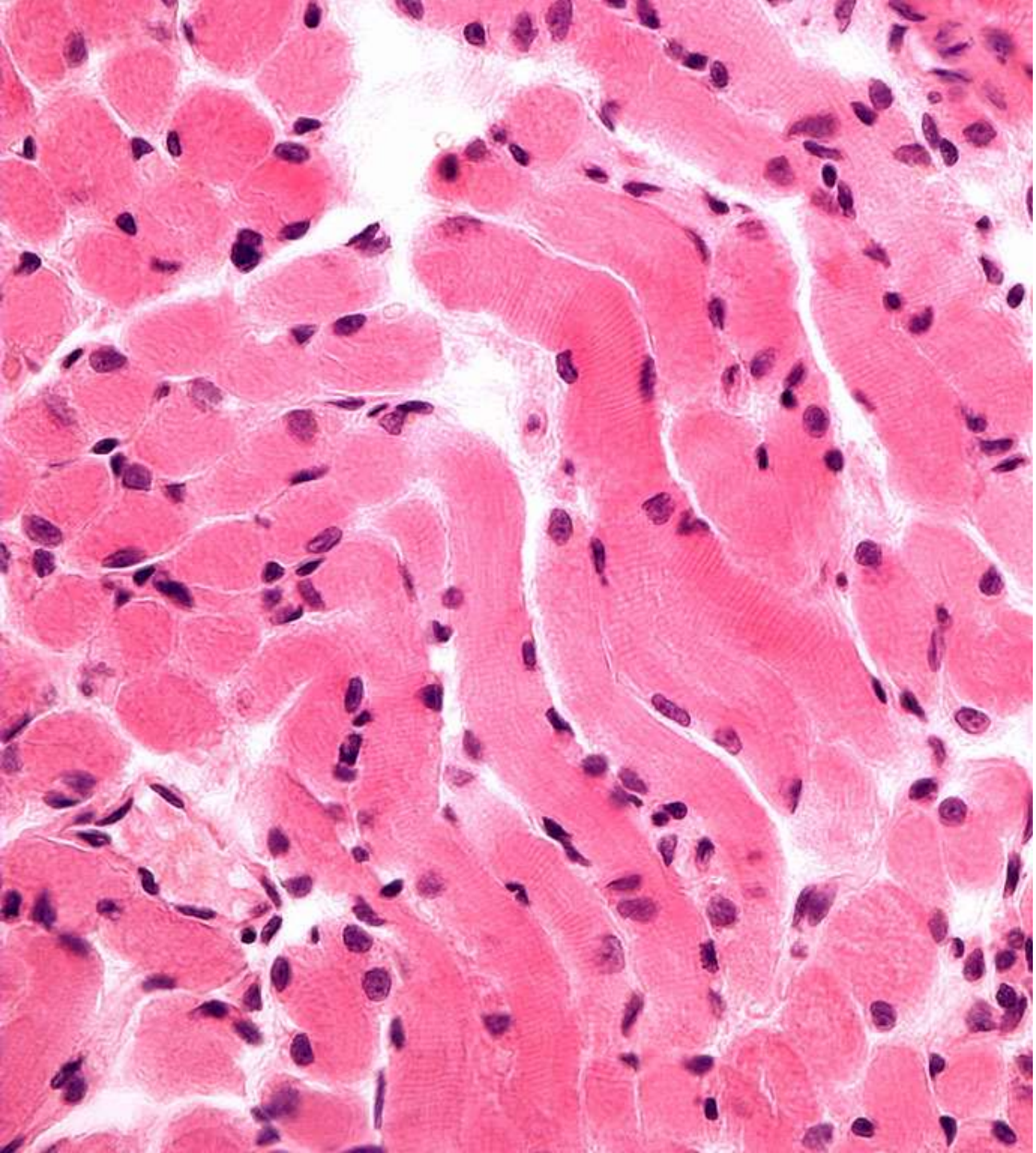

MUSCLE TISSUE

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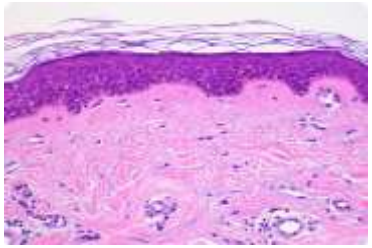
CONTEMPORARY TISSUE CLASSIFICATION

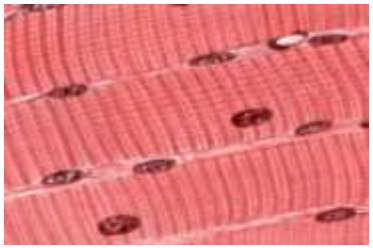
Based on morphology and function:

Epithelium



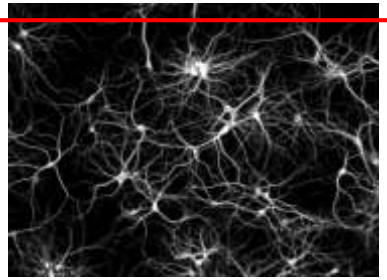
Continual, avascular layers of cells with different function, oriented to open space, with specific junctions and minimum of ECM and intercellular space.
Derivates of all three germ layers

Muscle



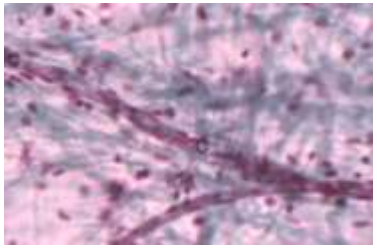
Cytoskeleton → contraction
Mesoderm – skeletal muscle, myocard, mesenchyme – smooth muscles
Rarely ectoderm (eg. m. sphincter a m. dilatator pupillae)

Nerve



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

Connective



Dominant extracellular matrix
Connective tissue, cartilage, bone…
Mesenchyme

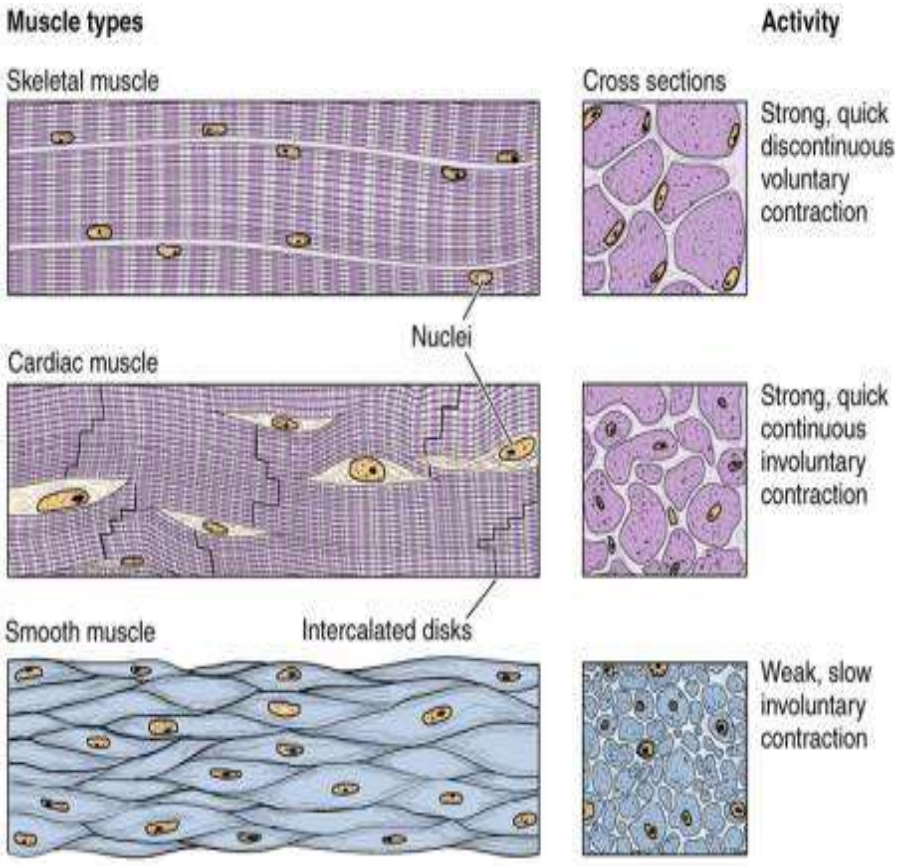
GENERAL CHARACTERISTIC OF MUSCLE TISSUE

Hallmarks

- Unique cell architecture
- Excitability and contraction
- Mesodermal origin

Muscle tissue

- Skeletal
- Cardiac
- Smooth



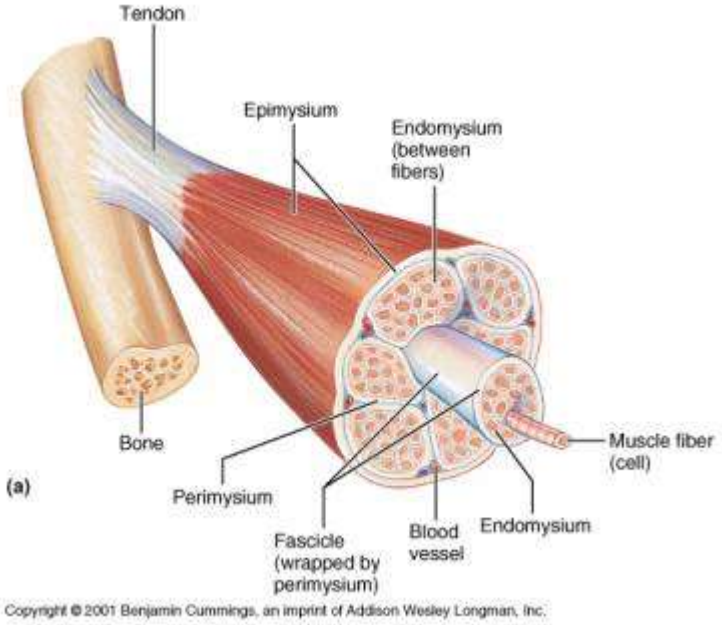
HISTOLOGY OF SKELETAL MUSCLE TISSUE

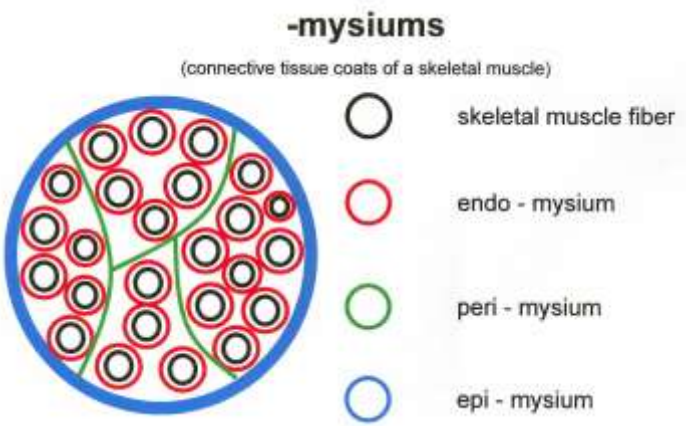
- Composition: muscle cells + connective tissue, blood vessels
- Unique cell architecture – long multinuclear cells – muscle fibers (rhabdomyocytes)
- Long axis of cells is oriented parallel with direction of contraction
- Specific terminology:
  - cell membrane = sarcolemma
  - cytoplasm = sarcoplasm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

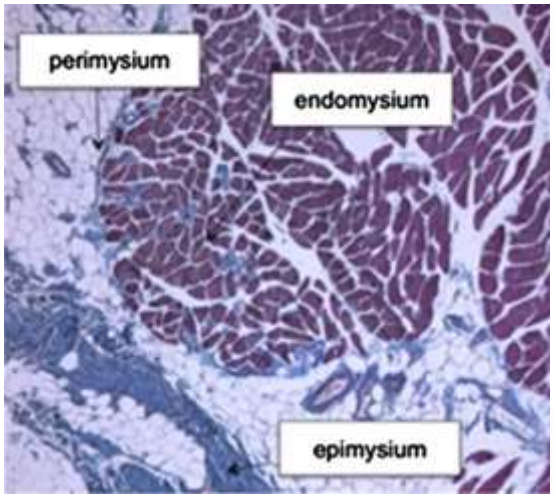
  - Muscle fiber – microscopic unit of skeletal muscle
  - Myofibril – LM unit – myofilaments – unit of muscle fibers
  - Myofilaments – filaments of actin and myosin (EM)

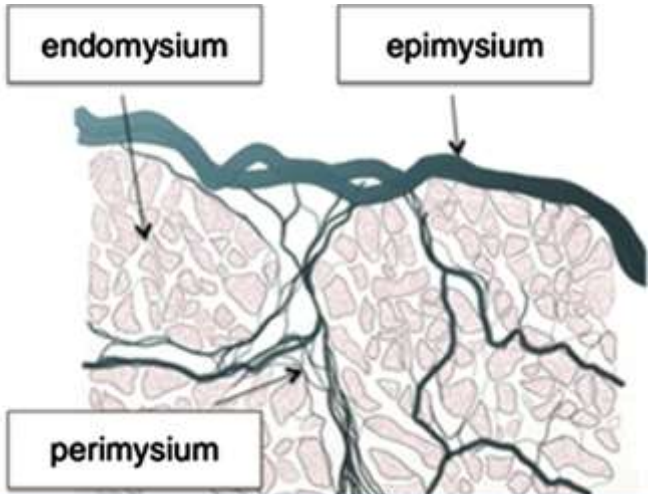
CONNECTIVE TISSUE OF SKELETAL MUSCLE

- 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.

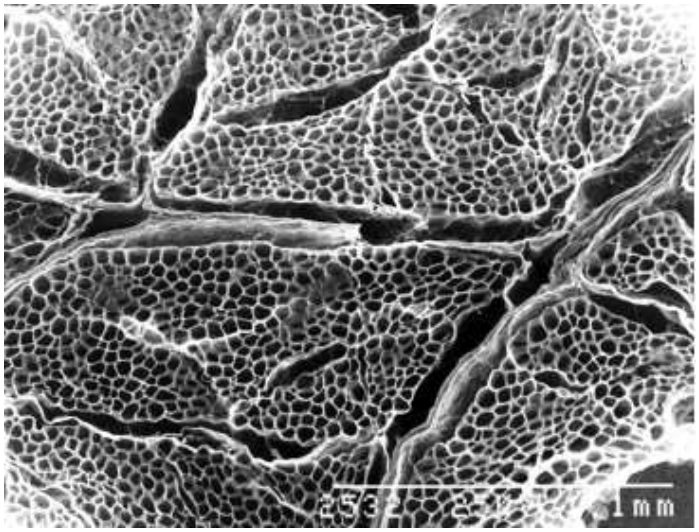


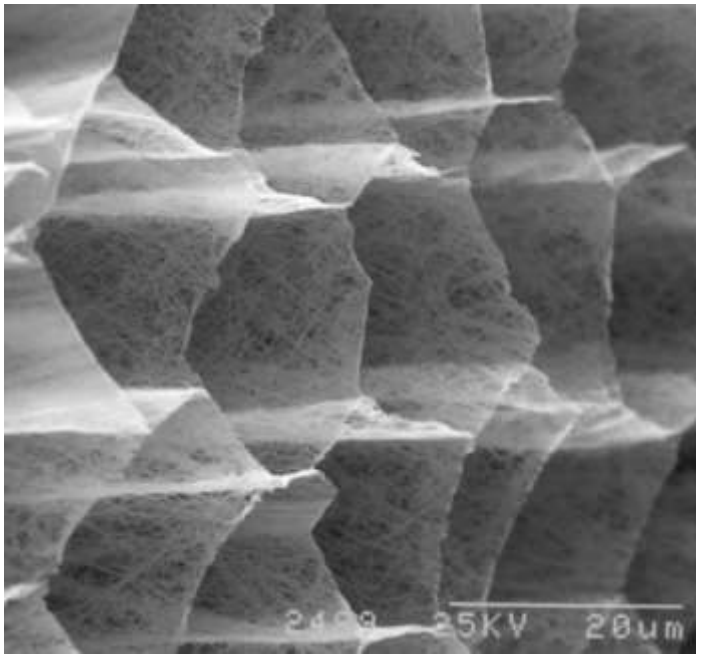


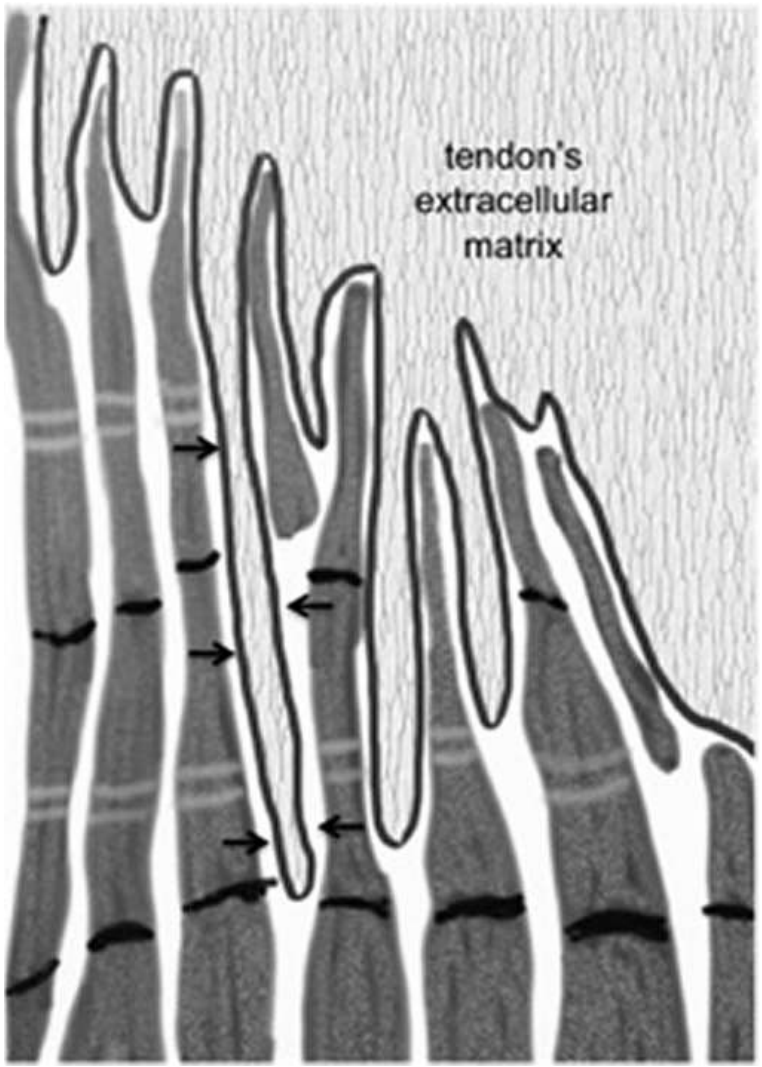




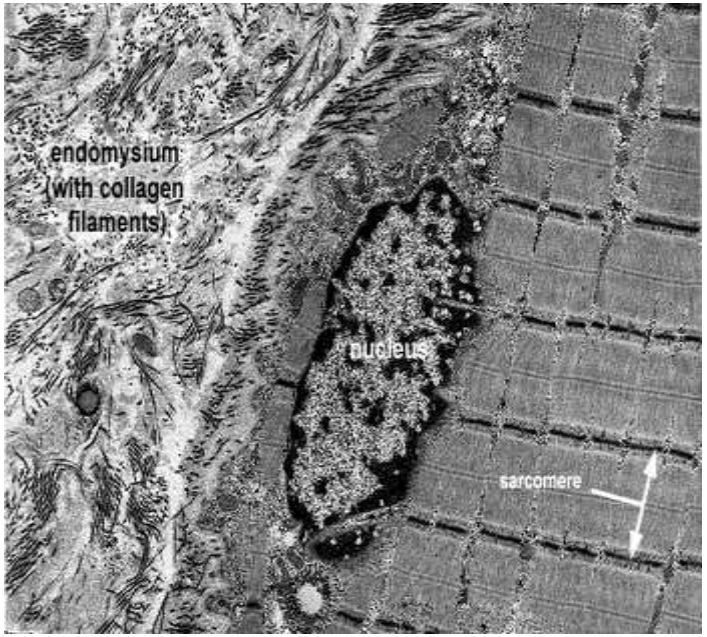
CONNECTIVE TISSUE OF SKELETAL MUSCLE

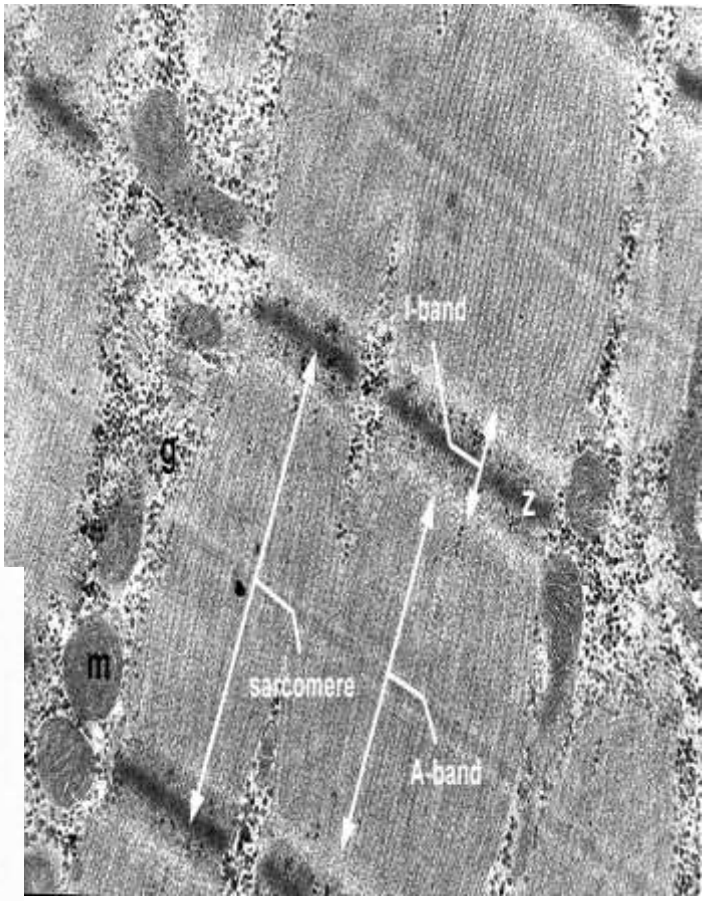


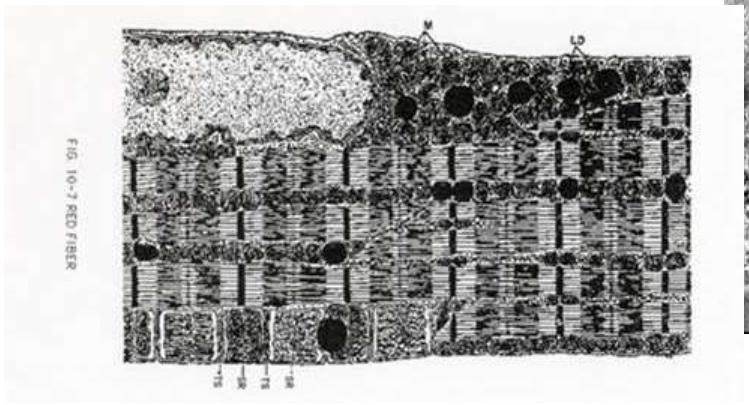




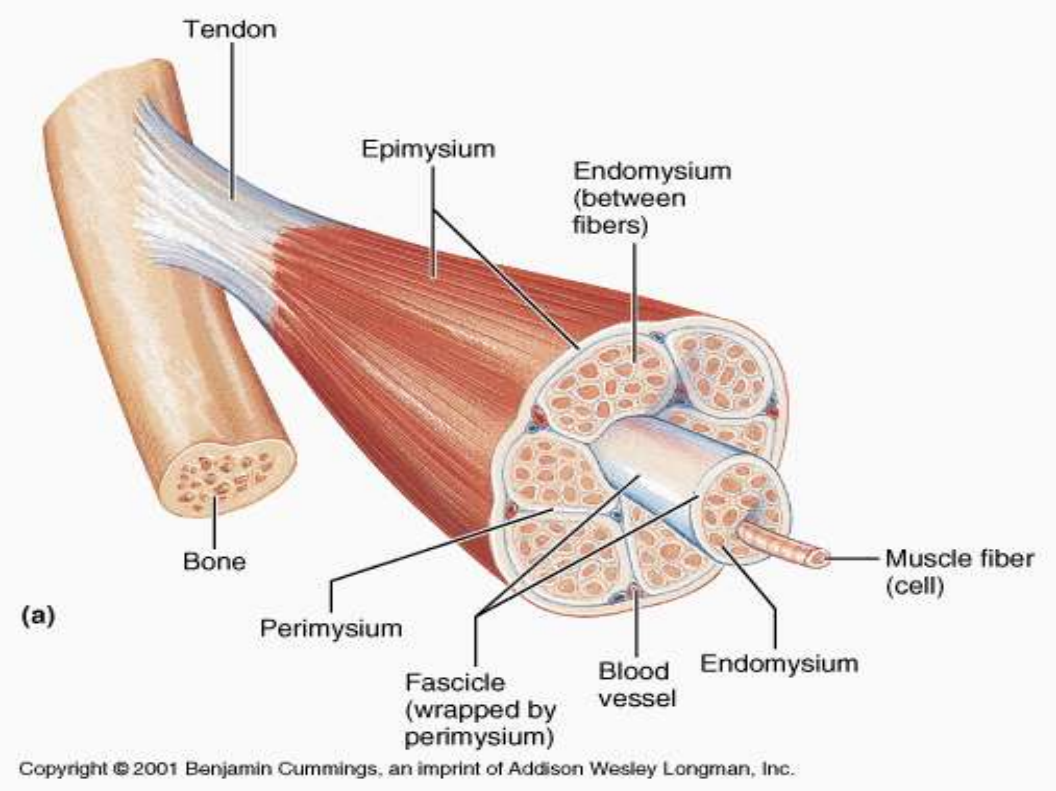
CONNECTIVE TISSUE OF SKELETAL MUSCLE

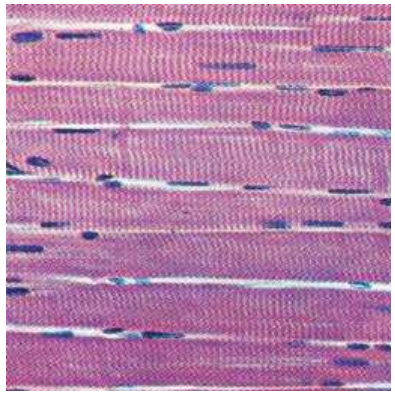


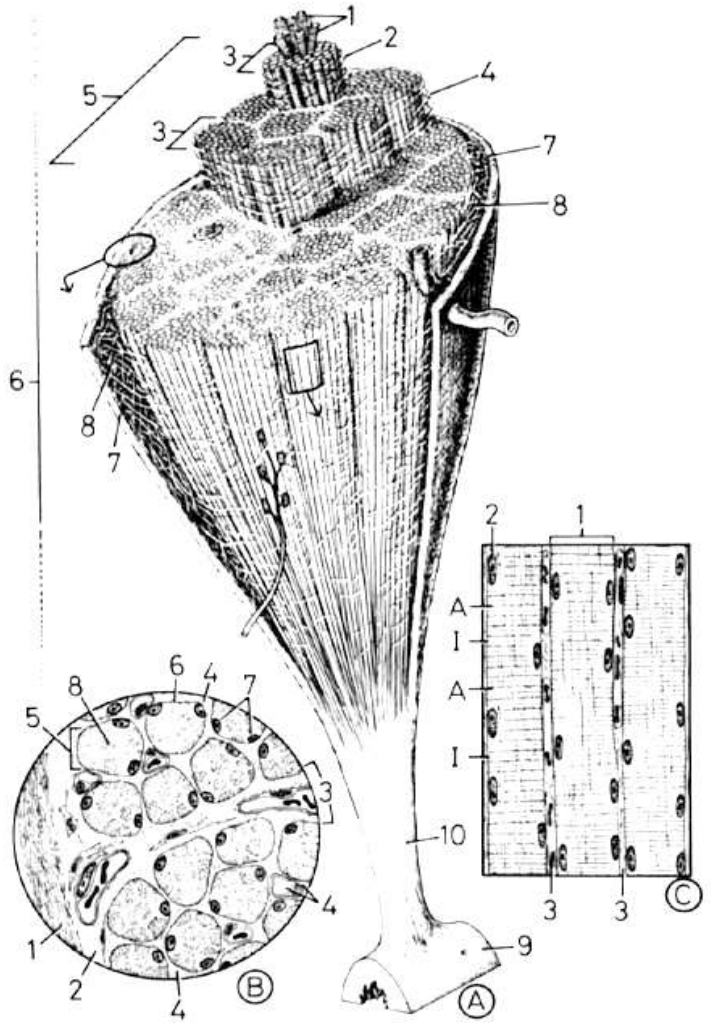




STRUCTURE OF SKELETAL MUSCLE

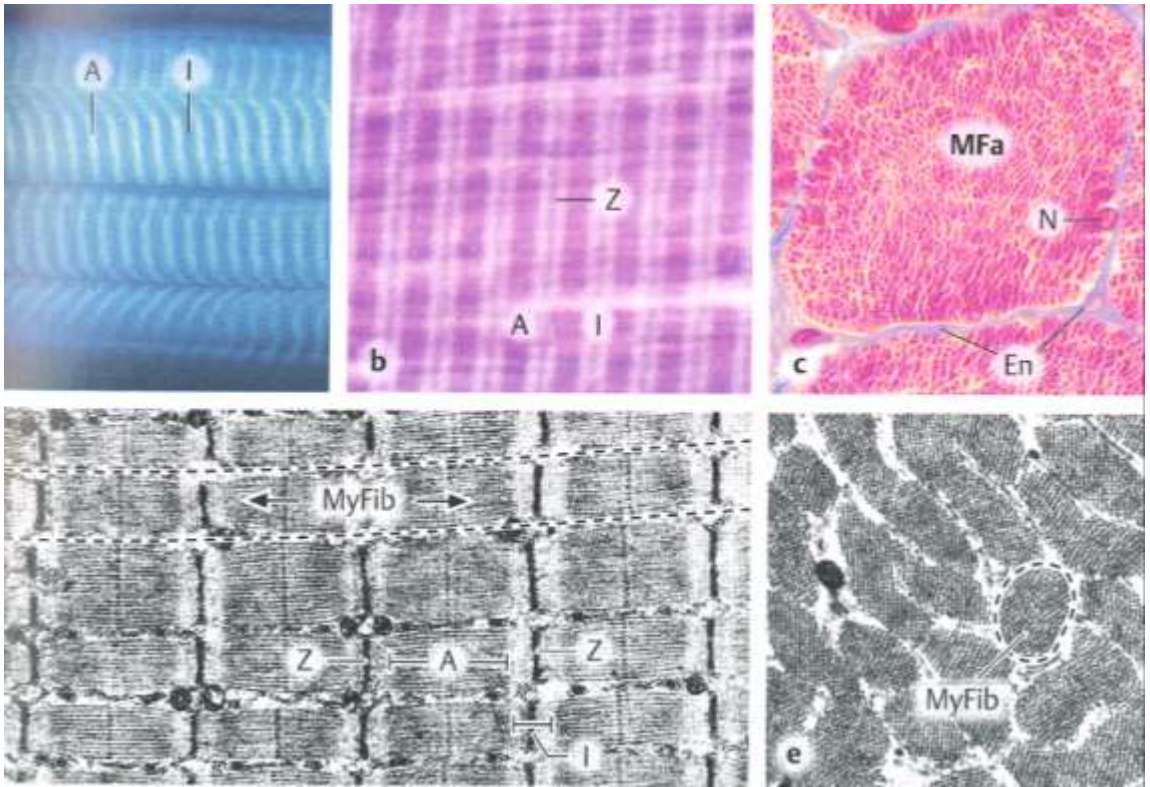






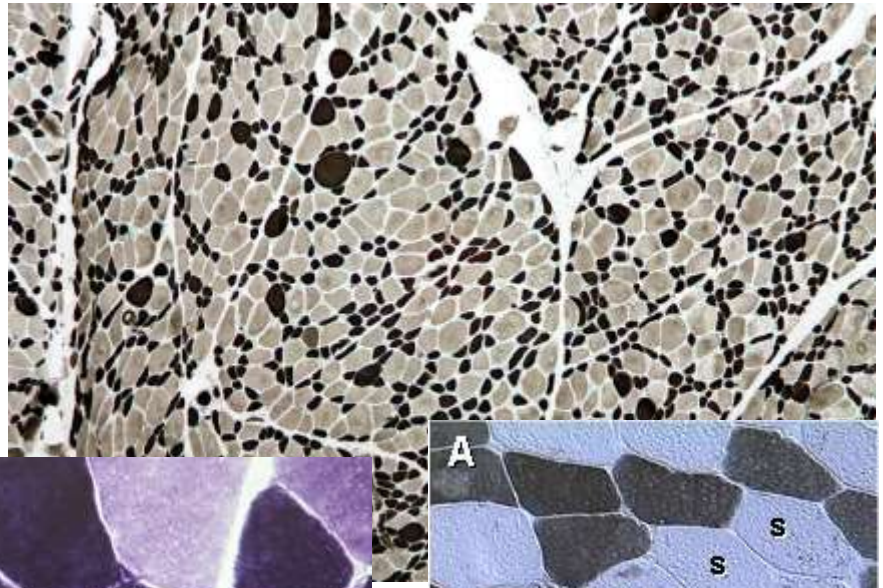
STRUCTURE OF SKELETAL MUSCLE

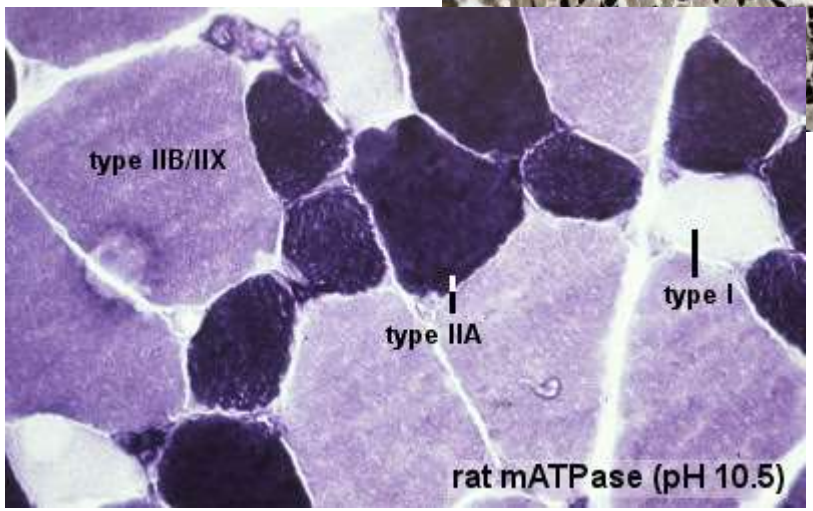
- morphological and functional unit: **muscle fiber (rhabdomyocyte)** – elongated, cylindrical-shaped, multinucleated cell (syncytium)
- nuclei are located at the periphery (under sarcolemma)
- **myofibrils** show cross striation
- diameter of muscle fiber: 25-100 μm
- length: millimeters - centimeters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

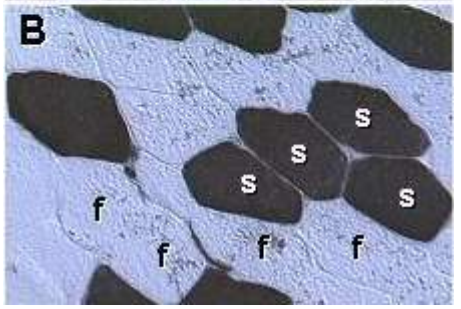


CLASSIFICATION OF SKELETAL MUSCLE FIBERS

- **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**







CLASSIFICATION OF SKELETAL MUSCLE FIBERS

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

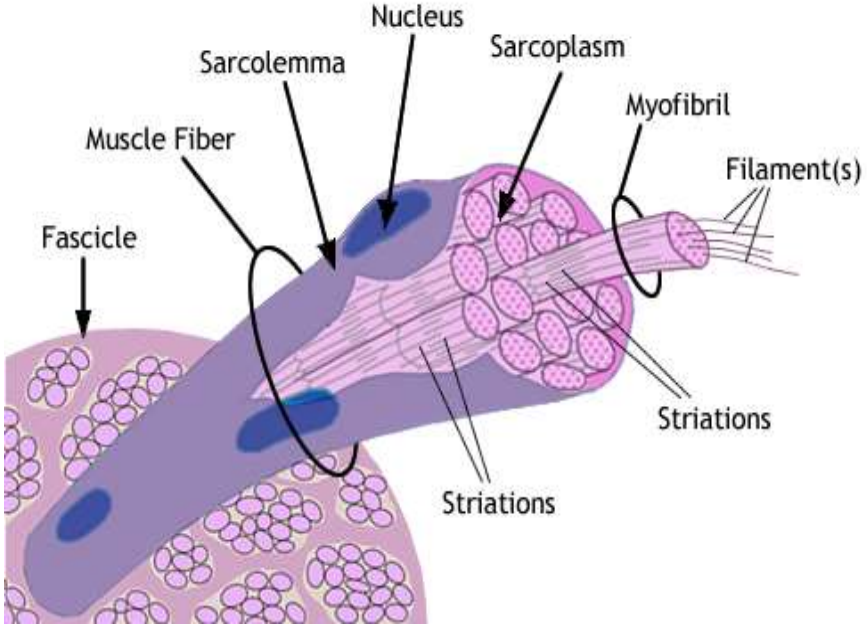
Muscle fiber = myofiber = syncitium = rhabdomyocyte

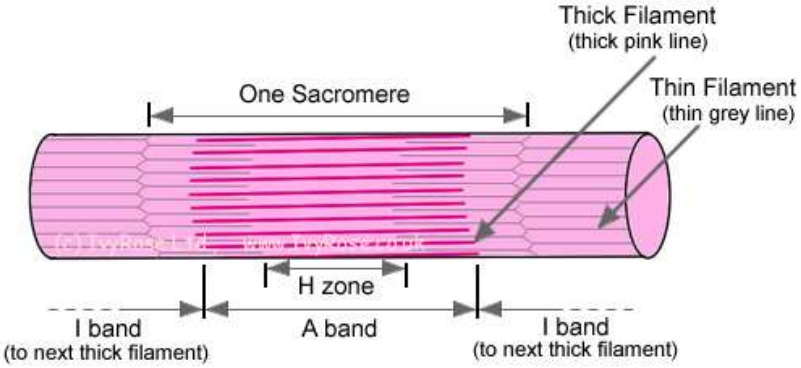
Muscle fiber – morphological and functional unit of skeletal muscle [Ø 25 – 100 μm]

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]





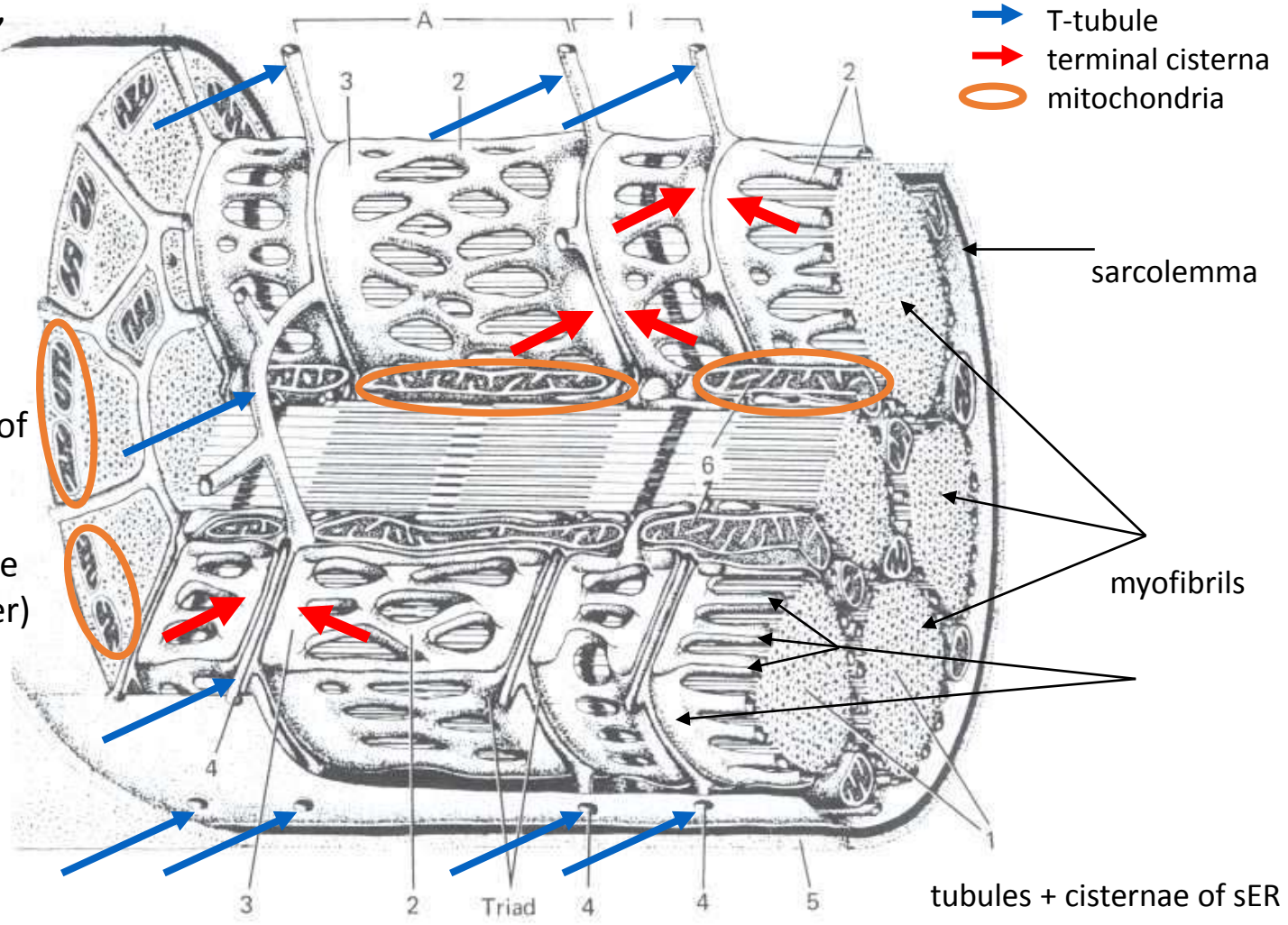
ULTRASTRUCTURE OF RHABDOMYOCYTE

Sarcolemme + **t-tubules**,

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

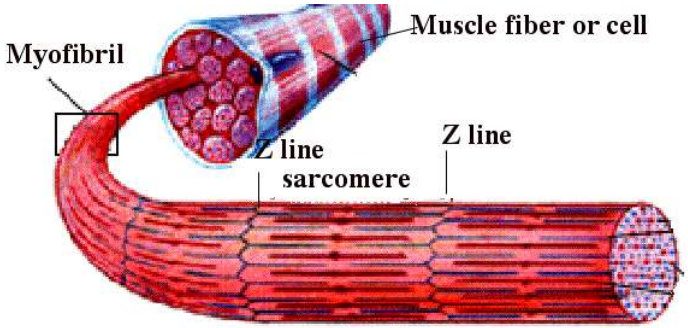
Sarcoplasmic reticulum (smooth ER) – reservoir of Ca^{2+}

Myofibrils (parallel to the length of the muscle fiber)

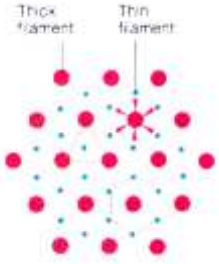


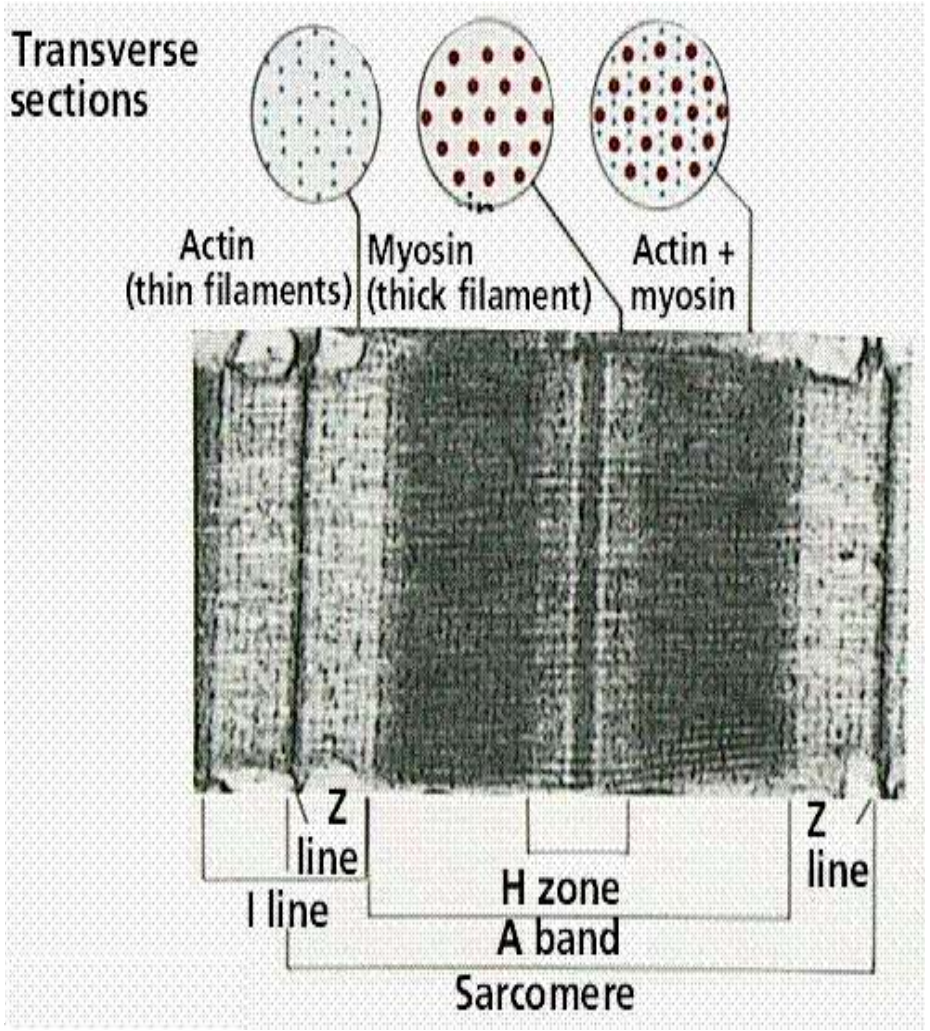
MYOFIBRILS

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

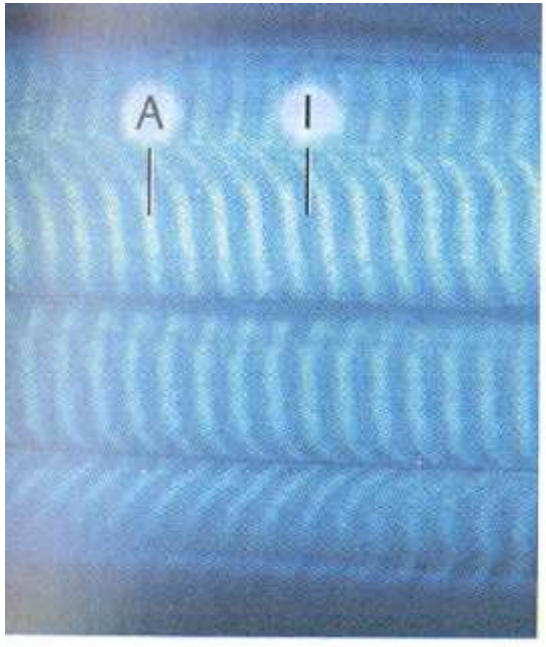


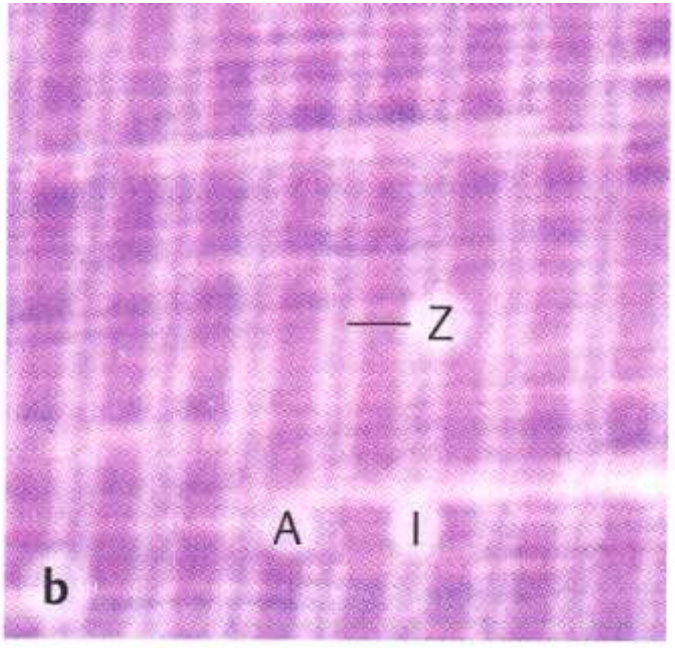
- Actin + myosin myofilaments
- Sarcomere
- Z-line
- M-line and H-zone
- I-band, A-band

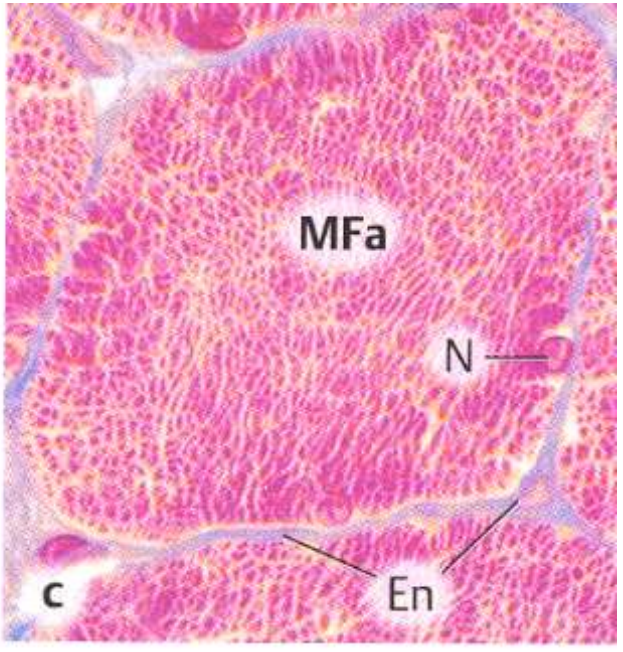


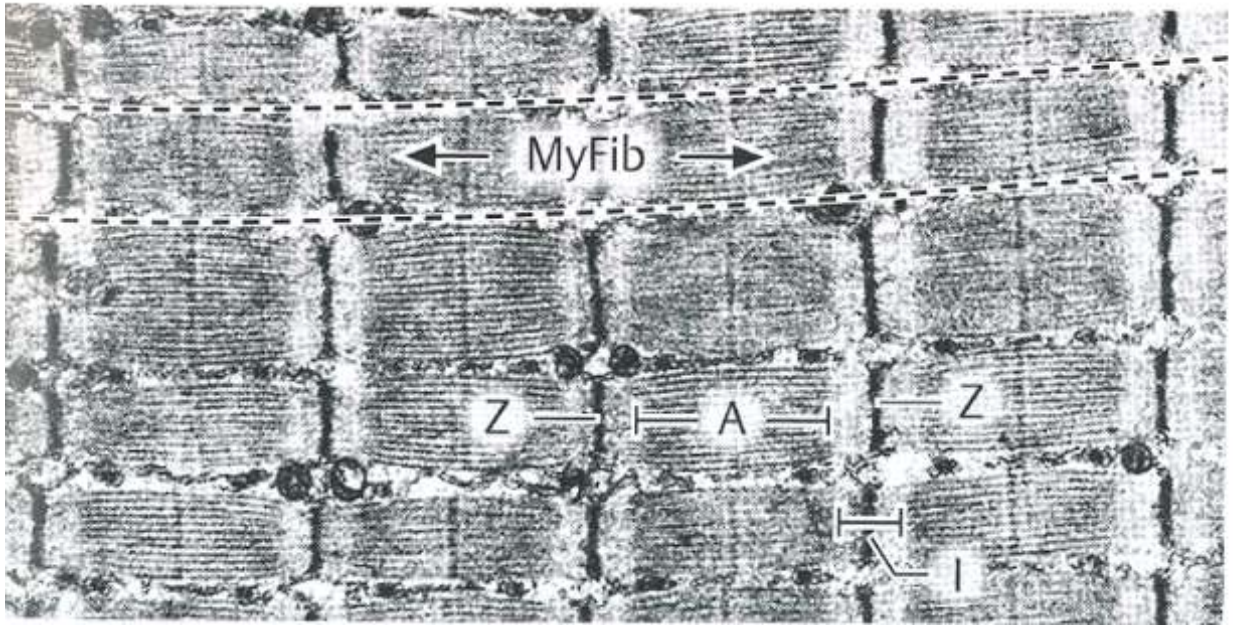


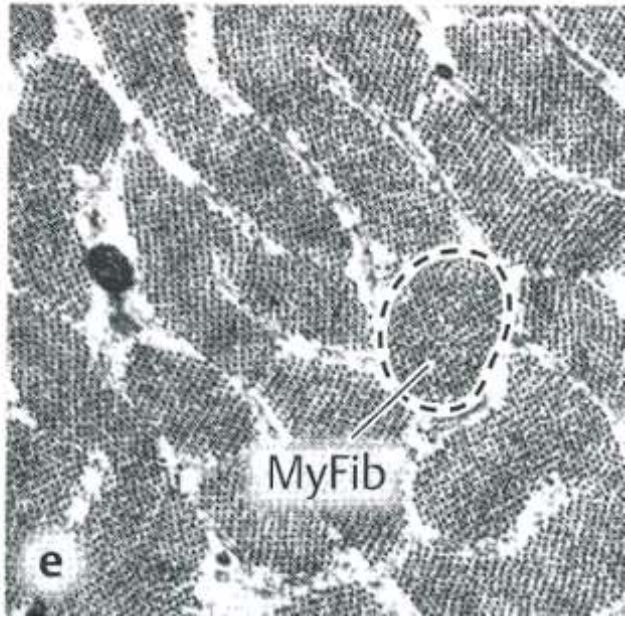
MYOFIBRILS



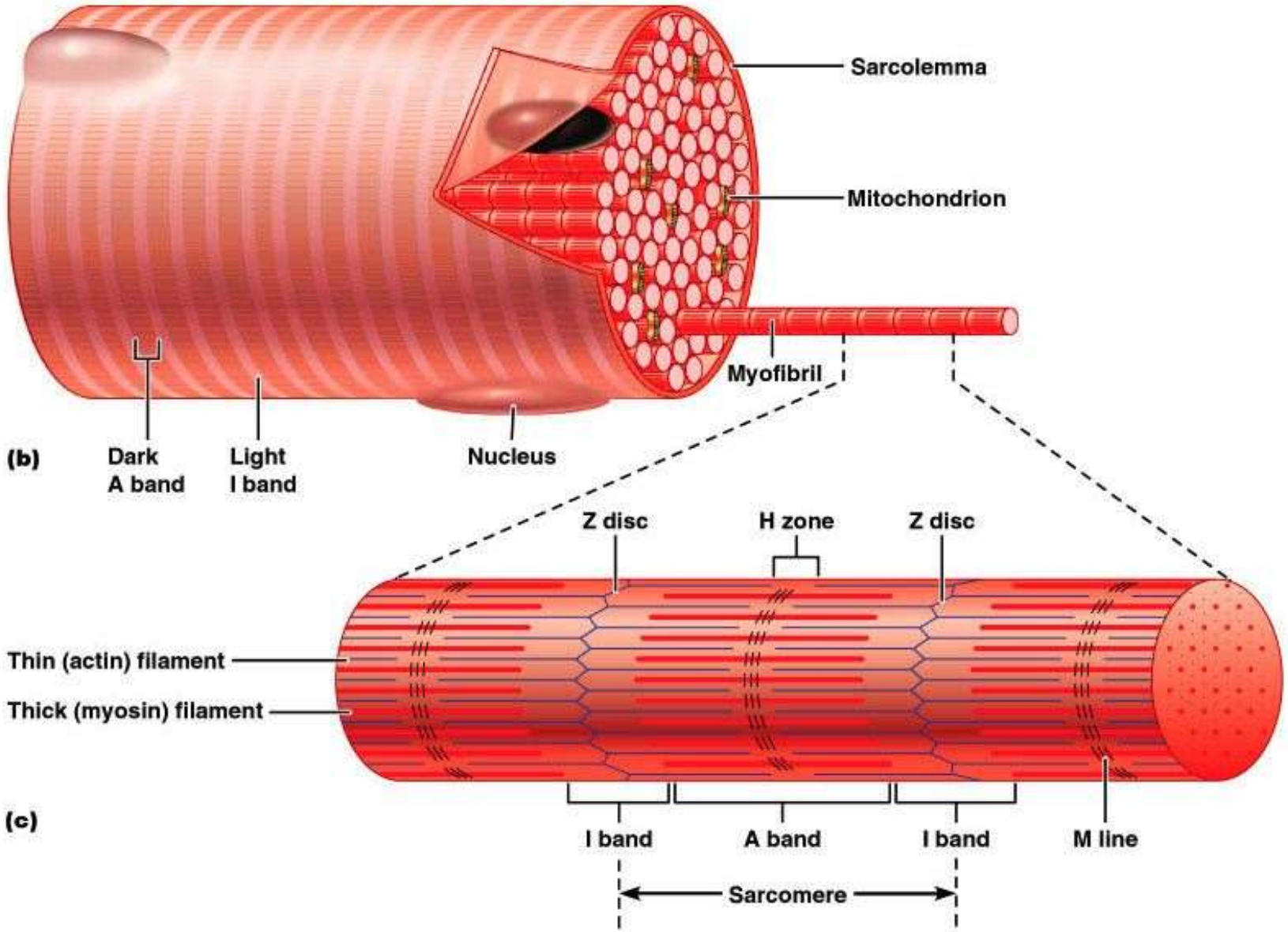




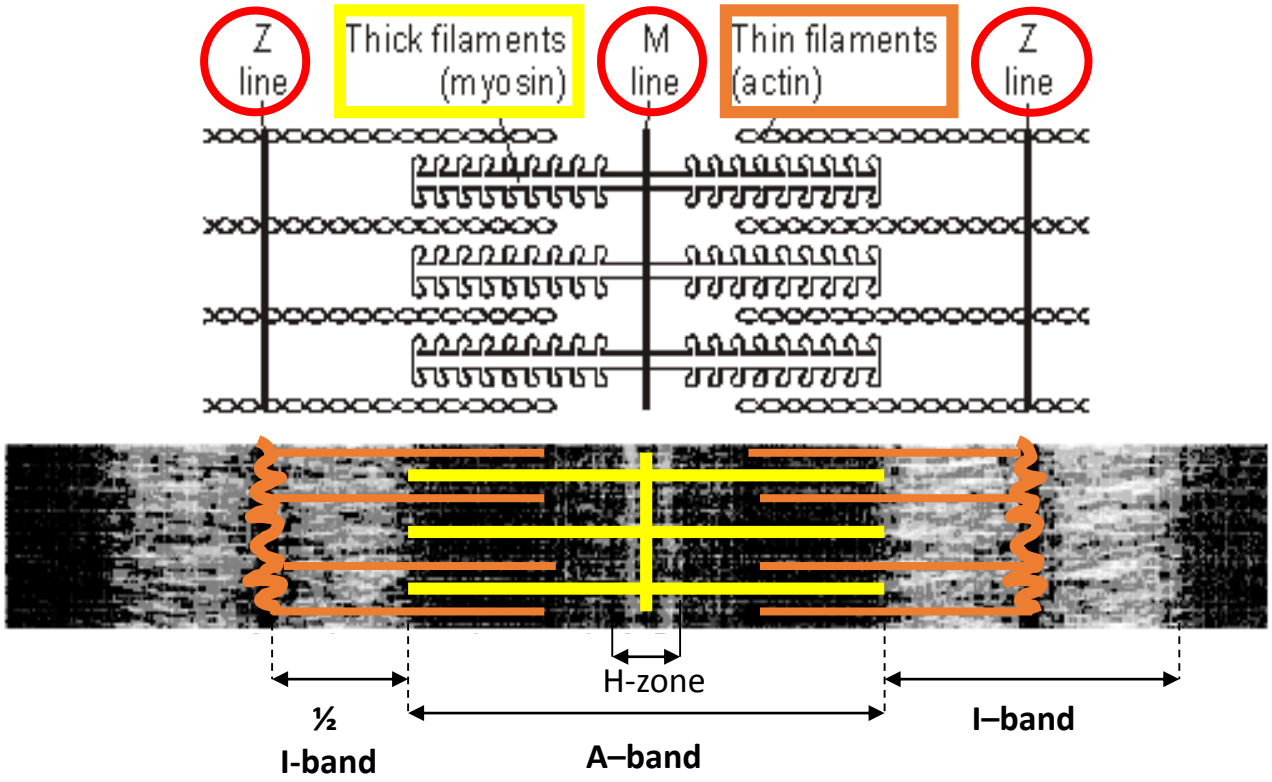




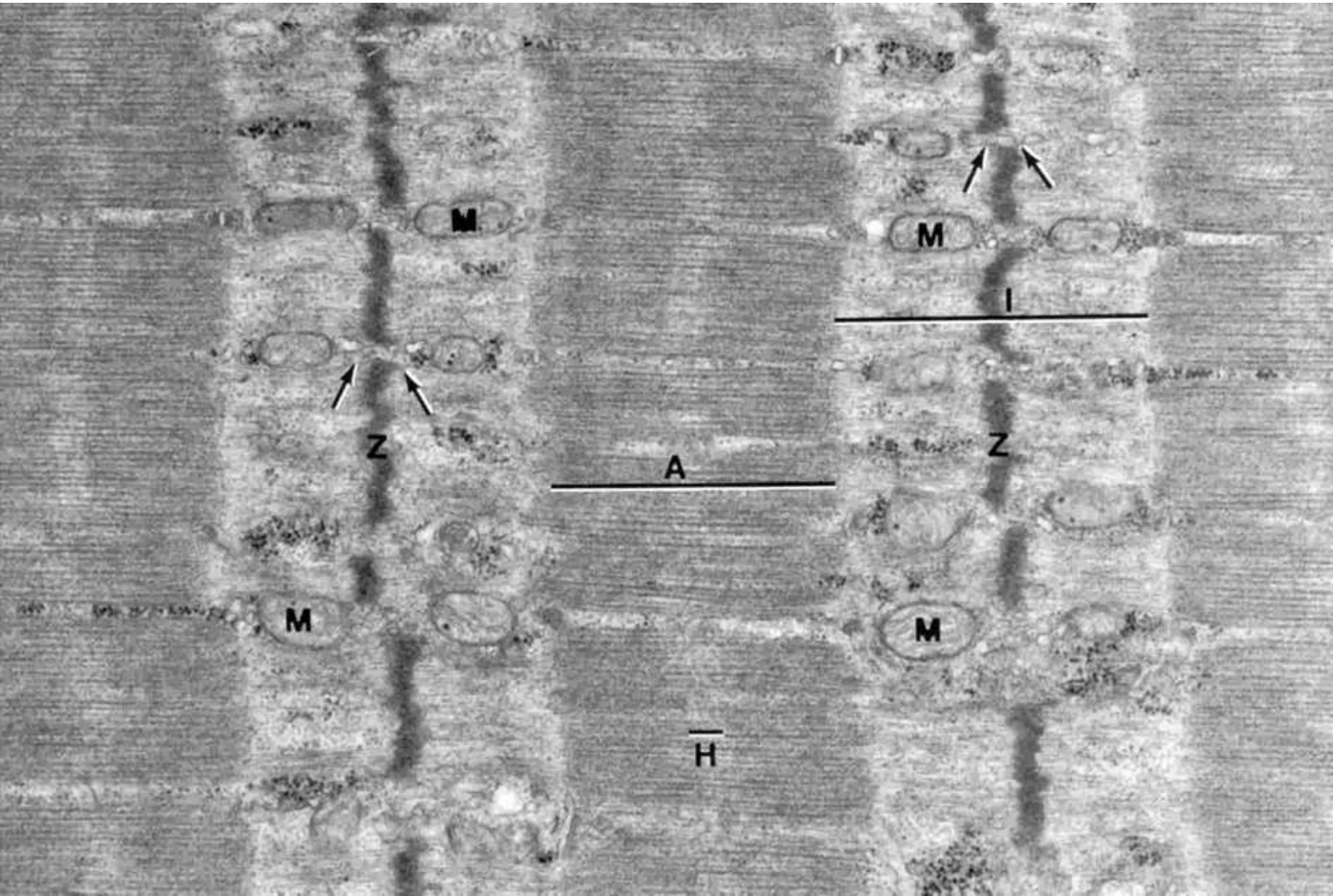
SARCOMERE



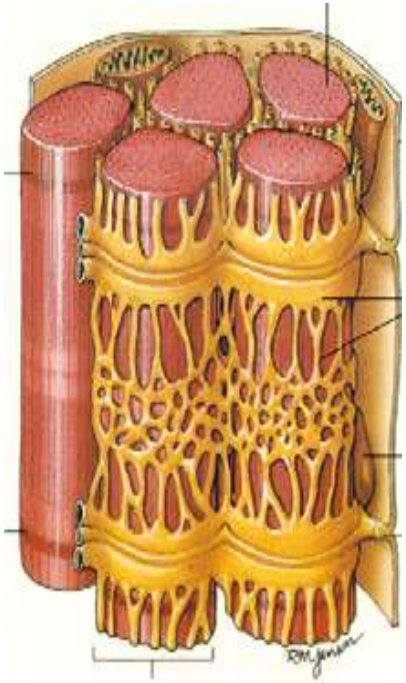
SARCOMERE

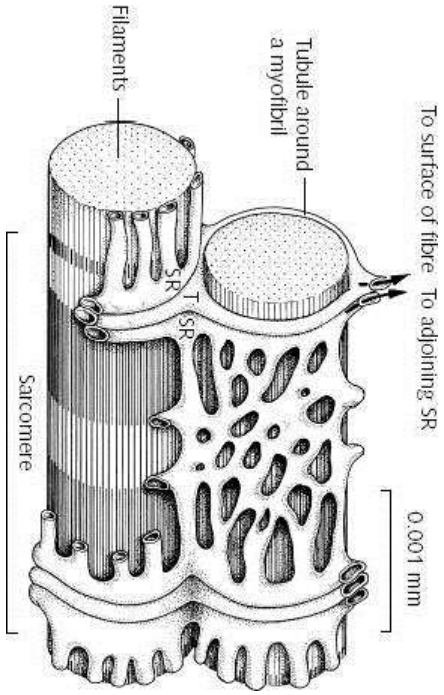

Z line
Thick filaments (myosin)
M line
Thin filaments (actin)
Z line
H-zone
½ I-band
A–band
I–band

SARCOMERE



SARCOPLASMIC RETICULUM



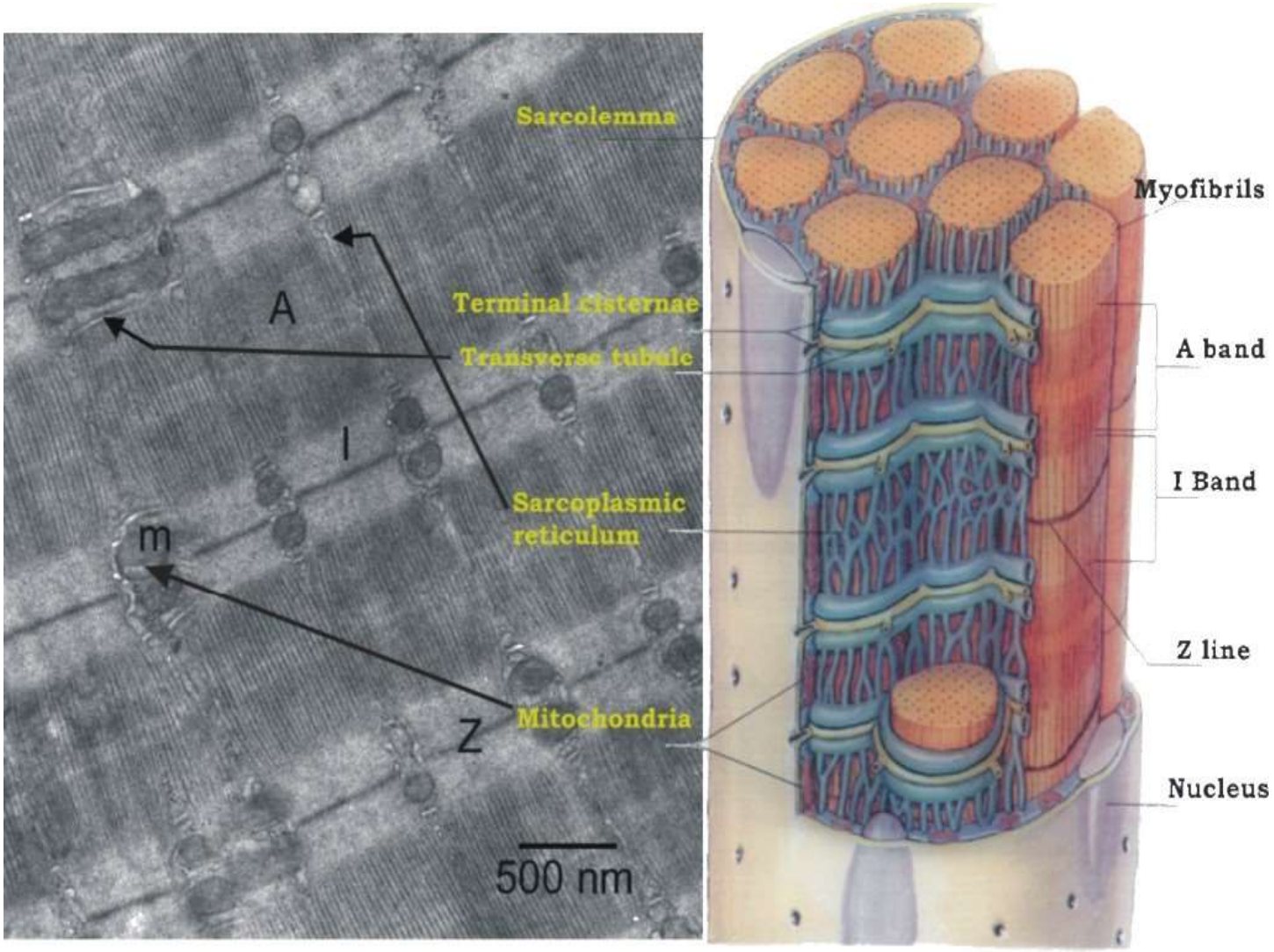


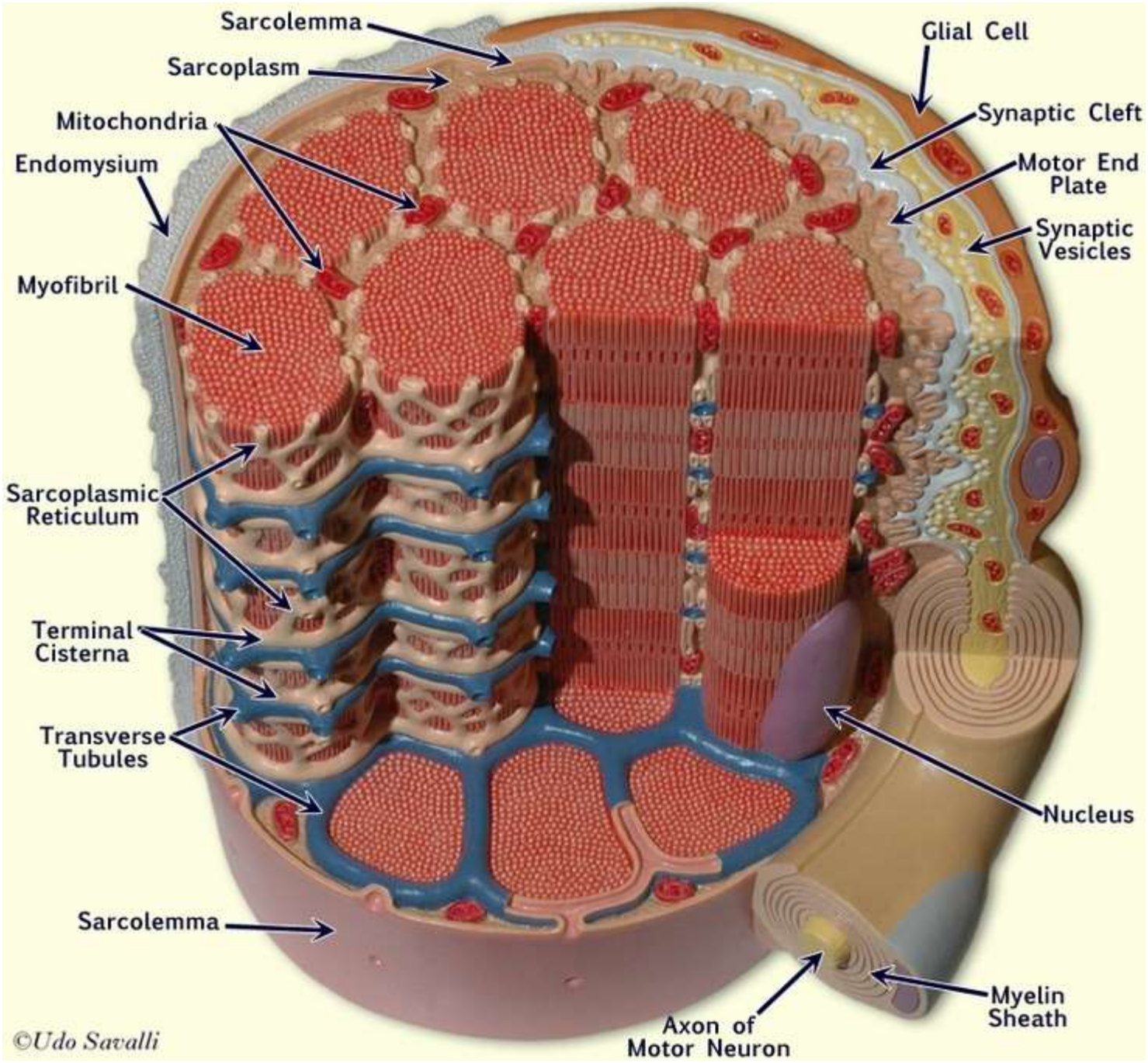
Terminal cisterna
T-tubule
Terminal cisterna
} **TRIAD**

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 sarcoplasm and bring action potential to terminal cisternae change permeability of membrane for Ca^{II+} ions

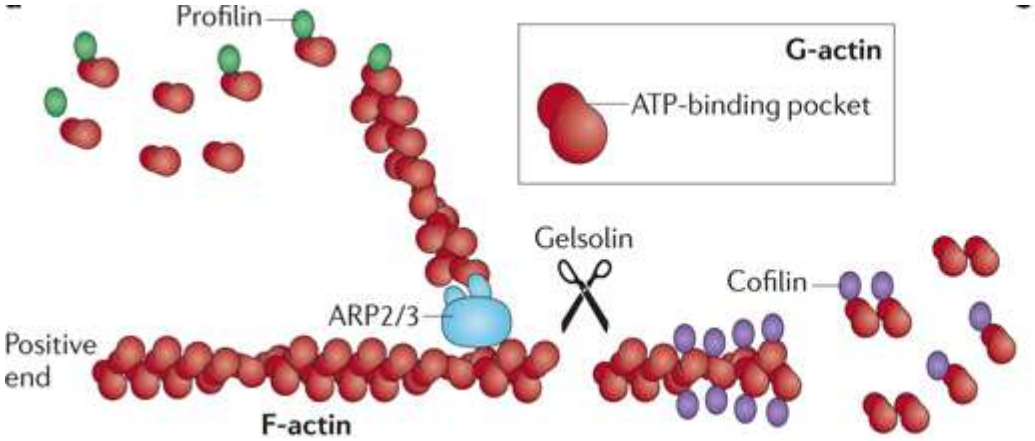
SARCOPLASMIC RETICULUM



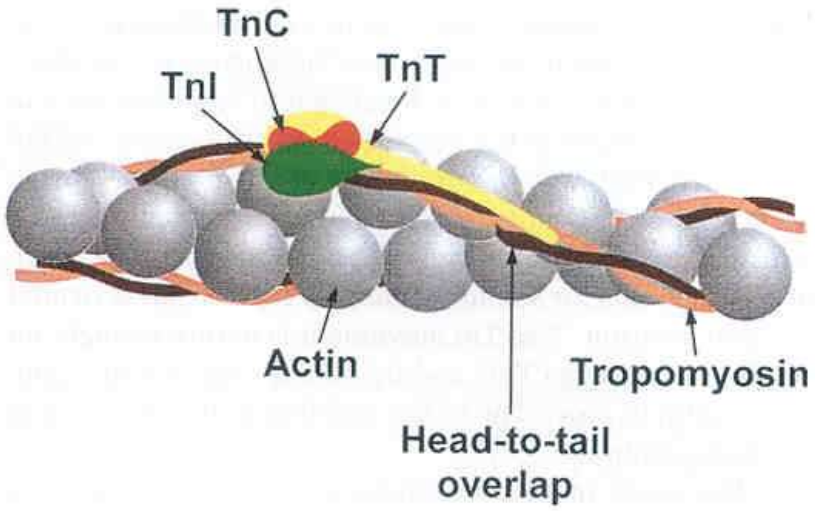

Sarcolemma
Sarcoplasm
Mitochondria
Endomysium
Myofibril
Sarcoplasmic Reticulum
Terminal Cisterna
Transverse Tubules
Sarcolemma
Glial Cell
Synaptic Cleft
Motor End Plate
Synaptic Vesicles
Nucleus
Myelin Sheath
Axon of Motor Neuron
©Udo Savalli

THIN MYOFILAMENTS

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



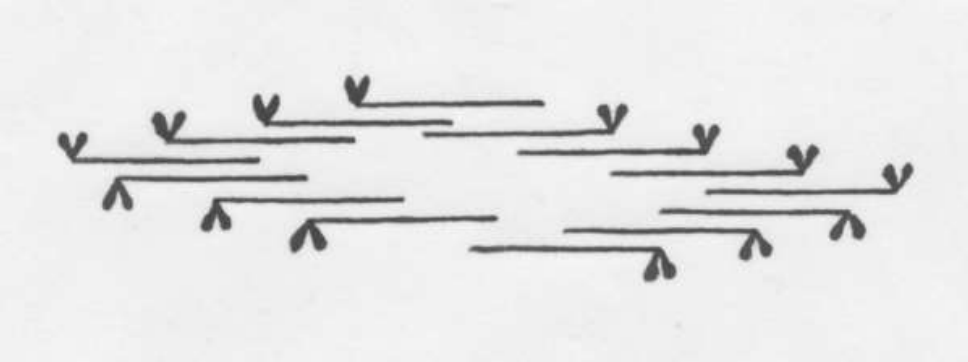
- Tropomyosin – thin double helix in groove of actin double helix, spans 7 monomers of G-actin
- Troponin – complex of 3 globular proteins
  - TnT (Troponin T) – binds tropomyosin
  - TnC (Troponin C) – binds calcium
  - TnI (Troponin I) inhibits interaction between thick and thin filaments

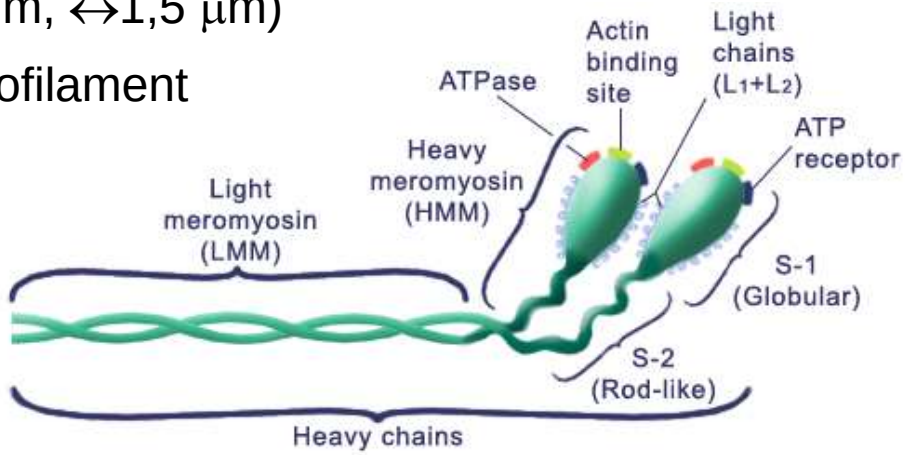


THICK MYOFILAMENTS

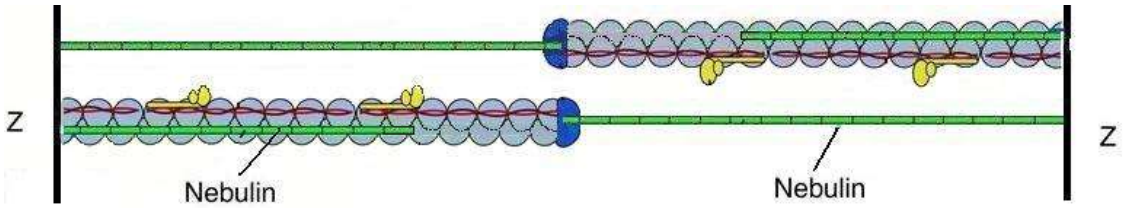
- **Myosin II**

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

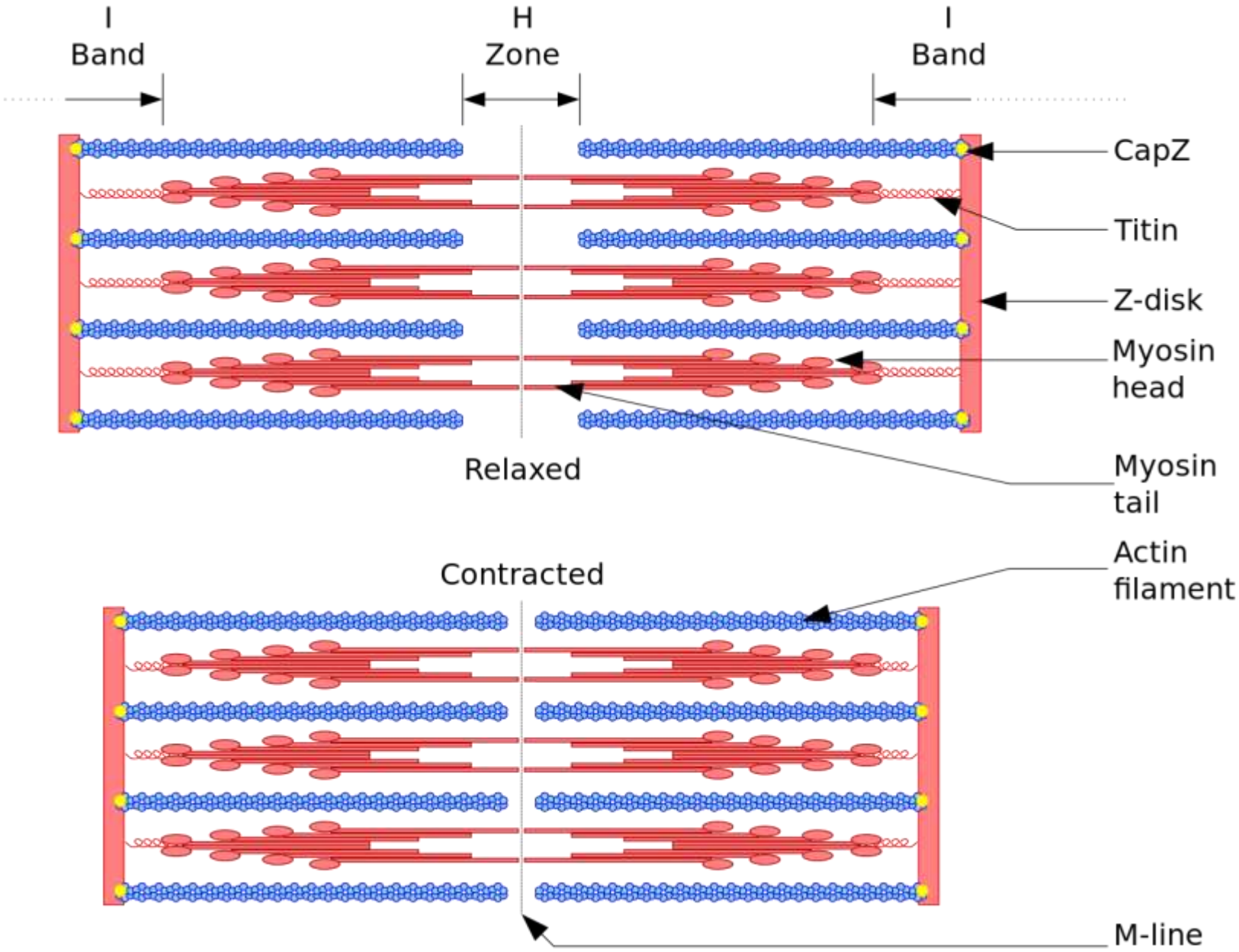




- **Nebulin**
- 600-900kDa
- F-actinu stabilization

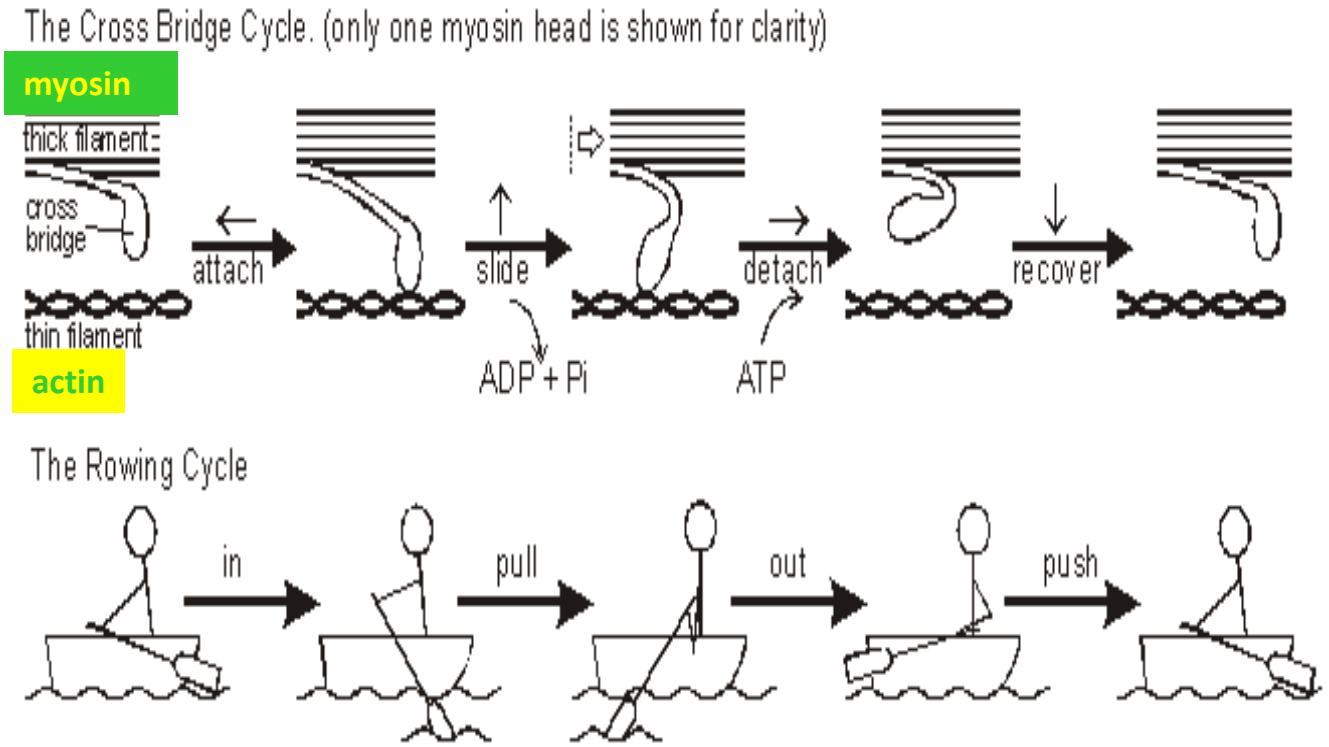


- **Titin**
- >MDa
- Myosin II stabilization


I
Band
H
Zone
I
Band
CapZ
Titin
Z-disk
Myosin
head
Myosin
tail
Relaxed
Contracted
Actin
filament
M-line

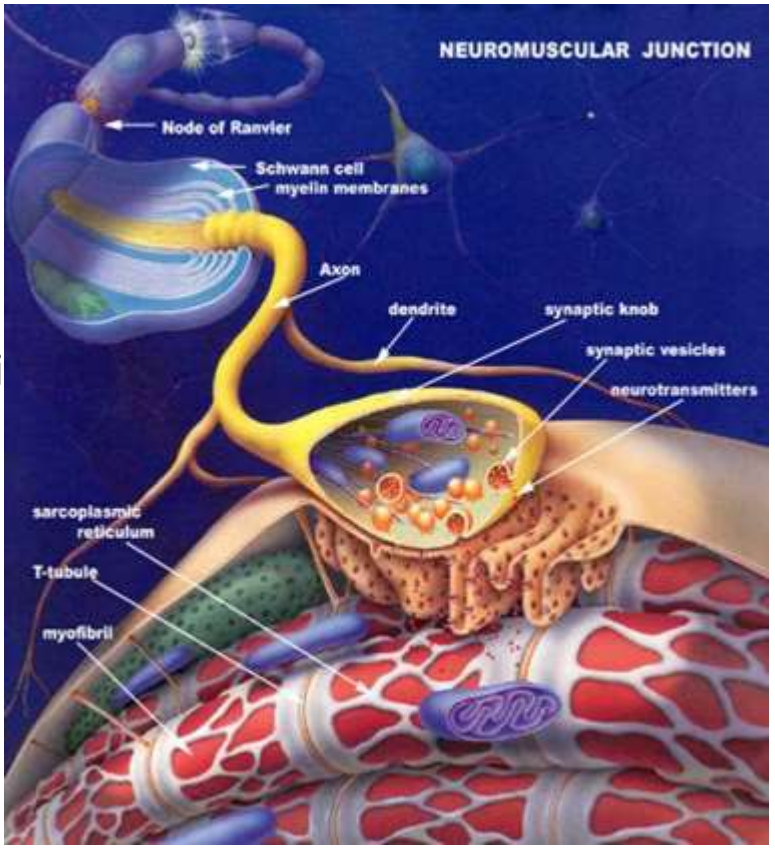
CONTRACTION

- 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



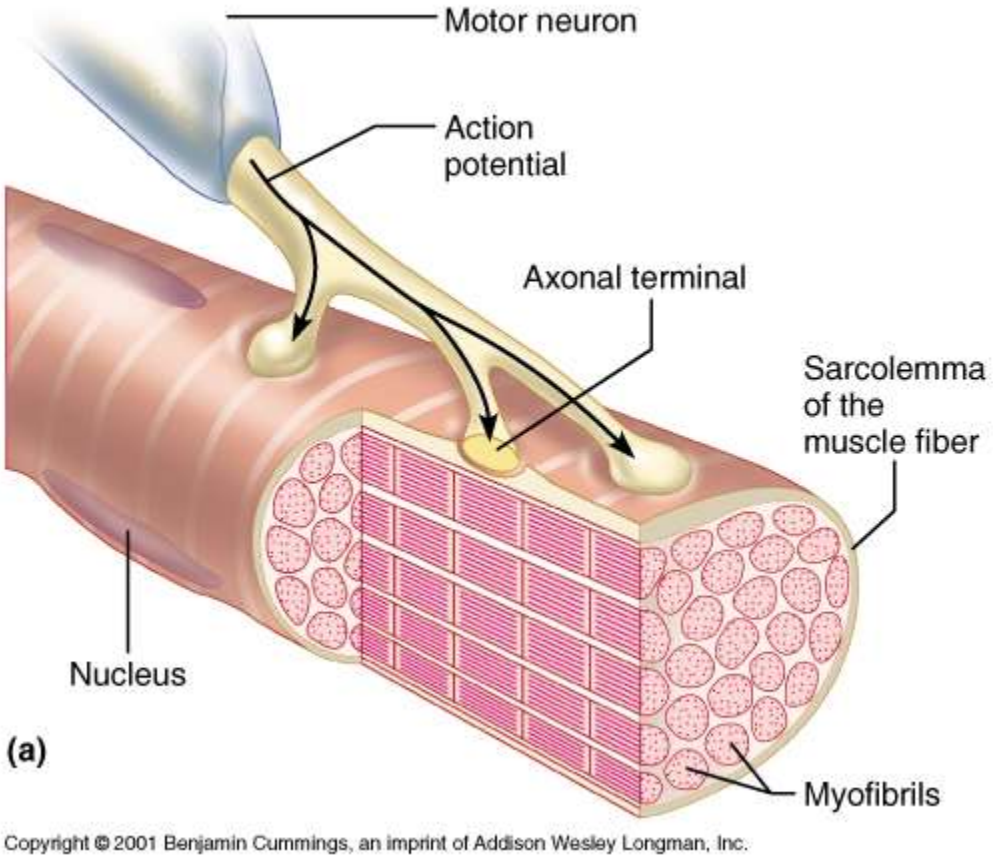
CONTRACTION

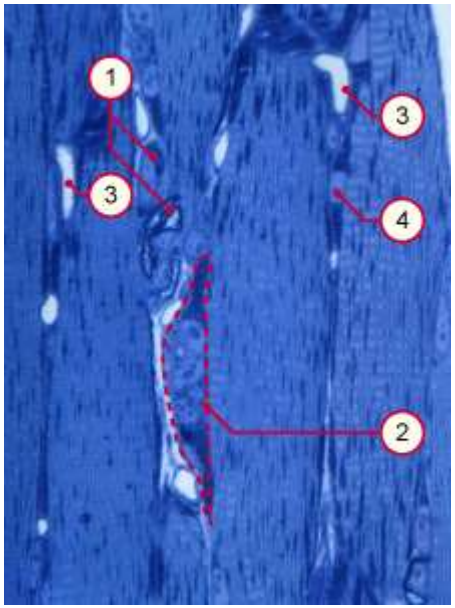
1. Impulse along motor neuron axon
2. Depolarization of presynpatic membrane (Na^+ influx)
3. Synaptic vesicles fuse with presynaptic membrane
4. Acetylcholine exocyted to synaptic cleft
5. Acetylcholine diffuses over synaptic cleft
6. Acetylcholine binds to receptors in postsynaptic membrane
7. Depolarization of presynaptic 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 removed from actin-myosin binding si
15. Globular parts of myosin bind to actin
16. ATPase in globular parts of myosin activated
17. Energy generated from ATP$\rightarrow$ADP + Pi
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 contracted
22. Muscle fiber contracted



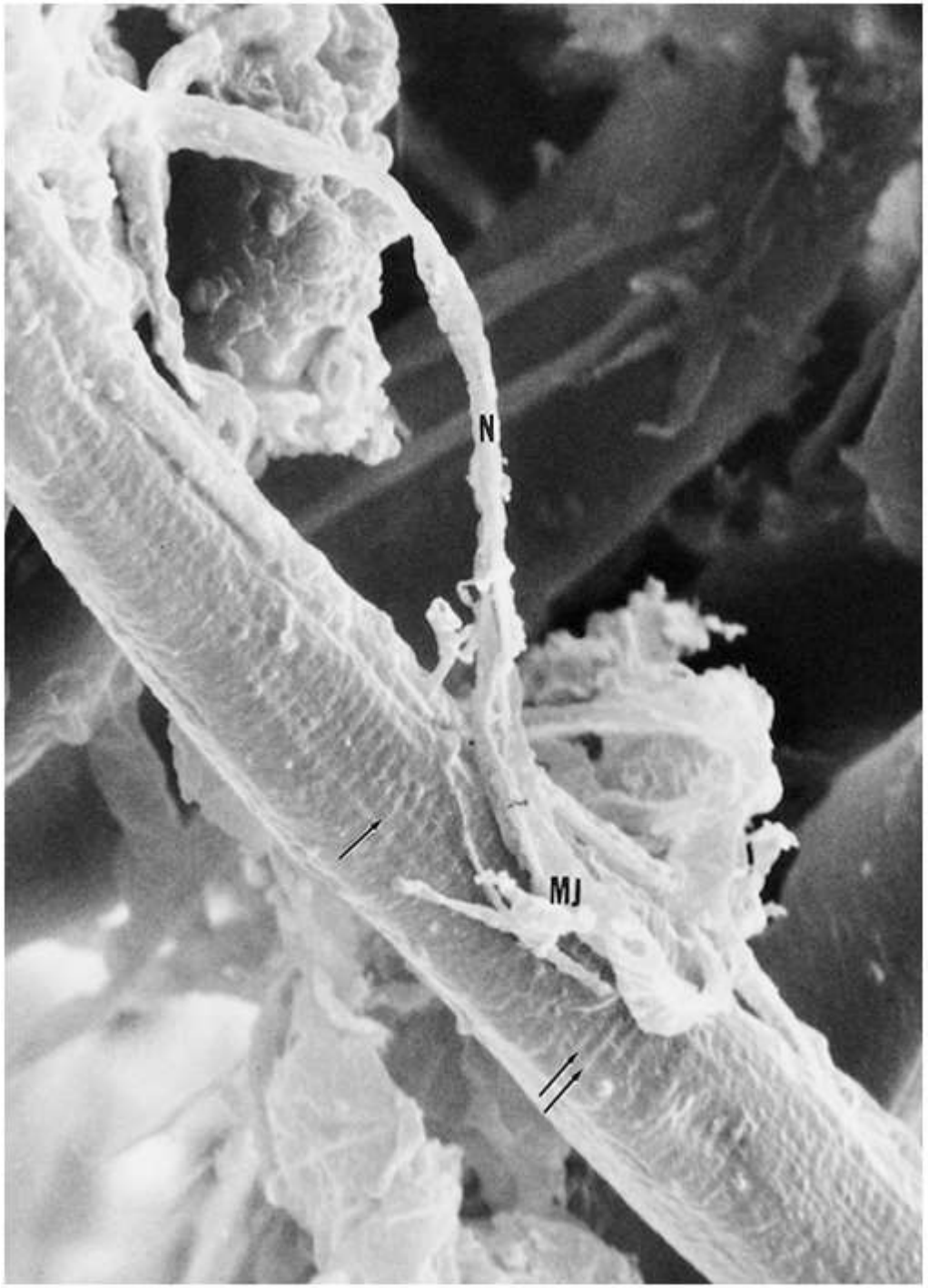
http://highered.mheducation.com/sites/0072495855/student_view0/chapter10/animation__breakdown_of_atp_and_cross-bridge_movement_during_muscle_contraction.html

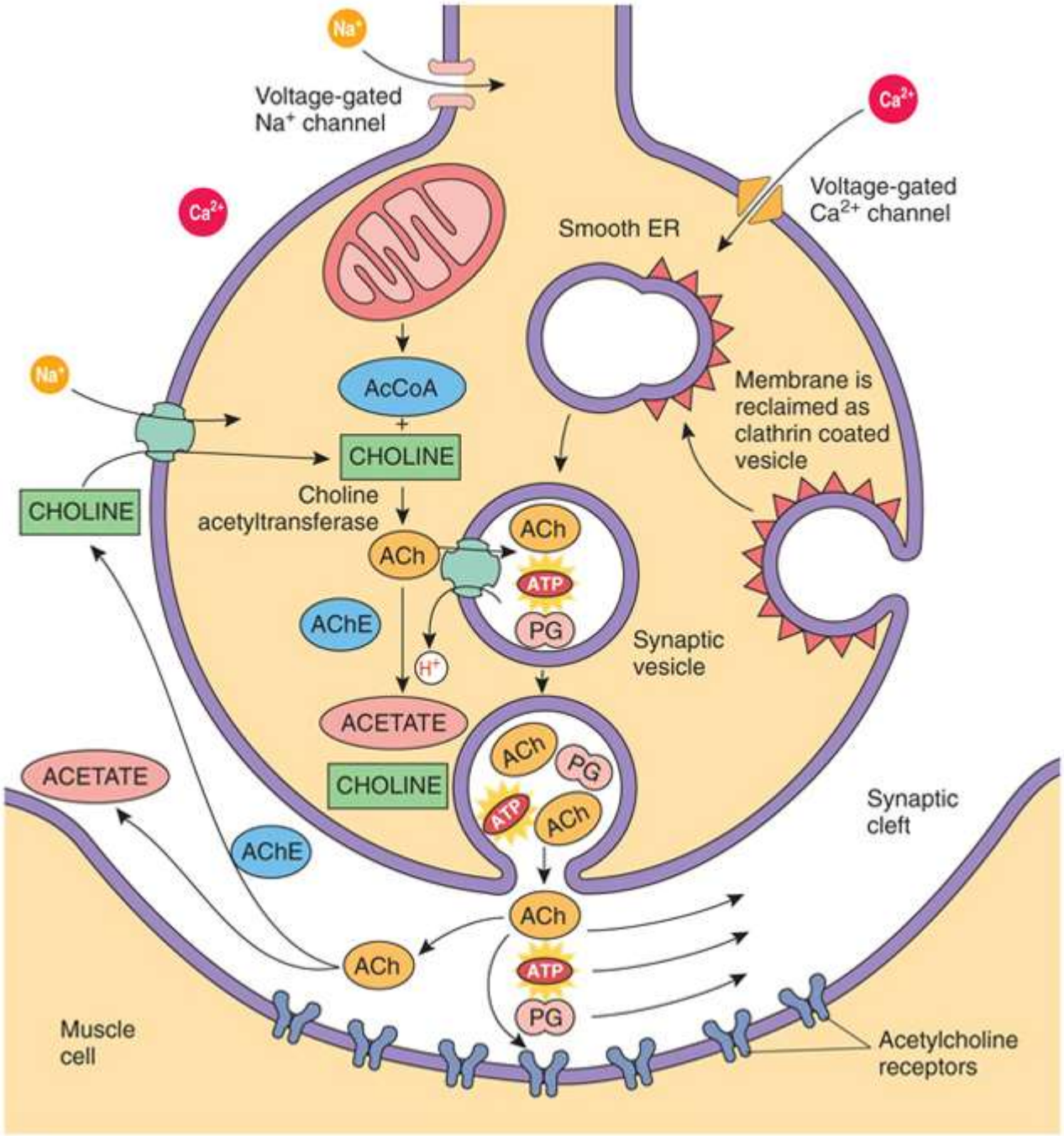
NEUROMUSCULAR JUNCTION



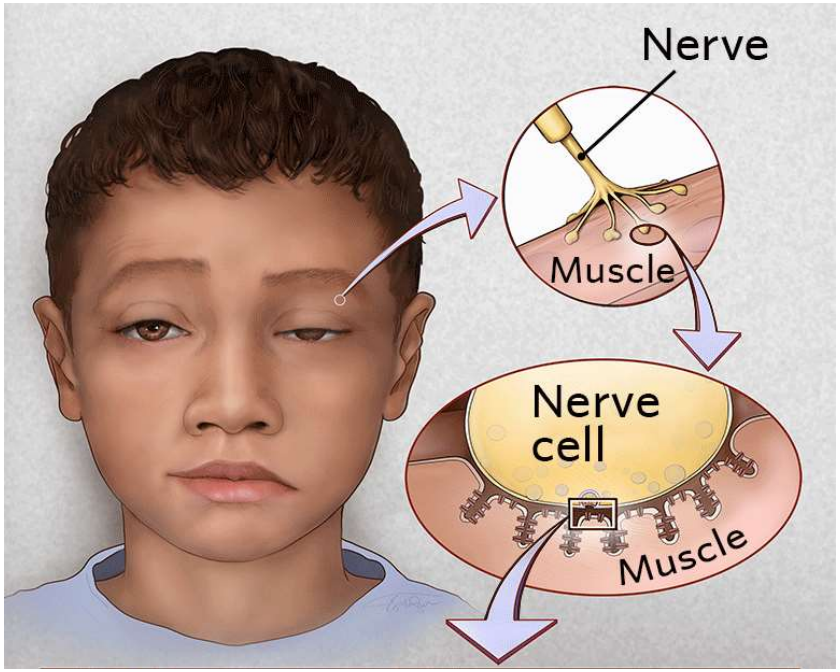


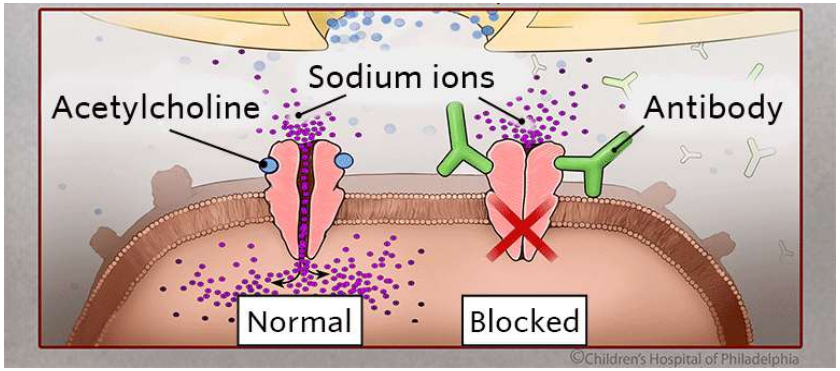
1 Myelinated axons
2 Neuromuscular junction
3 Capillaries
4 Muscle fiber nucleus


N
MJ

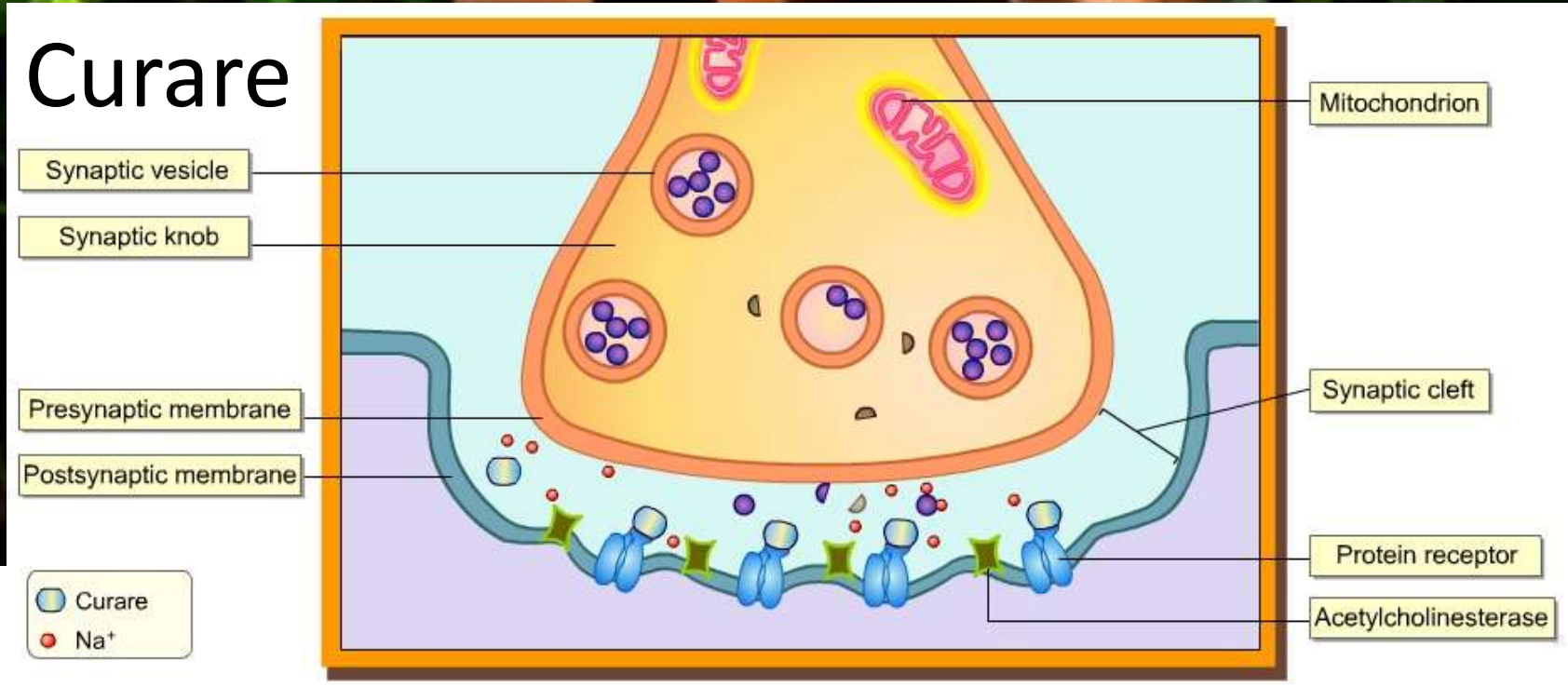

Na+
Voltage-gated
Na+ channel
Ca2+
Voltage-gated
Ca2+ channel
Ca2+
Smooth ER
Na+
AcCoA
+
CHOLINE
Membrane is
reclaimed as
clathrin coated
vesicle
CHOLINE
Choline
acetyltransferase
ACh
ACh
ATP
PG
AChE
H+
Synaptic
vesicle
ACETATE
ACh
PG
CHOLINE
ATP
ACh
ACETATE
Synaptic
cleft
AChE
ACh
ACh
ATP
PG
Muscle
cell
Acetylcholine
receptors

MYASTHENIA GRAVIS



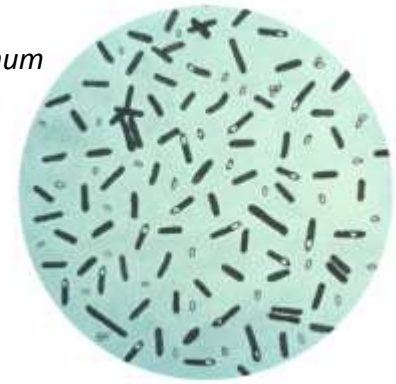


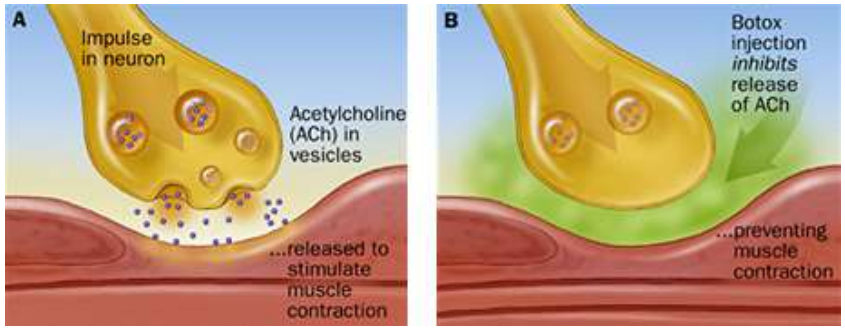
Curare


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

Botulotoxin

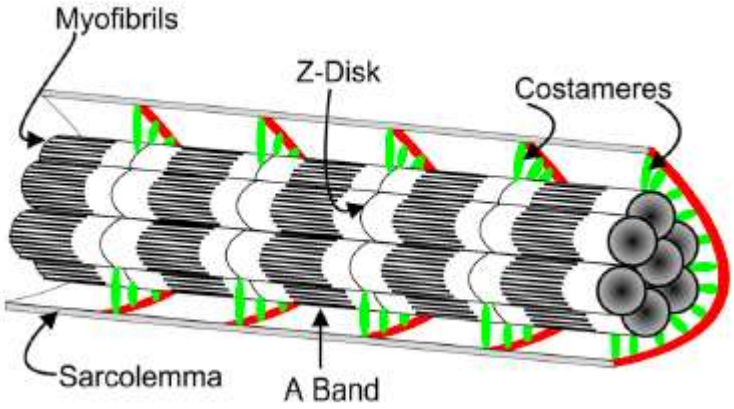
Clostridium botulinum

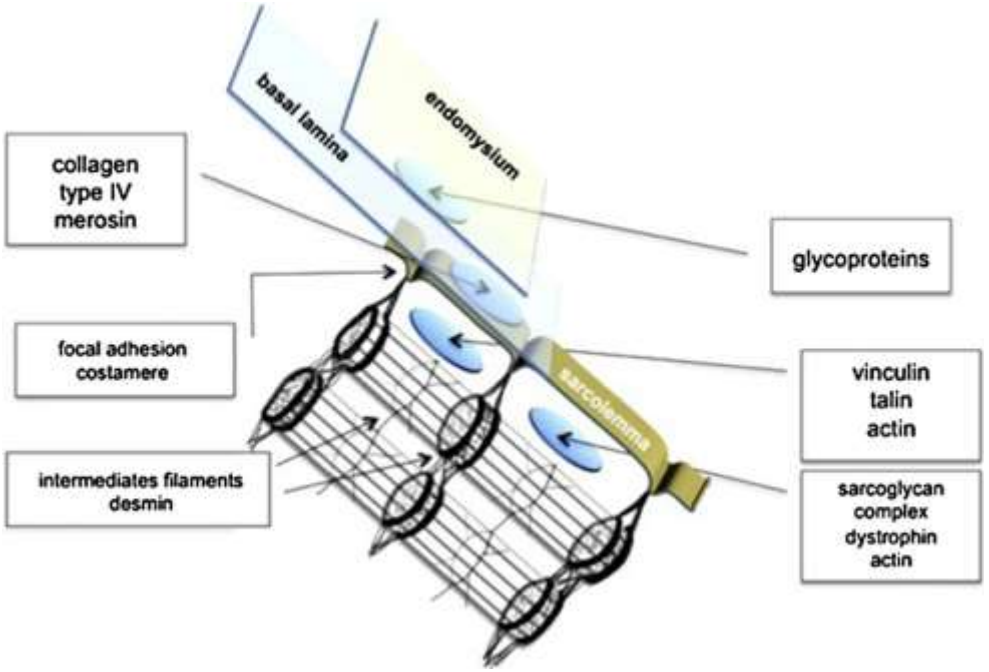




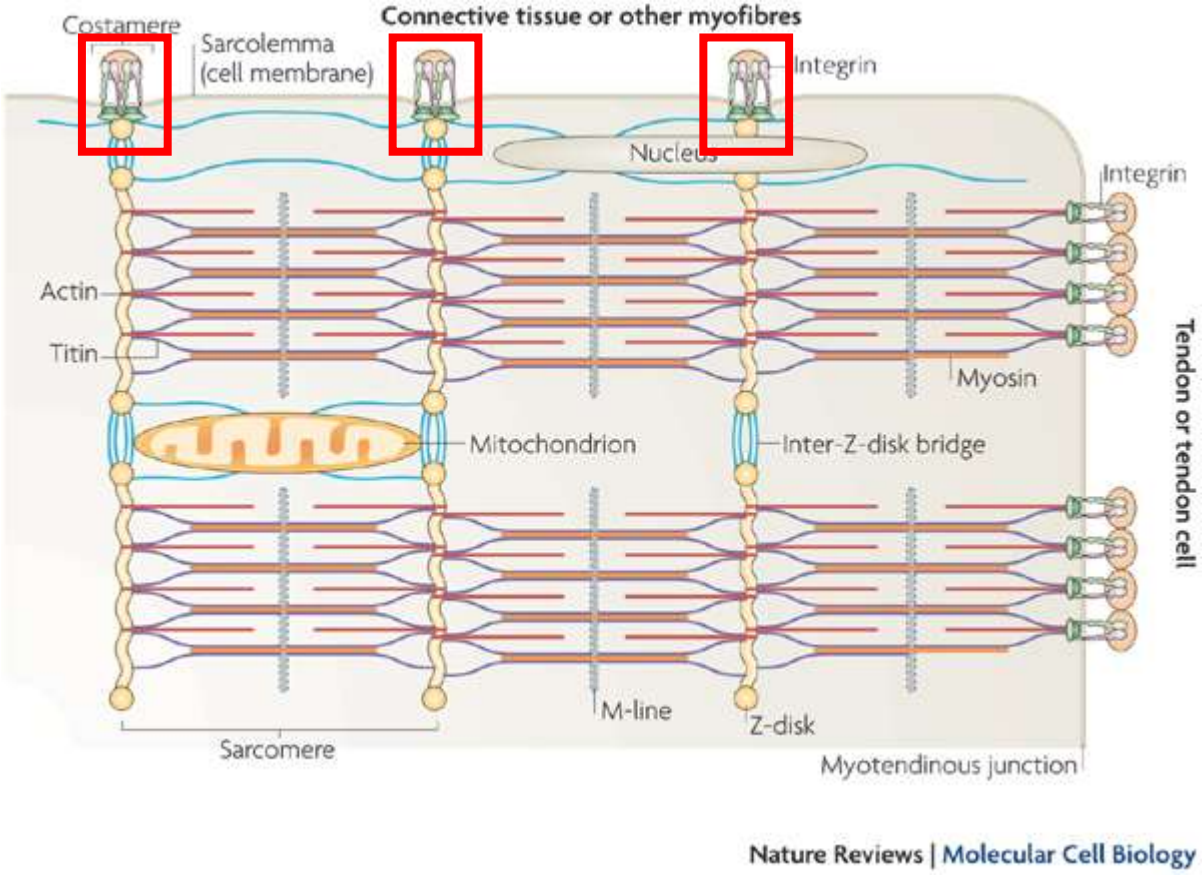
COSTAMERES

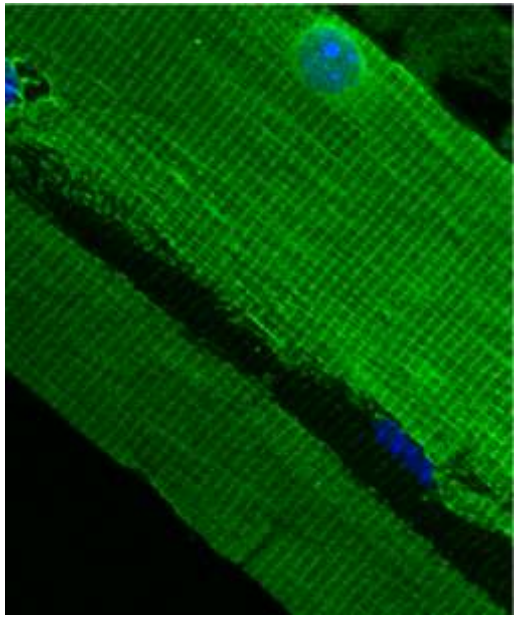
- Structural components linking myofibrils to sarcolemma
- Circumferential alignment
- **dystrophin-associated glycoprotein (DAG) complex**
  - links internal cytoskelet to ECM
  - Integrity of muscle fiber



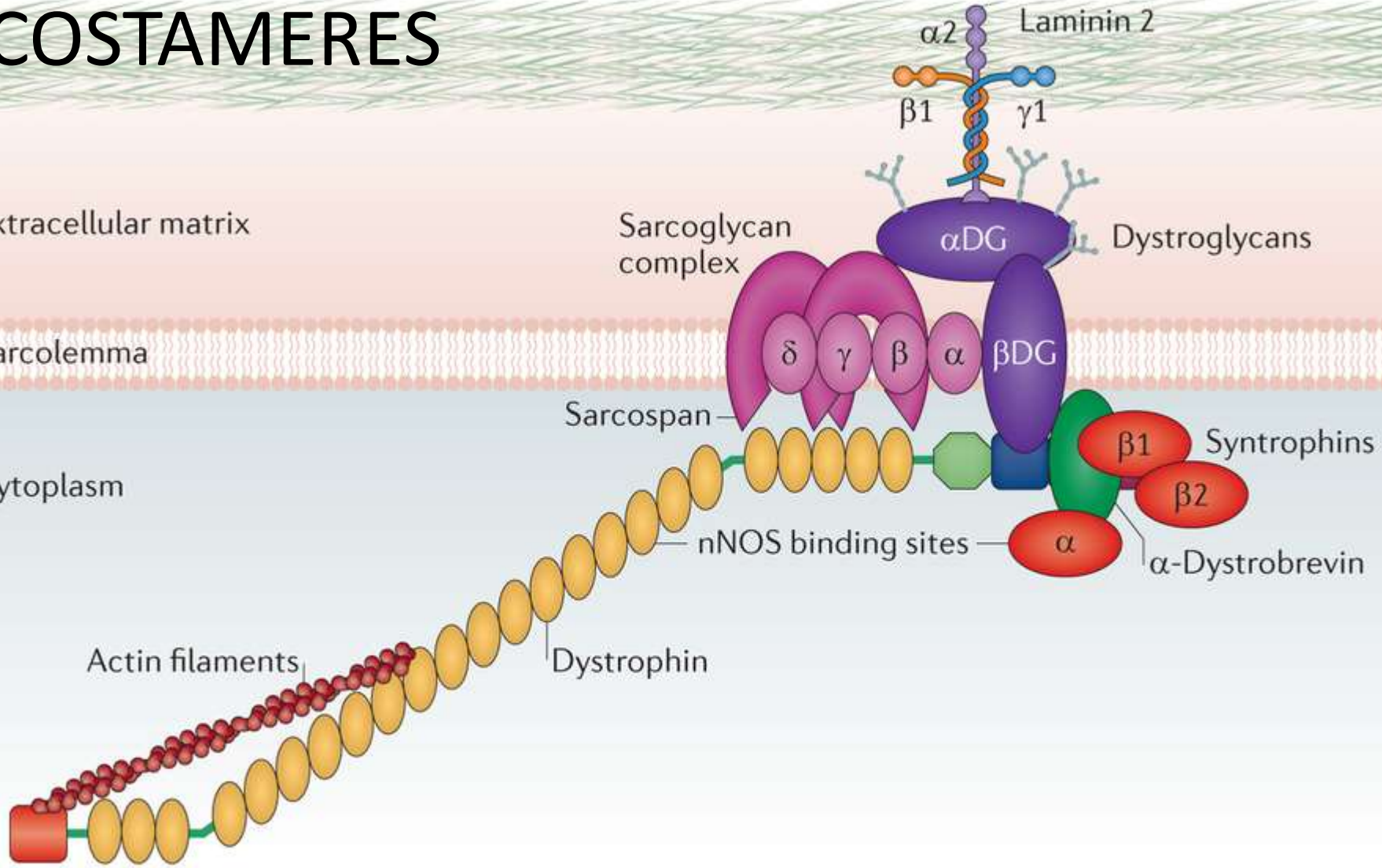


COSTAMERES


Costamere
Sarcolemma
(cell membrane)
Connective tissue or other myofibres
Integrin
Nucleus
Integrin
Actin
Titin
Myosin
Mitochondrion
Inter-Z-disk bridge
Tendon or tendon cell
M-line
Z-disk
Sarcomere
Myotendinous junction
Nature Reviews | Molecular Cell Biology

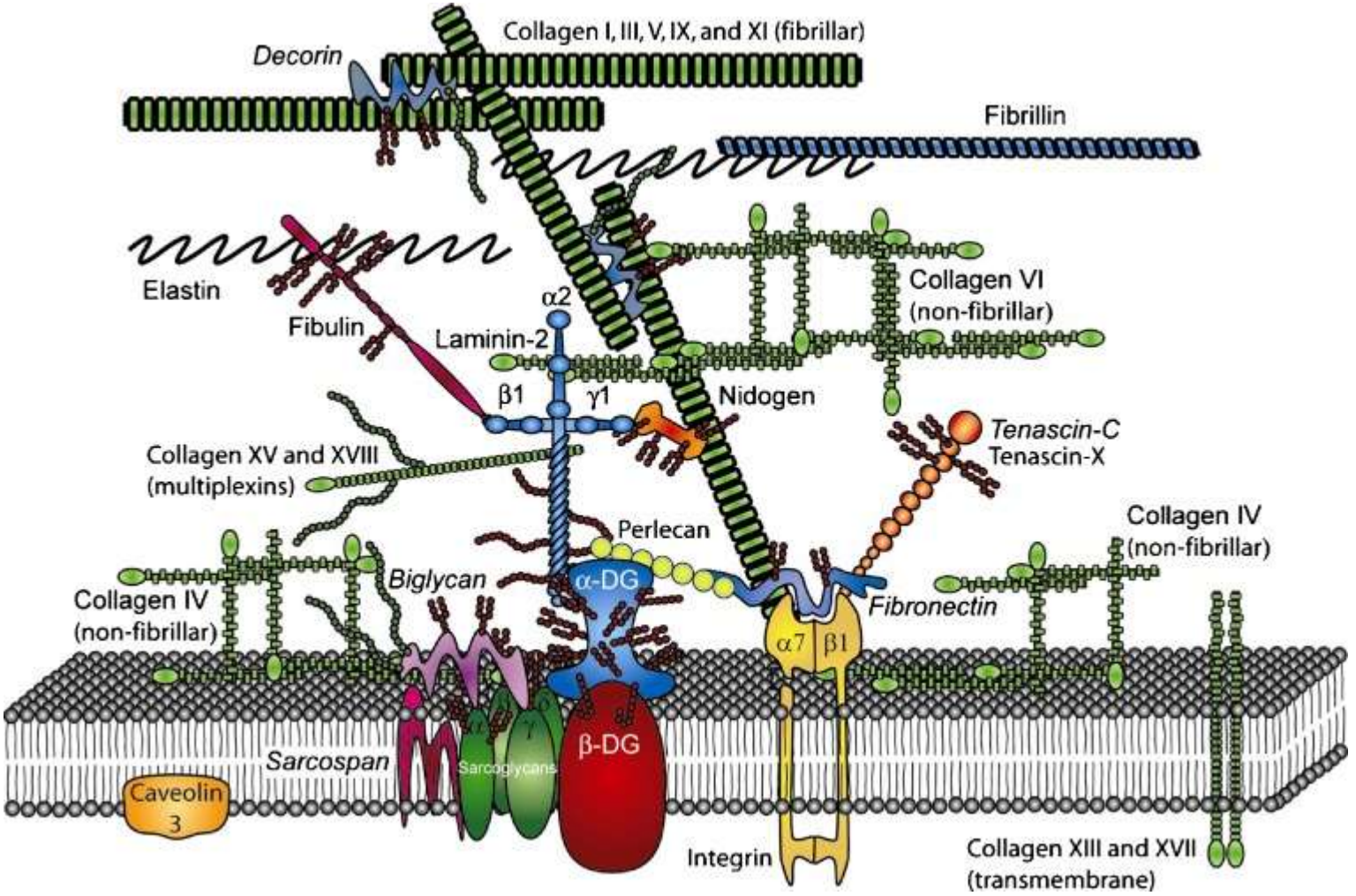


COSTAMERES

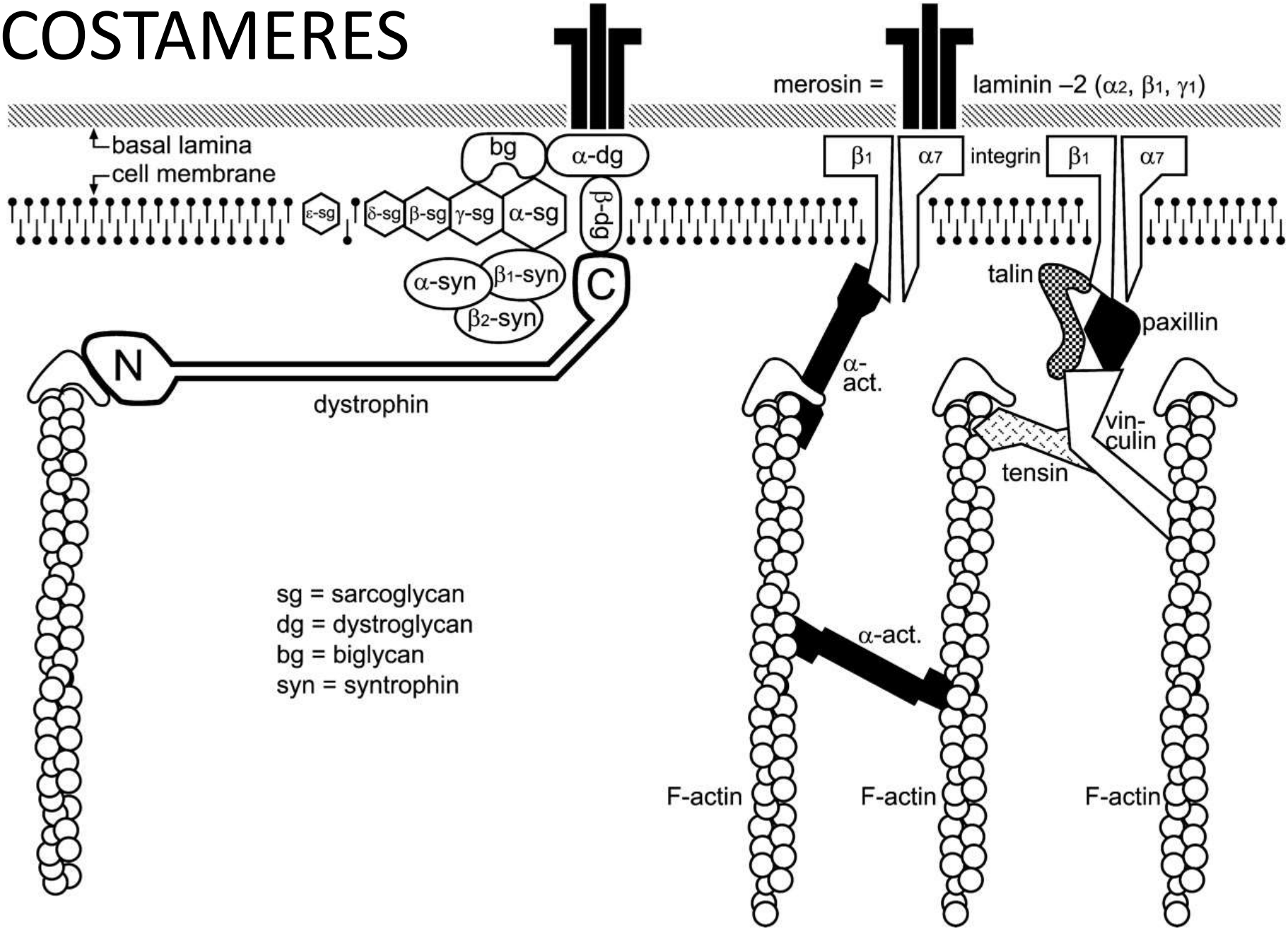


Nature Reviews | Genetics

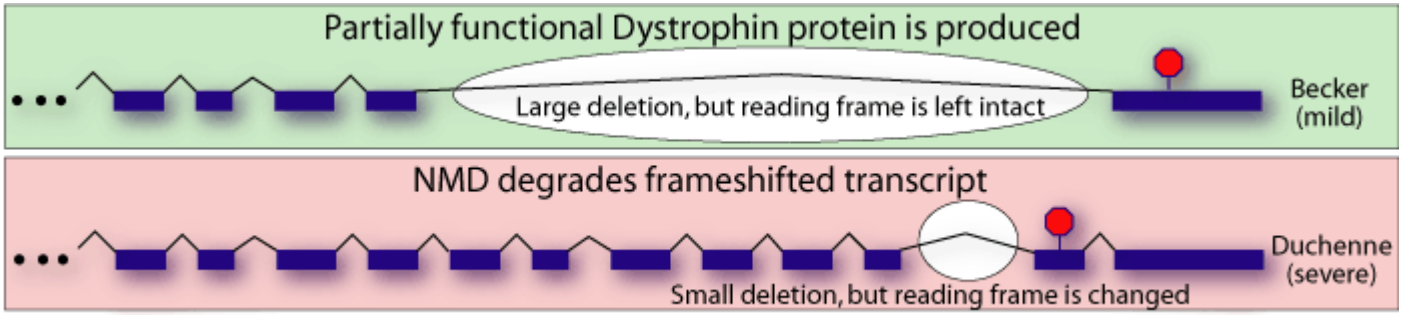
COSTAMERES

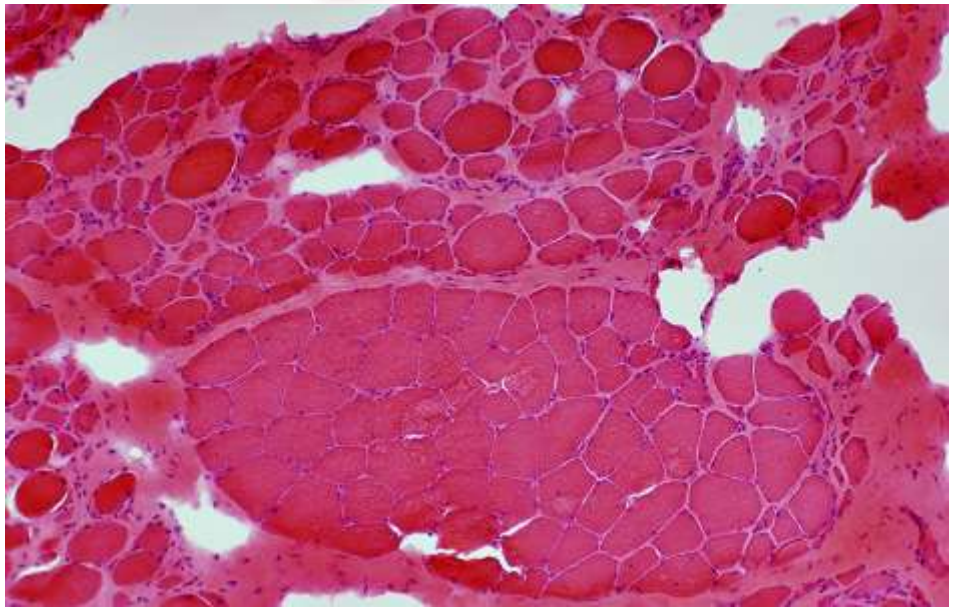

Collagen I, III, V, IX, and XI (fibrillar)
Decorin
Fibrillin
Elastin
Fibulin
α2
Laminin-2
β1
γ1
Nidogen
Collagen VI
(non-fibrillar)
Tenascin-C
Tenascin-X
Collagen XV and XVIII
(multiplexins)
Perlecan
Collagen IV
(non-fibrillar)
Biglycan
α-DG
Collagen IV
(non-fibrillar)
Fibronectin
α7
β1
Sarcospan
Sarcoglycans
β-DG
Caveolin
3
Integrin
Collagen XIII and XVII
(transmembrane)

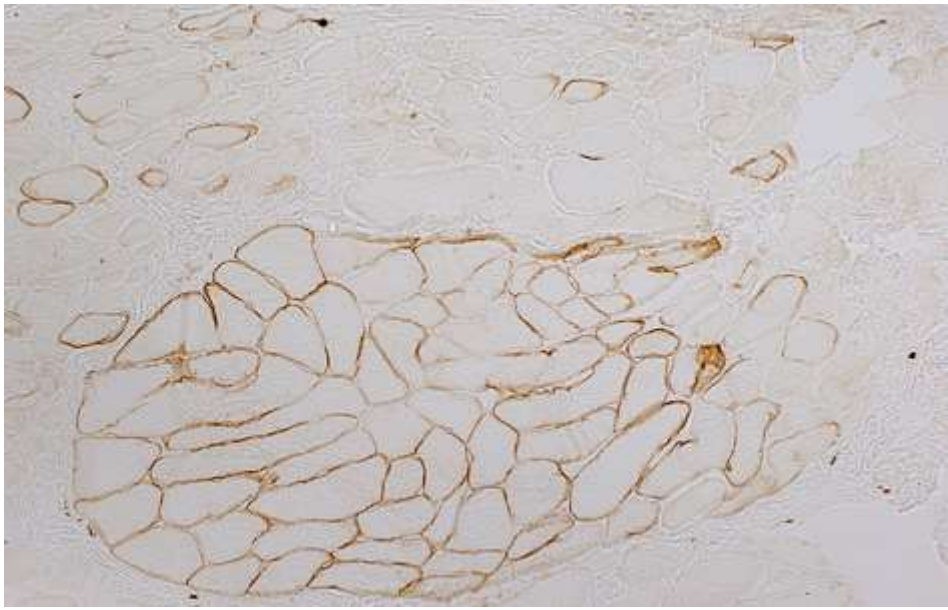
COSTAMERES

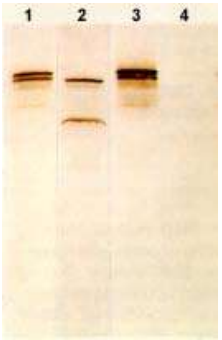

merosin =
laminin –2 (α2, β1, γ1)
basal lamina
cell membrane
bg
α-dg
β-dg
ε-sg
δ-sg
β-sg
γ-sg
α-sg
α-syn
β1-syn
β2-syn
C
N
dystrophin
β1
α7
integrin
β1
α7
talin
paxillin
α-
act.
vin-
culin
tensin
α-act.
F-actin
F-actin
F-actin
sg = sarcoglycan
dg = dystroglycan
bg = biglycan
syn = syntrophin

DUCHENNE MUSCULAR DYSTROPHY





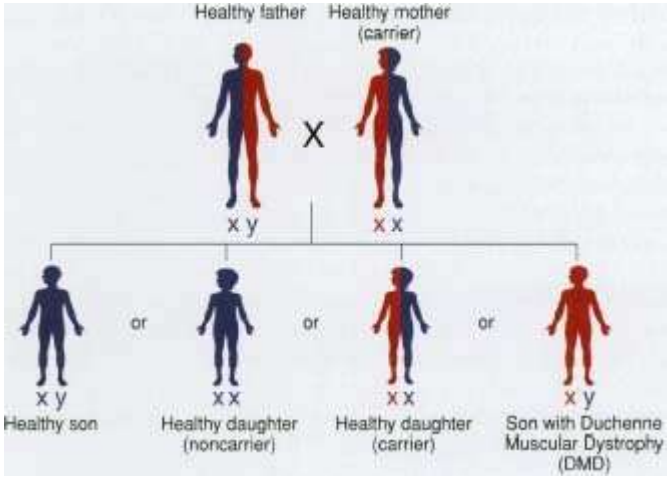


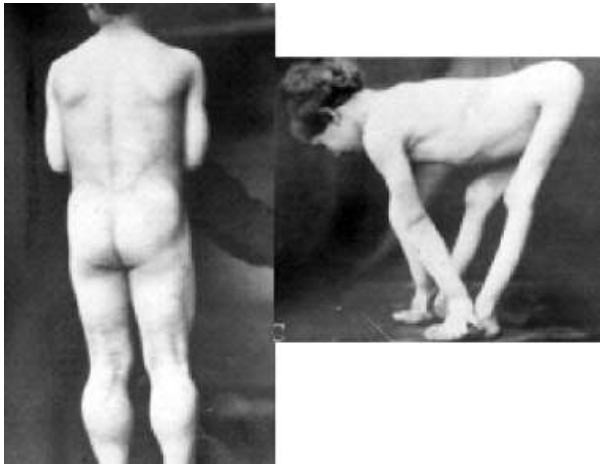


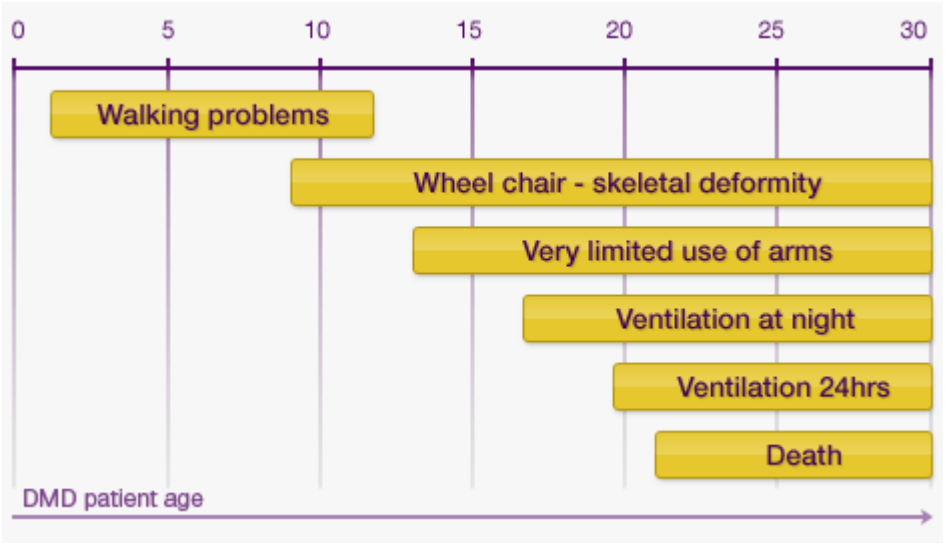
Lane 1: Becker dystrophy; Dystrophin has reduced abundance but normal size.
Lane 2: Becker dystrophy; Dystrophin has reduced size and abundance.
Lane 3: Normal; Dystrophin has normal size and amount.
Lane 4: Duchenne dystrophy; Almost no protein is present.

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

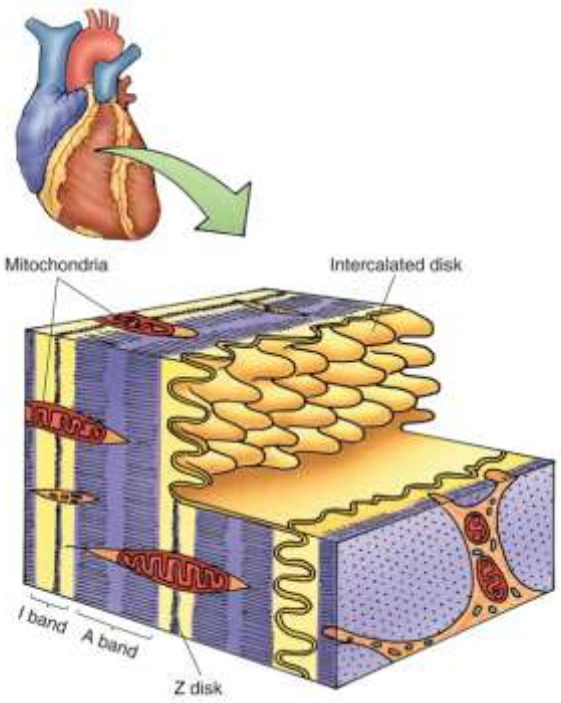
DUCHENNE MUSCULAR DYSTROPHY



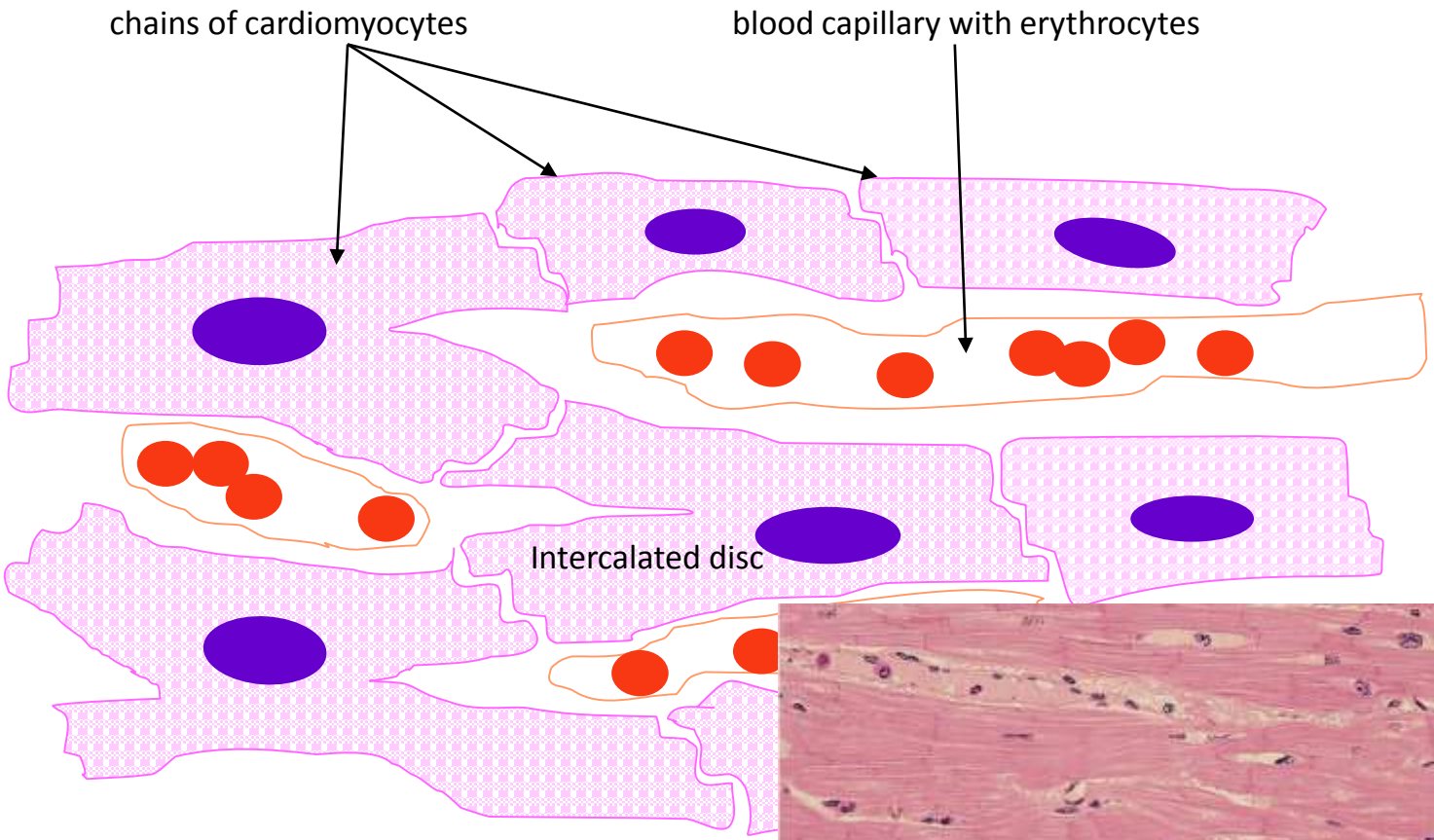


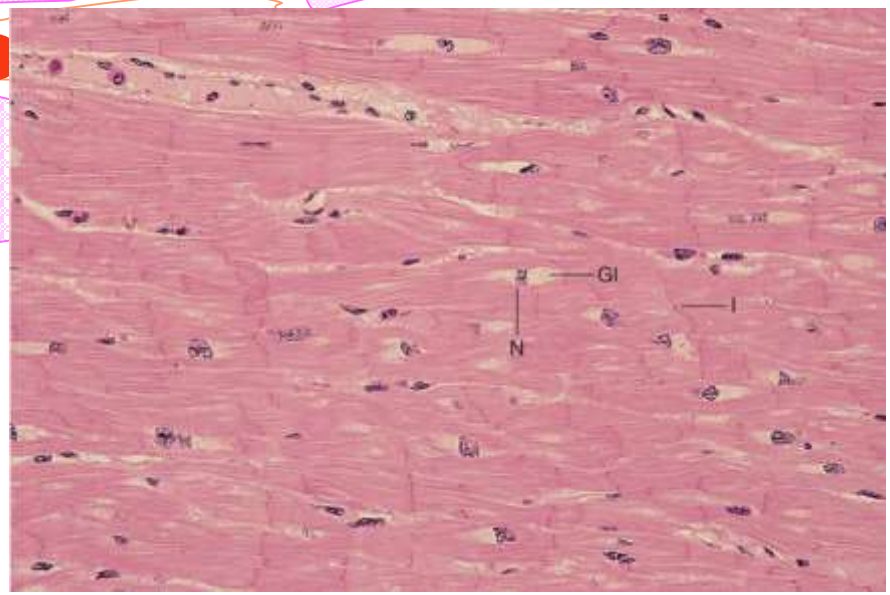


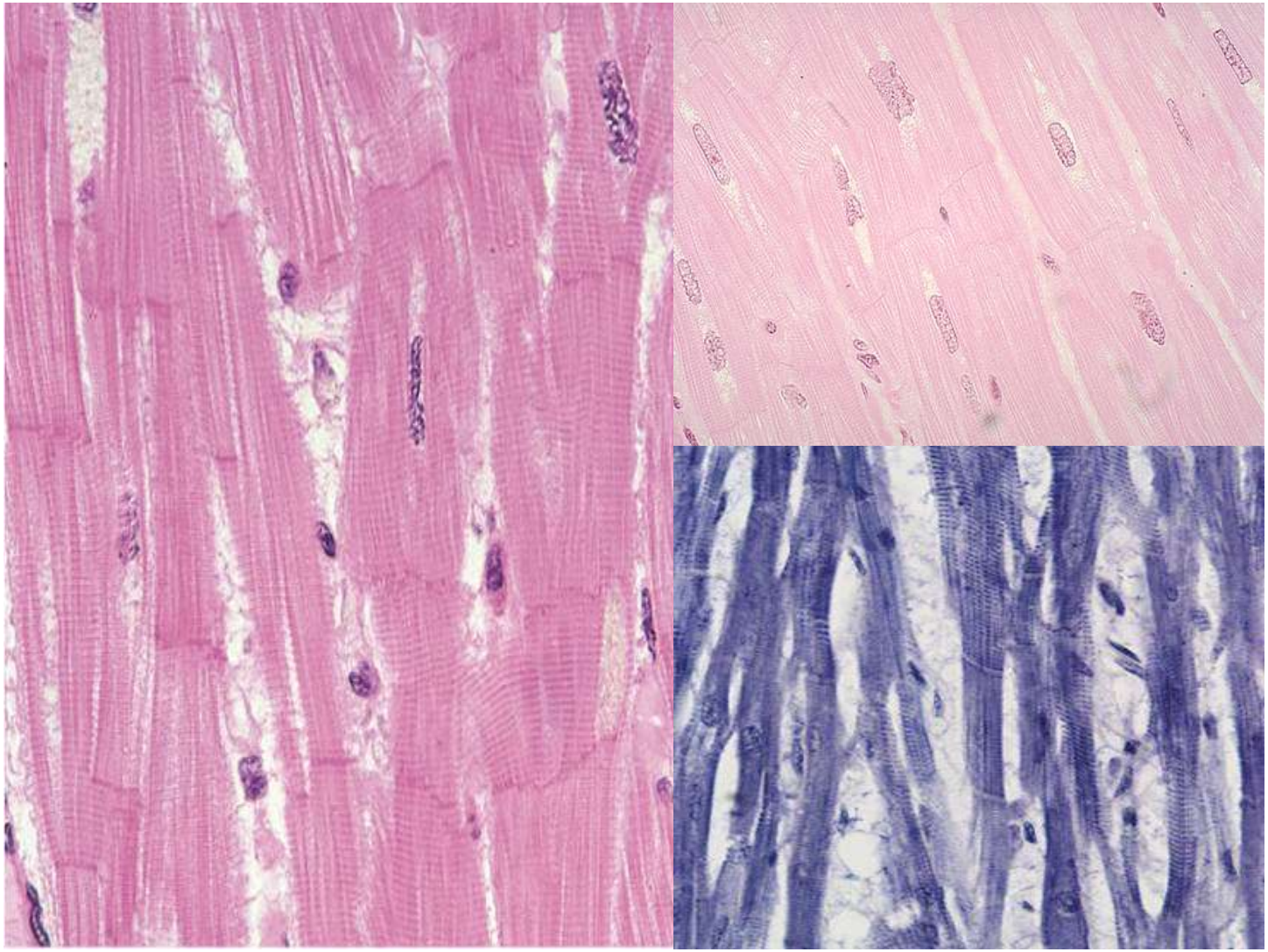
HISTOLOGY OF CARDIAC MUSCLE TISSUE

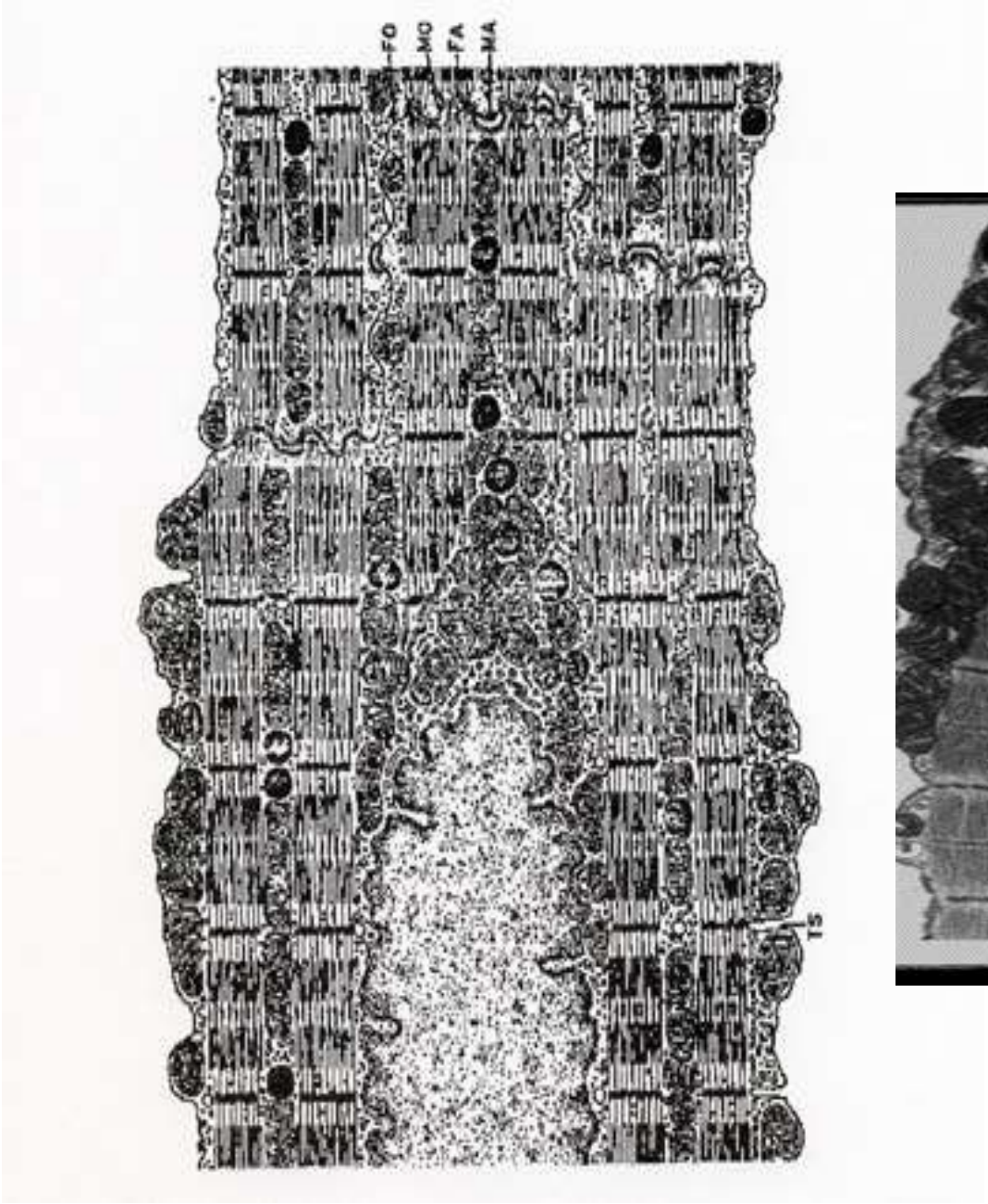


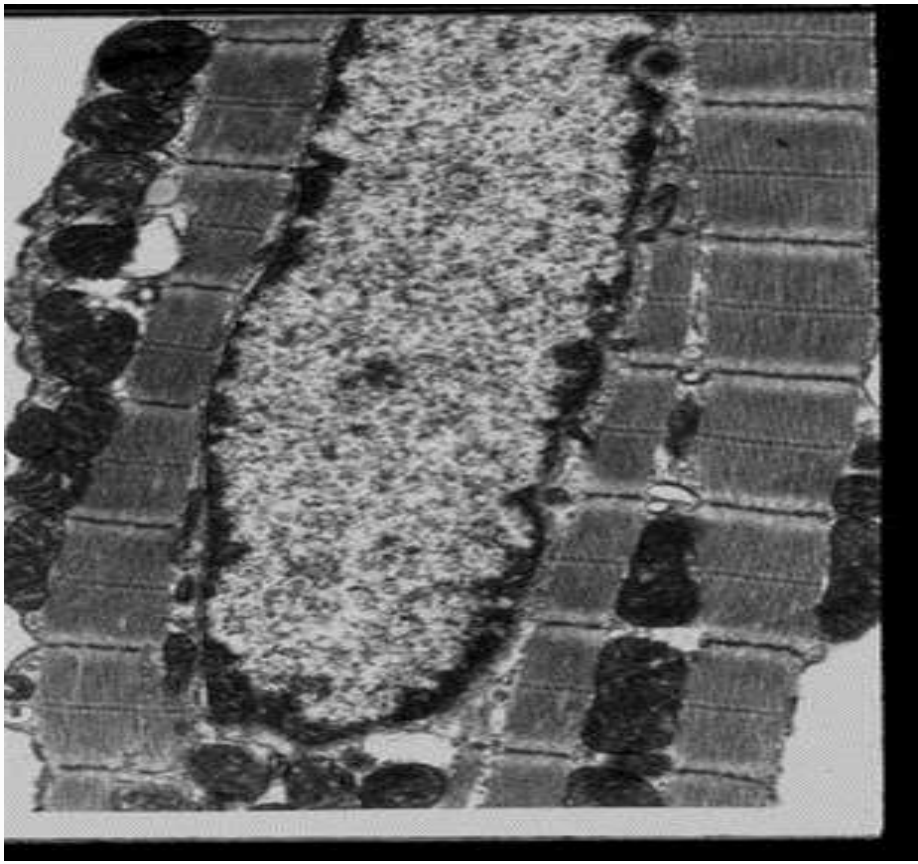
- made up of long branched fiber (cells) – **cardiomyocytes**,
- cardiomyocytes are cylindrical cells, branched on one or both ends (Y, X shaped cells),
- sarcoplasm: single nucleus in the center of cell, striated myofibrils, numerous mitochondria,
- cells are attached to one another by end-to-end junctions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


chains of cardiomyocytes
blood capillary with erythrocytes
Intercalated disc


GI
I
N

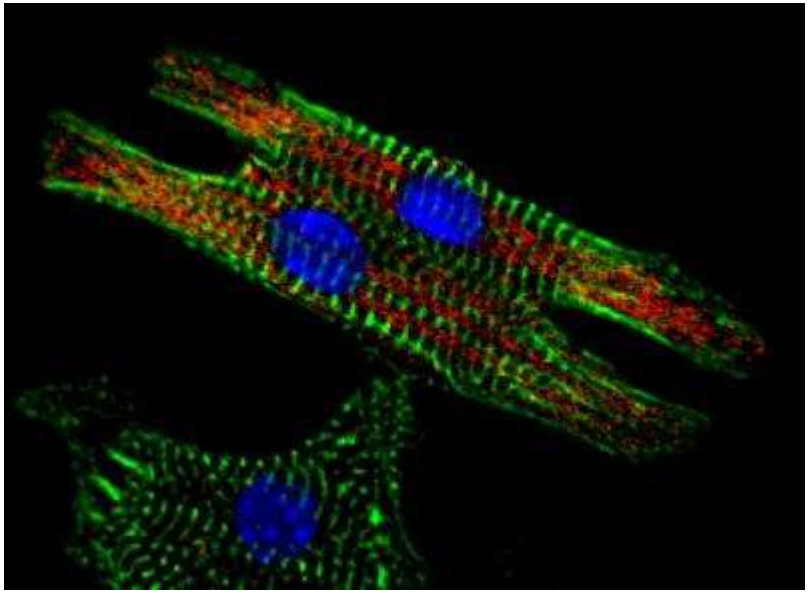


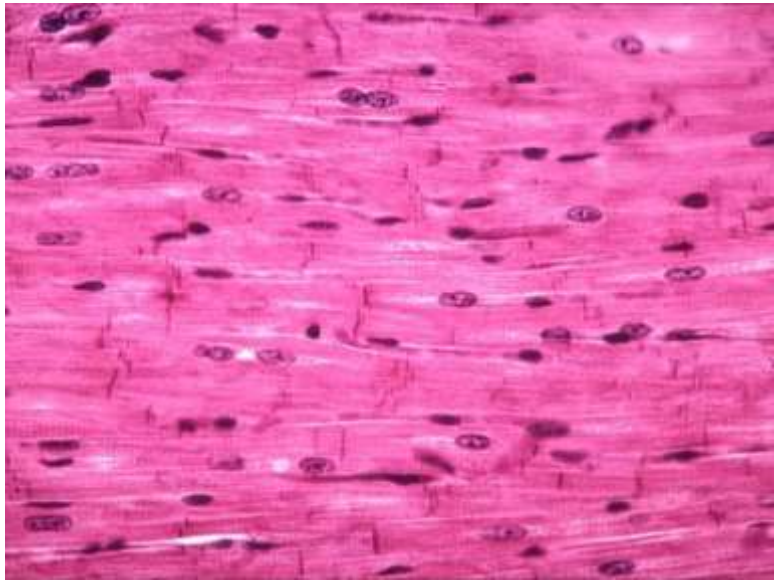

FO
MO
FA
MA
T5



CARDIAC MUSCLE COMPARED TO SKELETAL

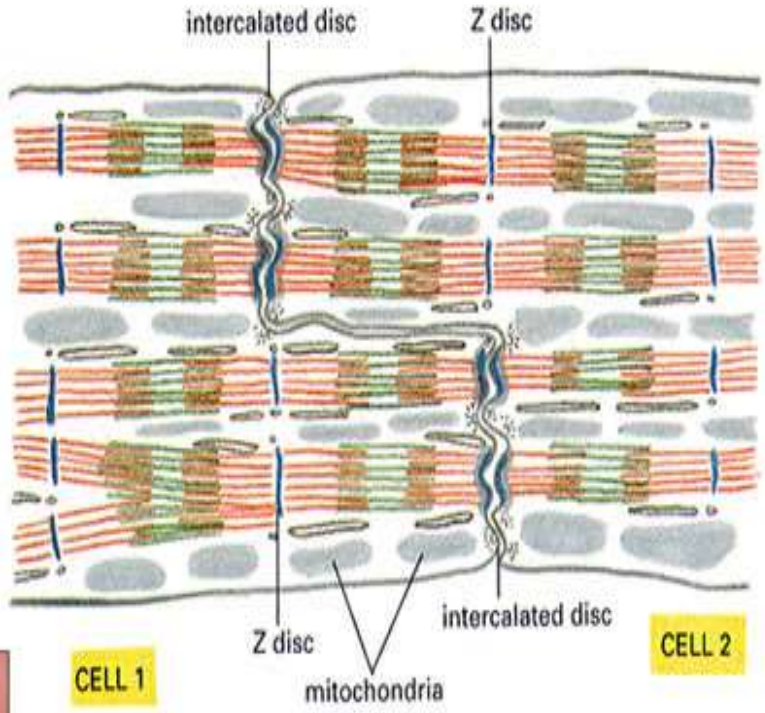
- no triads, but diads: 1 t-tubule + 1 cisterna
- t-tubules around the sarcomeres at the Z lines rather than at the zone of overlap
- sarcoplasmic reticulum via its tubules contact sarcolemma as well as the t-tubules
- cardiac muscle cells are totally dependent on aerobic metabolism to obtain the energy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

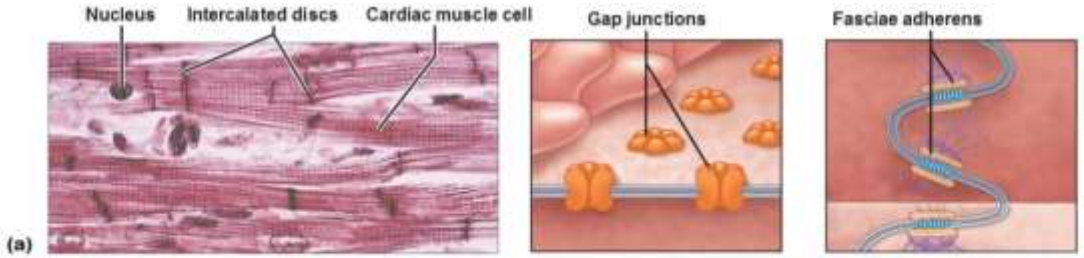


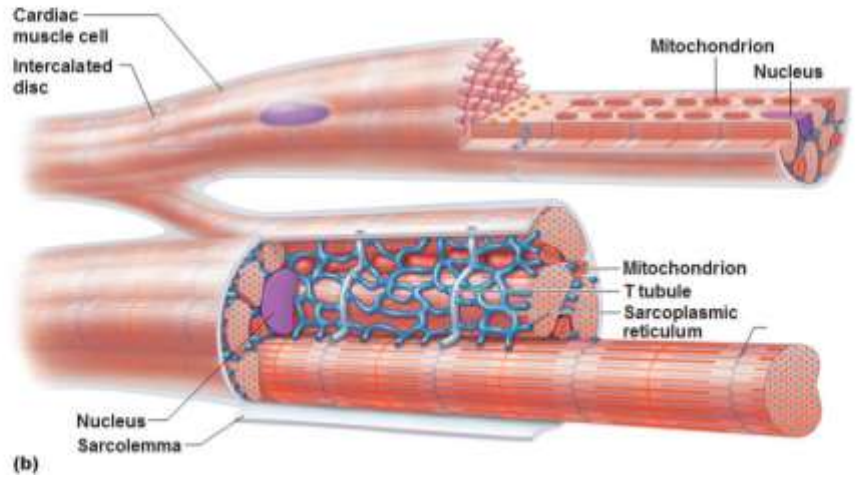


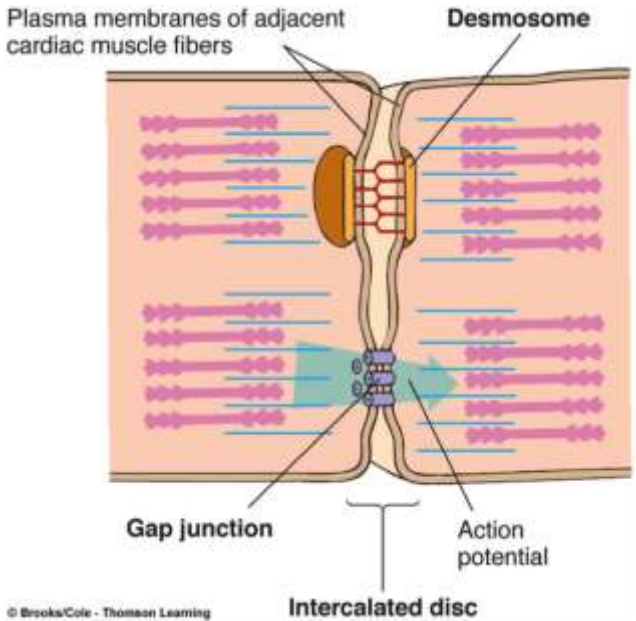
INTERCALATED DISC

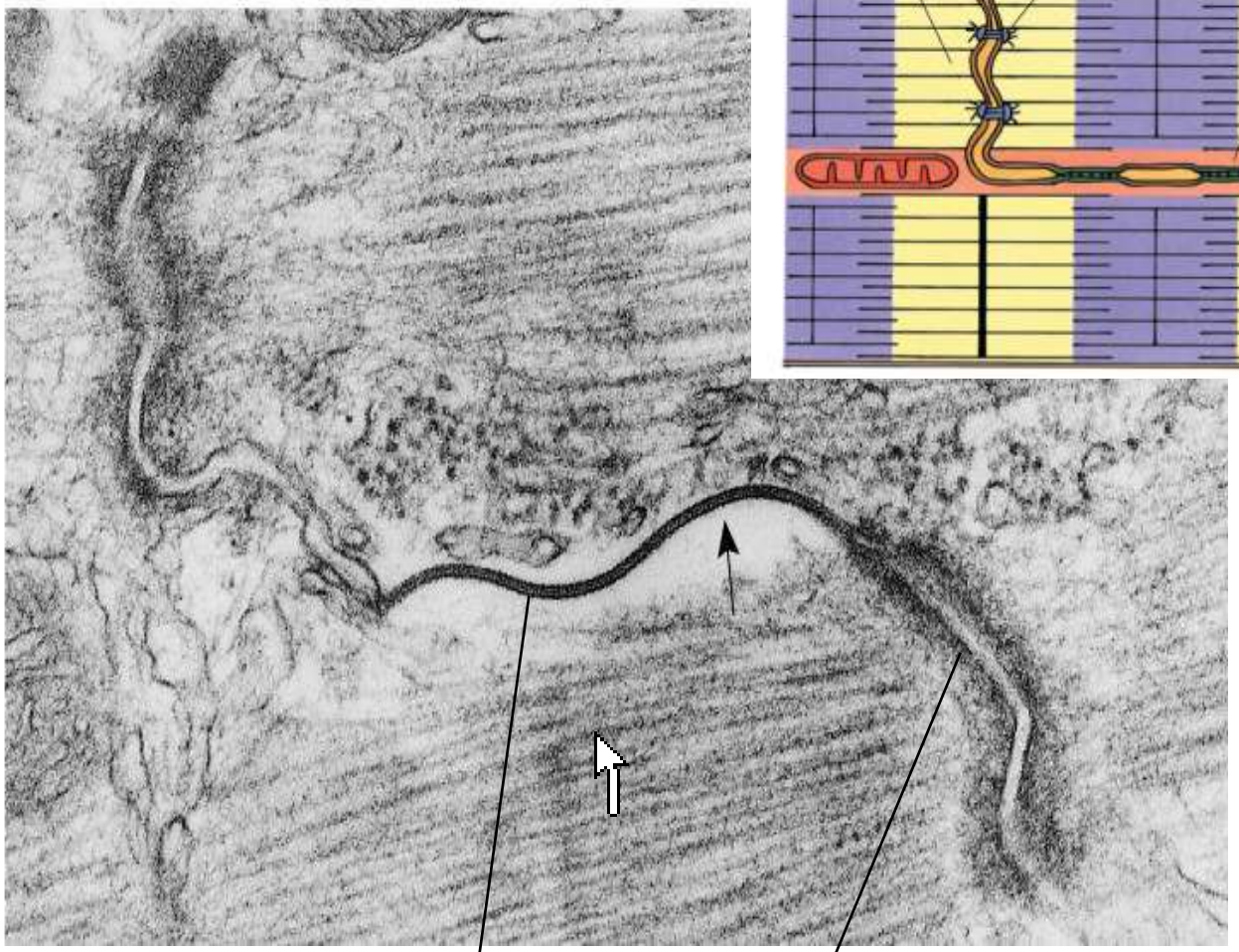
- „scalariform“ shape of cell ends
- fasciae adherentes (*adhesion of cells*)
- Nexus (quick intercellular communication – transport of ions, electric impulses, information)







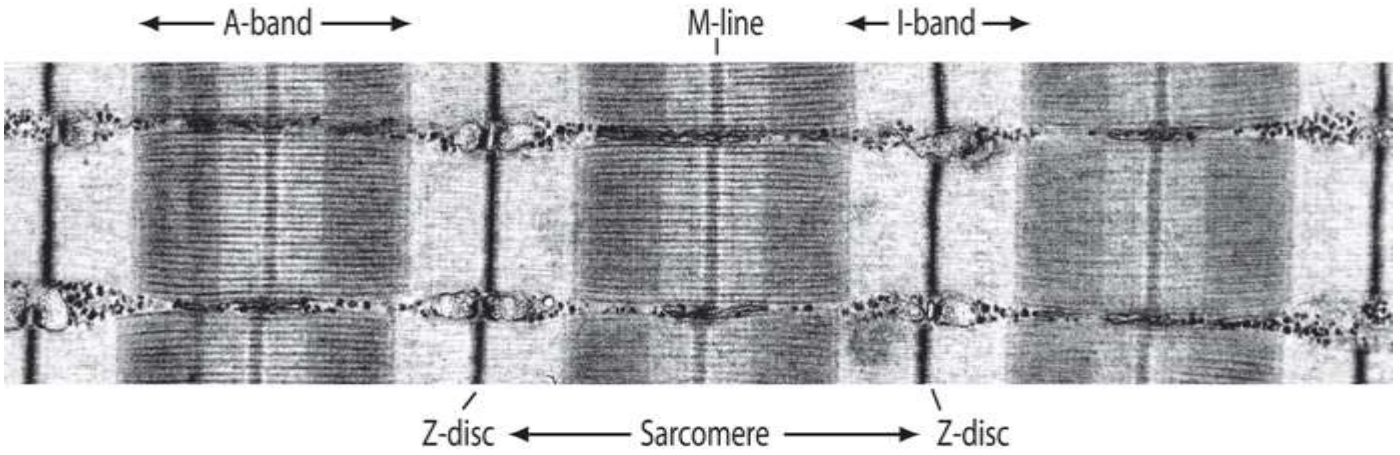


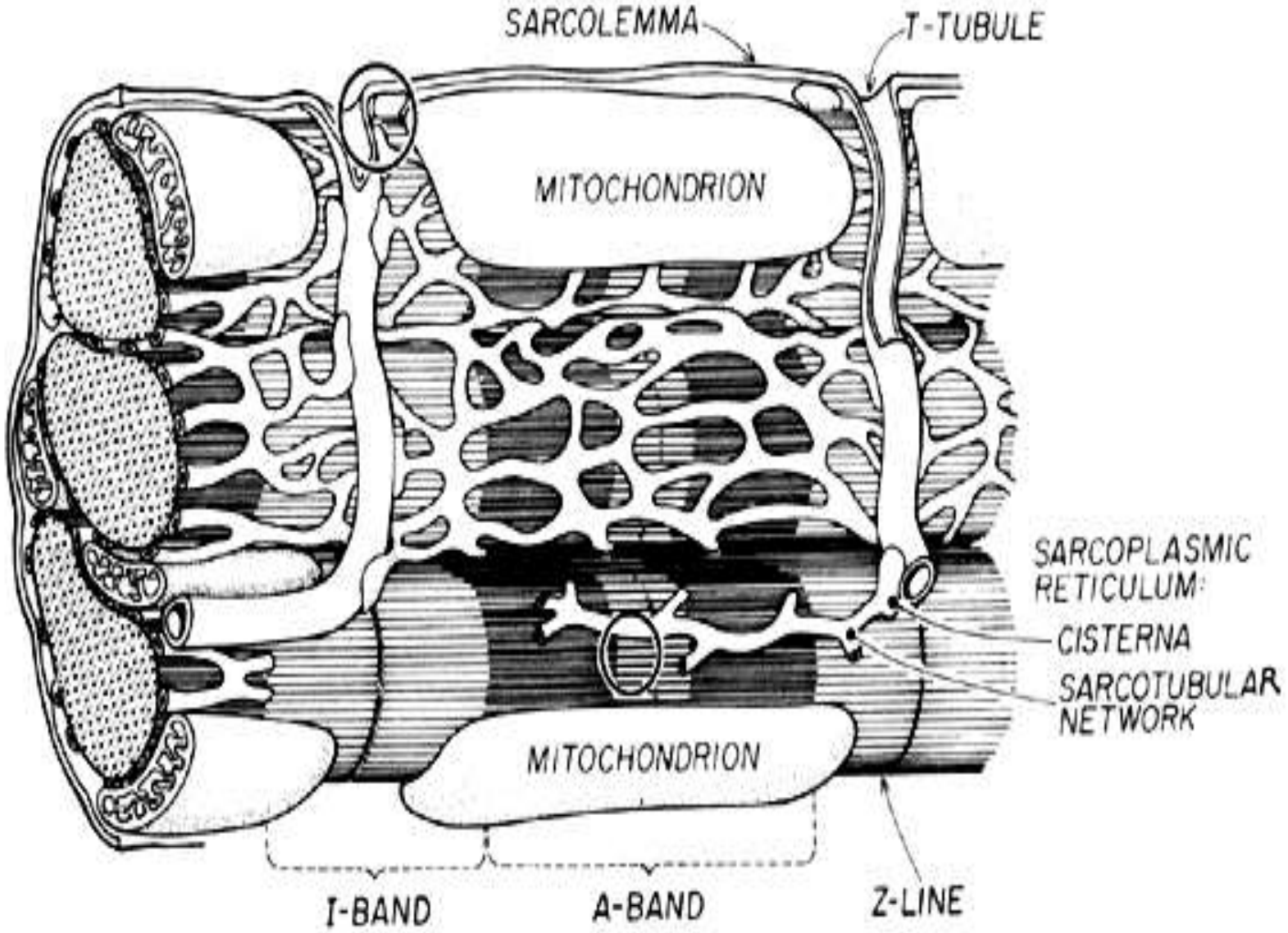


Intercalated disc: nexus fascia adherens

MYOFIBRIL OF CARDIOMYOCYTE

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

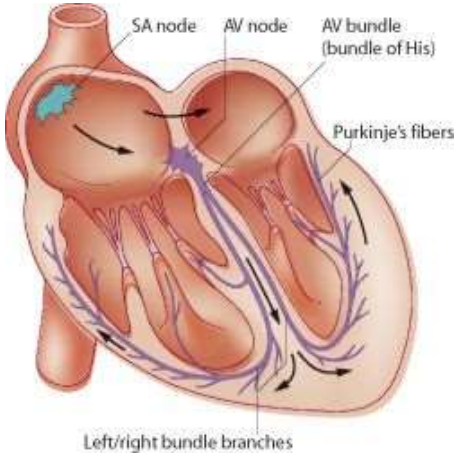


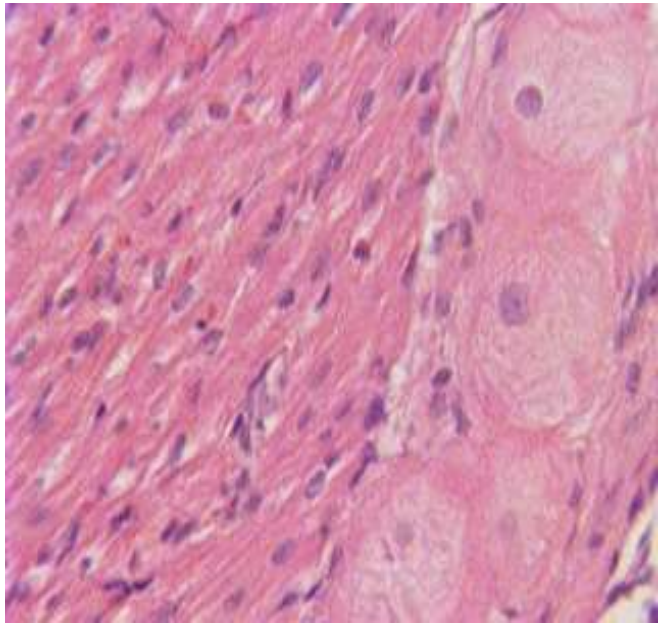

SARCOLEMMA
T-TUBULE
MITOCHONDRION
SARCOPLASMIC RETICULUM:
CISTERNA
SARCOTUBULAR NETWORK
MITOCHONDRION
I-BAND
A-BAND
Z-LINE

PURKINJE FIBERS

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

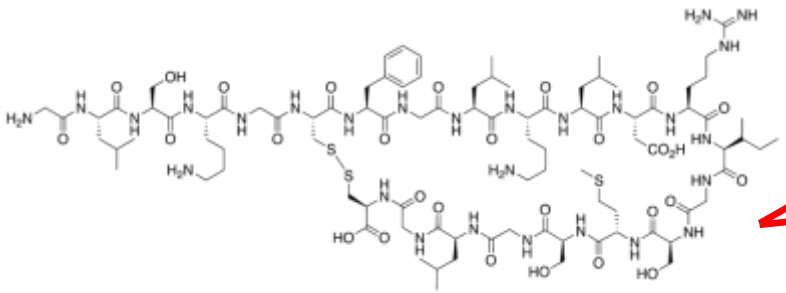
  mitochondria, fewer myofibrils

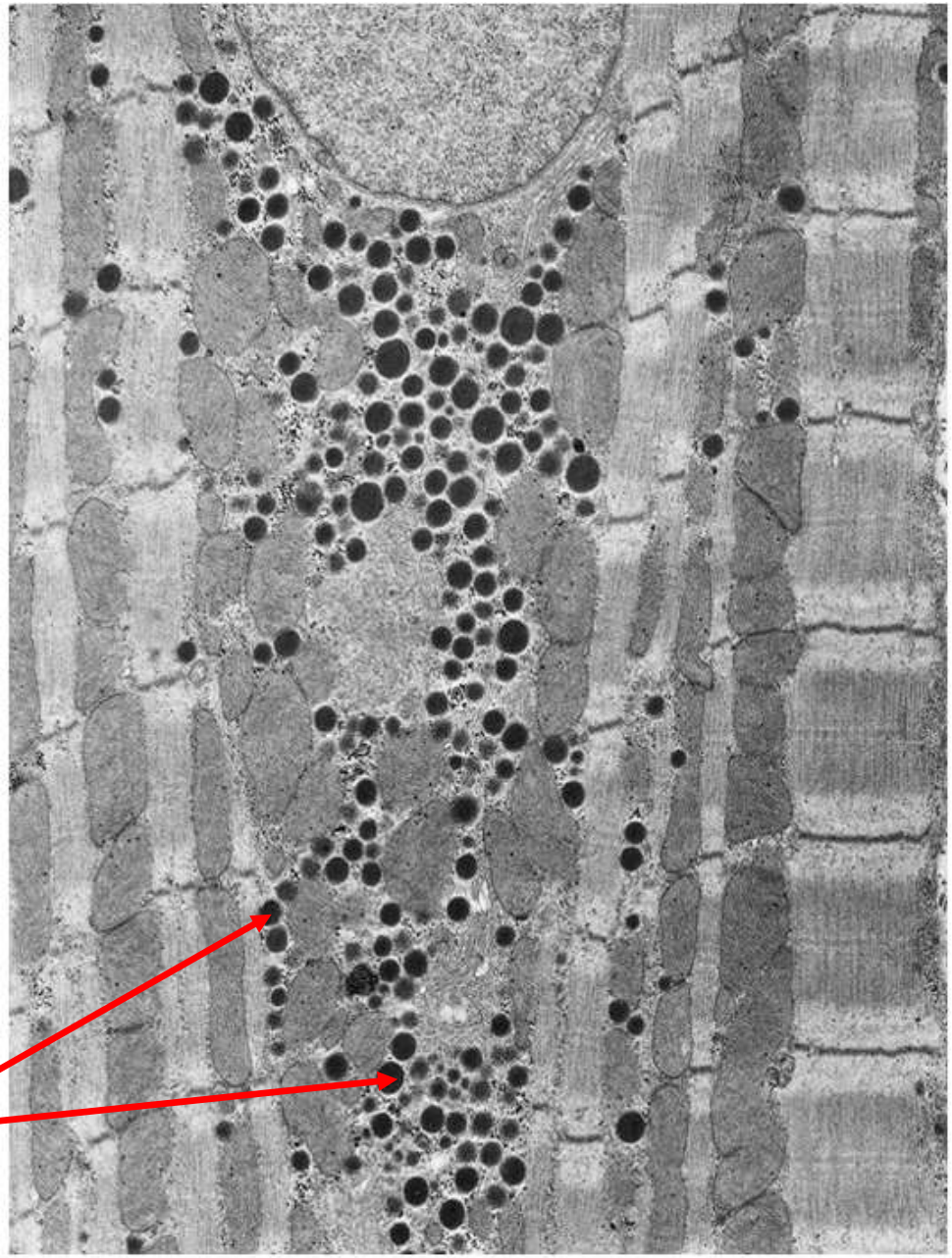




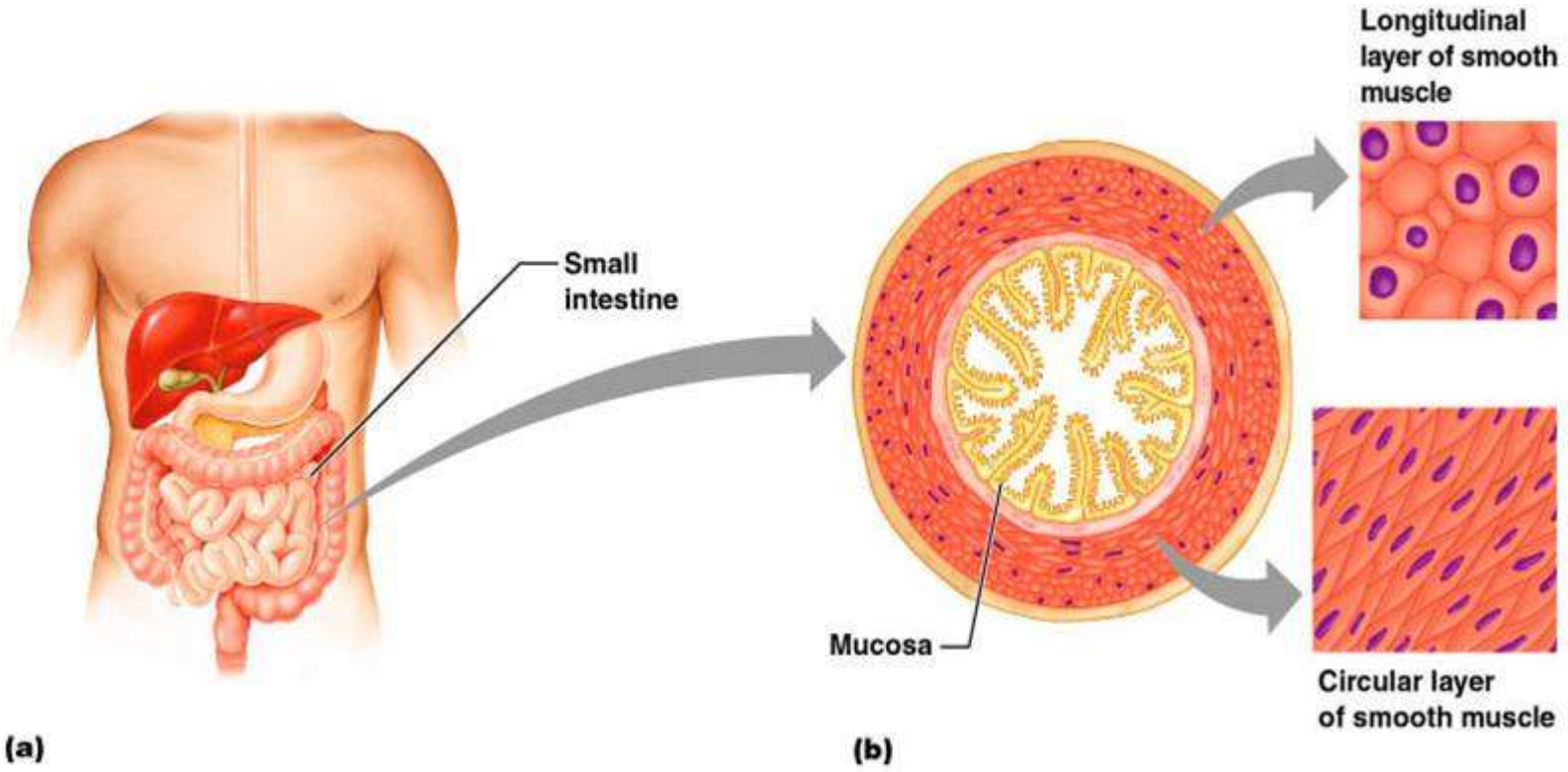
ATRIAL CARDIOMYOCYTES

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



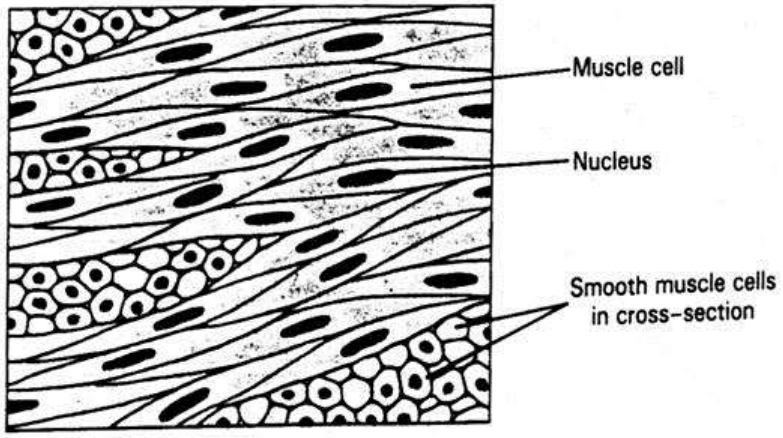


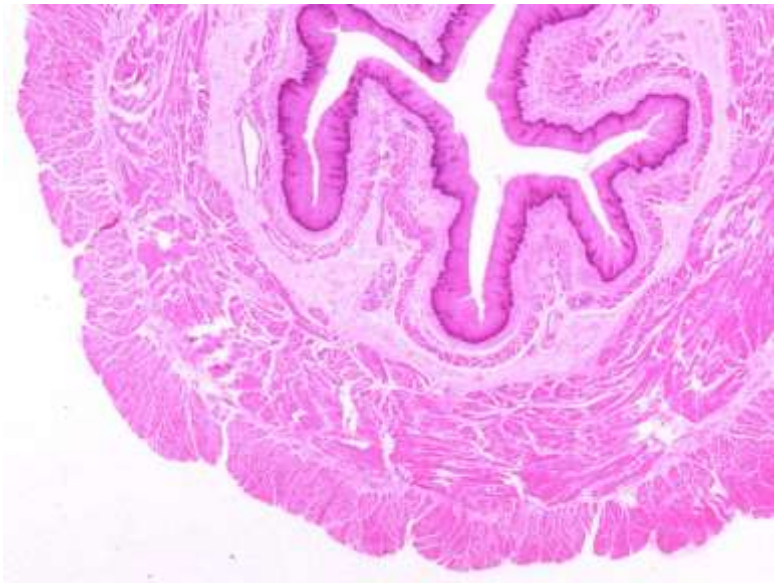
SMOOTH MUSCLE TISSUE

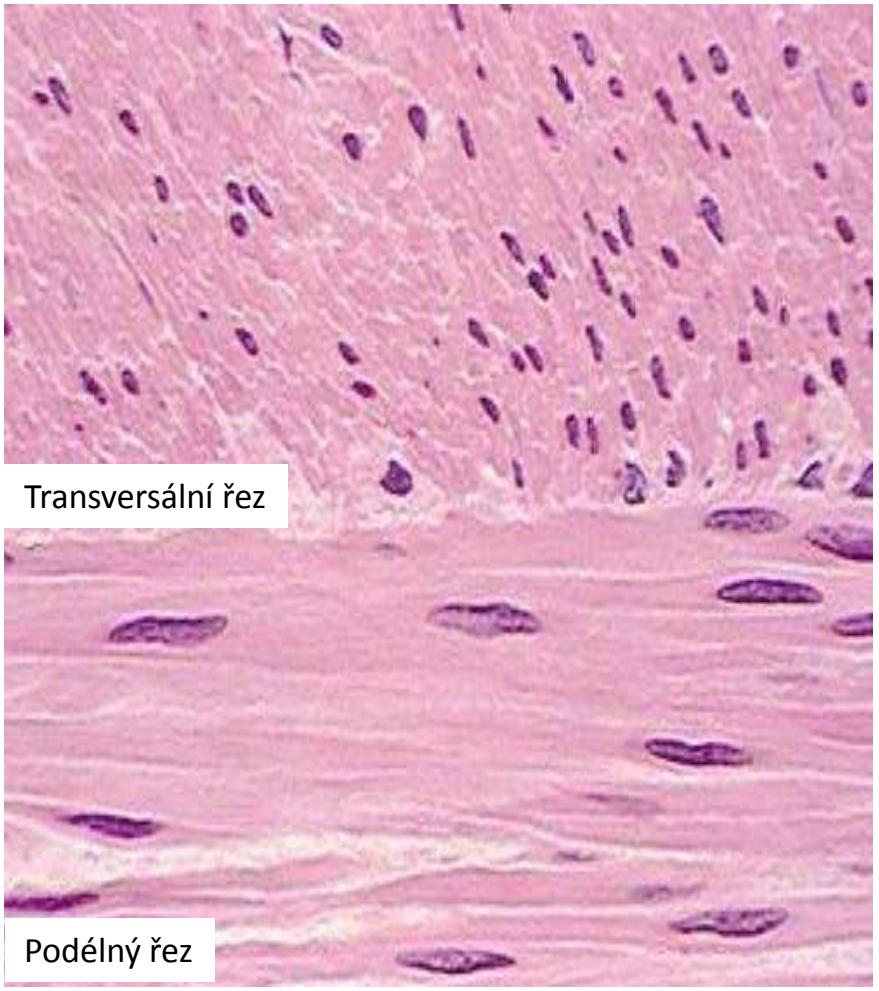


SMOOTH MUSCLE TISSUE

- Cells (leiomyocytes) form layers - eg. in walls of hollow organs





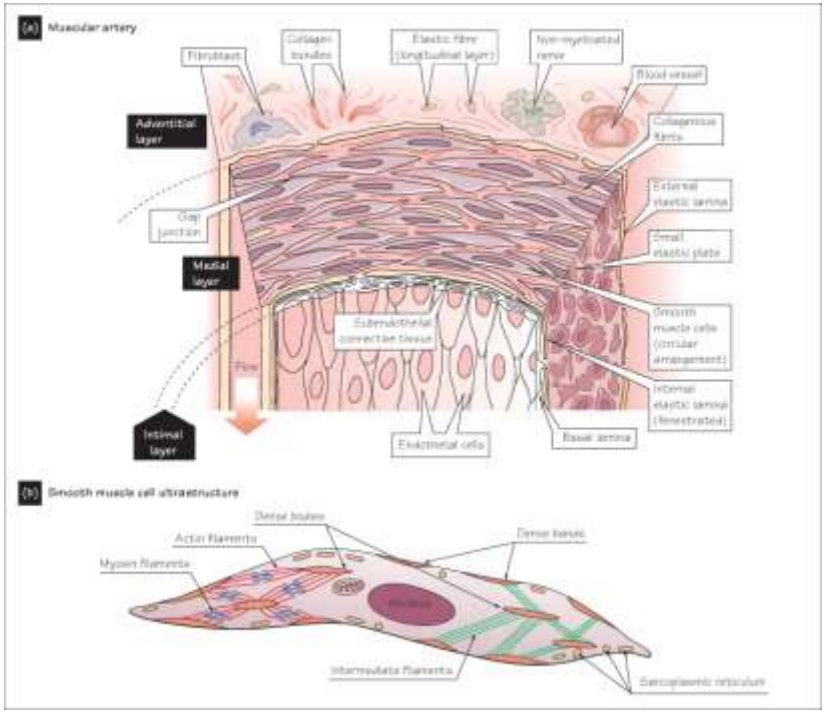


Transversální řez

Podélný řez

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 pinocytic vesicles
- zonulae occludentes and nexuses connect cells
- calmodulin



CAVEOLI

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

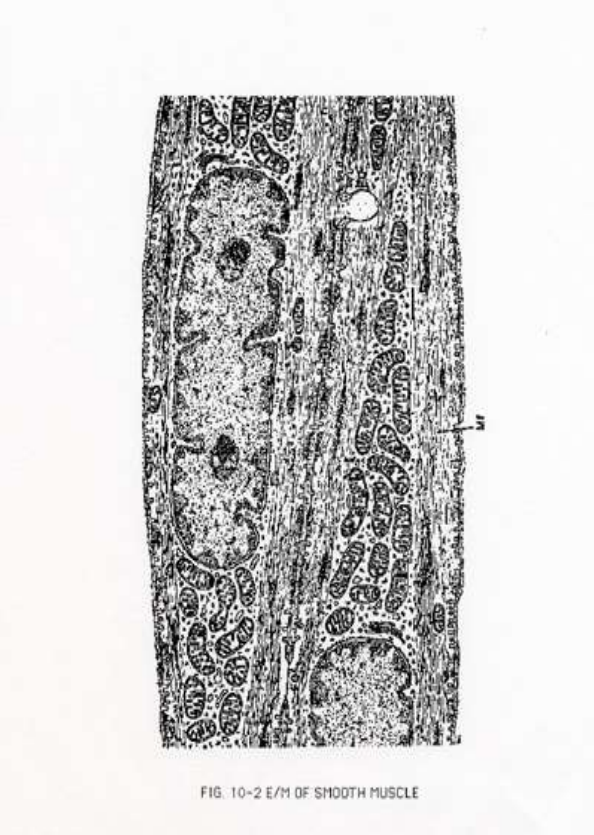
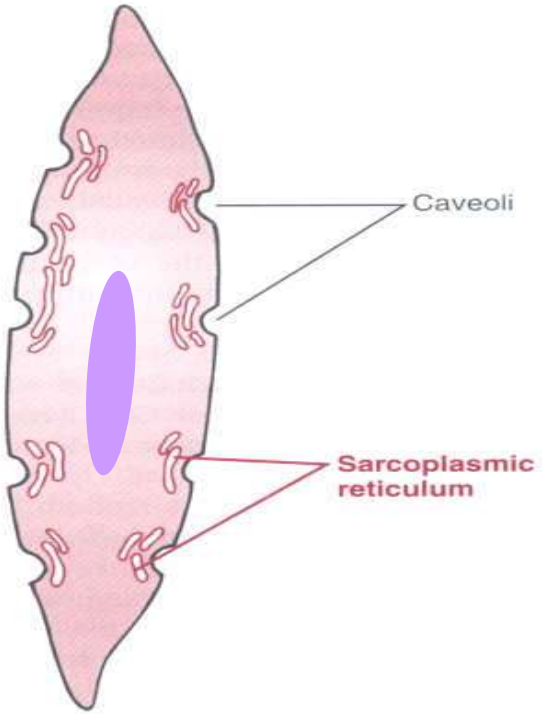
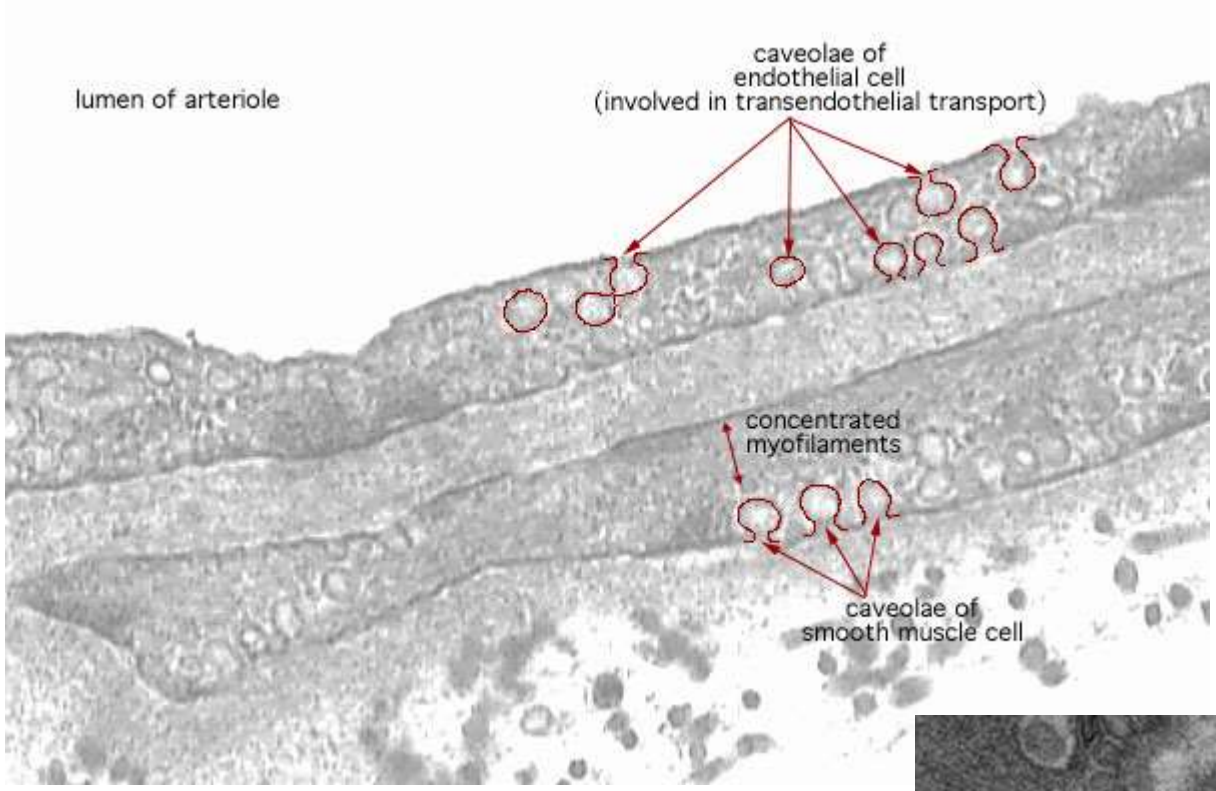
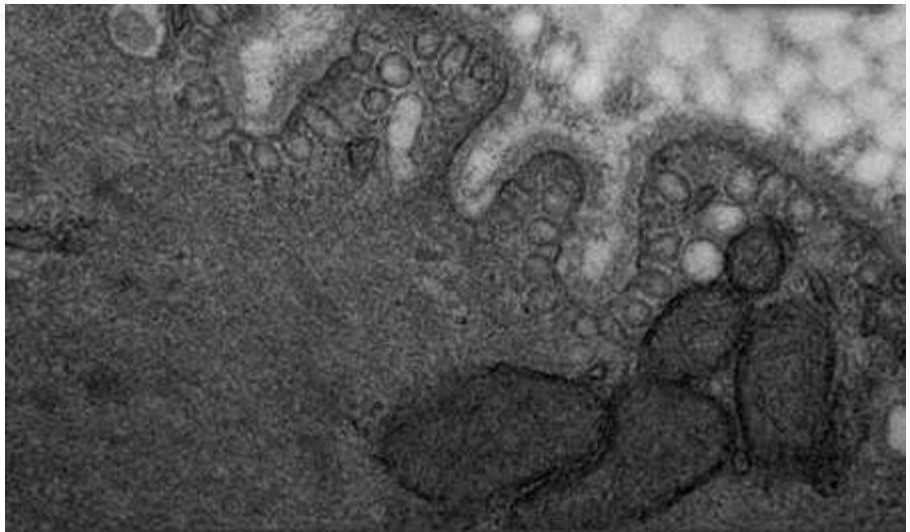


FIG. 10-2 E/M OF SMOOTH MUSCLE

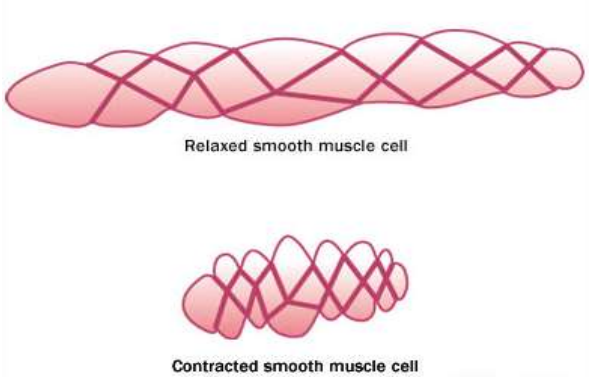


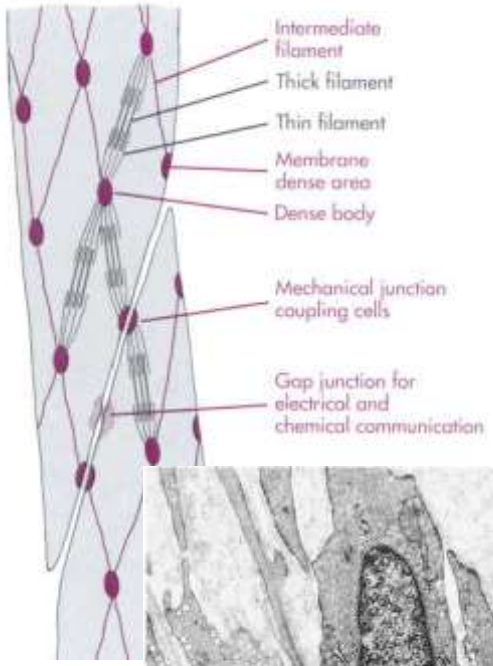
CAVEOLI

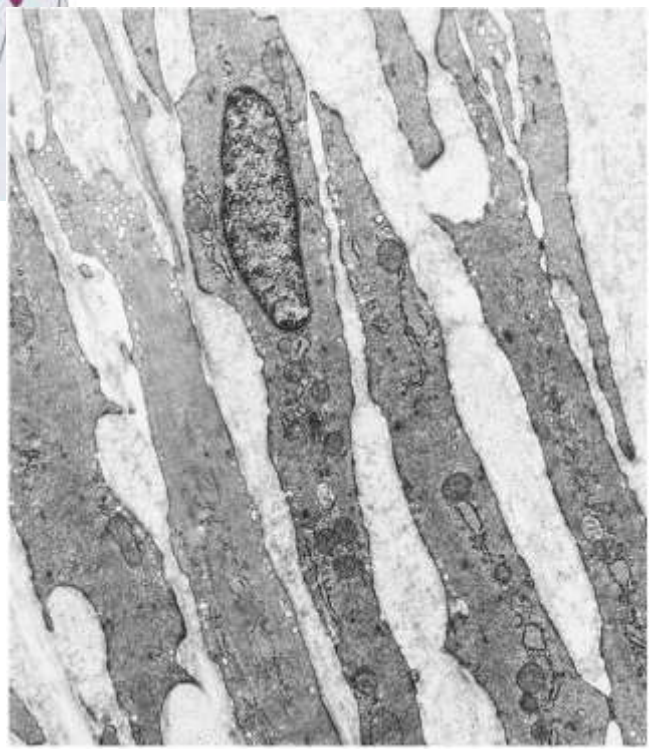

lumen of arteriole
caveolae of
endothelial cell
(involved in transendothelial transport)
concentrated
myofilaments
caveolae of
smooth muscle cell

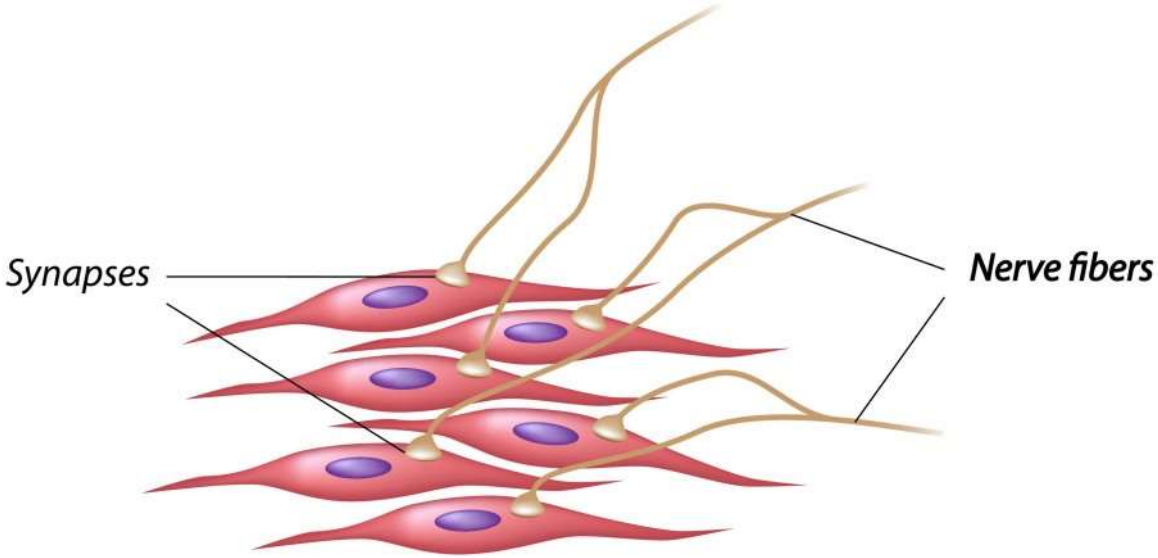


SMOOTH MUSCLE TISSUE

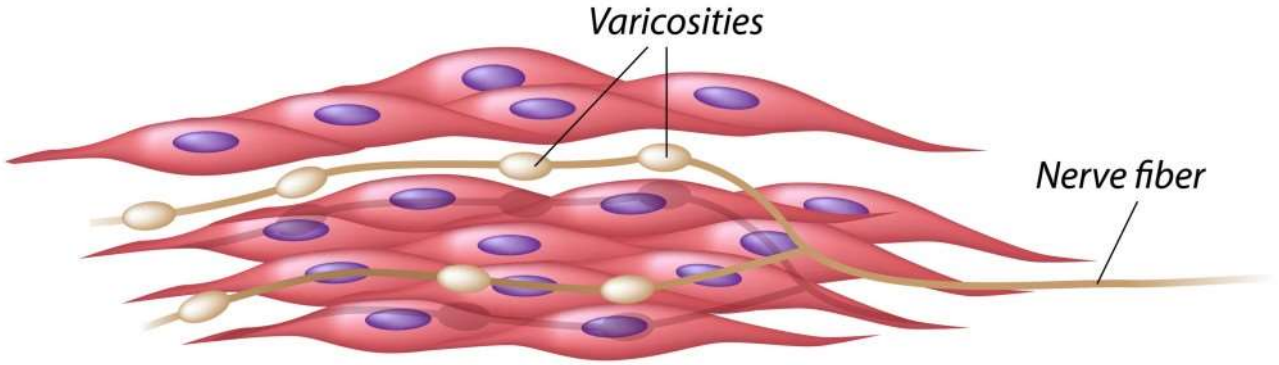




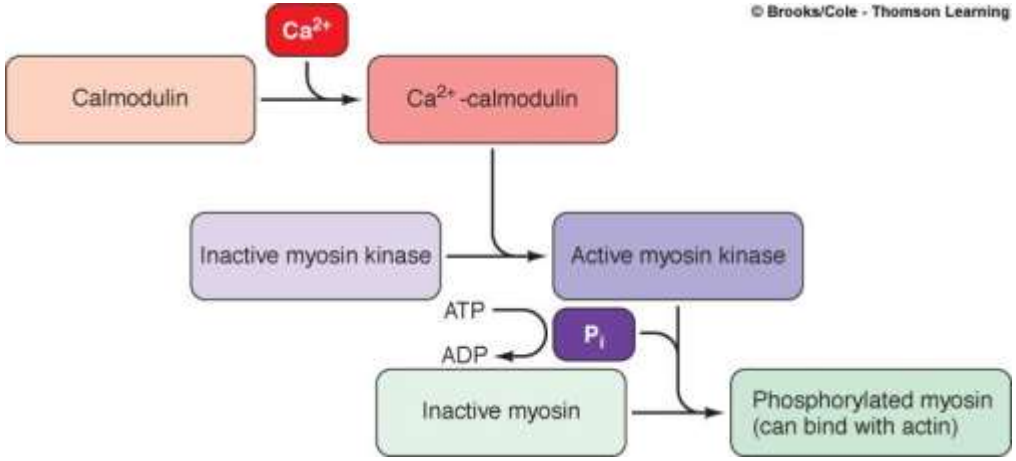


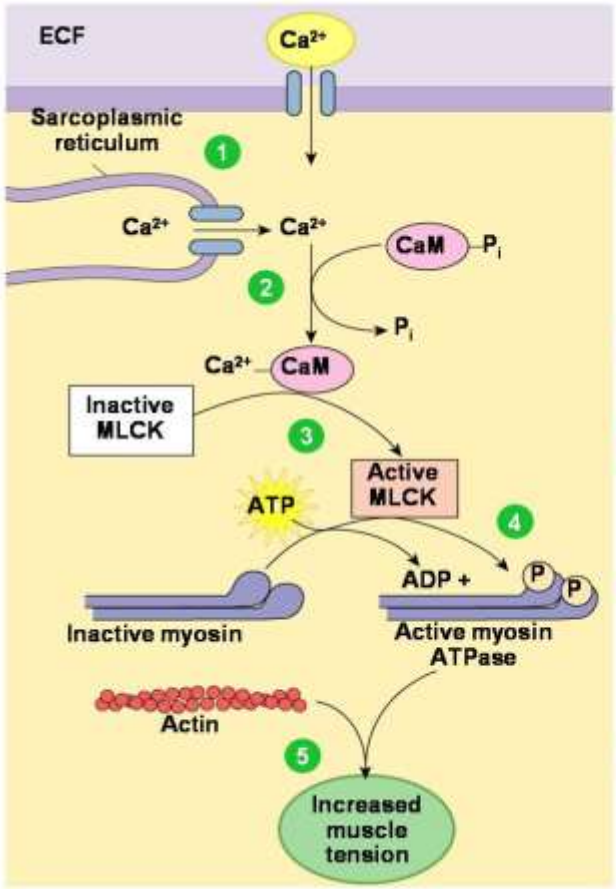


Multiunit Smooth Muscle

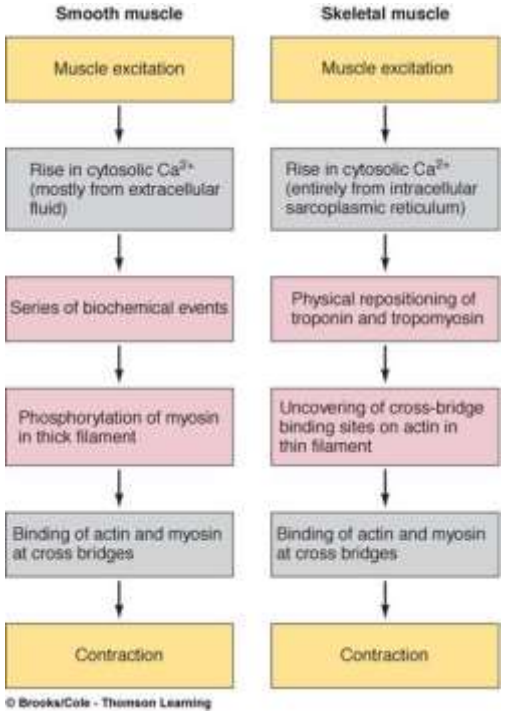


Single-unit Smooth Muscle





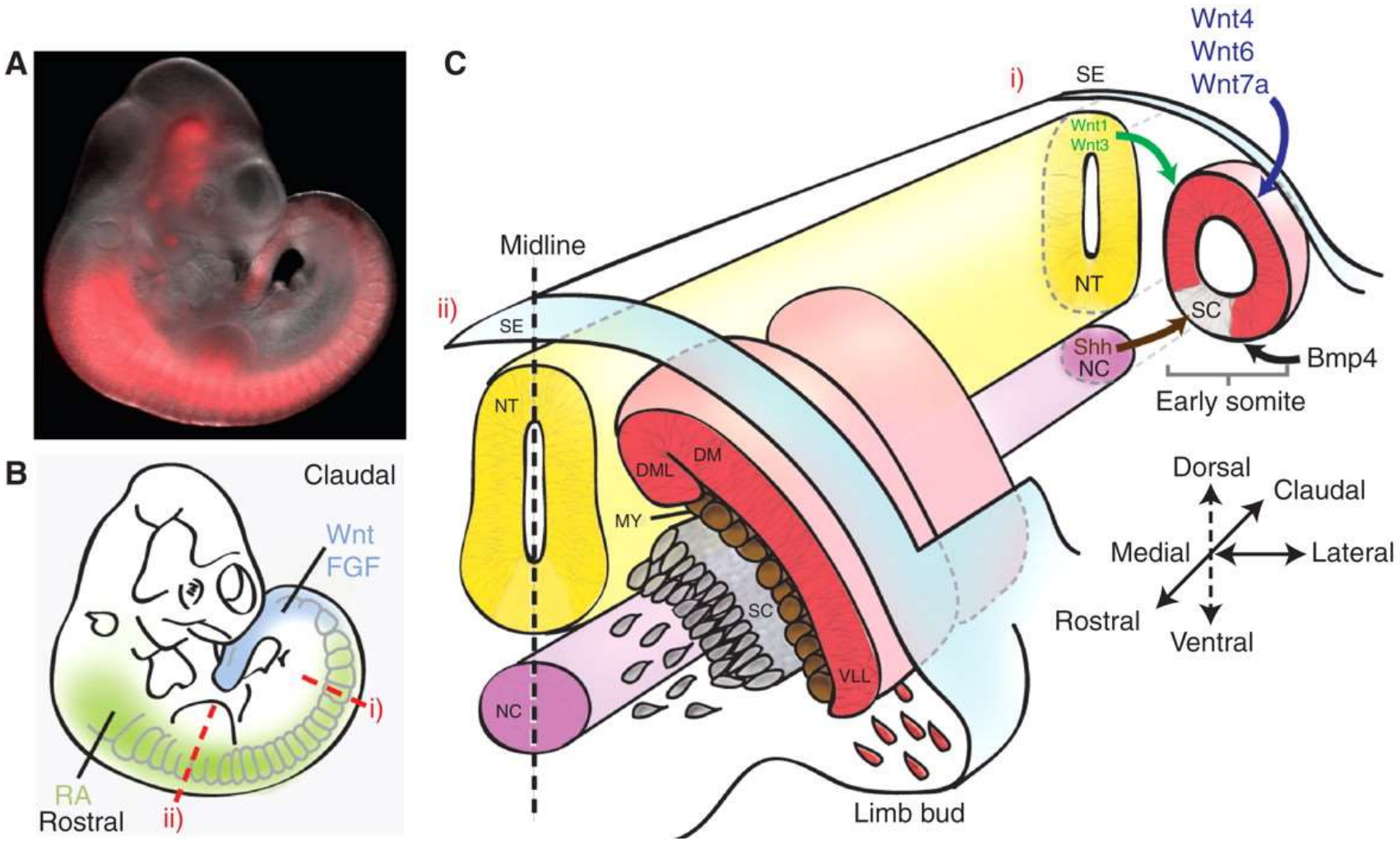
1. **Intracellular Ca^{2+} concentrations increase when Ca^{2+} enters cell and is released from sarcoplasmic reticulum.**
2. **Ca^{2+} binds to calmodulin (CaM).**
3. **Ca^{2+}–calmodulin activates myosin light chain kinase (MLCK).**
4. **MLCK phosphorylates light chains in myosin heads and increases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

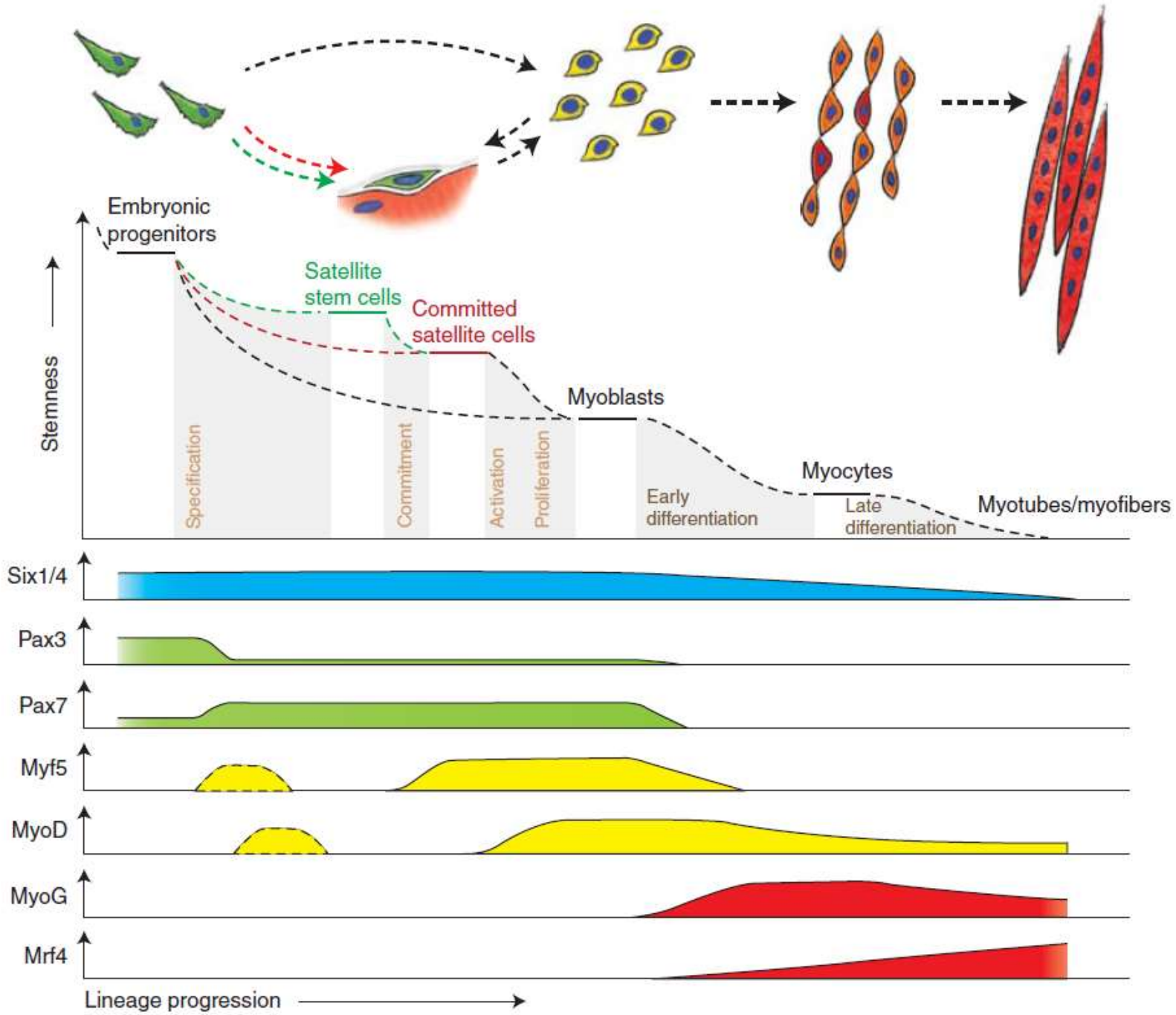


SUMMARY

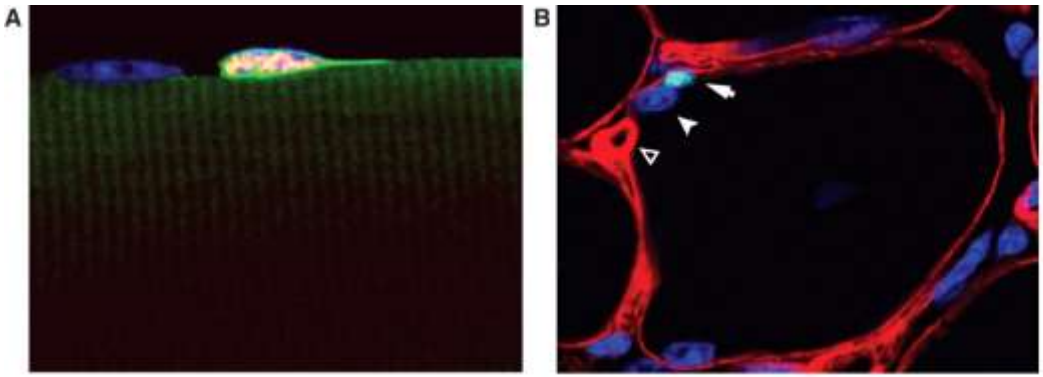
Hallmark	Skeletal muscle	Cardiac muscle	Smooth muscle
Cells	Thick, long, cylindrical, non-branched	Branched, cylindrical	Small, spindle-shaped
Nuclei	Abundant, peripherally	1-2, centrally	1, centrally
Filaments ratio (thin:thick)	6:1	6:1	12:1
sER and myofibrils	Regular sER around myofibrils	Less regular 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	Bundles, c.t.	Intercalated discs	Caveoli, overlapping cells

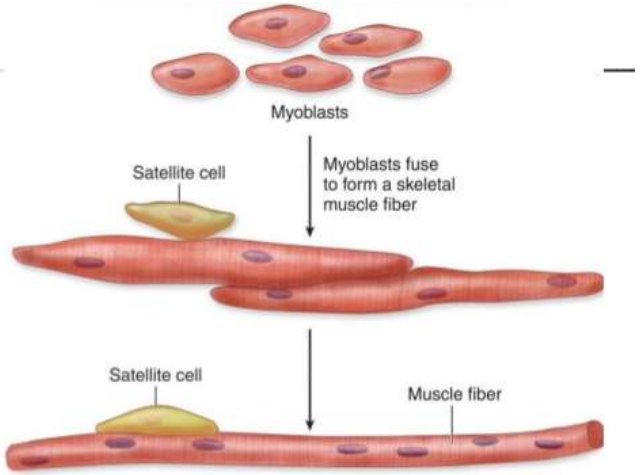
EMBRYONIC DEVELOPMENT

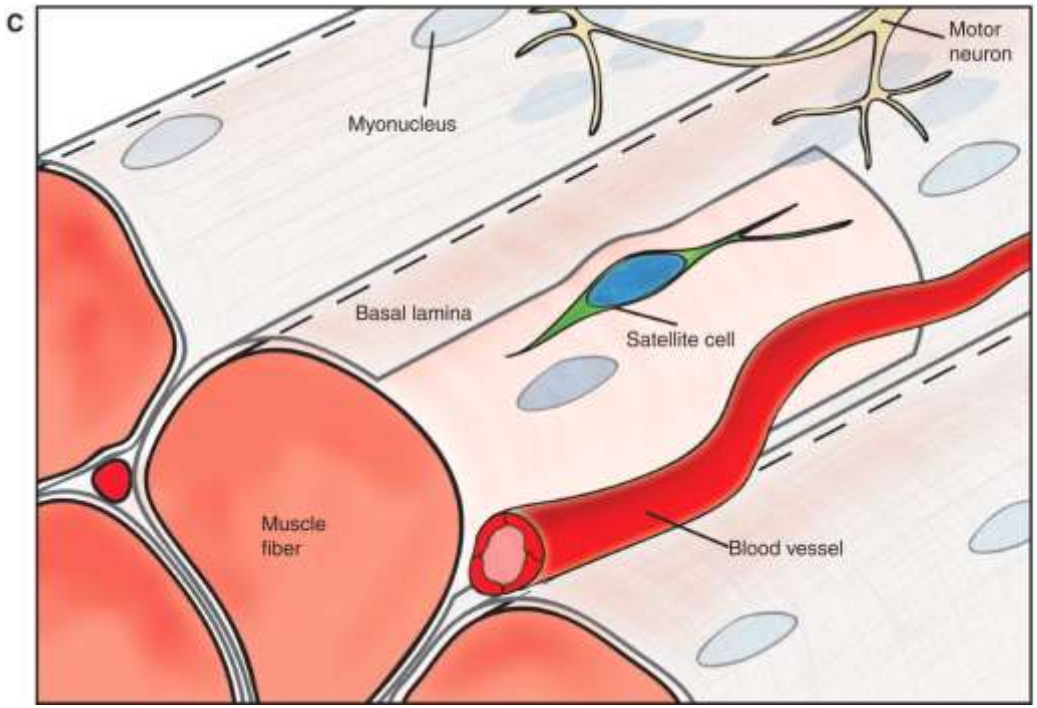



Embryonic progenitors
Satellite stem cells
Committed satellite cells
Myoblasts
Myocytes
Myotubes/myofibers
Stemness
Specification
Commitment
Activation
Proliferation
Early differentiation
Late differentiation
Six1/4
Pax3
Pax7
Myf5
MyoD
MyoG
Mrf4
Lineage progression

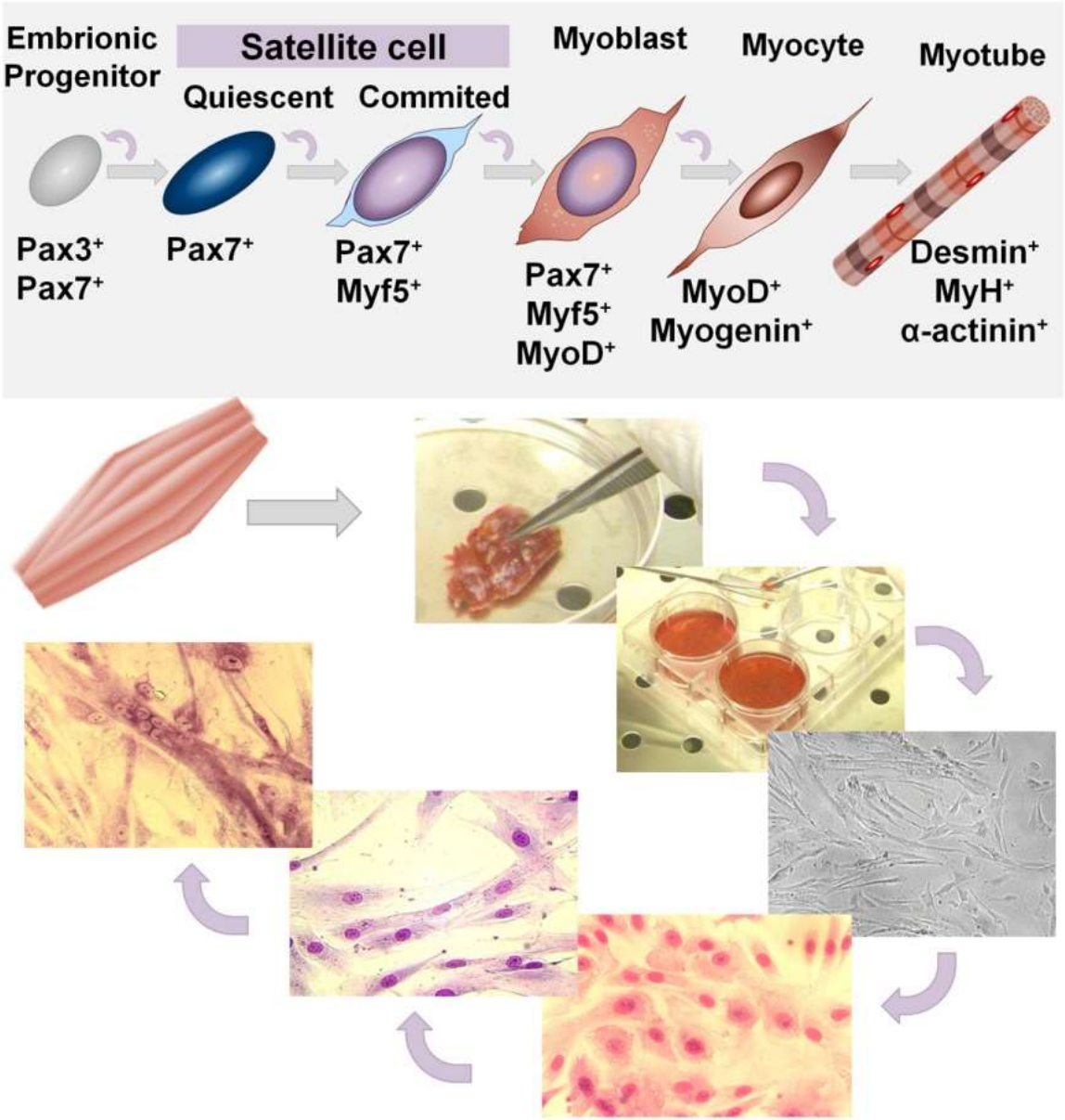
REGENERATION

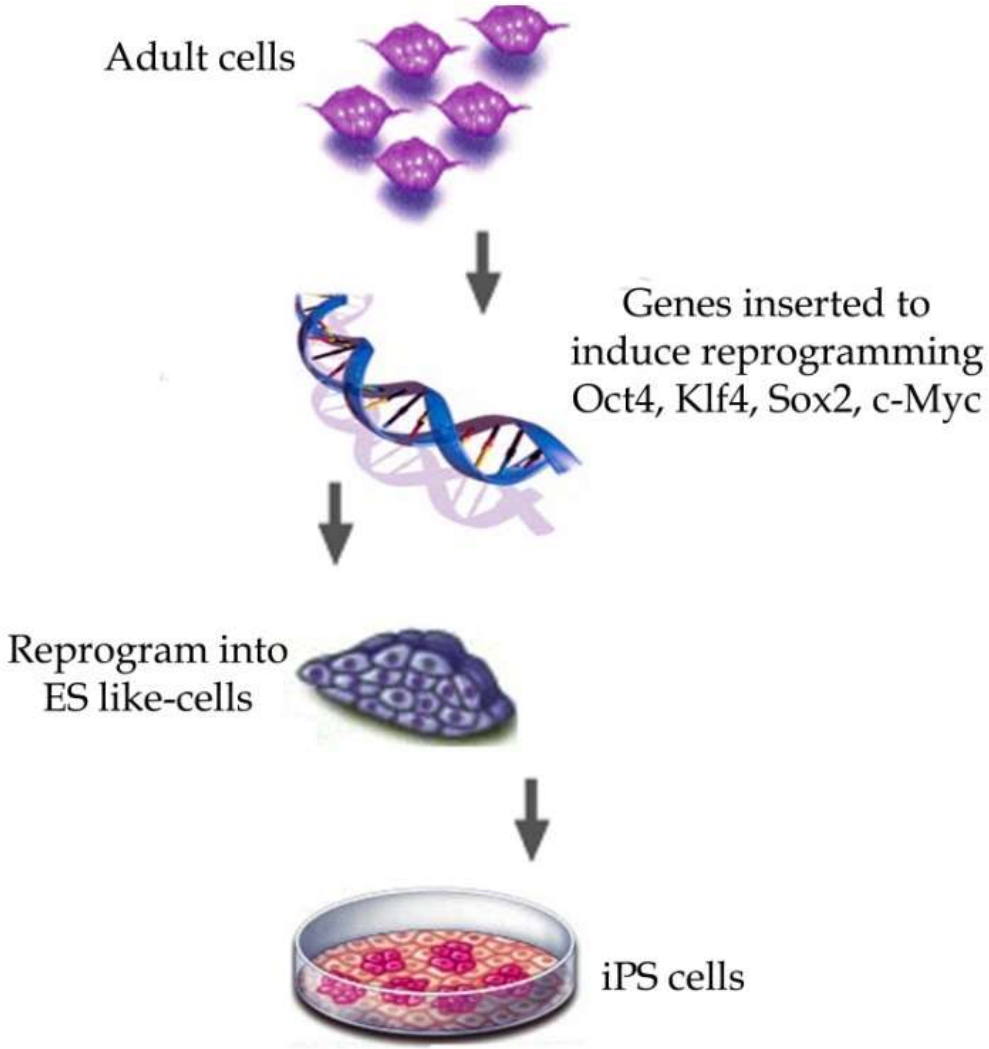






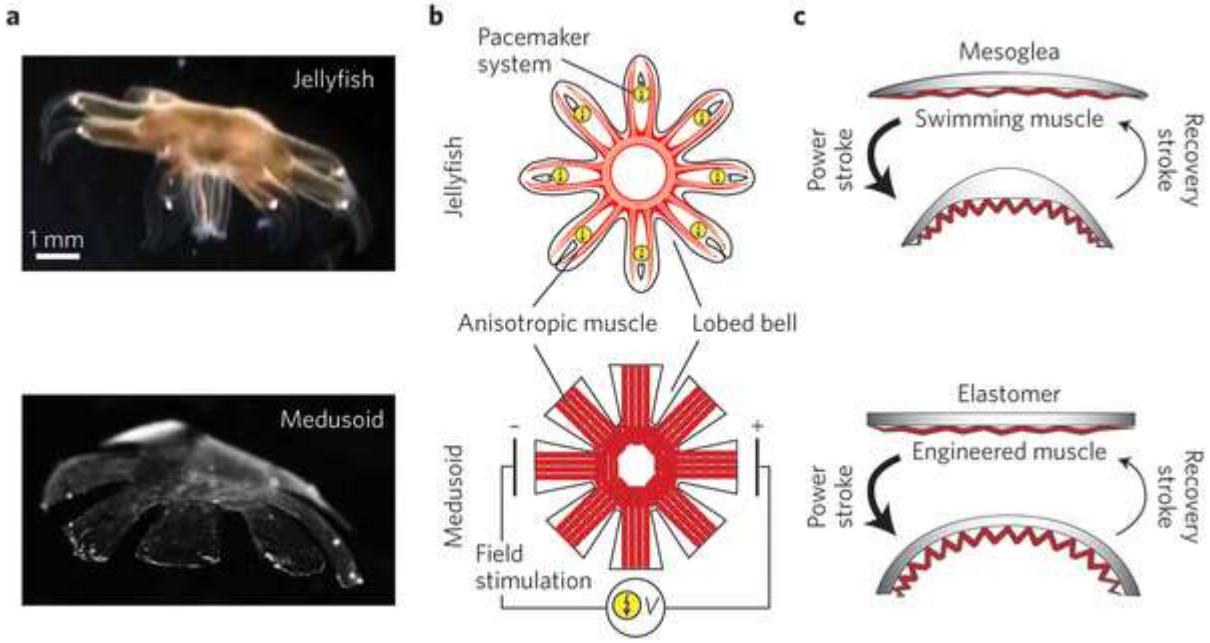
REGENERATION

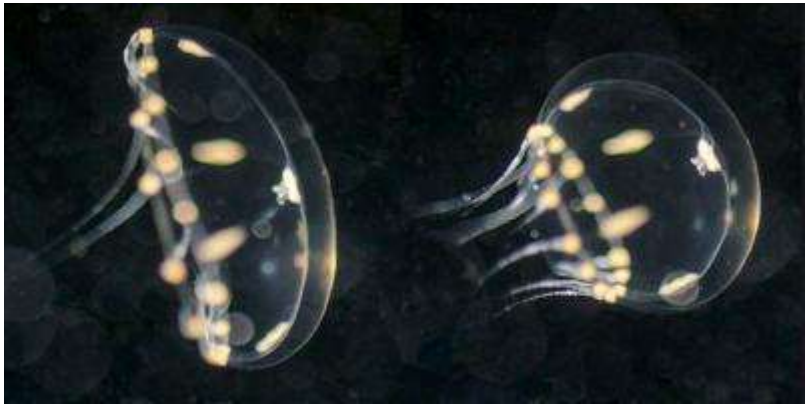




https://www.youtube.com/watch?v=b1WD564sjWw

TISSUE ENGINEERING





https://www.youtube.com/watch?v=ay0fIASNGik

Thank you for attention

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