General physiology
Second Semester 2023-2024
Lecture 26
Skeletal Muscle Contraction I

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Lecture objectives

- List the three types of muscles and their primary function
- Review the gross anatomy of the muscle skeletal muscles and microscopic of the muscle fibers
- Identify the structural features of muscle fibers and the components of myofibril
- Define the sarcomere and identify the arrangements of contractile and structural proteins within the sarcomere
- Describe the contractile proteins in the myofibril and their molecular arrangement of Actin and Myosin
- List the cytoskeleton proteins within the sarcomere and their function
- Describe the events in a muscle contraction cycle and the myosin ATPase cycle
- Define the role of ATP in muscle contraction
- Describe the sliding-filament model of sarcomere contraction
- Describe the role of calcium ions in muscle contraction and excitation contraction coupling
- Define Rigor Mortis Phenomenon

Types of Muscle

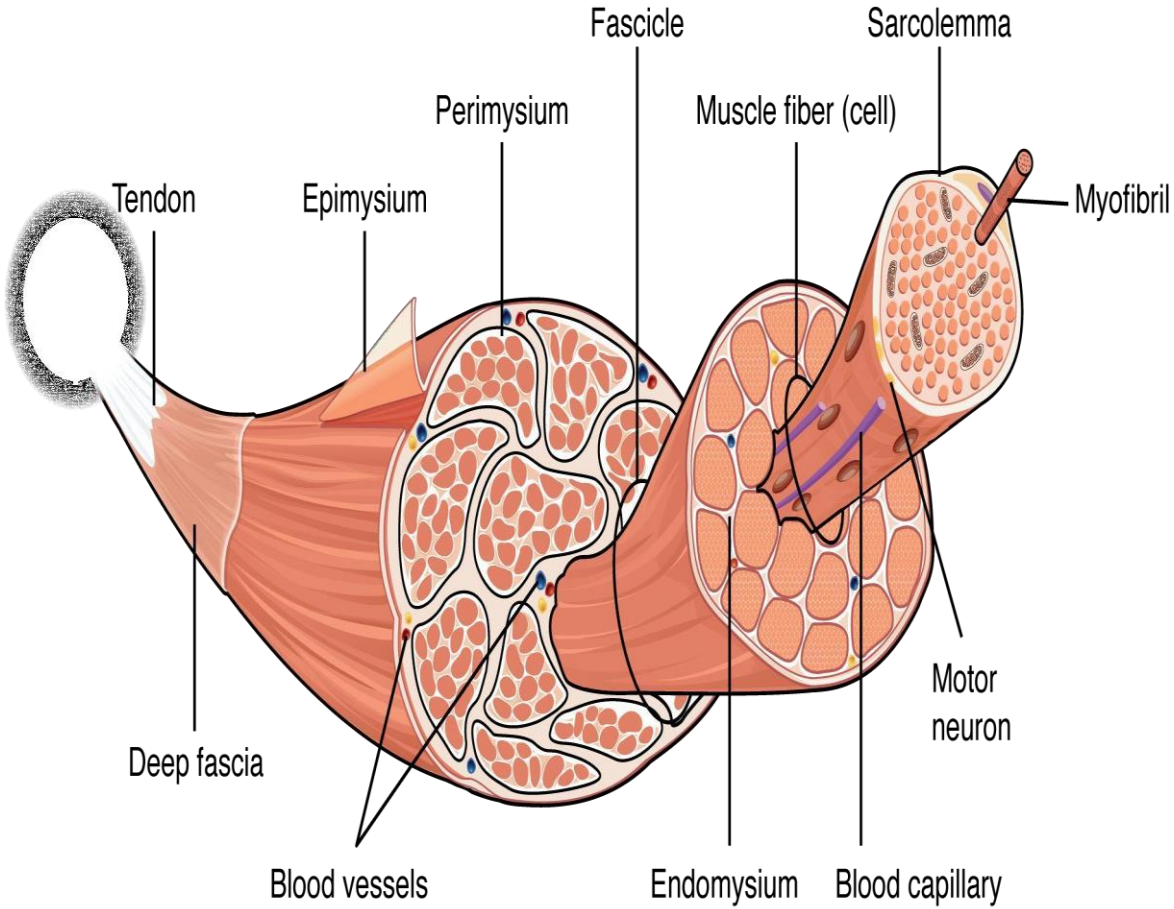
- **Skeletal**
  - Attached to bones of skeleton
  - Makes up 40% of body weight
  - Responsible for locomotion, facial expressions, posture, respiratory movements, vocalization
  - Joints stabilization etc.
  - Voluntary in action; controlled by somatic motor neurons
  - Striated
  - Heat production
  - Excitable tissue
  - Contract in response to nerve stimulation

Types of muscles

- **Smooth**
- In the walls of hollow organs, blood vessels, eye, uterus, skin
  - Some functions: propel urine, mix food in digestive tract, dilating/constricting pupils, regulating blood flow, regulate airways resistance etc
  - In some locations, autorhythmic
  - Controlled involuntarily by endocrine and autonomic nervous systems
  - Some have spontaneous activity
  - Non striated
- **Cardiac**
  - Striated
  - Heart: major source of pumping blood and movement of blood in circulatory system
  - Autorhythmic
  - Controlled involuntarily by endocrine and autonomic nervous systems

Functional Anatomy of skeletal muscles .

- Epimysium – loose connective tissue sheath surrounding each skeletal muscle
- Muscle Fasciculi – visible bundles that compose the muscle – these bundles are composed of multiple muscle fibers (cells)
- Perimysium – loose connective tissue surrounding the muscle fasciculi
- Endomysium – loose connective tissue surrounding each muscle fiber – functions to separate and electrically isolate each cell

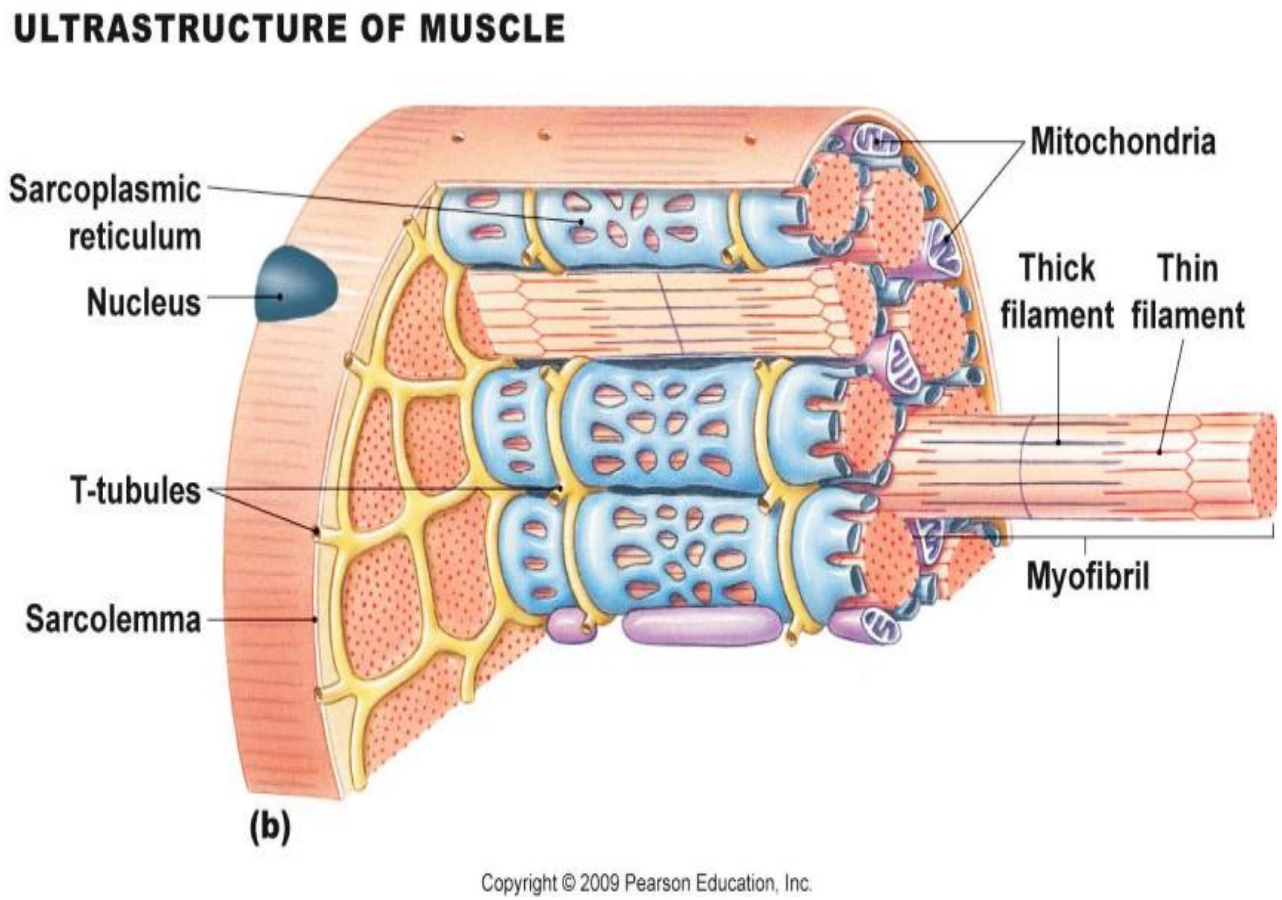


Ultrastructure of muscle fiber

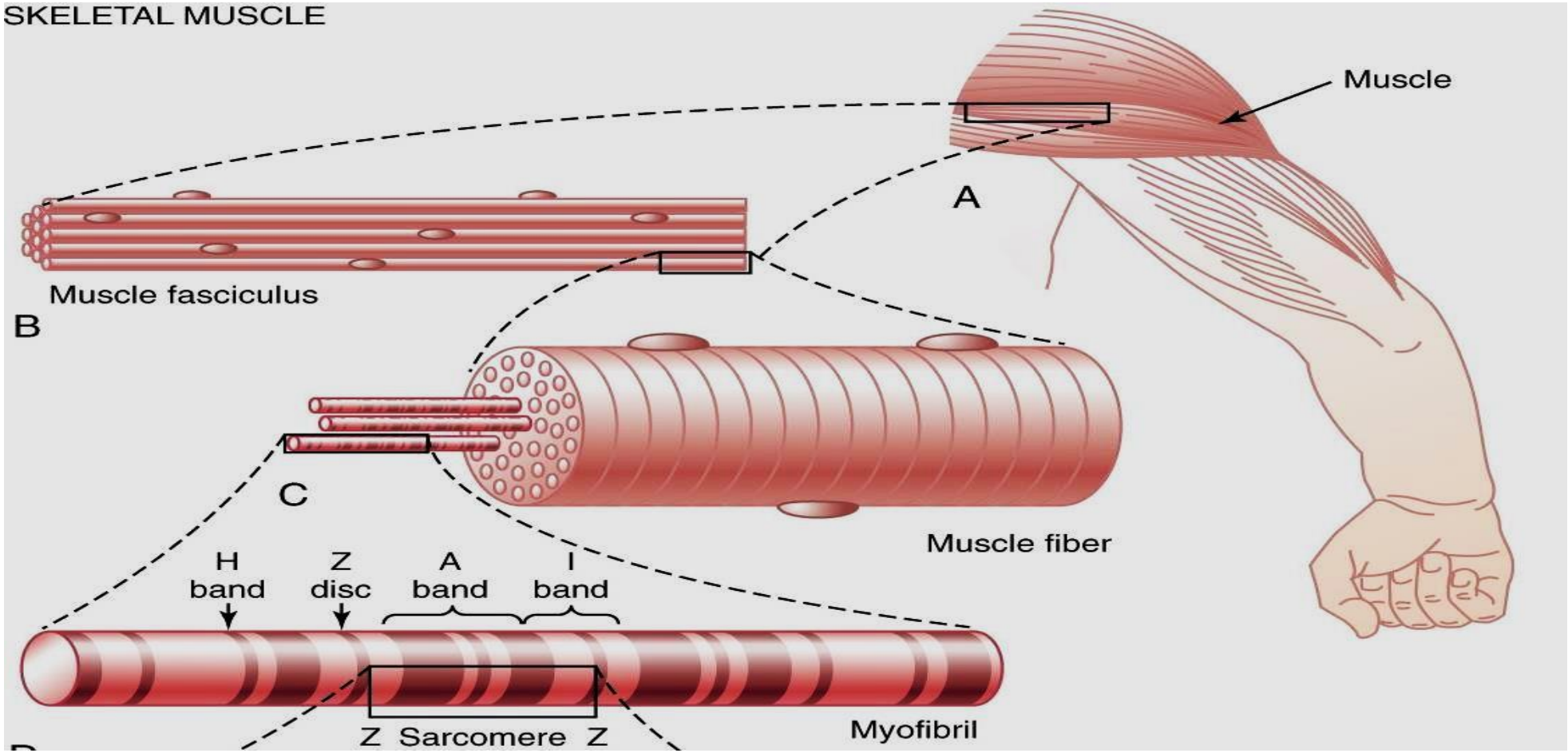
Muscle Fiber – a single cylindrical cell that contains several nuclei located at the periphery (edge) of the cell – largest are up to 30cm long, .15mm in diameter, and containing several thousand nuclei

Myofibril – thread like structure extending through the muscle fiber from one end to the other in the sarcoplasm – composed of two myofilaments (protein fibers)-actin and myosin

Sarcolemma – cell membrane of a muscle fiber



Skeletal muscle organization and Ultrastructure of muscle fiber



Structure of Skeletal Muscle : Functional Anatomy

- all skeletal muscles are composed of numerous fibers ranging from 10 to 80 micrometers in diameter.
- In most skeletal muscles, each fiber extends the entire length of the muscle.
- Each of these fibers is made up of successively smaller subunits know as myofibril.
- Each muscle fiber contains several hundred to several thousand myofibrils which are thread like structure extending through the muscle fiber from one end to the other in the sarcoplasm

Ultrastructure of muscle fibers

- Each myofibril is composed of about 1500 adjacent myosin filaments and 3000 actin filaments, which are large polymerized protein molecules that are responsible for the muscle contraction
- The thick filaments are myosin, and the thin filaments are actin
- Actin myofilaments – thin filaments resembling two strands of pearls twisted together
- Myosin myofilaments – thick filaments resembling bundles of miniature golf clubs
- The myosin and actin myofilaments , partially interdigitate and thus cause the myofibrils to have alternate light and dark

- The light bands contain only actin filaments and are called *I bands* because they are *isotropic* to polarized light.
- The dark bands contain myosin filaments, as well as the ends of the actin filaments, where they overlap the myosin, and are called *A bands* because they are *anisotropic* to polarized light. Note also the small projections from the sides of the myosin filaments in
- . These projections are *cross-bridges.* It is the interaction between these cross-bridges and the actin filaments that causes contraction

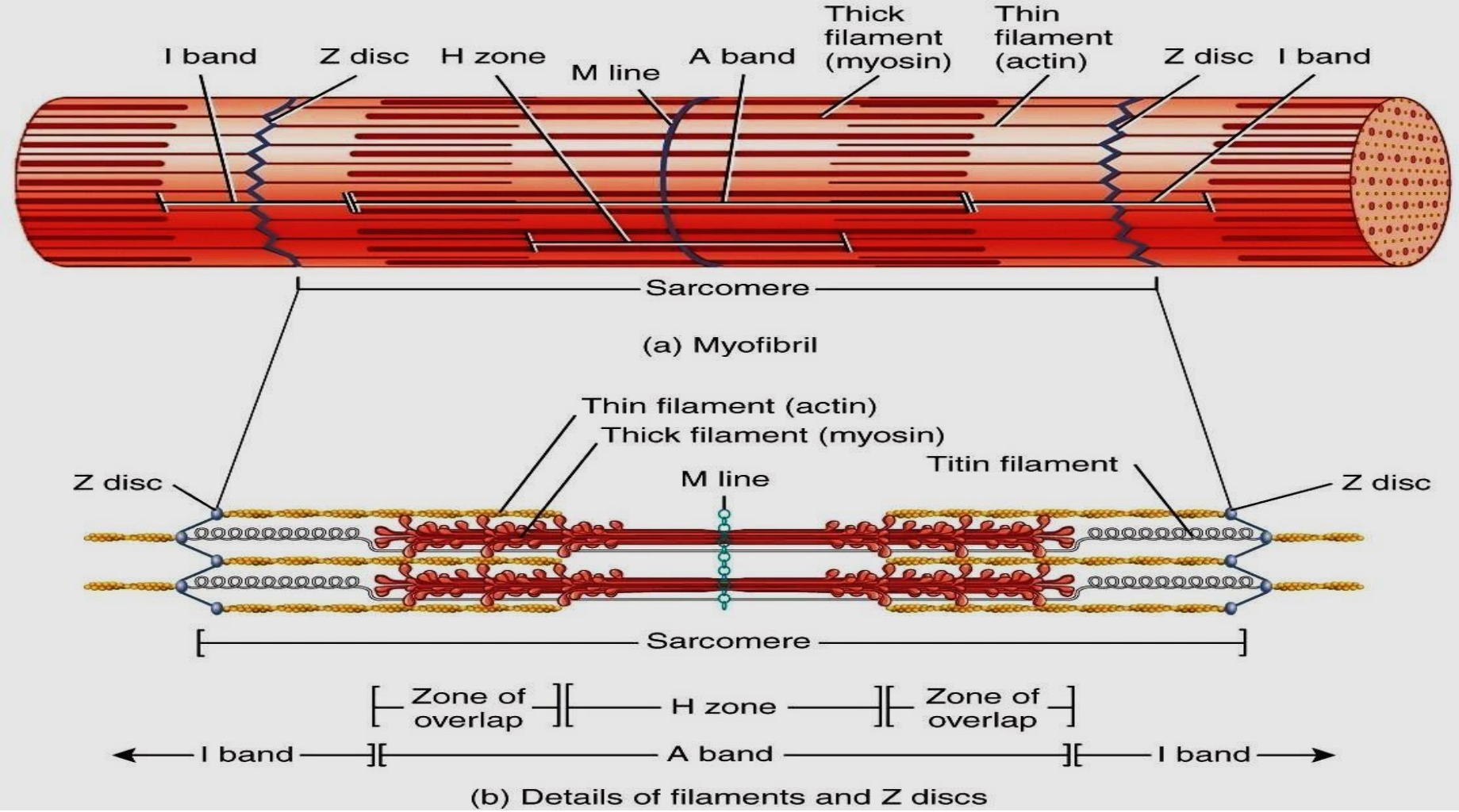
Z disks

- .The Z disk, which is composed of filamentous proteins, passes crosswise across the myofibril and also crosswise from myofibril to myofibril, attaching the myofibrils to one another all the way across the muscle fiber.
- Therefore, the entire muscle fiber has light and dark bands, as do the individual myofibrils. These bands give skeletal and cardiac muscle their striated appearance.
- From Z disc, actin filaments extend in both directions to interdigitate with the myosin filaments.

Ultrastructure of muscle fiber
Sarcomere

- Sarcomere – the basic structural and functional unit of skeletal muscle – the smallest portion of skeletal muscle capable of contraction
- It is he portion of the myofibril (or of the whole muscle fiber) that lies between two successive Z disks. When the muscle fiber is contracted, as shown at the bottom of the length of the sarcomere is about 2 micrometers.
- At this length, the actin filaments completely overlap the myosin filaments, and the tips of the actin filaments are just beginning to overlap one another.
- At this length the muscle can generate its greatest force of contraction

The Arrangement of a Sarcomere



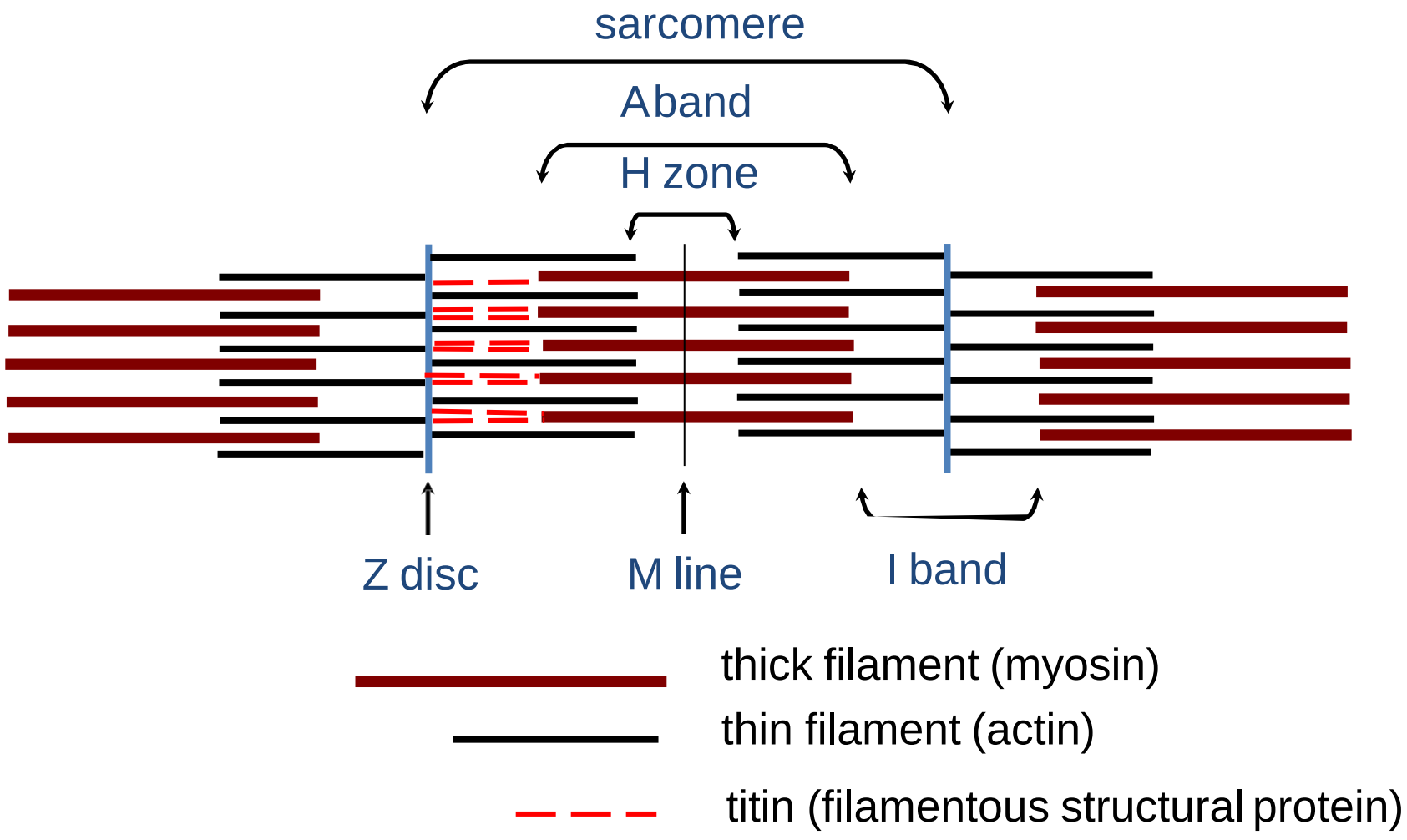
Titin filaments and its functions

- **Titin Filamentous Molecules Keep the Myosin and Actin Filaments in Place**
- The side-by-side relationship between the myosin and actin filaments is maintained by a large number of filamentous molecules of a protein called *titin*
- Also, because it is filamentous, it is very *springy.* These springy titin molecules act as a framework that holds the myosin and actin filaments in place so that the contractile machinery of
- One end of the titin molecule is elastic and is attached to the Z disk, acting as a spring and changing length as the sarcomere contracts and relaxes.
- The other part of the titin molecule tethers it to the myosin thick filament.
- The titin molecule may also act as a template for the initial formation of portions of the contractile filaments of the sarcomere, especially the myosin filaments.

Ultrastructure of sarcomeres
Zones and bands of myofibril

- Zones – areas of measurement that make up the sarcomere to show contraction in the sliding filament model
- M line – center line of a sarcomere and attachment site for myosin filaments
- H zone – area of the sarcomere extending out from the M line on either side - composed of myosin only (no actin)
- A band – area of the sarcomere extending from one end of the myosin to the other end, includes the M line, the H zone, and the area where actin and myosin overlap
- Z disk – the area of the sarcomere indicating the ends of the sarcomere and the attachment site for actin filaments.
- I band – area that includes the Z disk , made out of 2 ends of adjoining sarcomeres, and composed of actin only (no myosin)
- Sliding filament model – used to show/explain muscle contraction with one sarcomere – in this model myosin and actin filaments slide past one another shortening or narrowing the H zone and I band, the filaments themselves do not shorten

The Sarcomere



The Actin Filament

Form the I band
- Anchored at one end to Z disc

Overlap with myosin filament in a portion of the A band

1 µm long: very uniform, *nebulin* forms guide for synthesis

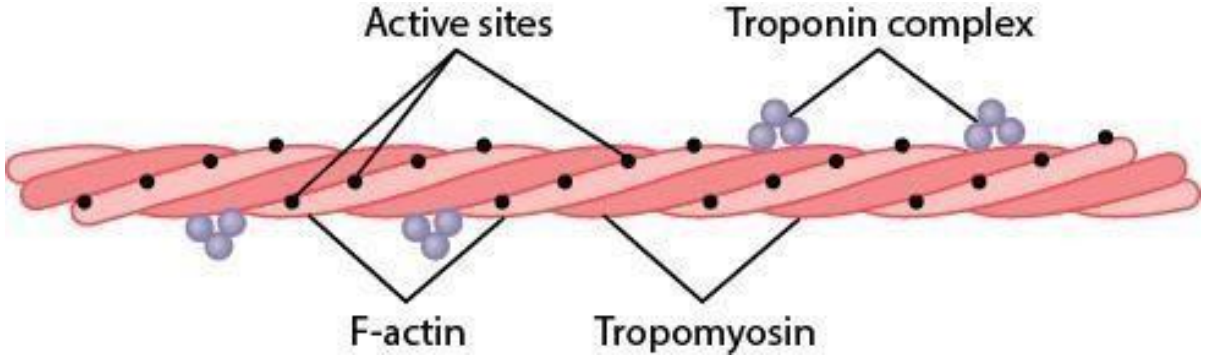


Figure 6-7

F-actin is The backbone of the actin filament is a double-stranded *F-actin protein molecule*

- composed of polymerized G-actin
- ADP bound to each G-actin (active sites)
- myosin heads bind to active sites

Tropomyosin

- covers active sites
- prevents interaction with myosin

Troponin

- **I** - binds actin
- **T** - binds tropomyosin
- **C - binds Ca^{2+}**

The Myosin filaments and myosin molecule

- Present in the A band
- Myosin Filaments are composed of multiple myosin molecules which is six polypeptide chain
- Two heavy chains Spirally around each other to form the tail
- The four light chains are also part of the myosin head, two to each head. .
- Thus each myosin molecule has two “heads” attached to a single “tail
- “head” region - site of ATPase activity

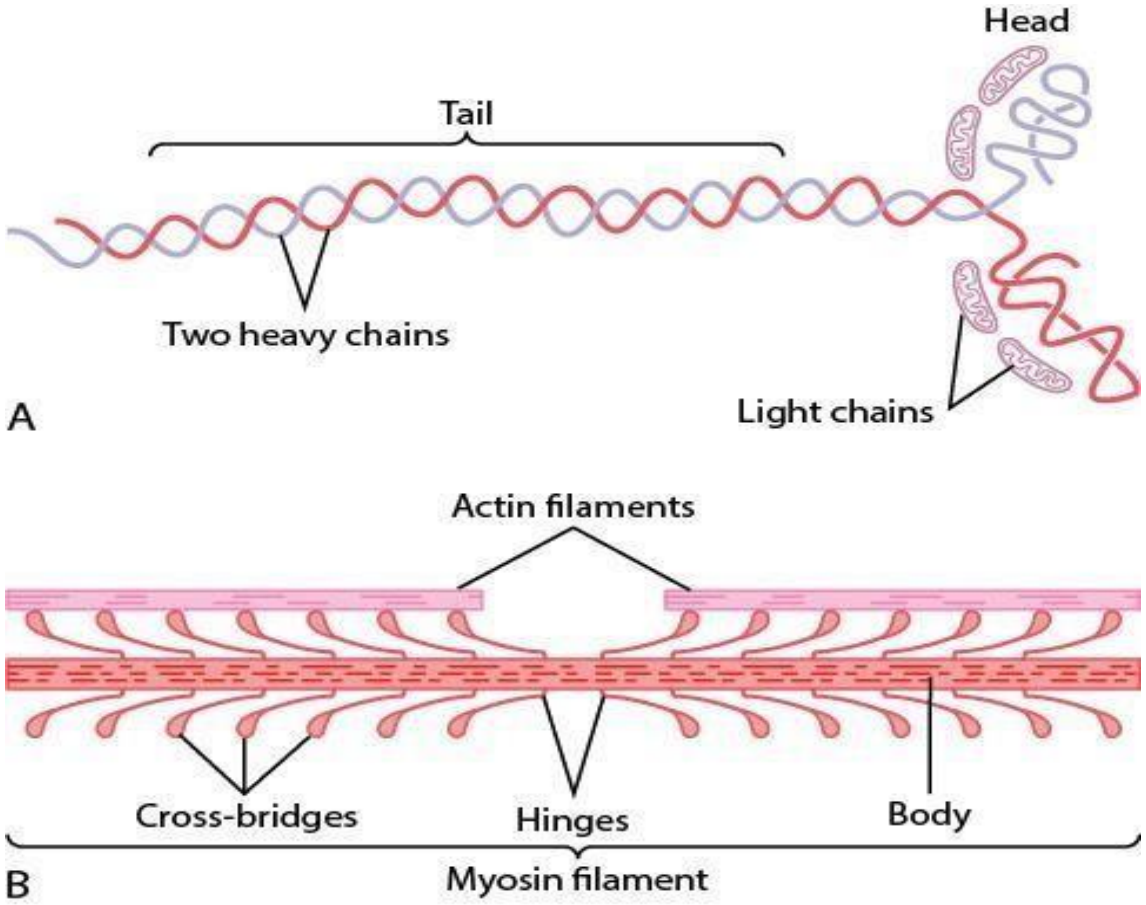
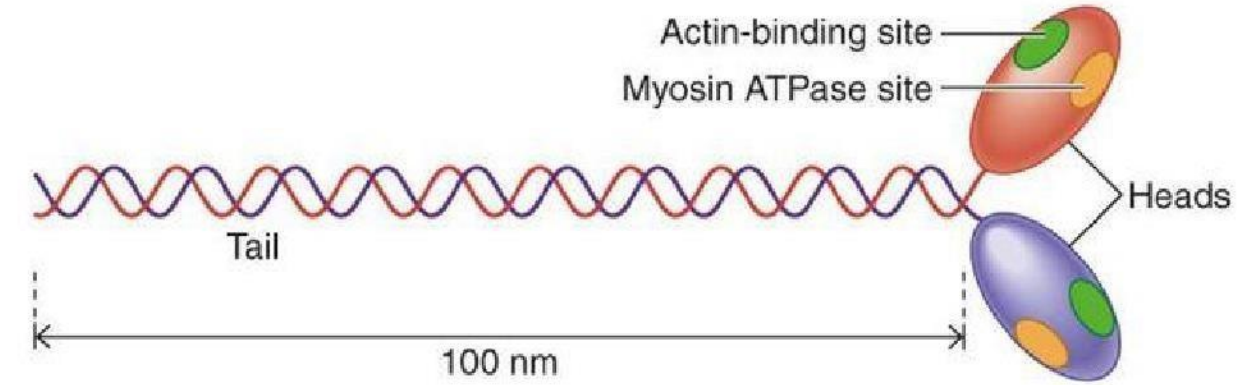
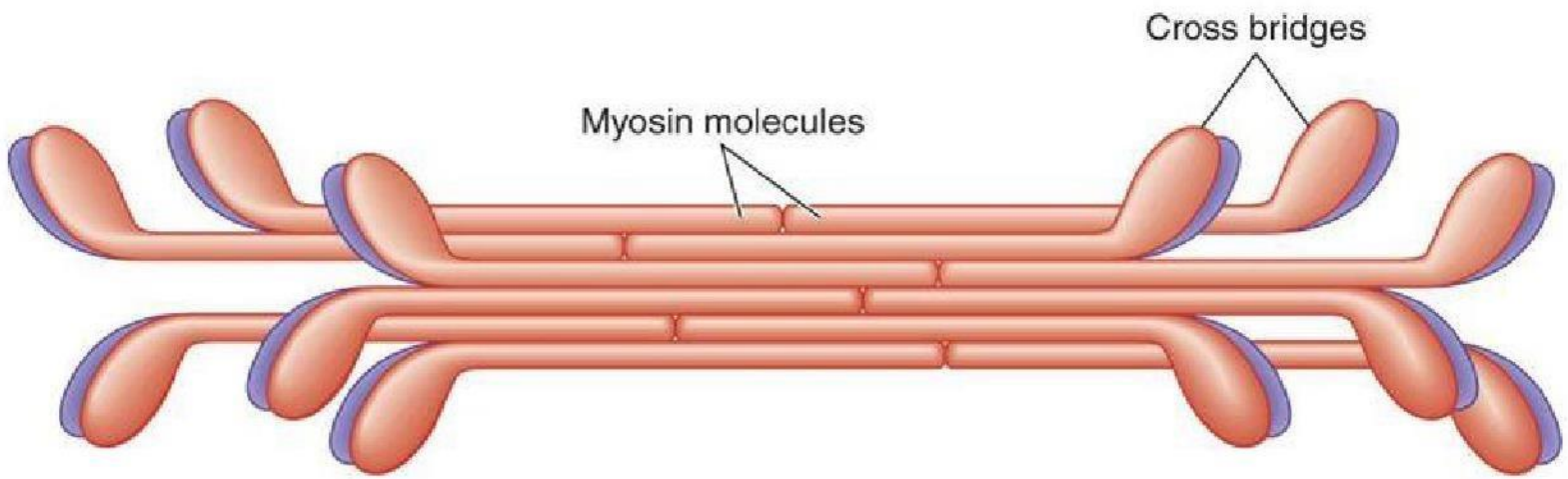


Fig. 6.5

Structure and Arrangement of Myosin Molecules Within Thick Filament

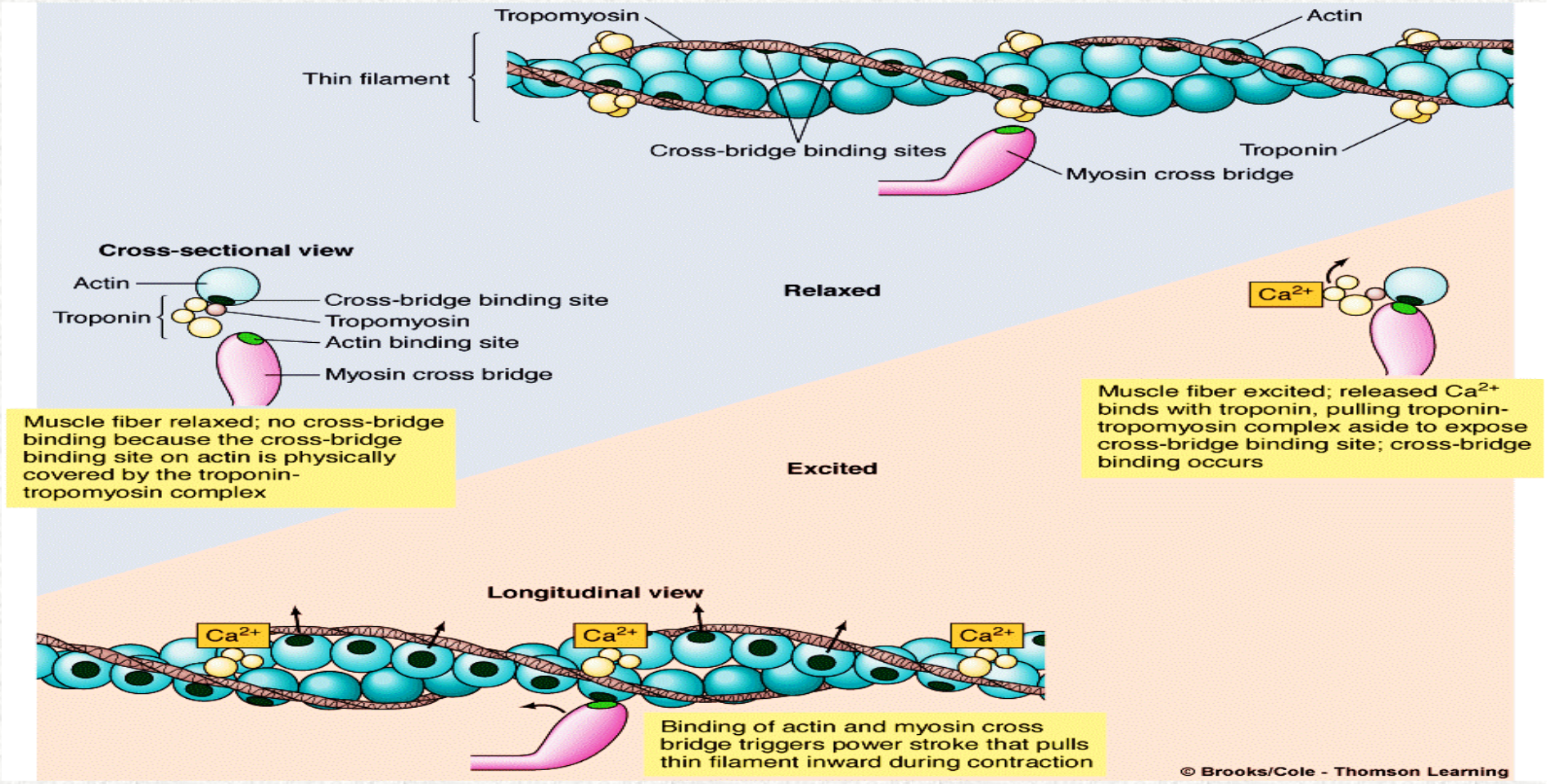


(a) Myosin molecule

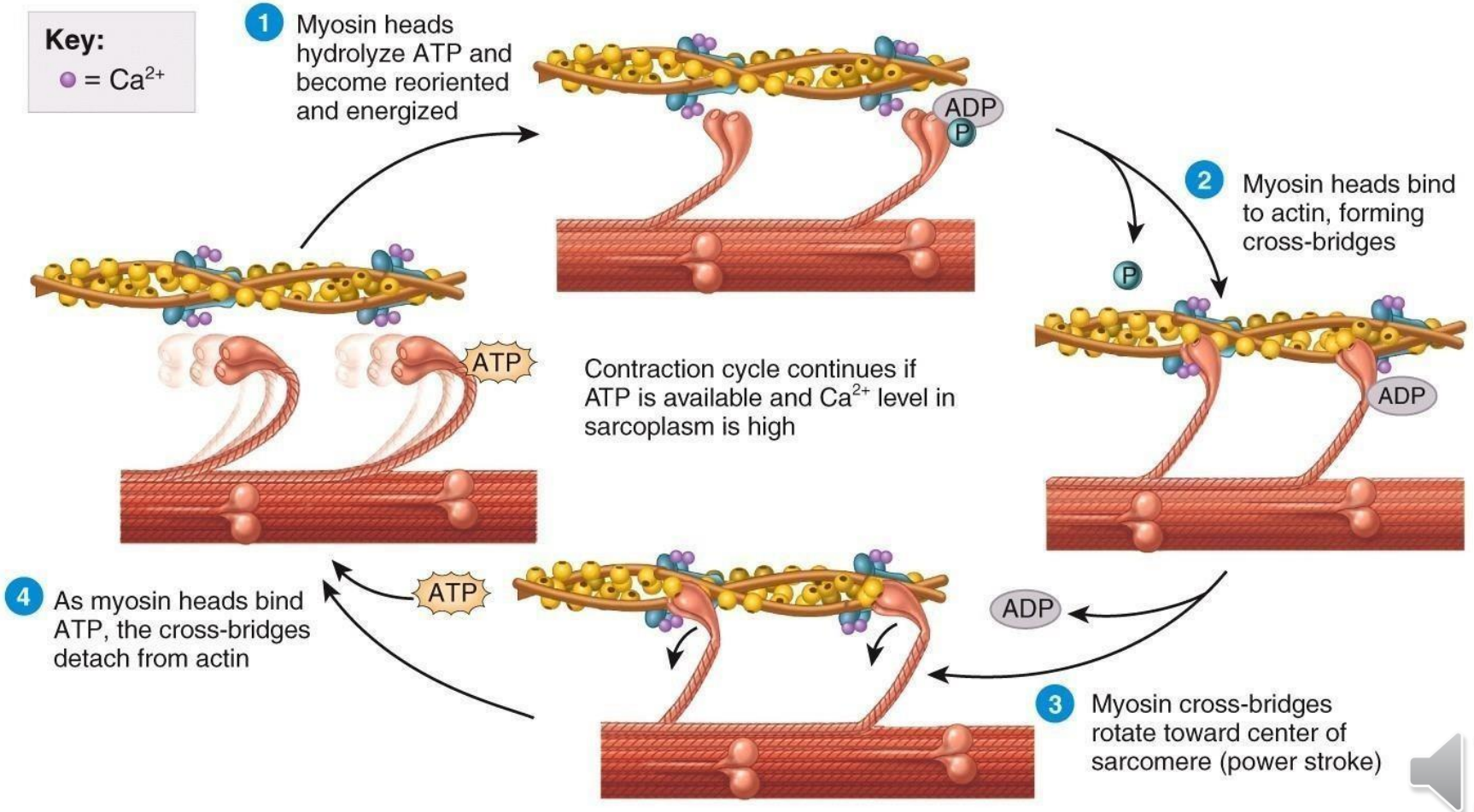


(b) Thick filament

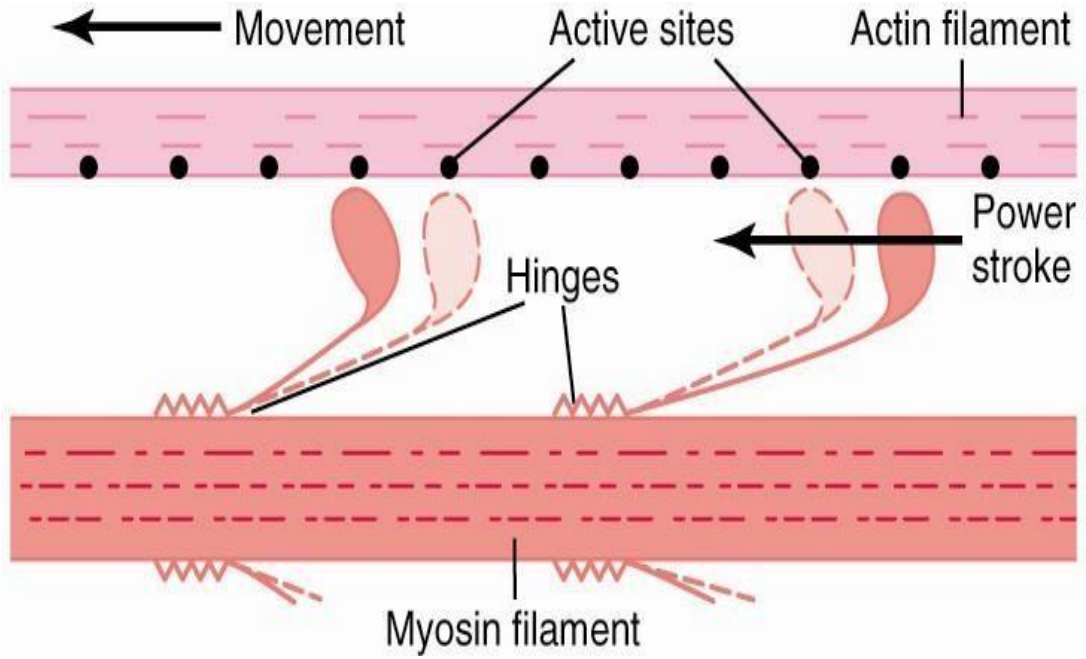
Contraction and relaxation cycle



Contraction and relaxation cycle



“Walk-Along” Theory



The new alignment of forces causes the head to tilt toward the arm and to drag the actin filament along with it. This tilt of the head is called the *power stroke.*

The 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 toward the center of the myosin filament

The greater the number of cross-bridges in contact with the actin filament at any given time, the greater the force of contraction.

The Sliding Filament Mechanism
Relaxed and Contracted States of sarcomeres

Contraction results from the sliding action due to engagement and coupling of actin and myosin filaments
It shows the relaxed state of a sarcomere (top) and the contracted state (bottom). In the relaxed state, the ends of the actin filaments extending from two successive Z disks barely overlap one another.
Conversely, in the contracted state, these actin filaments have been pulled inward among the myosin filaments, so their ends overlap one another to their maximum extent. Also, the Z disks have been pulled by the actin filaments up to the ends of the myosin filaments. Thus, muscle contraction occurs by a *sliding filament mechanism.*

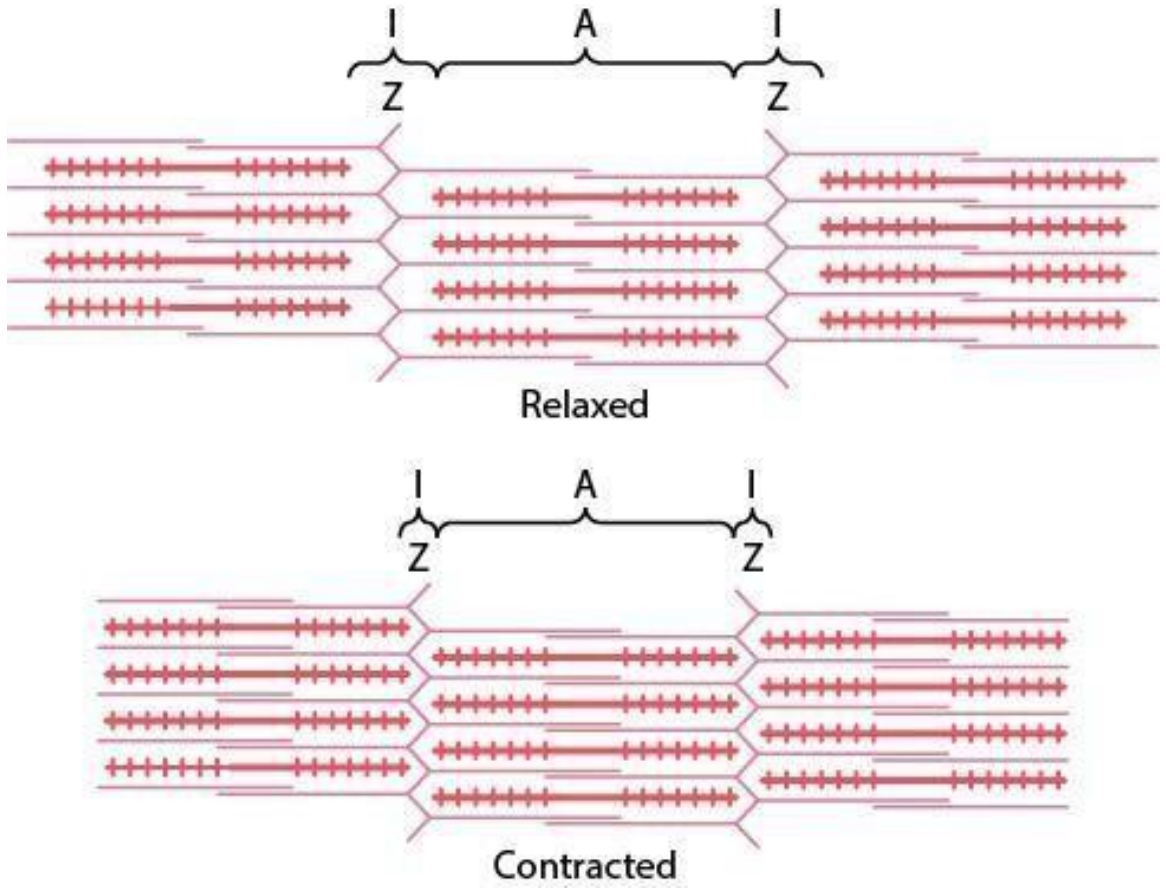
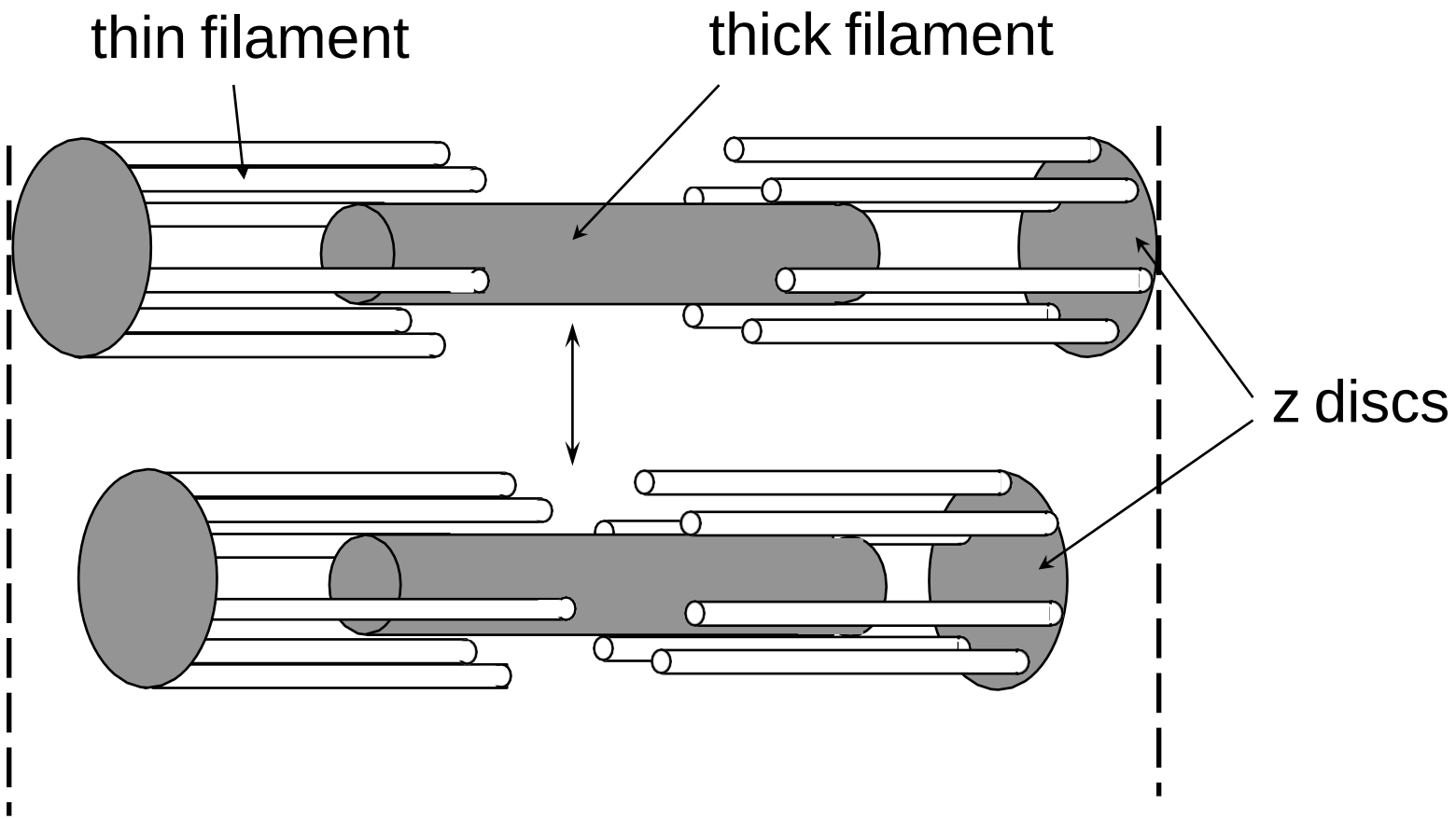


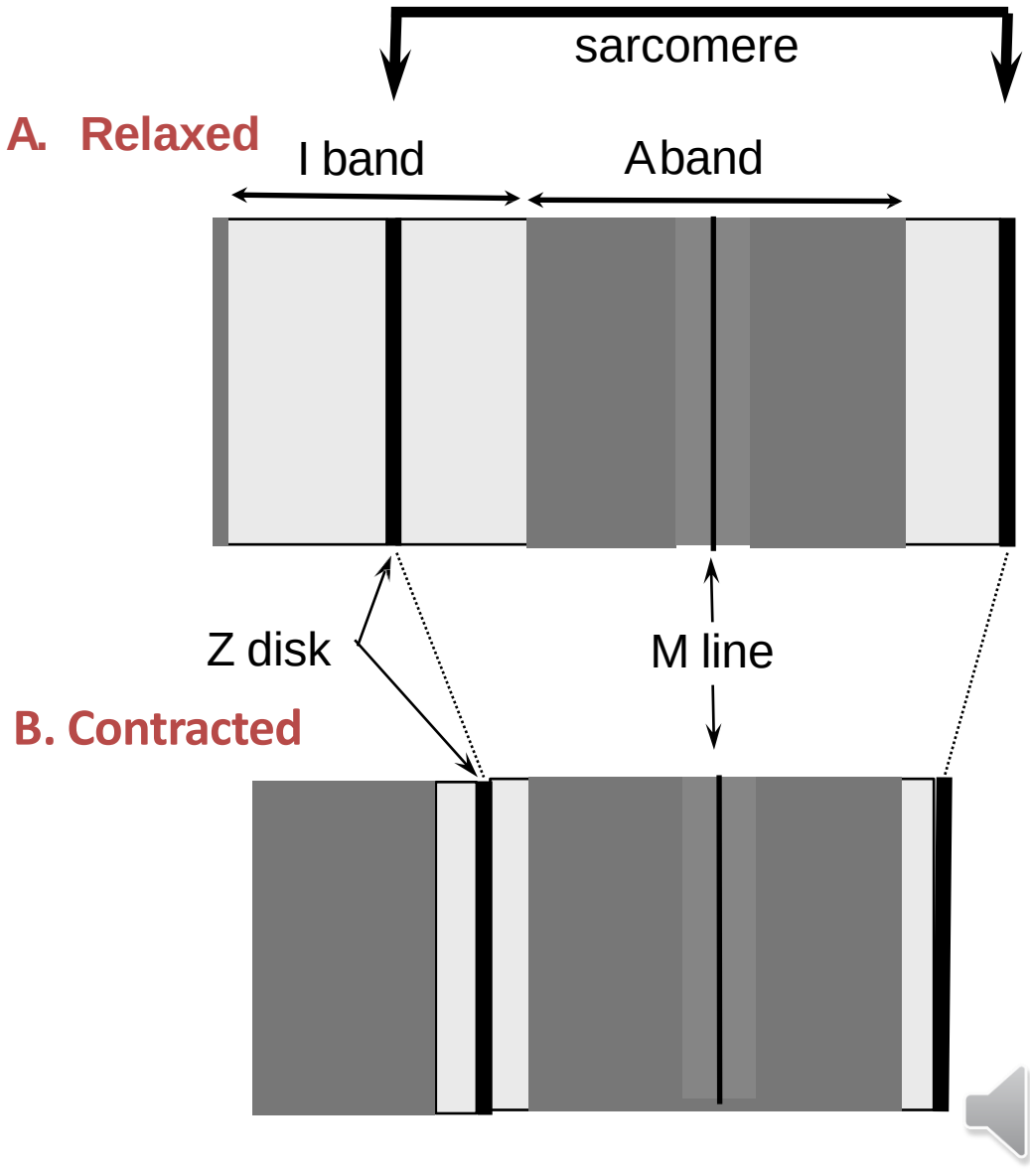
Figure 6-5

Which band shortens - I or A?



Which band shortens - I or A?

- The A band appearsdark
- The I band appears light
  - So, when the I band filament is pulled into the A band, the I band is obscured!
- The I band appears to shorten.



Role of ATP and Fenn effect

- Large amounts of ATP are cleaved to form ADP during the contraction process, and the greater the amount of work performed by the muscle, the greater the amount of ATP that is cleaved; this phenomenon is called the *Fenn effect*
- Before contraction begins, the heads of the cross bridges bind with ATP. The ATPase activity of the myosin head immediately cleaves the ATP but leaves the cleavage products, ADP plus phosphate ion, bound to the head. In this state, the conformation of the head is such that it extends perpendicularly toward the actin filament but is not yet attached to the actin
- When the troponin-tropomyosin complex binds with calcium ions, active sites on the actin filament are uncovered and the myosin heads then bind with these sites
- When Cross bridges formed the energy previously stored by cleavage of ATP in the relaxed state is used for the power stroke

Role of ATP : Continue

- Once the head of the cross-bridge tilts, release of the ADP and phosphate ion that were previously attached to the head is allowed.
- At the site of release of the ADP, a new molecule of ATP binds. This binding of new ATP causes detachment of the head from the actin.
- After the head has detached from the actin, the new molecule of ATP is cleaved to begin the next cycle, leading to a new power stroke.
- That is, the energy again “cocks” the head back to its perpendicular position ready to begin the new power stroke cycle

Rigor Mortis

1. Myosin head attached to actin

RIGOR

Rigor mortis:

- state of contracture that occurs following death
- due to loss of ATP

Cytoskeletal Proteins

- Longitudinal cytoskeletal proteins include two large proteins called titin and nebulin
- Titin
  - elastic anchor protein
  - Helps align the thick filament
  - Adds an elastic element to the sarcomere.
    - Titin is anchored at the M-Line, runs the length of myosin, and extends to the Z disc.
- Nebulin
  - stabilizing protein associated with the thin filament
  - None elastic
  - Spans the length of the thick filament
- Myomesin plays an important in the structure of sarcomeres. They are found in the M-band region of the sarcomere, between the thick filaments (myosin).
- It's main purpose in this setting is to provide structural integrity by linking the antiparallel myosin fibers and titin filaments which are connected to the Z-discs

Cytoskeletal Proteins : Transverse cytoskeletal proteins

- Transverse cytoskeletal proteins link thick and thin filaments, forming a “scaffold” for the myofibrils and linking sarcomeres of adjacent myofibrils
- A system of intermediate filaments holds the myofibrils together, side by side
- **Dystrophin:** An acting binding protein which anchors he entire
- myofibrillar array to the cell membrane
- In patients with muscular dystrophy, dystrophin is defective or absent