Skeletal Muscles

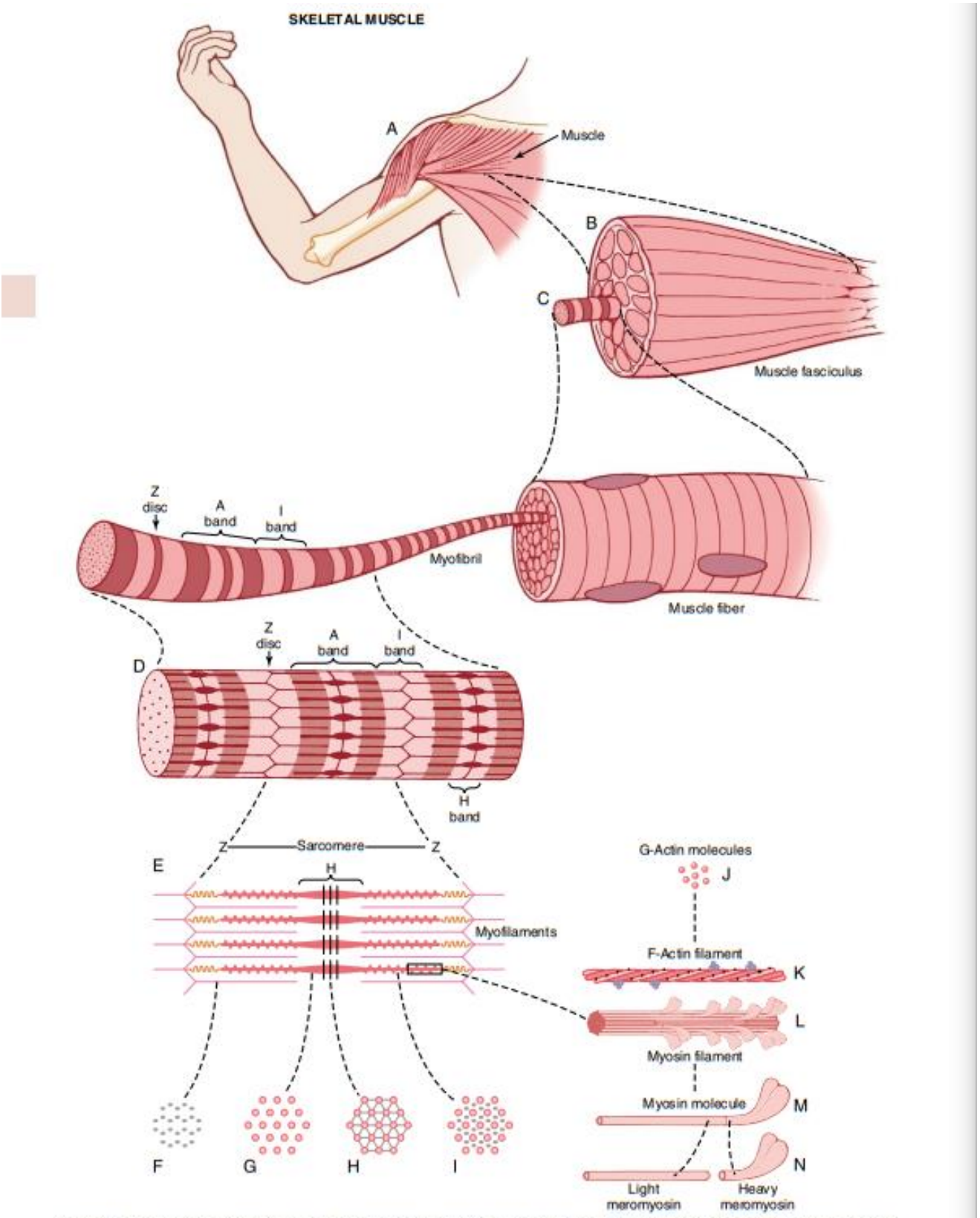


Figure 6-1 Organization of skeletal muscle, from the gross to the molecular level. *F*, *G*, *H*, and *I* are cross sections at the levels indicated.

Molecular Characteristics of the Contractile Filaments

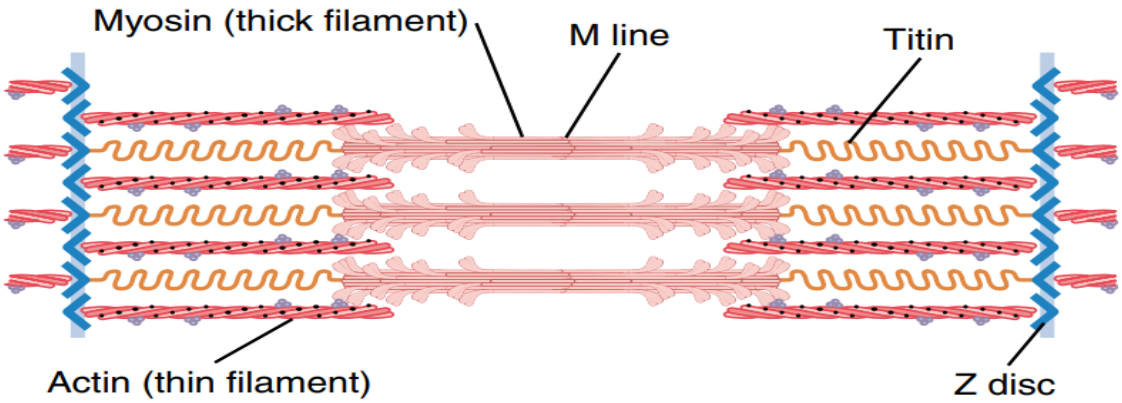


Figure 6-3 Organization of proteins in a sarcomere. Each titin molecule extends from the *Z disc* to the *M line*. Part of the titin molecule is closely associated with the myosin thick filament, whereas the rest of the molecule is springy and changes length as the sarcomere contracts and relaxes.

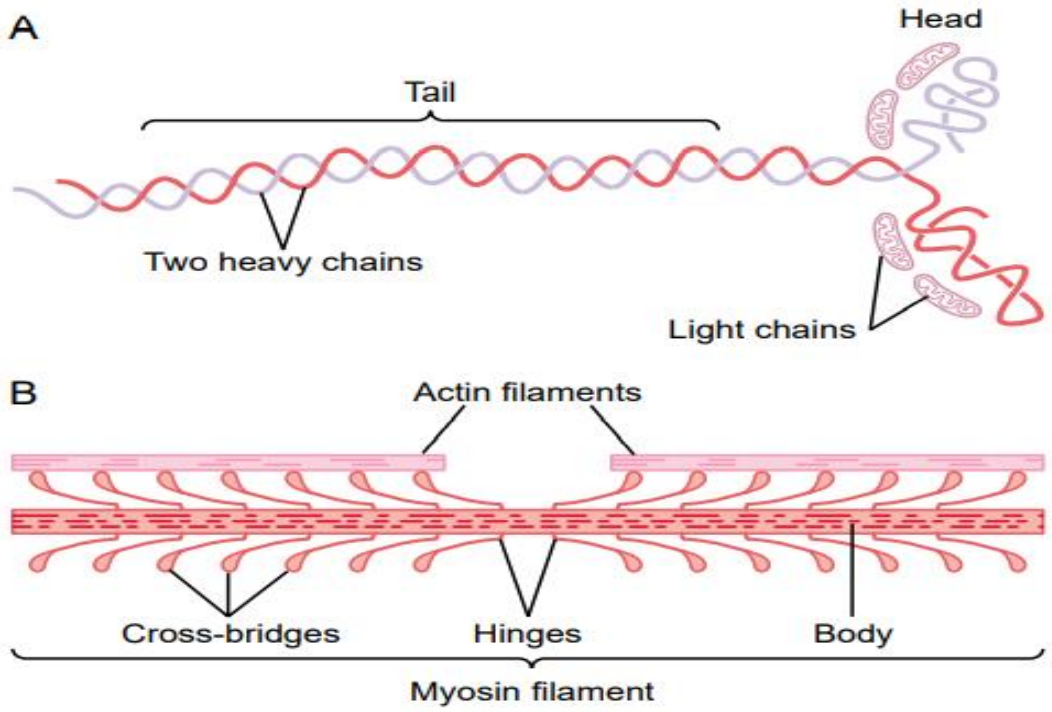


Figure 6–5

A, Myosin molecule. *B*, Combination of many myosin molecules to form a myosin filament. Also shown are thousands of myosin *cross-bridges* and interaction between the *heads* of the cross-bridges with adjacent actin filaments.

Myosin Filament. The myosin filament is composed of multiple myosin molecules. Figure 6–5A shows an individual molecule; Figure 6–5B shows the organization of many molecules

to form a myosin filament, as well as interaction of this filament on one side with the ends of two actin filaments.

- The myosin molecule (see Figure 6–5A) is composed of six polypeptide chains—two heavy chains, and four light chains.
- The two heavy chains wrap spirally around each other to form a double helix, which is called the tail of the myosin molecule.
- One end of each of these chains is folded bilaterally into a globular polypeptide structure called a myosin head. **Thus, there are two free heads at one end of the double-helix myosin molecule.**
- The four light chains are also part of the myosin head, two to each head. These light chains help control the function of the head during muscle contraction.
- The myosin filament is made up of 200 or more individual myosin molecules. The central portion of one of these filaments is shown in Figure 6–5B, displaying the tails of the myosin molecules bundled together to form the body of the filament, while many heads of the molecules hang outward to the sides of the body.
- Also, part of the 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, as shown in the figure. The protruding arms and heads together are called cross-bridges.
- Each cross-bridge is flexible at two points called hinges—one where the arm leaves the body of the myosin filament, and the other where the head attaches to the arm.
- The hinged arms allow the heads either to be extended far outward from the body of the myosin filament or to be brought close to the body. The hinged heads in turn participate in the actual contraction process.
- **ATPase Activity of the Myosin Head**: Another feature of the myosin head that is essential for muscle contraction is that it functions as an ATPase enzyme. As explained later, this property allows the head to cleave ATP and to use the energy derived from the ATP's high-energy phosphate bond to energize the contraction process

Actin Filament

It is composed of three protein components: actin, tropomyosin, and troponin. The backbone of the actin filament is a doublestranded F-actin protein molecule, represented by the two lighter-colored strands in Figure 6–6. The two strands are wound in a helix in the same manner as the myosin molecule.

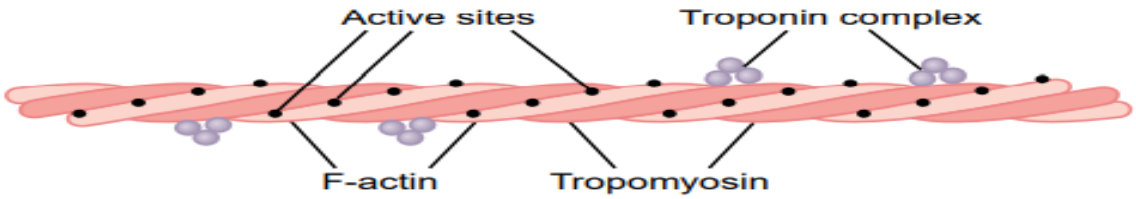


Figure 6–6

Actin filament, composed of two helical strands of *F-actin* molecules and two strands of *tropomyosin* molecules that fit in the grooves between the actin strands. Attached to one end of each tropomyosin molecule is a *troponin* complex that initiates contraction.

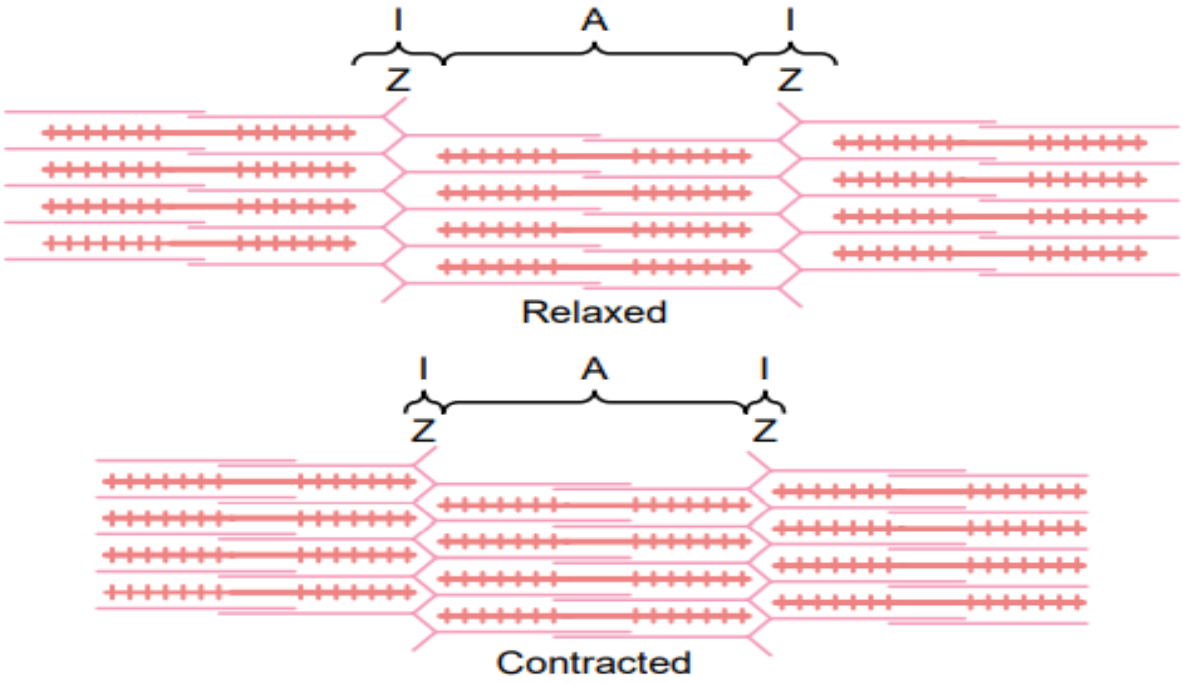


Figure 6–4

Relaxed and contracted states of a myofibril showing *(top)* sliding of the actin filaments *(pink)* into the spaces between the myosin filaments *(red)*, and *(bottom)* pulling of the Z membranes toward each other.

- Each strand of the double F-actin helix is composed of polymerized G-actin molecules.
- Attached to each one of the G-actin molecules is one molecule of ADP. It is believed that these ADP molecules are the active sites on the actin filaments with which the crossbridges of the myosin filaments interact to cause muscle contraction.
- Each actin filament is about 1 micrometer long.
- The bases of the actin filaments are inserted strongly into the Z discs; the ends of the filaments protrude in both directions to lie in the spaces between the myosin molecules, as shown in Figure 6–4.

Tropomyosin Molecules

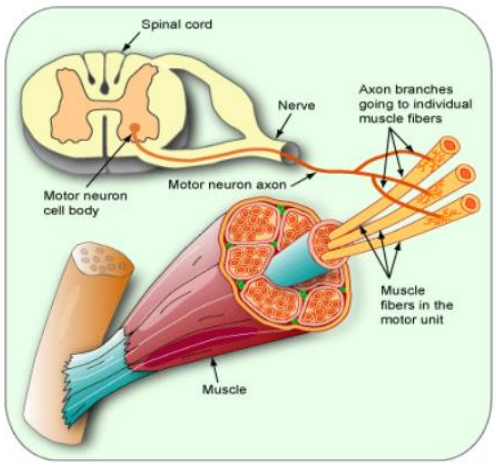
- The actin filament also contains another protein, tropomyosin.
- These molecules are wrapped spirally around the sides of the F-actin helix.
- In the resting state, the tropomyosin molecules lie on top of the active sites of the actin strands, so that attraction cannot occur between the actin and myosin filaments to cause contraction.

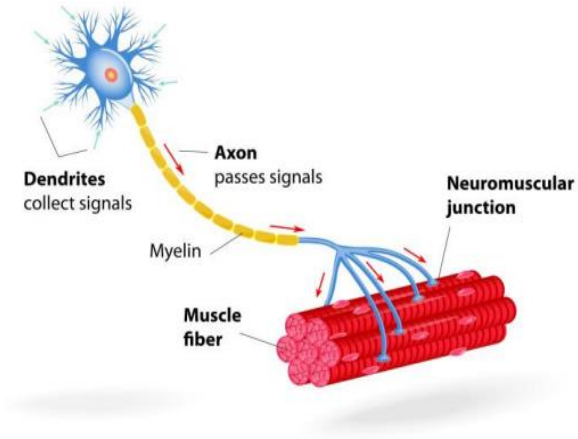
Troponin and Its Role in Muscle Contraction

- Attached intermittently along the sides of the tropomyosin molecules are still other protein molecules called troponin.
- These are actually complexes of **three loosely bound protein subunits**, each of which plays a specific role in controlling muscle contraction.
- One of the subunits (troponin I) has a strong affinity for actin, another (troponin T) for tropomyosin, and a third (troponin C) for calcium ions.
- This complex is believed to attach the tropomyosin to the actin. The strong affinity of the troponin for calcium ions is believed to initiate the contraction process,

Motor Unit

- Each motor neuron that leaves the spinal cord innervates multiple muscle fibers, the number depending on the type of muscle.
- **All the muscle fibers innervated by a single nerve fiber are called a motor unit.**
- In general, small muscles that react rapidly and whose control must be exact, have more nerve fibers for fewer muscle fibers (for instance, as few as two or three muscle fibers per motor unit in some of the laryngeal muscles).
- Conversely, large muscles that do not require fine control, such as the soleus muscle, may have several hundred muscle fibers in a motor unit.
- An average figure for all the muscles of the body is about 80 to 100 muscle fibers to a motor unit.
- The muscle fibers in each motor unit are not all bunched together in the muscle but overlap other motor units in microbundles of 3 to 15 fibers.
- This interdigitation allows the separate motor units to contract in support of one another rather than entirely as individual segments.





○ Typically the larger the muscle the more muscle fibers are innervated by each motor neuron. Allows a single motor neuron to generate large muscular forces

○ A small number of muscle fibers per motor neuron gives a small force but great precision (ex eye). ○ When the motor unit is innervated all the muscle fibers attached to it are contracted.

Types of motor units (fast/slow twitch)

a. Type I - slow twitch motor units consist of mainly slow twitch muscle fibers and have slower nerve transmission speeds and small muscle forces.
   ■ Can maintain contractions for a long period of time
   ■ Fatigue resistant
   ■ aerobic
b. Type IIa - fast twitch oxidative (uses oxygen)
   motor units consist mainly of type IIa muscle fibers and have fast nerve transmissions
   ■ Stronger contraction forces and are more resistant to fatigue
   ■ Anaerobic and aerobic
   ○ Type IIb - fast twitch motor units with mostly fast twitch muscle fibers.
   ■ Fastest contraction times and largest forces
   ■ High fatigue rate and can't maintain contractions for a long period of time
   ■ Anaerobic

General Mechanism of Muscle Contraction

The initiation and execution of muscle contraction occur in the following sequential steps.

1. An action potential travels along a motor nerve to its endings on muscle fibers.

2. At each ending, the nerve secretes a small amount of the neurotransmitter substance acetylcholine.

3. The acetylcholine acts on a local area of the muscle fiber membrane to open multiple "acetylcholinegated" channels through protein molecules floating in the membrane.

4. Opening of the acetylcholine-gated channels allows large quantities of sodium ions to diffuse to the interior of the muscle fiber membrane. This initiates an action potential at the membrane.

5. The action potential travels along the muscle fiber membrane in the same way that action potentials travel along nerve fiber membranes.

6. The action potential depolarizes the muscle membrane, and much of the action potential electricity flows through the center of the muscle fiber. Here it causes the sarcoplasmic reticulum to release large quantities of calcium ions that have been stored within this reticulum.

7. The calcium ions initiate attractive forces between the actin and myosin filaments, causing them to slide alongside each other, which is the contractile process.

8. After a fraction of a second, the calcium ions are pumped back into the sarcoplasmic reticulum by a Ca++ membrane pump, and they remain stored in the reticulum until a new muscle action potential comes along; this removal of calcium ions from the myofibrils causes the muscle contraction to cease.

Chemical Events in the Motion of the Myosin Heads

When a muscle contracts, work is performed and energy is required. Large amounts of ATP are cleaved to form ADP during the contraction process; the greater the amount of work performed by the muscle, the greater the amount of ATP that is cleaved, which is called the Fenn effect.

The following sequence of events is believed to be the means by which this occurs:

1. Before contraction begins, the heads of the crossbridges 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.

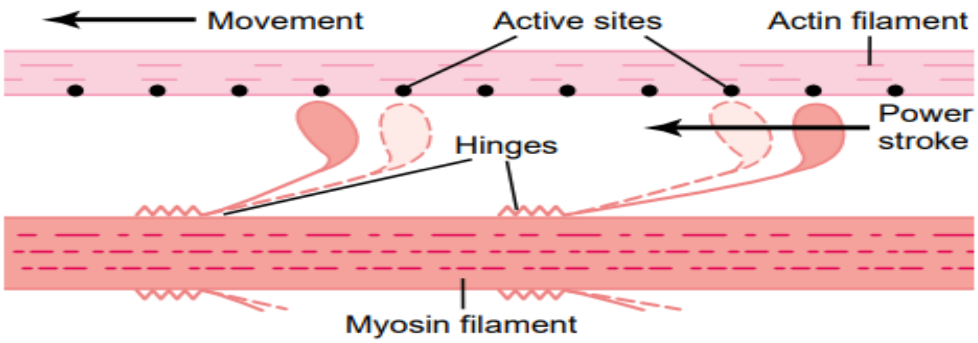


Figure 6–7

"Walk-along" mechanism for contraction of the muscle.

2. 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, as shown in Figure 6–7.

3. The bond between the head of the cross-bridge and the active site of the actin filament causes a conformational change in the head, prompting the head to tilt toward the arm of the cross-bridge. This provides the power stroke for pulling the actin filament. The energy that activates the power stroke is the energy already stored, like a "cocked" spring, by the conformational change that occurred in the head when the ATP molecule was cleaved earlier.

4. Once the head of the cross-bridge tilts, this allows release of the ADP and phosphate ion that were previously attached to the head. 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.

5. 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 condition, ready to begin the new power stroke cycle.

6. When the cocked head (with its stored energy derived from the cleaved ATP) binds with a new active site on the actin filament, it becomes uncocked and once again provides a new power stroke.

Thus, the process proceeds again and again until the actin filaments pull the Z membrane up against the ends of the myosin filaments or until the load on the muscle become

Muscle Contractions of Different Force—Force Summation.

- Summation means the adding together of individual twitch contractions to increase the intensity of overall muscle contraction.
- Summation occurs in two ways:
  (1) by increasing the number of motor units contracting simultaneously, which is called multiple fiber summation, and
  (2) by increasing the frequency of contraction, which is called frequency summation and can lead to tetanization.

Multiple Fiber Summation

- When the central nervous system sends a weak signal to contract a muscle, the smaller motor units of the muscle may be stimulated in preference to the larger motor units. Then, as the strength of the signal increases, larger and larger motor units begin to be excited as well, with the largest motor units often having as much as 50 times the contractile force of the smallest units. This is called the **size principle**.
- It allows the gradations of muscle force during weak contraction to occur in small steps, whereas the steps become progressively greater when large amounts of force are required. The cause of this size principle is that the smaller motor units are driven by small motor nerve fibers, and the small motoneurons in the spinal cord are more excitable than the larger ones, so they naturally are excited first.
- Another important feature of multiple fiber summation is that the different motor units are driven asynchronously by the spinal cord, so that contraction alternates among motor units one after the other, thus providing smooth contraction even at low frequencies of nerve signals.

Frequency Summation and Tetanization

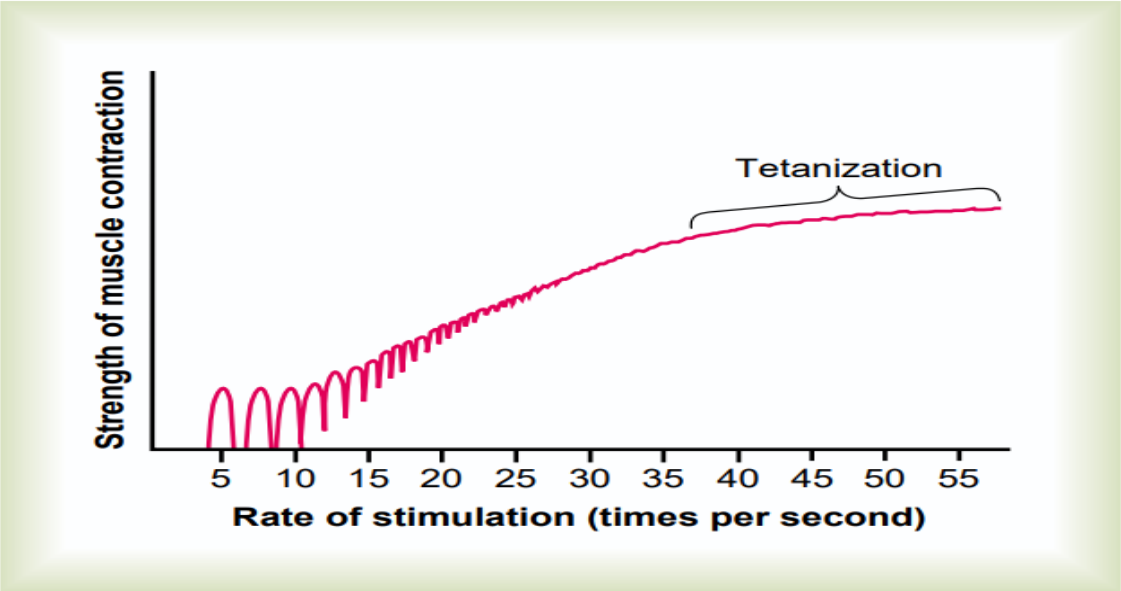


Figure 6–13

Figure 6–13 shows the principles of frequency summation and tetanization. To the left are displayed individual twitch contractions occurring one after another at low frequency of stimulation. Then, as the frequency increases, there comes a point where each new contraction occurs before the preceding one is over. As a result, the second contraction is added partially to the first, so that the total strength of contraction rises progressively with increasing frequency. When the frequency reaches a critical level, the successive contractions eventually become so rapid that they fuse together, and the whole muscle contraction appears to be completely smooth and continuous, as shown in the figure. This is called tetanization. At a slightly higher frequency, the strength of contraction reaches its maximum, so that any additional increase in frequency beyond that point has no further effect in increasing contractile force. This occurs because enough calcium ions are maintained in the muscle sarcoplasm, even between action potentials, so that full contractile state is sustained without allowing any relaxation between the action potentials.