MUNI MED
Department of Histology and Embryology

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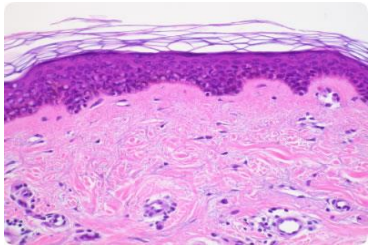
MUSCLE TISSUE

Petr Vaňhara

CONTEMPORARY TISSUE CLASSIFICATION

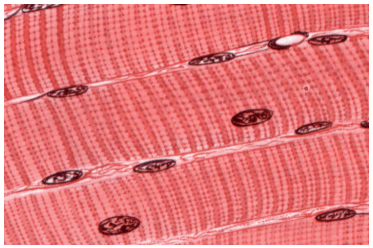
Based on morphology and function:

Epithelium



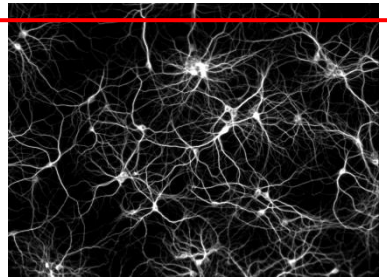
Continual, avascular layers of cells with different functions, oriented to open space, with specific junctions and minimum of ECM and intercellular space.
Derivates of all three germ layers

Muscle



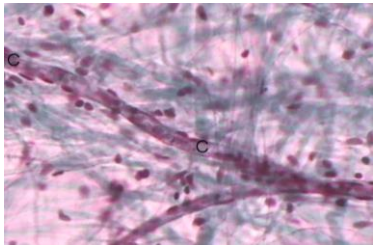
Cytoskeleton → contraction
Mesoderm – skeletal muscle, myocard, mesenchyme – smooth muscles
Rarely ectoderm (eg. m. sphincter a m. dilatator pupillae)

Nerve



Neurons and neuroglia
Reception and transmission of electric signals
Ectoderm, rarely mesoderm (microglia)

Connective



Dominant extracellular matrix
Connective tissue, cartilage, bone…
Mesenchyme

GENERAL CHARACTERISTIC OF MUSCLE TISSUE

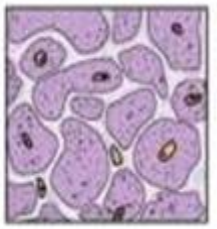
Hallmarks

- Unique cell architecture
- Excitability and contraction
- Mesodermal origin

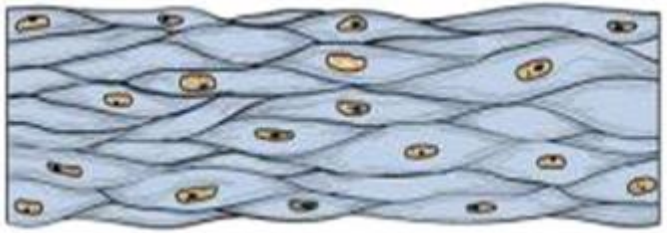
Classification according to cell and tissue structure

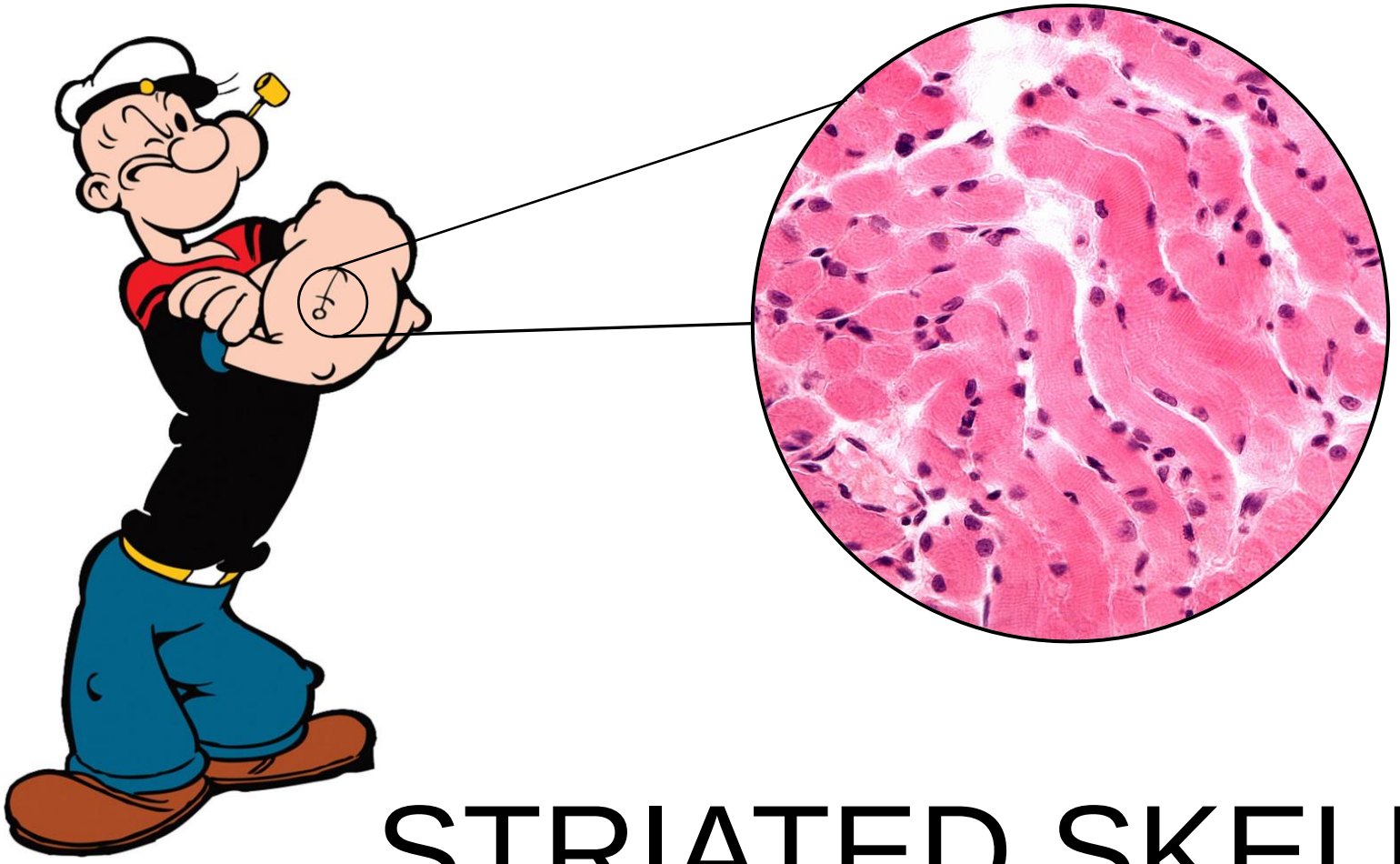
Striated skeletal

Striated cardiac



Smooth





STRIATED SKELETAL MUSCLE TISSUE

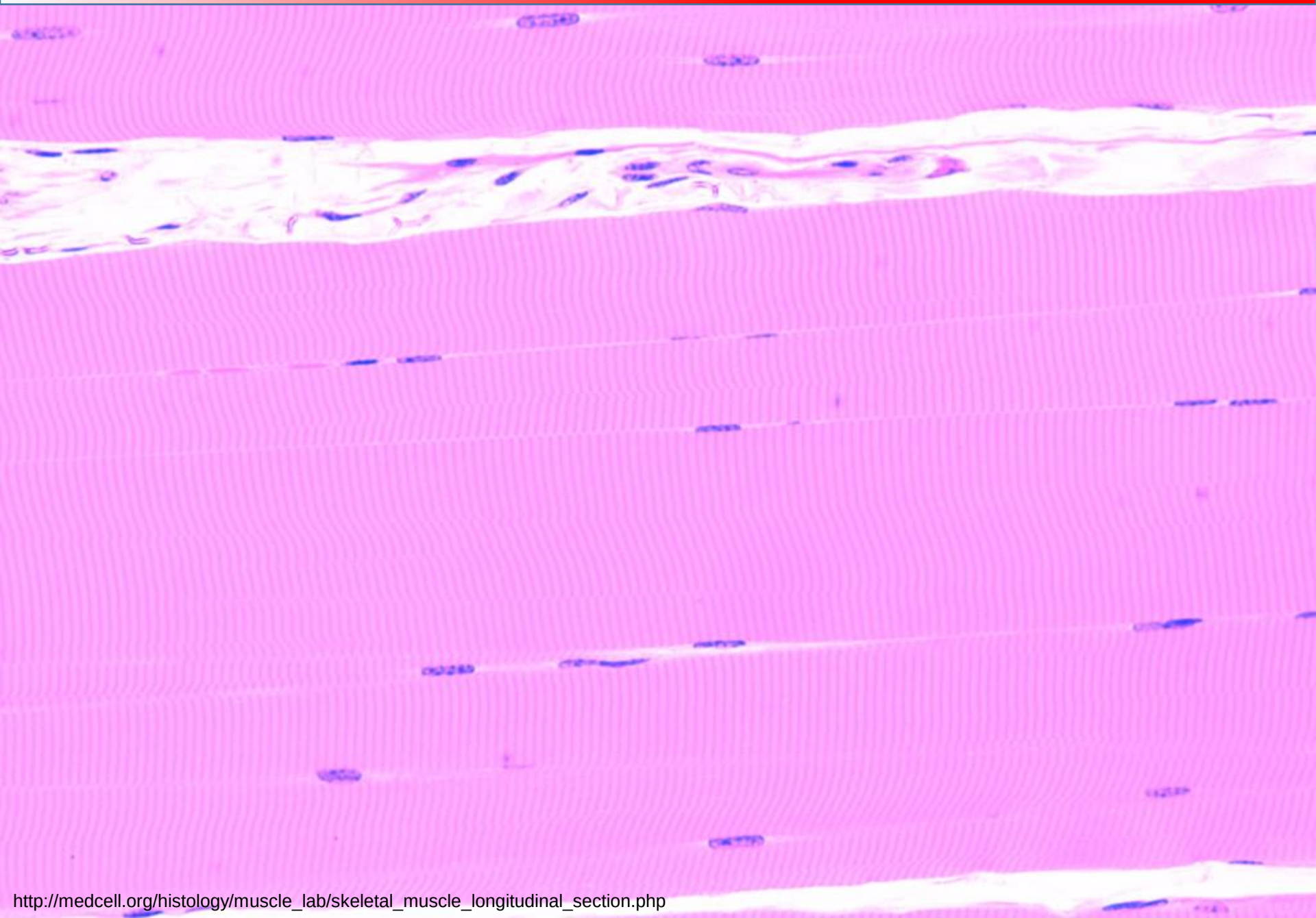
TERMINOLOGY OF SKELETAL MUSCLE TISSUE

- Composition: muscle cells + connective tissue, blood vessels
- Unique cell architecture: long multinuclear cells – **muscle fibers** (**rhabdomyocytes**)
- Long axis of cells is oriented in parallel with direction of contraction
- Specific terminology:
  - cell membrane = **sarcolemma**
  - cytoplasm = **sarcoplasm**
  - sER = **sarcoplasmic reticulum**

  - **Muscle fiber** – microscopic unit of skeletal muscle
  - **Myofibril** – LM unit – myofilaments – unit of muscle fibers
  - **Myofilaments** – filaments of actin and myosin (EM)

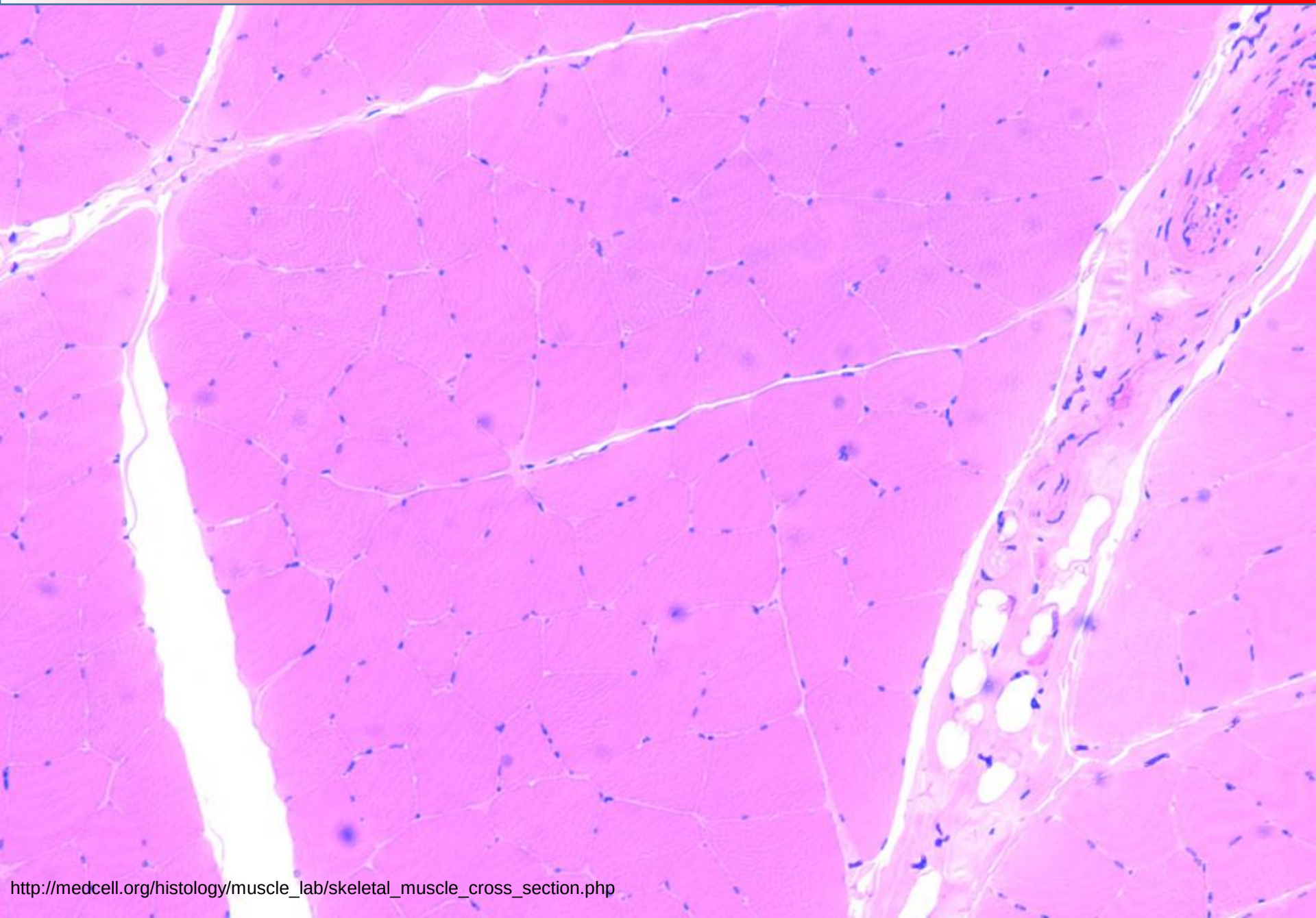
TERMINOLOGY OF SKELETAL MUSCLE TISSUE

SKELETAL MUSCLE TISSUE



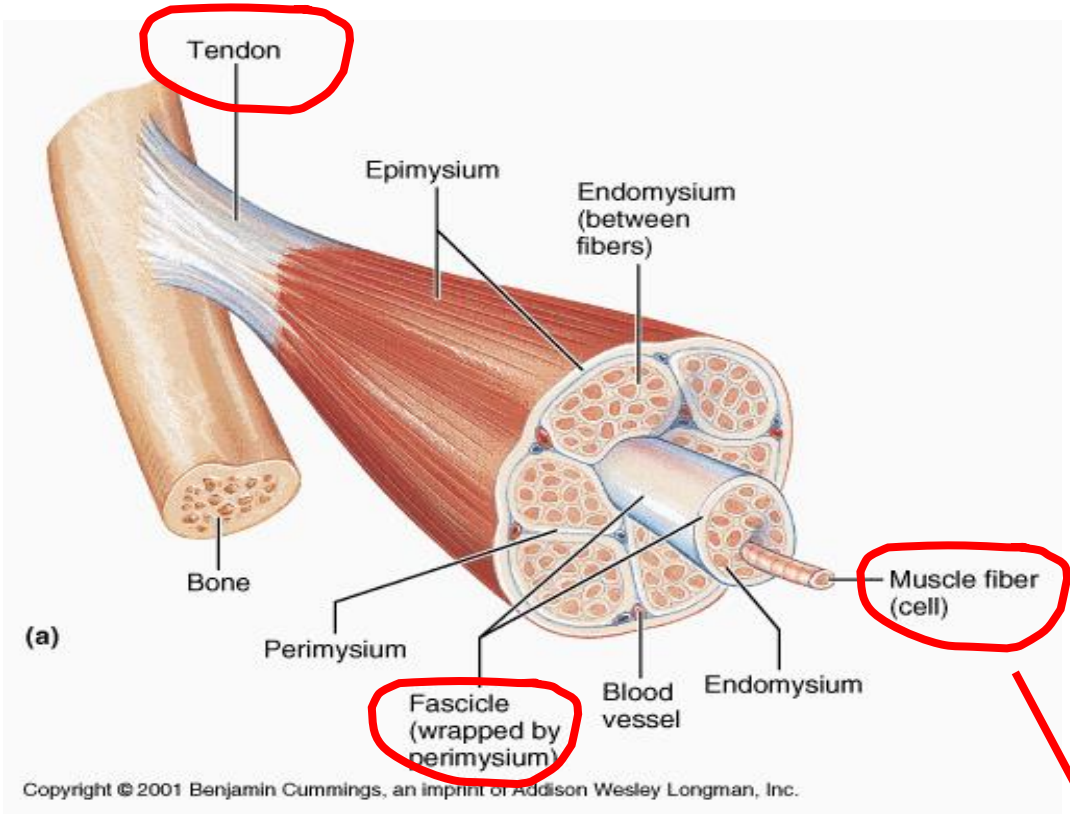
http://medcell.org/histology/muscle_lab/skeletal_muscle_longitudinal_section.php

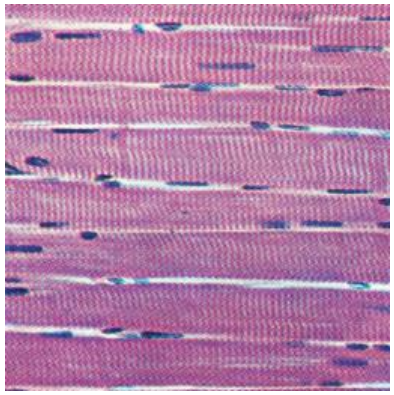
SKELETAL MUSCLE TISSUE



http://medcell.org/histology/muscle_lab/skeletal_muscle_cross_section.php

STRUCTURE OF SKELETAL MUSCLE





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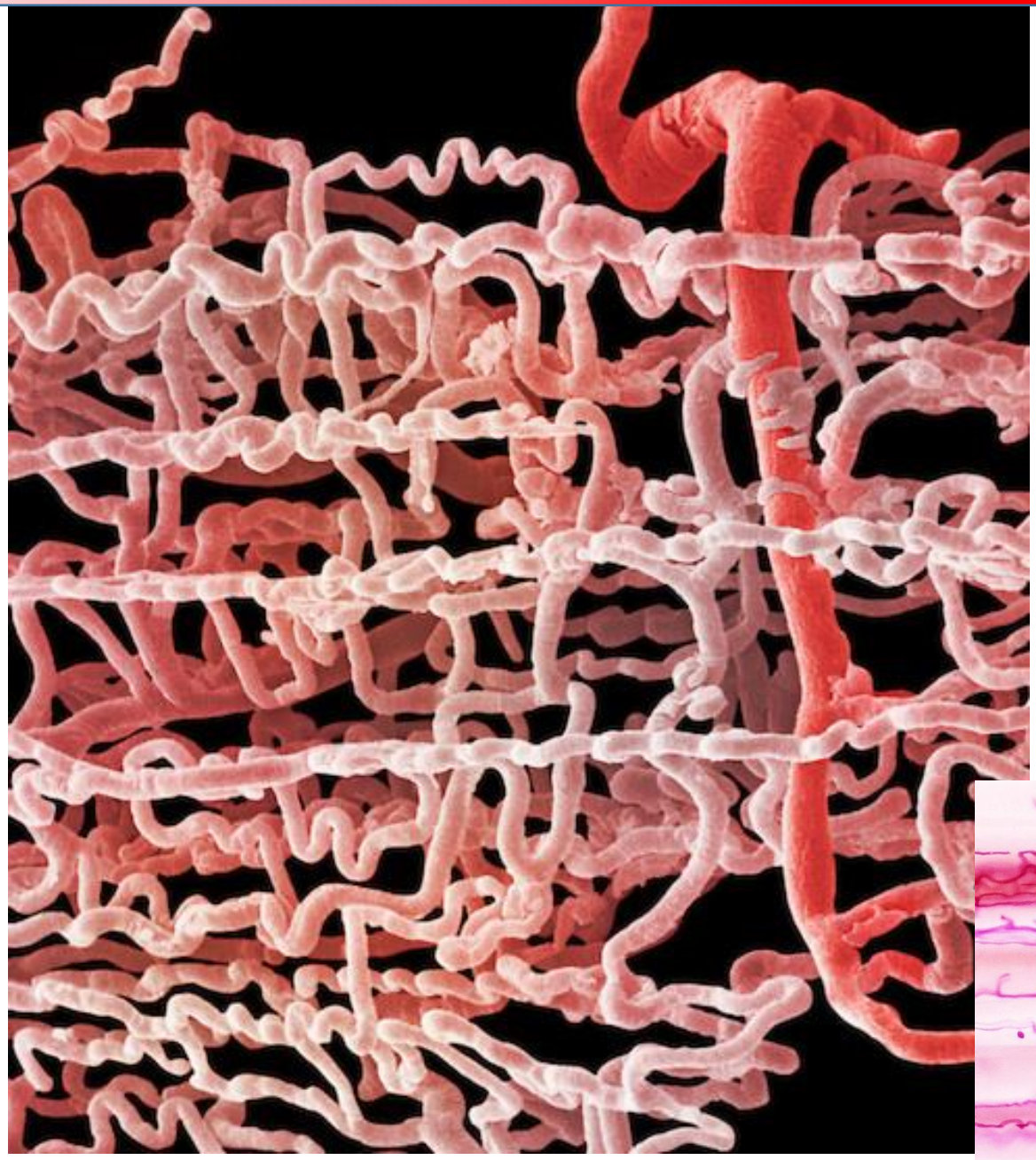
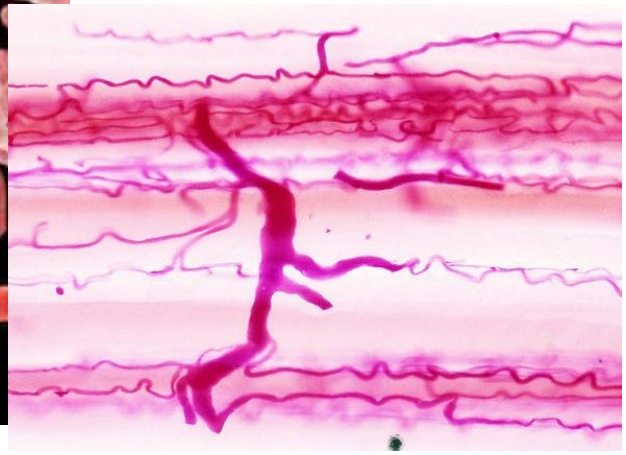
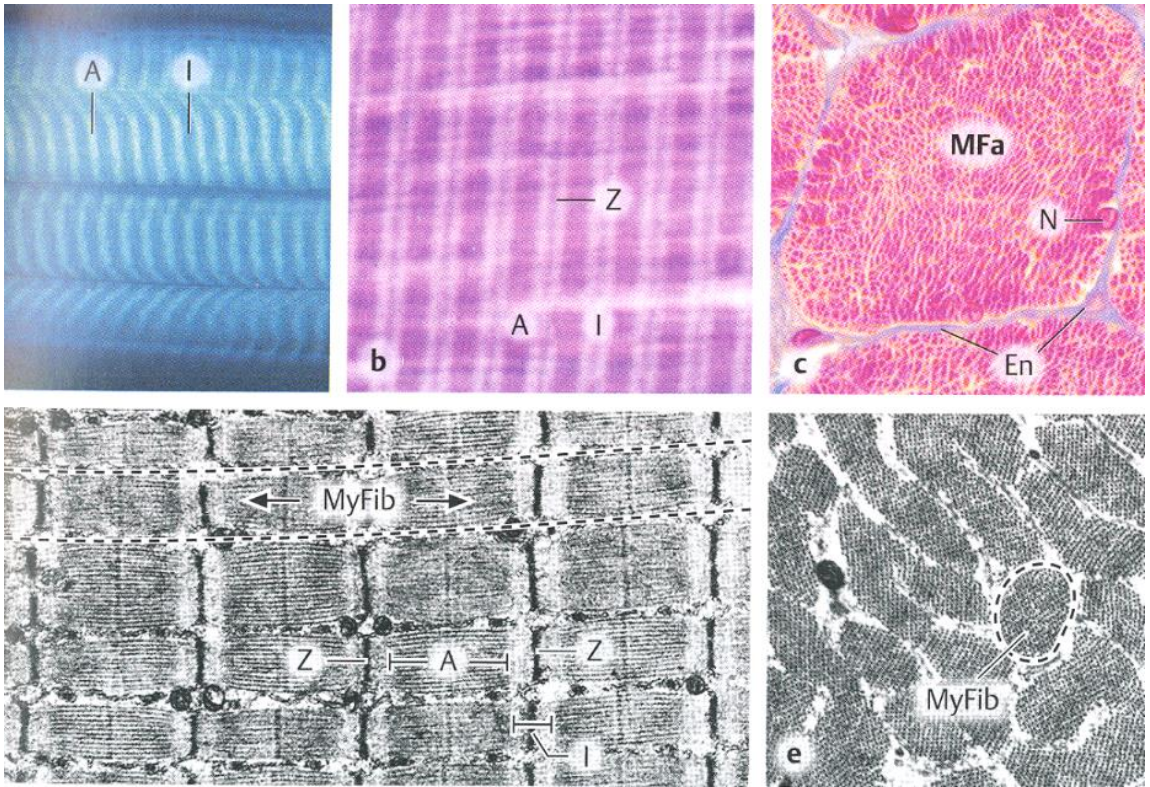




STRUCTURE OF SKELETAL MUSCLE

- morphological and functional unit: **muscle fiber (rhabdomyocyte)** – elongated, cylindrical-shaped, multinucleated cell (syncytium)
- nuclei are located at the periphery (under sarcolemma)
- **myofibrils** show cross striation
- diameter of muscle fiber: 25-100 μm
- length: millimeters - centimeters (up to 15)



ULTRASTRUCTURE OF RHABDOMYOCYTE

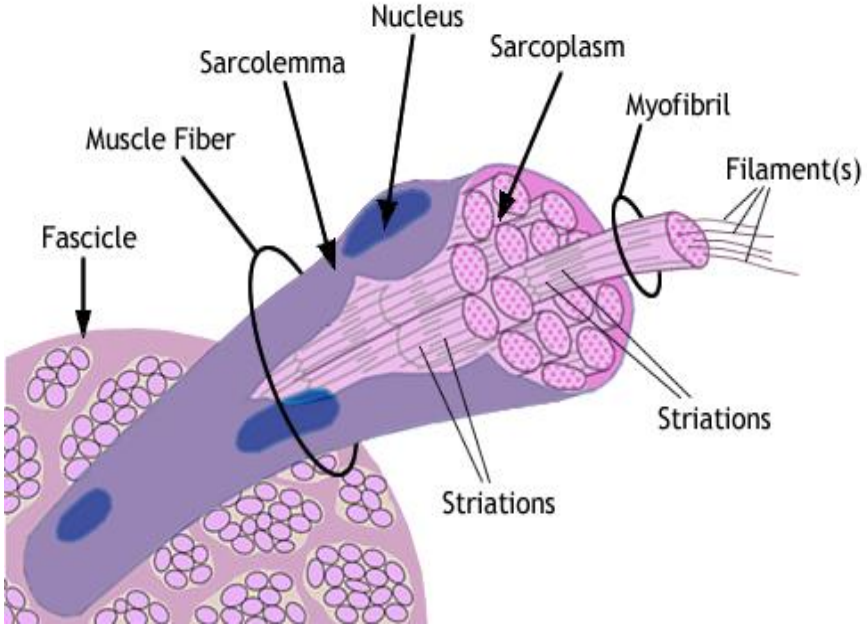
Muscle fiber = myofiber = syncitium = rhabdomyocyte

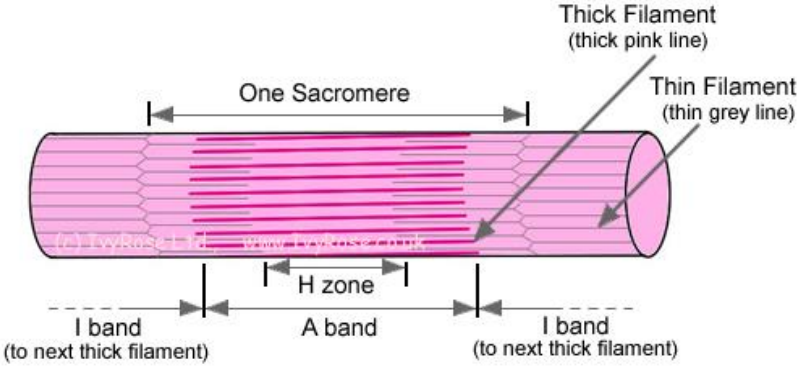
Muscle fiber – morphological and functional unit of skeletal muscle [Ø 25 – 100 μm]

Myofibrils – compartment of fiber sarcoplasm [Ø 0.5 – 1.5 μm]

Sarcomere – the smallest contractile unit [2.5 μm], serial arrangement in myofibrils

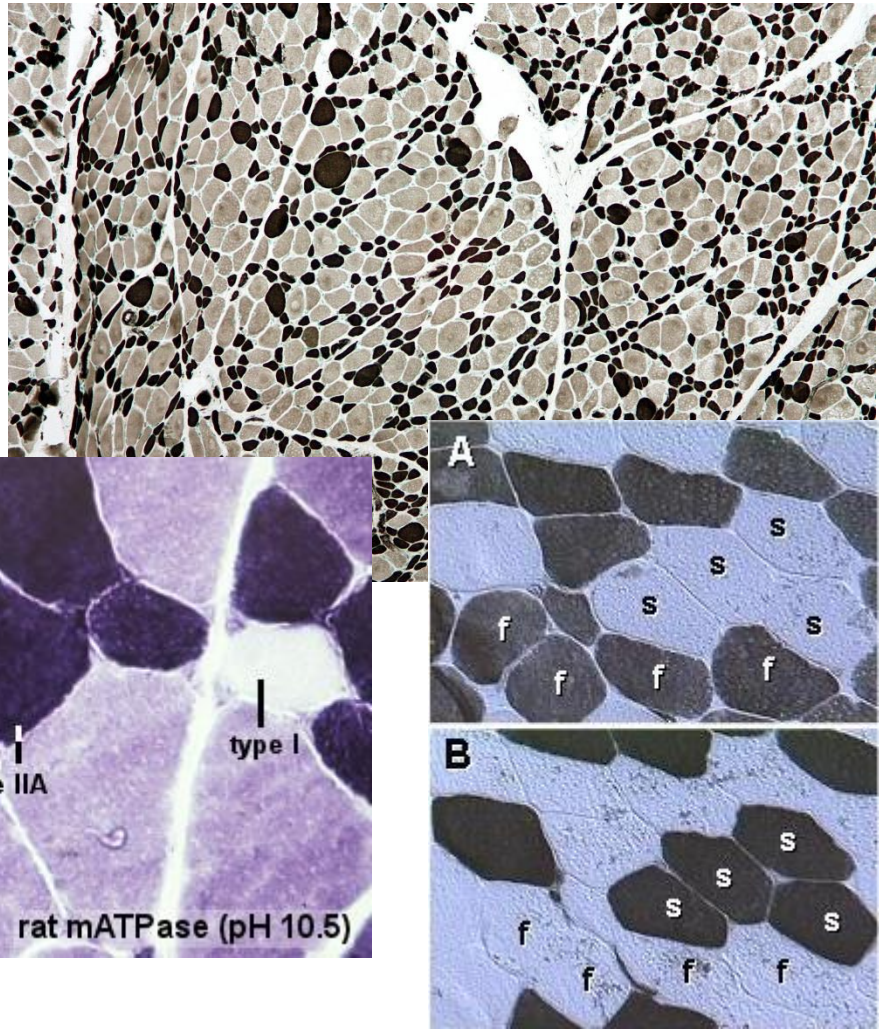
Myofilaments – actin and myosin, are organized into sarcomeres [Ø 8 and 15 nm]



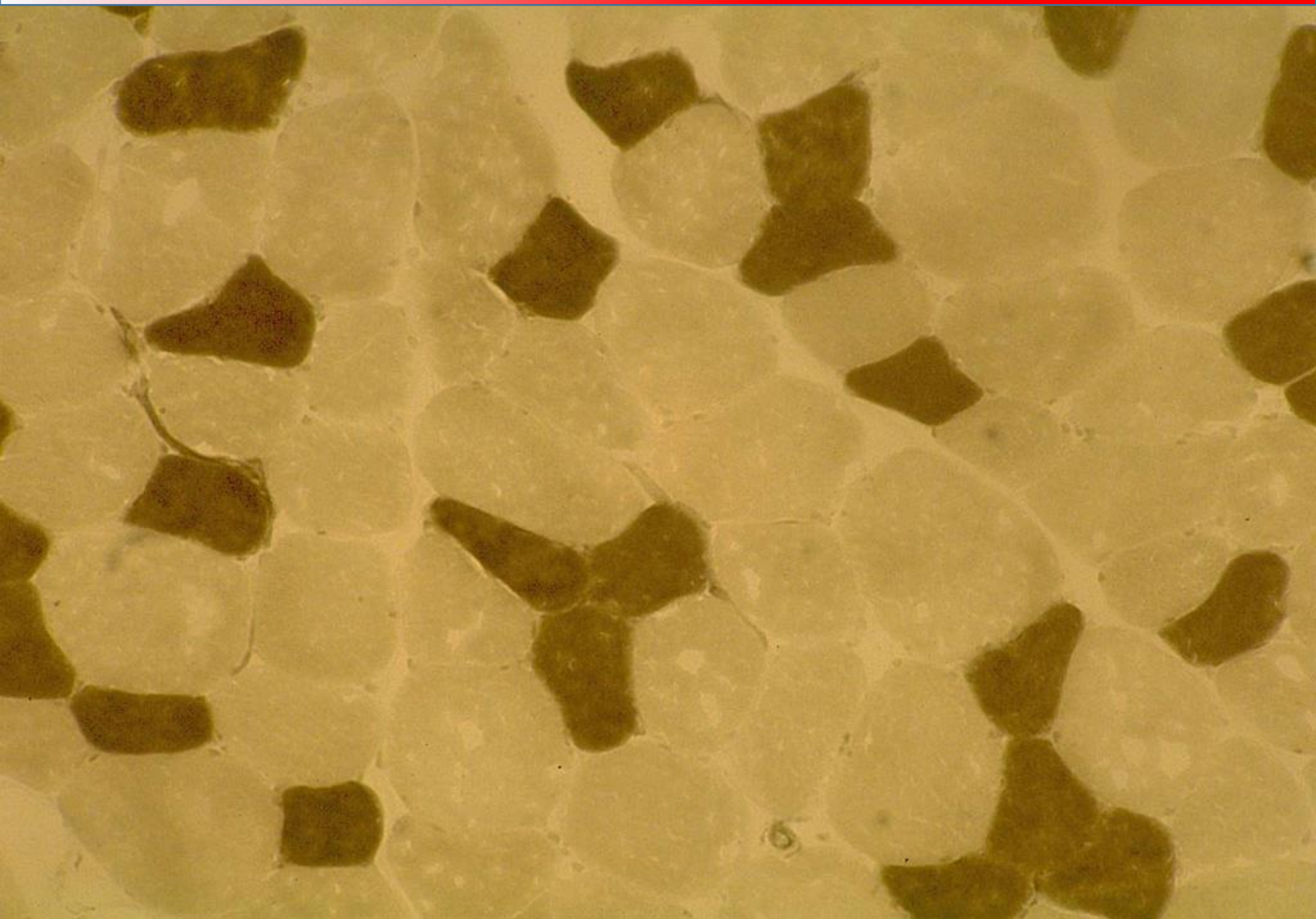


PHYSIOLOGICAL TYPES OF SKELETAL MUSCLES

- **Myosin heavy chain (MHC) type I and II**
- distinct metabolic, contractile, and motor-unit properties
- ATPase activity
- **Twitch type**
- Fast vs. slow
- **Fiber color**
- Red vs. white
- **Myoglobin content**
- **Glycogen content**
- **Energy metabolism**
- **Endurance**



PHYSIOLOGICAL TYPES OF SKELETAL MUSCLES



PHYSIOLOGICAL TYPES OF SKELETAL MUSCLES

Properties	Type I fibers	Type IIA fibers	Type IIX fibers
Motor Unit Type	Slow Oxidative (SO)	Fast Oxidative/Glycolytic (FOG)	Fast Glycolytic (FG)
Twitch Speed	Slow	Fast	Fast
Twitch Force	Small	Medium	Large
Resistance to fatigue	High	High	Low
Glycogen Content	Low	High	High
Capillary Supply	Rich	Rich	Poor
Myoglobin	High	High	Low
Red Color	Dark	Dark	Pale
Mitochondrial density	High	High	Low
Capillary density	High	Intermediate	Low
Oxidative Enzyme Capacity	High	Intermediate-high	Low
Z-Line Width	Intermediate	Wide	Narrow
Alkaline ATPase Activity	Low	High	High
Acidic ATPase Activity	High	Medium-high	Low

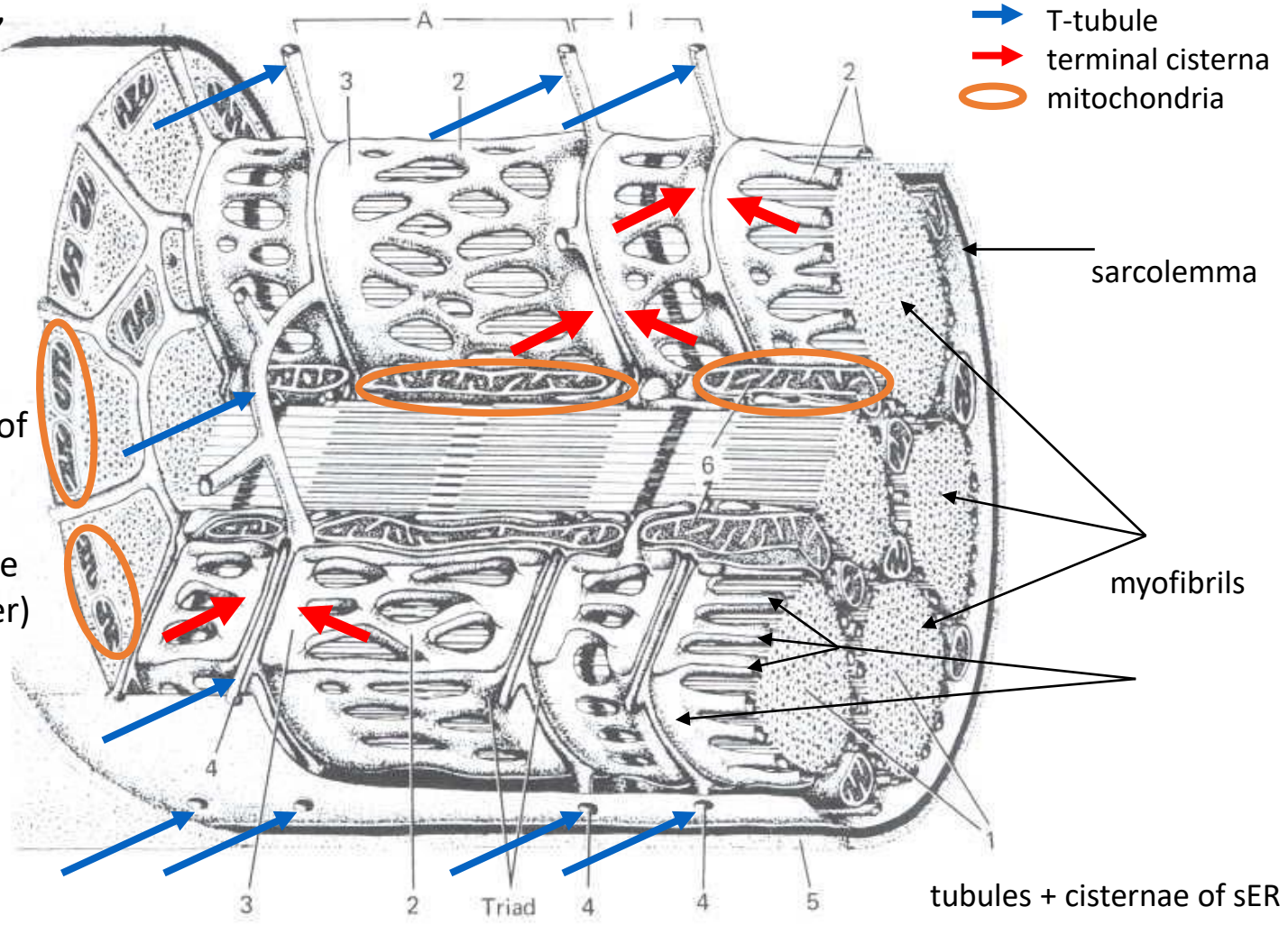
ULTRASTRUCTURE OF RHABDOMYOCYTE

Sarcolemma + **t-tubules**,

Sarcoplasm:
Nuclei,
Mitochondria,
Golgi apparatus,
Glycogen (β granules)

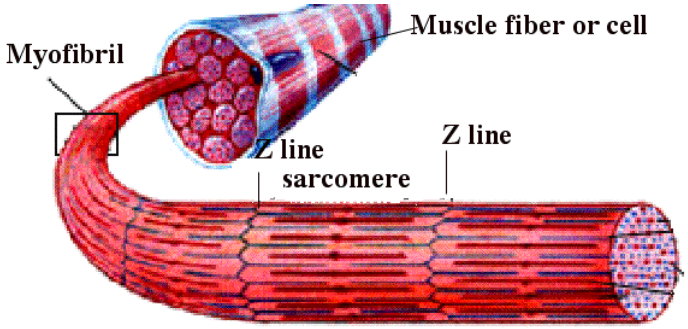
Sarcoplasmic reticulum (smooth ER) – reservoir of Ca^{2+}

Myofibrils (parallel to the length of the muscle fiber)

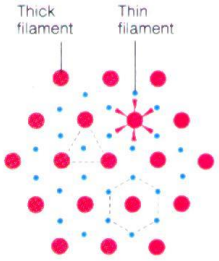


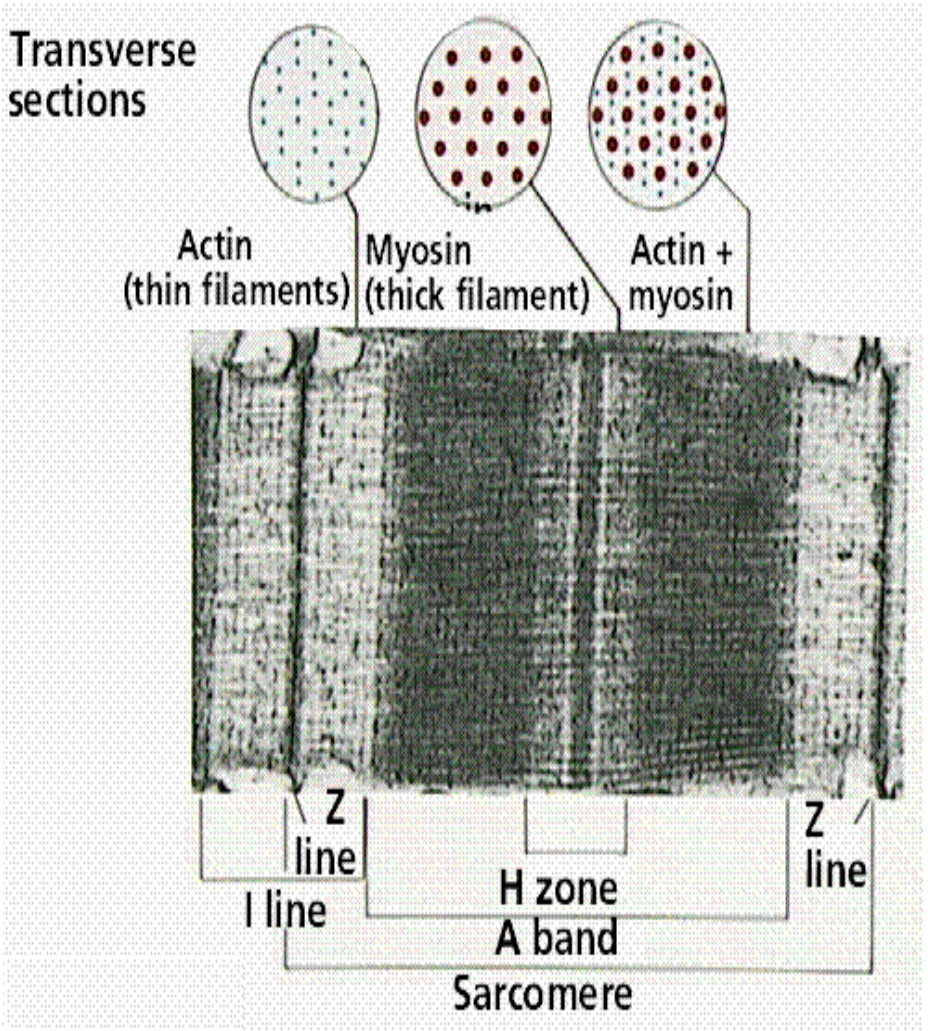
MYOFIBRILS

– elongated structures [Ø 0.5 – 1.5 μ] in sarcoplasm of muscle fiber oriented in parallel to the length of the fiber,

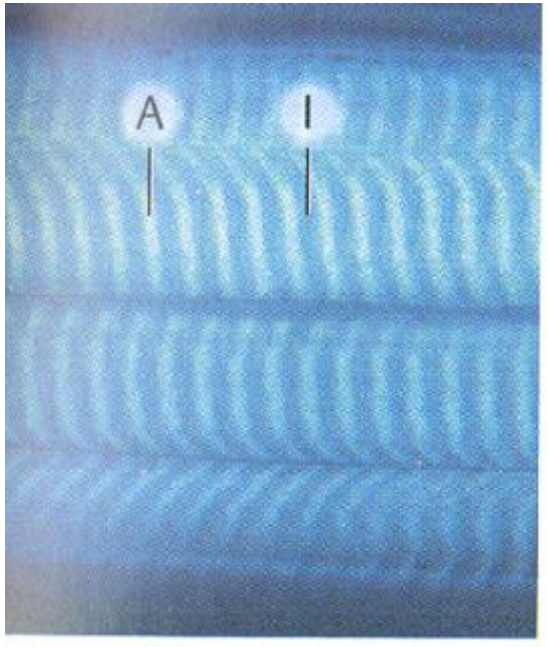


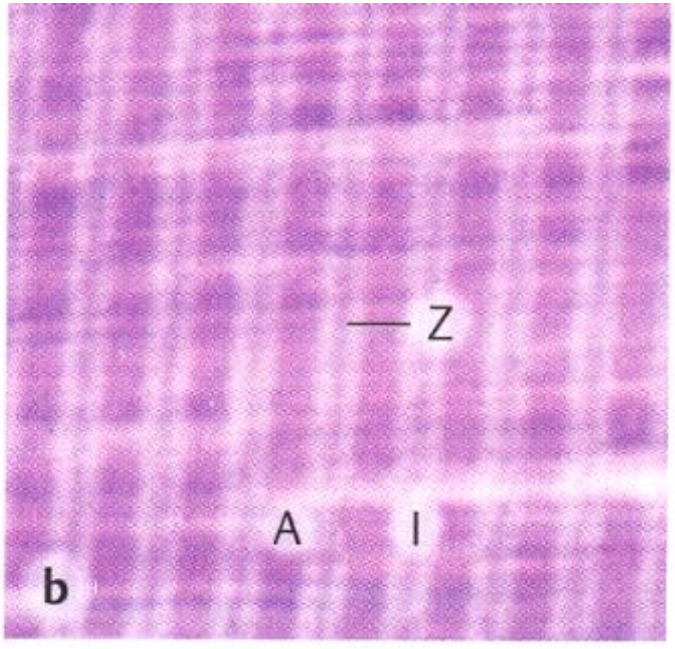
– Actin + myosin myofilaments
– Sarcomere
– Z-line
– M-line and H-zone
– I-band, A-band

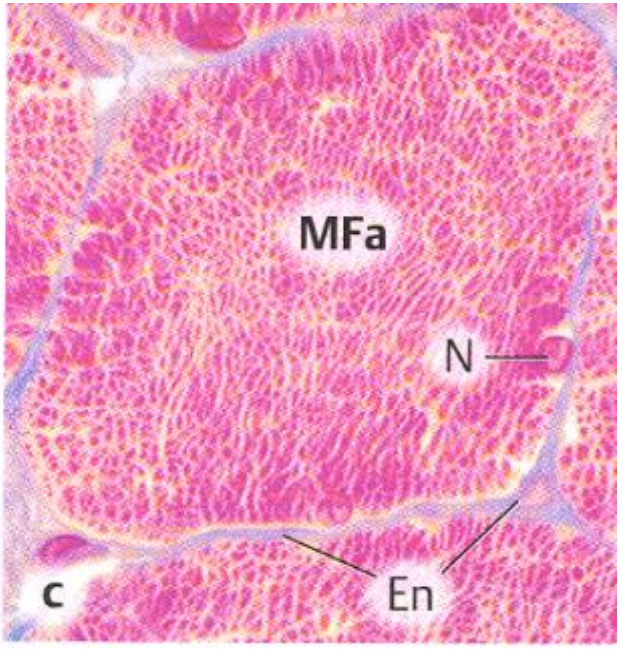


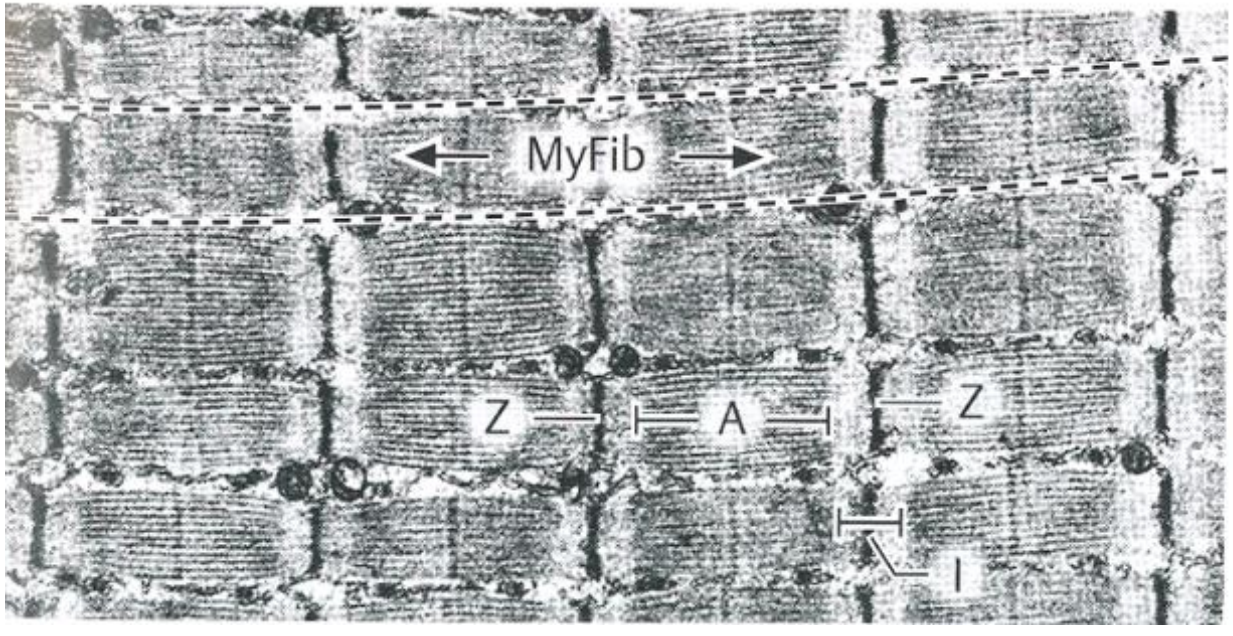


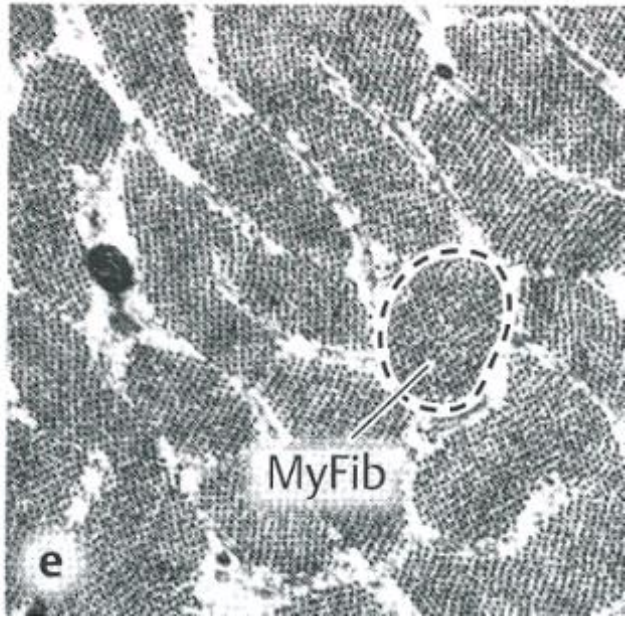
MYOFIBRILS



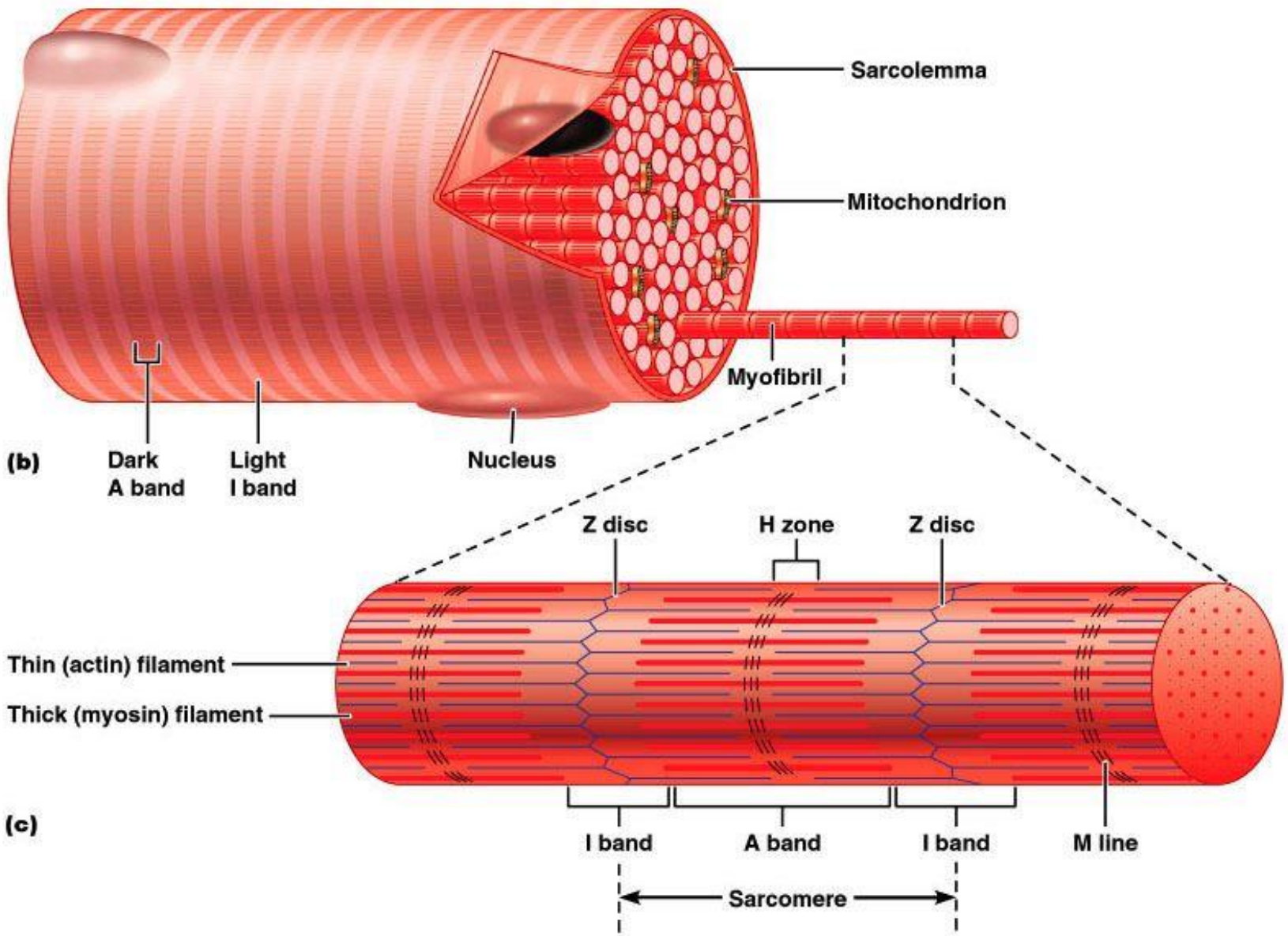




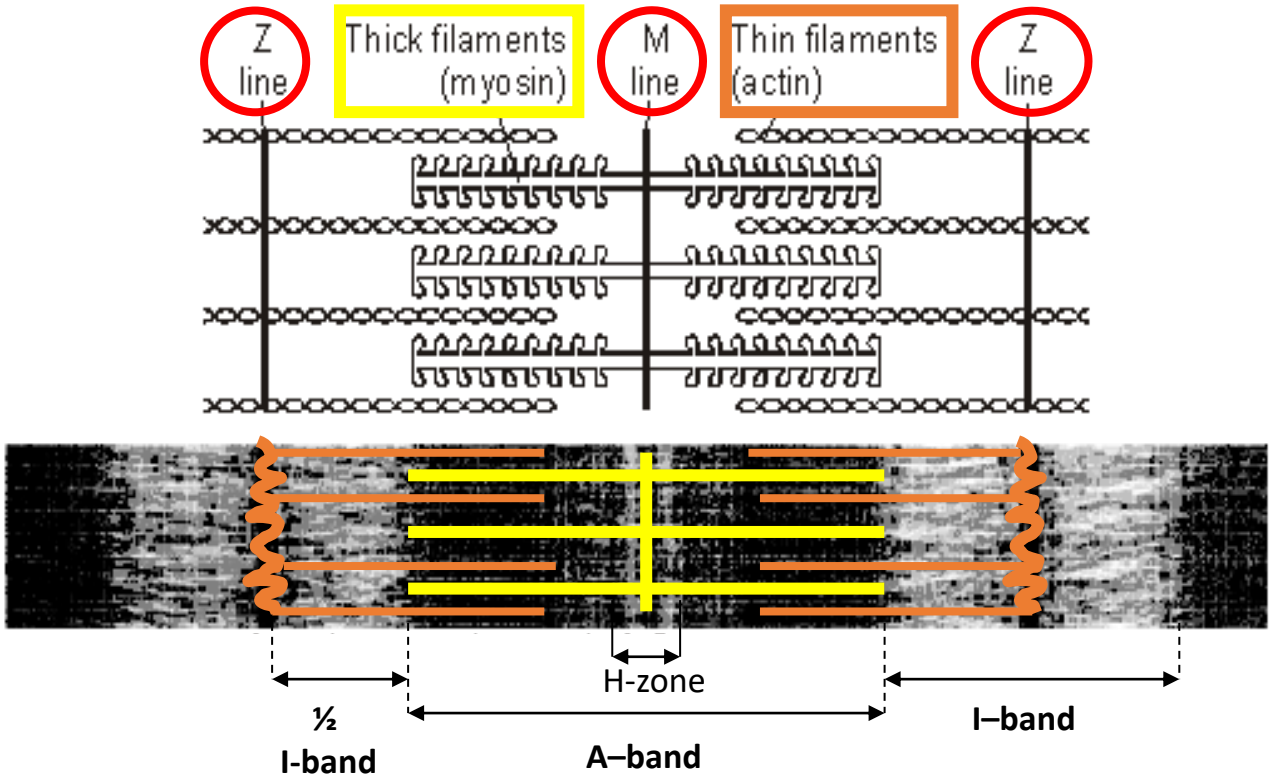




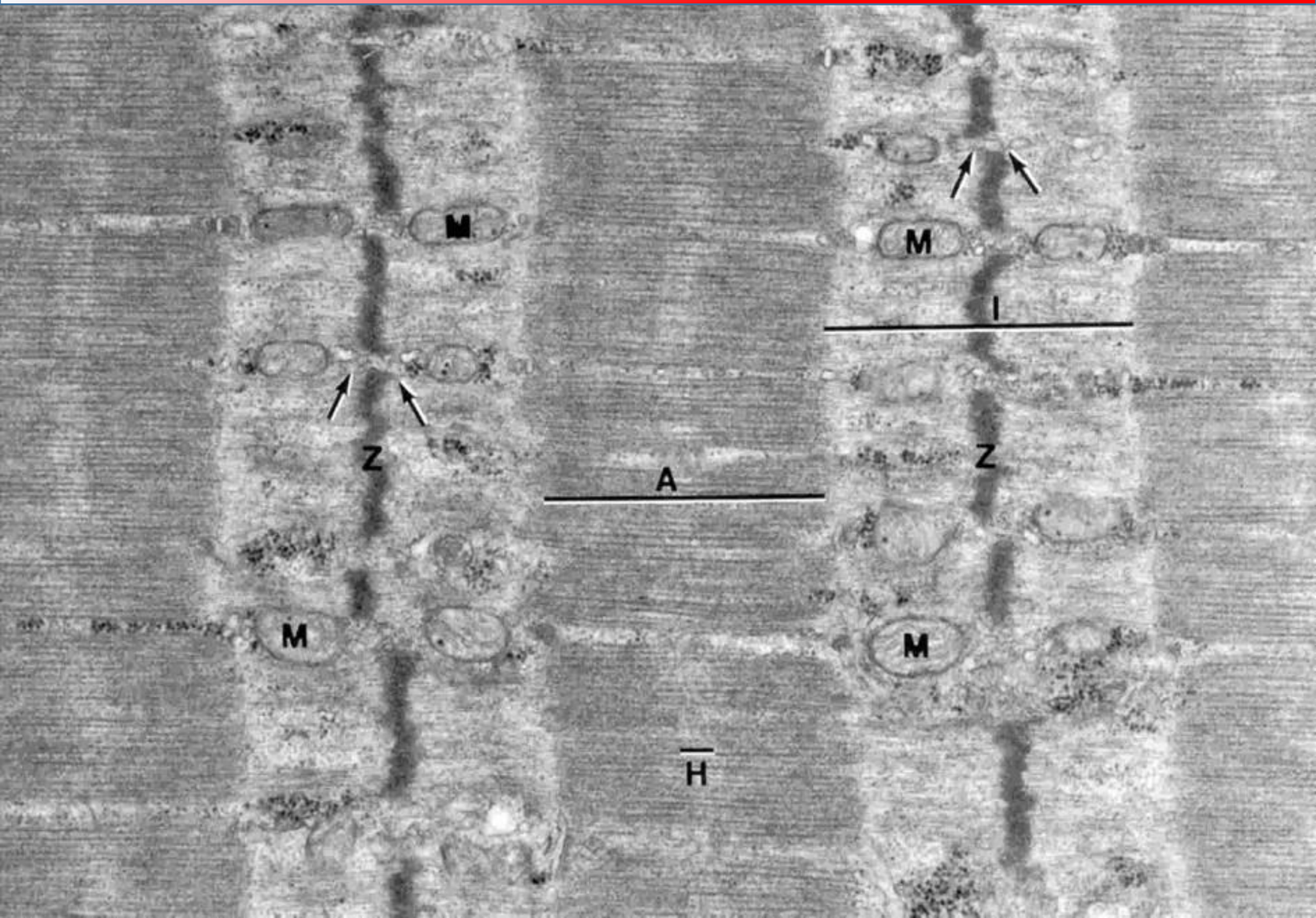
SARCOMERE



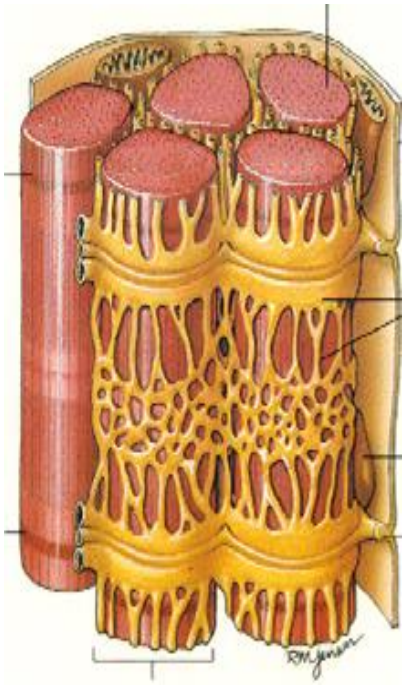
SARCOMERE

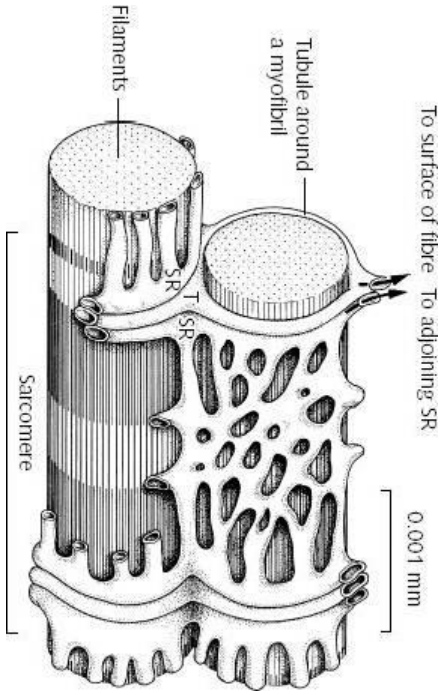

Z line
Thick filaments (myosin)
M line
Thin filaments (actin)
Z line
H-zone
½ I-band
A–band
I–band

SARCOMERE



SARCOPLASMIC RETICULUM





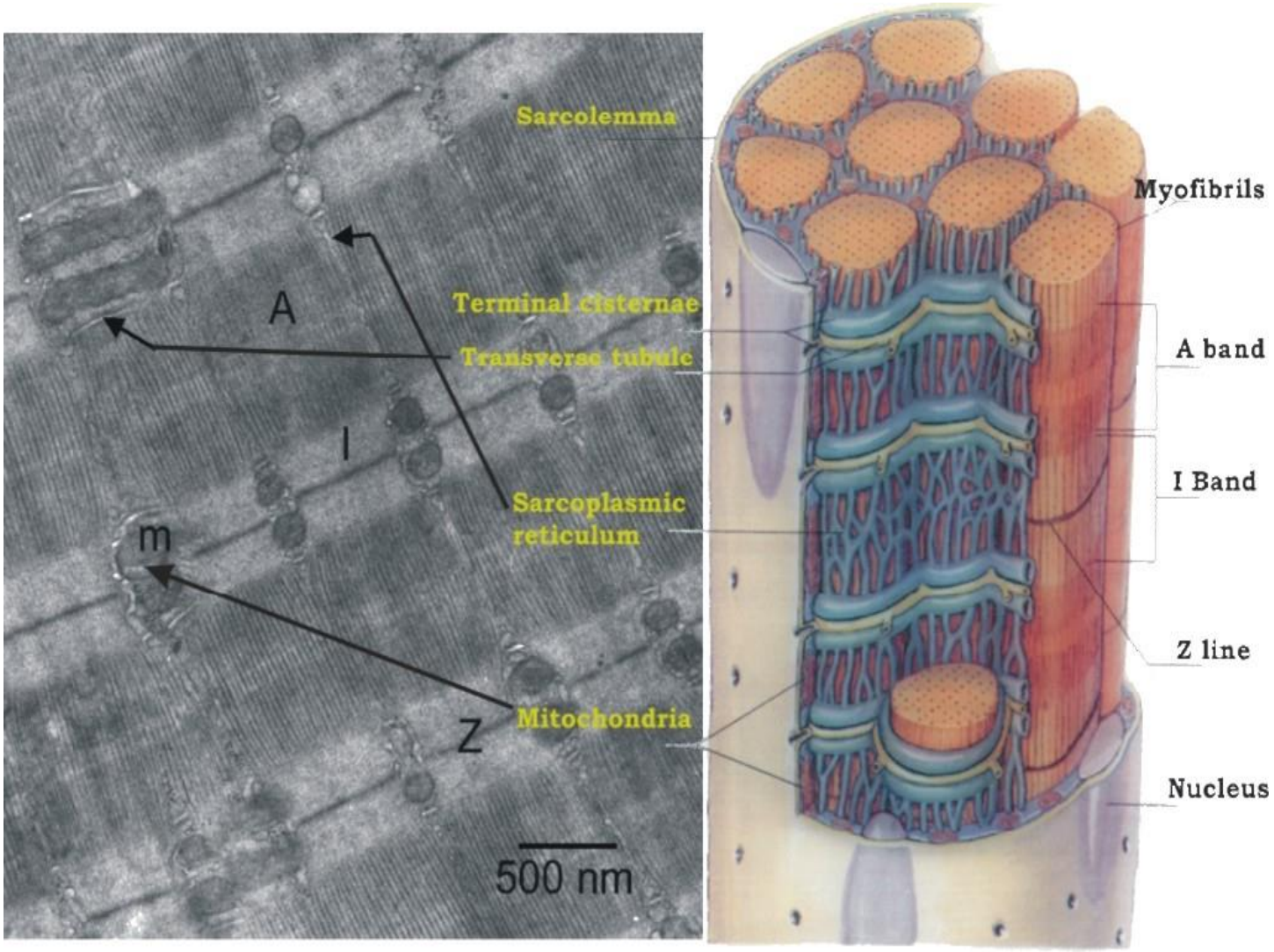
- Terminal cistern
- T-tubule
- Terminal cistern

TRIAD

- communicating intracellular cavities around myofibrils, separated from cytosol
- **terminal cisternae** (“junction”) and **longitudinal tubules** (“L” system).
- reservoir of Ca^{II+} ions

- **T-tubules** (“T” system) are invaginations of sarcolemma and bring action potential to terminal cisternae change permeability of membrane for Ca^{II+} ions

SARCOPLASMIC RETICULUM



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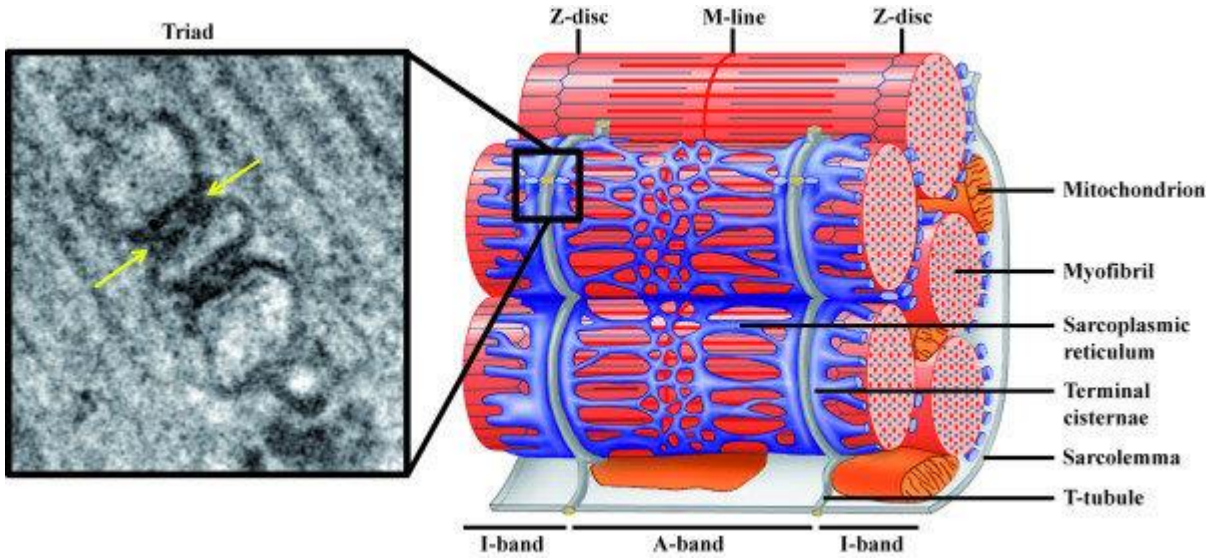

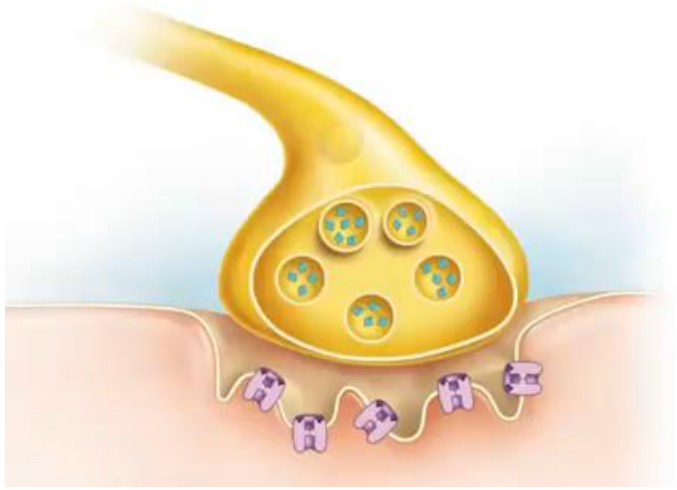

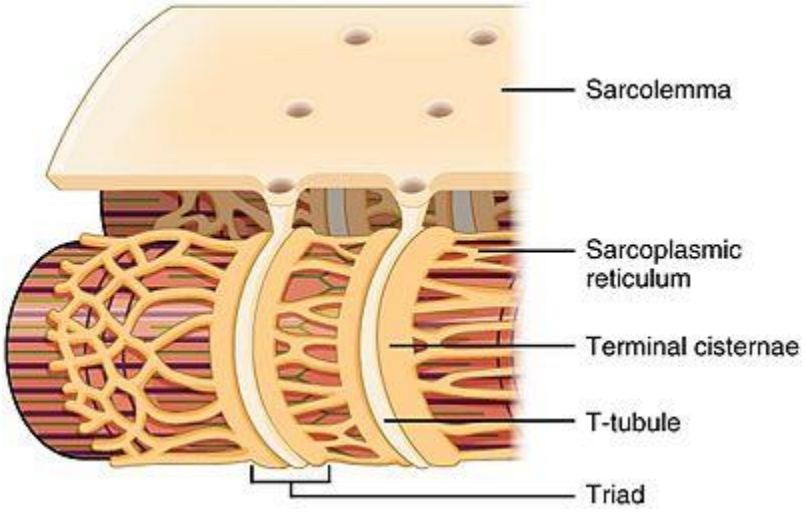

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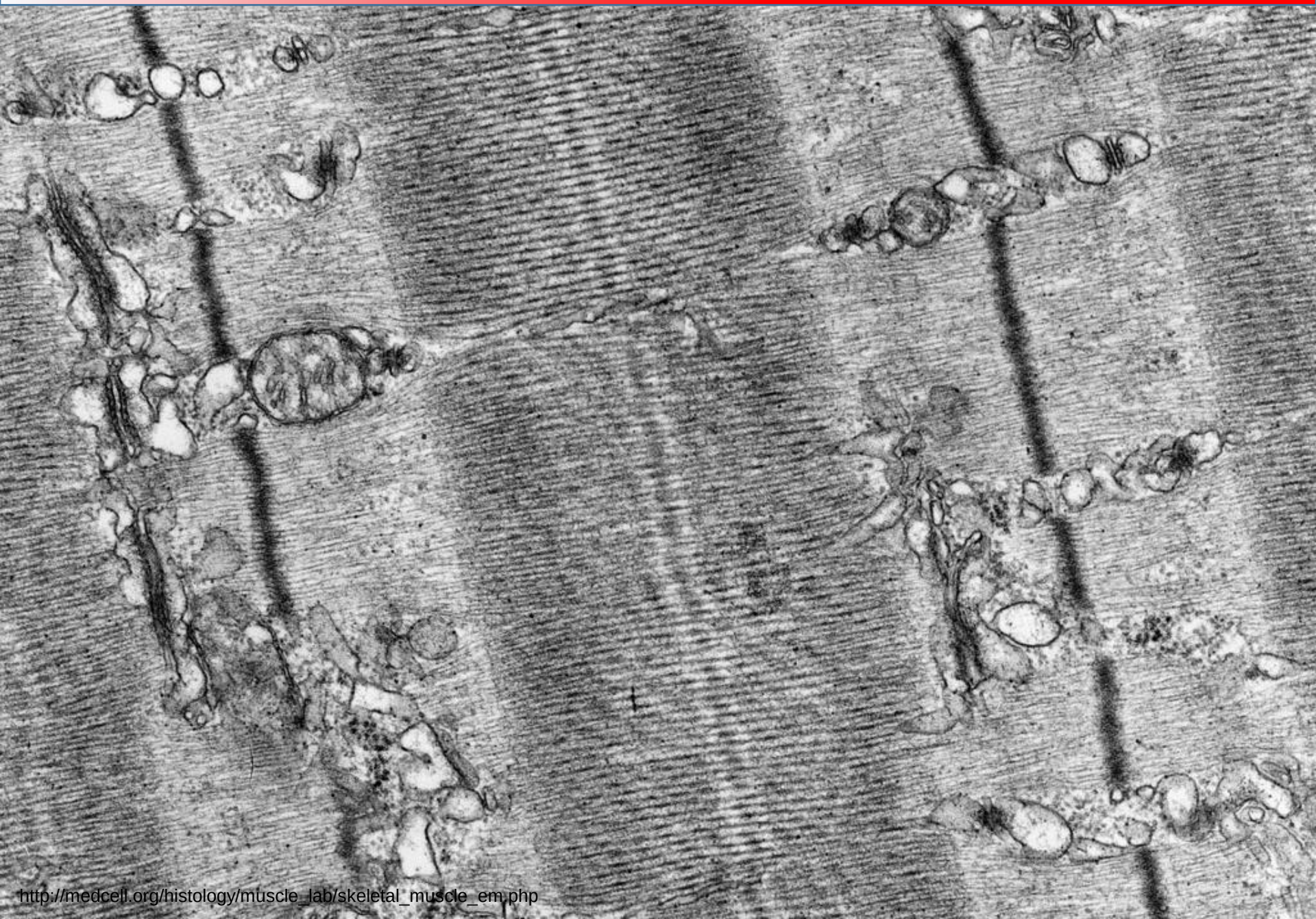
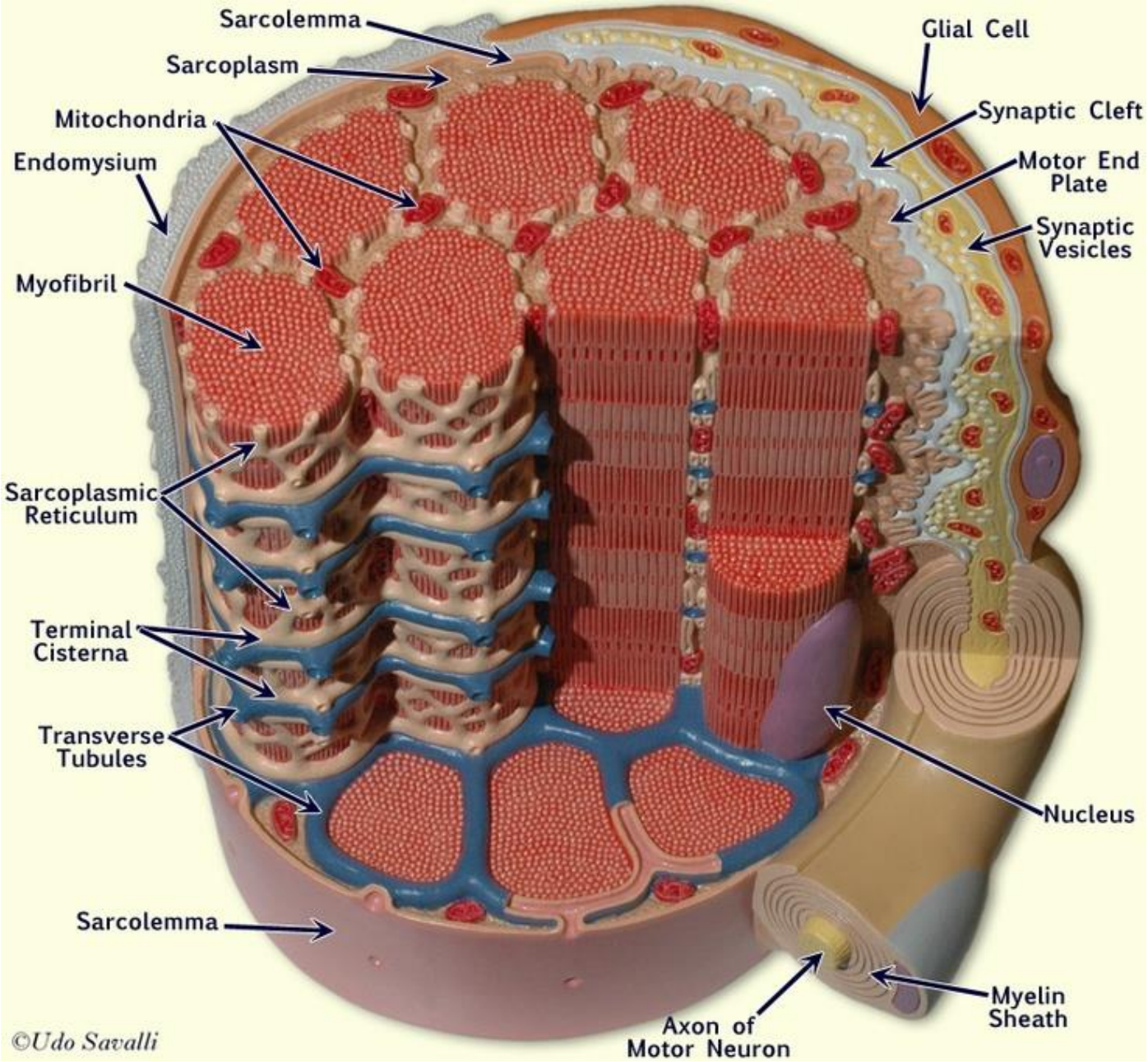
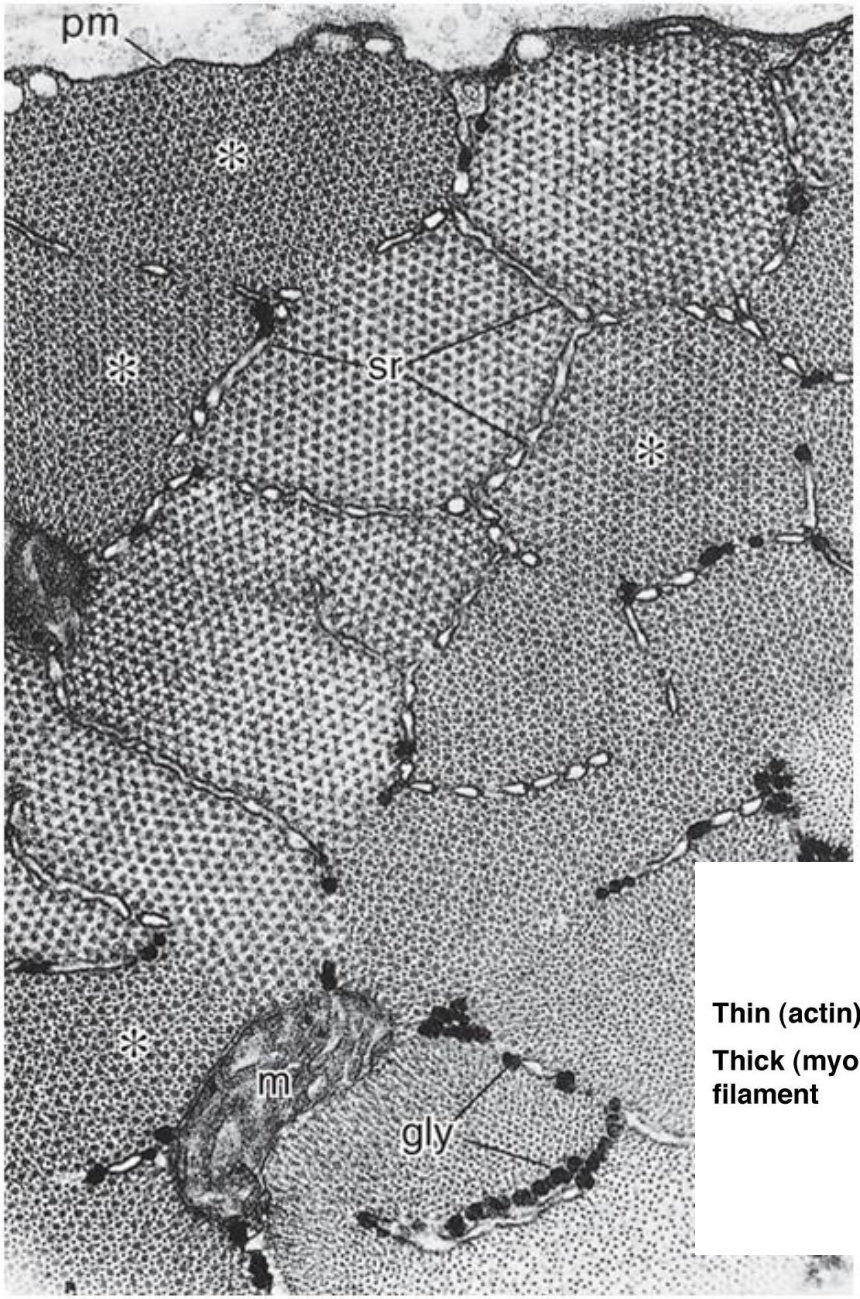


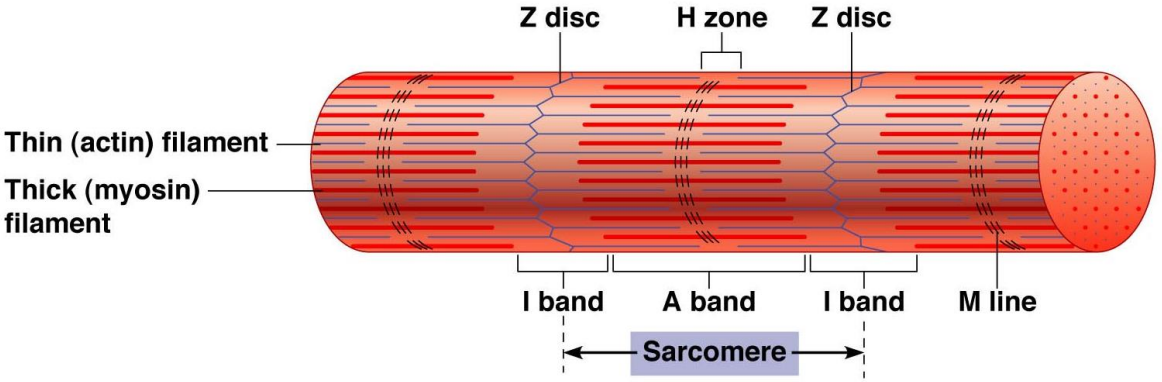
http://medcell.org/histology/muscle_lab/skeletal_muscle_em.php

ULTRASTRUCTURE OF RHABDOMYOCYTE



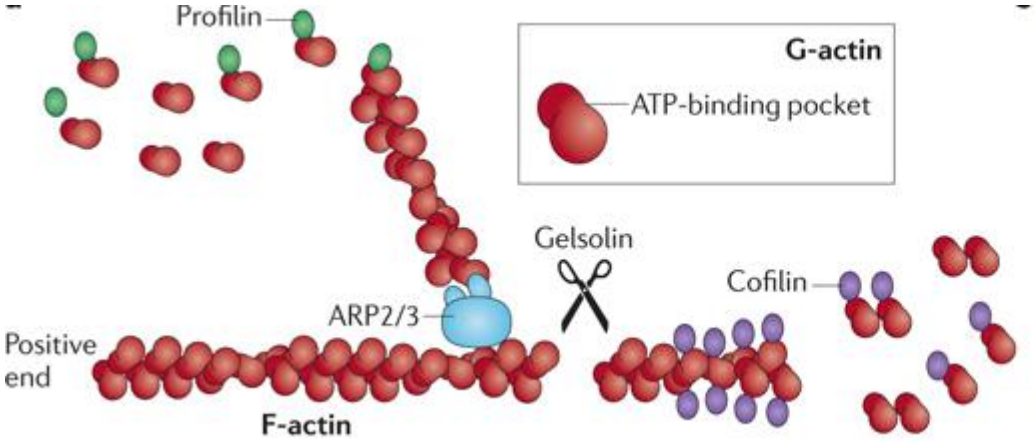
MYOFILAMENTS

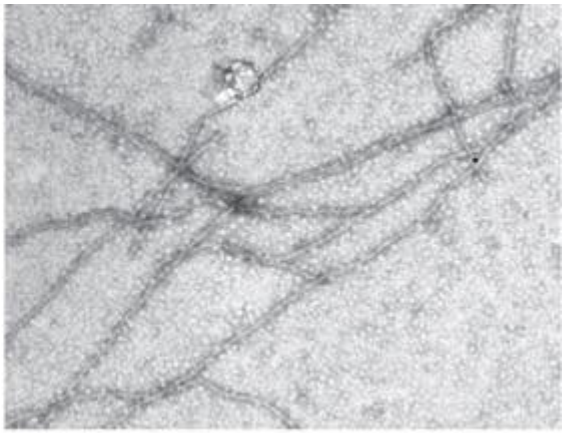




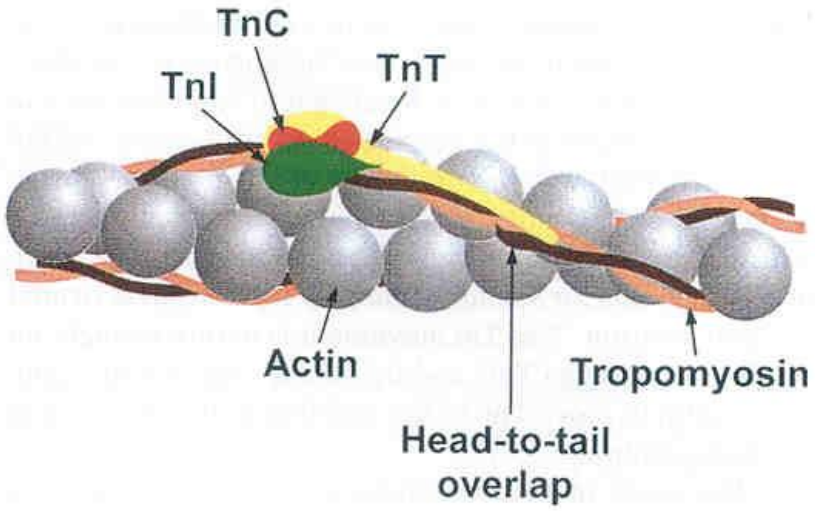
THIN MYOFILAMENTS

- **Fibrilar actin (F-actin),** (∅ 7 nm, ↔1 μm)





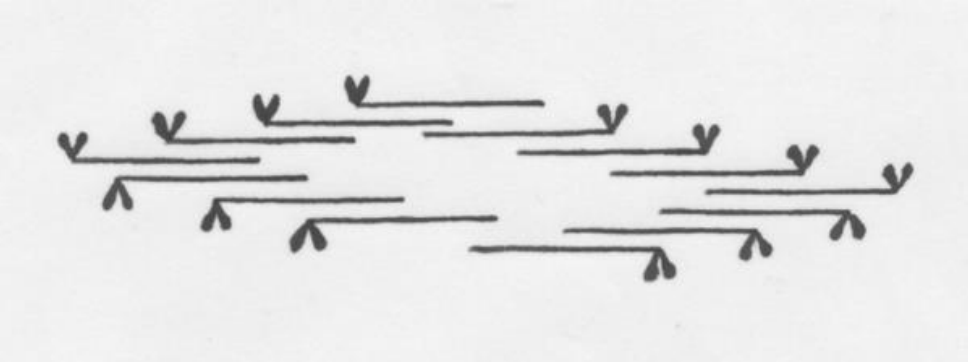
- Tropomyosin – thin double helix in groove of actin double helix, spans 7 monomers of G-actin
- Troponin – complex of 3 globular proteins
  - TnT (Troponin T) – binds tropomyosin
  - TnC (Troponin C) – binds calcium
  - TnI (Troponin I) inhibits interaction between thick and thin filaments

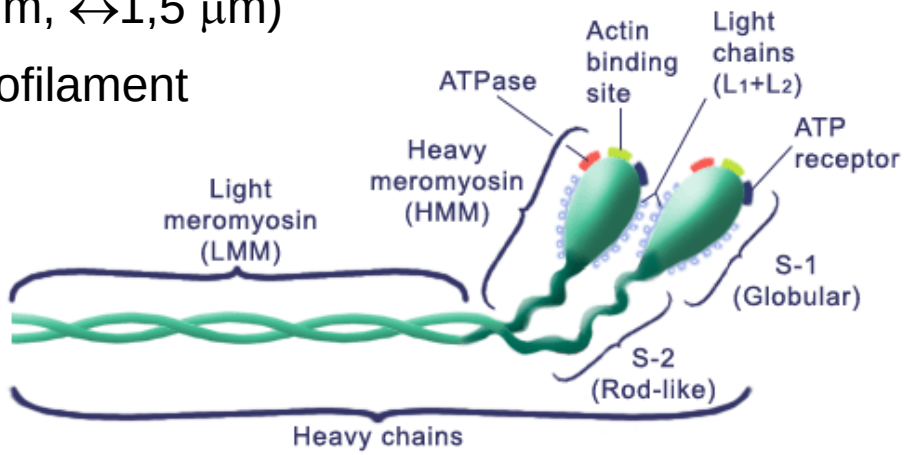


THICK MYOFILAMENTS

- **Myosin II**

- Large polypeptide, golf stick shape, (∅ 15 nm, ↔1,5 μm)
- Bundles of myosin molecules form thick myofilament

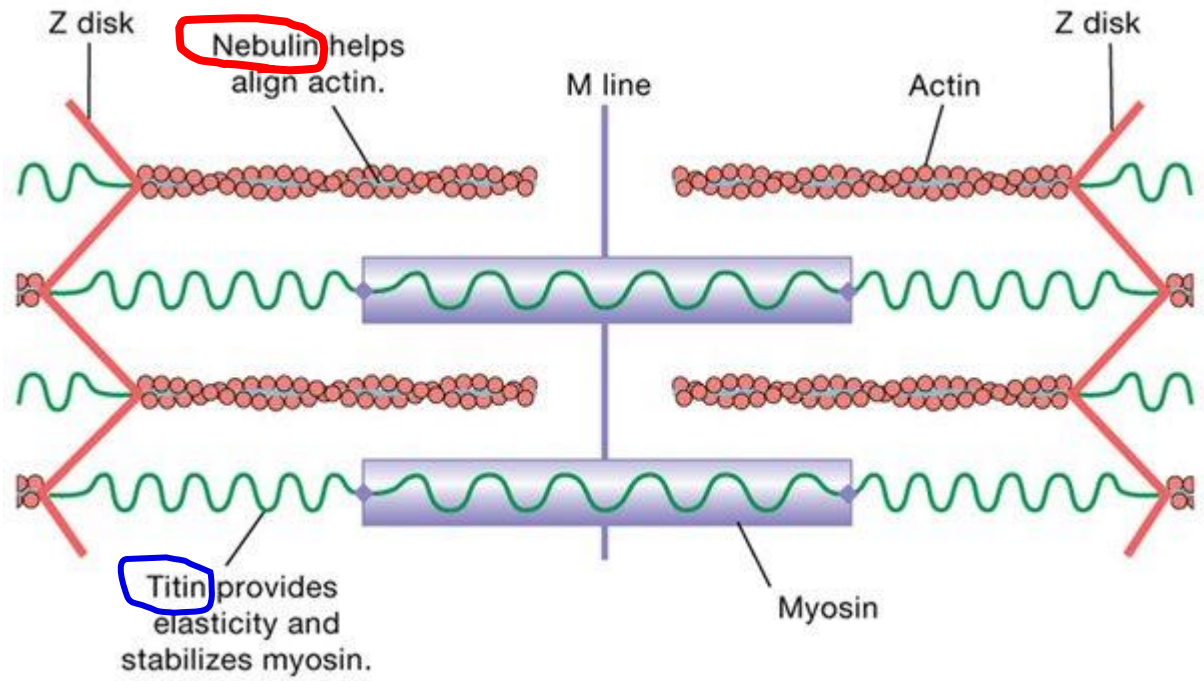




OTHER PROTEINS ASOCIATED WITH MYOFILAMENTS

- **Nebulin**
- 600-900kDa
- F-actin stabilization
- length of sarcomere

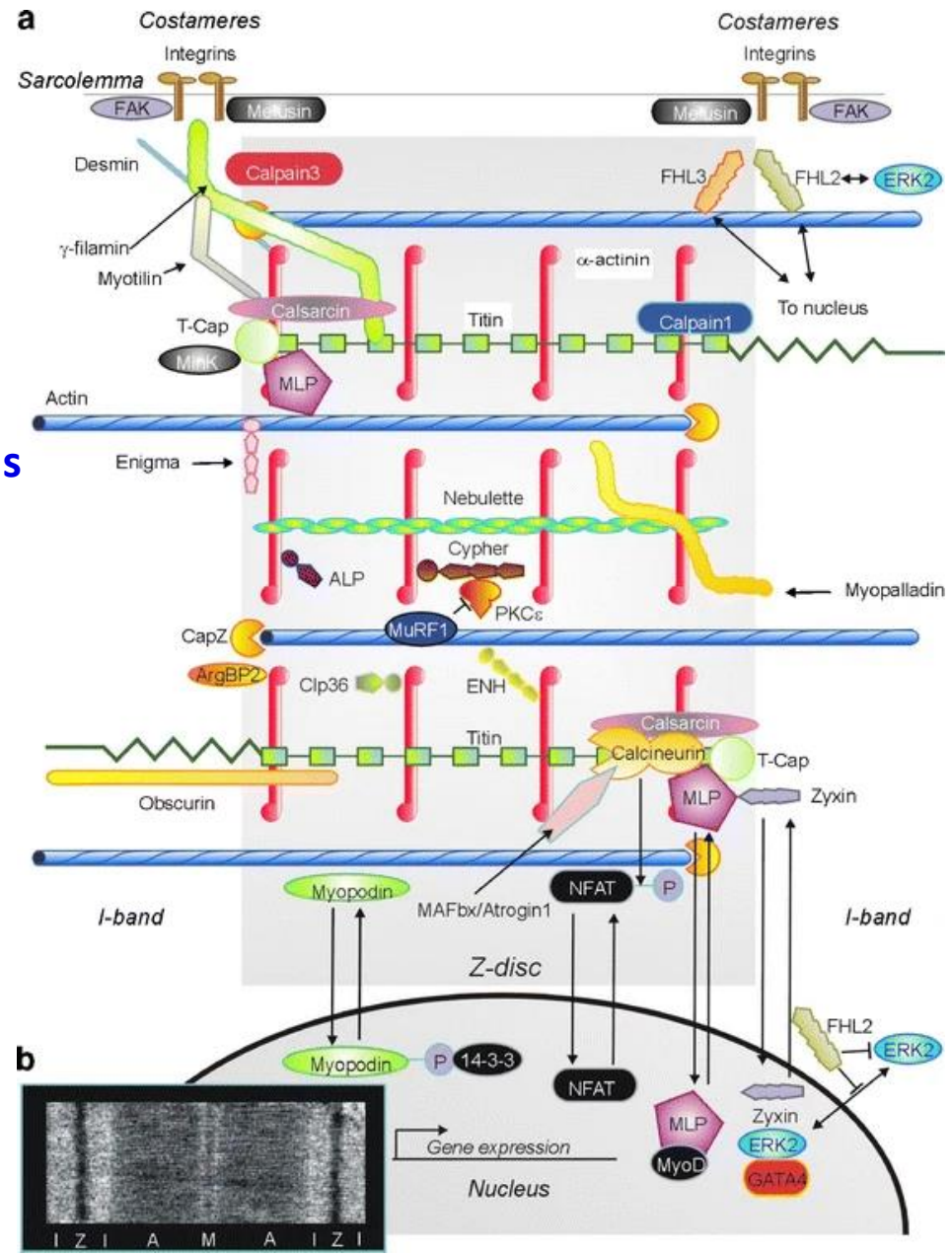
- **Titin** (konektin)
- >MDa
- myosin stabilization
- elastic



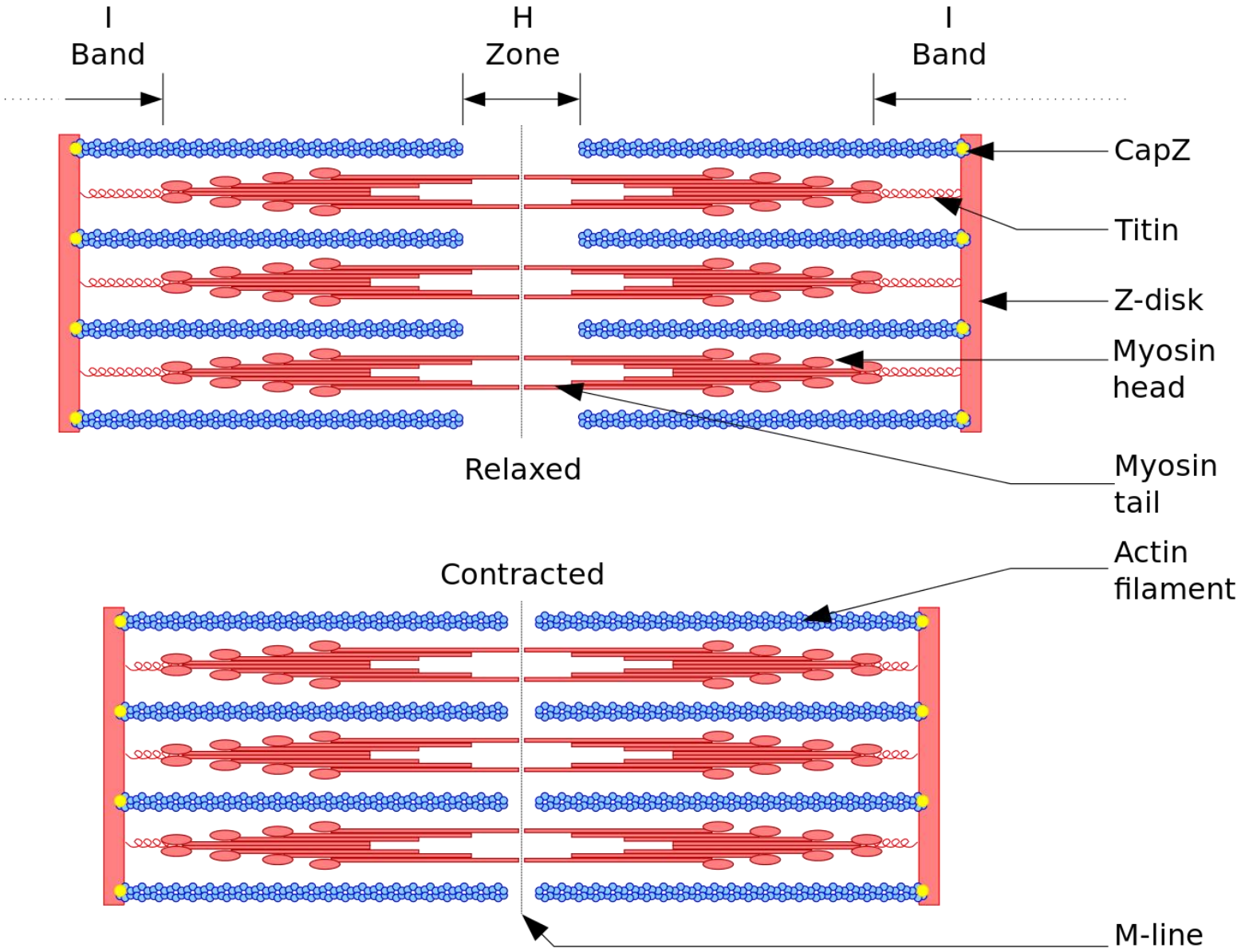
- **α-actinin**
- Z-line
- binds actin

OTHER PROTEINS ASOCIATED WITH MYOFILAMENTS

- **Sarcomere is a complex structure. Defects caused by mutations in sarcomere proteins are linked to various myopathies.**

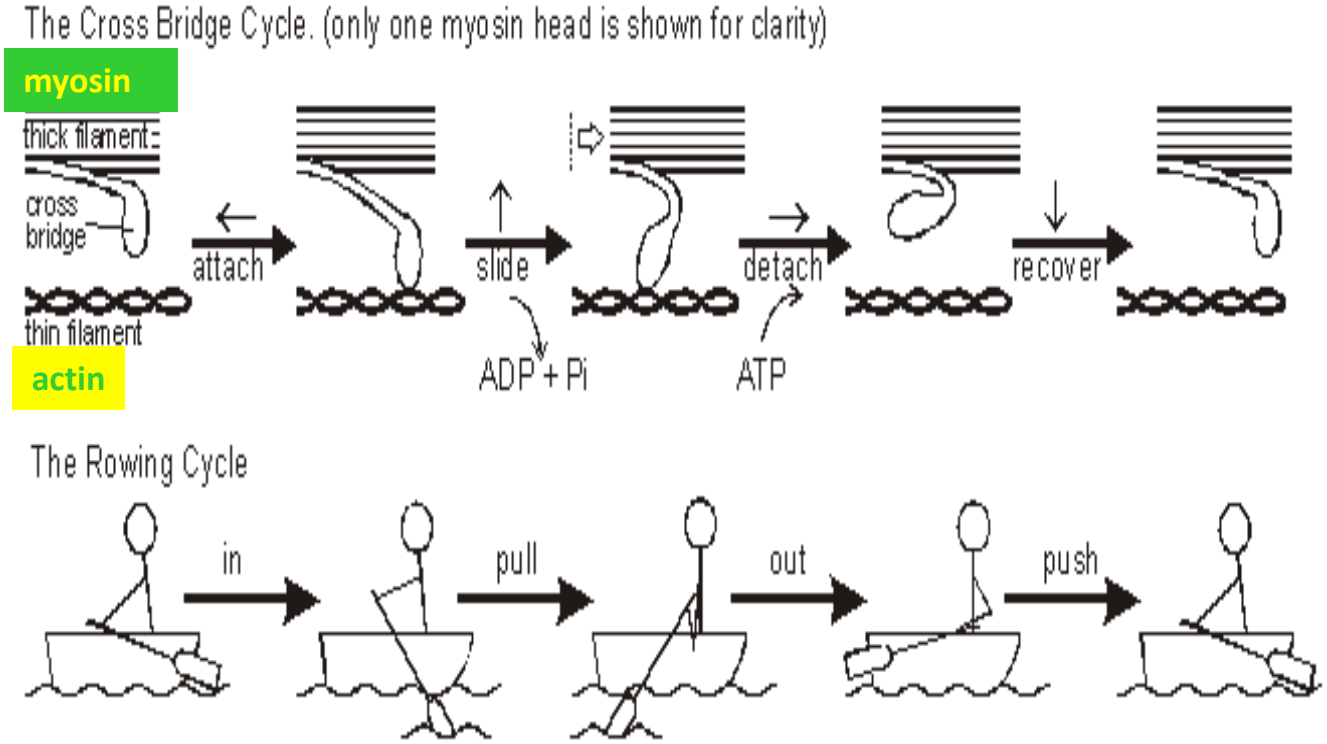


MYOFILAMENTS ASSEMBLE TO CONTRACTIVE STRUCTURES

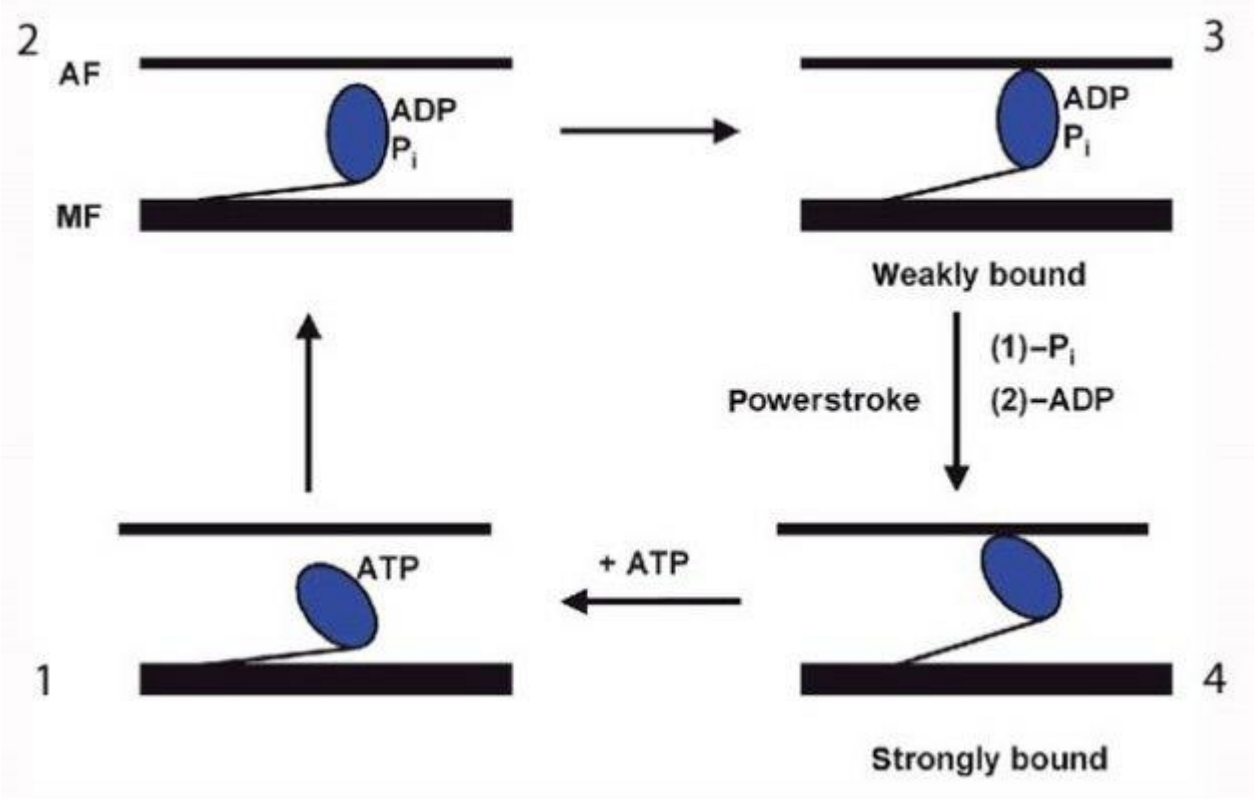


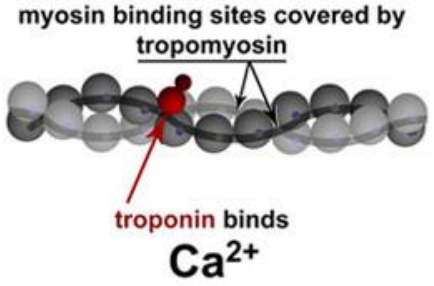
MYOFILAMENTS ASSEMBLE TO CONTRACTIVE STRUCTURES

- Propagation of action potential (depolarization) via T-tubule (= invagination of sarcolemma)
- Change of terminal cisternae permeability – releasing of Ca^{+} ions increases their concentration in sarcoplasm
- Myosin binds actin - sarcomera then shortens by sliding movement – contraction
- Relaxation: repolarization, decreasing of Ca^{2+} ions concentration, inactivation of binding sites of actin for myosin



CROSS BRIDGE CYCLE



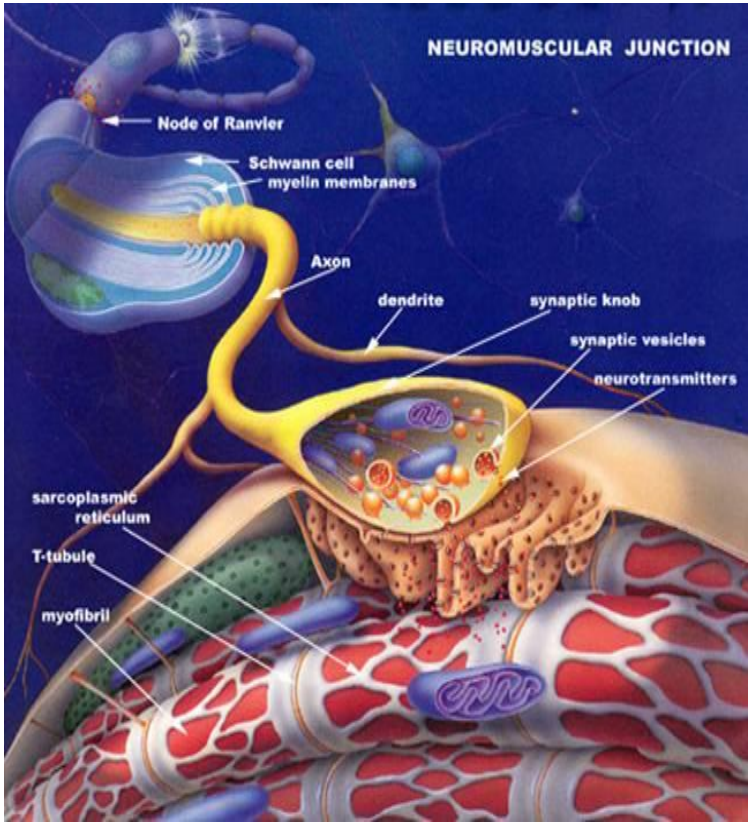


Huxley, H. E. & Hanson, J. Changes in the cross-striations of muscle during contraction and stretch and their structural interpretation. Nature 173, 973–976 (1954) doi:10.1038/173973a0.

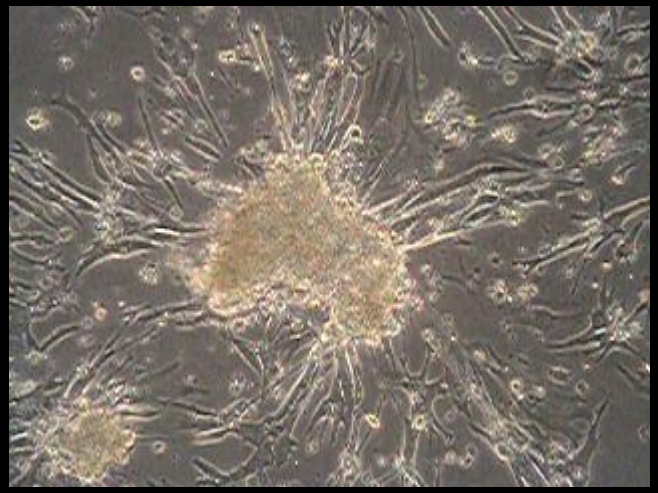
Huxley, A. F. & Niedergerke, R. Structural changes in muscle during contraction: Interference microscopy of living muscle fibres. Nature 173, 971–973 (1954) doi:10.1038/173971a0.

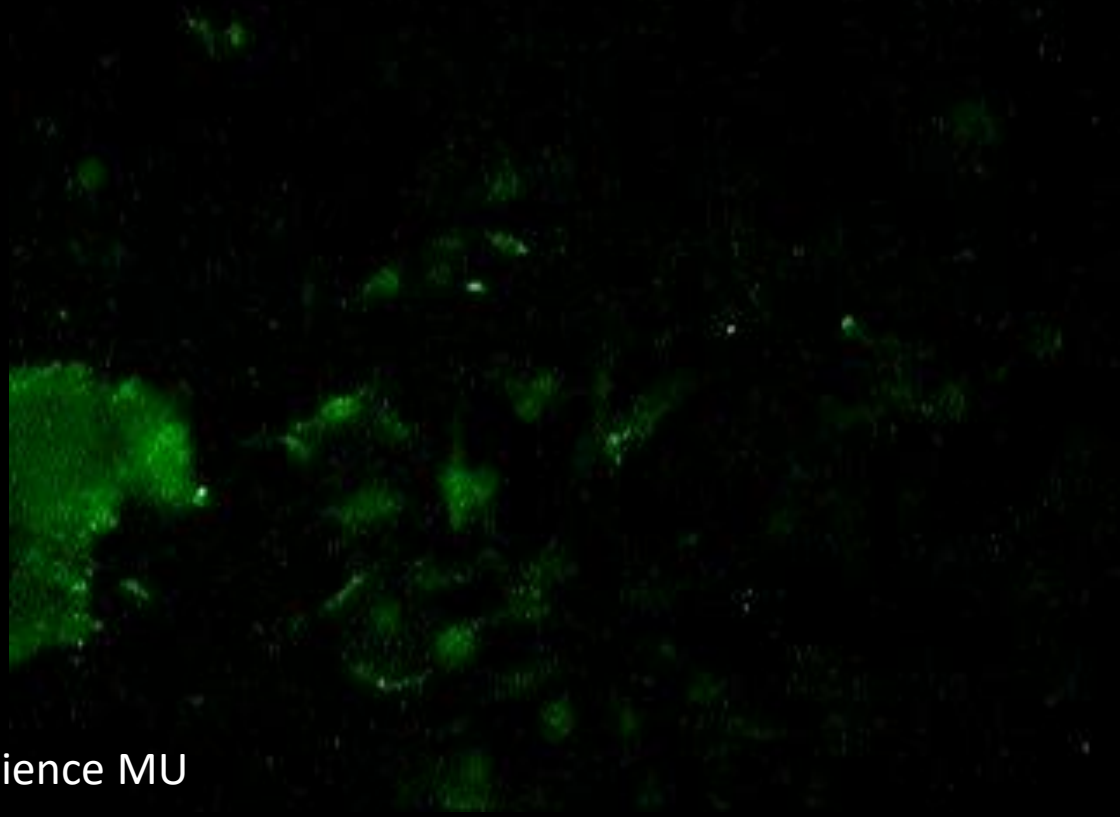
MECHANISM OF CONTRACTION

1. Impulse along motor neuron axon
2. Depolarization of presynaptic membrane (Na^+ influx)
3. Synaptic vesicles fuse with presynaptic membrane
4. Acetylcholine is exocyted to synaptic cleft
5. Acetylcholine diffuses over synaptic cleft
6. Acetylcholine binds to receptors in postsynaptic membrane
7. Depolarization of postsynaptic membrane and sarcolemma (Na^+ influx)
8. T-tubules depolarization
9. Depolarization of terminal cisternae of sER
10. Depolarization of complete sER
11. Release of Ca^{II+} from sER to sarcoplasm
12. Ca^{II+} binds TnC
13. Troponin complex changes configuration
14. Tropomyosin allows binding of actin and myosin
15. Globular parts of myosin bind to actin
16. ATPase in globular parts of myosin activated
17. Energy generated from ATP→ADP + Pi enables cross-bridge cycling
18. Movement of globular parts of myosin
19. Actin myofilament drag to the center of sarcomere
20. Sarcomeres contract (H-zone, I-band shorten)
21. Myofibrils contract
22. Muscle fiber contract



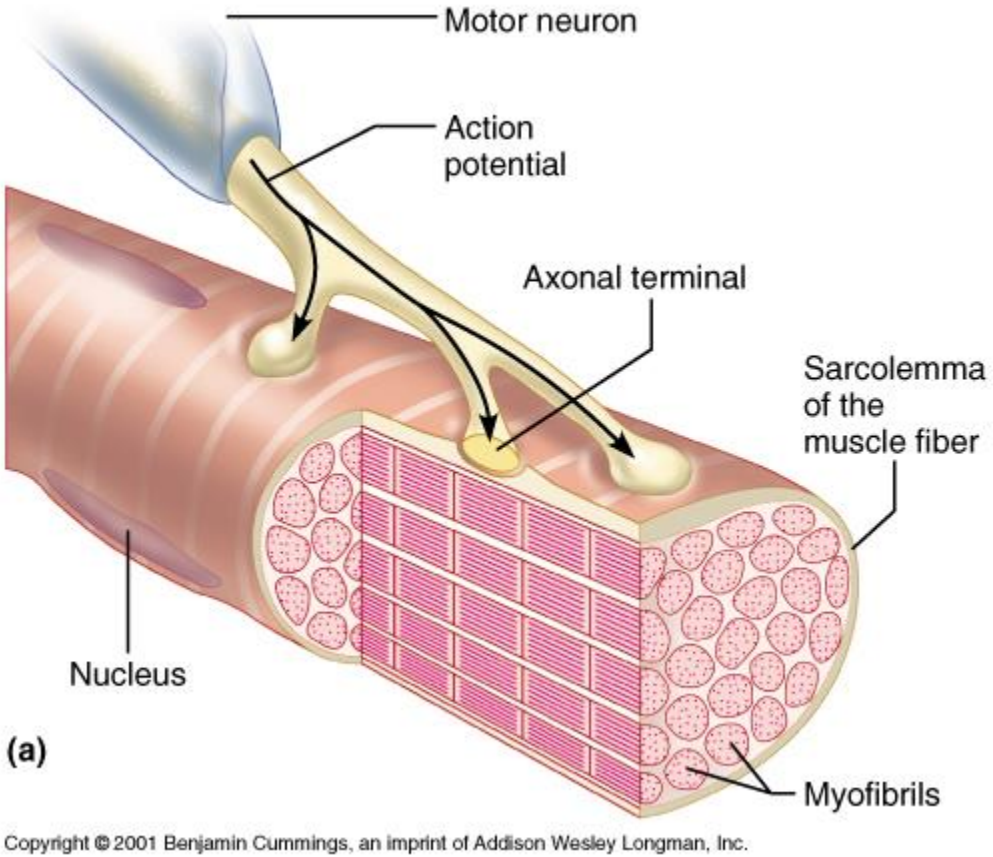
CALCIUM FLOW FROM SARCOPLASMIC RETICULUM

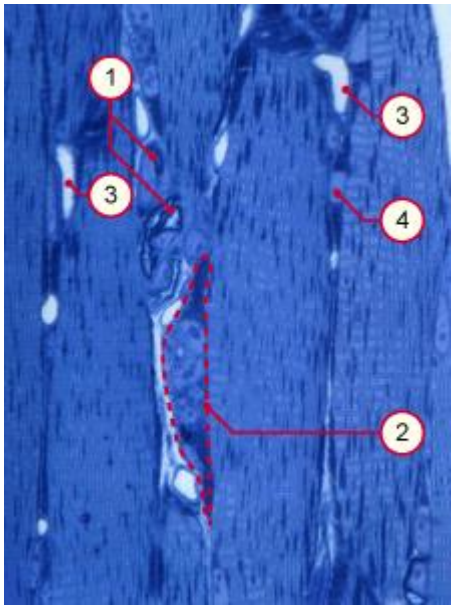




Courtesy Dr. Pacherník, Faculty of Science MU

NEUROMUSCULAR JUNCTION



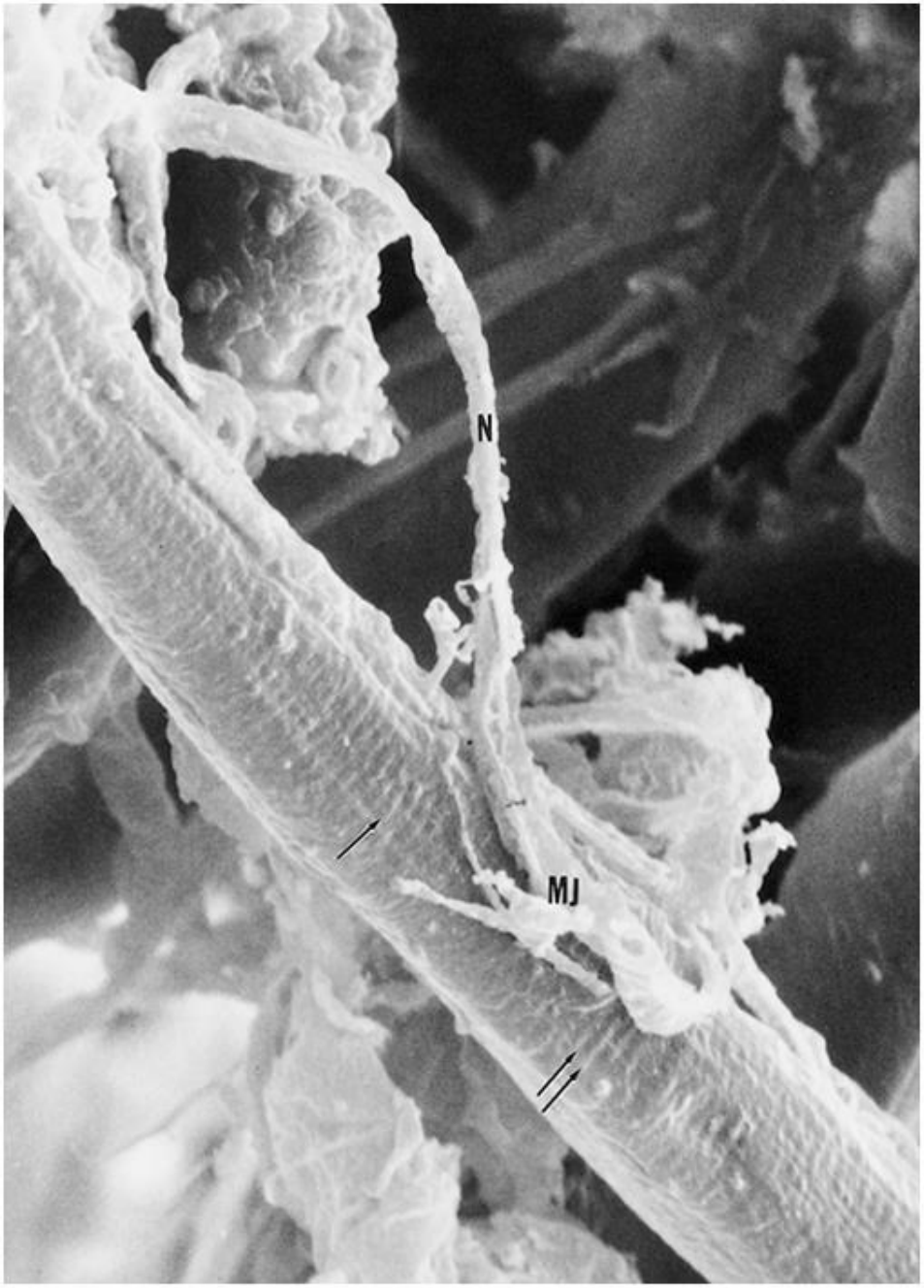


1 Myelinated axons
2 Neuromuscular junction
3 Capillaries
4 Muscle fiber nucleus

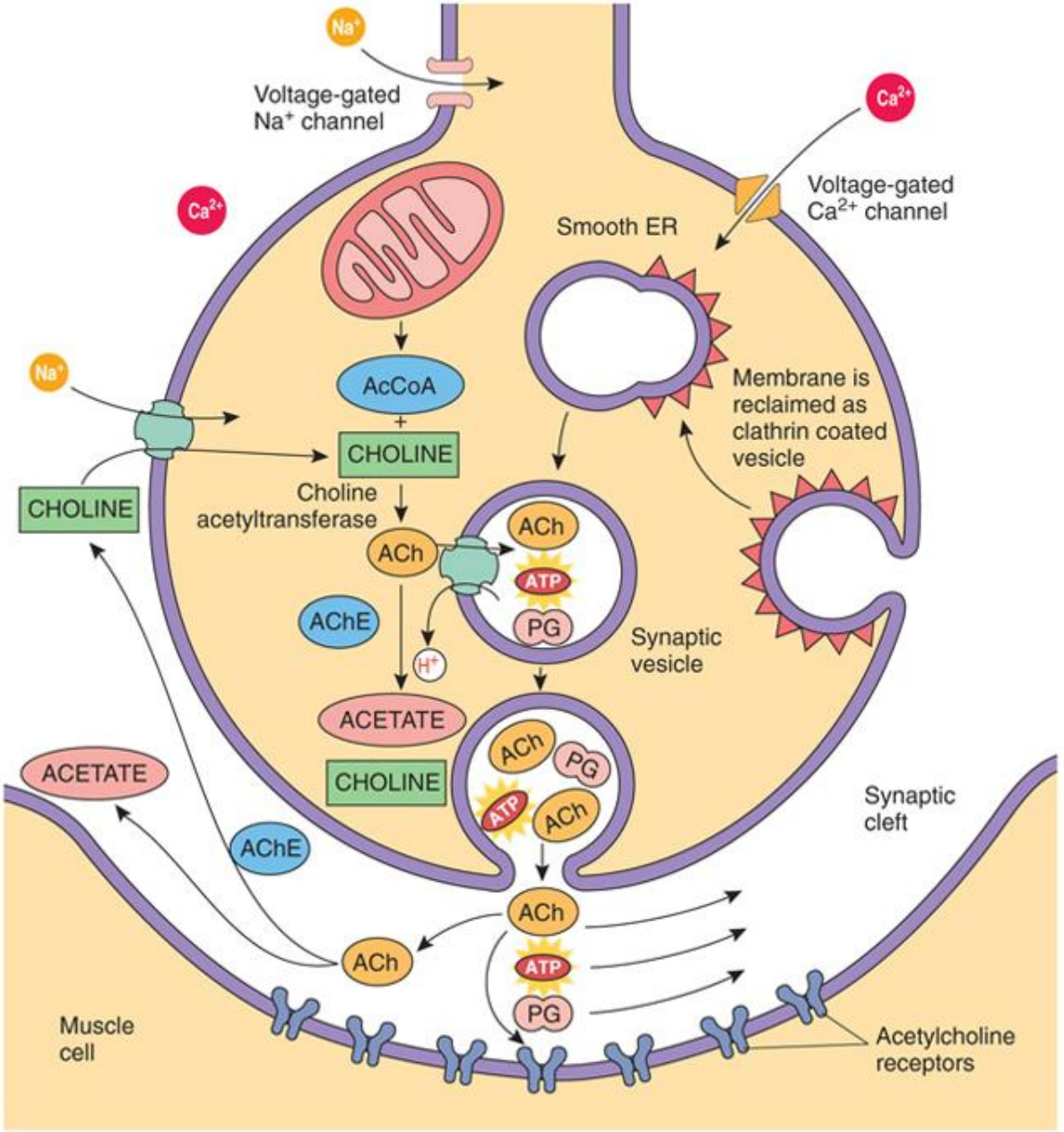
NEUROMUSKULÁRNÍ SPOJENÍ

http://medcell.org/histology/muscle_lab/neuromuscular_junction.php

NEUROMUSCULAR JUNCTION



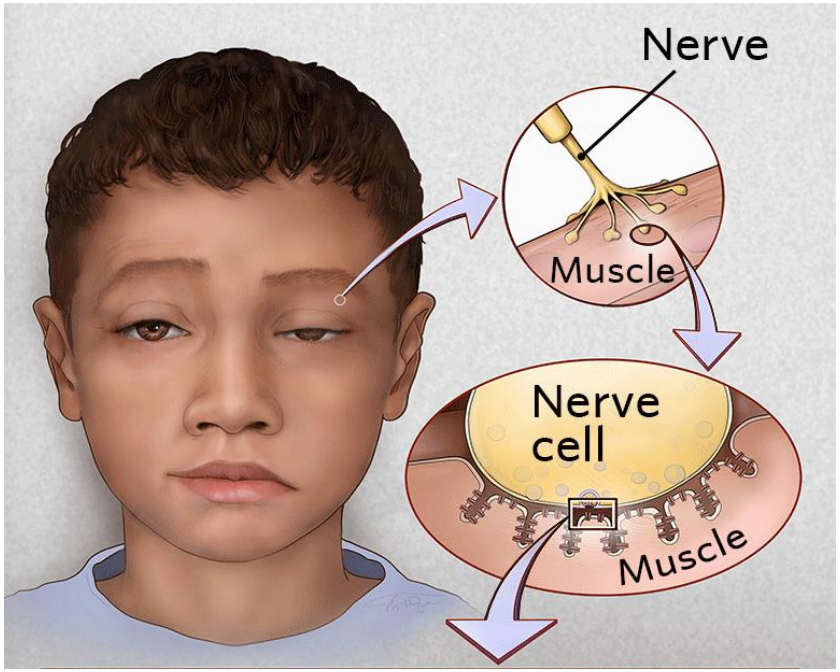
NEUROMUSCULAR JUNCTION

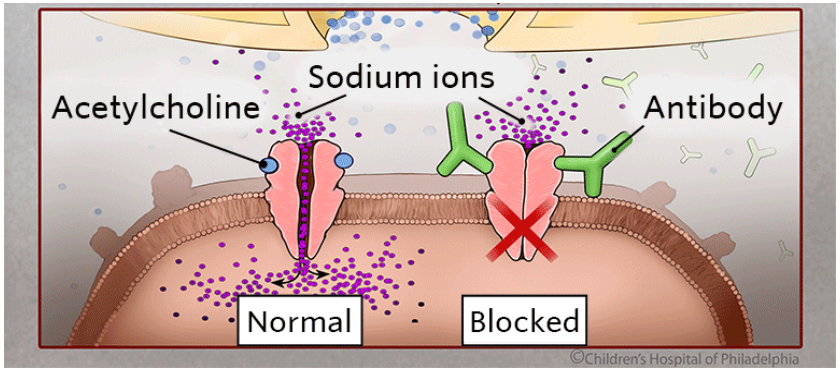


NEUROMUSCULAR JUNCTION

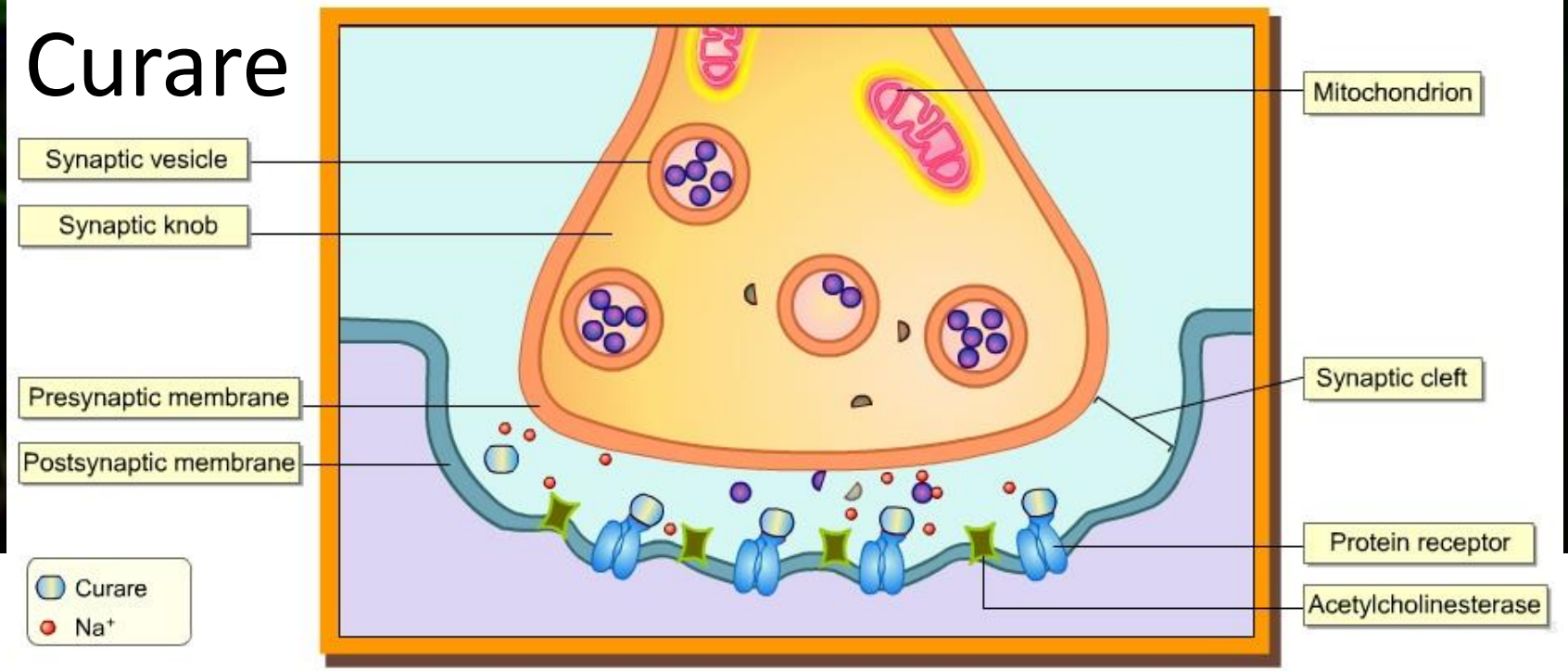
http://medcell.org/histology/muscle_lab/neuromuscular_junction_em.php

MYASTHENIA GRAVIS



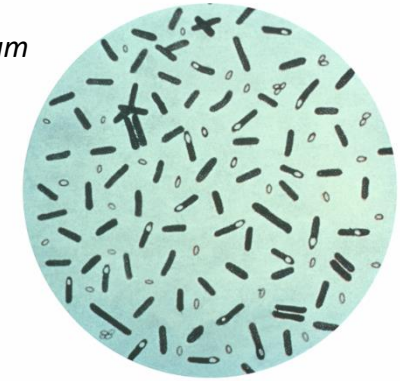


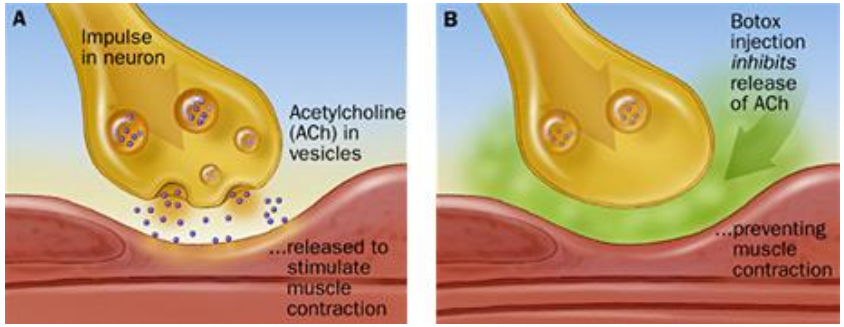
Curare


Synaptic vesicle
Synaptic knob
Presynaptic membrane
Postsynaptic membrane
Mitochondrion
Synaptic cleft
Protein receptor
Acetylcholinesterase
Curare
Na+

Botulotoxin

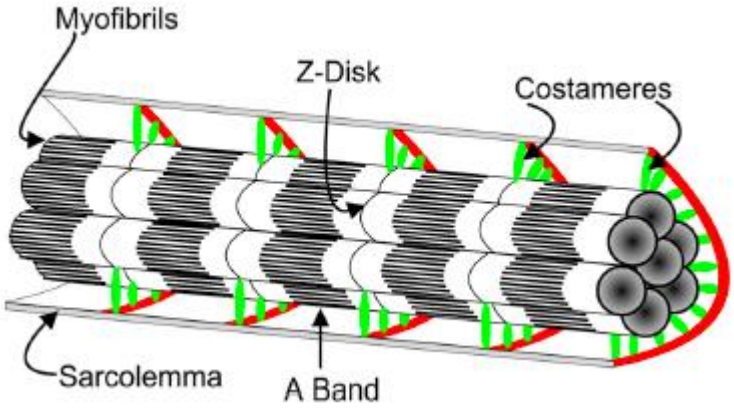
Clostridium botulinum

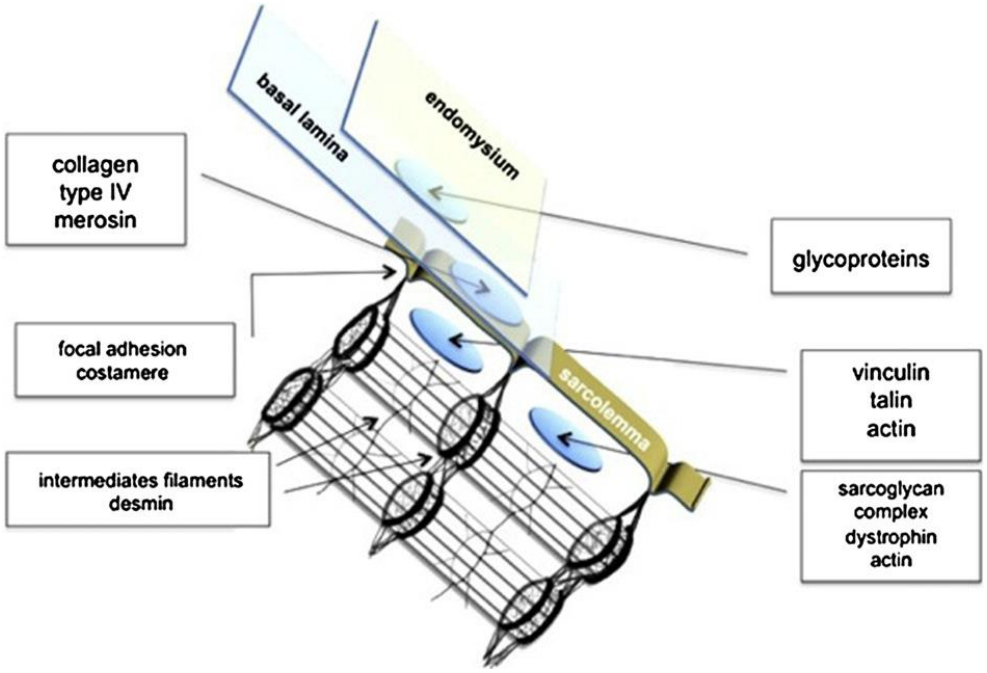




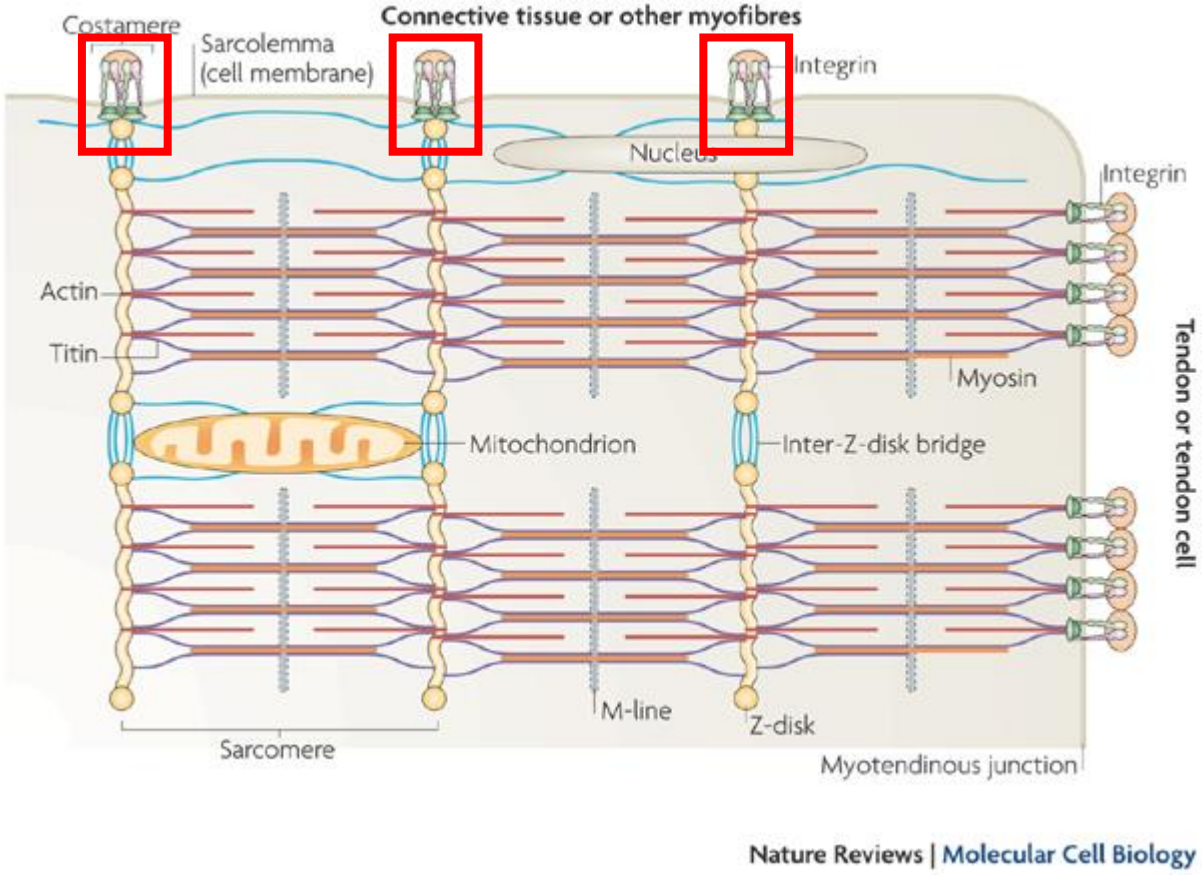
COSTAMERES

- Structural components linking myofibrils to sarcolemma
- Circumferential alignment
- **dystrophin-associated glycoprotein (DAG) complex**
  - links internal cytoskelet to ECM
  - Integrity of muscle fiber

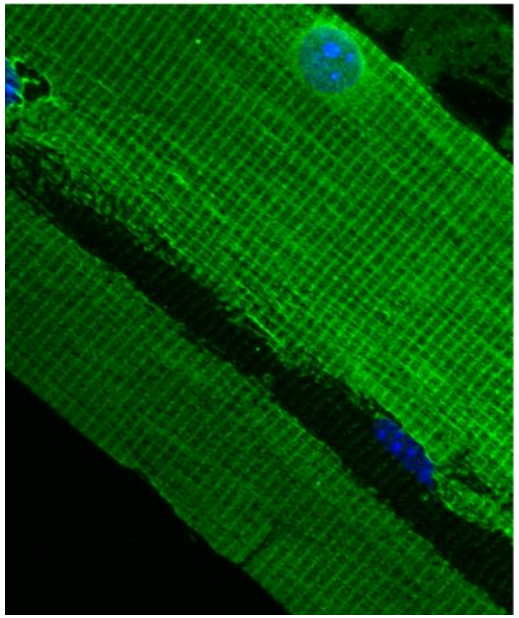




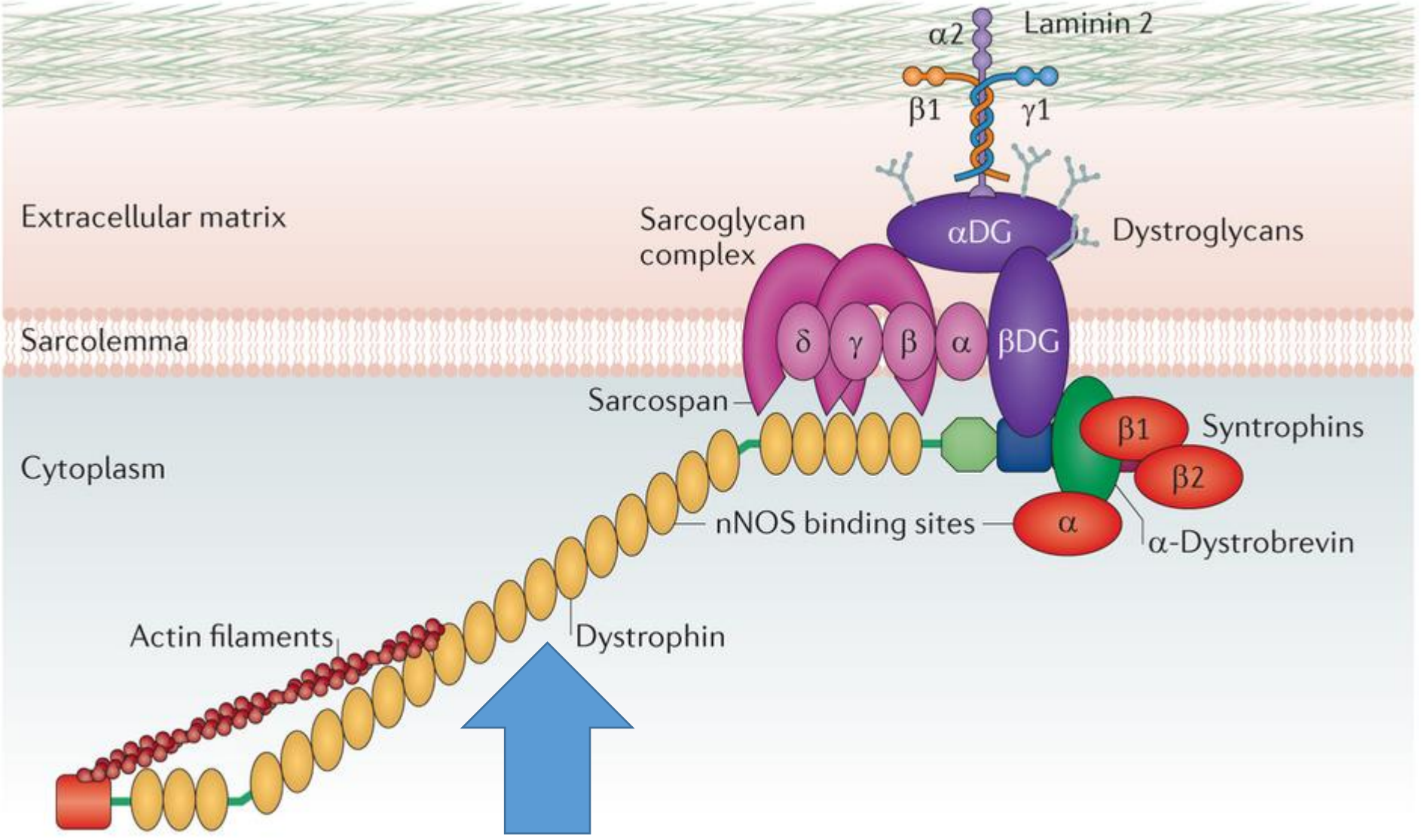
COSTAMERES



Nature Reviews | Molecular Cell Biology

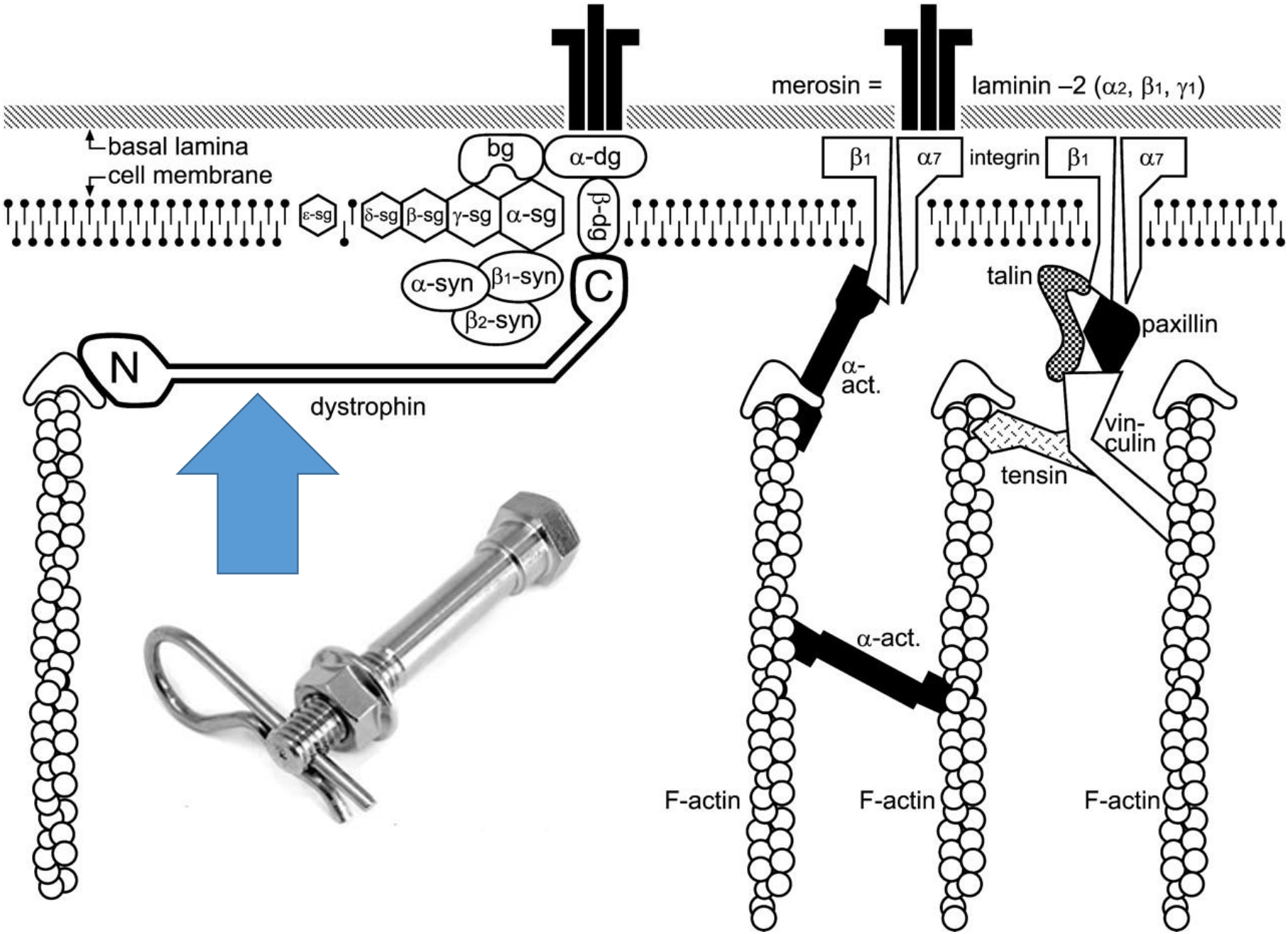


COSTAMERES AND DYSTROPHIN

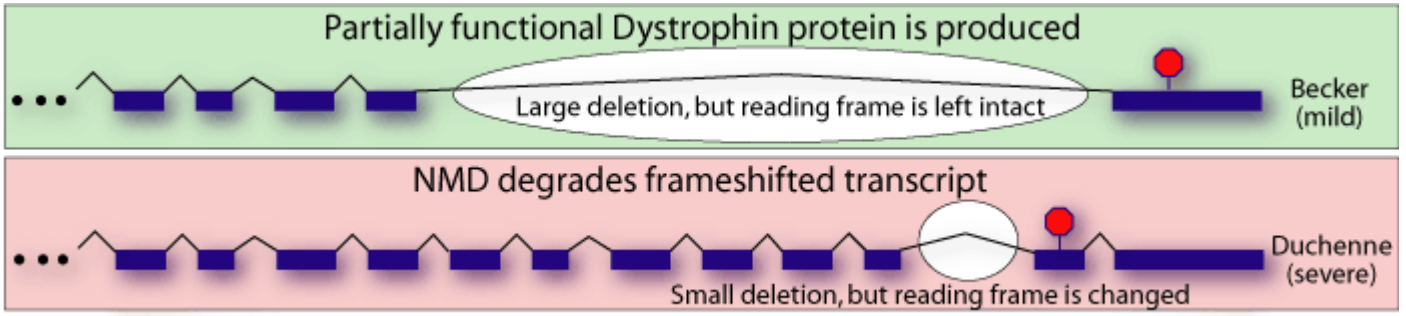


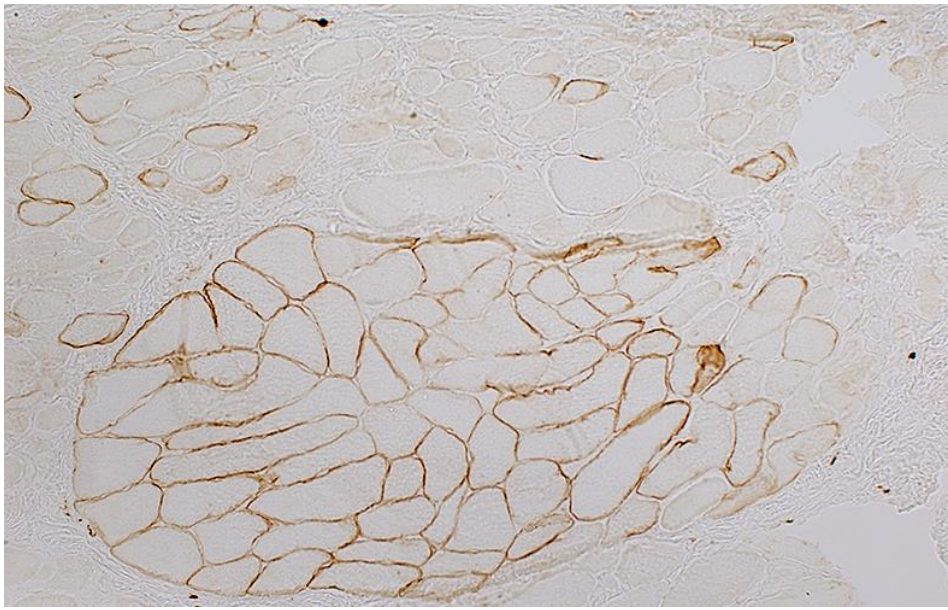
Nature Reviews | Genetics

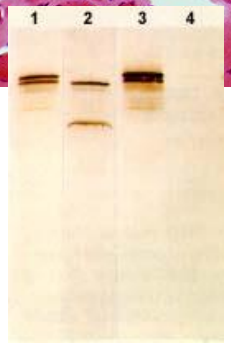
COSTAMERES AND DYSTROPHIN



DUCHENNE MUSCULAR DYSTROPHY



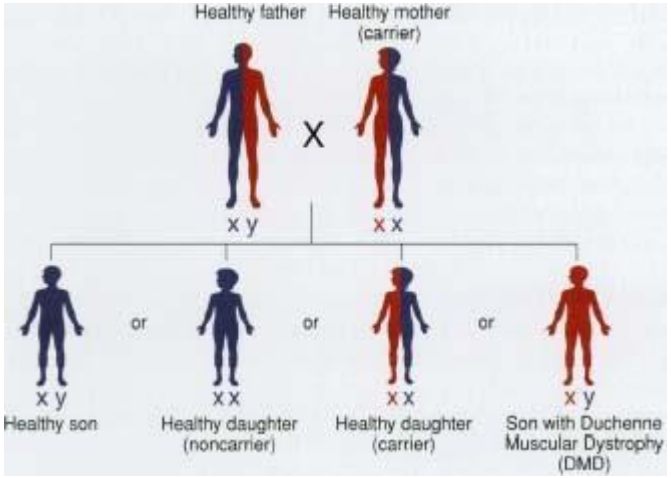


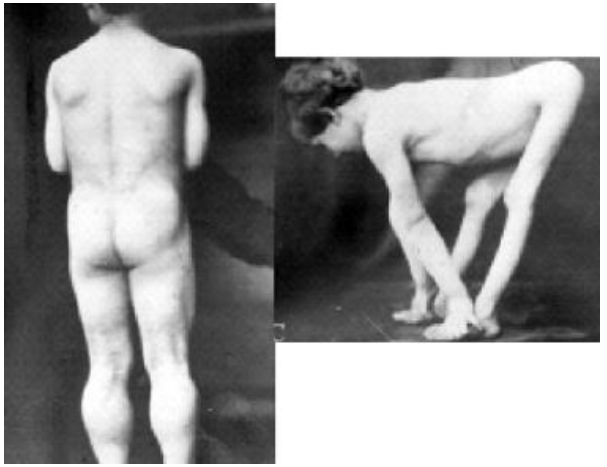


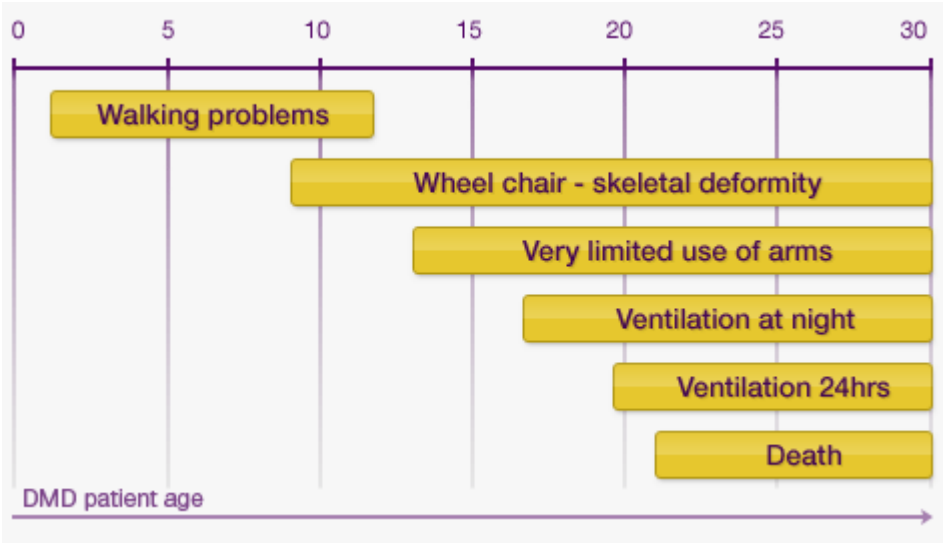
Lane 1: Becker dystrophy; Dystrophin has reduced abundance but normal size.
Lane 2: Becker dystrophy; Dystrophin has reduced size and abundance.
Lane 3: Normal; Dystrophin has normal size and amount.
Lane 4: Duchenne dystrophy; Almost no protein is present.

http://neuromuscular.wustl.edu/pathol/dmdpath.htm

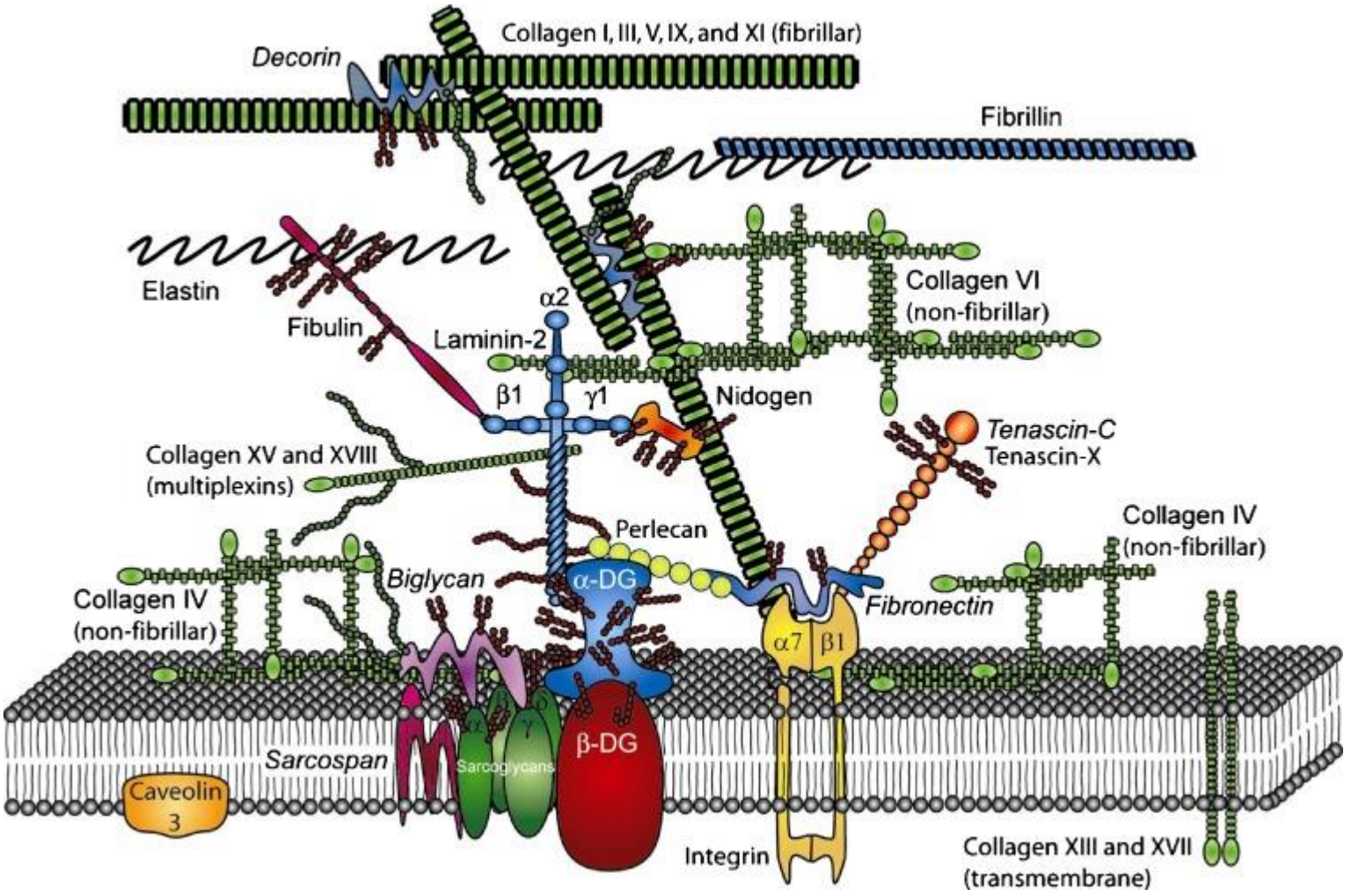
COSTAMERES AND DYSTROPHIN





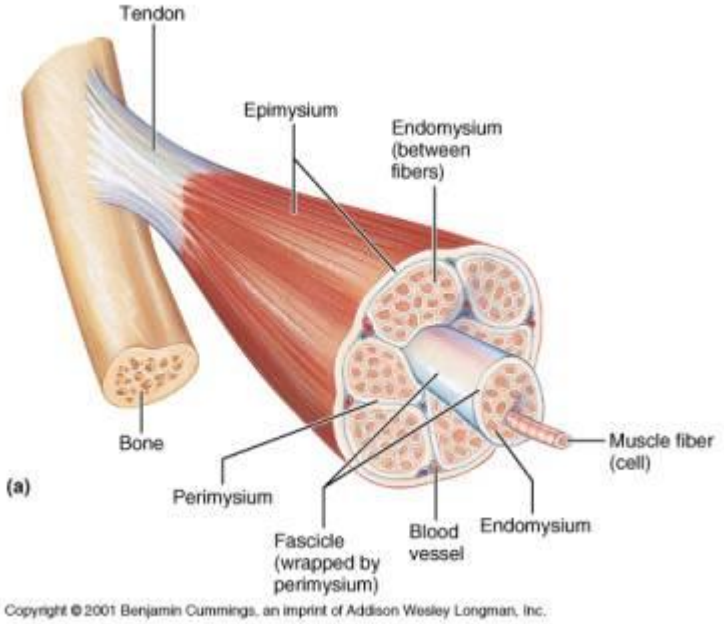


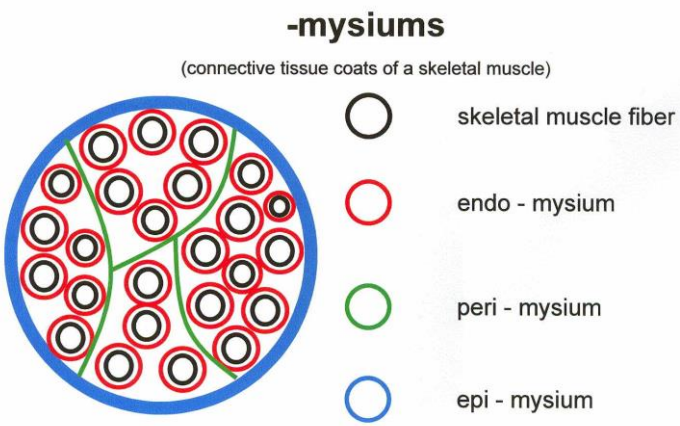
COSTAMERES - ATTACHMENT TO ECM

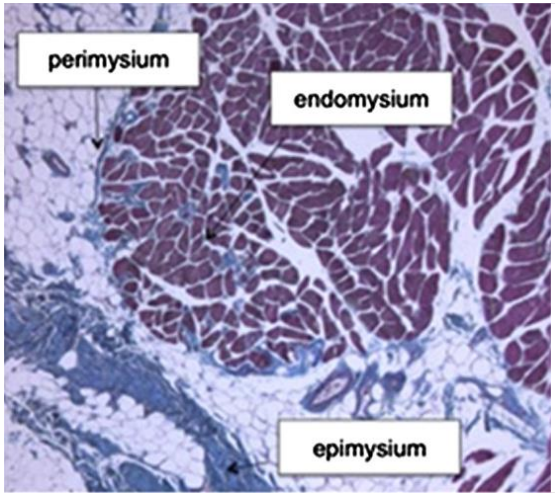


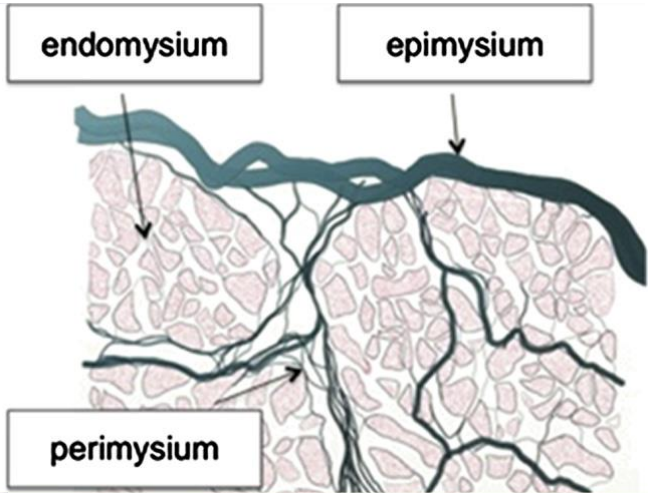
CONNECTIVE TISSUE OF SKELETAL MUSCLE

- Containment
- Limit of expansion of the muscle
- Transmission of muscular forces
- **Endomysium** – around each muscle cell (fiber)
- **Perimysium** – around and among the primary bundles of muscle cells
- **Epimysium** – dense irregular collagen c.t., continuous with tendons and fascia
- Fascia – dense regular collagen c.t.



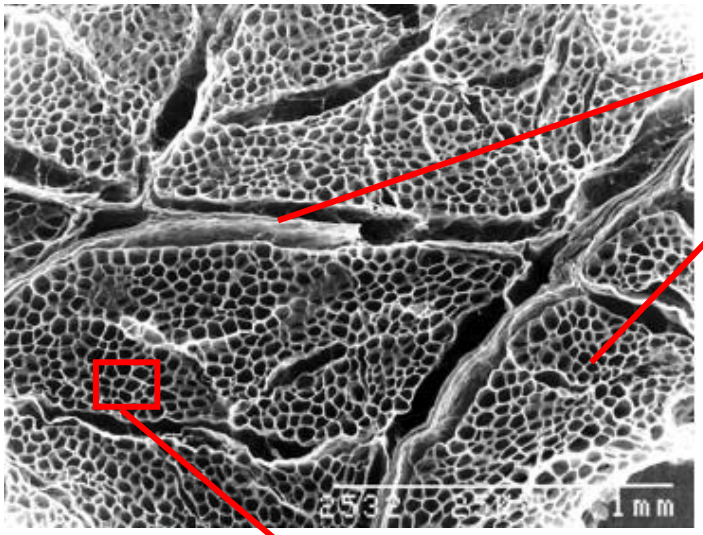


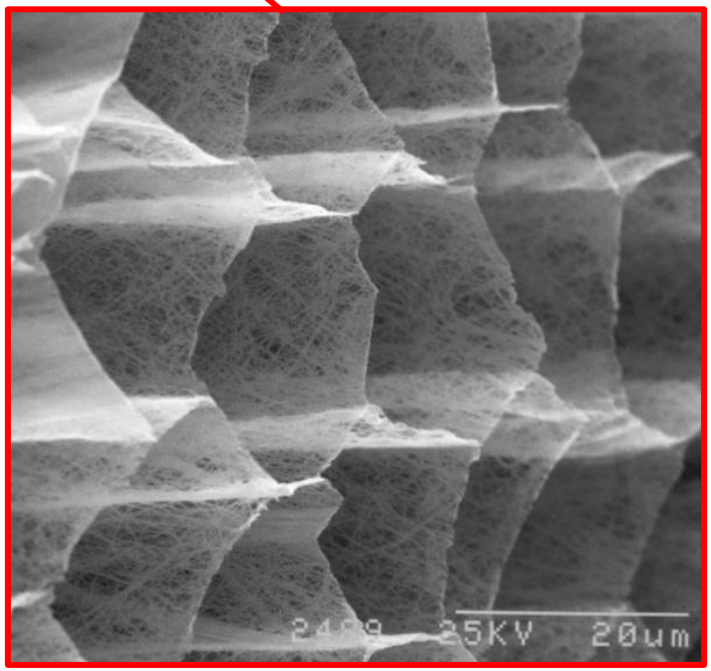


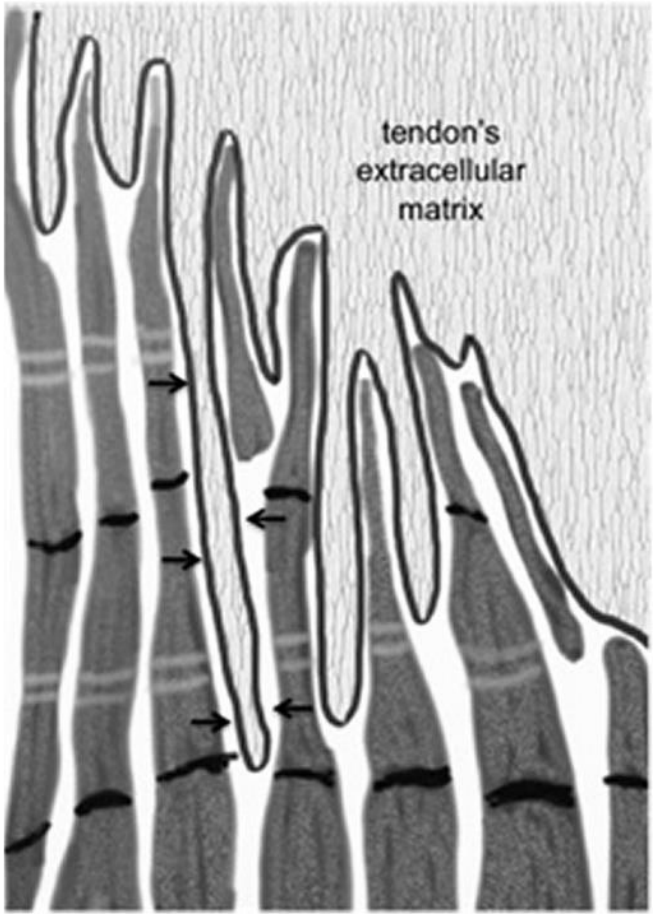


CONNECTIVE TISSUE OF SKELETAL MUSCLE

Connective tissue around muscle bundles and muscle fibers

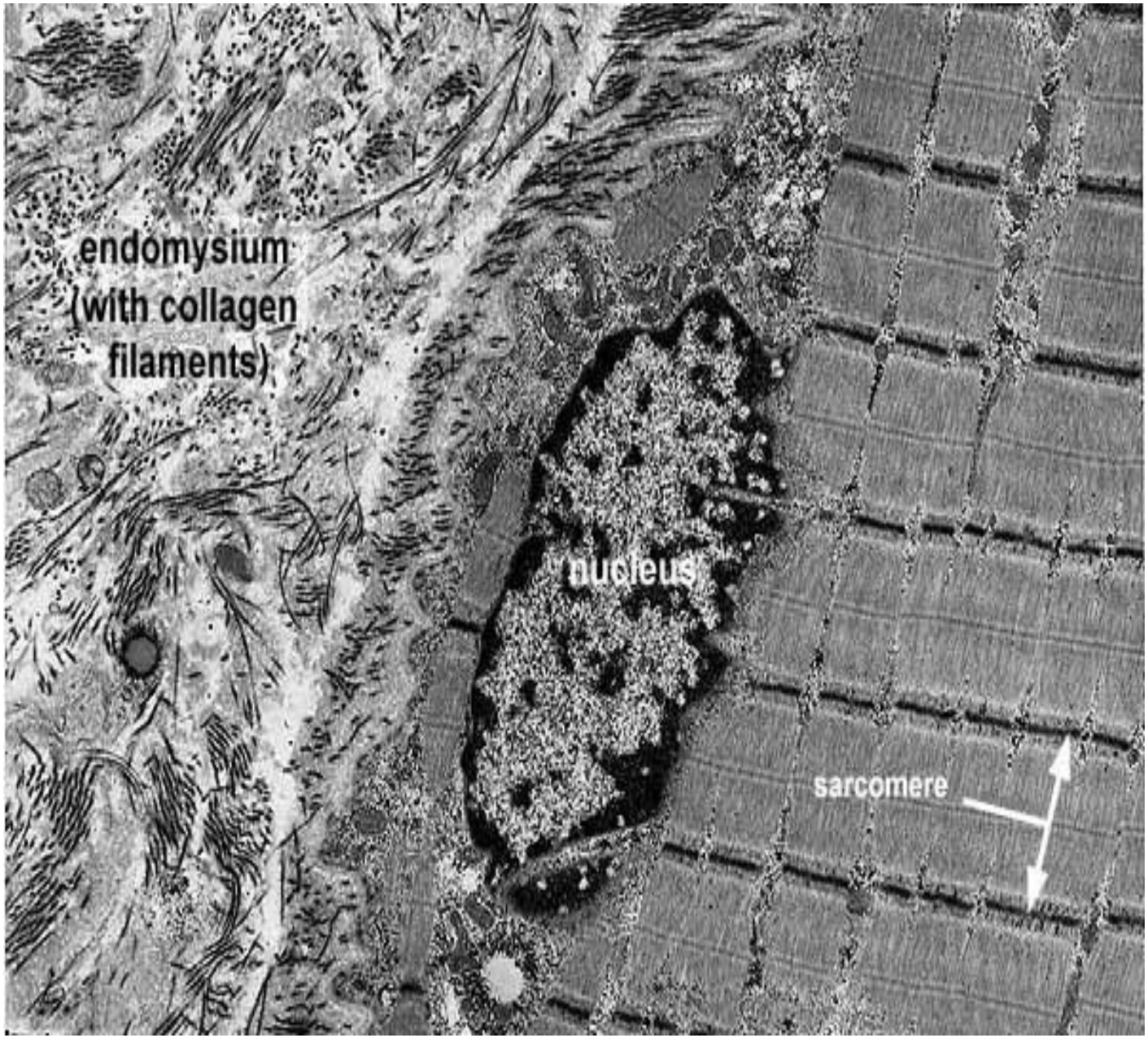




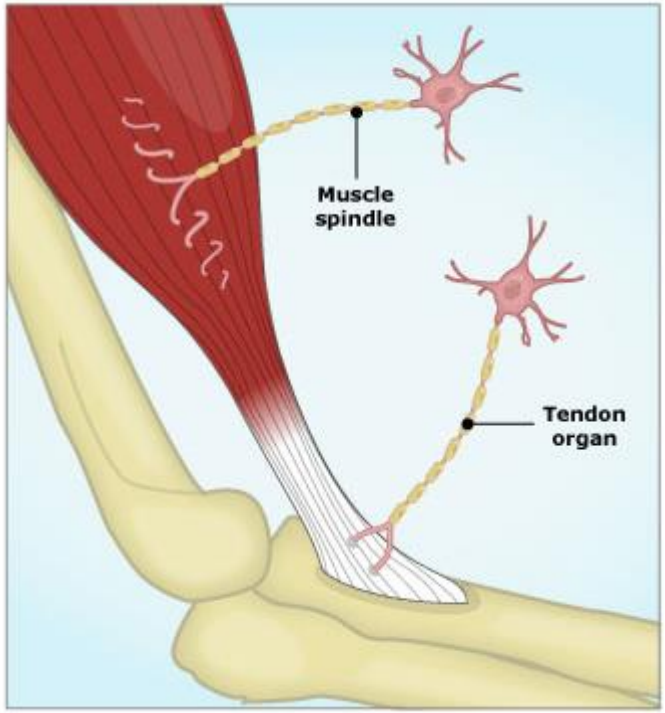


Myotendinous junction

CONNECTIVE TISSUE OF SKELETAL MUSCLE

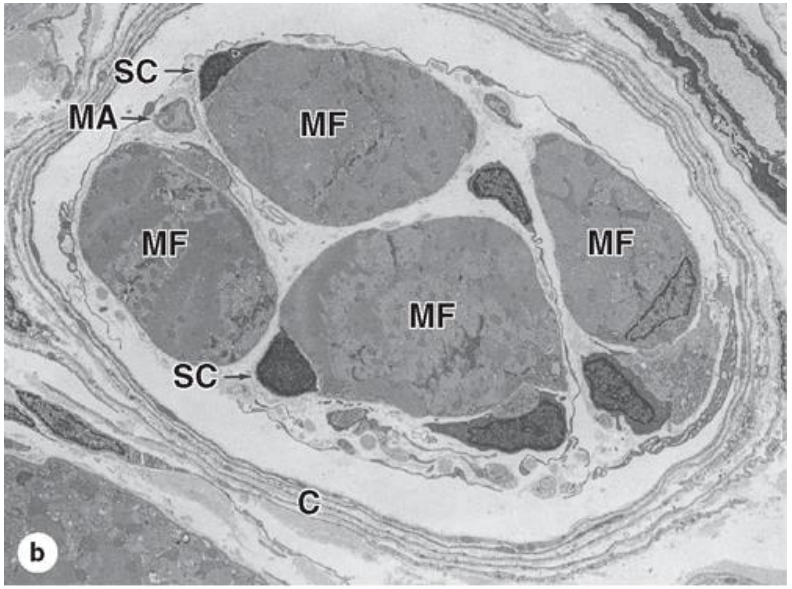


PROPRIORECEPTORS



Muscle spindles

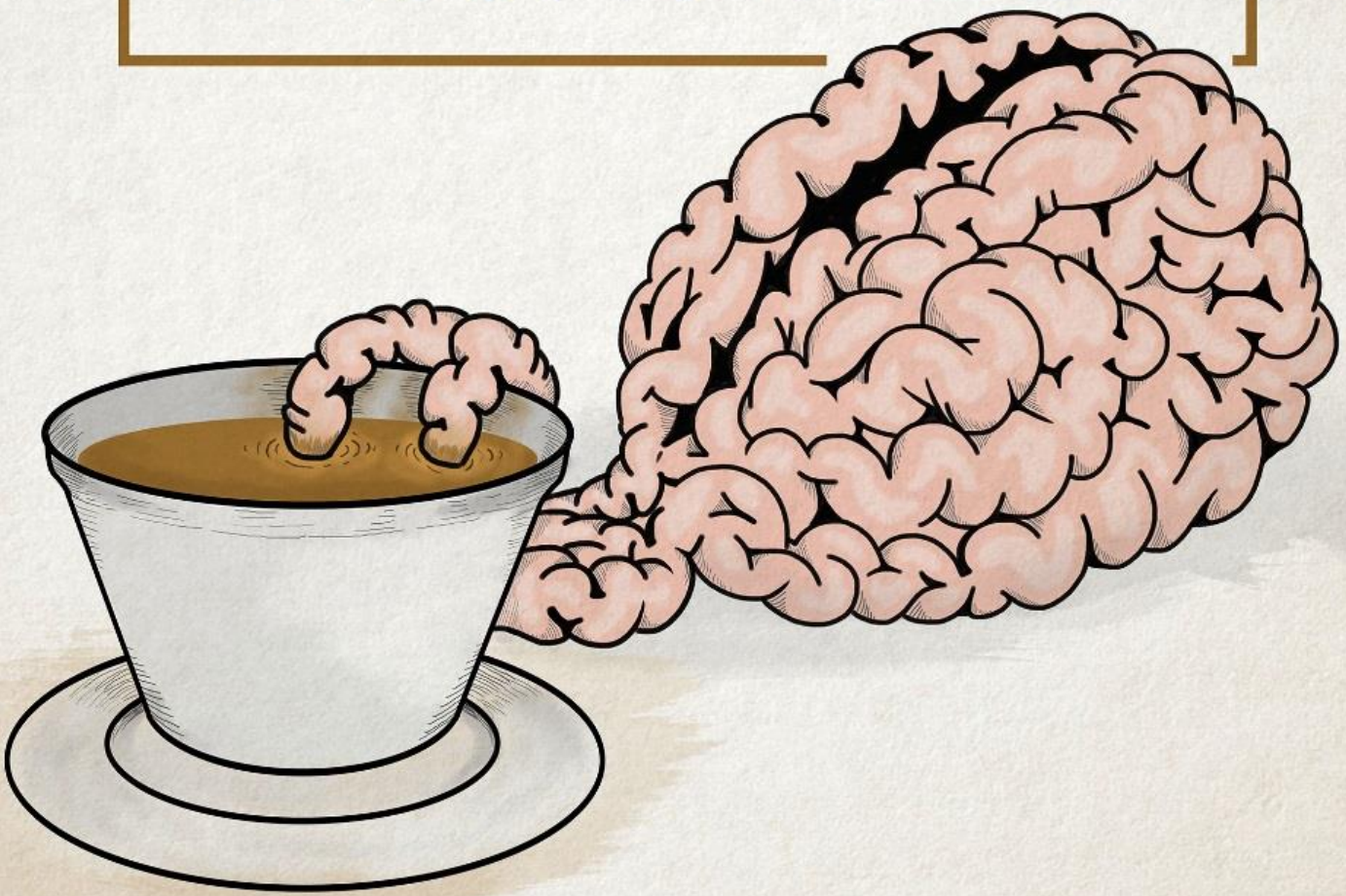
- change in muscle elongation (stretch)
- modified perimysium
- thin muscle (intrafusal) fibers
- sensory endings
- reflexes, coordination of muscle groups



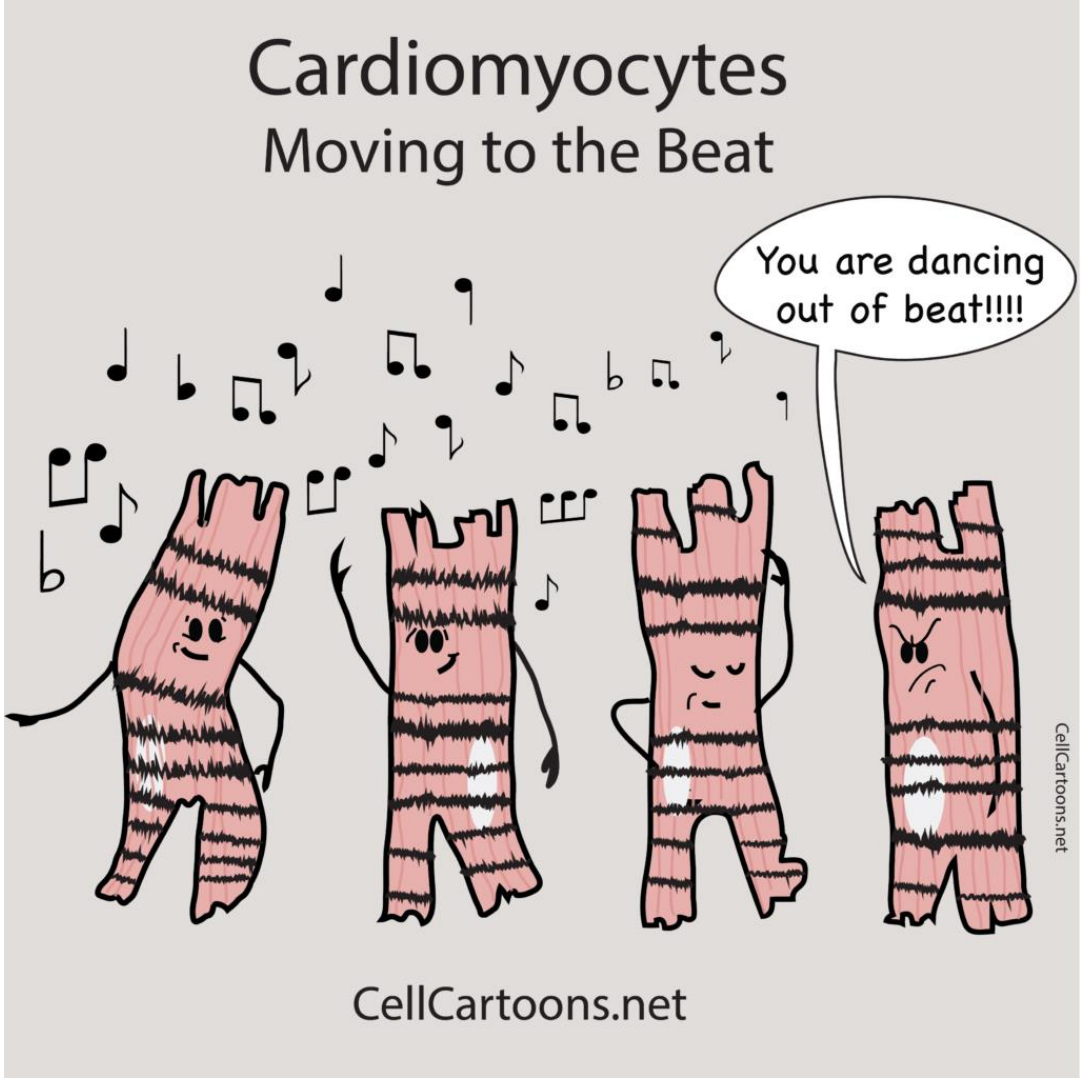
Golgiho tendon organs

- myotendineous junction
- senzory endings synapsed with inhibitory neurons
- tension, stretch

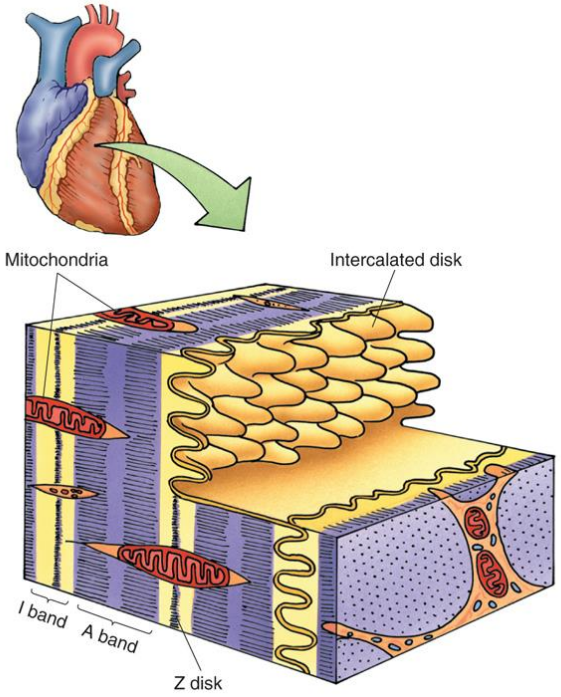
COFFEEBREAK



CARDIAC MUSCLE TISSUE

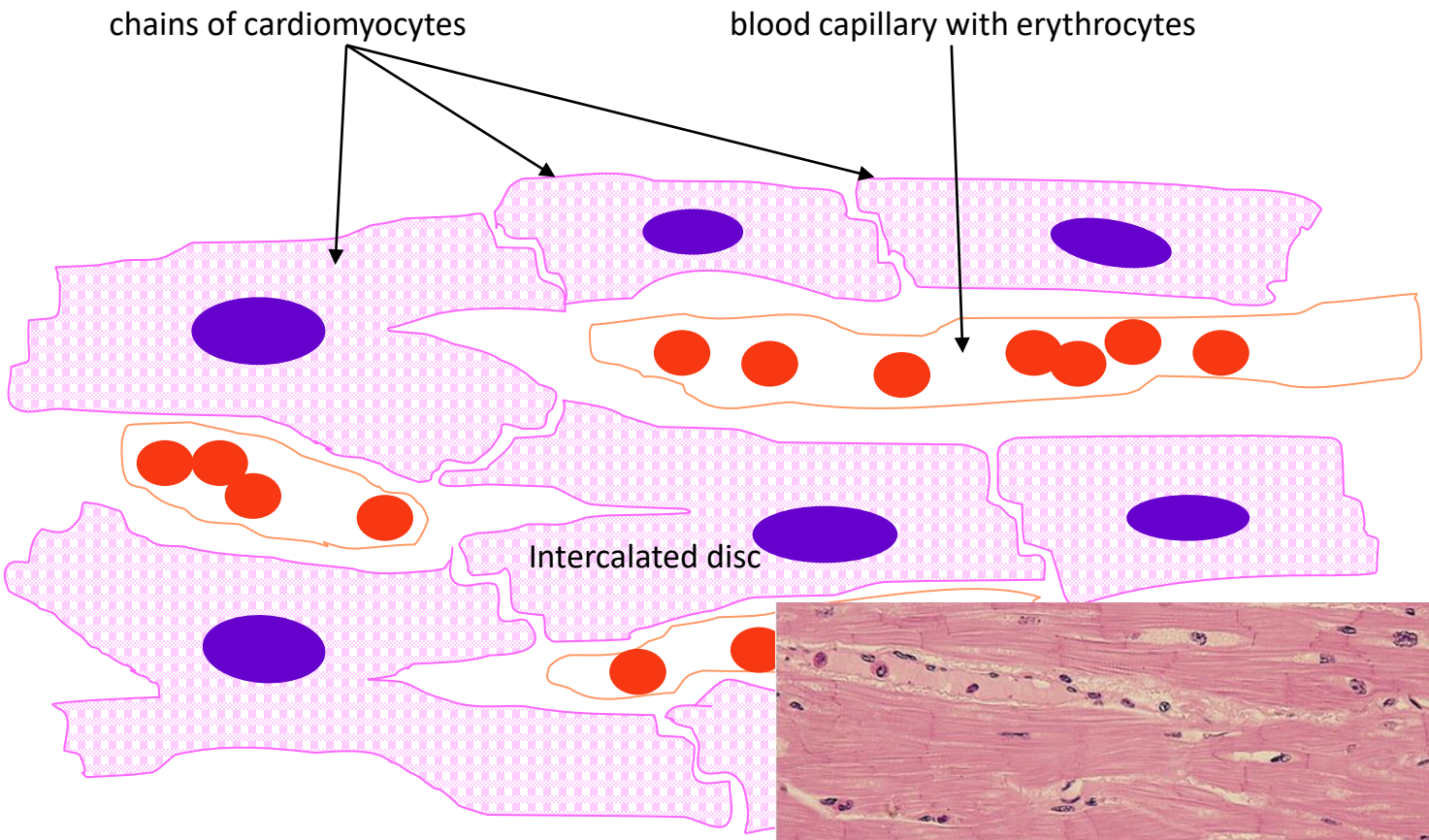


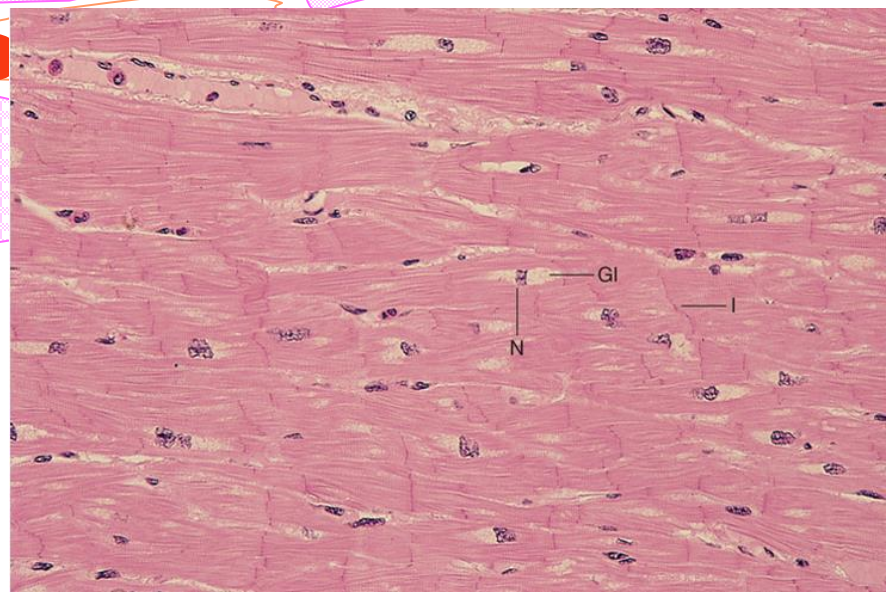
HISTOLOGY OF CARDIAC MUSCLE TISSUE



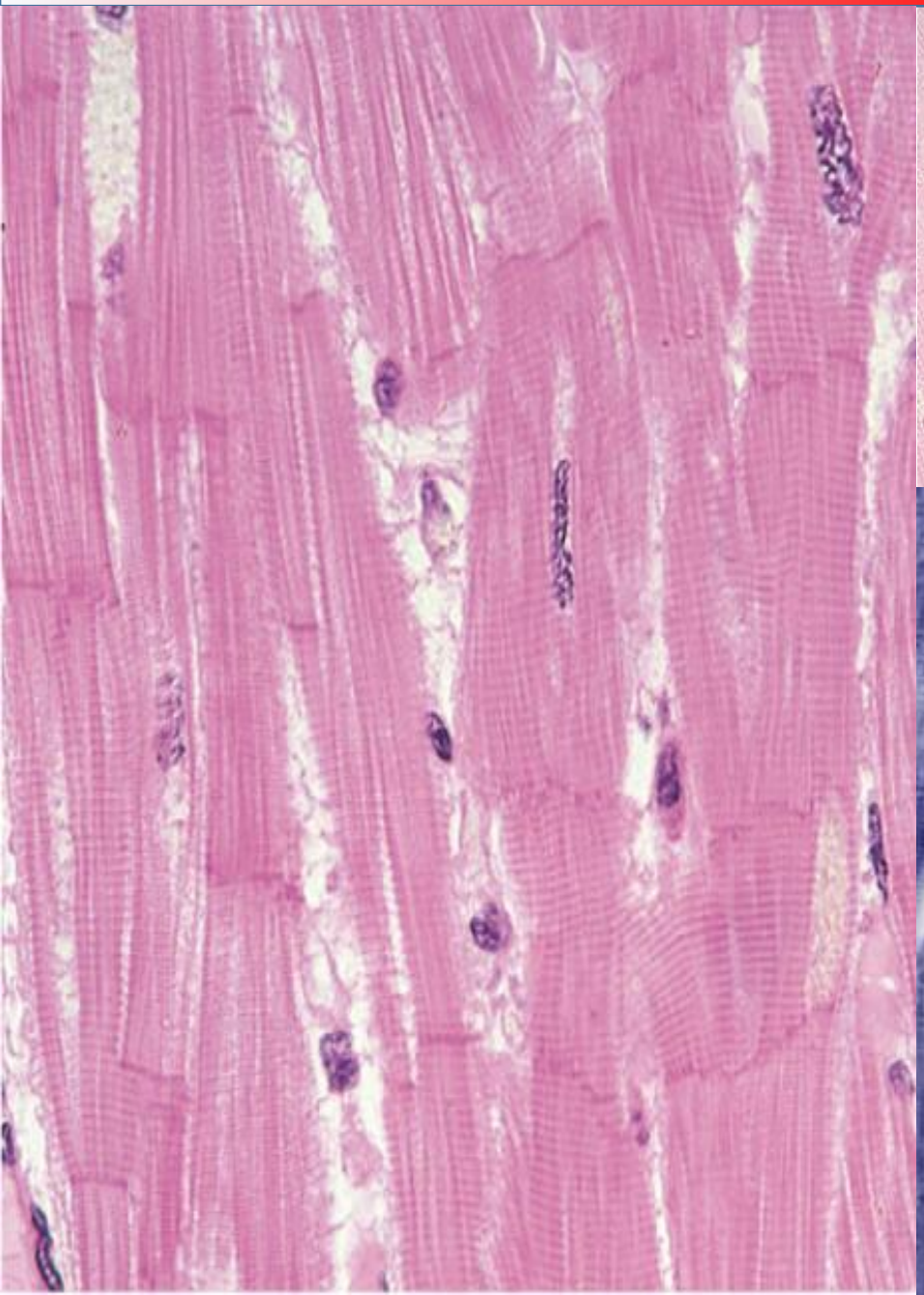
- made up of long branched fiber (cells) – **cardiomyocytes**,
- cardiomyocytes are cylindrical cells, branched on one or both ends (Y, X shaped cells),
- sarcoplasm: single nucleus in the center of cell, striated myofibrils, numerous mitochondria,
- cells are attached to one another by end-to-end junctions – intercalated discs.

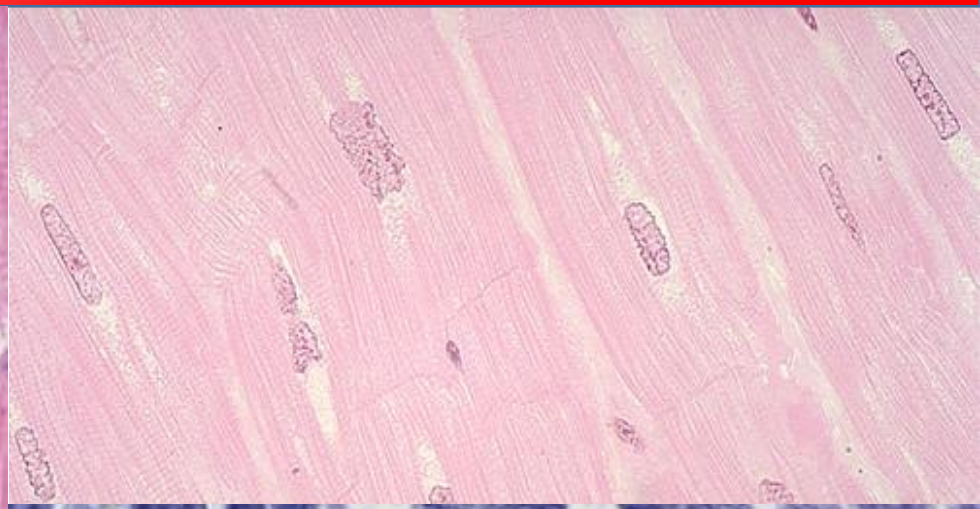
HISTOLOGY OF CARDIAC MUSCLE TISSUE

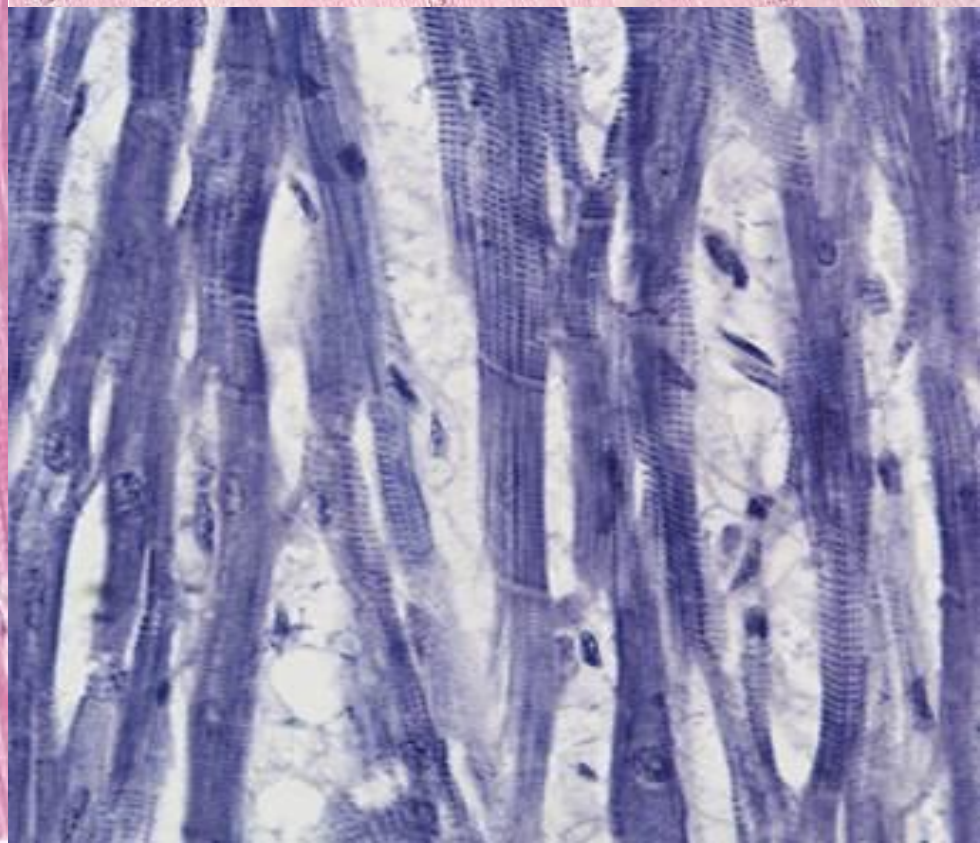




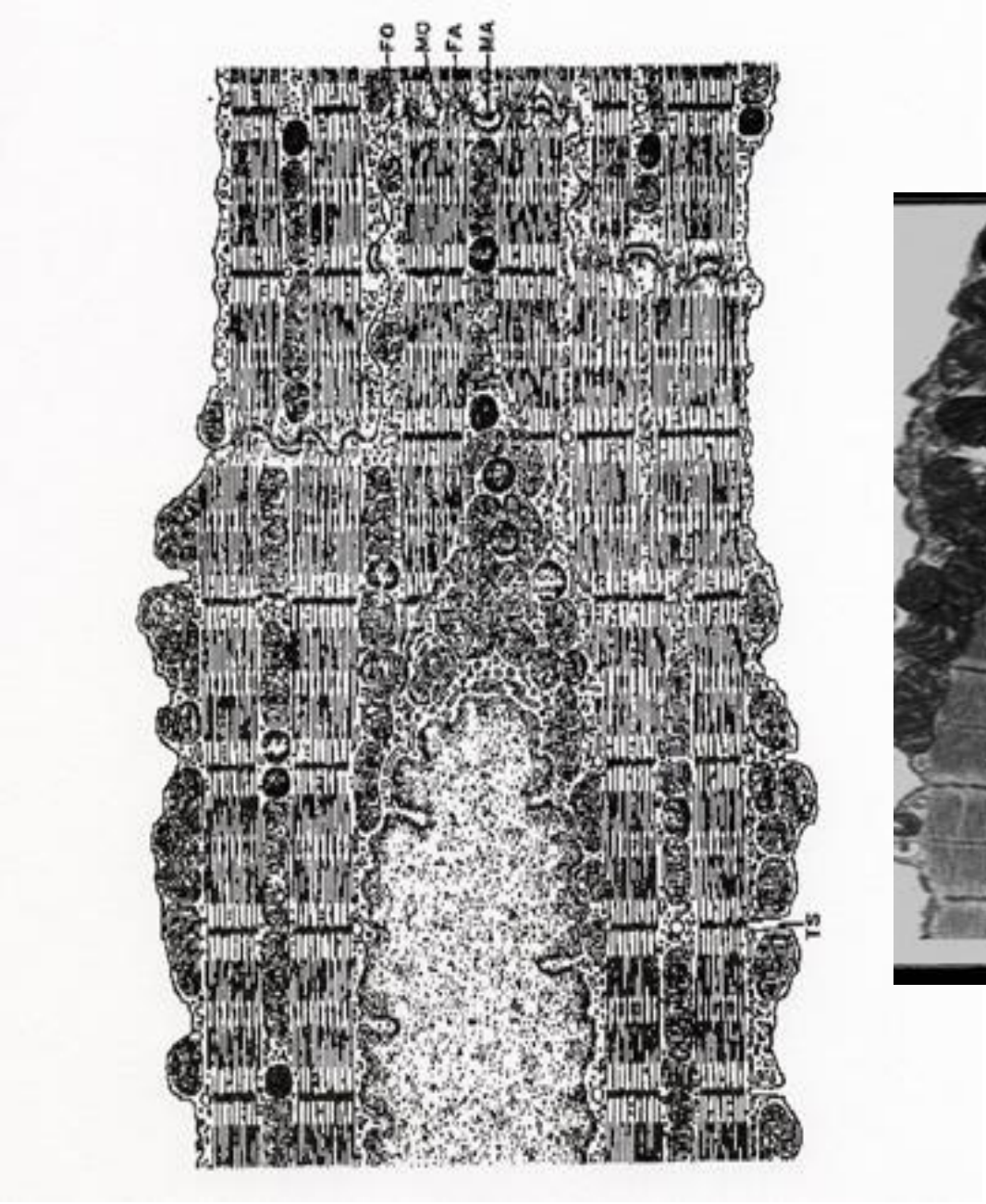
HISTOLOGY OF CARDIAC MUSCLE TISSUE

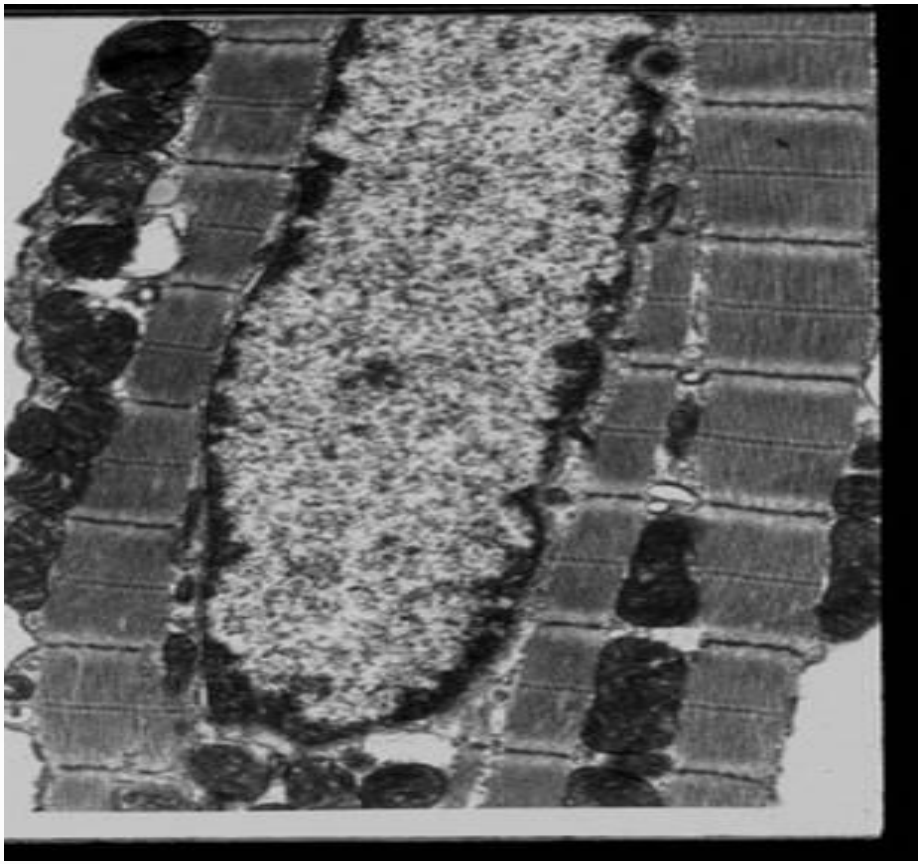






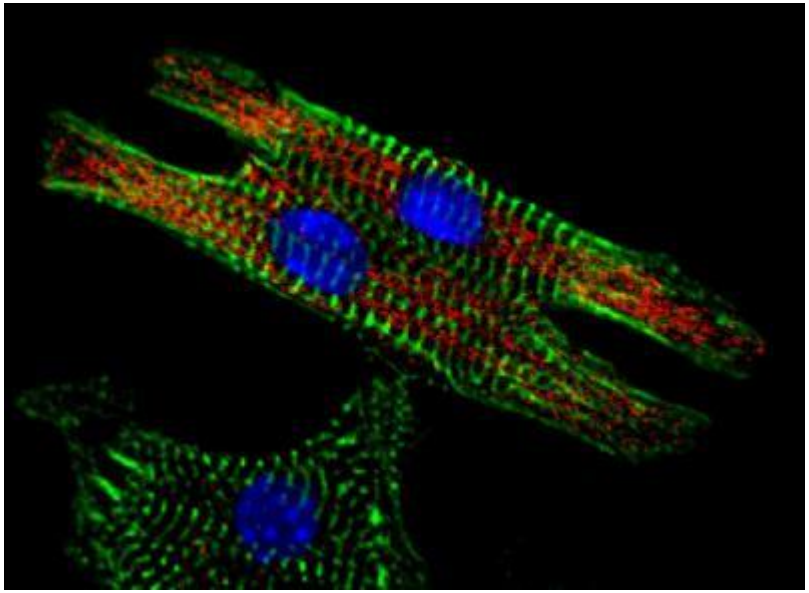
ULTRASTRUCTURE OF CARDIOMYCYTE

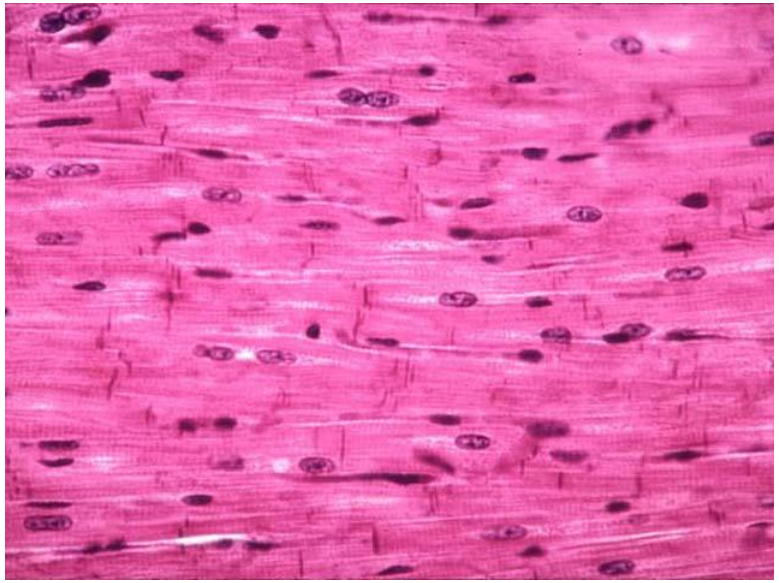




CARDIAC MUSCLE COMPARED TO SKELETAL

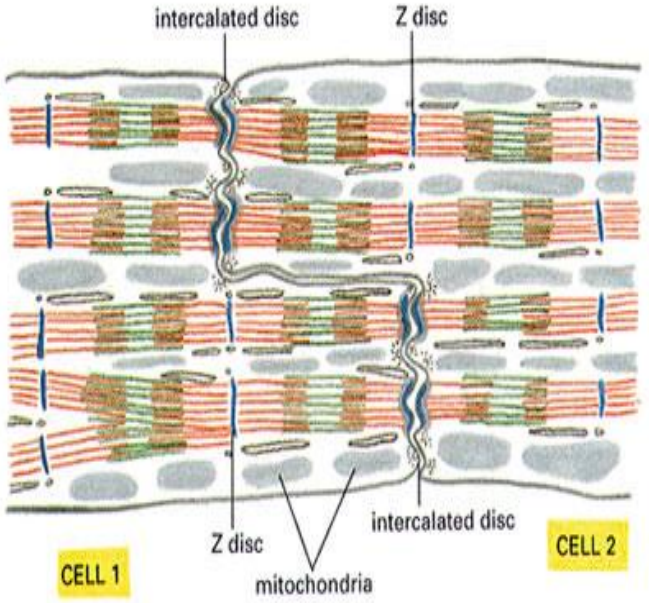
- no triads, but diads: 1 t-tubule + 1 cisterna
- t-tubules around sarcomeres at Z lines rather than at zone of overlap
- sarcoplasmic reticulum via its tubules contact sarcolemma as well as the t-tubules
- cardiac muscle cells are totally dependent on aerobic metabolism to obtain the energy
- large numbers of mitochondria in sarcoplasm and abundant reserves of myoglobin (to store oxygen)
- abundant glycogen and lipid inclusions

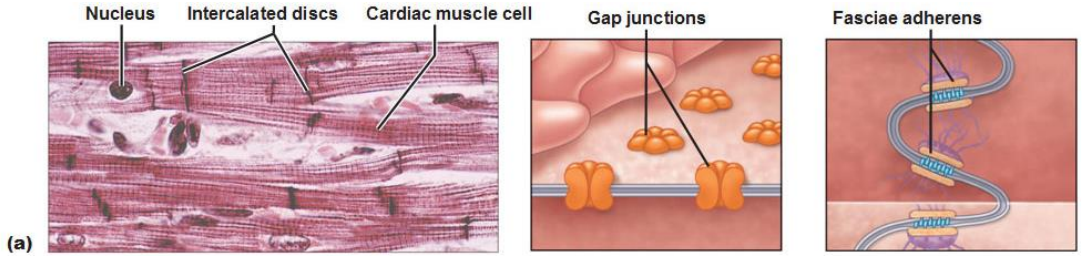


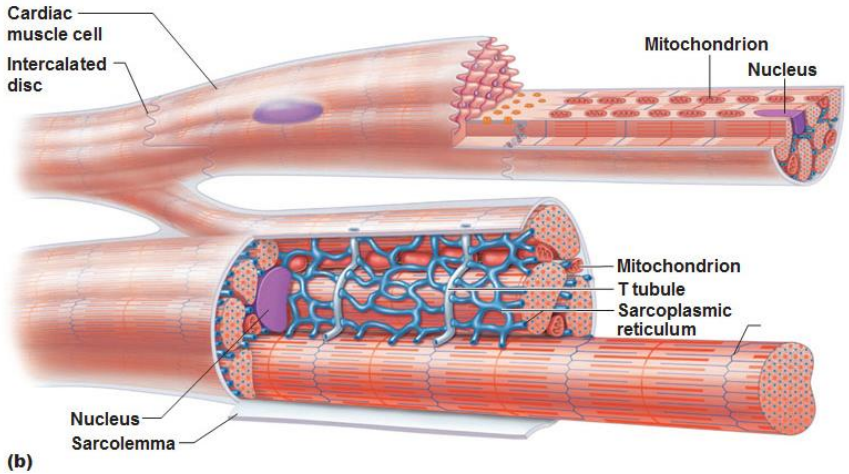


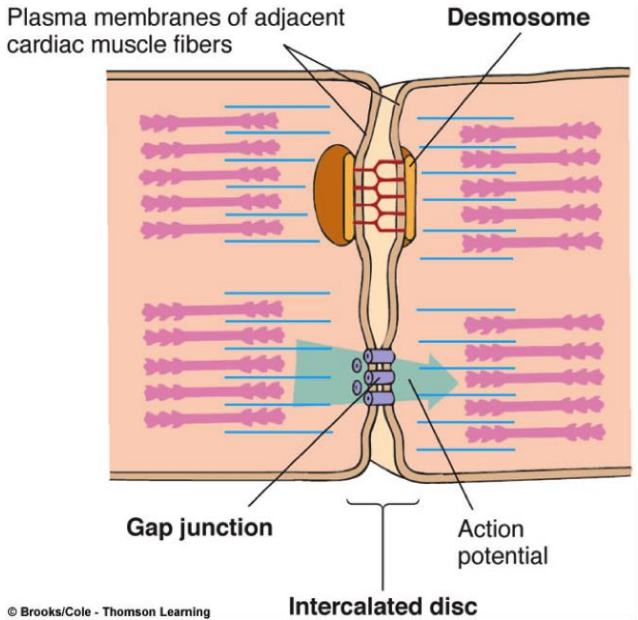
INTERCALATED DISC

- **fasciae adherentes** (*adhesion of cells*)
- **nexus** (quick intercellular communication – transport of ions, electric impulses, information)
- „scalariform“ shape of cell ends

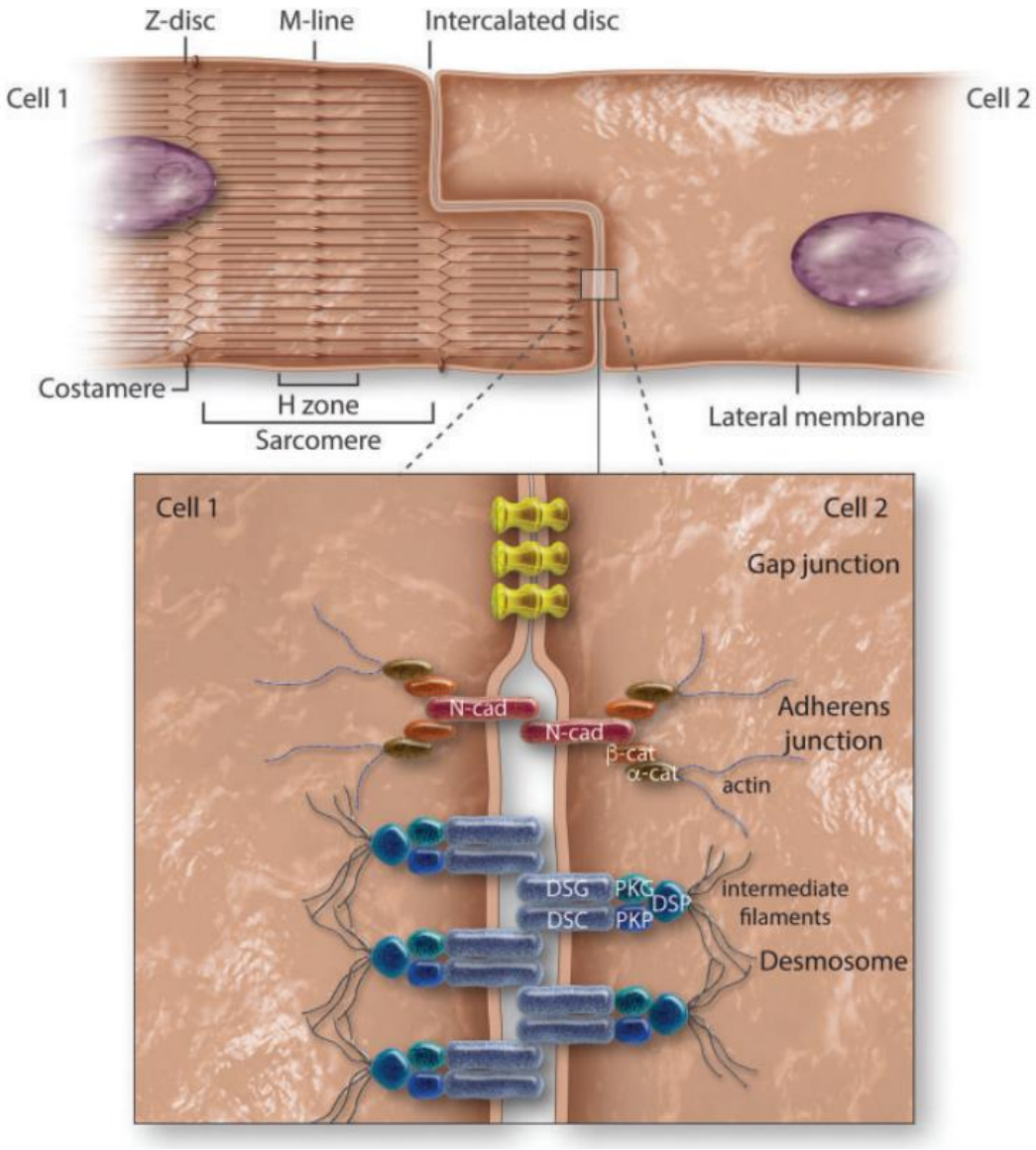








INTERCALATED DISC



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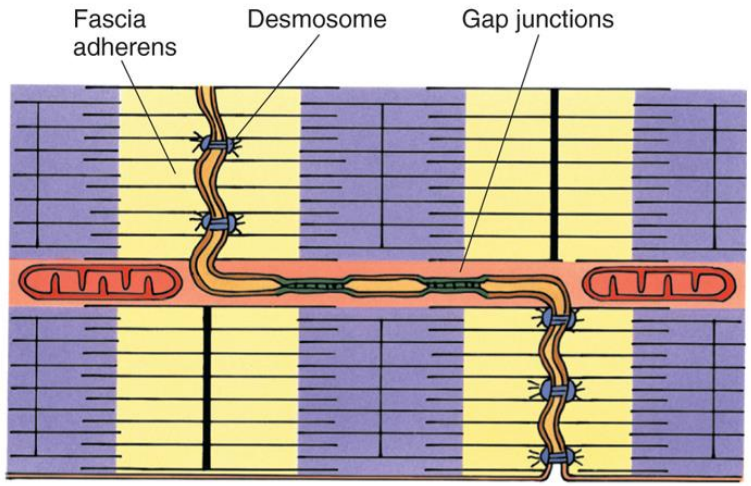
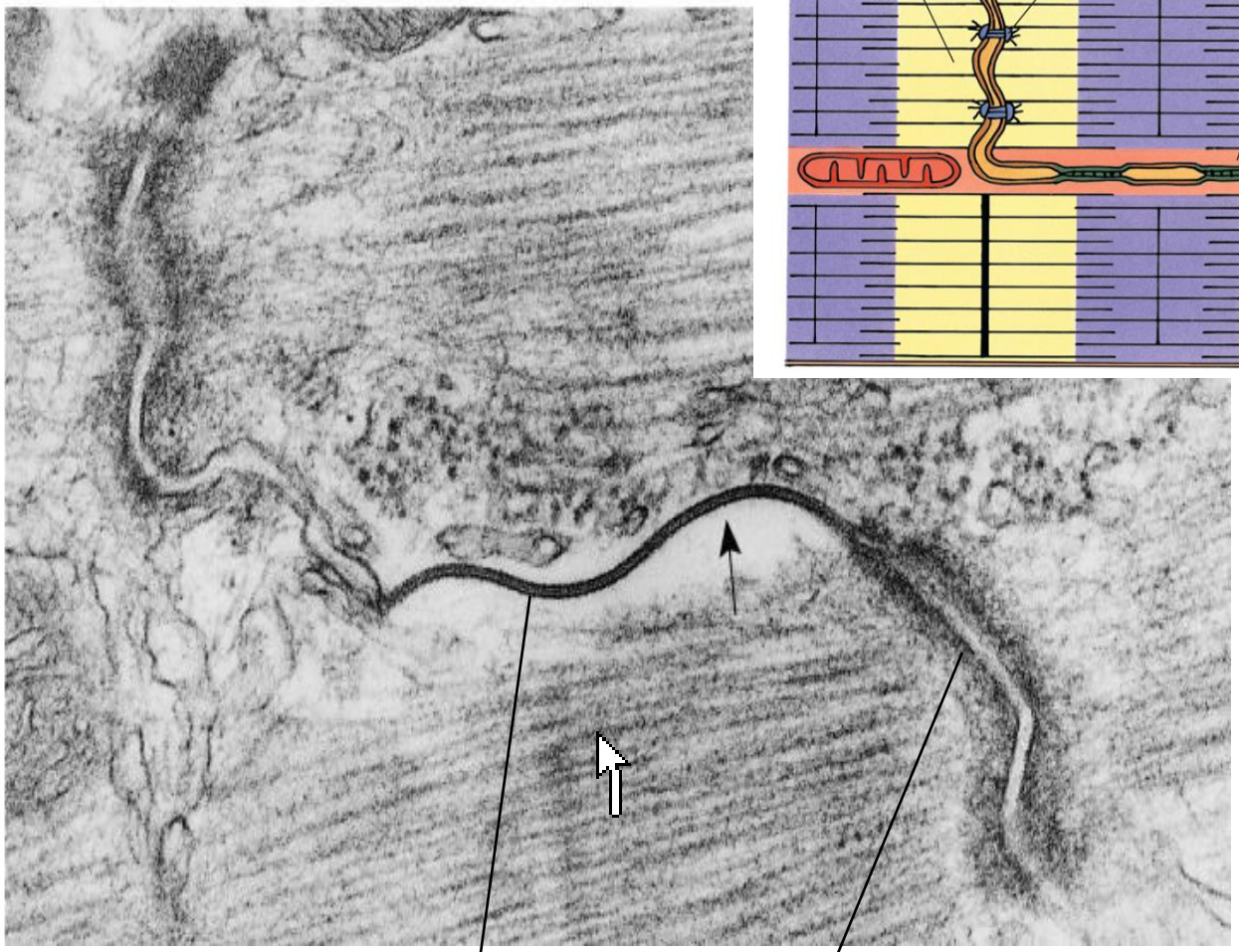
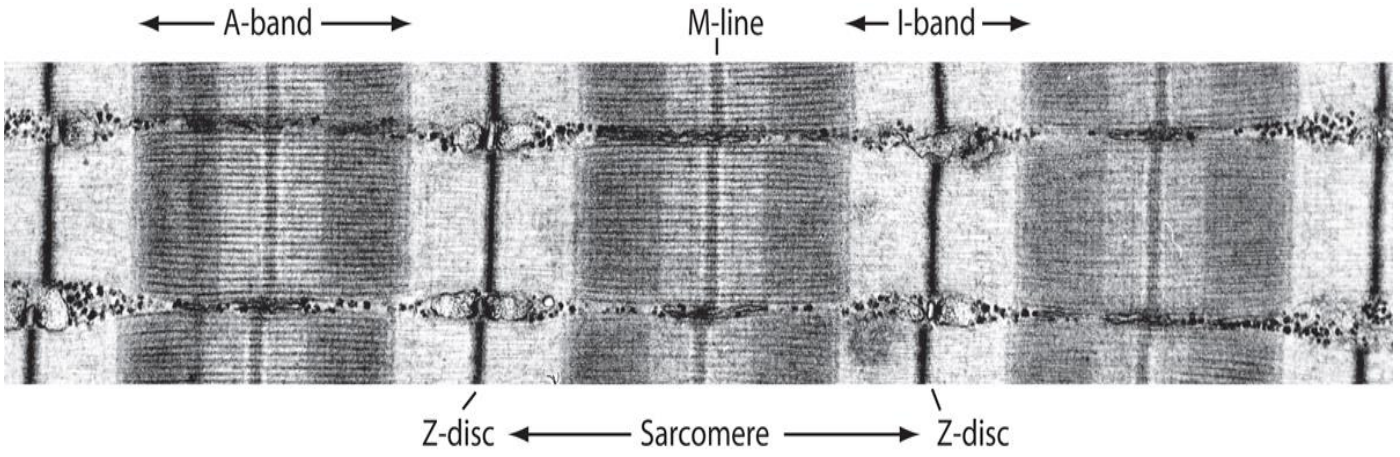




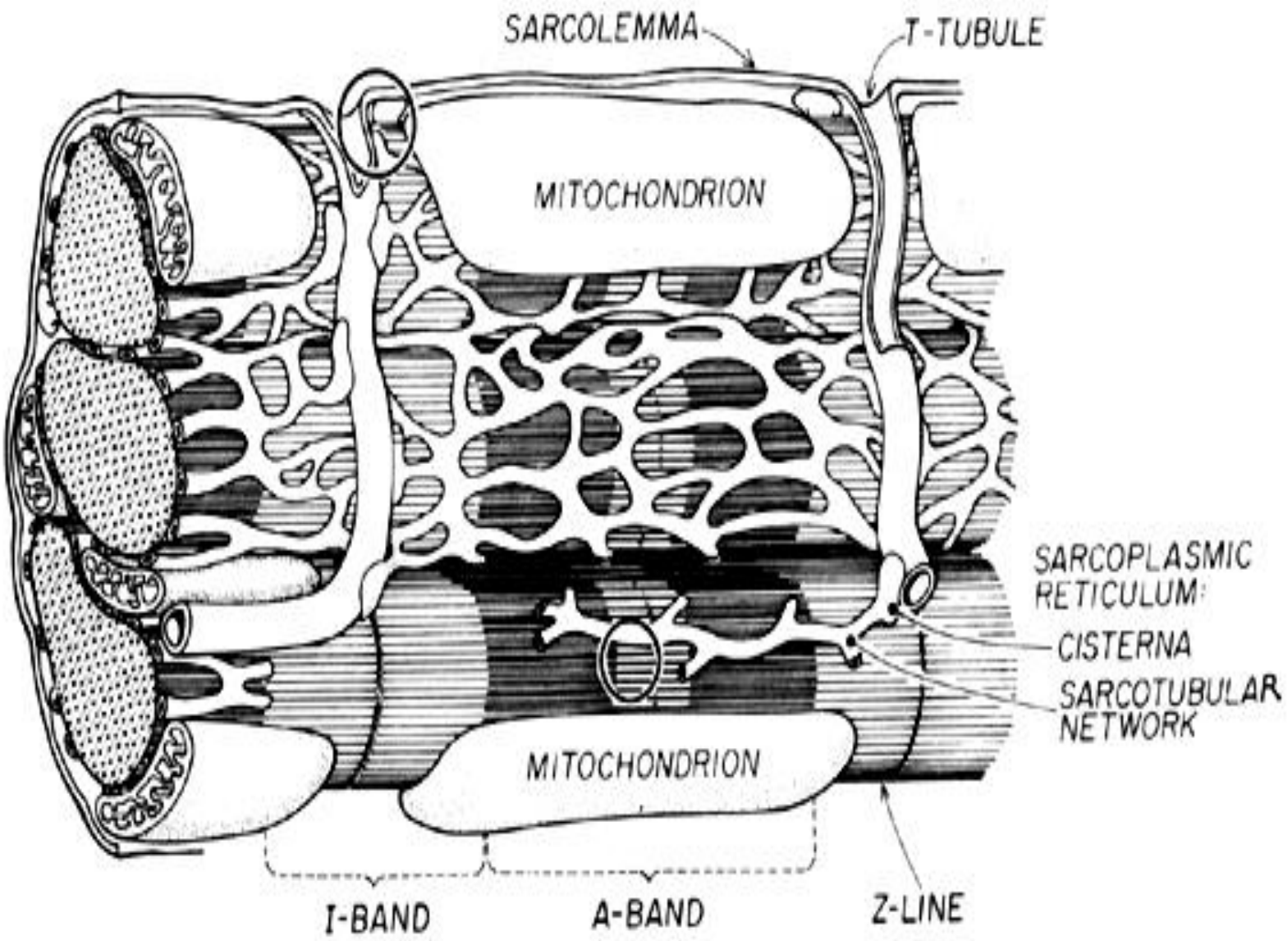
Intercalated disc: nexus fascia adherens

MYOFIBRILS IN CARDIOMYOCYTE

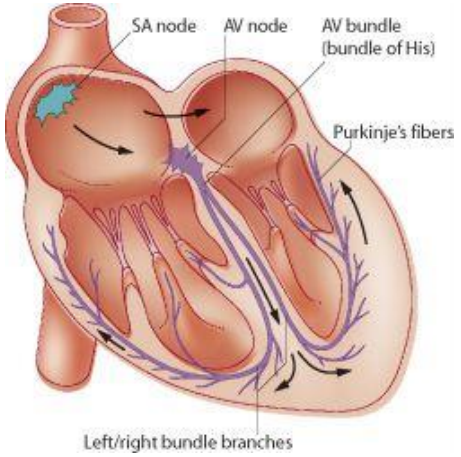
- Actin + myosin myofilaments
- Sarcomere
- Z-line
- M-line and H-zone
- I-band, A-band
- T-tubule + 1 cistern = diad (around Z-line)



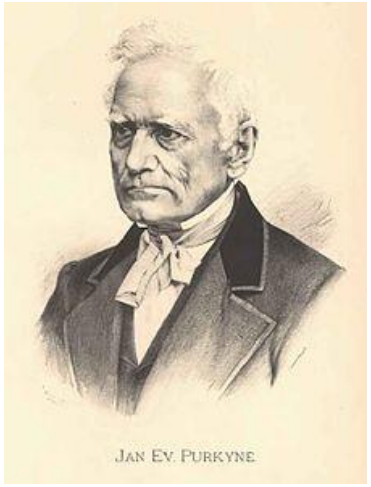
MYOFIBRILS IN CARDIOMYOCYTE

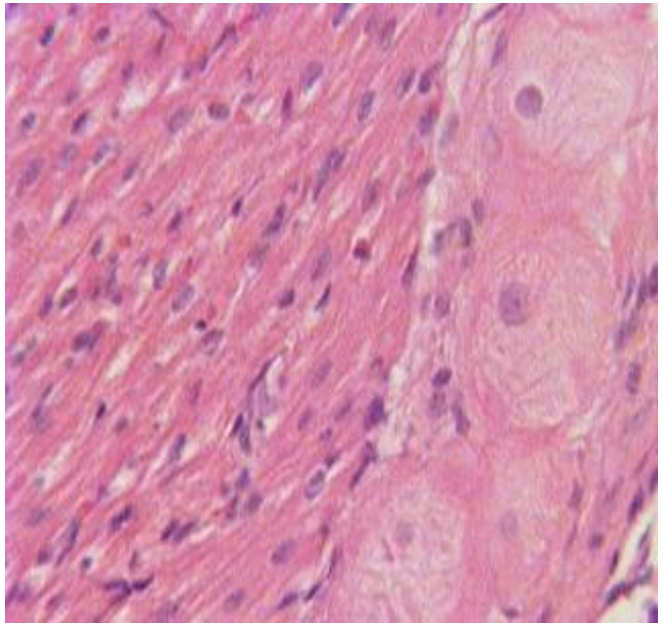


PURKINJE FIBERS

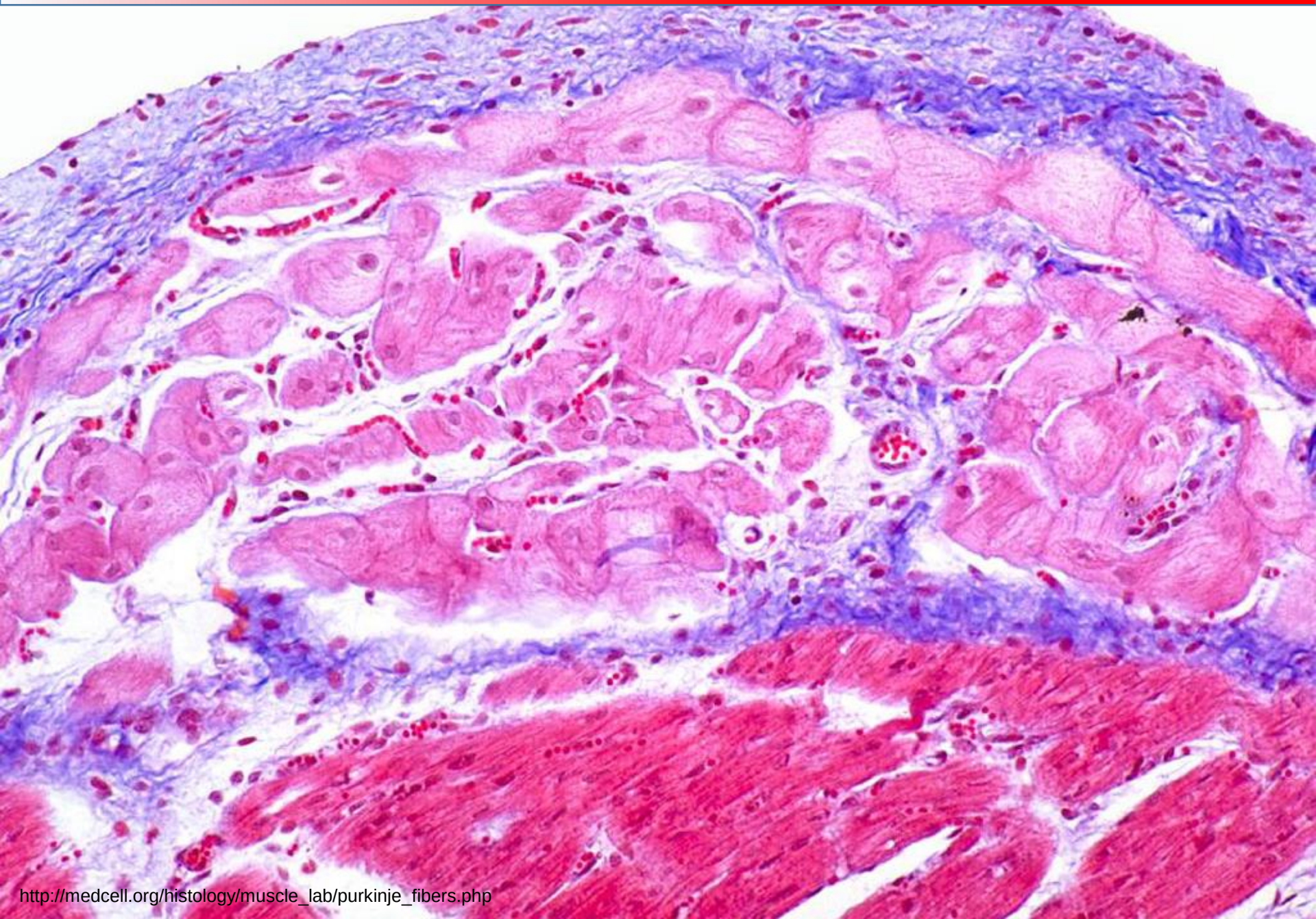


- are located in the inner layer of heart ventricle wall
- are specialized cells fibers that conduct electrical stimuli or impulses that enables the heart to contract in a coordinated fashion
- numerous sodium ion channels and mitochondria, fewer myofibrils





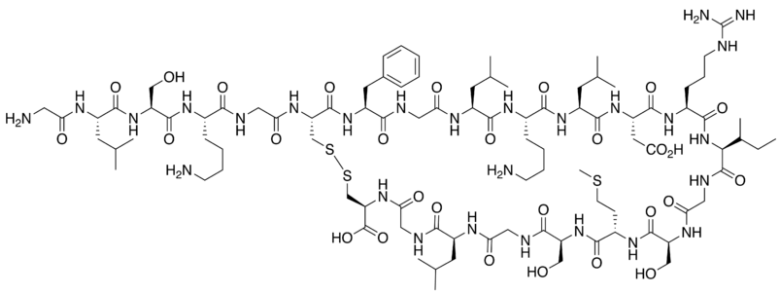
PURKINJE FIBERS

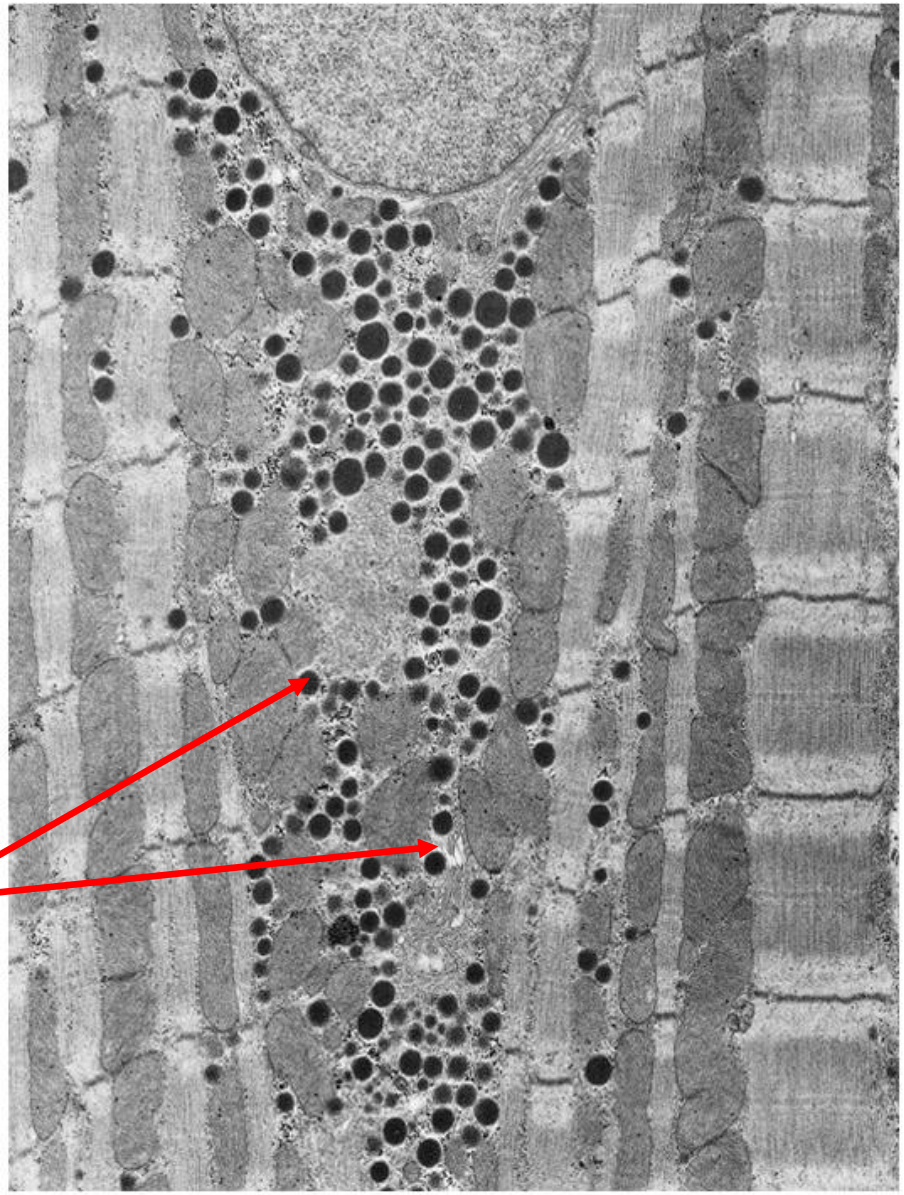


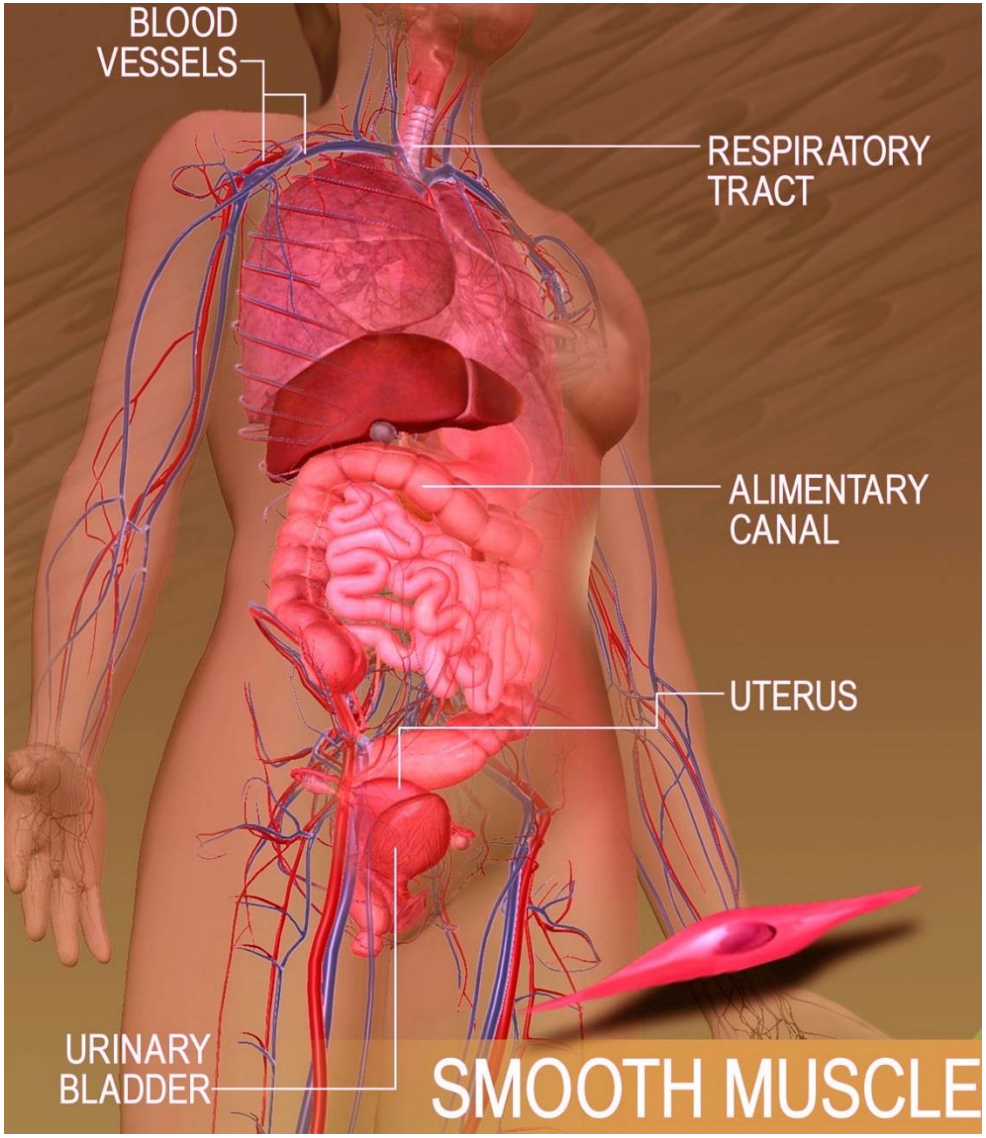
http://medcell.org/histology/muscle_lab/purkinje_fibers.php

ATRIAL CARDIOMYOCYTES

- **Natriuretic peptide A** (ANP)
- atrial cardiomyocytes
- vasodilatation, diuresis



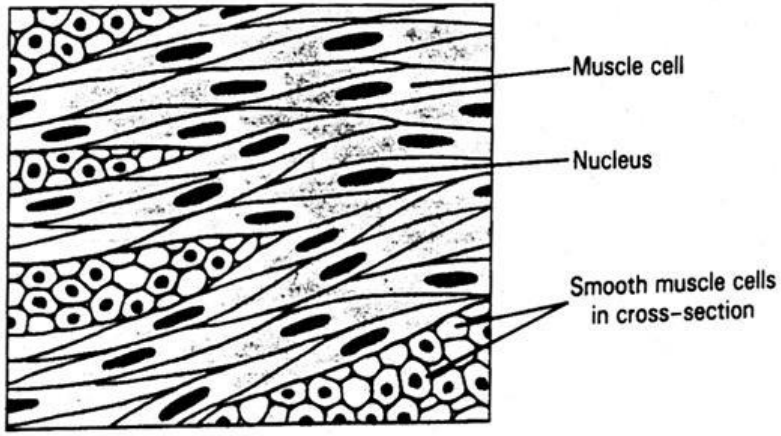


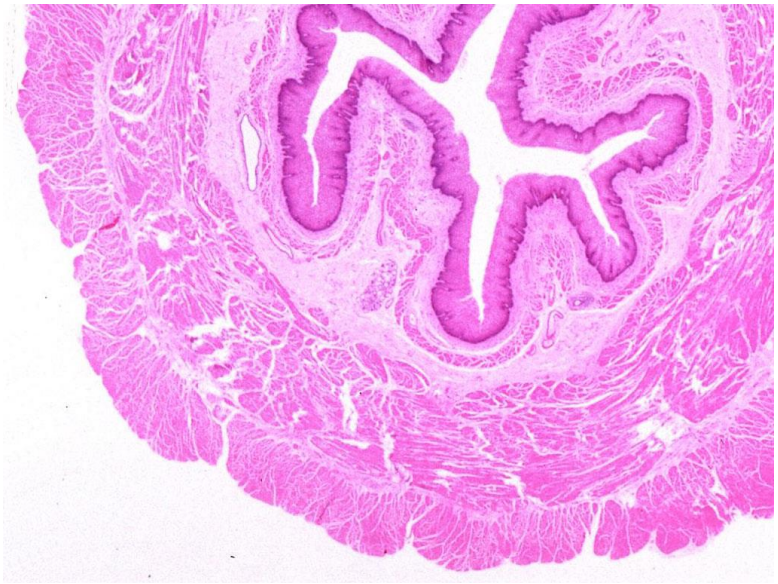


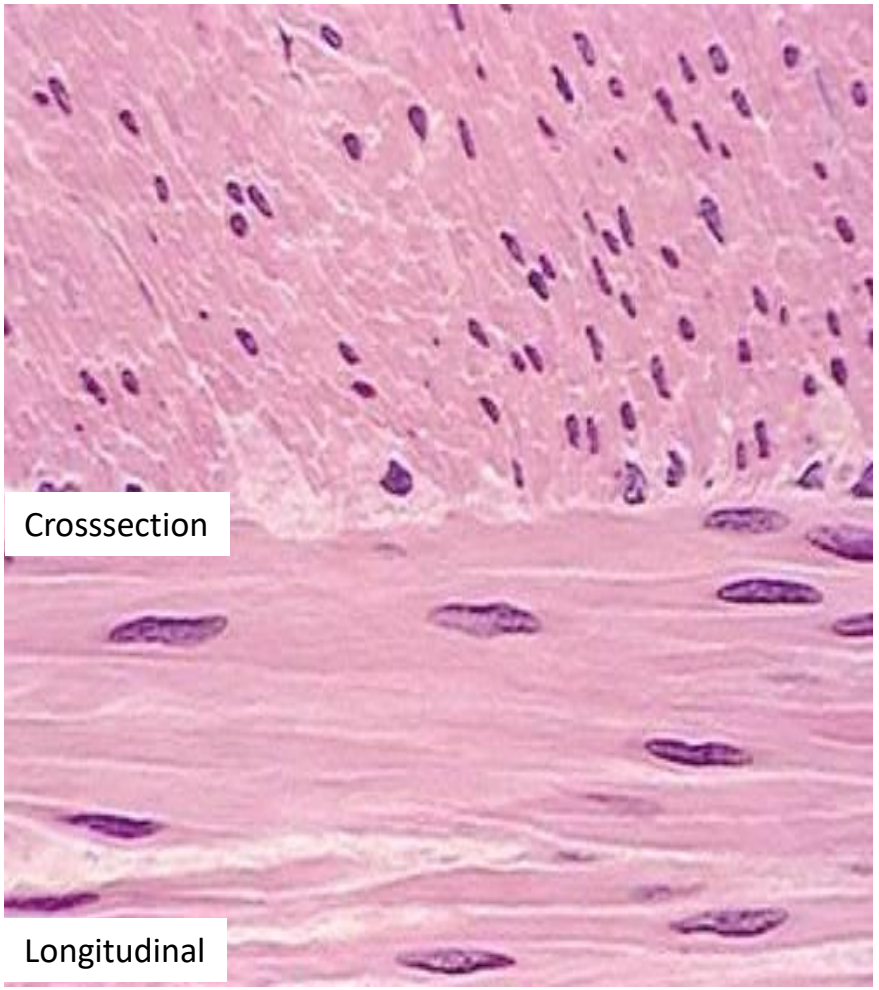
SMOOTH MUSCLE TISSUE

SMOOTH MUSCLE TISSUE

- Cells – **leiomyocytes** - form layers - eg. in walls of hollow organs

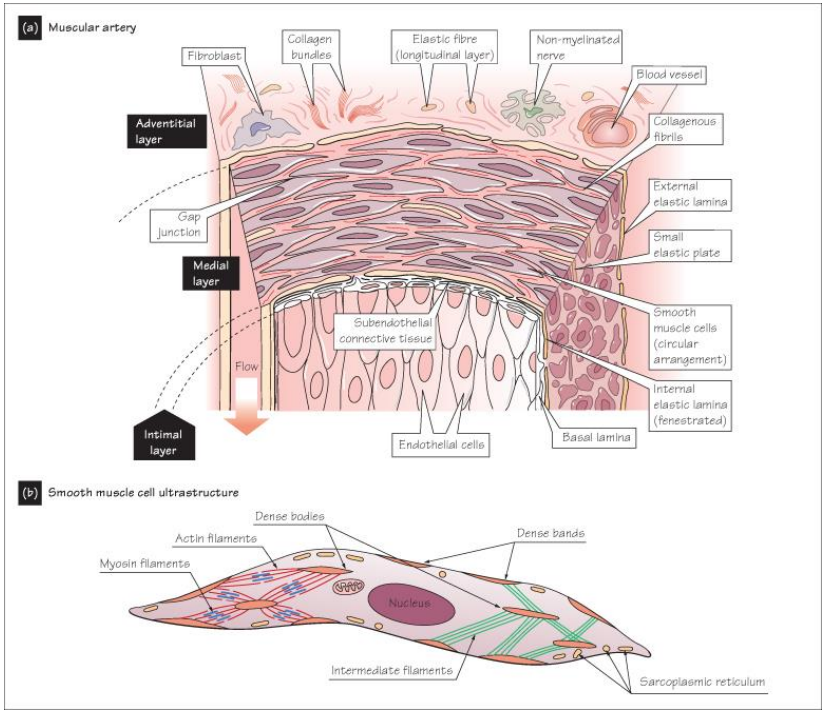






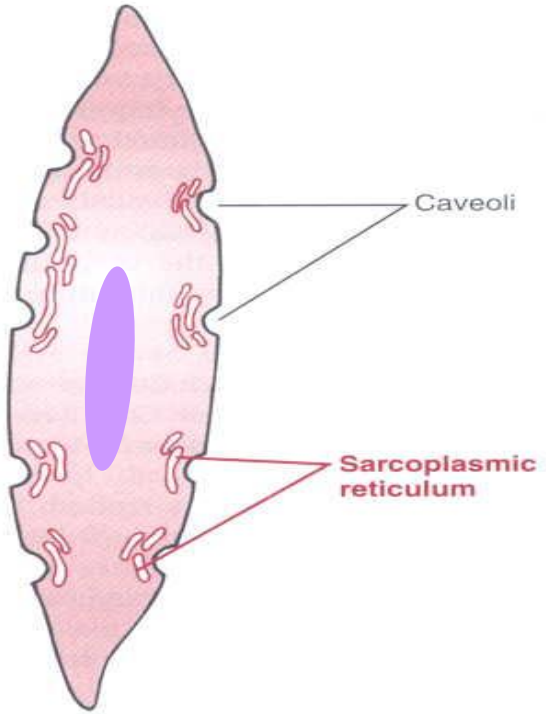
SMOOTH MUSCLE TISSUE

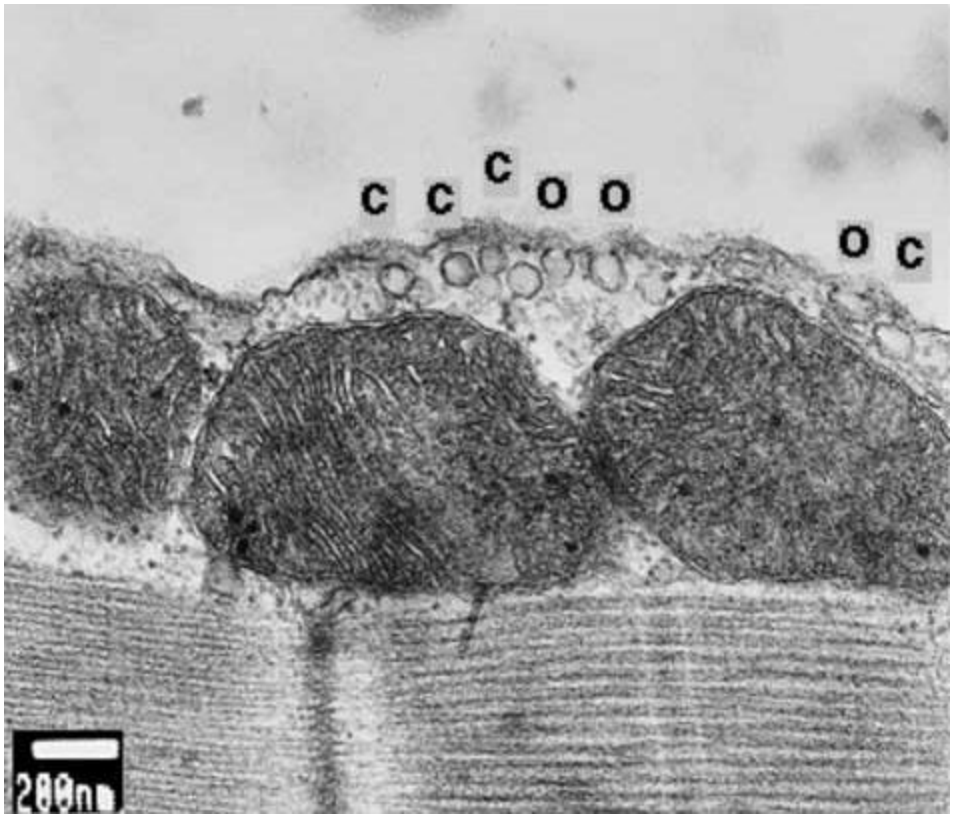
- spindle shaped cells (leiomyocytes) with myofilaments not arranged into myofibrils (no striation), 1 nucleus in the centre of the cell
- myofilaments form bands throughout the cell
- actin filaments attach to the sarcolemma by focal adhesions or to the dense bodies substituting Z-lines in sarcoplasm
- sarcoplasmic reticulum forms only tubules, Ca^{II+} ions are transported to the cell via caveolae and pinocytic vesicles
- zonulae occludentes and nexuses connect cells
- calmodulin

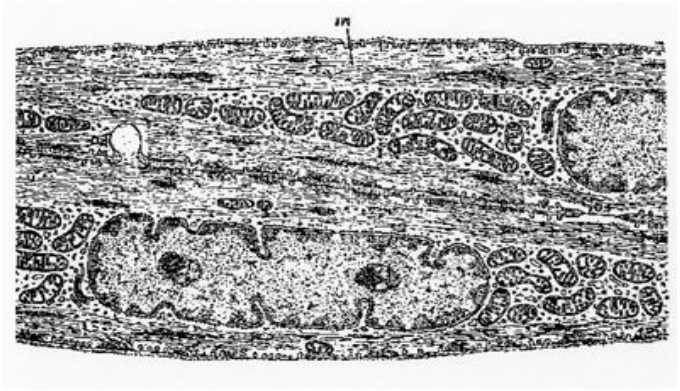


CAVEOLAE

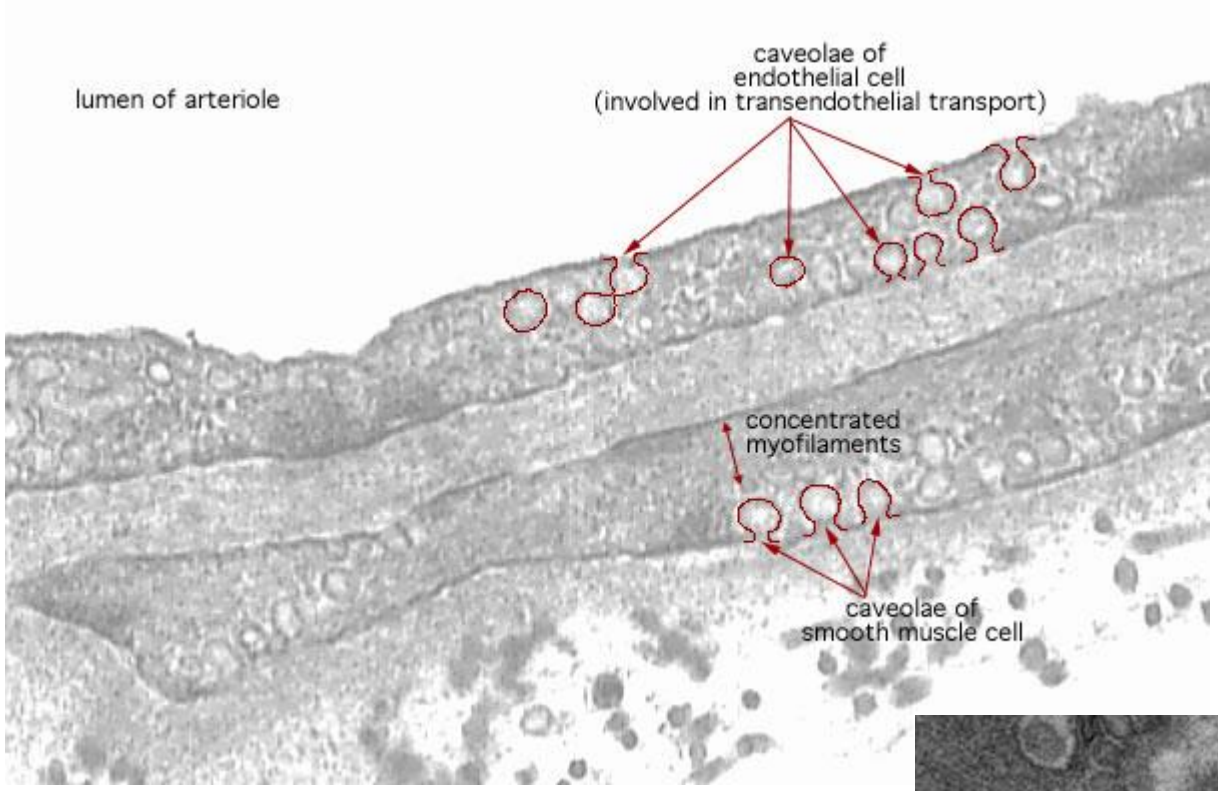
- caveolae are equivalent to t-tubules
- transmembrane ion channels

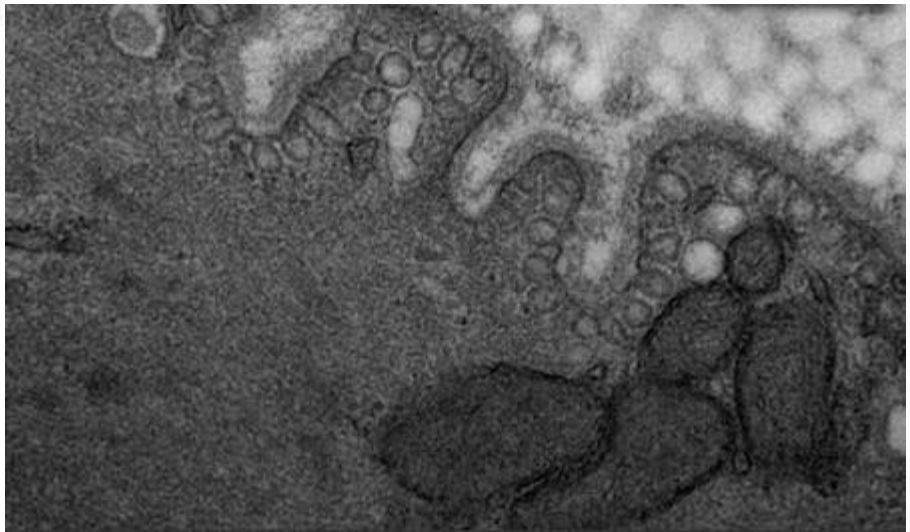




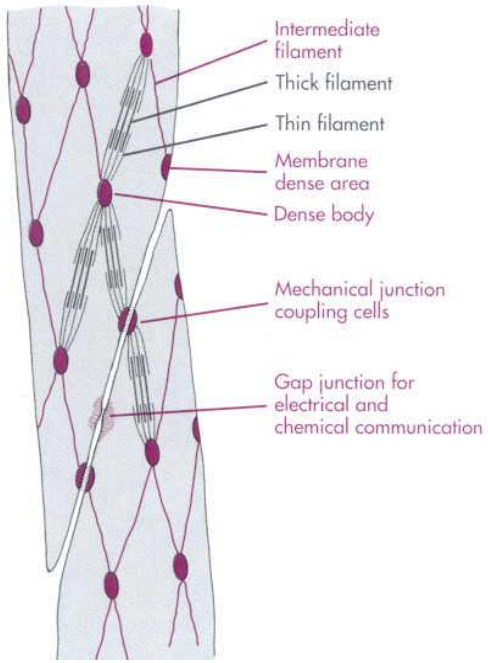


CAVEOLAE


lumen of arteriole
caveolae of
endothelial cell
(involved in transendothelial transport)
concentrated
myofilaments
caveolae of
smooth muscle cell

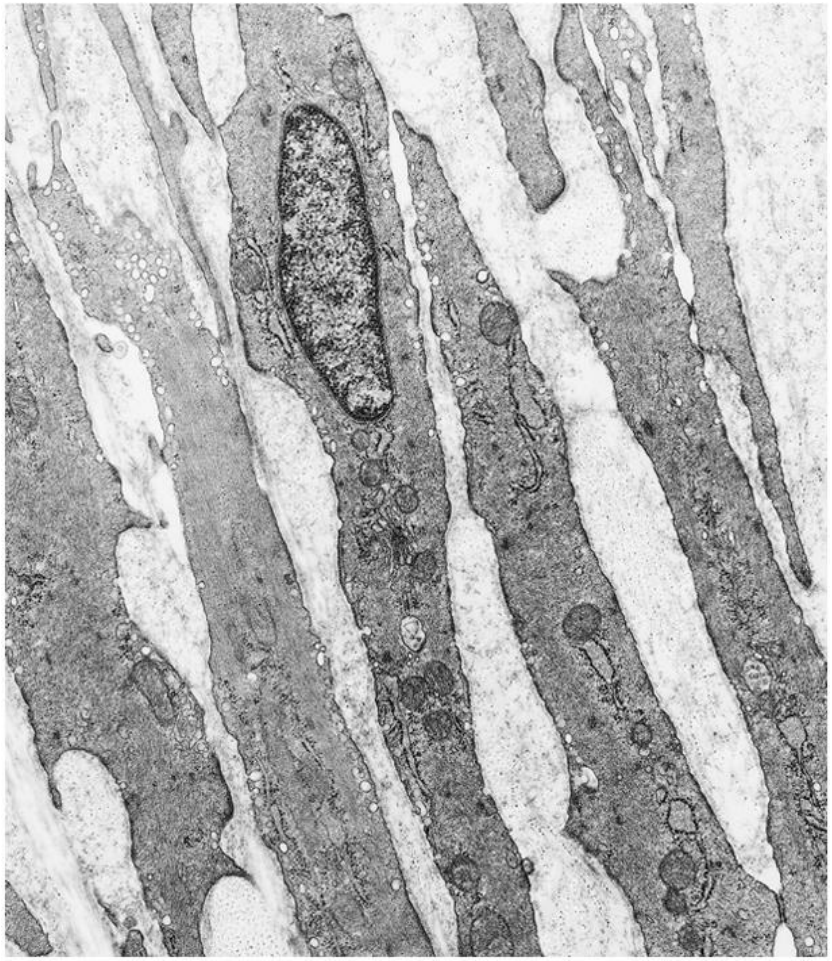


CONTRACTION OF LEIOMYCYTES

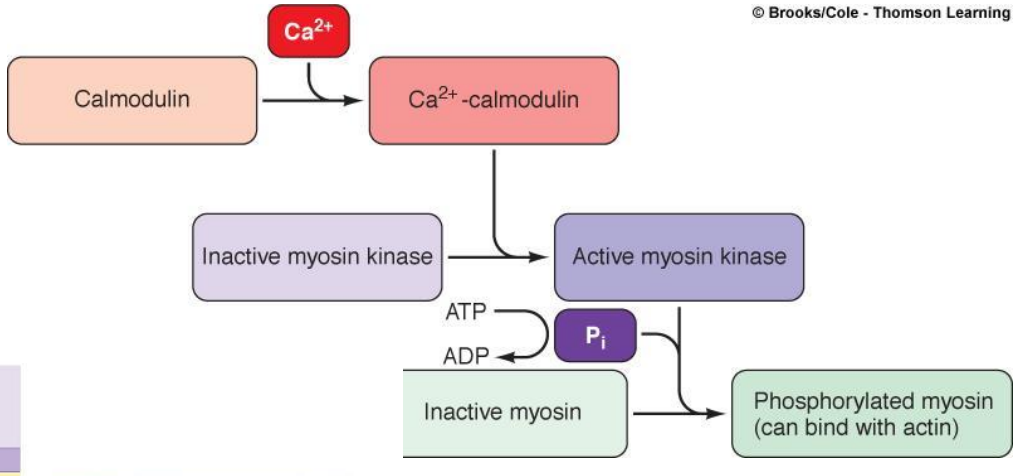


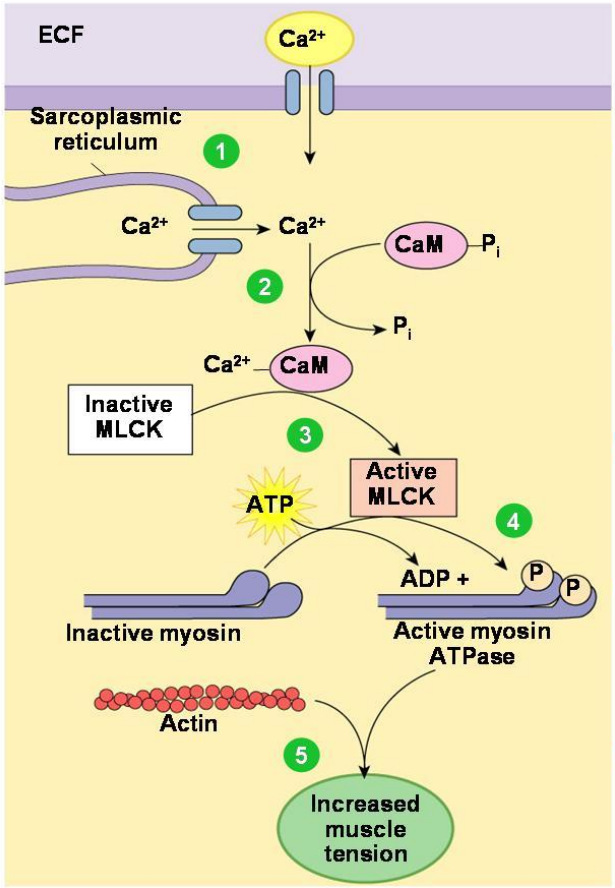
Relaxed smooth muscle cell

Contracted smooth muscle cell

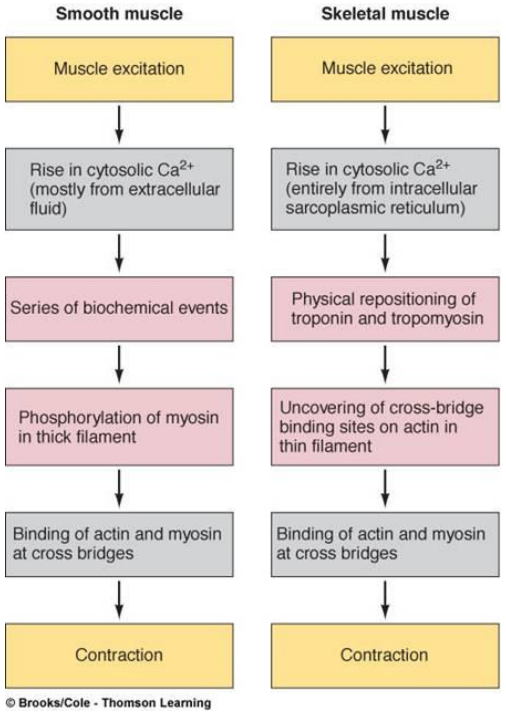


CONTRACTION OF LEIOMYCYTES

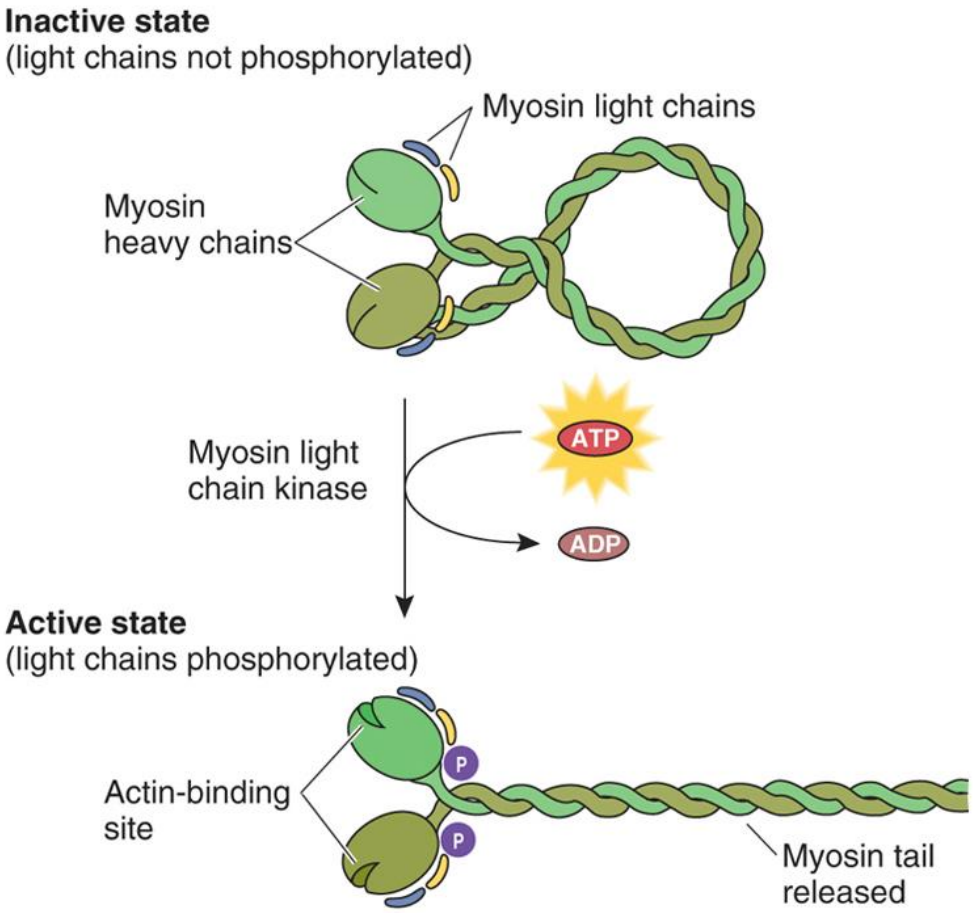




1. Intracellular Ca^{2+} concentrations increase when Ca^{2+} enters cell and is released from sarcoplasmic reticulum.
2. Ca^{2+} binds to calmodulin (CaM).
3. Ca^{2+}–calmodulin activates myosin light chain kinase (MLCK).
4. MLCK phosphorylates light chains in myosin heads and increases myosin ATPase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



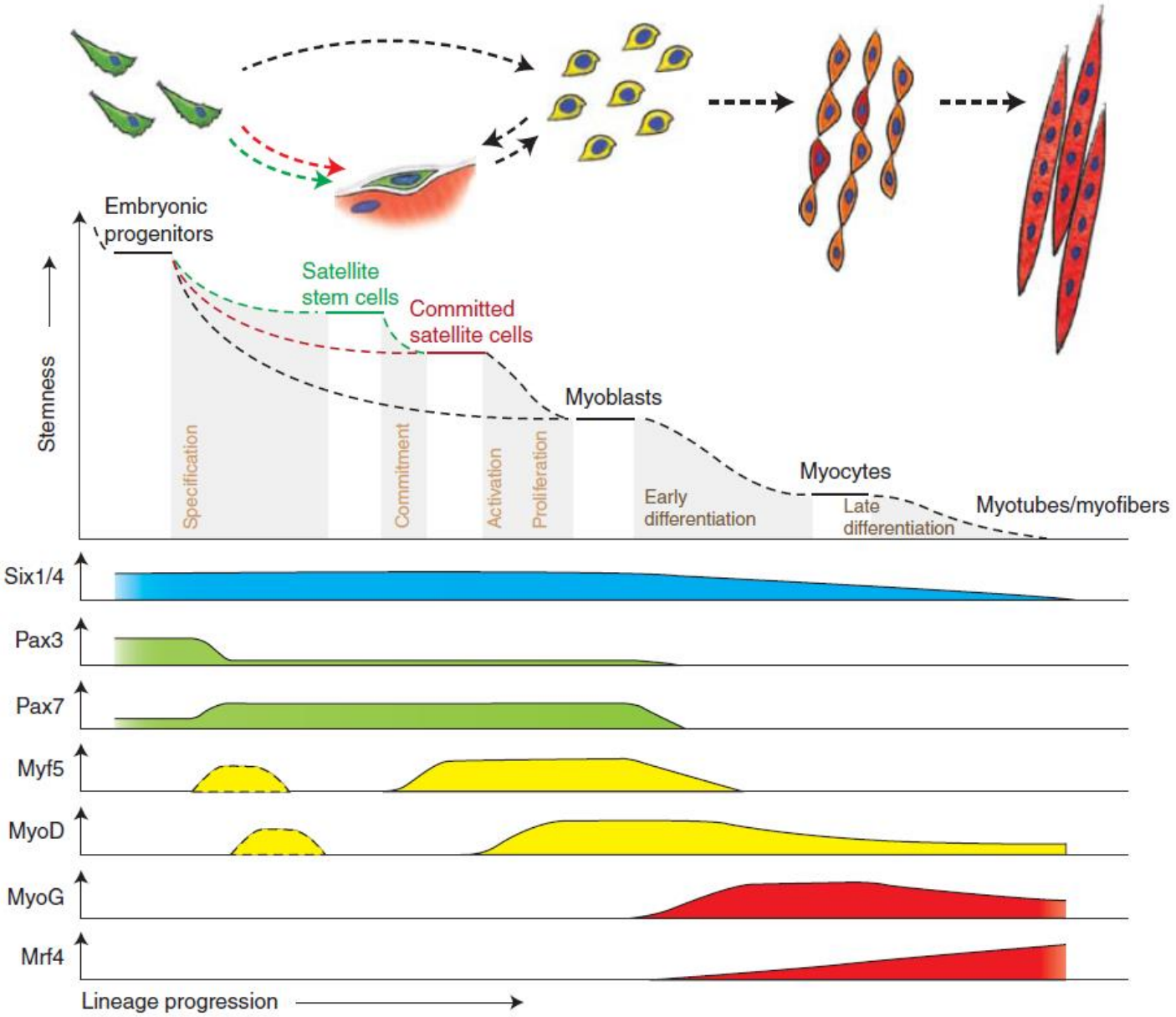
SMOOTH MUSCLE TISSUE



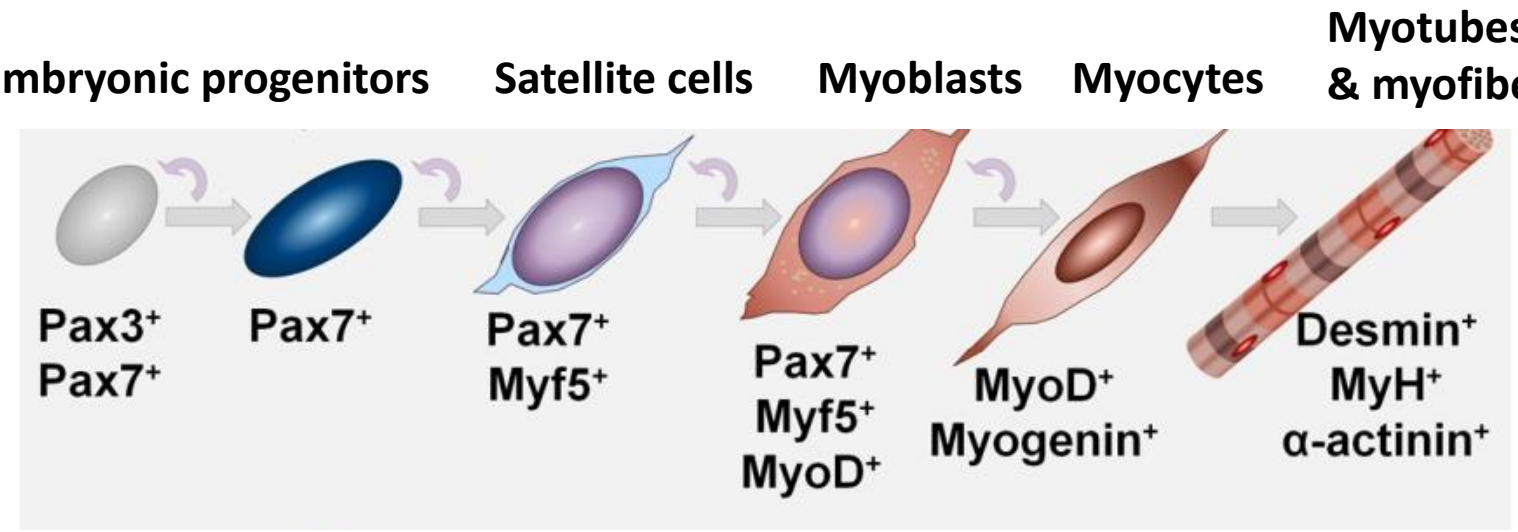
SUMMARY

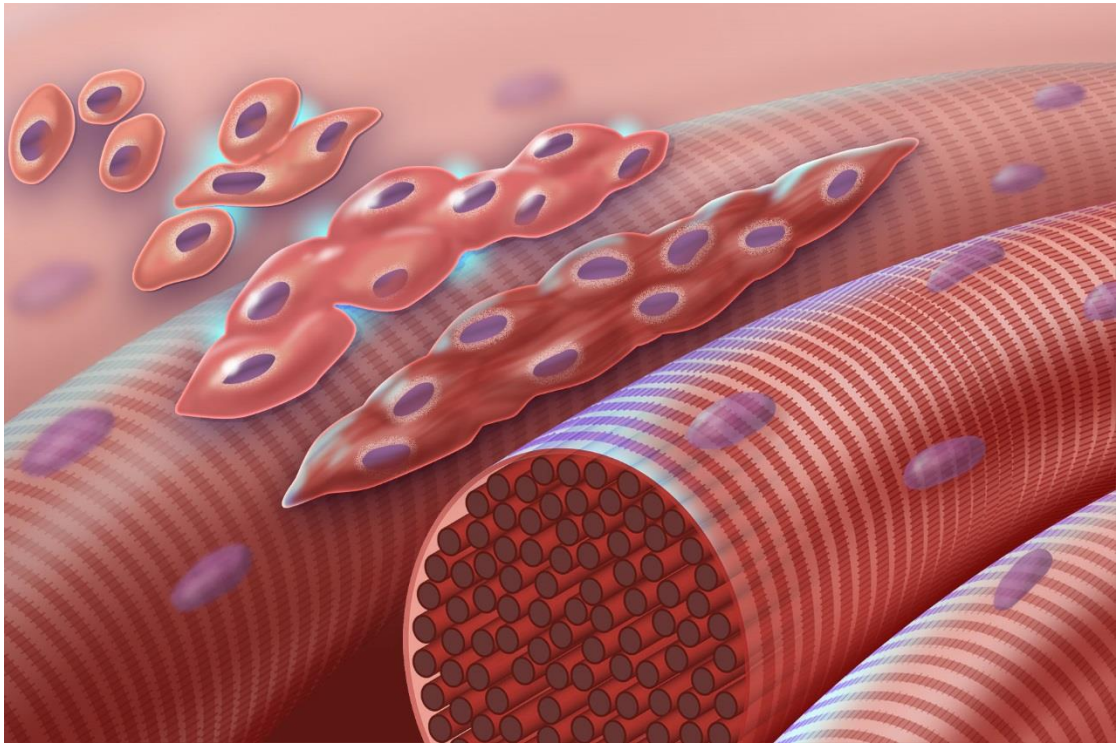
Hallmark	Skeletal muscle	Cardiac muscle	Smooth muscle
Cells	Thick, long, cylindrical, non-branched	Branched, cylindrical	Small, spindle-shaped
Nuclei	Abundant, peripherally	1-2, centrally	1, centrally
Filaments ratio (thin:thick)	6:1	6:1	12:1
sER and myofibrils	Regular sER around myofibrils	Less regular sER, myofibrils less apparent	Less regular sER, myofibrils not developed
T tubules	Between A-I band, triads	Z lines, diads	Not developed
Motor end plate	Present	Not present	Not present
Motor regulation	Voluntary control	No voluntary control	No voluntary control
Other	Large multinucleated cells in bundles, c.t.	Intercalated discs, working and specialized cardiomyocytes	Caveolae, overlapping cells in layers

HISTOGENESIS OF SKELETAL MUSCLE TISSUE

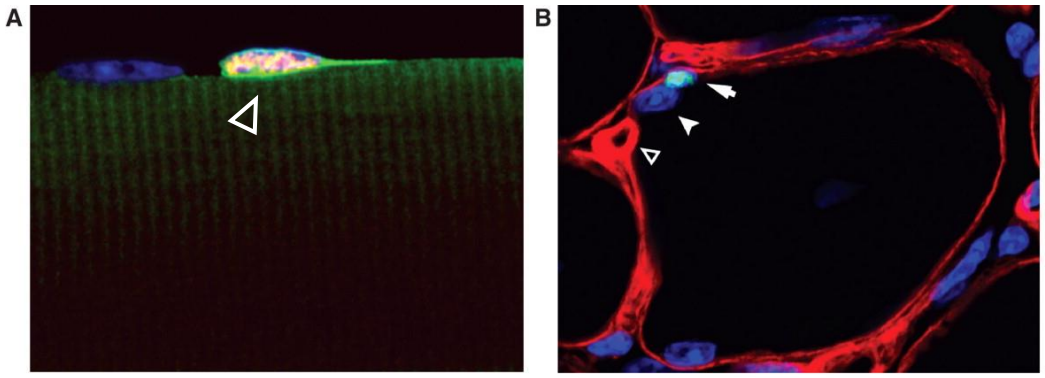


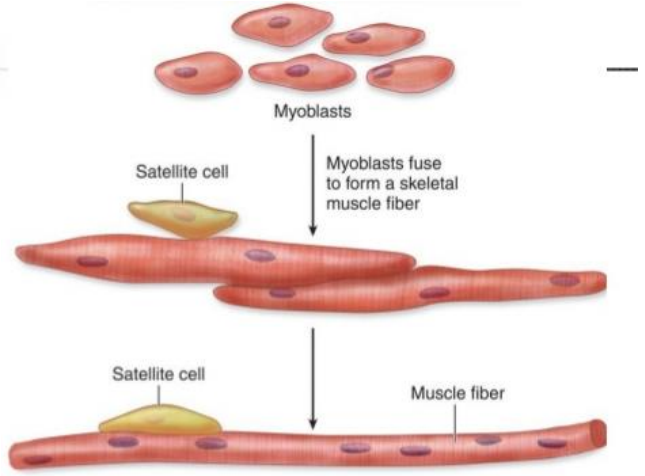
HISTOGENESIS OF SKELETAL MUSCLE TISSUE

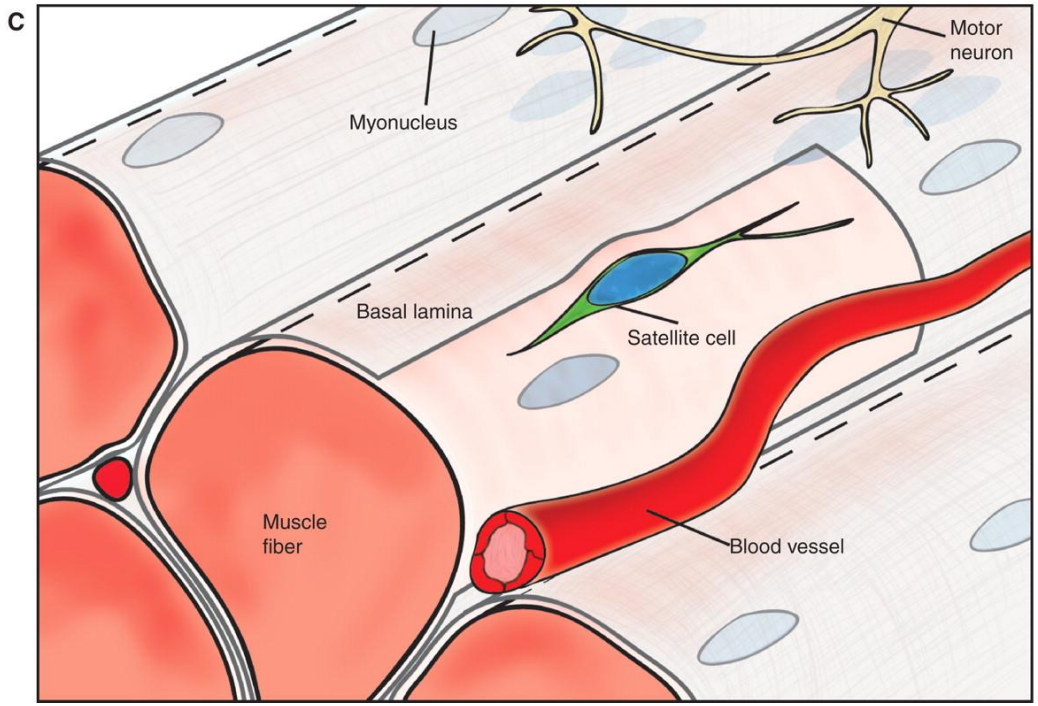




SATELLITE CELLS ARE REQUIRED FOR REGENERATION

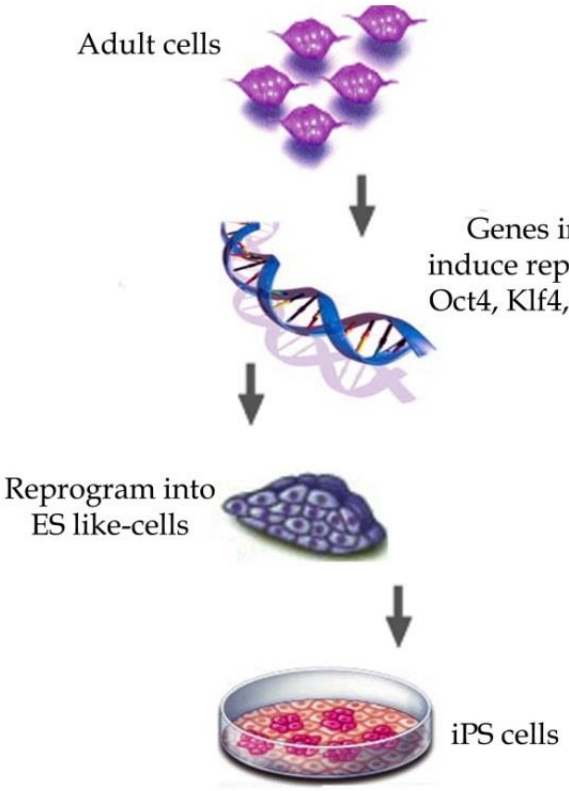


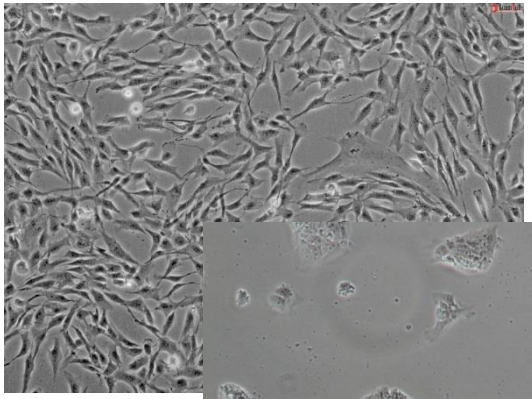


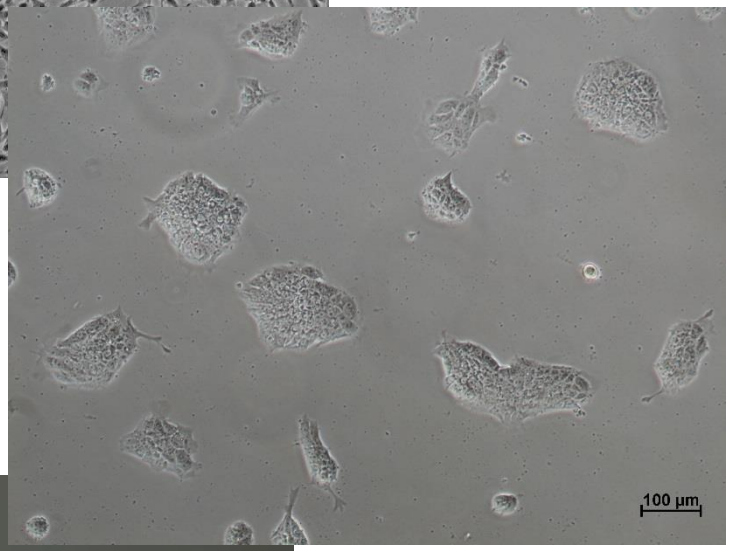


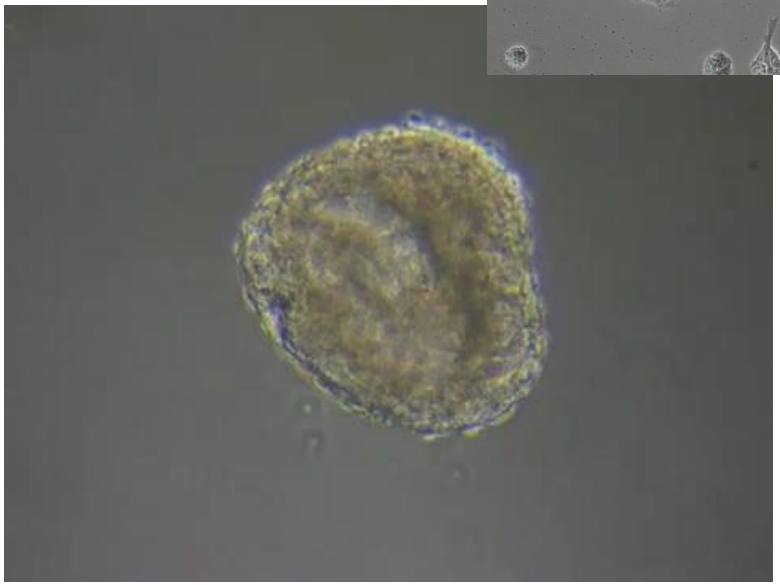
Satellite cells are equivalent to embryonic precursors of muscle fibers

DIFERENTIATION IN VITRO

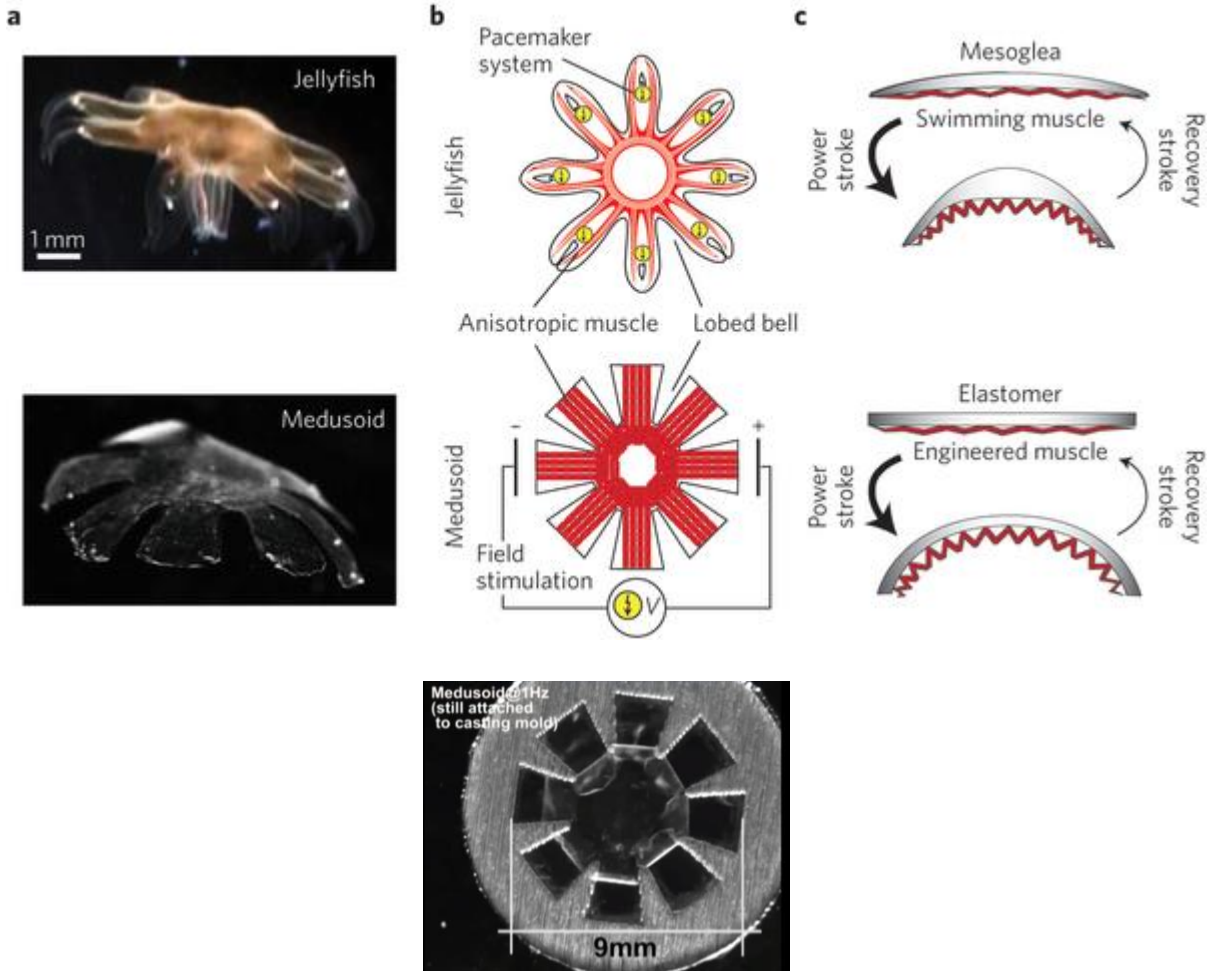








TISSUE ENGINEERING



https://www.nature.com/articles/nbt.2269

https://www.nature.com/news/artificial-jellyfish-built-from-rat-cells-1.11046

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