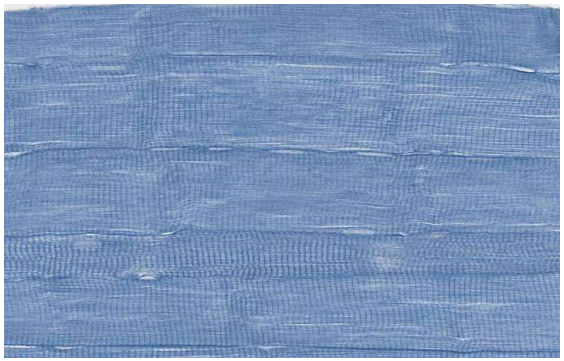
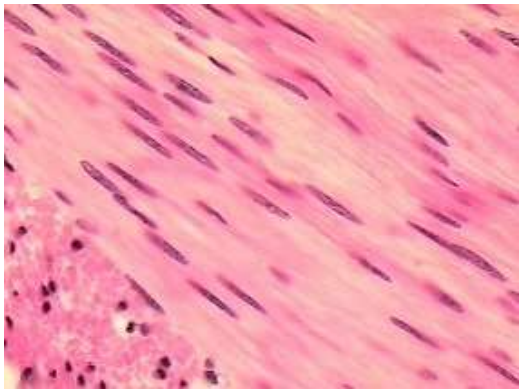
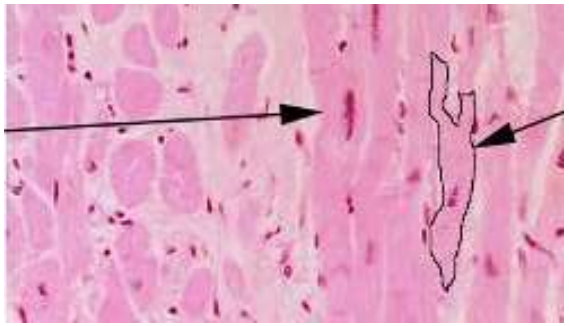
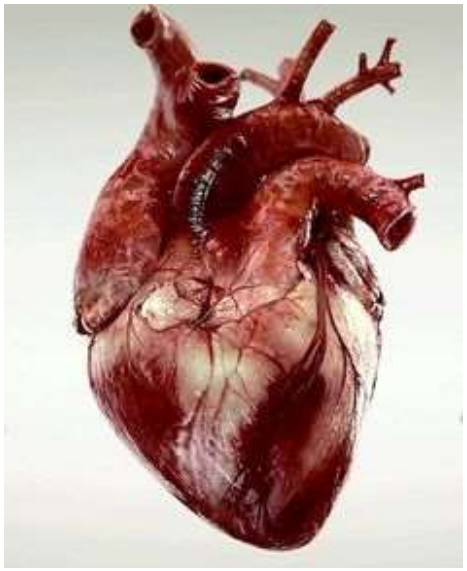




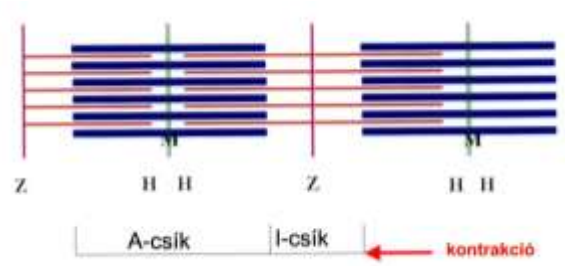


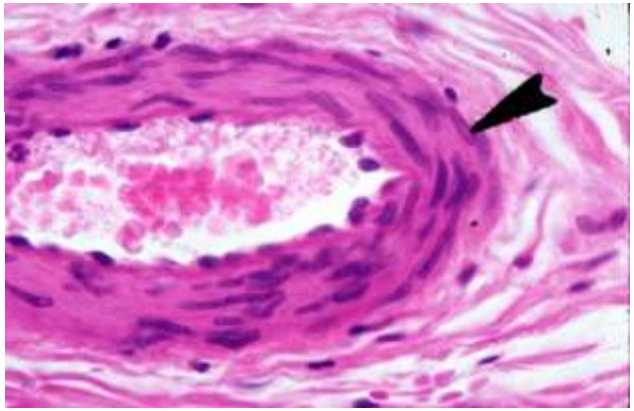


Muscle tissues

By Krisztina H.-Minkó
Semmelweis University
Department of Anatomy, Histology and Embryology

2020. 02 28.





Introduction

- Function: contraction
- Mainly cellular, small amount of ECM
- Contractile filaments, Actin, Miozin
- Well developed citoskeleton
- High energy requirement– Mitochondria
- high Ca^{2+}-demand– smooth ER, Ca^{2+}-ion channels, Ca^{2+}-pumps
- Membrana basalis

Types of muscle tissue

- Striated muscle

  Sceletal: -histological unit: muscle fiber
  -origin and insertion on bony structures
  -contraction is due to nerve stimulation

  Visceral: - histological unit: muscle fiber
  - independent of sceletal elements (muscles of tongue, muscles of esophagus upper third)
  - contraction is due to nerve stimulation

- Cardiac muscle (cellular, shows striation)

- Smooth muscle (no striation)

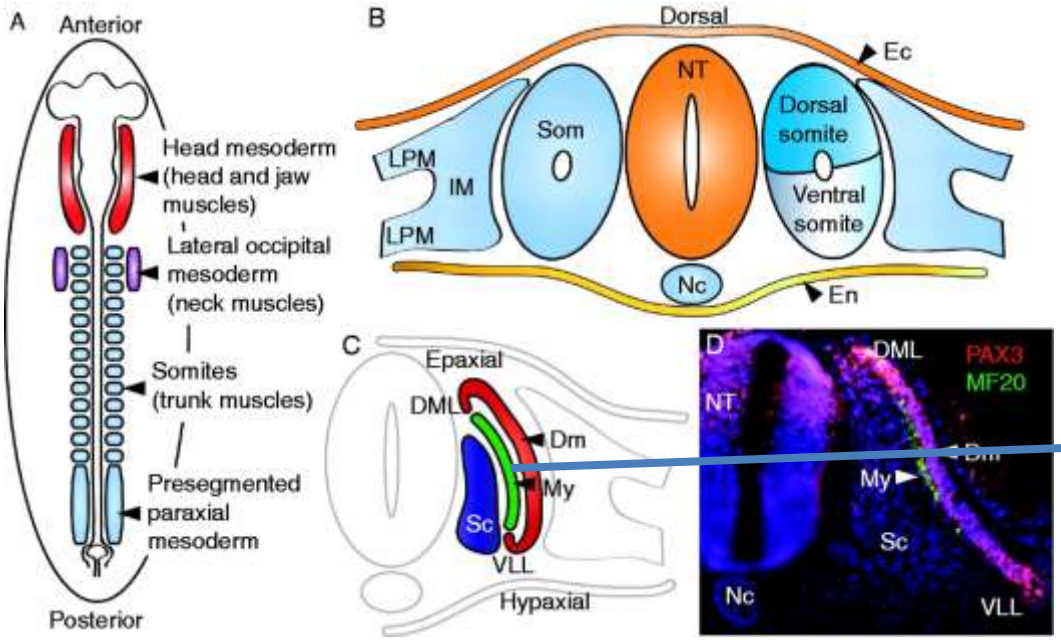
Transitional forms (these are not muscular tissues)

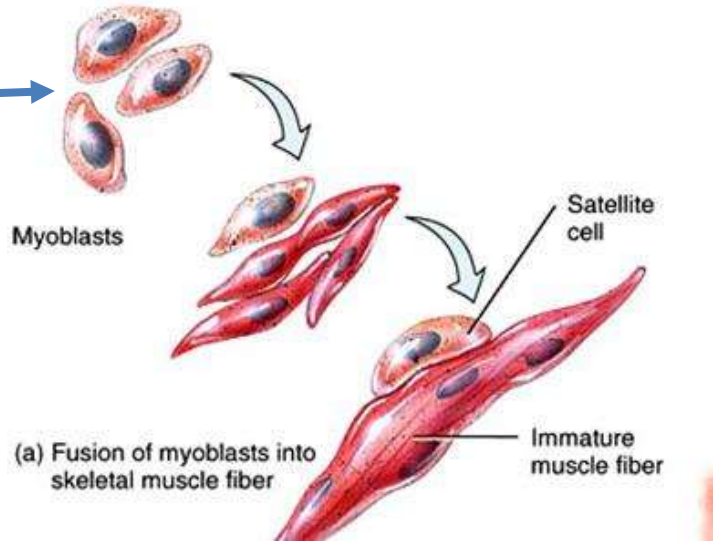
Myoepithel (glands)

Myofibroblast (pericytes, mesangial cells)

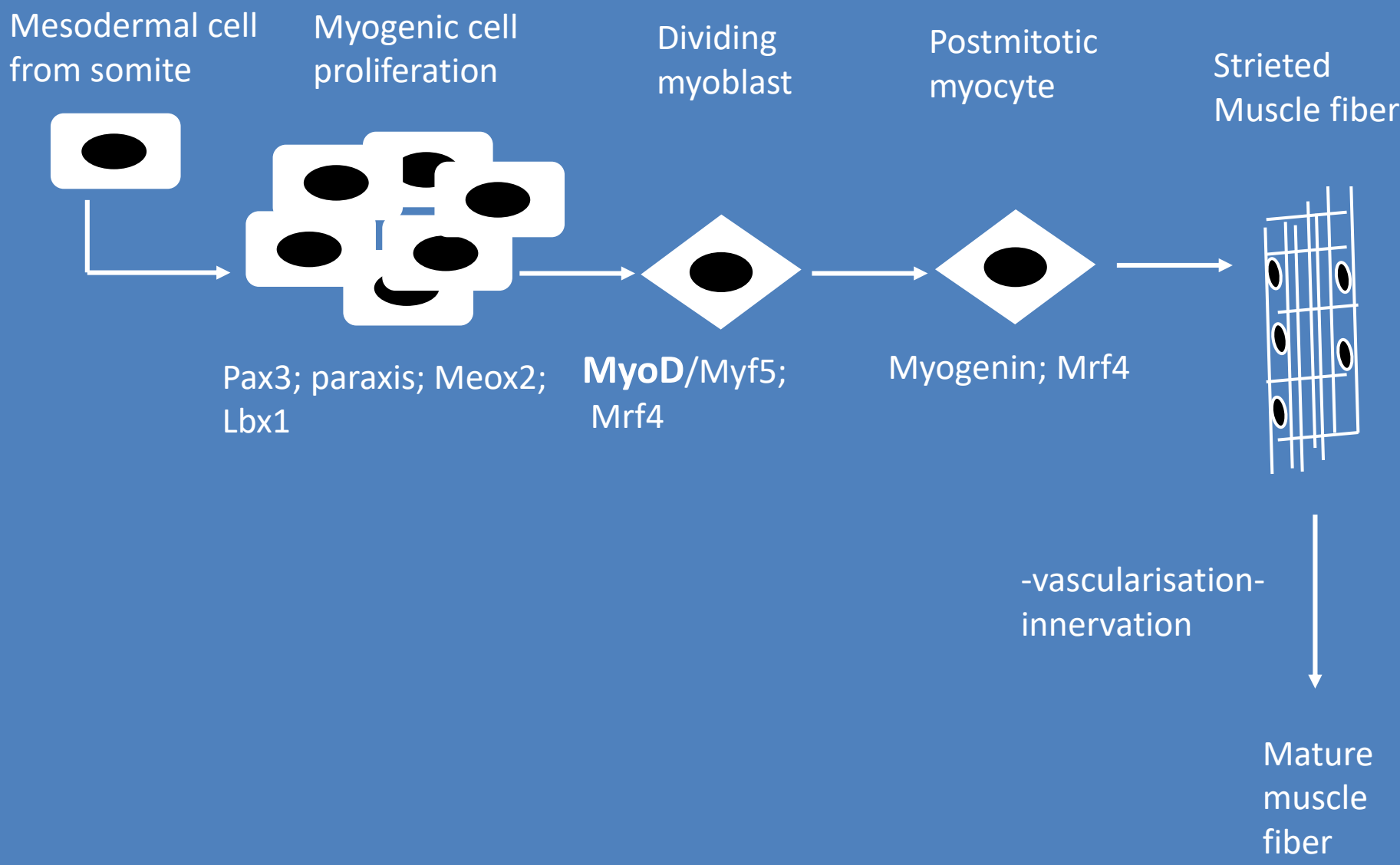
Development of muscle tissue

Mesodermal origin in the body
Neural crest origin in the head





Order of activation of transcription factors during muscle development

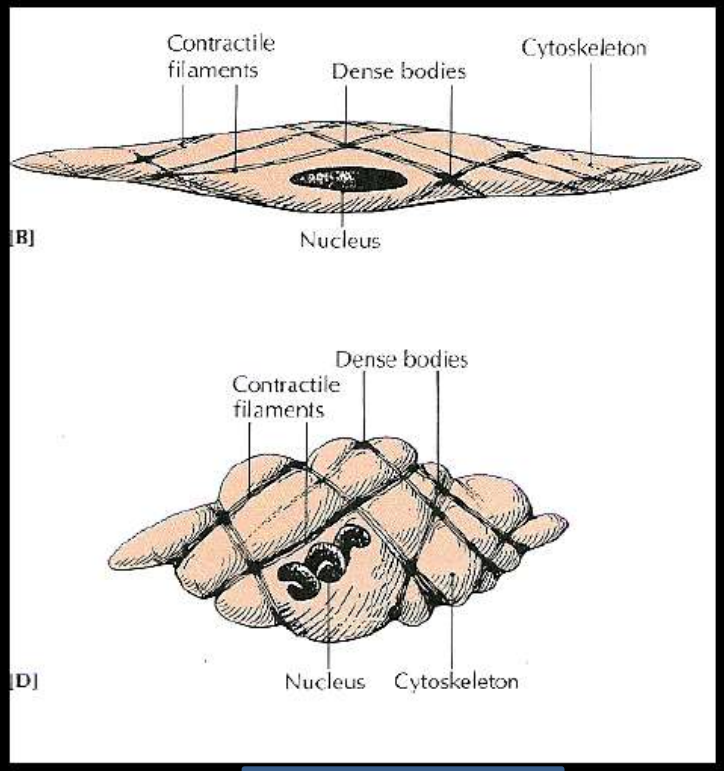


After Shahragim Tajbakhsh Current Opinion in Genetics & Development 2003, 13:413–422 és Charge´Sophie B. P. and Michael A. Rudnicki. *Physiol Rev* 84: 209–238, 2004;

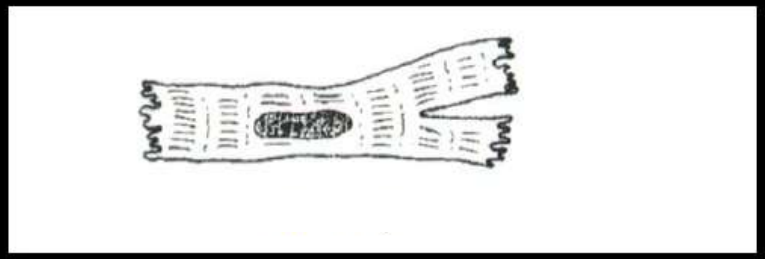
Smooth muscle

Units of different muscle types

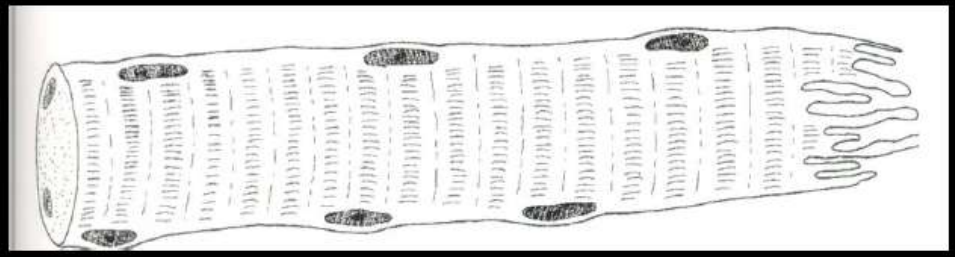
unit of smooth muscle



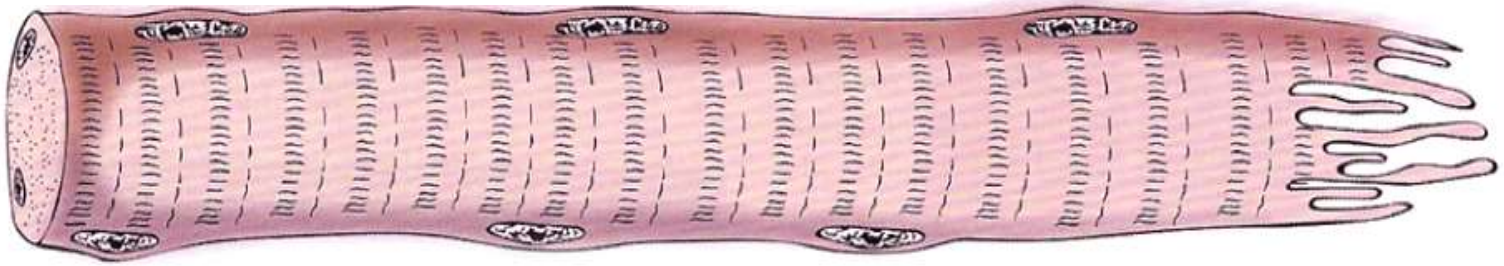
unit of cardiac muscle



unit of sceletal muscle



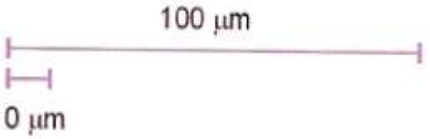
striated muscle fiber (up to several cms)

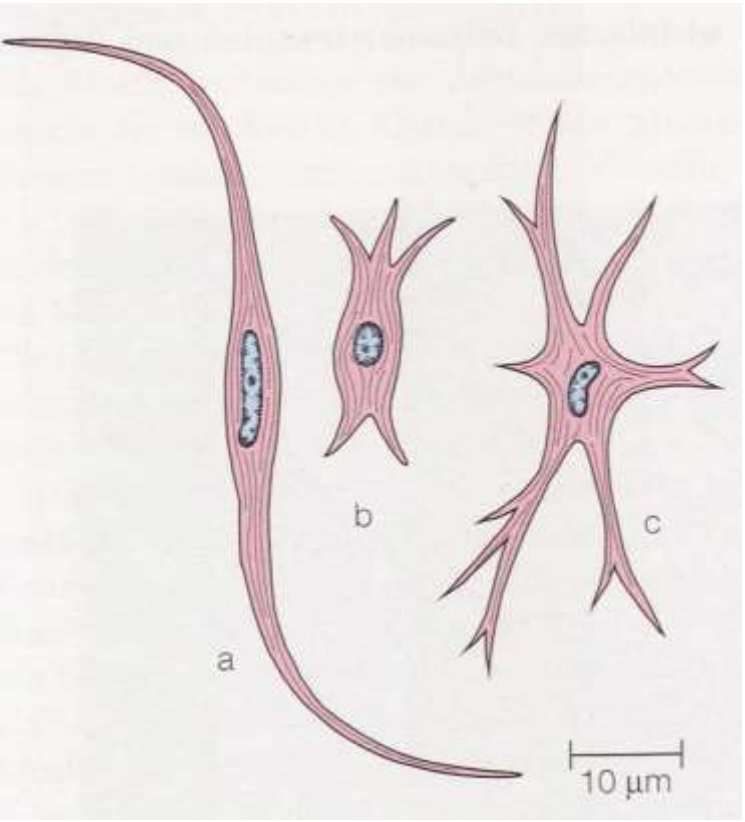


cardiomyocyte

smooth muscle cell from pregnant uterus

normal smooth muscle cell





Cells with spindle like morphology

Cell nucelus is flattened, central, euchromatic with rounded ends

Length: 20-500 µm, diameter: 5-10 µm

Membrana basalis

Forms layers

Spontaneous activity– pacemaker activity

Under control of autonomic nervous system

Under hormonal control

slow but persistent contraction

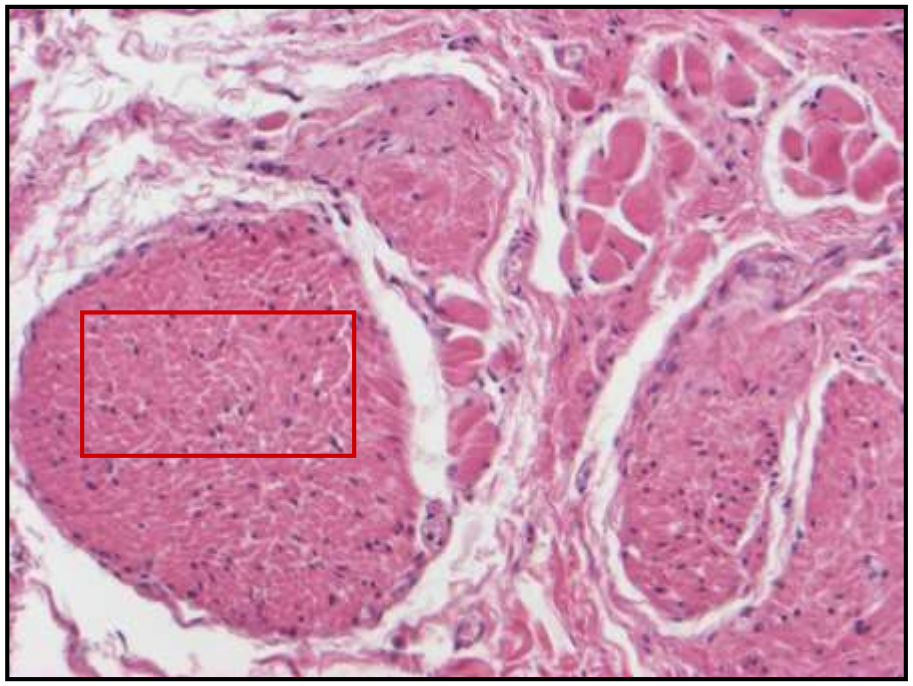
Minimal need of energy

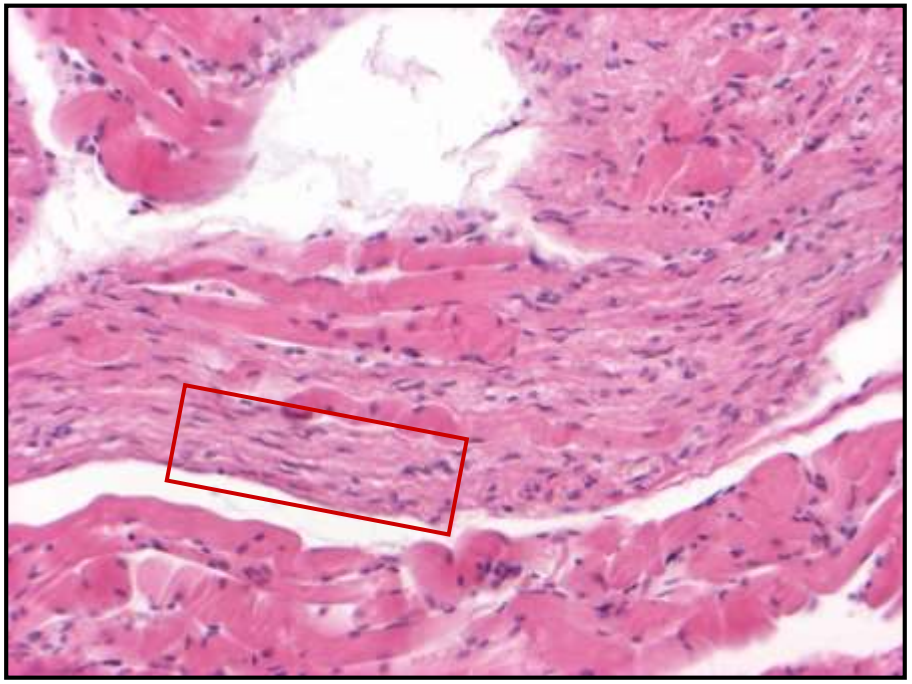
No striation

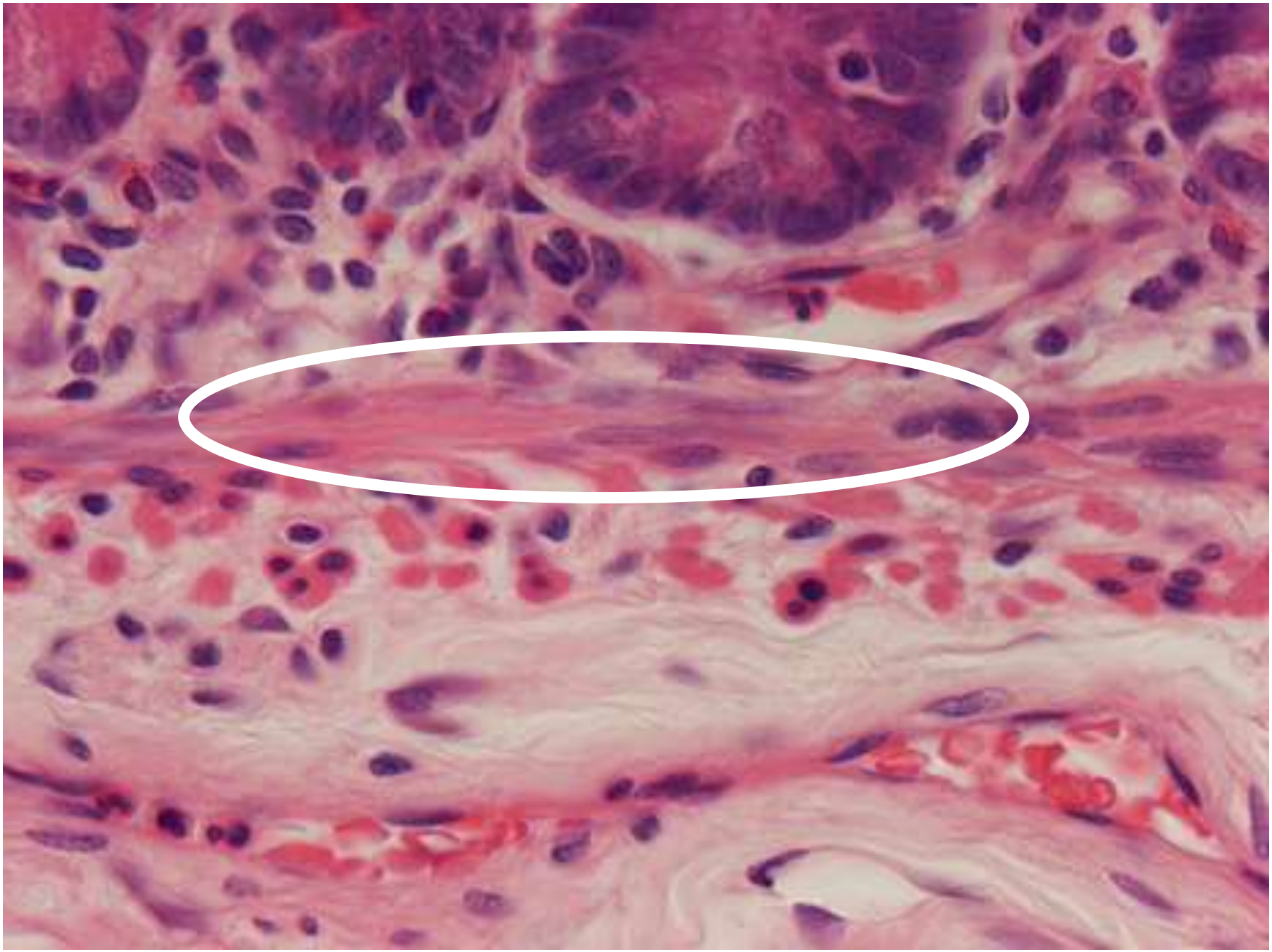
No Troponin

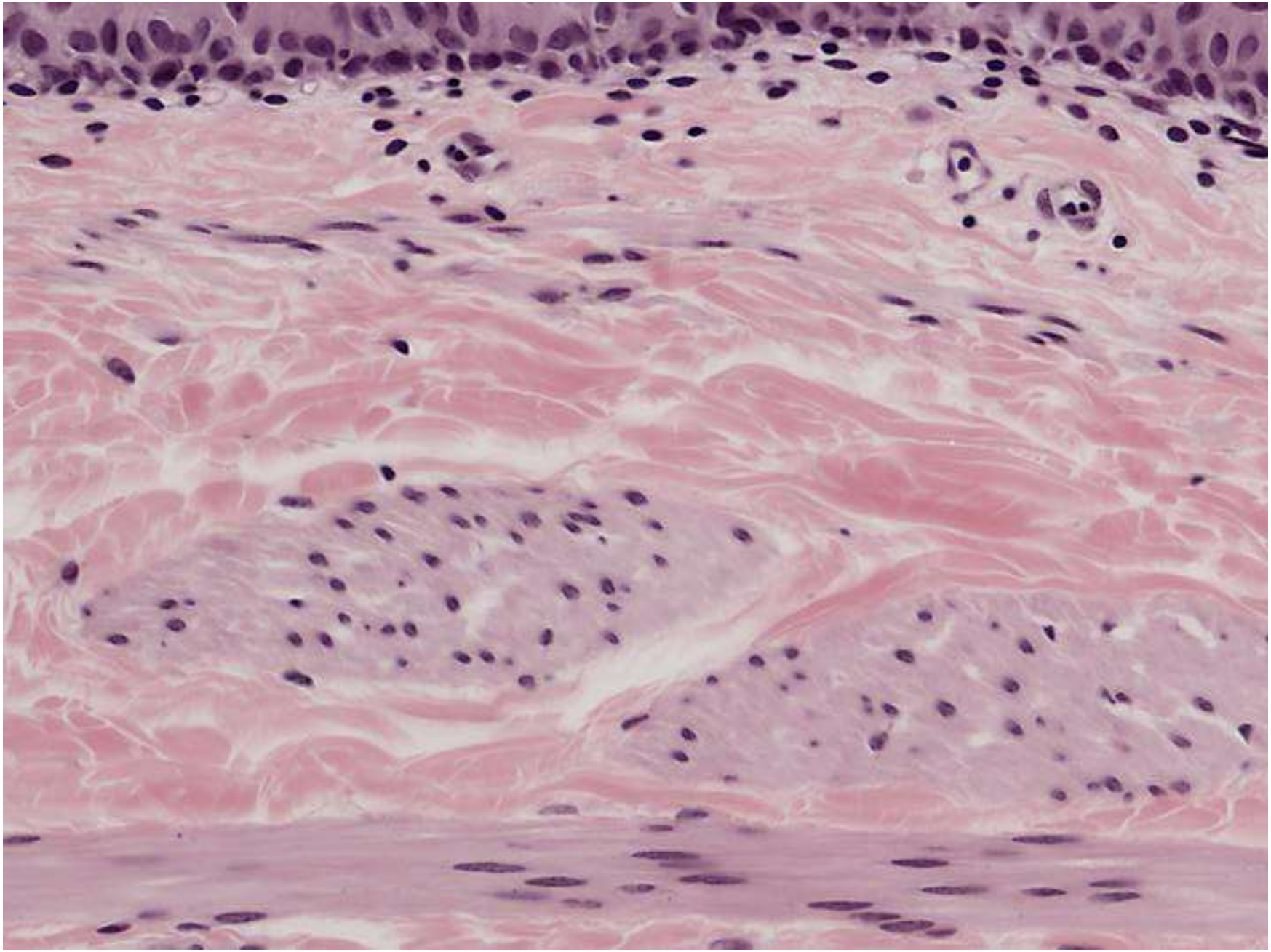
Where? In wall of splanchnic organs (like intestine)

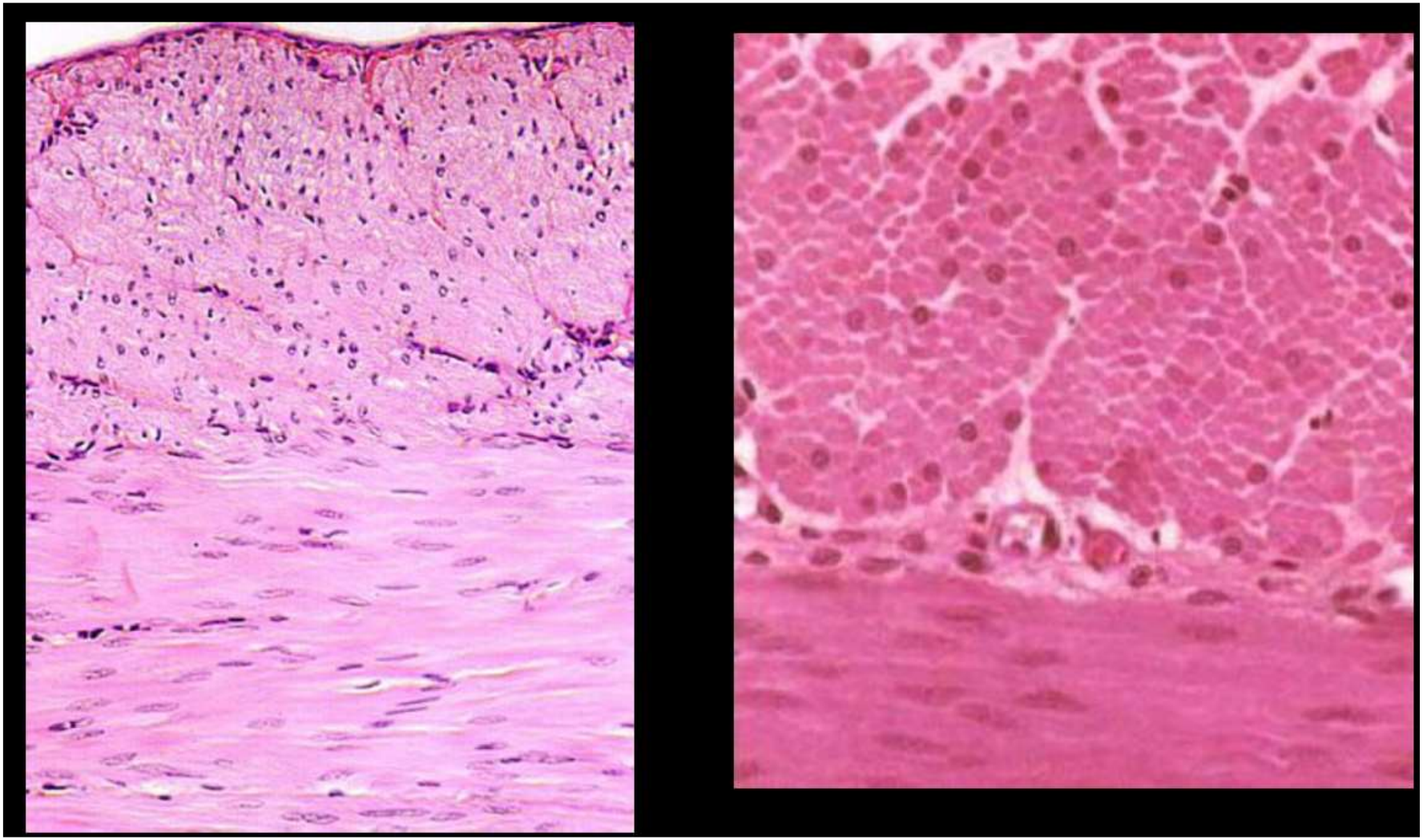
Smooth muscle – light microscopy

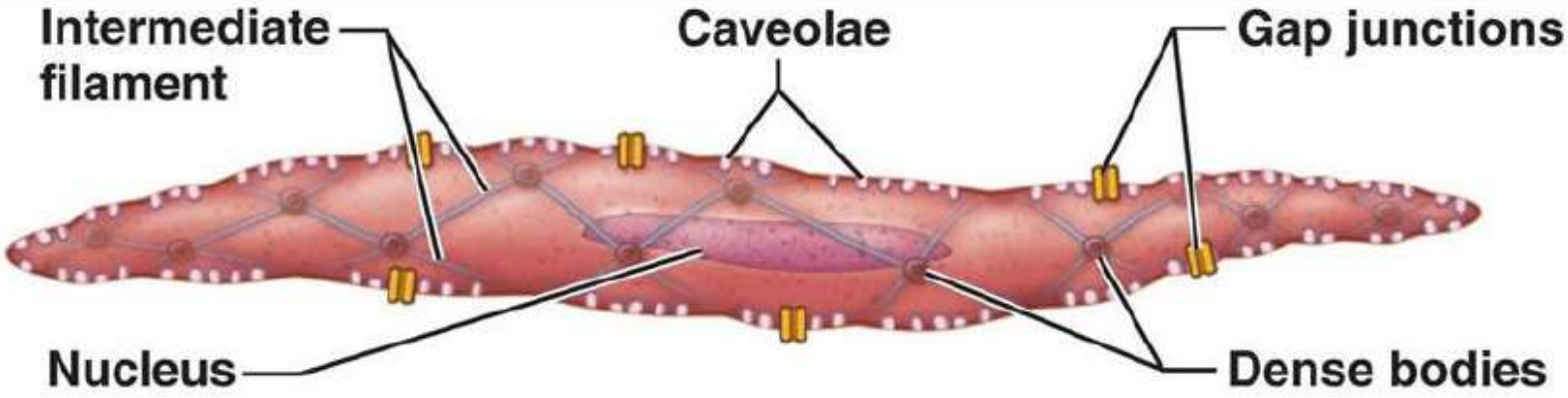




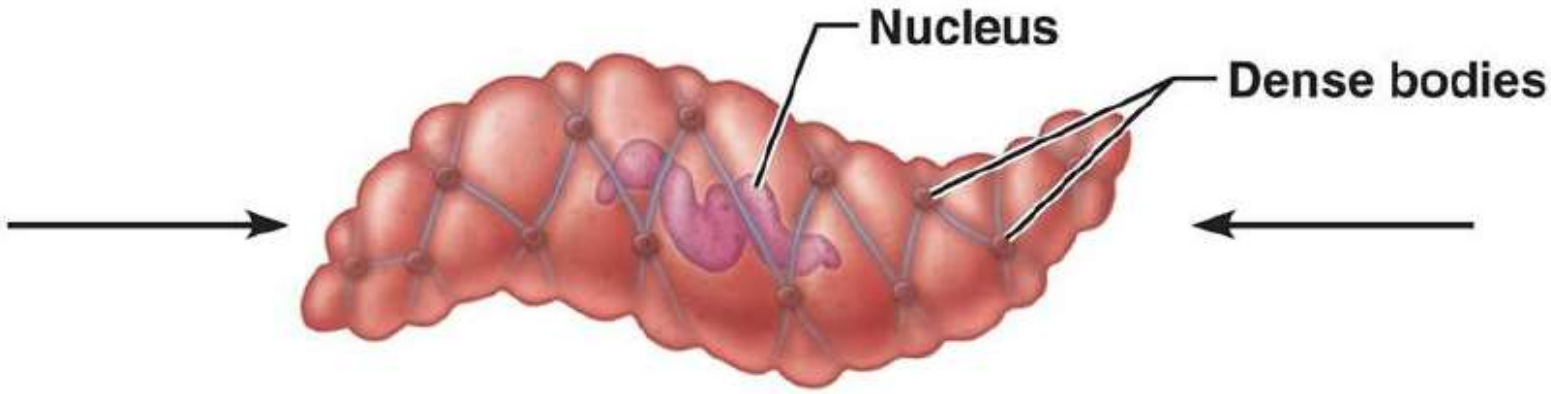






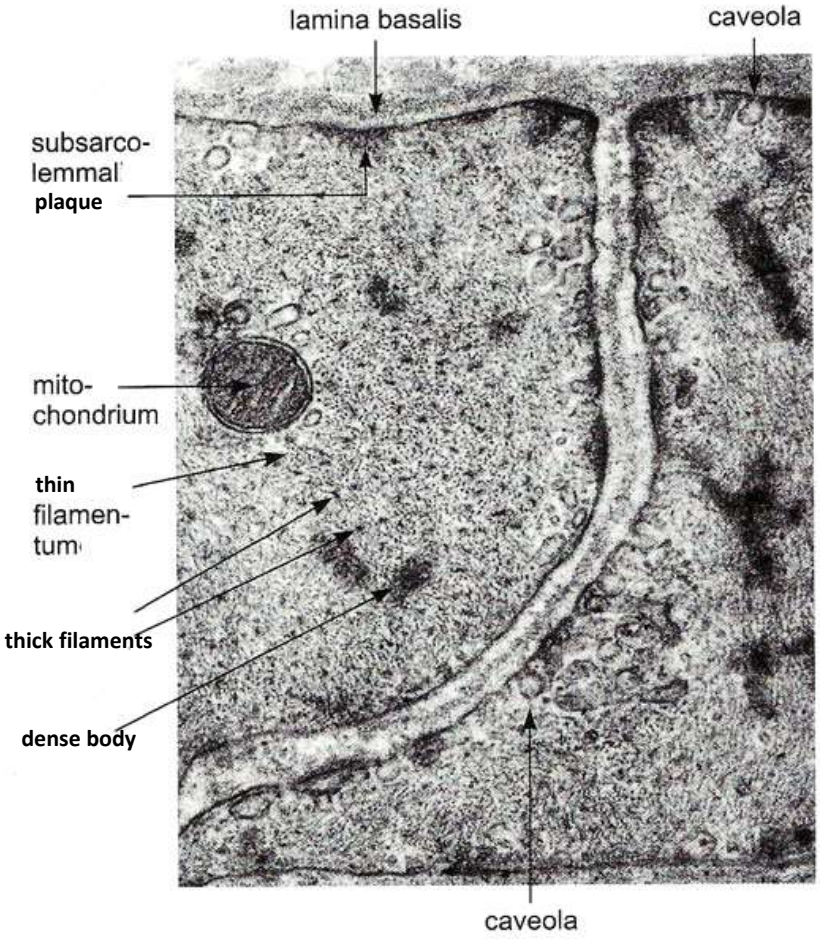


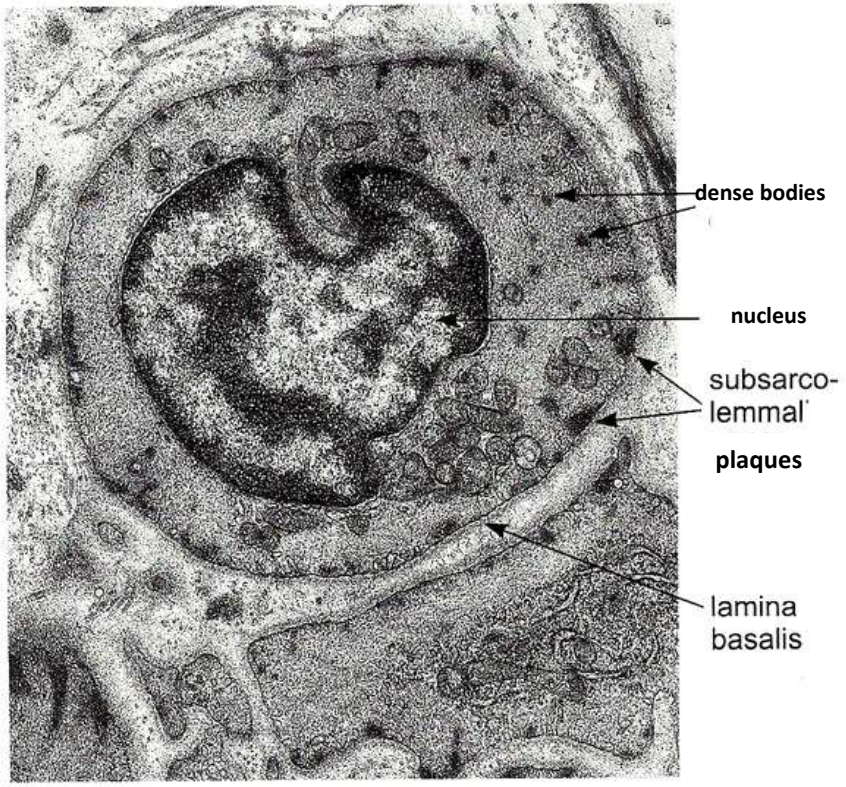
(a) Relaxed smooth muscle cell (note that gap junctions connect adjacent fibers)



(b) Contracted smooth muscle cell

Smooth muscle by TEM

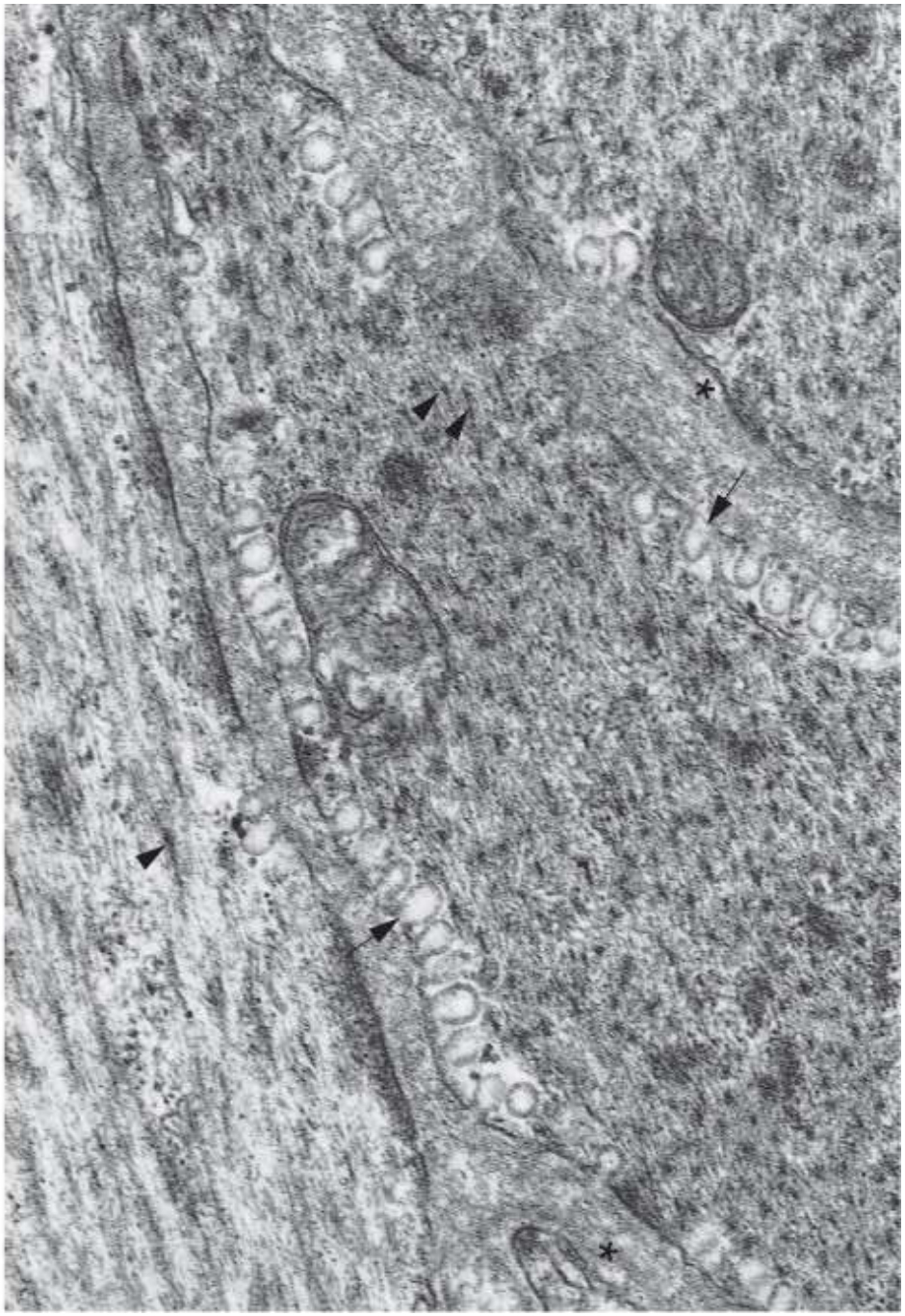


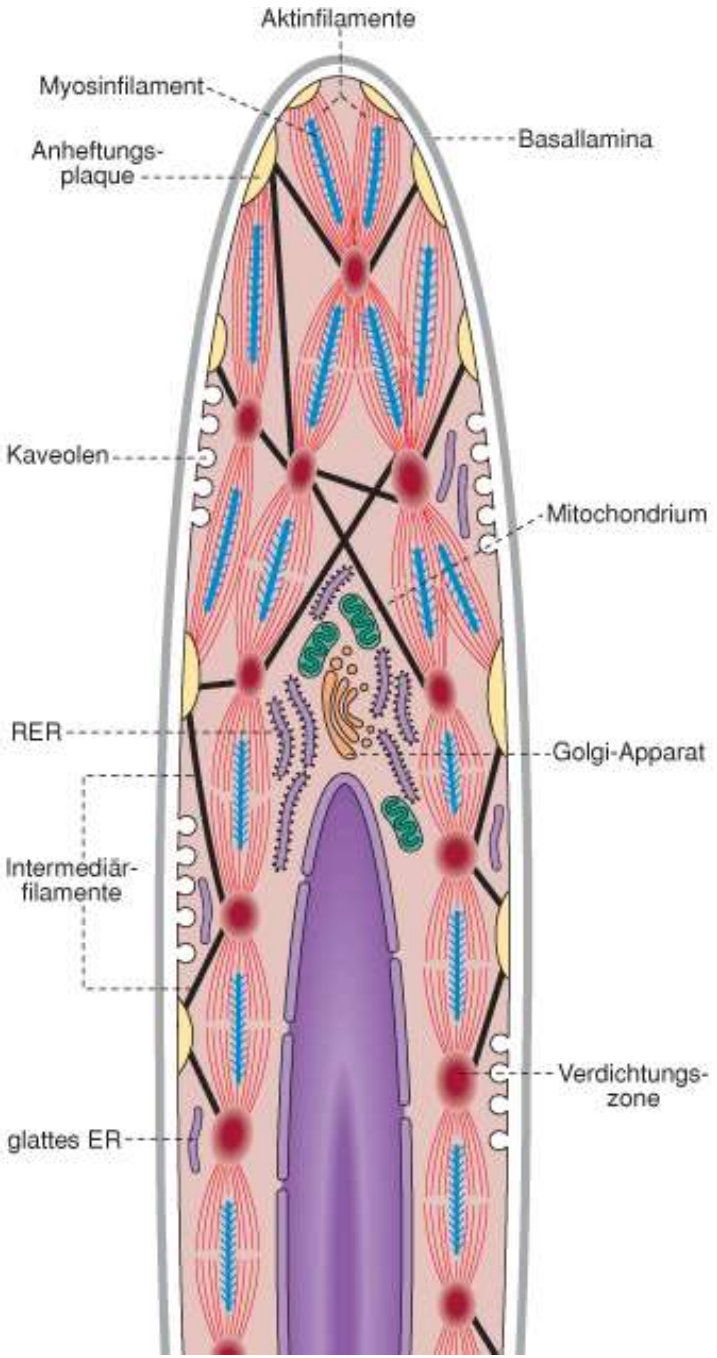


Dense bodies - actin filaments of contractile units are attached to *dense bodies*

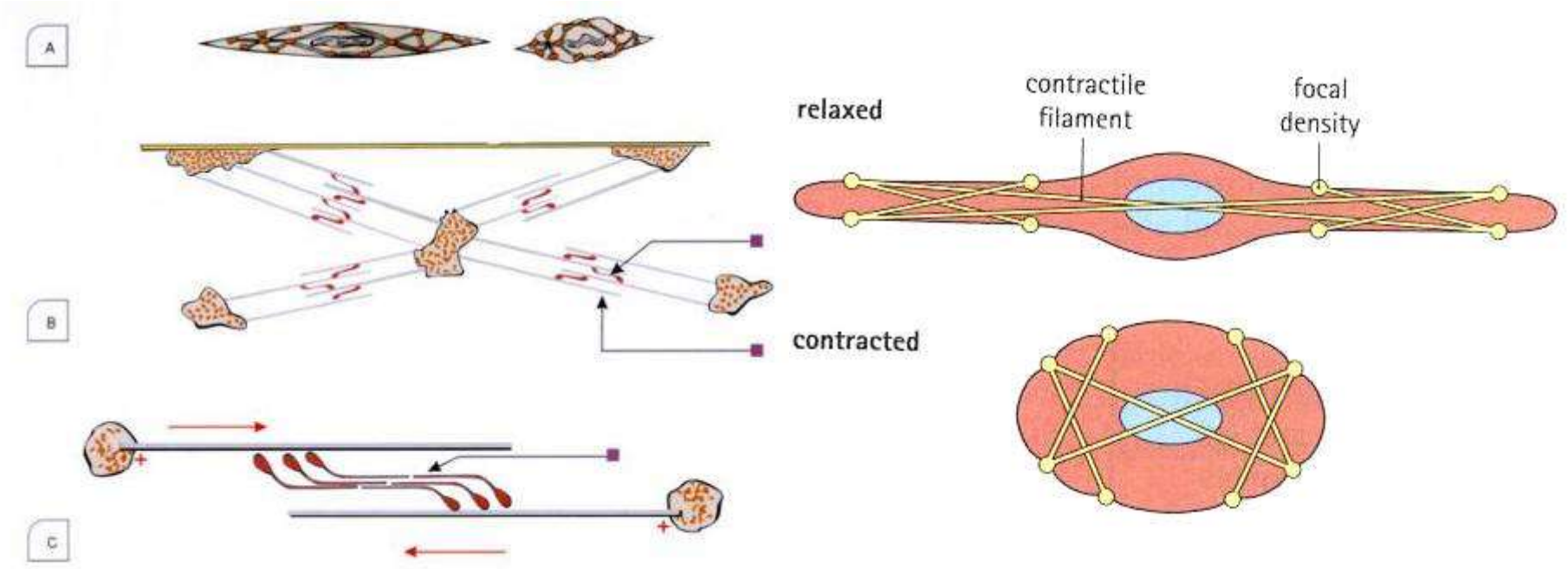
Dense bands (or dense subsarcolemmal plaques) - are circumfering the smooth muscle cell in a rib-like pattern

areas alternate with regions of membrane containing numerous caveolae




Aktinfilamente
Myosinfilament
Anheftungs-
plaque
Basallamina
Kaveolen
Mitochondrium
RER
Golgi-Apparat
Intermediär-
filamente
Verdichtungs-
zone
glattes ER

Mechanism of contraction



increase of Ca^{2+} concentration→ Ca^{2+} binds to calmodulin (instead of troponin) → calmodulin activates myosin light chain kinase (MLCC) → the enzime phosphorilates myosin→ activated myosine binds to actin→ contraction

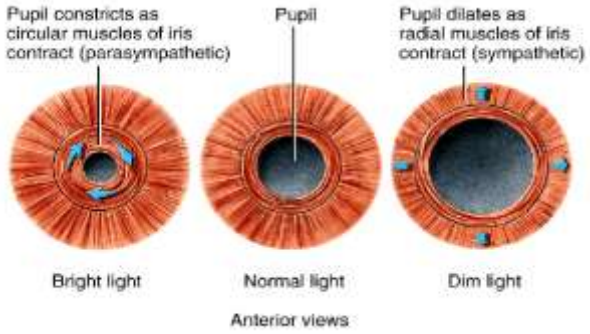
If myosin is dephosphorylated in the actin-bound state, it remains bound to the actin lasting contraction without additional energy input!

Types of smooth muscle

Multiunit:

- individual cells, each has its own innervation (no electric connection)
- well regulated
- contraction due to innervation

example: m. sphincter pupillae, m. ciliaris



Single unit:

- electrical and mechanical connection (gap junction)
- functional unit, functional syncitium
- innervation has secondary importance *(except in yogis* ☺)
-almost all smooth muscle

example: wall of organs like intestine

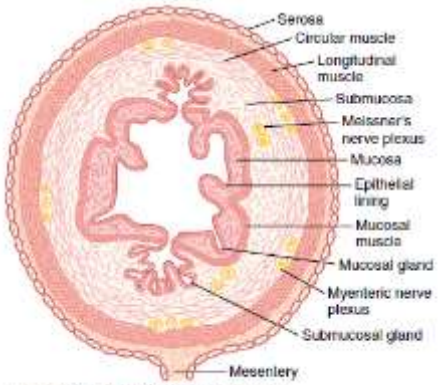
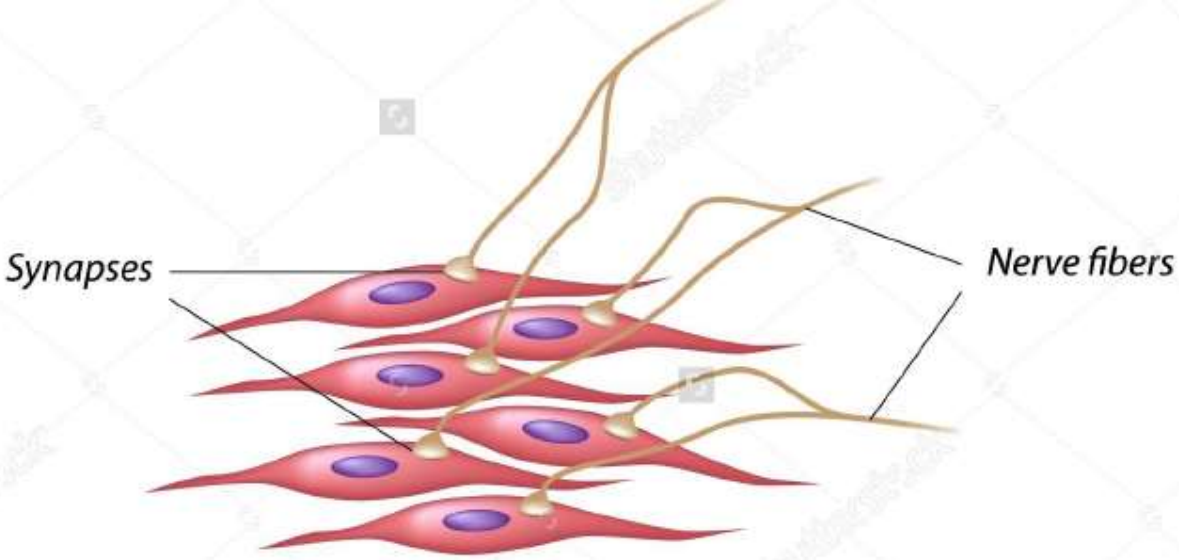
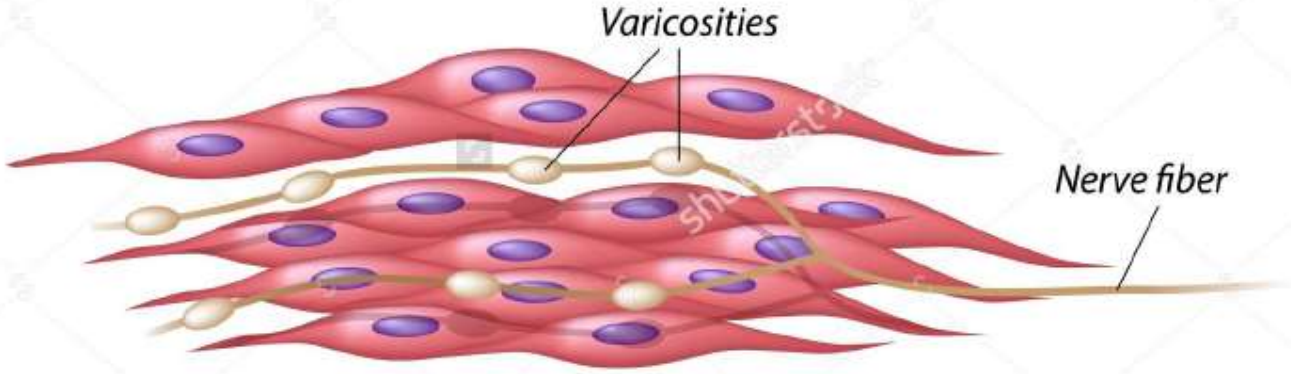


Figure 62-2 Typical cross section of the gut.



Multiunit Smooth Muscle



Single-unit Smooth Muscle

Striated muscle

Multi-nucleated giant cells, forming by fusion of myoblasts (syncytium) – **muscle fiber**

Membrana basalis

Stem cells – **Satellite cells**

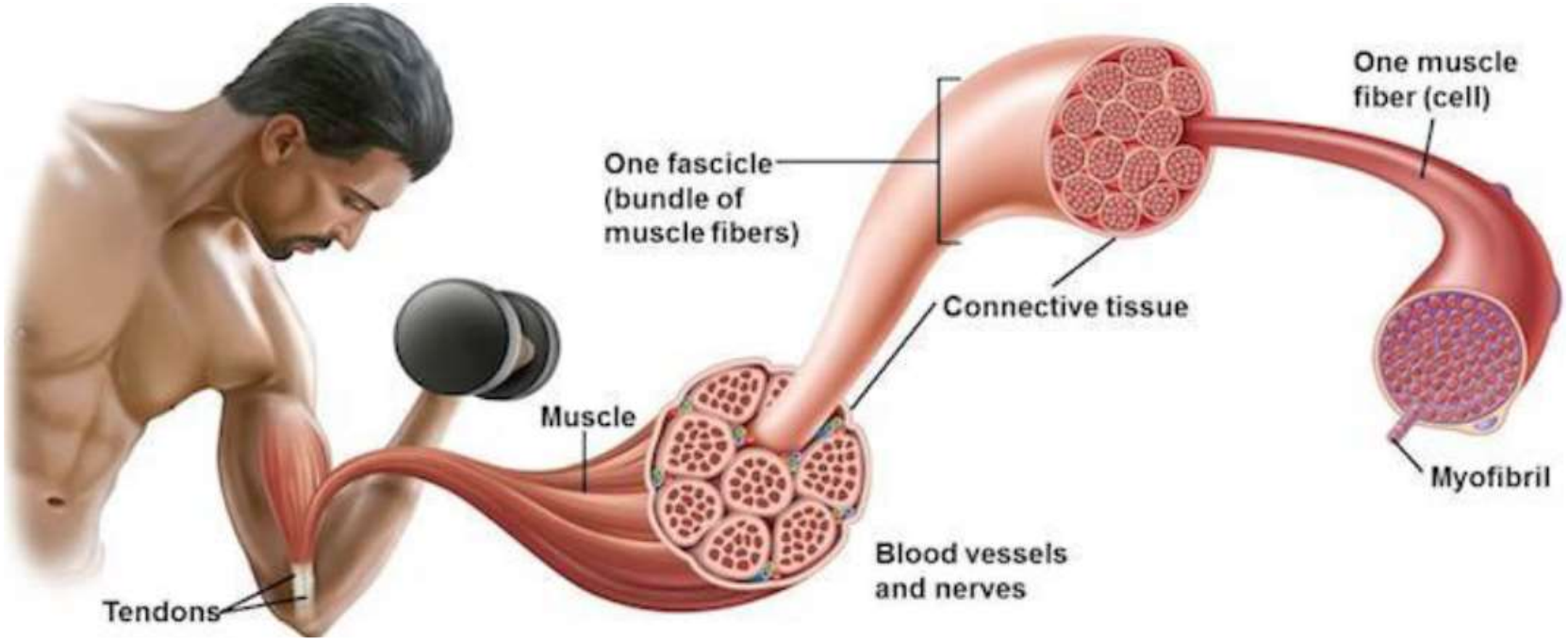
Plasmamembrane - **Sarcolemma**

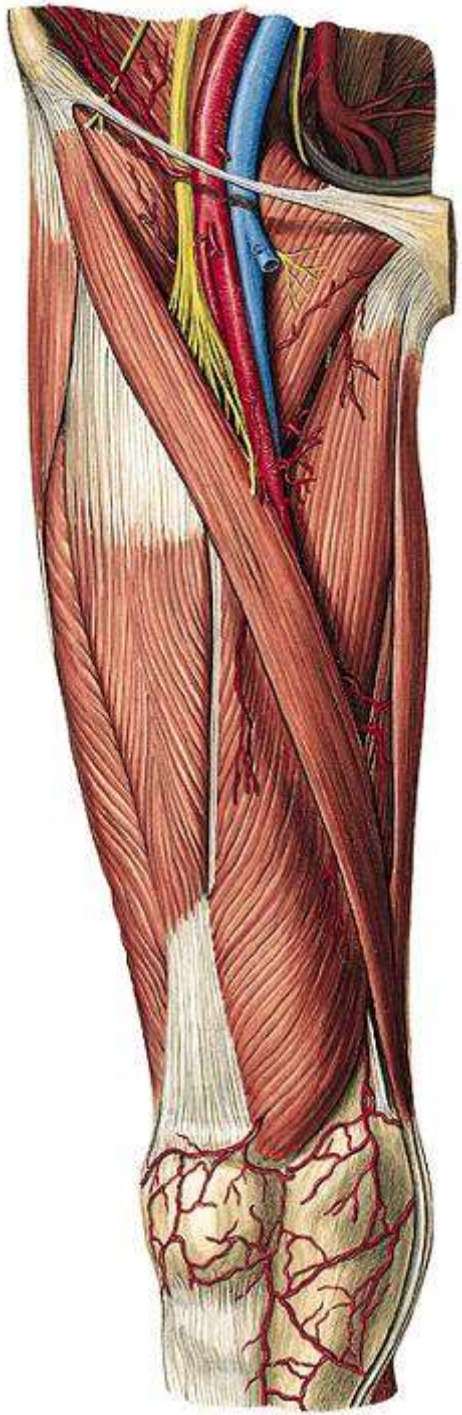
Cytoplasme **- Sarcoplasme**

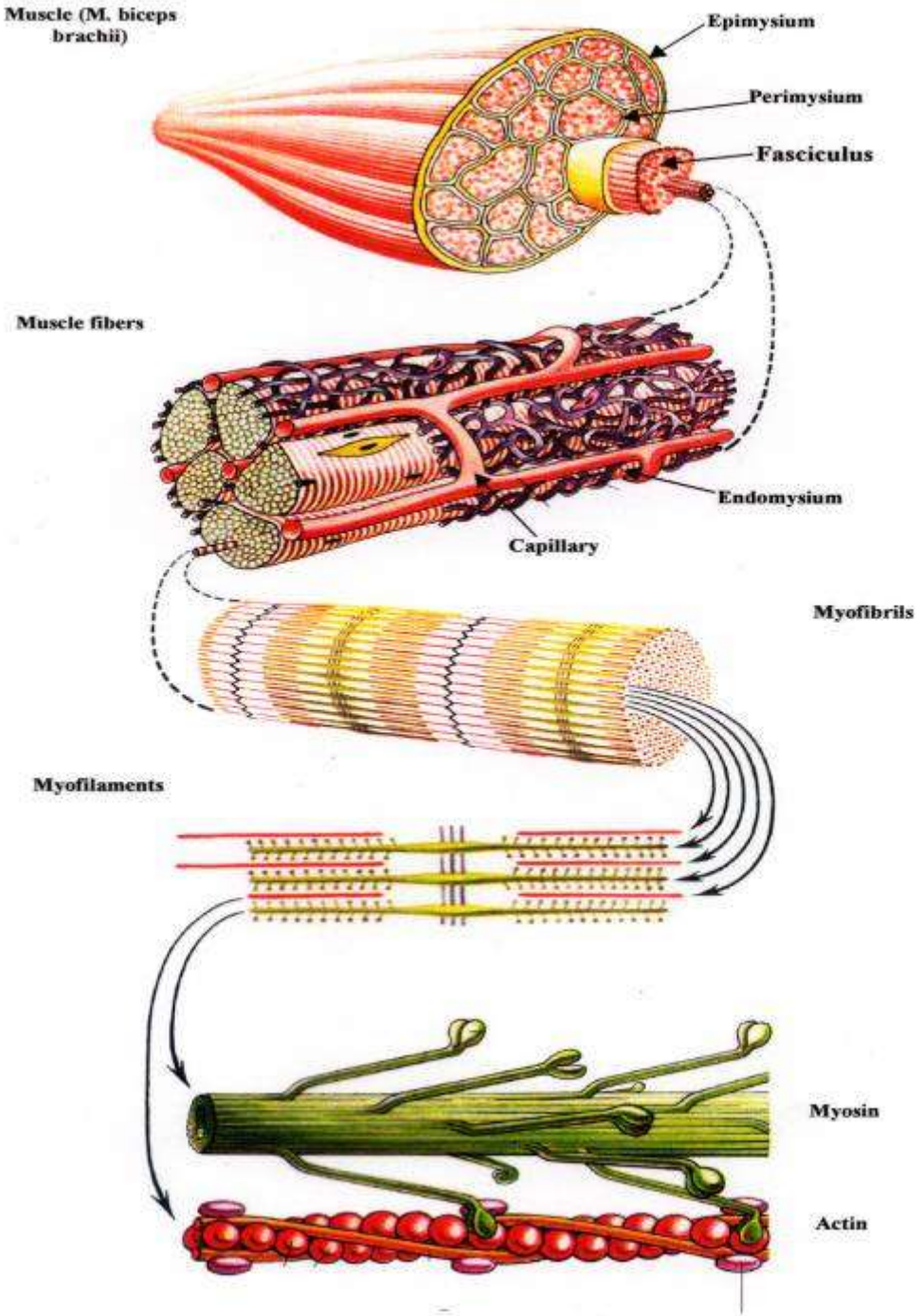
Smooth ER – **Sarcoplasmic reticulum**

Mitochondria **- Sarcosome**

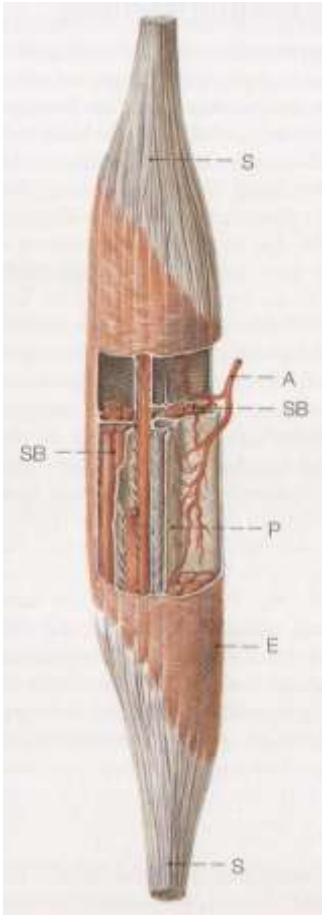
Contractile unit- **Sarcomer**


One muscle fiber (cell)
One fascicle (bundle of muscle fibers)
Connective tissue
Muscle
Myofibril
Blood vessels and nerves
Tendons

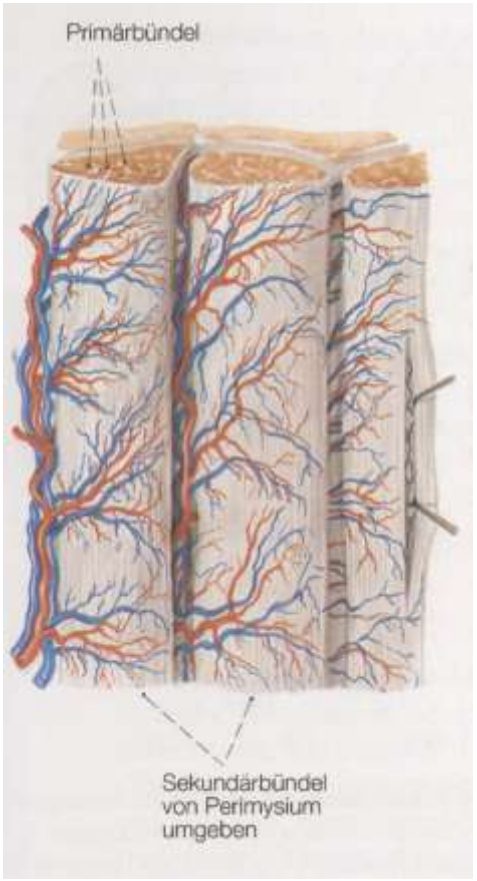



Muscle (M. biceps brachii)
Epimysium
Perimysium
Fasciculus
Muscle fibers
Endomysium
Capillary
Myofibrils
Myofilaments
Myosin
Actin

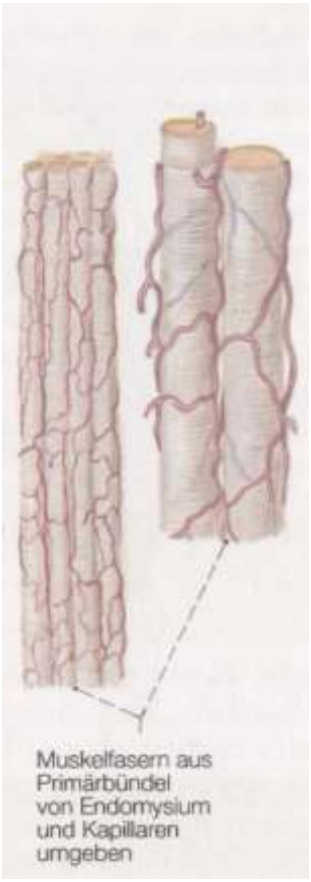
Connective tissue surronding sceletal muscle



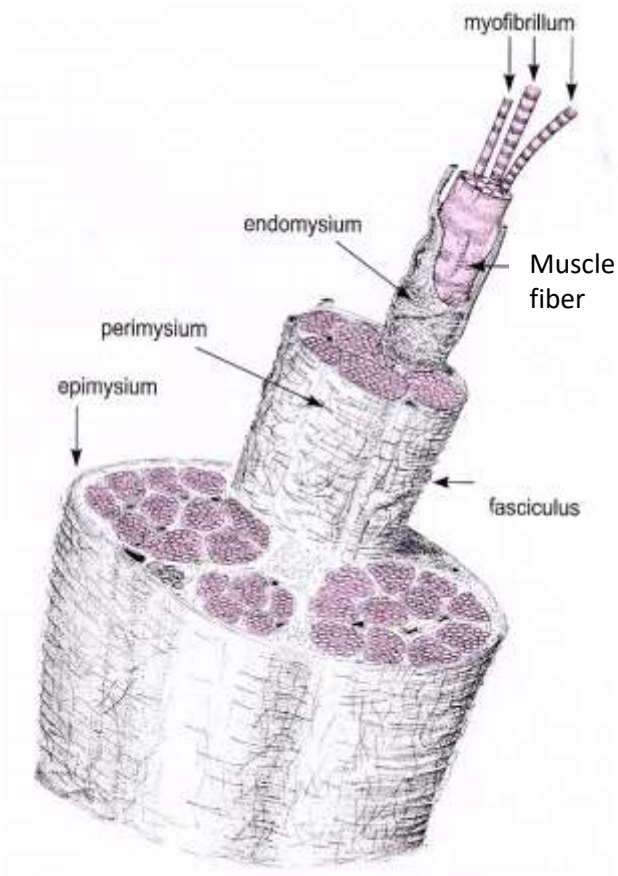
Epimysium
Dense CT

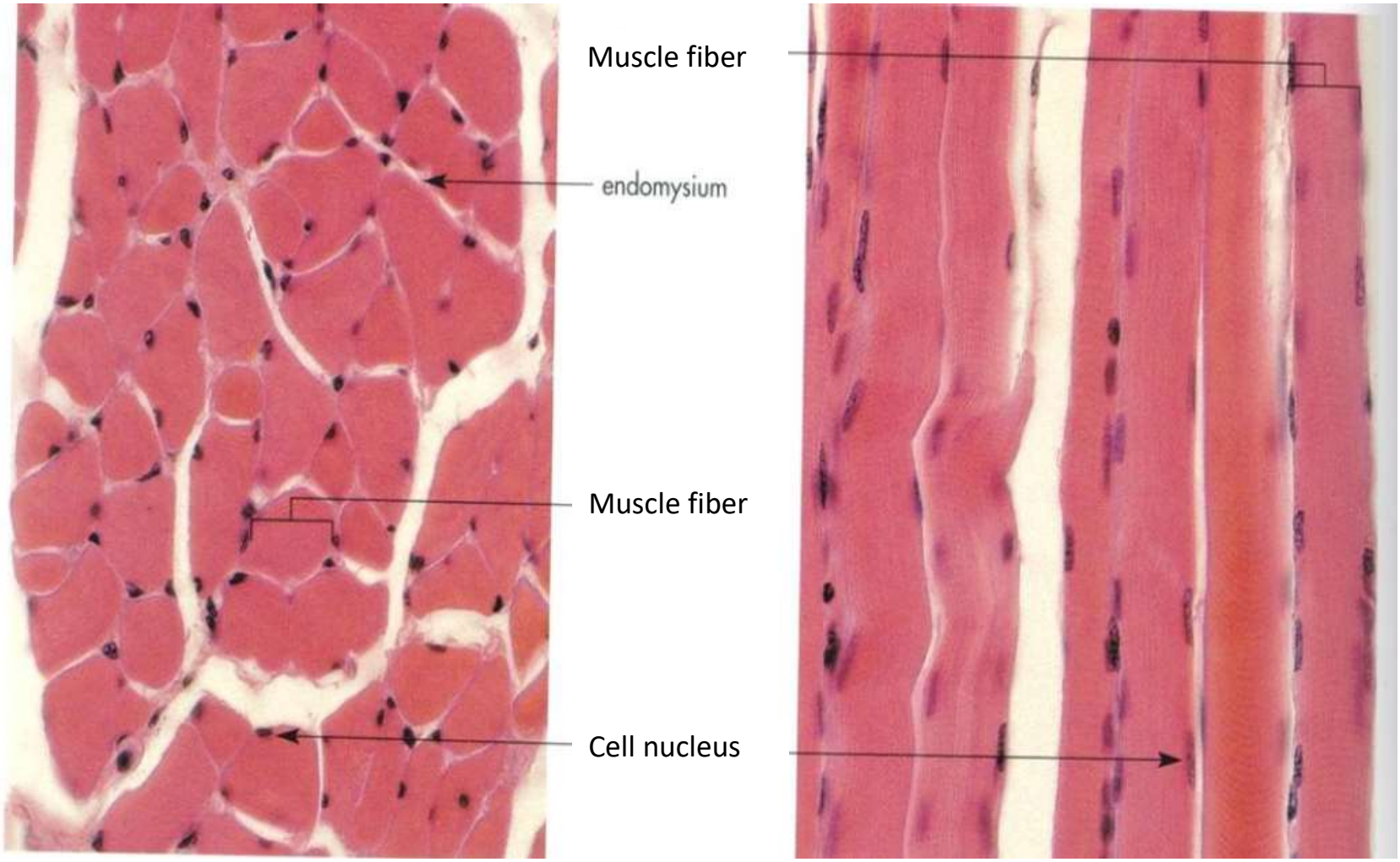


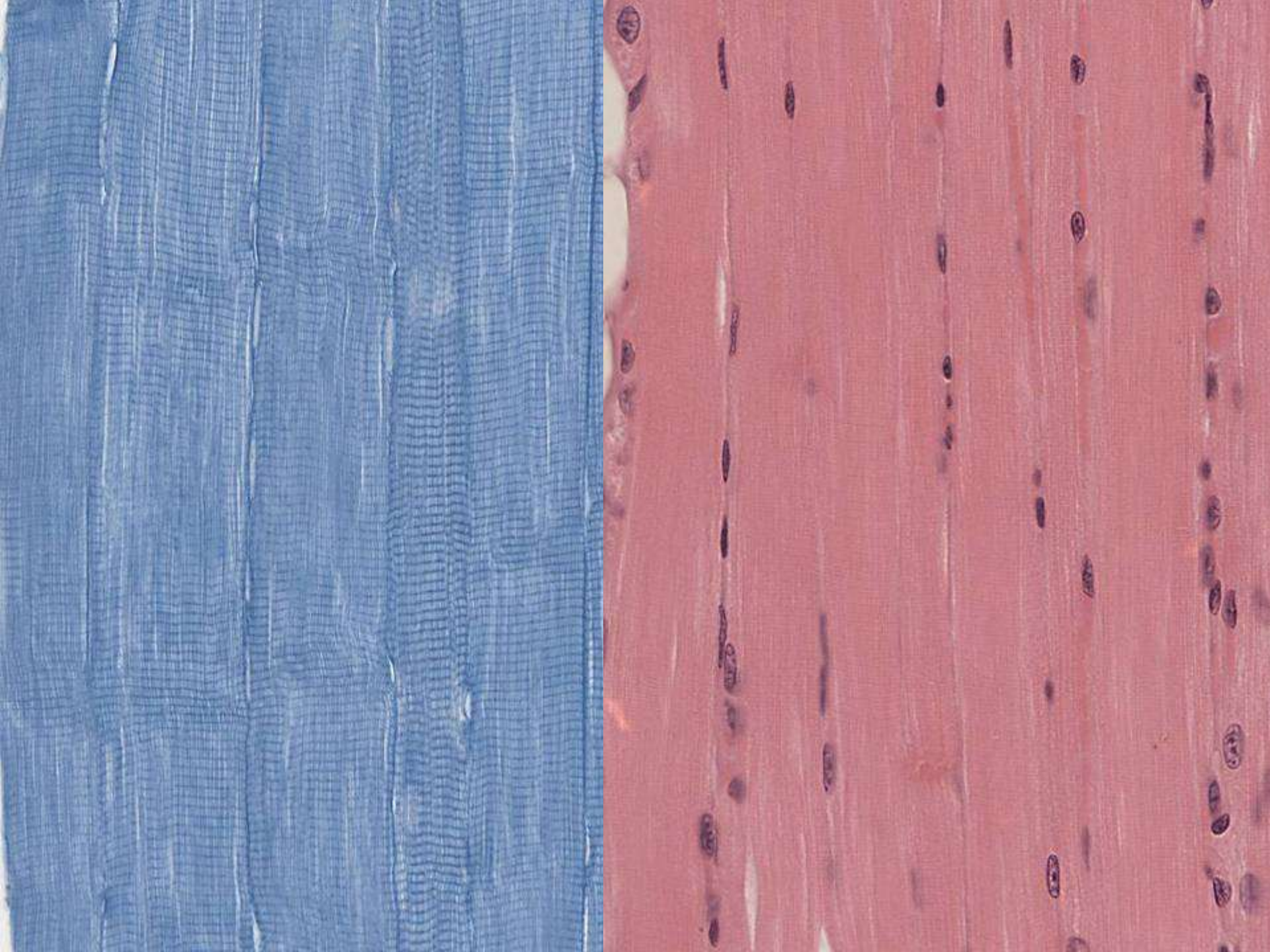
Perimysium
derives from epimysium

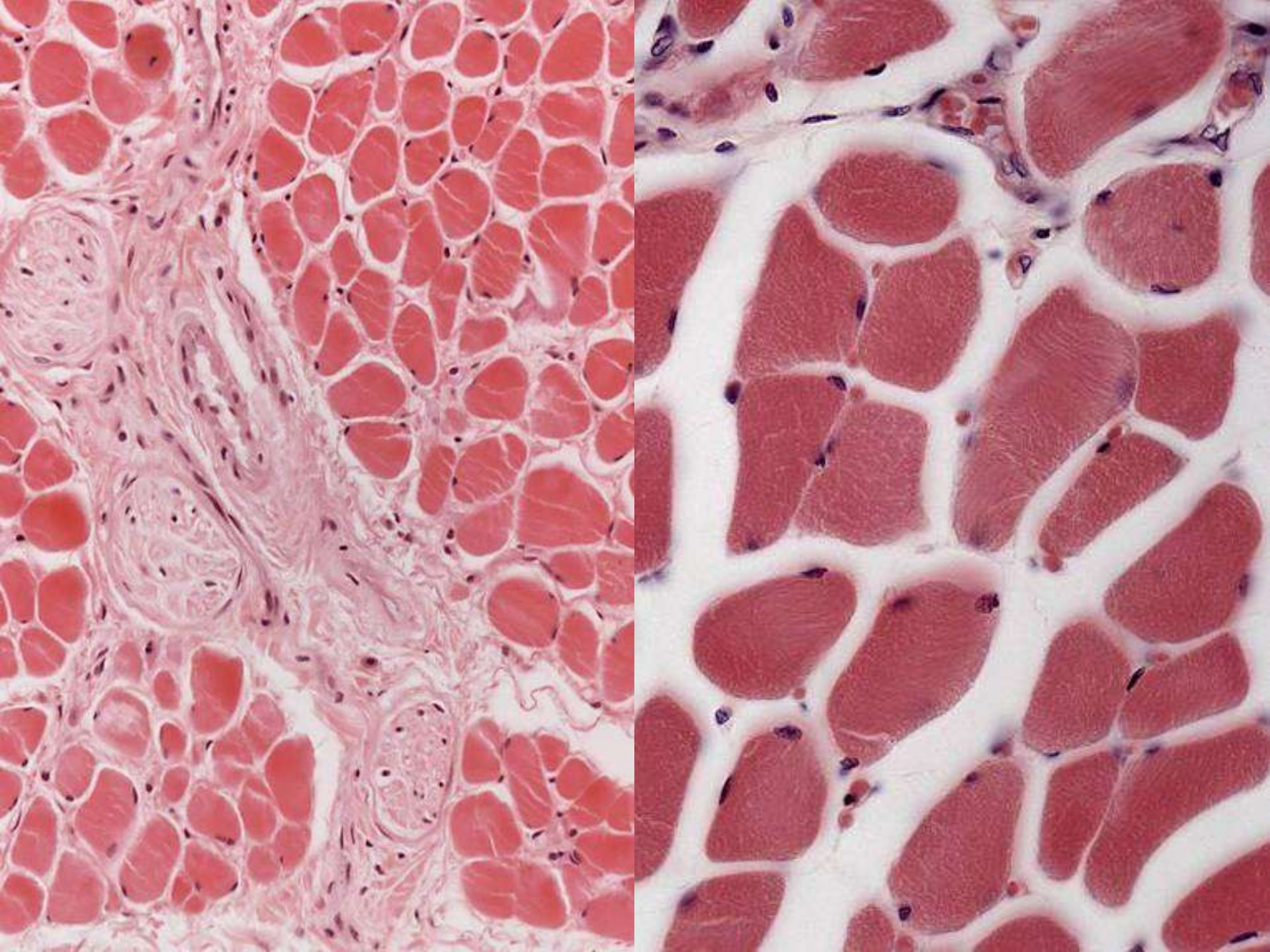


Endomysium
Reticular fibers and ECM

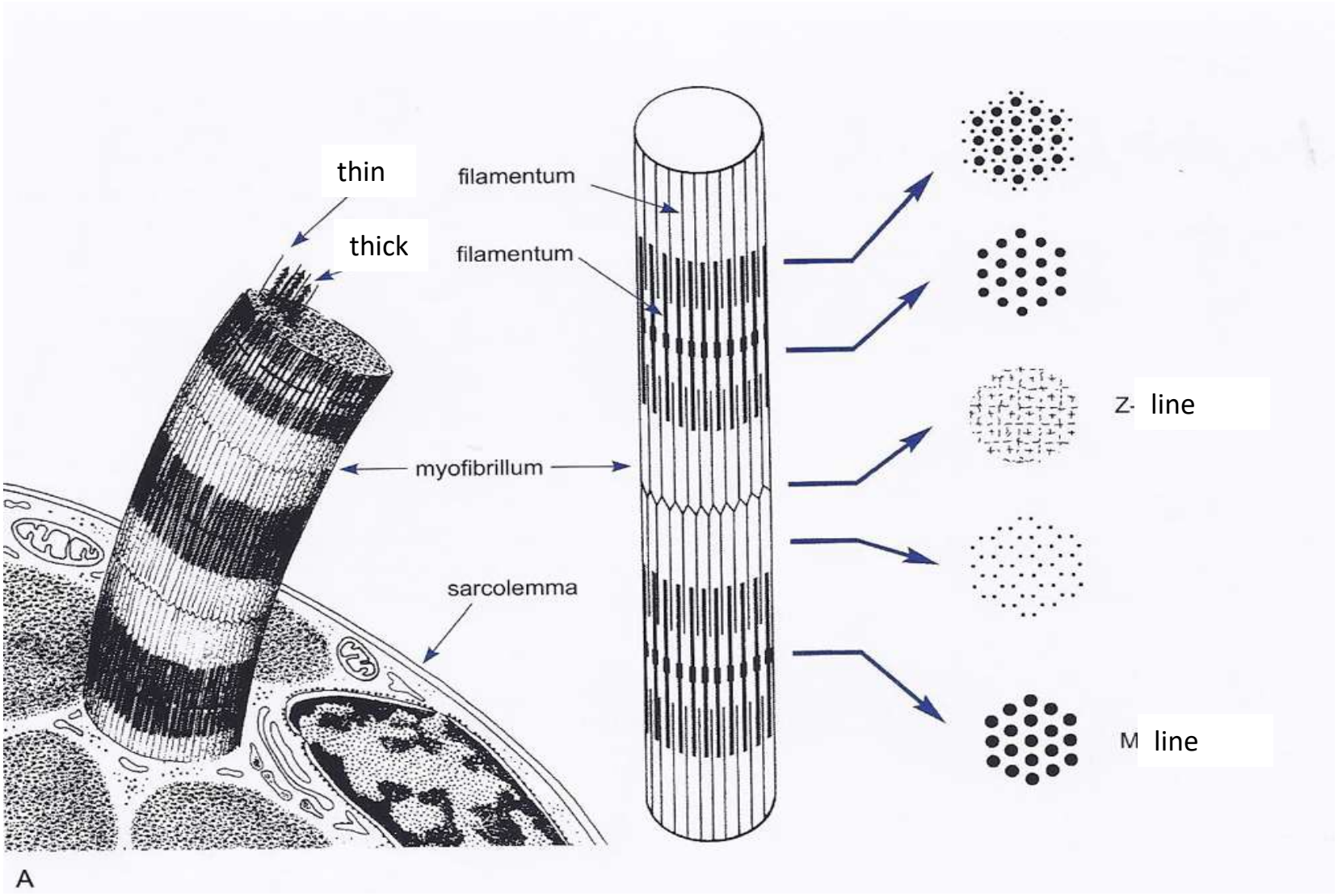


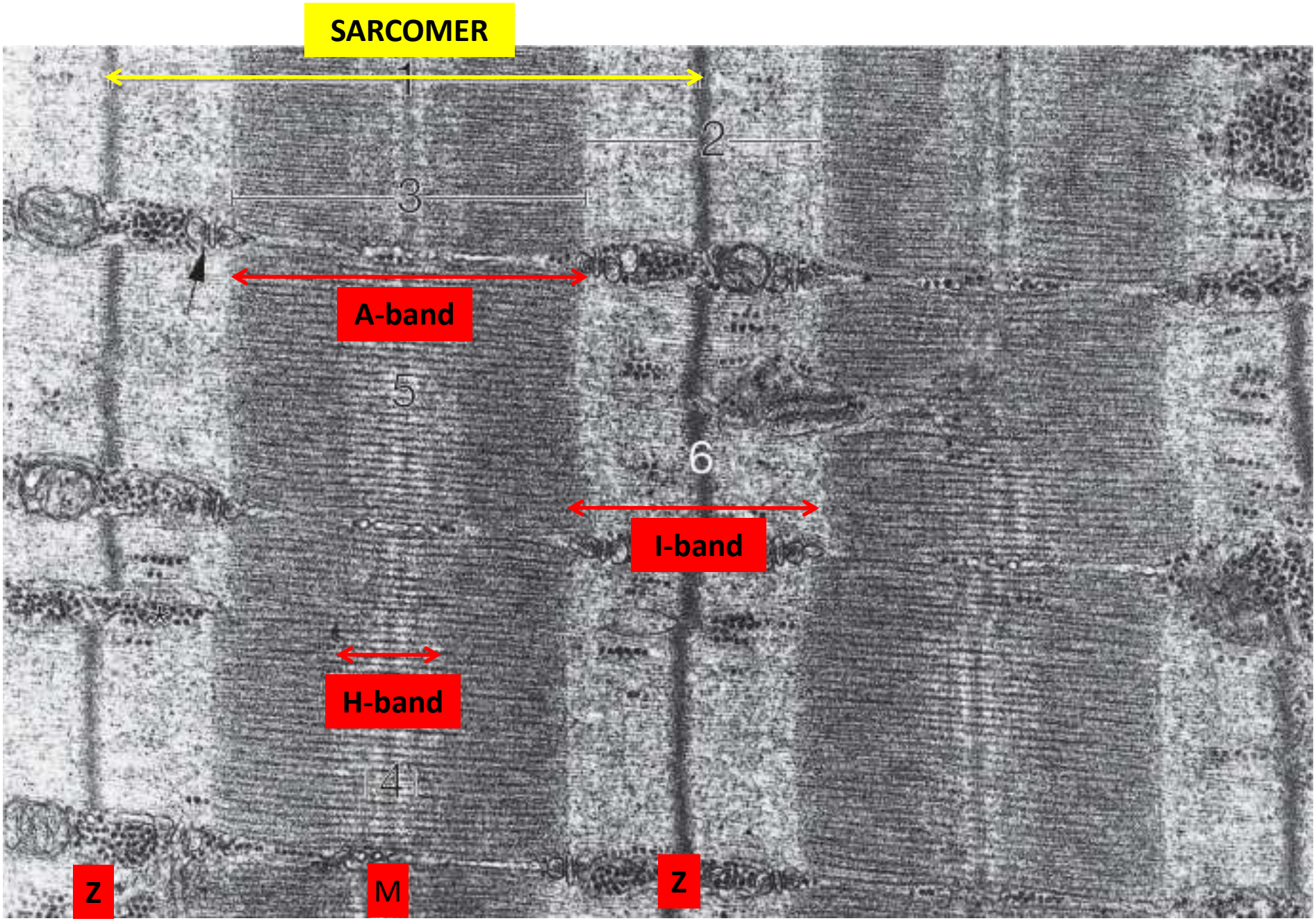

Muscle fiber
endomysium
Muscle fiber
Cell nucleus



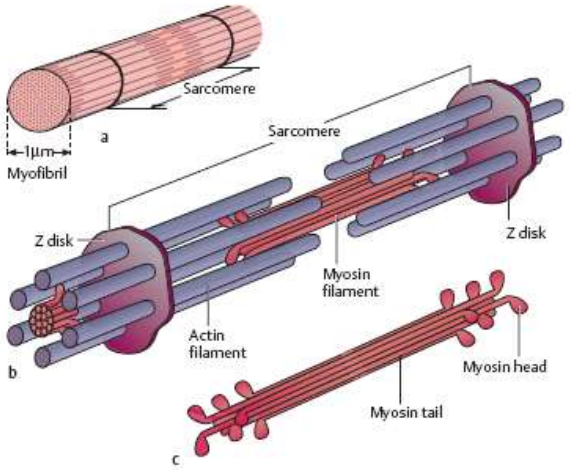


Structure of myofibrillum




SARCOMER
1
2
3
A-band
5
6
I-band
H-band
4
Z
M
Z

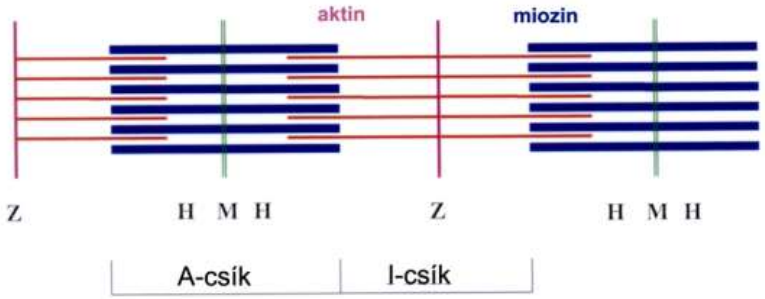
Sarcomer: (2-3 µm) between Z lines



A-band: anisotrop, double refractive, thick, dense
(1,5 µm long, 15 nm thick)
mainly myosin + overlapping actin filaments
its length remains unchanged during contraction

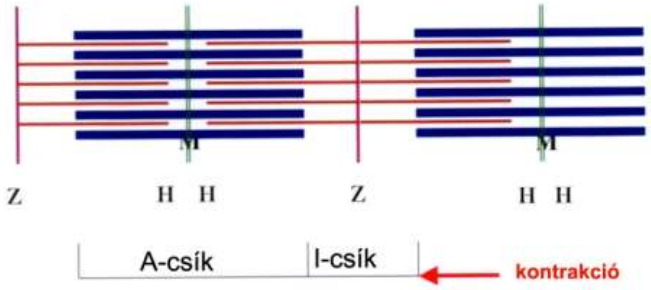
I-band: isotrop, simple refractive, thinner, ligther
(1 µm long, 7 nm thick)
mainly actin
shortens during contraction

Z-line: (Zwischenstreifen, intermediate tapes)
border of sarcomer
α-Actinin, Desmin molecules

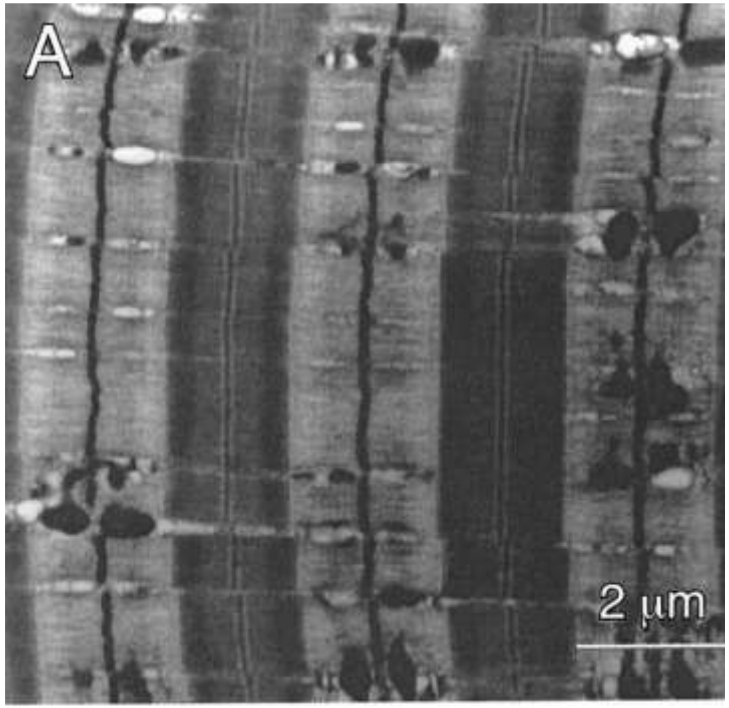


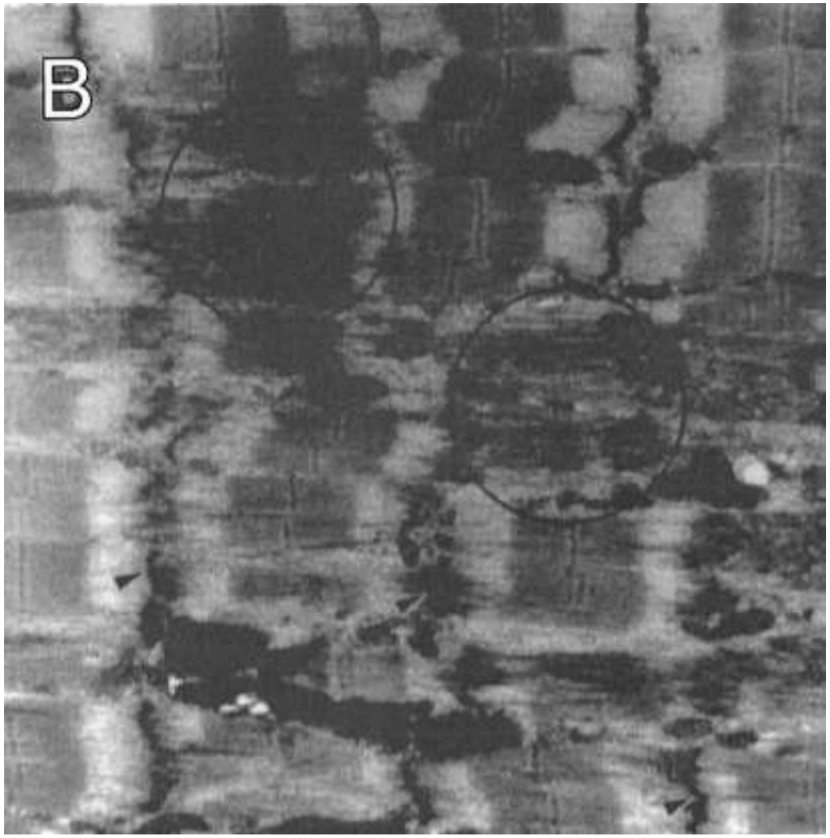
H-band: (Hensen-Streifen)
lighter area in A-band
only Myosin

M-line: (Mittenmembran) middle membrane
in the middle of A-band
attachement of myosin bundles



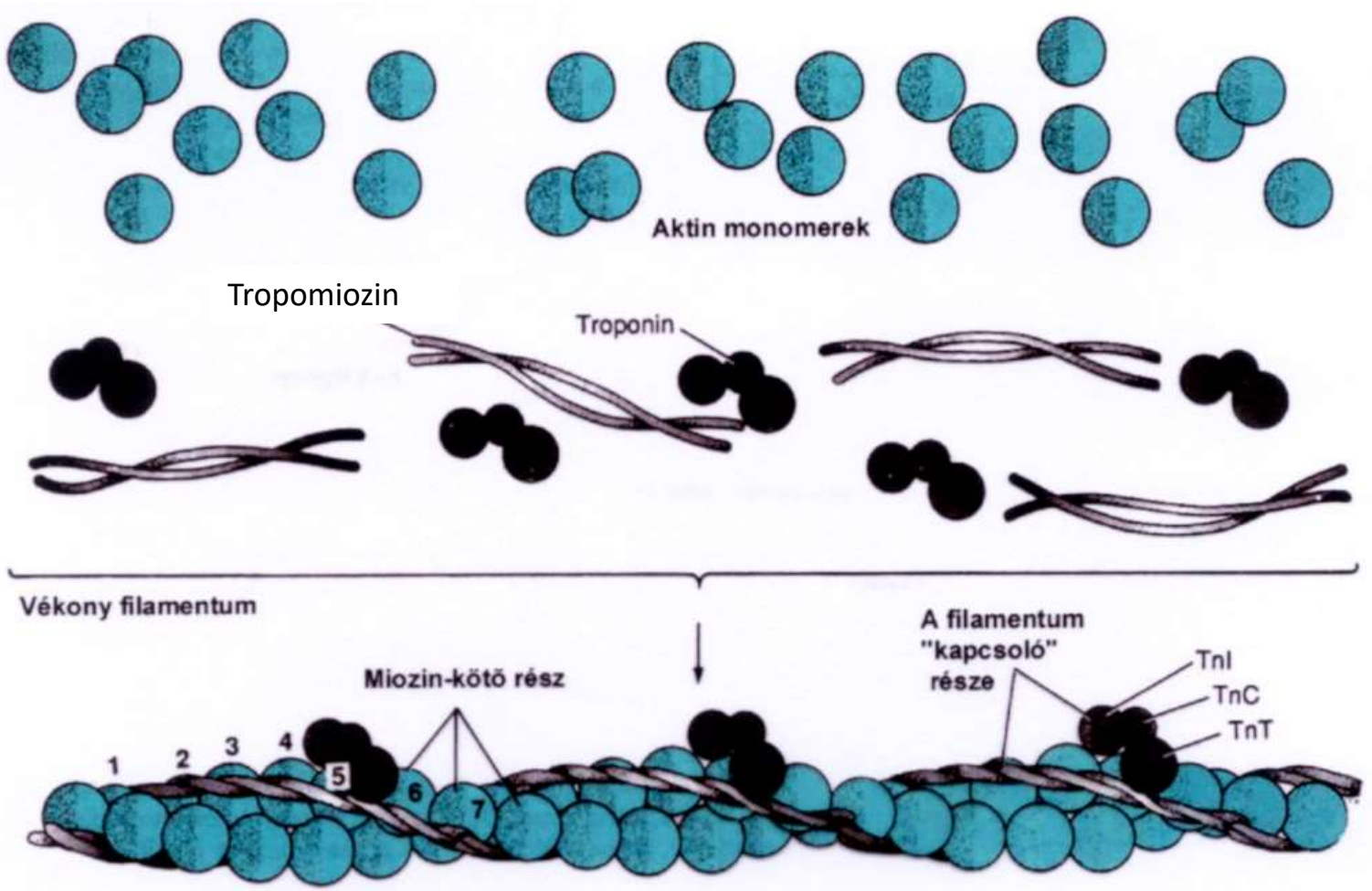
Muscle fever





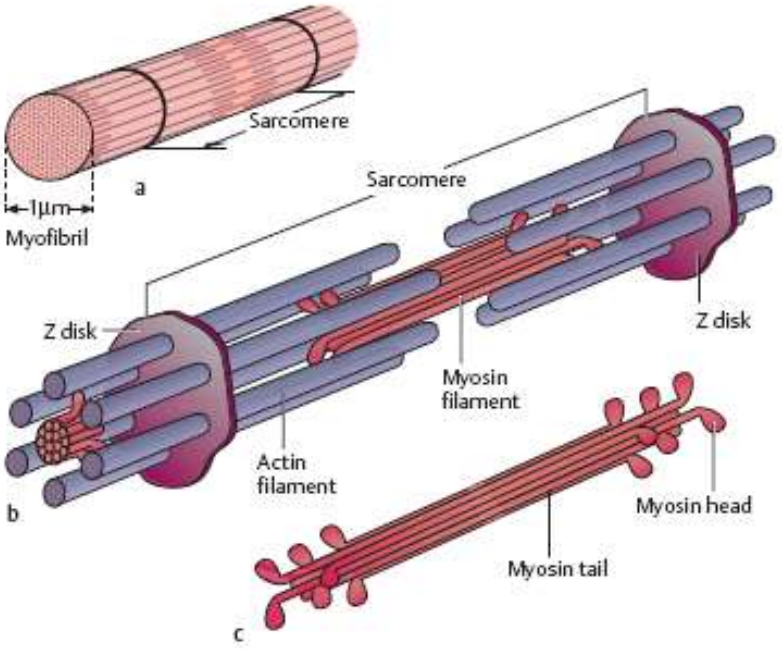
- micro tears
- Inflammation – leukocytes, monocytes
- cytokins – directly activate
- nociceptive receptors

Miofilament: Actin



Troponin, Tropomyosin, Nebulin: needed for structural identity

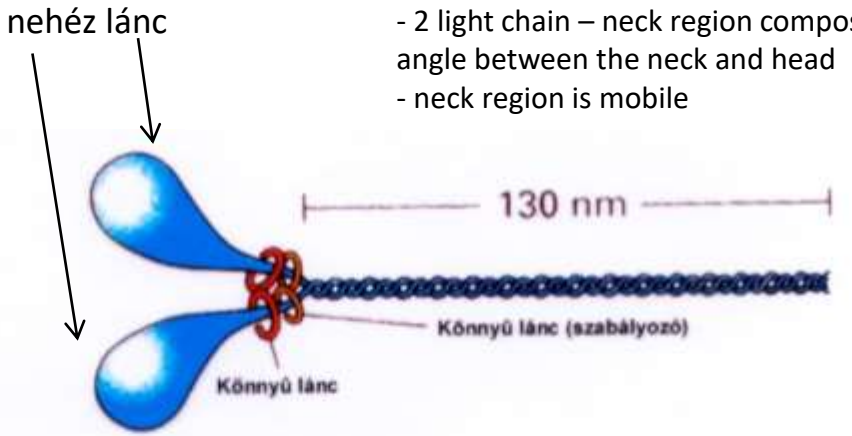
Miofilament: type II. myosin

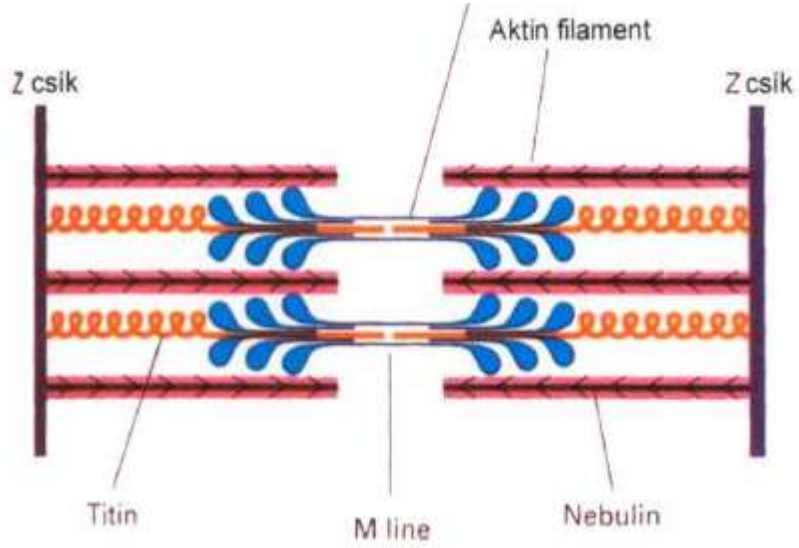


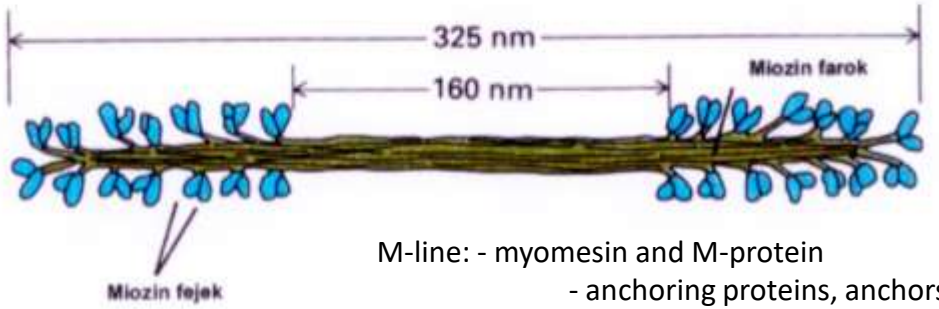
Thick filament:

-main components are bands of myosin filaments

- ATP dependent motor protein
  - myosin molecule is composed of 4 chains
  - 2 heavy chains forming a curled tail and a globular head
  - 2 light chain – neck region compose angle between the neck and head
  - neck region is mobile



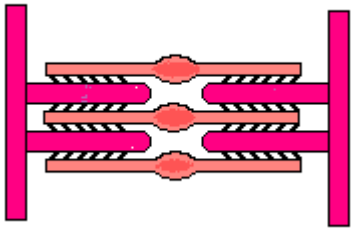




M-line: - myomesin and M-protein

- anchoring proteins, anchors to titin

Mechanism of contraction
Sliding filament theory



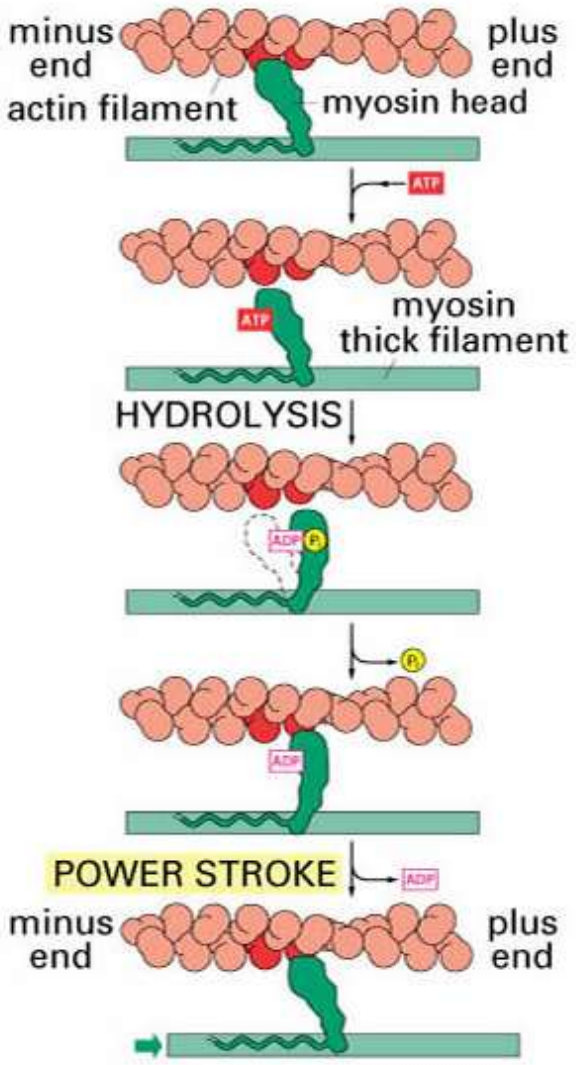
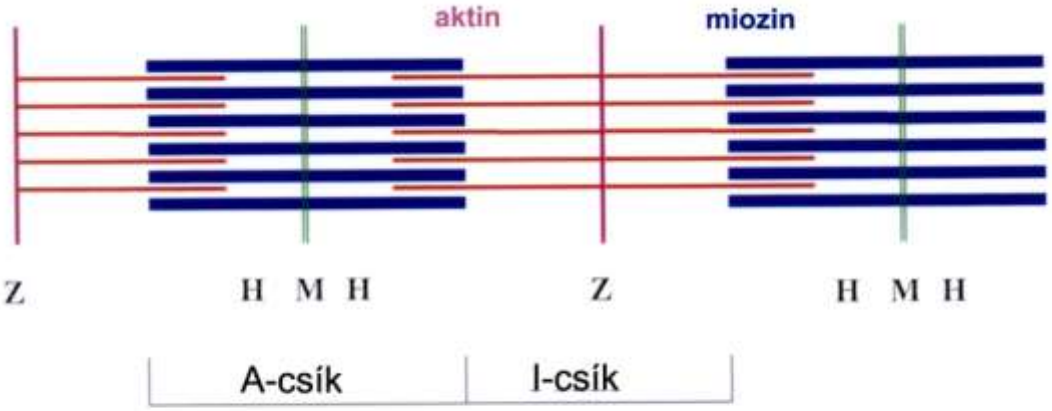
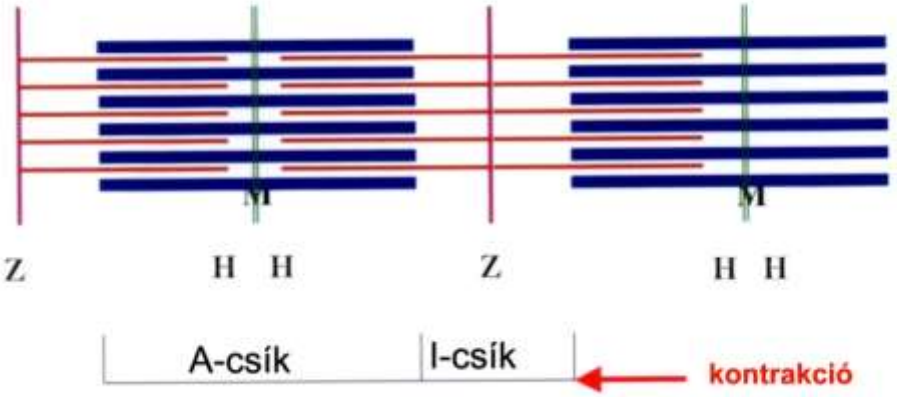


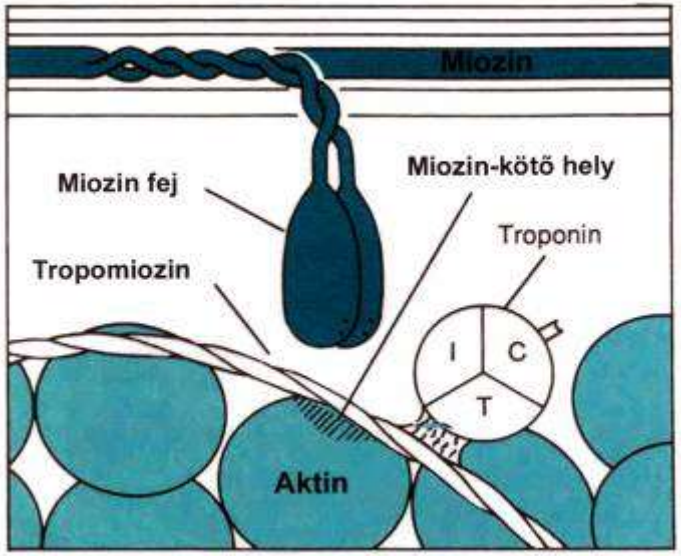
Figure 17-45 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Chemical energy transforms into mechanical energy during ATP hydrolysis





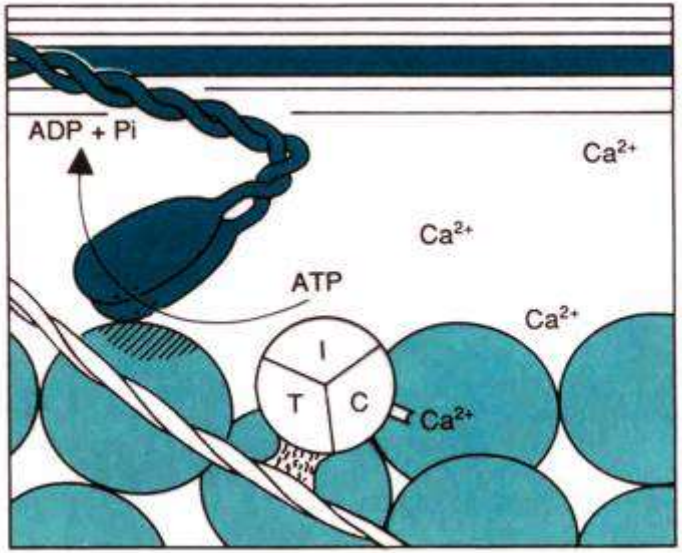
Regulation of contraction



Tropomyosin – blocks myosin binding sites

Troponin – 3 subunit

Troponin T – binds to Tropomyosin
Troponin I – inhibítory
Troponin C – can bind Ca^{2+}



Ca^{2+} binds to troponin→ conformation changes
→ tropomyosin moves out from actin myosin-binding sites → myosin can bind to az actin

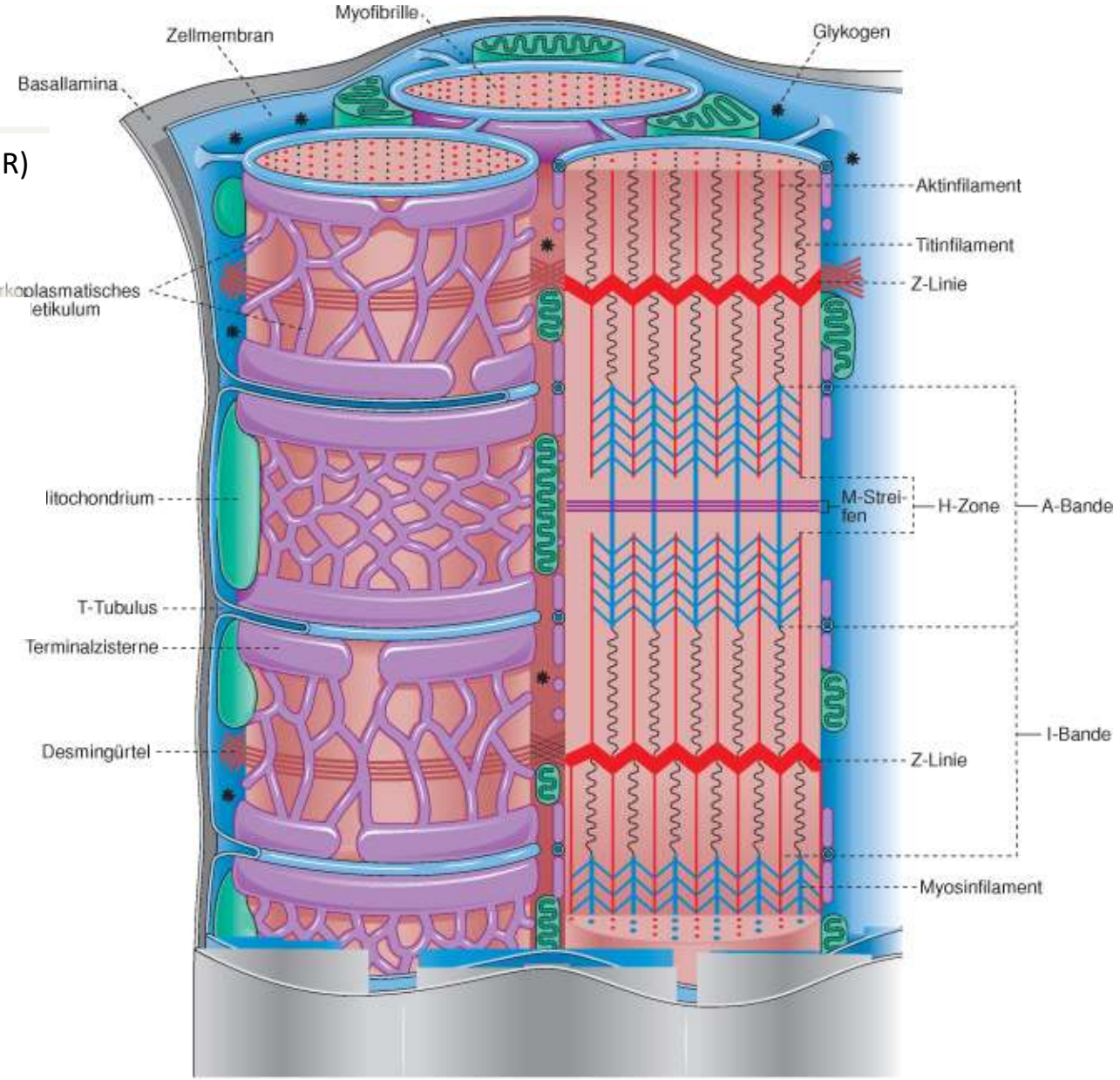
Transversal (T)–Tubule, Triad

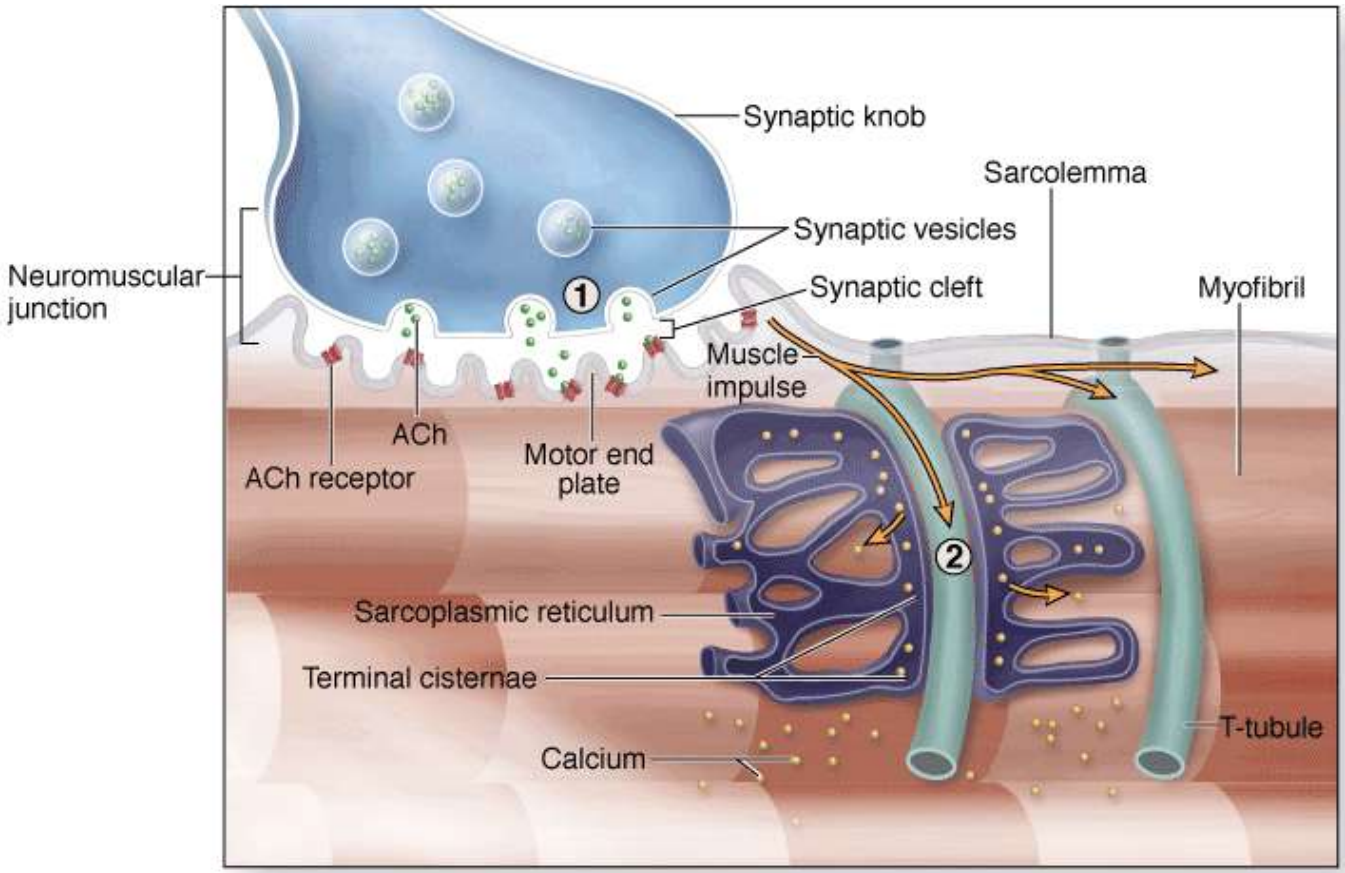
excitation-contraction connection

-**sarcoplasmic reticulum** (smooth ER)
- store Ca++ and pump them

Releases Ca++ during contraction and absorb it during relaxation

T-tubule
-deep invagination of plasmamembrane of the muscle fiber





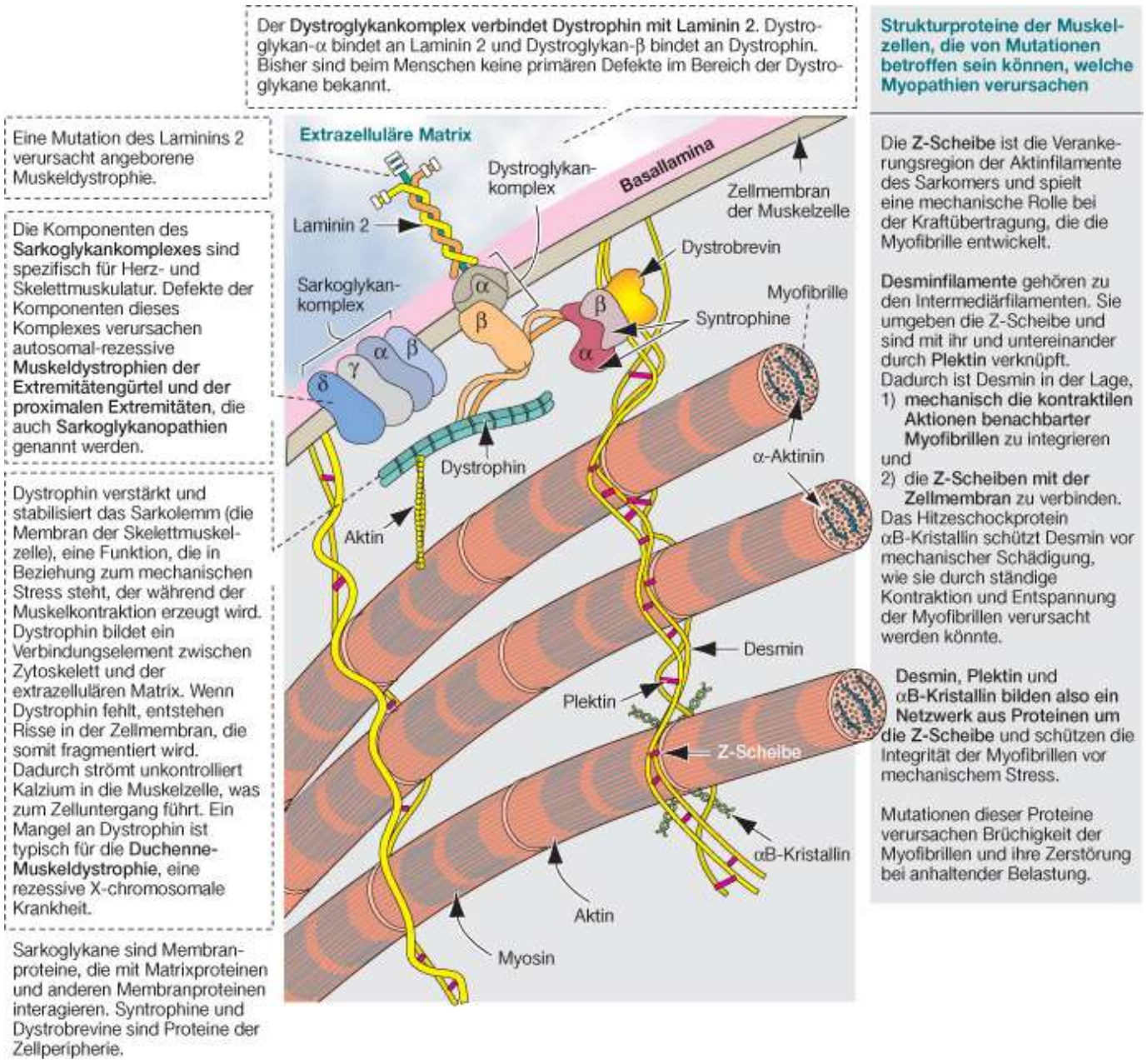
① A nerve impulse triggers release of ACh from the synaptic knob into the synaptic cleft. ACh binds to ACh receptors in the motor end plate of the neuromuscular junction, initiating a muscle impulse in the sarcolemma of the muscle fiber.

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

Muscle Contraction Process Molecular Mechanism

https://www.youtube.com/watch?v=S5uFaqpEPMI

Desmin, Distrofin



Desmin (Intermediate fil.)

connects myofibrills to sacrolemma at the level of the Z-lines

Connects sarcomer to ECM across desmosomes

anchors mitochondria in sarcomers

Distrofin

stabilising protein between ECM and cytoskeleton

If mutated sarcolemma disintegrates and muscle fiber die

Titin molecule– from Z-disk to M-line

- big protein
- binds to the surface of thick filament in A band
- **spring-like part** of titin in I band
- stabilise thick filaments position in the center

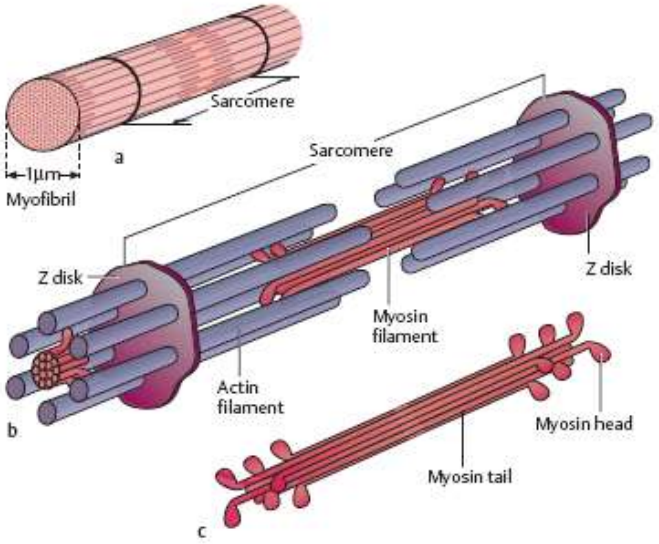
Nebulin – from Z-line along the actin molecules

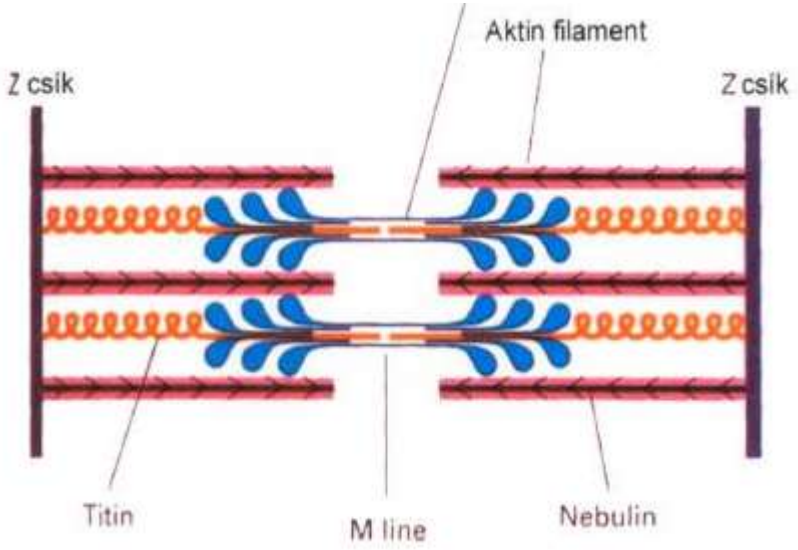
- regulates length of thin filaments

α-actinin – Z-filaments in Z-lines

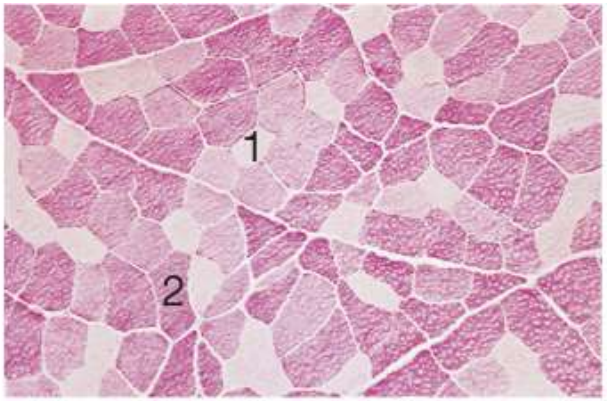
- fix + ends of actin filaments (barbed end) to Z-discs
- **very strong binding**

Myomesin and M-protein – anchor thick filament to other filaments (titin)





Types of striated muscle



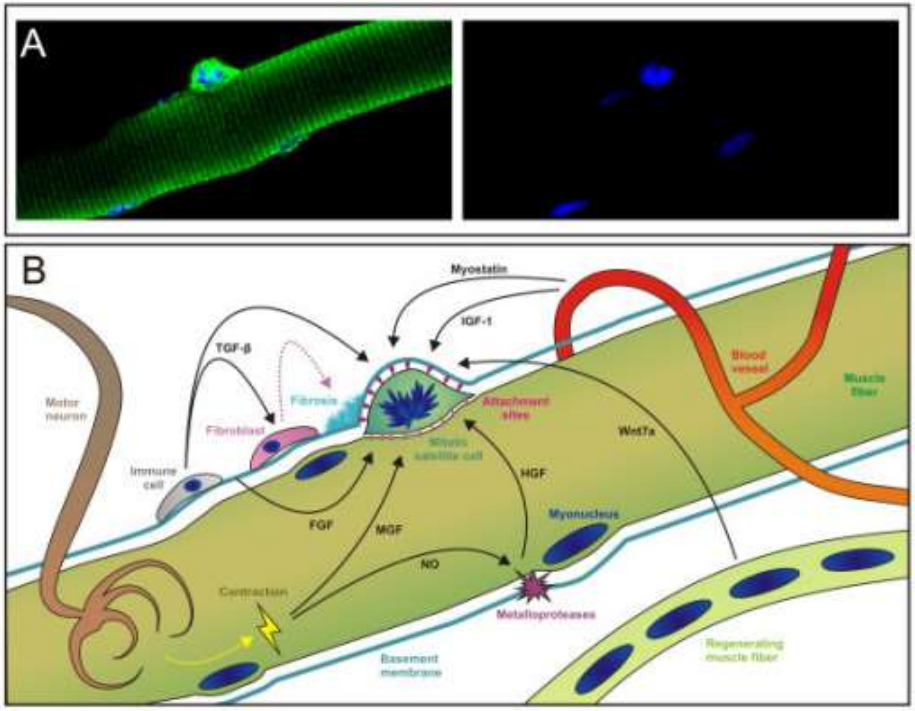
RED MUSCLE FIBRE

- High content of myoglobin & cytochrome
- Many mitochondria
- Rich blood supply
- Slow & continuous contraction
- Smaller in diameter
- E.g: postural muscles

WHITE MUSCLE FIBRE

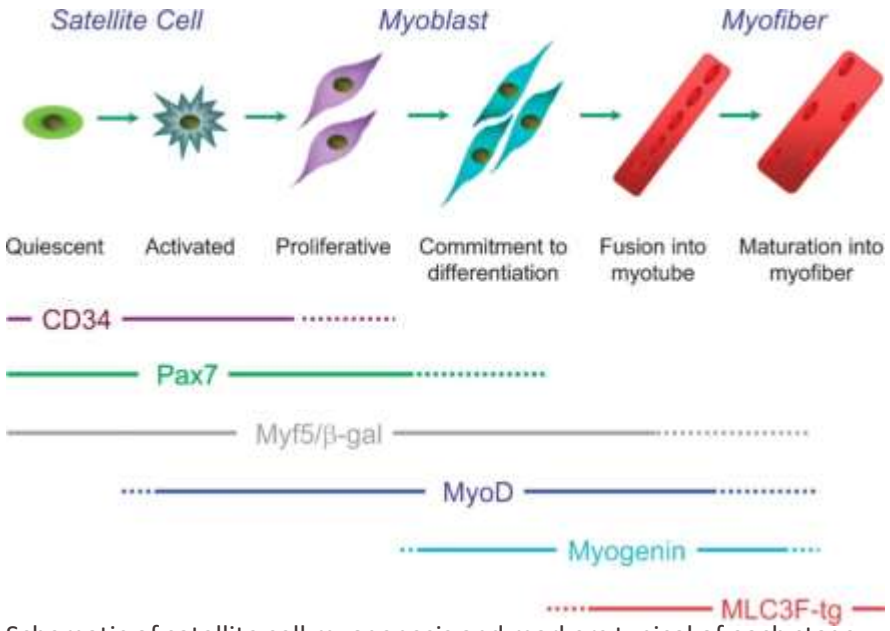
- Low content of myoglobin & cytochrome
- Few mitochondria
- Poor blood supply
- Rapid contractions
- Larger in diameter
- E.g: extra ocular muscles

Metaphase satellite cell on mouse muscle fiber fluorescent labelling



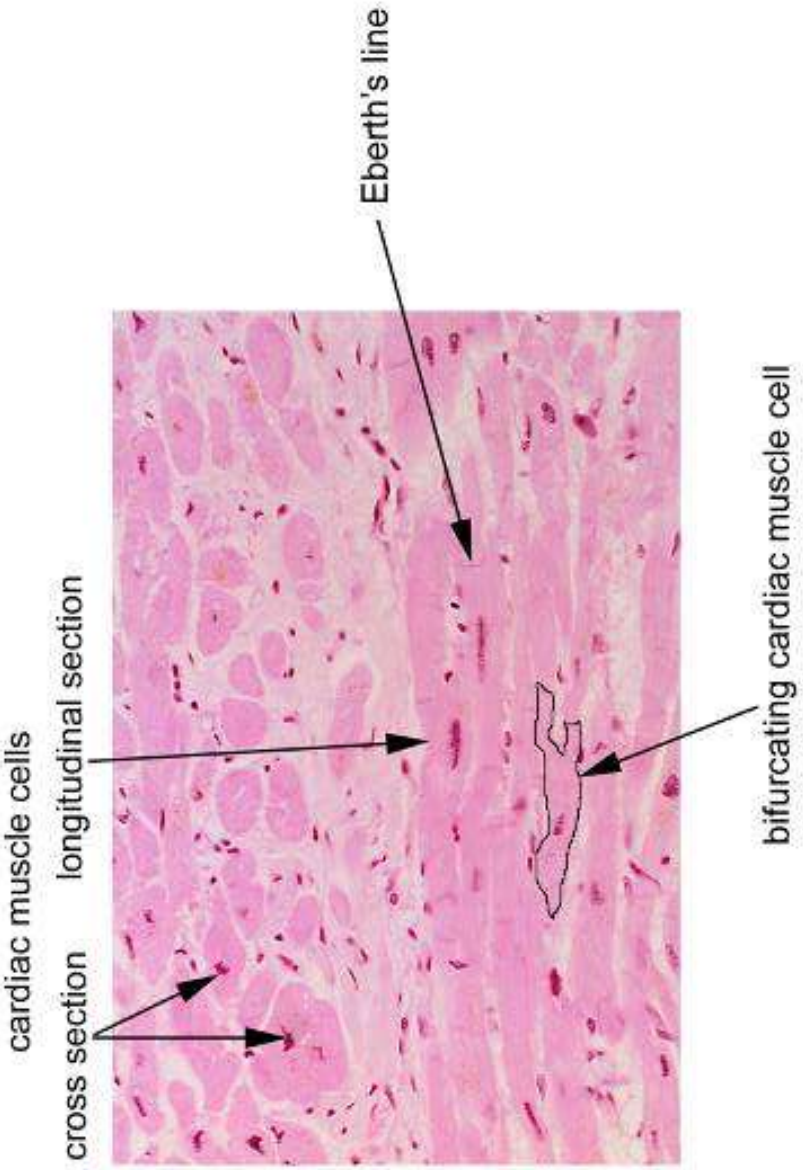
The satellite cell niche and regulatory factors. (a) Fluorescence microscopic image of a mitotic satellite cell (metaphase) on a mouse muscle fiber. The satellite cell is labeled by the expression of a yellow fluorescent protein and DNA is stained in blue. (b) Schematic of the different environmental cues influencing a satellite cell in its niche. FGF, fibroblast growth factor, HGF, hepatocyte growth factor, IGF, insulin-like growth factor, MGF, mechano-growth factor, NO, nitric oxide, TGF, transforming growth factor.

Myogenesis from satellite cells



Schematic of satellite cell myogenesis and markers typical of each stage. Satellite cells are quiescent in normal adult muscle and can be activated by, for example, muscle damage. Once activated, satellite cells divide to produce satellite cell-derived myoblasts that further proliferate, before committing to differentiation and fusing to form myotubes, which then mature into myofibers (for clarity, satellite cell self-renewal is not included). CD34, Pax7, and Myf5/β-gal are expressed in quiescent satellite cells. Satellite cell activation is marked by the rapid onset of MyoD expression, whereas myogenin later marks the commitment to differentiation. The temporal expression pattern of MLC3F-tg is typical of many structural muscle genes such as skeletal muscle actin and MyHC, which mark sarcomeric assembly in the later stages of differentiation. Myf5/β-gal denotes the fusion protein product of the targeted allele of the *Myf5*$^{nlacZ/+}$ mouse (Tajbakhsh et al. 1997), whereas MLC3F-tg is the product of the *3F-nlacZ-E* transgene (Kelly et al. 1995). (Adapted from Miller et al. 1999with modifications by J. Beauchamp and the authors.)

Cardiac muscle



Branching cells

length: 85-100 µm

Big nucleus in the middle of the cells, euchromatic

Membrana basalis

striated

Eberth's line– cells connected electrically and mechanically functional syntitium

Pacemaker activity

Conduction system in heart

Under regulation of autonomic NS

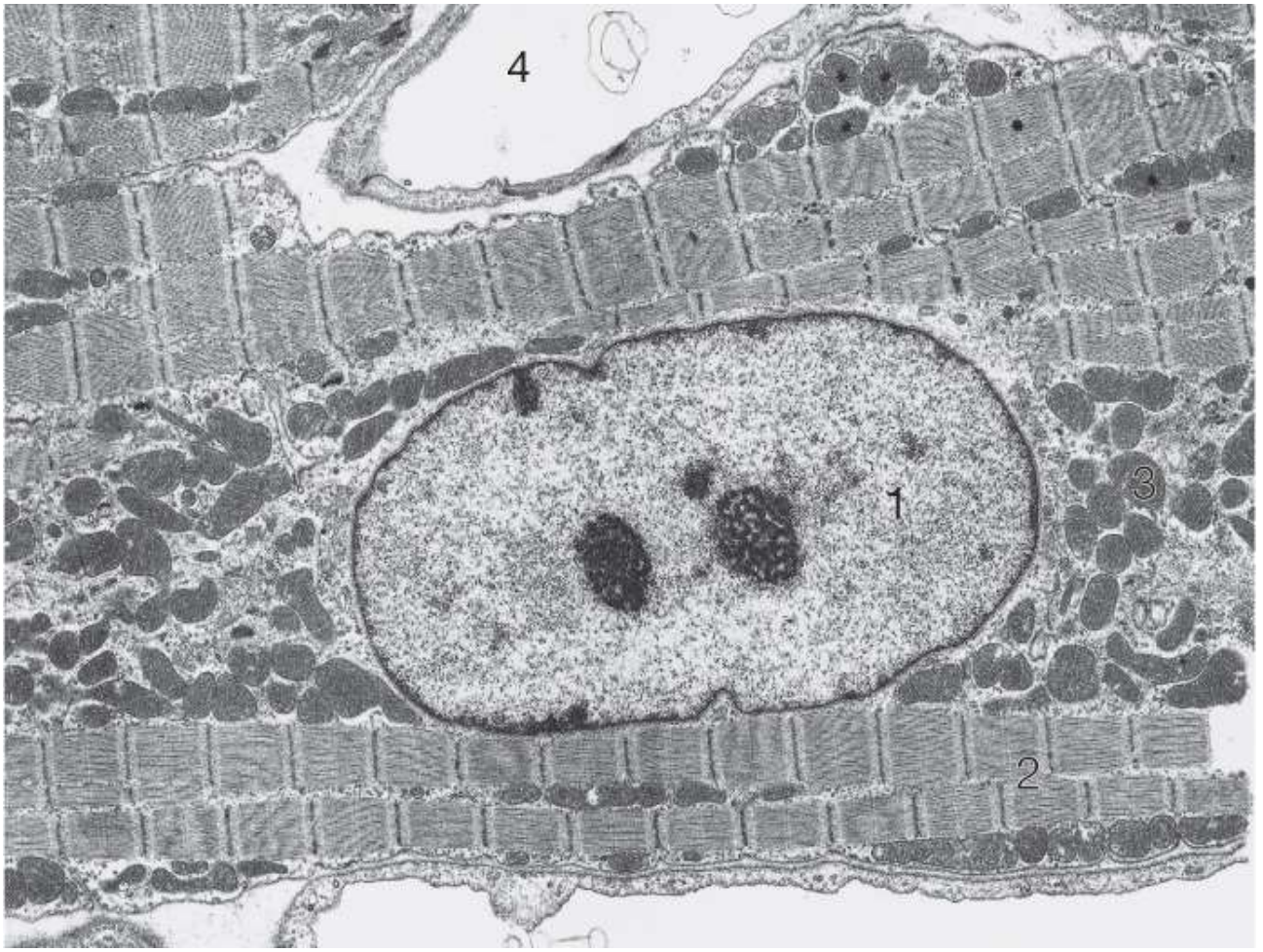
Persistent work

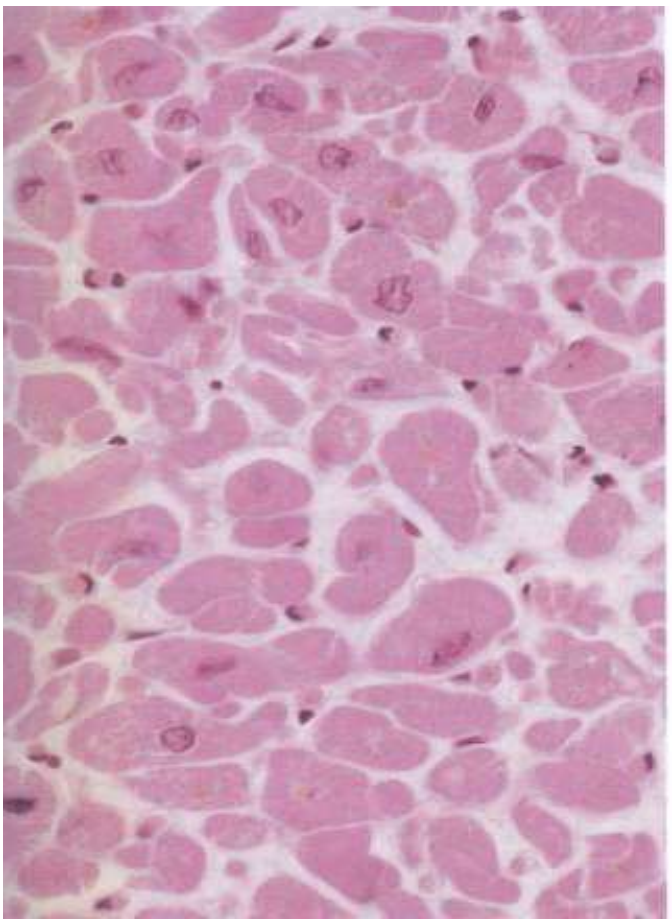
Needs lot of energy

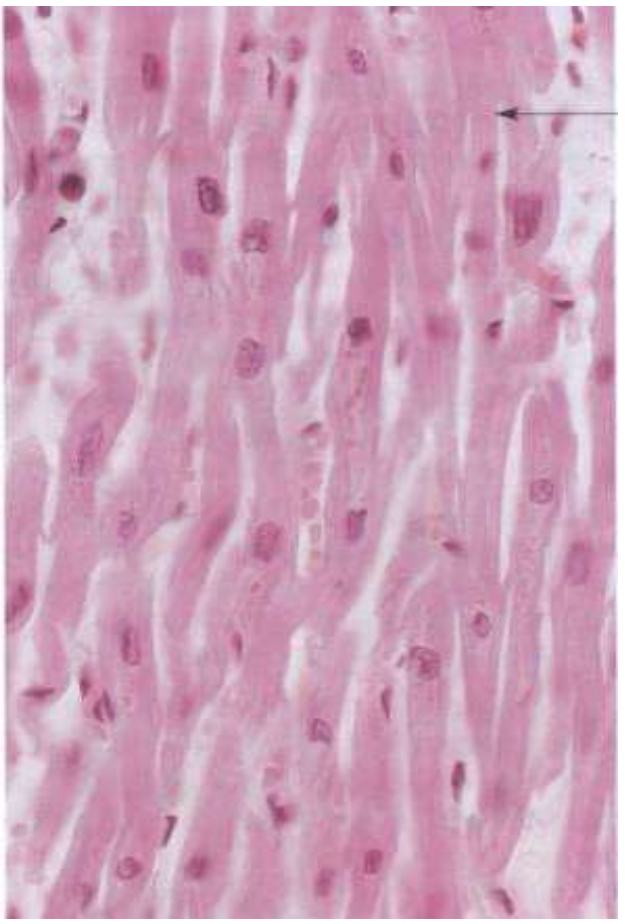
Lipofuscin granules

No (?) Regeneration

Heart tissue

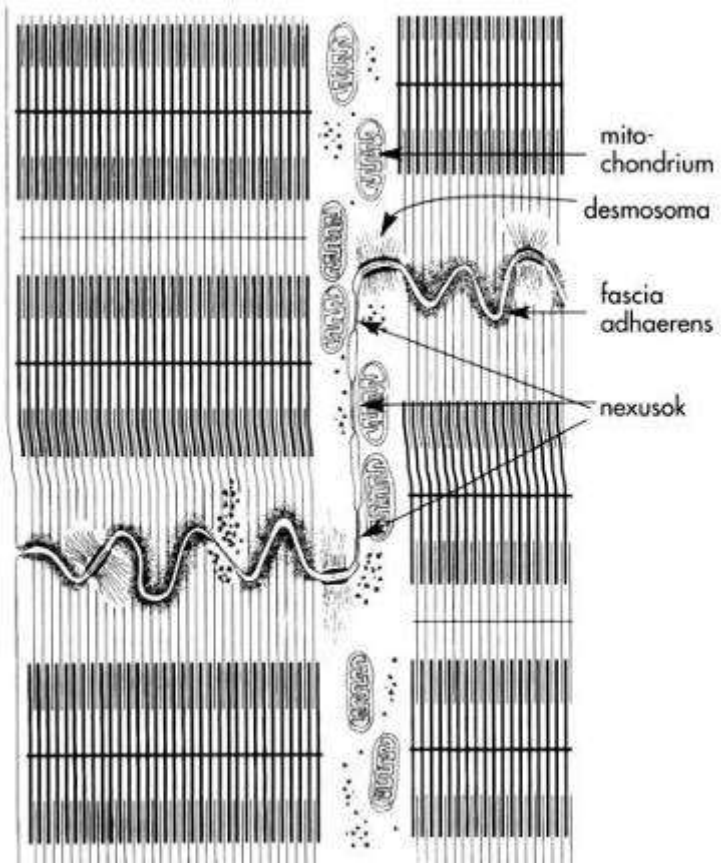

4
1
3
2

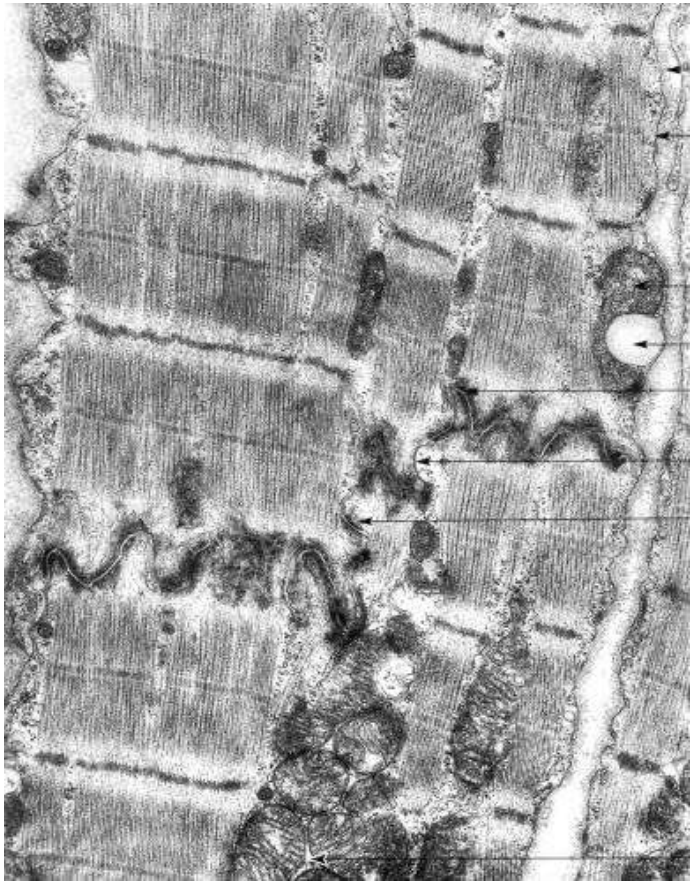




Eberth's line (Discus intercalaris)

Karl Joseph Eberth
1835 - 1926

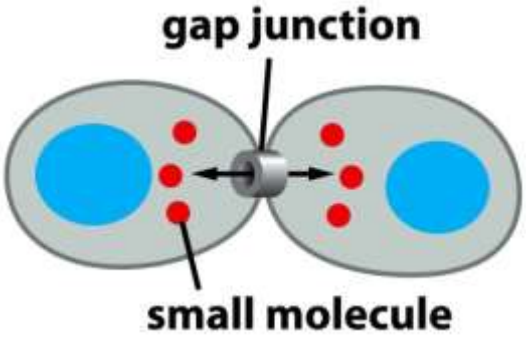


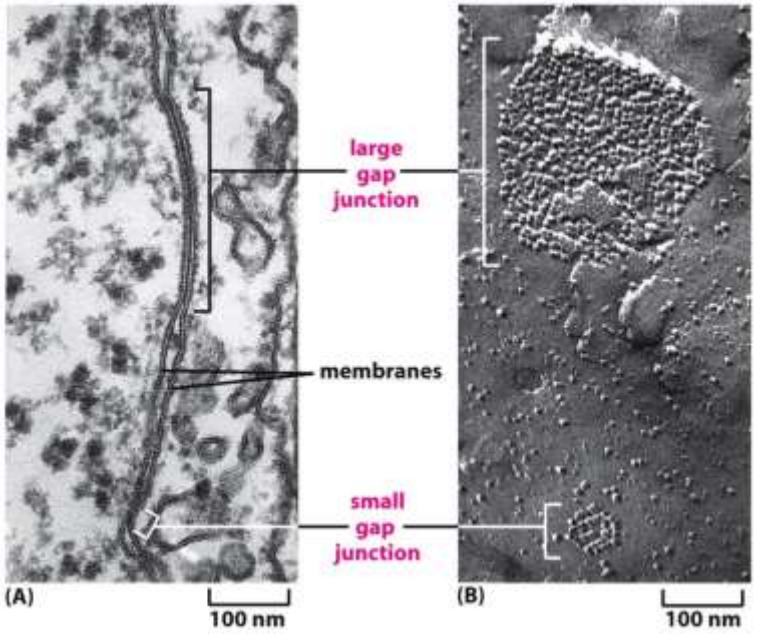


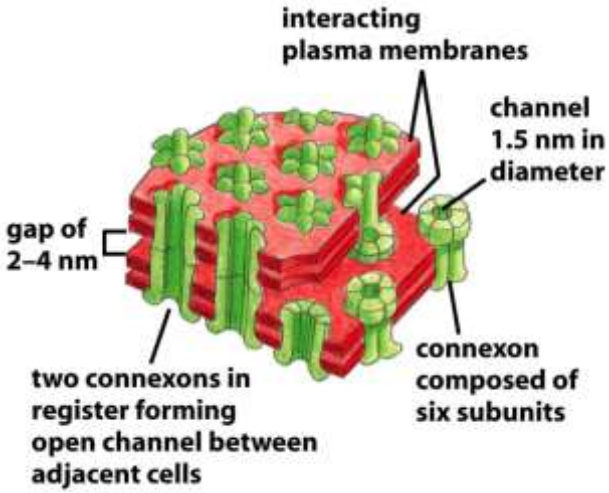
Cell adhesion structures along Eberth's line: fascia adherens (actin), desmosoma (IF), gap juncion=nexus (electric synapse)

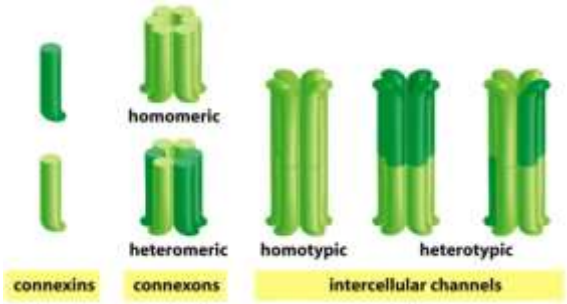
Gap junction=nexus

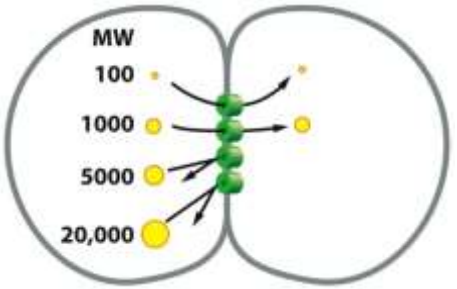
Place of cellular exchange (small molecules, ions, glucose, intracellular mediators: IP_3, cAMP)
Electric synapse,
Enable ionic communication between cells leading to synchronous muscle contraction.







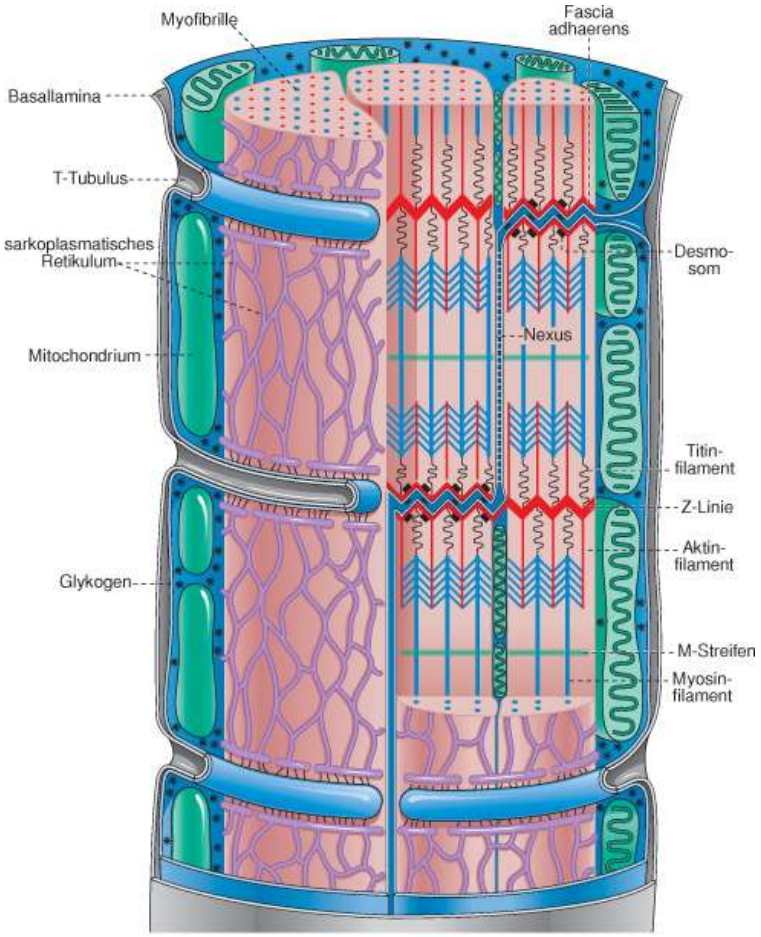


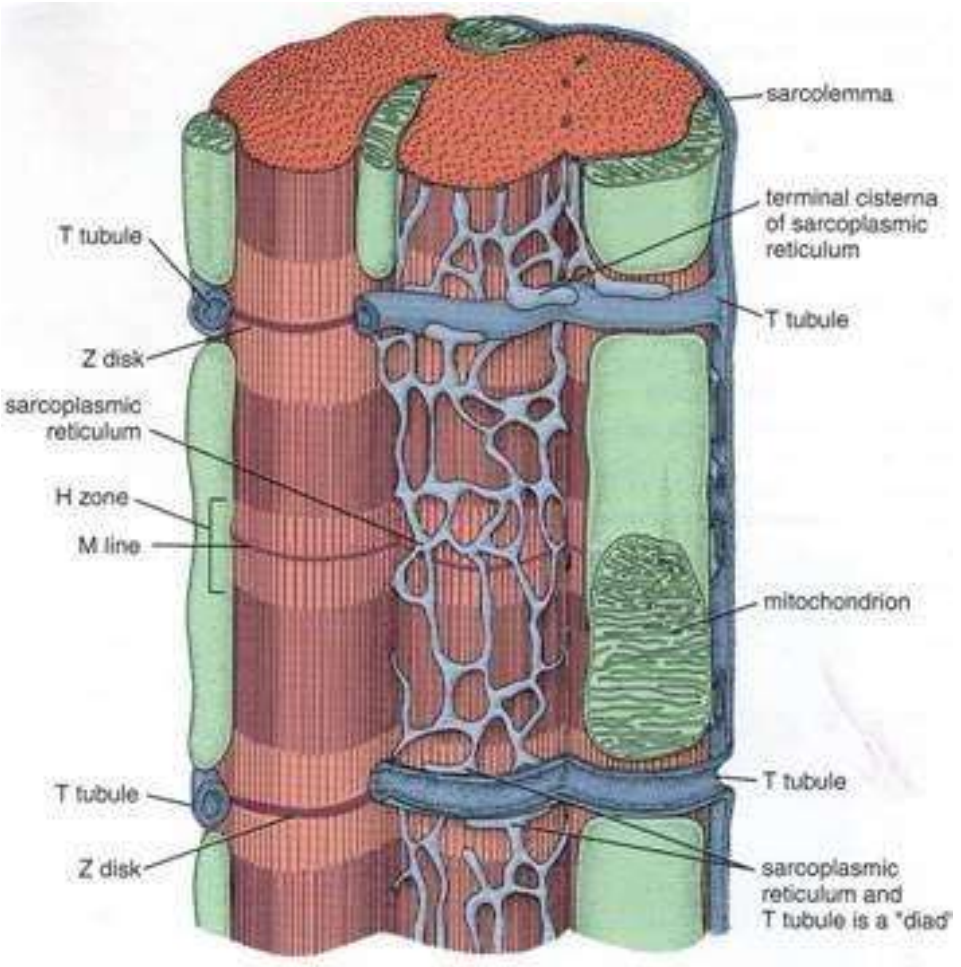


Transversal (T)–Tubule in cardiac muscle, Diad

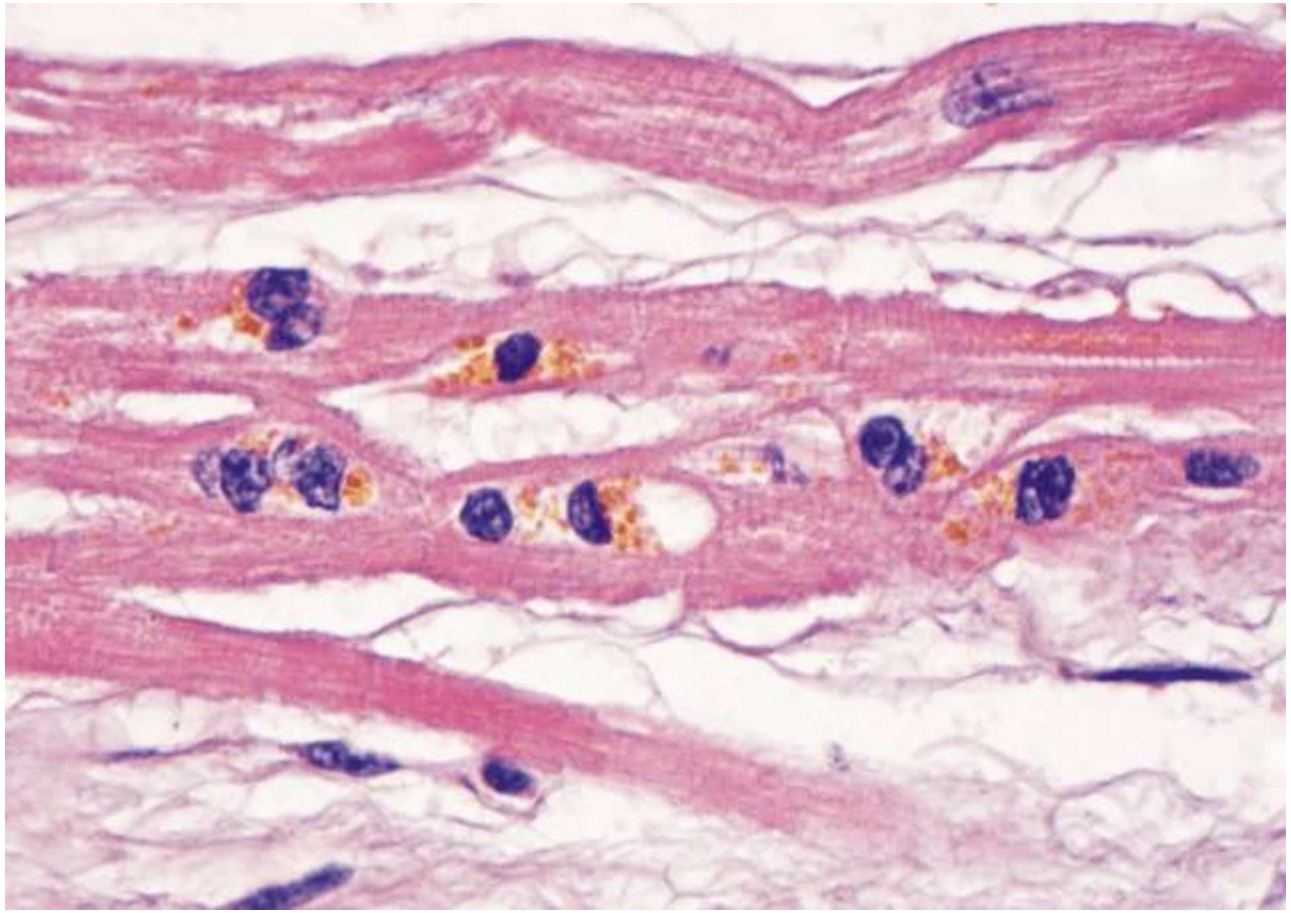
DIAD

-at Z line
- Terminal cistern of sarcoplasmic reticulum on T tubule





Lipofuscin granules



yellow-brown pigment granules

lipid containing residues of lysosomal digestion

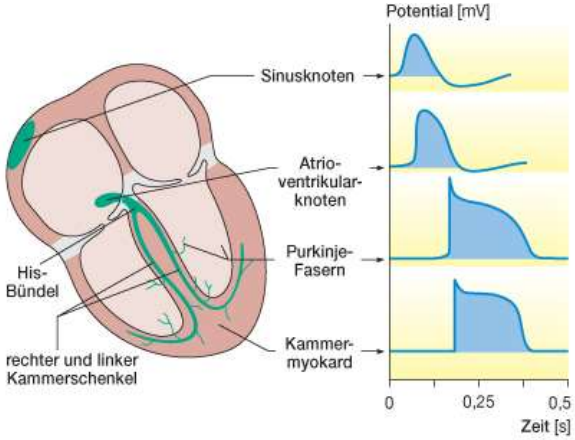
„aging” pigments

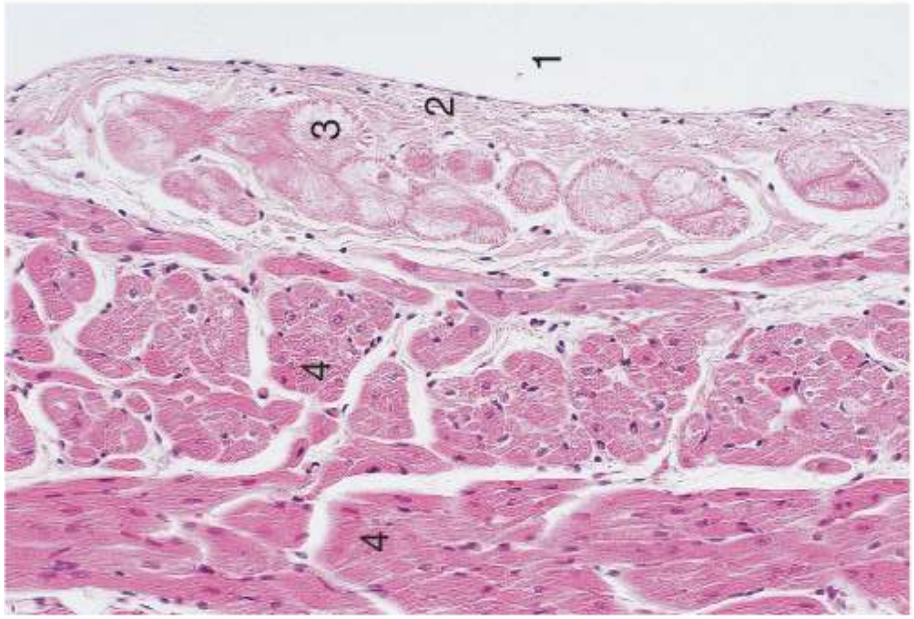
arranged around the nucleus

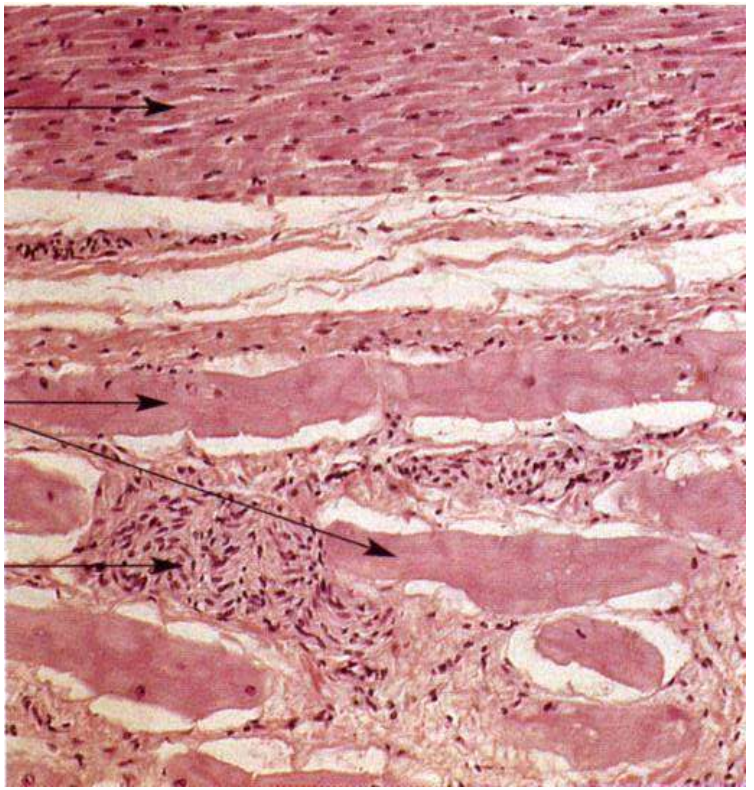
Myocardiocytes with lipofuscin granules (HE stain, ×400).

Pacemaker activity, Purkinje fibers

Jan Evangelista Purkyně
1787 - 1869







Thank you for your attention!

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