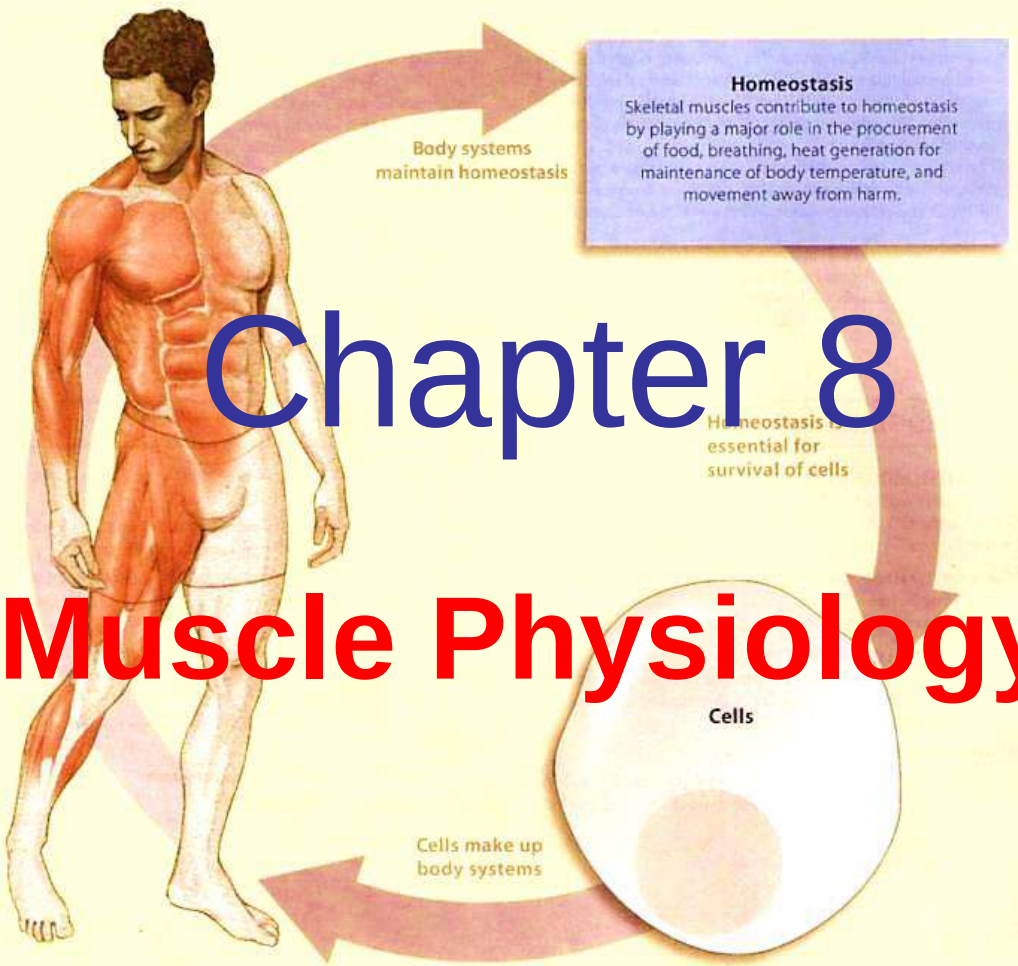
Chapter 8

Muscle Physiology



Muscles are the contraction specialists of the body. **Skeletal muscle** attaches to the skeleton. Contraction of skeletal muscles moves bones to which they are attached, allowing the body to perform a variety of motor activities. Skeletal muscles that support homeostasis include those important in acquiring, chewing, and swallowing food and those essential for breathing. Skeletal muscle contraction is also used to move the body away from harm. Heat-generating muscle contractions are important in temperature regulation. Skeletal muscles are also used for nonhomeostatic activities, such as dancing or operating a computer. **Smooth muscle** is found in the walls of hollow organs and tubes. Controlled contraction of smooth muscle regulates movement of blood through blood vessels, food through the digestive tract, air through respiratory airways, and urine to the exterior. **Cardiac muscle** is found only in the walls of the heart, whose contraction pumps life-sustaining blood throughout the body.

Introduction

- Cell division and WBCs are examples of intracellular machinery for movement.

- Muscle cells are the contraction specialists of the body due to the ability of there components to contract by developing tension and shortening.

Control contractive of the muscle types allows

1. **Purposeful movement of part or whole body.**
2. **Manipulation of external objects (e.g. driving, moving things, ..etc)**
3. **Propulsion of content through various hollow internal organs.**
4. **Emptying. (e.g. urination and giving birth).**

- Muscles comprises approximately half of the body weight:
  - 40% skeletal muscle in men, 32% in women.
  - 10 % smooth and cardiac muscles.
- **Muscles classified into:**
  - Striated or non-striated.
  - Voluntary or involuntary.

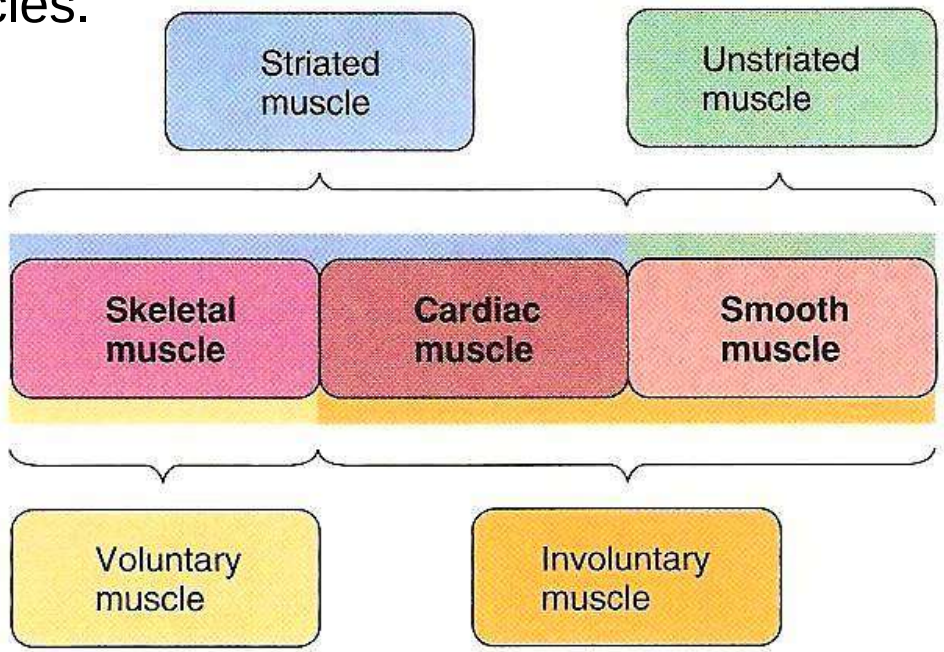


FIGURE 8-1
Categorization of muscle

Structure of skeletal muscle

From molecular to cellular to whole muscle

- **Relatively large, elongated and cylinder shaped.**
- **10-100 µm diameter and 750000 µm in length.**
- **A skeletal muscle consists of a number of muscle fibers lying parallel to each other and bundled together by connective tissue.**
- **Presence of multiple nuclei in a single muscle cell as it is formed by the fusion of many smaller cells during embryonic development and abundance of mitochondria.**

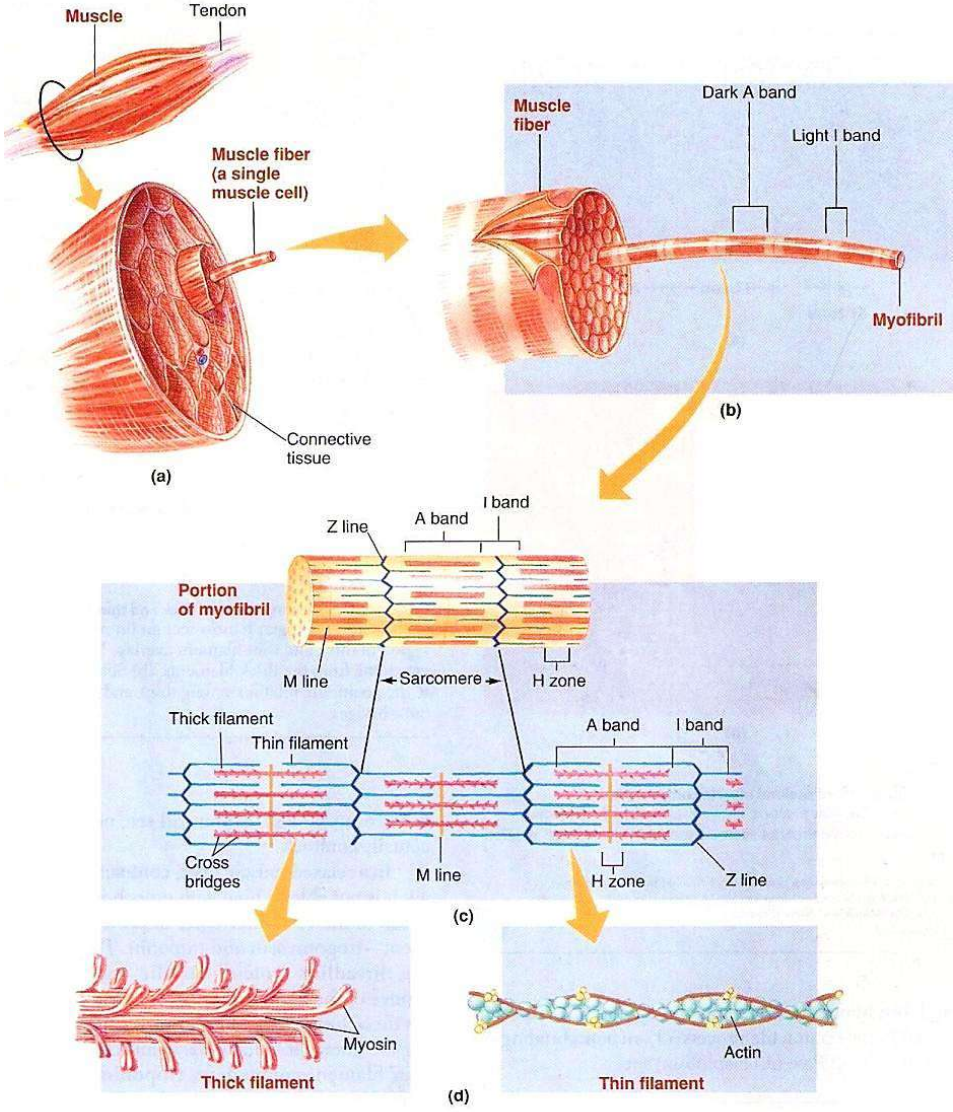


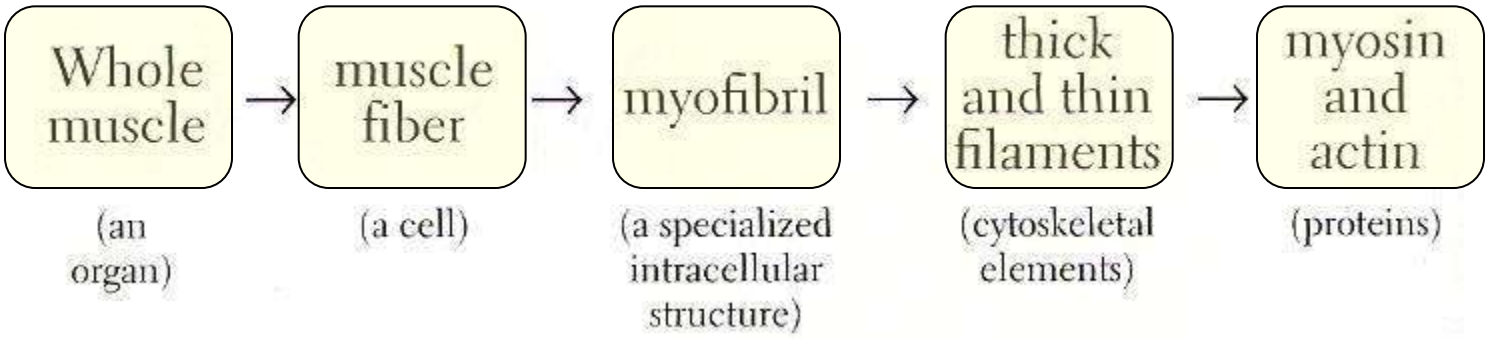
FIGURE 8-2

Levels of organization in a skeletal muscle

(a) Enlargement of a cross section of a whole muscle. (b) Enlargement of a myofibril within a muscle fiber. (c) Cytoskeletal components of a myofibril. (d) Protein components of thick and thin filaments.

Skeletal muscle fiber are striated by a highly organized internal arrangement

- 80% of muscle fiber constitute of myofibrile; cylindrical intercellular structures.
- Each myofibrile consists of a regular arrangement of **Thick filaments** made of **Myosin**(12-18 μm × 1.6 μm) and **Thin filaments** made of **Actin**(5-8 μm × 1 μm).

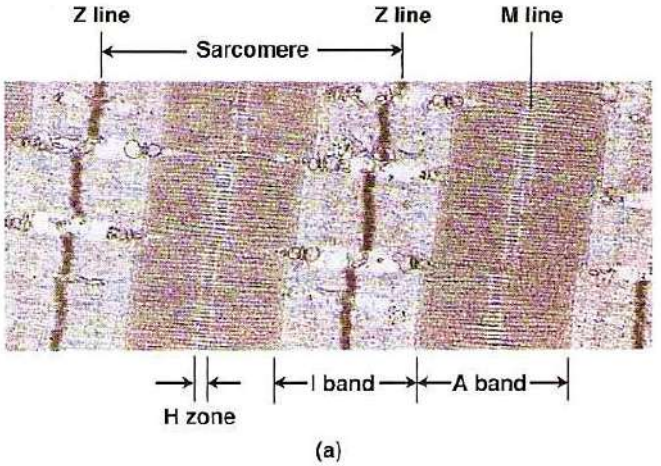


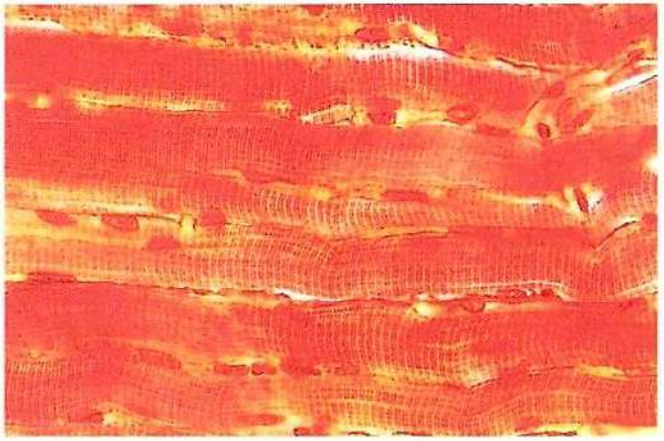
A and **I** band

A myofibrile displays alternating dark bands **A** and light band **I**.

A band :

- Consists of a stacked set of thick filaments along with the thin filaments that overlap on both ends of the thick filaments.
- That is, the two ends of the tick filaments within a stack define the outer limits of a given **A** band.
- The lighter area within the middle of the **A** band is known as the **H** band, **Why ?**
- **M** line is a supporting protein system to hold the thick filaments together vertically within each stack.





● FIGURE 8-3

Light-microscope view of skeletal muscle components

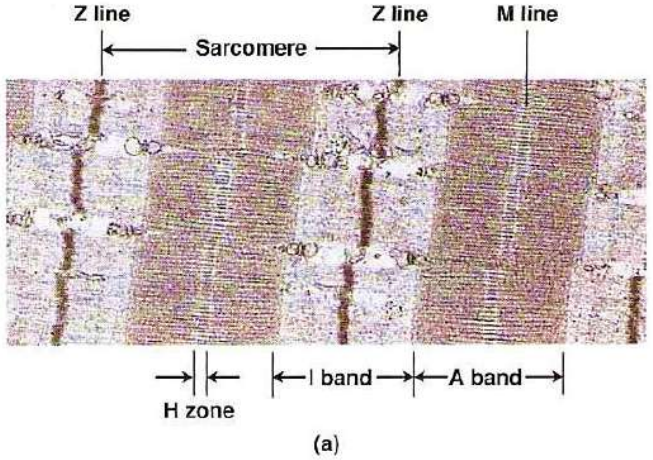
(a) High-power light-microscope view of a myofibril. (b) Low-power light-microscope view of skeletal muscle fibers. Note striated appearance.

[SOURCE: Reprinted with permission from Sydney Schochet Jr., M.D., Professor, Department of Pathology, School of Medicine, West Virginia University: *Diagnostic Pathology of Skeletal Muscle and Nerve* (Stamford, Connecticut: Appleton & Lange, 1986), ● Figure 1-13.]

A and **I** band

I band :

- The **I** band contains only thin filaments.
- In the middle of each **I** band, a dense vertical **Z** line.
- The area between two **Z** lines is called a **sarcomere**.
- **Sarcomere** is the functional unit of skeletal muscle that is capable of contraction.
- During growth, a muscle increases in length by adding **sarcomeres**, not by increasing the size of each **sarcomeres**.



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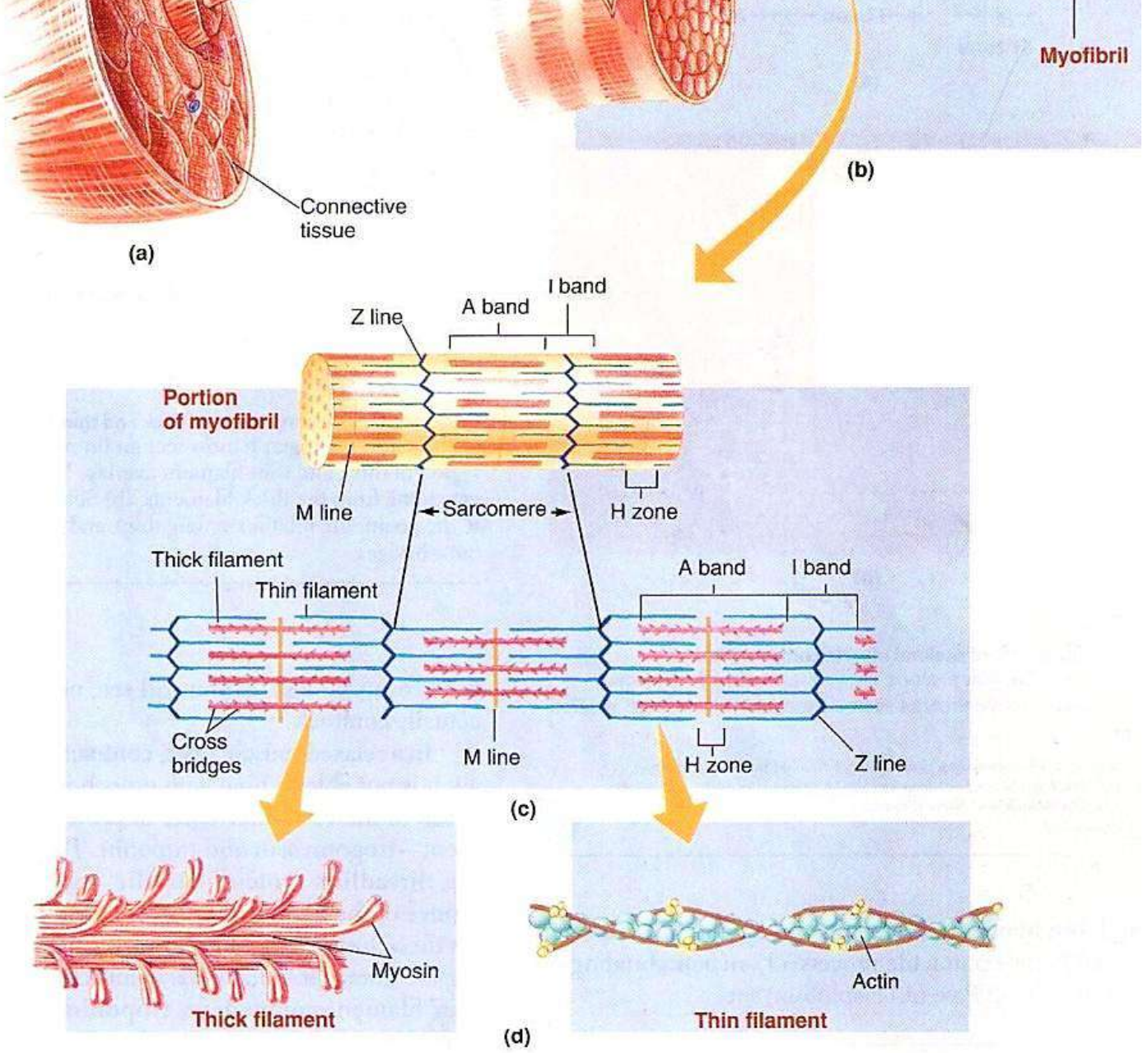

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Cross bridges

- With an electron microscope, fine cross bridges can be seen.
- Three-dimensionally, the fine filaments are arranged hexagonally around the thick filaments.
- A single muscle fiber contain 16b thick and 32b thin filament.

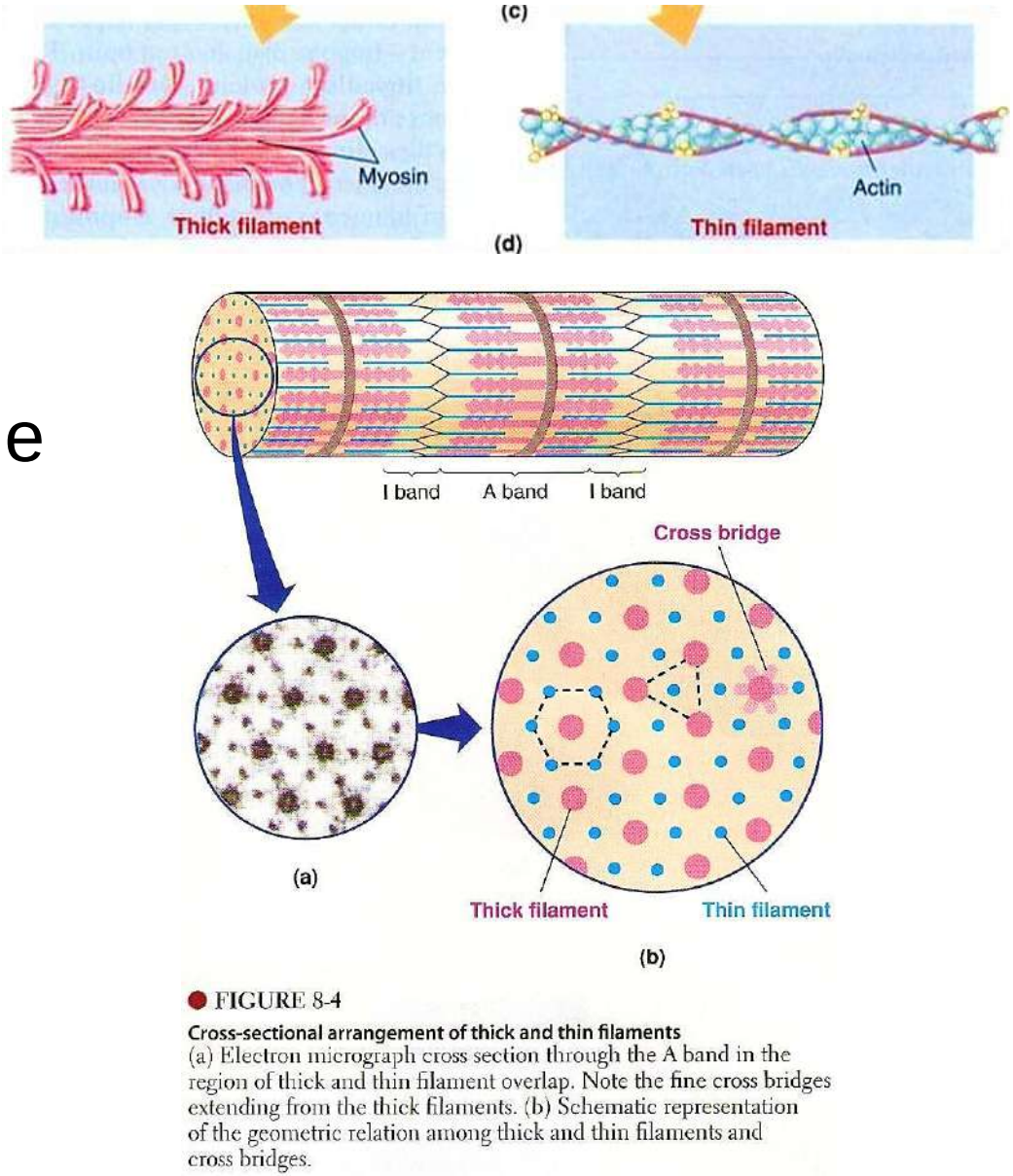


FIGURE 8-4

Cross-sectional arrangement of thick and thin filaments
(a) Electron micrograph cross section through the A band in the region of thick and thin filament overlap. Note the fine cross bridges extending from the thick filaments. (b) Schematic representation of the geometric relation among thick and thin filaments and cross bridges.

Myosin forms the thick filaments

- A myosin molecule is a protein consisting of two identical subunits, with their tails interwinds and their globular heads.
- Each of which contains an actin-binding site and a myosin ATPase site.

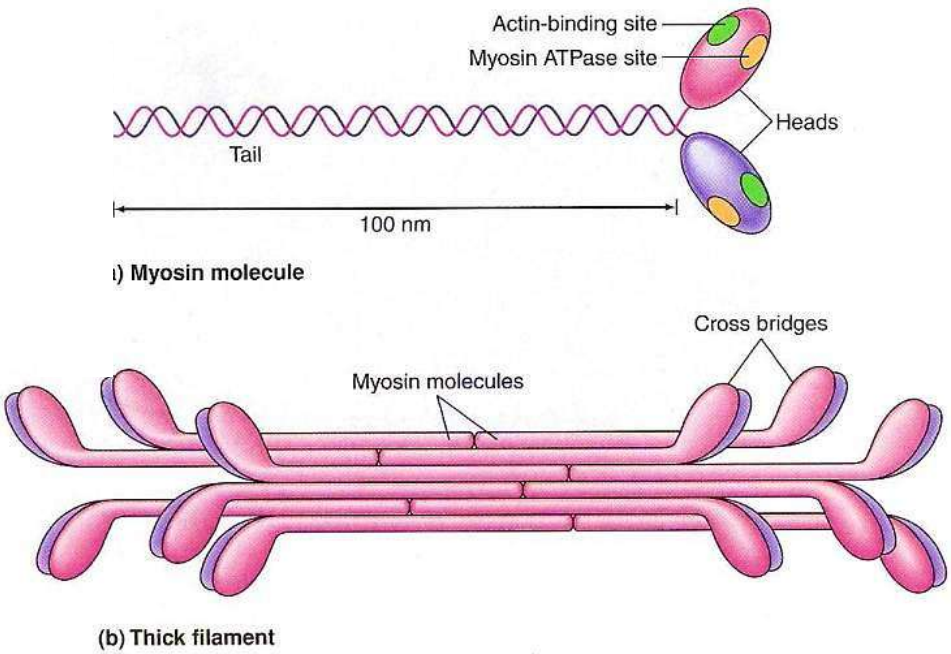
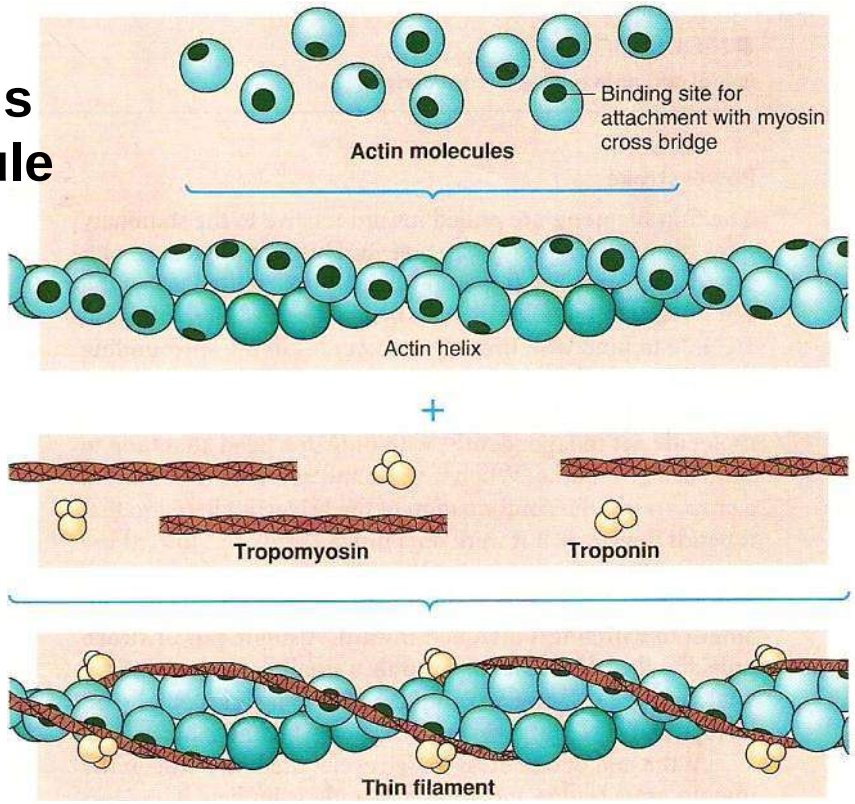
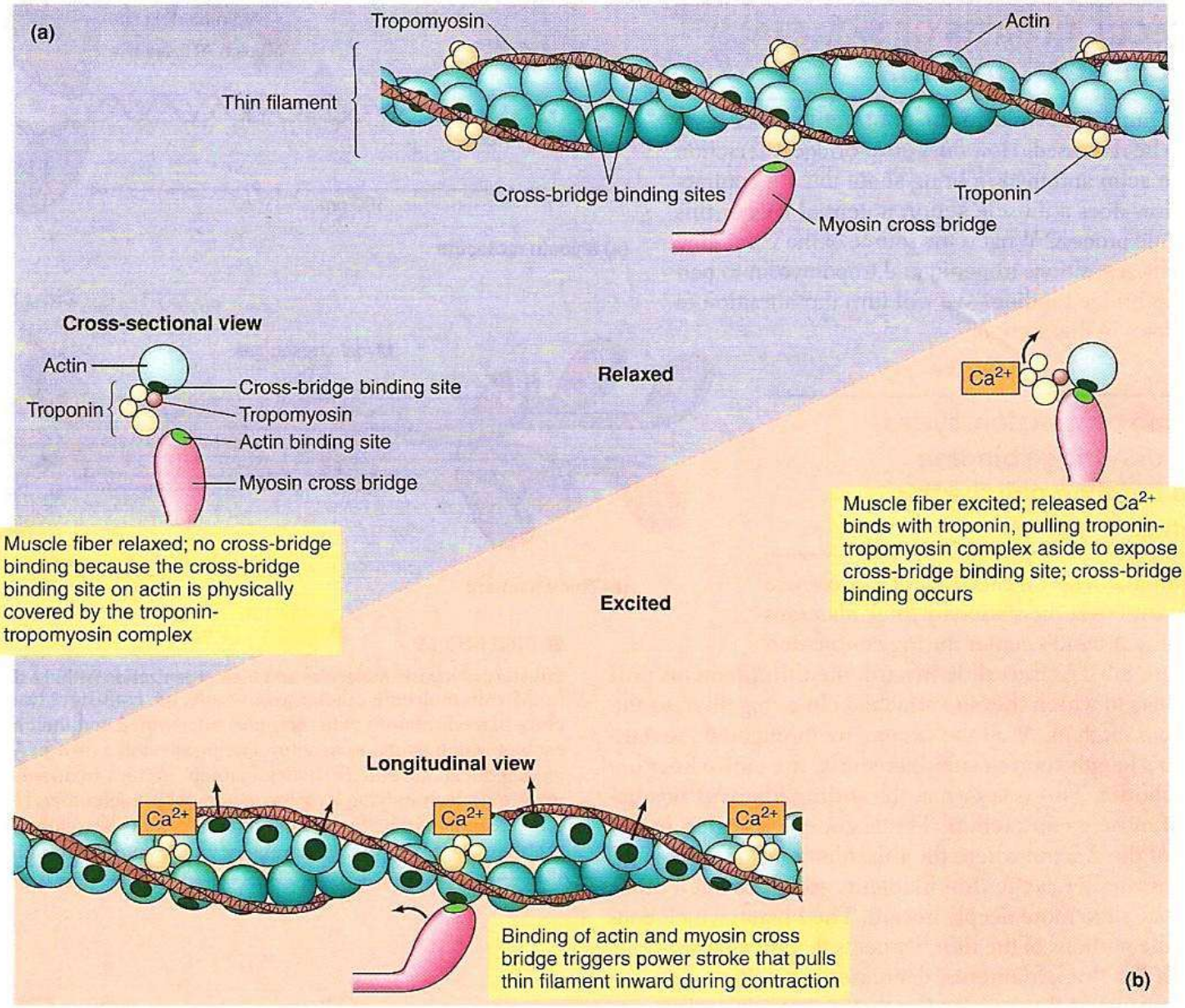


FIGURE 8-5
tructure of myosin molecules and their organization within a thick filament
a) Myosin molecule. Each myosin molecule consists of two identical golf club–shaped subunits with their tails intertwined and their globular heads, each of which contains an actin-binding site and a myosin ATPase site, projecting out at one end. (b) Thick filament. A thick filament is made up of myosin molecules lying lengthwise parallel to each other. Half are oriented in one direction and half in the opposite direction. The globular heads, which protrude at regular intervals along the thick filament, form the cross bridges.

Actin is the main structural component of the thin filaments

- **Thin filaments are composed of three proteins: Actin, Tropomycin and Troponin.**
- **Actin molecules joined into two strands and twisted together, and each molecule has a special binding site for myosin attachment forming the cross bridge results in energy-consuming contraction of the muscle fibers.**
- **Tropomysin molecules are thread like proteins, covers the actin sites, thus blocking the interaction that lead to muscle contraction.**
- **Troponin is a protein complex consisting of three polypeptides units: one that binds toTropomysin,one to Acin and third with Ca^{2+}.**





● FIGURE 8-7

Role of calcium in turning on cross bridges

Molecular bases of skeletal muscle contraction

- Q1. How dose cross-bridge interaction between actin and myosin bring about muscle contraction?
- Q2. How does a muscle action potential trigger this contractile process?
- Q3. What is the source of the Ca^{2+} that physically repositions troponin and tropomysin to permit cross-bridge binding?

During contraction cycles of cross-bridge binding and bending pull the thin filament inward

- As the thin filaments slide inward toward A bands, they pull Z lines closer together, so the sarcomere shortens.
- As all the sarcomeres shorten simultaneously, the entire muscle fiber becomes shorter (the sliding filament mechanism of muscle contraction.
- Note that neither the thick nor thin filaments decrease in length to shorten the sarcomere.

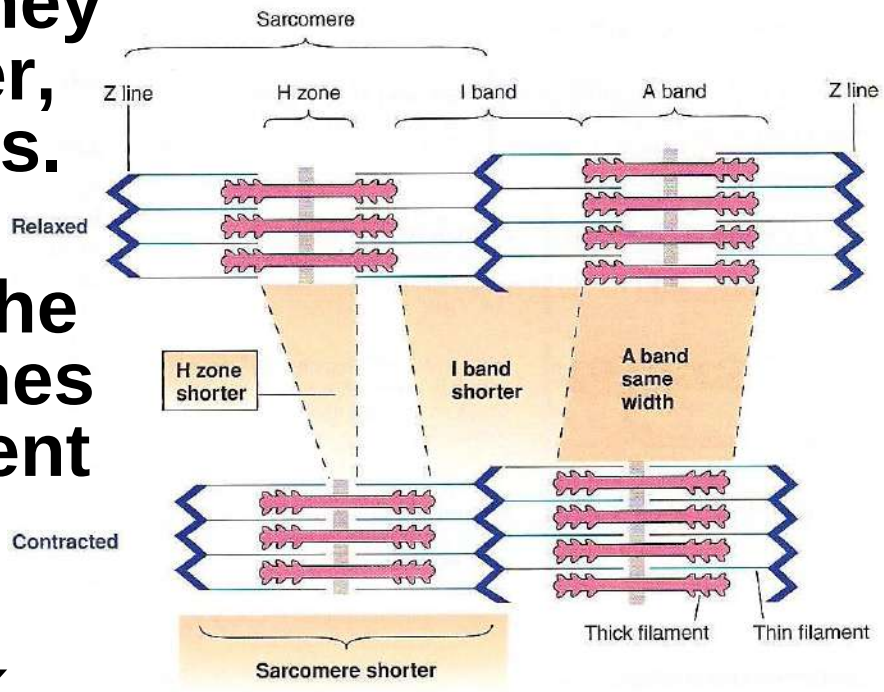
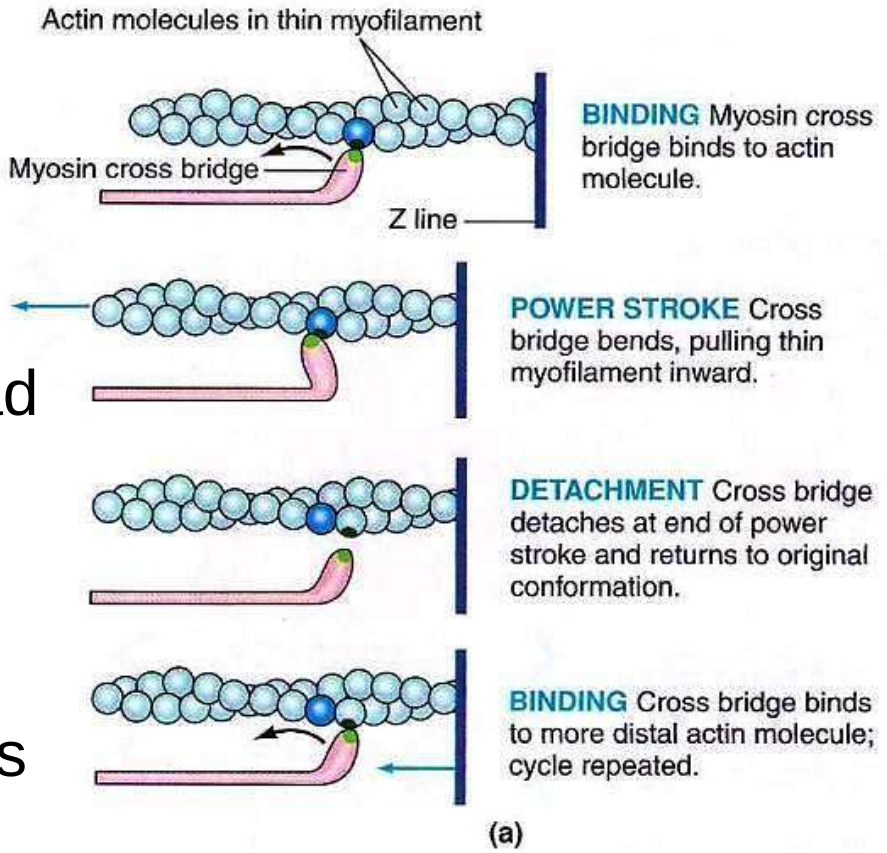


FIGURE 8-8
Changes in banding pattern during shortening
During muscle contraction, each sarcomere shortens as the thin filaments slide closer together between the thick filaments so that the Z lines are pulled closer together. The width of the A bands does not change as a muscle fiber shortens, but the I bands and H zones become shorter.

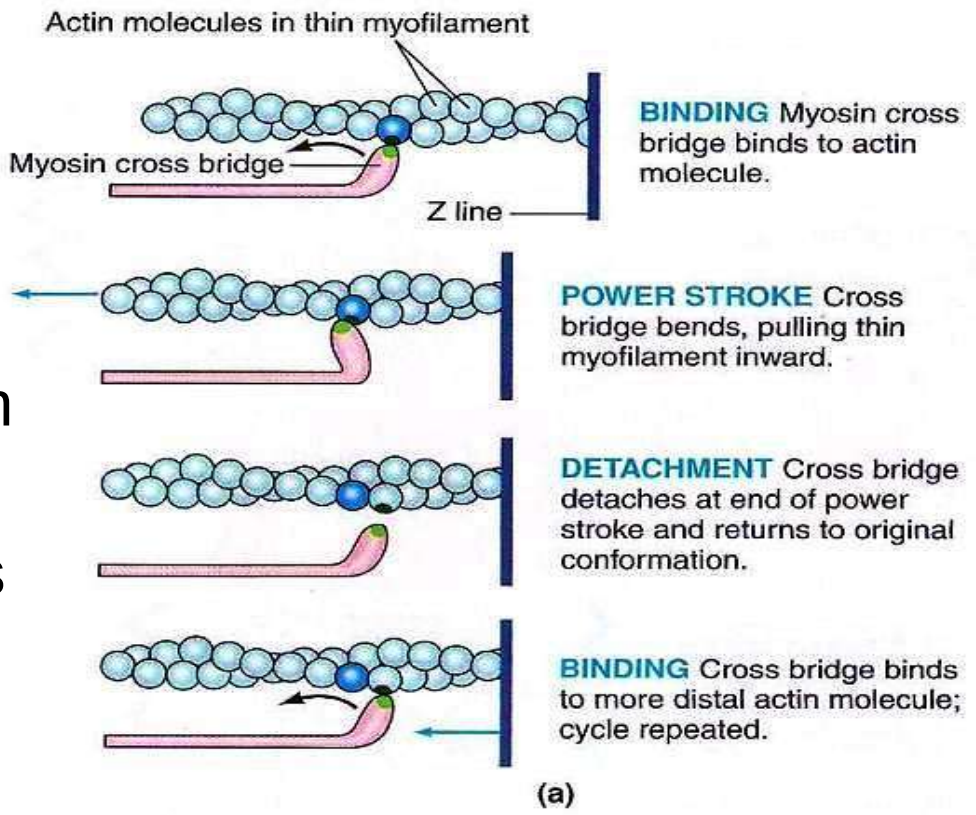
Power stroke

- The thin filaments are pulled inward relative to the stationary thick filaments by cross-bridge activity.
- The two myosin heads of each myosin molecule act independently, with only one head attaching to actin at a given time.
- When myosin and actin make contact at a cross bridge, the conformation of the bridge is altered so that it bends in ward as if it were on a hinge رزة , stroking toward the center of the sarcomere, similar to the stroking of a boat oar (**power stroke**).



Power stroke

- Complete shortening is accomplished by repeated cycles of cross-bridge binding and bending, then at the end of one cross-bridge cycle the link between actin and myosin molecules broken.
- The cross bridge returns to its original conformation and binds to the next actin molecules, much like pulling in a rope hand over hand.



Power stroke

- At any time during contraction, part of the cross-bridges are attached while others are returning to their original conformation, thus, some cross bridges are "**holding on**" to the thin filaments, whereas others "**let go**" to bind with new actin.
- **Excitation-contraction coupling:**

Refers to the series of events linking muscle excitation (**action potential**) to muscle contraction.

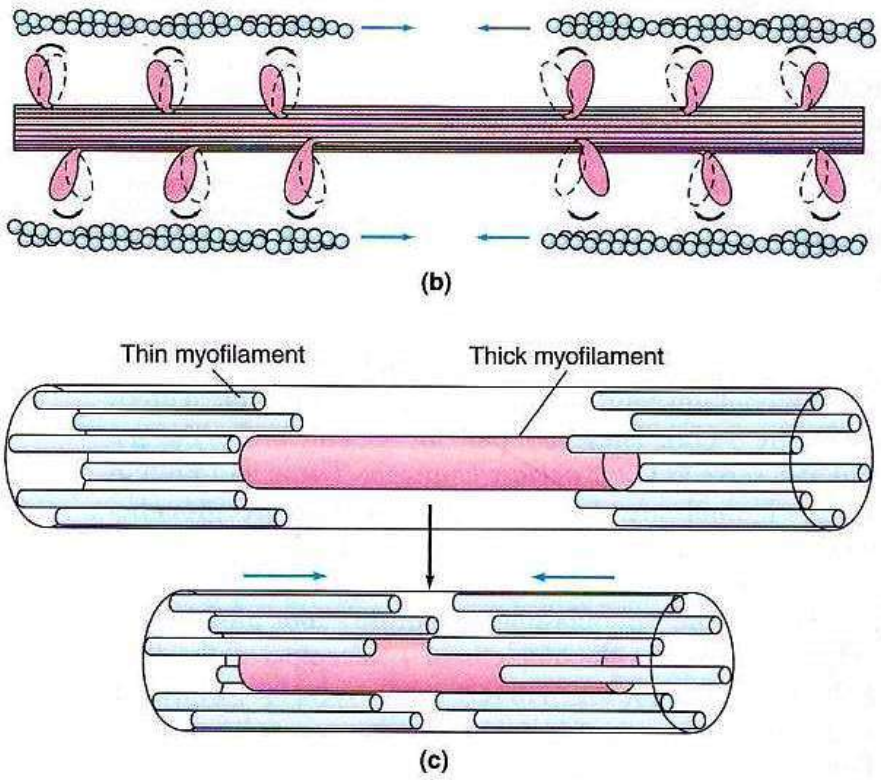


FIGURE 8-9
Cross-bridge activity

Calcium is the link between excitation and contraction

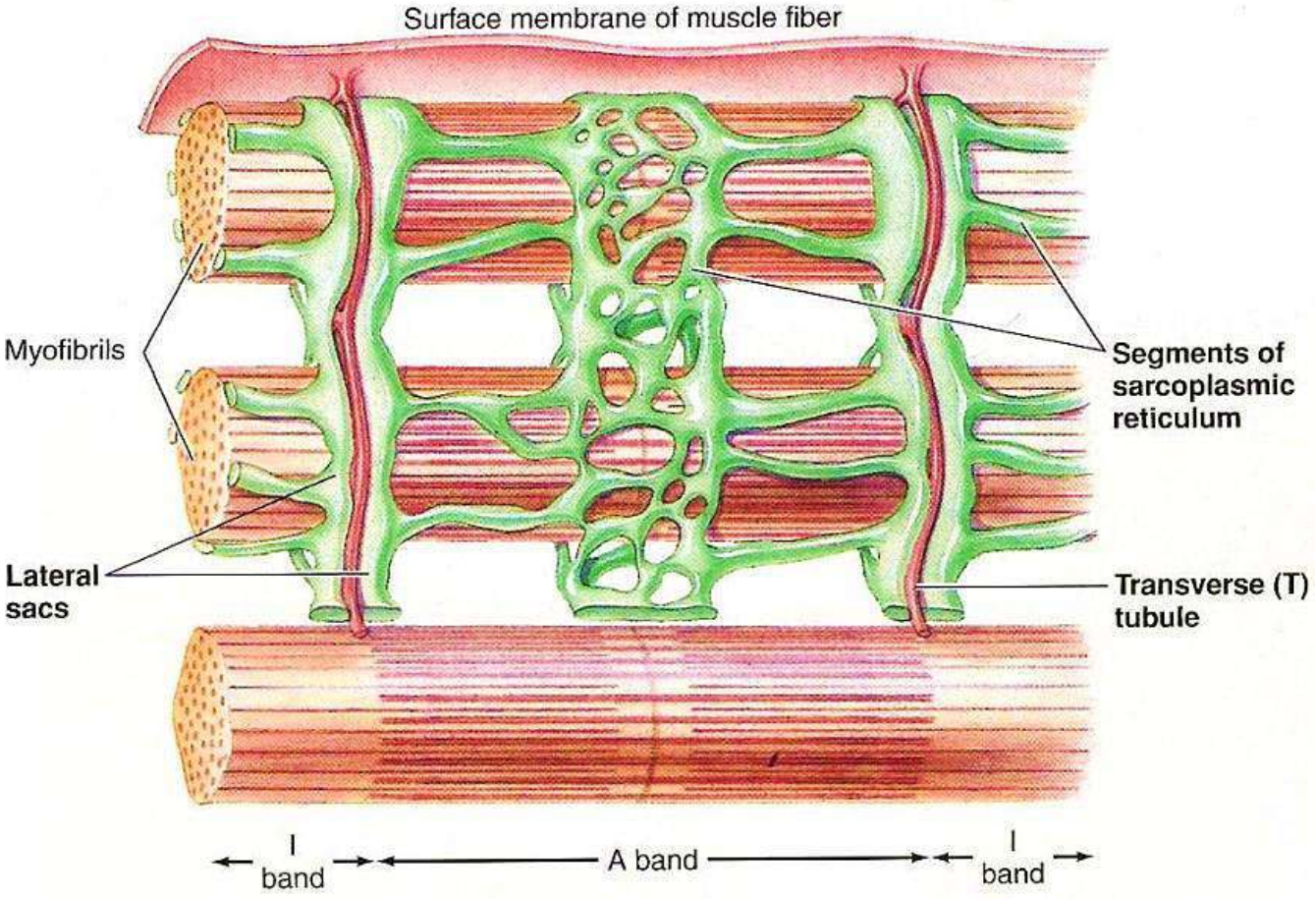
- Skeletal muscle are stimulated to contract by release of acetylcholin (Ach) at neuromuscular junctions between motor neuron terminals and muscle fibers.

- Figure 7-6, page 249 (Animation).

- Two membrane structures play an important role in linking this excitation to contraction within the muscle fiber:
  - -1- Transverse tubules and
  - -2- The sarcoplasmic reticular.

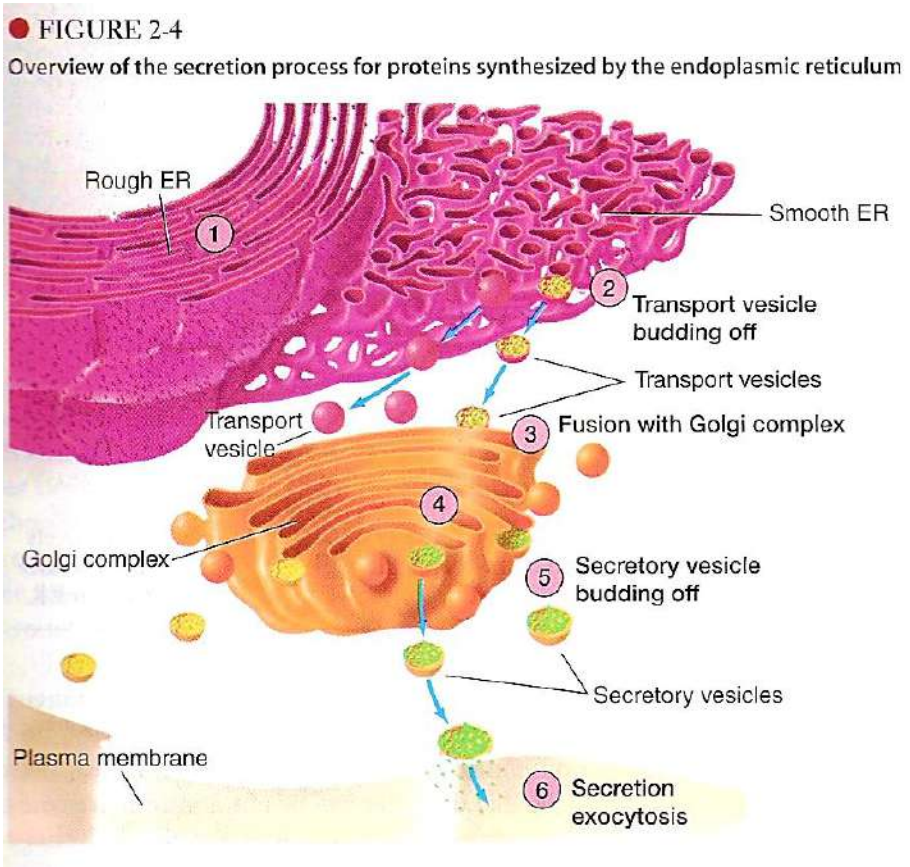
Spread of the action potential down the T tubules

- Because the T tubule membrane is continuous with the surface membrane, an Action potential on the surface membrane also spreads down into the T tubule, providing a means of rapidly transmitting the surface electric activity into the central portions of the fiber.



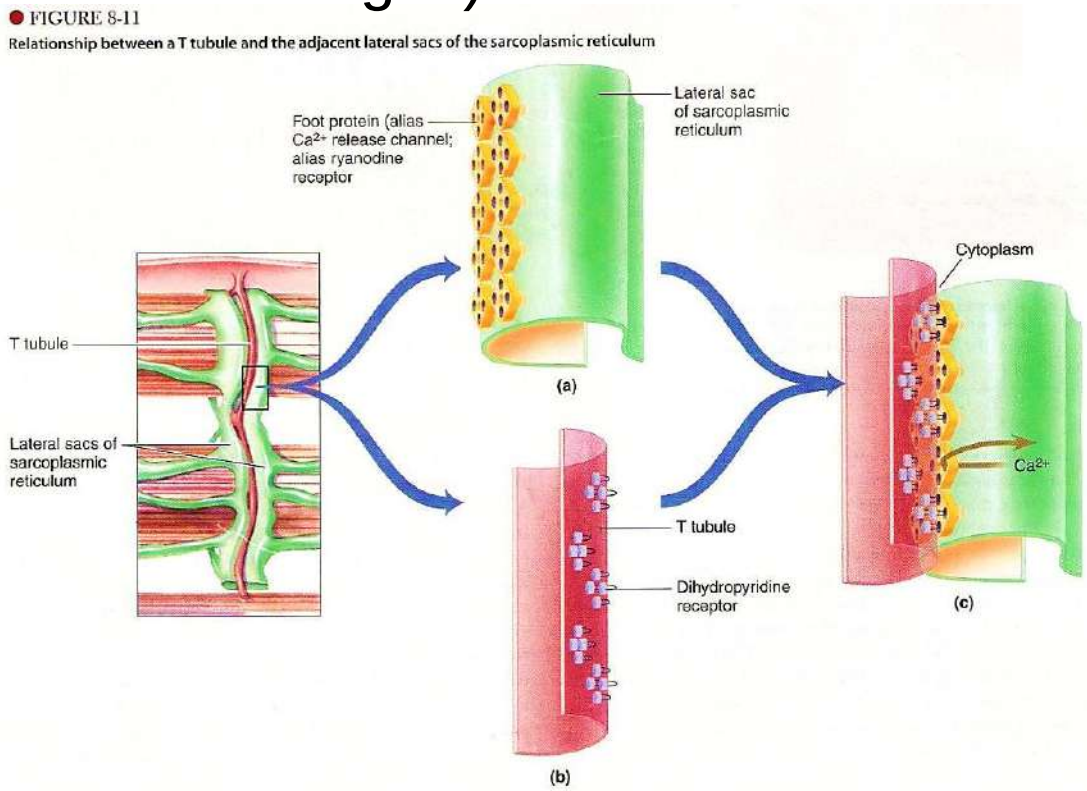
Release of calcium from the sarcoplasmic reticulum

- The sarcoplasmic reticulaum is a modified endoplasmic reticulum (fig 2-4 page 28) that consists of a fine network of interconnected compartments surrounding each myofibril like a mesh sleeve.
- The end of each segment expand to form sac-like regions, **the lateral sacs** (terminal costernae), that stores Ca^{2+}.



How is a change in T tubule protein linked with the release of Ca^{2+} from the lateral sacs?

- **Foot proteins** extends from the sarcoplasmic reticulum and spans the gap between the lateral sac and T tubule.
- The foot proteins not only bridge the gap but also serve as Ca^{2+}-release channels (also known as **ryanodine** receptors).
- **Dihydropyridine** receptors (voltage gated channels), are made up of four subunits in exactly the same pattern as the foot proteins (like mirror images) but to half of it.



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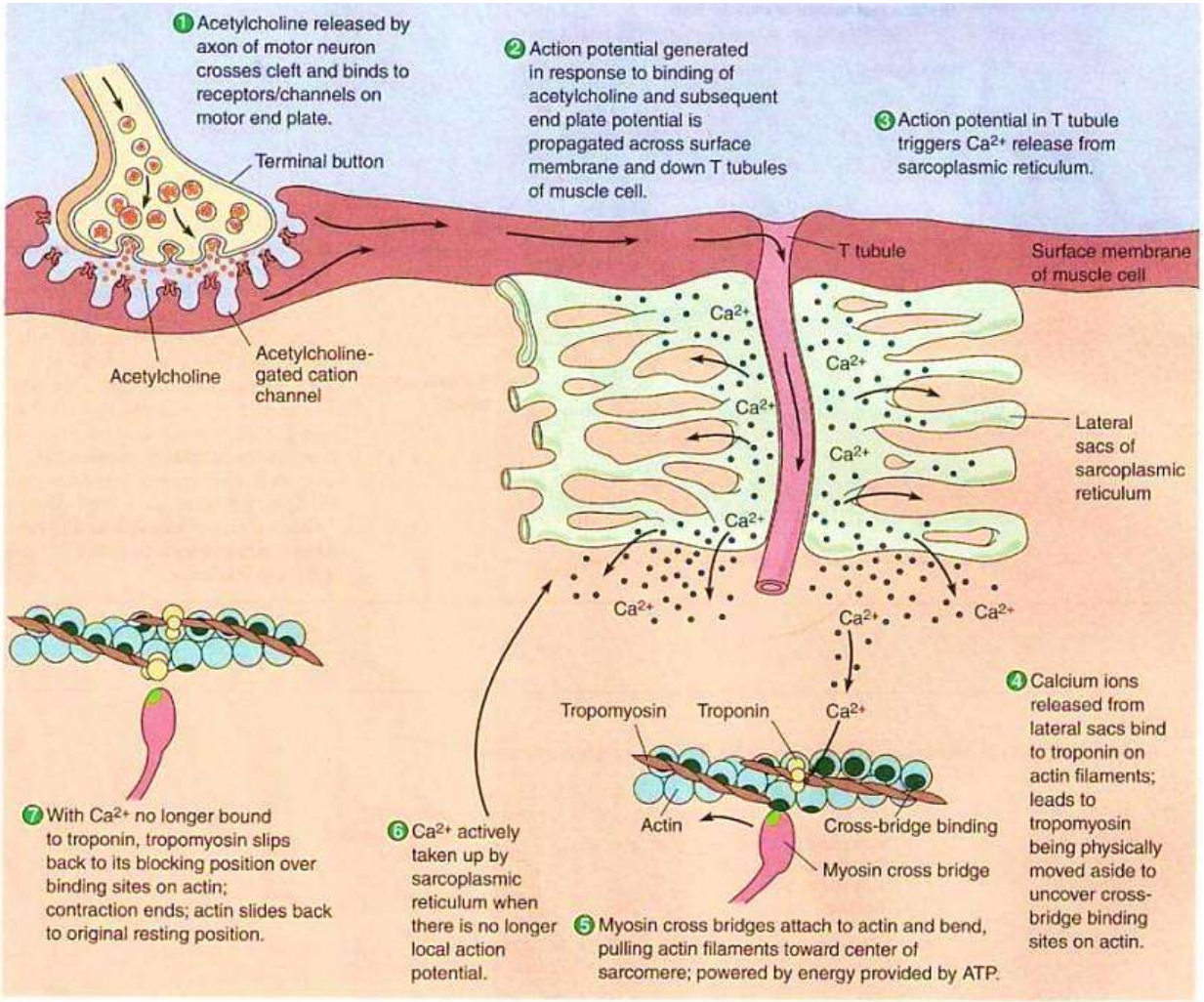
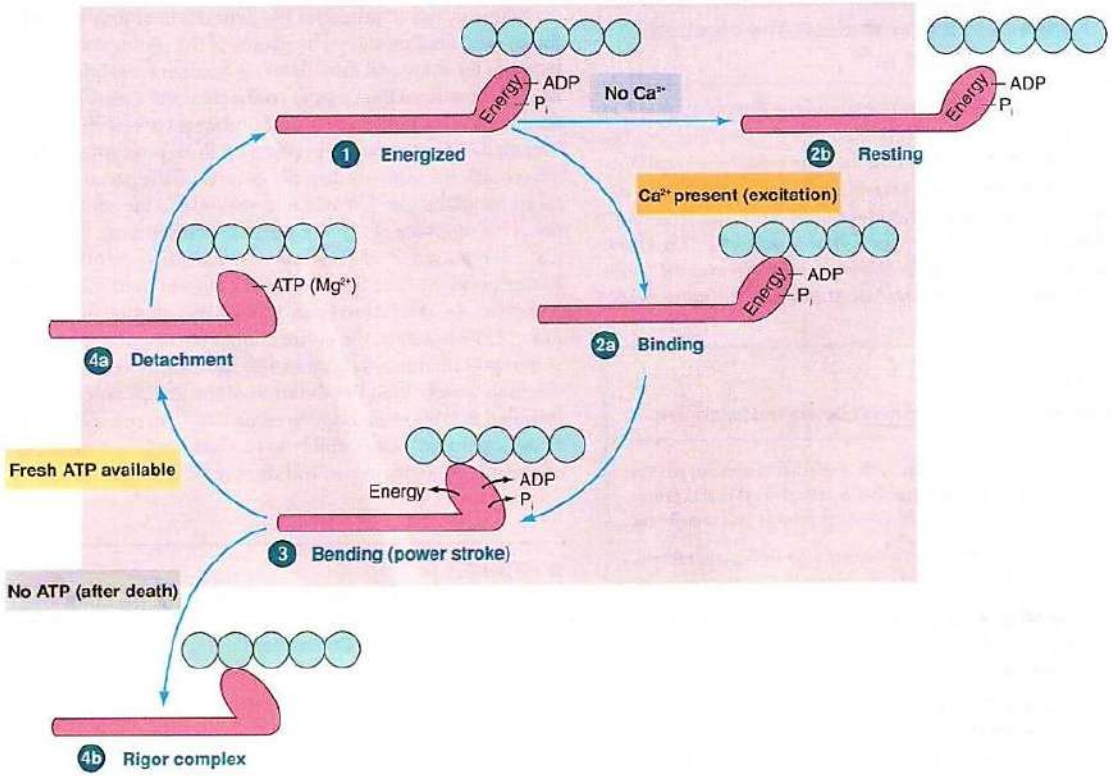


● FIGURE 8-12

Calcium release in excitation–contraction coupling

Steps 1 through 5 depict the events that couple neurotransmitter release and subsequent electrical excitation of the muscle cell with muscle contraction. Steps 6 and 7 depict events associated with muscle relaxation.

ATP-powered cross-bridge cycling



1 ATP split by myosin ATPase; ADP and P_i remain attached to myosin; energy stored in cross bridge.

...or...

2a Ca^{2+} released on excitation; removes inhibitory influence from actin, enabling it to bind with cross bridge.

2b No excitation; no Ca^{2+} released; actin and myosin prevented from binding; no cross-bridge cycle; muscle fiber remains at rest.

3 Power stroke of cross bridge triggered on contact between myosin and actin; P_i and ADP released.

...or...

4a Linkage between actin and myosin broken as fresh molecule of ATP binds to myosin cross bridge; cross bridge assumes original conformation; ATP hydrolyzed (cycle starts again at step 1).

4b If no fresh ATP available (after death), actin and myosin remain bound in rigor complex.

● FIGURE 8-13
Cross-bridge cycle

Relaxation

- **The contractile process is turned off when Ca^{2+} is returned to the lateral sacs on cessation of local electrical activity.**
- **The sarcoplasmic reticulum possesses an energy-consuming carrier, a Ca^{2+}-ATPase pump, which activly transports Ca^{2+} from the cytosol and concentrates it in the lateral sacs.**
- **The thin filaments, freed from cycles of cross bridge attachment and pulling, are able to return passively to their resting position.**

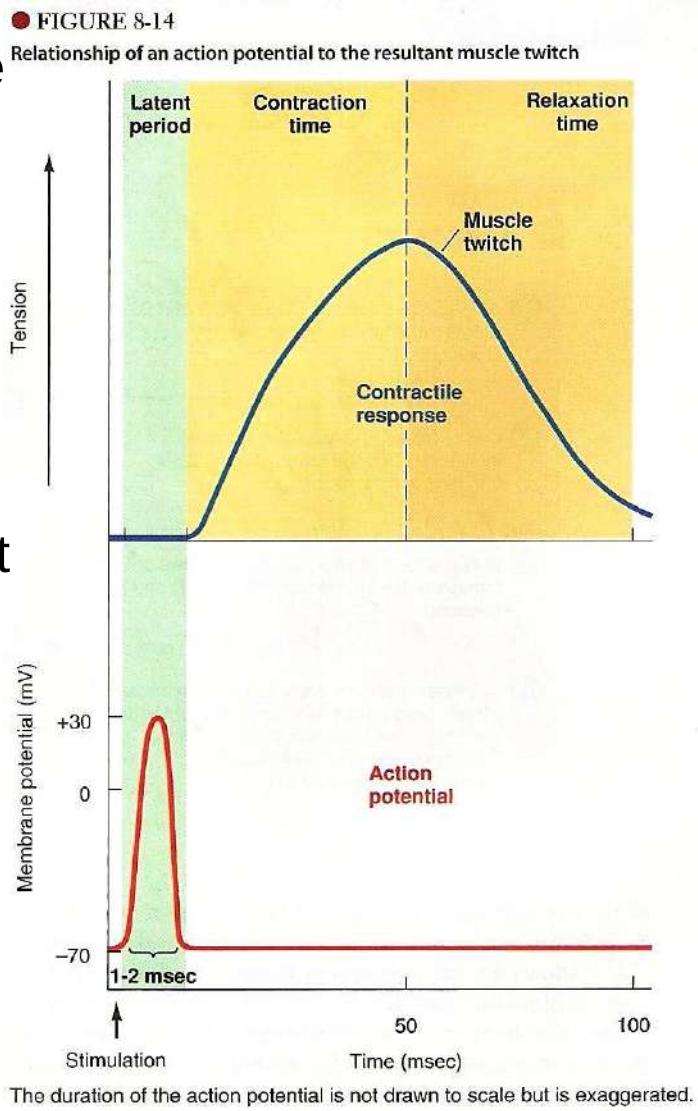
▲ TABLE 8-1
Steps of Excitation–Contraction Coupling and Relaxation

1. Acetylcholine released from the terminal of a motor neuron initiates an action potential in the muscle cell that is propagated over the entire surface of the muscle cell membrane.
2. The surface electric activity is carried into the central portions of the muscle fiber by the T tubules.
3. Spread of the action potential down the T tubules triggers the release of stored Ca^{2+} from the adjacent lateral sacs of the sarcoplasmic reticulum.
4. Released Ca^{2+} binds with troponin and changes its shape so that the troponin-tropomysin complex is physically pulled aside, uncovering actin's cross-bridge binding sites.
5. Exposed actin sites bind with myosin cross bridges, which have previously been energized by the splitting of ATP into ADP + P_i + energy by the myosin ATPase site on the cross bridges.
6. Binding of actin and myosin at a cross bridge causes the cross bridge to bend, producing a power stroke that pulls the thin filament inward. Inward sliding of all the thin filaments surrounding a thick filament shortens the sarcomere (causes muscle contraction).
7. P_i is released from the cross bridge during the power stroke; ADP is released after the power stroke is complete.
8. Attachment of a new molecule of ATP permits detachment of the cross bridge, which returns to its original conformation.
9. Splitting of the fresh ATP molecule by myosin ATPase energizes the cross bridge once again.
10. If Ca^{2+} is still present so that the troponin-tropomyosin complex remains pulled aside, the cross bridges go through another cycle of binding and bending, pulling the thin filament in even further.
11. When there is no longer a local action potential and Ca^{2+} has been actively returned to its storage site in the sarcoplasmic reticulum's lateral sacs, the troponin-tropomyosin complex slips back into its blocking position, actin and myosin no longer bind at the cross bridges, and the thin filaments passively slide back to their resting position as relaxation takes place.

Contractile activity far out let the electrical activity that initiated it

- The onset of the resultant contractile response lags behind the action potential because the entire excitation contraction coupling process must take place before cross-bridge activity begins.

1. **The latent period:** is the time delay of a few milliseconds between stimulation and onset of contraction.
2. **The contraction time:** the time from the onset of contraction until peak tension is developed, its averages about 50 msec, depending on the type of muscle fiber in which the lateral sacs have reuptake of Ca^{2+}, and time for the filaments to return to their resting position.
3. **The relaxation time:** the time from peak tension until relaxation is complete.



الحمد لله رب العالمين