Muscle Physiology

Muscular System Functions

- Body movement
- Maintenance of posture
- Respiration
- Production of body heat
- Communication
- Constriction of organs and vessels
- Heart beat

Properties of Muscle

- Contractility
  - Ability of a muscle to shorten with force
- Excitability
  - Capacity of muscle to respond to a stimulus
- Extensibility
  - Muscle can be stretched to its normal resting length and beyond to a limited degree
- Elasticity
  - Ability of muscle to recoil to original resting length after stretched

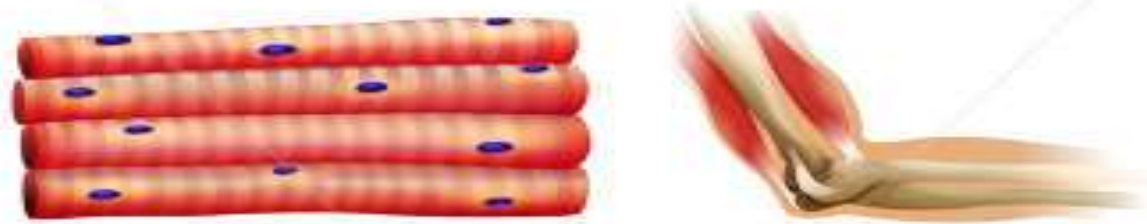
Muscle Tissue Types

- Skeletal
  - Attached to bones
  - Nuclei multiple and peripherally located
  - Striated, Voluntary and involuntary (reflexes)
- Smooth
  - Walls of hollow organs, blood vessels, eye, glands, intestines
  - Single nucleus centrally located
  - Not striated, involuntary
- Cardiac
  - Heart
  - Single nucleus centrally located
  - Striations, involuntary, intercalated disks

Skeletal Muscle

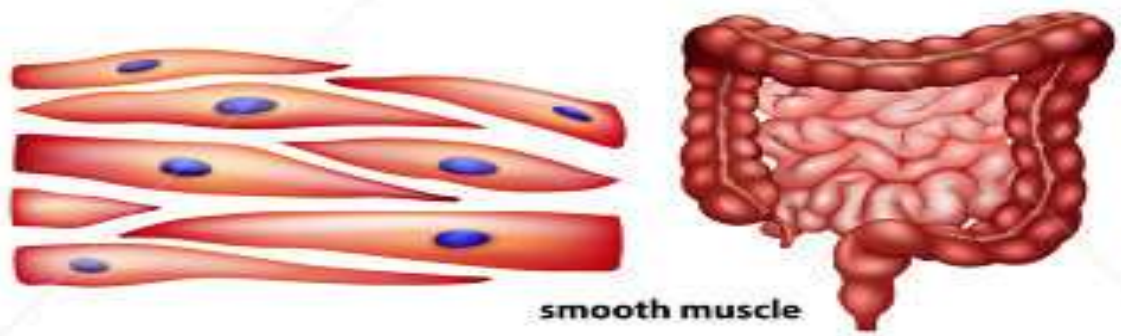
- Long cylindrical cells
- Many nuclei per cell
- Striated
- Voluntary
- Attached to bones or occasionally to the skin
- Rapid contractions

Types of Muscle Cells



skeletal muscle

cardiac muscle



smooth muscle

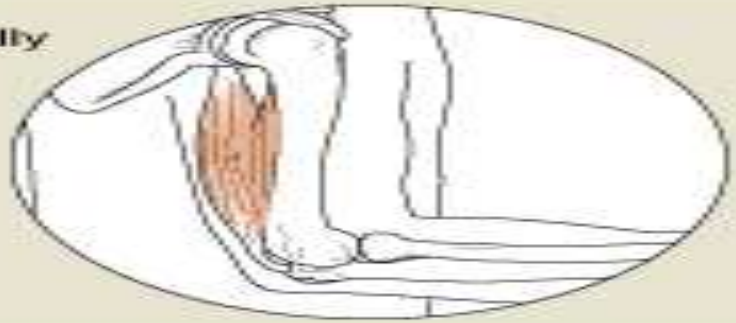
Skeletal Muscle

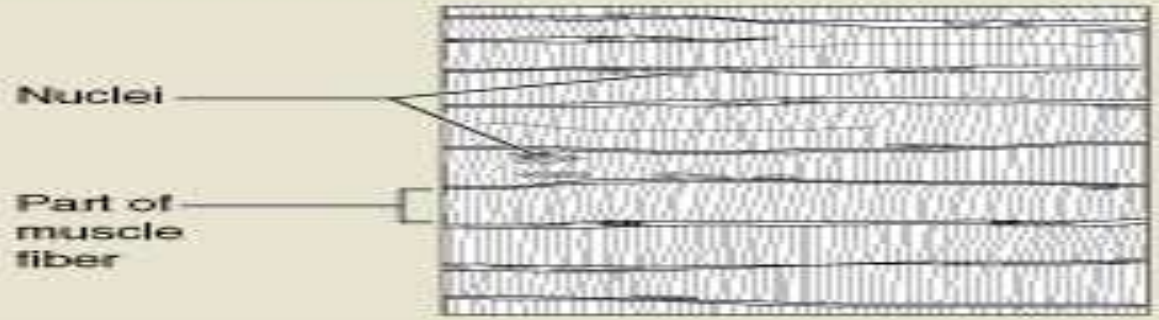
(a) Skeletal muscle

Description: Long, cylindrical, multinucleate cells; obvious striations.

Function: Voluntary movement; locomotion; manipulation of the environment; facial expression; voluntary control.

Location: In skeletal muscles attached to bones or occasionally to skin.

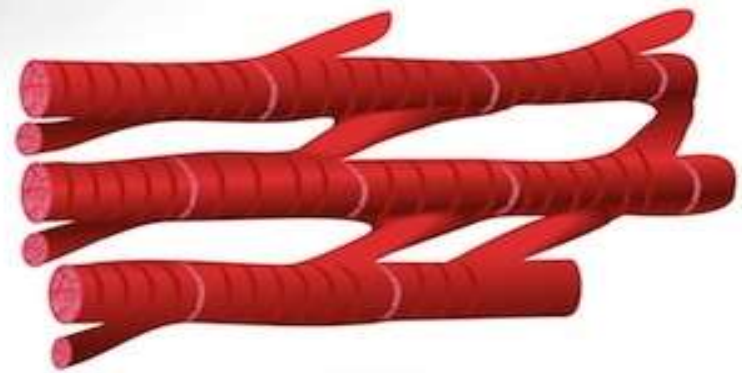




Skeletal muscle

Smooth muscle

Cardiac muscle



Skeletal Muscle

- Produce movement
- Maintain posture & body position
- Support Soft Tissues
- Guard entrance / exits
- Maintain body temperature
- Store nutrient reserves

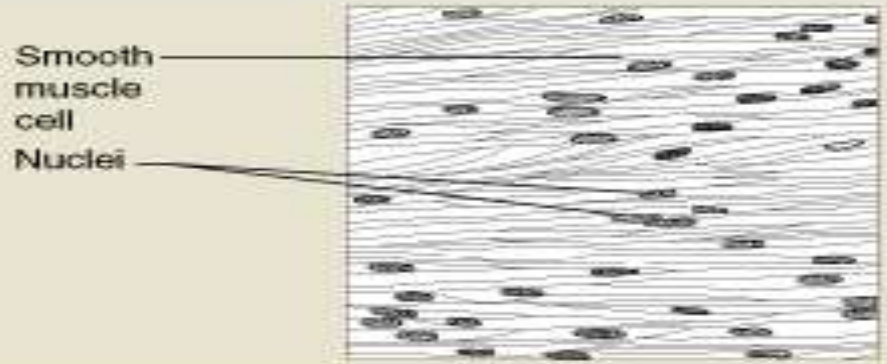
Smooth Muscle

(c) Smooth muscle

Description: Spindle-shaped cells with central nuclei; cells arranged closely to form sheets; no striations.

Function: Propels substances or objects (foodstuffs, urine, a baby) along internal passageways; involuntary control.

Location: Mostly in the walls of hollow organs.

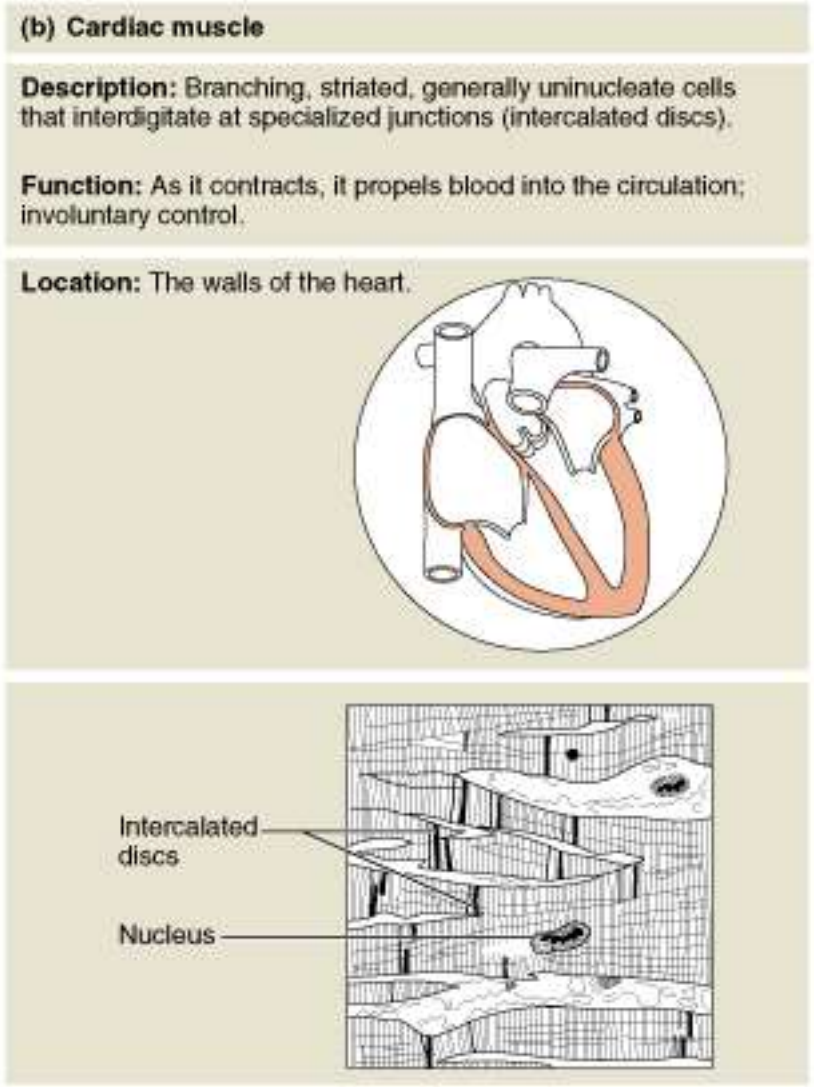


Smooth muscle

- Fusiform cells
- Spindle shaped with central nuclei
- Cells arranged closely to form sheets
- No striations
- Involuntary
- Slow wave like
- Propels substances or objects eg foodstuffs,blood urine
- Mostly in walls of hollow organs

Cardiac Muscle

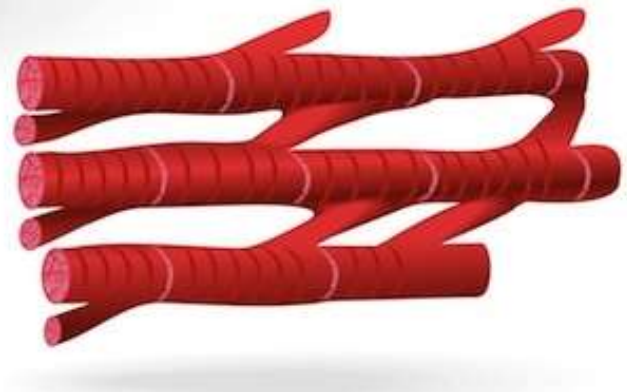
- Branching cells
- One/two nuclei per cell
- Striated
- Involuntary
- Medium speed contractions



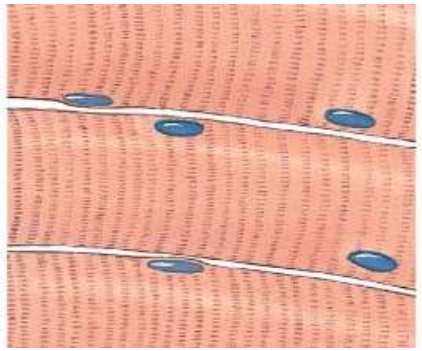
Skeletal muscle

Smooth muscle

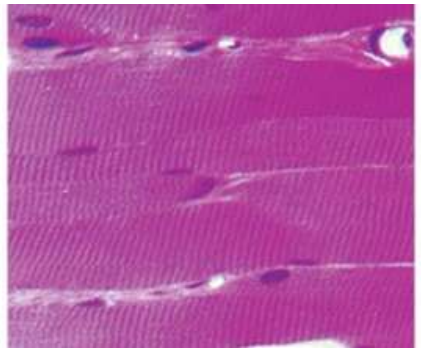
Cardiac muscle

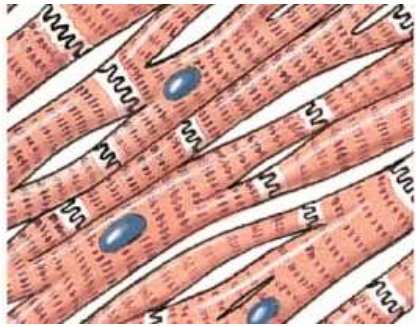


Muscle Tissue Types

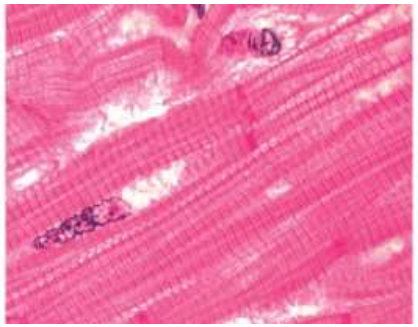


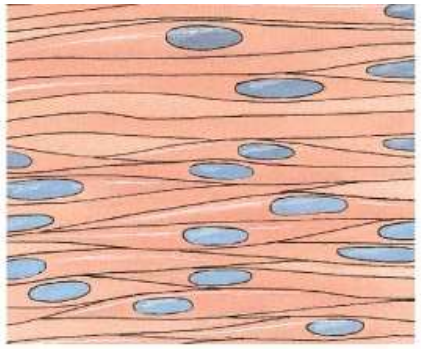
Skeletal



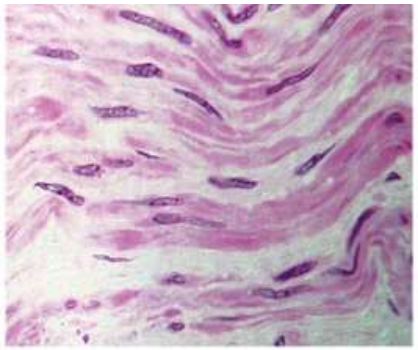


Cardiac





Smooth



Muscle Comparison Chart

Muscle Tissue	Cell Shape	Striae	Nucleus	Control	Special structures
Skeletal	Cylindrical	Yes	Multi-nucleate & peripheral	Voluntary	none
Cardiac	Cylindrical & branched	Yes	Uninucleate & central	Involuntary	Intercalated discs
Smooth	Fusiform	No	Uninucleate & central	Involuntary	May be single-unit or multi-unit

Structure and Function of Skeletal Muscle

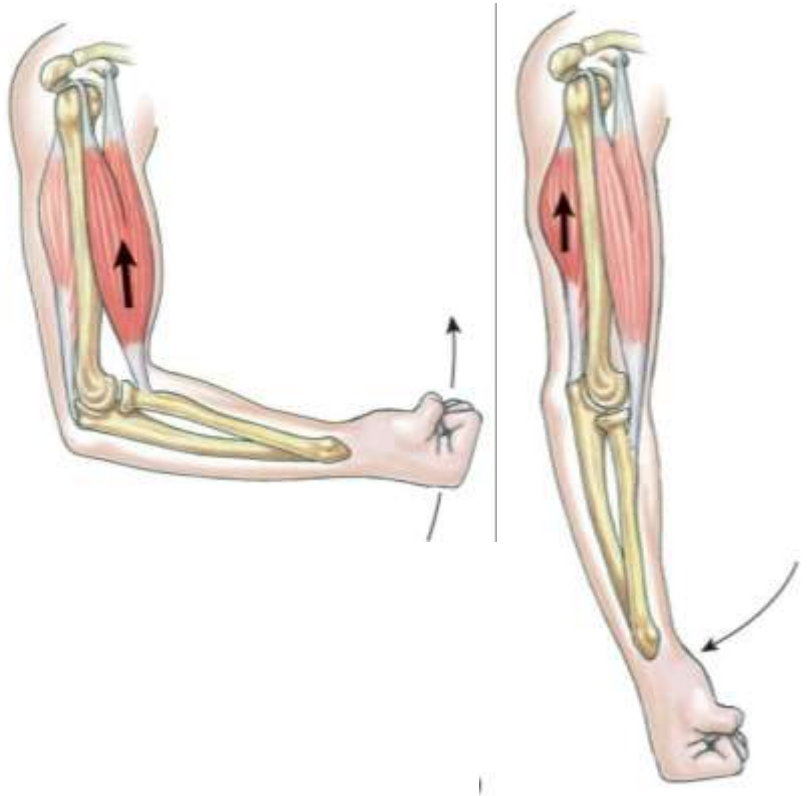
Skeletal Muscle

- Human body contains over 400 skeletal muscles
  - 40-50% of total body weight
- Functions of skeletal muscle
  - Force production for locomotion and breathing
  - Force production for postural support
  - Heat production during cold stress

Skeletal Muscle

General Functions - Voluntary

- Movement
  - Only have contractility in one direction
    - Requires multiple muscles to create movements from the simple
      - flexion and extension
    - To the complex
      - Circumduction
- Stabilizing Movements & Joints
  - The result of synergistic muscles



Skeletal Muscle

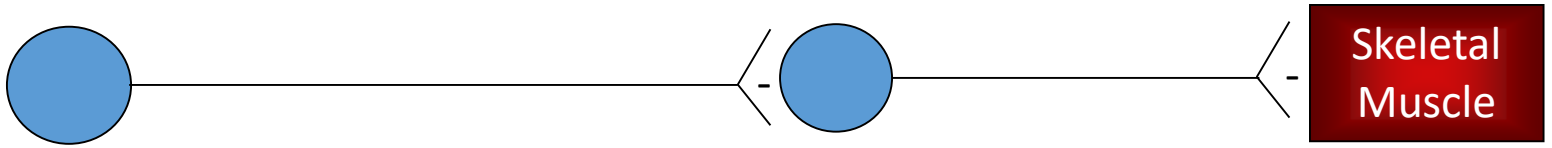
General Functions

- Protection
  - of underlying structures
    - abdominal viscera
  - Stronger muscles = greater protection, increased joint stability

Skeletal Muscle

General Functions - Involuntary

- Shivering Thermogenesis (shivering reflex)
  - asynchronous & involuntary
  - Initiated by hypothalamic nuclei in the primary motor center for shivering (posterior nuclei)
    - Normally inhibited by the heat center in the hypothalamus (preoptic nuclei) when body temp is in range (96.8-99.5)
      - Receives cold signals from skin and spinal cord



preoptic nucleus

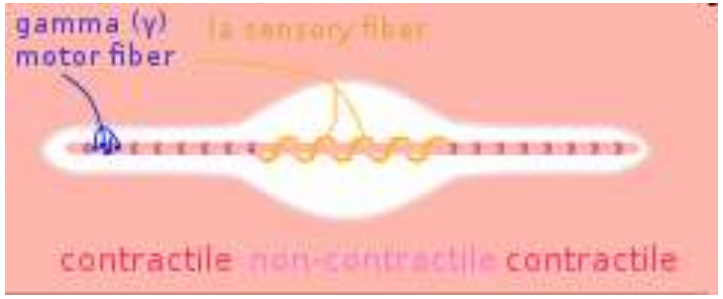
posterior nucleus

Damage to the posterior nuclei would cause?

Skeletal Muscle

General Functions - Involuntary

- Maintenance of Posture
  - Involves stretch reflexes
    - Static reflexes
      - Long term sustained contractile events
    - Phasic reflexes
      - Dynamic and short term corrective responses
    - Regulated by gamma neurons which adjust tension in the muscle spindles



- A single skeletal-muscle cell is known as a muscle fiber.
- Each muscle fiber is formed during development by the fusion of a number of undifferentiated, mononucleated cells, known as myoblasts, into a single cylindrical, multinucleated cell.
- Skeletal muscle differentiation is completed around the time of birth
- The differentiated fibers continue to increase in size during growth from infancy to adult stature
- No new fibers are formed from myoblasts.
- Adult skeletal muscle fibers have diameters between 10 and 100 µm
- Lengths may extend up to 20 cm

- If skeletal-muscle fibers are destroyed after birth as a result of injury, they cannot be replaced by the division of other existing muscle fibers.
- New fibers can be formed from undifferentiated cell known as satellite cells, located adjacent to the muscle fibers and undergo differentiation similar to that followed by embryonic myoblasts.
- This capacity for forming new skeletal-muscle fibers is considerable but will not restore a severely damaged muscle to full strength.
- Much of the compensation for a loss of muscle tissue occurs through an increase in the size of the remaining muscle fibers

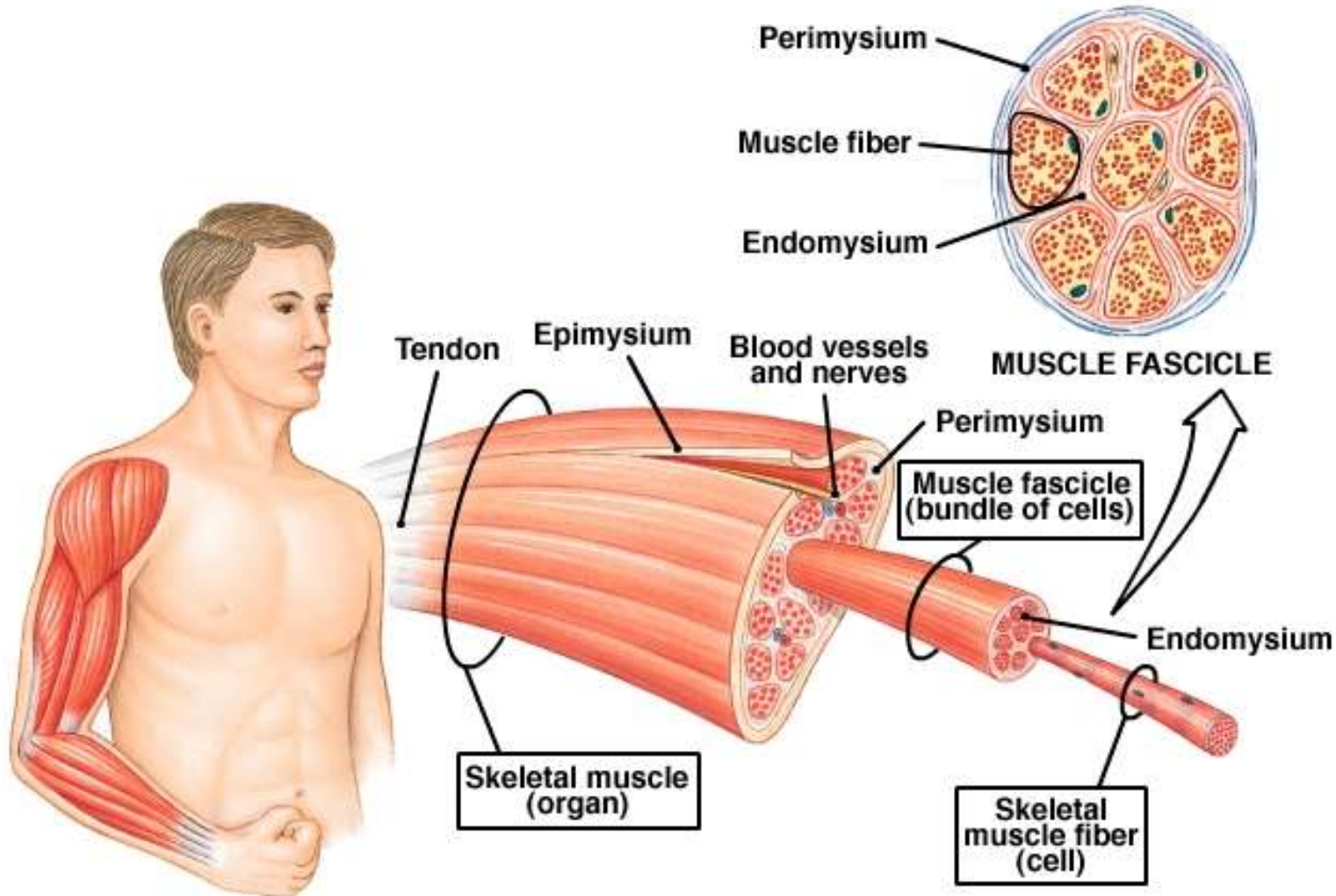
16th nov

- Muscles usually linked to bones by bundles of collagen fibers known as tendons are located at each end of the muscle.
- Some tendons are very long, with the site of tendon attachment to bone far removed from the end of the muscle.
- Eg- some of the muscles that move the fingers are in the forearm, as one can observe by wiggling one's fingers and feeling the movement of the muscles in the lower arm.
- These muscles are connected to the fingers by long tendons

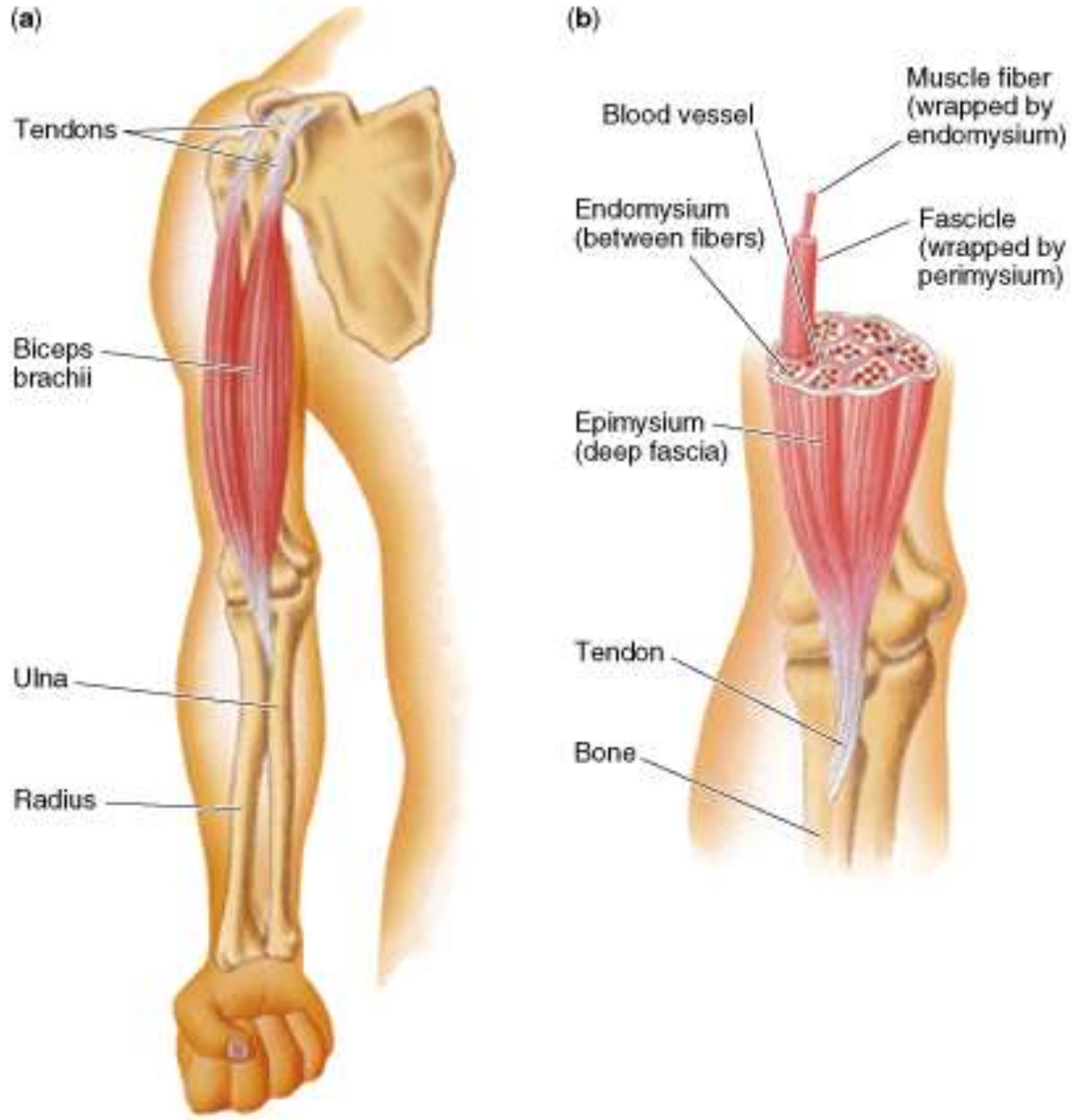
Structure of Skeletal Muscle: *Connective Tissue Covering*

- Epimysium
  - Surrounds entire muscle
- Perimysium
  - Surrounds bundles of muscle fibers
    - Fascicles
- Endomysium
  - Surrounds individual muscle fibers

Organization II:



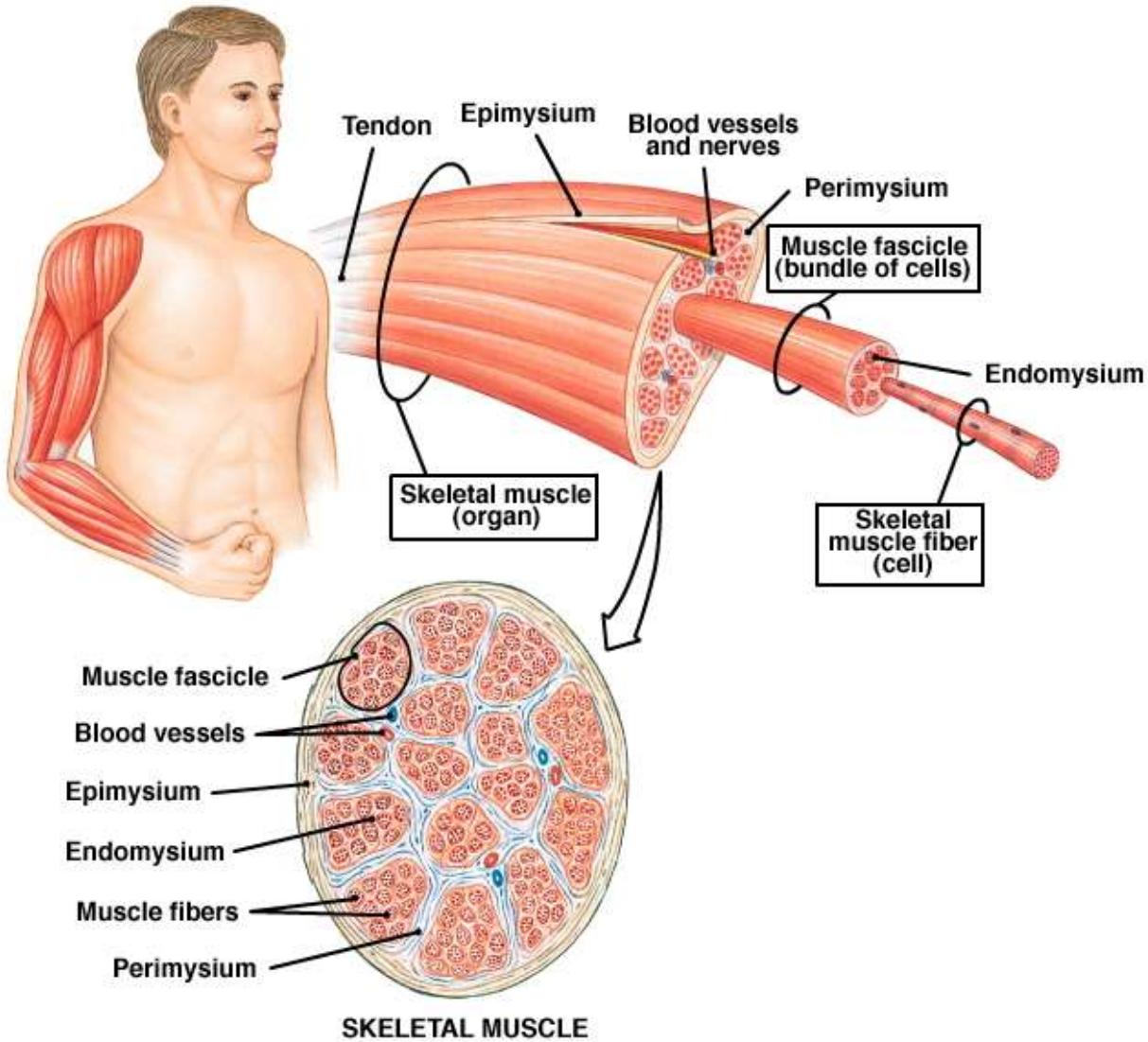
▶ Organization of Skeletal Tissue



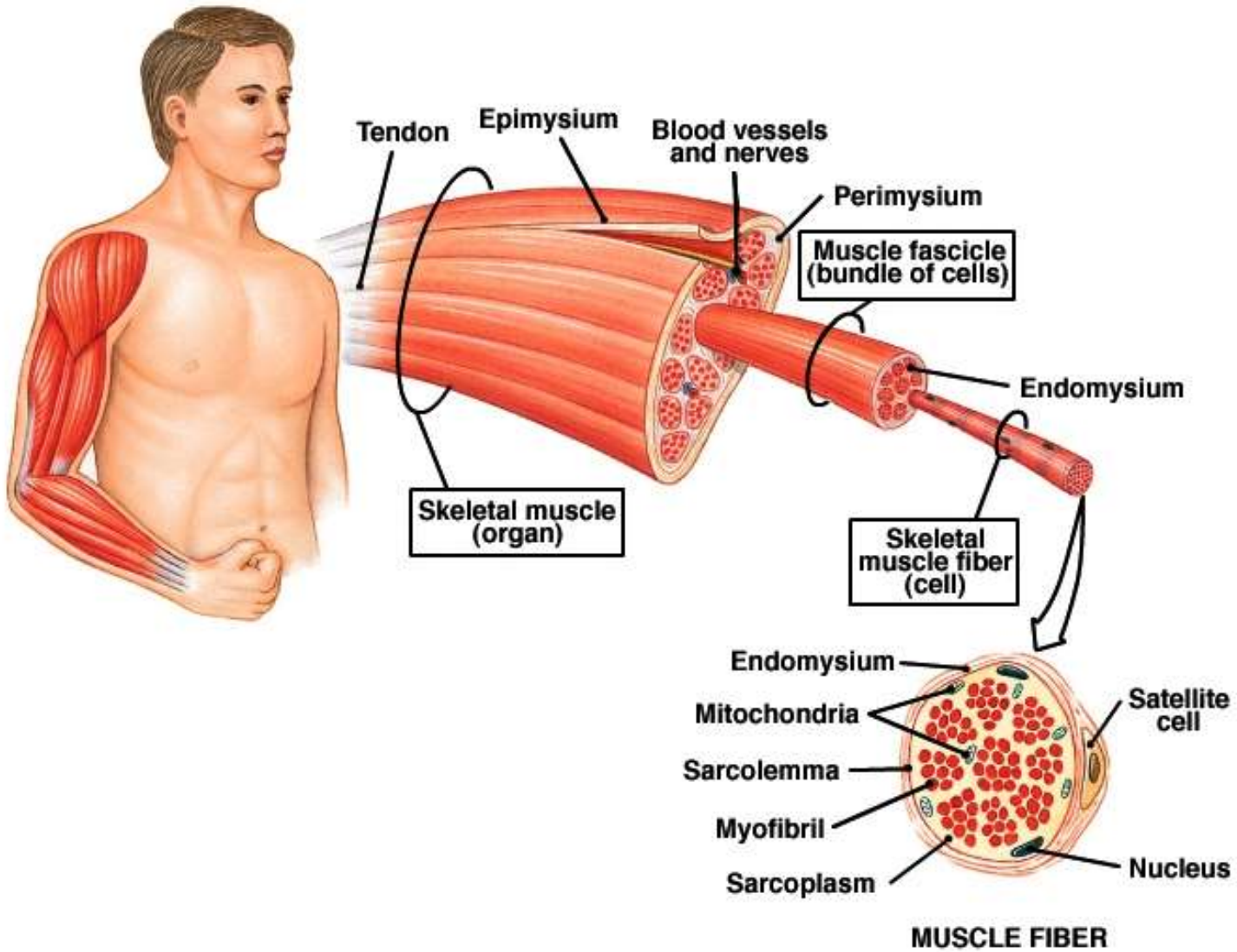
Structure of Skeletal Muscle

- Illustrates skeletal muscle spanning the elbow joint
- Muscle attached to bone on either side of joint
- Pt of attachment closest to spine called origin and distal called insertion
- Pt of attachment occur through tendons
- At end of the muscle fiber, surface layer of sarcolemma fuses with a tendon fiber which in turn collect into bundles to form muscle tendons that in turn insert into bones

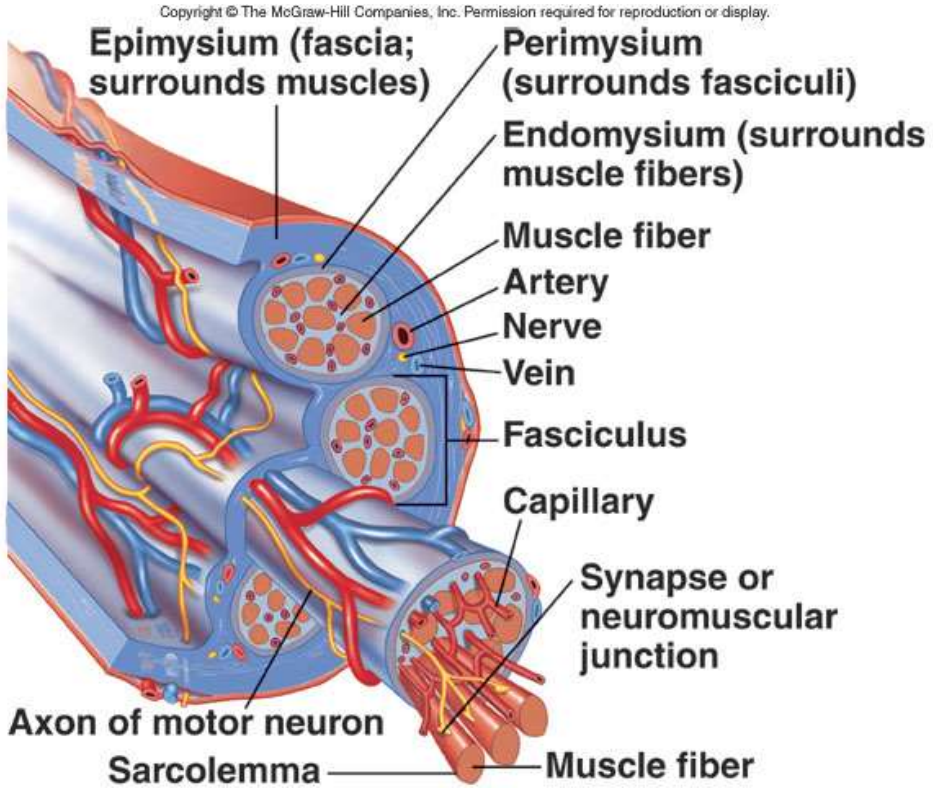
Organization I:



Organization III:

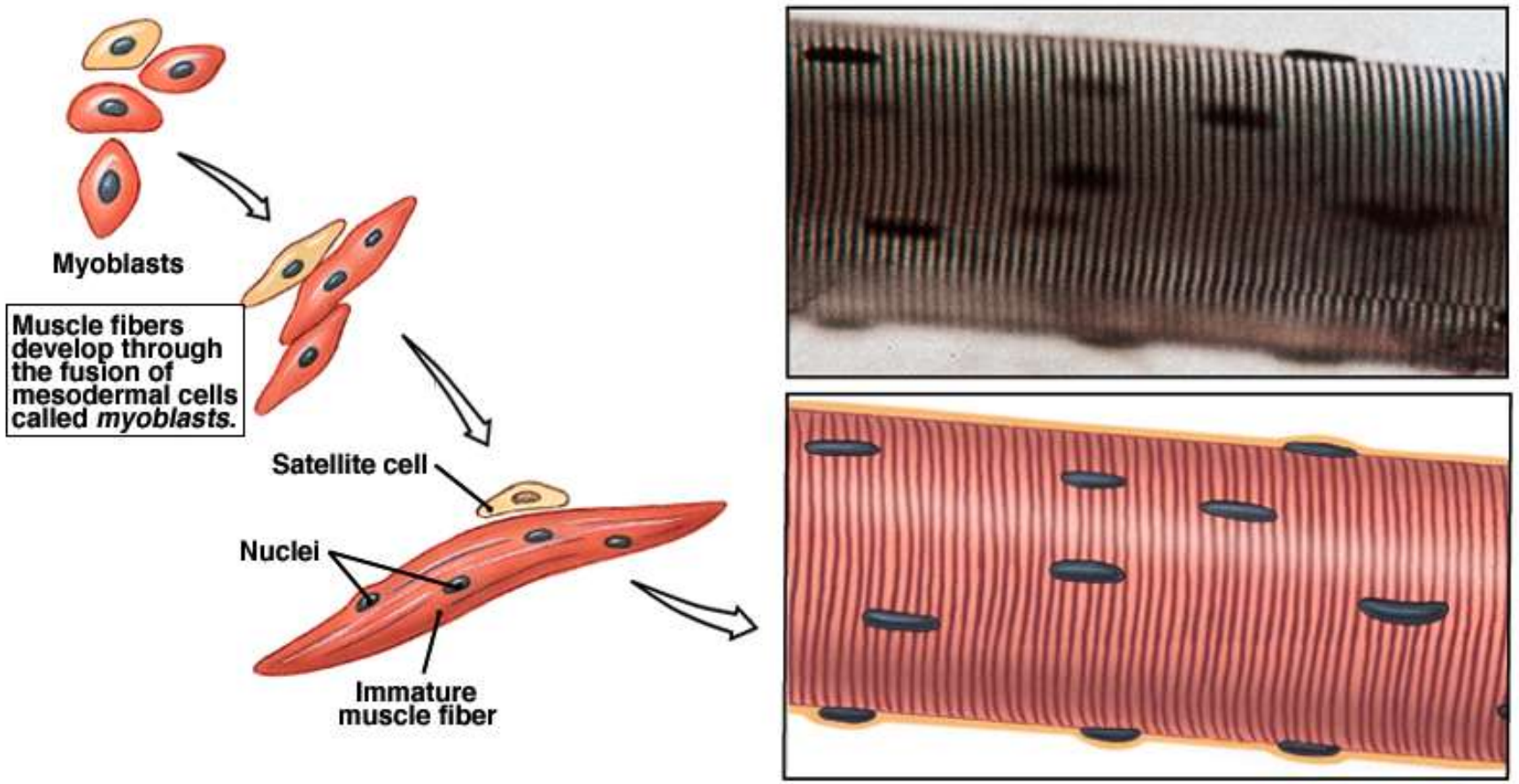


Connective Tissue, Nerve, Blood Vessels



- Connective tissue
  - External lamina
  - Endomysium
  - Perimysium
  - Fasciculus
  - Epimysium
- Fascia
- Nerve and blood vessels
  - Abundant

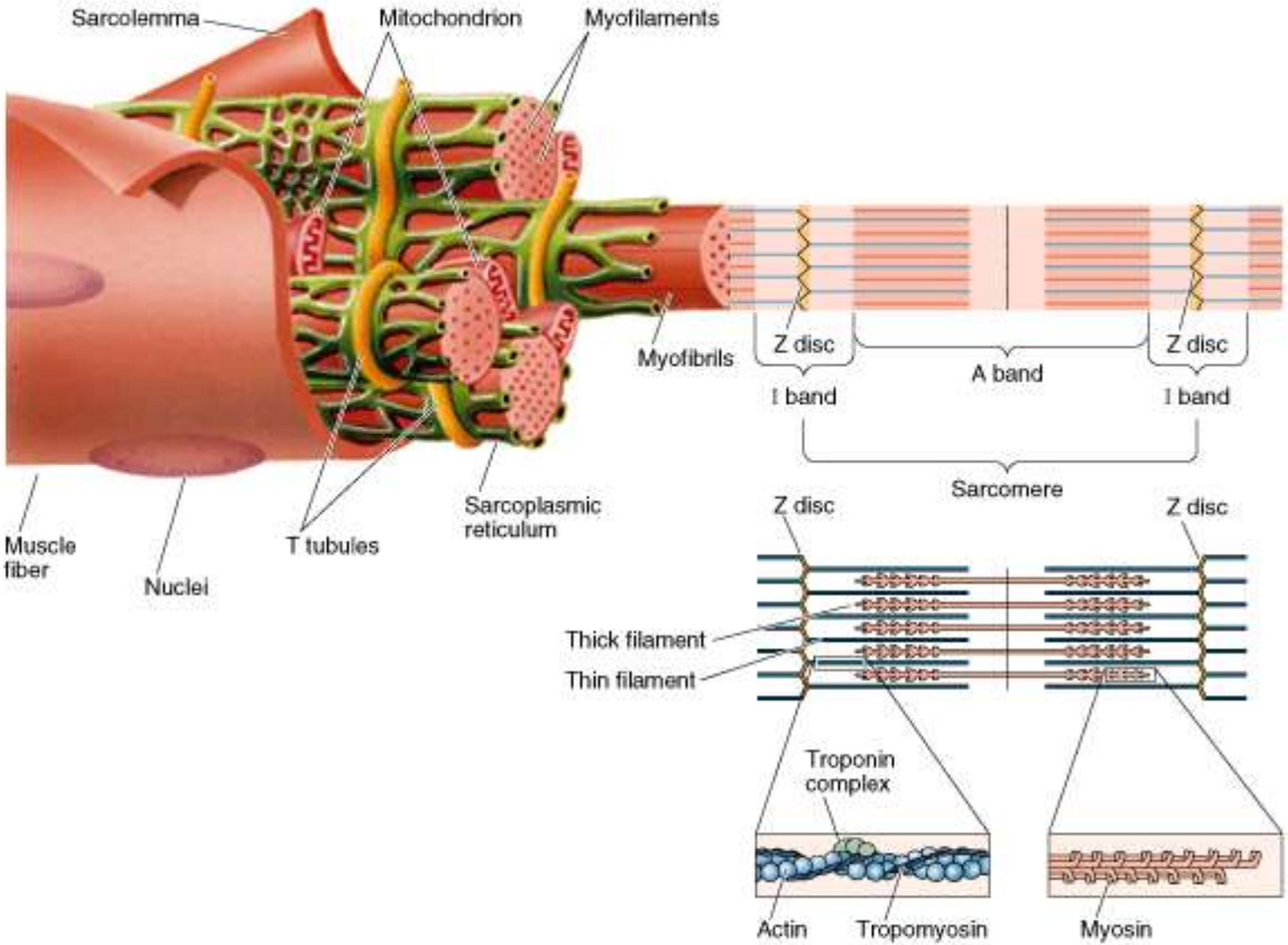
Embryologic origin:



Structure of Skeletal Muscle: *Microstructure*

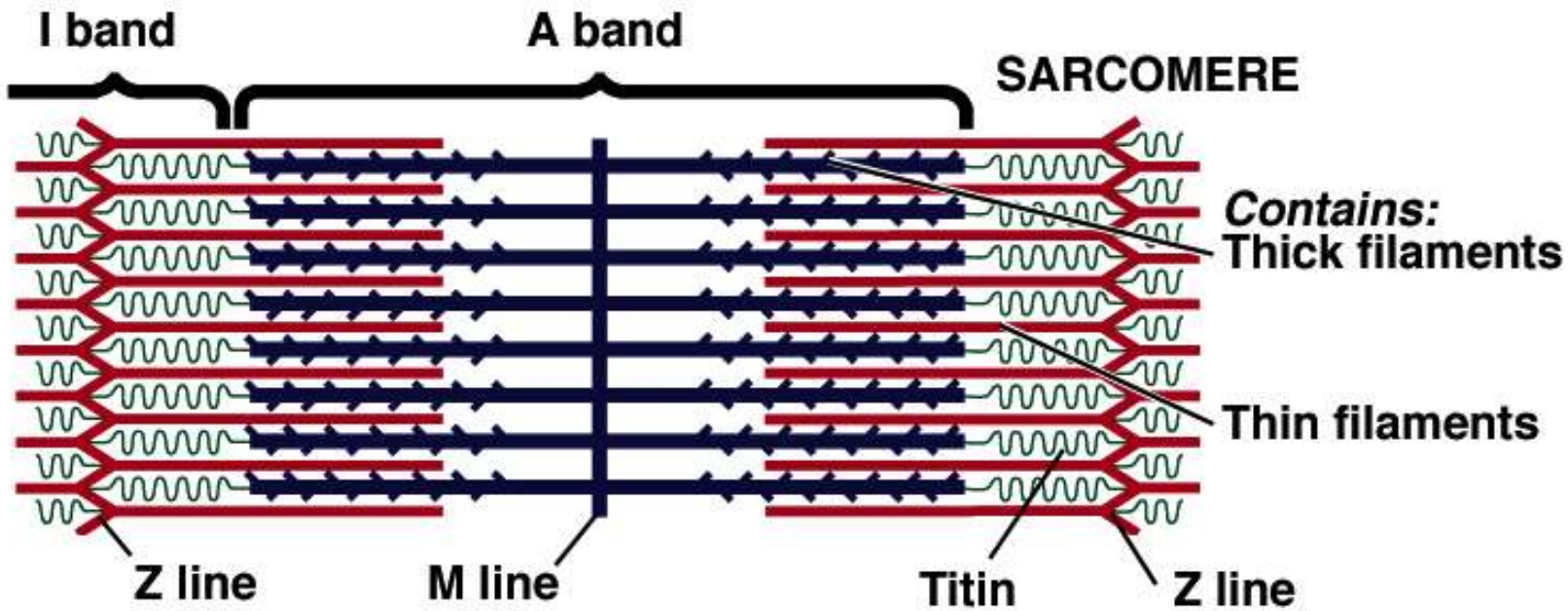
- Sarcolemma
  - Muscle cell membrane
- Each muscle fiber contains hundreds to thousands of myofibrils which are
  - Threadlike strands within muscle fibers
  - Actin (thin filament)
    - Troponin
    - Tropomyosin
  - Myosin (thick filament)

► Organization of a Muscle Fiber



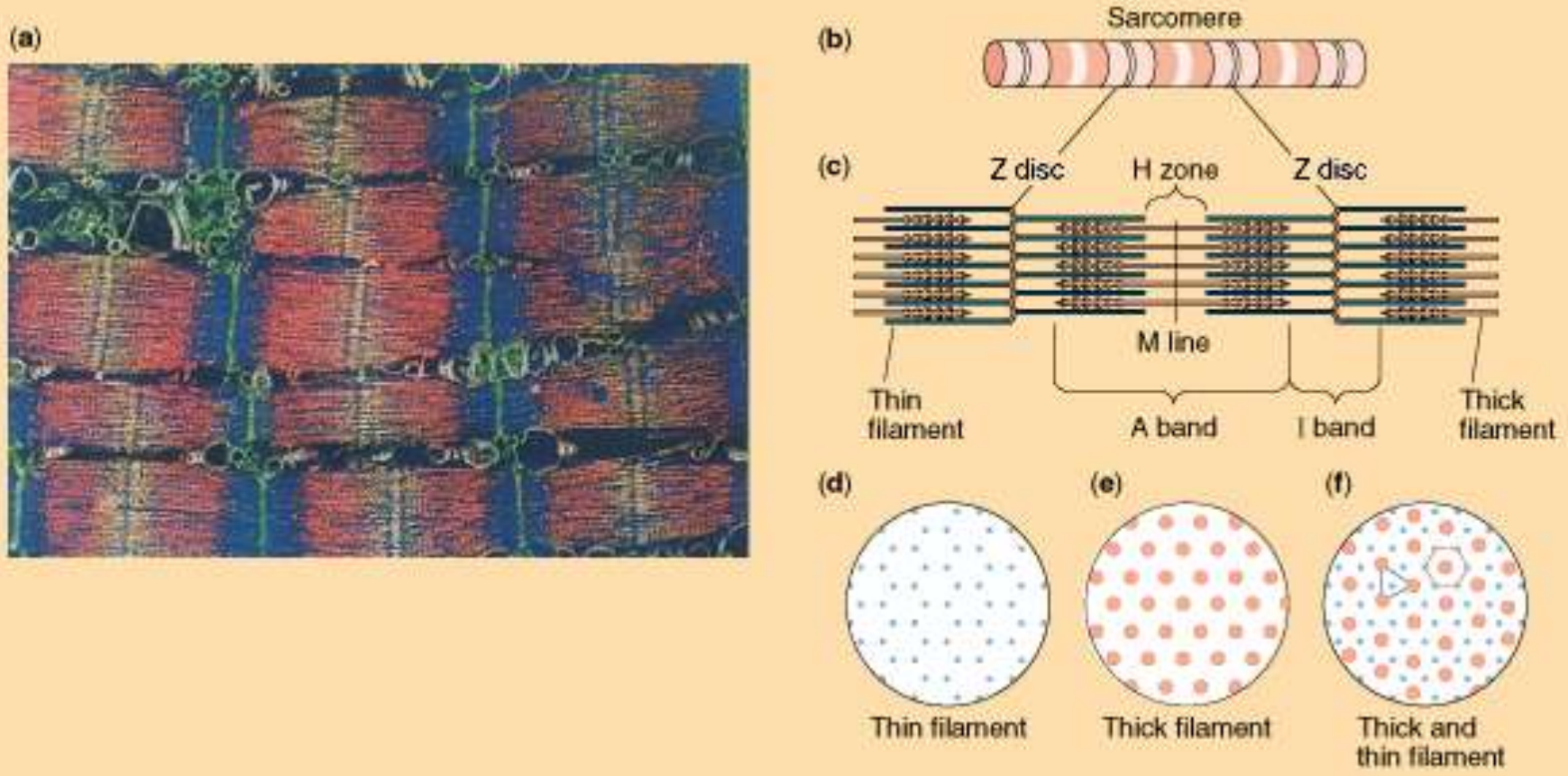
- Actin and myosin partially interdigitate causing myofibrils to have alternate light and dark bands
- Light bands contain only actin – I Bands
- Dark bands contain myosin and ends of actin where they overlap with myosin
- Small projections from myosin – called cross bridges whose interaction with actin cause actual muscle contraction

Organization of myofilaments I:

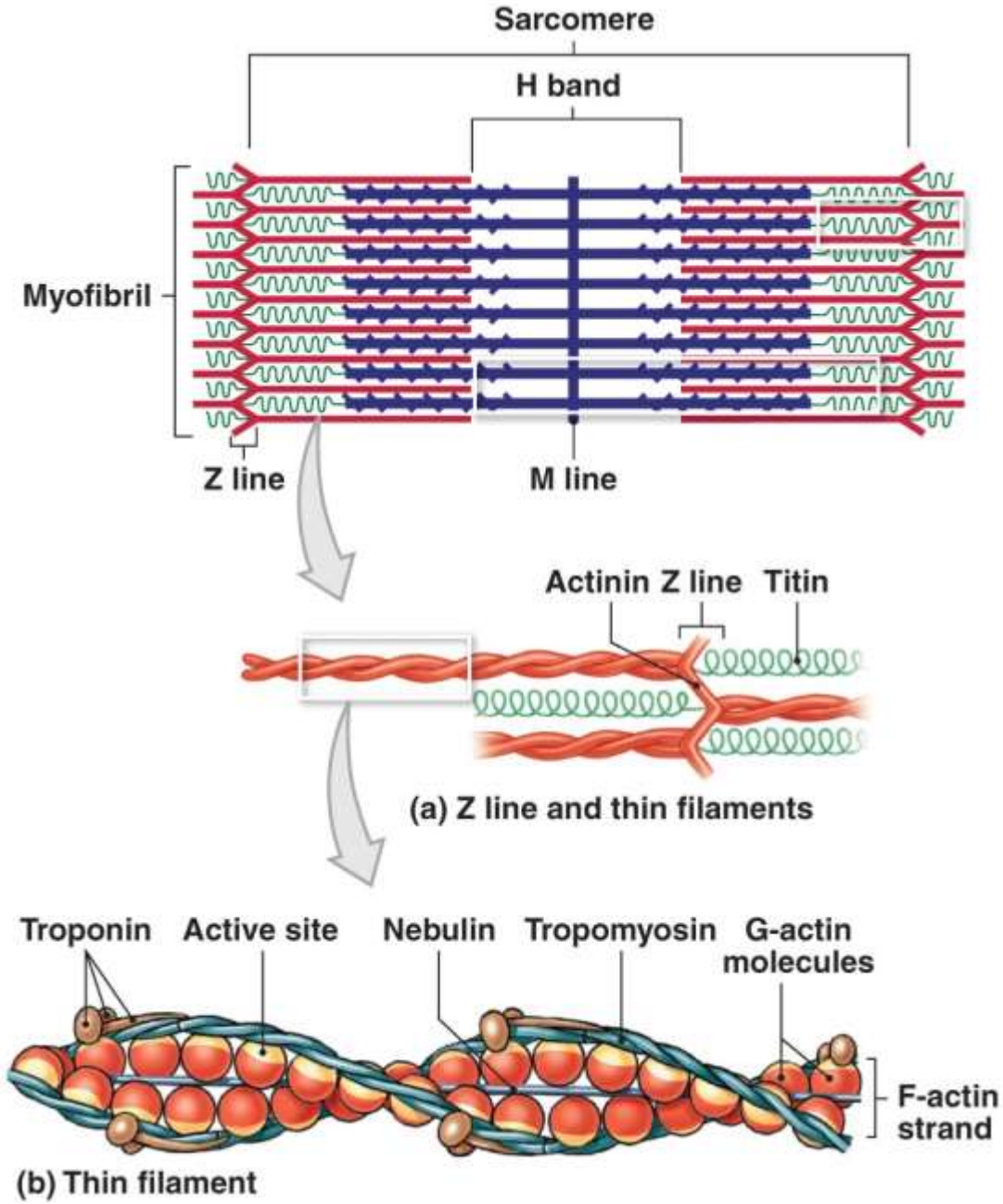


- Ends of actin filaments attached to Z-Disc.
- Extend in both directions to interdigitate with myosin
- Z-Disc made of filamentous proteins extends cross wise across myofibrils and also cross wise from myofibril to myofibril attaching myofibrils to one another all the way across a muscle fiber
- Entire muscle has dark and light bands as so do indivitual myofibrils
- Bands give skeletal and cardiac muscle striated appearance

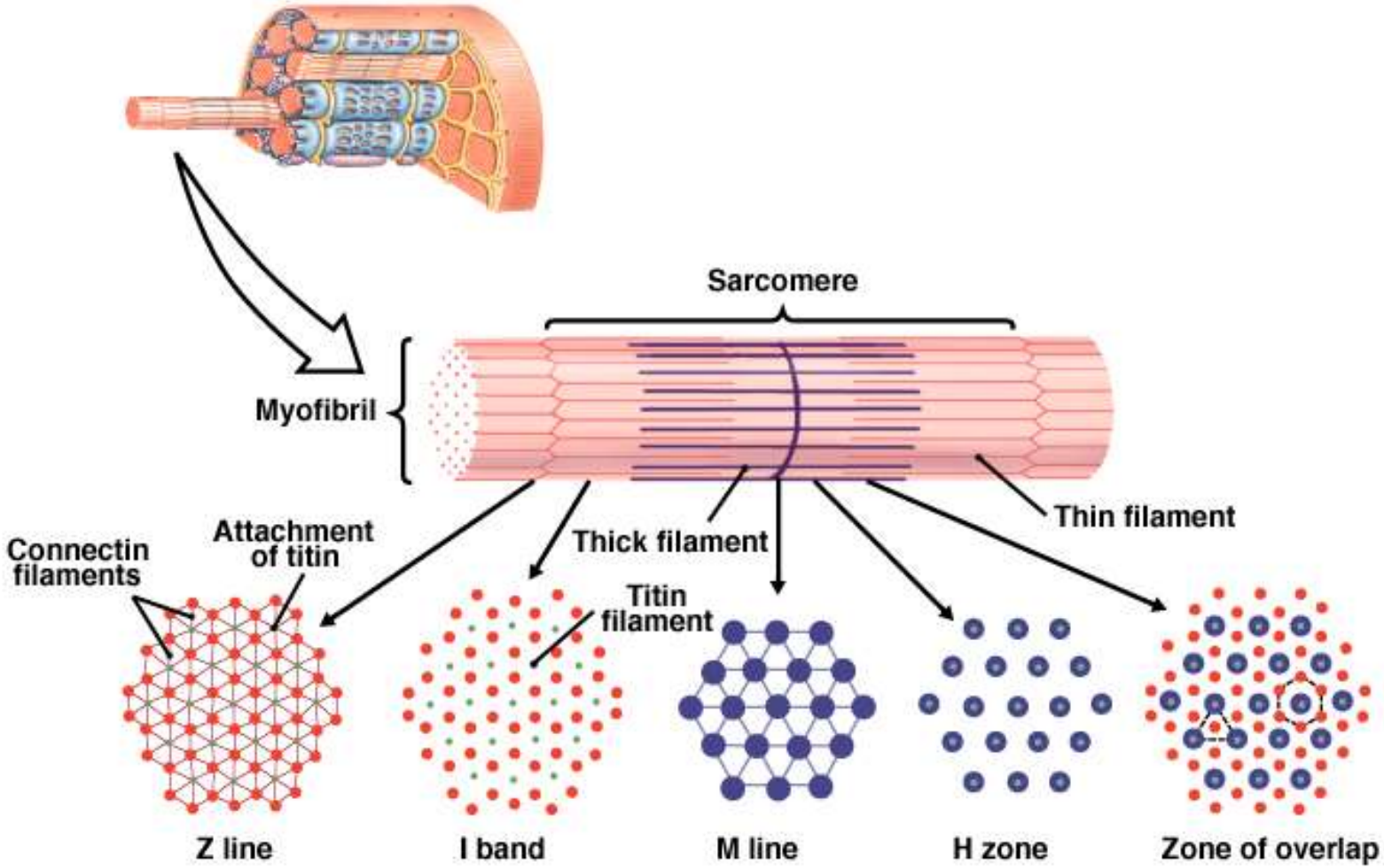
► Arrangements of Myofilaments in a Sarcomere



- Portion of myofibril between 2 successful Z-Discs called sarcomere
- Difficult to maintain side by side relationship between actin and myosin
- Maintained by large no.of filamentous protein molecules called titin – mwgt 3million – one of largest protein molecule in body.
- Since filamentous, is very springy
- Acts as framework that holds the myosin and actin together for the contractile machinery of sarcomere to work


Sarcomere
H band
Myofibril
Z line
M line
Actinin Z line
Titin
(a) Z line and thin filaments
Troponin
Active site
Nebulin
Tropomyosin
G-actin molecules
F-actin strand
(b) Thin filament

Organization of myofilaments II:



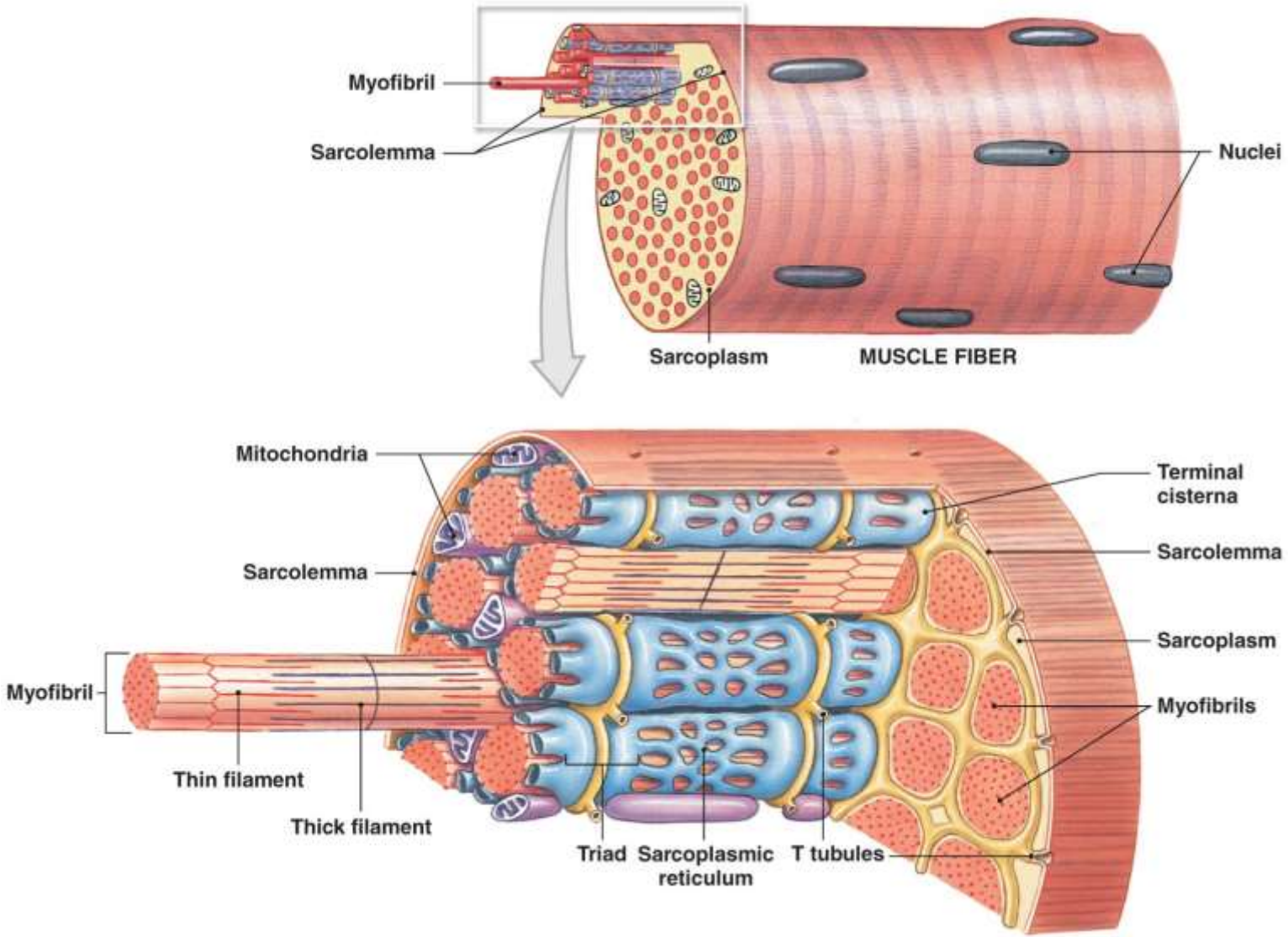
Muscle fiber contains sarcoplasm

Contains large quantities of K^+, Mg^{++} Phospates and multiple protein enzymes

Lot of mitochondria parallel to myofibrils to provide energy for contraction

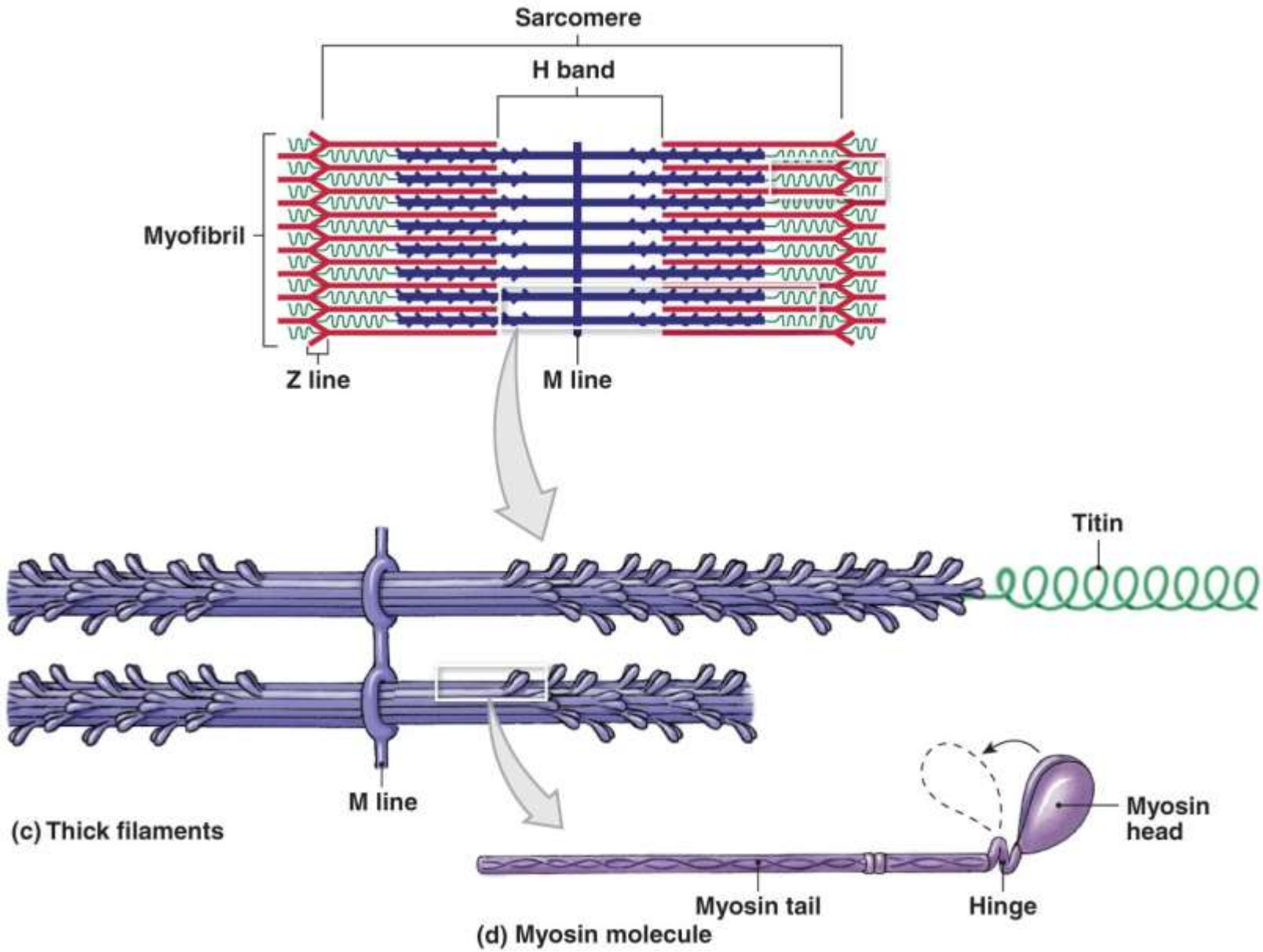
An extensive reticulum – the sarcoplasmic reticulum which is extremely important in muscle contraction

Skeletal Muscle Fiber;



Structure of Skeletal Muscle: *The Sarcomere*

- Further divisions of myofibrils
  - Z-line
  - A-band
  - I-band
- Within the sarcoplasm
  - Sarcoplasmic reticulum
    - Storage sites for calcium
  - Transverse tubules
  - Terminal cisternae

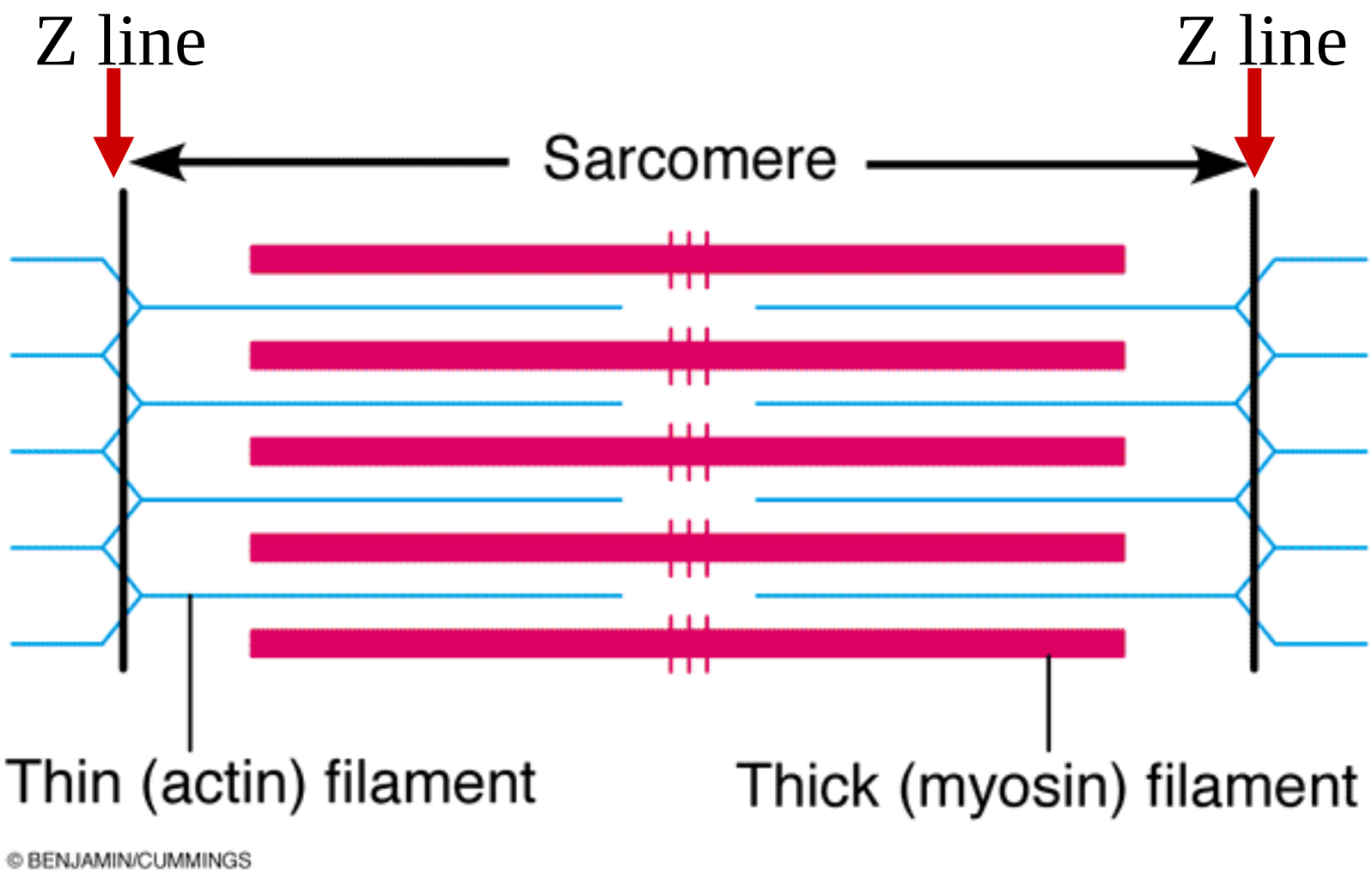

Sarcomere
H band
Myofibril
Z line
M line
Titin
M line
(c) Thick filaments
Myosin head
Myosin tail
Hinge
(d) Myosin molecule

Mechanism of contraction

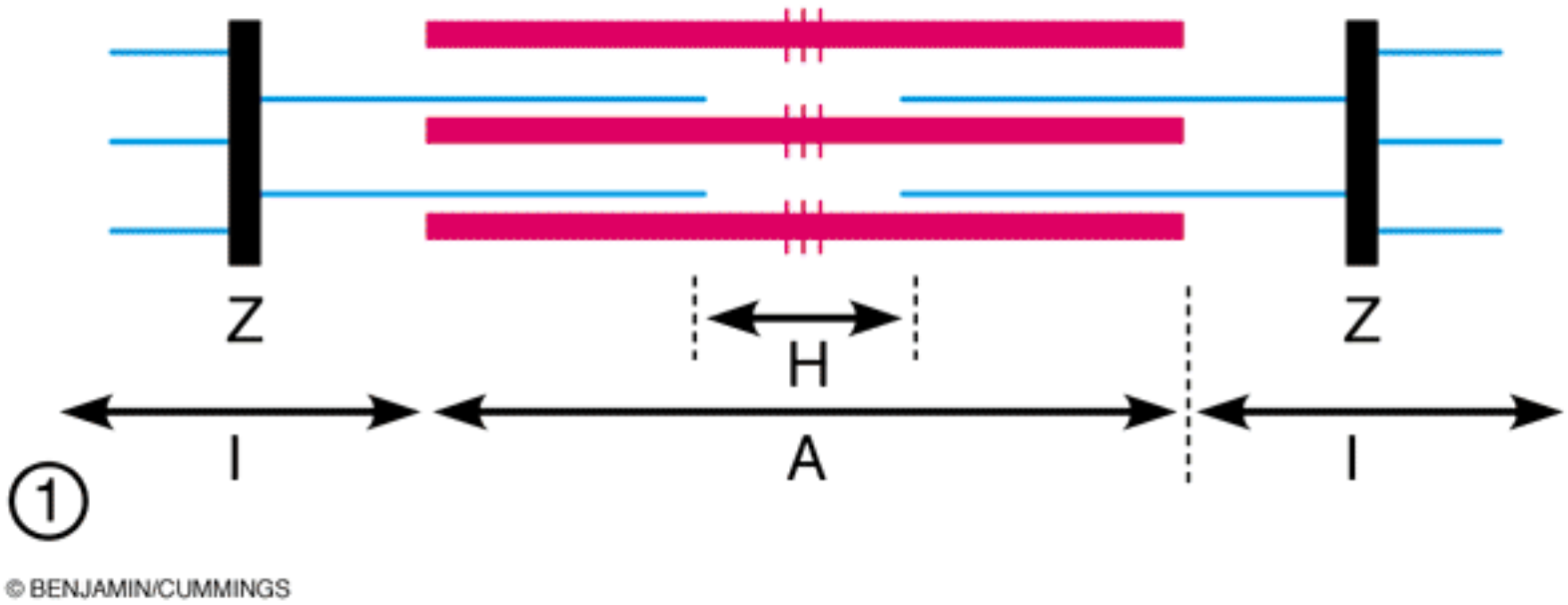
- In relaxed state, ends of actin filament extending from 2 successive Z-Discs barely begin to overlap one another
- In contracted state, they have pulled inward among the myosin filaments so that their ends overlap one another to maximum effects
- Also, Z –Discs have been pulled up to the ends of myosin filaments
- This is the sliding filament mechanism

Muscular Contraction

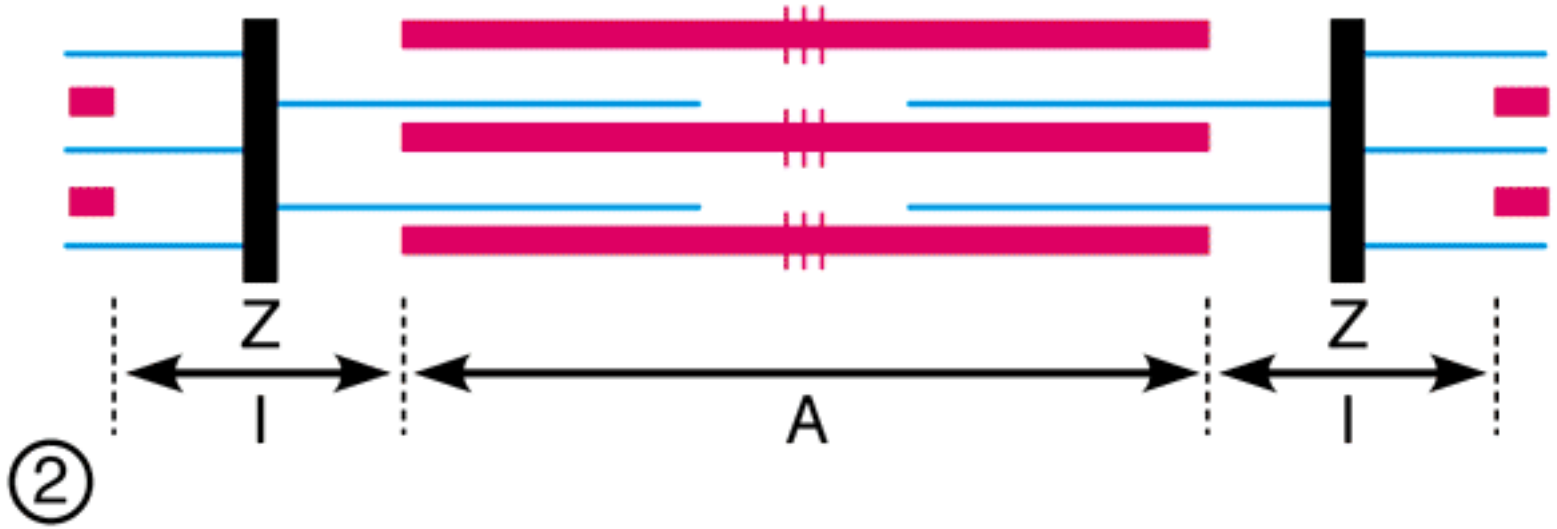
- The sliding filament model
  - Muscle shortening occurs due to the movement of the actin filament over the myosin filament
  - Formation of cross-bridges between actin and myosin filaments
  - Reduction in the distance between Z-lines of the sarcomere


Z line
Z line
Sarcomere
Thin (actin) filament
Thick (myosin) filament
© BENJAMIN/CUMMINGS

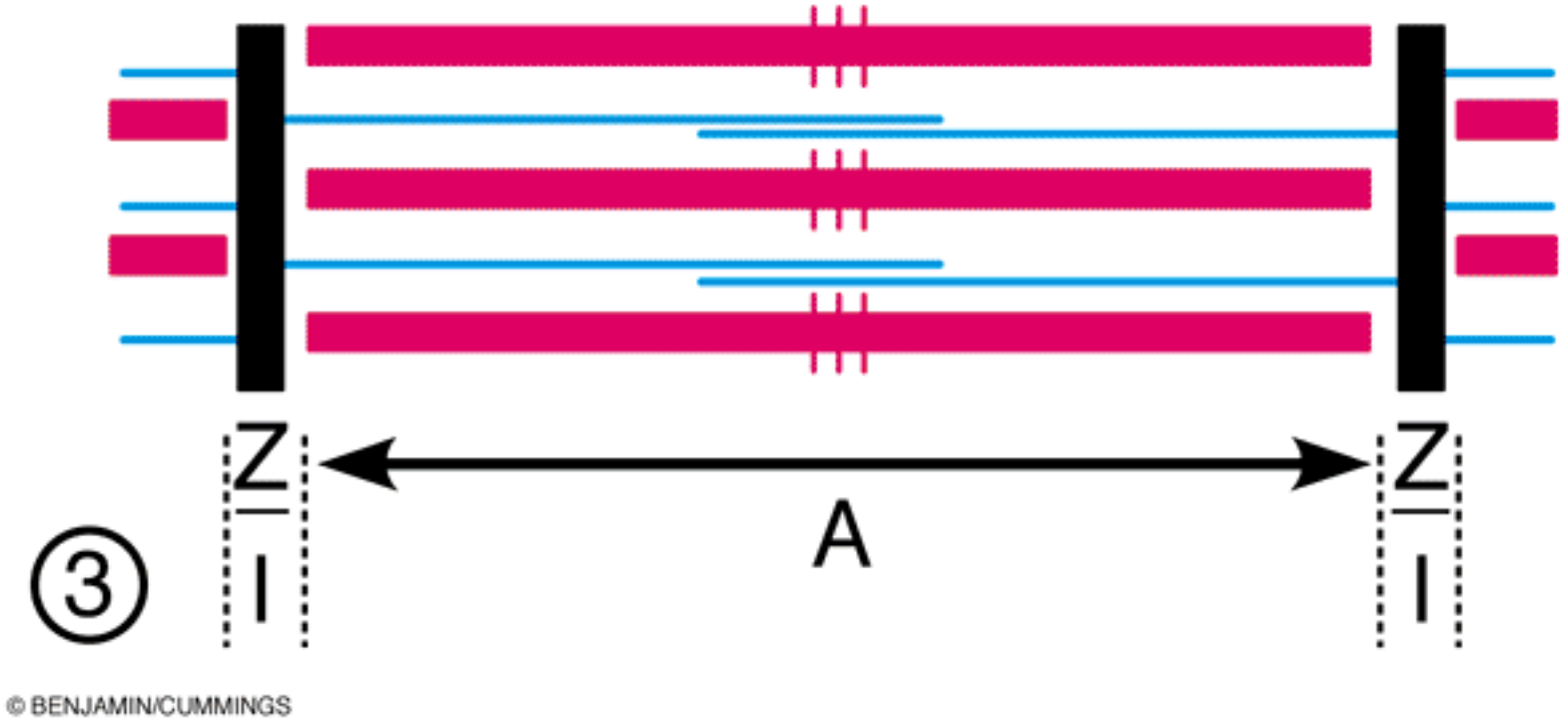
Sarcomere Relaxed

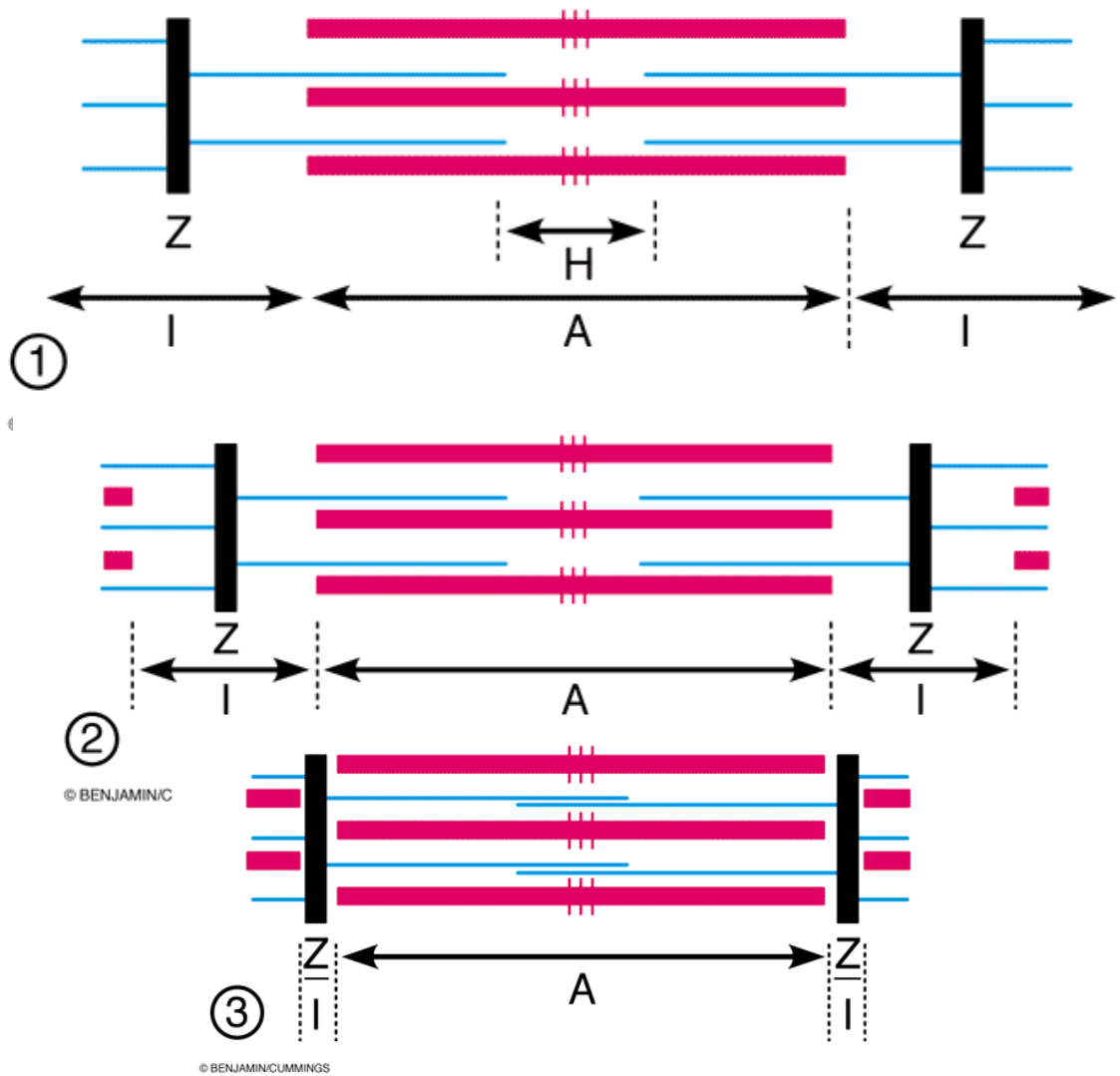


Sarcomere Partially Contracted



Sarcomere Completely Contracted

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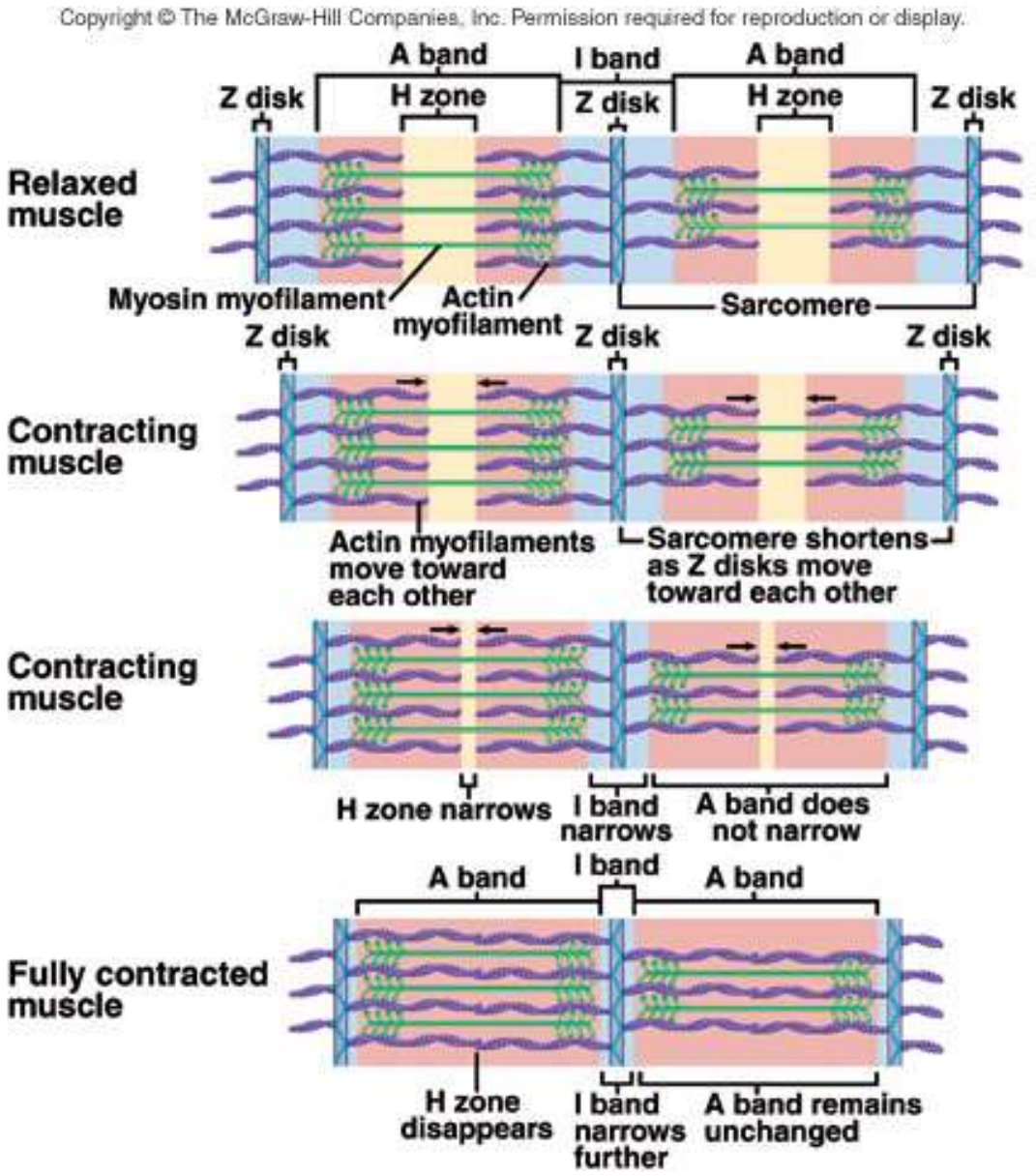
Sarcomere Shortening- 7th February



Mechanism of Muscle Contraction

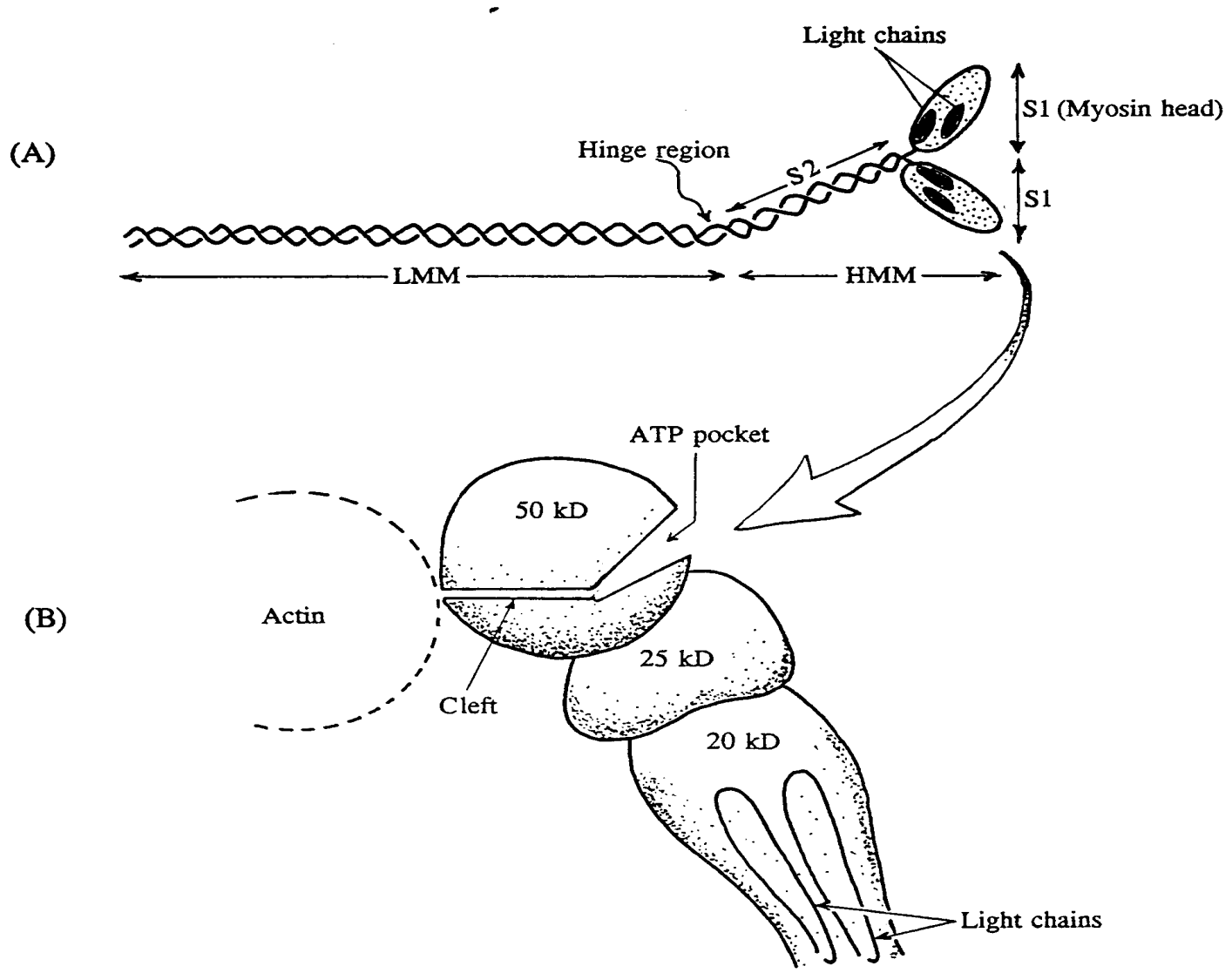
- Caused by forces generated by interaction of the cross bridges from the myosin filaments with the actin filaments
- Normally this forces inactive
- When action potential travels along muscle fiber, it causes sarcoplasmic reticulum to produce lots of Ca^{+} which rapidly surround the myofibrils

- The Ca^{++} ions activate the forces between myosin and actin initiating contraction
- Energy required for the process comes from conversion of ATP to ADP

- Myosin filament comprises of many myosin molecules
- Each myosin molecule consists of 2 heavy chains and four light chain
- Heavy chains wrap spirally around each other to form a double helix – Tail,
- One end of each chain folded bilaterally into globular head hence two heads at one end of the double helix myosin molecule

- The 4 light chains part of the myosin head, 2 on each head and help to control function of head during contraction
- Myosin filament made up of 200 or more myosin molecules
- Tails of the myosin bundled together to form body of the filament while many heads hang outside to the side of body

Myosin structure: Karatina

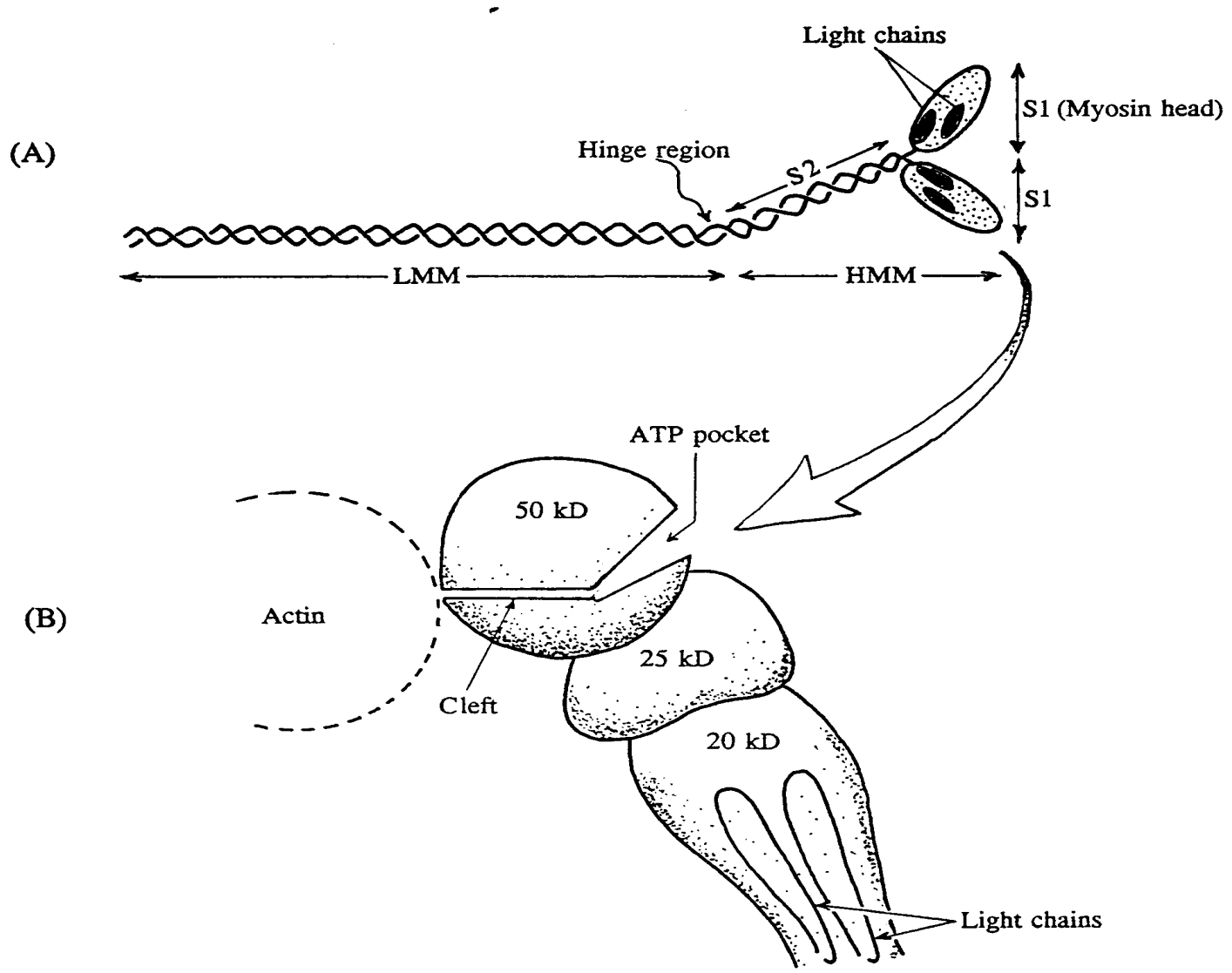


- Part of body of each myosin molecule hangs to the side along with the head, thus providing an arm that extends the head outward from the body
- Protruding arm and head called the cross-bridges
- Each cross bridge flexible at two points called hinges- one where the body leaves the filament and the other where the head attached to the arm

- Hinged arm allows the heads either to be extended far outward from the body of the myosin molecule or to be brought close to the body.
- The hinged heads in turn participate in the actual contraction process

- Myosin filament twisted such that each successful pair of cross-bridges is axially displaced from the previous pair by 120 degrees
- This ensures that cross bridges extend in all directions

Myosin structure: Karatina



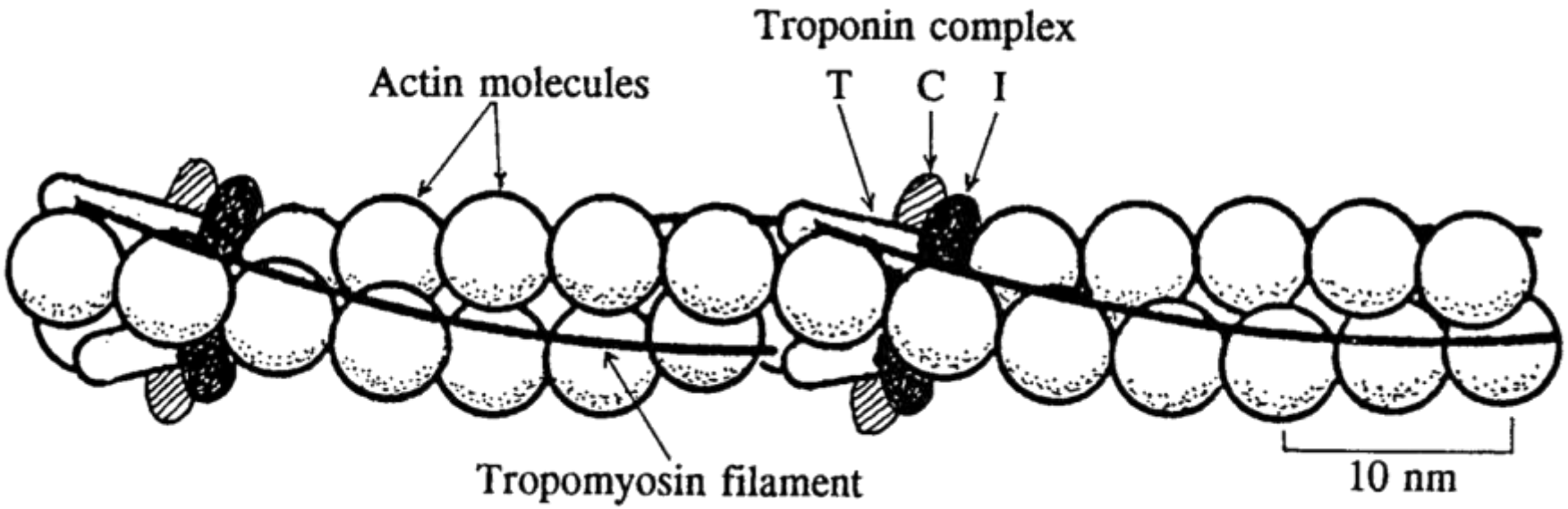
- Myosin head acts as ATPase enzyme
- This allows head to cleave ATP and to use energy derived from this ATP to energize contractile process

Actin Filaments

- Three proteins
- Actin
- Troponin and
- Tropomyosin

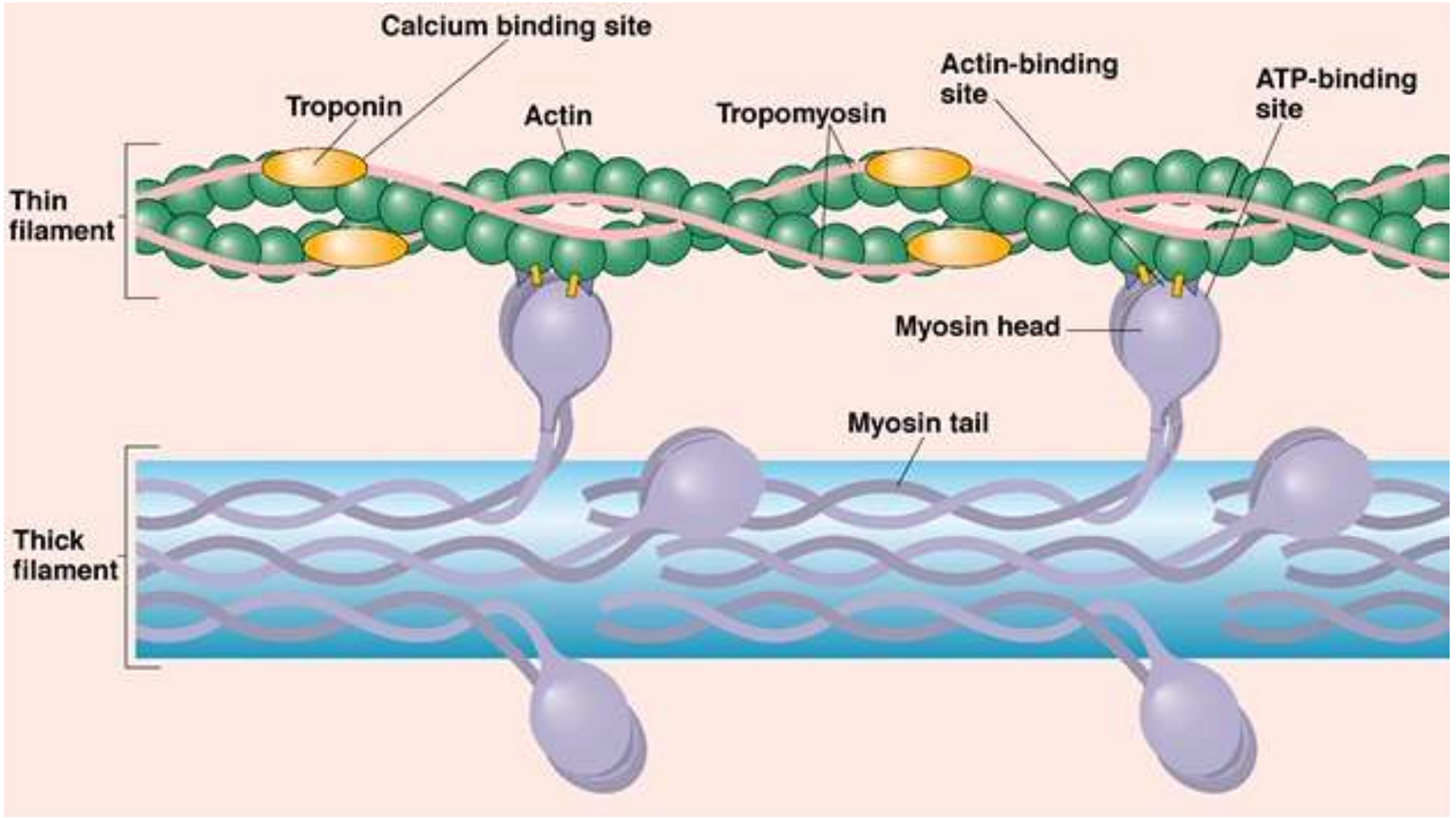
Consists of a double stranded *F-Actin* molecule wound in a helix.

Structure of thin filament:



- Each strand of F-Actin strand comprised of polymerized G-Actin molecules
- Attached to each G actin molecule is a molecule of ADP
- This ADP is active site on actin filaments with which the cross-bridges of the myosin filament interact to cause contraction

Cross-Bridge Formation in Muscle Contraction



- Active sites on the 2 f-actin filaments staggered giving one active site on the overall actin molecule every 2.7 nanometers
- Each actin filament about 1 micrometer long
- Base inserted strongly into the Z- discs
- End of filaments protrude into both directions to lie in spaces between the myosin

Tropomyosin

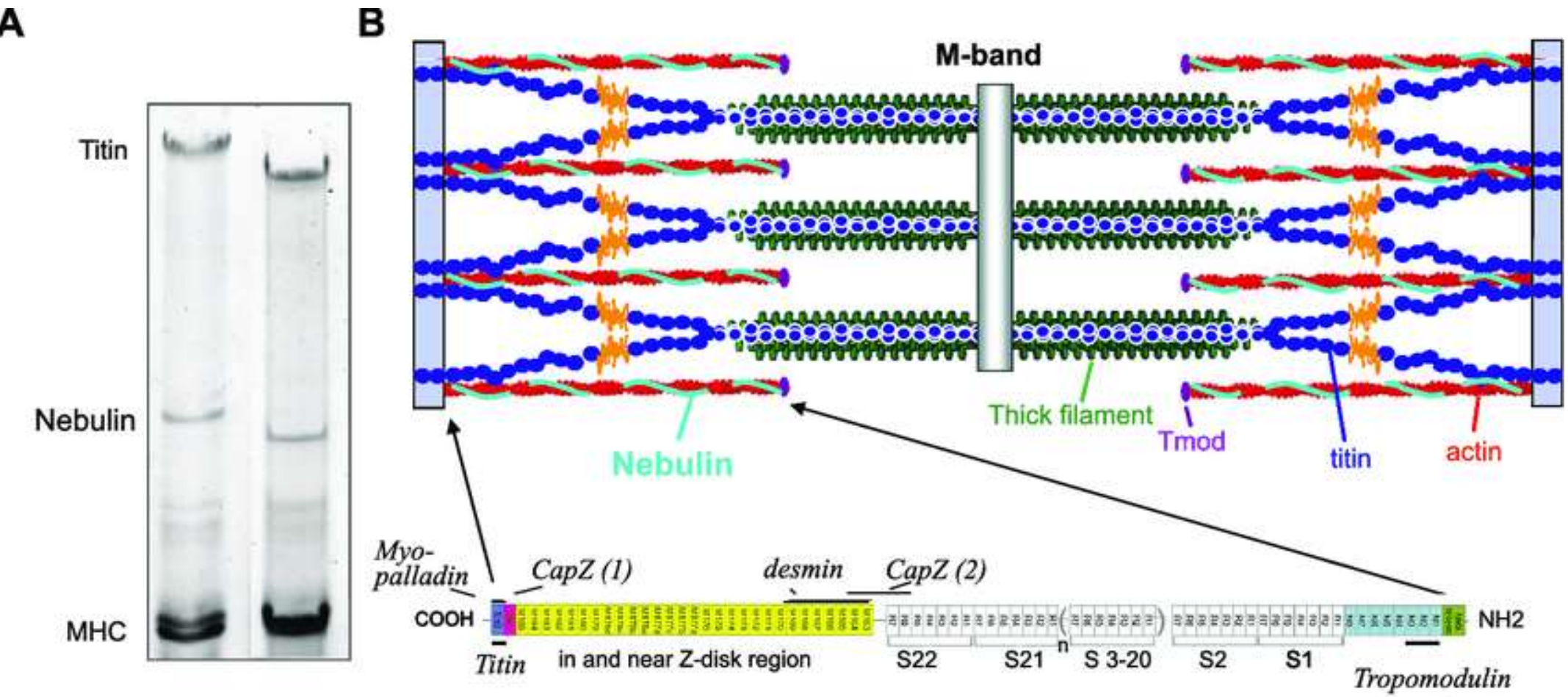
- Actin also contains tropomyosin molecules
- Wrapped spirally around the sides of the F-actin helix
- In resting state, lie on active sites of actin strands
- No attraction between actin and myosin

Troponin

- Attached intermittently along the sides of tropomyosin molecules
- Complex of 3 loosely bound proteins

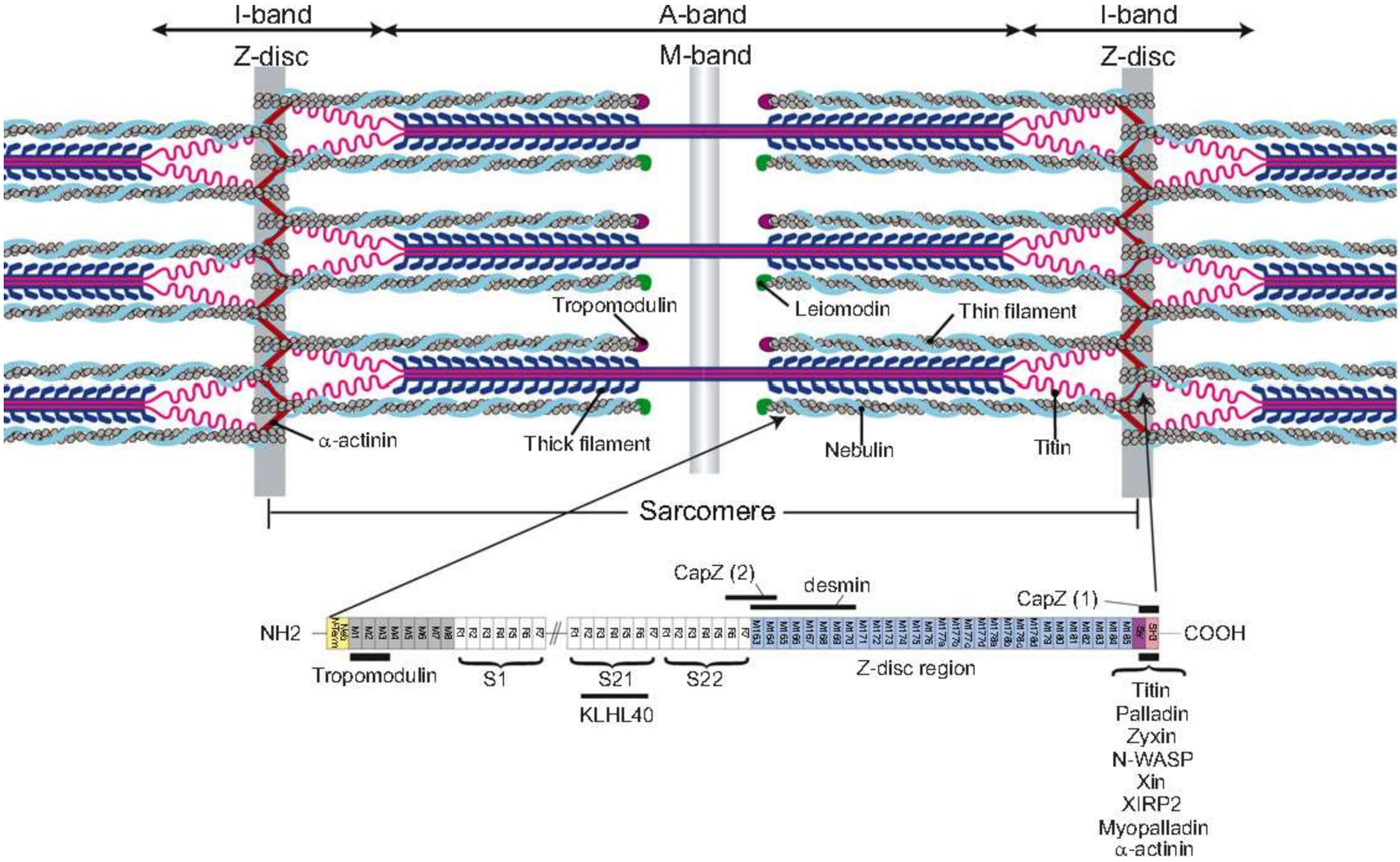
1) Troponin I which has strong affinity for actin
2) Troponin T which has strong affinity for tropomyosin &
3) Troponin C with strong affinity for Ca^{++}

- Strong affinity of troponin for Ca^{++} believed to initiate contraction process

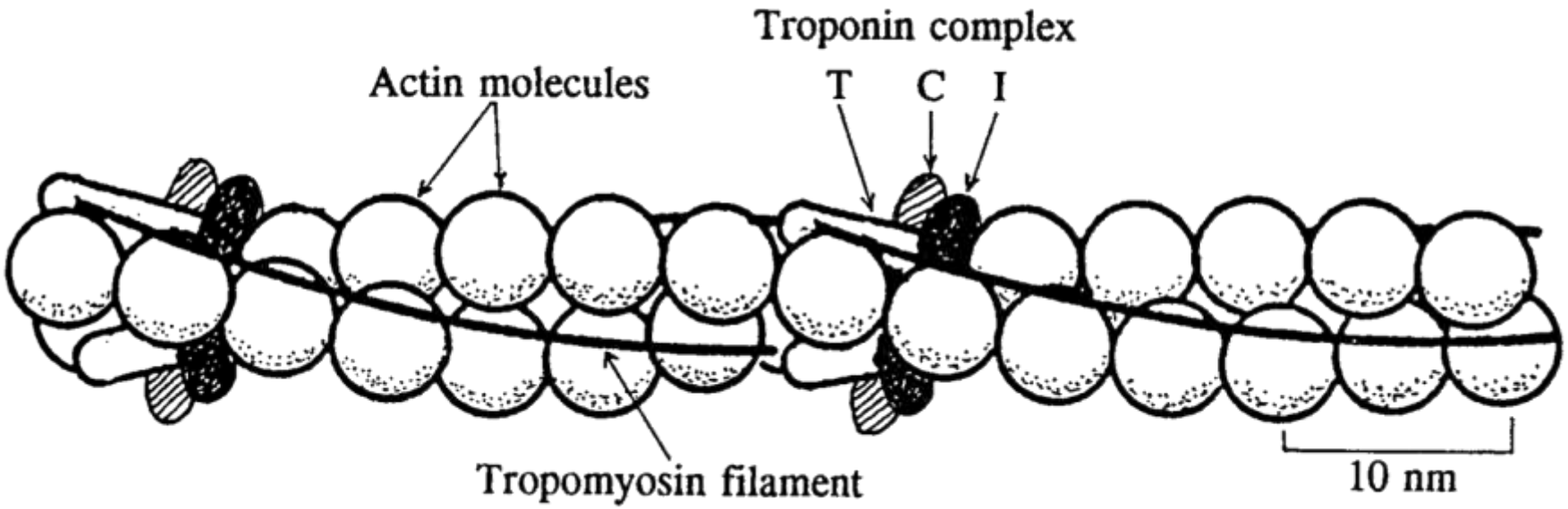

A
Titin
Nebulin
MHC
B
M-band
Thick filament
Tmod
titin
actin
Nebulin
Myo-palladin
CapZ (1)
desmin
CapZ (2)
COOH
NH2
Titin
in and near Z-disk region
S22
S21
n
S 3-20
S2
S1
Tropomodulin

Nebulin

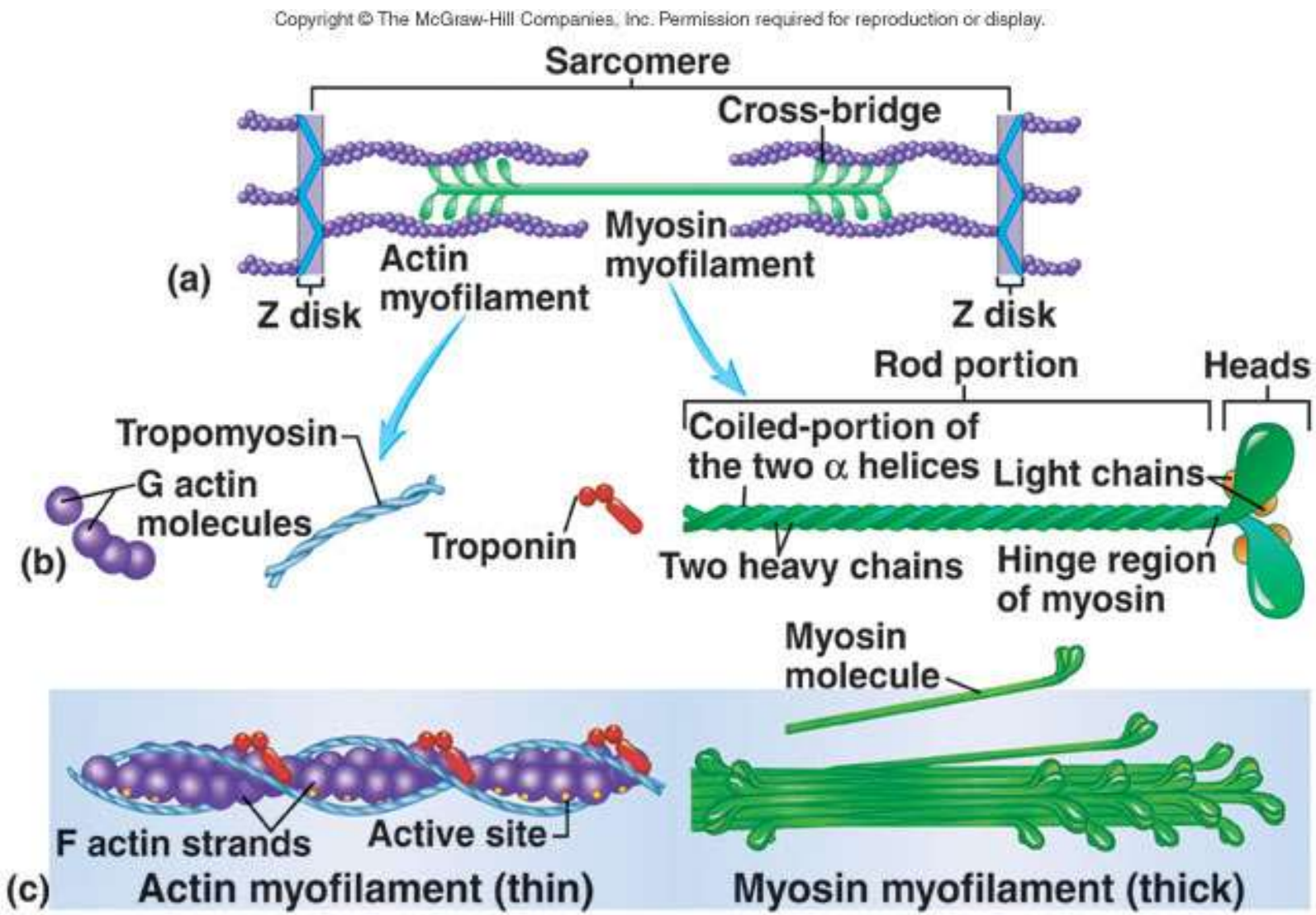
- It is an actin-binding protein localized to actin in skleetal muscle
- It is a giant filamentous protein that is an integral component of the skeletal muscle actin
- Functions could be
- Play a major role in thin-filament length specification, nebulin also functions in the
- Regulation of muscle contraction
- Muscle fibers deficient in nebulin have a higher tension cost, and develop less force due to reduced myofilament calcium sensitivity and altered crossbridge cycling kinetics.
- May have a role in calcium homeostasis.
- May have a role in the assembly and alignment of the Z disks.

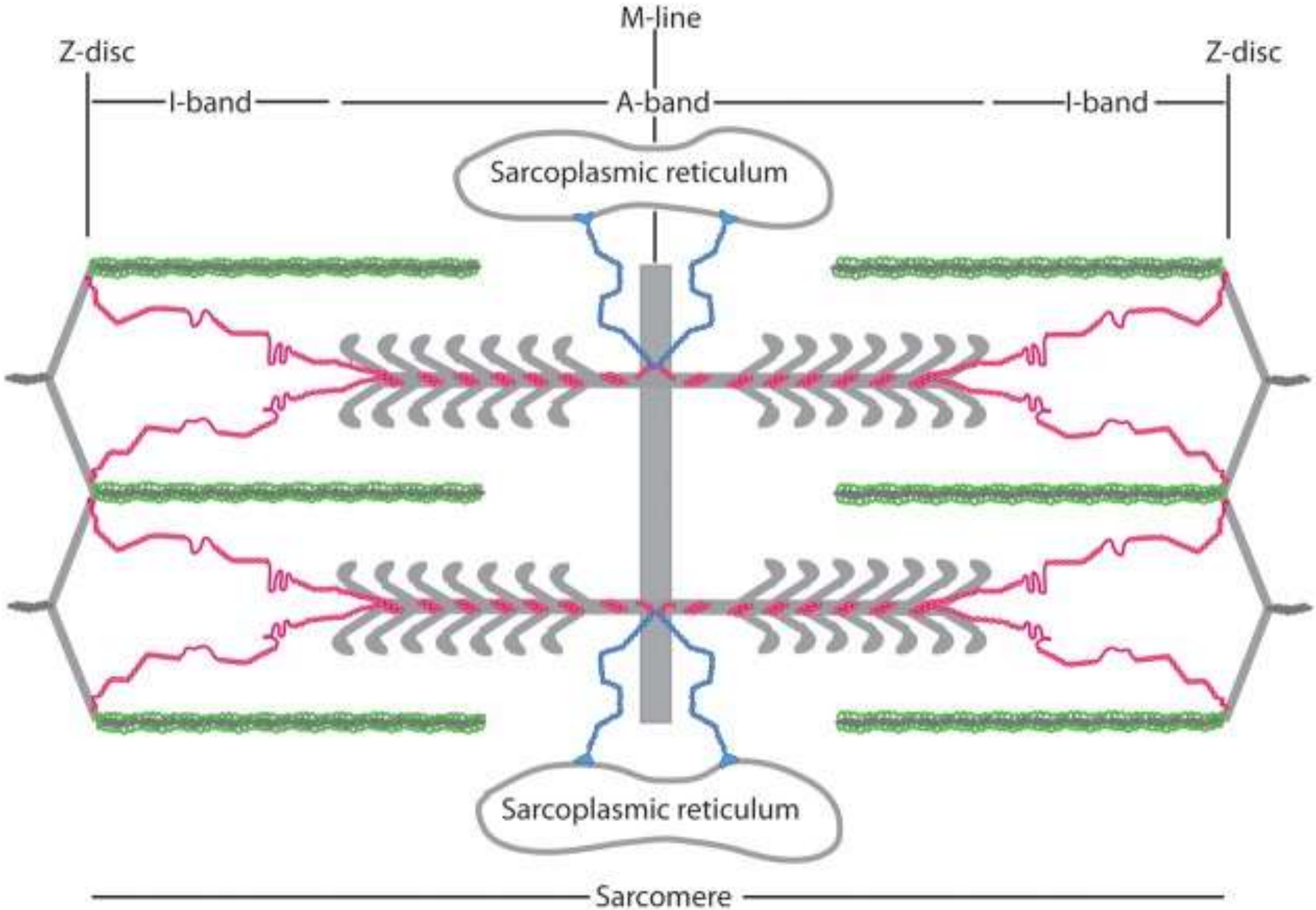

I-band
A-band
I-band
Z-disc
M-band
Z-disc
Tropomodulin
Leiomodin
Thin filament
α-actinin
Thick filament
Nebulin
Titin
Sarcomere
CapZ (2)
desmin
CapZ (1)
NH2
COOH
Tropomodulin
S1
S21
S22
KLHL40
Z-disc region
Titin
Palladin
Zyxin
N-WASP
Xin
XIRP2
Myopalladin
α-actinin

Structure of thin filament:



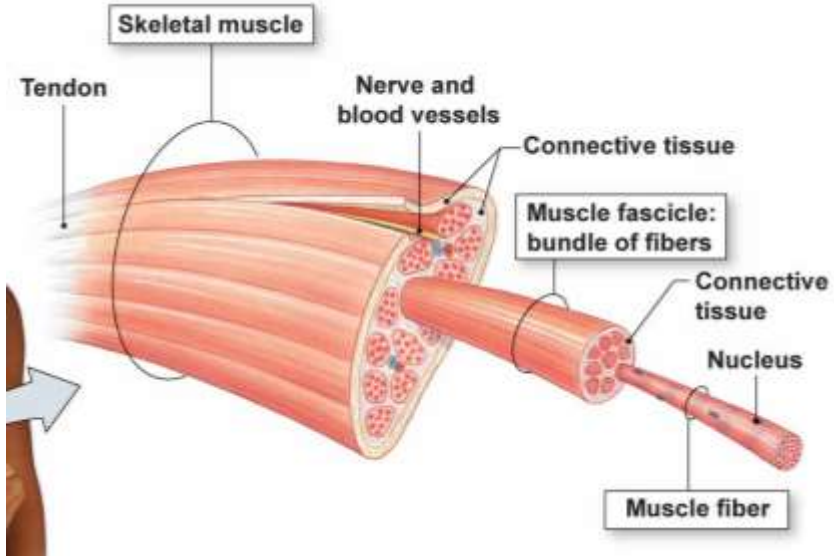
Structure of Actin and Myosin

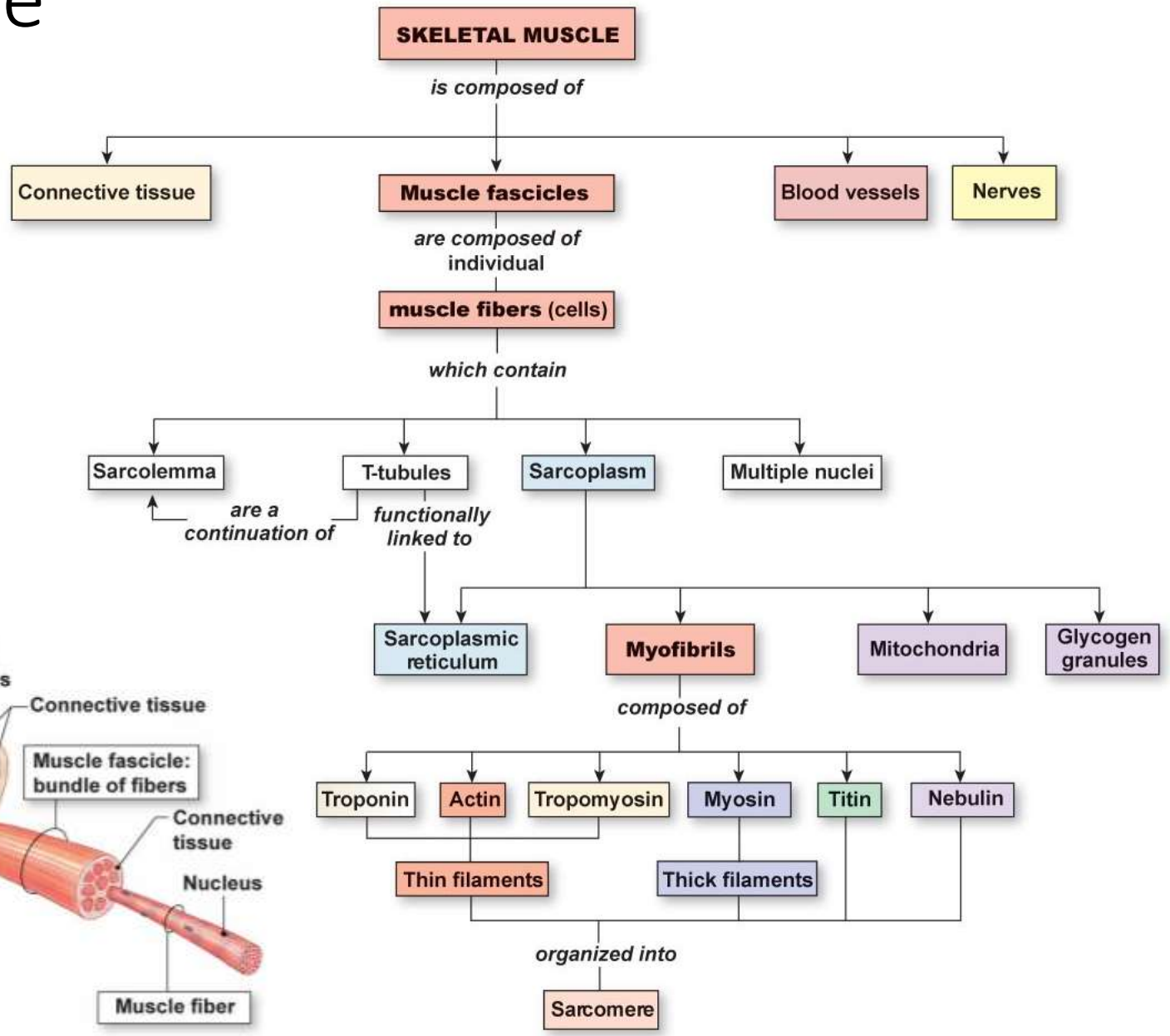



M-line
Z-disc
Z-disc
I-band
A-band
I-band
Sarcoplasmic reticulum
Sarcoplasmic reticulum
Sarcomere

Skeletal Muscle

Functional Anatomy





Muscle contraction

- Active sites on actin inhibited or covered by the troponin-tropomyosin complex
- Ca^{++} ions in huge quantities inhibit the troponin-tropomyosin complex inhibitory effect on the actin
- When Ca^{++} ions combine with troponin C, troponin complex undergoes a conformational change that in some ways tugs the tropomyosin molecule moving it deeper in the groove between actin strands

- This uncovers the active sites allowing this to attract the myosin cross-bridge heads causing contraction to proceed
- Once actin activated, heads of cross-bridges become attracted to the active sites this causing contraction to occur.
- Precise manner how this causes contraction not known

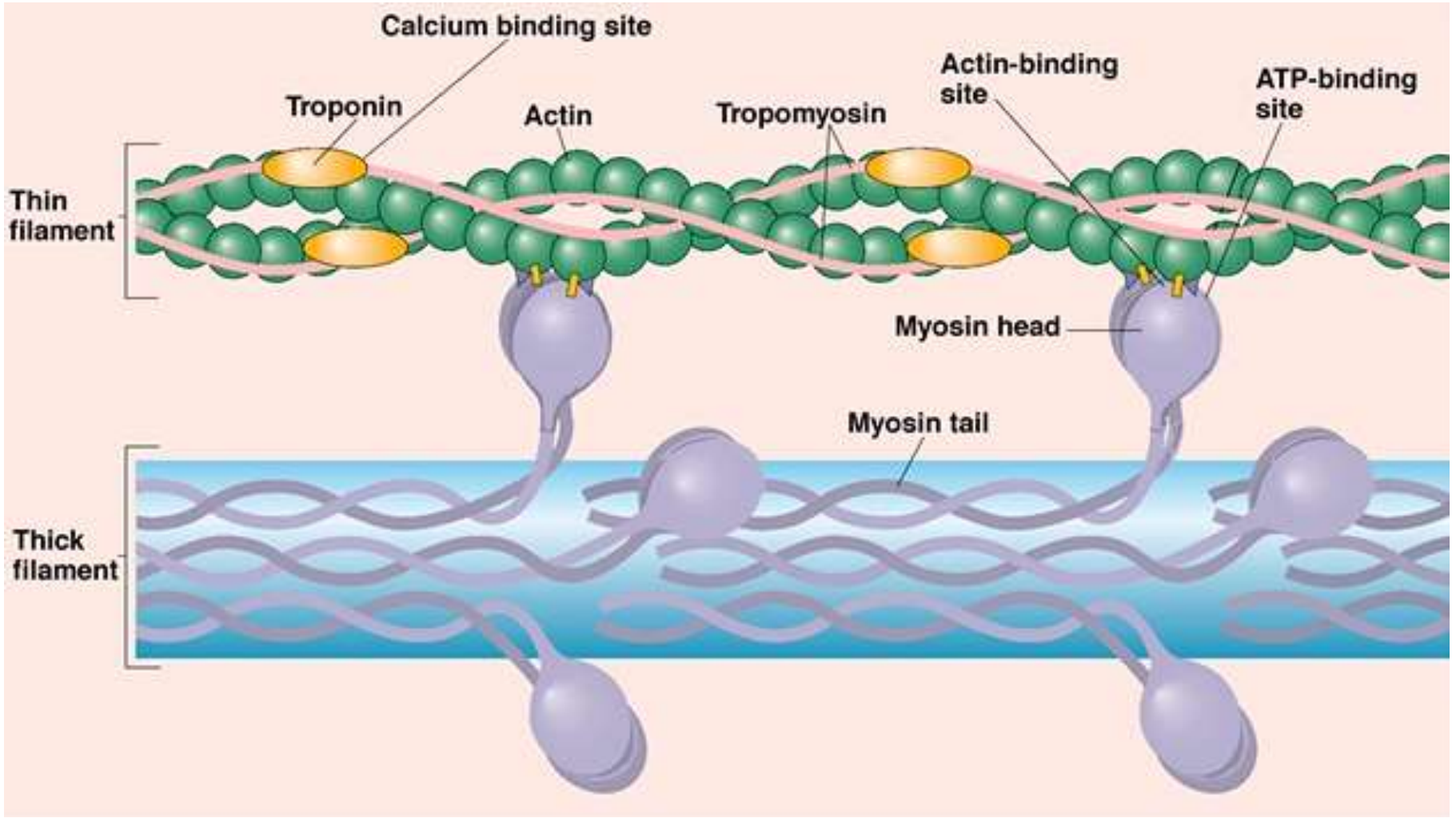
Interaction between active Actin and Myosin cross bridge

- Hypothesis for this is the walk along theory or ratchet theory
- When head attaches to active site, this attachment simultaneously causes profound changes in molecular forces between the head and arm of the cross bridge
- This causes the head to tilt towards the arm and to drag the actin filament with it

- This tilt of head is called the power stroke
- Immediately after tilting, the head automatically breaks away from the active site
- Next, the head returns to its extended direction
- In this post’n it combines with new active site further down along the actin filament: then head tilts again to cause a new power stroke; then the actin filament moves another step

- Thus, heads of the cross bridges bend back and forth and step by step walk along the actin filament pulling the ends of two successive actin filaments towards the center of myosin filament
- Each cross bridge believed to operate independently of others , each attaching and pulling in a continuous repeated cycle.
- The greater the number of cross bridges with actin at any given time, the greater the force of contraction

Cross-Bridge Formation in Muscle Contraction



Muscular Contraction

- The sliding filament model
  - Muscle shortening occurs due to the movement of the actin filament over the myosin filament
  - Formation of cross-bridges between actin and myosin filaments
  - Reduction in the distance between Z-lines of the sarcomere

Sliding Filament Theory

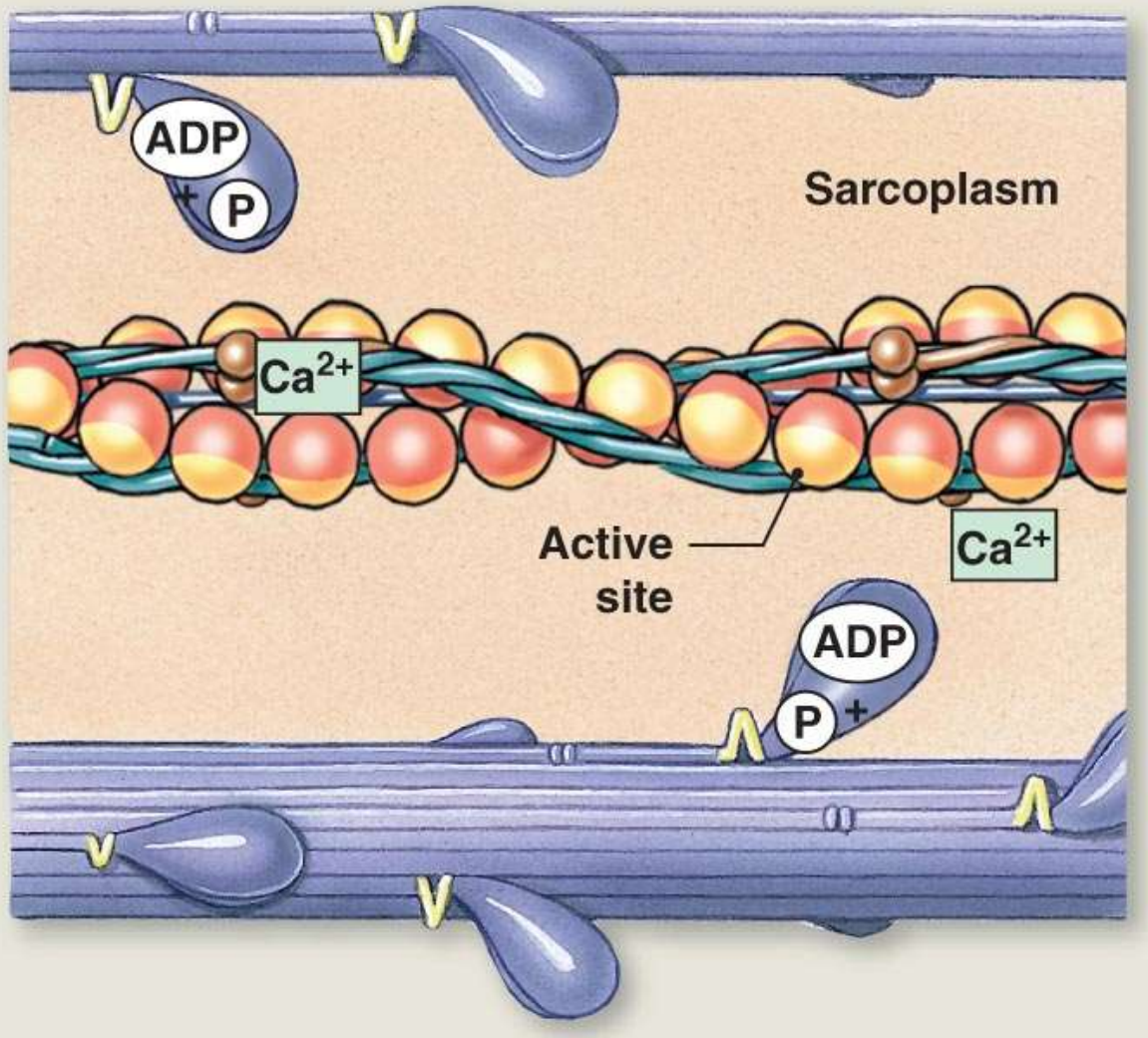
- Rest – uncharged ATP cross-bridge complex
- Excitation-coupling – charged ATP cross-bridge complex, “turned on”
- Contraction – actomyosin – ATP > ADP & Pi + energy
- Recharging – reload cross-bridge with ATP
- Relaxation – cross-bridges “turned off”

Sequence of events

1

- B4 contraction begins, head of cross bridges bind with ATP
- ATPase activity of myosin head cleaves ATP leaving cleavage products ADP & phosphate ions bound to head

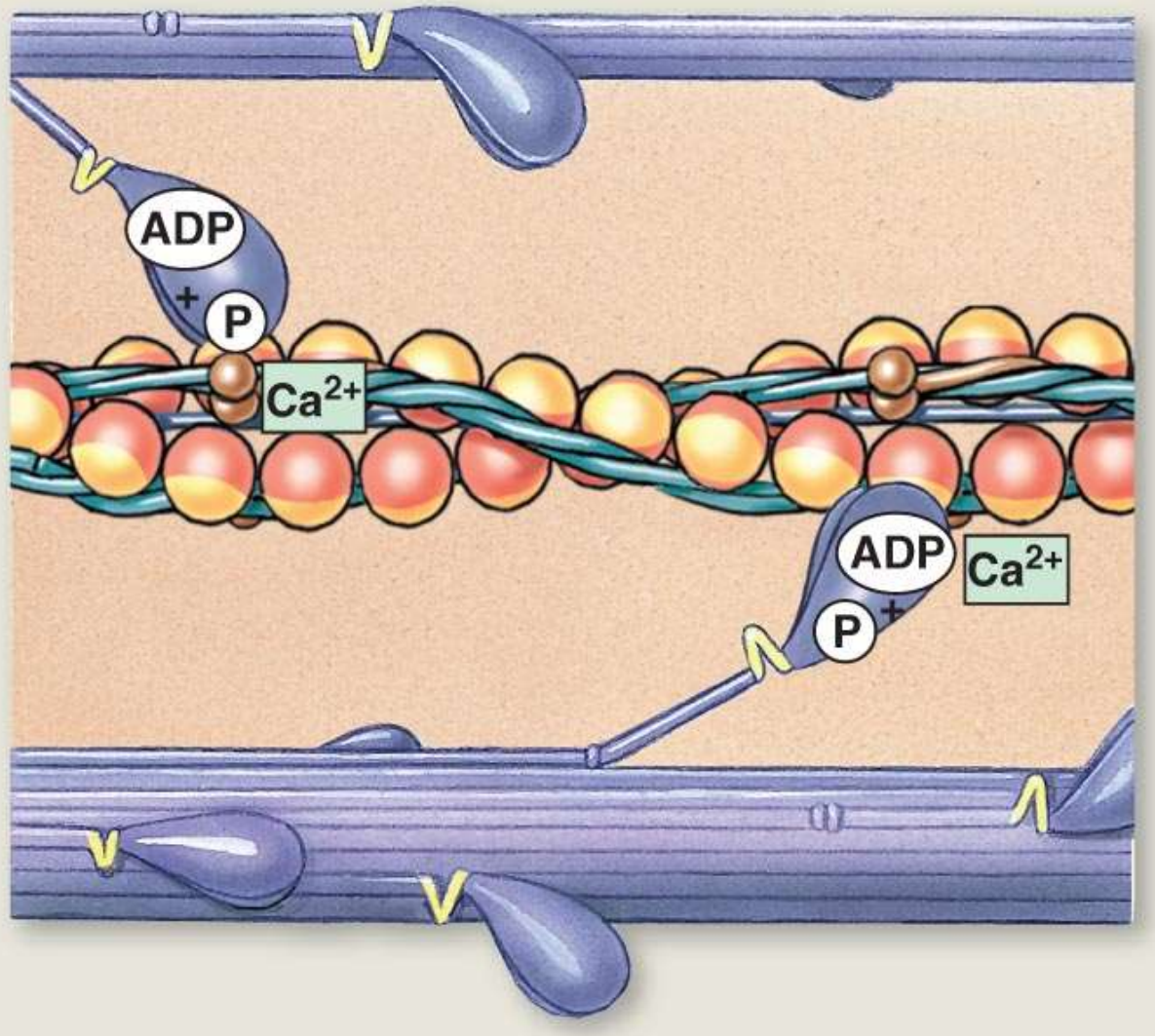
STEP 1 ACTIVE-SITE EXPOSURE



2

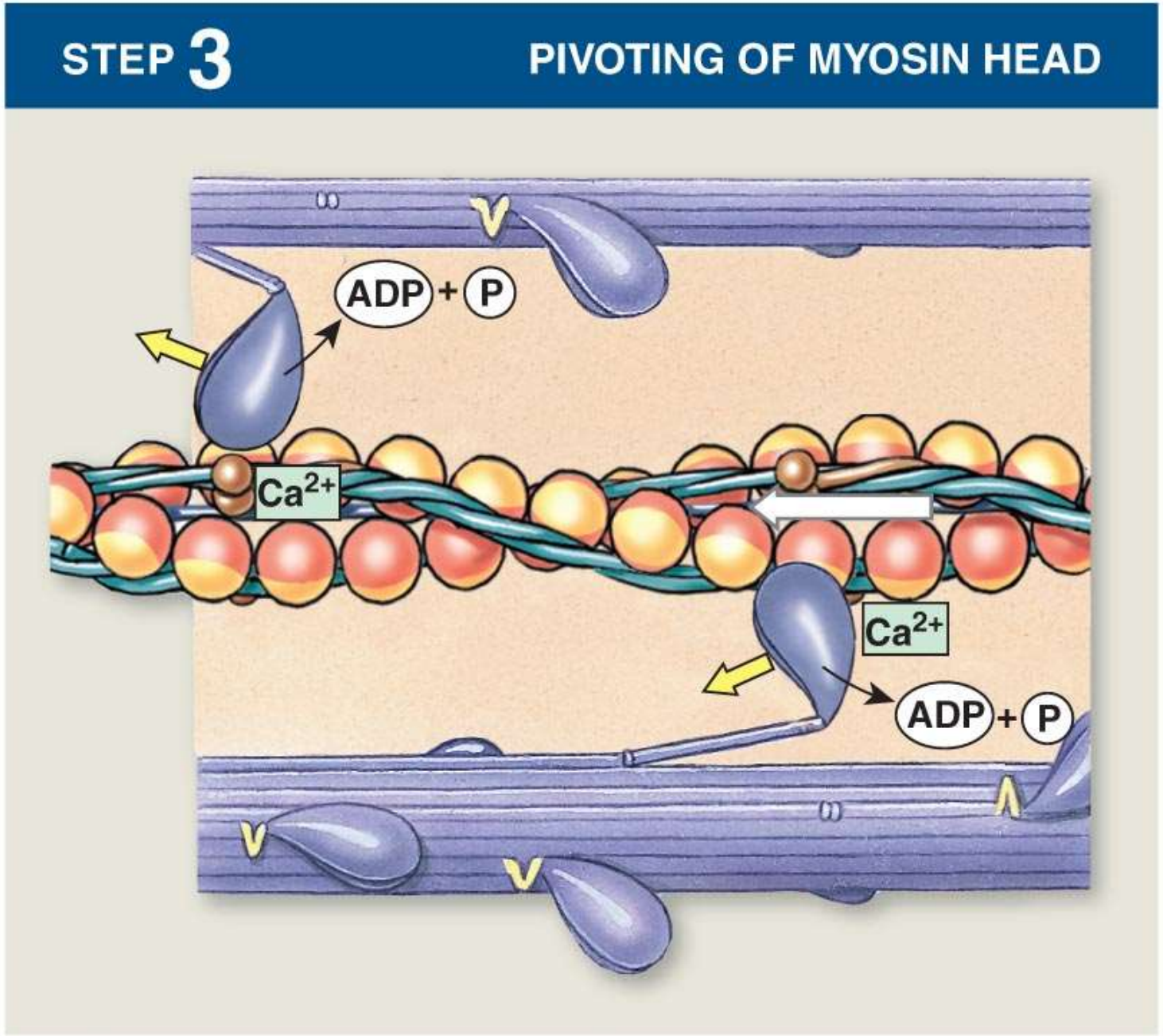
- When troponin-tropomyosin complex binds to Ca^{++} ions, active sites on the actin filament are uncovered and the myosin head binds with this

STEP 2 CROSS-BRIDGE FORMATION



3

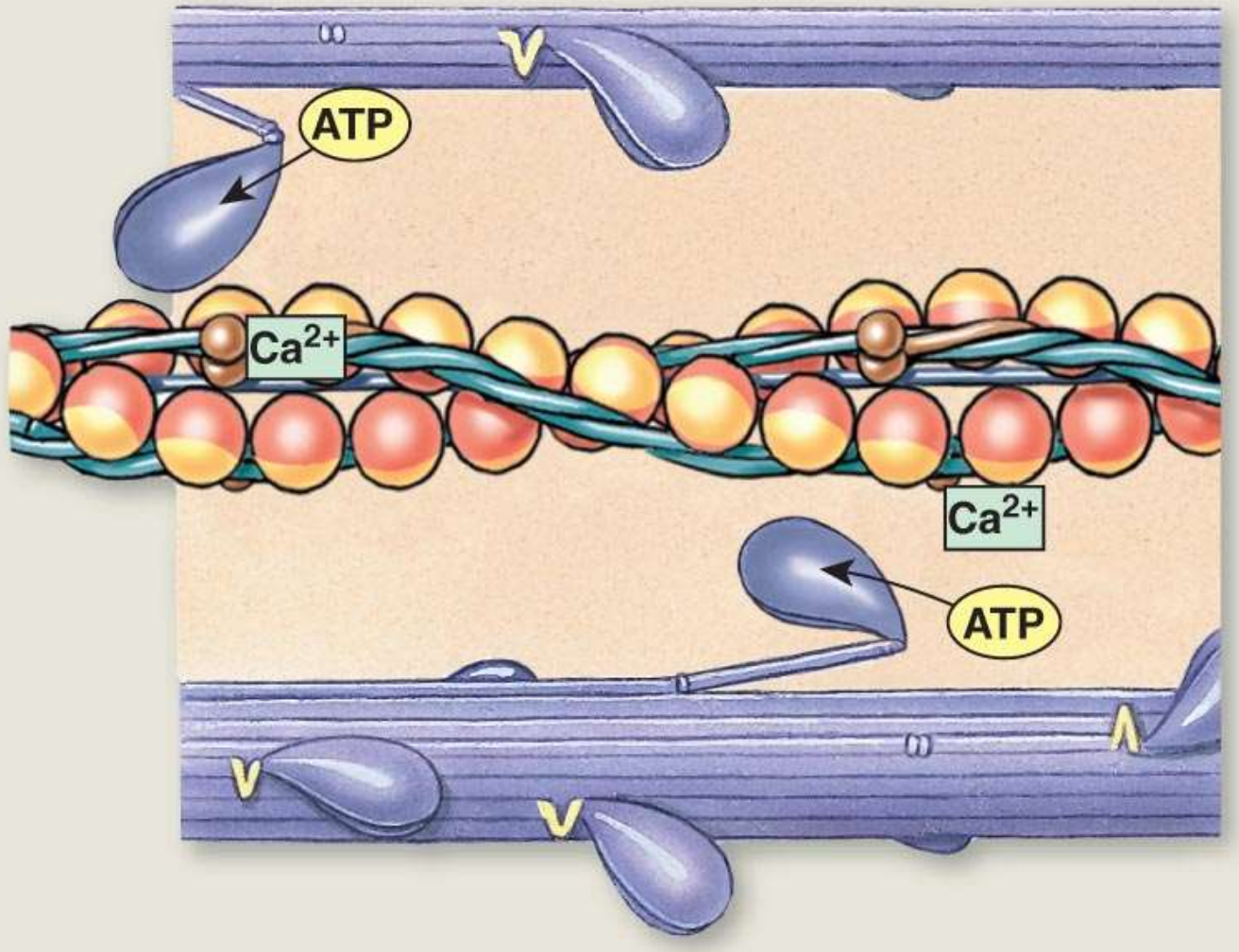
- Bond between head of cross bridge and active site of actin filament causes conformation change in the head prompting it to tilt towards arm of cross bridge
- This provides power stroke for pulling actin filament
- Energy activating power stroke is already stored by conformational changes which occurred when the ATP molecule was cleaved earlier


STEP 3
PIVOTING OF MYOSIN HEAD
ADP + P
Ca2+
Ca2+
ADP + P

4

- Once the head tilts, this allows release of ADP & Phosphate ions previously attached to the head
- At this site, a new ATP molecule binds
- This binding causes detachment of the head from actin

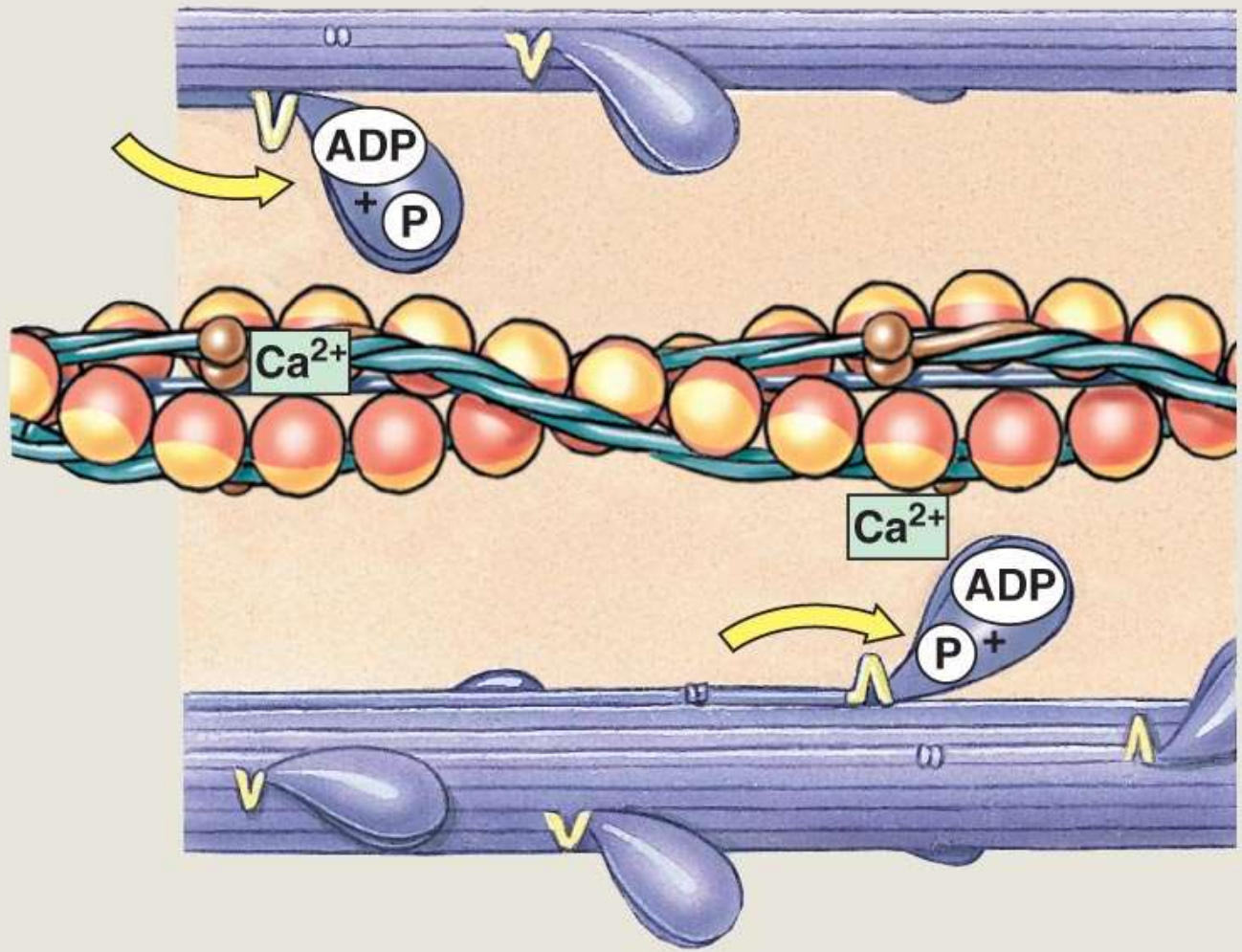
STEP 4 CROSS-BRIDGE DETACHMENT

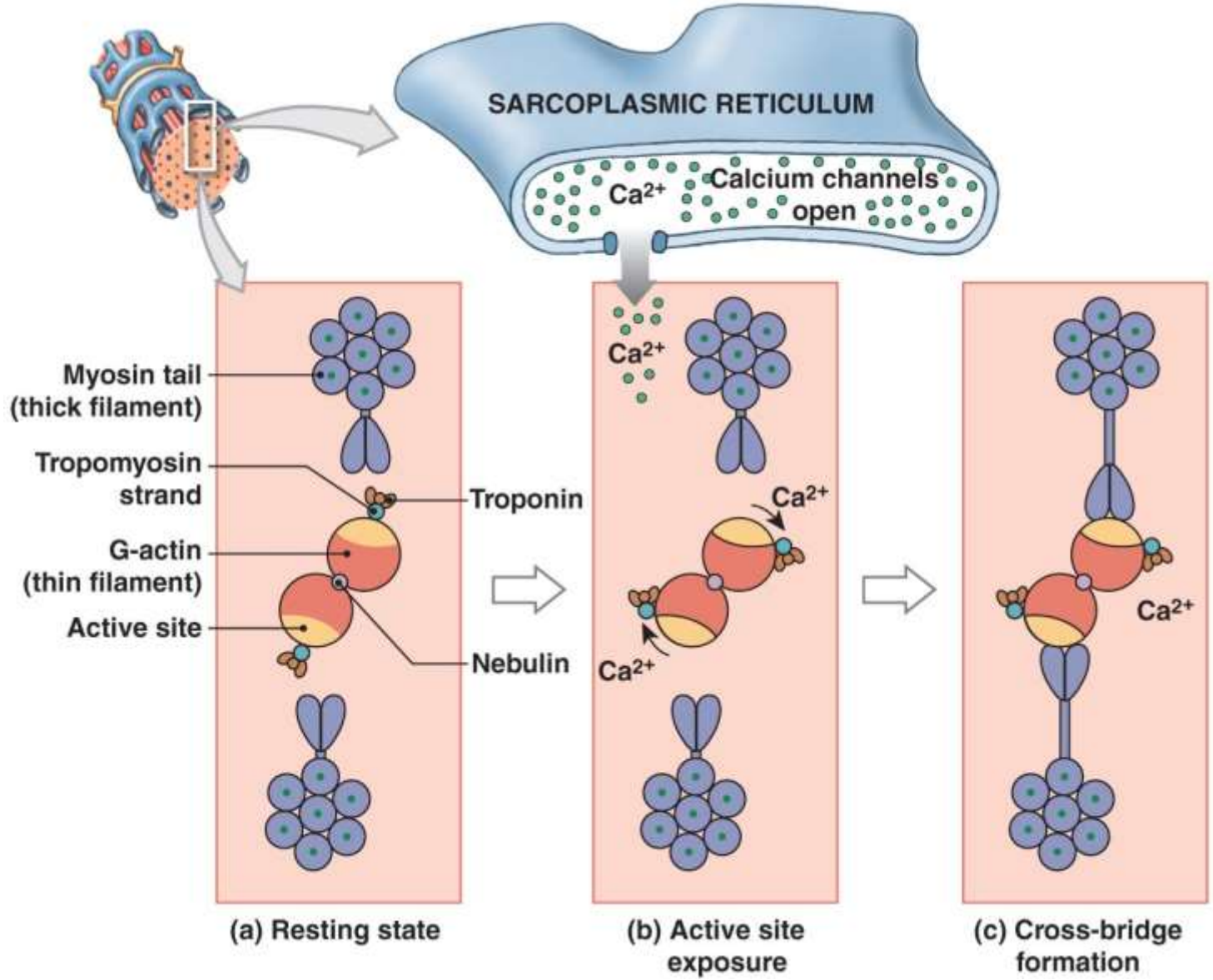


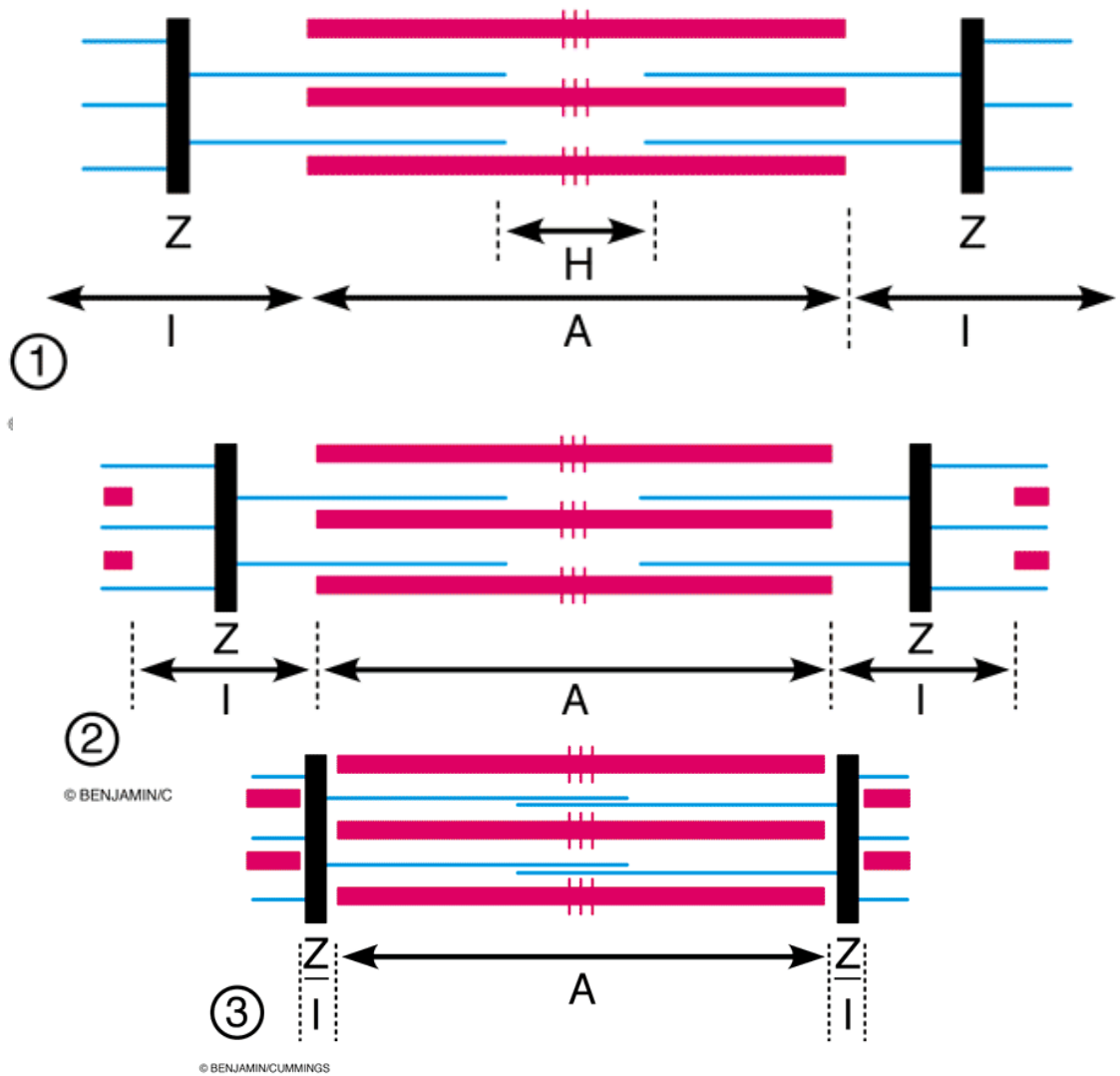
5

- After head has detached from actin, the new ATP molecule is cleaved to begin a new cycle leading to a new power stroke
- This process proceeds again and again until the actin filaments pull the Z membrane up against the ends of myosin filaments or until the load on the muscle becomes too great for further pulling to occur.

STEP 5 MYOSIN REACTIVATION




SARCOPLASMIC RETICULUM
Ca2+
Calcium channels open
Myosin tail (thick filament)
Tropomyosin strand
Troponin
G-actin (thin filament)
Active site
Nebulin
Ca2+
Ca2+
Ca2+
Ca2+
(a) Resting state
(b) Active site exposure
(c) Cross-bridge formation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