500 myosin.
- Myosin is a large complex with two identical heavy chains and two pairs of light chains.
- Globular projections containing the four myosin light (**the two pairs**) 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.



- The myosin head has 2 binding sites, one for actin and the other for ATP, and that is what we need to contract the muscle.
- Contraction happens when the myosin heads bind with actin and ATP. conformational changes will lead to bending the myosin heads over the tail and then they drag the actin filaments to the center (the thin filaments contain actin, which means that during contraction, the thin filaments will be dragged to the middle of the sarcomere, this will be discussed later on slide 30). Then the actin will be released and it will go back to its normal location and that's when muscle relaxation happens.

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 Ca^{2+} ; and TnI, which regulates the actin-myosin interaction.

- We need calcium for contraction.
- This calcium will bind to troponin TnC subunit of the troponin

- From where does this calcium come?
It is usually stored in the smooth ER

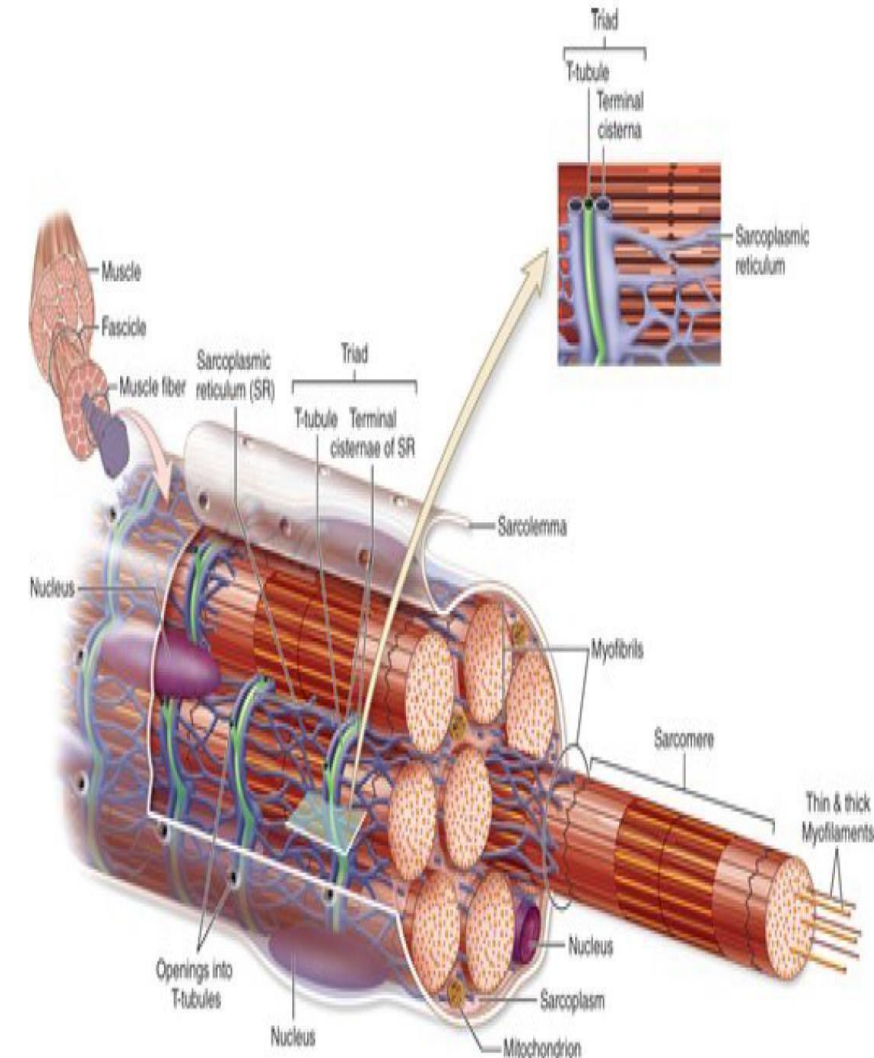
What does that mean?

We said that the muscle fibers are very long compared with conventional cell types. These fibers need calcium throughout the entire length of the myofibrils. This smooth ER has two spreads and reaches each individual myofibril. (There is a complex relationship between the SER and the myofilaments). The SER creates a complex structure with the aid of the sarcolemma (the plasma membrane of muscle fibers). This structure is created to ensure the uniform diffusion of calcium to the thin and thick filaments in the sarcomeres in order to contract at the same time.

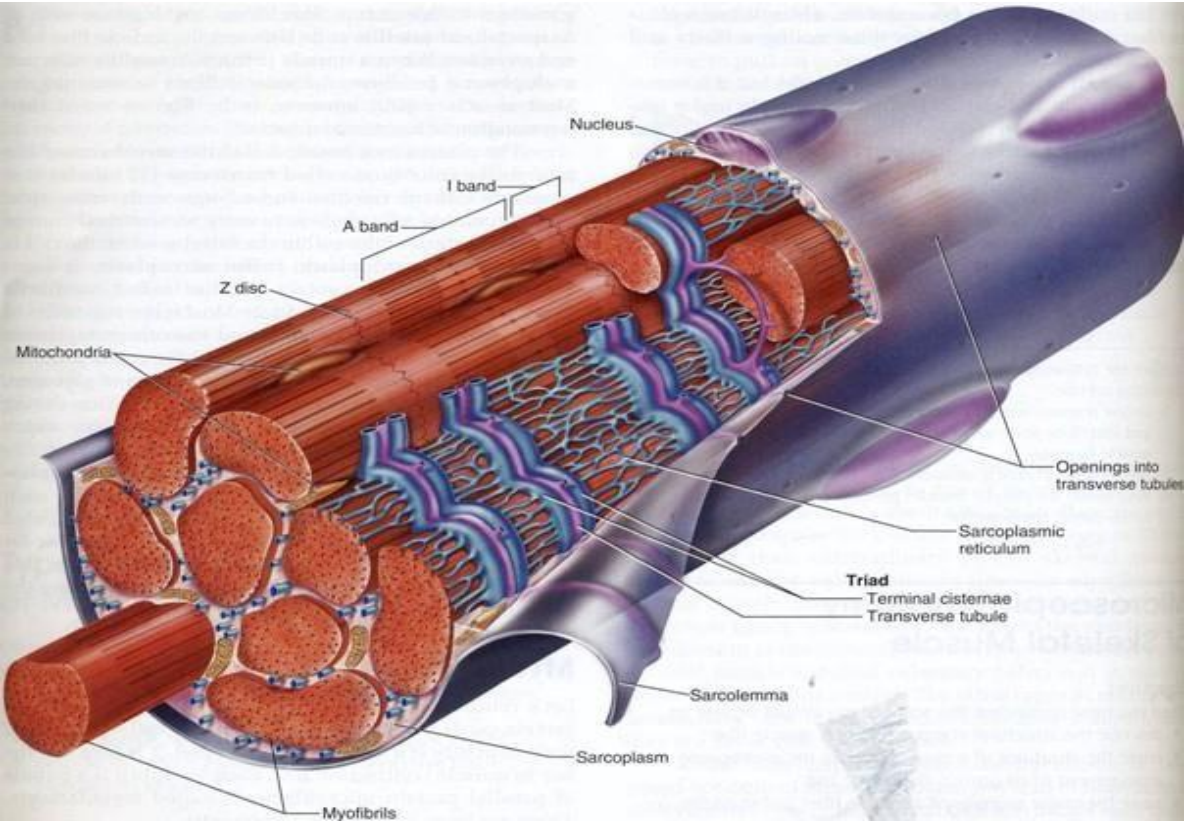
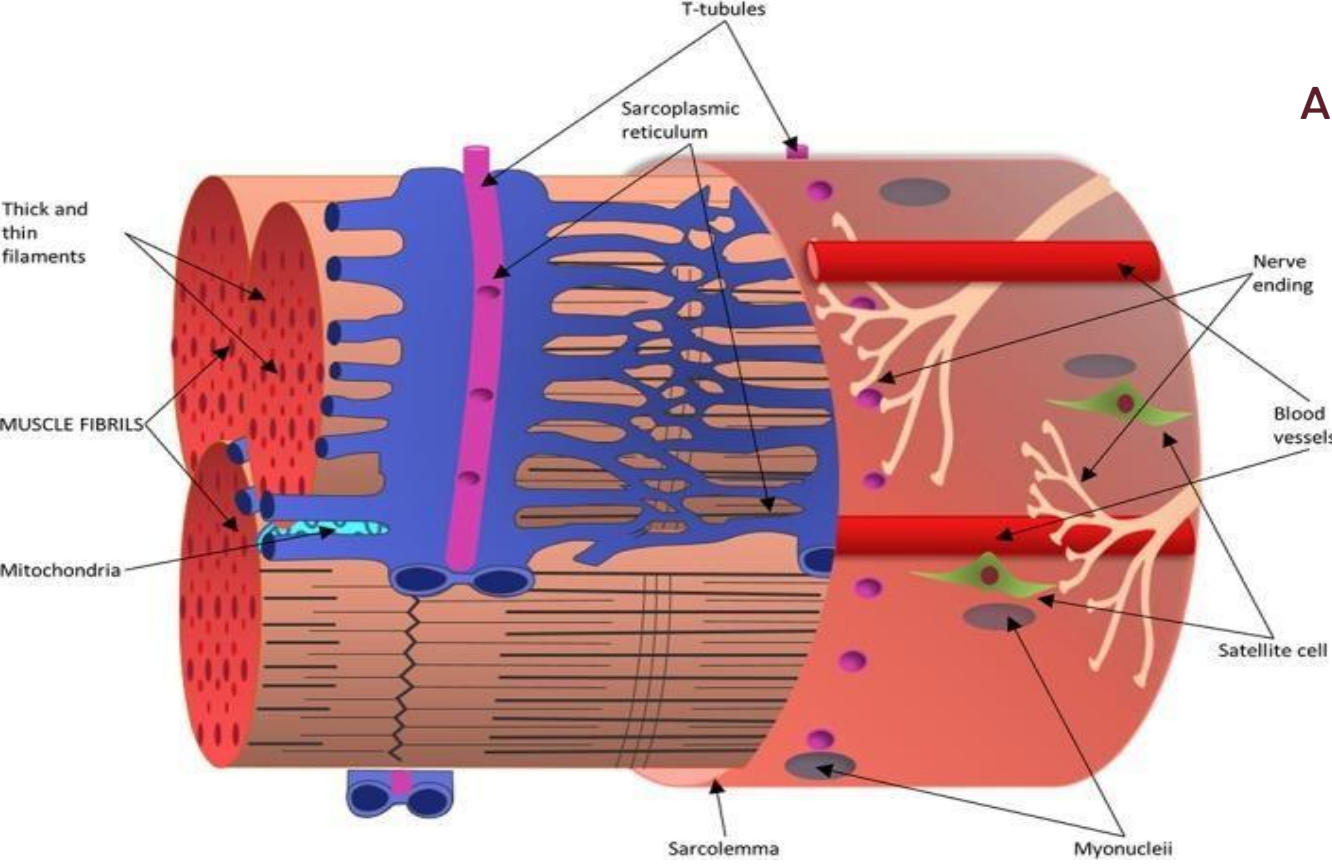
This arrangement is called the **Triad** (because there is **3** tubes in this structure). In the model in the next slide, we see purple color (**2** terminal cisternae - created by SER) and green color in between (**1** T-tubule - scattered throughout the entire length of the myofibril. It is a deep invagination of the sarcolemma. It - the sarcolemma - creates a tiny tunnel that reaches deeper in the sarcoplasm; this will ensure the uniform access of the action potential of the muscle fibers down to the sarcolemma so we can ensure the quick release of the calcium toward the myofibrils, so it can diffuse and bind to the troponin). The triad in skeletal muscles is the most sophisticated structure among the other two types (smooth and cardiac - later in the slides)

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**



As we see, the myofibrils are covered by the SER

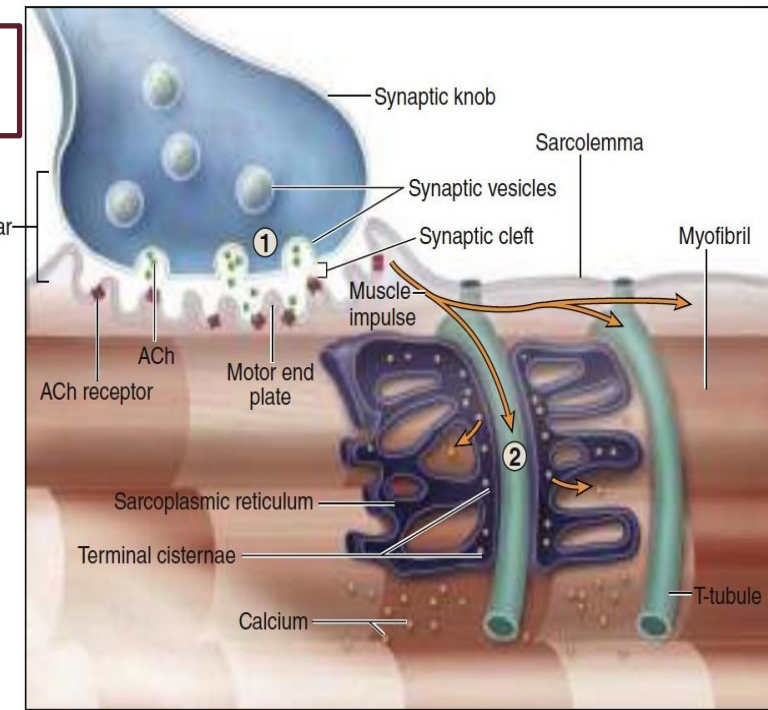


Innervation/contraction

The neuromuscular junction (NMJ) or (MEP)

- 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).

Neurons communicate with each other and with muscles through synapses.



The main purpose of the action potential in muscle fibers is to open calcium channels. The triad, especially the T-tubules, helps spread the action potential deep into the muscle fiber. This ensures a uniform release of calcium (Ca^{2+}), which is important for proper muscle contraction.

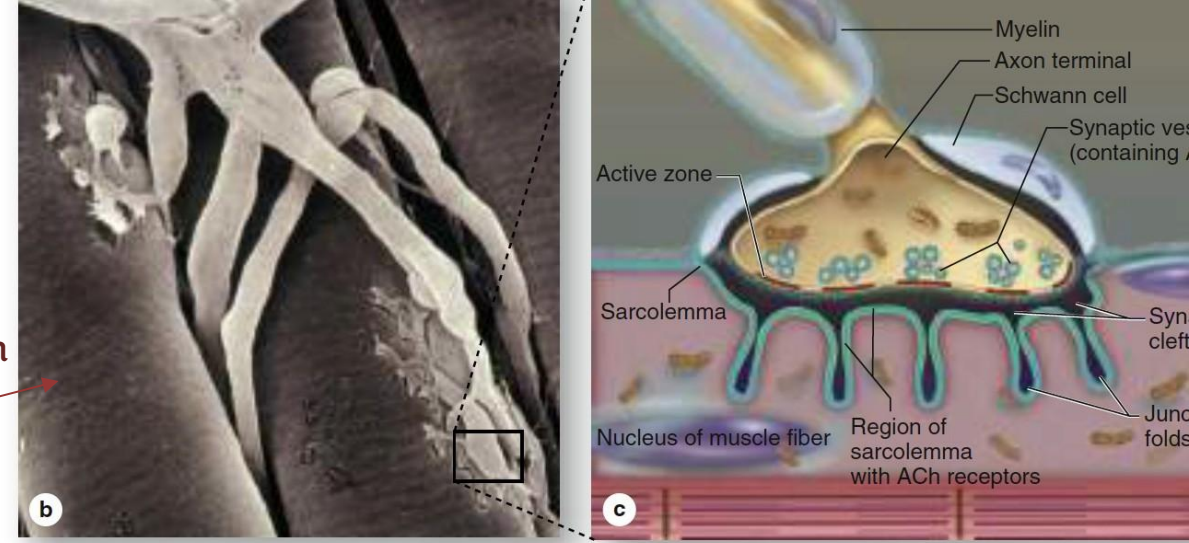
- The axon terminal contains mitochondria and numerous synaptic vesicles----neurotransmitter acetylcholine.
- Between the axon and the muscle is the synaptic cleft.
- Adjacent to the synaptic cleft---the sarcolemma---- deep junctional folds--- **greater postsynaptic surface area and more acetylcholine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

Innervation/contraction

Sarcolemma creates the junctional folds which increase the number of receptors.

b) This image was taken with SEM.

Skeletal muscle fiber



- Acetylcholine (the neurotransmitter) + 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 MEJs with one or many muscle fibers.
- Innervation of **single** muscle fibers by **single** motor neurons (**axon**) --- **precise** control of muscle activity --- extraocular muscles (**eye movements**).
- Larger muscles --- motor axons branch profusely --- **1 axon** innervate **100 or more** muscle fibers (**motor unit**).

Innervation/contraction

- **The motor unit: A group (number) of muscle fibers are innervated by a single axon.**
- **The more precise the muscle, the smaller its motor unit and vice versa**
(In general, the larger the muscle the less precise its function)
- **In the Extraocular muscles (muscles of moving the eye) each single muscle fiber is innervated by a single motor neuron (which means an axon)**
- **Large (bulky) muscles such as gluteus maximus and quadriceps femoris are less precise, so axons branch extensively** (each axon (motor neuron) may innervate 100 or even more muscle fibers).

Regardless the size of motor unit, each muscle fiber (skeletal muscles) must have its own MEP to deliver the action potential to it (no gap junctions)

The doctor said (by accident) that the motor unit is how many axon per muscle fiber which is incorrect because in the previous slide it is written that the extraocular muscles have a small motor unit which is not consistent with this.

Innervation/contraction

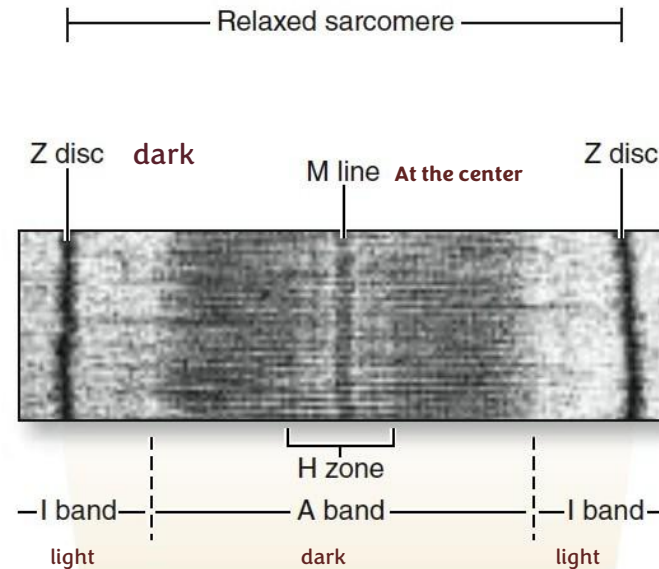
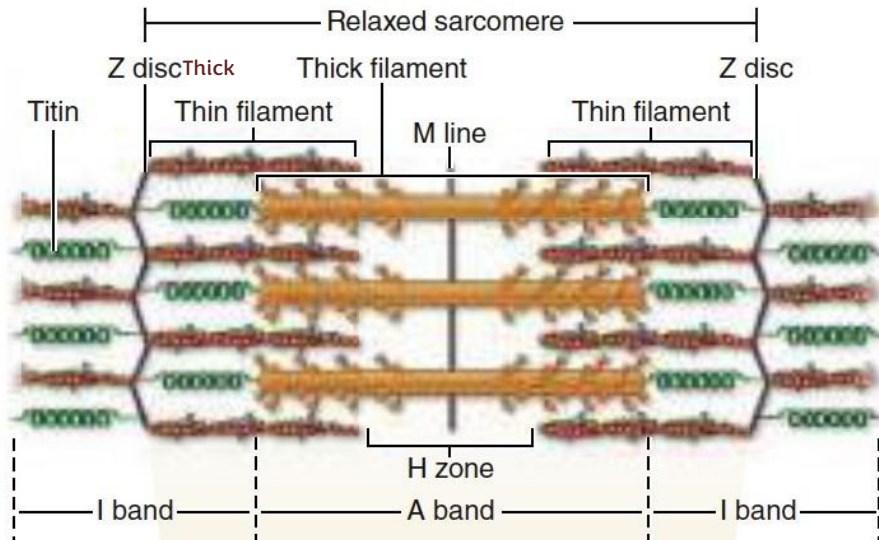
If a fiber receives an action potential, all the fiber contracts. But the fibers in a fascicle do not contract simultaneously

- 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. **Usually seen in the muscles of the back**
- 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



a Relaxed skeletal muscle

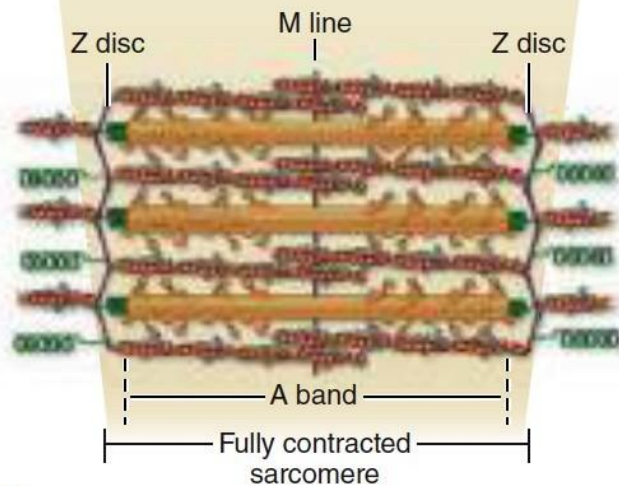


Contraction

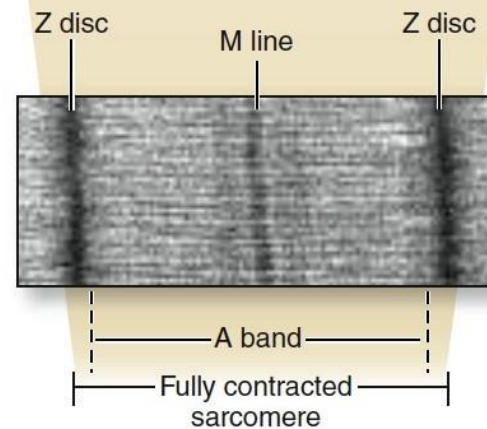
Contraction



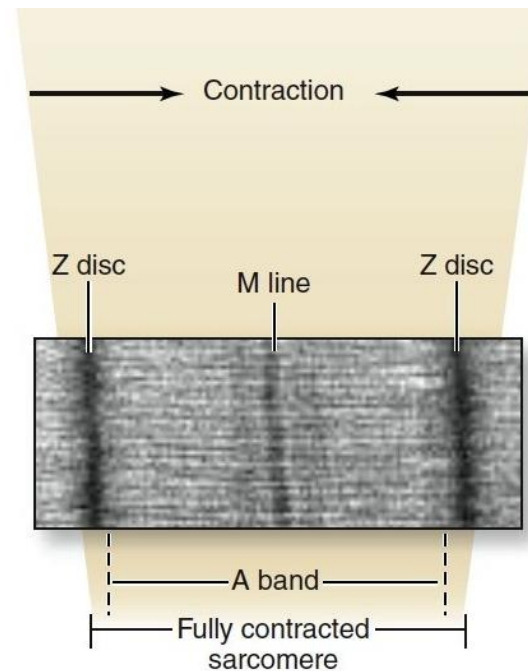
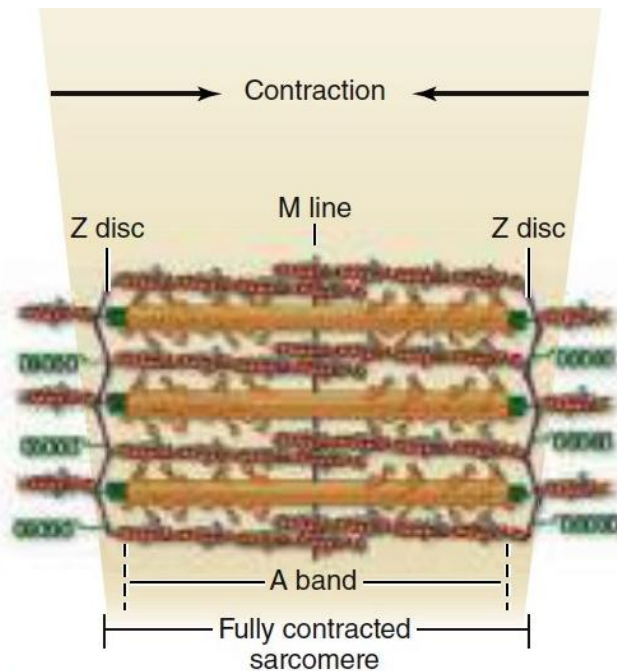
b Fully contracted skeletal muscle



We could barely identify the I band here



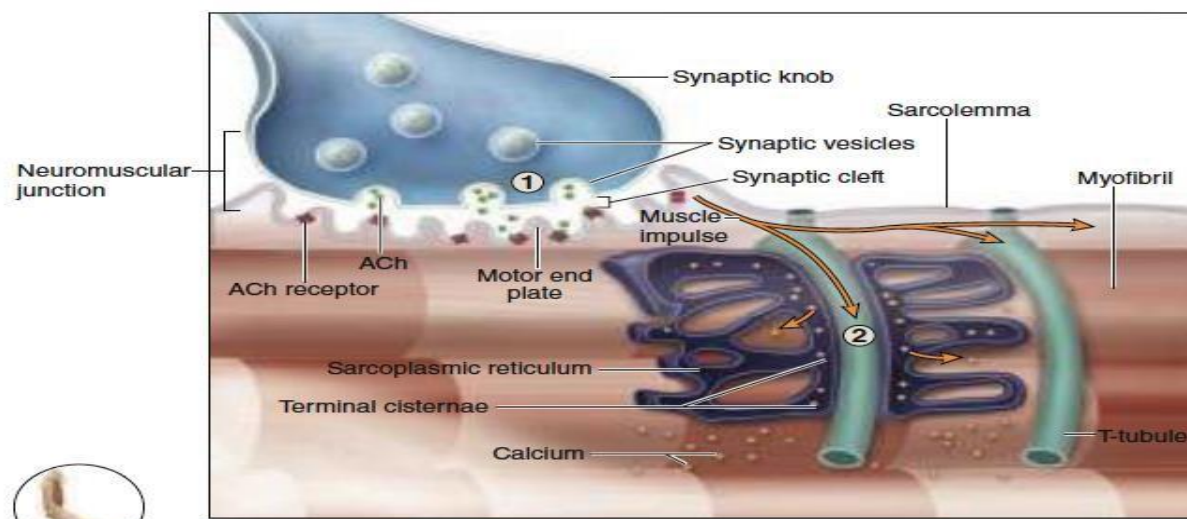
- During contraction, the myosin heads will bind to the actin and conformational changes will happen, they will drag the thin filaments towards the center of the sarcomere (towards the M line). The left and right thin filaments will be dragged to the point that they overlap with each other as you can see in the diagram.
- The Z discs become closer to the M line during contraction, the I band is barely visible because most of the thin filaments are overlapping with the thick filaments to form the A band. It seems like the whole length of the sarcomere is just the A band, but we still have a very very small area of the I band in a fully contracted muscle.



SUMMARY:

During contraction, the following will change:

1. The length of the sarcomere is shortened .
2. The I band is significantly shortened .
3. The A band length stays the same (remember the A band is the area occupied with the thick filaments, and their length didn't change during contraction!).
4. The distance between the 2 Z discs is shortened.
5. The H zone **DISSAPEARS** during full muscle contraction.(the H zone is the zone where it is only occupied by thick filaments, and when full muscle contraction happens, the thin filaments are going to completely overlap the thick filaments , you can see this in the previous diagram) (The doctor didn't mention this in the lecture but this should be known by logic).

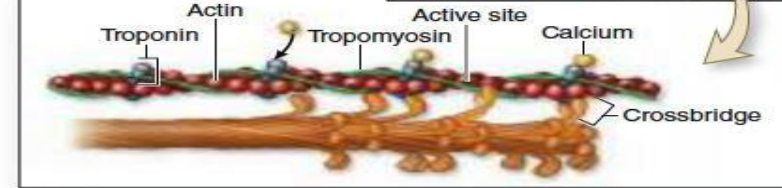
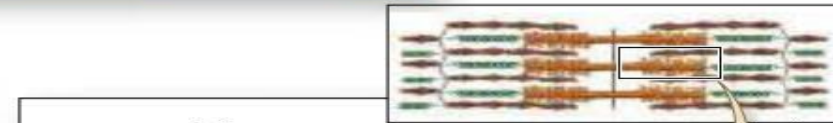


① A nerve impulse triggers release of ACh from the synaptic knob into the synaptic cleft. ACh binds to ACh receptors in the motor end plate of the neuromuscular junction, initiating a muscle impulse in the sarcolemma of the muscle fiber.

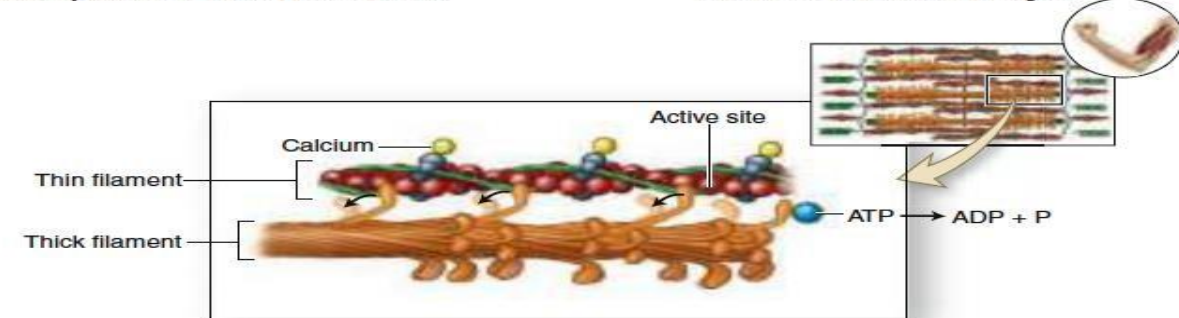
② As the muscle impulse spreads quickly from the sarcolemma along T tubules, calcium ions are released from terminal cisternae into the sarcoplasm.



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.



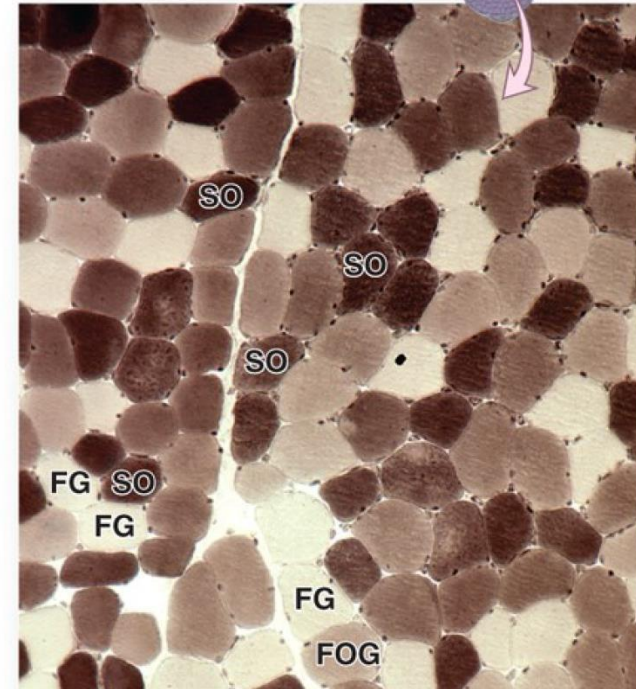
④ Myosin heads pivot, moving thin filaments toward the sarcomere center. ATP binds myosin heads and is broken down into ADP and P. Myosin heads detach from thin filaments and return to their prepivot position. The repeating cycle of *attach-pivot-detach-return* slides thick and thin filaments past one 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 fibers

Different types of fibers are based on:

1. **Maximal rate of contraction** (fast or slow fibers)---**depends on** myosin isoforms.
2. **Major pathway for ATP synthesis** (oxidative phosphorylation or **anaerobic** glycolysis).
3. **Others:** capillary density, number of mitochondria, content of glycogen and myoglobin (O₂ storage).

3 types (next slide) according to the type of myosin ATPase Isoform



The darker color means the myosin ATPase has more proteins

Stained with immunohistochemistry

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.
Two mechanisms to guarantee the constant flow of oxygen
1- surrounding capillaries
2- myoglobin

Fast glycolytic:

- Fibers are specialized for rapid, short term 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.**

The first and the second part of the name indicates the speed (maximal rate) of contraction and the major pathway of ATP synthesis respectively

	Slow, Oxidative Fibers (Type I) Slow contraction	Fast, Oxidative-Glycolytic Fibers (Type IIa)	Fast, Glycolytic Fibers (Type IIb) Fast contraction
Mitochondria	Numerous	Numerous	Sparse Less mitochondria because it relies on anaerobic glycolysis
Capillaries	Numerous It needs high amount of oxygen	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 Muscle fibers store glucose in the form of glycogen
Major source of ATP	Oxidative phosphorylation	Oxidative phosphorylation They use glycolysis sometimes	Anaerobic glycolysis Less efficient
Glycolytic enzyme activity	Low	Intermediate	High The pathway of generating ATP IS RELATED TO THE TYPE OF ENZYMES
Rate of fatigue How fast do the muscle fibers make us feel tired	Slow	Intermediate	Fast The faster the release of lactic acid, the faster the fatigue rate
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 O₂ storage
It has a heme group that binds to oxygen (like hemoglobin)

Chicken legs are darker than its breast, that due to the high content of myoglobin in the legs. They use their legs a lot -----> low fatigue rate (the leg muscles are formed from the slow oxidative type)

Note: What is written in the table in slide 35 about the motor unit is related to the type of fibers is generally correct, but the examples of muscles (postural and extraocular) make it confusing

For clarity:

Postural muscles: large motor unit and at the same time, it is composed of slow oxidative fibers (Type I)

Extraocular muscles: small motor unit and at the same time, it is composed of fast glycolytic fibers (Type IIb)

Generally, Type I fibers have small motor units and type IIb fibers have large motor units

The only muscle type that represents in the heart

Cardiac Muscle

Unique characteristics : Branched cells , intercalated discs

- 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. **(Sometimes 2 but we'll stick with one)**
- Each muscle cells is a surrounded by endomysium with a rich capillary network.

So they've good blood supply

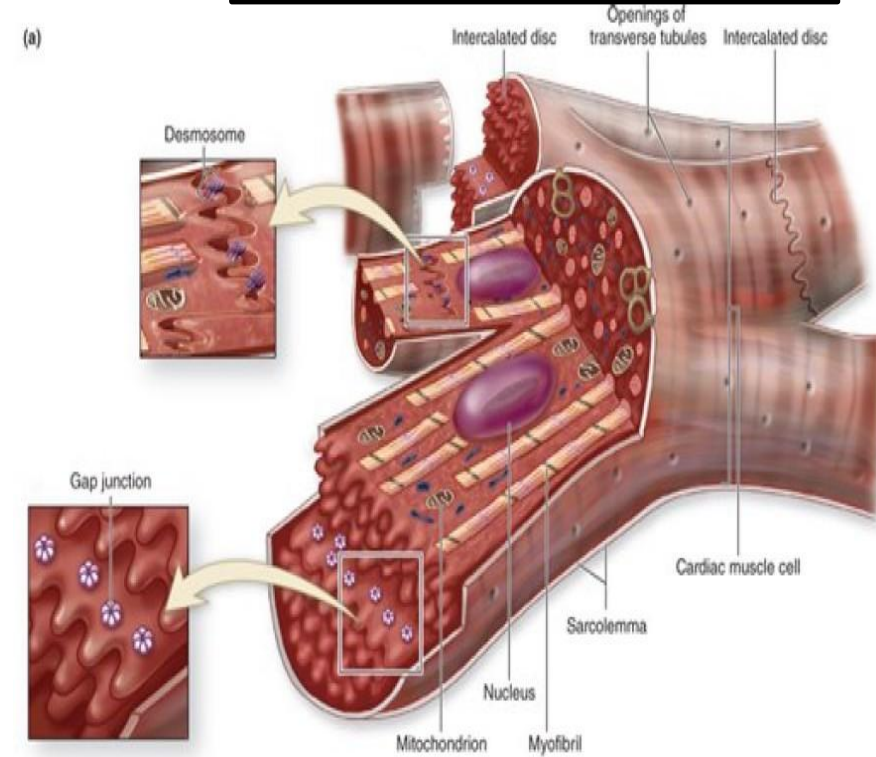
We have to remember that cardiac muscle contracts continuously from the moment it starts functioning until death, so it requires a constant blood supply to maintain its activity and perform its function.

- A thicker perimysium separates bundles and layers of muscle fibers (functional separation) and in specific areas (larger masses of fibrous connective tissue: cardiac skeleton) **(this is extremely important for the insulation of atria from the ventricles)**

Cardiac muscle.

- Gap junction are important

لمرور أيونات الصوديوم



The heart itself is a little bit different from skeletal muscle, so although you may expect the same arrangement of epimysium, endomysium, and perimysium, it is not exactly the same. We do have endomysium, but the perimysium part is actually part of the fibrous connective tissue system of the heart that creates other structures within the heart. It might cover and separate other bundles, but this separation is more functional, not just anatomical, and it is important for the function of the heart.

Cardiac Muscle

Also we have some myoglobin in Cardiac muscles.

Myofibril in cardiac muscles are way less than the skeletal muscles cuz I don't want to move a whole joint. I just need to shorten the muscle to push the blood out.

How these muscle cells do not separate from each others ? Because of the intercalated discs (inside them we have junctional complexes)

There is a delay that allows the atria to complete their contraction.

Contraction : down → up

- Mitochondria occupy up to 40% cuz these cells got to do a lot of work, heart needs more energy to keep pumping.

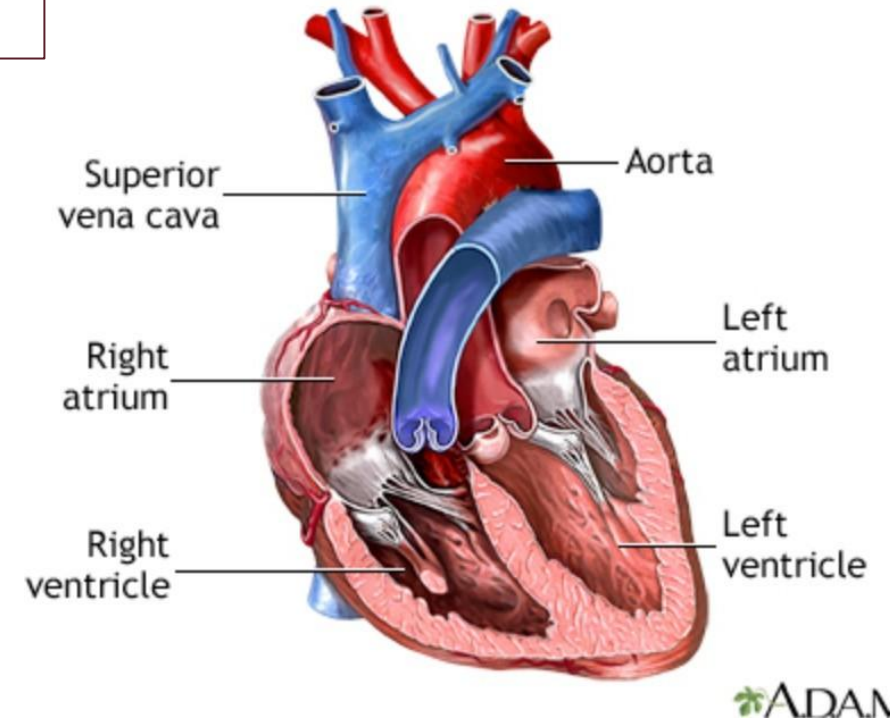


Cardiac Muscle

* If I need to control the heart rate, I should control the SA node

- Muscle of the heart ventricles is much thicker Due to amount of cardiac muscle fibers in it
- 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**) (the same mechanism as triads but less developed resulting in its association with the T-tubule forming a single cisterna rather than encompassing it from all directions.)

*They are called dyads because they are two structures (1 T-tubule & 1 cisterna, and triads because they are 3 structures.)



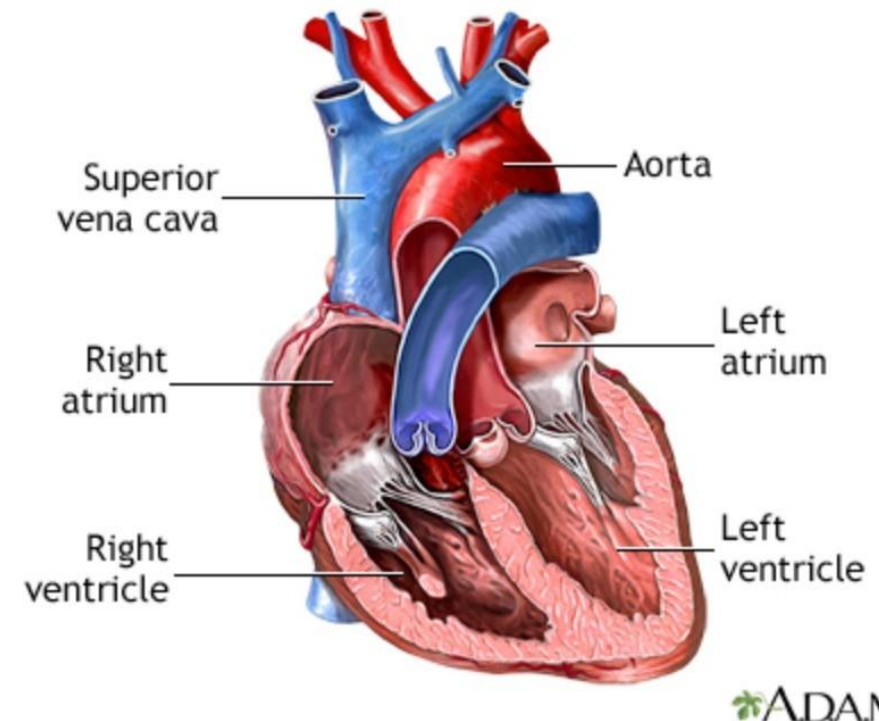
Cardiac Muscle

- 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

If we recall skeletal muscle, we said that inside the sarcoplasm we have an extensive amount of myofibrils. We also said that the sarcolemma creates T-tubules through invagination of the sarcolemma to be closer to the smooth endoplasmic reticulum, which already forms an extensive network around the myofibrils. So, the T-tubules of the sarcolemma together with the cisternae of the smooth endoplasmic reticulum create triads.

Now, in cardiac muscle fibers or cells, we have something similar but a little bit less advanced. So, we are not going to see three different structures, one T-tubule and two cisternae; instead, we see what is called dyads, where we have one T-tubule and one terminal cisterna from the smooth endoplasmic reticulum. This is because we do not need the same force of contraction that we usually have in skeletal muscle. Instead, we need a steady, small, rhythmic contraction. In the heart, the contraction is not slow, but rhythmic, because we need it for as long as we are alive. So, dyads are the organized structures of the sarcolemma and smooth endoplasmic reticulum that help perform this function.

*The idea in skeletal muscles -where stretch as long as we need- that I need it to contract now so we need a faster action potential (the pressure of the Calcium ions to be faster) and this is not what we need in the heart, we actually need continuity.



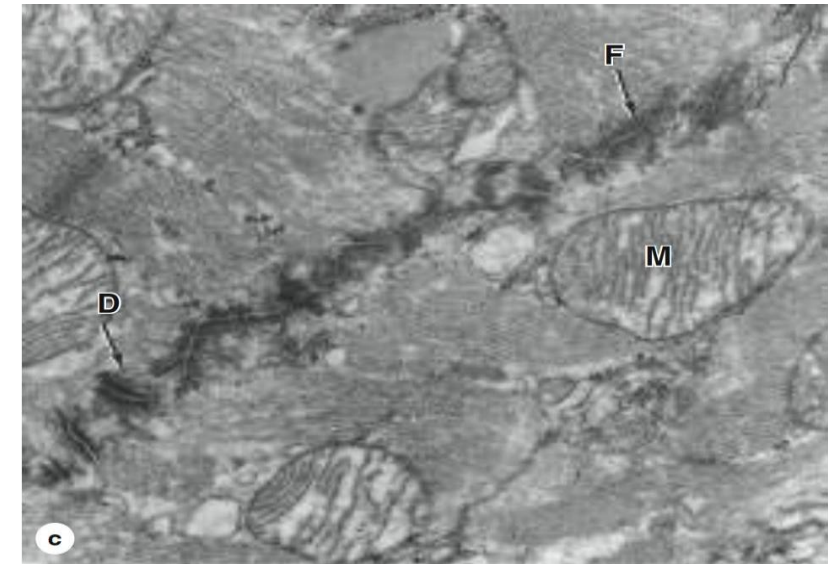
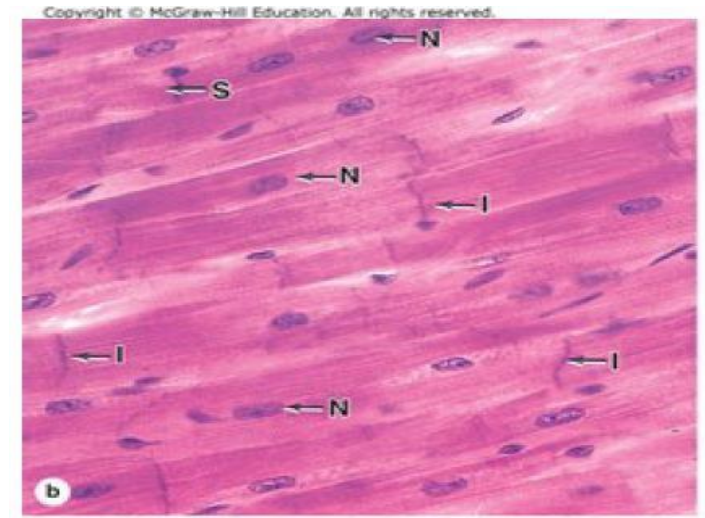
Cardiac muscle

- The fibers consist of separate cells joined at interdigitating regions called the **intercalated discs** (most distinguishing features of the **cardiac muscle**).
- Intercalated discs: transverse lines that cross the fibers at irregular intervals where the myocardial cells join (junctional complexes).

Most important junction is the gap junction as it is needed for the propagation of action potential.

- 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

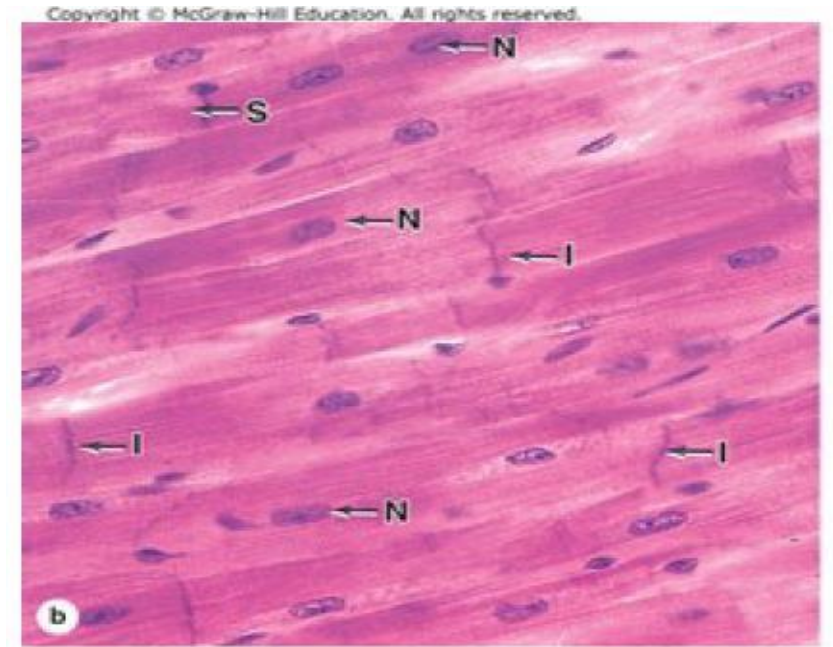
***One extra feature is that cardiac cells have significantly fewer myofibrils than skeletal muscle cells, because these cells do not need the same force of contraction provided by skeletal muscle. Therefore, they need fewer myofibrils. They still need contraction, specifically a rhythmic contraction, but to a lesser extent. This also creates extra space for other organelles, such as mitochondria.**



Cardiac muscle

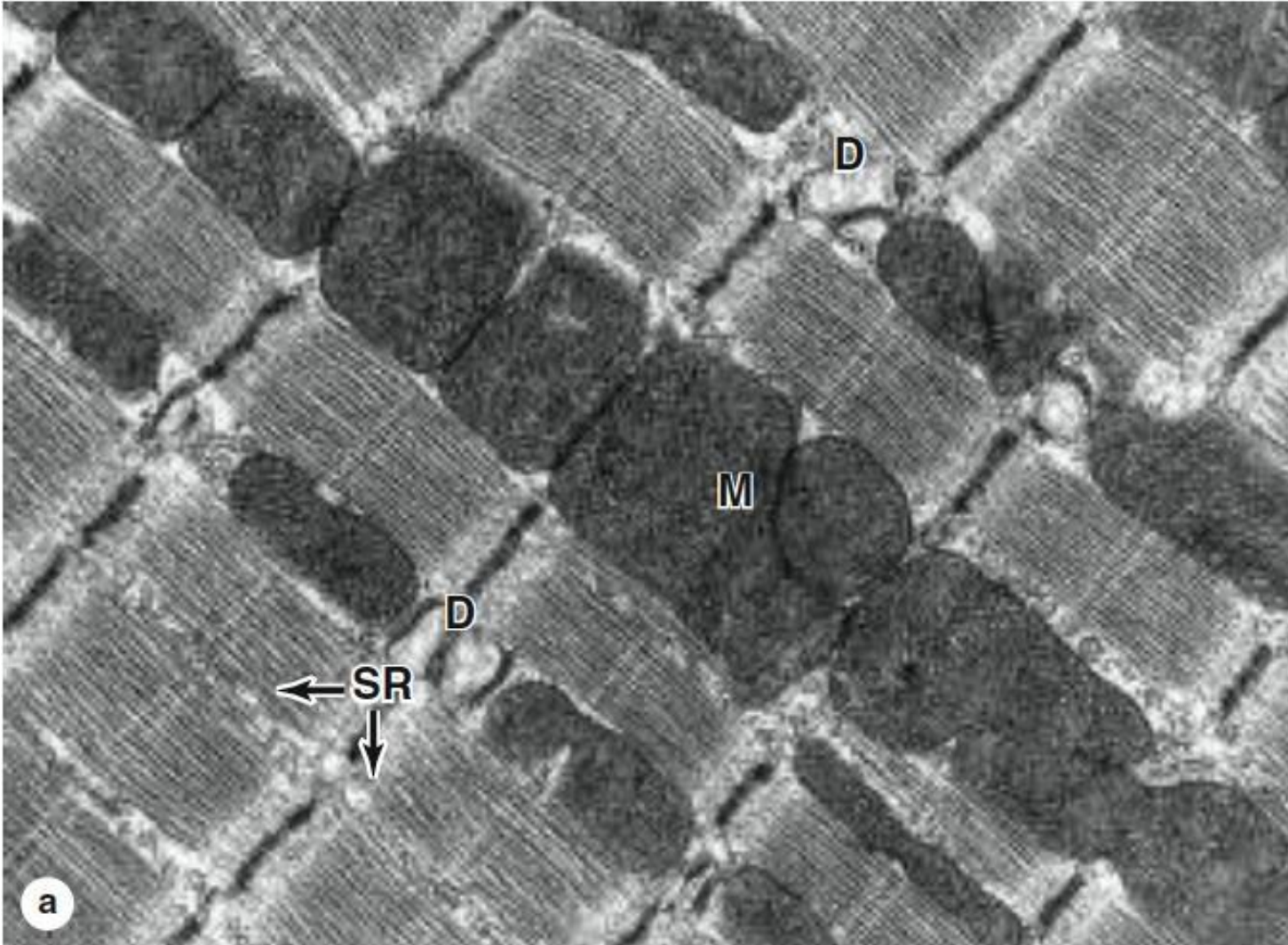
If we look at this image, we can recognize the transversely running lines, which are called intercalated discs. These are one of the most distinguishing features of cardiac muscle. So, what are intercalated discs? Look at this diagram: this is the area where two muscle cells meet. This is the area we are looking at here, and this is the intercalated disc, including how it is arranged and structured.

So, this is where two cells meet. What is unique about intercalated discs? As we can see, this is not one flat surface opposite another flat surface; instead, it is more like interdigitation between the two cells to enhance adhesion between them. Not only that, but this area is also rich in junctional complexes. One of the most important junctions here is the gap junction, which is very important for the transmission of action potentials between cells. This is actually how action potentials are transmitted from one cell to another. So again, the intercalated disc is the area where two cells meet, and it is rich in junctional complexes, particularly gap junctions and fascia adherens.



M = mitochondria
SR = sarcoplasmic reticulum
D = dyad

Where was this take from?



Transmission electron microscope
of the cardiac muscle

What is unique about it?

- First, let's identify the sarcomeres and myofibrils. These structures here represent the sarcomeres.
- However, we can also notice a large number of other structures, which are actually mitochondria.

Mitochondria in cardiac muscle:

- Around 40% of the cytoplasm of cardiac muscle cells is occupied by mitochondria.
- This is because cardiac muscle requires a constant supply of energy to maintain continuous contraction throughout life.

Internal arrangement:

- If you recall, in skeletal muscle we talked about the triad, which consists of:
 - *One T-tubule
 - *Two terminal cisternae from the smooth endoplasmic reticulum
- In cardiac muscle, instead of a triad, we have a dyad, which consists of:
 - *One T-tubule (an invagination of the membrane)
 - *One terminal cisterna

Always remember that cardiac muscle cells contain a large amount of mitochondria to meet their high energy demands.

The last type we will talk about is smooth muscle. Smooth muscle is quite unique in many ways. It shares some similarities with cardiac muscle regarding innervation and the presence of gap junctions, but other than that, it is quite different from both cardiac and skeletal muscle.

- **Slow and steady contraction.**

unlike the rhythmic contraction seen in cardiac muscle and the forceful contraction seen in skeletal muscle.

- **Under the control of autonomic nerves and various hormones.**

These cells do not contract on their own; they require either a neural impulse or another external stimulus to initiate contraction. This is considered another unique feature of smooth muscle cells.

- **Present in blood vessels, digestive, respiratory, urinary, and reproductive tracts.**

In fact, within the gastrointestinal, urinary, and reproductive tracts, we can distinguish a separate thick layer in the wall of these organs that is responsible for their contraction.

- **Fibers of smooth muscle are elongated, tapering, and unstriated cells.**

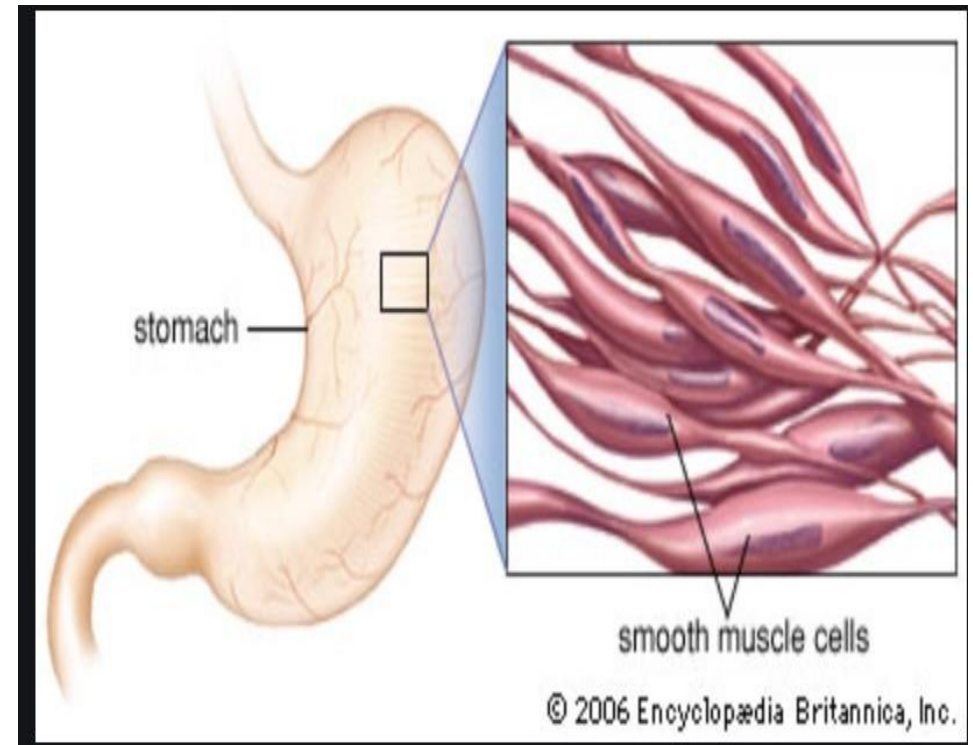
As shown, smooth muscle fibers are spindle-shaped (fusiform). The nucleus is located in the center of the cell, while both ends of the cell are narrower and thinner than the middle portion. These cells are surrounded by reticular fibers, which represent the equivalent of endomysium found in the other two muscle types.

- **Enclosed by an endomysium (a network of type I and type III).**

- **Length is 20 μm - 500 μm .**

Smooth muscle cells are relatively small, usually measuring around 20 micrometers. However, in certain cases, they can stretch and reach up to 500 micrometers in length.

Smooth Muscle

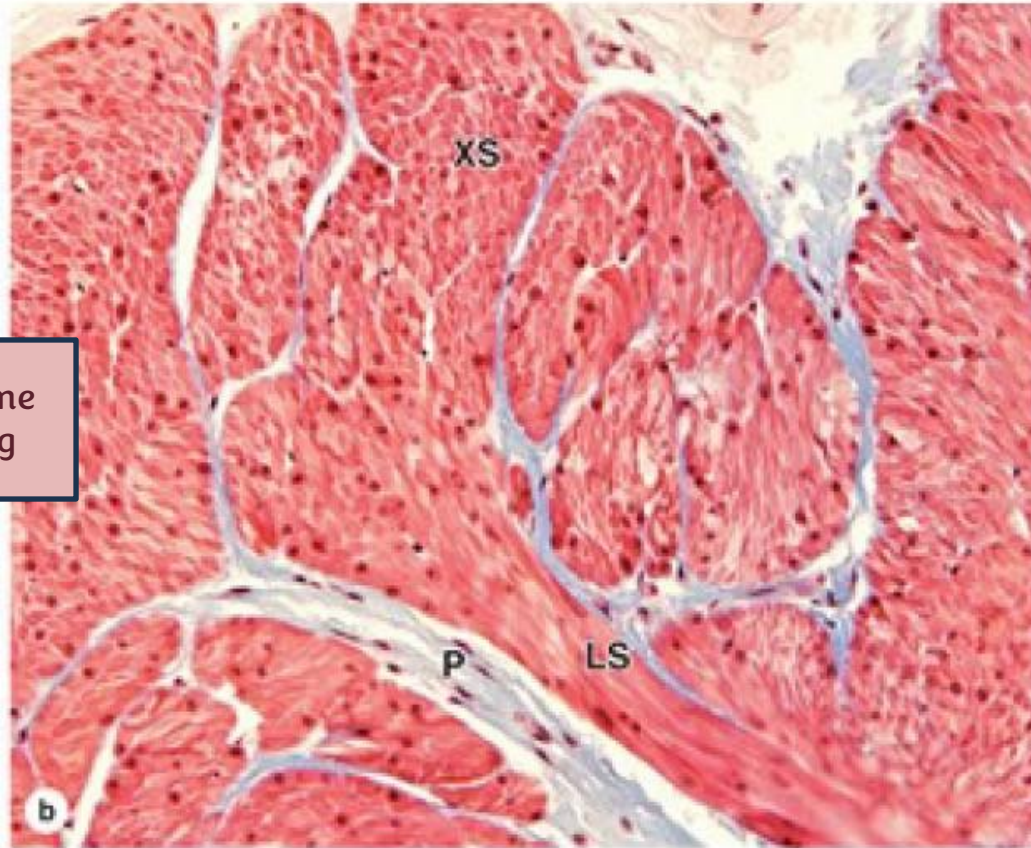


Smooth muscles are present everywhere even in your skin, for example, when you're cold, the hair on your body stand on end in what we call piloerection.

This is due to the attachment of the hair shaft to a smooth muscle that is called arrector pili, when this muscle contracts it pulls the skin downward so the hair erect (stand).

Smooth Muscles

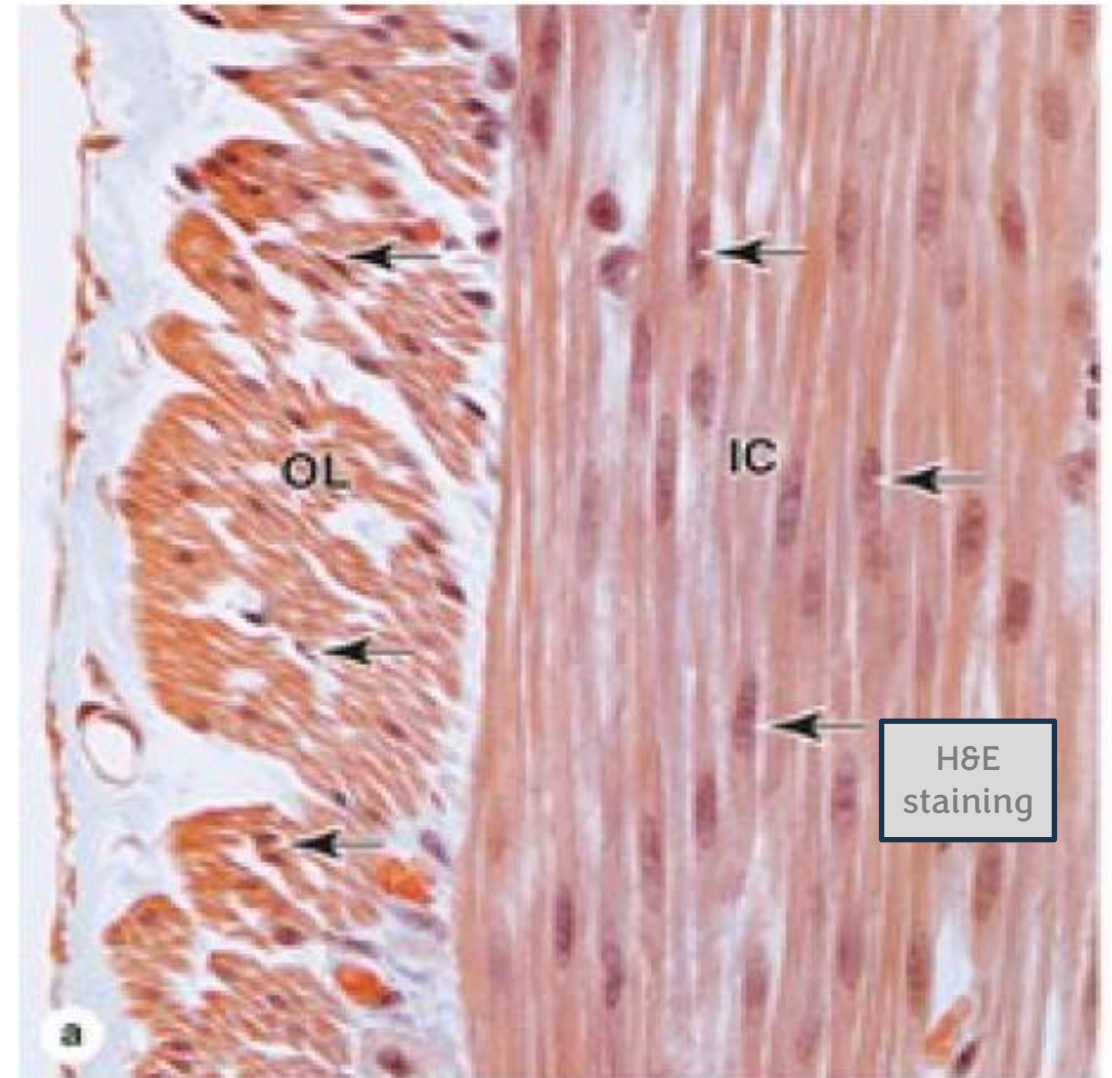
Relaxed smooth muscle



Trichrome staining

- The red colored part is the muscle
- The blue part is connective tissue with fibroblasts in between
- Spindle-shaped nuclei in response to spindle-shaped muscles

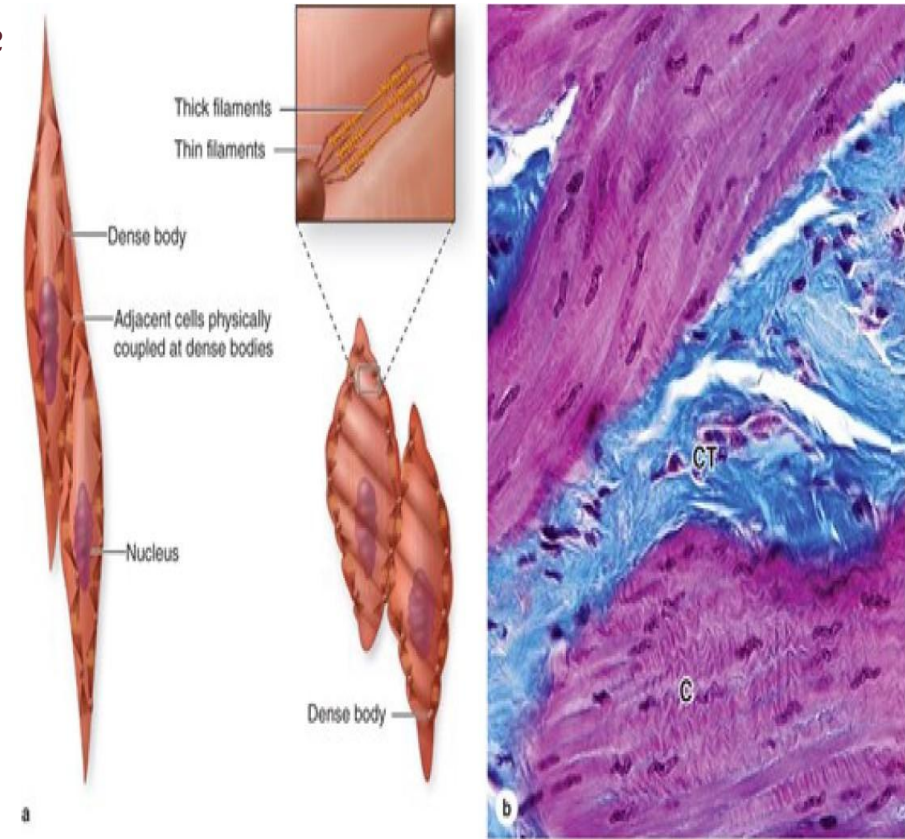
Contracted smooth muscle



H&E staining

Characteristics and Contraction

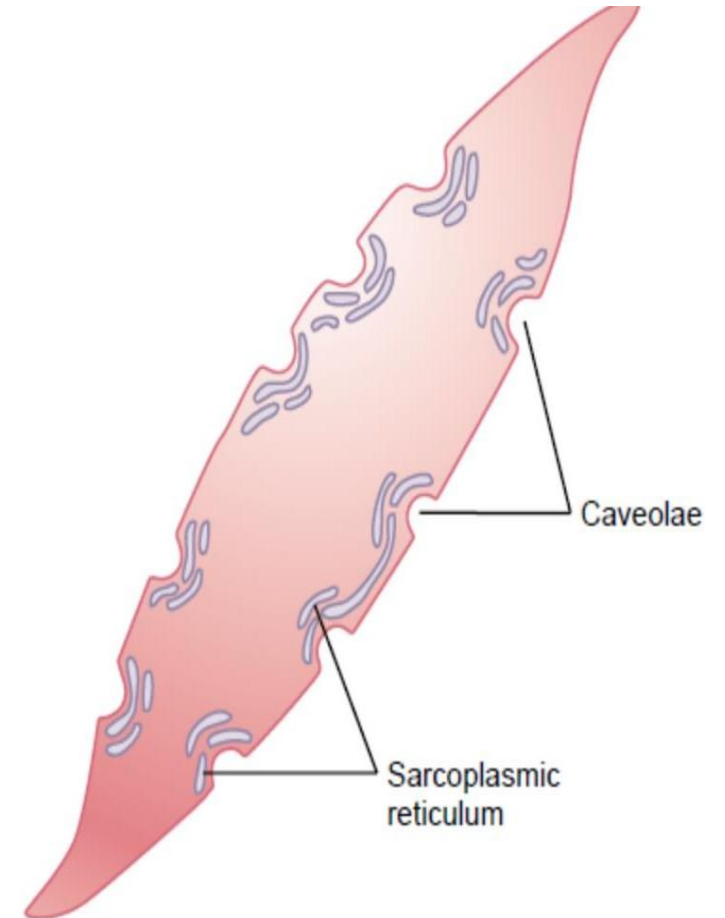
- Dense bodies (similar to Z discs) is located in the cytoplasm and at the cell membrane. (They are globular proteins that are scattered throughout the entire length of the muscle's membrane, dense bodies compensate for z discs.)--> **LACKING Z DISCS = NO STRIATION**
- Both thin filaments and intermediate (for adhesive junctions between cells).
- *Thin filaments and intermediate ones are attached to the dense bodies, and thick filaments are in between (this arrangement is the most unique feature in smooth muscles)
- 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.



Smooth muscle cells shorten when contracted.

Characteristics and Contraction

- Rudimentary sarcoplasmic reticulum **and lack of T-tubules, so we describe smooth muscles as rudimental** (incompletely developed)
- Rich in gap junction.
- Caveolae are small plasmalemma invaginations which contain signaling components (ion channels). **Caveolae increase and accelerate the spread of the action potential (as the role of T-tubules in the cardiac & skeletal).**
- NO troponin (**TnC**) and tropomyosin instead there are calmodulin (**which binds to the calcium**) and Ca^{2+} -sensitive myosin light-chain kinase (MLCK)

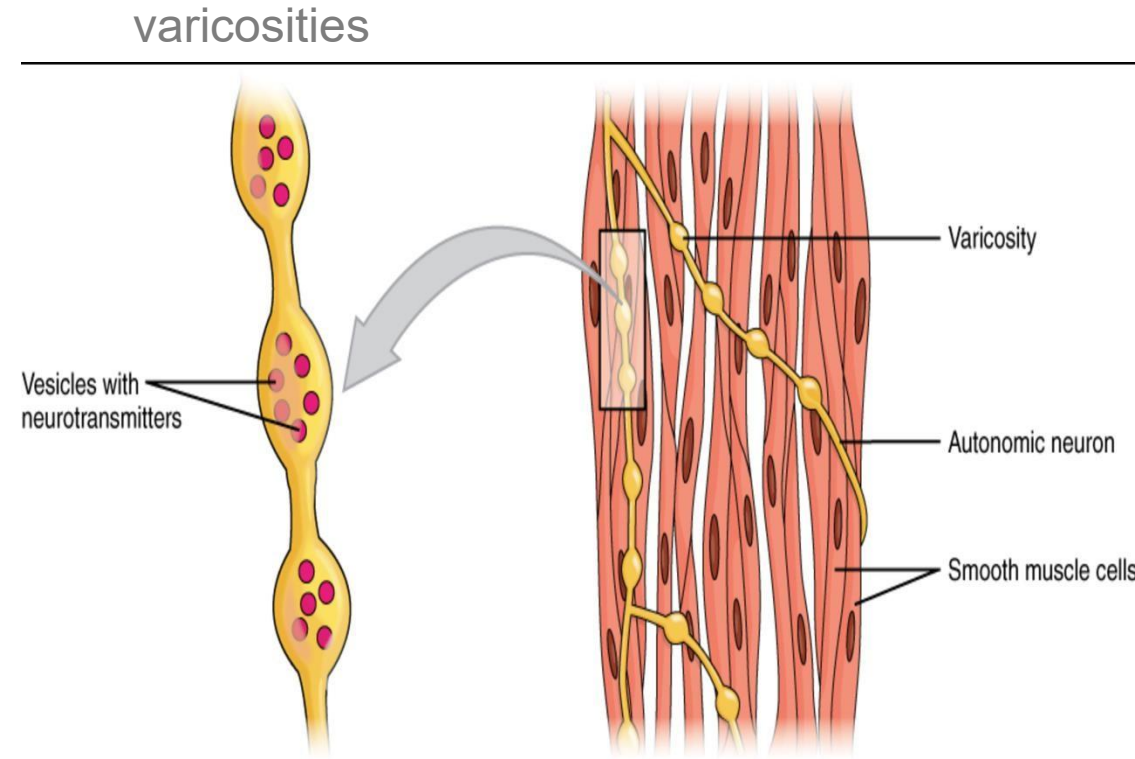


Characteristics and Contraction

- Smooth muscles fibers (or muscle cells as it's more accurate to say) are fusiform in shape with a center-located nucleus and the cytoplasmic components are just like any other muscular cell.
- Contraction of smooth muscles is described slow and steady.
- It's somehow similar to the contraction of the heart.
- While contraction, the desne bodies will be closer to each other, the thin filaments will slide over the thick and undergo the same mechanism as other muscles (we need calcium, ATP, and all other things mentioned earlier in skeletal & cardiac.)
- While contraction, there is shortening but actually, shortening from one side and a bit of stretching in the other because it's a collective change in shape (it's not linear orientation as in skeletal muscles).

Smooth Muscle

- Lack well-defined neuromuscular junctions and motor end plates (MEP)
- 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



Innervation of smooth muscles

The nerve synapses with the smooth muscle but there is no motor end plate as in the skeletal.

HOW??

In the end of the axon its terminals will sprinkle the neurotransmitter on the surface of the smooth muscles and the transmitter will bind to receptors and they will contract.

When the neurotransmitter is sprinkled it doesn't reach all the muscle cells, so it spreads to the rest by gap junctions (smooth muscles are rich in gap junctions as heart muscles.)

Since we are talking about smooth muscles, then the neurotransmitter is epinephrine.

Innervation

```
graph TD; A[Innervation] --> B[Cardiac:]; A --> C[Skeletal:]; A --> D[Smooth:];
```

Cardiac:

In the heart there is no motor end plate, instead there is specialized cells that initiate the depolarization, which then spreads throughout via gap junctions.

Skeletal:

Every skeletal muscle fiber must have its own motor end plate (each one must receive a neurotransmitter then it contracts)

Smooth:

Some parts are similar to skeletal; they receive the neurotransmitter directly. Others are like the mechanism in the cardiac; spreading of the transmitter via gap junctions.

contraction

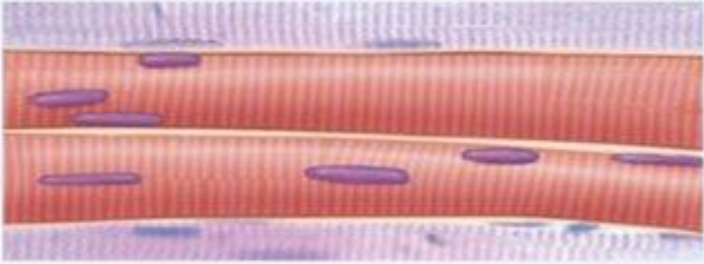

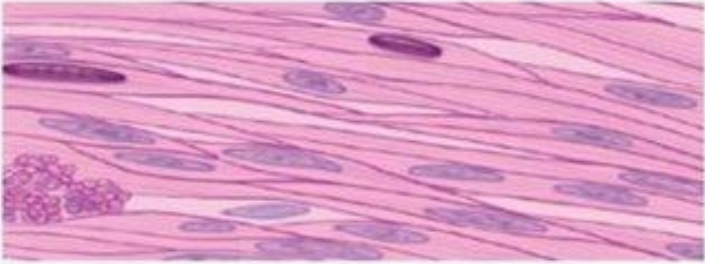
↳ Cardiac & skeletal: all or none

↳ Smooth muscles: graded contraction

For example:

In the GI tract the movement is steady and slow and continuous (one cell contracts then relaxes then the other contracts when the transmitter is transported to it via gap junctions, and so on until it spreads throughout the entire length of the GI tract.

The peristaltic movement starts from the second third of the esophagus (not from the first one because it's skeletal (the 1st third is purely skeletal/ the 2nd one is mixed skeletal & smooth/ the last one is purely smooth and after it we no longer see skeletal muscles except when we need control again in the external anal sphincter)

	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,

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

Cardiac muscle (the worst in regeneration)

- lacks satellite cells and there is a very small number of stem cells (so they are the worst in regeneration)
- Very little regenerative capacity beyond early childhood.
- Defects or damage replaced by proliferating fibroblasts and CT formation leading to myocardial scars.

Smooth muscle (the best in regeneration)

- Is capable of a more active regenerative response.
- Can undergo mitosis and replace the damaged tissue.
- it regenerates as if nothing has happened even if $\frac{3}{4}$ of it was damaged.

If there is a massive damage in the tissue, no way that the cells will compensate the muscle tissue, but if it's minor they might do).

>> 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.

QUIZ!!

Good luck!



START

For any feedback, scan the code or click on it.



Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:

Reference Used:

Dr. Ghada's face-to-face and online lectures of muscle tissue

قال الله تعالى :

وَالْفَجْرِ ١
وَاللَّيْلِ إِذَا يَسْرِ ٢
وَالشَّفْعِ وَالْوَتْرِ ٣
وَالْأَيْلِ إِذَا يَسْرِ ٤
هَلْ فِي ذَلِكَ قَسَمٌ لِّذِي حَبْرِ ٥

سورة القدر

أي أقسم الله سبحانه بوقت الفجر، والليالي العشر الأول من ذي الحجة وما شرفت به، وبكل شفع وفرد، وبالليل إذا يسري بظلامه، أليس في الأقسام المذكورة مقنع لذي عقل؟

(التفسير المنير)

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قَالَ رَسُولُ اللَّهِ ﷺ

«أفضل الدعاء دعاء يوم عرفة، وأفضل ما قلت أنا والنبيون من قبلي، لا إله إلا الله وحده لا شريك له، له الملك، وله الحمد، وهو على كل شيء قدير»

يوم الترمذي (١٥٤) وحسنه الألباني في "صحيح الترمذي" (١٣٩) .

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