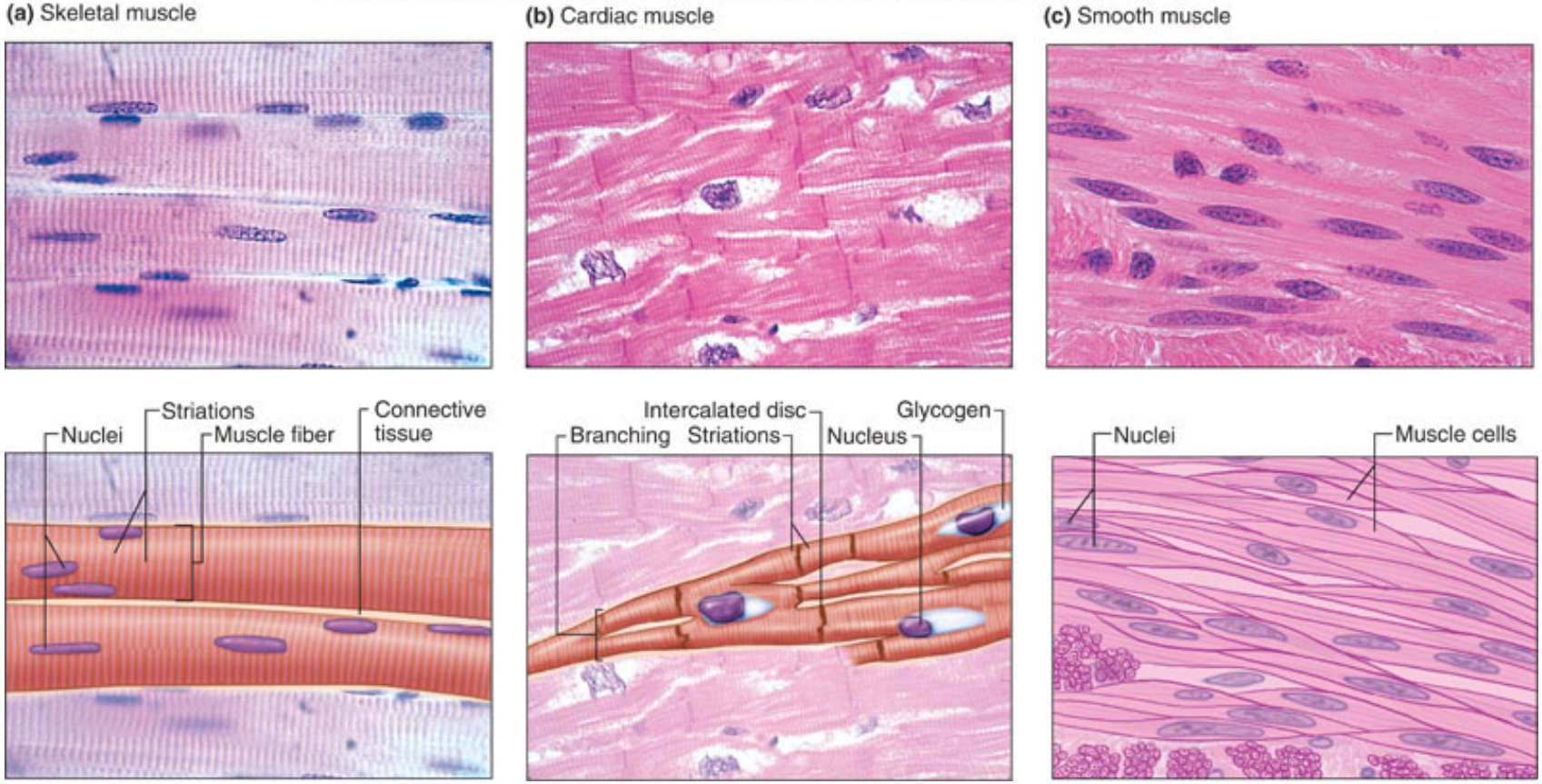
# Chapter 9
# Muscle

Types of muscle

- Skeletal muscle
- Cardiac muscle

} Striated muscle

- Smooth muscle



# Chapter 9
# Muscle (cont.)

- The sliding filament mechanism, in which myosin filaments bind to and move actin filaments, is the basis for shortening of stimulated skeletal, smooth, and cardiac muscles.

- In all three types of muscle, myosin and actin interactions are regulated by the availability of calcium ions.

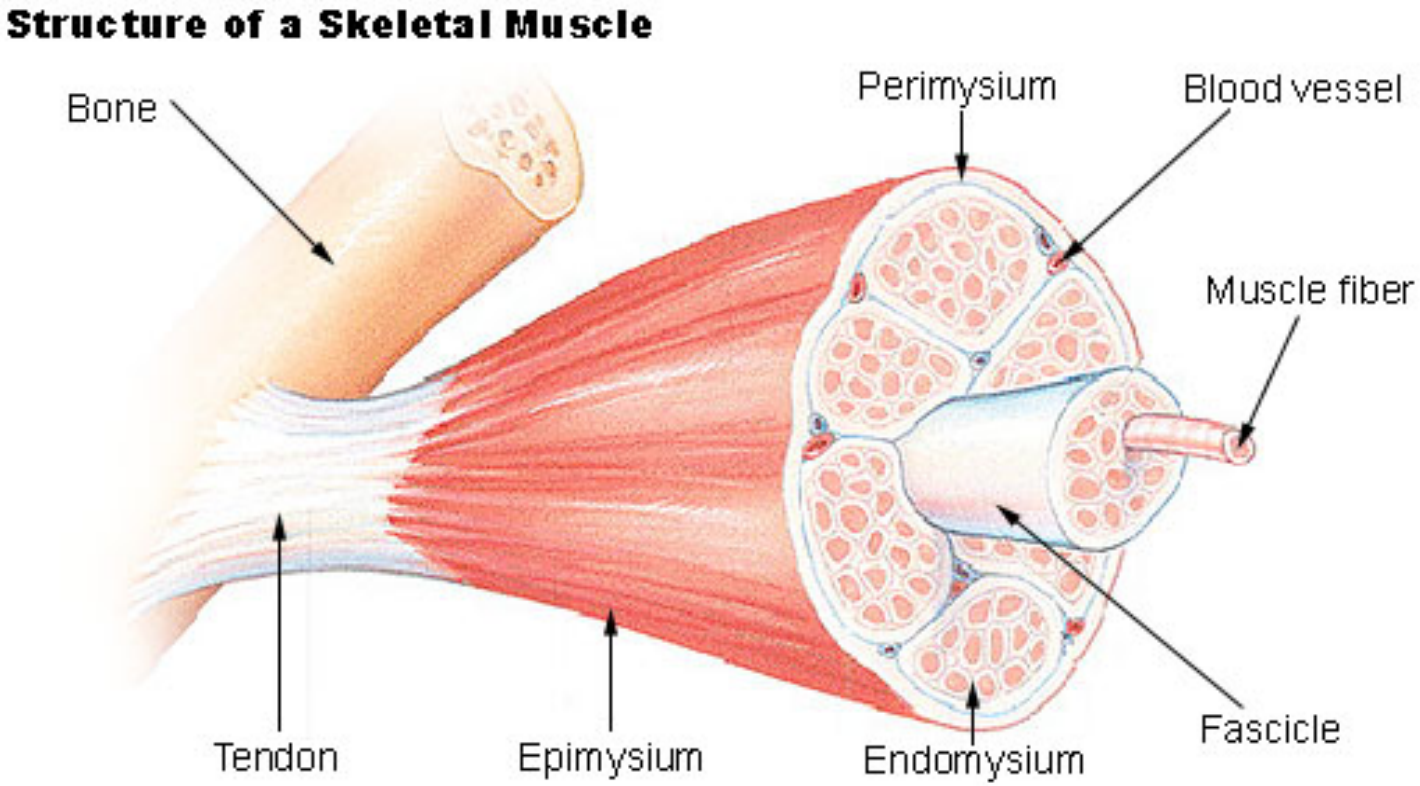
- Changes in the membrane potential of muscles are linked to internal changes in calcium release (and contraction).

# Chapter 9
# Muscle (cont.)

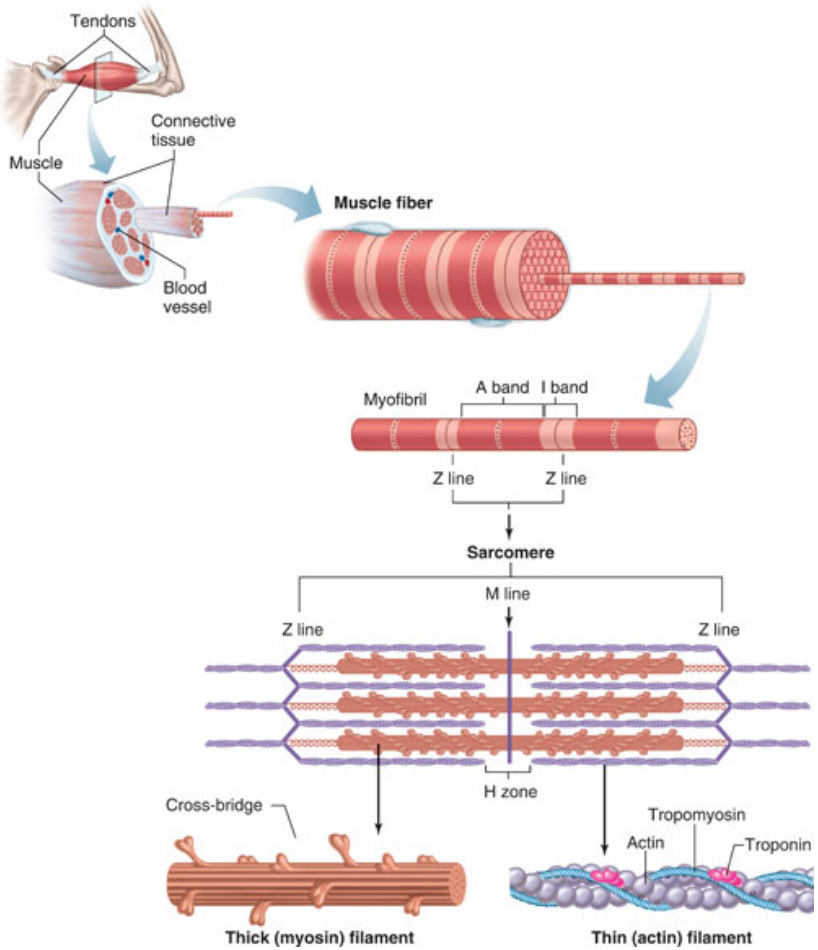
- Neuronal influences on the contraction of muscles is affected when neural activity causes changes in the membrane potential of muscles.

- Smooth muscles operate in a wide variety of involuntary functions such as regulation of blood pressure and movement of materials in the gut.

# Structure of skeletal muscle



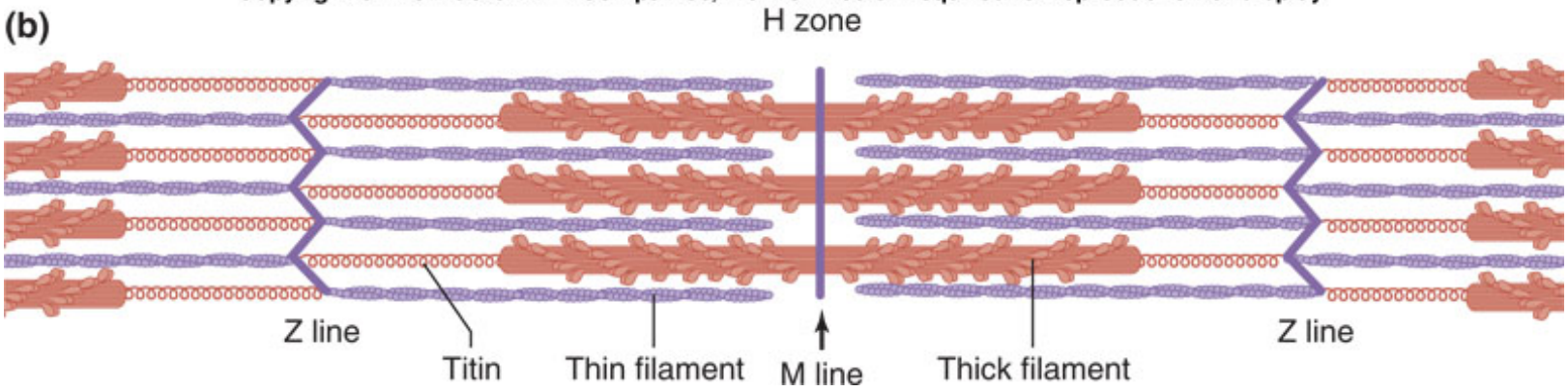
Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.




**Skeletal muscles are attached to the skeleton by tendons.**

**Skeletal muscles typically contain many, many muscle fibers.**

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.




**The sarcomere is composed of:**

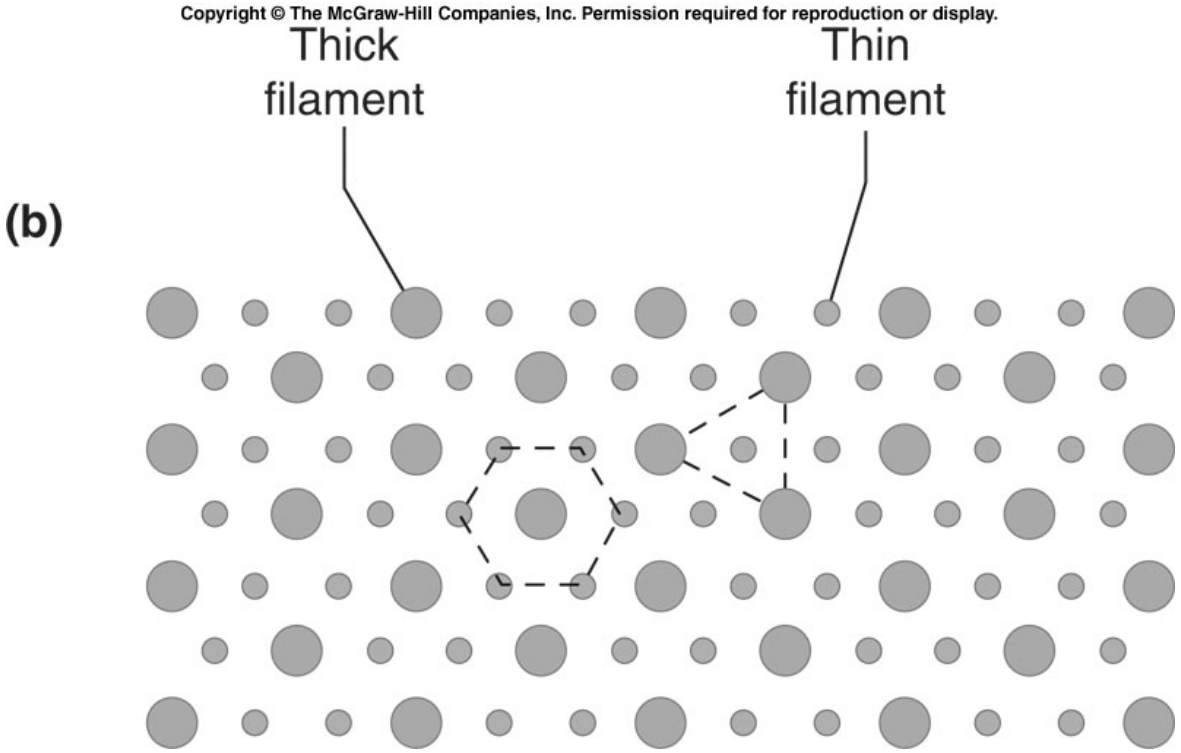
**thick filaments called myosin, anchored in place by titin fibers, and**

**thin filaments called actin, anchored to Z-lines .**

Figure 9-4b



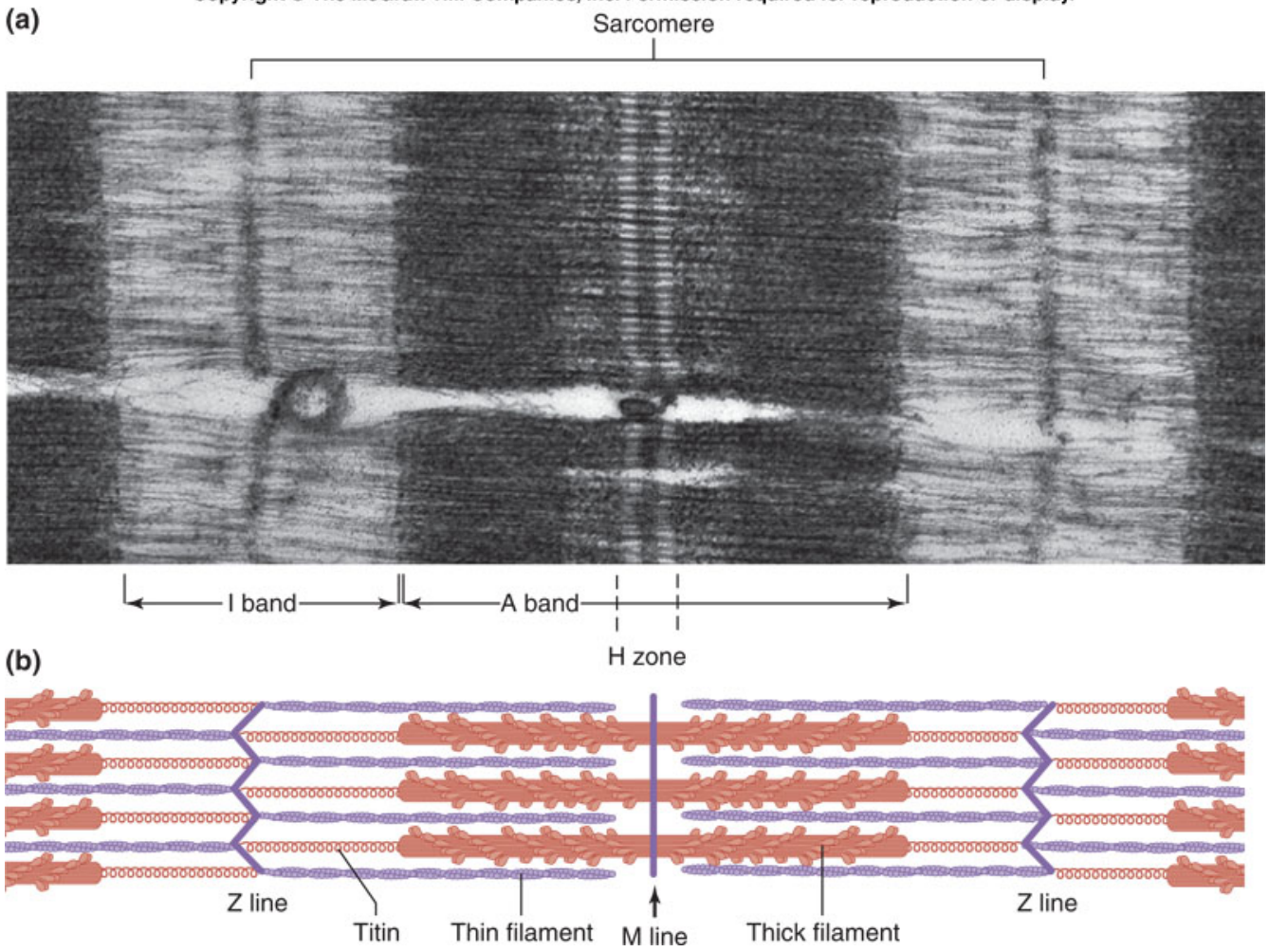
Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.




**A cross section through a sarcomere shows that:**

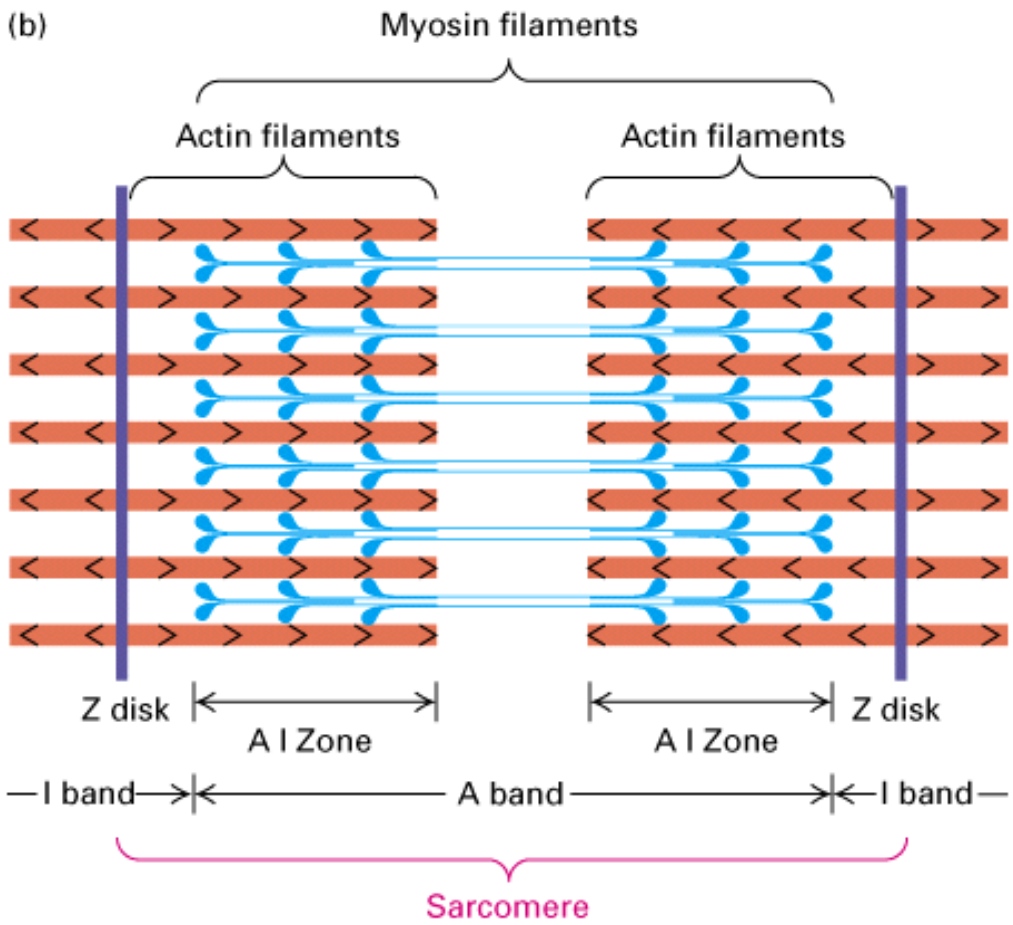
- **each myosin can interact with 6 actin filaments, and**
- **each actin can interact with 3 myosin filaments.**

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



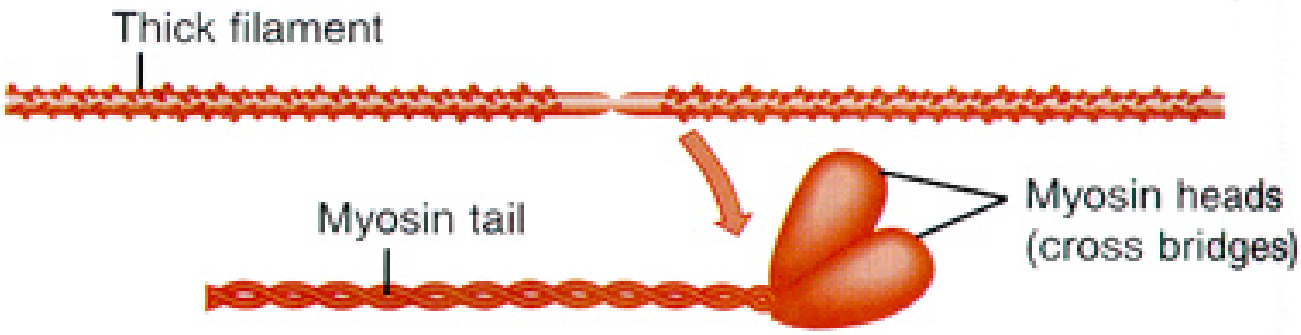

**Sarcomere  structures in an electron micrograph.**

# Filaments


(b)
Myosin filaments
Actin filaments
Actin filaments
Z disk
A I Zone
A I Zone
Z disk
I band
A band
I band
Sarcomere

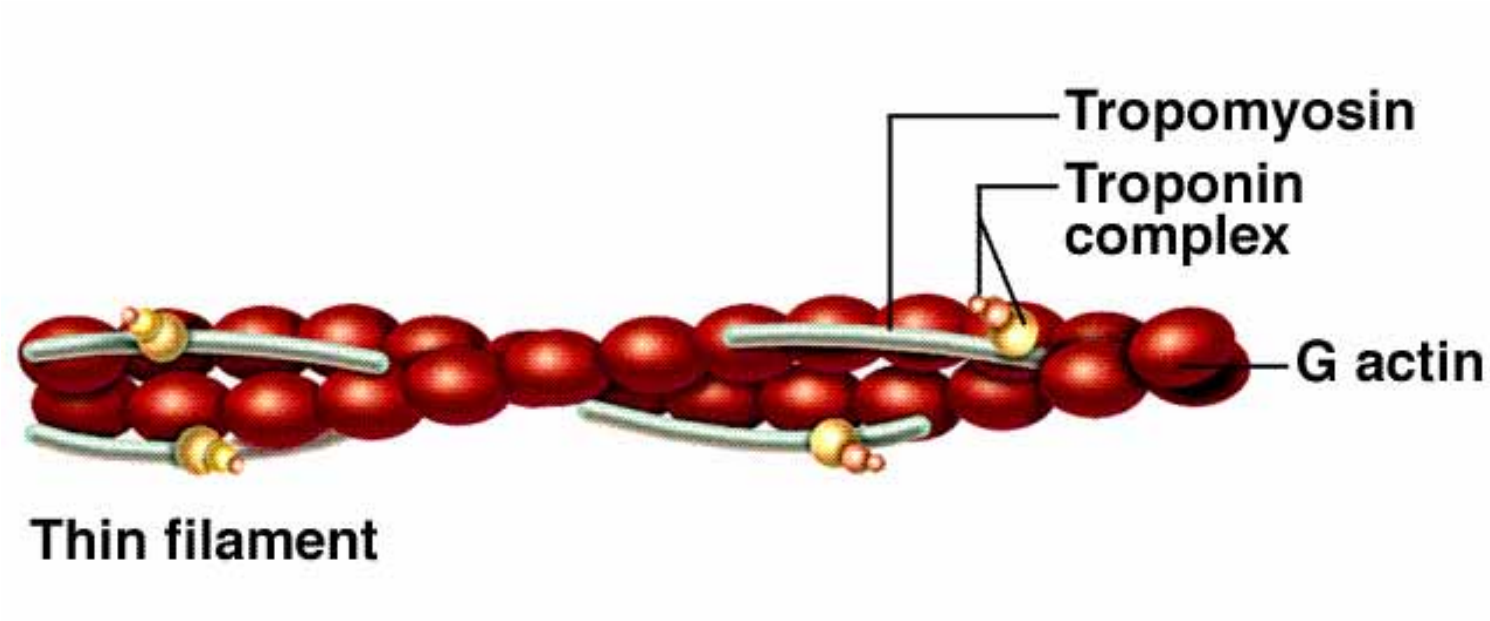
# Myosin filament (thick filament)

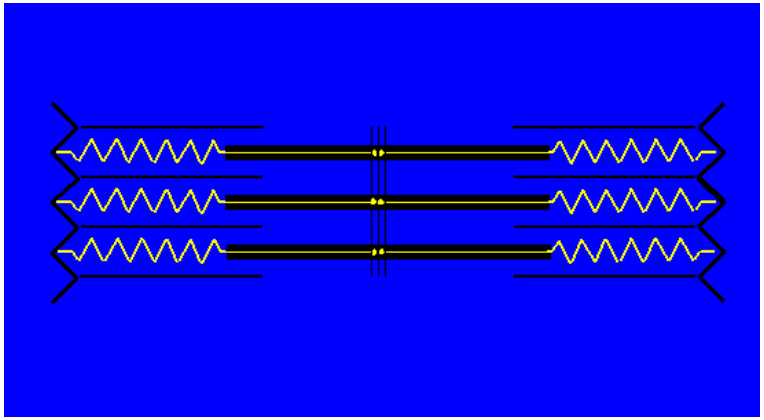
- Myosin



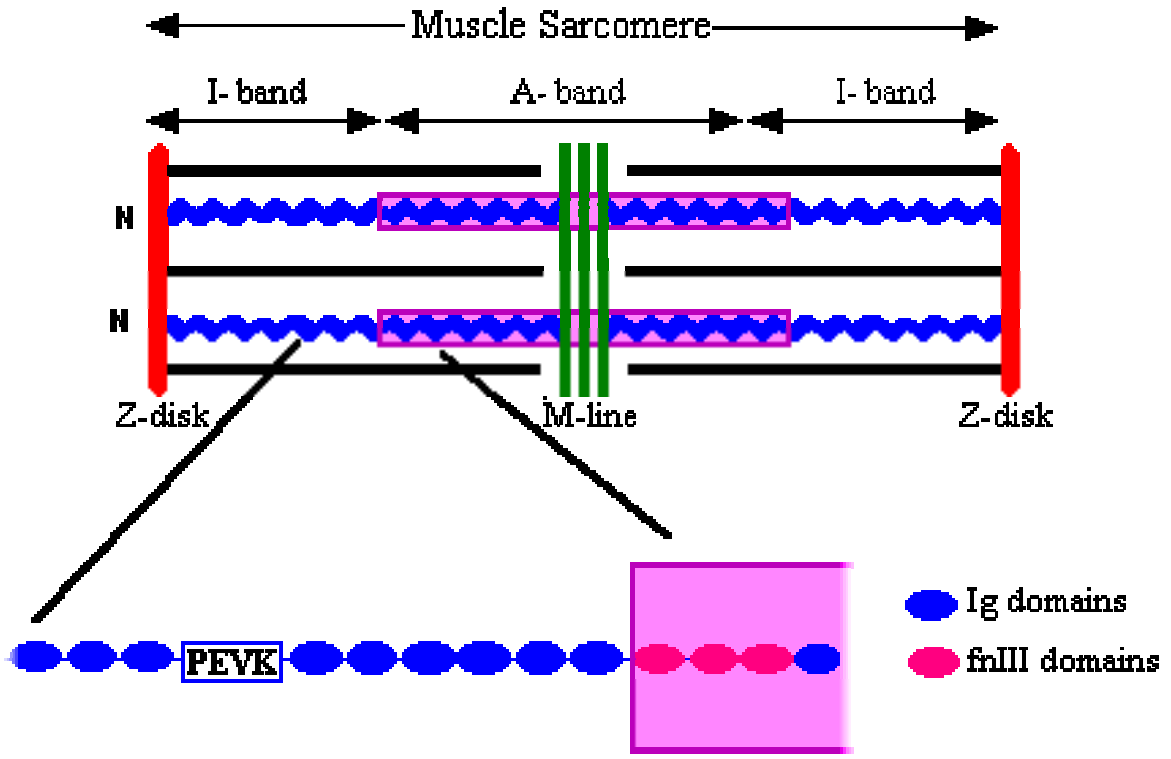
# Actin filament (thin filament)

- Actin
- Tropomyosin
- Troponin





# Titin

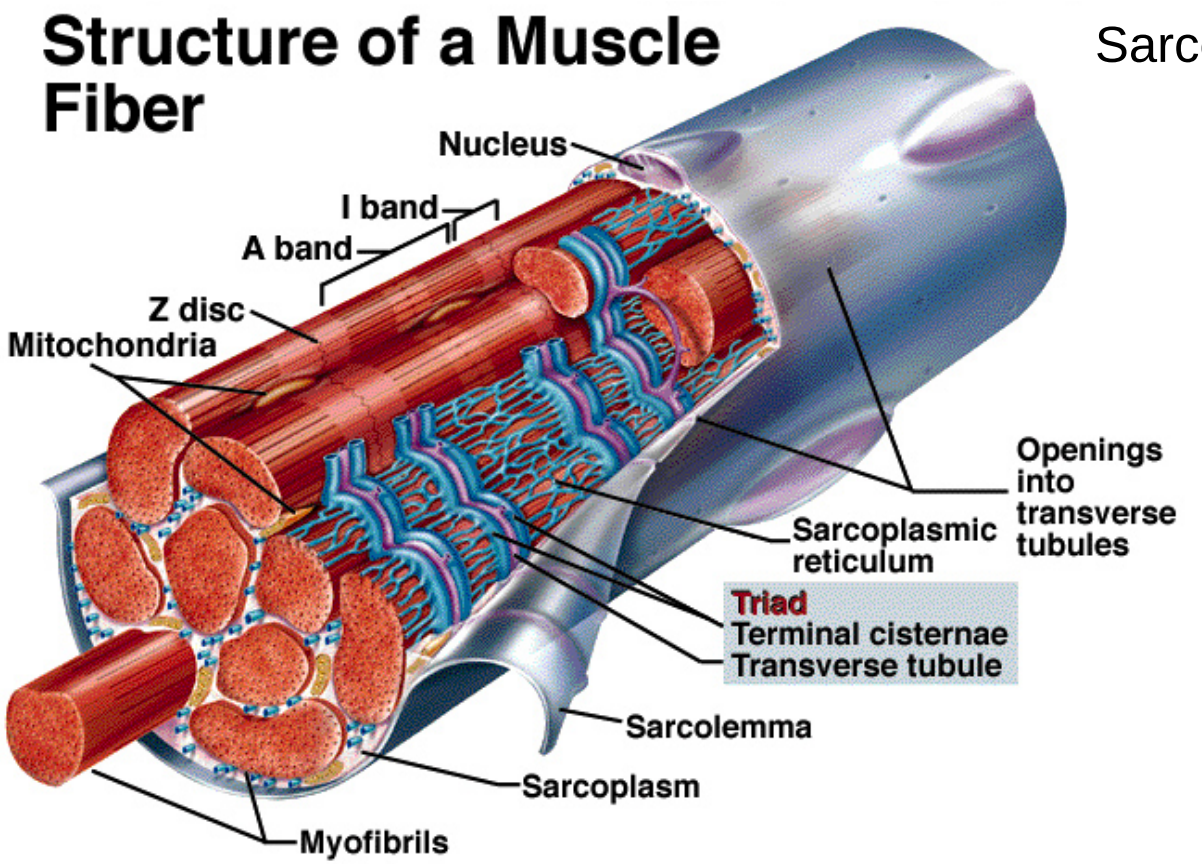

Muscle Sarcomere
I- band
A- band
I- band
N
N
Z-disk
M-line
Z-disk
PEVK
Ig domains
fnIII domains

# Sarcotubular system

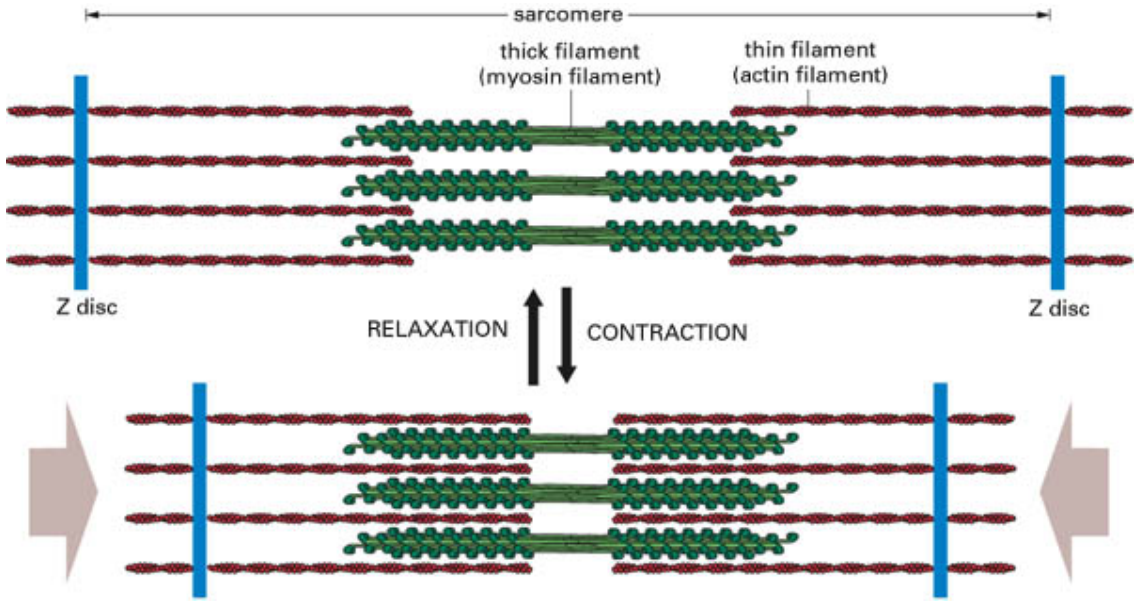
(1) Transverse Tubule

(2) Longitudinal Tubule

Sarcoplasmic reticulum



# Molecular mechanisms of contraction




Sliding-filament mechanism

Figure 9-5



## Contraction (shortening):

**myosin binds to actin, and slides it, pulling the Z-lines closer together, and reducing the width of the I-bands.**

***Note that filament lengths have not changed.***

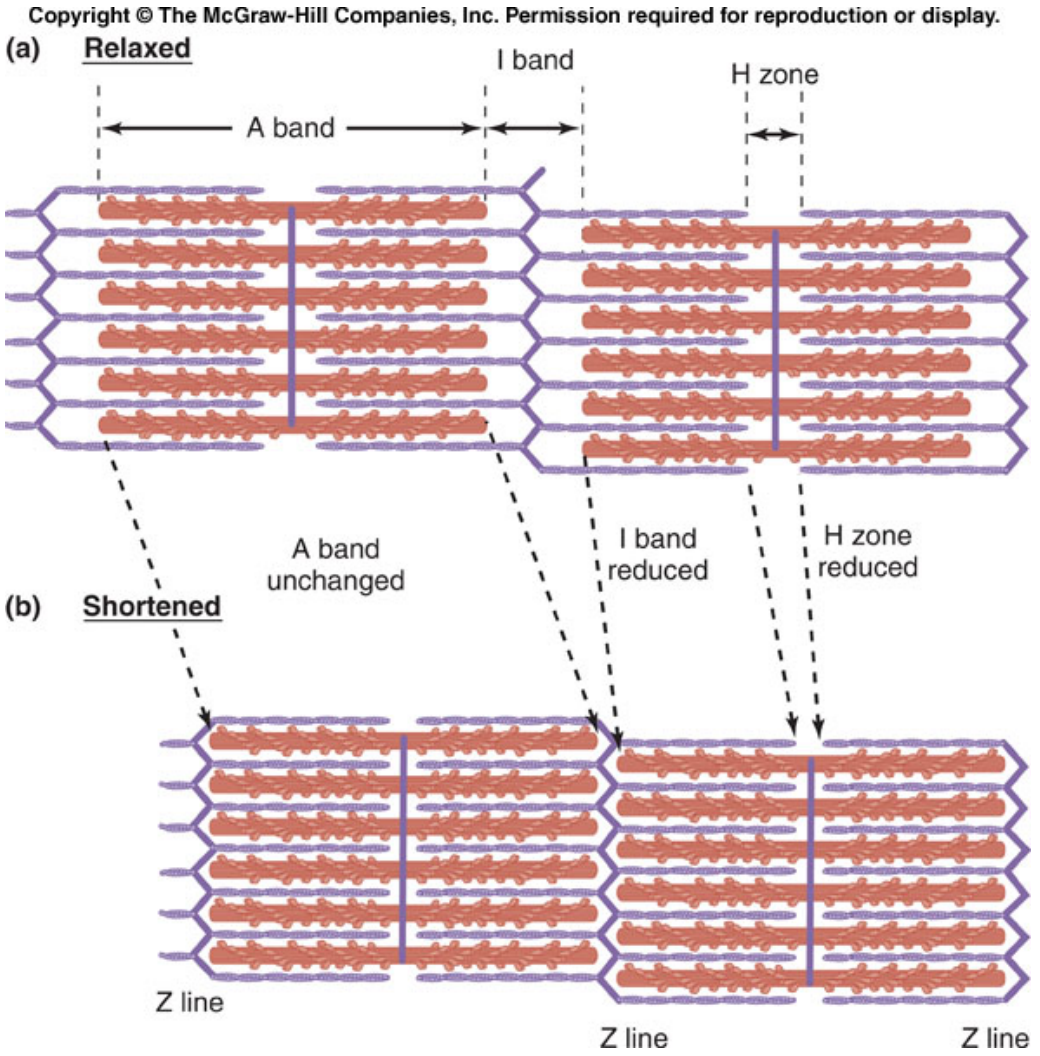
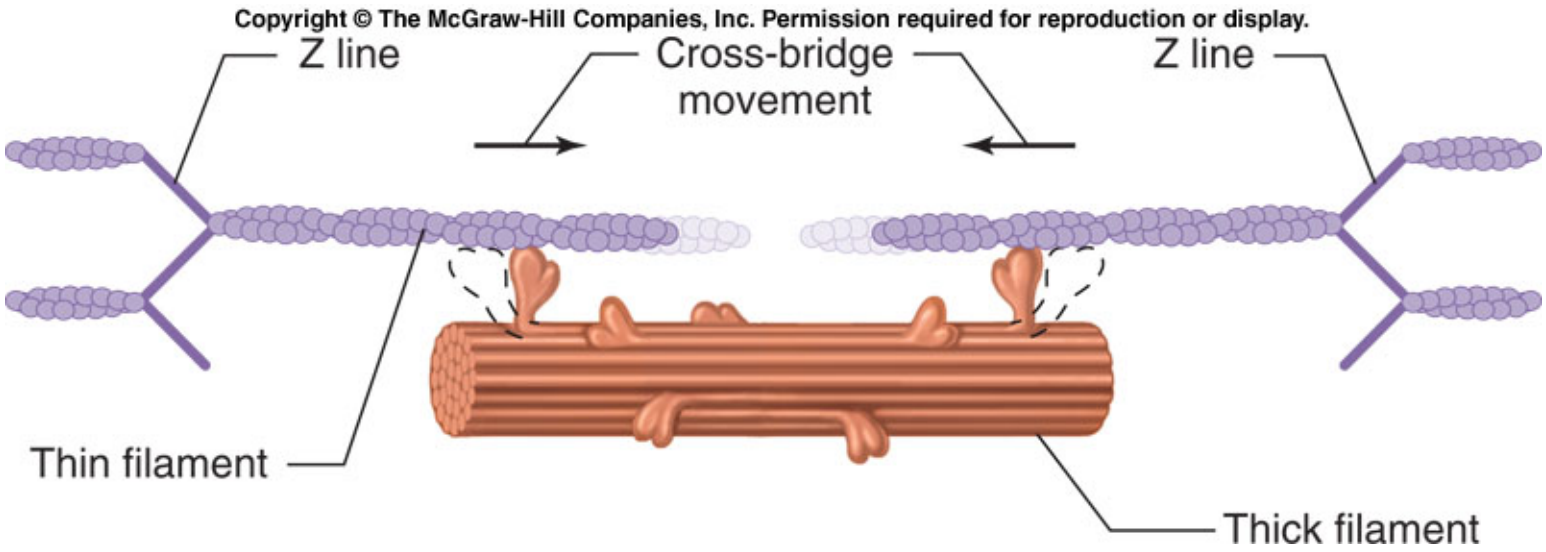


Figure 9-6






**Contraction:**

**myosin's cross-bridges bind to actin;**

**the crossbridges then flex to slide actin.**

Click here to play the Sarcomere Shortening Flash Animation

# Sliding-filament mechanism

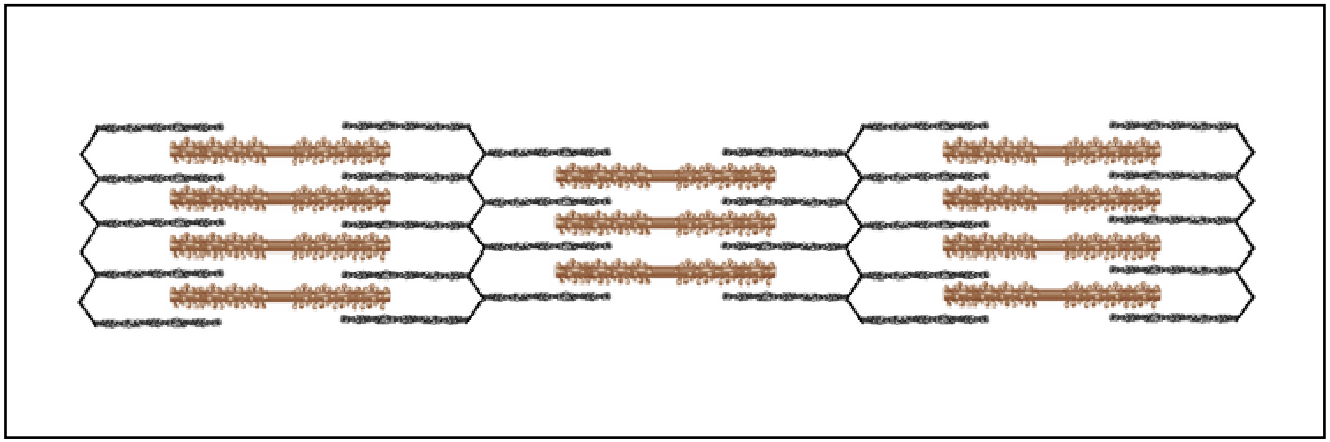
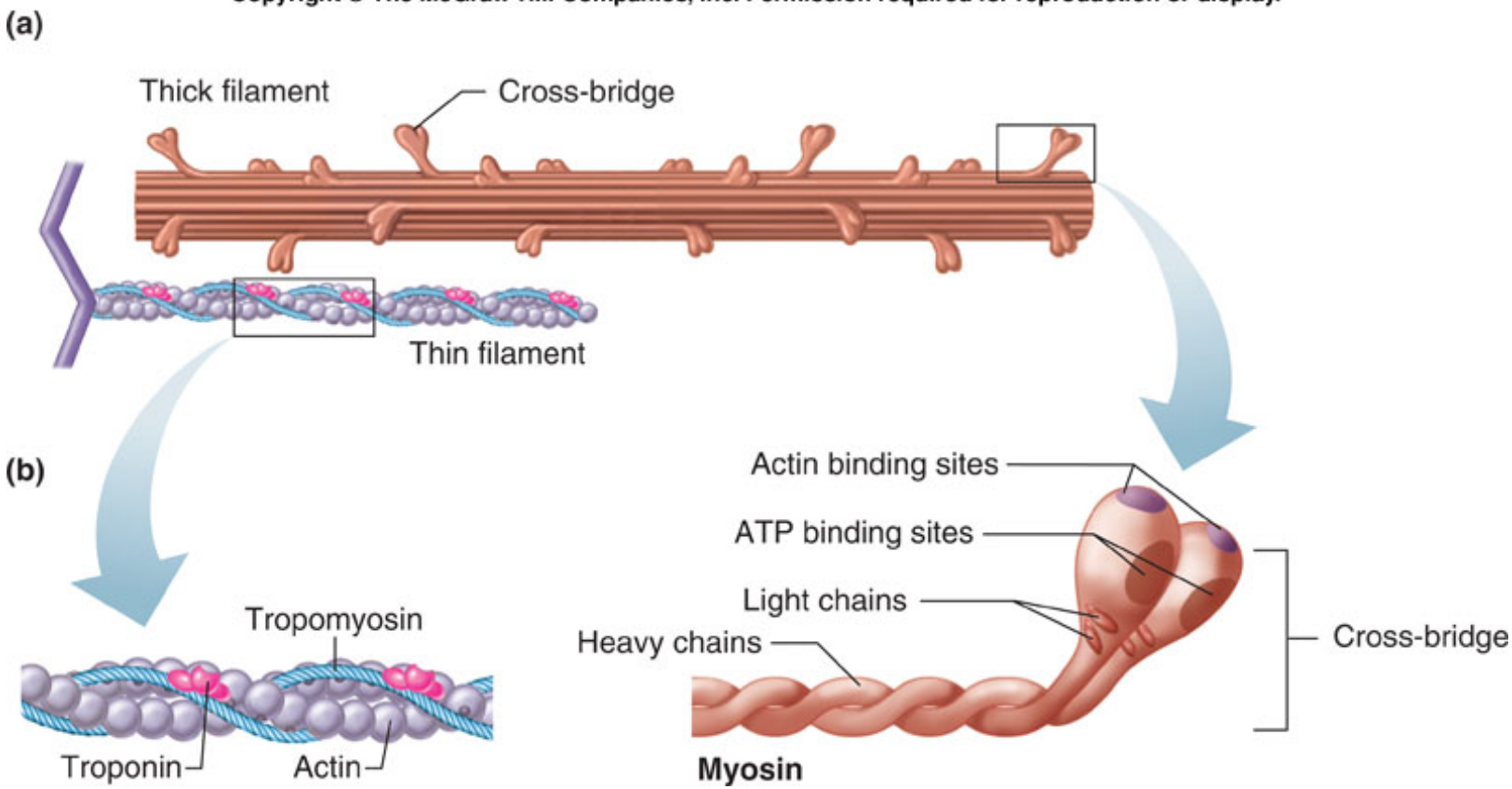


Figure 9-7



Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

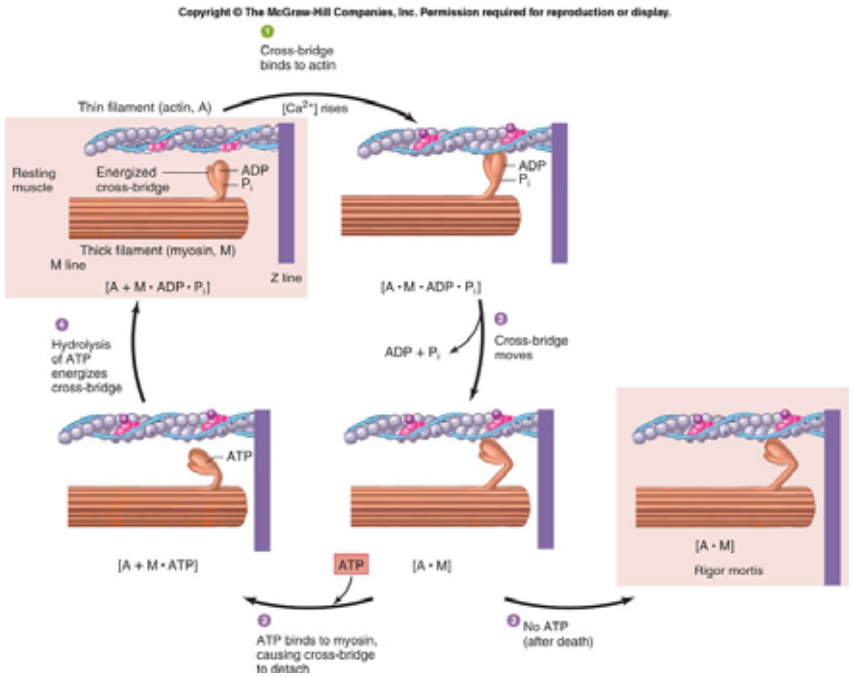



**The thick filament called myosin is actually a polymer of myosin molecules, each of which has a flexible cross-bridge that binds ATP and actin.**

# Figure 9-8

## The cross-bridge cycle requires ATP

**1.** The myosin-binding site on actin becomes available, so the energized cross-bridge binds.

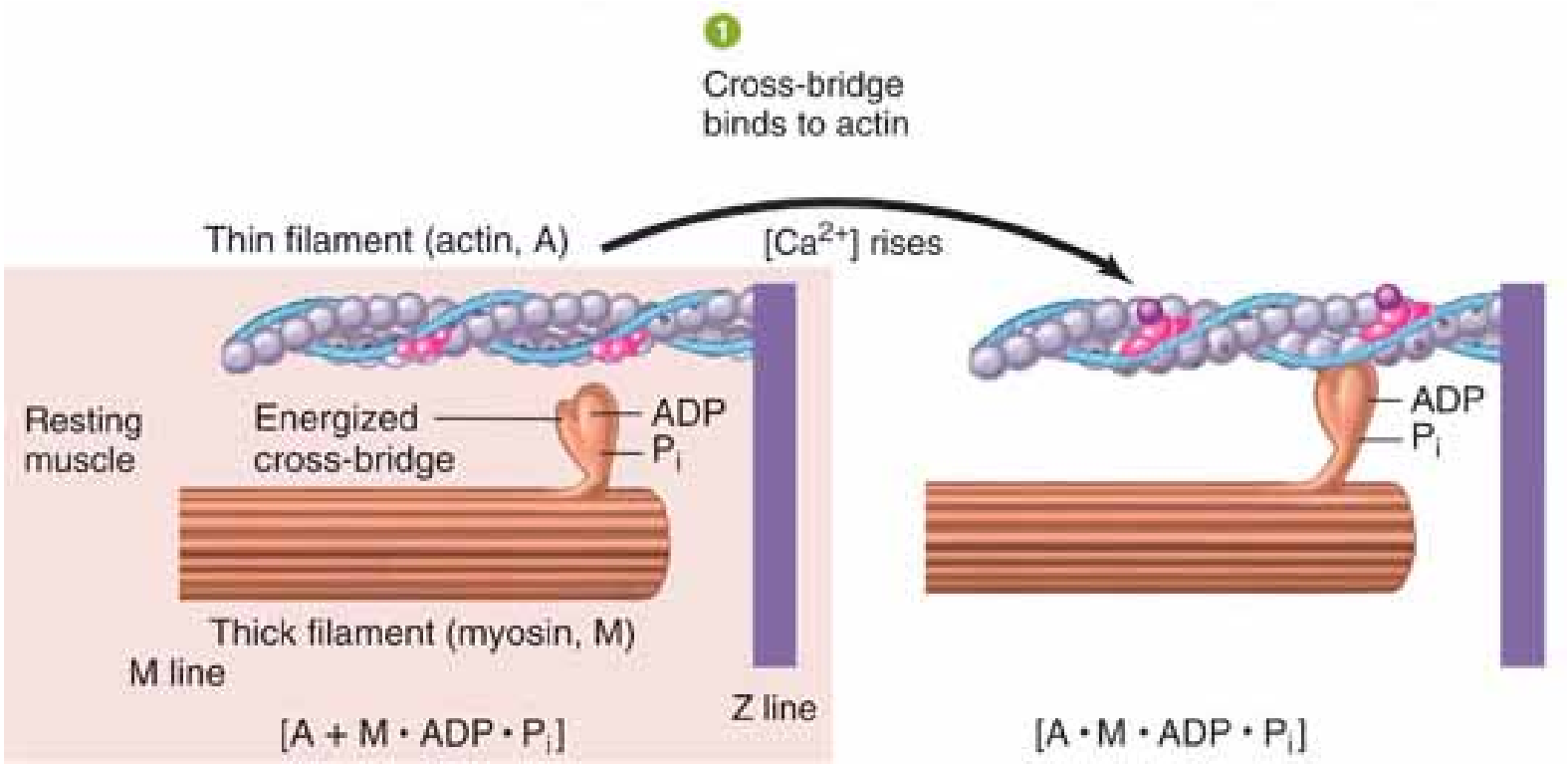


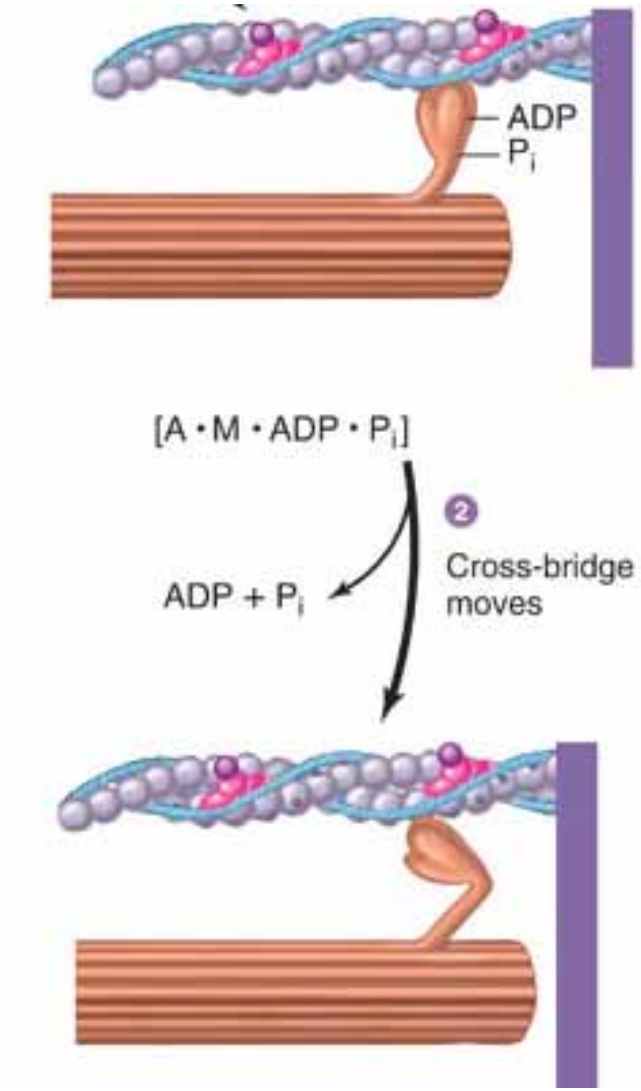

**2.** The full hydrolysis and departure of ADP + $P_i$ causes the flexing of the bound cross-bridge.

**3.** Binding of a "new" ATP to the cross-bridge uncouples the bridge.

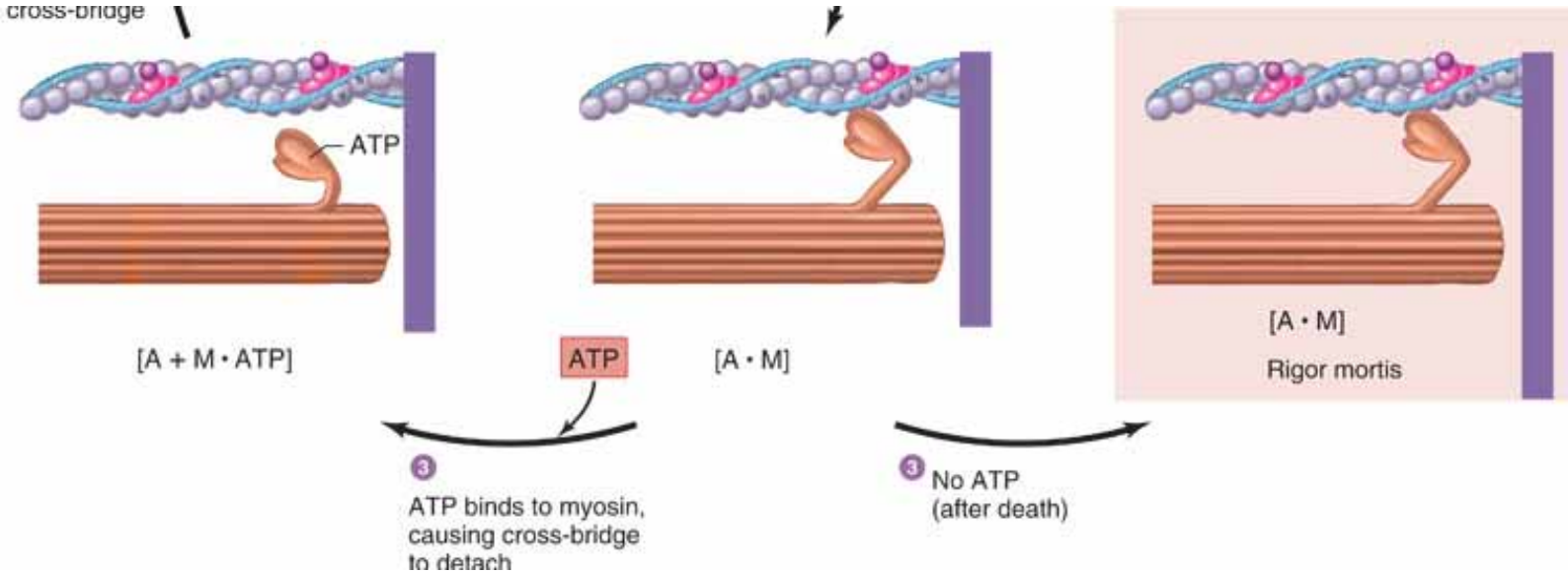
**4.** Partial hydrolysis of the bound ATP energizes or "re-cocks" the bridge.

**1.** **The myosin-binding site on actin becomes available, so the energized cross-bridge binds.**



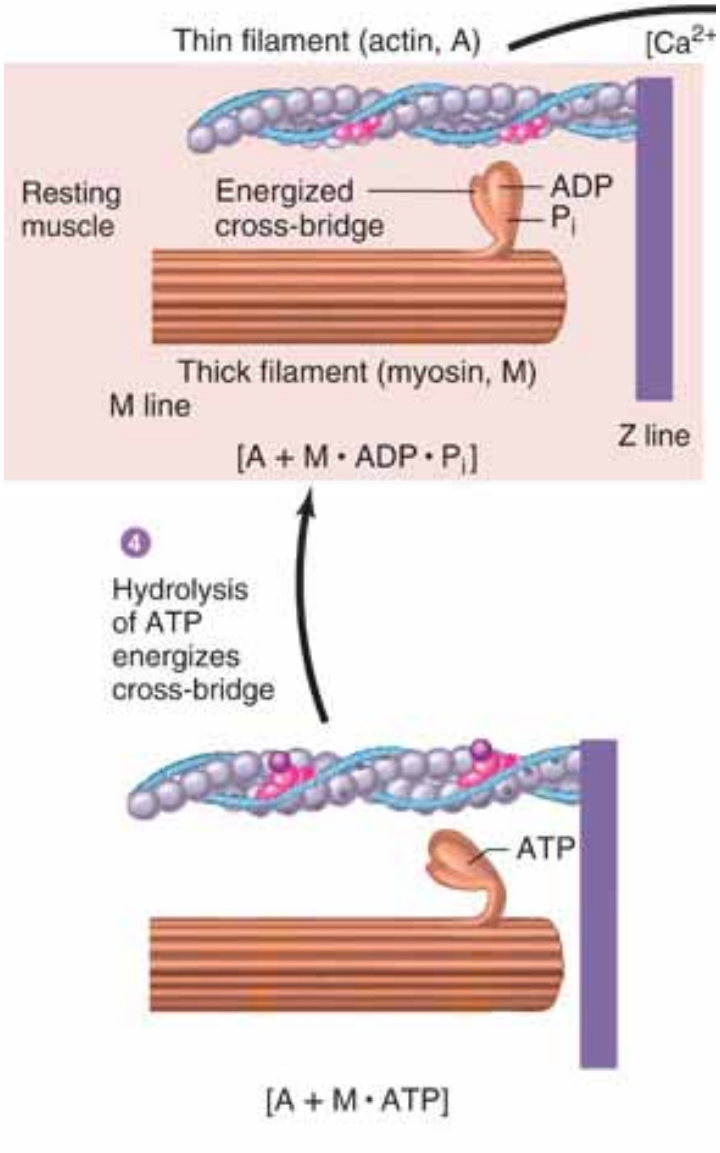



**2.** **The full hydrolysis and departure of ADP + $P_i$ causes the flexing of the bound cross-bridge.**




**3.** **Binding of a "new" ATP to the cross-bridge uncouples the bridge.**

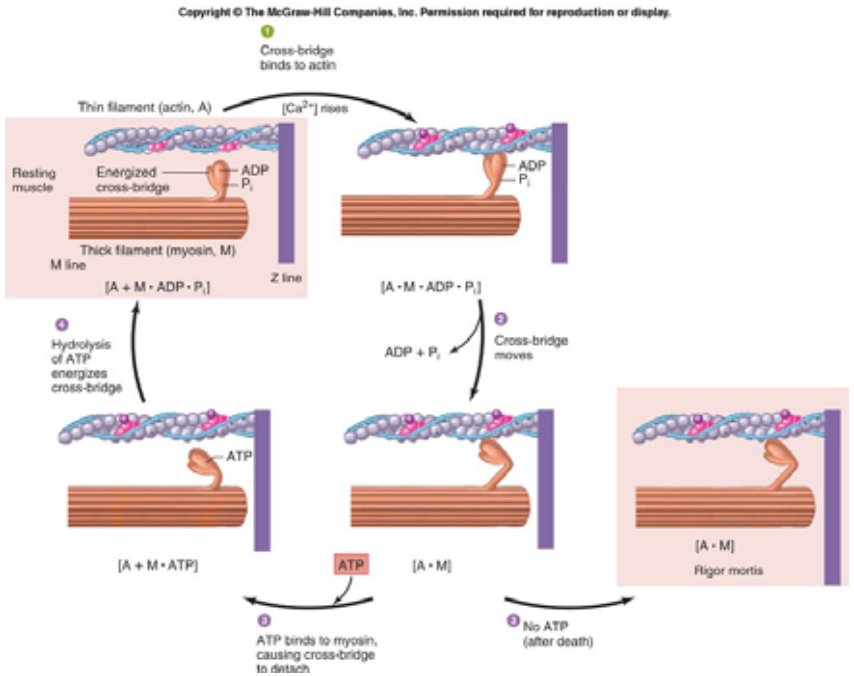
**4. Partial hydrolysis of the bound ATP energizes or "re-cocks" the bridge.**



# Figure 9-8

## The cross-bridge cycle requires ATP

**1.** The myosin-binding site on actin becomes available, so the energized cross-bridge binds.



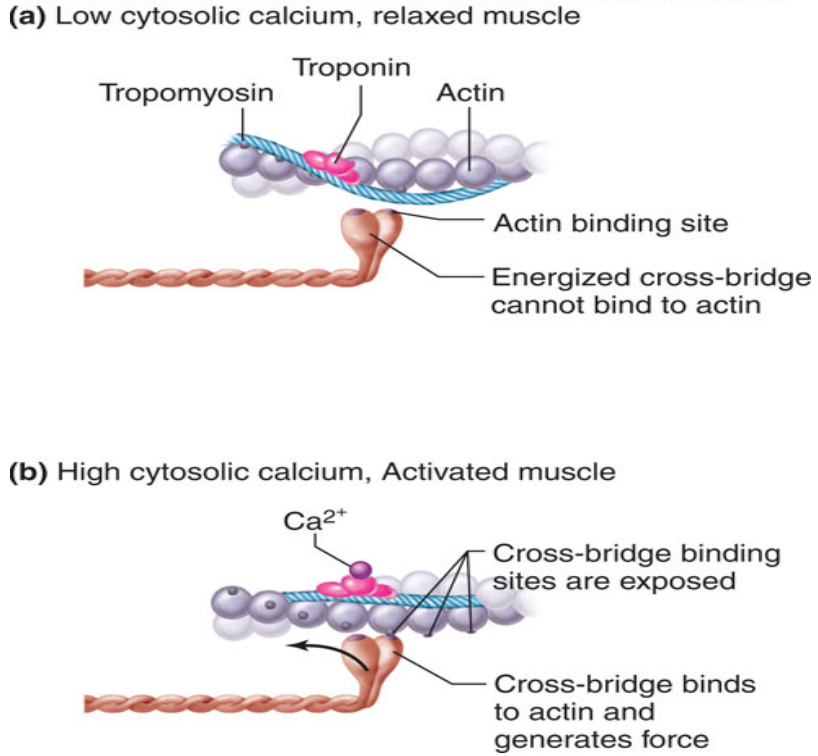

**2.** The full hydrolysis and departure of ADP + $P_i$ causes the flexing of the bound cross-bridge.

**3.** Binding of a "new" ATP to the cross-bridge uncouples the bridge.

**4.** Partial hydrolysis of the bound ATP energizes or "re-cocks" the bridge.

Click here to play the Cross-bridge cycle Flash Animation

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

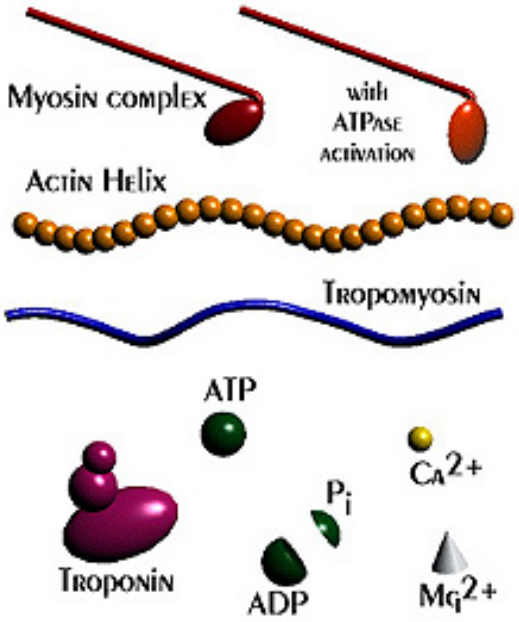


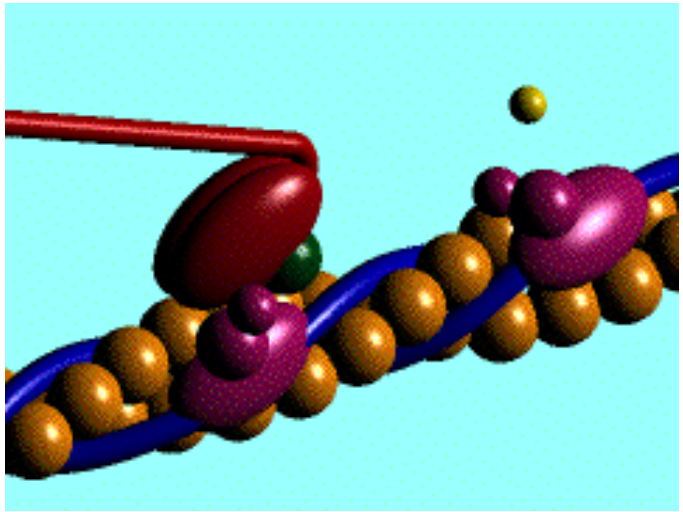

## Roles of troponin, tropomyosin, and calcium in contraction

**In relaxed skeletal muscle, tropomyosin blocks the cross-bridge binding site on actin.**

**Contraction occurs when calcium ions bind to troponin; this complex then pulls tropomyosin away from the cross-bridge binding site.**

# Interaction of myosin and actin



# Excitation-contraction coupling

- Transmission of action potential (AP) along T tubules
- Calcium release caused by T tubule AP
- Contraction initiated by calcium ions

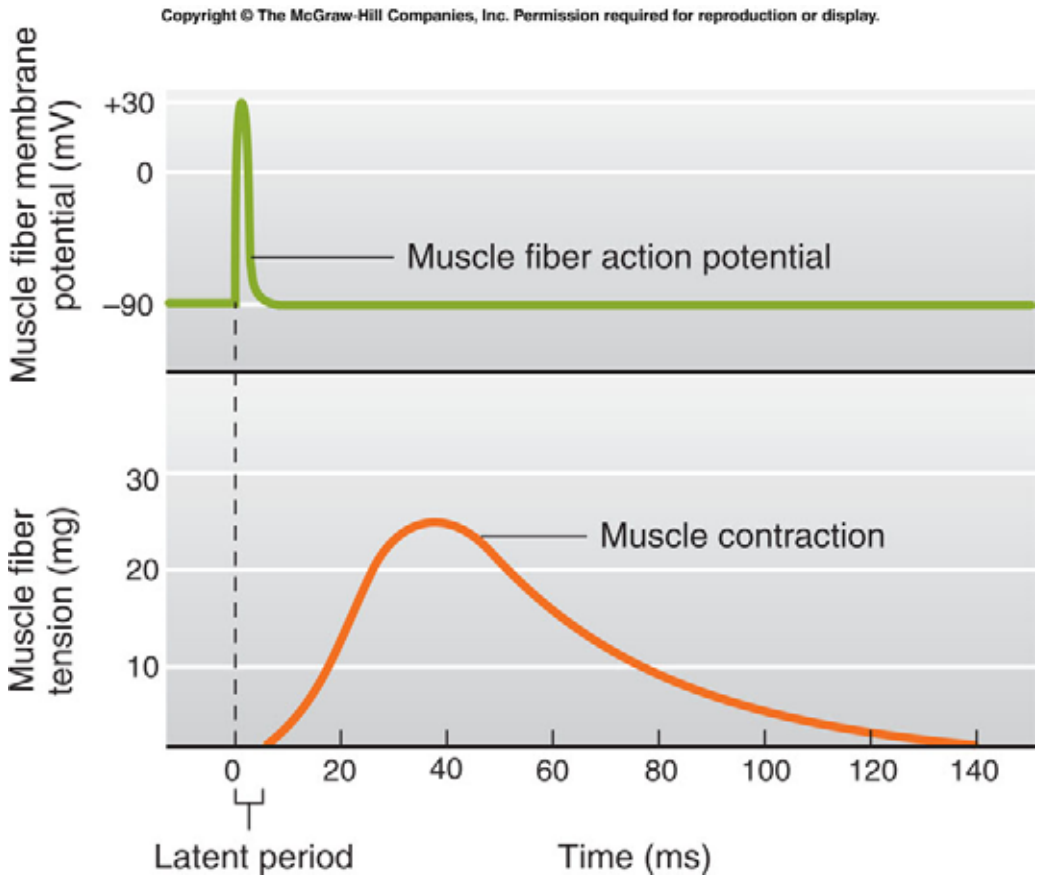
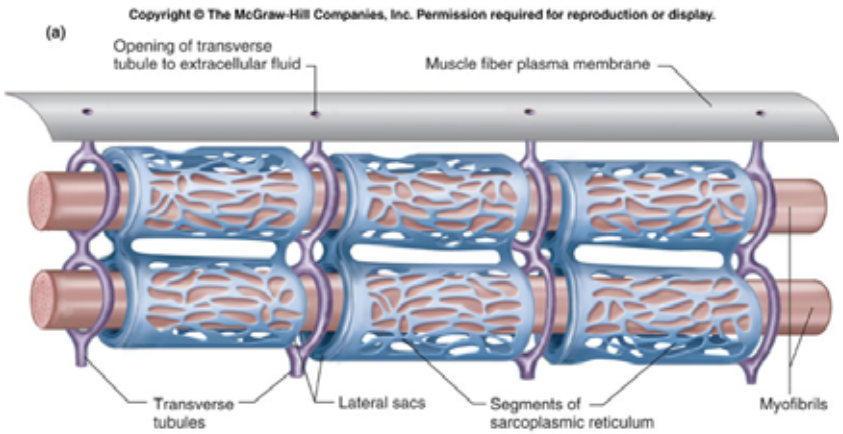



Figure 9-10

**The latent period between excitation and development of tension in a skeletal muscle includes the time needed to release $Ca^{++}$ from sarcoplasmic reticulum, move tropomyosin, and cycle the cross-bridges.**

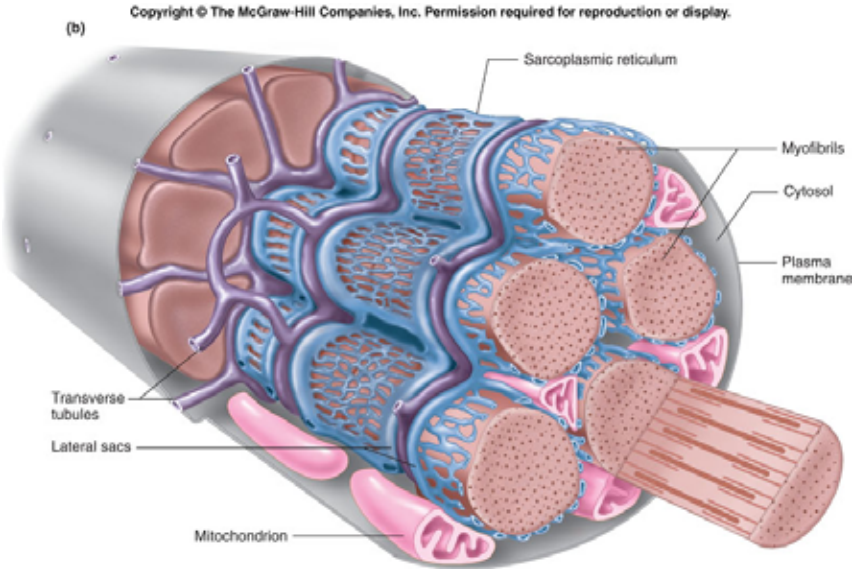
Figure 9-11





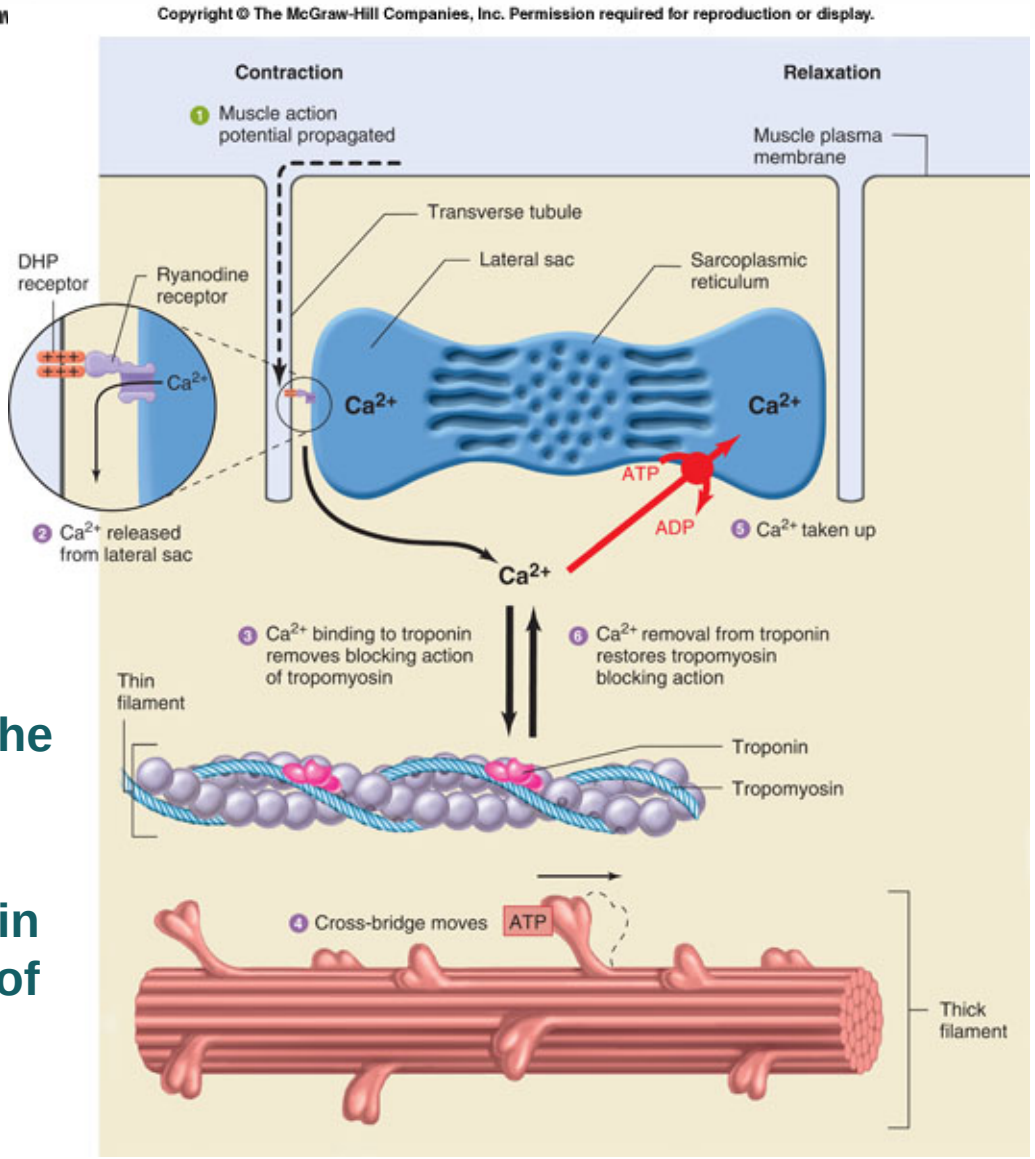

**The transverse tubules bring action potentials into the interior of the skeletal muscle fibers, so that the wave of depolarization passes close to the sarcoplasmic reticulum, stimulating the release of calcium ions.**

**The extensive meshwork of sarcoplasmic reticulum assures that when it releases calcium ions they can readily diffuse to all of the troponin sites.**



# Figure 9-12






**Passage of an action potential along the transverse tubule opens nearby voltage-gated calcium channels, the "ryanodine receptor," located on the sarcoplasmic reticulum, and**

**calcium ions released into the cytosol bind to troponin.**

**The calcium-troponin complex "pulls" tropomyosin off the myosin-binding site of actin, thus allowing the binding of the cross-bridge, followed by its flexing to slide the actin filament.**

## TABLE 9–1 Functions of ATP in Skeletal Muscle Contraction

1. Hydrolysis of ATP by myosin energizes the cross-bridges, providing the energy for force generation.
2. Binding of ATP to myosin dissociates cross-bridges bound to actin, allowing the bridges to repeat their cycle of activity.
3. Hydrolysis of ATP by the $Ca^{2+}$-ATPase in the sarcoplasmic reticulum provides the energy for the active transport of calcium ions into the reticulum, lowering cytosolic calcium to prerelease levels, ending the contraction, and allowing the muscle fiber to relax.

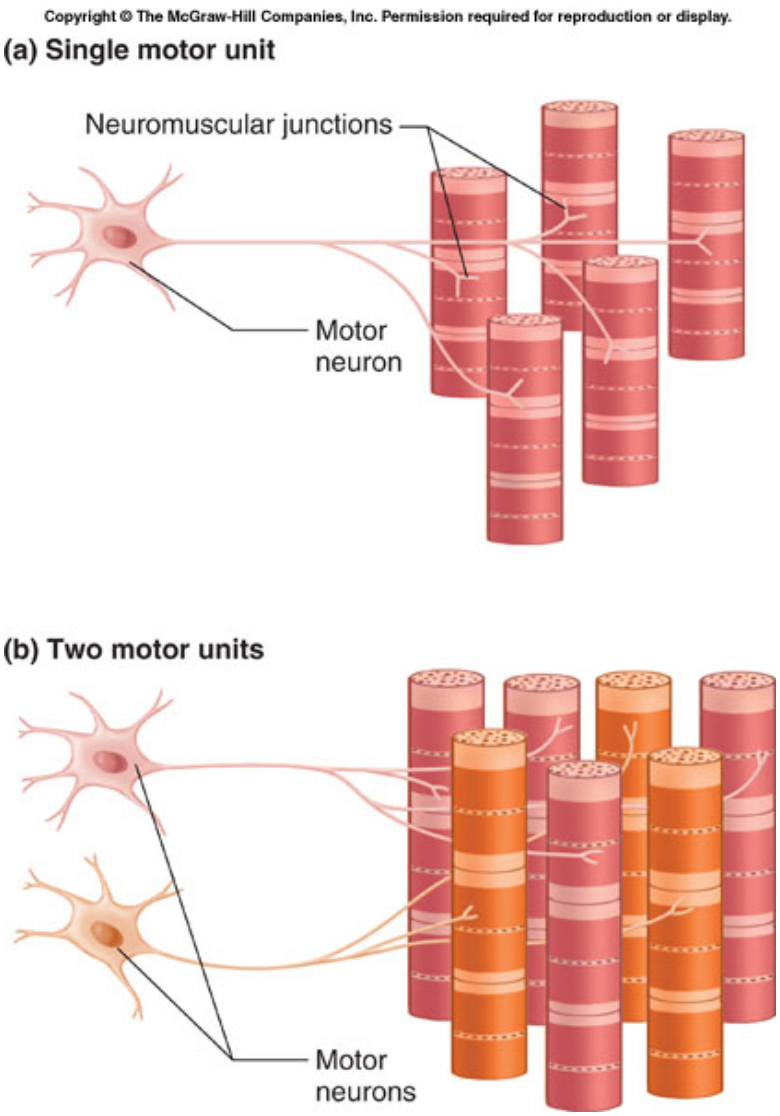
# General process of excitation and contraction in skeletal muscle

- Neuromuscular transmission
- Excitation-contraction coupling
- Muscle contraction

Figure 9-13



**A single motor unit consists of a motor neuron and all of the muscle fibers it controls.**

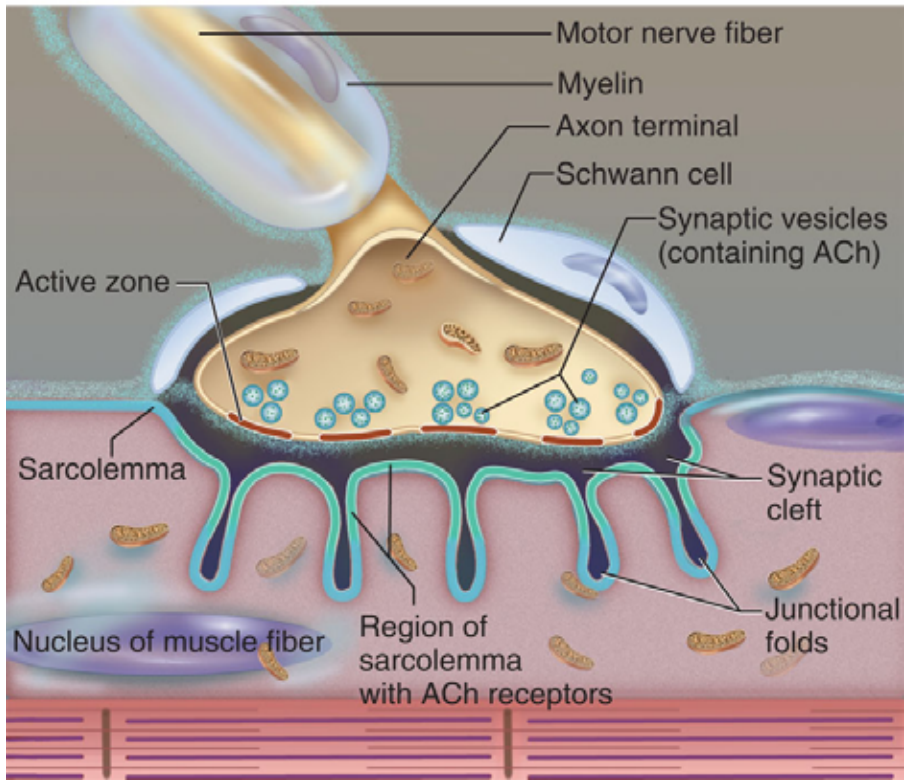


**The neuromuscular junction is the point of synaptic contact between the axon terminal of a motor neuron and the muscle fiber it controls.**

**Action potentials in the motor neuron cause acetylcholine release into the neuromuscular junction.**



(b)




**Muscle contraction follows the delivery of acetylcholine to the muscle fiber.**

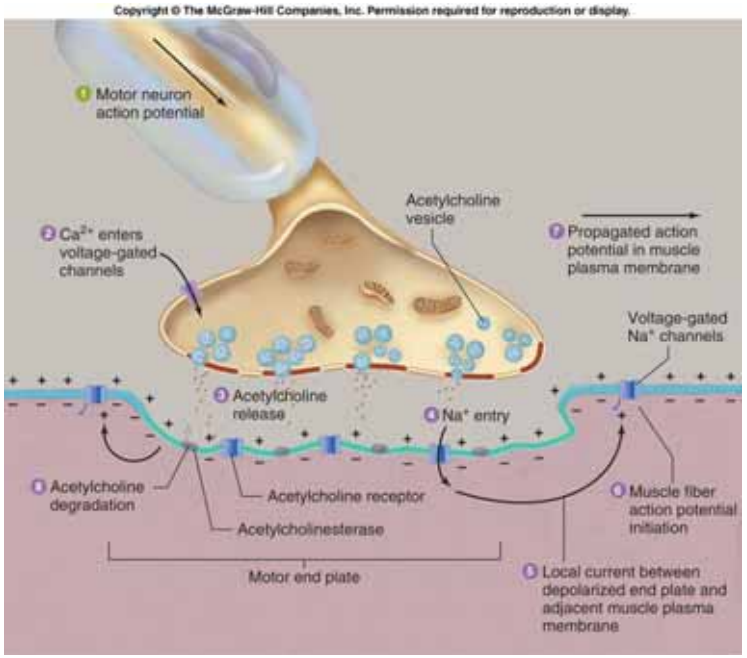


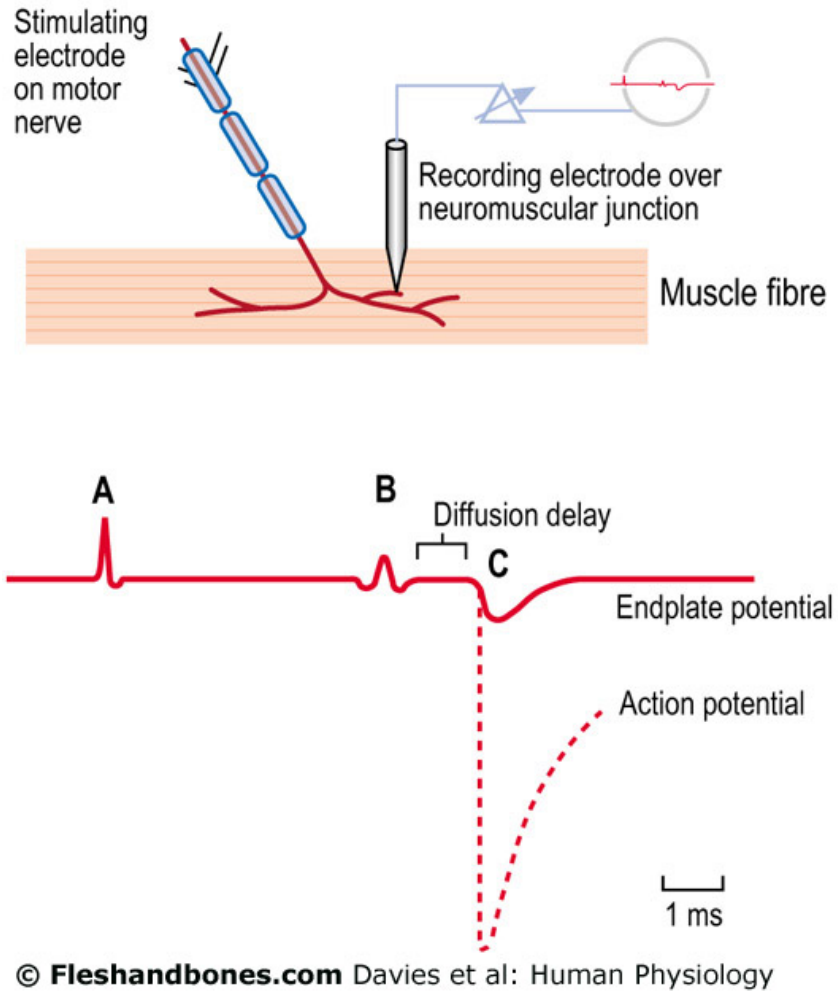

Figure 9-15

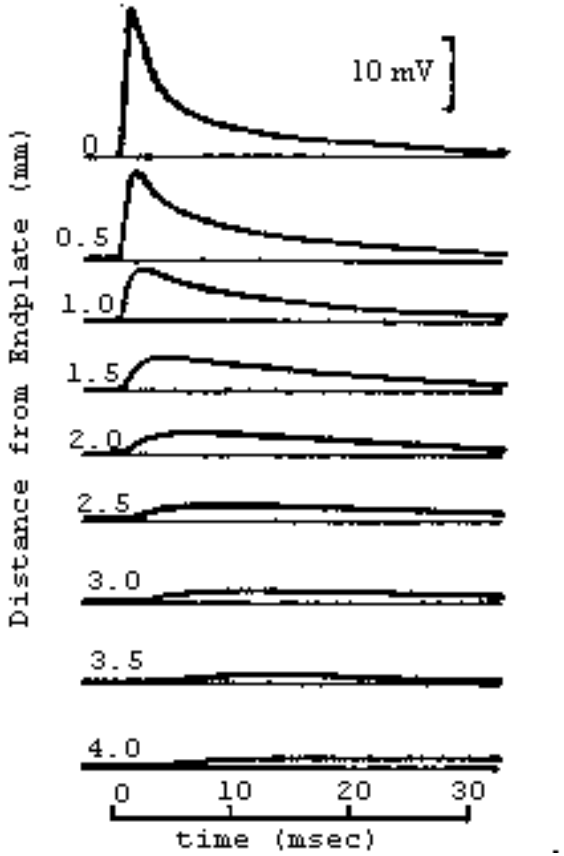
**1. The exocytosis of acetylcholine from the axon terminal occurs when the acetylcholine vesicles merge into the membrane covering the terminal.**

**2. On the membrane of the muscle fiber, the receptors for acetylcholine respond to its binding by increasing $Na^+$ entry into the fiber, causing a graded depolarization.**

**3. The graded depolarization typically exceeds threshold for the nearby voltage-gate $Na^+$ and $K^+$ channels, so an action potential occurs on the muscle fiber.**

# End plate potential (EPP)



Click here to play the Neuromuscular Junction Flash Animation

Click here to play the Action Potentials and Muscle Contraction Flash Animation

**TABLE 9–2** Sequence of Events Between a Motor Neuron Action Potential and Skeletal Muscle Fiber Contraction

1. Action potential is initiated and propagates to motor neuron axon terminals.
2. Calcium enters axon terminals through voltage-gated calcium channels.
3. Calcium entry triggers release of ACh from axon terminals.
4. ACh diffuses from axon terminals to motor end plate in muscle fiber.
5. ACh binds to nicotinic receptors on motor end plate, increasing their permeability to $Na^+$ and $K^+$.
6. More $Na^+$ moves into the fiber at the motor end plate than $K^+$ moves out, depolarizing the membrane, producing the end plate potential (EPP).
7. Local currents depolarize the adjacent muscle cell plasma membrane to its threshold potential, generating an action potential that propagates over the muscle fiber surface and into the fiber along the T-tubules.
8. Action potential in T-tubules triggers release of $Ca^{2+}$ from lateral sacs of sarcoplasmic reticulum.
9. $Ca^{2+}$ binds to troponin on the thin filaments, causing tropomyosin to move away from its blocking position, thereby uncovering cross-bridge binding sites on actin.
10. Energized myosin cross-bridges on the thick filaments bind to actin:

$$A + M \cdot ADP \cdot P_i \longrightarrow A \cdot M \cdot ADP \cdot P_i$$

11. Cross-bridge binding triggers release of ATP hydrolysis products from myosin, producing an angular movement of each cross-bridge:

$$A \cdot M \cdot ADP \cdot P_i \longrightarrow A \cdot M + ADP + P_i$$

12. ATP binds to myosin, breaking linkage between actin and myosin and thereby allowing cross-bridges to dissociate from actin:

$$A \cdot M + ATP \longrightarrow A + M \cdot ATP$$

13. ATP bound to myosin is split, energizing the myosin cross-bridge:

$$M \cdot ATP \longrightarrow M \cdot ADP \cdot P_i$$

14. Cross-bridges repeat steps 10 to 13, producing movement (sliding) of thin filaments past thick filaments. Cycles of cross-bridge movement continue as long as $Ca^{2+}$ remains bound to troponin.
15. Cytosolic $Ca^{2+}$ concentration decreases as $Ca^{2+}$ is actively transported into sarcoplasmic reticulum by $Ca^{2+}$-ATPase.
16. Removal of $Ca^{2+}$ from troponin restores blocking action of tropomyosin, the cross-bridge cycle ceases, and the muscle fiber relaxes.

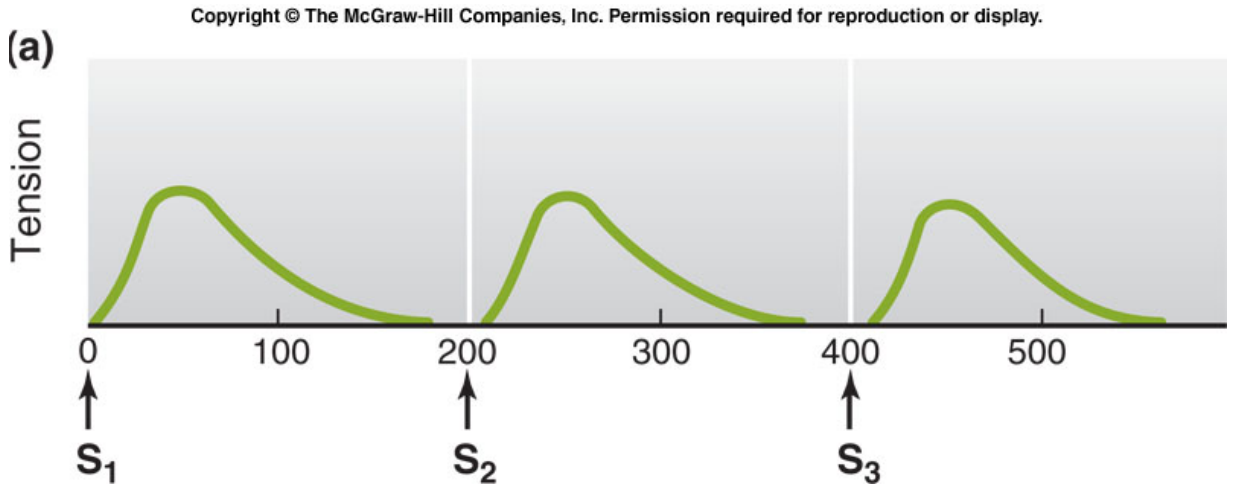
# Mechanics of single-fiber contraction

- Muscle tension – the force exerted on an object by a contracting muscle
- Load – the force exerted on the muscle by an object (usually its weight)

- Isometric contraction – a muscle develops tension but does not shorten (or lengthen) (constant length)
- Isotonic contraction – the muscle shortens while the load on the muscle remains constant (constant tension)

# Twitch contraction

- The mechanical response of a single muscle fiber to a single action potential is know as a **TWITCH**

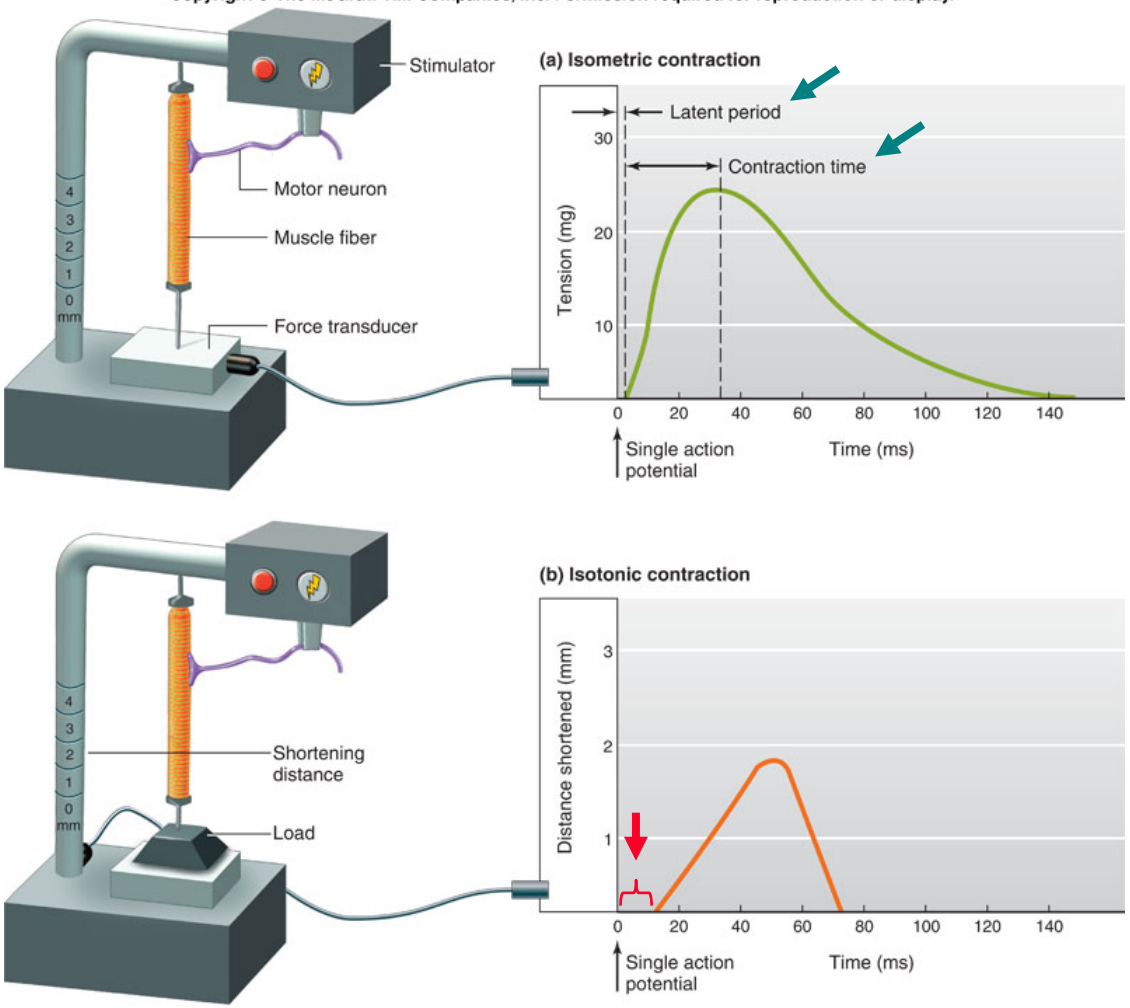


# Figure 9-20



***iso*** **= same** ***tonic*** **= tension** ***metric*** **= length**






**Tension increases rapidly and dissipates slowly**

**Shortening occurs slowly, only after taking up elastic tension; the relaxing muscle quickly returns to its resting length.**

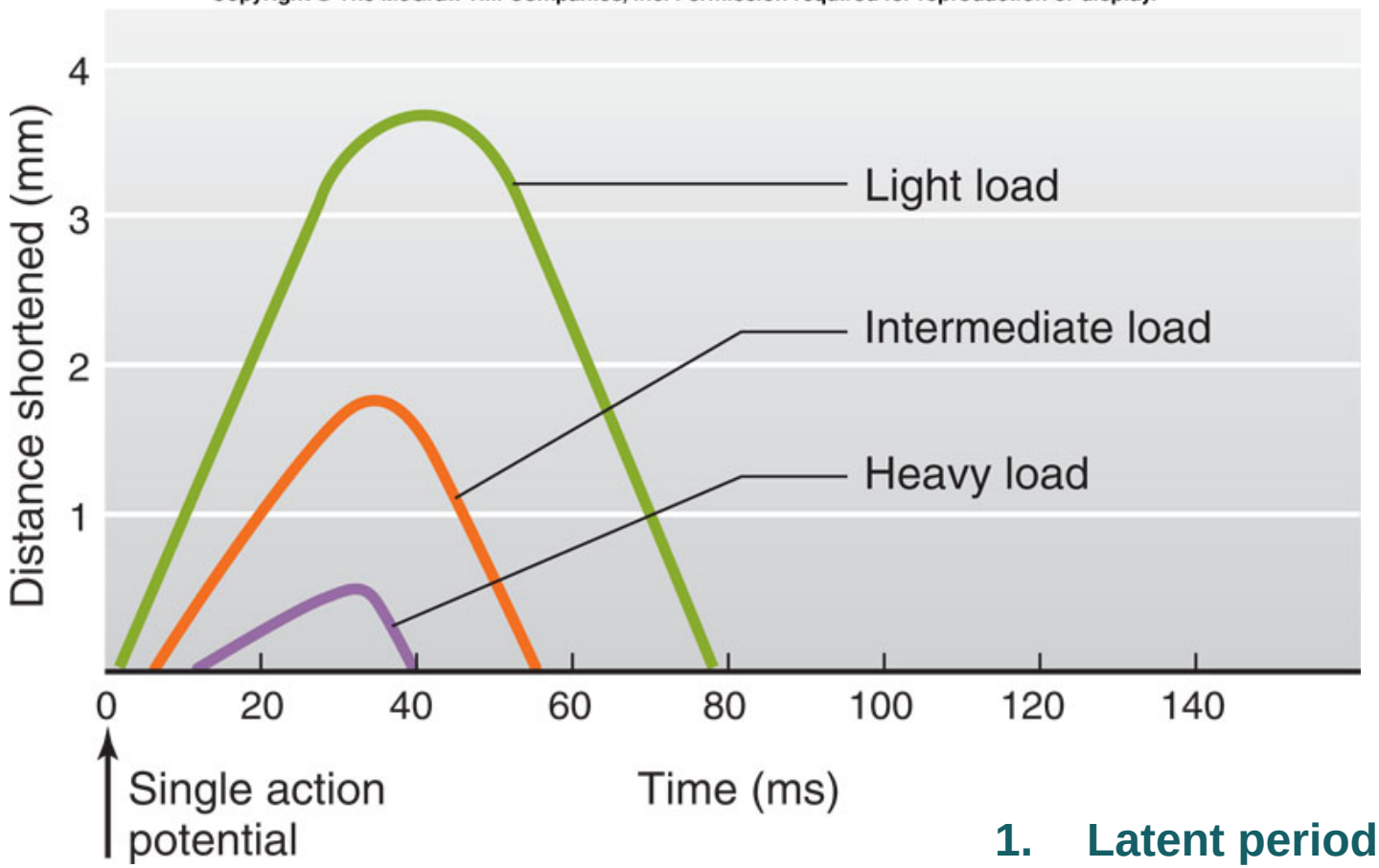
Click here to play the
Mechanisms of
Single Fiber Contraction
Flash Animation

Figure 9-17



**All three are isotonic contractions.**

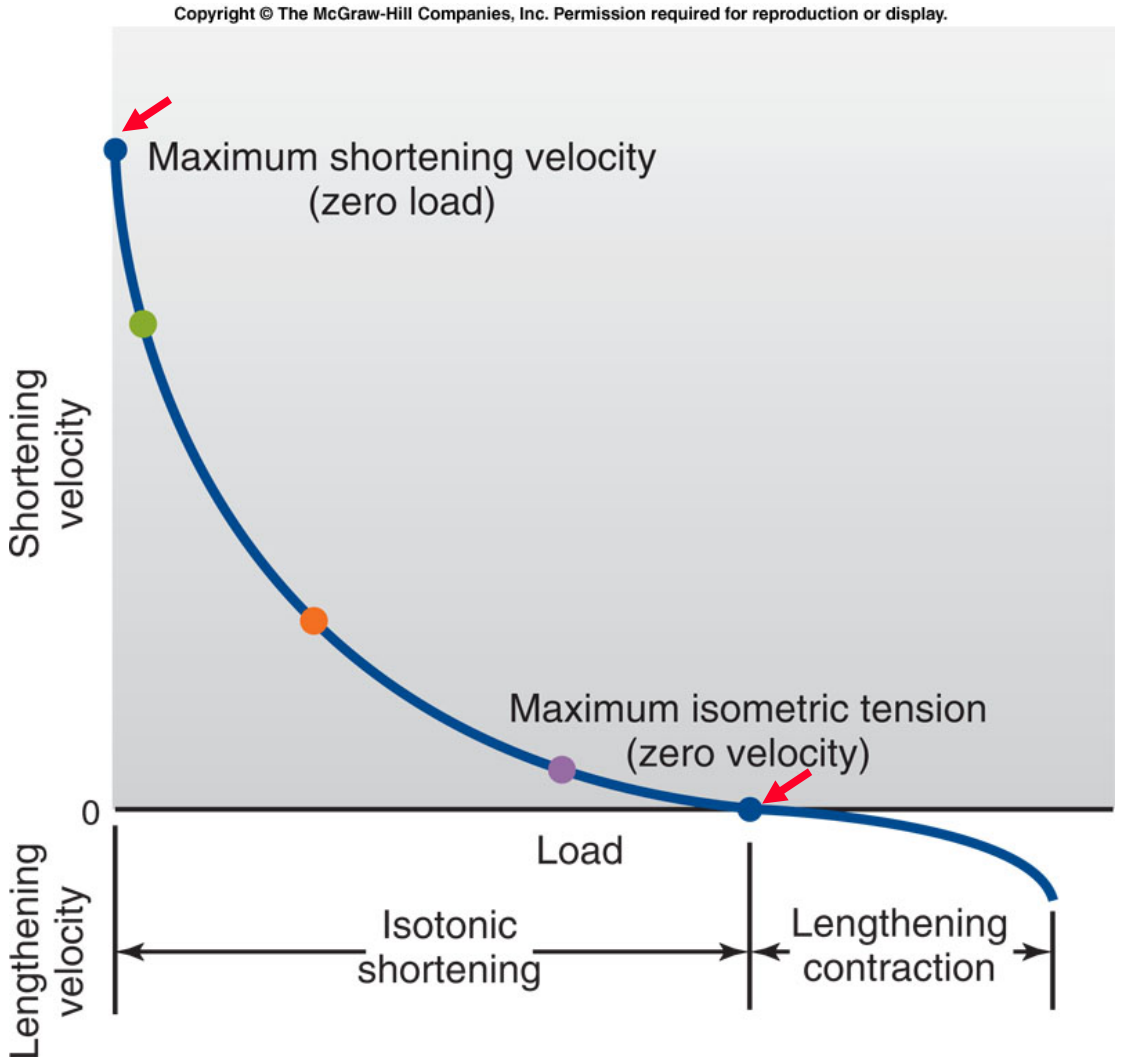
Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.




1. **Latent period**
2. **Velocity of shortening**
3. **Duration of the twitch**
4. **Distance shortened**

# Load-velocity relation





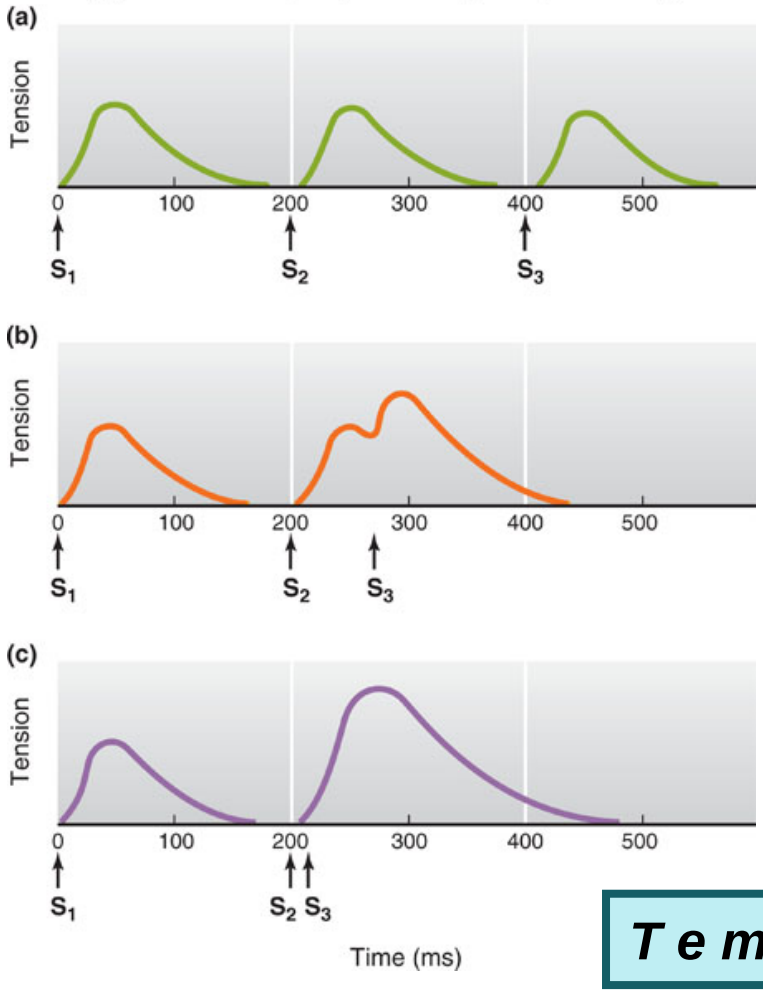
Click here to play the
Mechanisms of
Single Fiber Contraction
Flash Animation

Figure 9-19



# Frequency-tension relation






**Complete dissipation of elastic tension between subsequent stimuli.**

**$S_3$ occurred prior to the complete dissipation of elastic tension from $S_2$.**

**$S_3$ occurred prior to the dissipation of ANY elastic tension from $S_2$.**

***Temporal summation.***

Figure 9-20

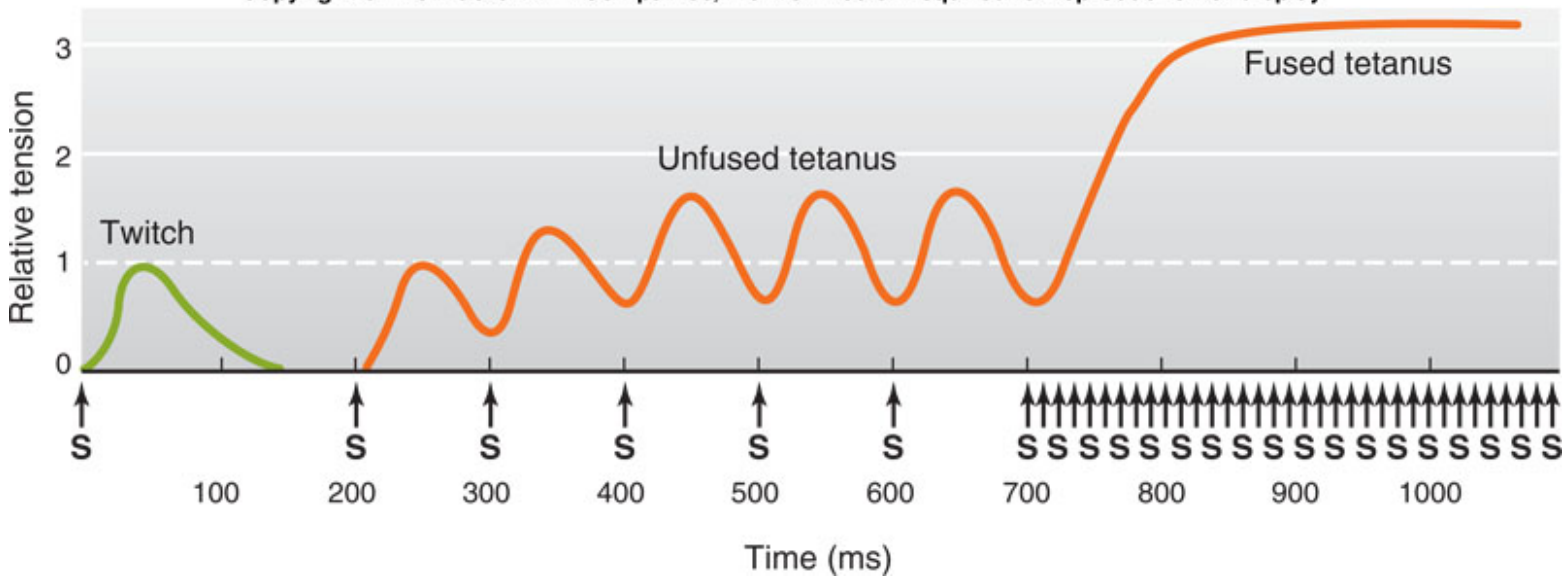


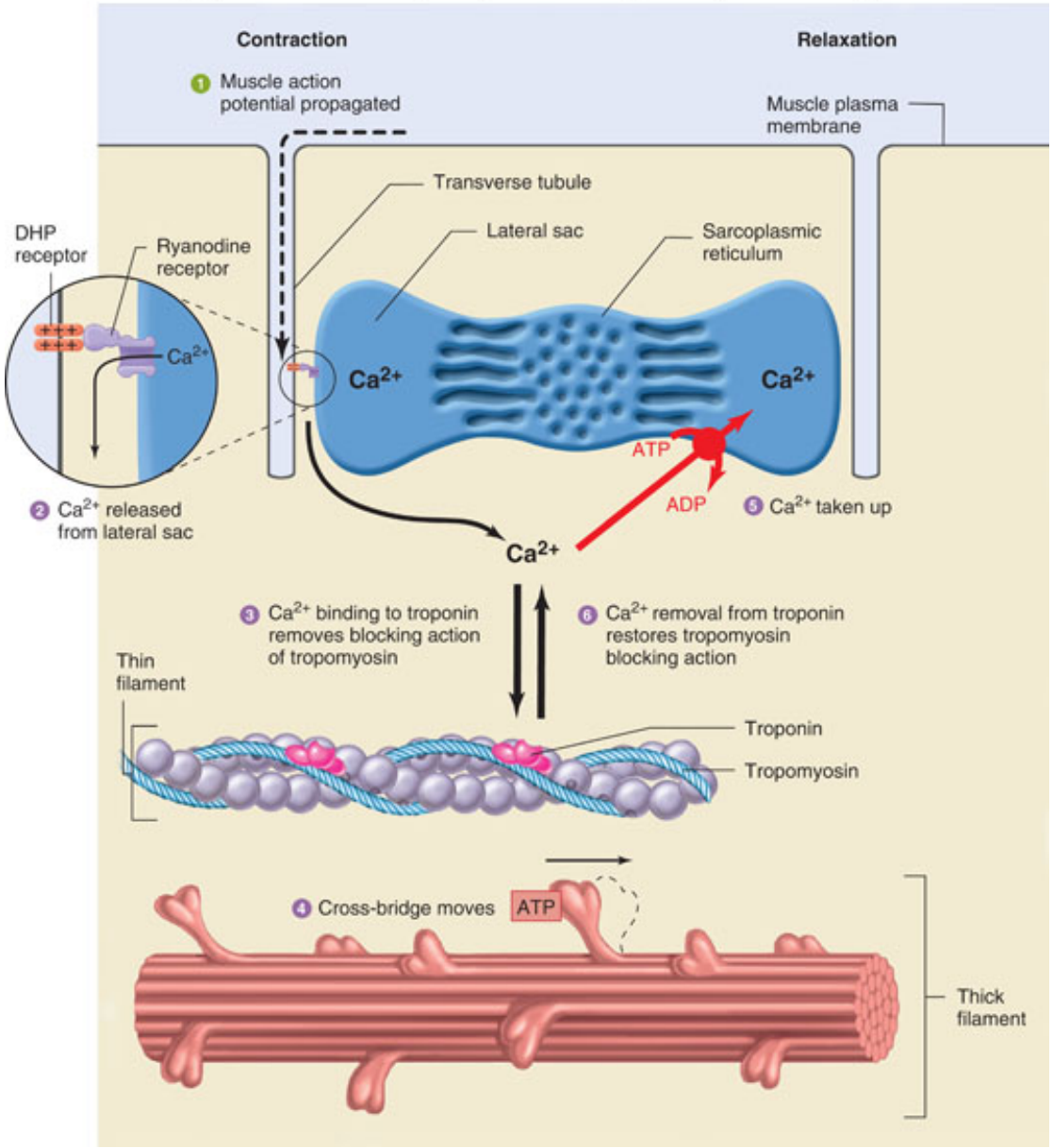
# Frequency-tension relation

**Unfused tetanus:**
**partial dissipation of elastic tension between subsequent stimuli.**

**Fused tetanus:**
**no time for dissipation of elastic tension between rapidly recurring stimuli.**








# Mechanism for greater tetanic tension

**Successive action potentials result in a persistent elevation of cytosolic calcium concentration**

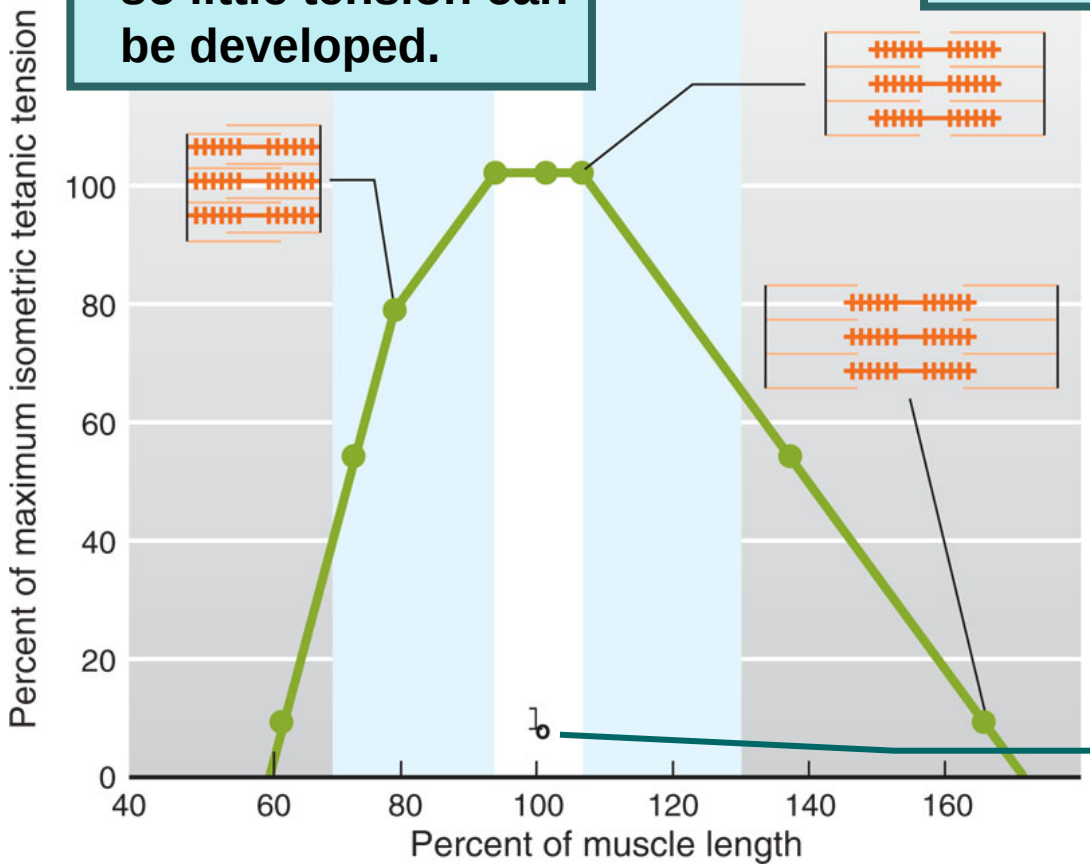
Figure 9-21



# Length-tension relation

**Short sarcomere: actin filaments lack room to slide, so little tension can be developed.**

**Optimal-length sarcomere: lots of actin-myosin overlap and plenty of room to slide.**




**Long sarcomere: actin and myosin do not overlap much, so little tension can be developed.**

**Optimal length**

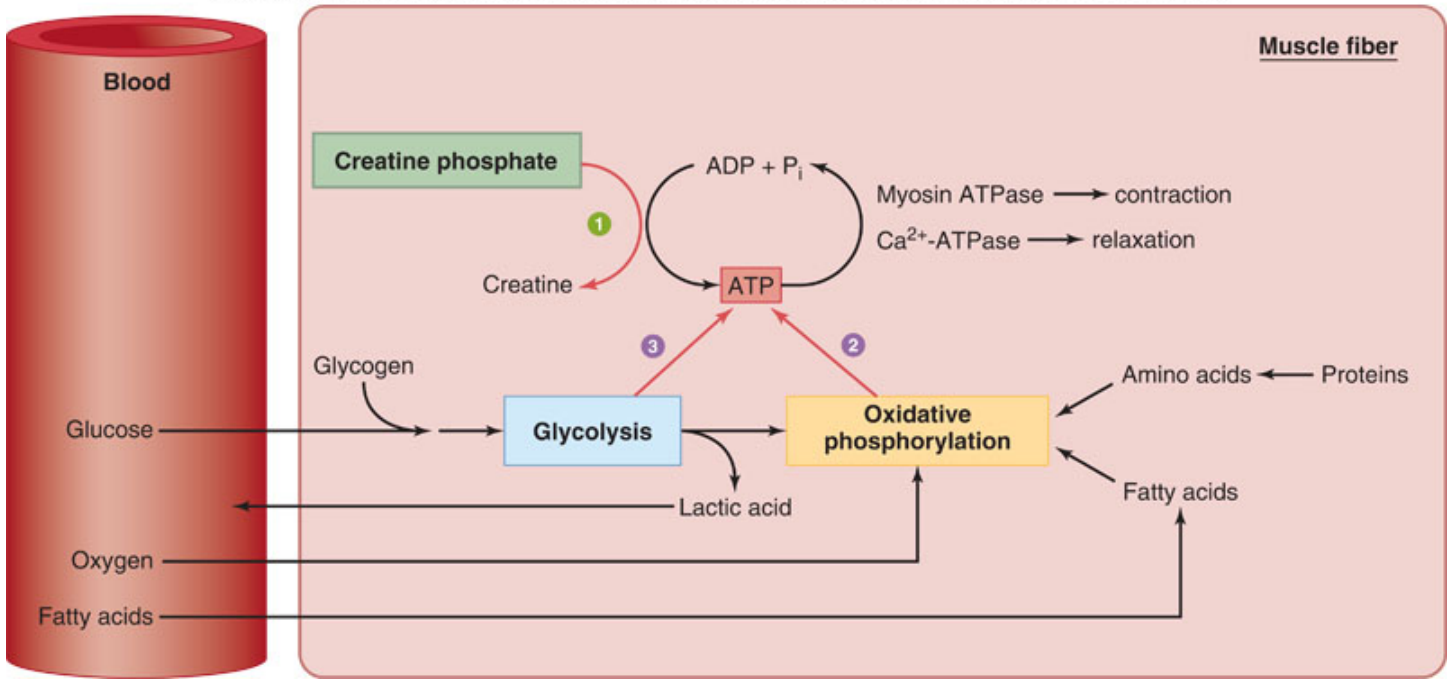
Click here to play the
Length-Tension Relation
in Skeletal Muscles
Flash Animation

Figure 9-22



**In skeletal muscle, ATP production via substrate phosphorylation is supplemented by the availability of creatine phosphate.**






**Skeletal muscle's capacity to produce ATP via oxidative phosphorylation is further supplemented by the availability of molecular oxygen bound to intracellular myoglobin.**

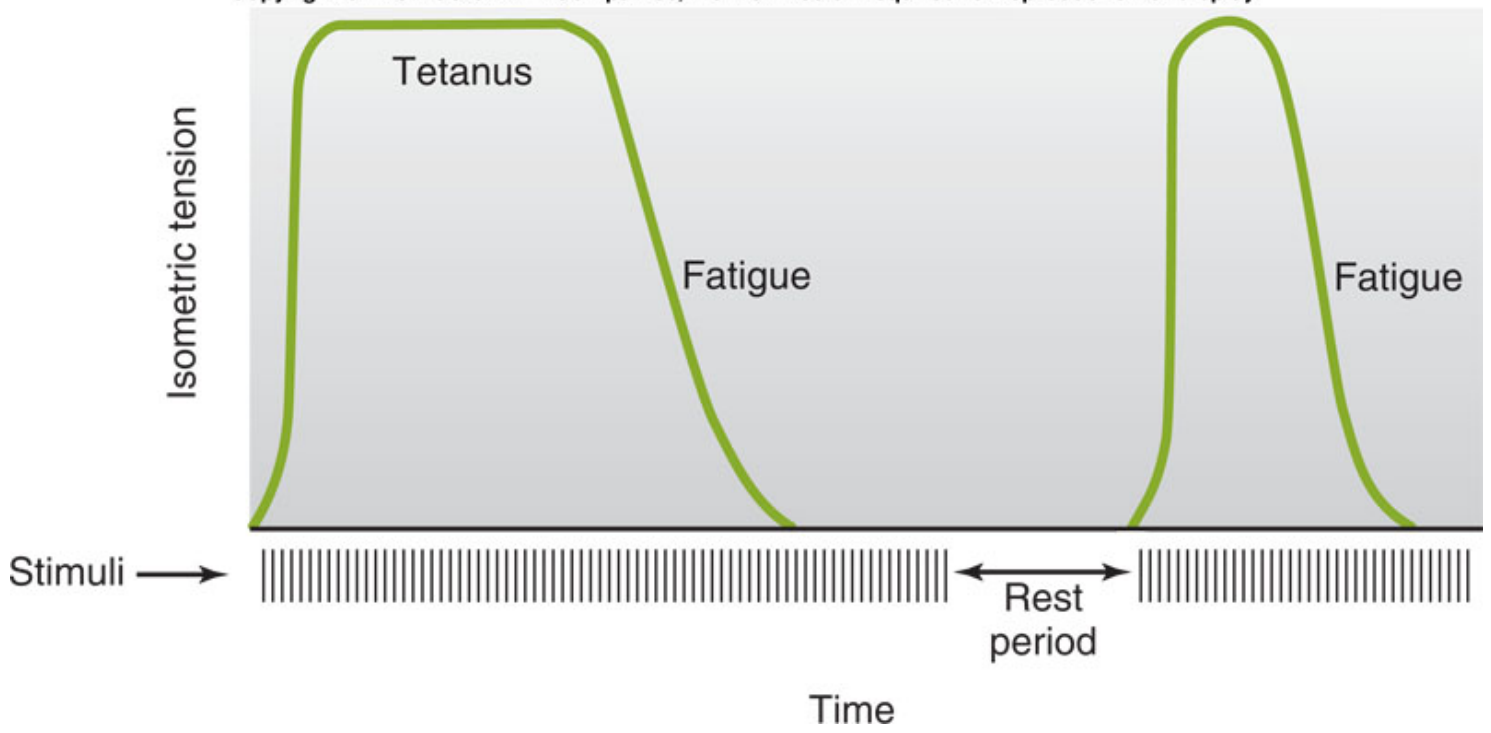
Figure 9-23



**In skeletal muscle, repetitive stimulation leads to fatigue, evident as reduced tension.**

**Rest overcomes fatigue, but fatigue will reoccur sooner if inadequate recovery time passes.**





# Types of skeletal muscle fibers

- On the basis of maximal velocities of shortening
  - Fast fibers – containing myosin with high ATPase activity (type II fibers)
  - Slow fibers -- containing myosin with low ATPase activity (type I fibers)
- On the basis of major pathway to form ATP
  - Oxidative fibers – containing numerous mitochondria and having a high capacity for oxidative phosphorylation, also containing large amounts of myoglobin (red muscle fibers
  - Glycolytic fibers -- containing few mitochondria but possessing a high concentration of glycolytic enzymes and a large store of glycogen, and containing little myoglobin (white muscle fibers)

# Types of skeletal muscle fibers

- Slow-oxidative fibers – combine low myosin-ATPase activity with high oxidative capacity
- Fast-oxidative fibers -- combine high myosin-ATPase activity with high oxidative capacity and intermediate glycolytic capacity
- Fast-glycolytic fibers -- combine high myosin-ATPase activity with high glycolytic capacity

**Slow-oxidative skeletal muscle responds well to repetitive stimulation without becoming fatigued; muscles of body posture are examples.**

**Fast-oxidative skeletal muscle responds quickly *and* to repetitive stimulation without becoming fatigued; muscles used in walking are examples.**

**Fast-glycolytic skeletal muscle is used for quick bursts of strong activation, such as muscles used to jump or to run a short sprint.**

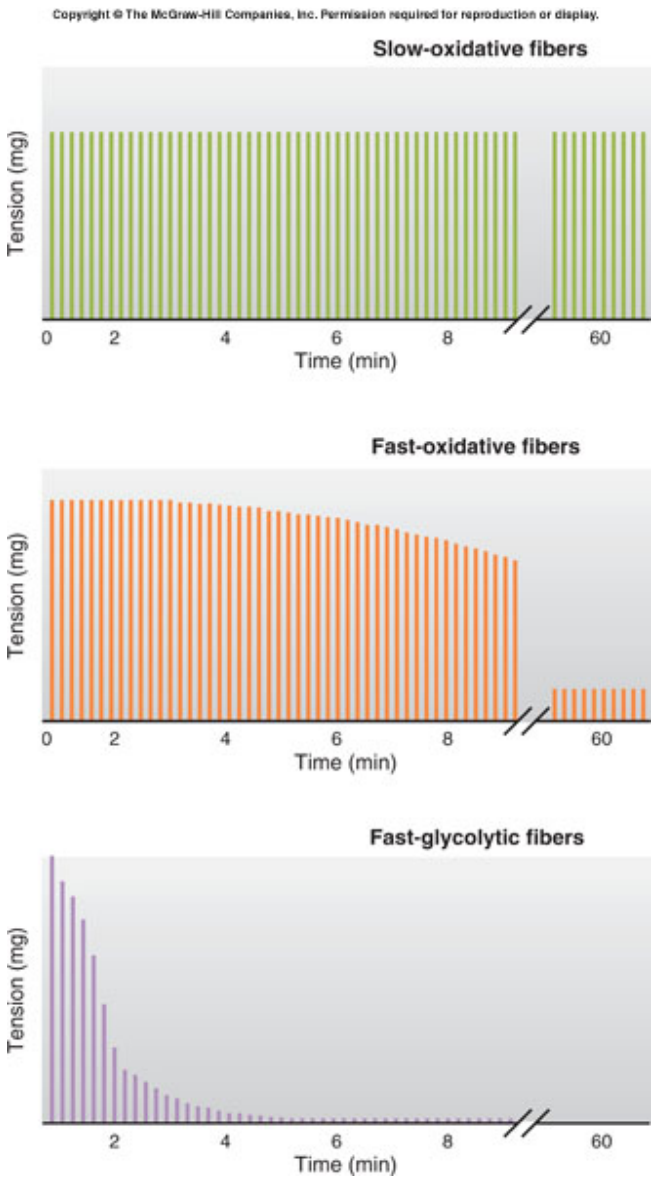



Figure 9-25

***Most skeletal muscles include all three types.***

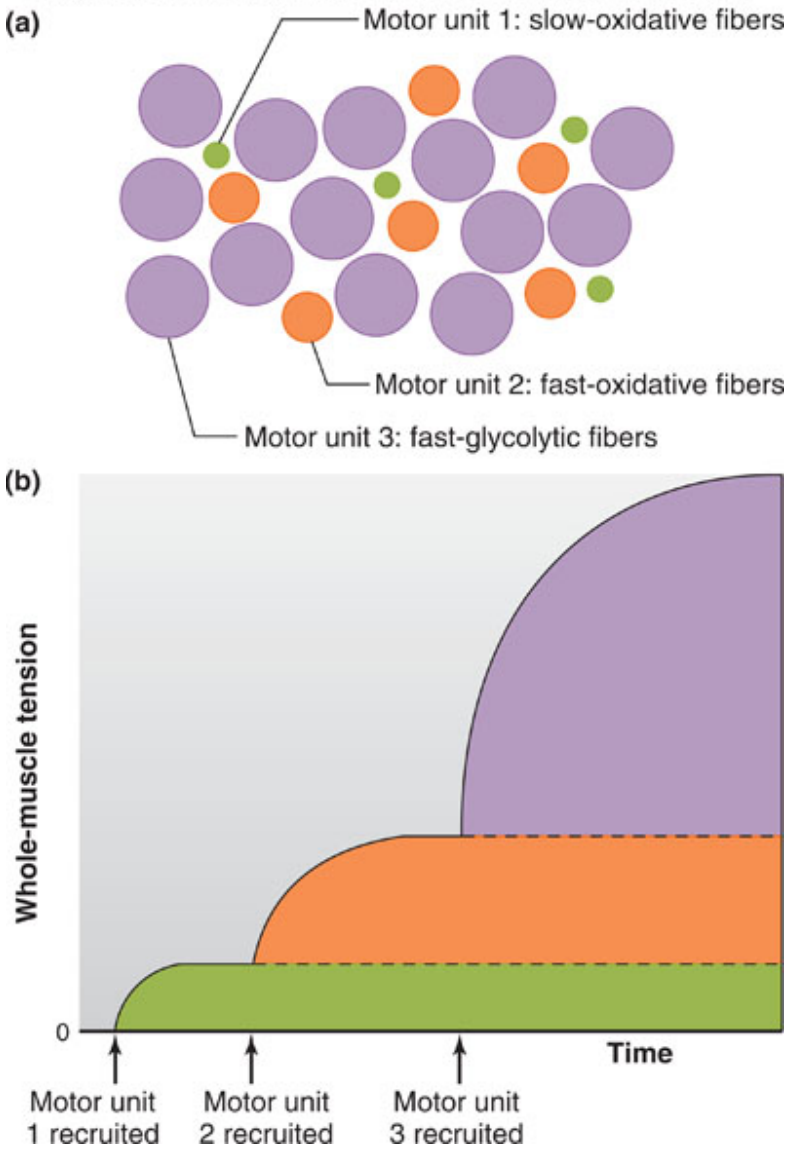
**TABLE 9–3** Characteristics of the Three Types of Skeletal Muscle Fibers

| | SLOW-OXIDATIVE FIBERS | FAST-OXIDATIVE FIBERS | FAST-GLYCOLYTIC FIBERS |
|---|---|---|---|
| Primary source of ATP production | Oxidative phosphorylation | Oxidative phosphorylation | Glycolysis |
| Mitochondria | Many | Many | Few |
| Capillaries | Many | Many | Few |
| Myoglobin content | High (red muscle) | High (red muscle) | Low (white muscle) |
| Glycolytic enzyme activity | Low | Intermediate | High |
| Glycogen content | Low | Intermediate | High |
| Rate of fatigue | Slow | Intermediate | Fast |
| Myosin-ATPase activity | Low | High | High |
| Contraction velocity | Slow | Fast | Fast |
| Fiber diameter | Small | Intermediate | Large |
| Motor unit size | Small | Intermediate | Large |
| Size of motor neuron innervating fiber | Small | Intermediate | Large |

**Note: Because fast-glycolytic fibers have significant glycolytic capacity, they are sometimes called "fast oxidative-glycolytic [FOG] fibers.**

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

# Whole-muscle contraction




**All three types of muscle fibers are represented in a typical skeletal muscle,**

**and, under tetanic stimulation, make the predicted contributions to the development of muscle tension.**

Figure 9-26

## TABLE 9–4 Factors Determining Muscle Tension

**I. Tension developed by each fiber**

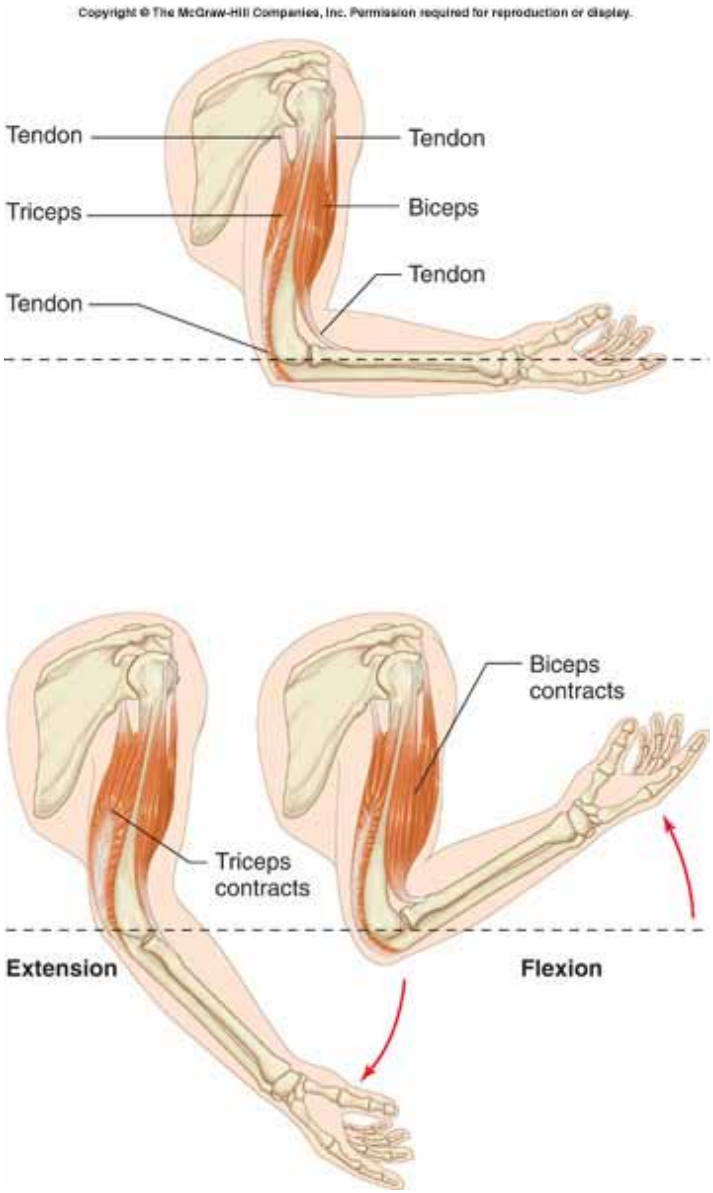
a. Action potential frequency (frequency-tension relation)
b. Fiber length (length-tension relation)
c. Fiber diameter
d. Fatigue

**II. Number of active fibers**

a. Number of fibers per motor unit
b. Number of active motor units

Figure 9-27





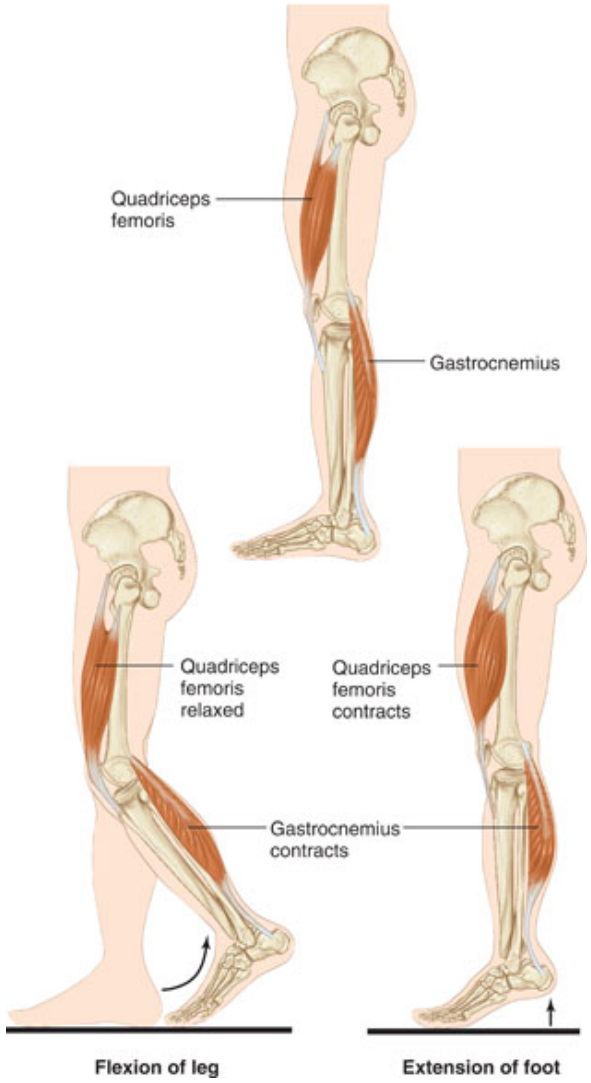

**Flexors and extensors work in antagonistic sets to refine movement,**

**and to allow force generation in two opposite directions.**

Figure 9-28



Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.




**How can gastrocnemius contraction result in two different movements?**

Figure 9-29



**The lever system of muscles and bones:**

**Here, muscle contraction must generate 70 kg force to hold a 10 kg object that is 30 cm away from the site of muscle attachment.**



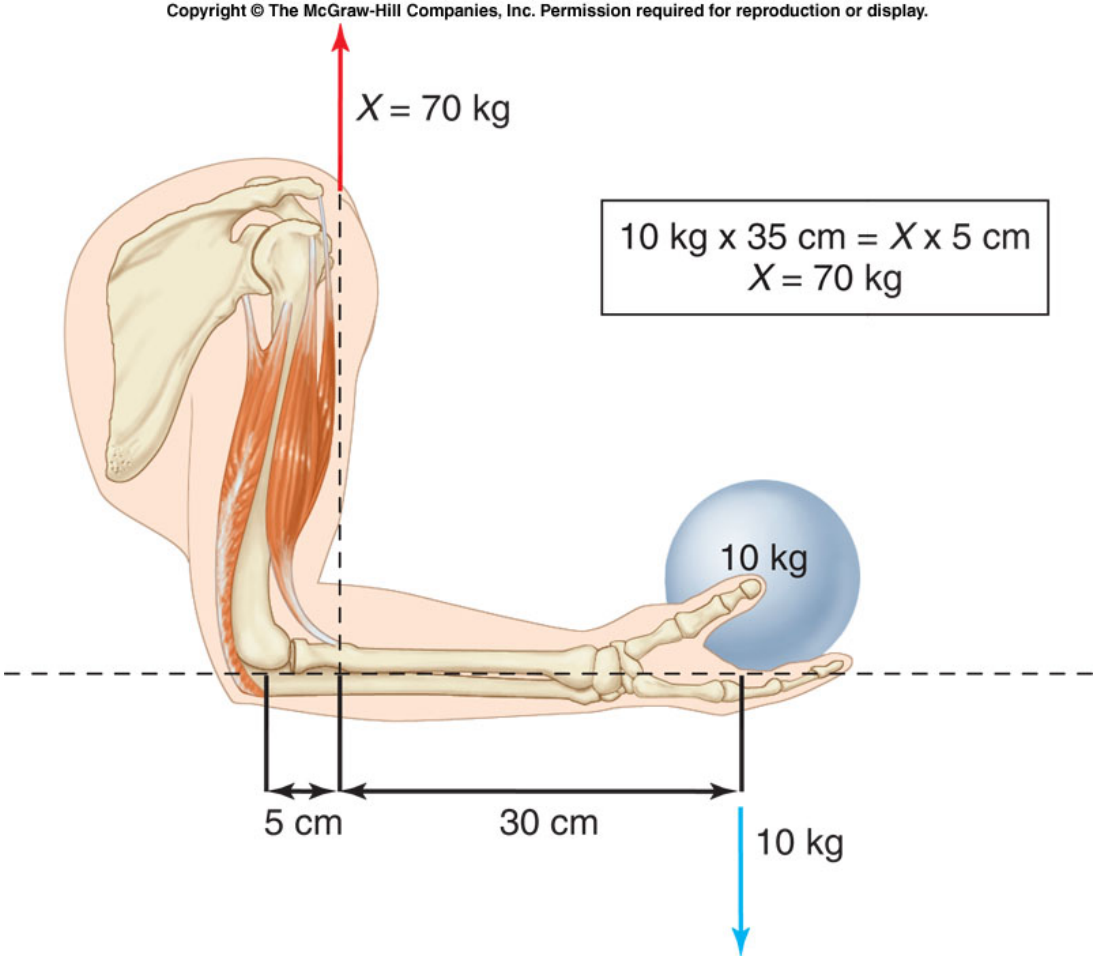
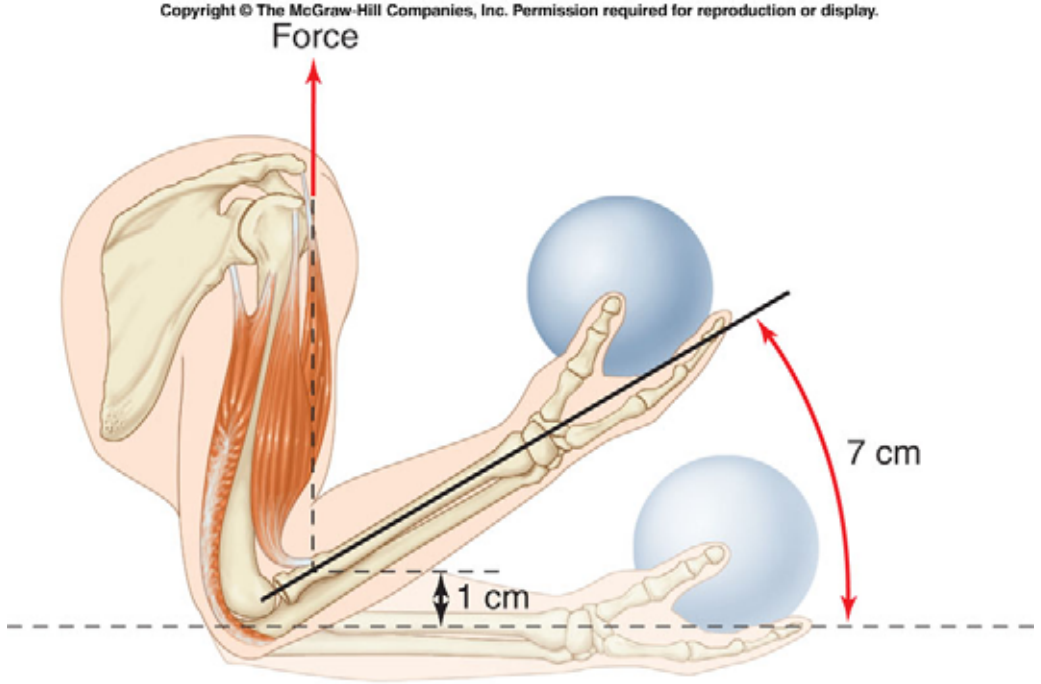


Figure 9-30



Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



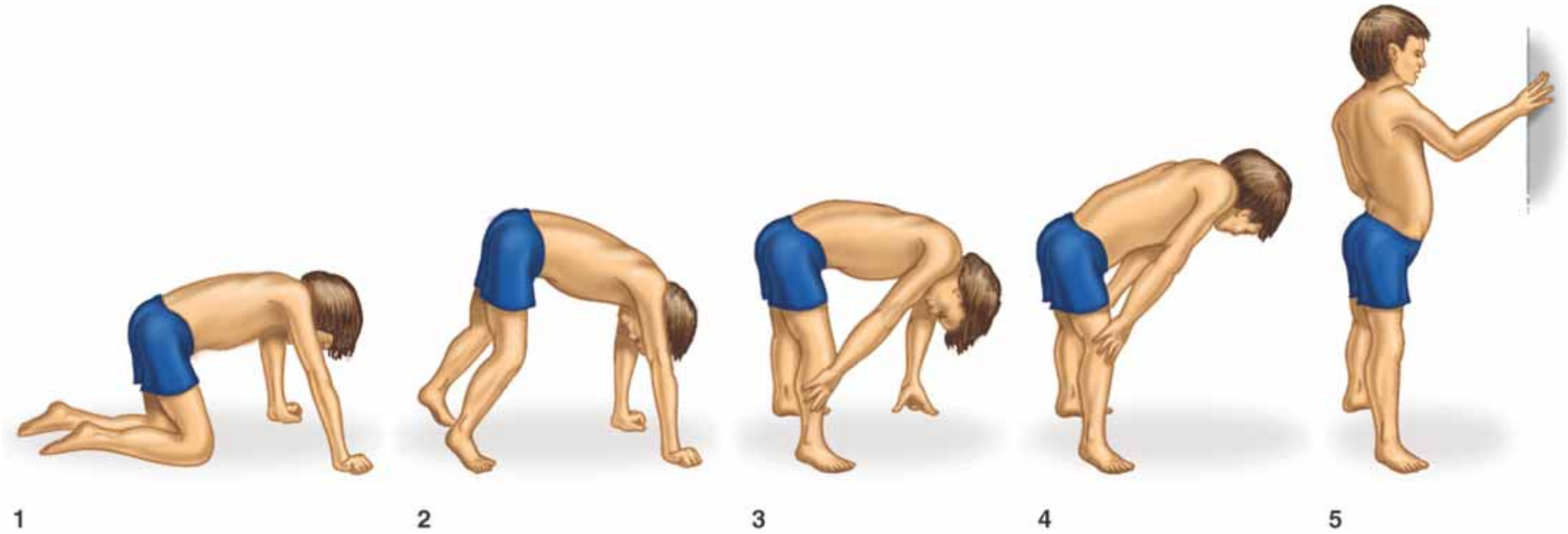

$V_m$ = muscle contraction velocity

$V_h$ = hand velocity = 7 x $V_m$

**Muscle contraction that moves the attachment site on bone 1 cm results in a 7 cm movement of the object 30 cm away from the site; similar gains in movement velocity occur.**

Figure 9-31






**Duchenne muscular dystrophy weakens the hip and trunk muscles, thus altering the lever-system relationships of the muscles and bones that are used to stand up.**

# Smooth muscle



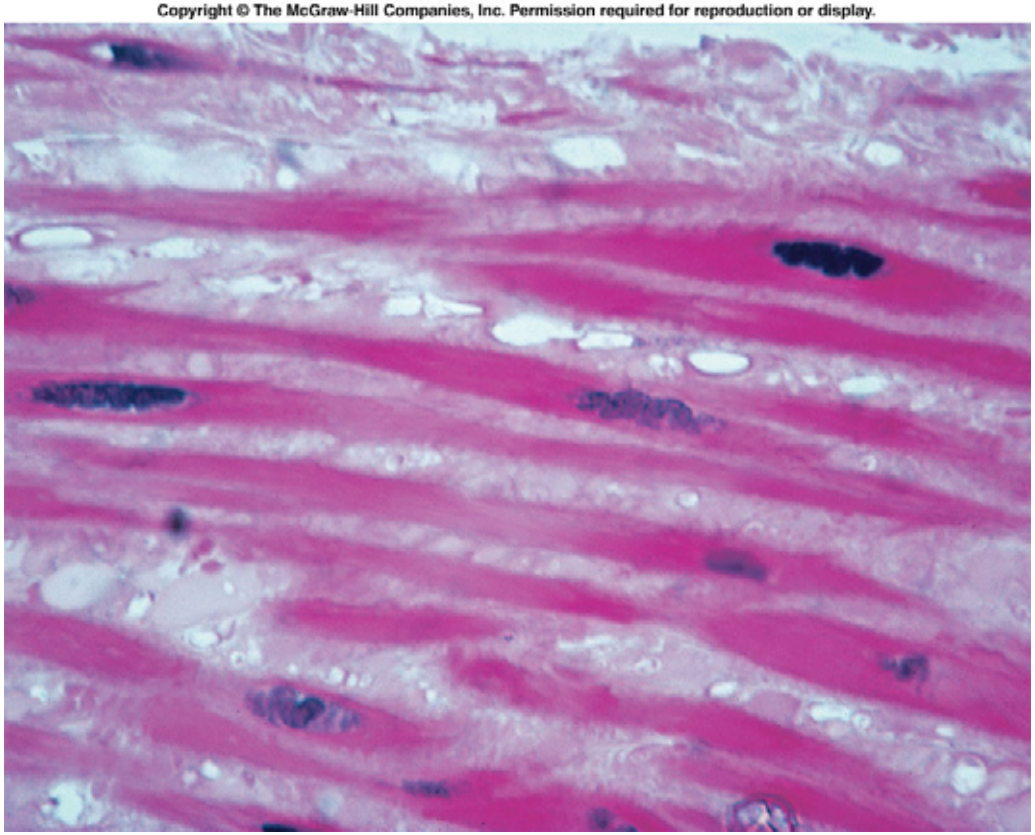
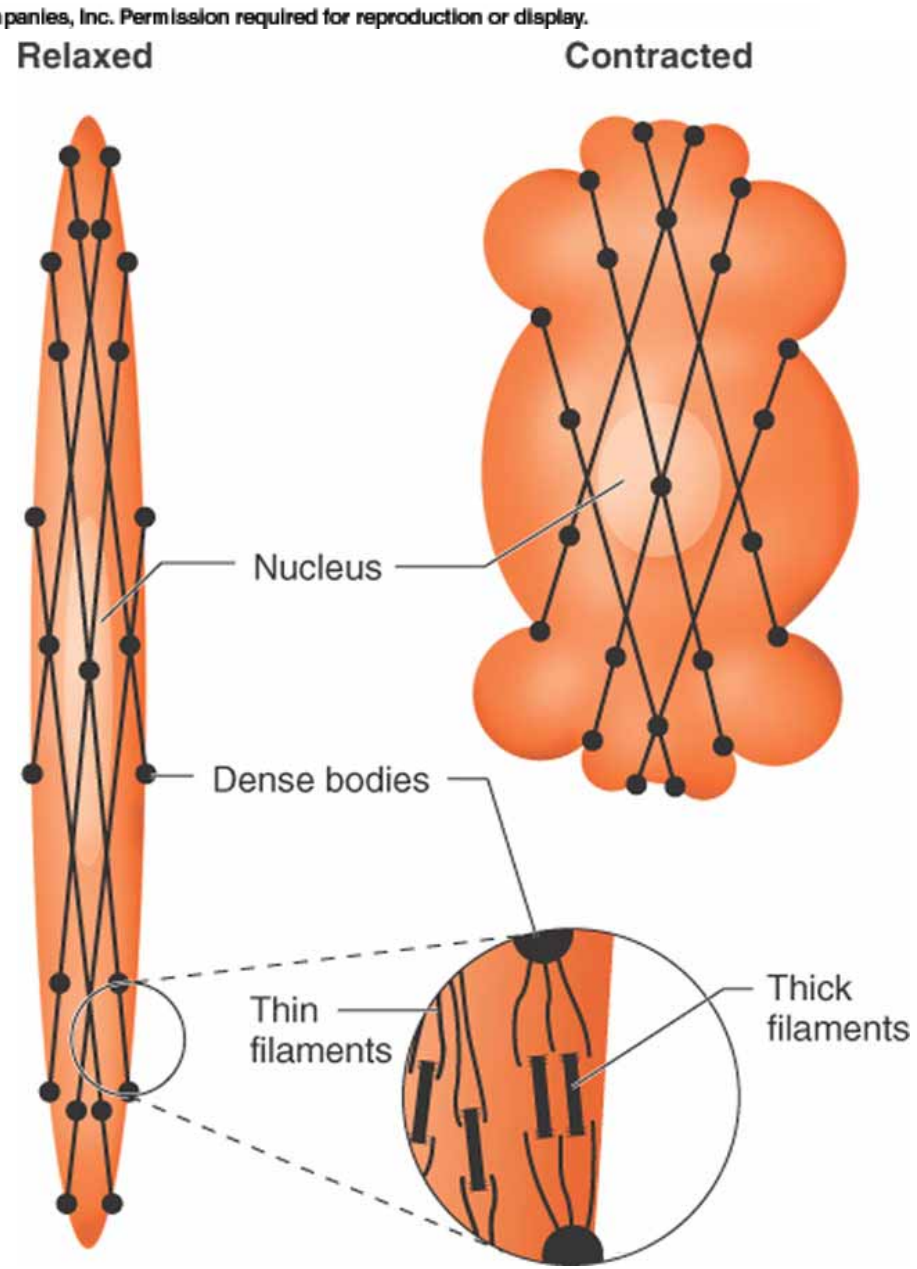
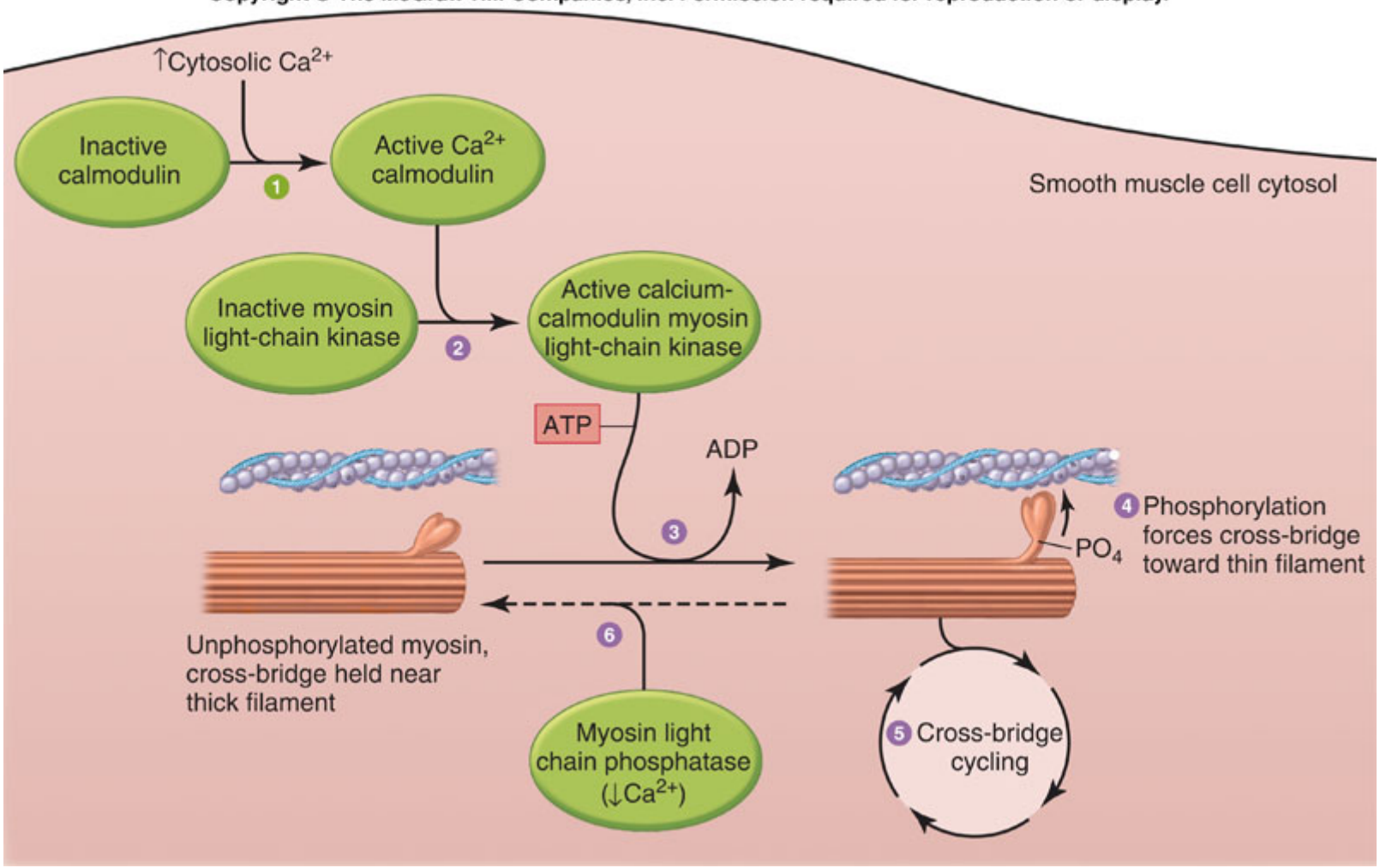


Figure 9-33



**Thick (myosin-based) and thin (actin-based) filaments, biochemically similar to those in skeletal muscle fibers, interact to cause smooth muscle contraction.**



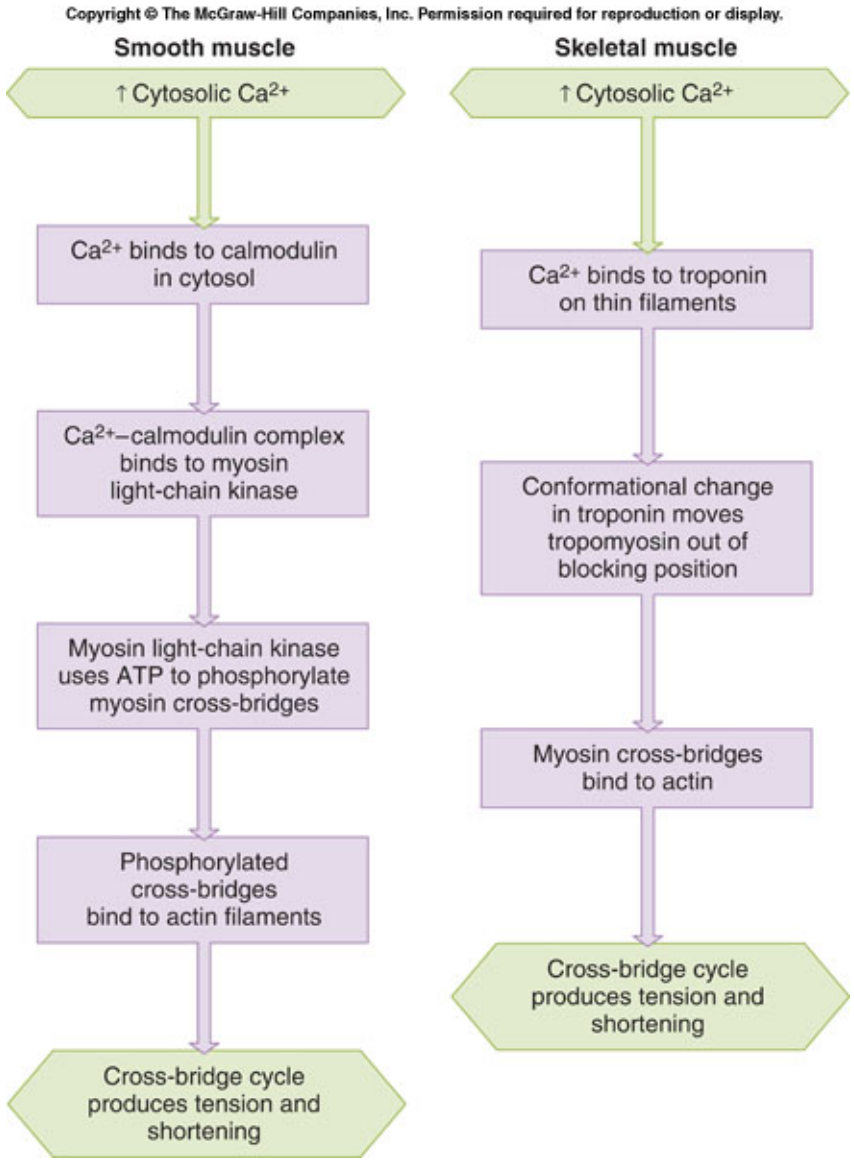



## Activation of smooth muscle contraction by calcium

Figure 9-35



**Calcium ions play major regulatory roles in the contraction of both smooth and skeletal muscle, but the calcium that enters the cytosol of stimulated smooth muscles binds to calmodulin, forming a complex that activates the enzyme that phosphorylates myosin, permitting its binding interactions with actin.**

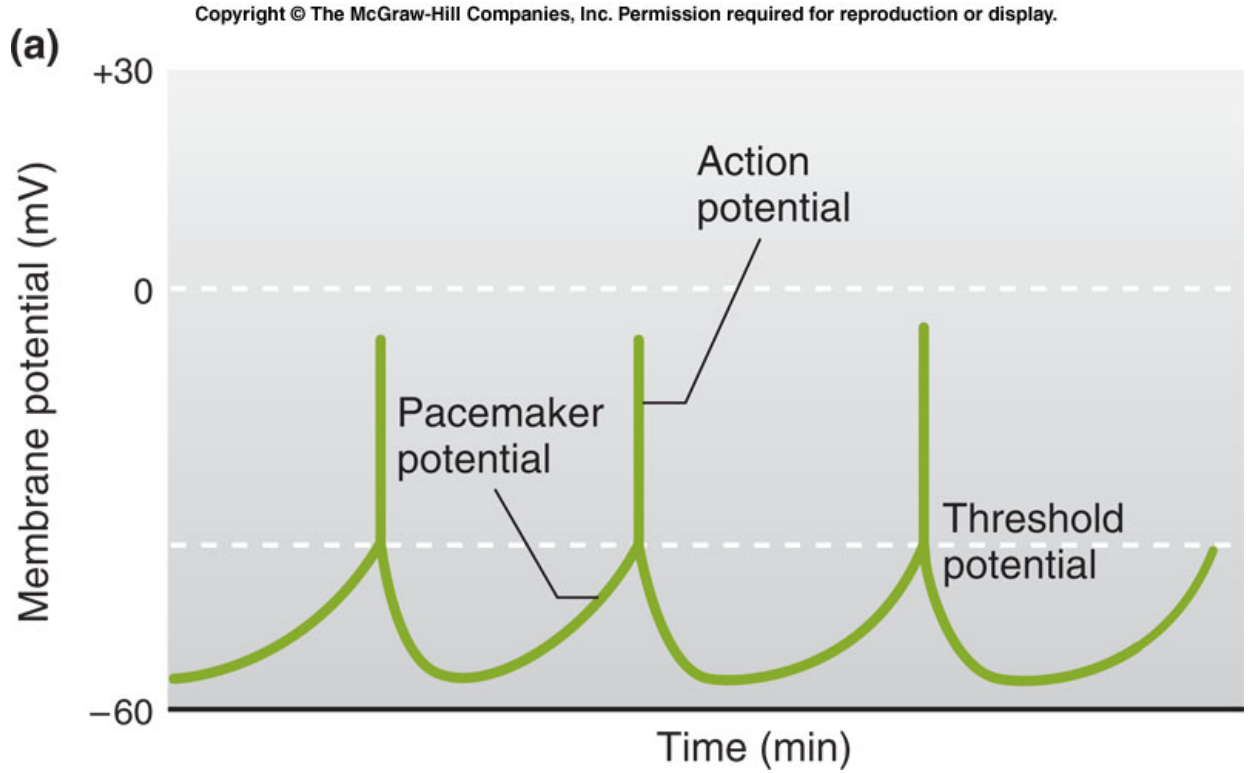


## TABLE 9–5 Inputs Influencing Smooth Muscle Contractile Activity

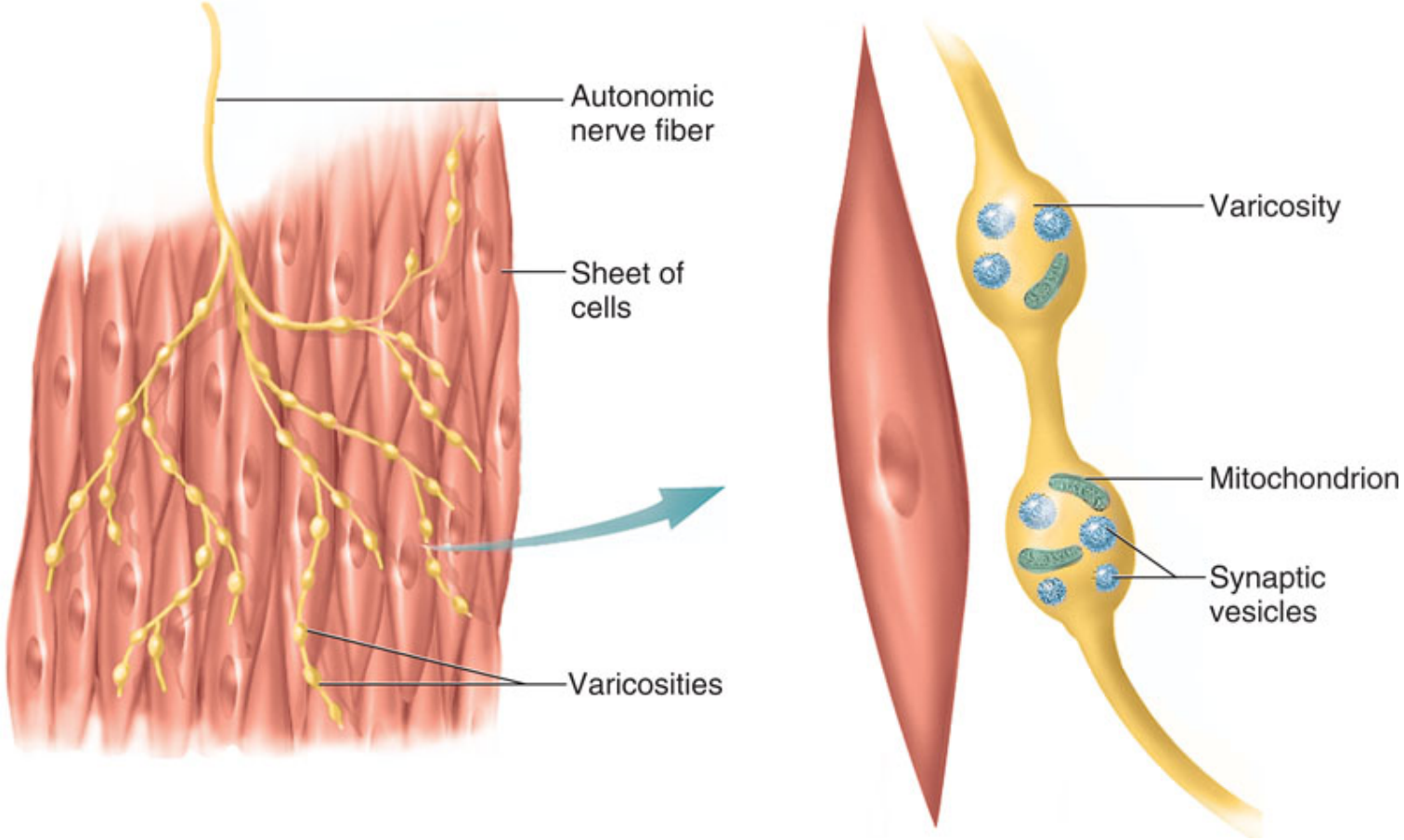
1. Spontaneous electrical activity in the plasma membrane of the muscle fiber
2. Neurotransmitters released by autonomic neurons
3. Hormones
4. Locally induced changes in the chemical composition (paracrine agents, acidity, oxygen, osmolarity, and ion concentrations) of the extracellular fluid surrounding the fiber
5. Stretch

Figure 9-36a

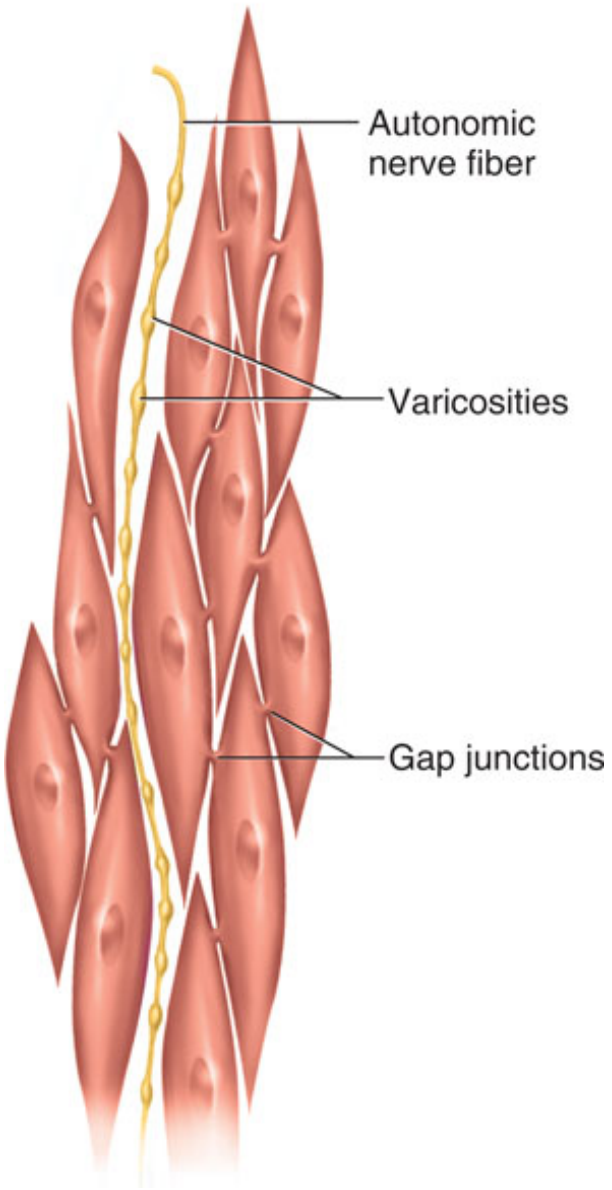





**Rhythmic changes in the membrane potential of smooth muscles results in rhythmic patterns of action potentials and therefore rhythmic contraction; in the gut, neighboring cells use gap junctions to further coordinate these rhythmic contractions.**




**Innervation of smooth muscle by a postganglionic neuron**




# Innervation of a single-unit smooth muscle

**TABLE 9–6** Characteristics of Muscle Fibers

| CHARACTERISTIC | SKELETAL MUSCLE | *Smooth Muscle* | | CARDIAC MUSCLE |
|---|---|---|---|---|
| | | SINGLE UNIT | MULTIUNIT | |
| Thick and thin filaments | Yes | Yes | Yes | Yes |
| Sarcomeres—banding pattern | Yes | No | No | Yes |
| Transverse tubules | Yes | No | No | Yes |
| Sarcoplasmic reticulum (SR)* | ++++ | + | + | ++ |
| Gap junctions between fibers | No | Yes | Few | Yes |
| Source of activating calcium | SR | SR and extracellular | SR and extracellular | SR and extracellular |
| Site of calcium regulation | Troponin | Myosin | Myosin | Troponin |
| Speed of contraction | Fast-slow | Very slow | Very slow | Slow |
| Spontaneous production of action potentials by pacemakers | No | Yes | No | Yes in certain fibers, but most not spontaneously active |
| Tone (low levels of maintained tension in the absence of external stimuli) | No | Yes | No | No |
| Effect of nerve stimulation | Excitation | Excitation or inhibition | Excitation or inhibition | Excitation or inhibition |
| Physiological effects of hormones on excitability and contraction | No | Yes | Yes | Yes |
| Stretch of fiber produces contraction | No | Yes | No | No |

*Number of plus signs (+) indicates the relative amount of sarcoplasmic reticulum present in a given muscle type.

The End.