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MUSCLE TISSUE

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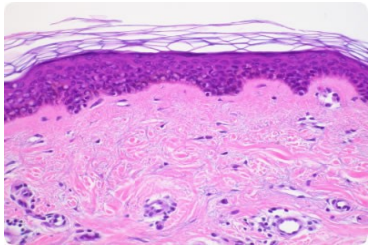
CONTEMPORARY TISSUE CLASSIFICATION

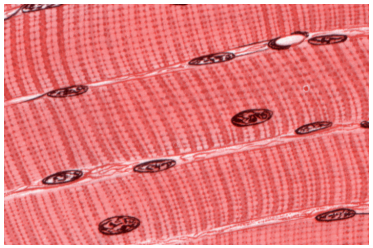
Based on morphology and function:

Epithelium



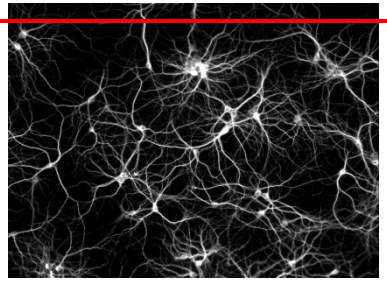
Continual, avascular layers of cells with different functions, oriented to open space, with specific junctions and minimum of ECM and intercellular space.
Derivates of all three germ layers

Muscle



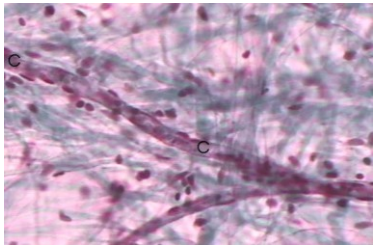
Cytoskeleton → contraction
Mesoderm – skeletal muscle, myocard, mesenchyme – smooth muscles
Rarely ectoderm (eg. m. sphincter a m. dilatator pupillae)

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

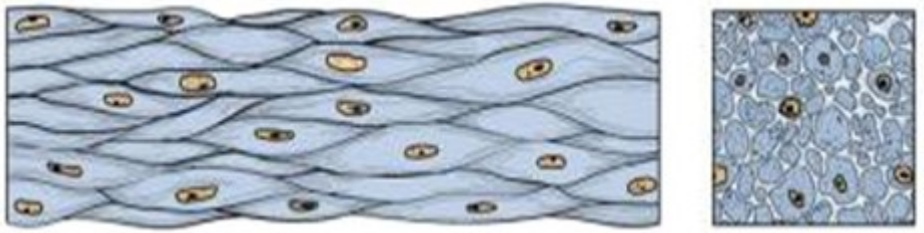
Hallmarks

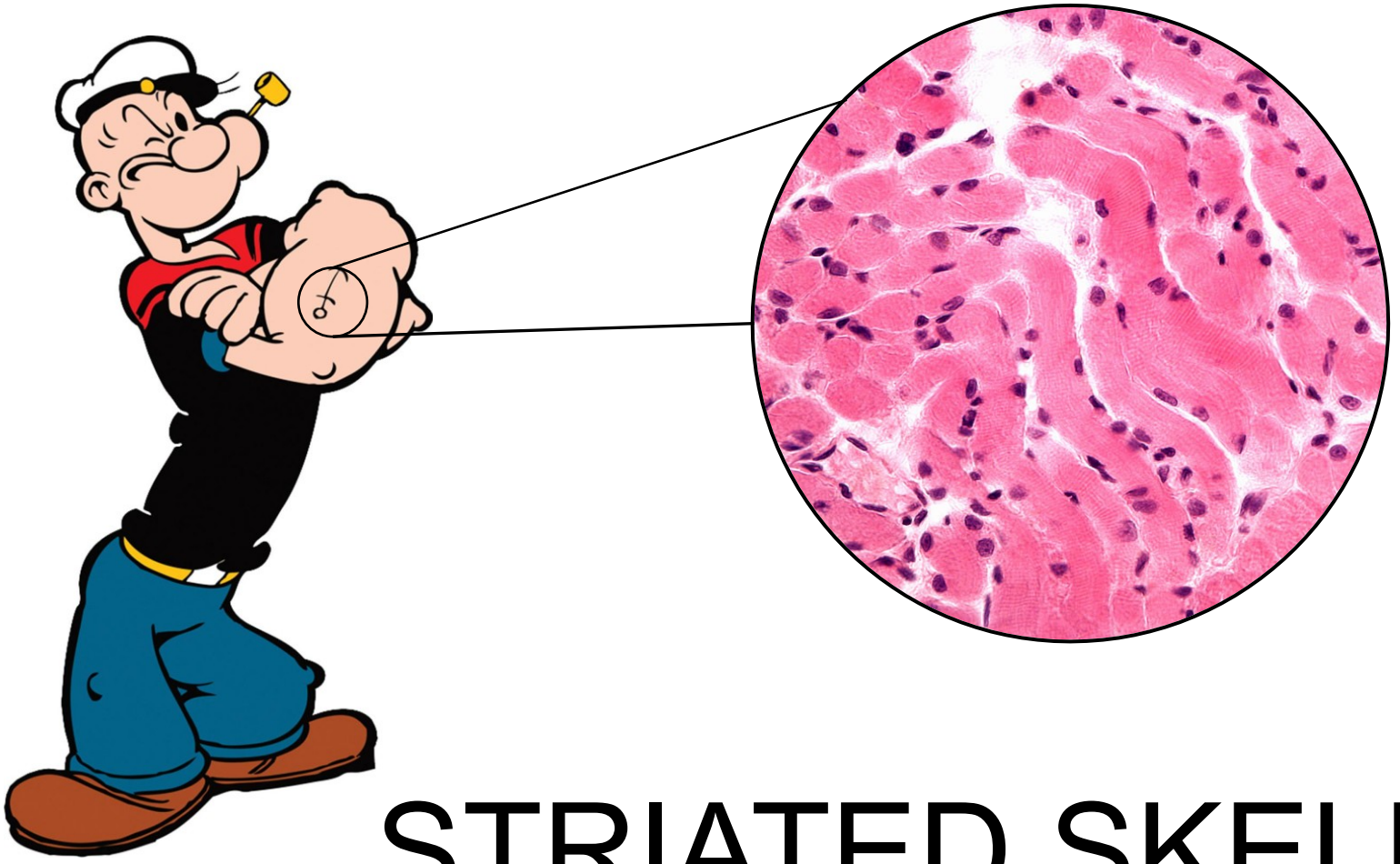
- Unique cell architecture
- Excitability and contraction
- Mesodermal origin

Striated skeletal

Striated cardiac

Smooth





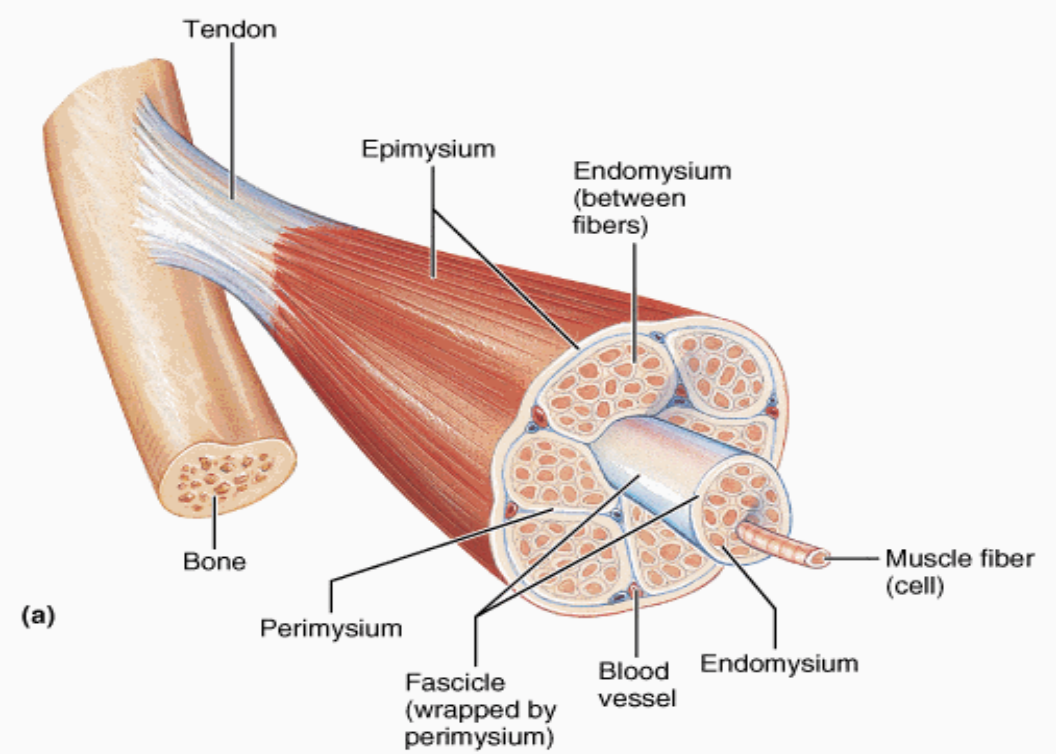
STRIATED SKELETAL MUSCLE TISSUE

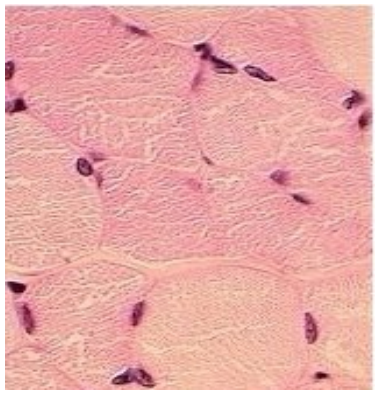
HISTOLOGY OF SKELETAL MUSCLE TISSUE

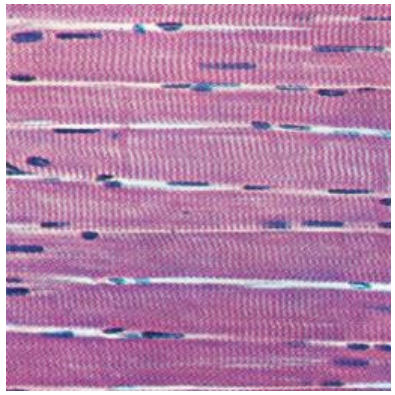
- Composition: muscle cells + connective tissue, blood vessels
- Unique cell architecture – long multinuclear cells – muscle fibers (rhabdomyocytes)
- Long axis of cells is oriented parallel with direction of contraction
- Specific terminology:
  - cell membrane = sarcolemma
  - cytoplasm = sarcoplasm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

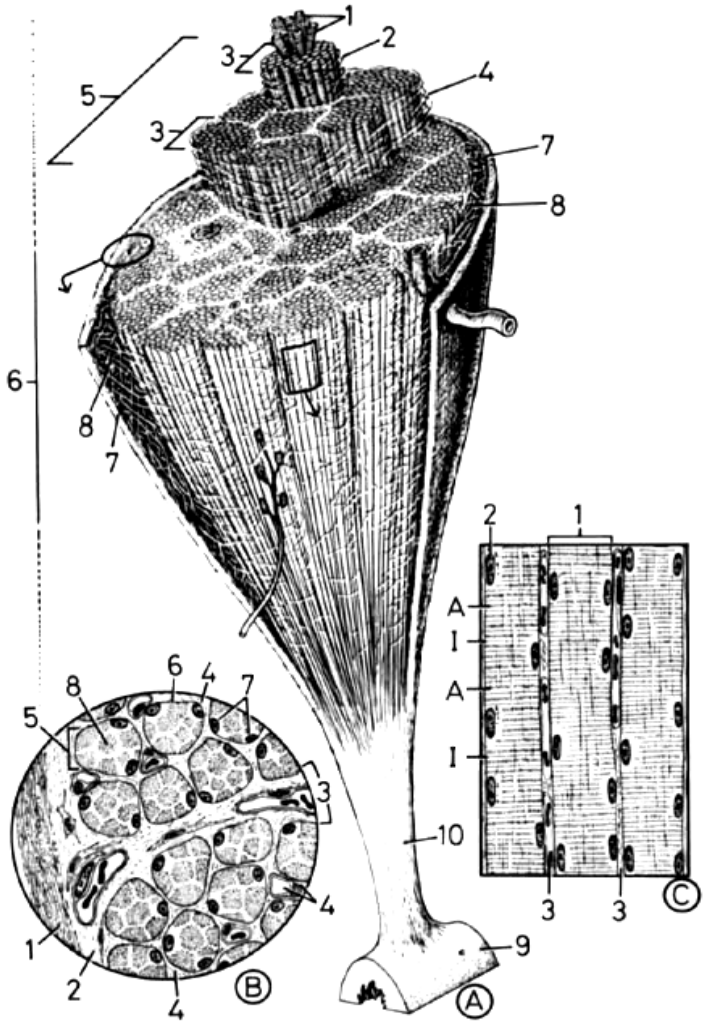
  - Muscle fiber – microscopic unit of skeletal muscle
  - Myofibril – LM unit – myofilaments – unit of muscle fibers
  - Myofilaments – filaments of actin and myosin (EM)

STRUCTURE OF SKELETAL MUSCLE



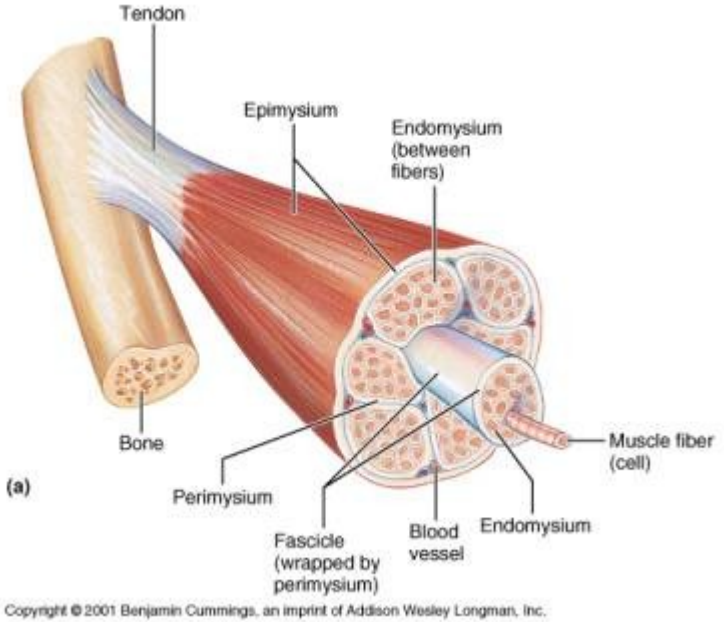


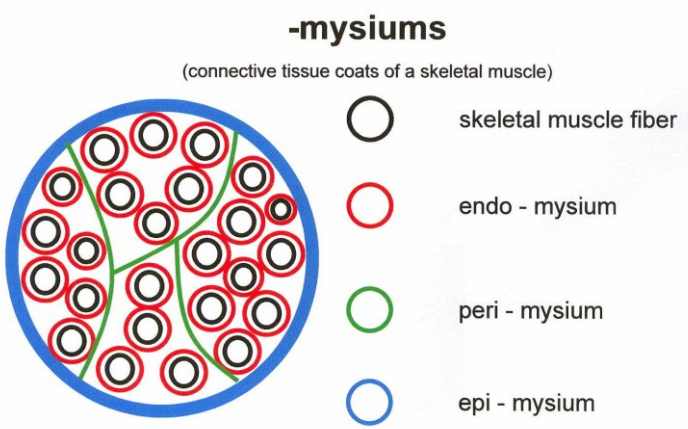


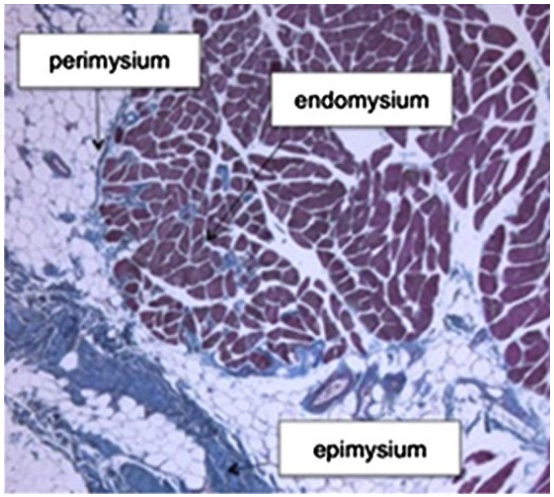


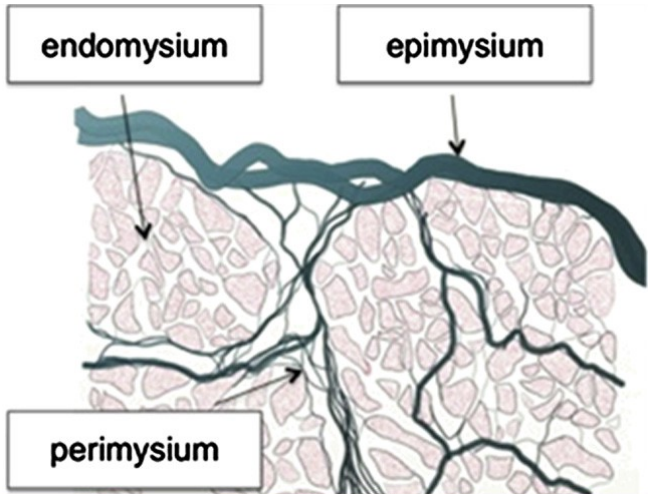
CONNECTIVE TISSUE OF SKELETAL MUSCLE

- 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.

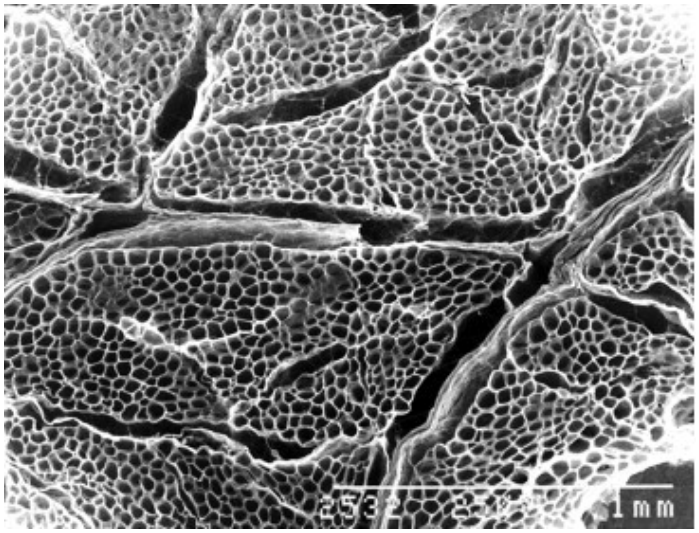


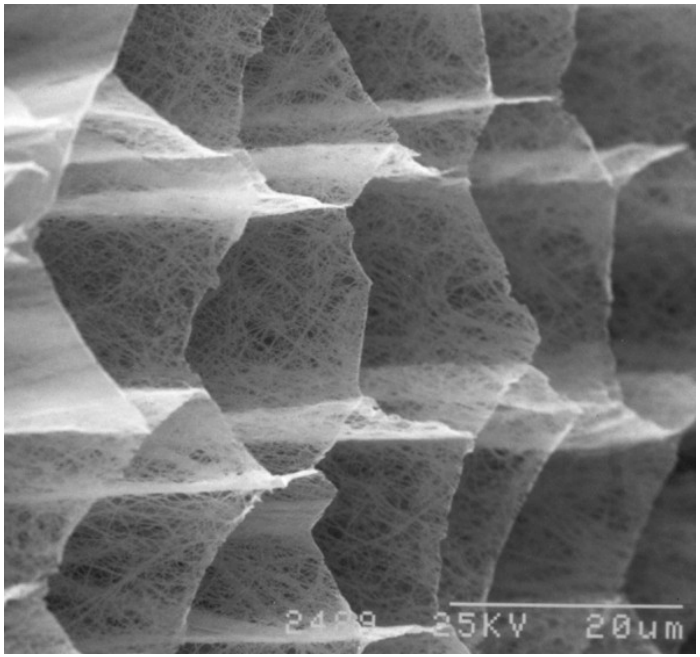


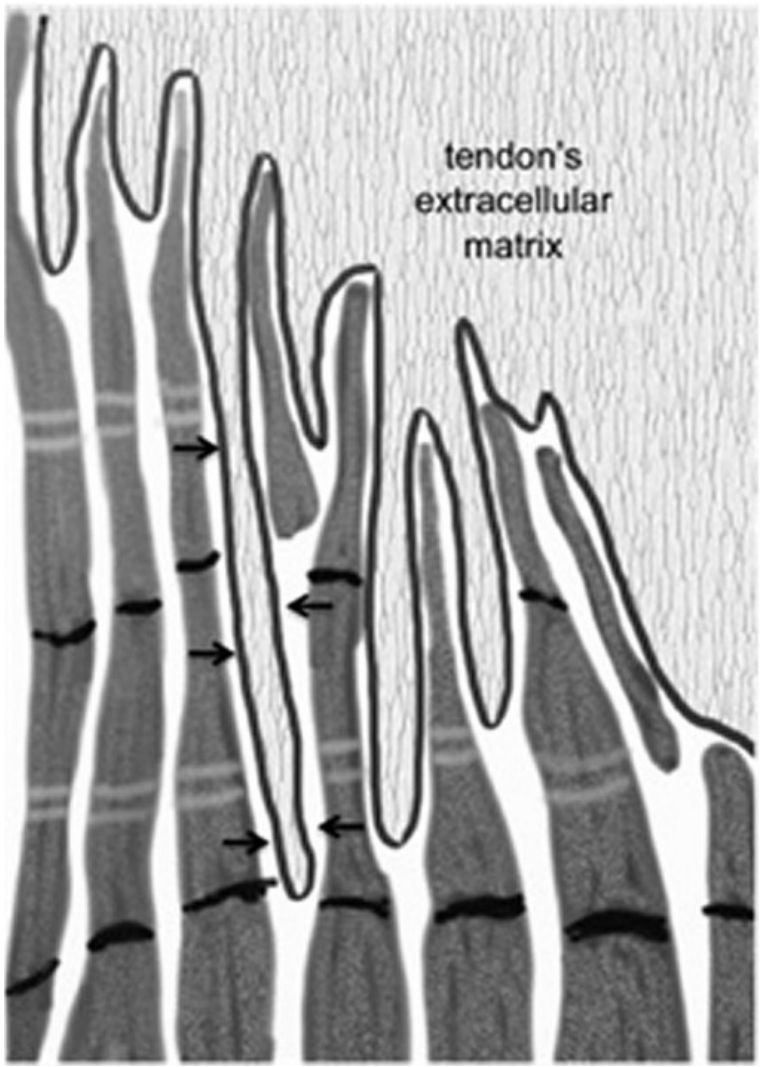




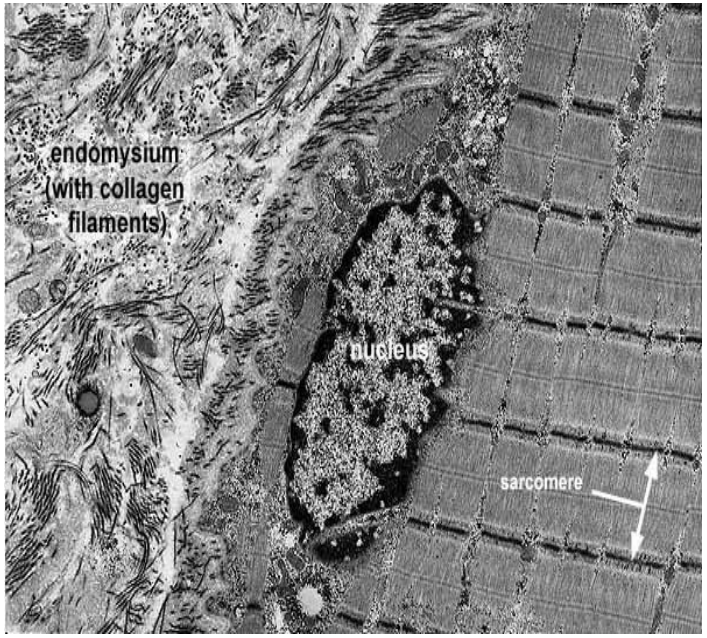
CONNECTIVE TISSUE OF SKELETAL MUSCLE

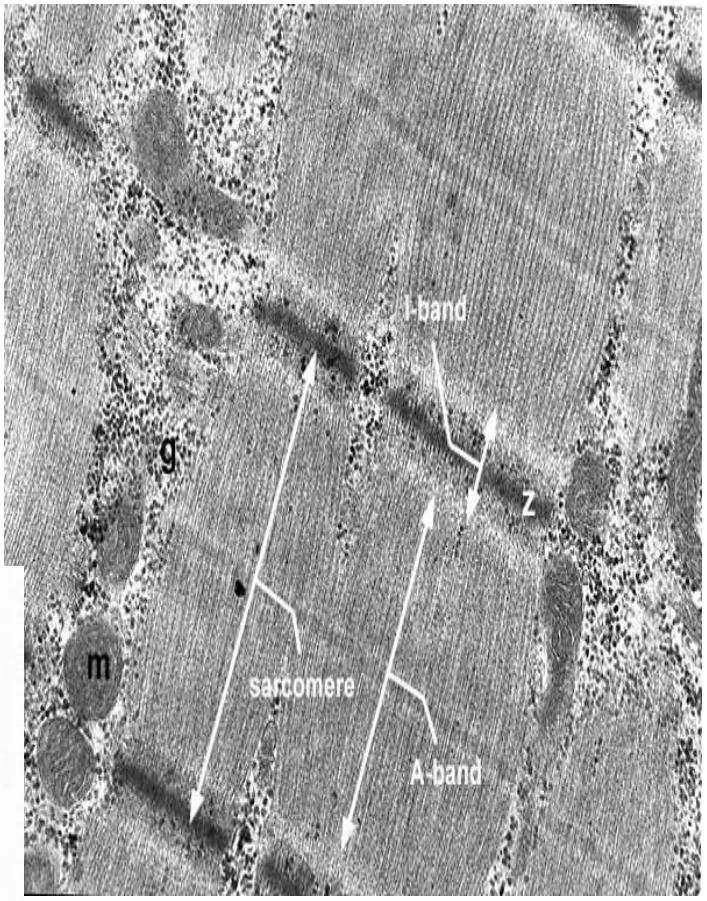


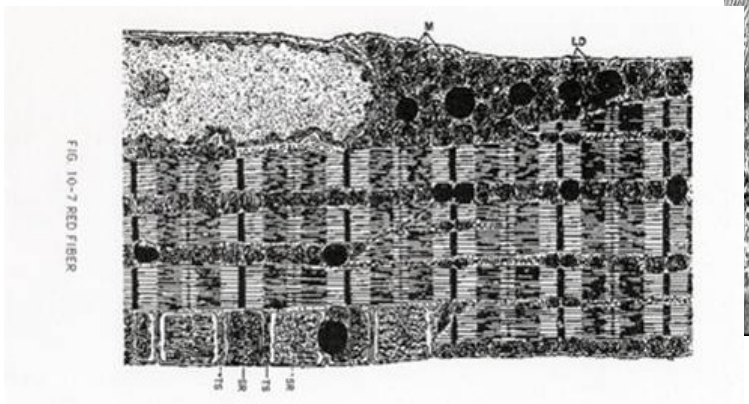




CONNECTIVE TISSUE OF SKELETAL MUSCLE

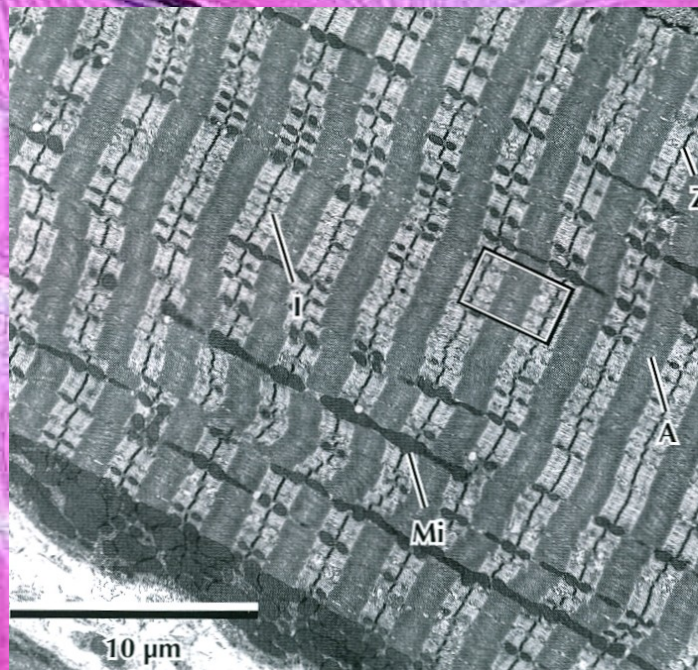






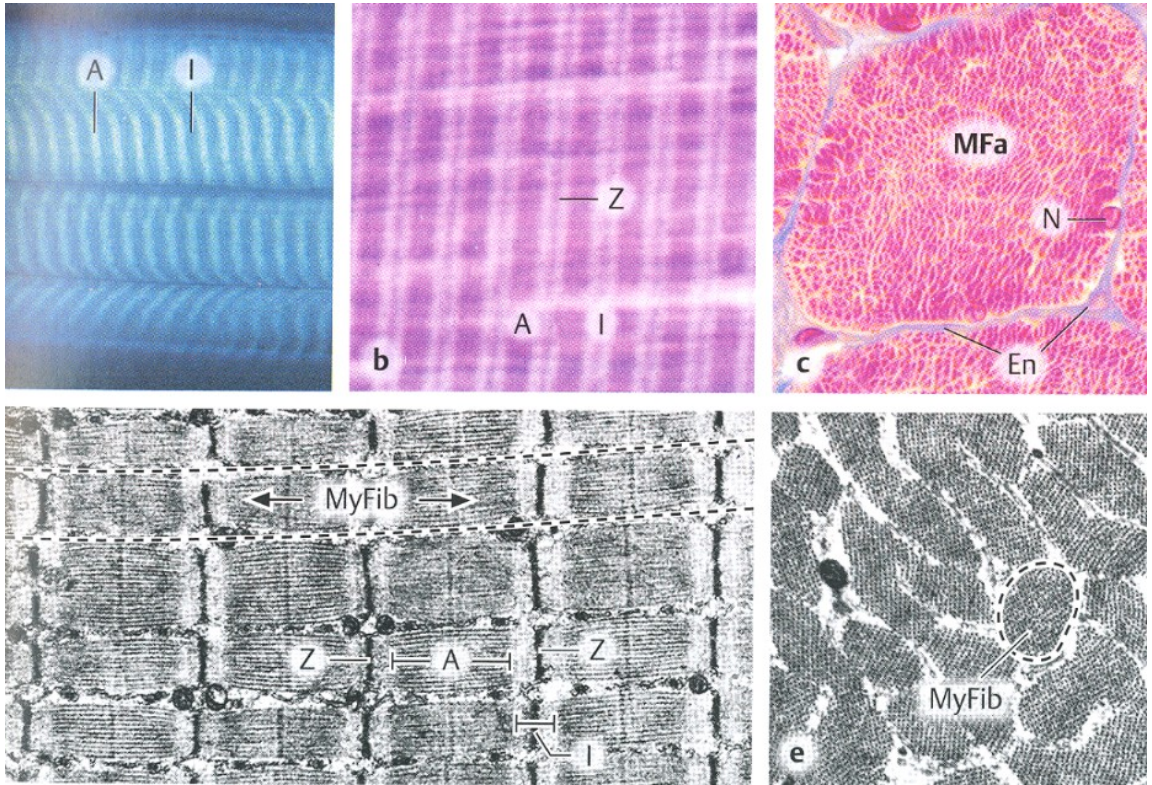
ORGANIZATION OF SKELETAL MUSCLE TISSUE

WHY IS SKELETAL MUSCLE TISSUE STRIATED?



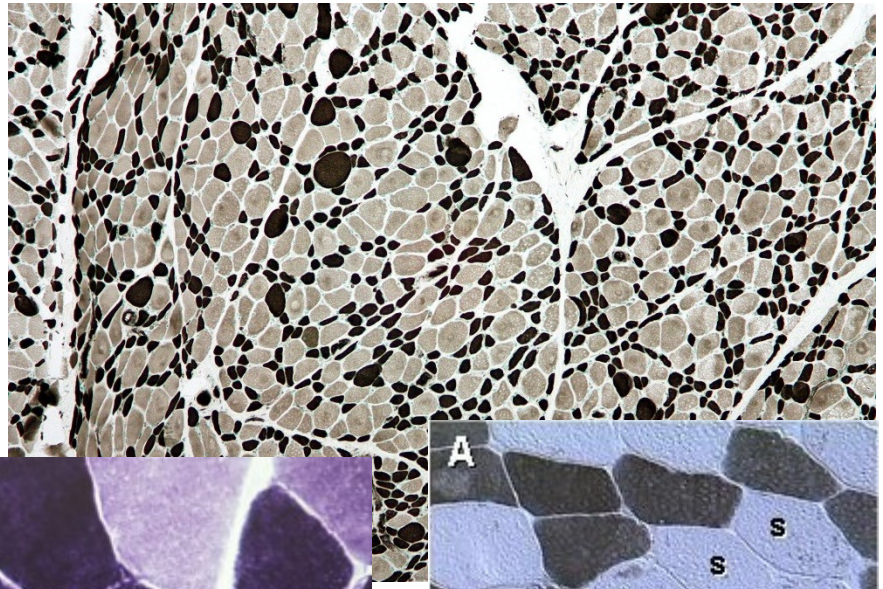
STRUCTURE OF SKELETAL MUSCLE

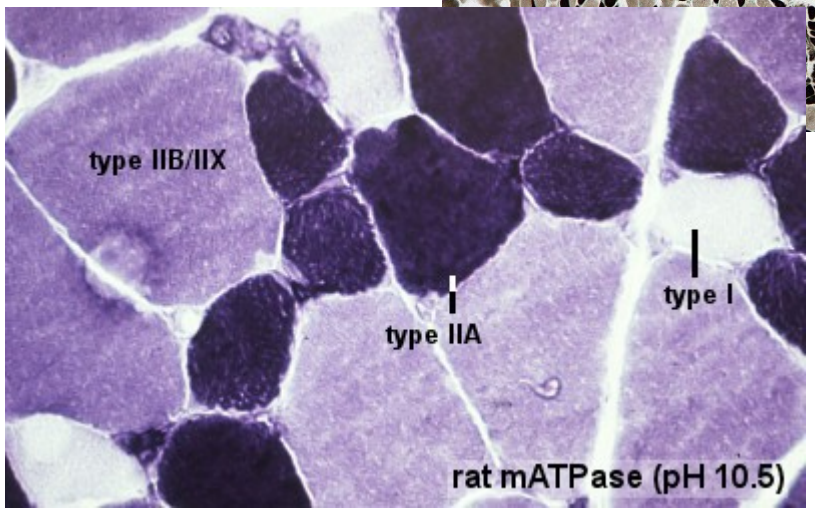
- morphological and functional unit: **muscle fiber (rhabdomyocyte)** – elongated, cylindrical-shaped, multinucleated cell (syncytium)
- nuclei are located at the periphery (under sarcolemma)
- **myofibrils** show cross striation
- diameter of muscle fiber: 25-100 μm
- length: millimeters - centimeters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

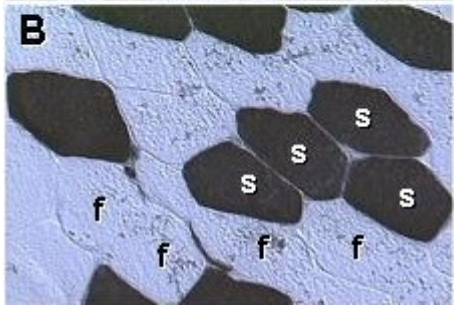


CLASSIFICATION OF SKELETAL MUSCLE

- **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

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

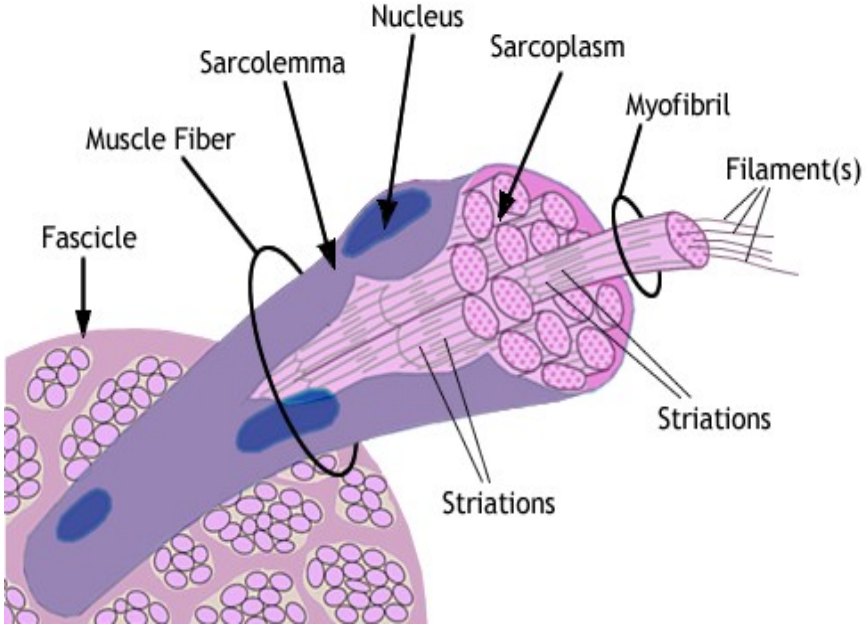
Muscle fiber = myofiber = syncitium = rhabdomyocyte

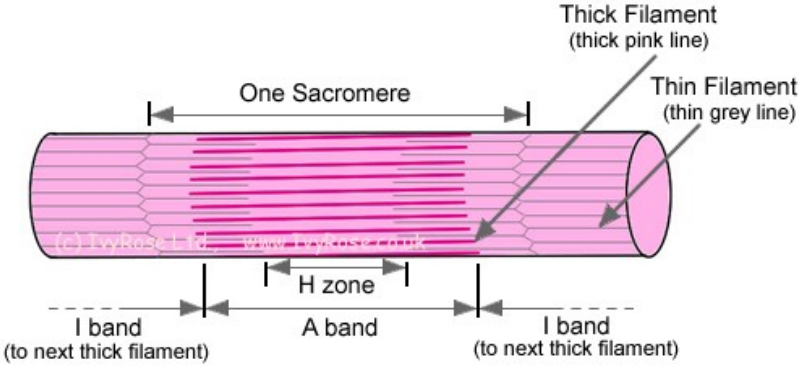
Muscle fiber – morphological and functional unit of skeletal muscle [Ø 25 – 100 μm]

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]





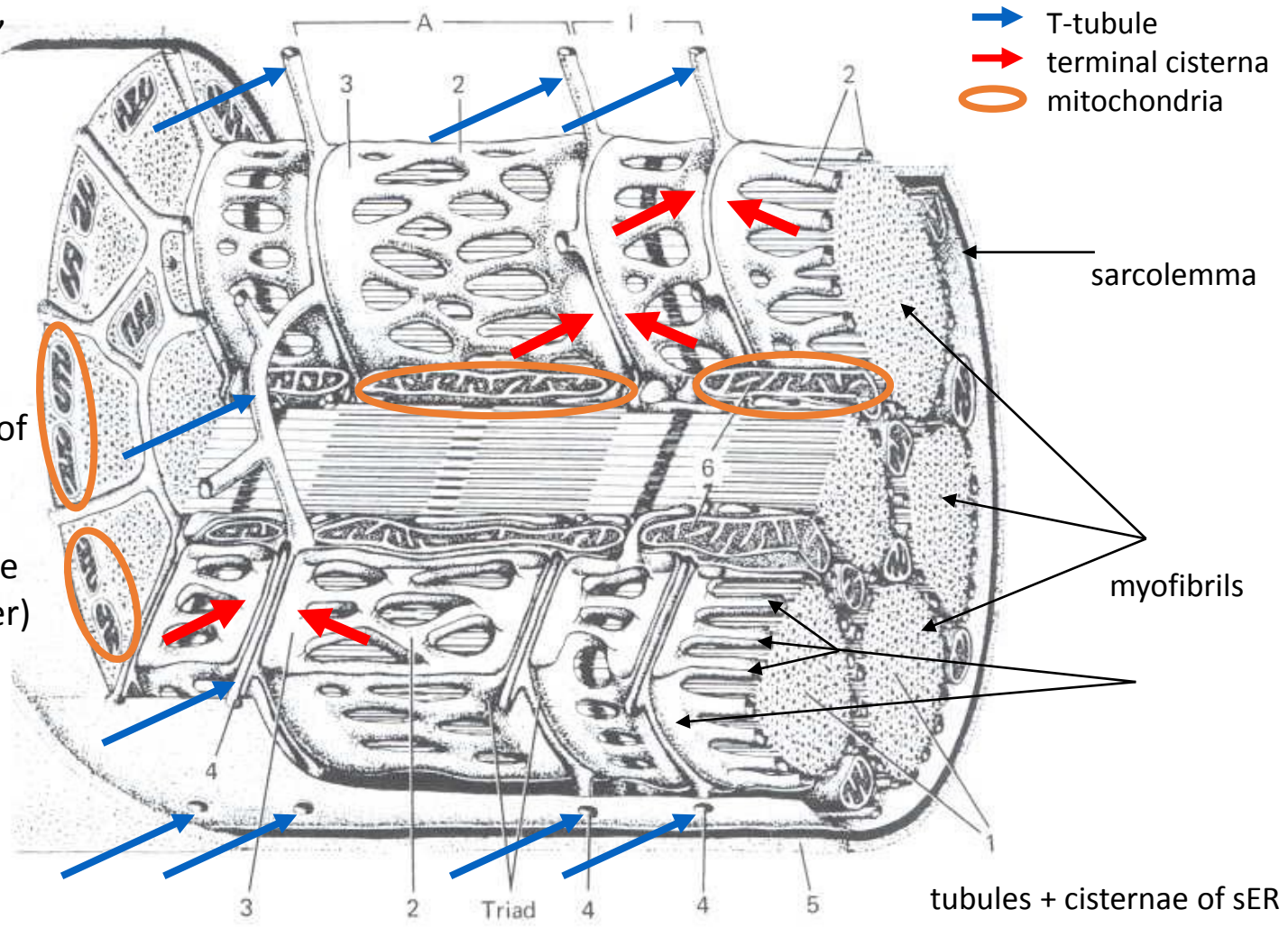
ULTRASTRUCTURE OF RHABDOMYOCYTE

Sarcolemma + **t-tubules**,

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

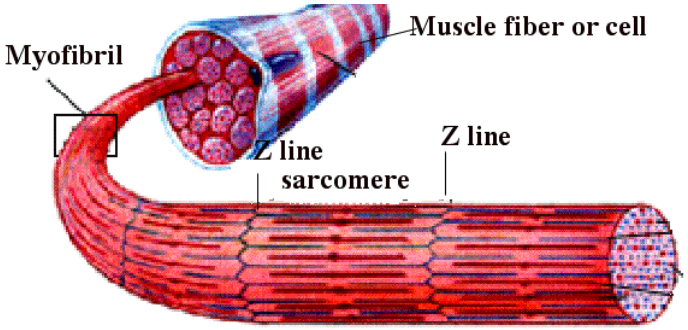
Sarcoplasmic reticulum (smooth ER) – reservoir of Ca^{2+}

Myofibrils (parallel to the length of the muscle fiber)

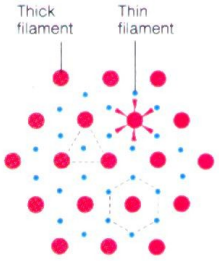


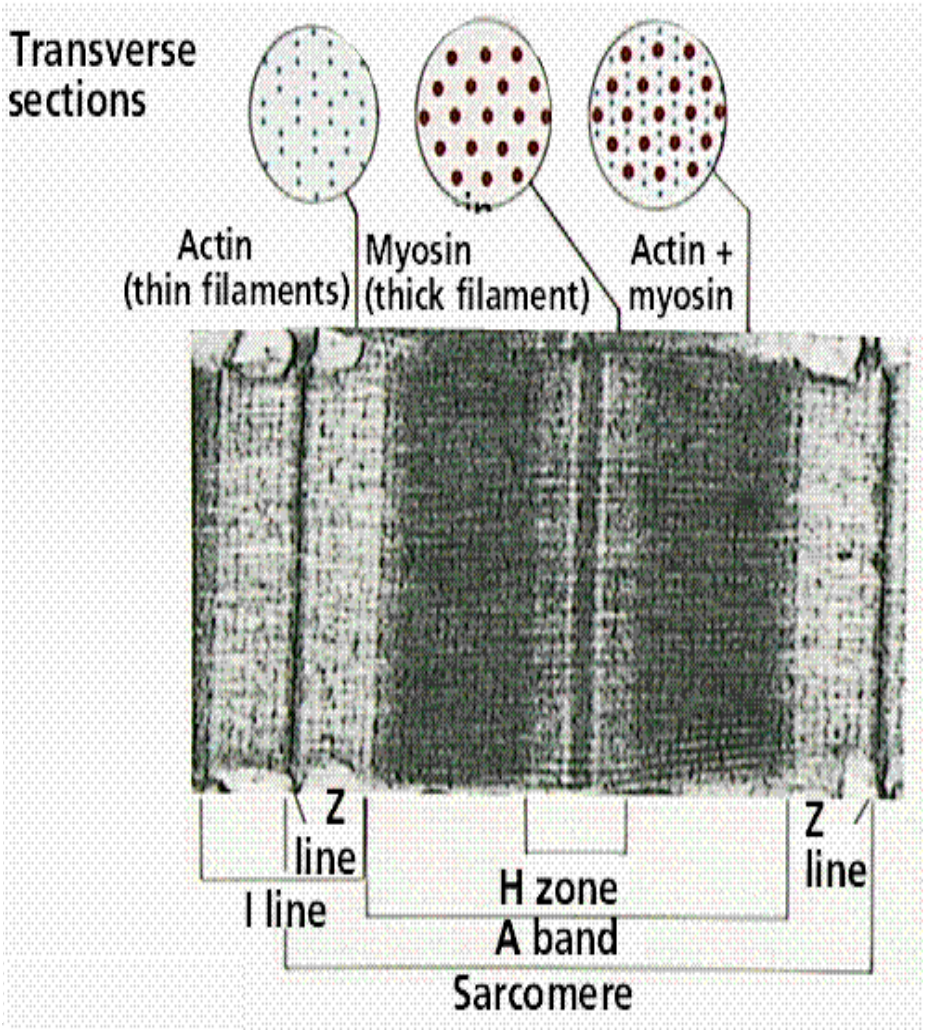
MYOFIBRILS

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

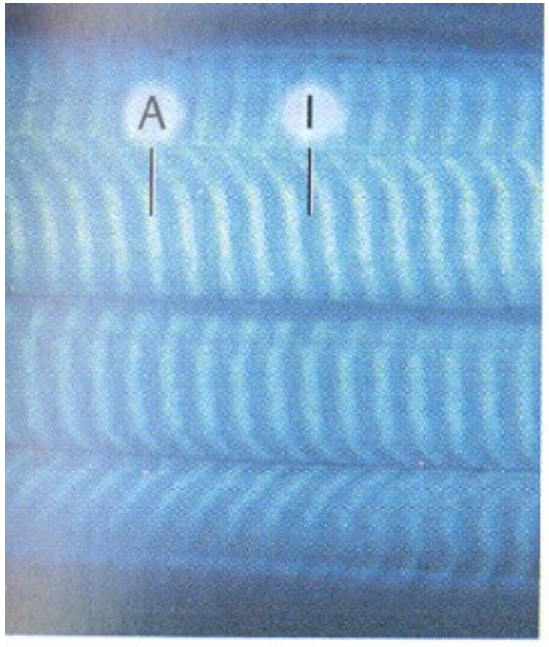


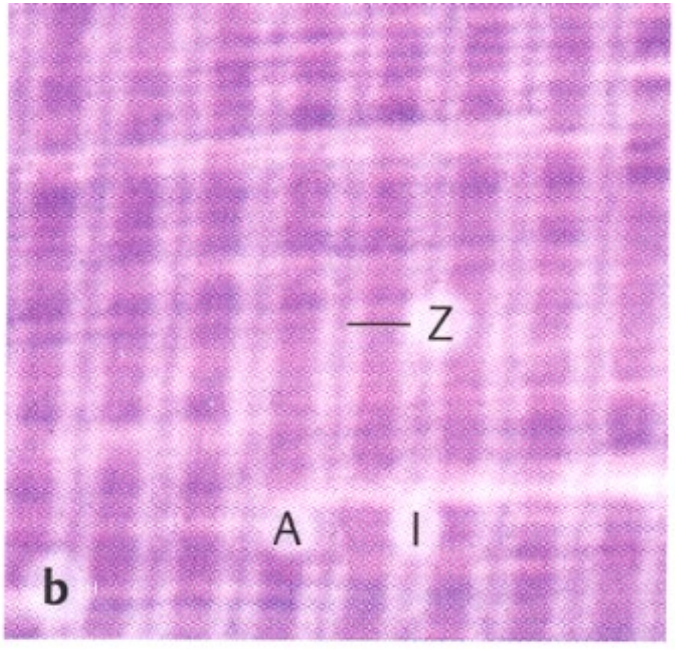
– Actin + myosin myofilaments
– Sarcomere
– Z-line
– M-line and H-zone
– I-band, A-band

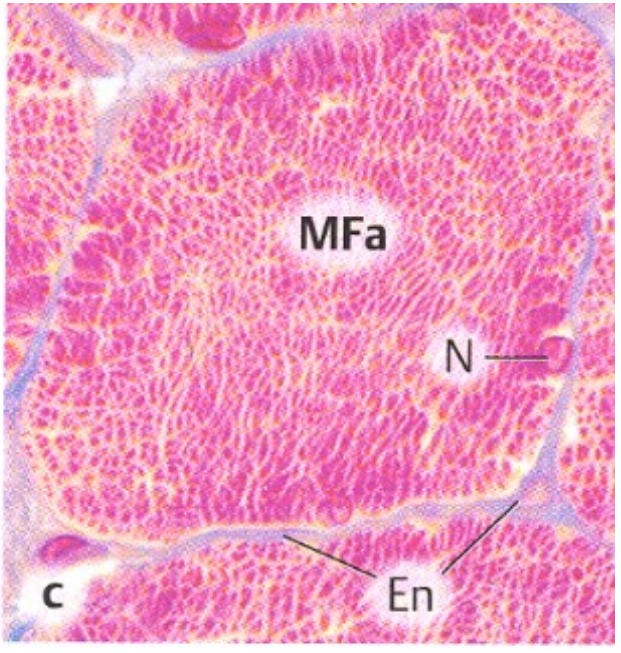


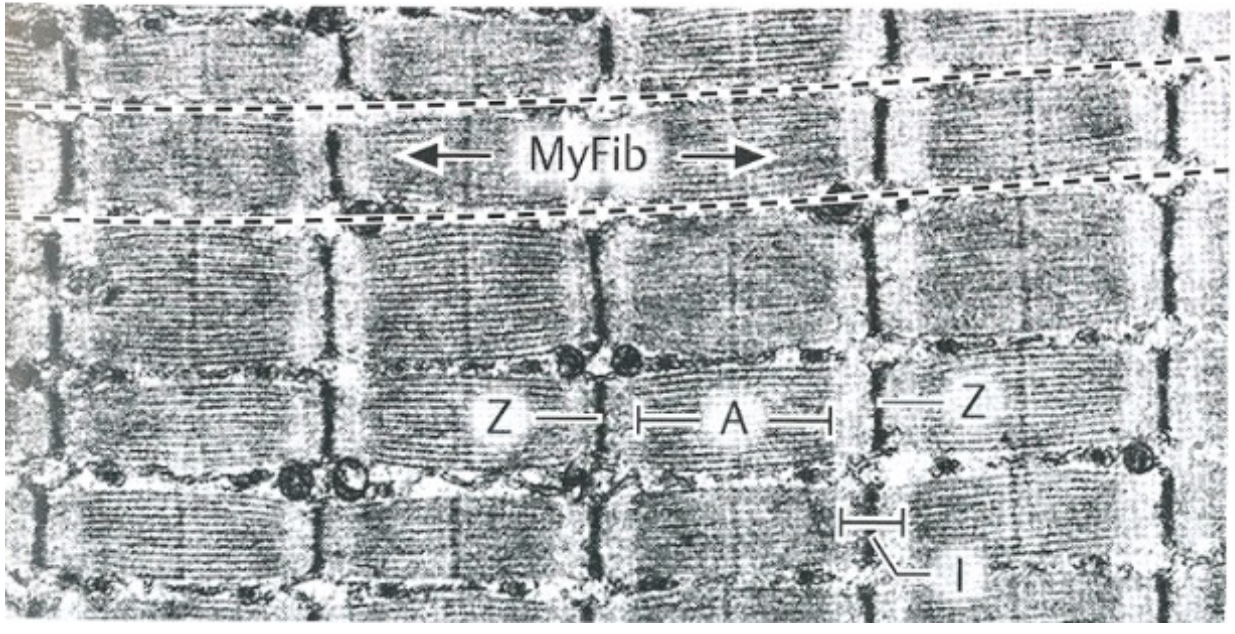


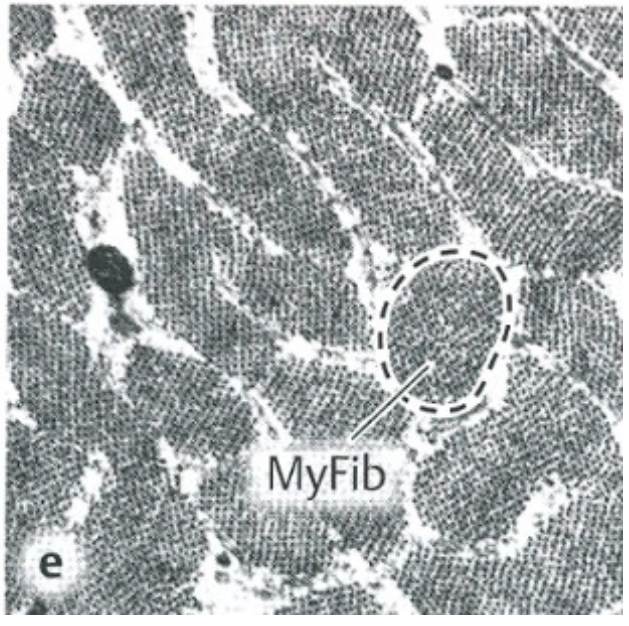
MYOFIBRILS



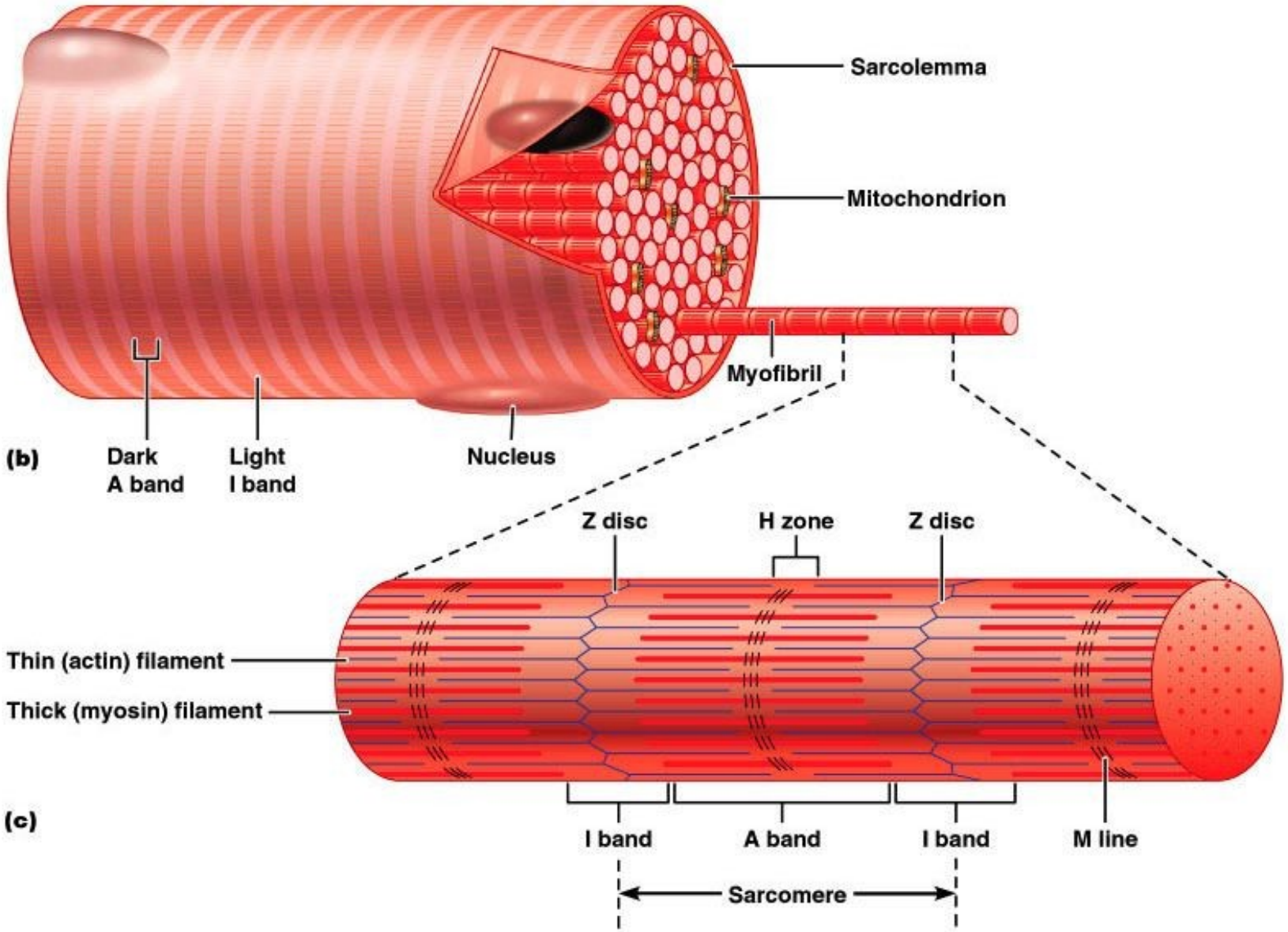








SARCOMERE



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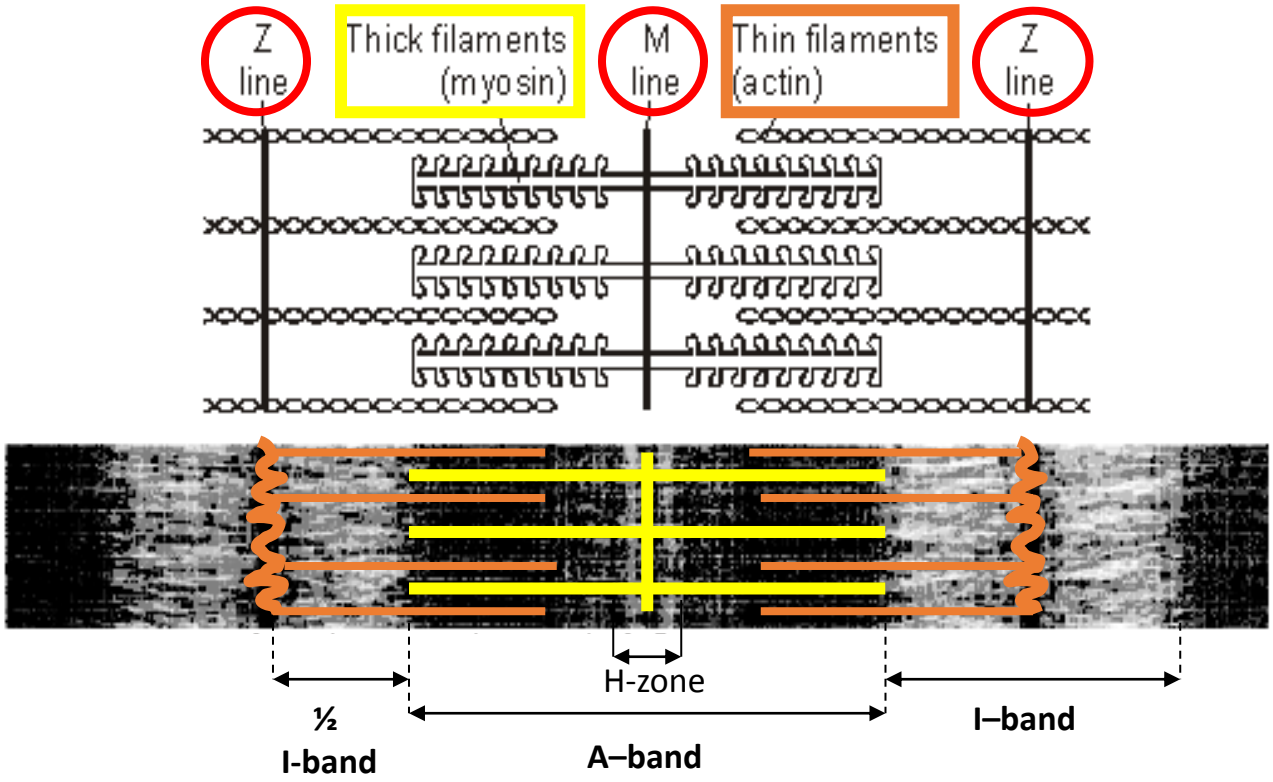
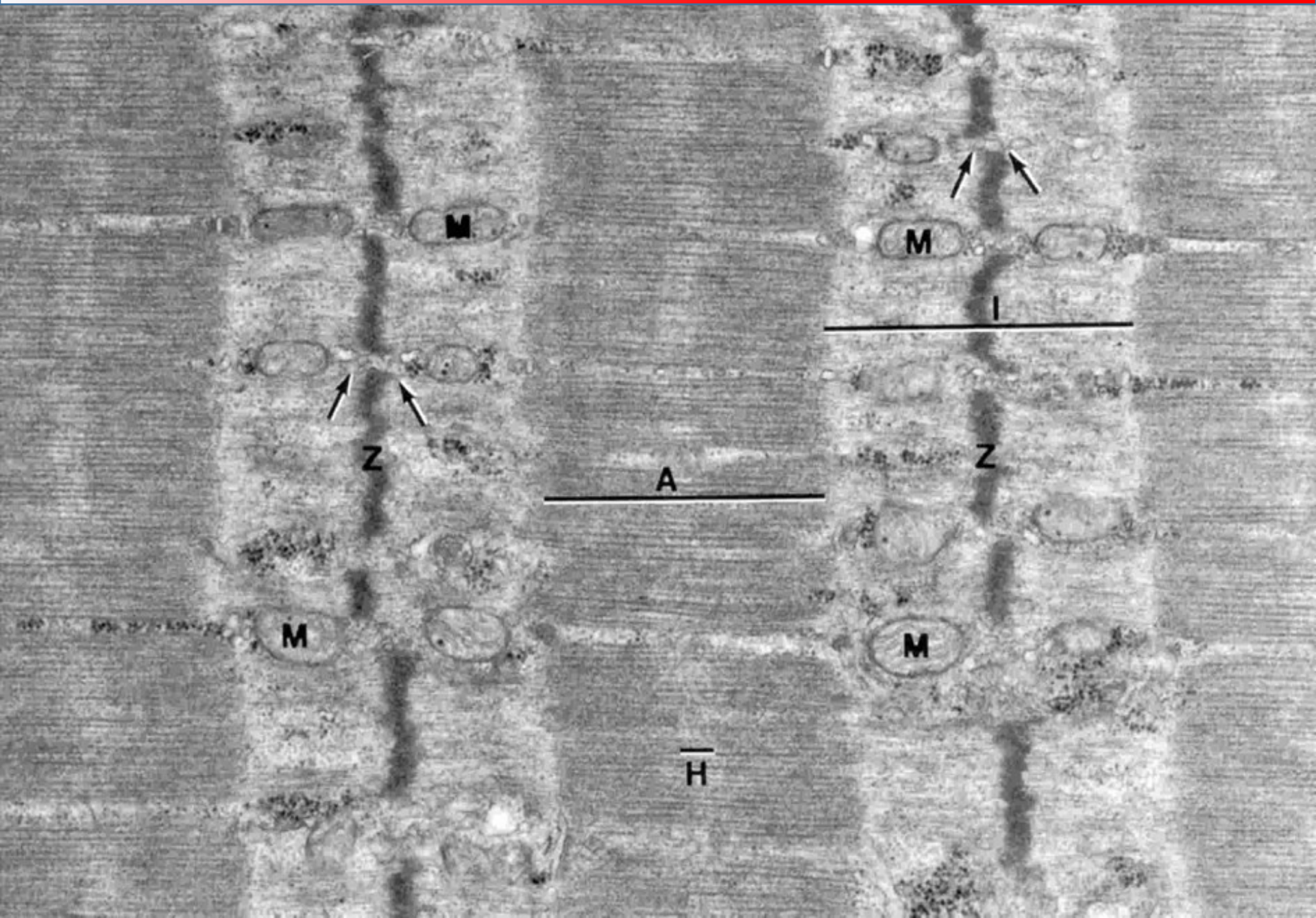
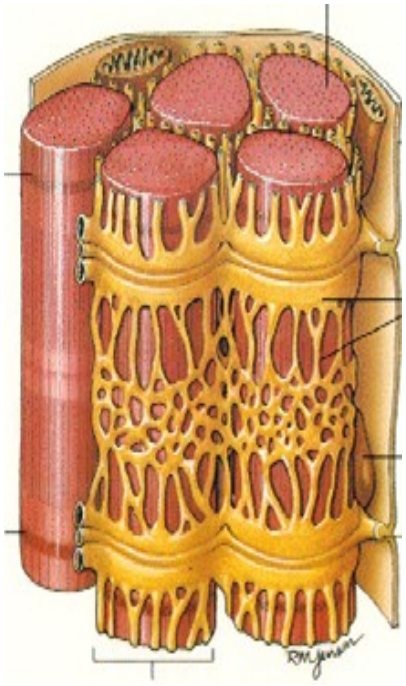
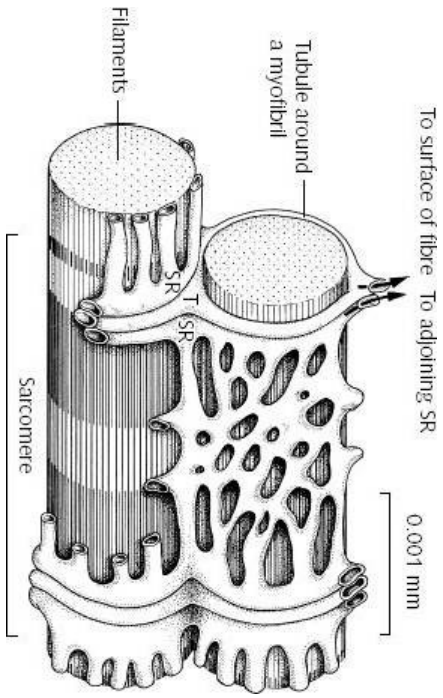

Z line
Thick filaments (myosin)
M line
Thin filaments (actin)
Z line
H-zone
½ I-band
A–band
I–band

SARCOMERE



SARCOPLASMIC RETICULUM





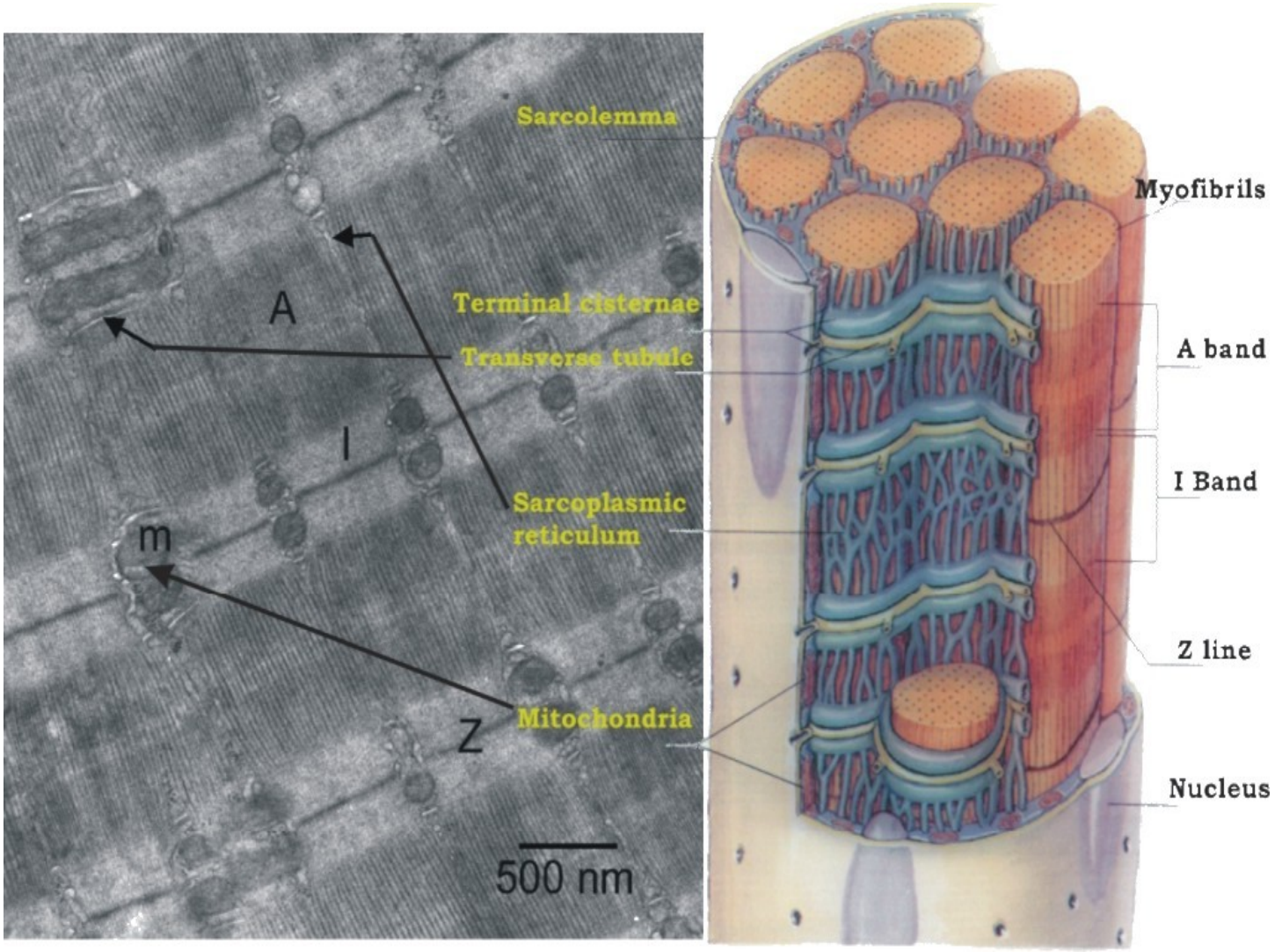
- Terminal cistern
- T-tubule
- Terminal cistern

TRIAD

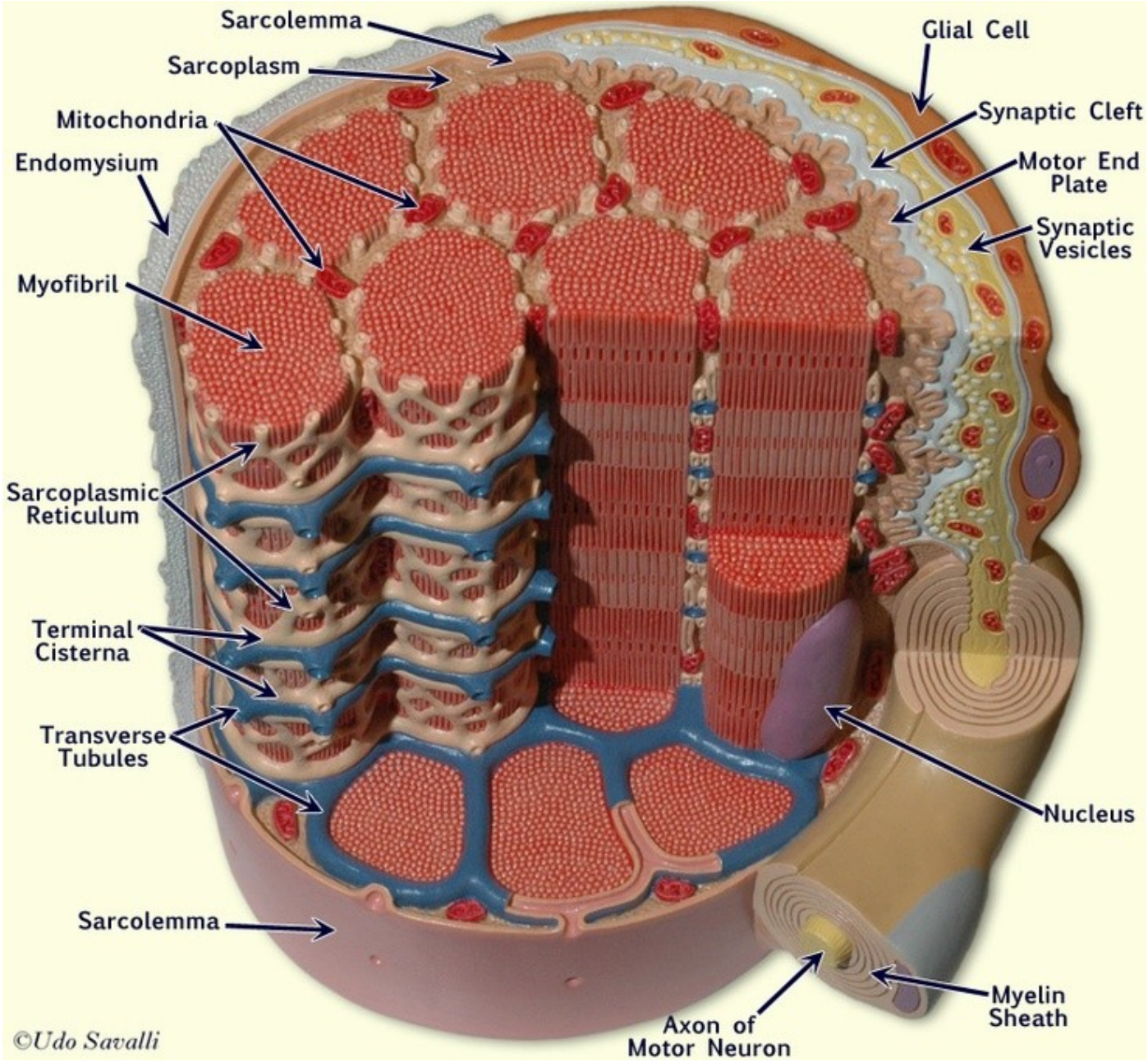
- communicating intracellular cavities around myofibrils, separated from cytosol
- **terminal cisternae** (“junction”) and **longitudinal tubules** (“L” system).
- reservoir of Ca^{II+} ions

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

SARCOPLASMIC RETICULUM

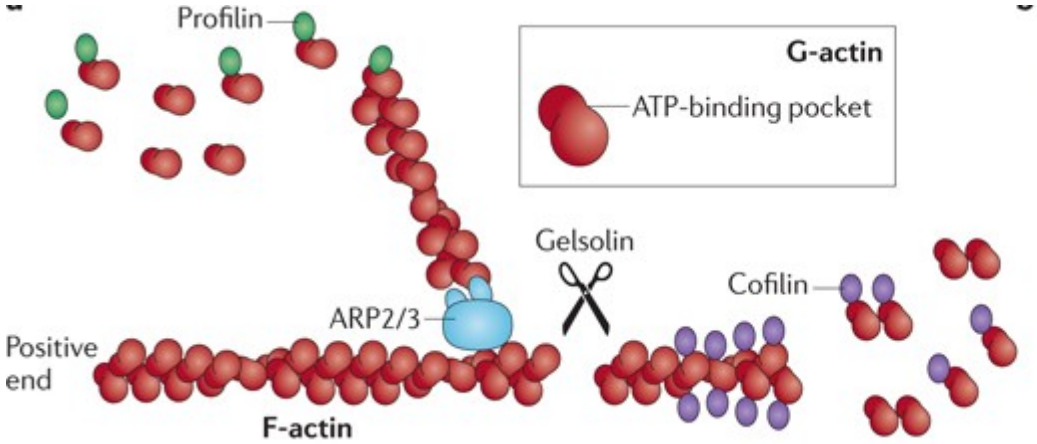


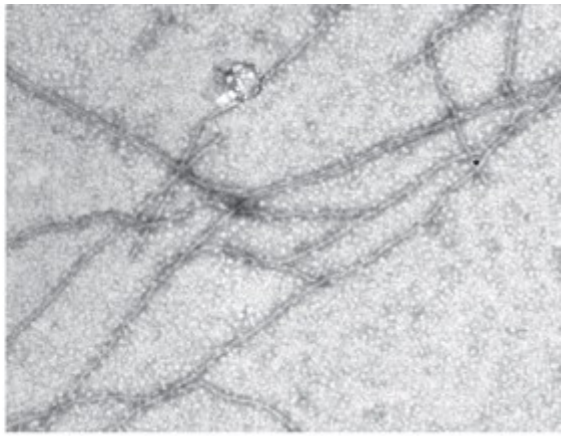
ULTRASTRUCTURE OF RHABDOMYOCYTE



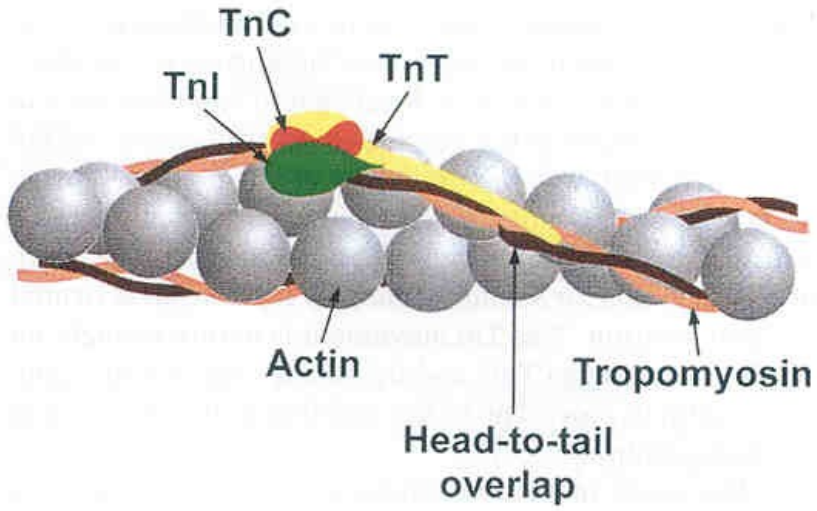
THIN MYOFILAMENTS

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





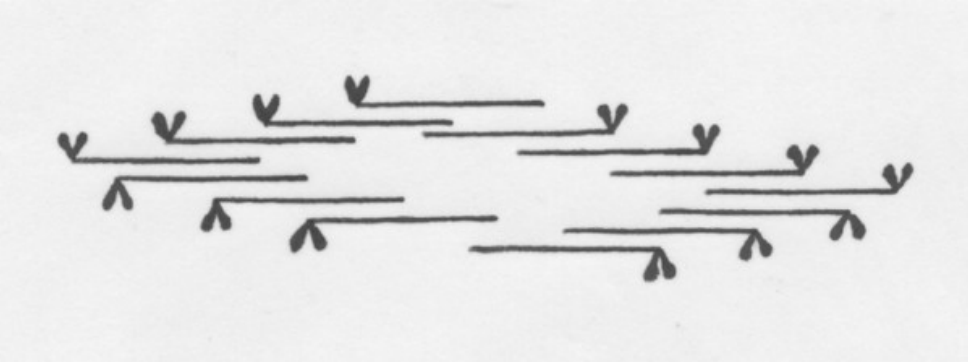
- Tropomyosin – thin double helix in groove of actin double helix, spans 7 monomers of G-actin
- Troponin – complex of 3 globular proteins
  - TnT (Troponin T) – binds tropomyosin
  - TnC (Troponin C) – binds calcium
  - TnI (Troponin I) inhibits interaction between thick and thin filaments

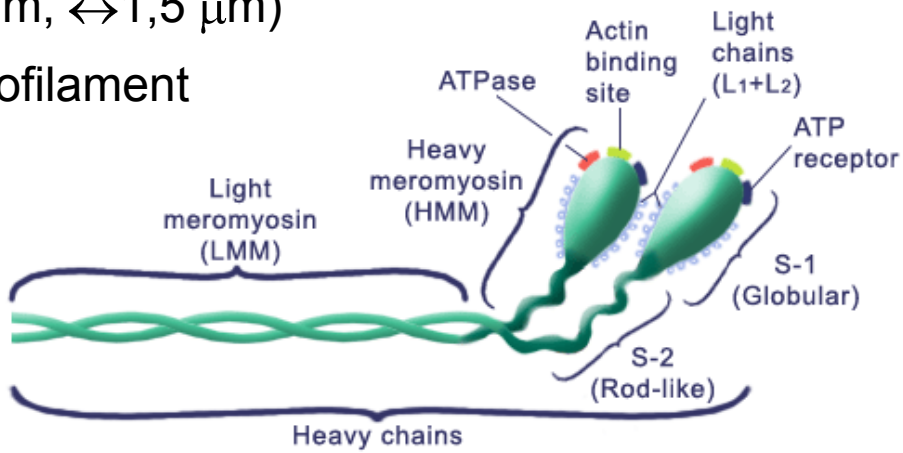


THICK MYOFILAMENTS

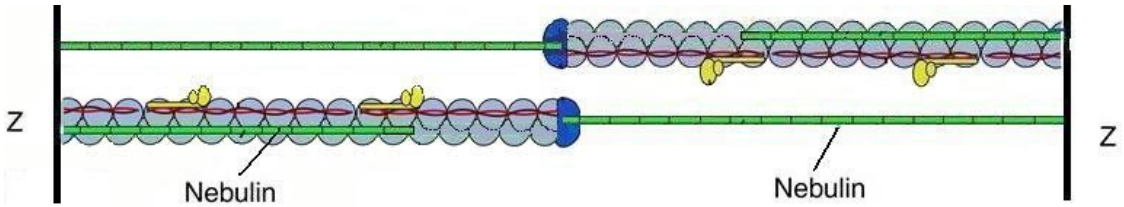
- **Myosin II**

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



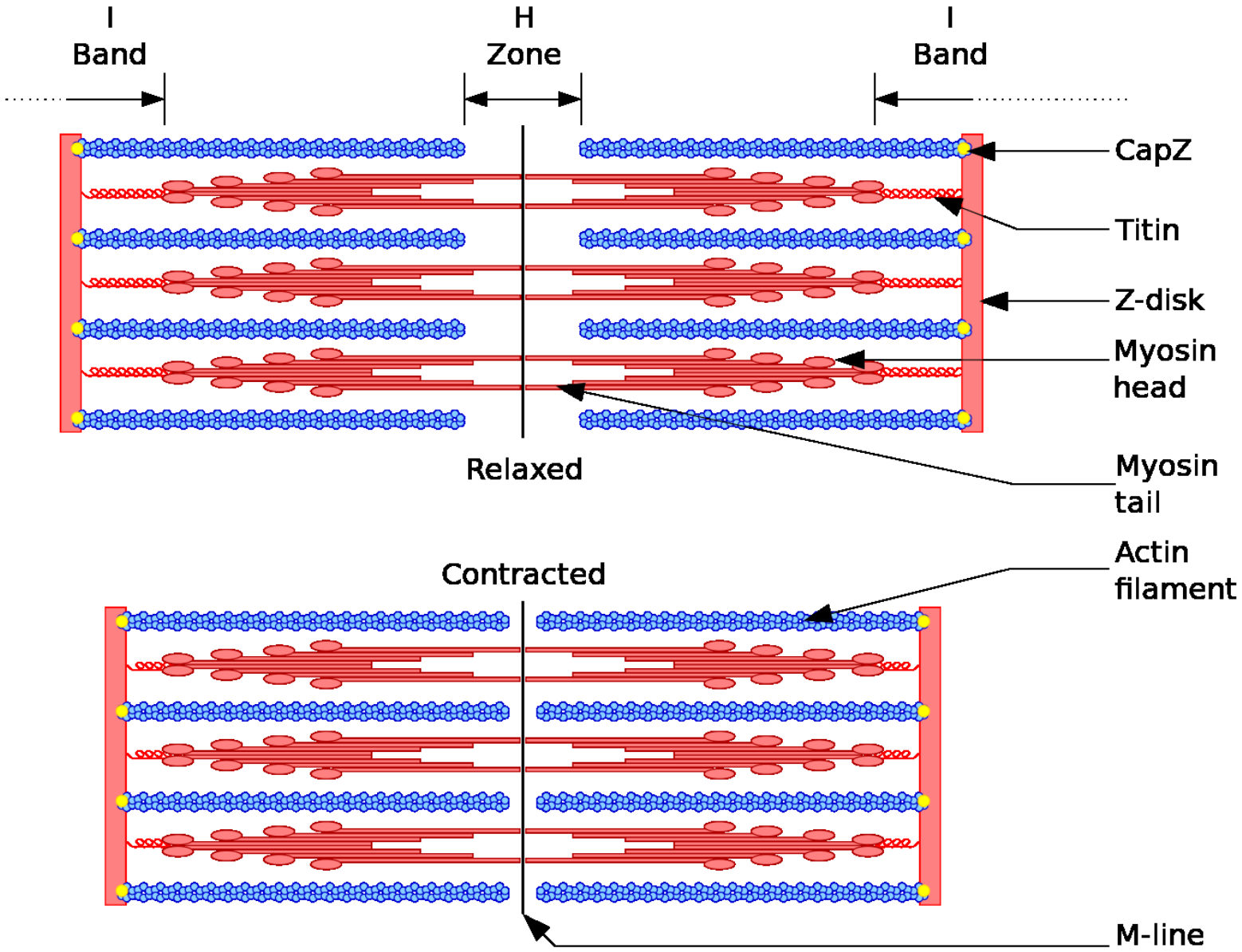


- **Nebulin**
  - 600-900kDa
  - F-actinu stabilization



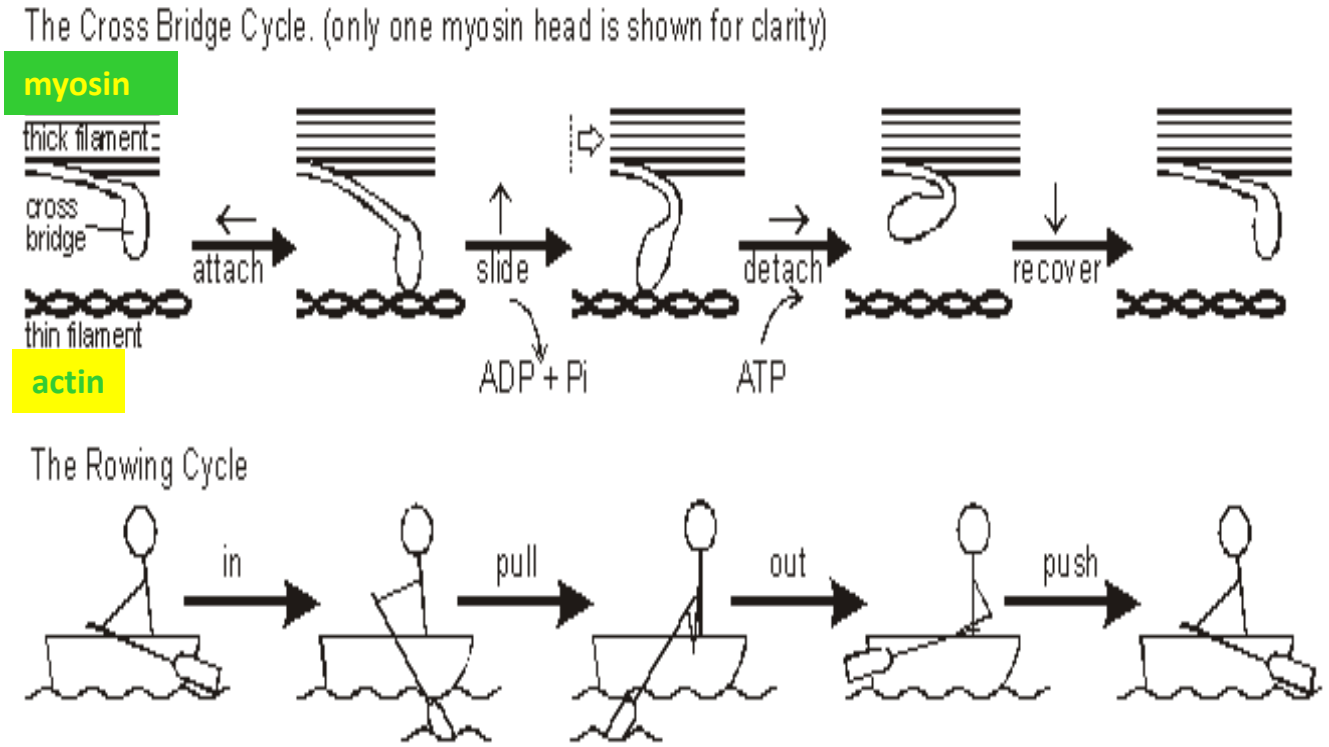
- **Titin**
  - >MDa
  - Myosin II stabilization

MYOFILAMENTS ASSEMBLE TO CONTRACTIVE STRUCTURES



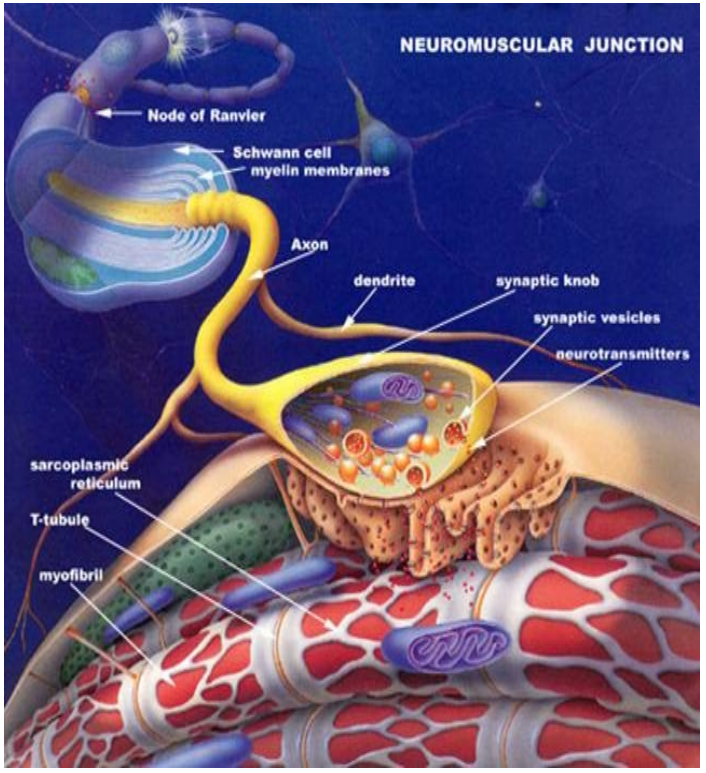
MYOFILAMENTS ASSEMBLE TO CONTRACTIVE STRUCTURES

- 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



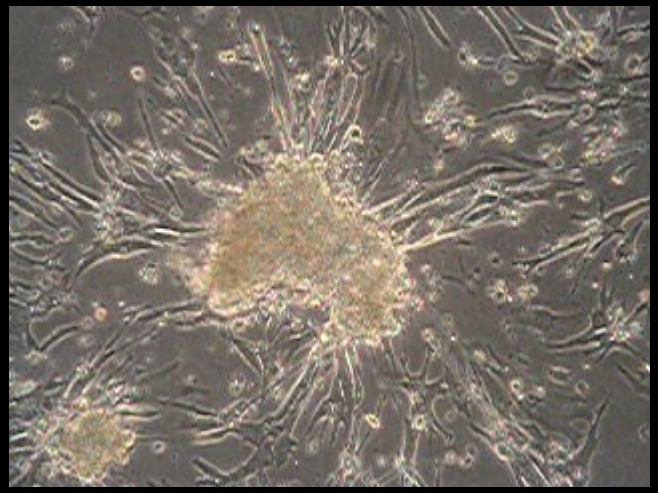
MECHANISM OF CONTRACTION

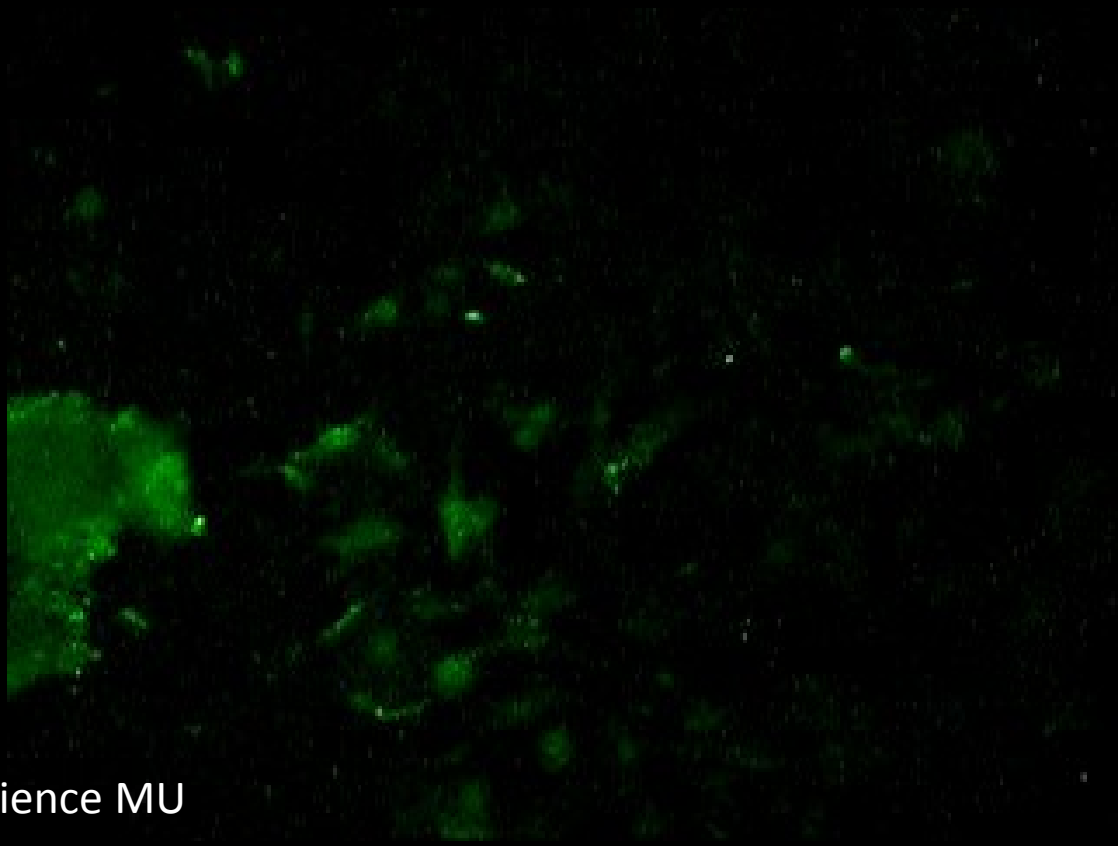
1. Impulse along motor neuron axon
2. Depolarization of presynaptic membrane (Na^+ influx)
3. Synaptic vesicles fuse with presynaptic membrane
4. Acetylcholine exocyted to synaptic cleft
5. Acetylcholine diffuses over synaptic cleft
6. Acetylcholine binds to receptors in postsynaptic membrane
7. Depolarization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



MECHANISM OF CONTRACTION

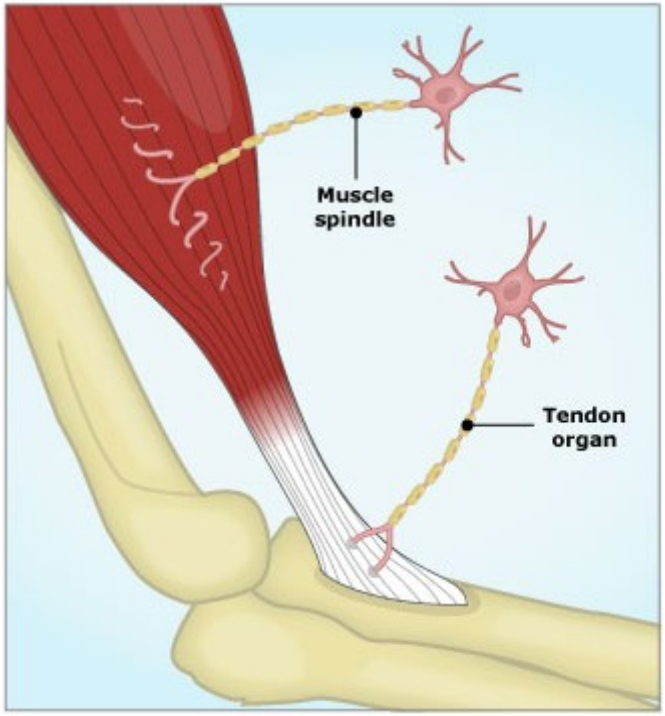
http://highered.mheducation.com/sites/0072495855/student_view0/chapter10/animation__breakdown_of_atp_and_cross-bridge_movement_during_muscle_contraction.html





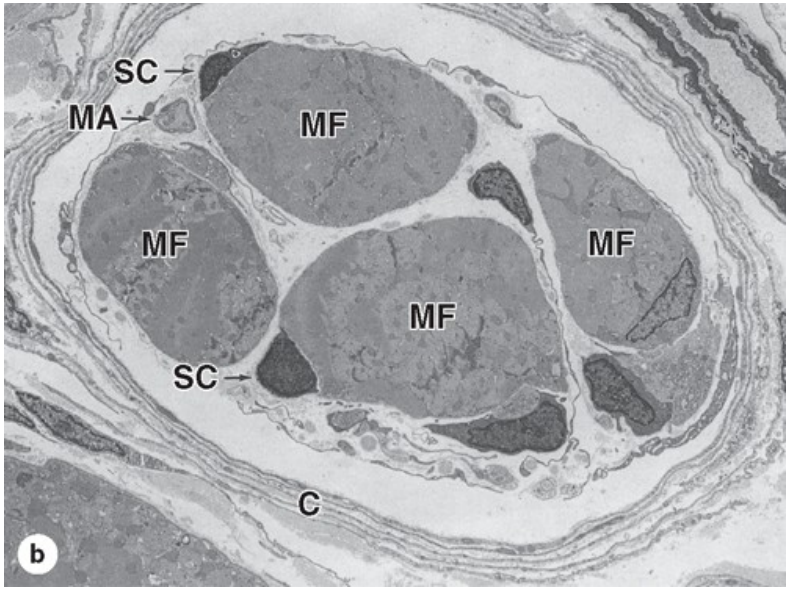
Courtesy Dr. Pacherník, Faculty of Science MU

PROPRIORECEPTORS



Muscle spindles

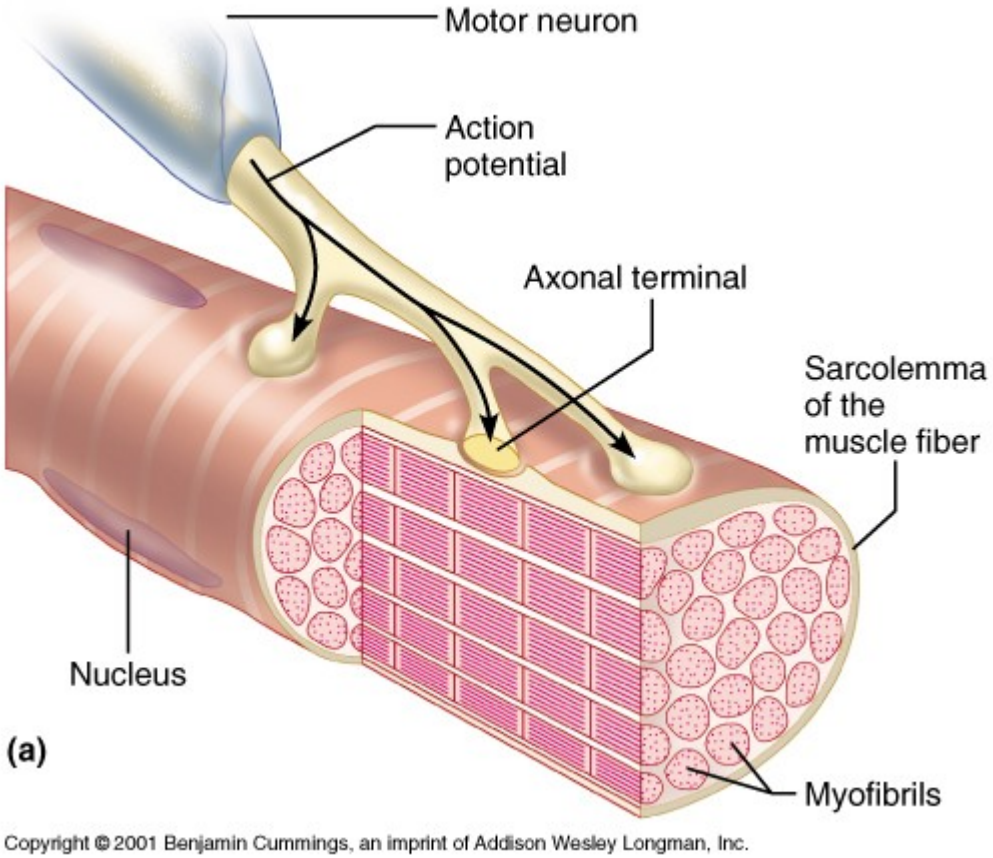
- change in muscle elongation (stretch)
- modified perimysium
- thin muscle (intrafusal) fibers
- sensory endings
- reflexes, coordination of muscle groups

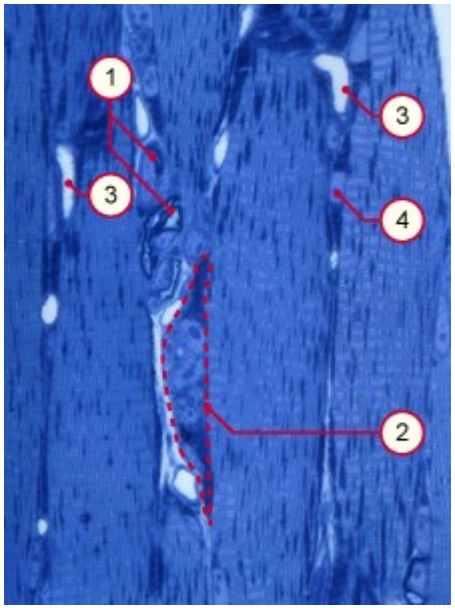


Golgiho tendon organs

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

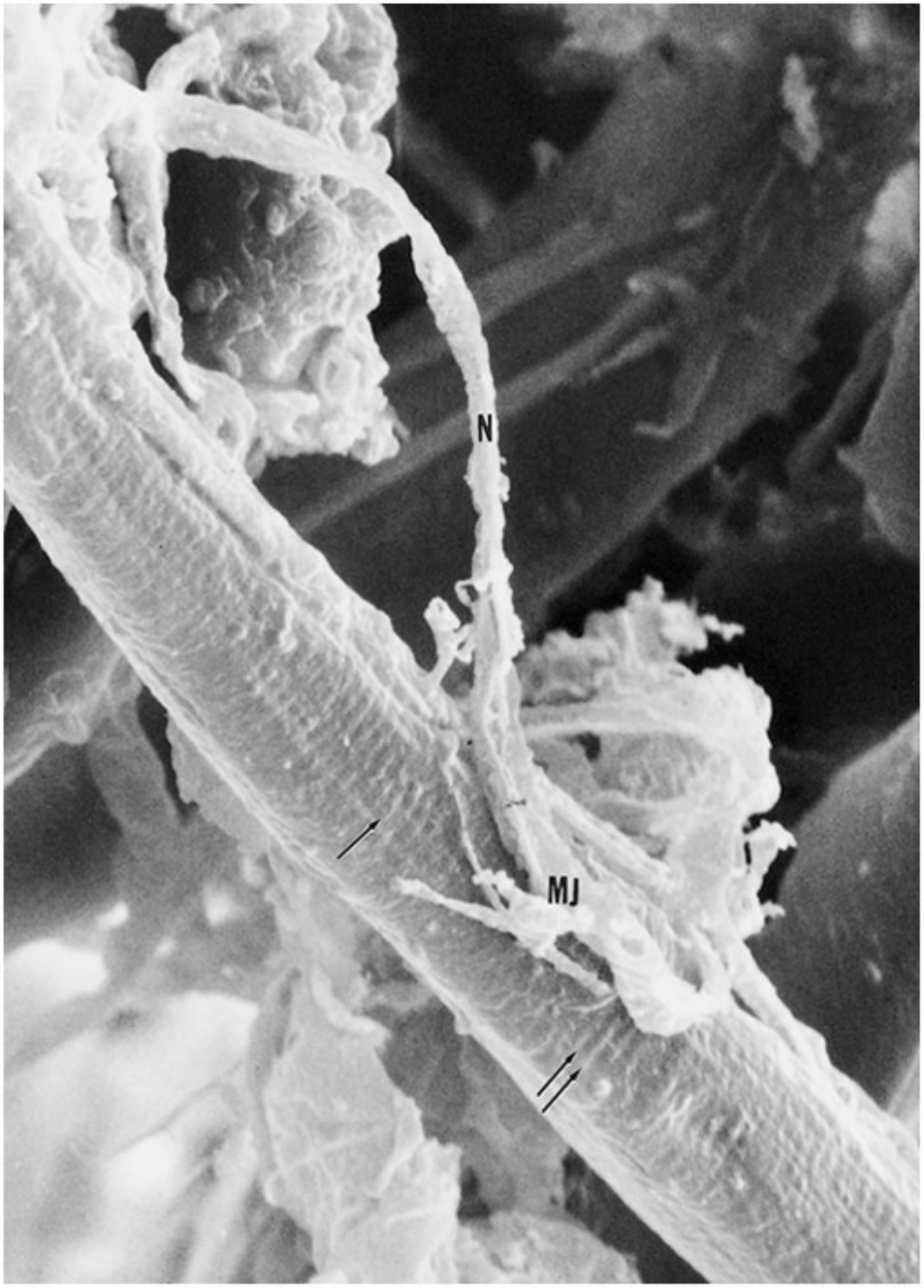
NEUROMUSCULAR JUNCTION



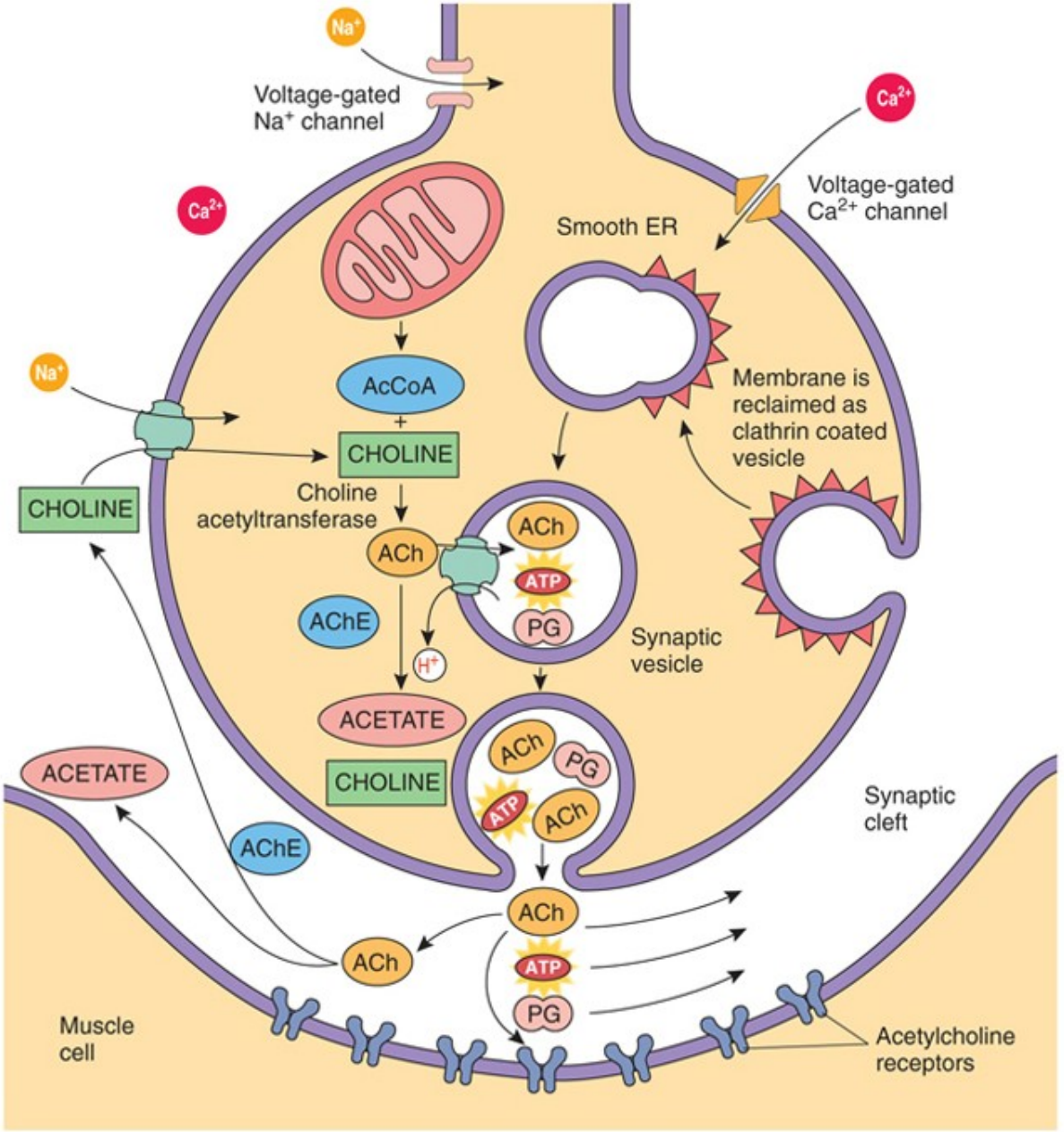


1 Myelinated axons
2 Neuromuscular junction
3 Capillaries
4 Muscle fiber nucleus

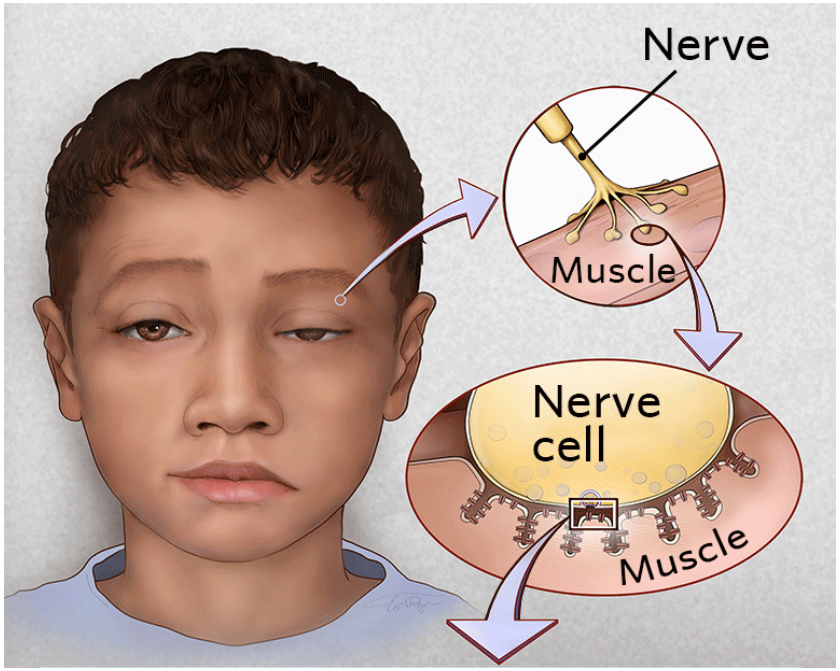
NEUROMUSCULAR JUNCTION

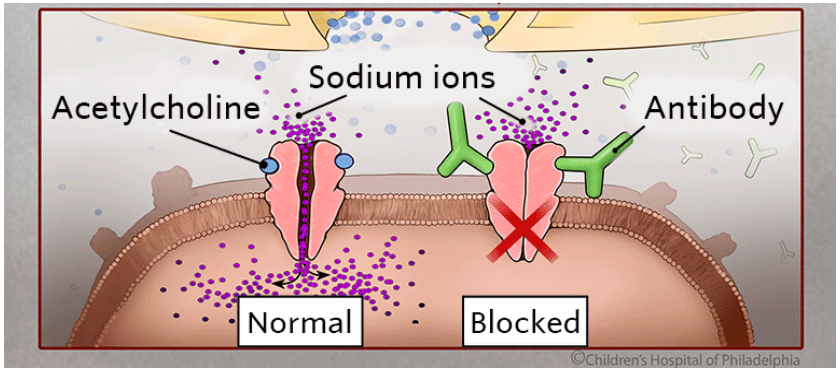


NEUROMUSCULAR JUNCTION

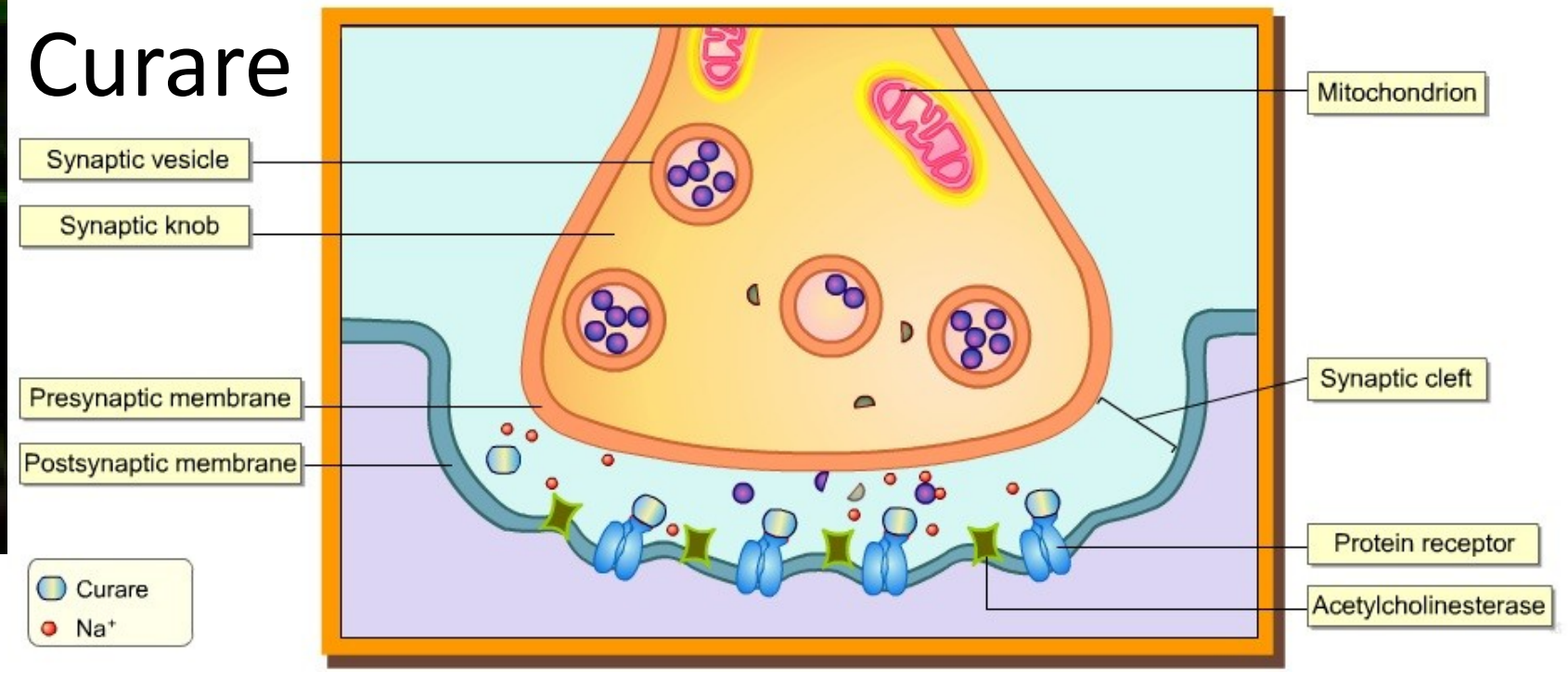


MYASTHENIA GRAVIS



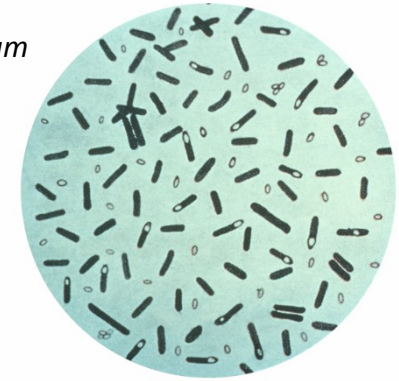


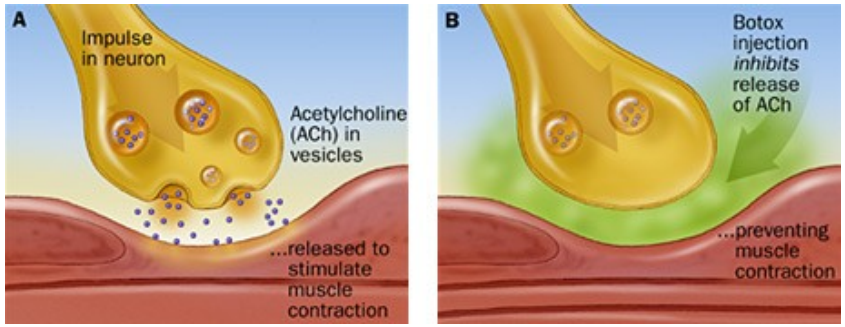
Curare


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

Botulotoxin

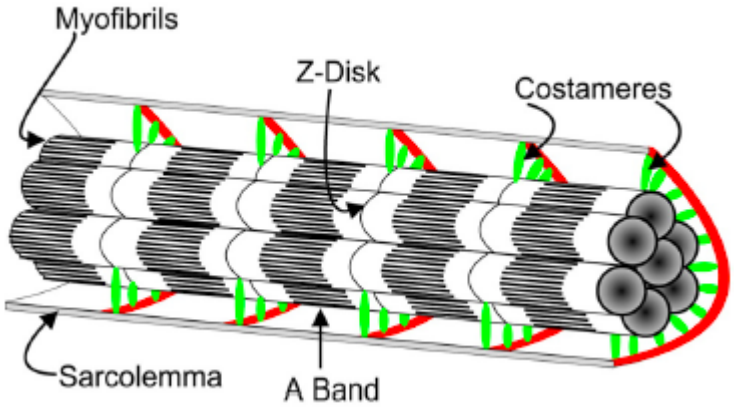
Clostridium botulinum

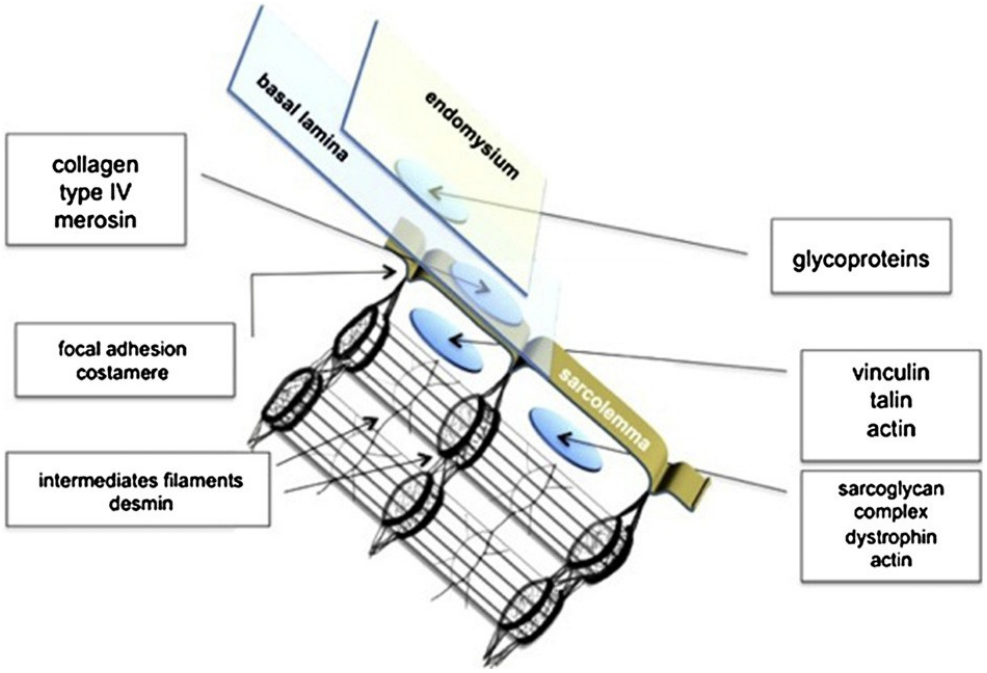




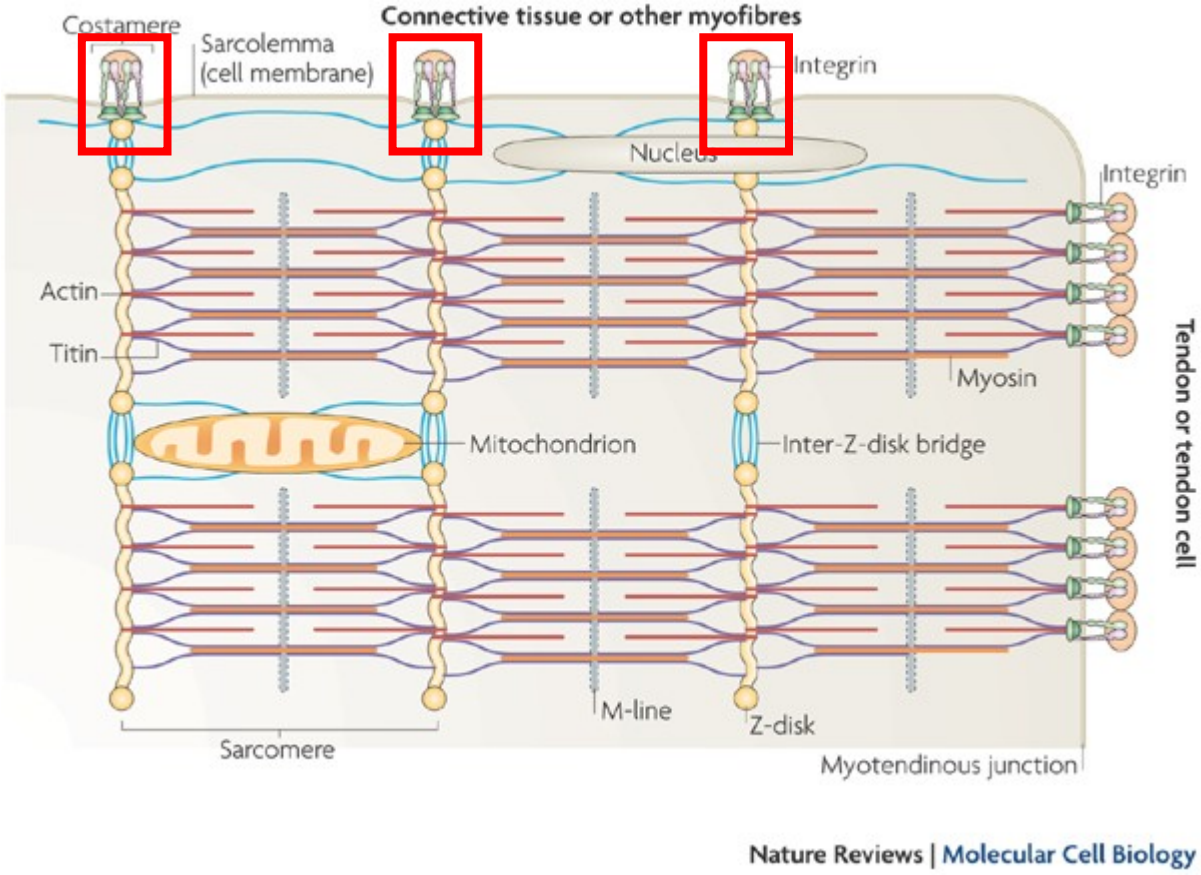
COSTAMERES

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

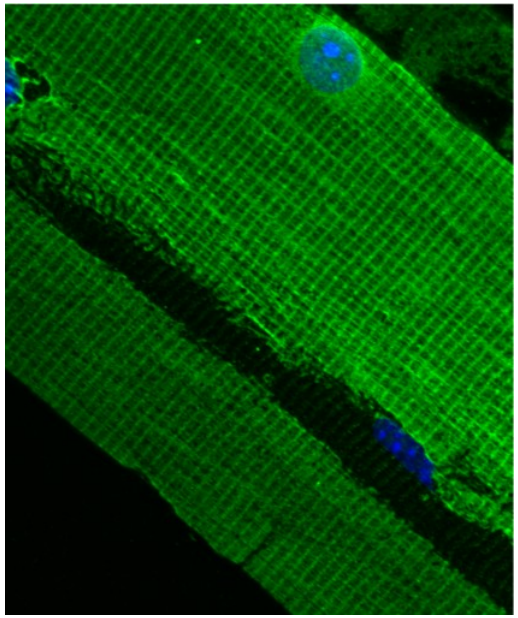




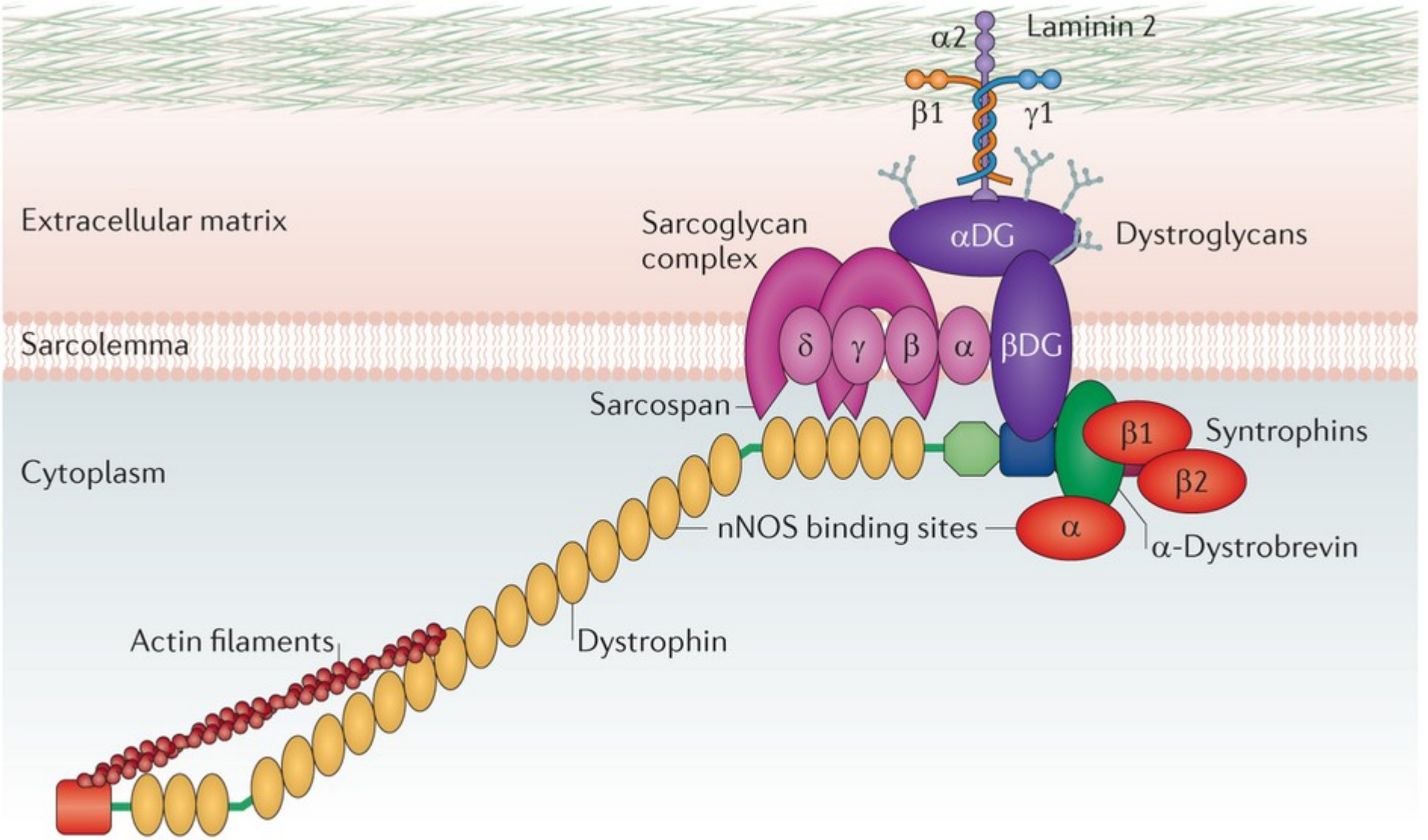
COSTAMERES



Nature Reviews | Molecular Cell Biology

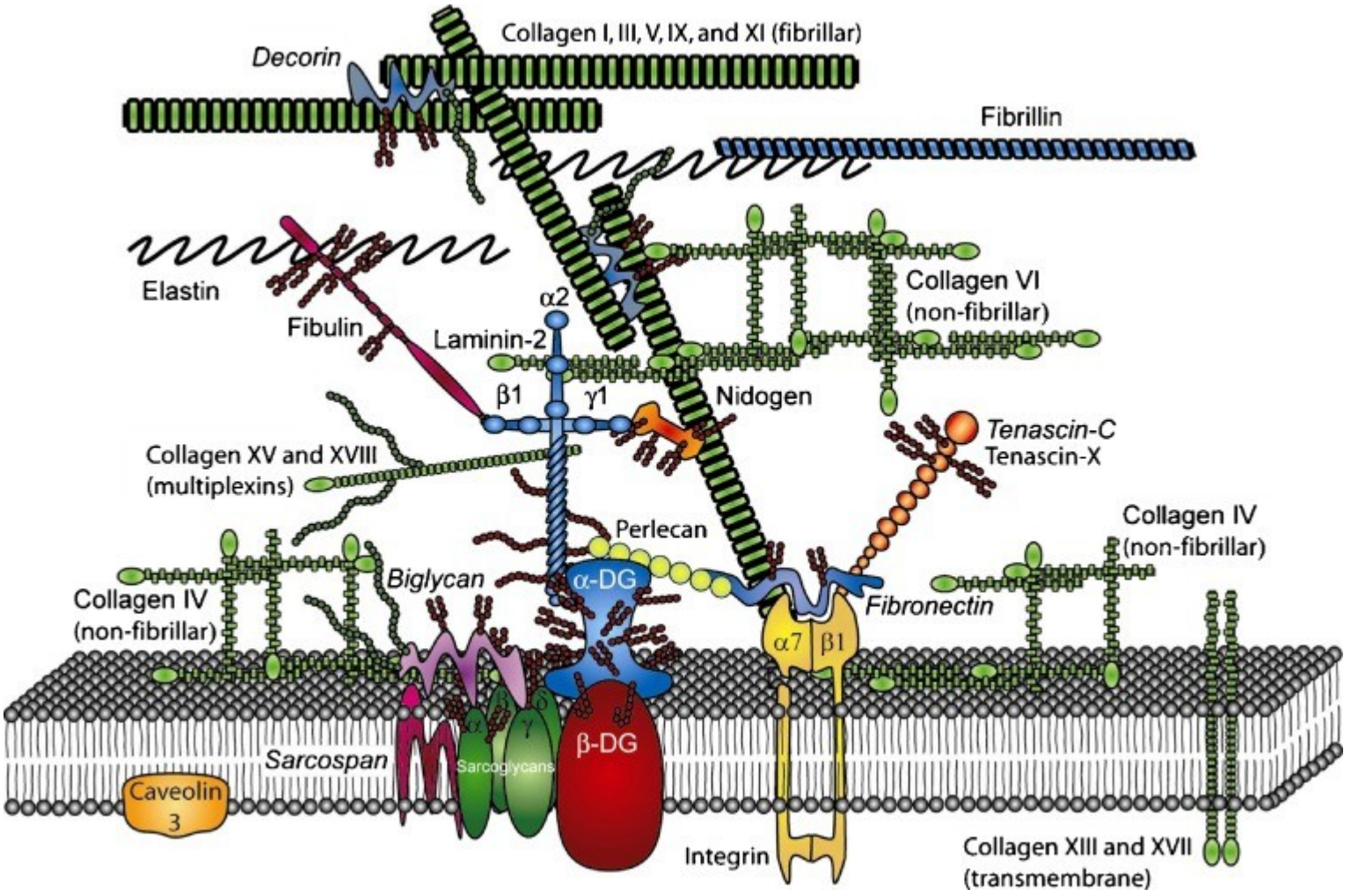


COSTAMERES

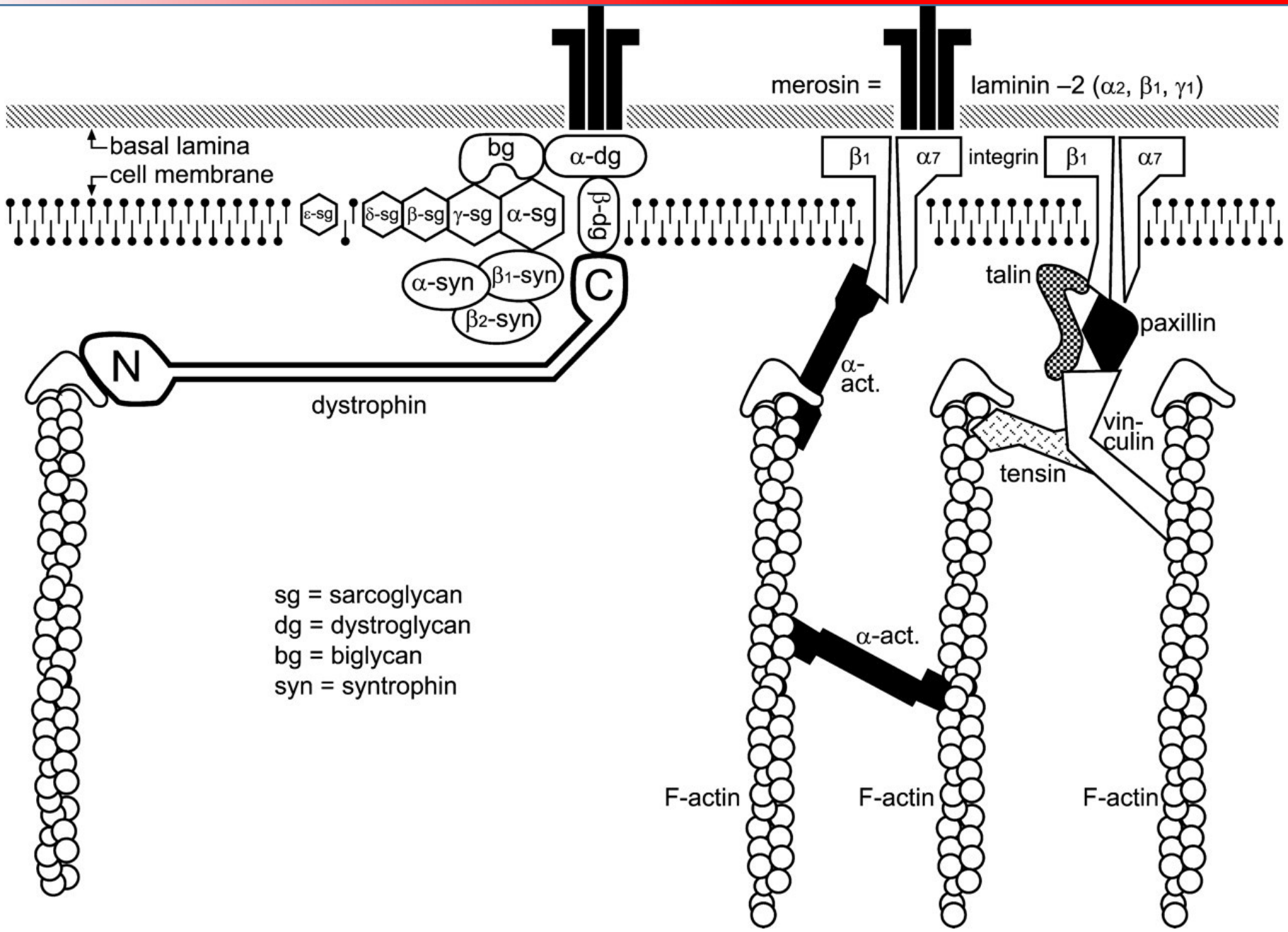


Nature Reviews | Genetics

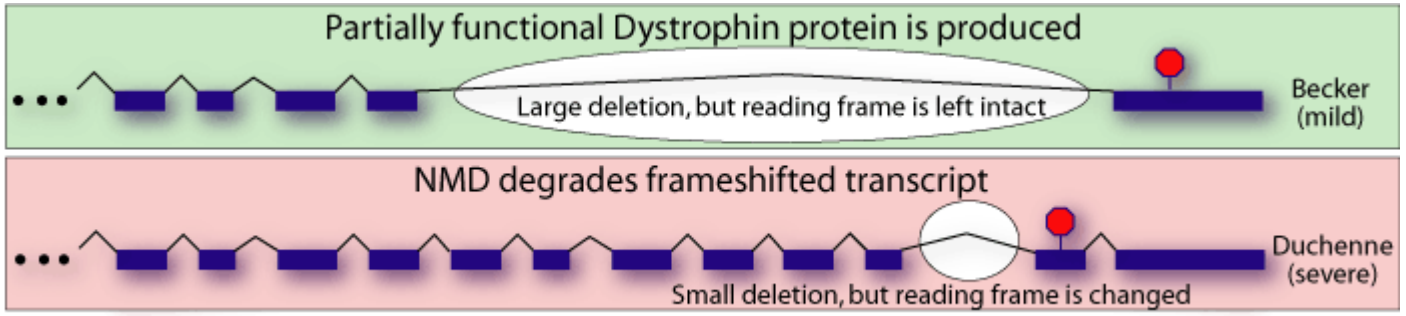
COSTAMERES

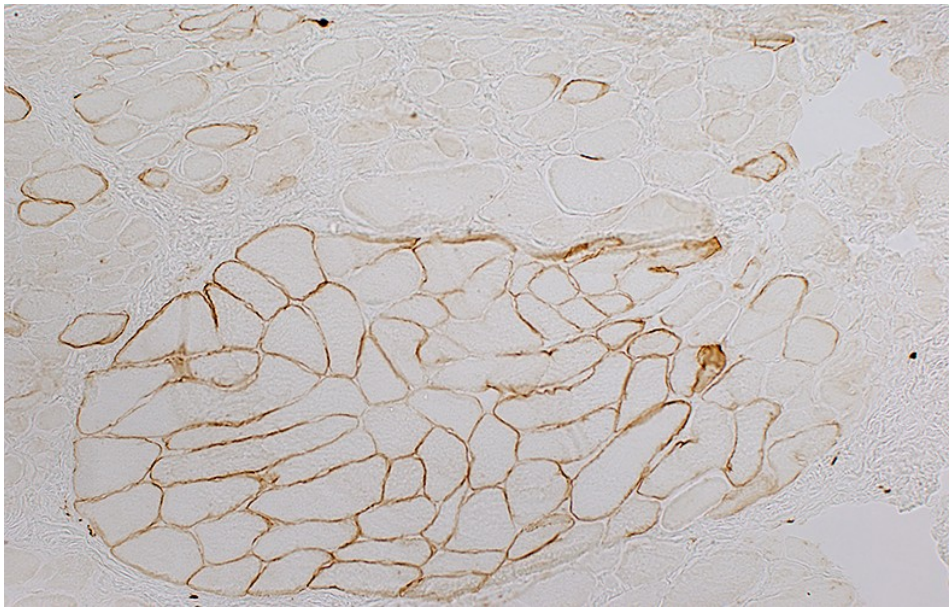

Collagen I, III, V, IX, and XI (fibrillar)
Decorin
Fibrillin
Elastin
Fibulin
α2
Laminin-2
β1
γ1
Collagen VI
(non-fibrillar)
Nidogen
Tenascin-C
Tenascin-X
Collagen XV and XVIII
(multiplexins)
Perlecan
Collagen IV
(non-fibrillar)
Biglycan
α-DG
Collagen IV
(non-fibrillar)
Fibronectin
α7
β1
Sarcospan
Sarcoglycans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

COSTAMERES


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
sg = sarcoglycan
dg = dystroglycan
bg = biglycan
syn = syntrophin
merosin =
laminin –2 (α2, β1, γ1)
β1
α7
integrin
β1
α7
talin
paxillin
α-
act.
vin-
culin
tensin
α-act.
F-actin
F-actin
F-actin

DUCHENNE MUSCULAR DYSTROPHY

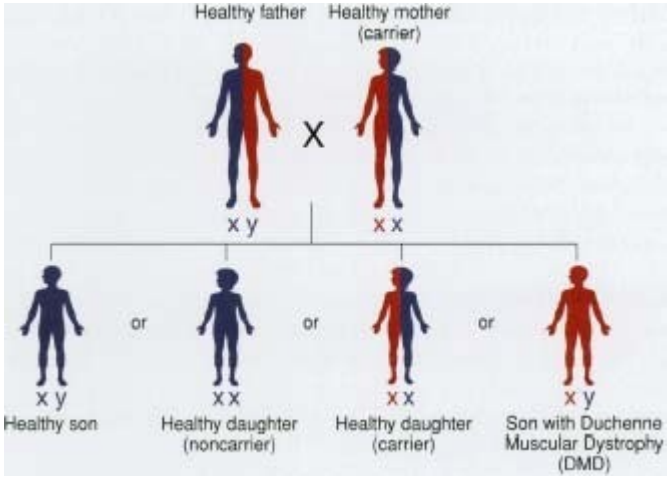


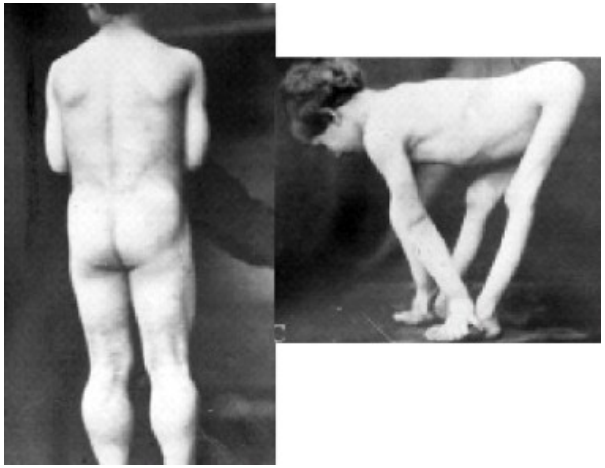


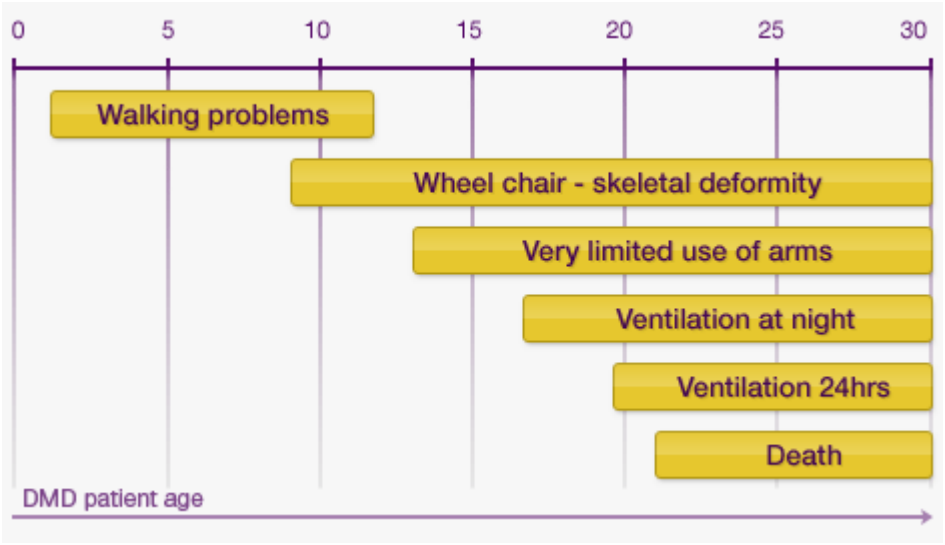
Lane 1: Becker dystrophy; Dystrophin has reduced abundance but normal size.
Lane 2: Becker dystrophy; Dystrophin has reduced size and abundance.
Lane 3: Normal; Dystrophin has normal size and amount.
Lane 4: Duchenne dystrophy; Almost no protein is present.

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

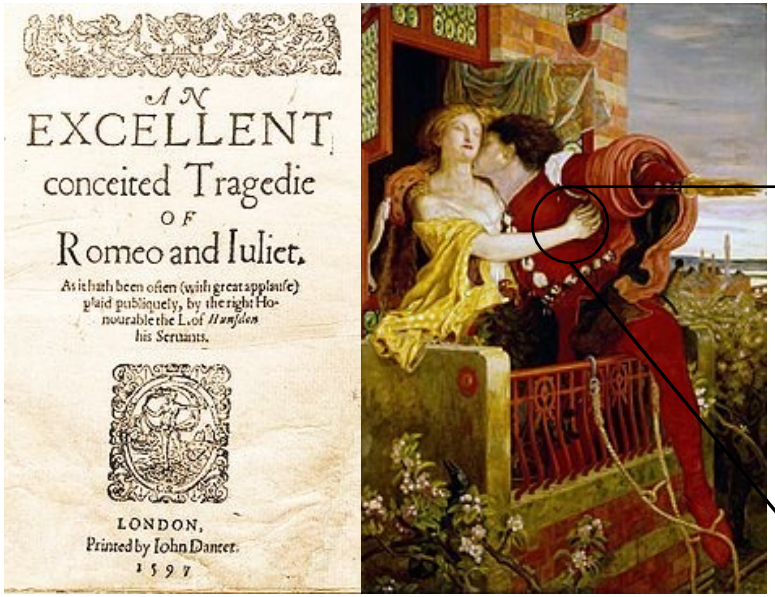
COSTAMERES

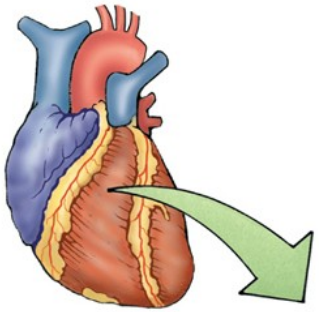

Healthy father
Healthy mother (carrier)
X
x y
x x
or
or
or
x y
Healthy son
x x
Healthy daughter (noncarrier)
x x
Healthy daughter (carrier)
x y
Son with Duchenne Muscular Dystrophy (DMD)

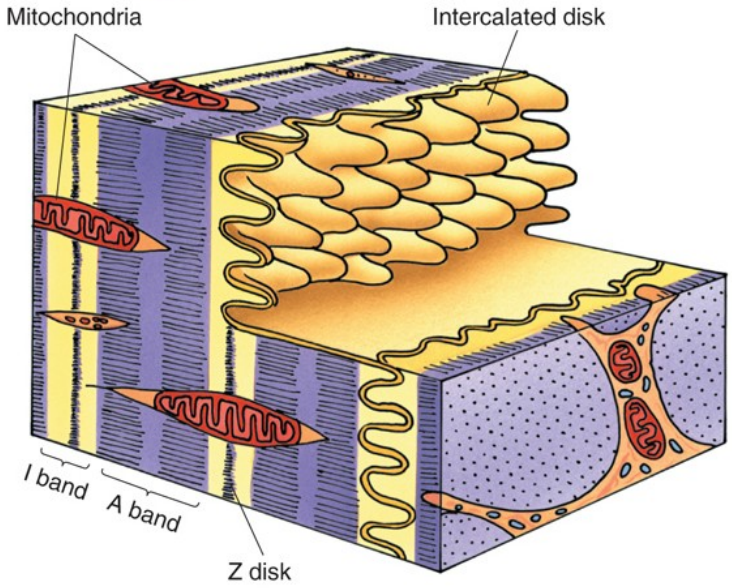



0
5
10
15
20
25
30
Walking problems
Wheel chair - skeletal deformity
Very limited use of arms
Ventilation at night
Ventilation 24hrs
Death
DMD patient age

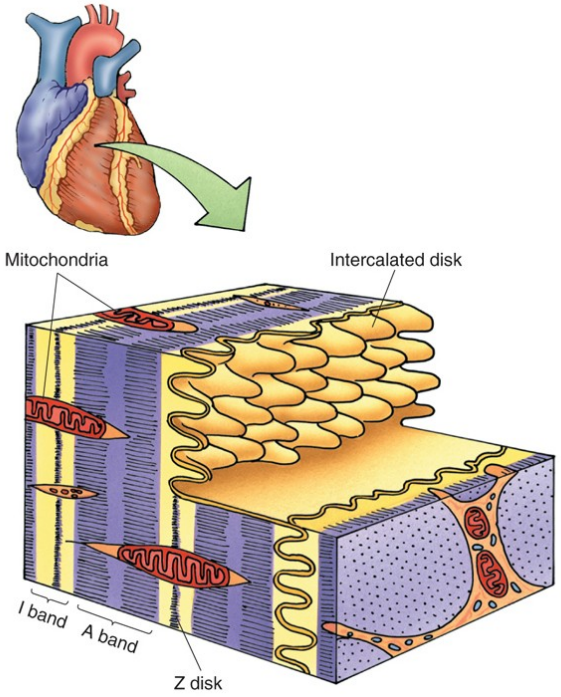
CARDIAC MUSCLE TISSUE





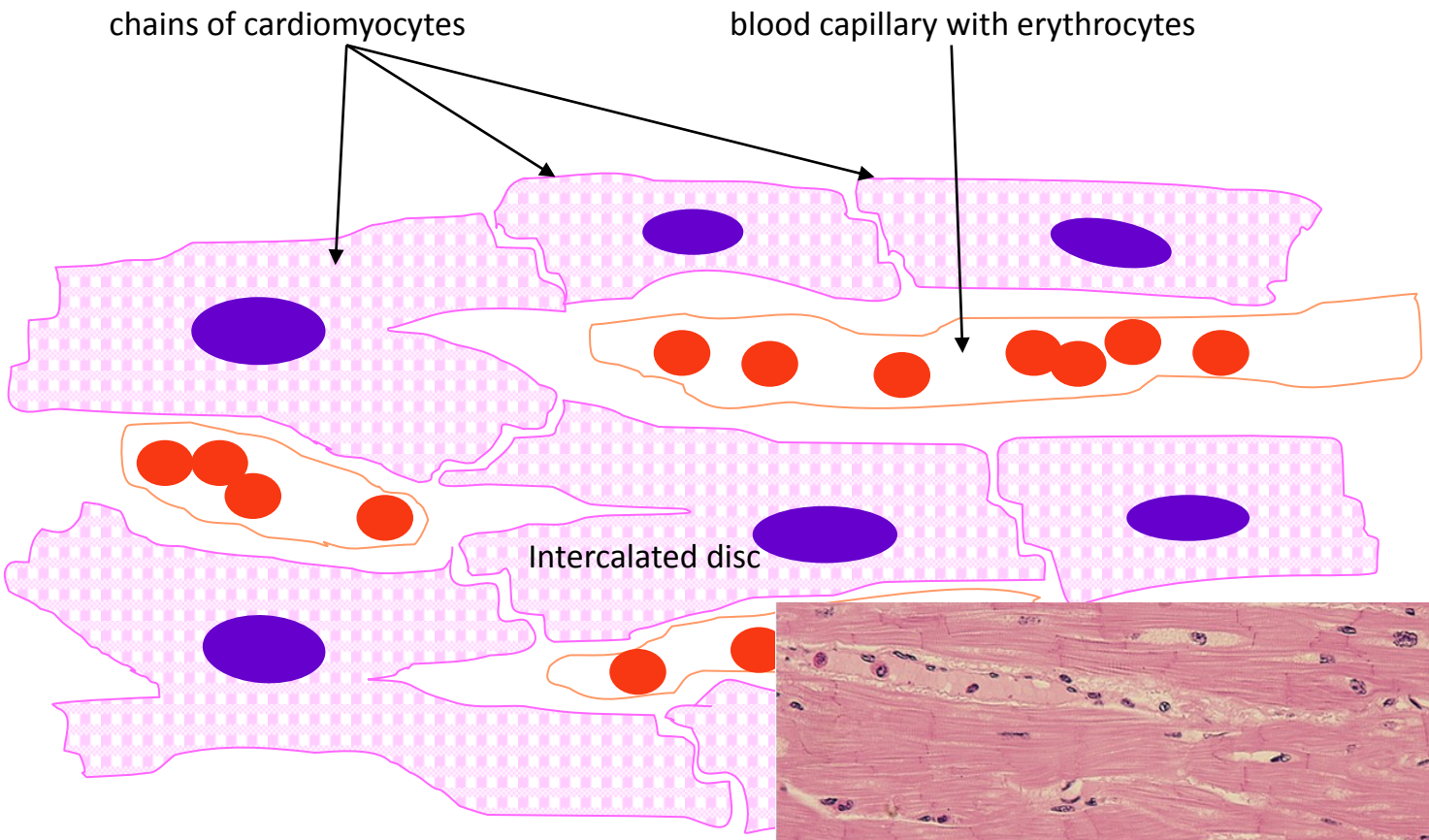


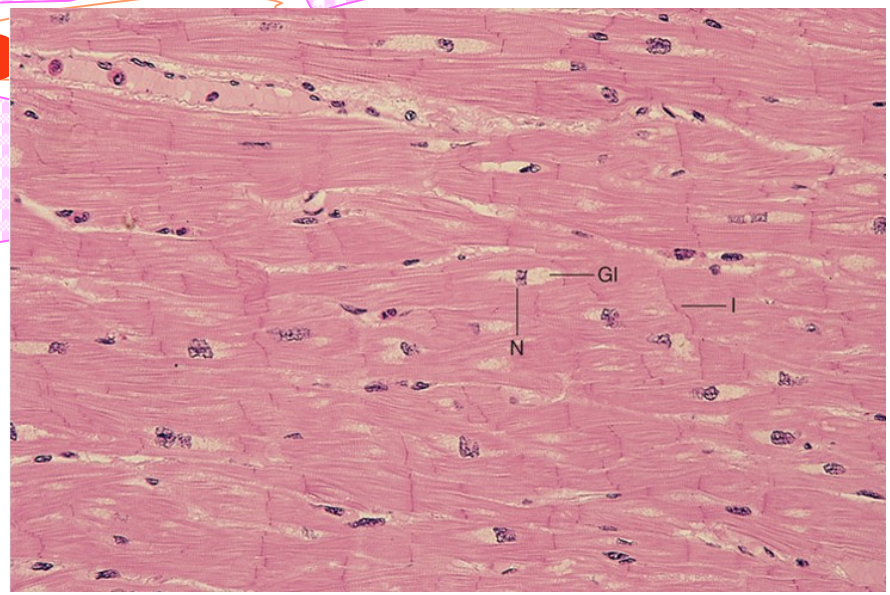
HISTOLOGY OF CARDIAC MUSCLE TISSUE



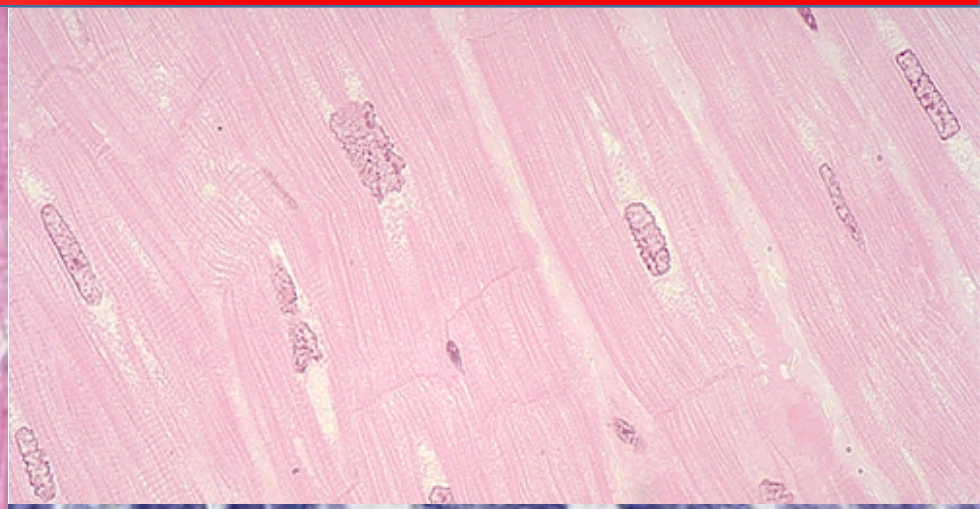
- made up of long branched fiber (cells) – **cardiomyocytes**,
- cardiomyocytes are cylindrical cells, branched on one or both ends (Y, X shaped cells),
- sarcoplasm: single nucleus in the center of cell, striated myofibrils, numerous mitochondria,
- cells are attached to one another by end-to-end junctions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

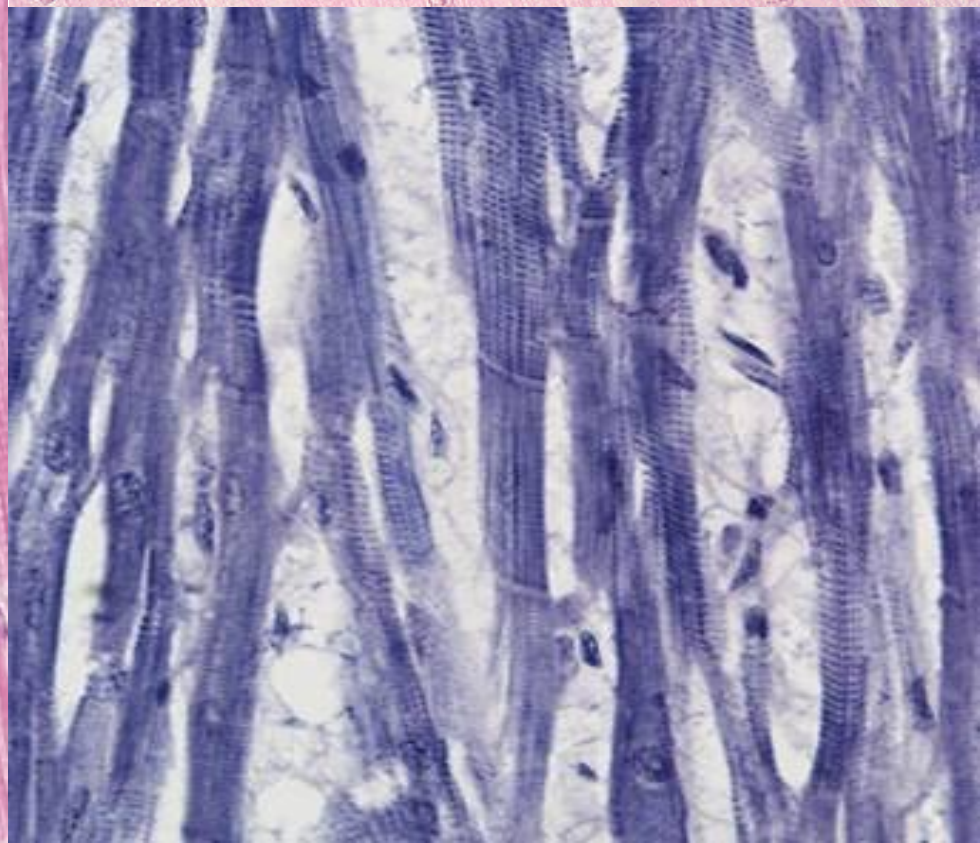
HISTOLOGY OF CARDIAC MUSCLE TISSUE



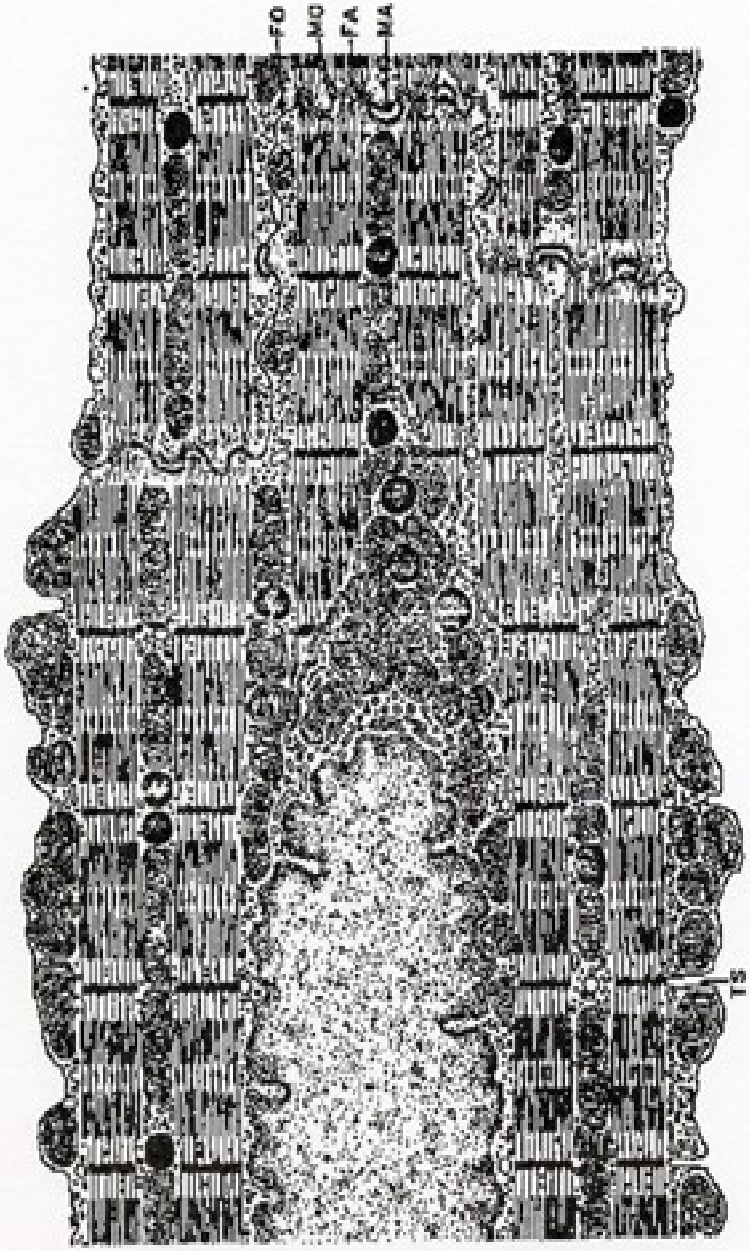


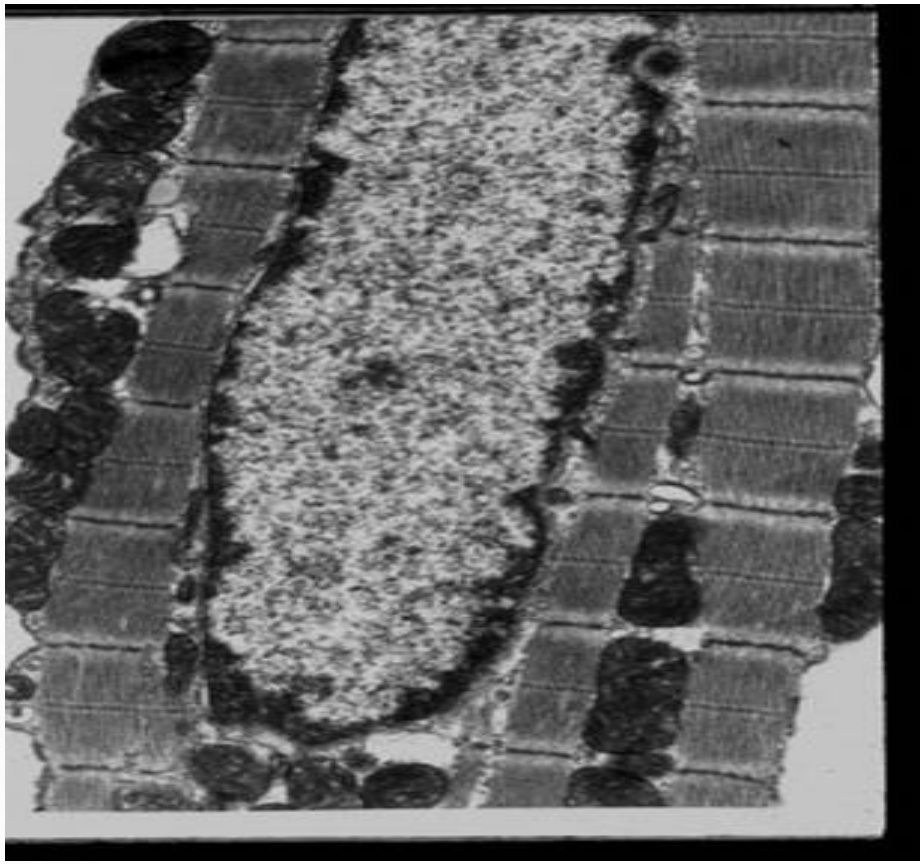
HISTOLOGY OF CARDIAC MUSCLE TISSUE





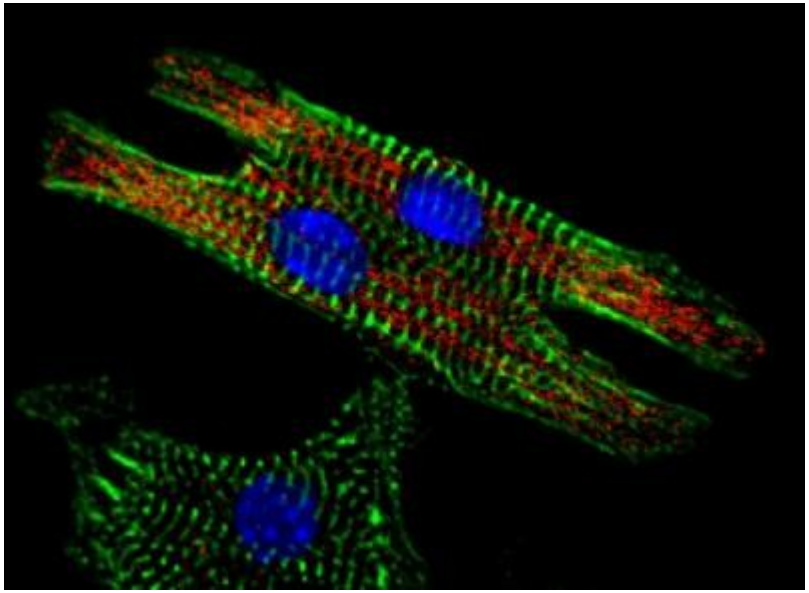
ULTRASTRUCTURE OF CARDIOMYCYTE

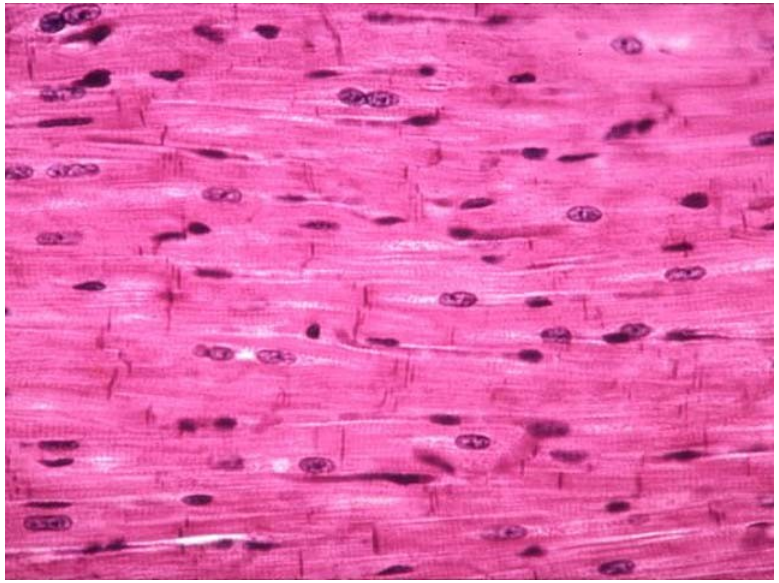




CARDIAC MUSCLE COMPARED TO SKELETAL

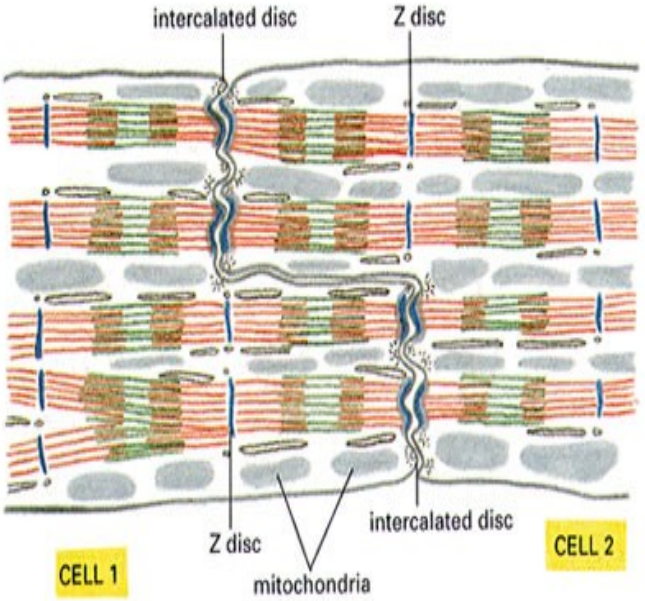
- no triads, but diads: 1 t-tubule + 1 cisterna
- t-tubules around sarcomeres at Z lines rather than at zone of overlap
- sarcoplasmic reticulum via its tubules contact sarcolemma as well as the t-tubules
- cardiac muscle cells are totally dependent on aerobic metabolism to obtain the energy
- large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

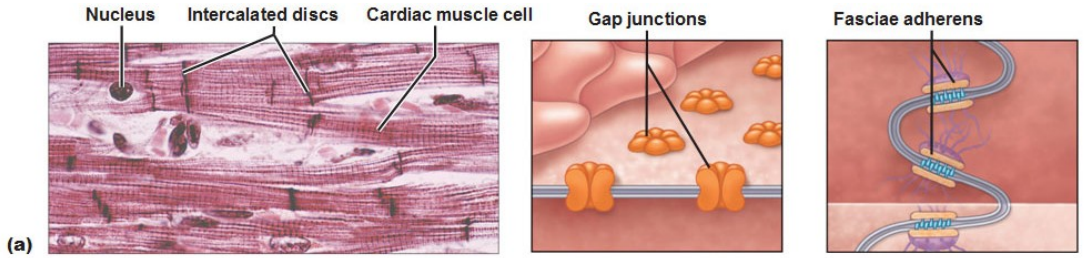


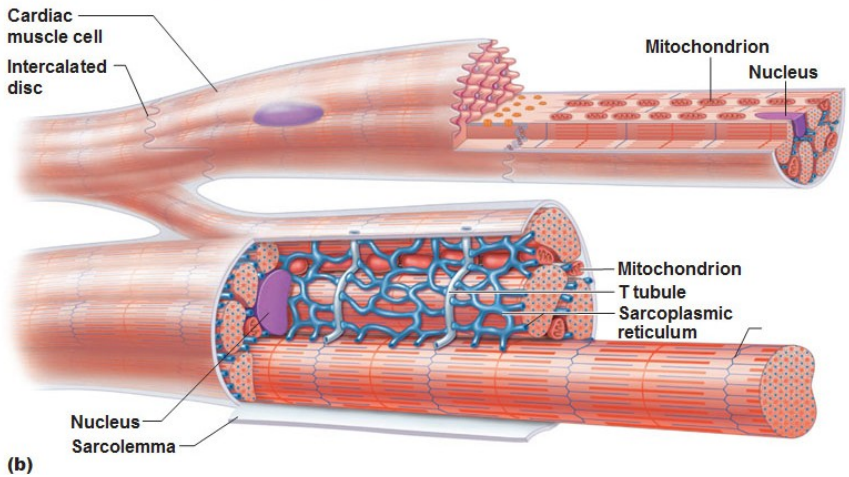


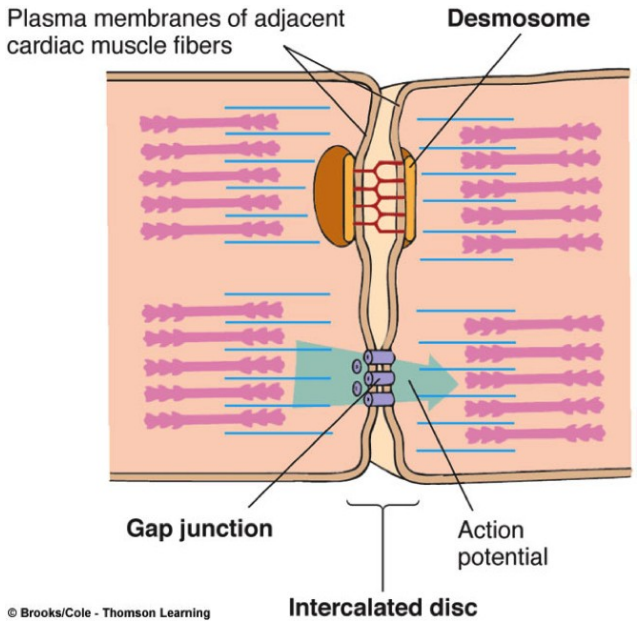
INTERCALATED DISC

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

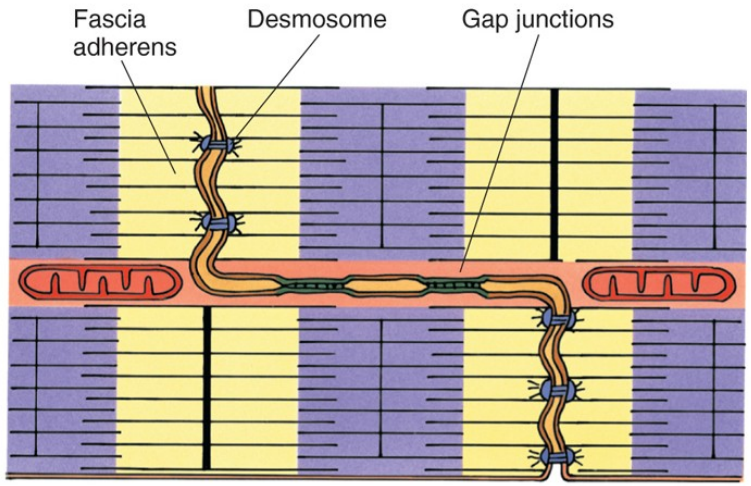


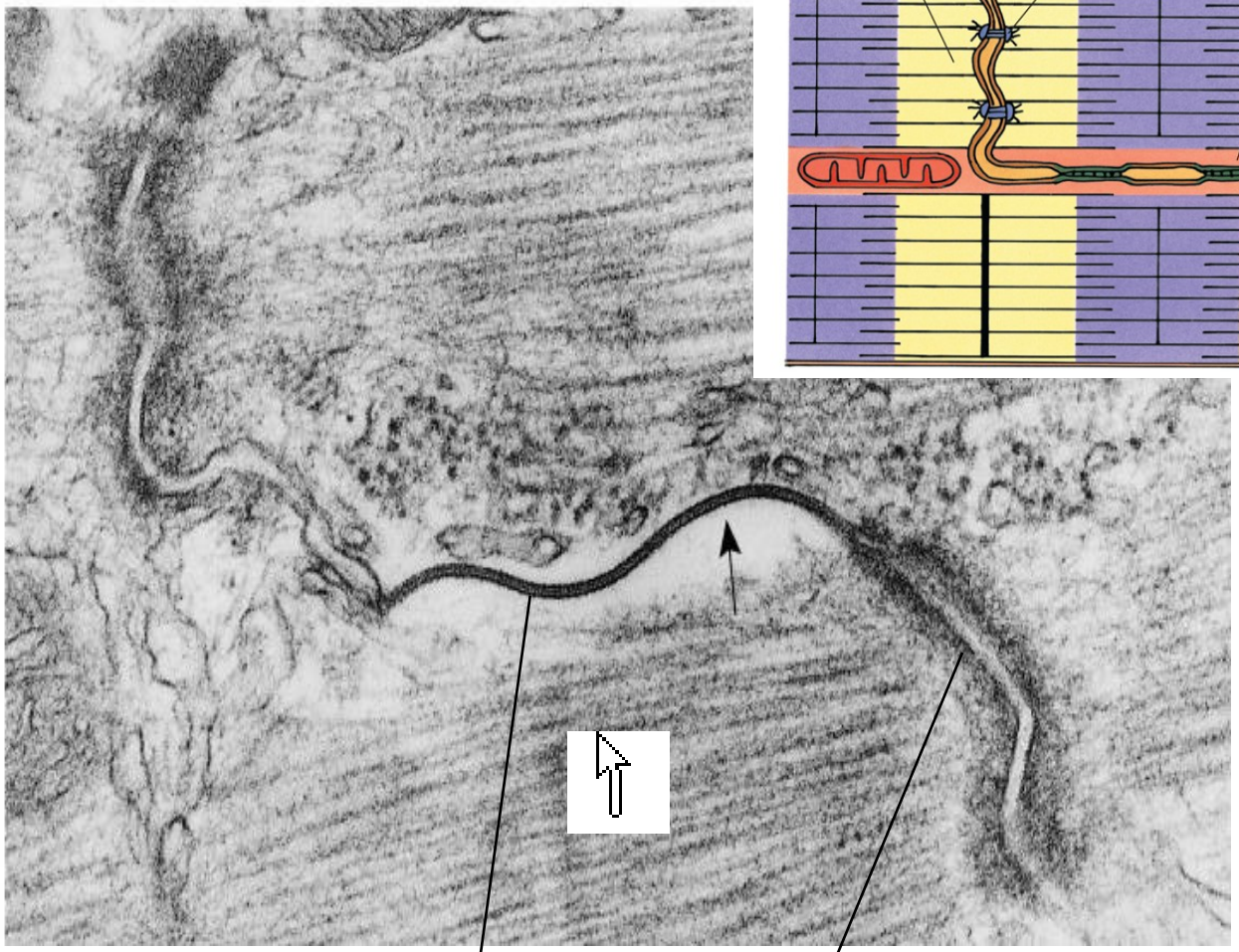






INTERCALATED DISC

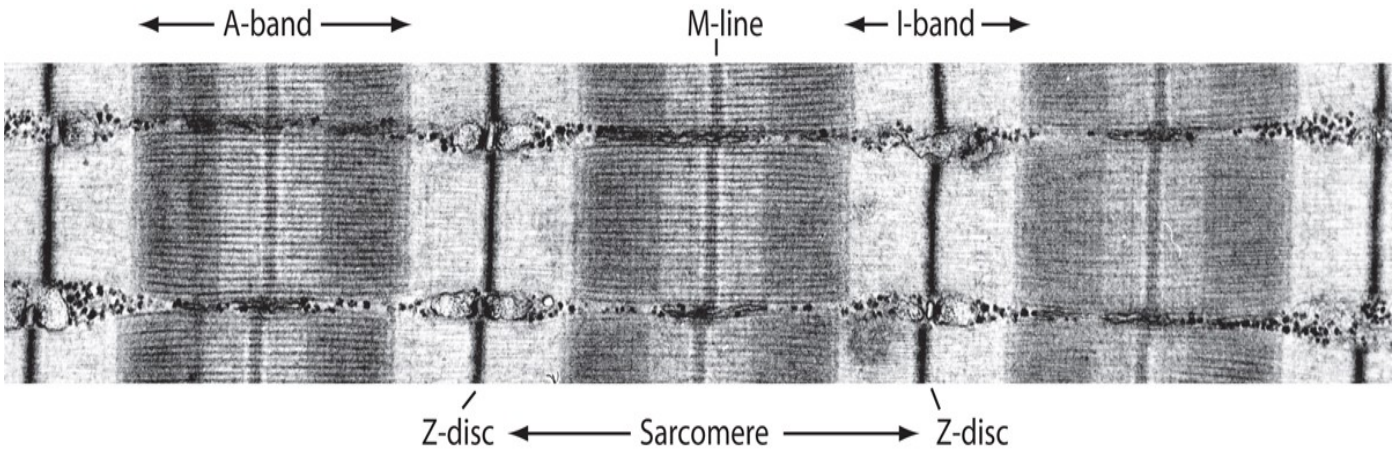




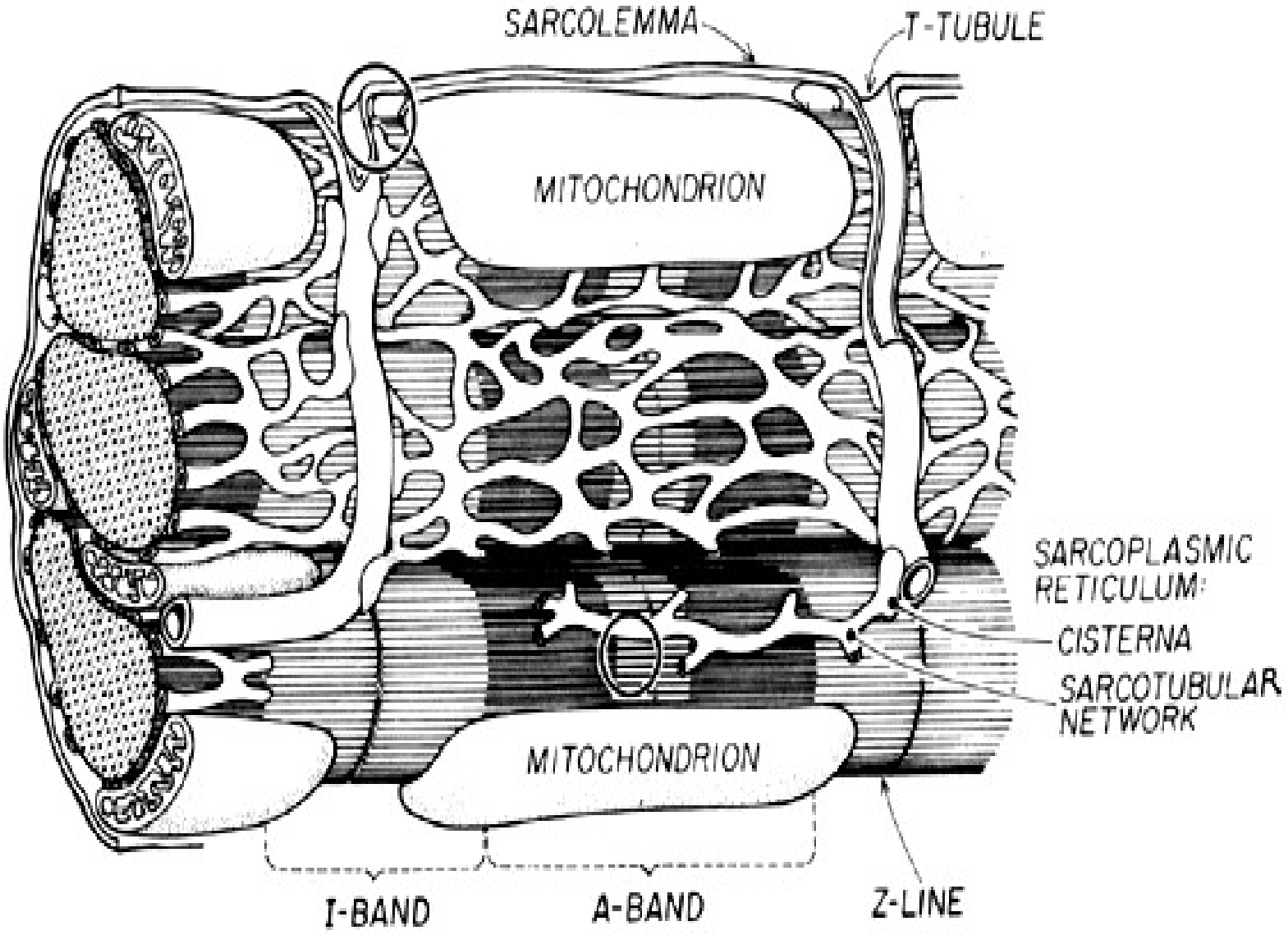
Intercalated disc: nexus fascia adherens

MYOFIBRILS IN CARDIOMYOCYTE

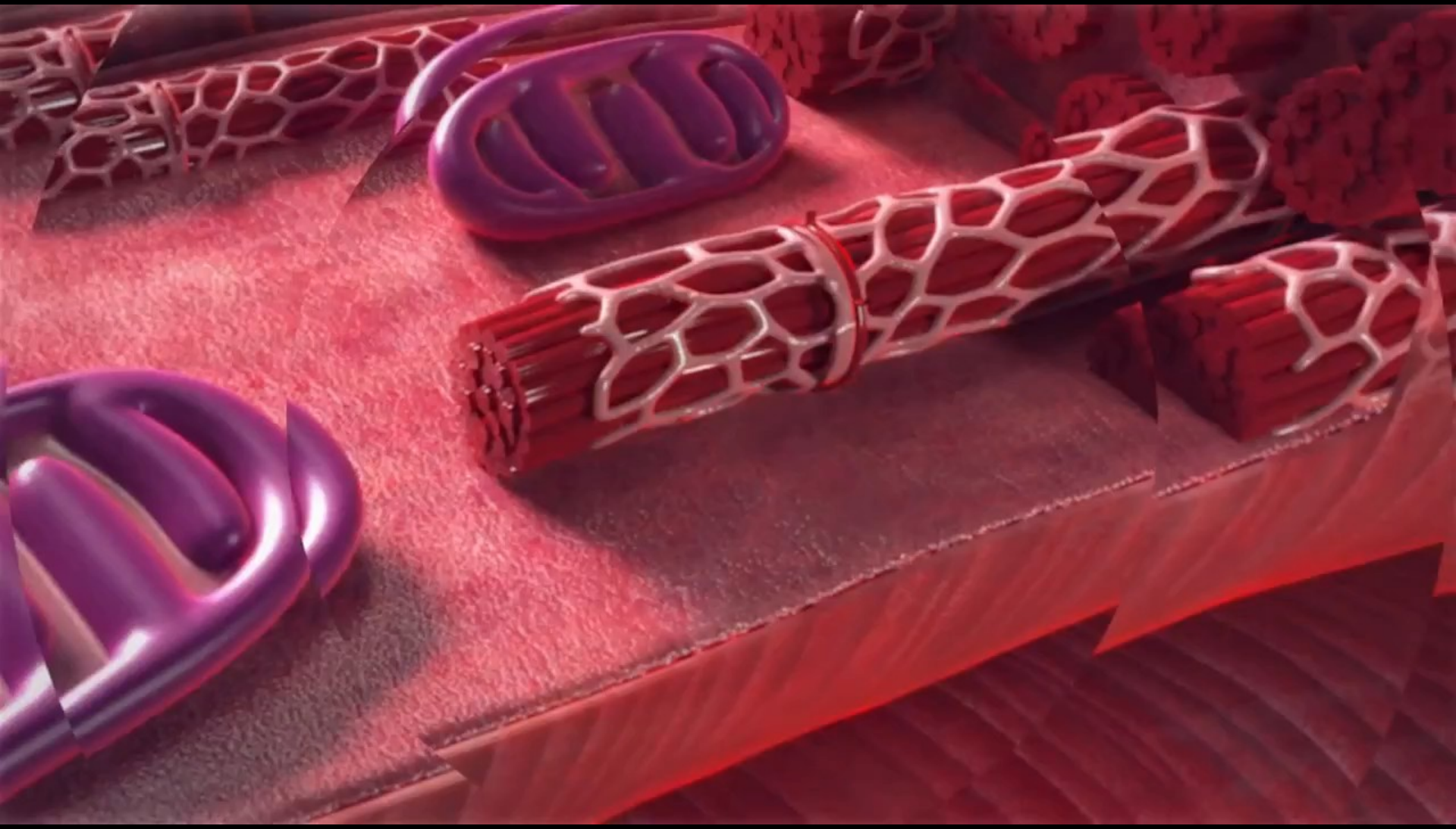
- Actin + myosin myofilaments
- Sarcomere
- Z-line
- M-line and H-zone
- I-band, A-band
- T-tubule + 1 cisterna = diad (around Z-line)



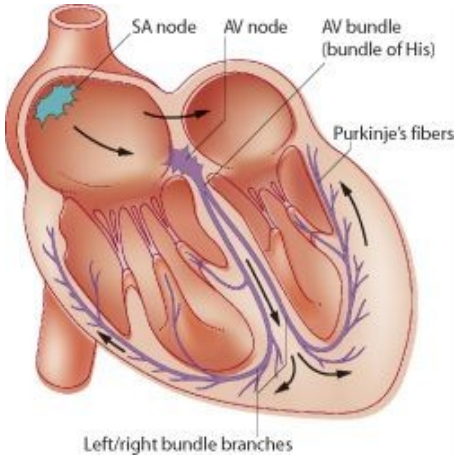
MYOFIBRILS IN CARDIOMYOCYTE



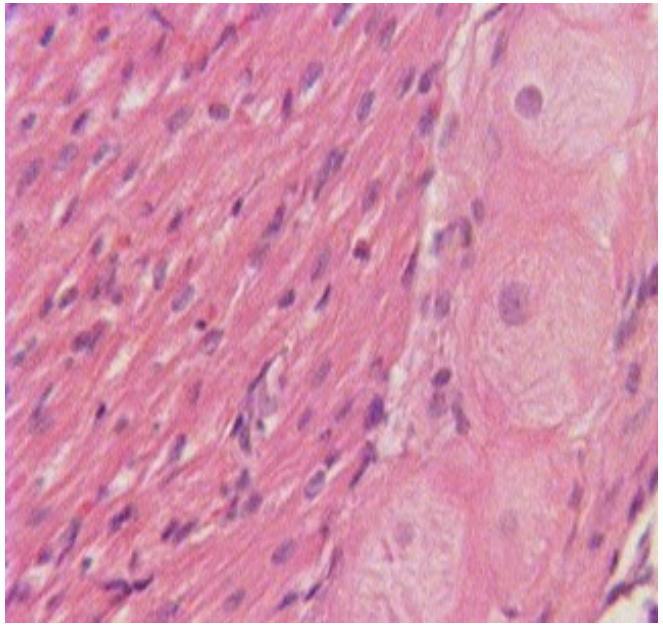
ULTRASTRUCTURE OF CARDIOMYOCYTES



PURKINJE FIBERS

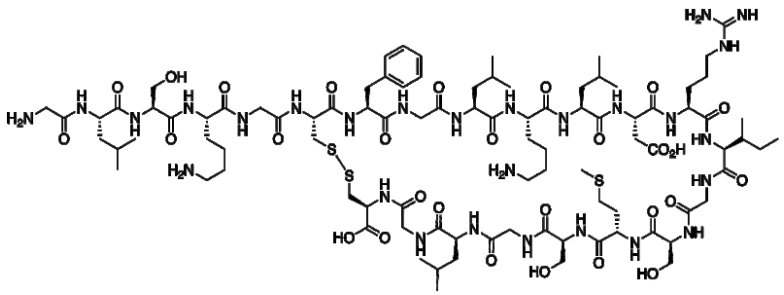


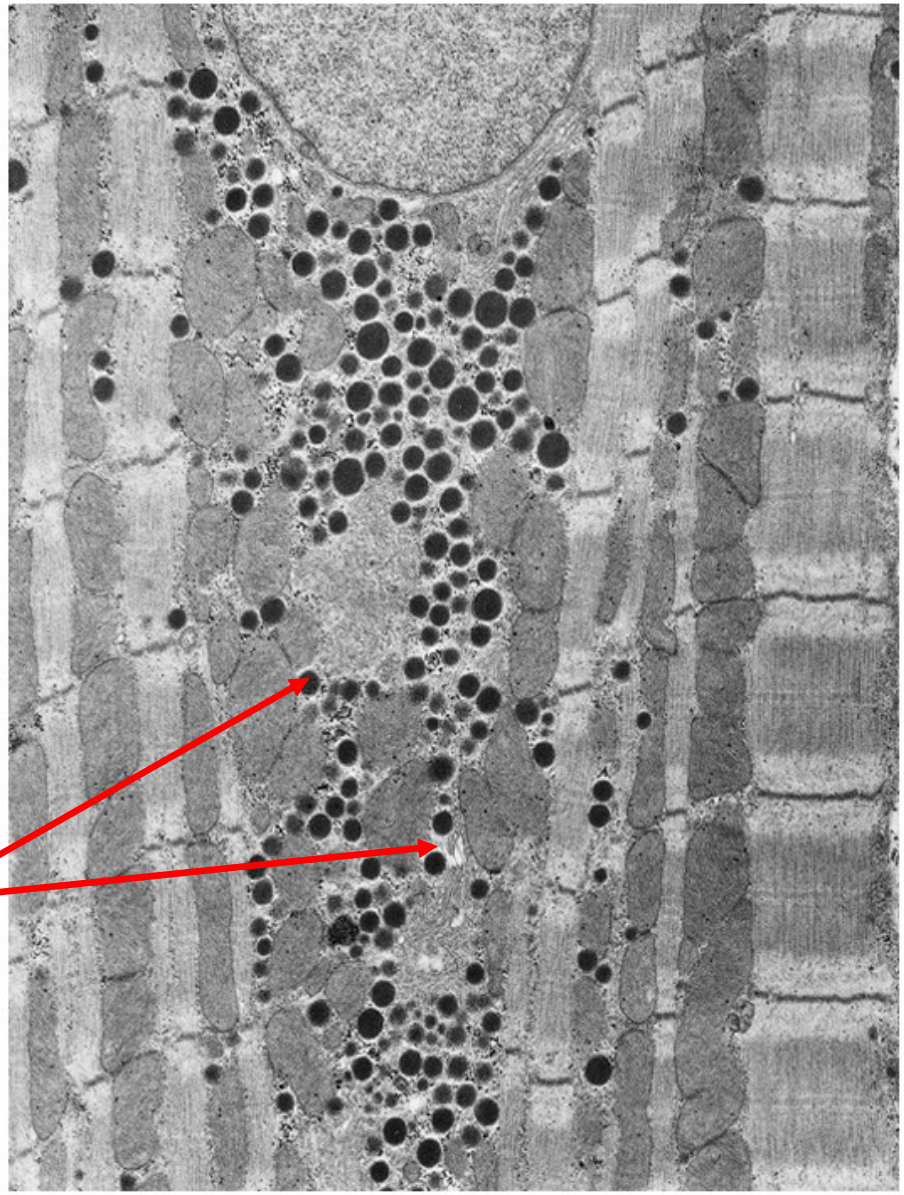
- are located in the inner layer of heart ventricle wall
- are specialized cells fibers that conduct electrical stimuli or impulses that enables the heart to contract in a coordinated fashion
- numerous sodium ion channels and mitochondria, fewer myofibrils

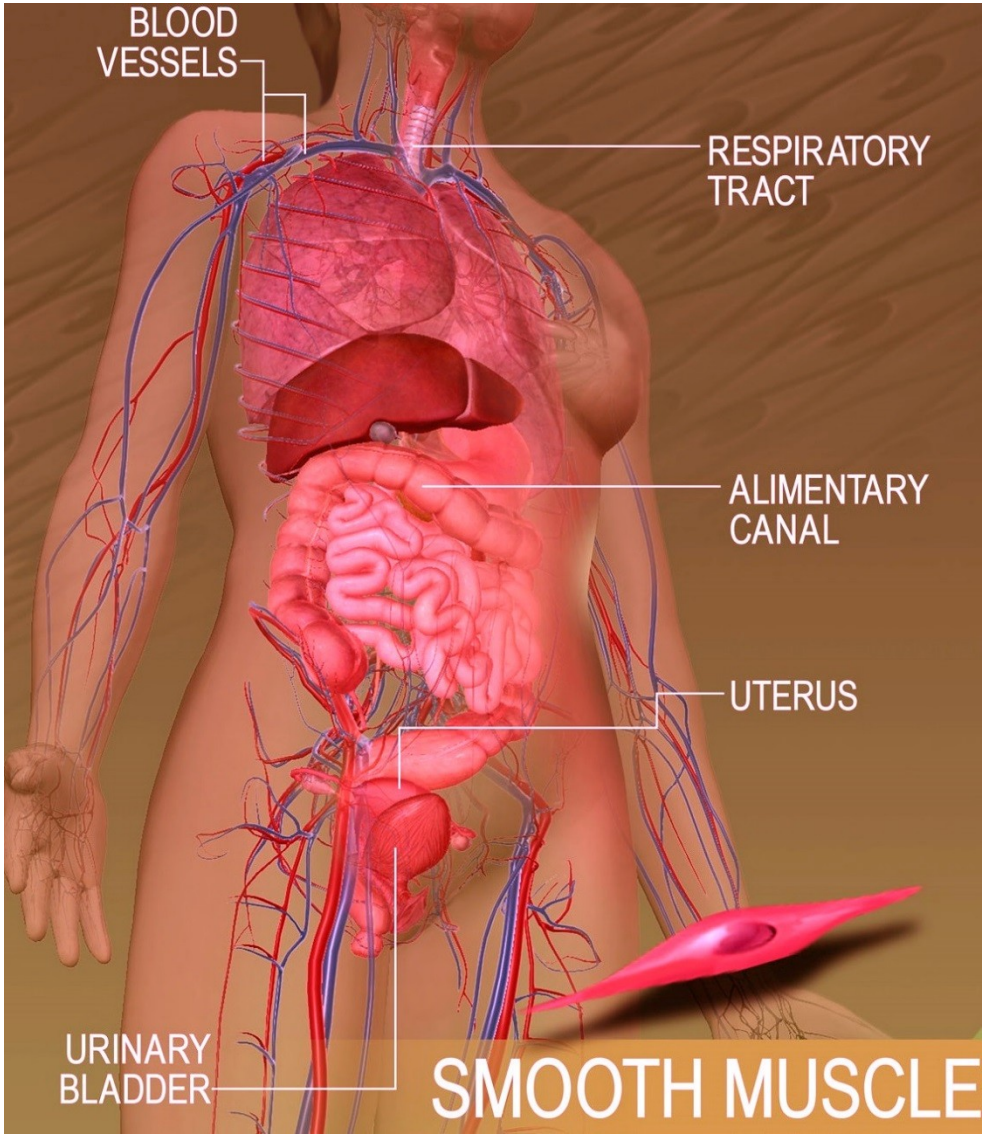


ATRIAL CARDIOMYOCYTES

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



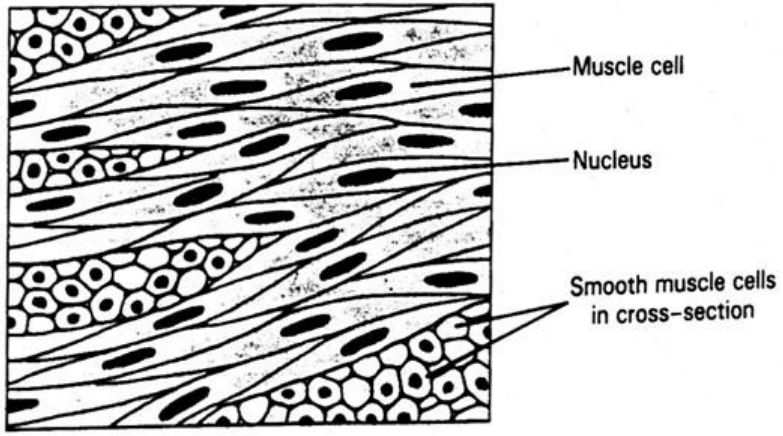


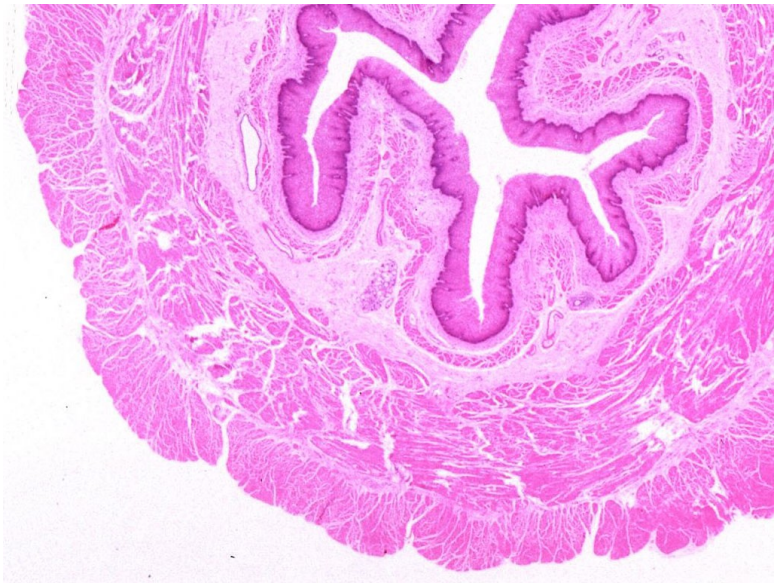


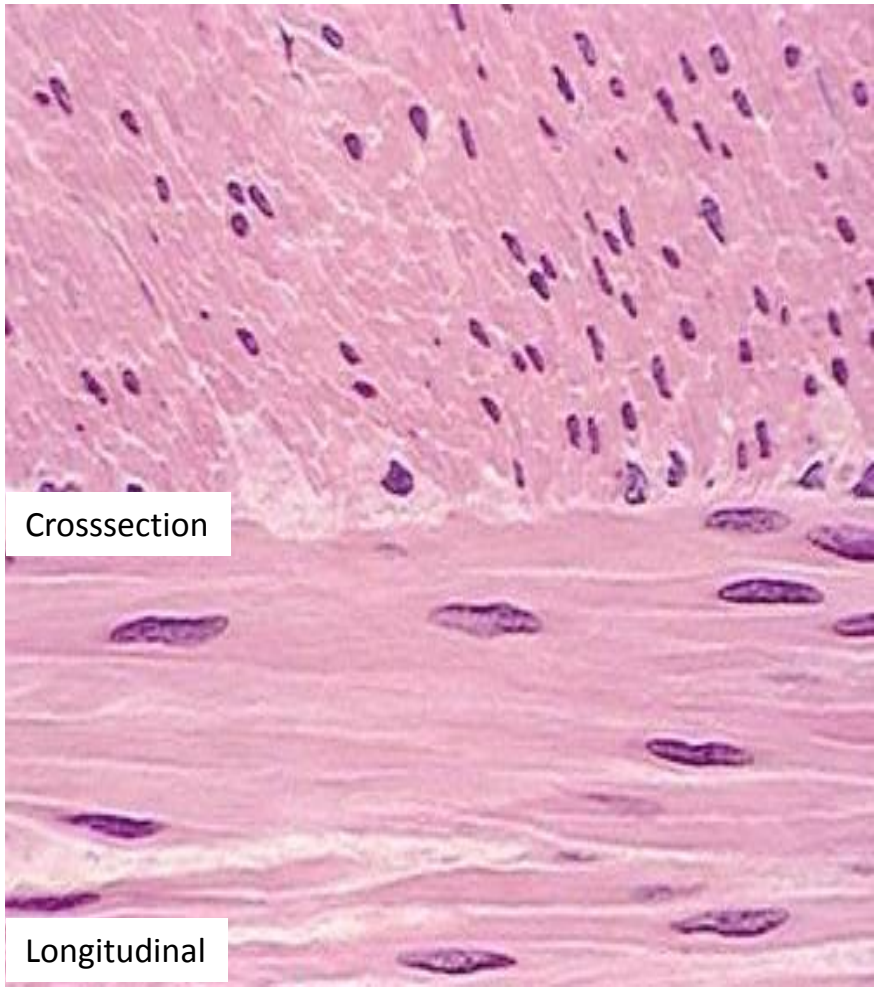
SMOOTH MUSCLE TISSUE

SMOOTH MUSCLE TISSUE

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

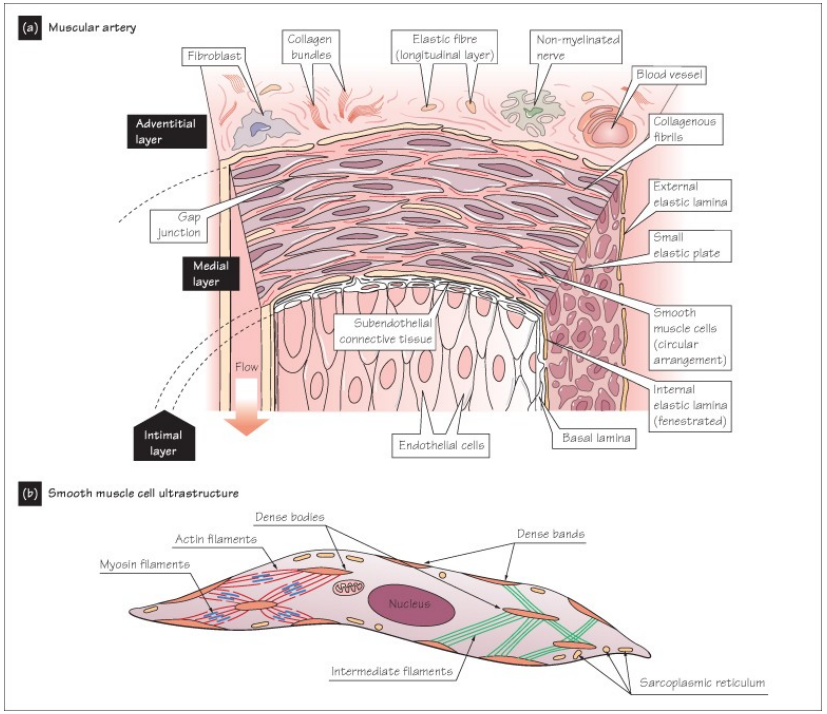






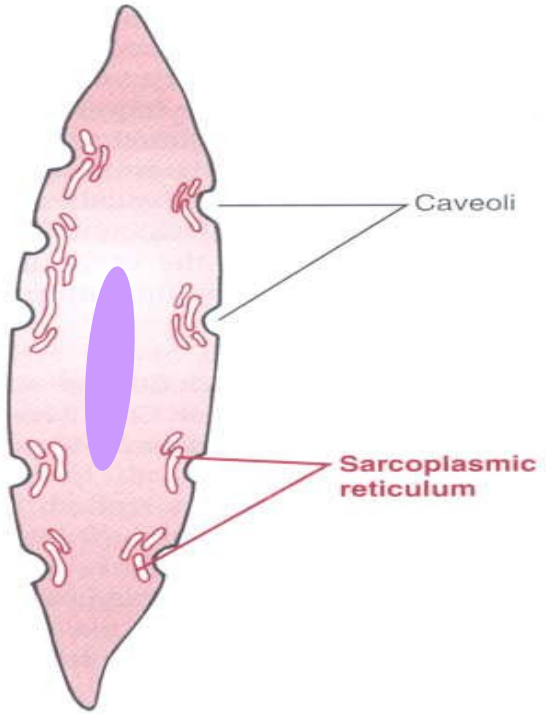
SMOOTH MUSCLE TISSUE

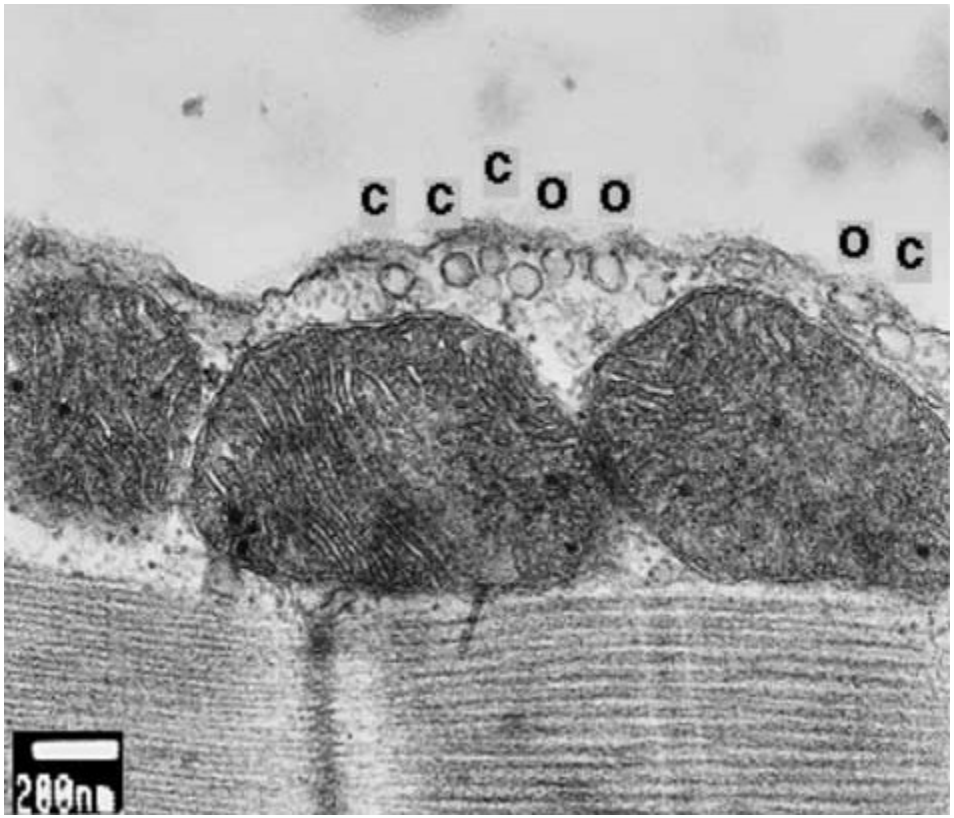
- spindle shaped cells (leiomyocytes) with myofilaments not arranged into myofibrils (no striation), 1 nucleus in the centre of the cell
- myofilaments form bands throughout the cell
- actin filaments attach to the sarcolemma by focal adhesions or to the dense bodies substituting Z-lines in sarcoplasm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

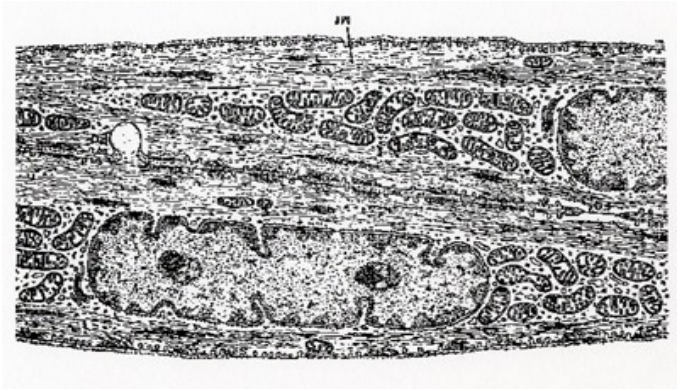


CAVEOLS

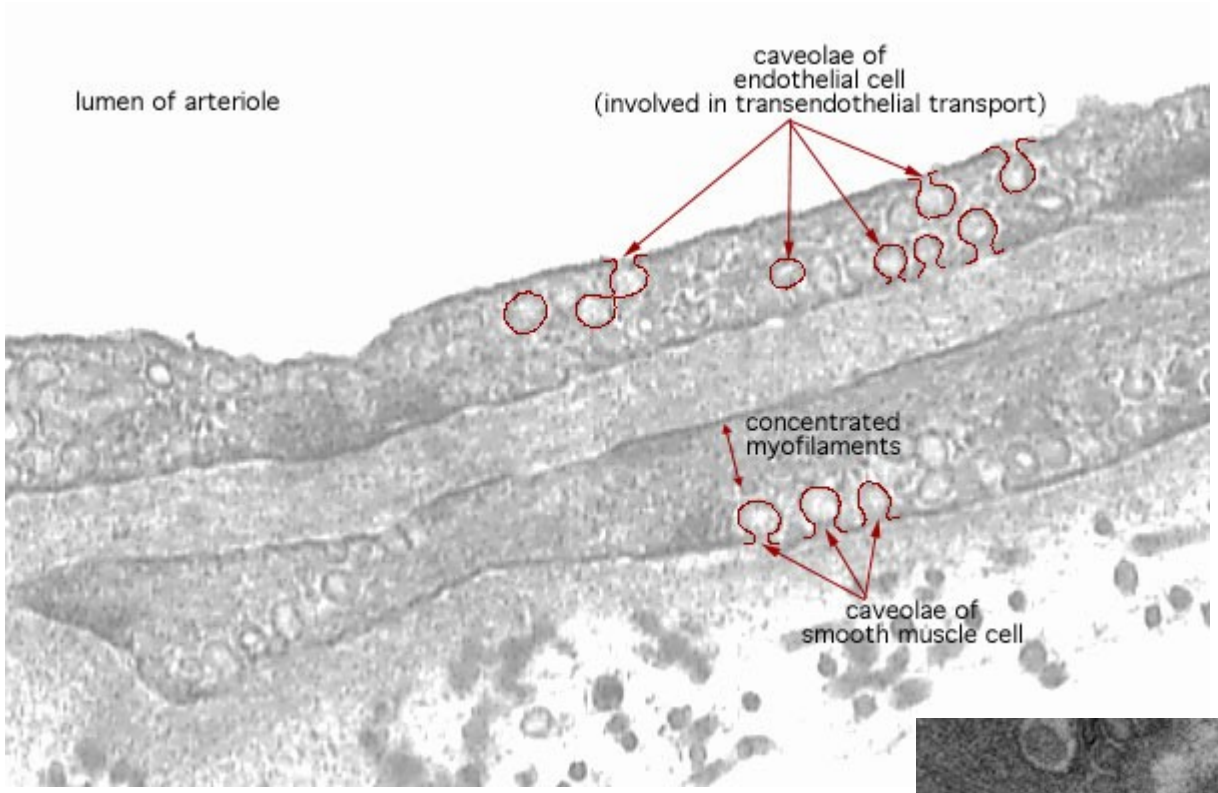
- caveolae are equivalent to t-tubules
- transmembrane ion channels

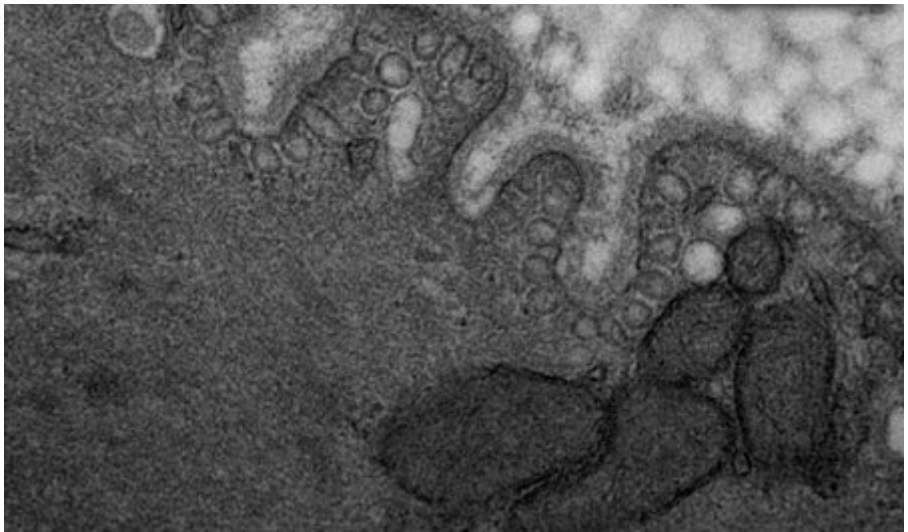




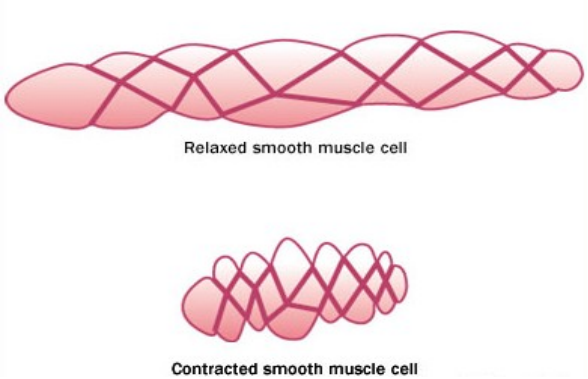


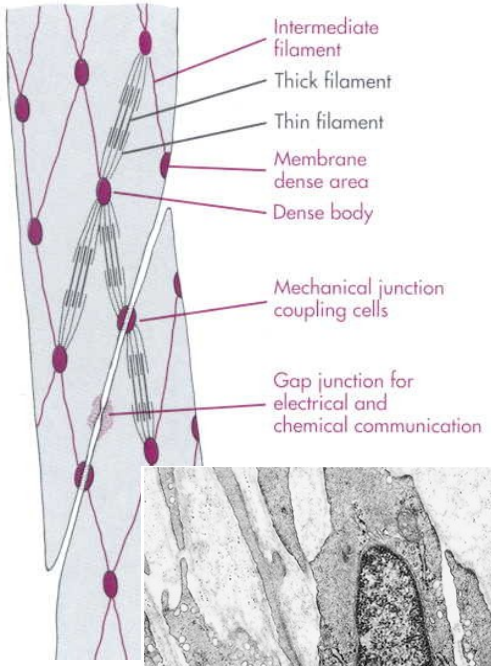
CAVEOLS

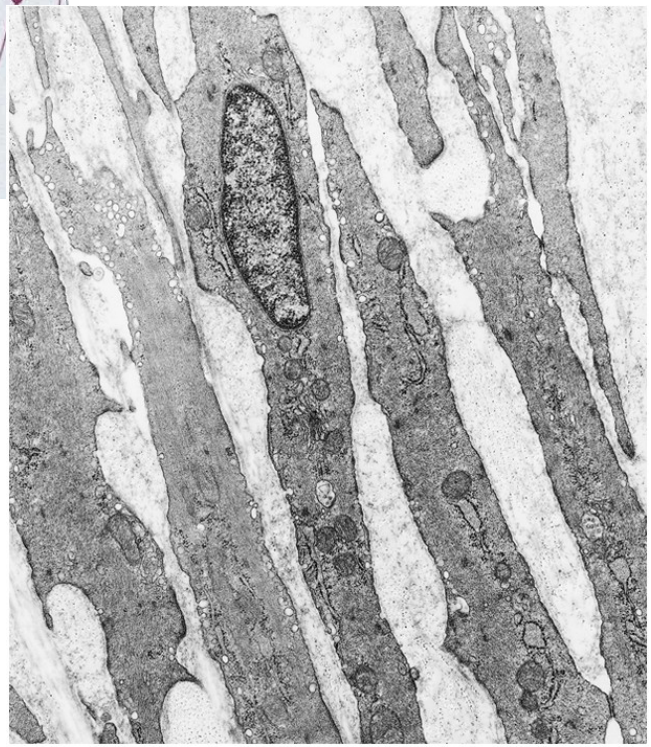

lumen of arteriole
caveolae of
endothelial cell
(involved in transendothelial transport)
concentrated
myofilaments
caveolae of
smooth muscle cell



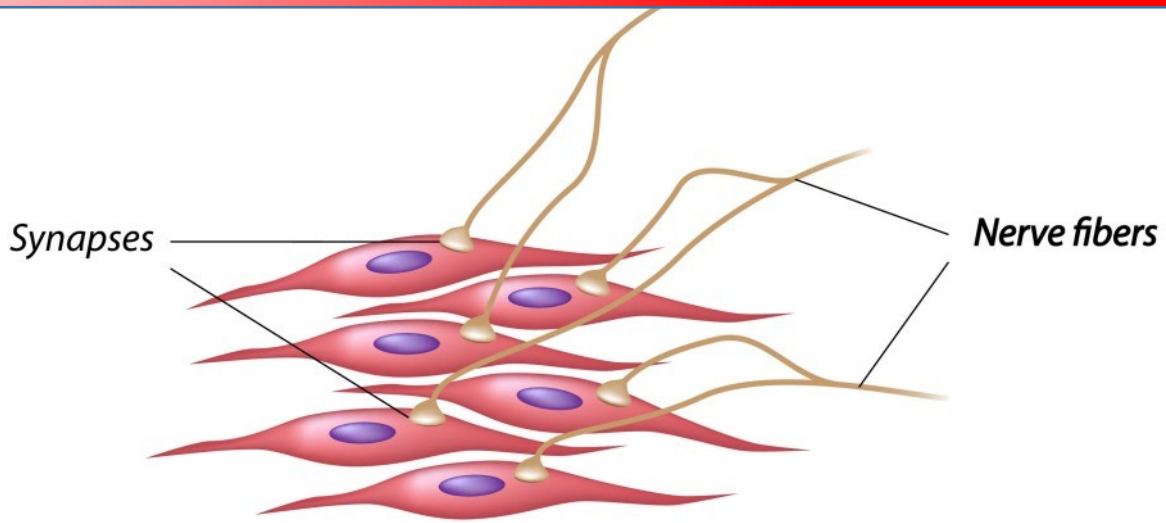
CONTRACTION OF LEIOMYCYTES



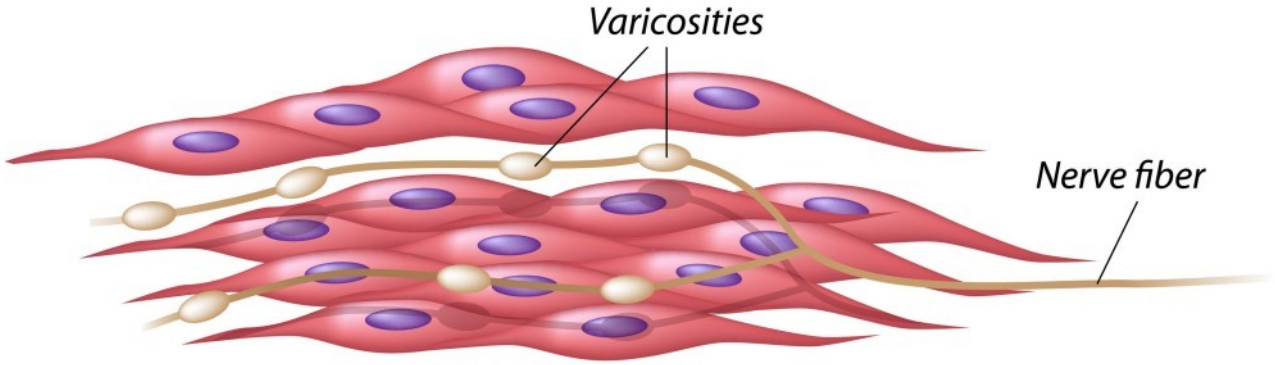




INNERVATION OF LEIOMYCYTES

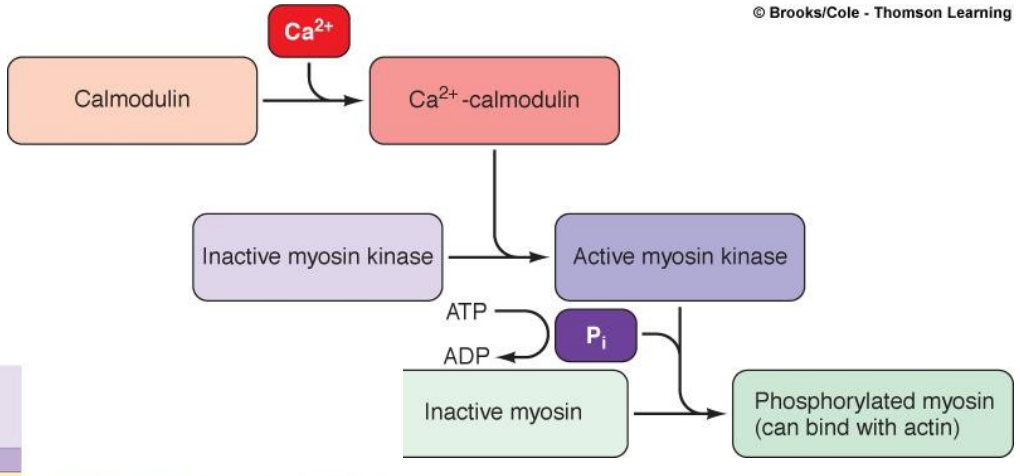


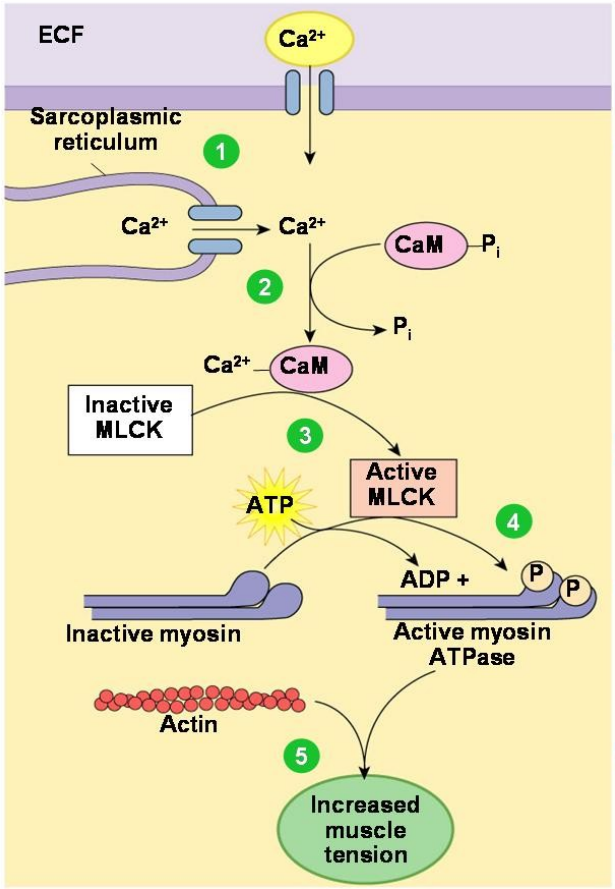
Multiunit Smooth Muscle



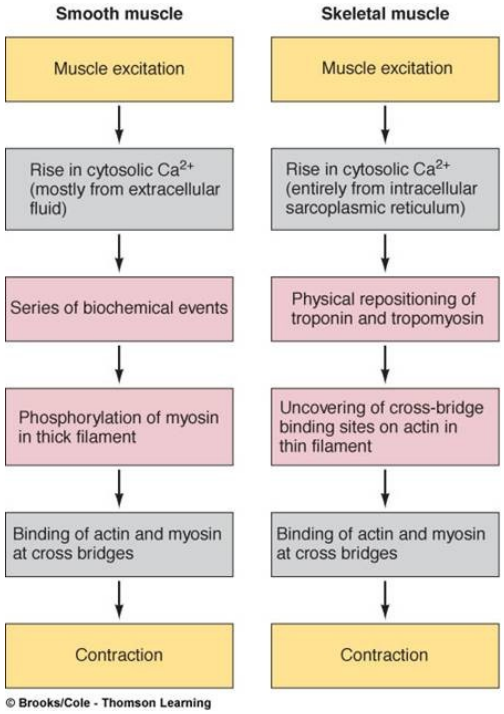
Single-unit Smooth Muscle

CONTRACTION OF LEIOMYCYTES

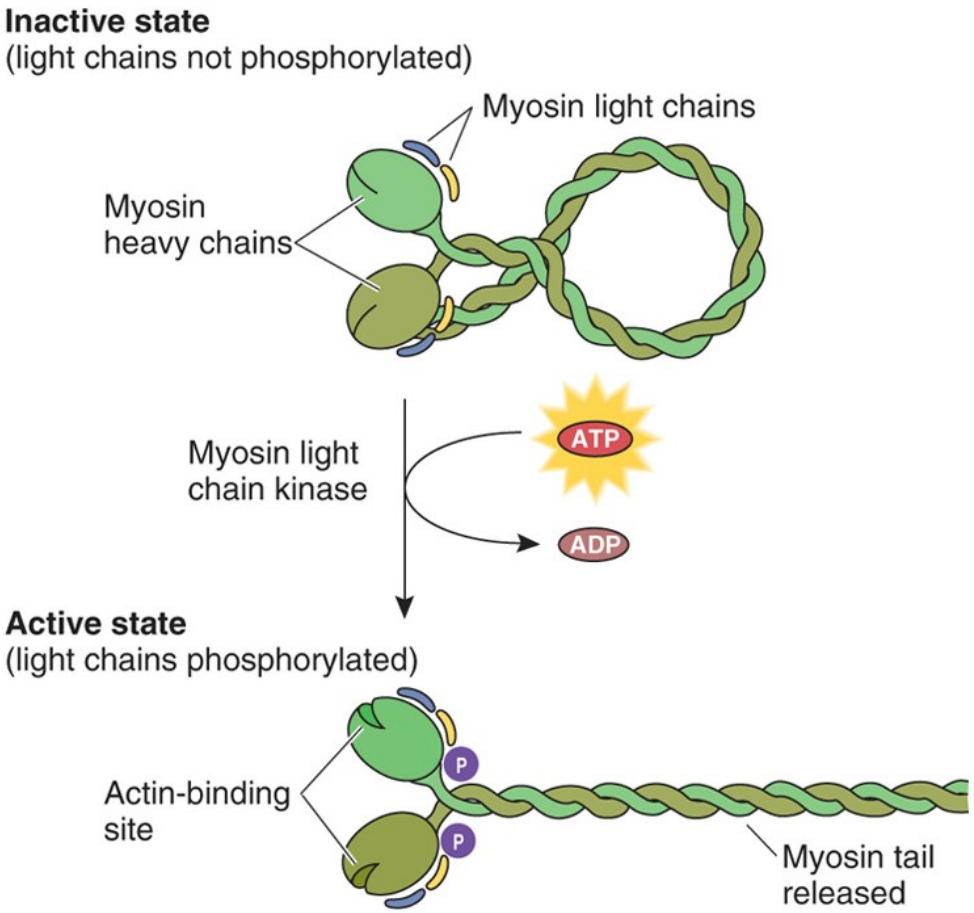




1. Intracellular Ca^{2+} concentrations increase when Ca^{2+} enters cell and is released from sarcoplasmic reticulum.
2. Ca^{2+} binds to calmodulin (CaM).
3. Ca^{2+}–calmodulin activates myosin light chain kinase (MLCK).
4. MLCK phosphorylates light chains in myosin heads and increases myosin ATPase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



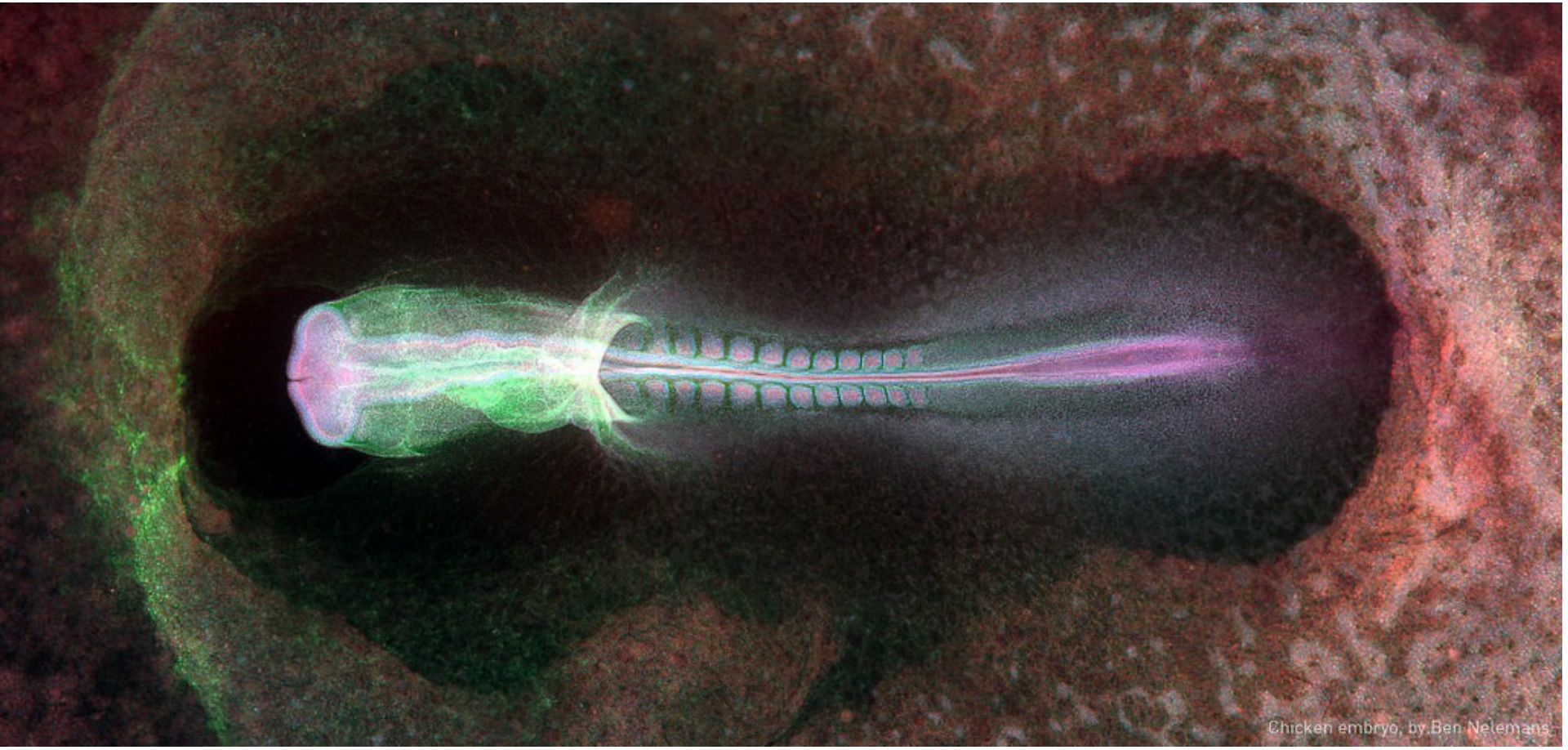
SMOOTH MUSCLE TISSUE



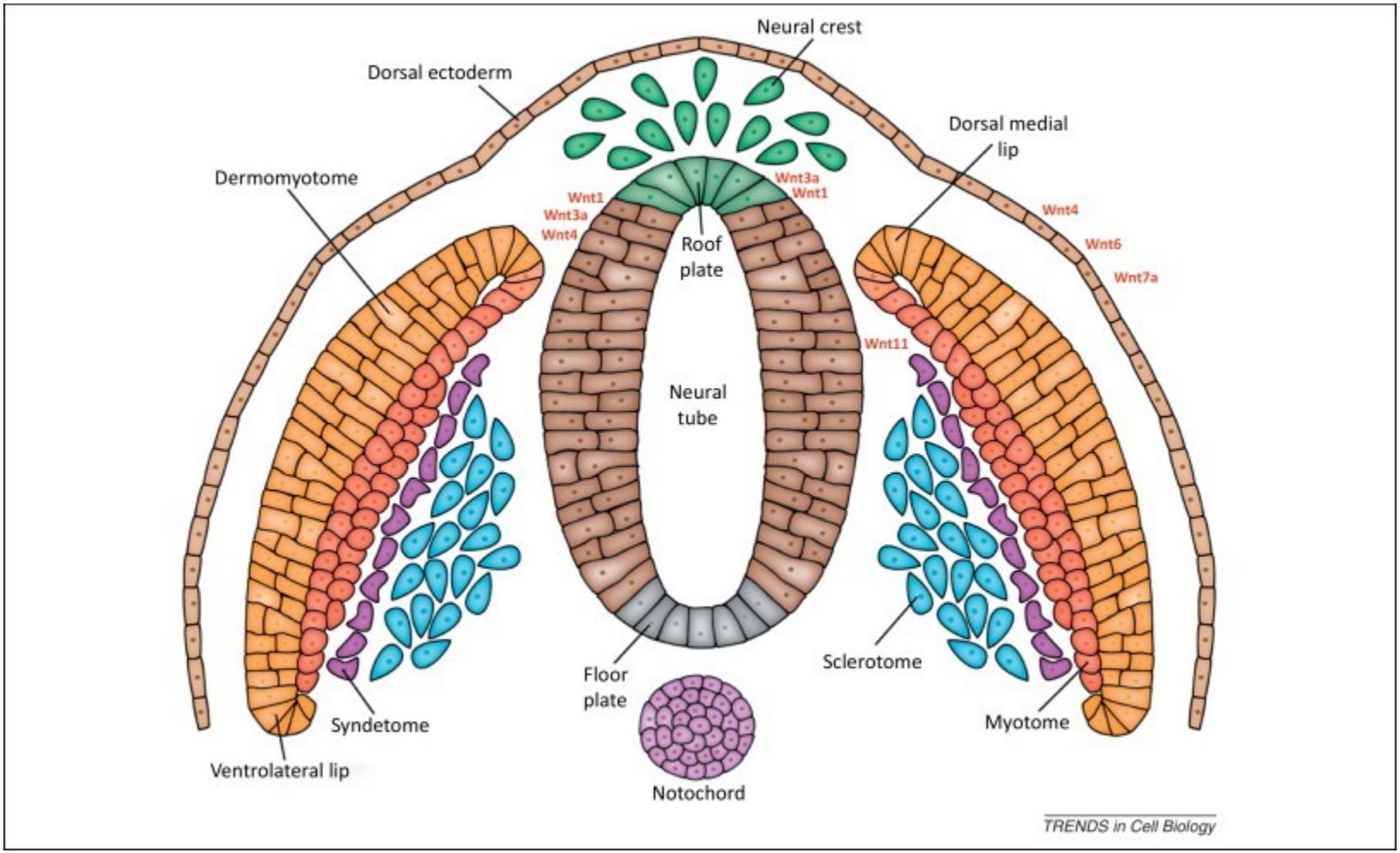
SUMMARY

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	Caveoli, overlapping cells in layers

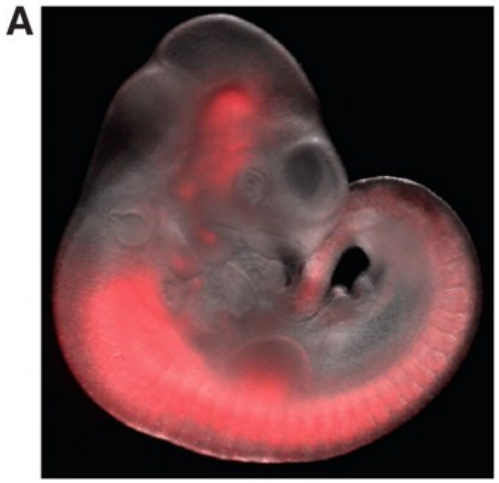
EMBRYONIC DEVELOPMENT OF MUSCLE SYSTEM

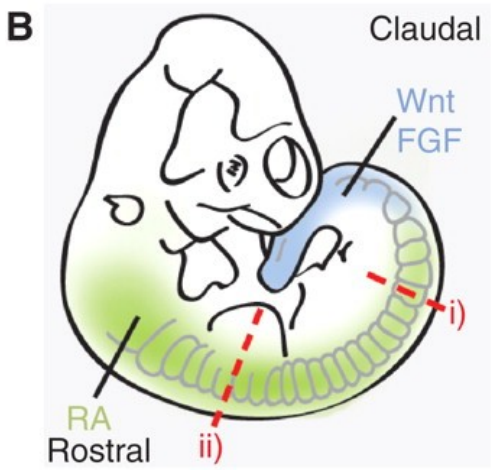


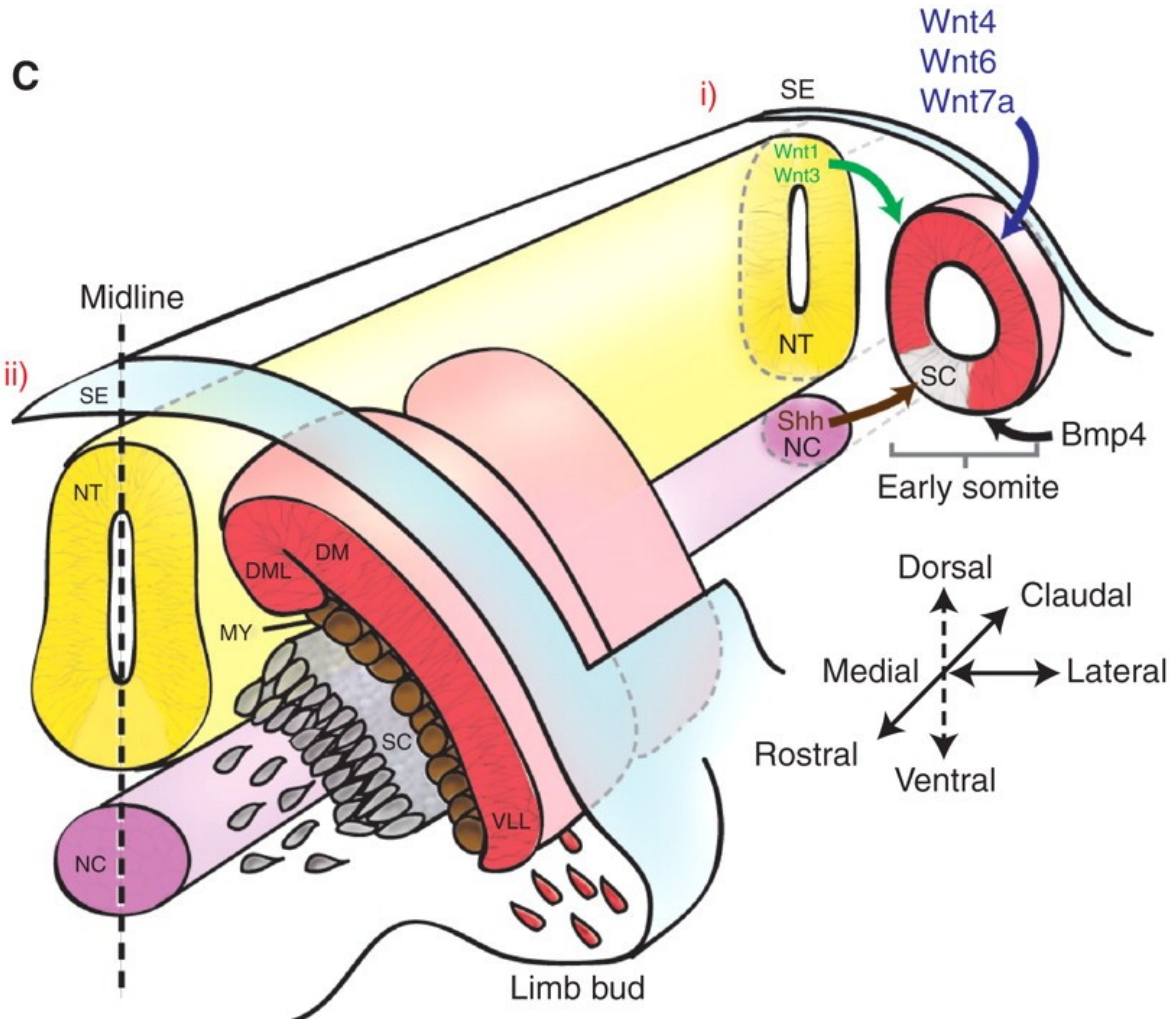
EMBRYONIC DEVELOPMENT OF MUSCLE SYSTEM



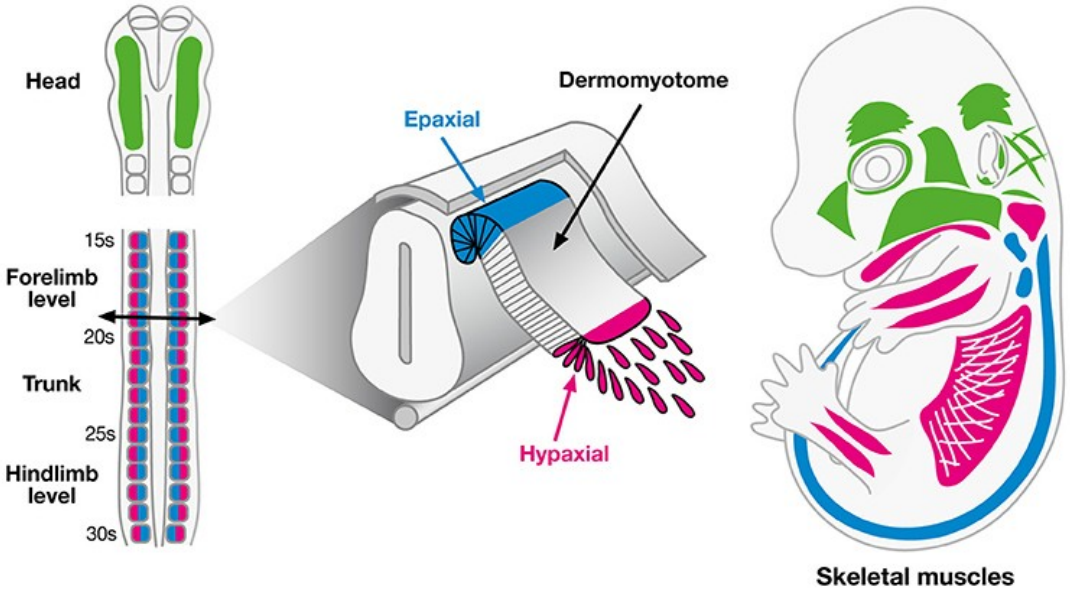
EMBRYONIC DEVELOPMENT OF MUSCLE TISSUE

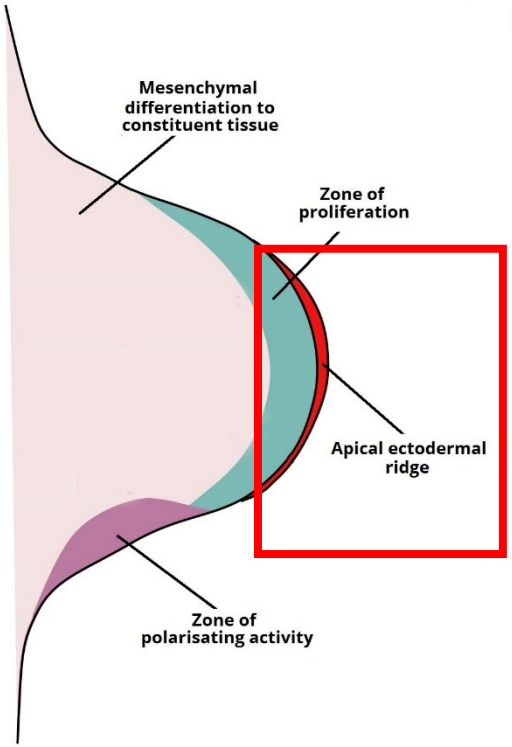


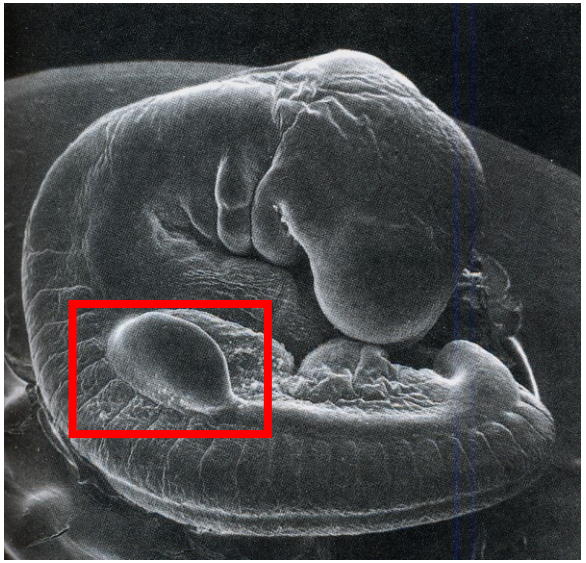


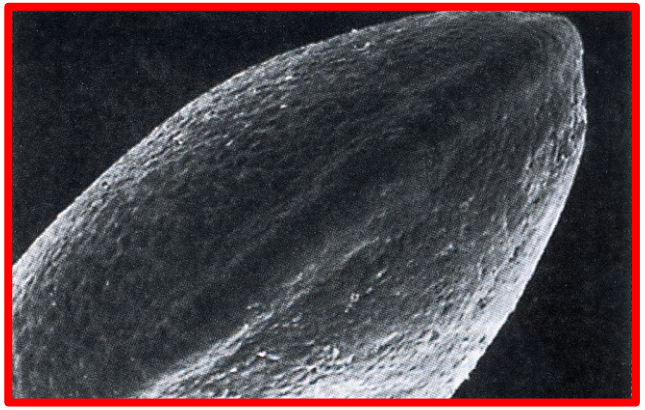


LIMB MUSCLES

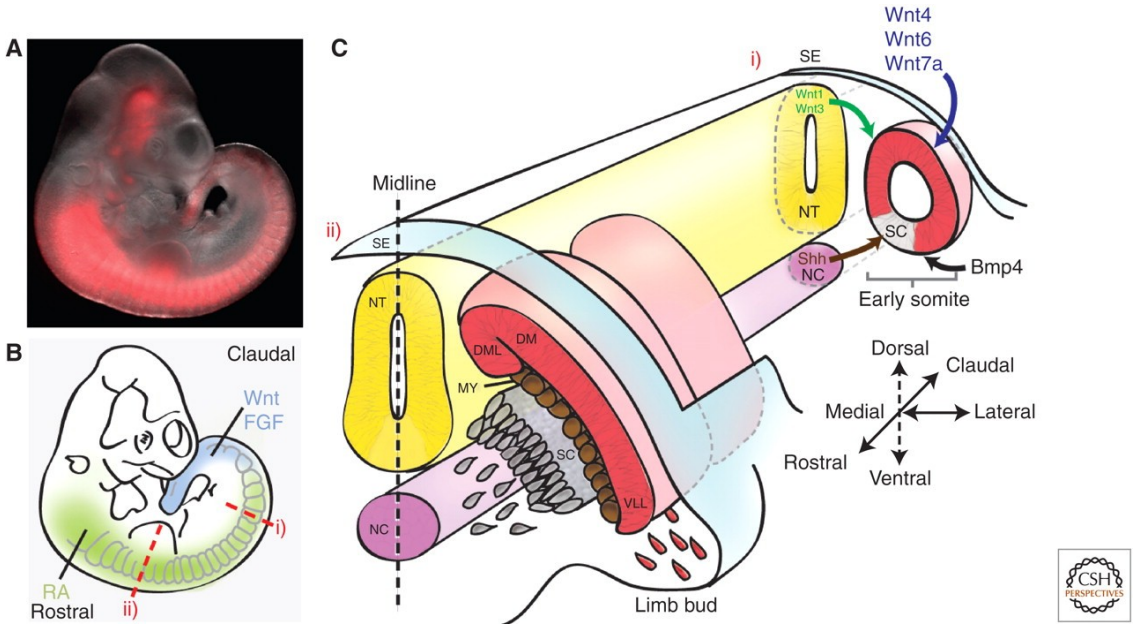


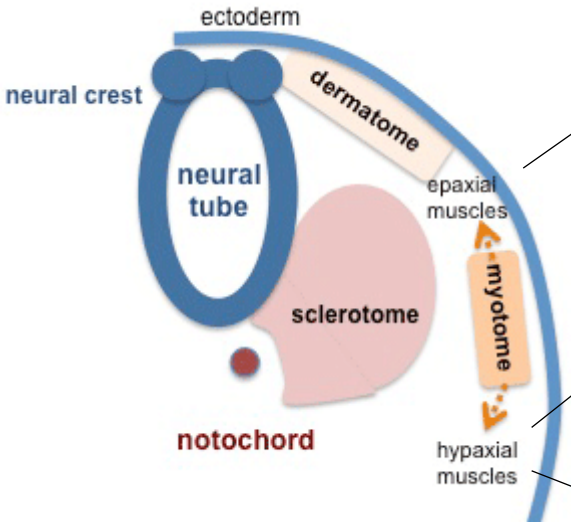






TRUNK MUSCLES





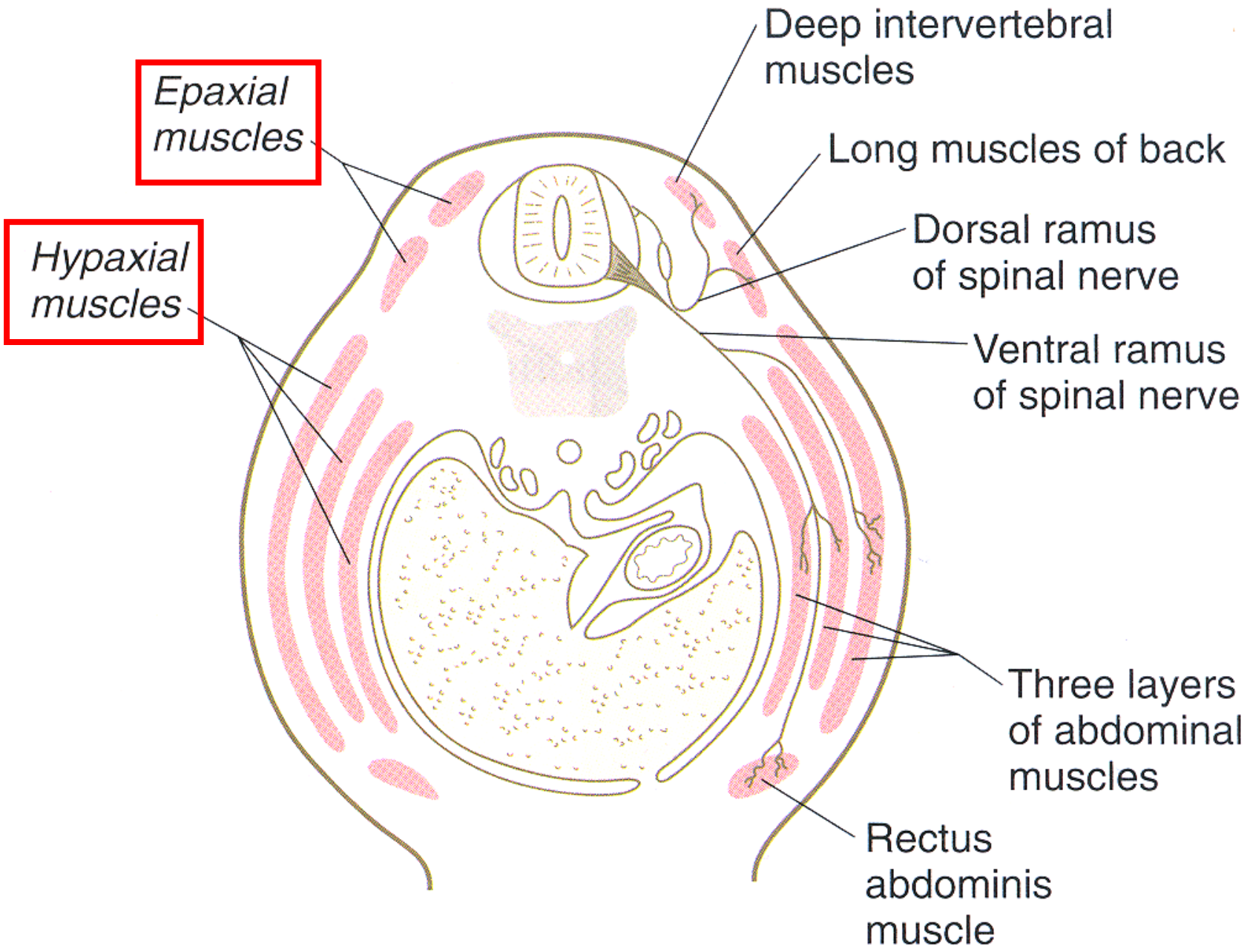
Deep back muscles

Spinocostal muscles

Surface back muscles: limb origin

Intercostal muscles

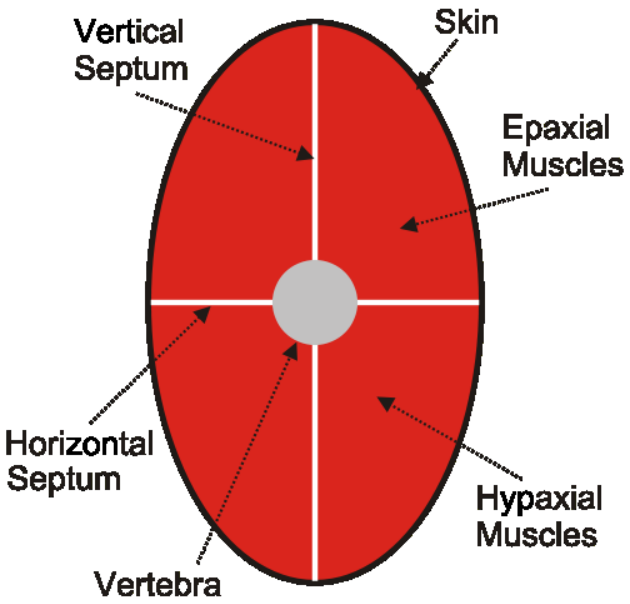
TRUNK MUSCLES



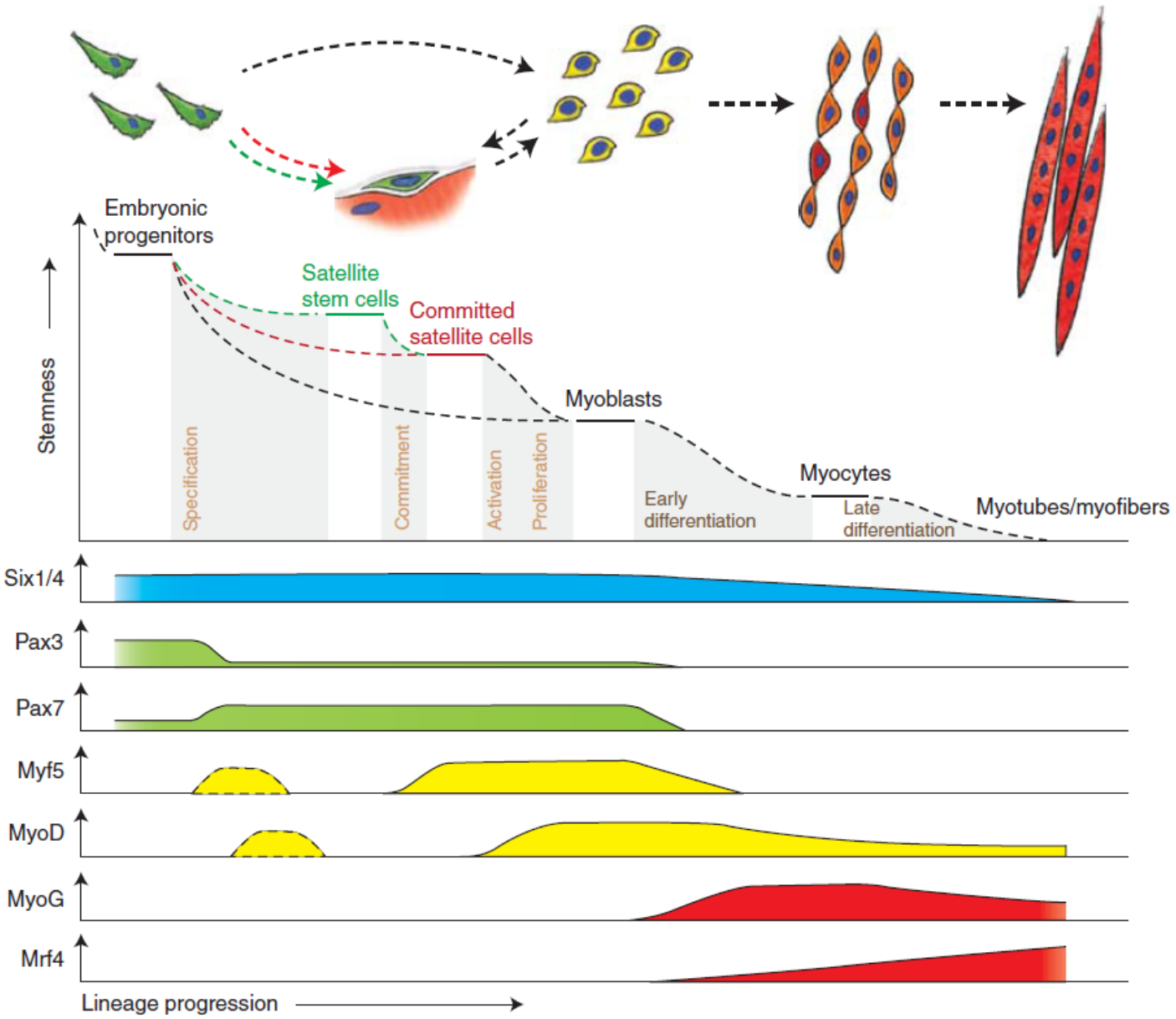
PRUNE BELLY SYNDROME

- Absence of abdominal muscles
- Failure of hypaxial specification
- VACTERL and aneuploidy association

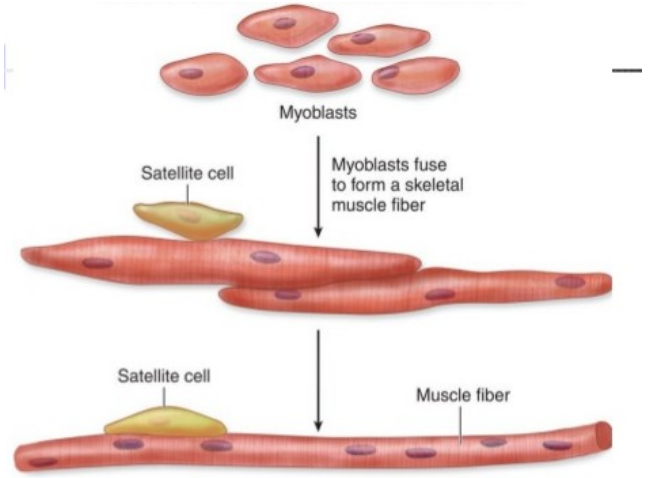
•V - Vertebral anomalies
•A - Anorectal malformations
•C - Cardiovascular anomalies
•T - Tracheoesophageal fistula
•E - Esophageal atresia
•R - Renal (Kidney) and/or radial anomalies
•L - Limb defects

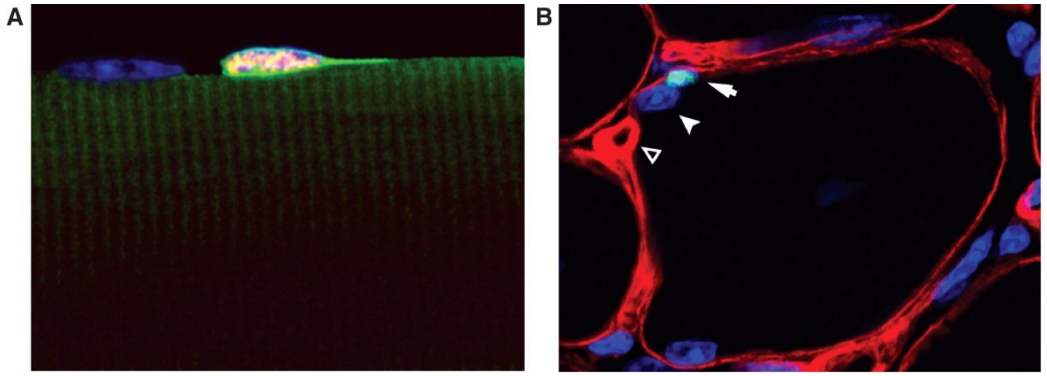


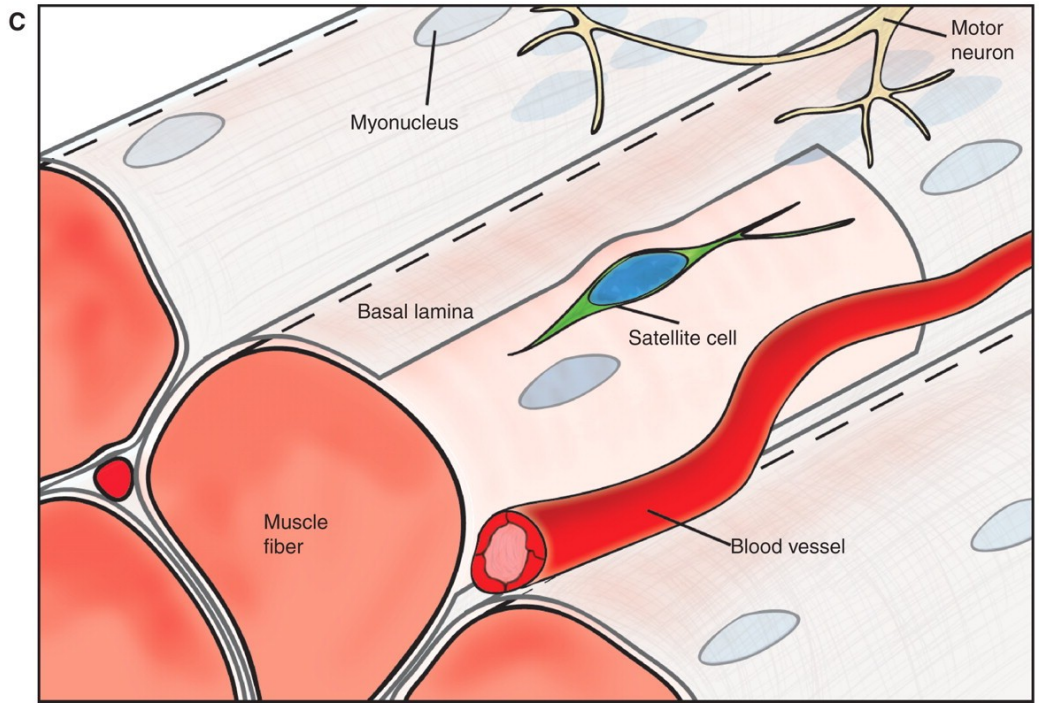
EMBRYONIC DEVELOPMENT OF SKELETAL MUSCLE TISSUE



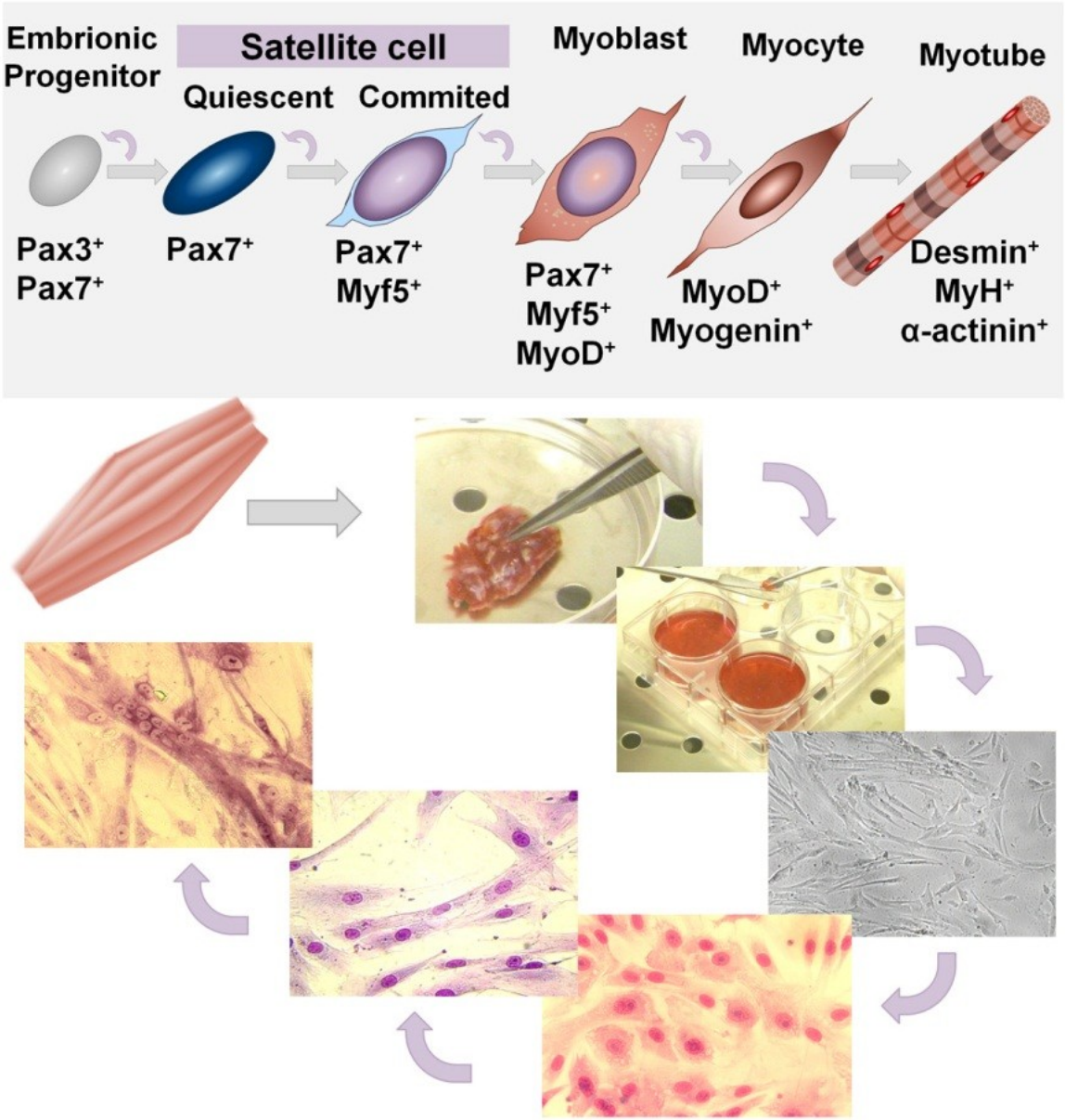
REGENERATION



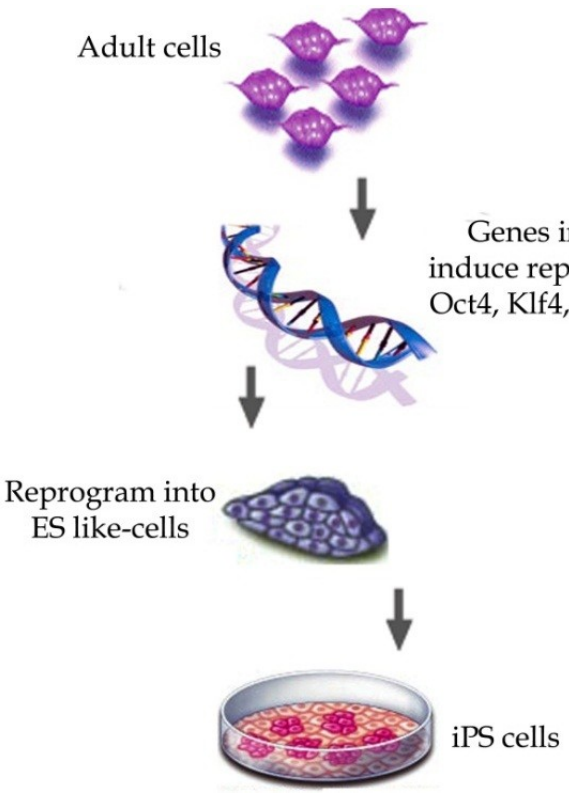


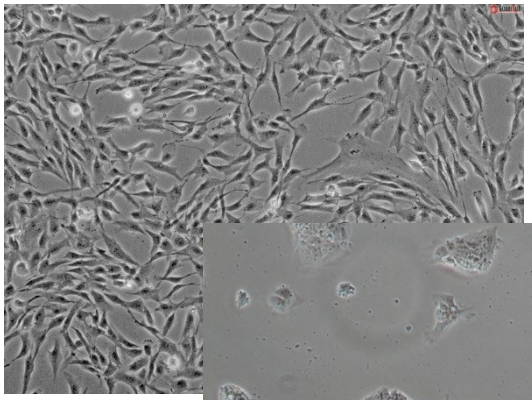


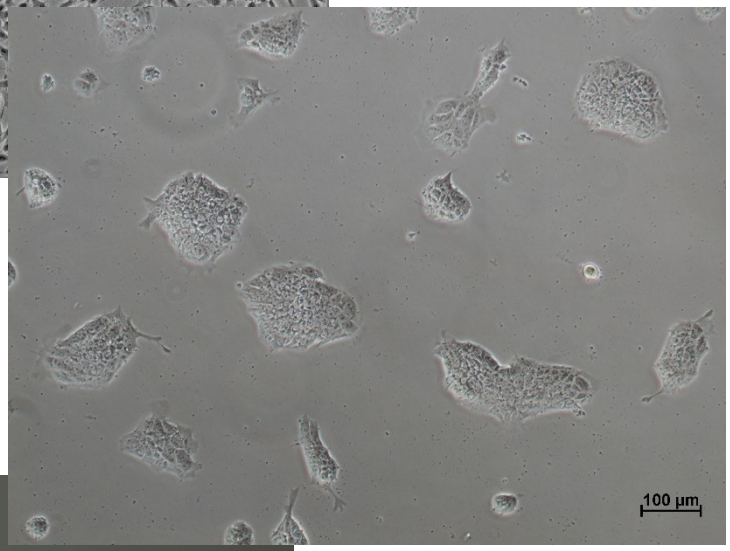
REGENERATION

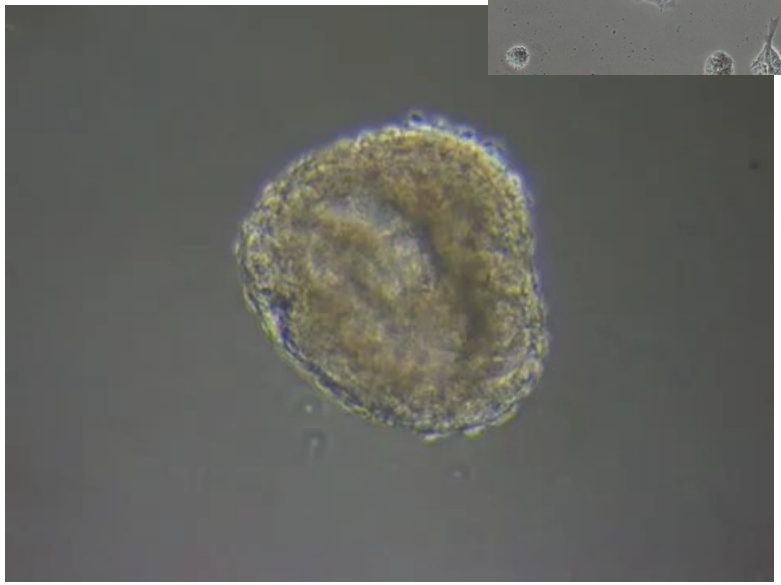


DIFFERENTIATION IN VITRO

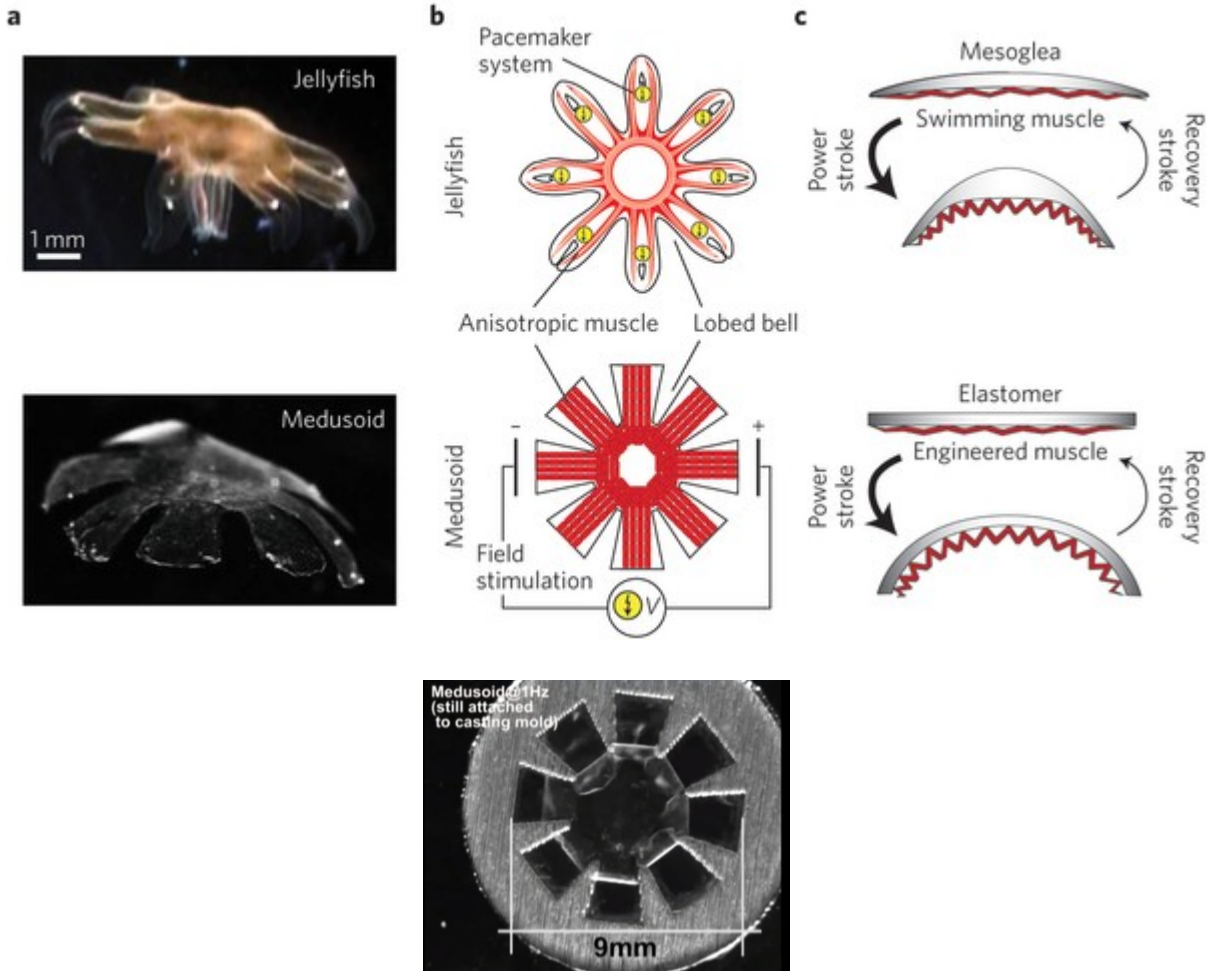








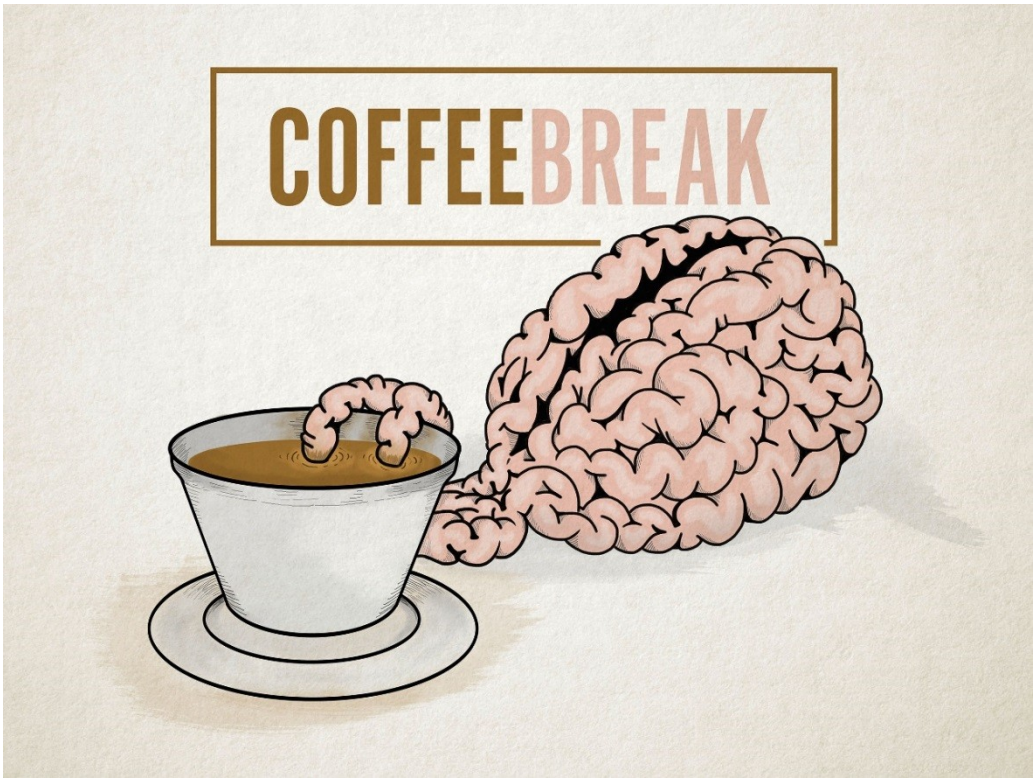
TISSUE ENGINEERING



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

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

BREAK 5 min.



Lecture 9

Nerve tissue

- Nerve tissue
- Neuron
- Synapse
- Neuroglia
- Nerve
- Saltatory signal propagation
- Development of nerve tissue
- Nerve regeneration

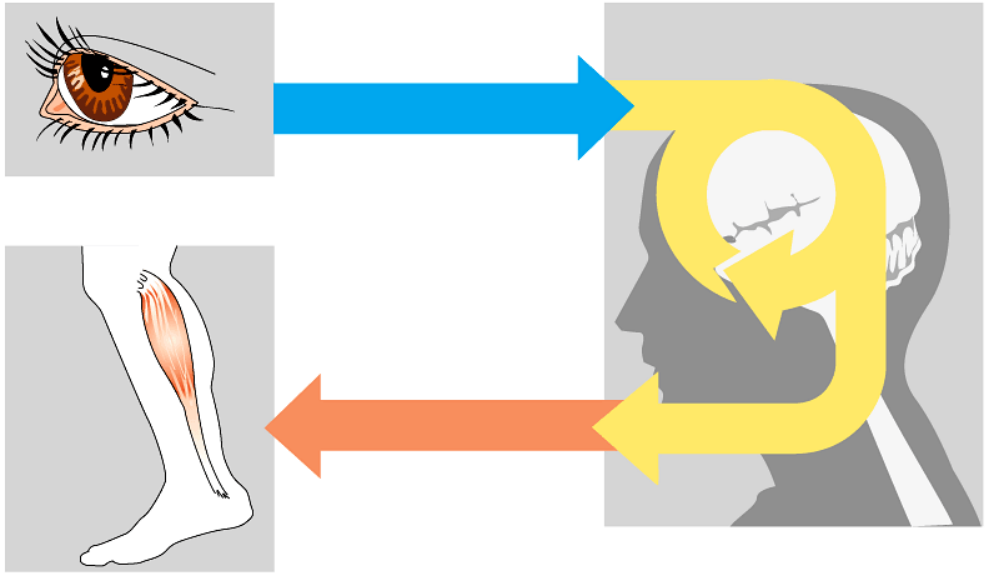
Brno, April 2020

Nerve tissue – general 1

Controls and integrates all body activities within limits that maintain life

Key functions

- sensing changes with sensory receptors
- interpreting and remembering those changes
- reacting to those changes with effectors



Somatic
X
Autonomous (vegetative)

Anatomical organization of nervous system 1

Central nervous system - CNS

Definition:
Unpaired, bilaterally symmetrical structures extending along the longitudinal axis of the midsagittal plane of the body.

Structures arising directly from the neural tube.

Includes:
- Brain
- Spinal cord

Peripheral nervous system - PNS

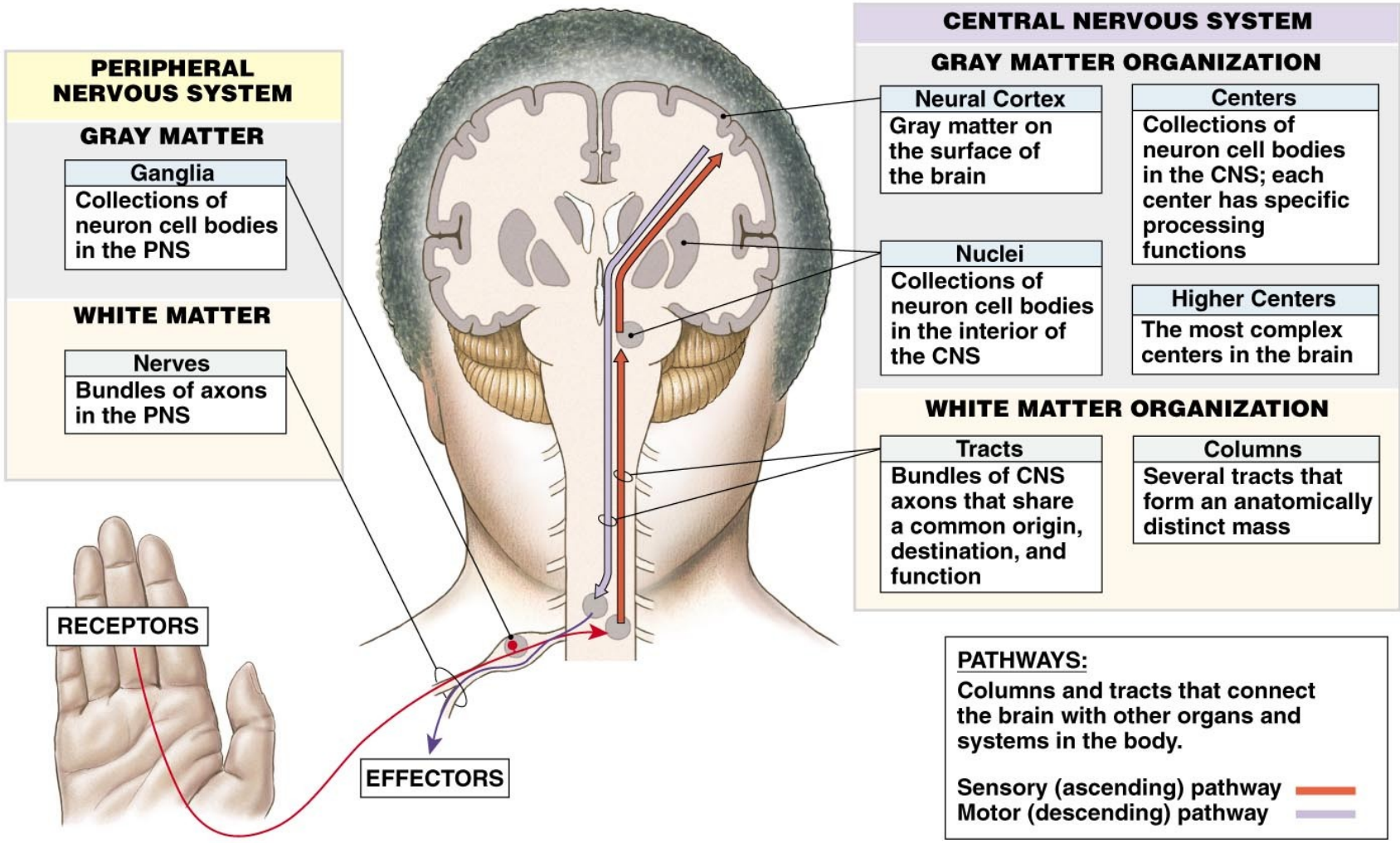
Definition:
Made up of transmission pathways carrying information between the CNS and external/internal environments.

Afferent (sensory) pathways:
Carry information to the CNS.

Efferent (motor) pathways:
Carry information from the CNS.

Includes:
- Cranial nerves (12 pairs)
- Spinal nerves (31 pairs)
- Peripheral nerves
- Ganglia

Anatomical organization of nervous system 2

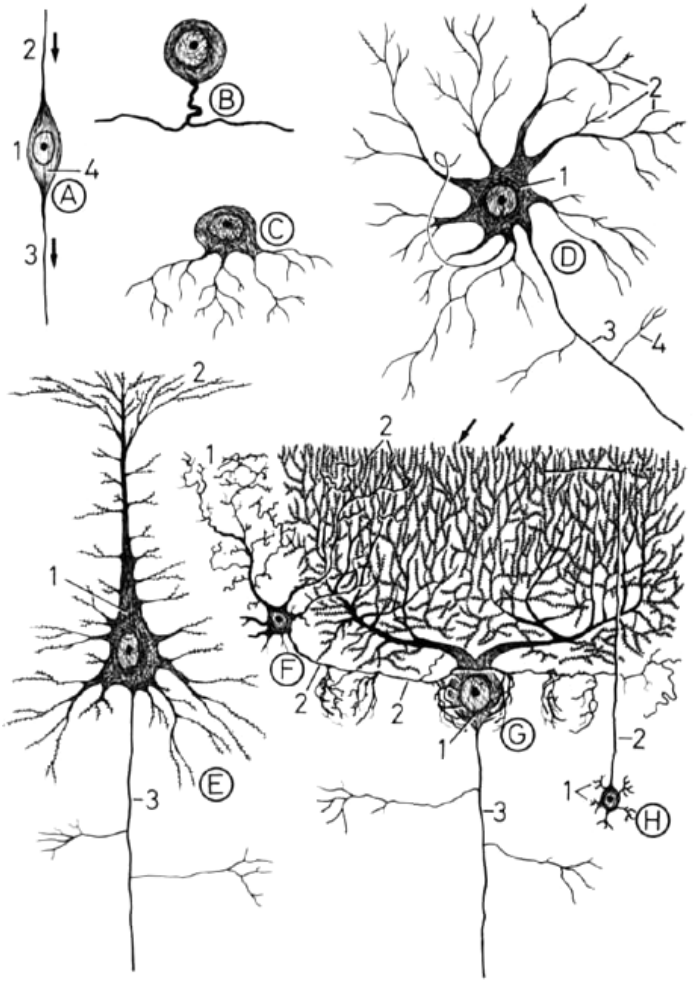


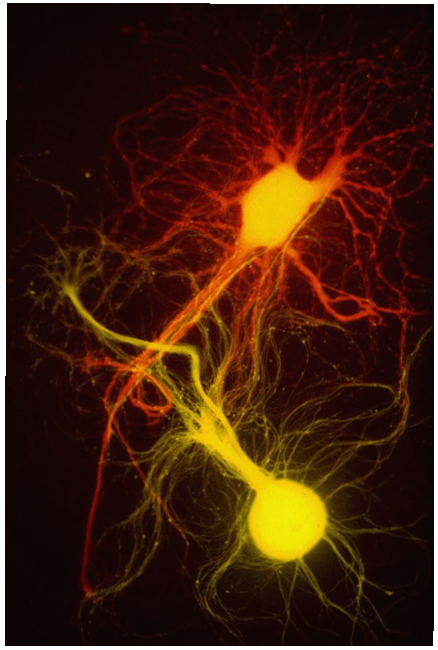
Nerve tissue – General – Neuron 1

Nervous tissue is made up of just 2 types of cells:

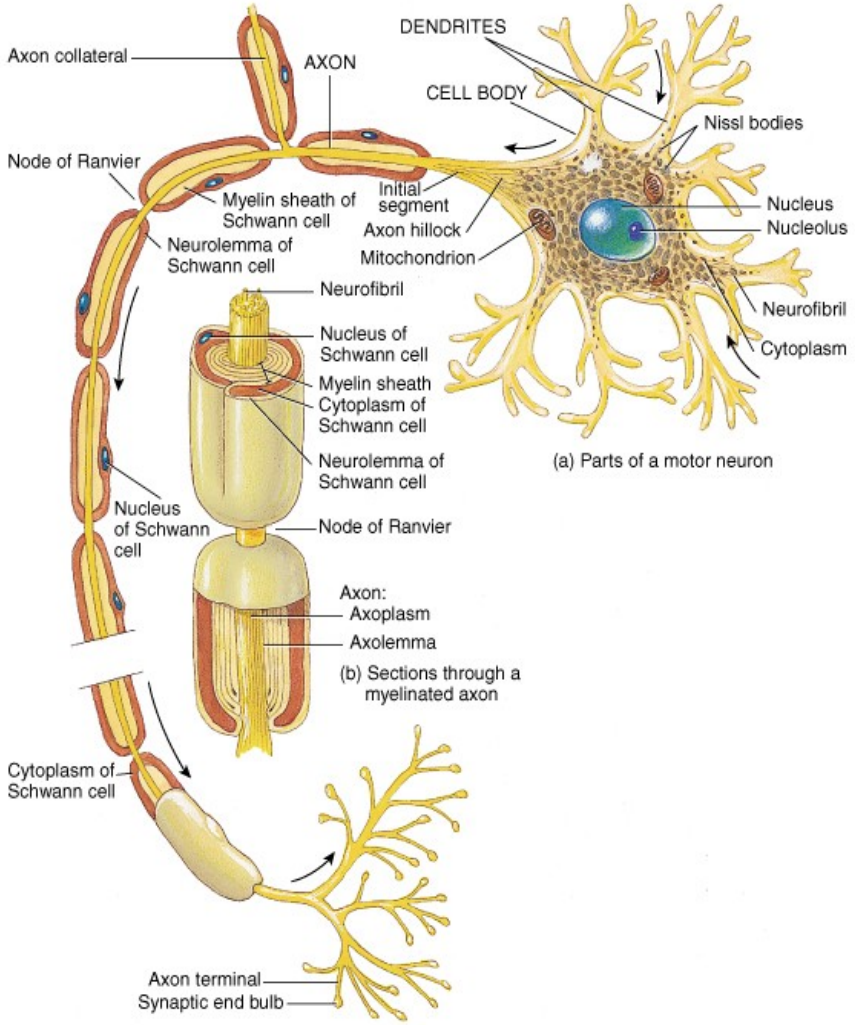
- Neurons
- Neuroglia - glial cells (supporting cells)

- Neurons are the basic functional units of nervous tissue.
- They are highly specialized to transmit nerve impulses.





Neuron 2



1. Perikaryon (neurocyte)

2. Processes:

   (one-way signal conduction)

- axon

(always only one; centrifugal conduction)

- dendrit(es)

(centripetal conduction)

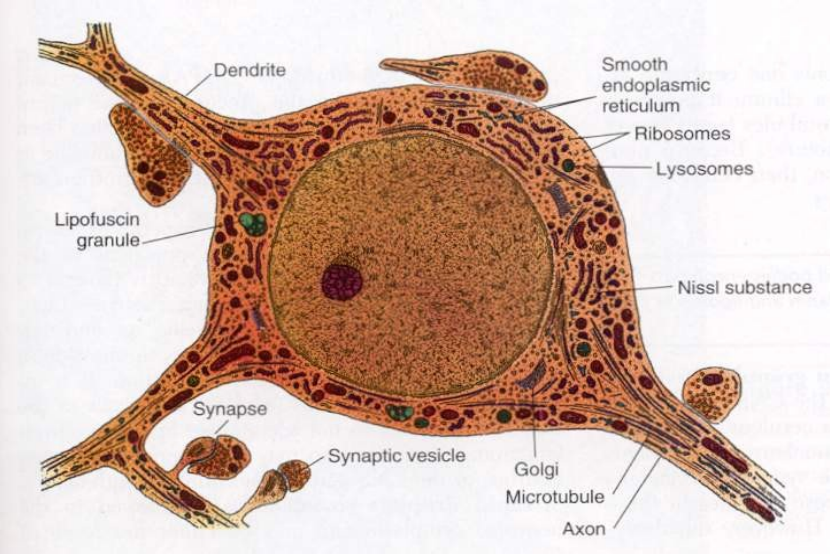
Neuron 3 - Perikaryon

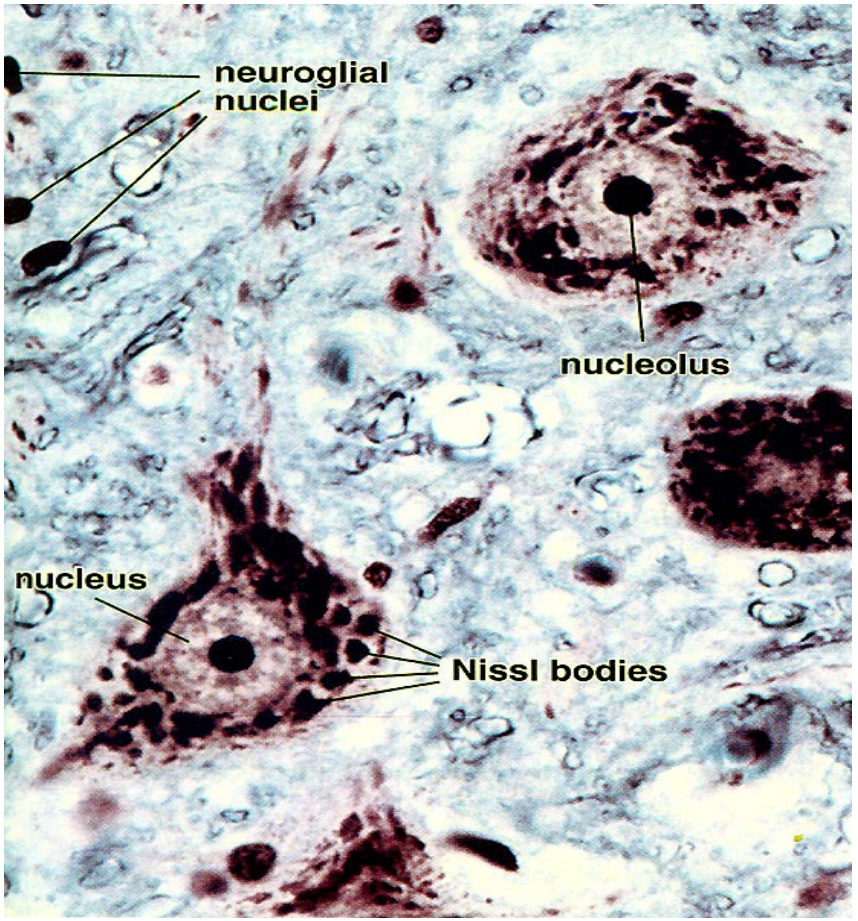
Position:
CNS – grey matter
PNS – ganglia

Shape:
pyramidal, shpherical, ovoid, peer-shaped

Size:
5 to 150 μm

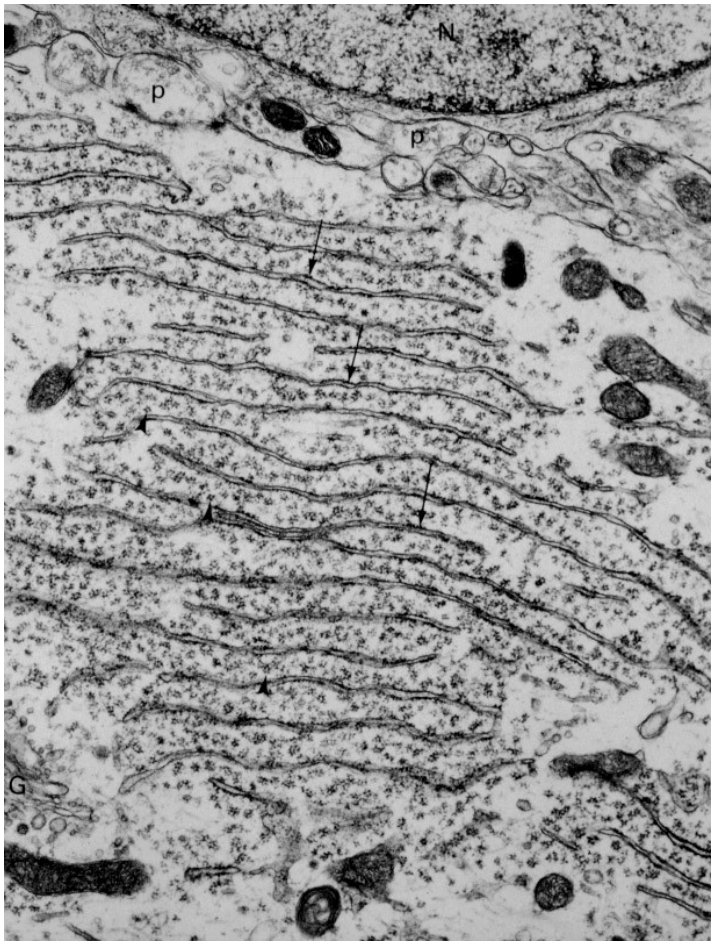
Organelles:
- Nuclues – large + pale + prominent nucleoli
- Nissl substance – rough ER
- Neurofibrils (neurofilaments + neurotubules + actin)
- Lipofuscin pigment clumps





Neuron 4 - Perikaryon

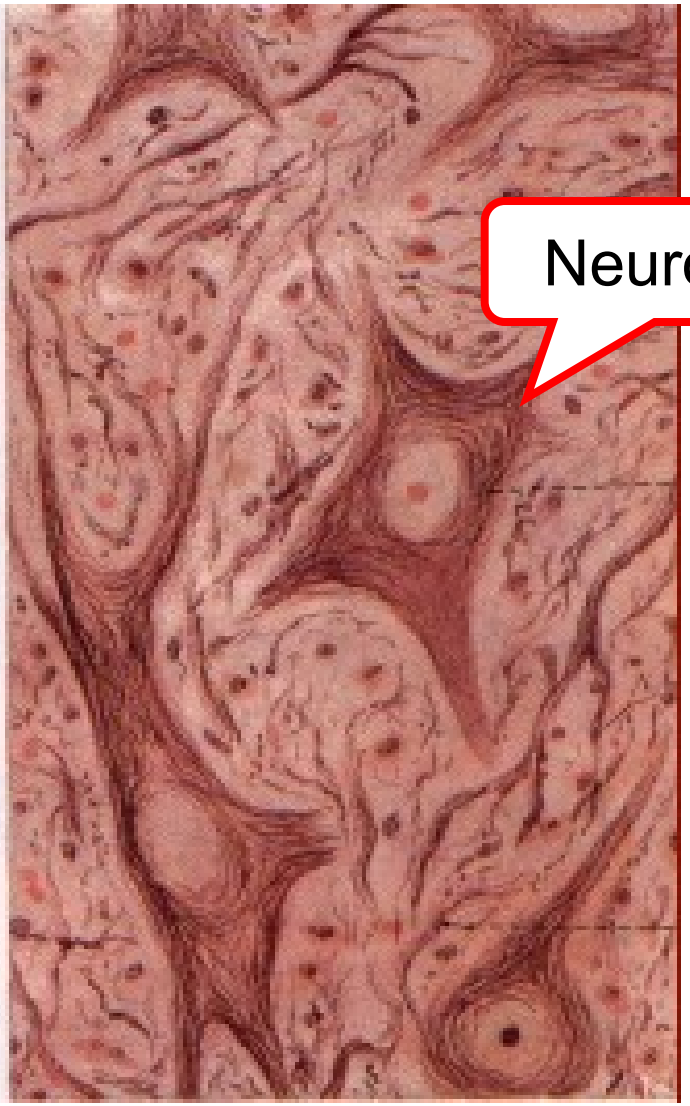
Nissl substance in TEM



Cell and Tissue Ultrastructure – A Functional Perspective; 1993; Cross and Mercer, Freeman and Co.; Page 127

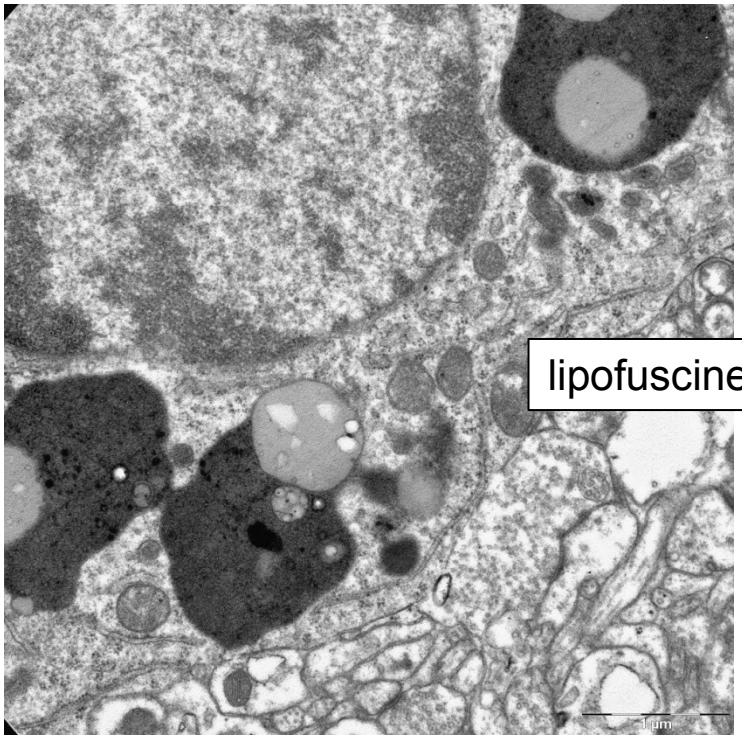
Neuron 5 - Perikaryon

H-E stains

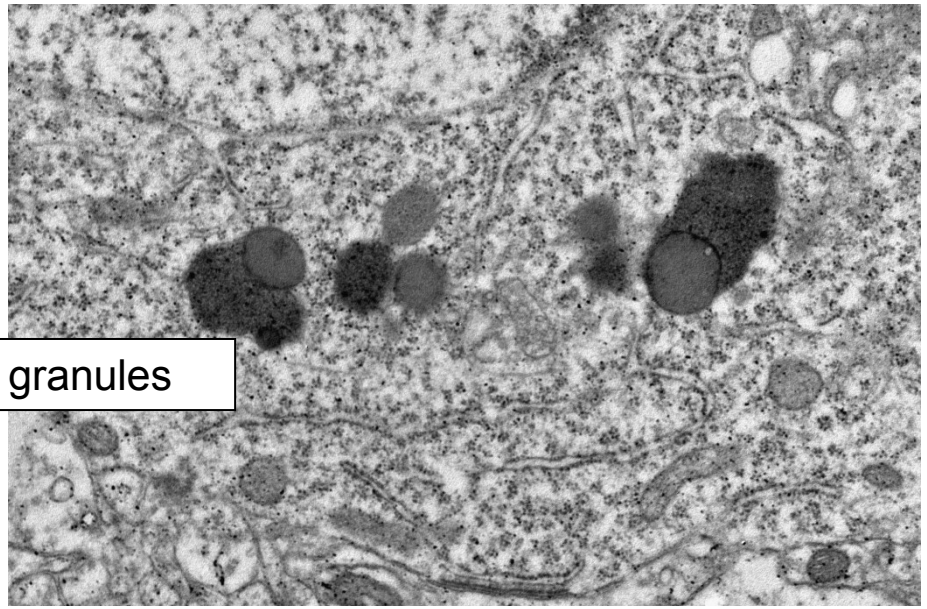


Silver nitrate

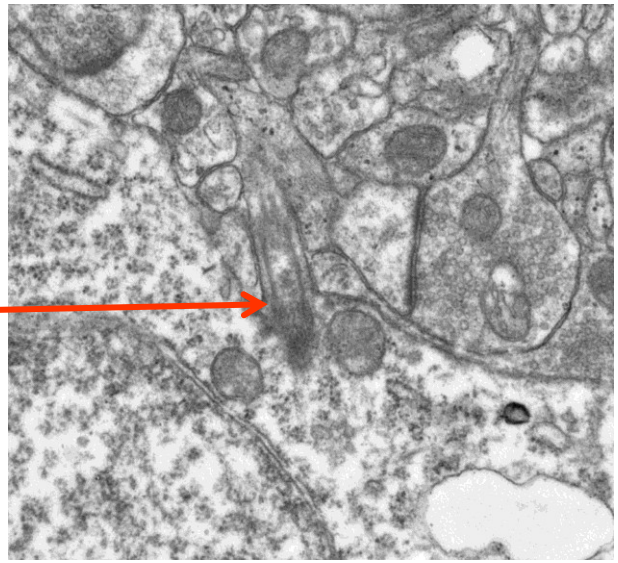
Neuron 6 - Perikaryon



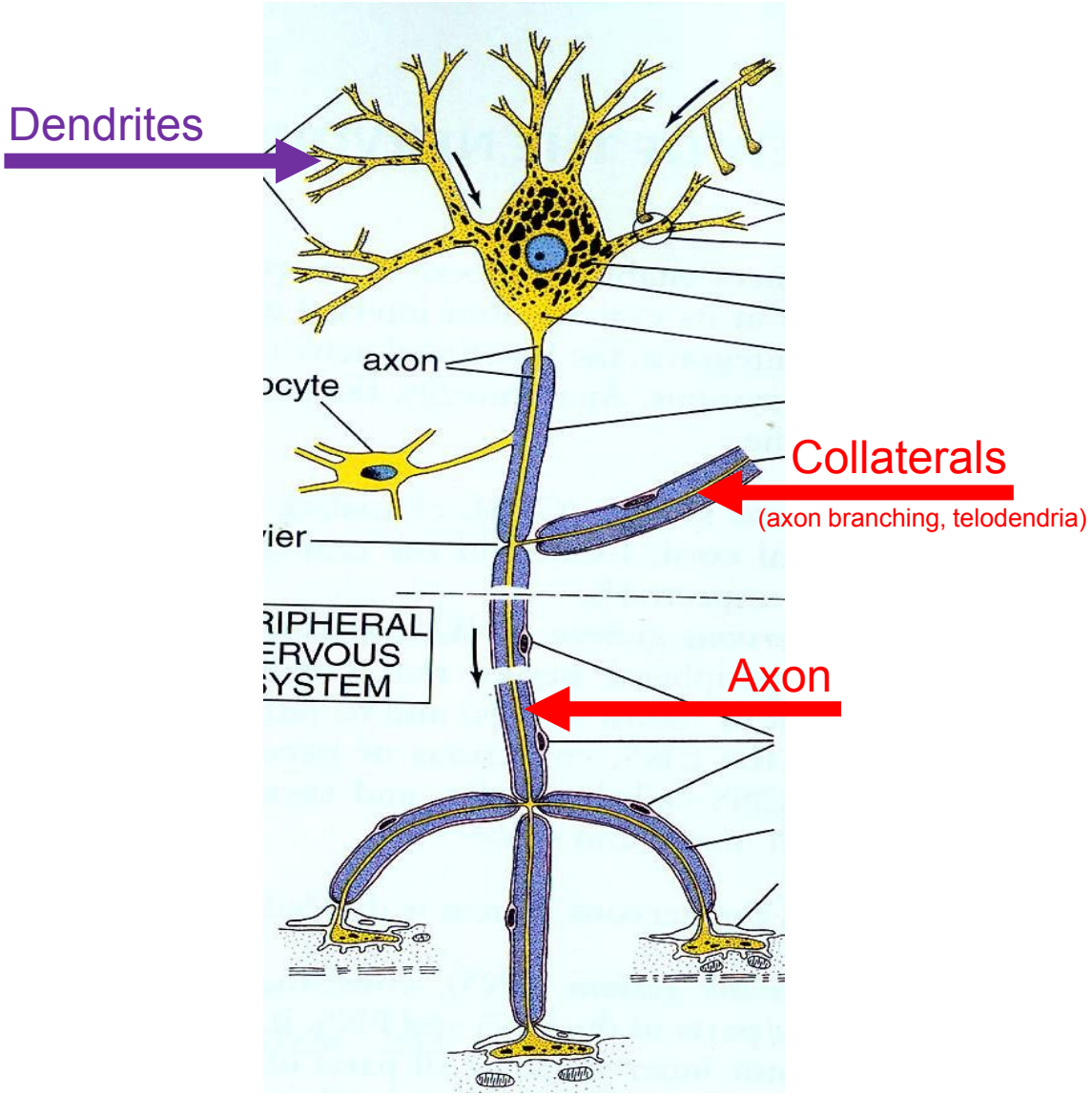
lipofuscine granules



Cilium derived from unused centriole



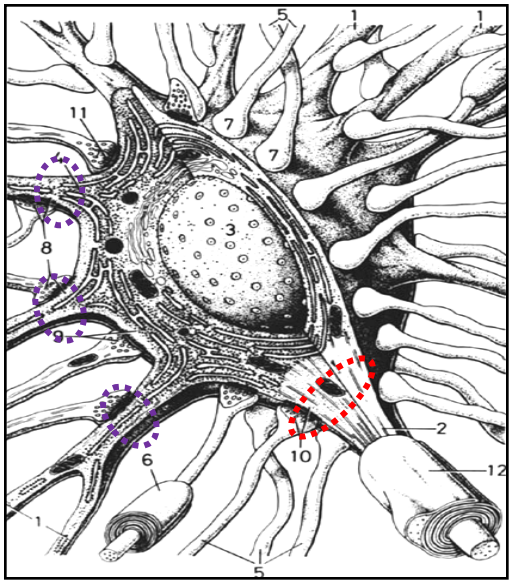
Neuron 7 – Neurites / Processes



Neuron 7 – Neurites / Processes

Dendrites

- Conducts impulses towards the cell body
- Typically short, highly branched & unmyelinated
- Surfaces specialized for contact with other neurons
- Contains neurofibrils & Nissl bodies
- Receptive surface for synaptic junctions
- Contain MAP-2 (distinction from axon)
- Tens of thousands of synapses on large dendrites
- Dendritic spines located on surface of some dendrites
- Spines diminish with age and poor nutrition

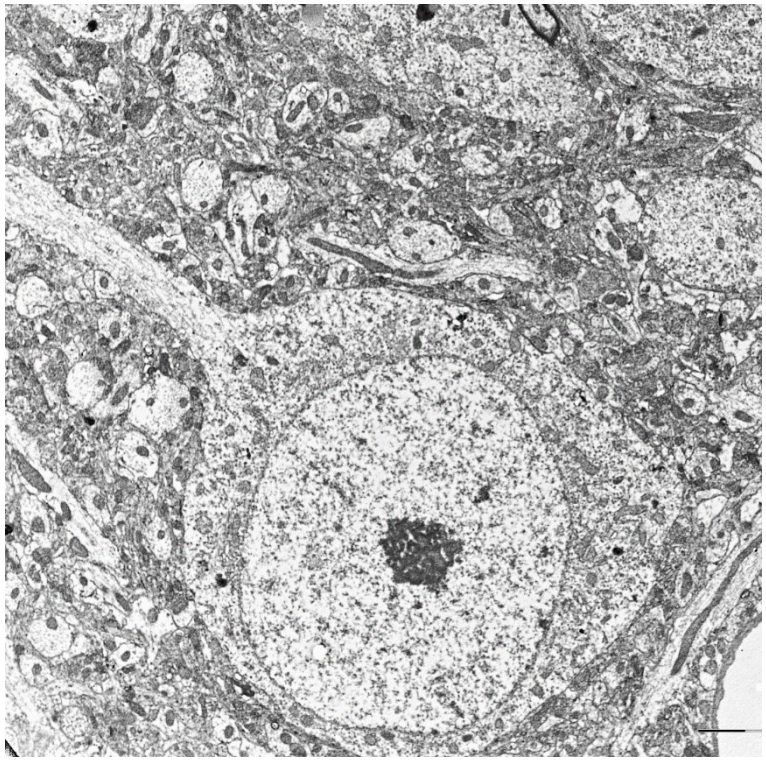


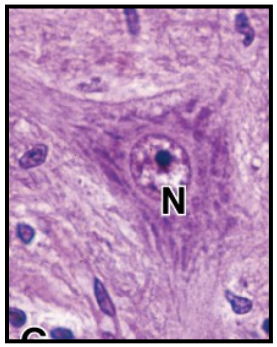
Axon (nerve fiber)

- 1 axon projects from cell body at axon hillock
- Axon hillock - pyramid shaped region of the soma that is devoid of RER
- Some axons are up to 100 cm
- Initial segment = Spike trigger zone (a portion of axon from its origin to the beginning of myelin sheath)
- At spike trigger zone trigger zone summation of excitatory and inhibitory impulses occurred
- Collateral branches, Terminal arbor
- Myelinated or Unmyelinated
- Conduct impulses away from cell body
- Swollen tips called synaptic knob (terminal button) contain synaptic vesicles filled with neurotransmitters
- Cell membrane = axolemma
- Cytoplasm = axoplasm

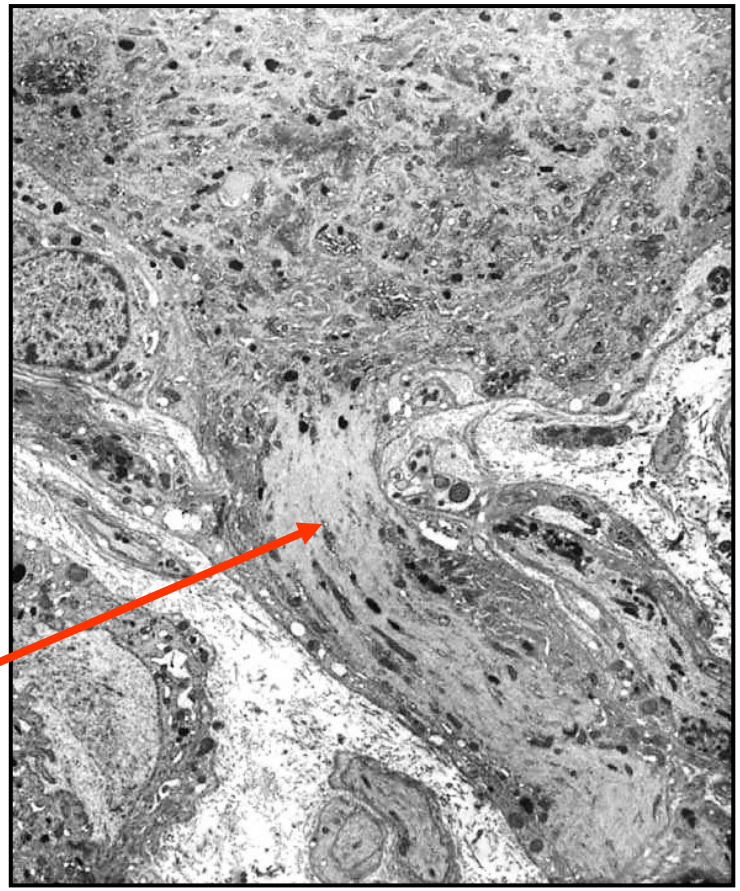
White matter: areas of myelinated axons
Gray matter: areas of unmyelinated axons, cell bodies, and dendrites

Neuron 8 – Neurites / Processes

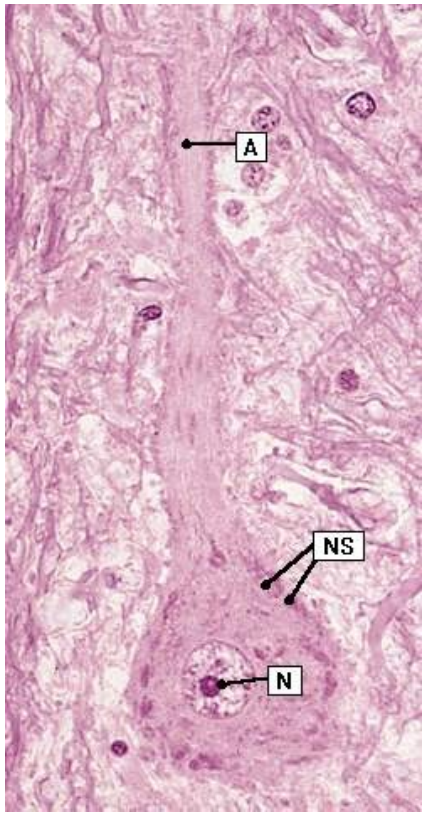




Neuron in TEM



Neuron 9 – Axonal transport



Why?
many proteins made in soma must be transported to axon and axon terminal to repair axolemma, serve as gated ion channel proteins, as enzymes or neurotransmitters

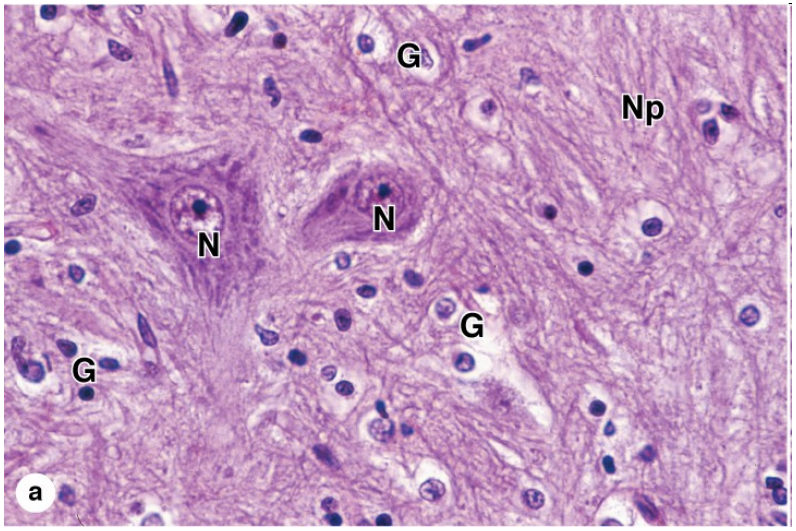
How?
axonal transport – two-way passage of proteins, organelles, and other material along an axon

- anterograde transport – movement down the axon away from soma (dynein)
- retrograde transport – movement up the axon toward the soma
- (kinesin)

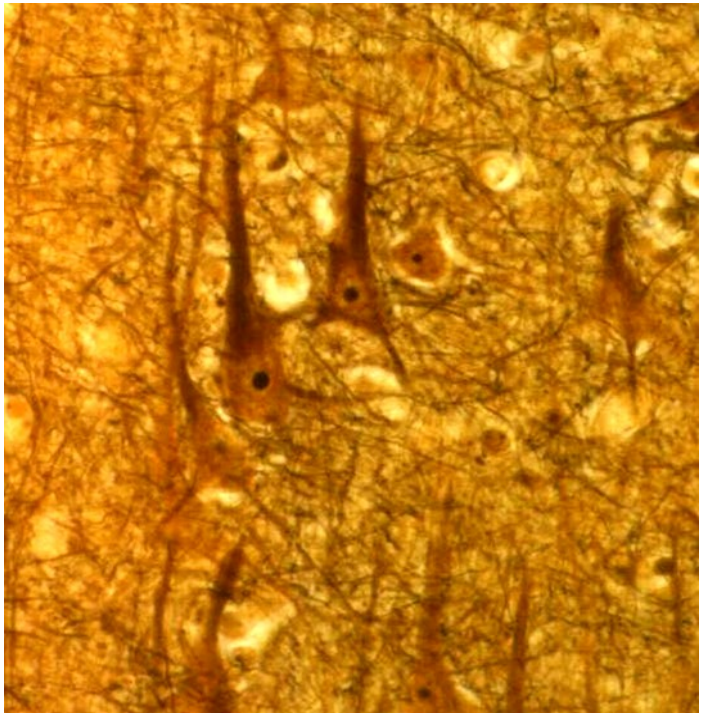
- Slow transport: 1-5 mm/day
- Fast transport: 200-400 mm/day

Nerve tissue – Neuropil 1

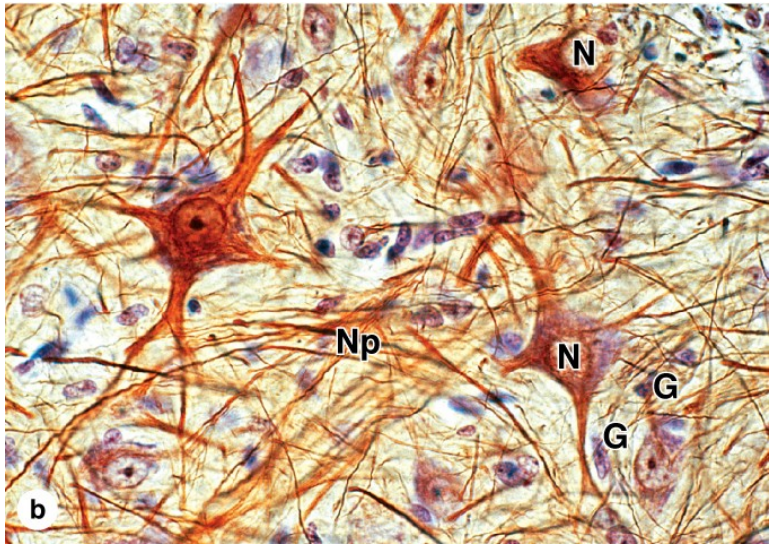
All the material filling space among the bodies of neurons and glial cells + ECM



motoneurons - HE



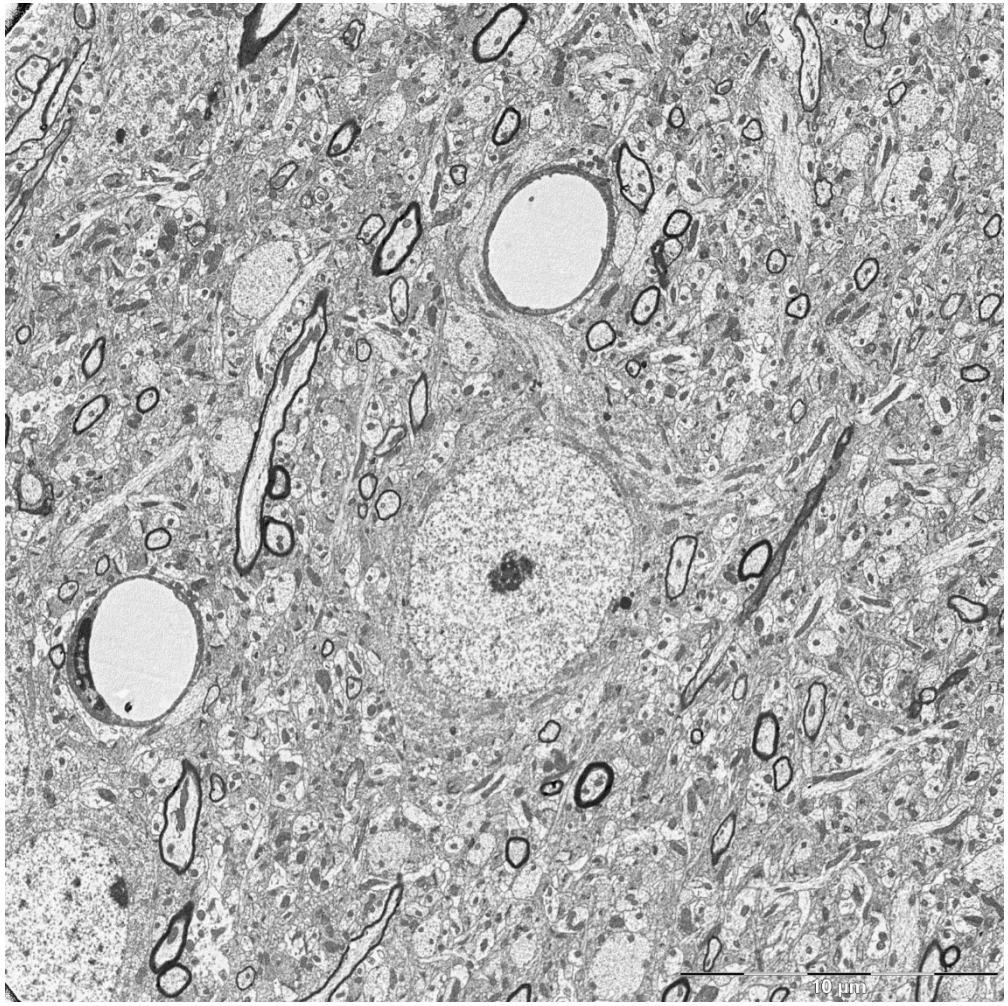
pyramidal cells - impregnation



motoneurons – combined method

Nerve tissue – Neuropil 2

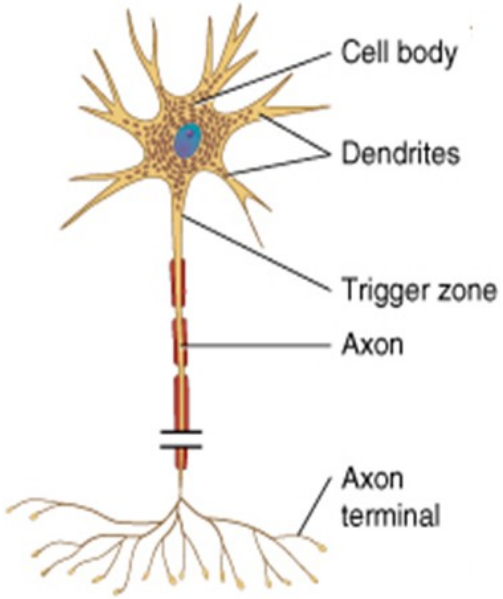
Neuropil in TEM



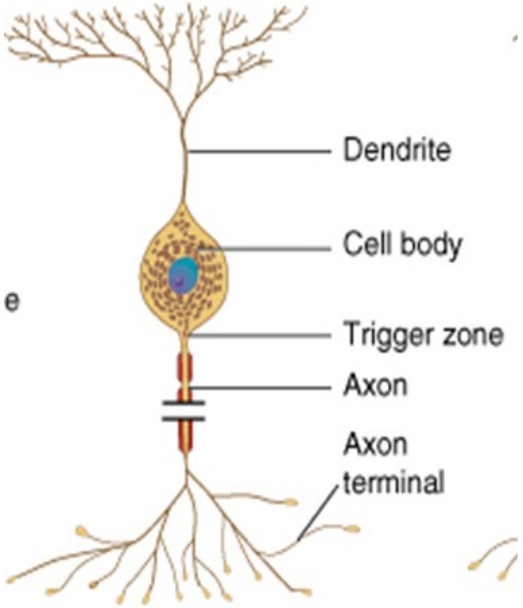
Neuron – Classification 1

According to the number of the processes

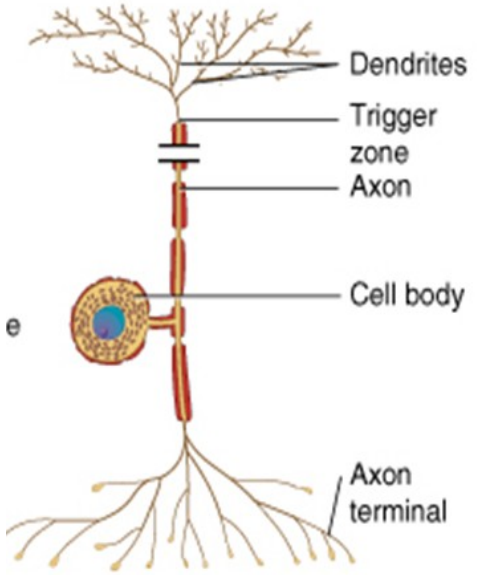
Multipolar
several dendrites & one axon
(most common cell type)



Bipolar
one main dendrite & one axon
(in retina, vestibular and cochlear ganglion)

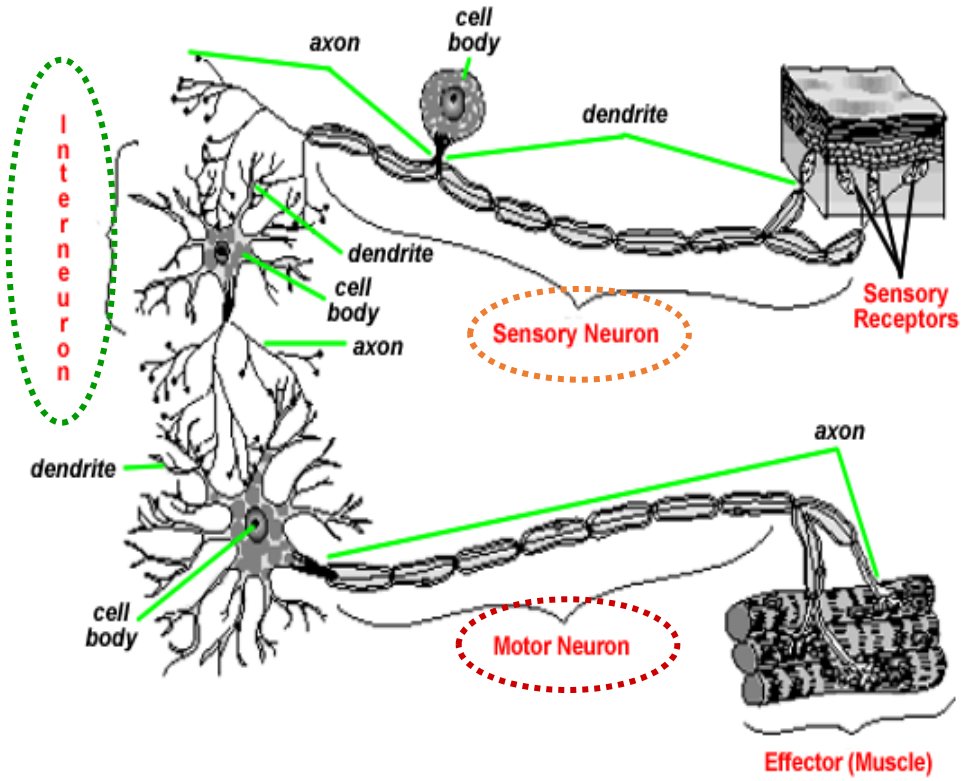


Unipolar (pseudounipolar)
one process only
(develop from a bipolar)
(always sensory, in spinal ganglia)



Neuron – Classification 2

According to the function



Motor (efferent) neurons:
- conduct impulses to muscles, neurons, glands

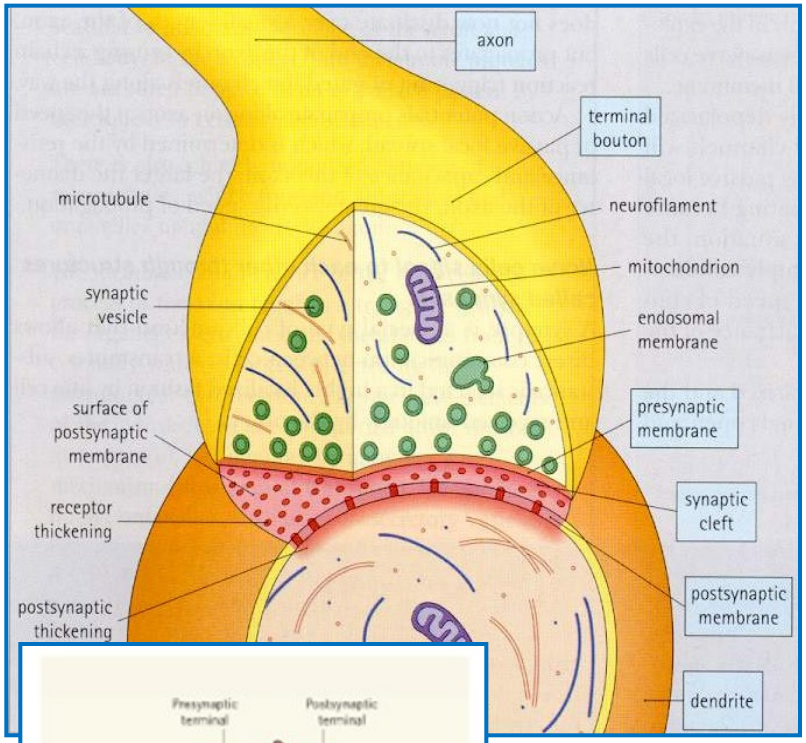
Sensory (afferent) neurons:
- receive sensation

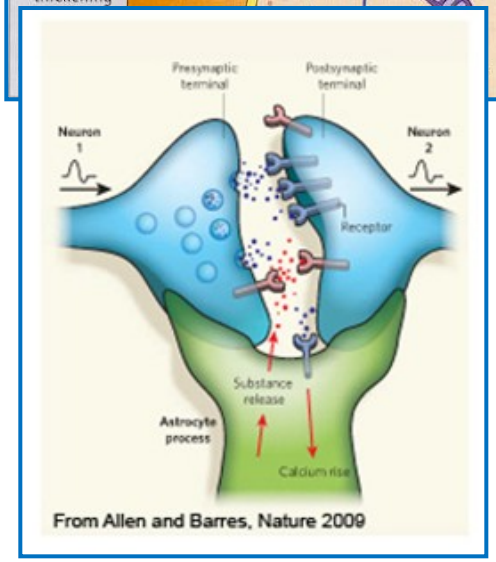
Interneurons:
- local circuit neurons

Synapse 1

Definition

Synapses are highly specialized intercellular junctions, which link the neurons of each nervous pathway





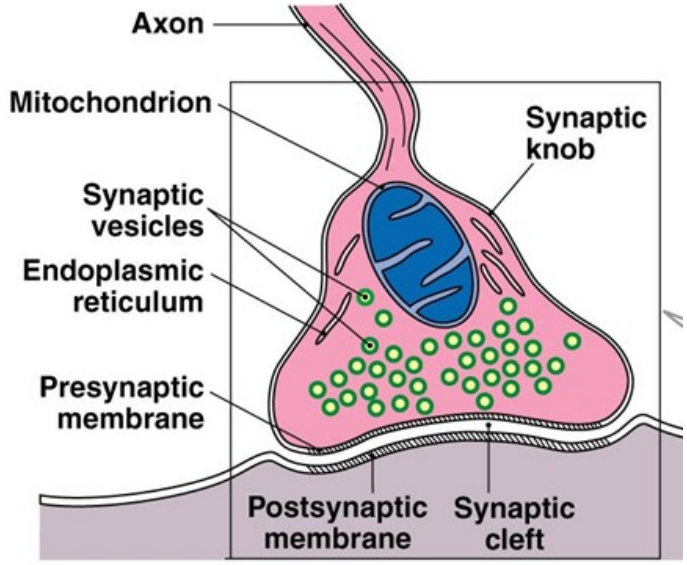
- Axon terminal forms bouton terminal
- Presynaptic membrane - contains mitochondria, and an abundance of synaptic vesicles with neurotransmitter
- Presynaptic dense projections - are associated with synaptic vesicles form active sites of synapse
- Synaptic vesicles (smaller + larger – storage)
- Postsynaptic membrane - contains receptors and some dense materials
- Synaptic cleft - 20-30 nm width, occupied by fine filaments
- Glial cells increase synaptic efficacy
- Asymmetric synapses are excitatory (a thick postsynaptic membrane and a 30 nm synaptic cleft)
- Symmetric synapses are inhibitory (thin postsynaptic membrane and a 20 nm synaptic cleft)
- Need special staining to see by light microscopy

Synapse 2

Excitatory synapses
- postsynaptic Na+ channels open
- influx of Na+
- depolarizition of membrane of postsynaptic neuron

X

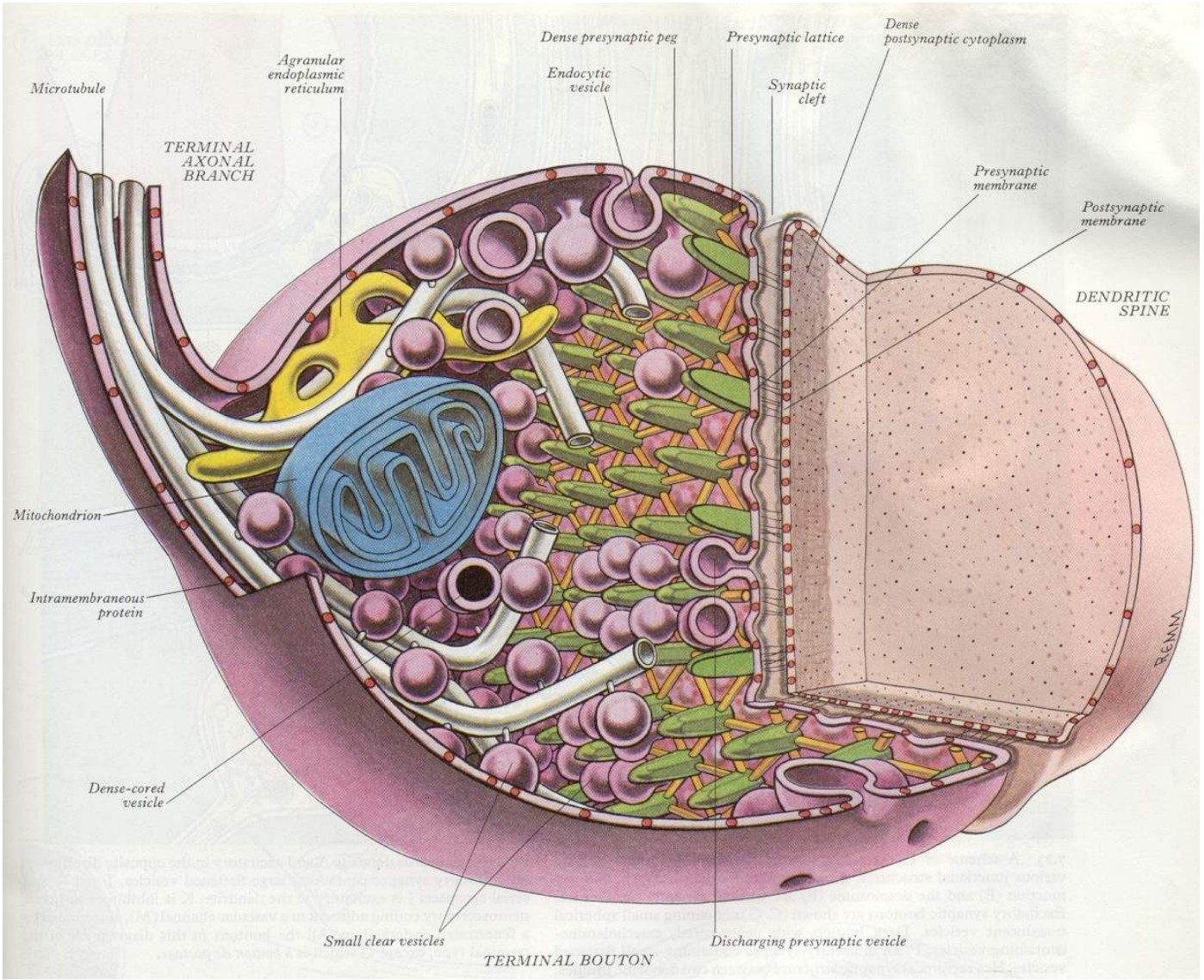
Inhibitory synapses
- postsynaptic Cl- (or other anion) channels open
- influx of anions
- hyperpolarizition of membrane of postsynaptic neuron



Neurotransmitters

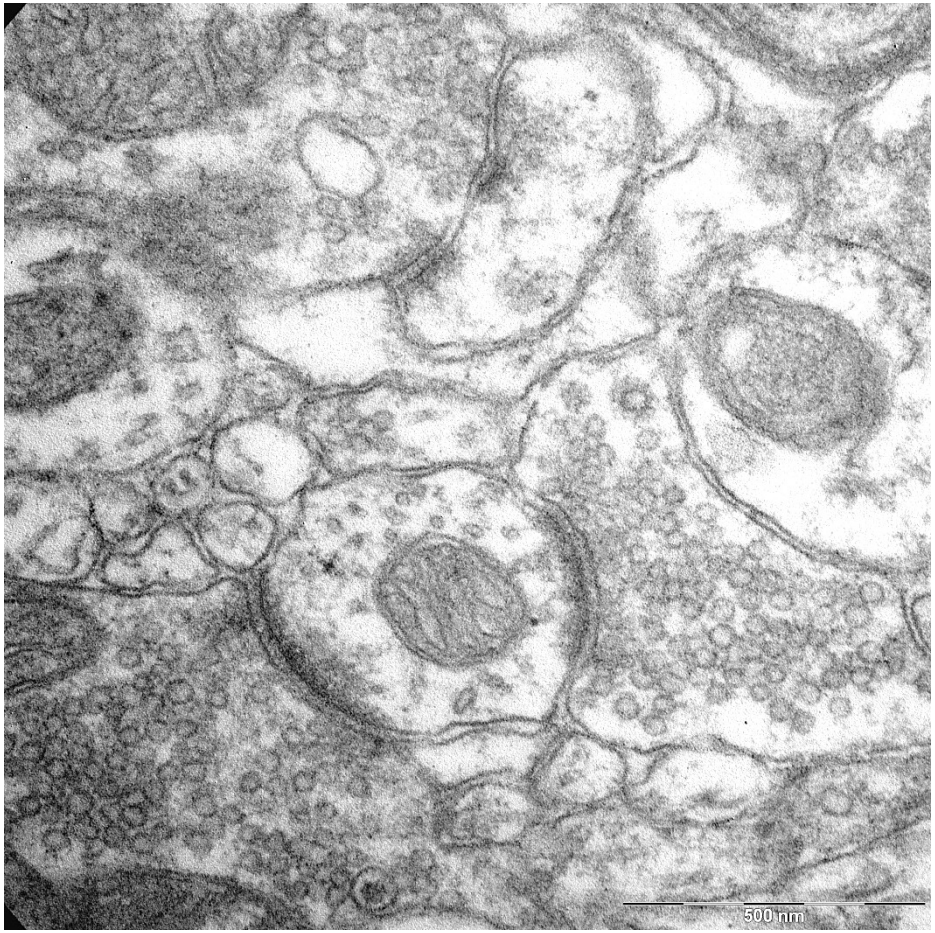
- Acetylcholine
- Amioacids – gluatamate, glycin, GABA (gamma-amminobutyric acid)
- Monoamines – serotonin, catecholamines, dopamine, adrenaline, …
- Neuropeptides – enkefalin, somatostatin, neurotensin, ….
- Others – adenosine, nitric oxide

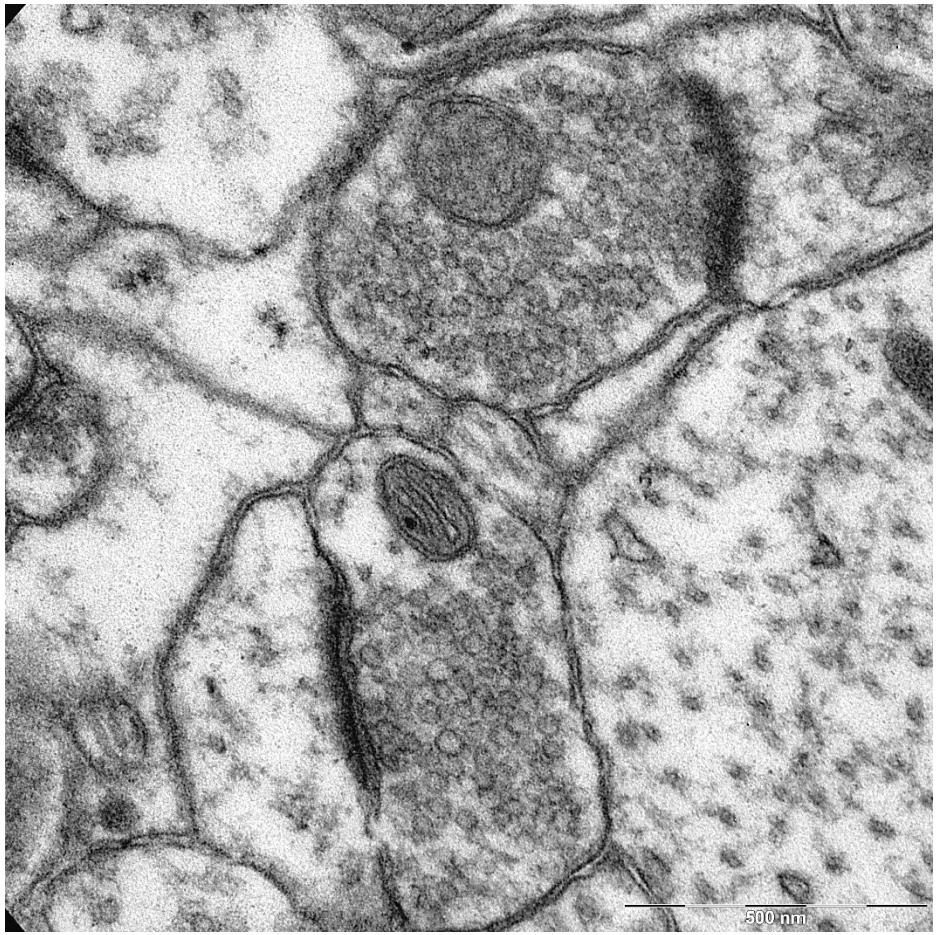
Synapse 3


Microtubule
Agranular endoplasmic reticulum
Dense presynaptic peg
Presynaptic lattice
Dense postsynaptic cytoplasm
Endocytic vesicle
Synaptic cleft
TERMINAL AXONAL BRANCH
Presynaptic membrane
Postsynaptic membrane
DENDRITIC SPINE
Mitochondrion
Intramembraneous protein
Dense-cored vesicle
Small clear vesicles
Discharging presynaptic vesicle
TERMINAL BOUTON
REMAK

Synapse 4

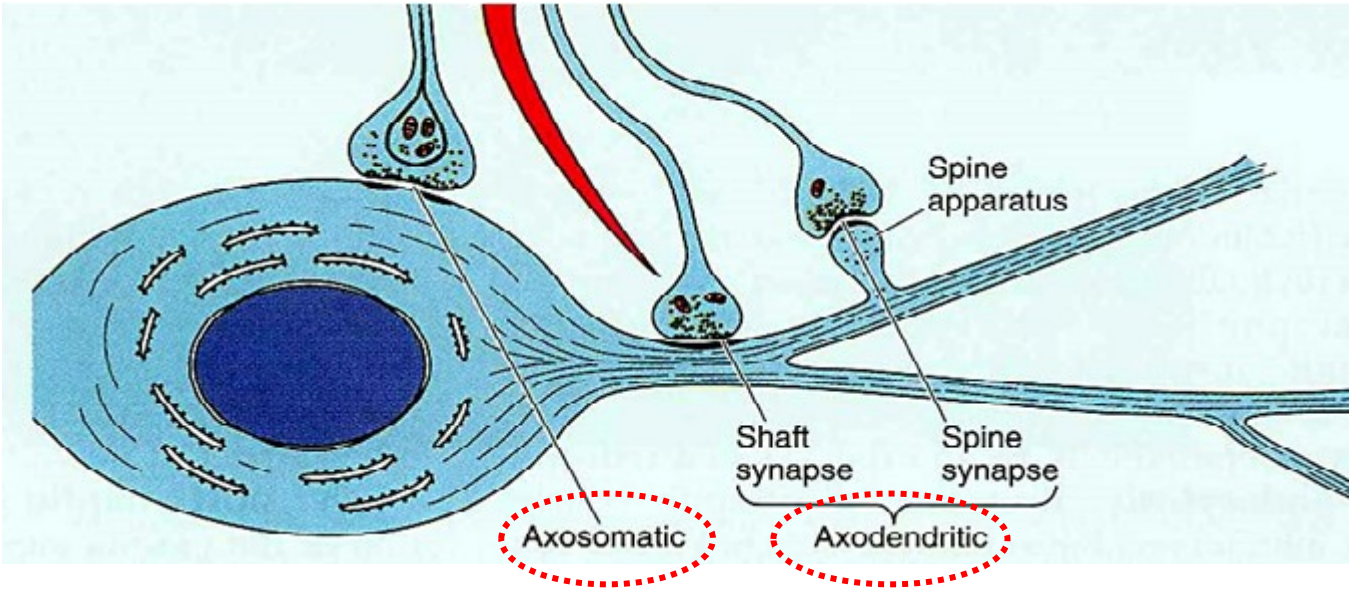
Synapse in TEM





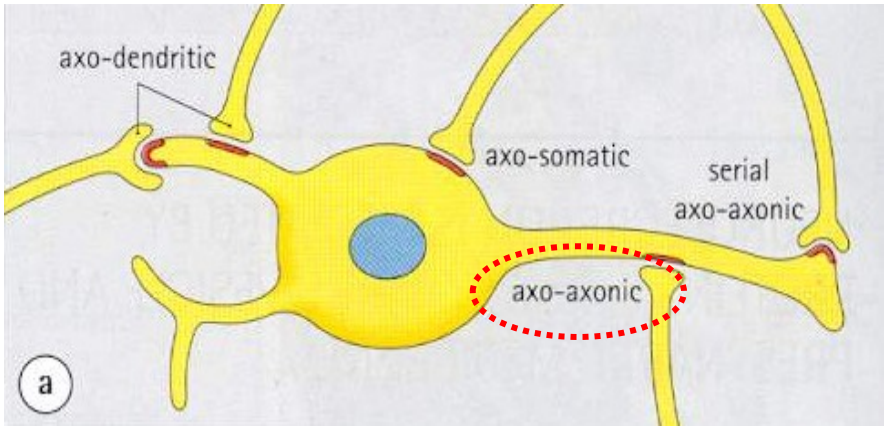
Synapse 5

Classification according to the constitution

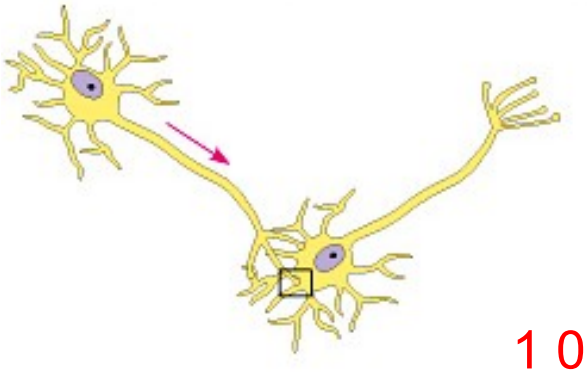


Axodendritic
Axosomatic
Axoaxonic

Note:
Neuromuscular junction – synapse between neuron and effector muscle fibre

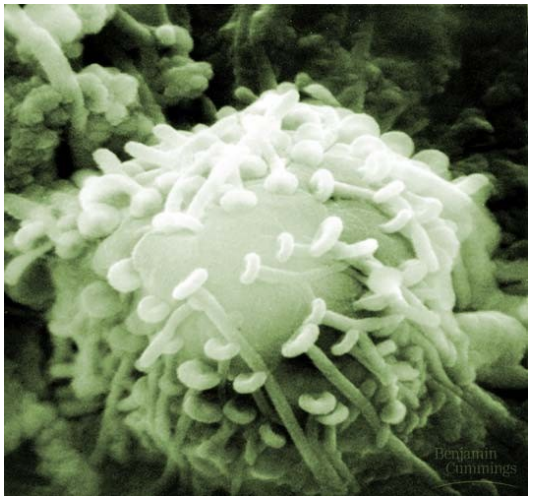


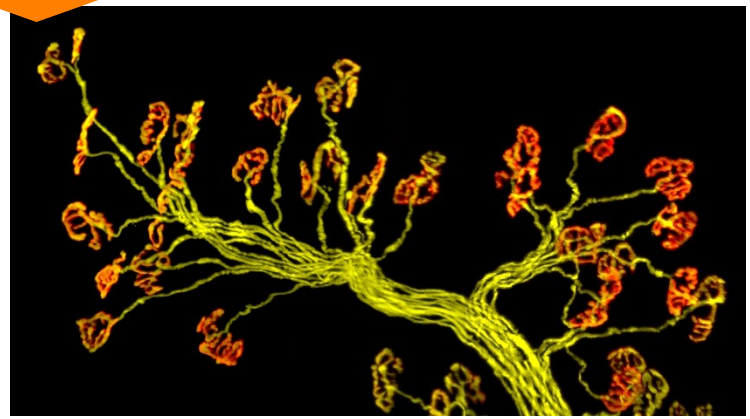
Synapse 7



One neuron may have

1 000 to 10 000 synapses !!!





Neuroglia

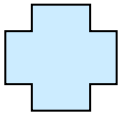
General features

- non-neuronal cells of several types
- support and protect the neurons
- bind neurons together and form framework for nervous tissue
- in fetus, guide migrating neurons to their destination
- if mature neuron is not in synaptic contact with another neuron it is covere
- prevents neurons from touching each other
- gives precision to conduction pathways
- only nucl… visible by light microscopy without special staining
- there are …

Number of neurons: about 100 billions to 1 trillion
Number of glial cells: 50x more then neurons

Central neuroglia

- Astrocytes
- Oligodendrocytes
- Microglia
- Ependymal cells



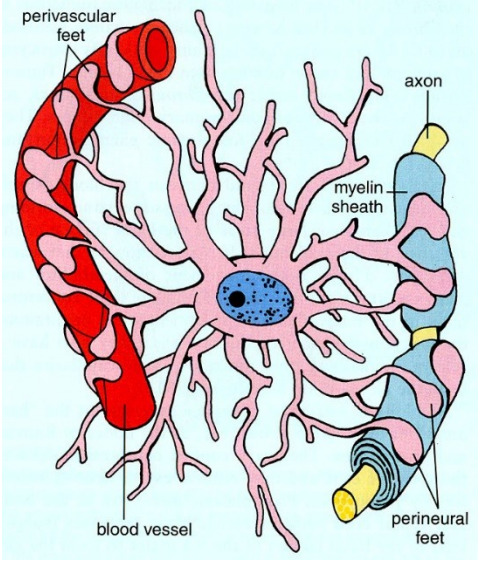
Peripheral neuroglia

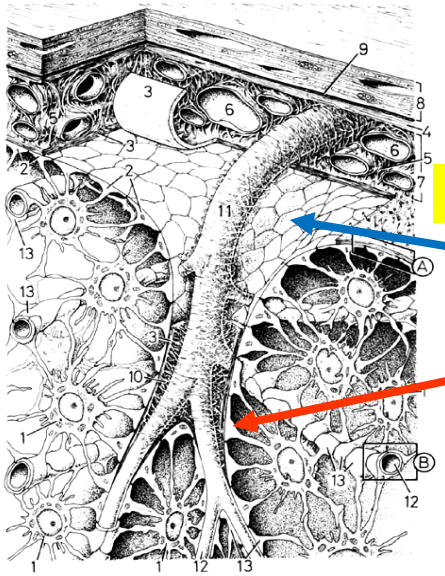
- Schwann cels
- Satelite cells

Neuroglia - Astrocytes

- most abundant glial cell in CNS
- covers entire brain surface and most non-synaptic regions of the neurons in the gray matter of the CNS

- diverse functions:
  - ✓ form a supportive framework of nervous tissue
  - ✓ have extensions (perivascular feet) that contact blood capillaries that stimulate them to form a tight seal called the blood-brain barrier
  - ✓ convert blood glucose to lactate and supply this to the neurons for nourishment
  - ✓ nerve growth factors secreted by astrocytes promote neuron growth and synapse formation
  - ✓ communicate electrically with neurons and may influence synaptic signaling
  - ✓ regulate chemical composition of tissue fluid by absorbing excess neurotransmitters and ions
  - ✓ astrocytosis or sclerosis – when neuron is damaged, astrocytes form hardened scar tissue and fill space formerly occupied by the neuron
  - ✓ contains GFAP



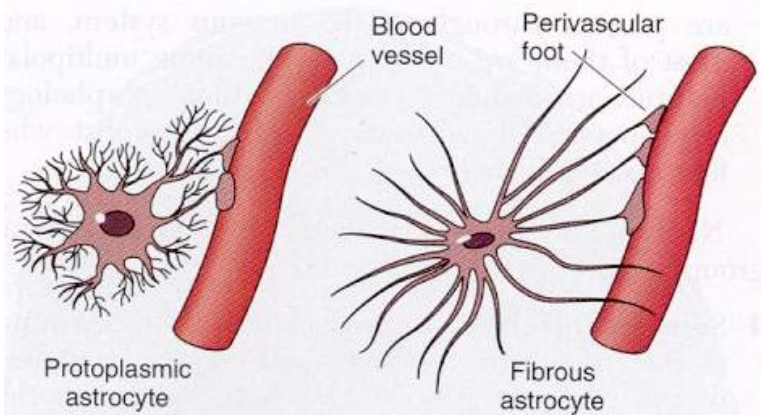


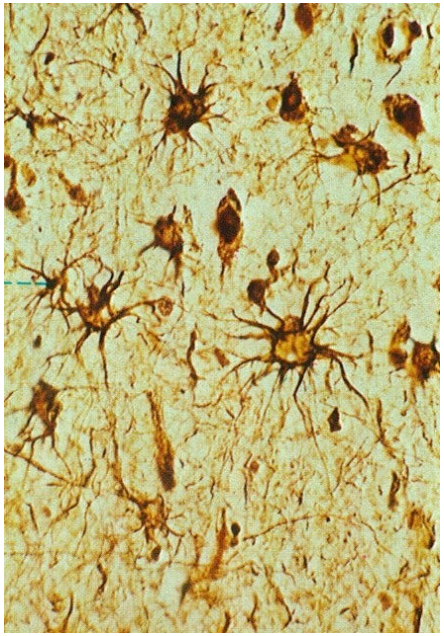
Membrana limitans gliae…

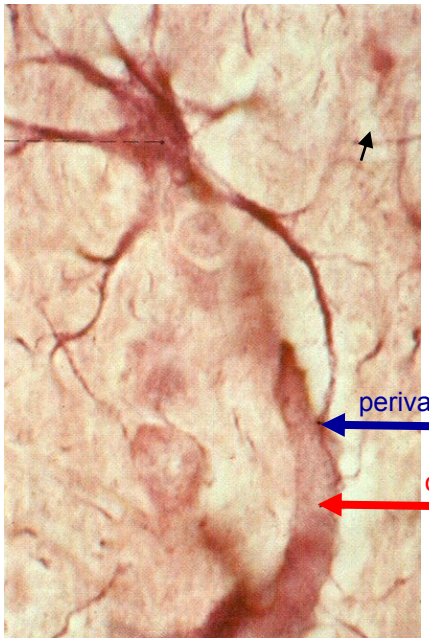
…superficialis

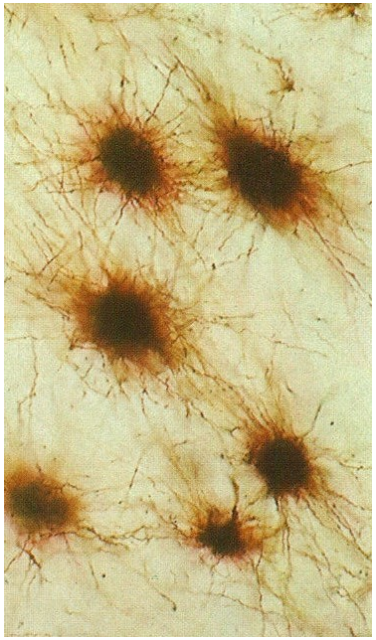
…perivascularis

Neuroglia - Astrocytes









protoplasmic astrocyte

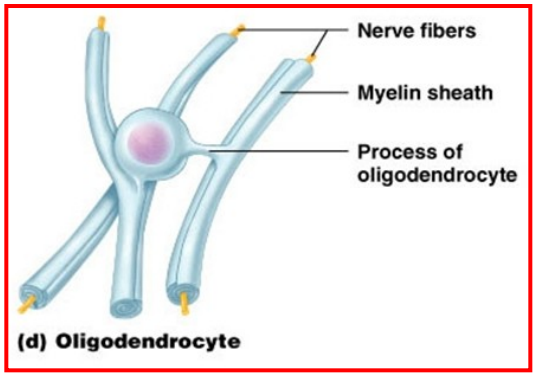
(predominant in grey matter)

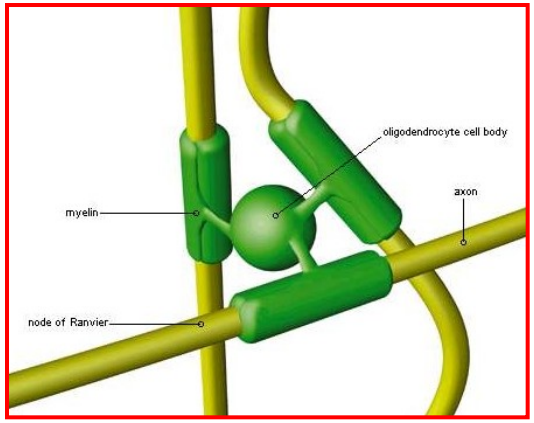
fibrous astrocyte

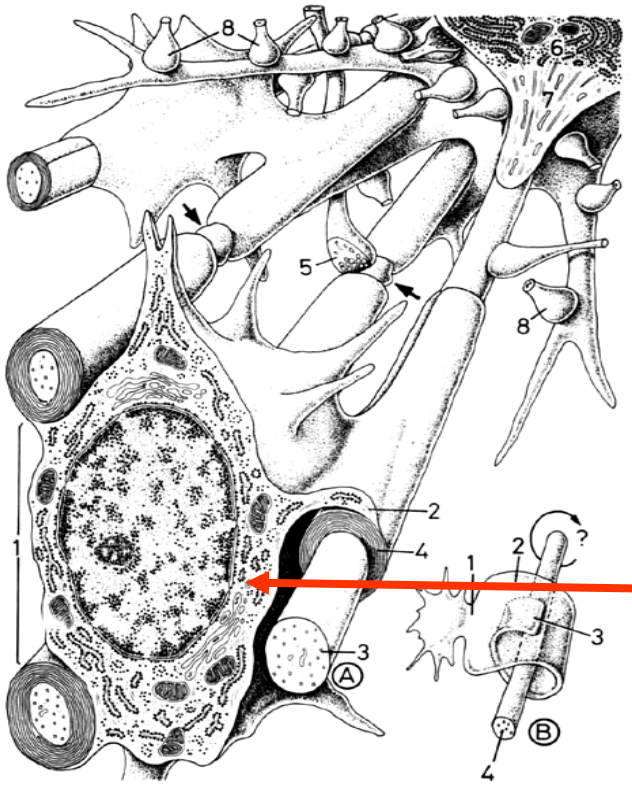
(predominant in white matter)

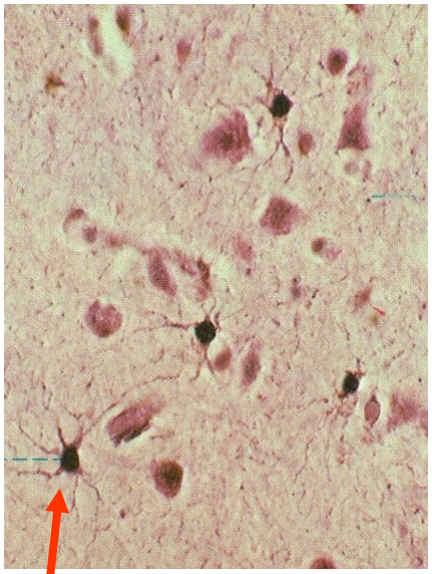
Neuroglia - Oligodendrocytes

- ✓ smaller than astrocytes; darker, round nucleus, abundant RER, well developed golgi apparatus
- ✓ form myelin sheaths in CNS
- ✓ one cell serves more then one axon
- ✓ cannot migrate around axons (unlike Schwann cells) must push newer layers of myelin under the older ones so myelination spirals inward toward nerve fiber
- ✓ nerve fibers in CNS have no Schwann sheath (neurilemma) or endoneurium
- ✓ each arm-like process wraps around a nerve fiber forming an insulating layer that speeds up signal conduction
- ✓ damaged in multiple sclerosis





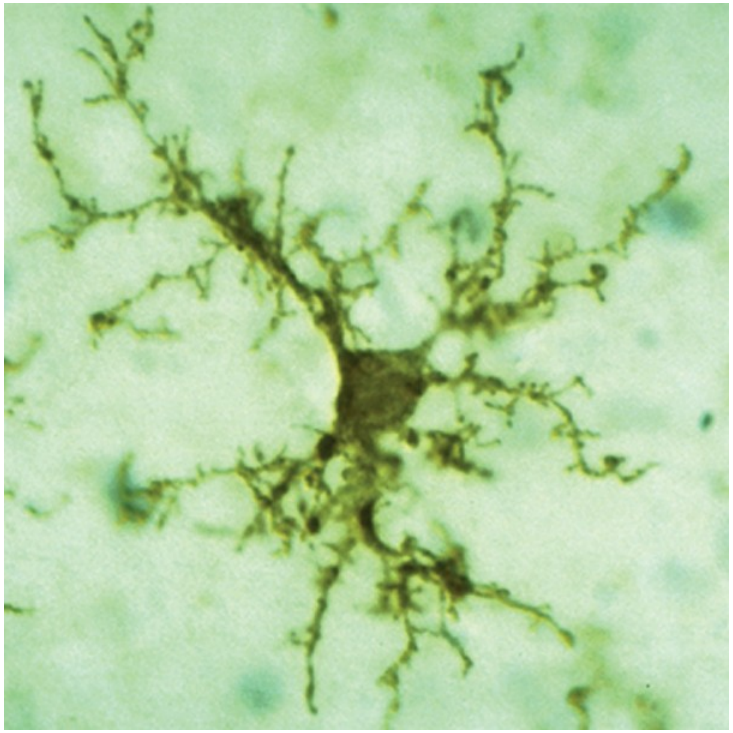


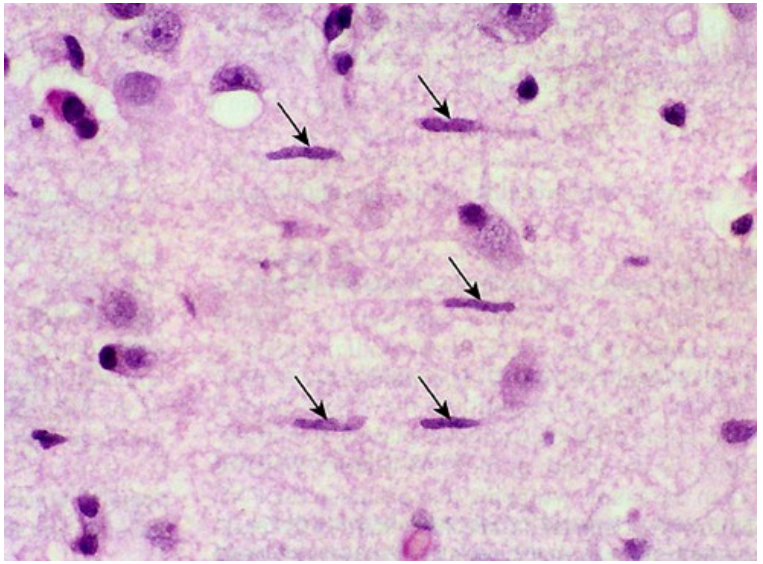


oligodendrocyte

Neuroglia - Microglia

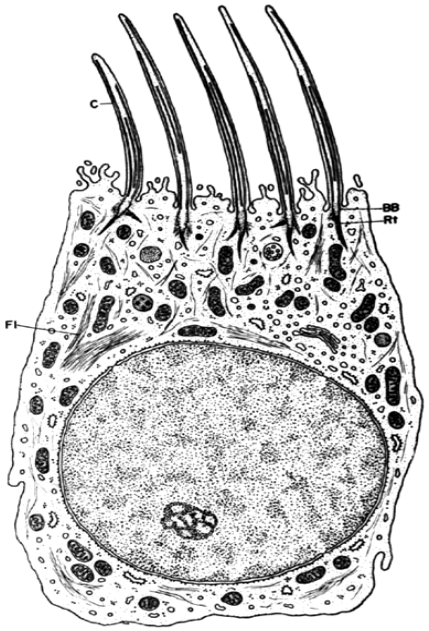
- ✓ smallest neuroglial cell
- ✓ small, dark, elongated nuclei
- ✓ possess phagocytotic properties
- ✓ when activated – antigen presenting cell
- ✓ originate in bone marrow (mesodermal origin)

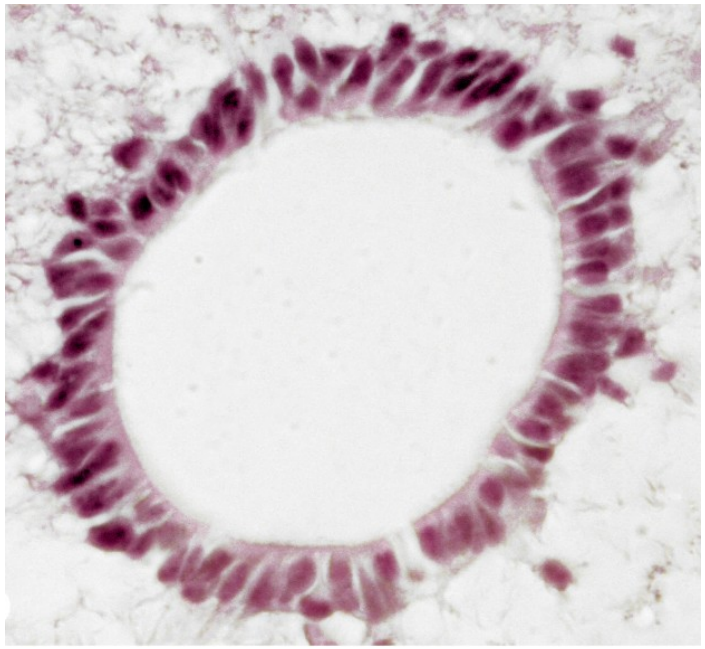




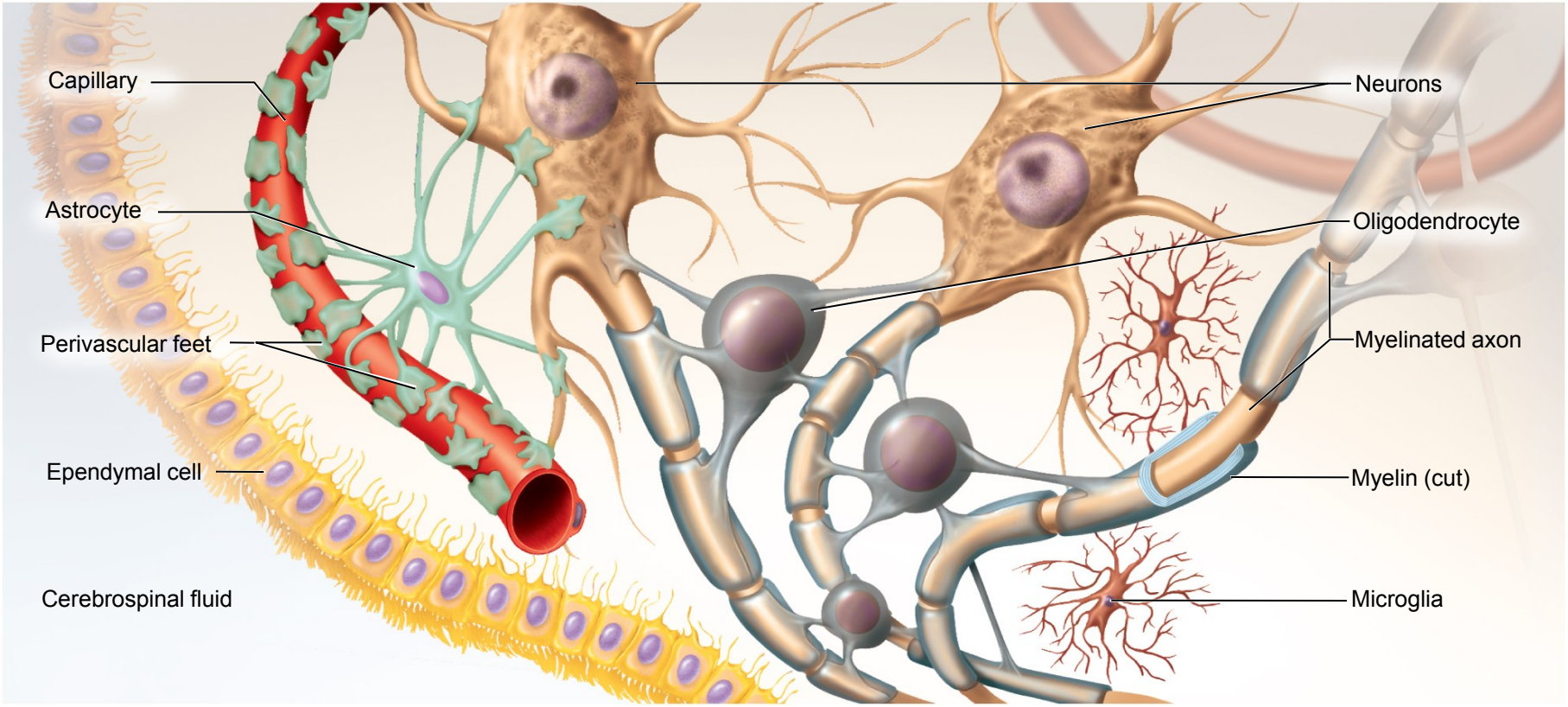
Neuroglia – Ependymal cells

- ✓ line ventricles of CNS and central canal of spinal cord
- ✓ cuboidal or low columnar shape
- ✓ no basal lamina
- ✓ secrete cerebrospinal fluid (CSF)
- ✓ some are ciliated, facilitate movement of CSF
- ✓ participate in formation of Choroid plexus





Neuroglia – Central - Summary

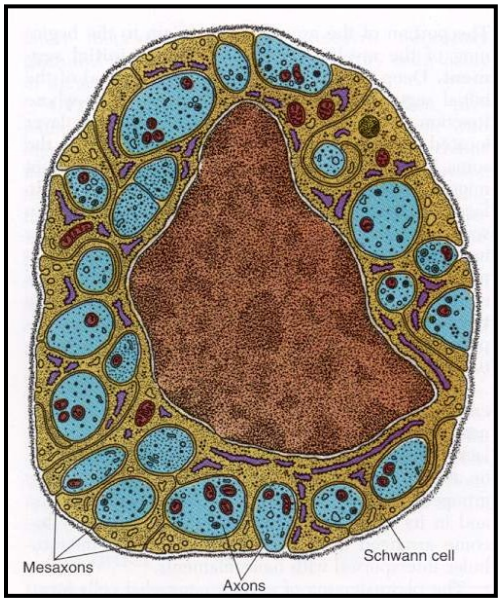


Neuroglia in PNS – Schwann cells 1

- cells that encircle all axons in PNS
- provide structural and metabolic support to axons
- provide guidance for axonal growth

Small diameter axons

Enveloping by only cytoplasm

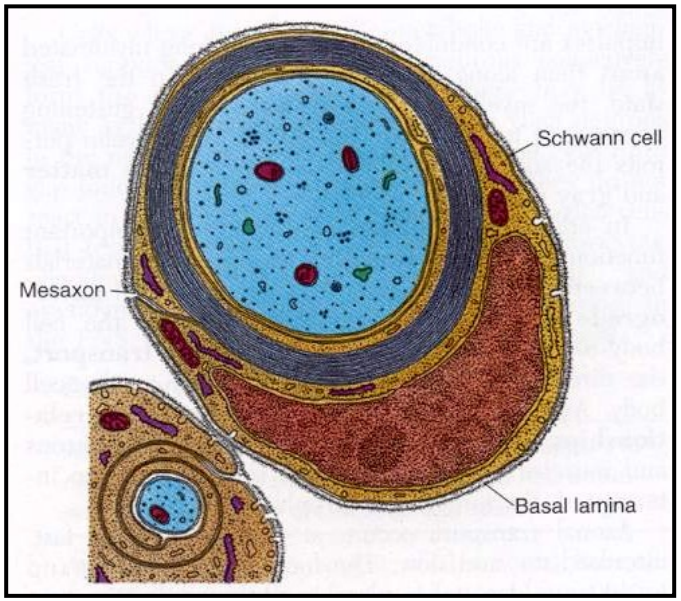


only Schwann sheath – gray nerve fiber

X

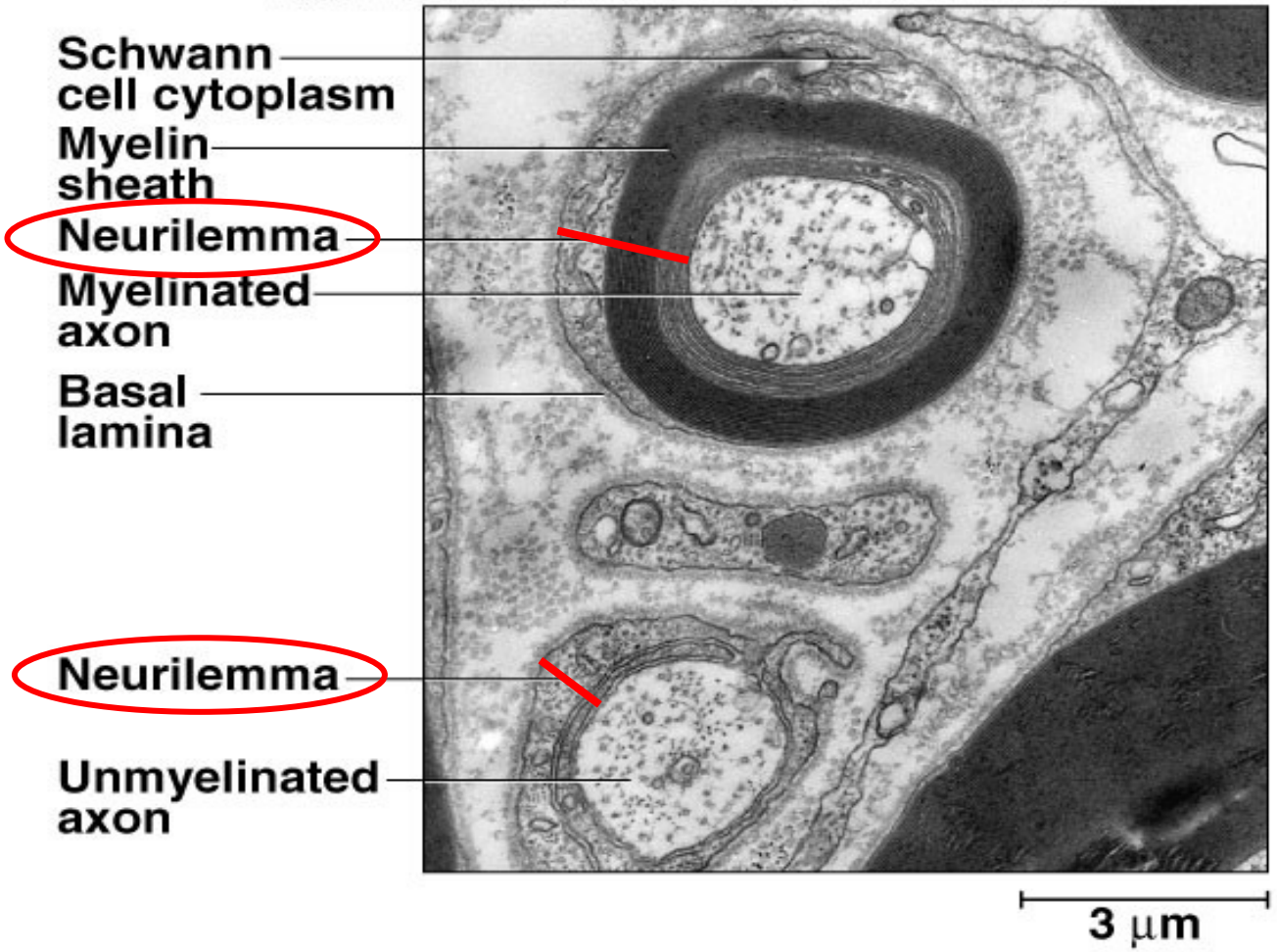
Large diameter axons

Wrapping by myelin sheaths



Schwann + myelin sheath– double contoured nerve fiber

Neuroglia in PNS – Schwann cells 2

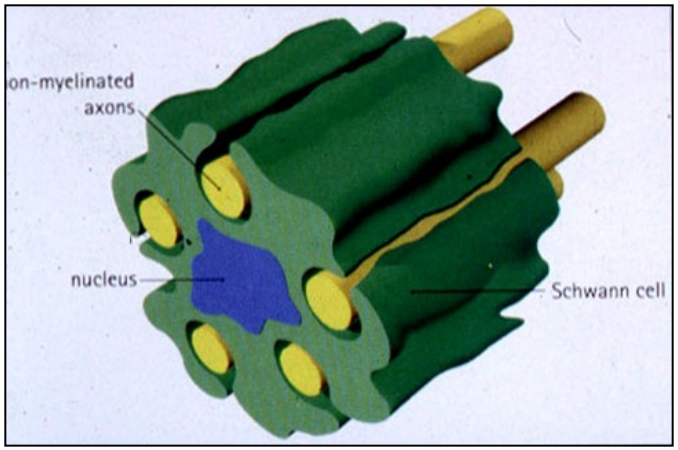


Neuroglia in PNS – Schwann cells 3

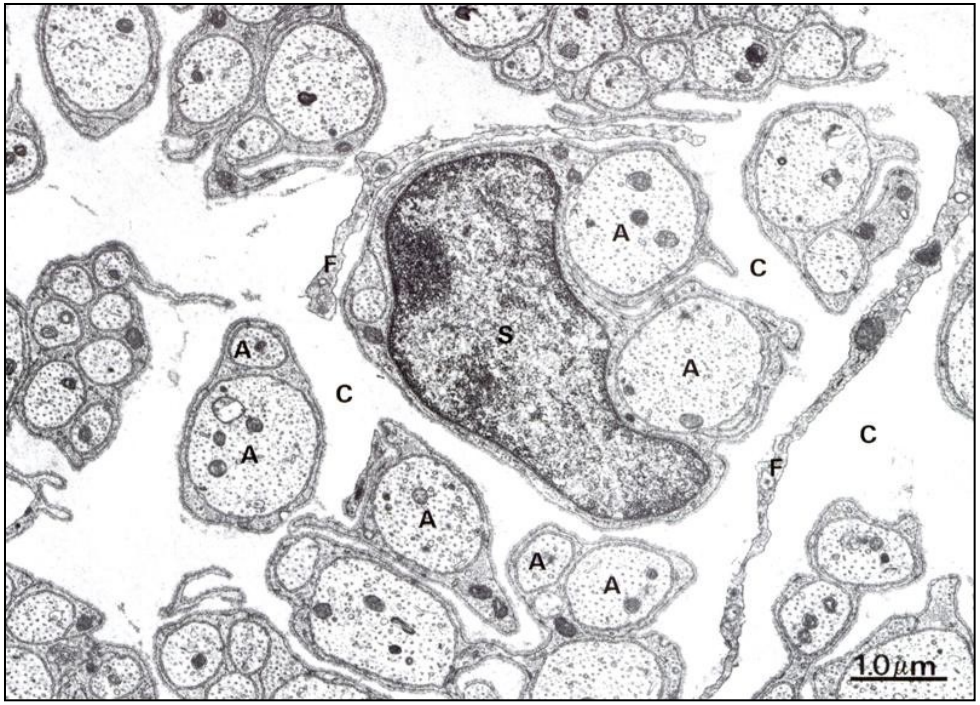
Small diameter axons ⇨ Non-myelinated fibers

(typical for autonomous nerve system)

only Schwann sheath – gray nerve fiber



One Schwann cell can ensheath multiple axons

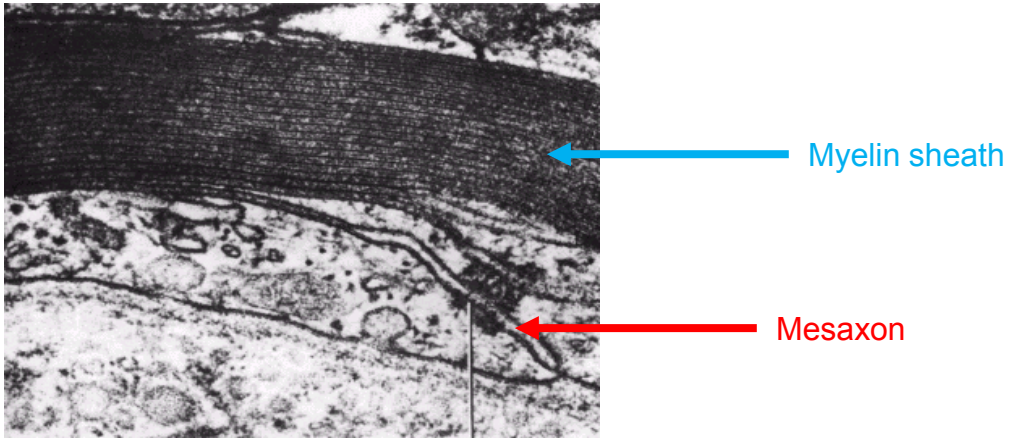


Neuroglia in PNS – Schwann cells 4

Large diameter axons ⇨ Myelinated fibers

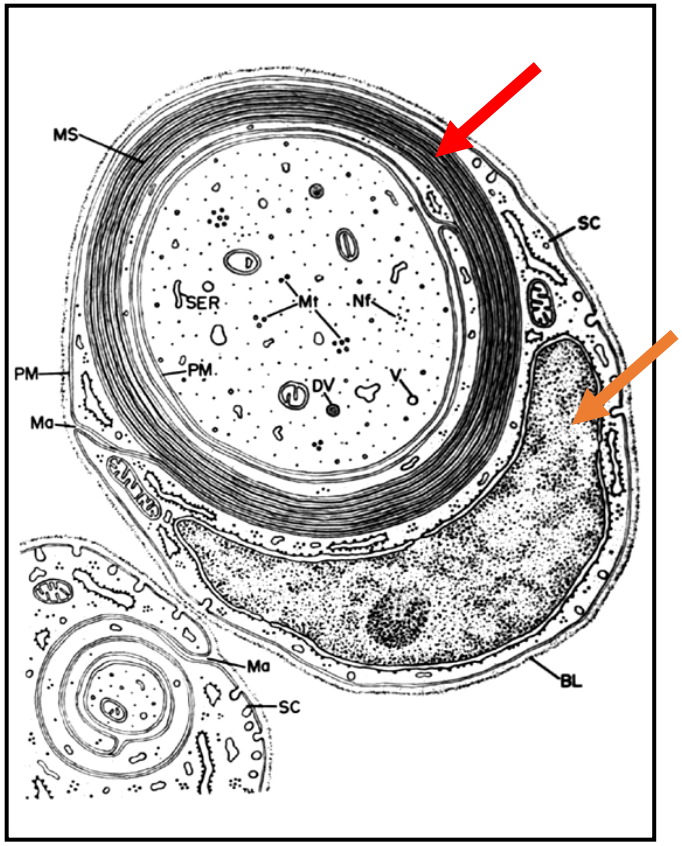
Myelination

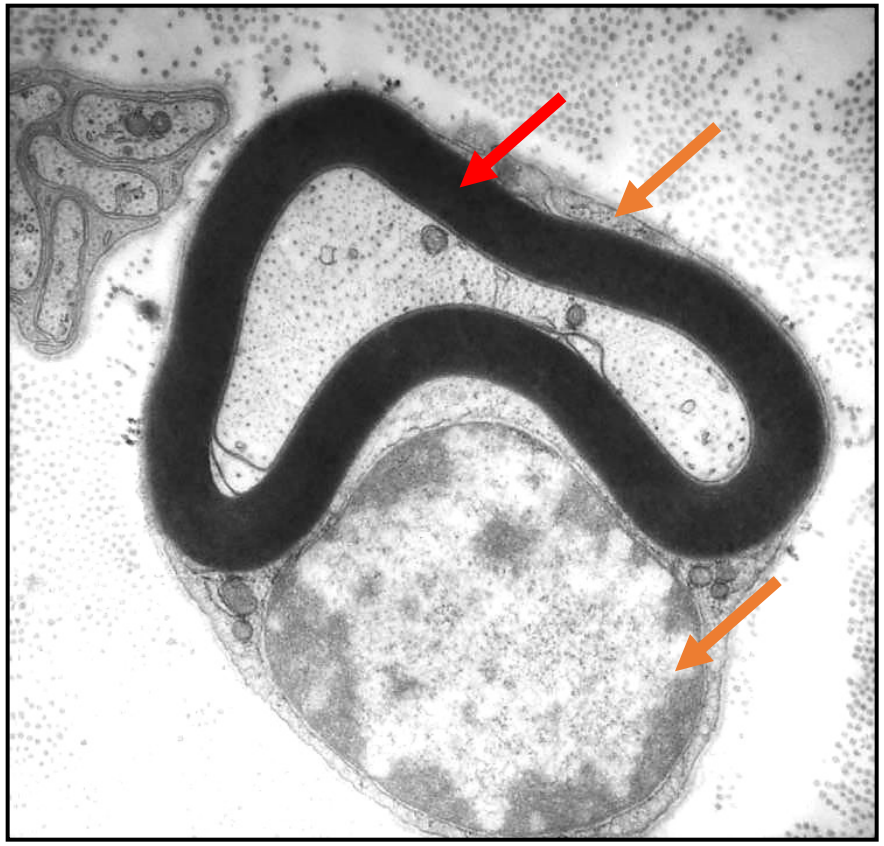
- begins 14th week of development
- proceeds rapidly during infancy
- completed in adolescence



Neuroglia in PNS – Schwann cells 5

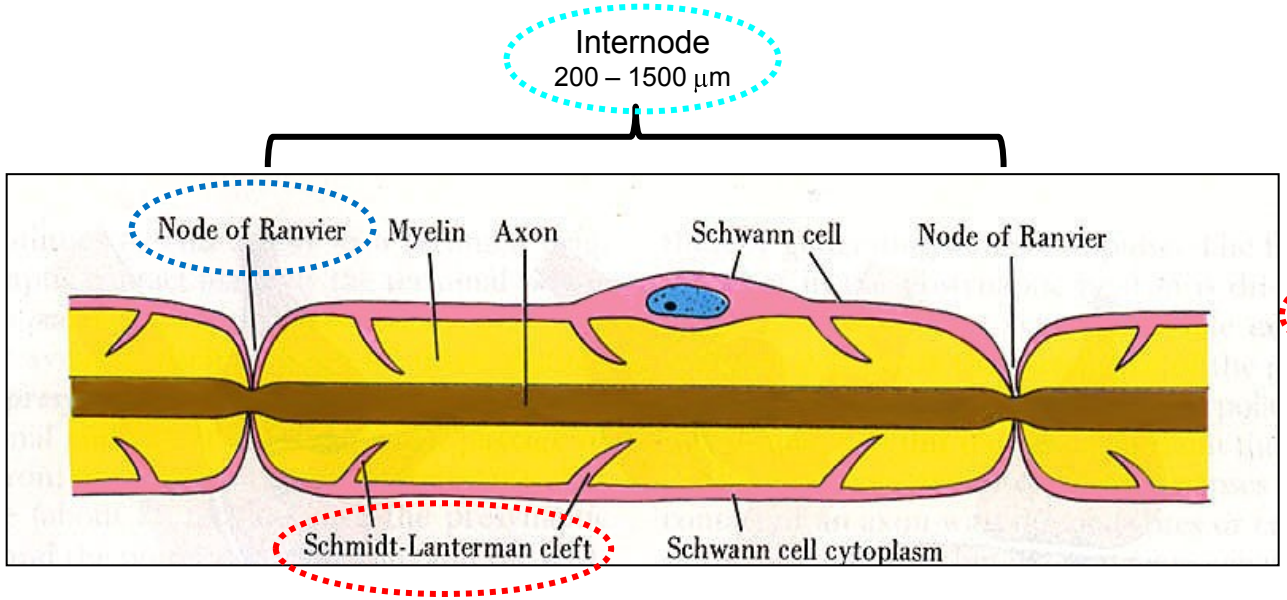
Double contoured nerve fiber ⇨ Schwann sheath + Myelin sheath = Neurilemma

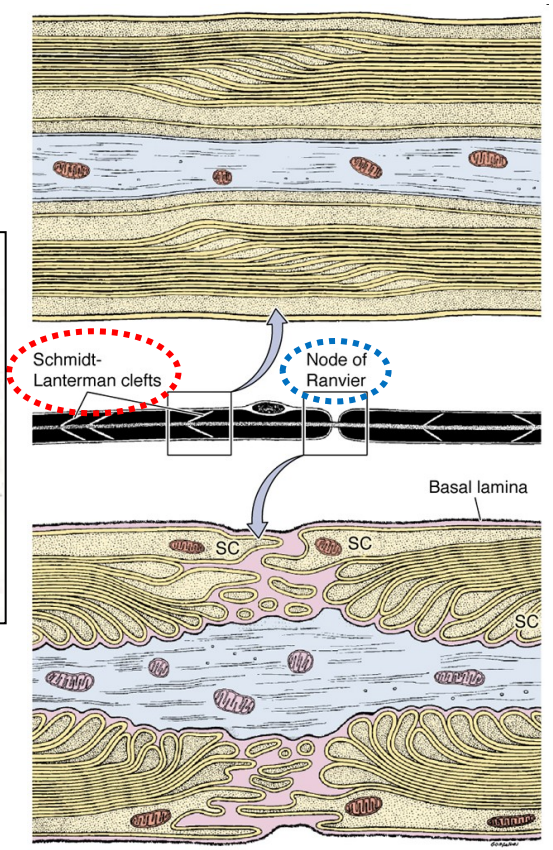




Neuroglia in PNS – Schwann cells 6

Myelin sheath is segmented = Many Schwann cells are needed to cover one nerve fibre

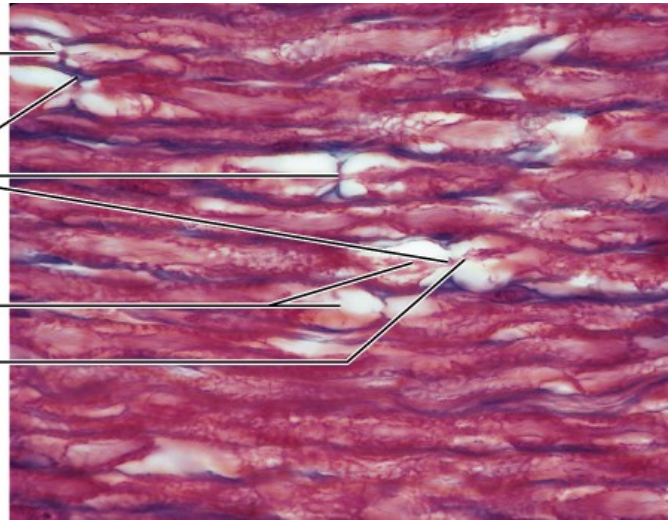


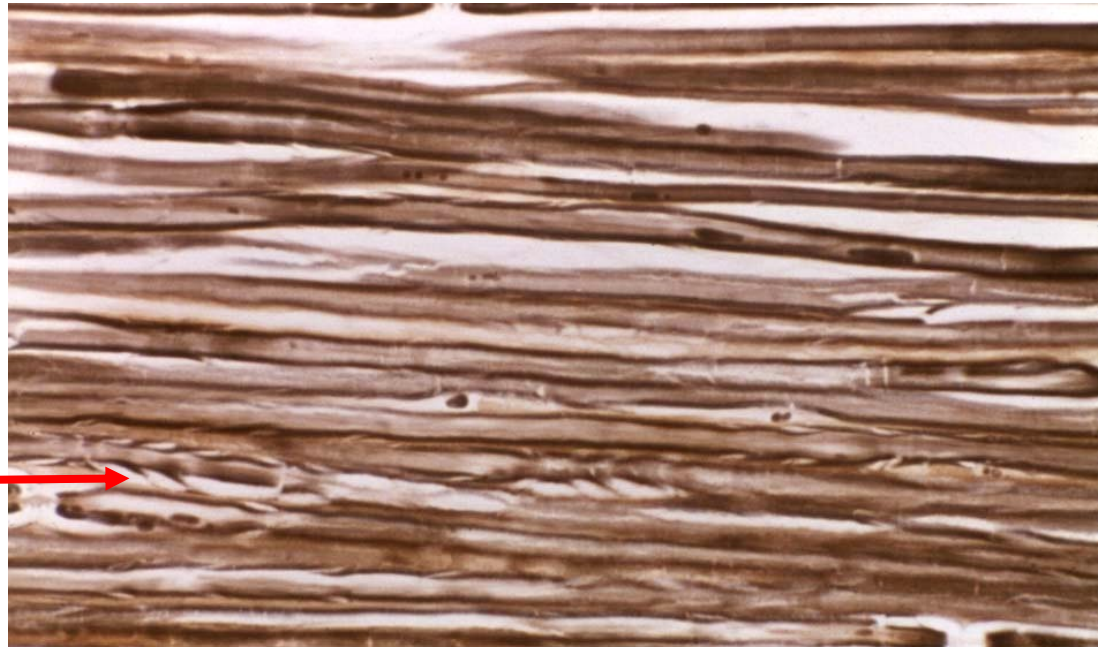


Schmidt-Lanterman clefts

- Schwann cell cytoplasm trapped within the lamellae of myelin

Neuroglia in PNS – Schwann cells 7



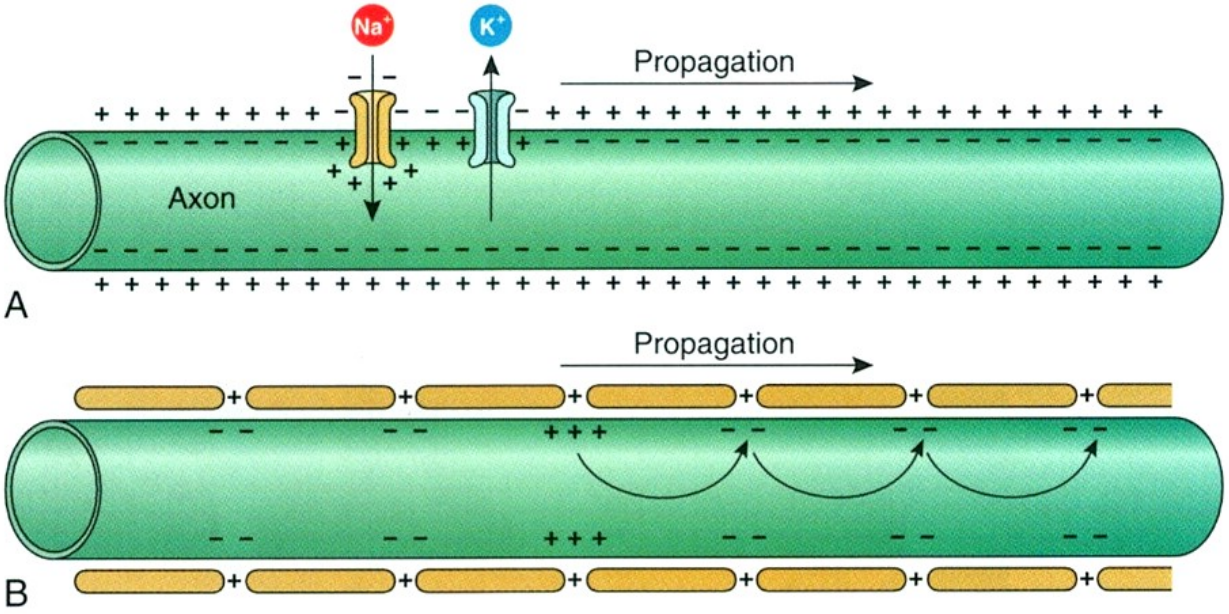


Neuroglia – Functional effect of myelination

Signal propagation

Non-myelinated axons – slow (0.5 – 2 m/s)

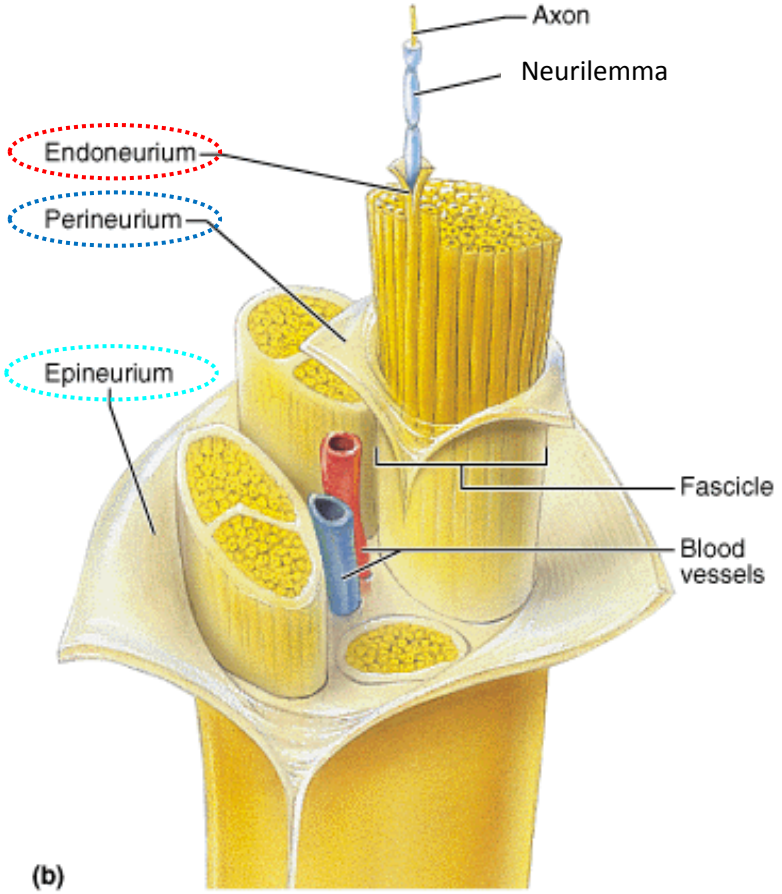
Myelinated axons – fast (15 – 20 m/s)



Saltatory (salta=jump)

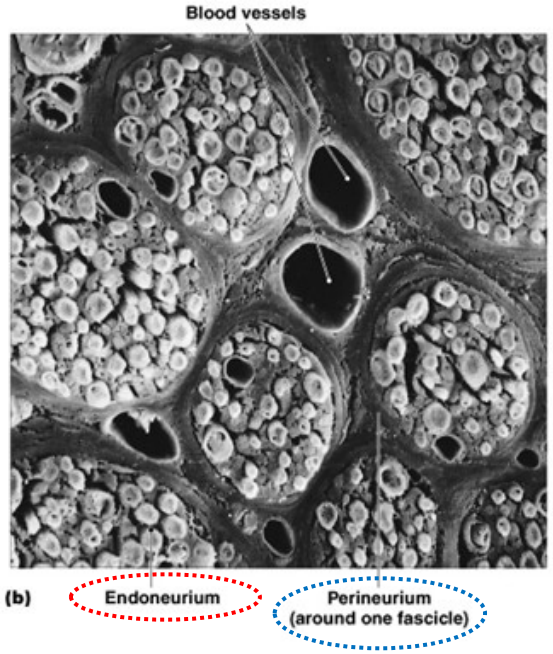
Peripheral nerve – Organization 1

Consists of 100's to 100,000's of myelinated and unmyelinated axons (nerve fibers).

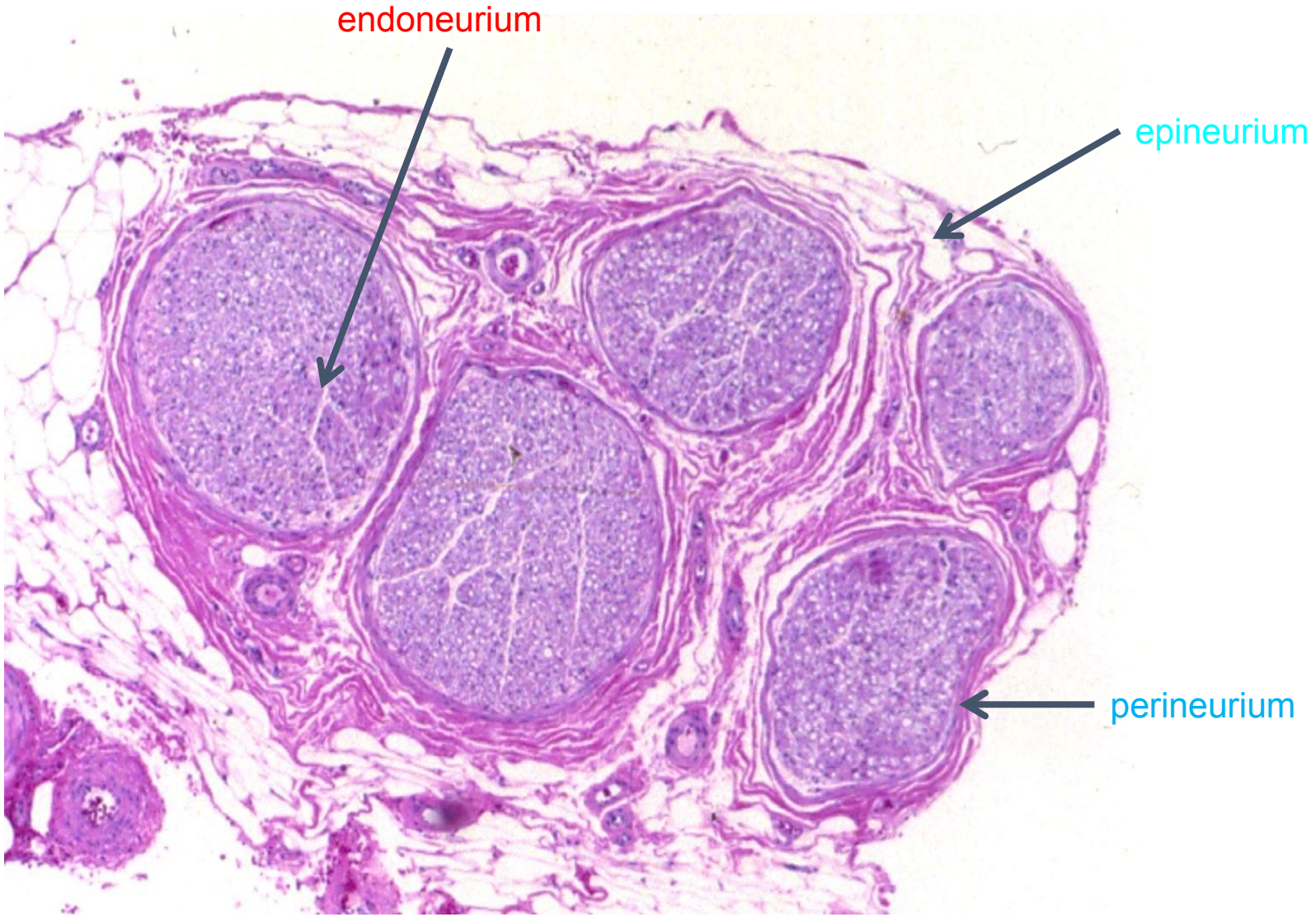


Connective tissue layers composing nerves:

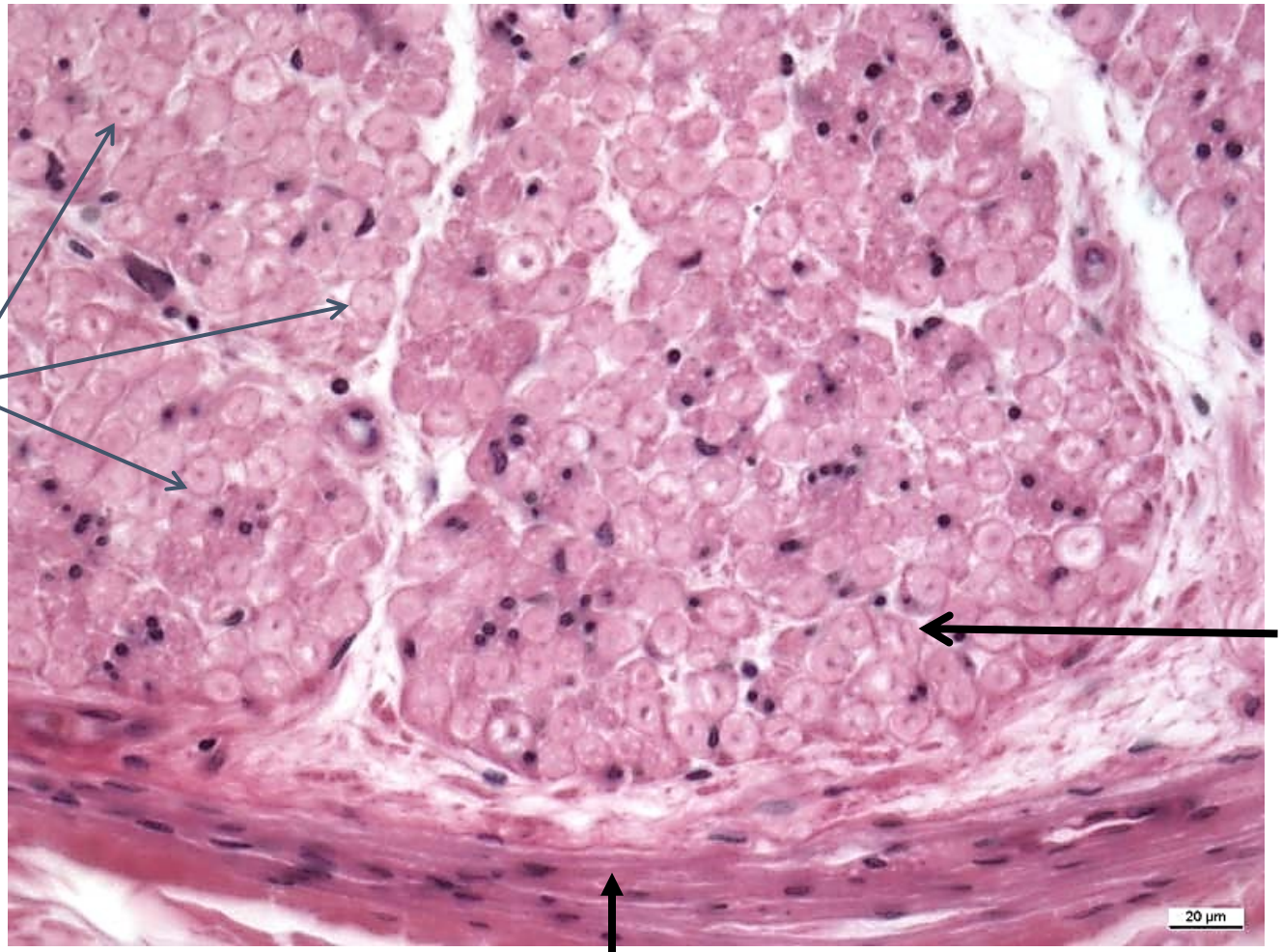
- Endoneurium - surrounds axons
- Pe
  fas
- Ep
  en



Peripheral nerve – Organization 2



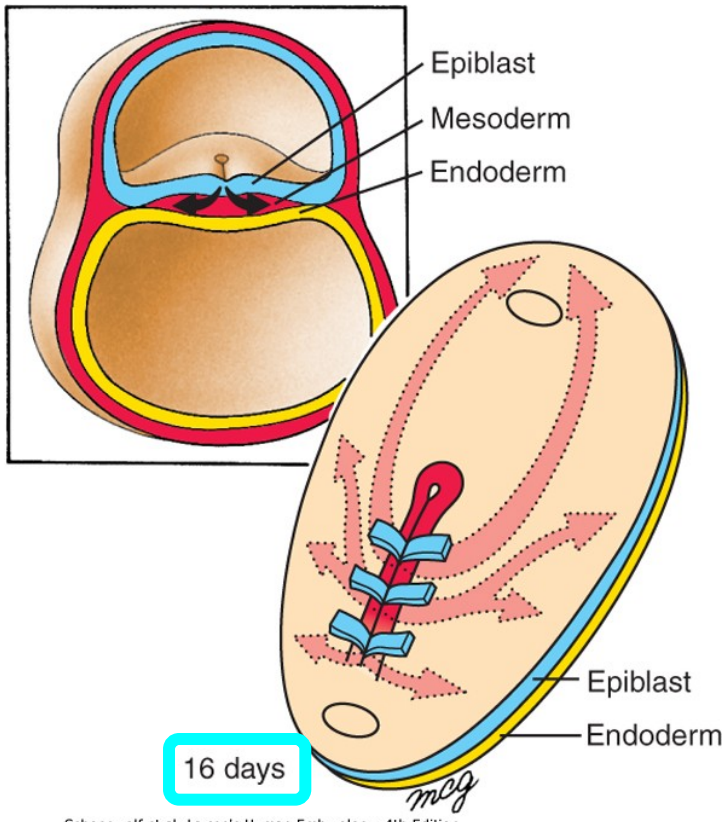
Peripheral nerve – Organization 3



Nerve tissue – Development 1

Gastrulation

Formation of the three germ layers



Ectoderm: outside, surrounds other layers later in development, generates **skin** and **nervous tissue.**

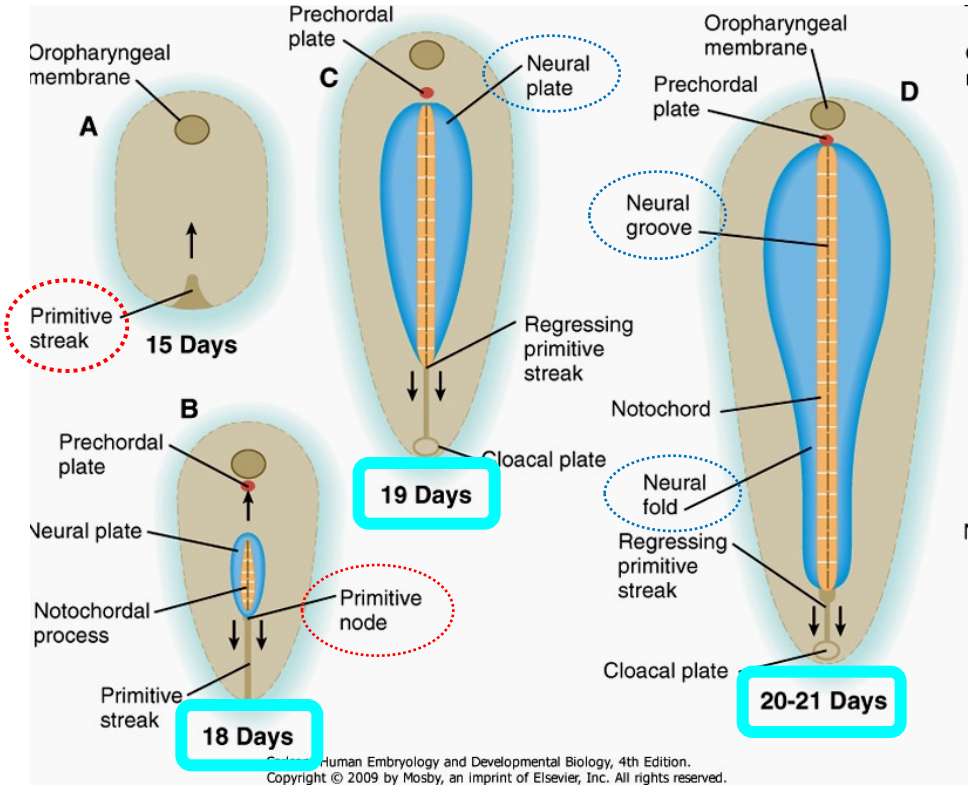
Mesoderm: middle layer, generates most of the **muscle, blood** and **connective tissues** of the body and placenta.

Endoderm: eventually most interior of embryo, generates the **epithelial lining** and associated **glands** of the **gut**, **lung**, and **urogenital tracts.**

Nerve tissue – Development 2

Neural Induction

In addition to patterning the forming mesoderm, the **primitive node** **also sets up the** **neural plate**



Endoderm + Mesoderm

BMP-4

Ectoderm to Skin

X

Primitive node

noggin
chordin
follistatin

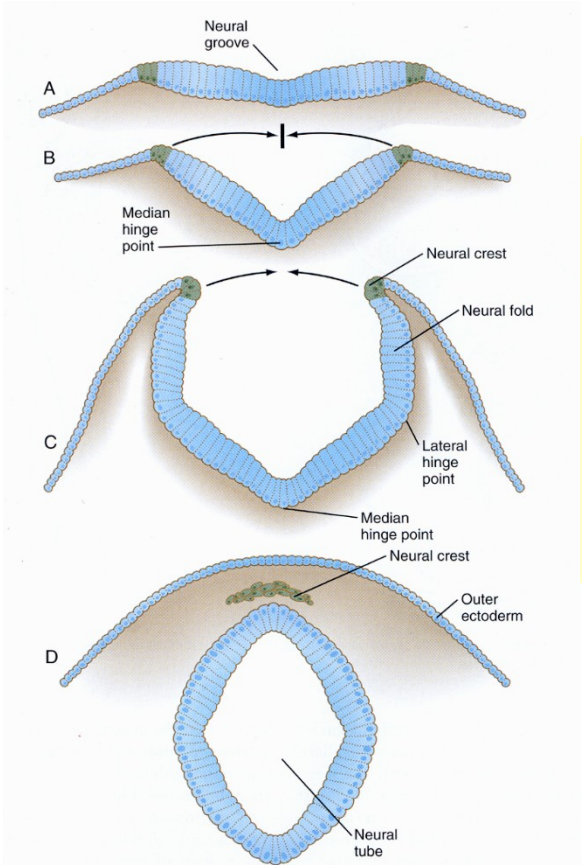
BMP-4 antagonists

Ectoderm to Nerve tissue

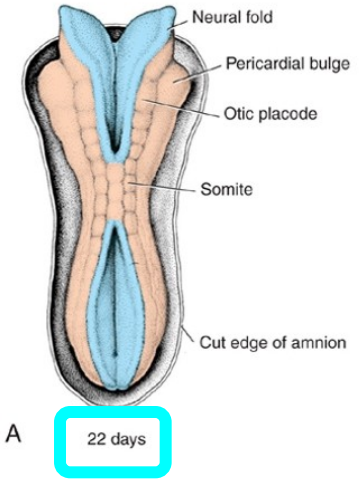
Nerve tissue – Development 3

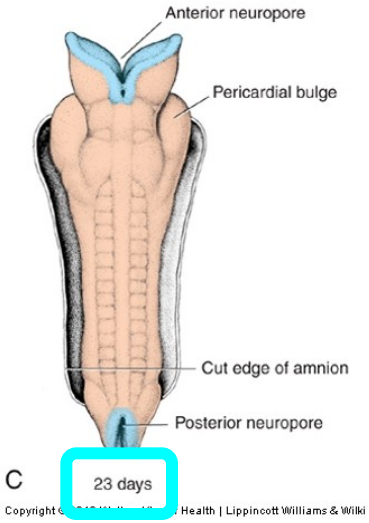
Neurulation

Folding and closure of the neural plate



- neural folds close
- neural crest delaminates and migrates away
- closure happens first in middle of the tube and then zips rostrally and caudally
- anterior neuropore closes around day 25
- posterior neuropore closes around day 28

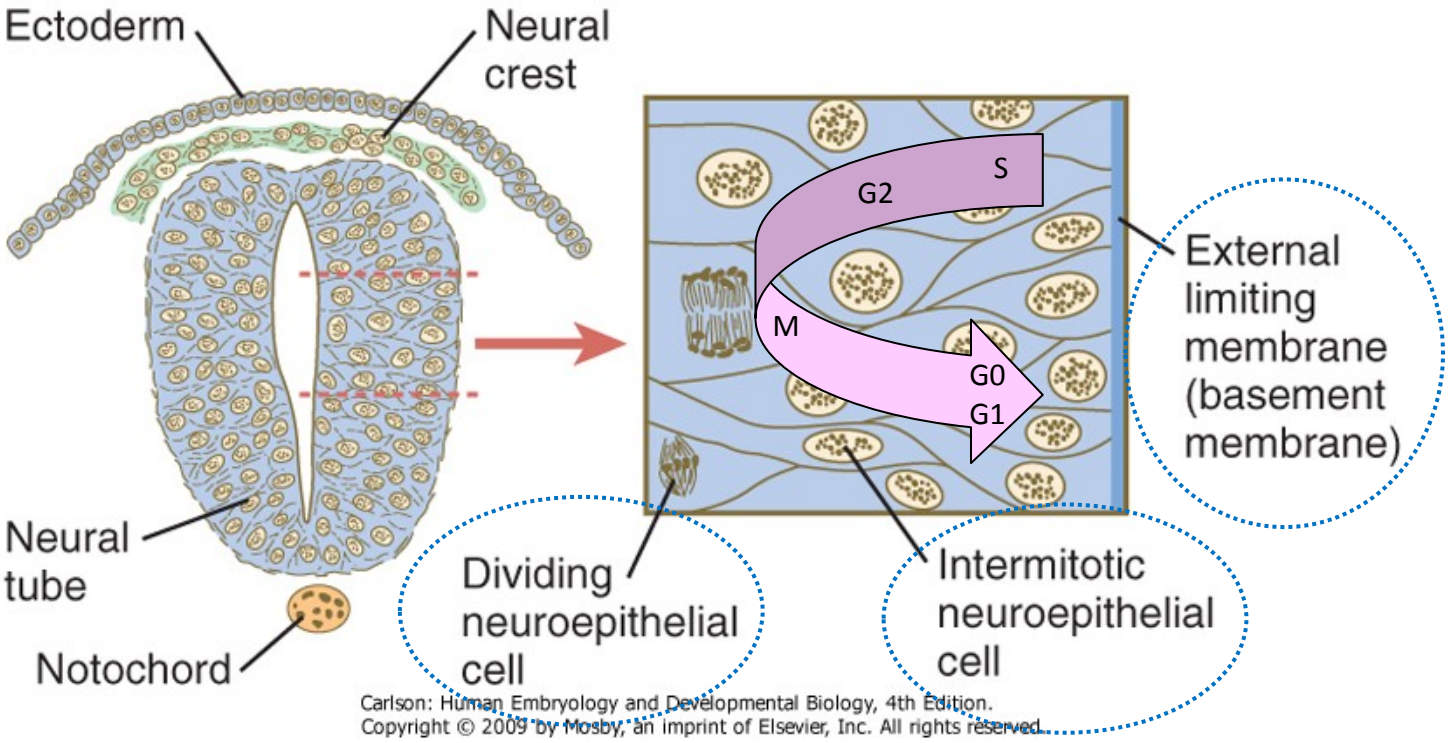




Nerve tissue – Development 4

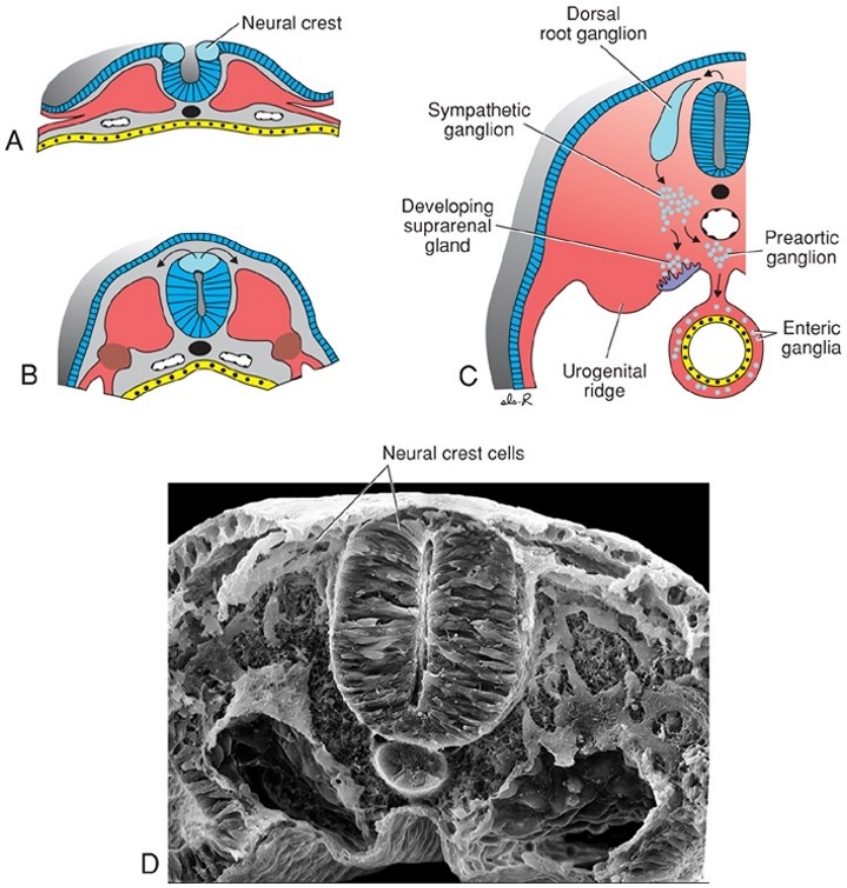
The **early neural tube** is a pseudostratified epithelium

- The **"apical" portion** abuts the **central canal**
- The **"basal" portion** abuts the **surrounding tissue** (e.g. somites, notochord, etc.).
- Cell division occurs in the apical portion.



Nerve tissue – Development 5

Neural crest
the "4th germ layer"



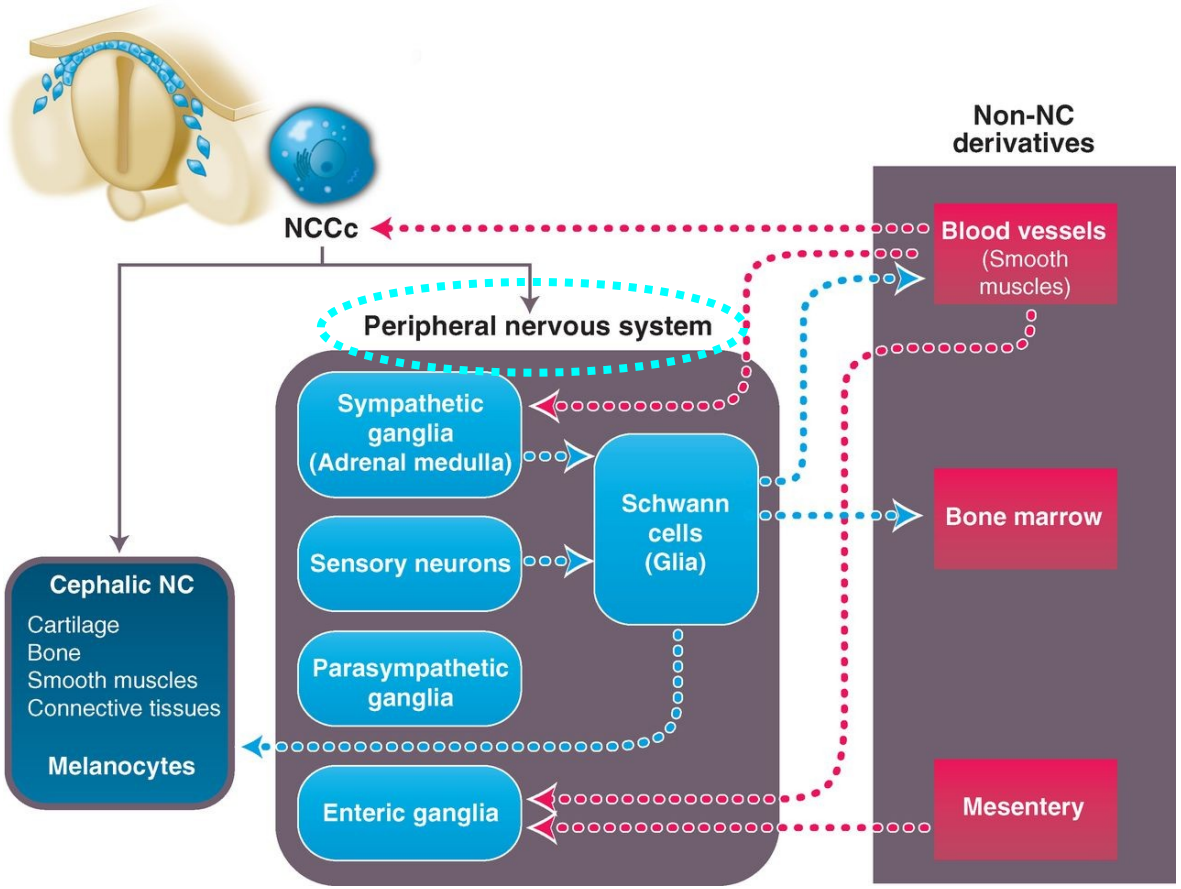
Signals from:
- Mesoderm
- Adjacent skin
- Neural plate

Neural crest cells

- Down-regulate cadherin
- Delaminate from neuroepithelium
- Transform into migratory mesenchymal cells
- Give rise to many cell types

Nerve tissue – Development 5

Neural crest derivatives

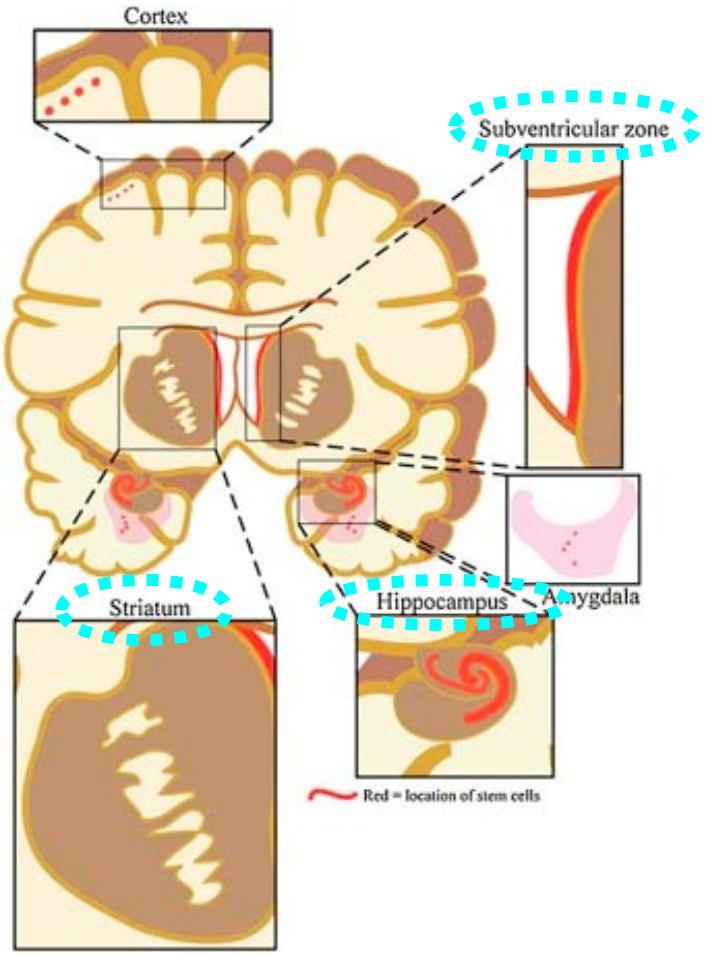


Nerve tissue regeneration - CNS

Stem / progenitor cells resiging in some areas of adult brain

Life-long plasticity of CNS

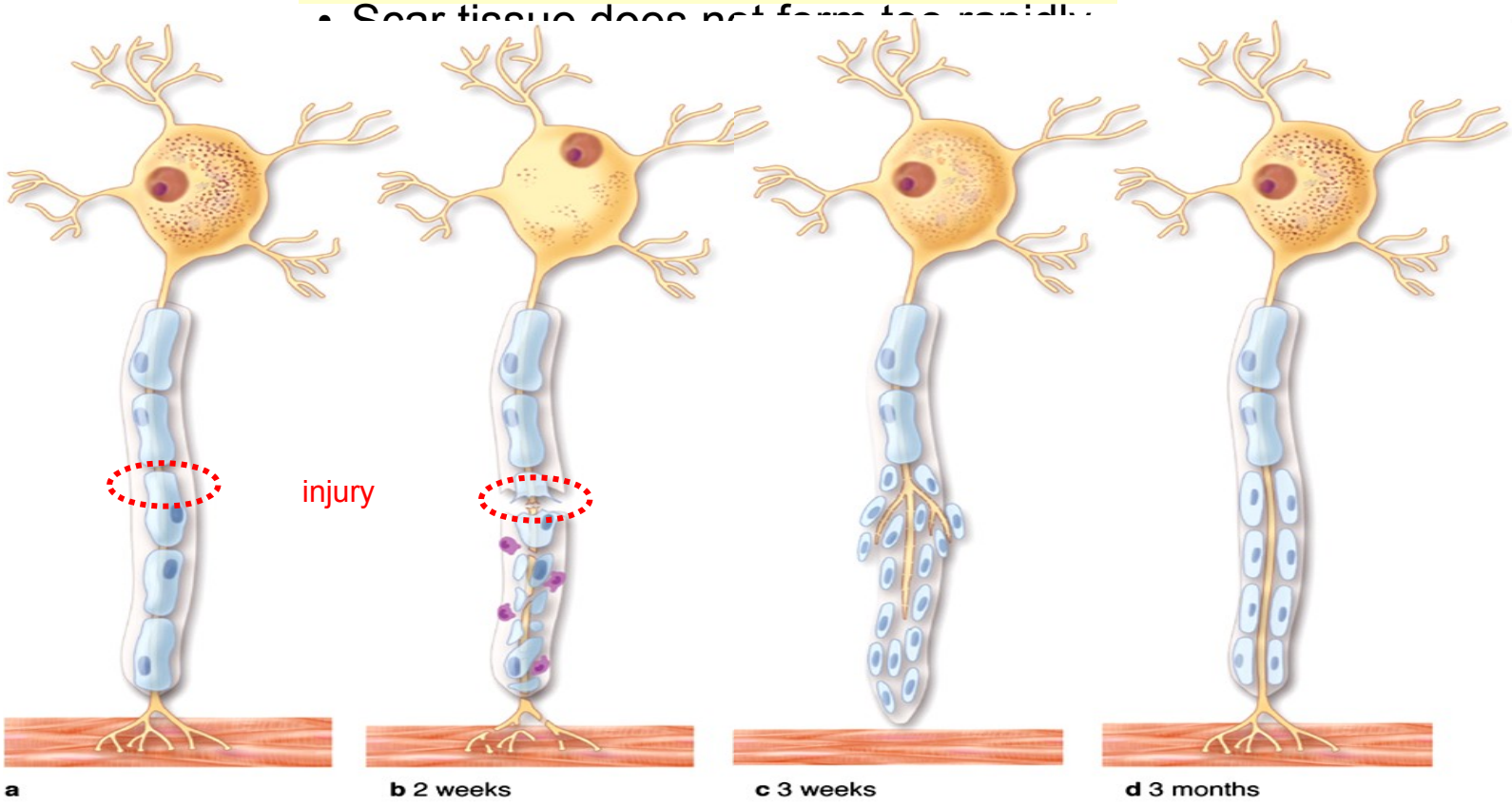
- Sprouting new dendrites
- Synthesis of new proteins
- Changes of synaptic contacts



Nerve tissue regeneration - PNS

Axons and dendrites may be repaired if:

- Neuron cell body remains intact
- Schwann cels remains active and form tube
- Scar tissue does not form too rapidly



Breakdown of axon
Breakdown of myelin sheath

Schwann cells divide
Axon begins to grow
(1.5 mm/day)
Navigaion by Schwann cells
Collaterals will die

Thank you for your attention !

Questions and comments at:
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THANK YOU FOR ATTENTION

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http://www.med.muni.cz/histology