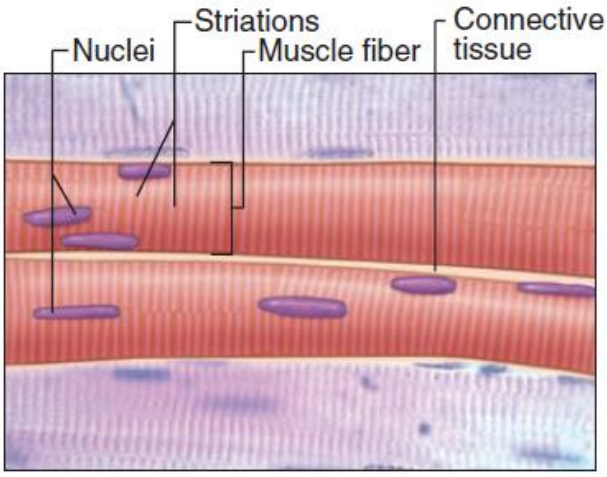
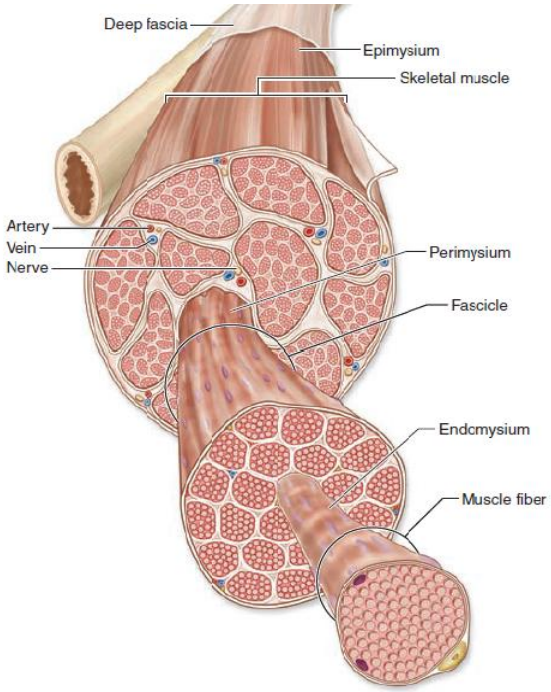
Skeletal (or **striated**) muscle consists of muscle fibers , which are long, cylindrical multinucleated cells with cross-striations having diameters of 10 to 100 µm. During embryonic muscle development, mesenchymal myoblasts (L. myo , muscle) fuse, forming myotubes with many nuclei. Myotubes then further diff erentiate to form striated muscle fibers (Figure 10–2). Elongated nuclei are found uniquely peripherally just under the sarcolemma. A small population of reserve progenitor cells called muscle **satellite cells** remains adjacent to most fibers of differentiated skeletal muscle.



a Skeletal muscle



Organization of a Skeletal Muscle

Three layers of connective tissues surround and organize skeletal muscle ----

- The **epimysium**, an external sheath of dense connective tissue, surrounds the entire muscle. Septa of this tissue extend inward, carrying the larger nerves, blood vessels, and lymphatics of the muscle.
- The **perimysium** is a thin connective tissue layer that immediately surrounds each bundle of muscle fibers termed a fascicle.
- Within fascicles a very thin, delicate layer of reticular fibers and scattered fibroblasts, the **endomysium**, surrounds the external lamina of individual muscle fibers.

Organization Within Muscle Fibers

Longitudinally sectioned skeletal muscle fibers show cross-striations of alternating light and dark bands. The dark bands are called **A bands** (anisotropic or birefringent in polarized light microscopy); the light bands are called **I bands** (isotropic, do not alter polarized light). In the TEM, each I band is seen to be bisected by a dark transverse line, the **Z disc** (Ger. zwischen, between). The repetitive functional subunit of the contractile apparatus, the **sarcomere**, extends from Z disc to Z disc and is about 2.5 µm long in resting muscle.

The sarcoplasm contains long cylindrical filament bundles, called **myofibrils**, running parallel to the long axis of the fiber. Mitochondria and sarcoplasmic reticulum are found between the myofibrils, which have a diameter of 1 to 2 μm. Myofibrils consist of an end-toend repetitive arrangement of
sarcomeres.The **A** and **I** banding pattern in sarcomeres is due mainly to the regular arrangement of **thick** and **thin myofilaments**, composed of **myosin** and **F-actin**, respectively.

- The **thick myosin** filaments are 1.6 μm long and 15 nm wide; they occupy the A band at the middle region of the sarcomere. Myosin is a large complex (~500 kDa) with two identical heavy chains and two pairs of light chains. Myosin heavy chains are thin, rodlike motor proteins (150 nm long and 2-3 nm thick) twisted together as myosin tails. Globular projections containing the four myosin light chains form a head at one end of each heavy chain. The myosin heads bind both actin forming transient crossbridges and ATP, catalyzing energy release (actomyosin ATPase activity). Several hundred myosin molecules are arranged within each thick filament with overlapping rodlike portions and the globular heads directed toward either end.

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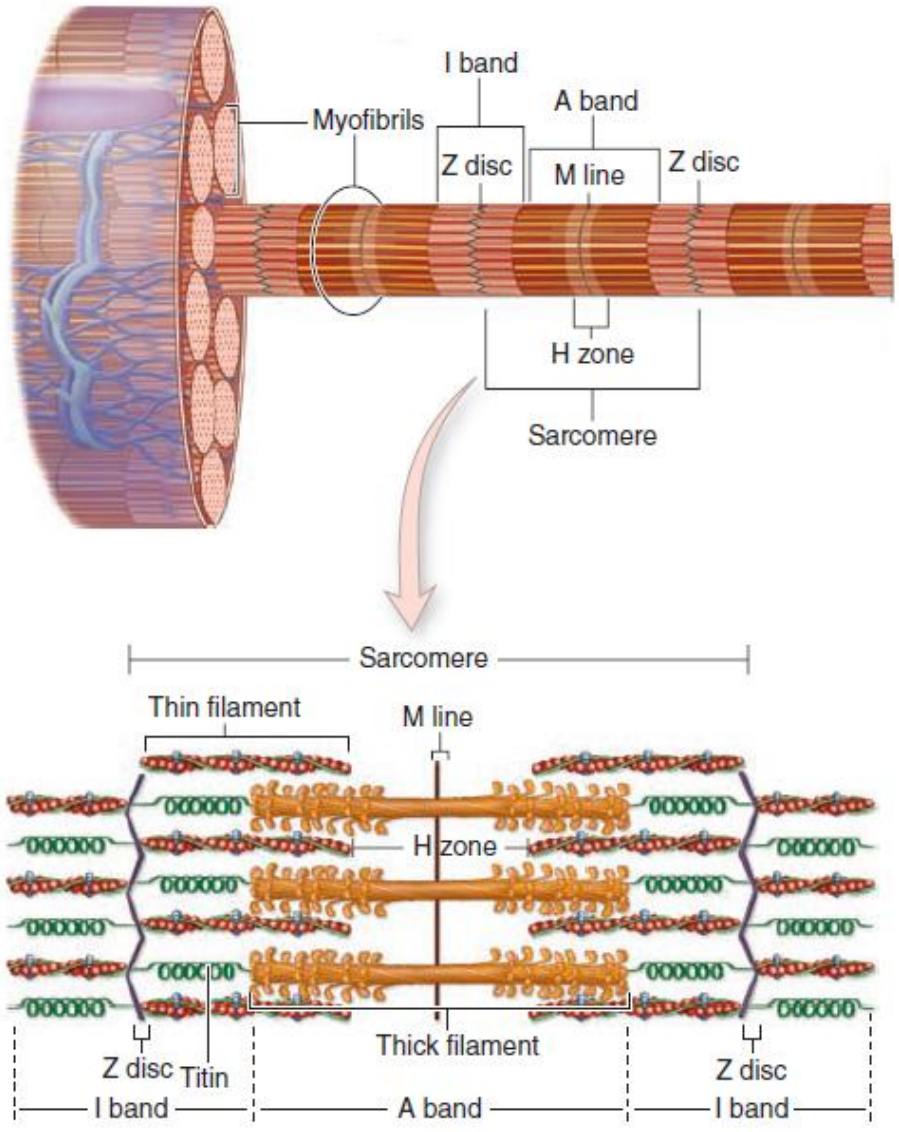
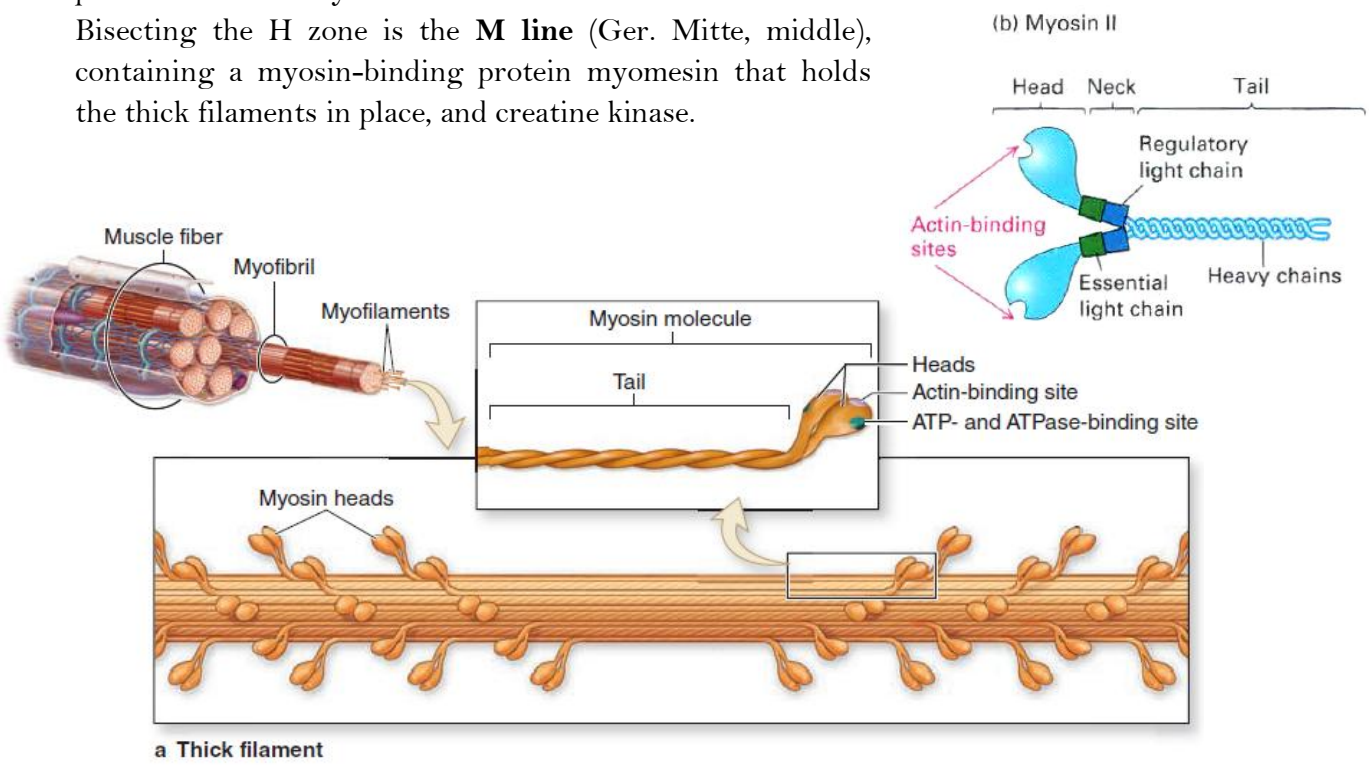


❖ The **thin**, helical **actin** filaments are each 1.0 μm long and 8 nm wide and run between the thick filaments. Actin filament is composed of G-actin monomer (globular)that contains a binding site for myosin. Actin filaments are anchored perpendicularly on the Z disc by the actin-binding protein**α-actinin.** Thin filaments are also tightly associated with two regulatory proteins --- (a) **Tropomyosin**, a 40-nm-long coil of two polypeptide chains located in the groove between the two twisted actin strands & (b) **Troponin**, a complex of three subunits: TnT, which attaches to tropomyosin; TnC, which binds Ca2+; and TnI, which regulates the actin-myosin interaction.

* **I** bands, each bisected by a **Z** disc, consist of the portions of the thin filaments that do not overlap the thick filaments.

* An important accessory protein in I bands is **titin** (3700 kDa), the largest protein in the body, which supports the thick myofilaments and connects them to the **Z** disc. Another very large accessory protein, nebulin (600-900 kDa), binds each thin myofilament laterally, helps anchor them to α-actinin.

* The A bands contain both thick filaments and the overlapping portions of thin filaments. A lighter zone in its center, the **H** zone, corresponds to a region with only the rodlike portions of the myosin molecule and no thin filaments. Bisecting the H zone is the **M line** (Ger. Mitte, middle), containing a myosin-binding protein myomesin that holds the thick filaments in place, and creatine kinase.



Sarcoplasmic Reticulum & Transverse Tubule System

In skeletal muscle fibers the smooth ER, or sarcoplasmic reticulum, is specialized for Ca2+ sequestration. The sarcolemma is folded into a system of transverse or T tubules forming long fingerlike invaginations that penetrate deeply into the sarcoplasm and encircle every myofibril. Motor nerve synapses on the sarcolemma controls release of Ca2+ ions from SR through depolarization. Adjacent to each side of every T tubule are expanded **terminal cisterns** of the sarcoplasmic reticulum that together form a **triad**.

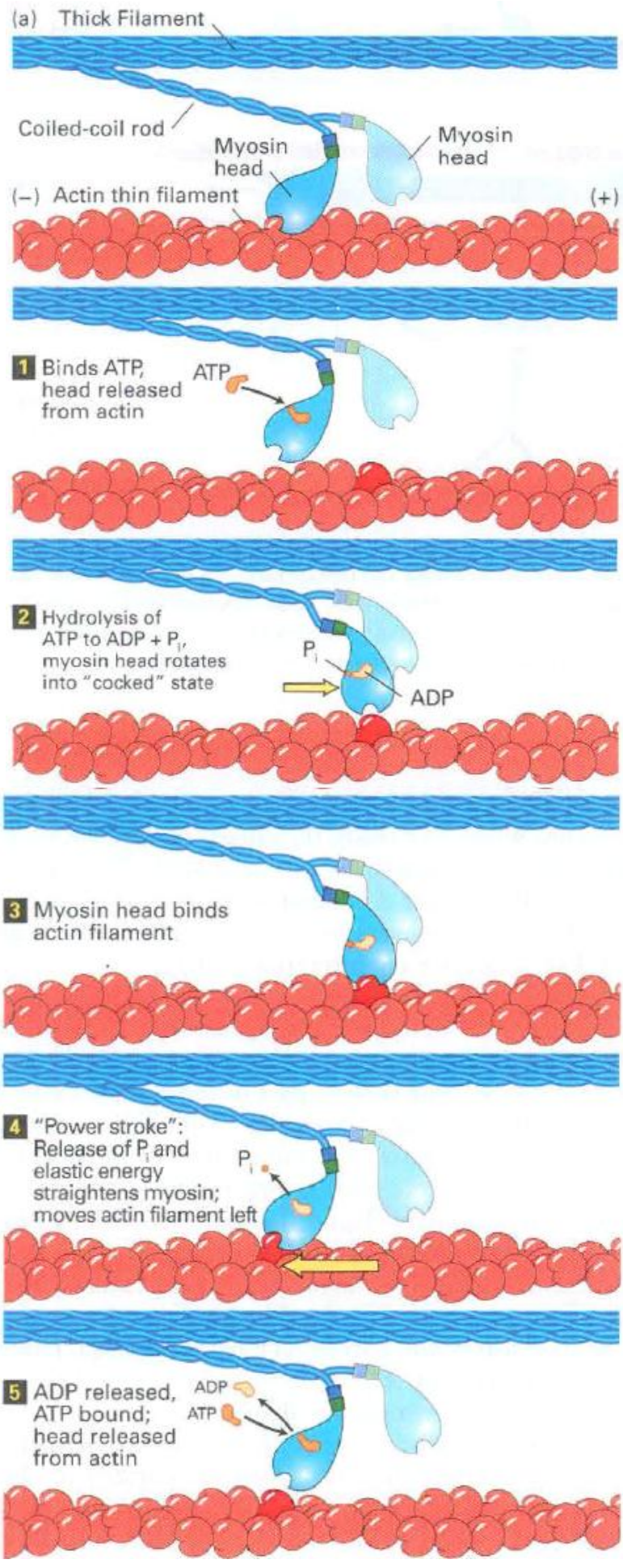
Mechanism of Contraction

During contraction, neither the thick nor thin filaments change their length. Contraction results as the overlapping thin and thick filaments of each sarcomere slide past one another. Contraction is induced when an action potential arrives at a synapse, the neuromuscular junction (NMJ), and is transmitted along the T tubules to the sarcoplasmic reticulum to trigger Ca2+ release.

In a resting muscle, the myosin heads cannot bind G-actin because the binding sites are blocked by the troponintropomyosin complex on the F-actin filaments. Calcium ions released upon neural stimulation bind troponin, changing its shape and moving tropomyosin on the F-actin to expose the myosin-binding active sites and allow crossbridges to form. Binding actin produces a conformational change or pivot in the myosins, which pulls the thin filaments farther into the A band, toward the Z disc. Energy for the pivot and pulling of actin is provided by hydrolysis of ATP bound to the myosin heads, after which myosin binds another ATP and detaches from actin. In the continued presence of Ca2+ and ATP, these **attach-pivot-detach** events occur in a repeating**cross-bridge cycle**, each lasting about 50 milliseconds, which shortens the sarcomere and contracts the muscle. A single muscle contraction results from hundreds of these cycles.

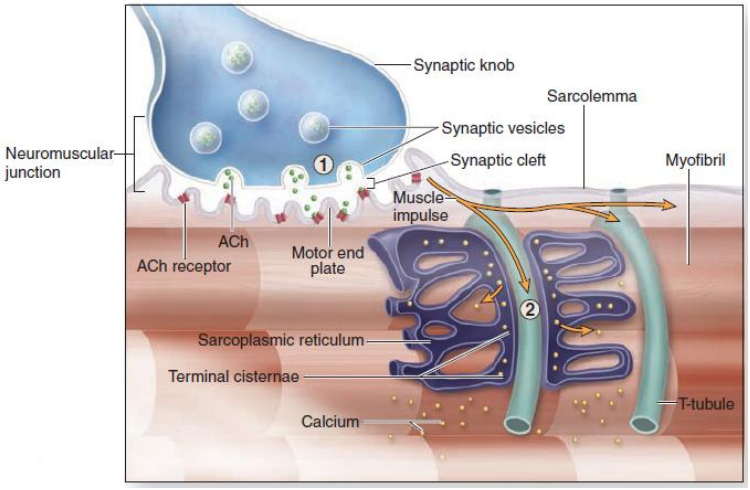
When the neural impulse stops and levels of free calcium diminish, tropomyosin again covers the myosin-binding sites on actin and the filaments passively slide back and sarcomeres return to their relaxed length. In the absence of ATP, the actinmyosin crossbridges become stable, which accounts for the rigidity of skeletal muscles (**rigor mortis**) that occurs as mitochondrial activity stops after death.

- Larger muscles with coarser movements have motor axons that typically branch profusely and innervate 100 or more muscle fibers. In this case the single axon and all the muscle fibers in contact with its branches make up a **motor unit.**



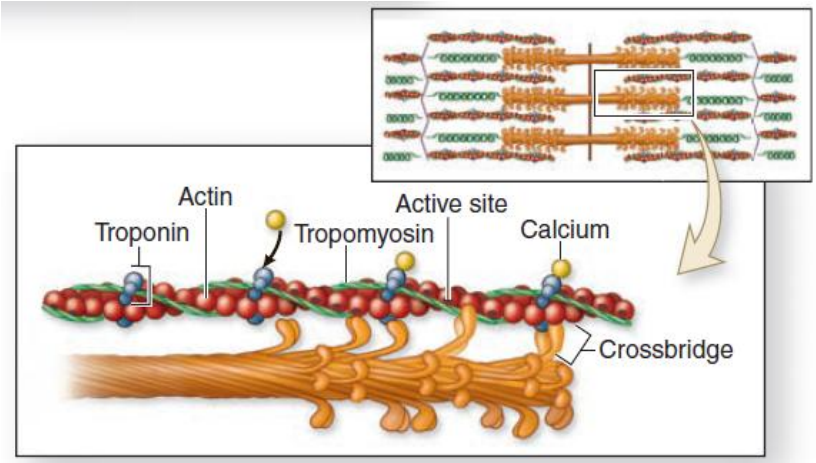
ATP-driven myosin movement along actin filaments.(a) In the absence of ATP, the myosin head is firmly attached to the actin filament. Although this state is very short-lived in living muscle, it is the state responsible for muscle stiffness in death (**rigor mortis**). **Step1 :** On binding ATP, the myosin head releases from the actin filament. **Step2:** The head hydrolyzes the ATP to ADP and P1, which induces a rotation in the head with respect to the neck. This **"cocked state"** stores the energy released by ATP hydrolysis as elastic energy, like a stretched spring. **Step 3:** Myosin in the "cocked" state binds actin. **Step 4:**When it is bound to actin, the myosin headcouples release of P with release of the elastic energy to move theactin filament. This is known as the **"power stroke,"**as it involvesmoving the actin filament with respect to the end of the myosin neckdomain. **Step5:** The head remains tightly bound to the filamentas ADP IS released and before fresh ATP is bound by the head.

1. A nerve impulse triggers release of ACh from the synaptic knob into the synaptic cleft. ACh binds to ACh receptors in the motor end plate of the neuromuscular junction, initiating a muscle impulse in the sarcolemma of the muscle fiber.

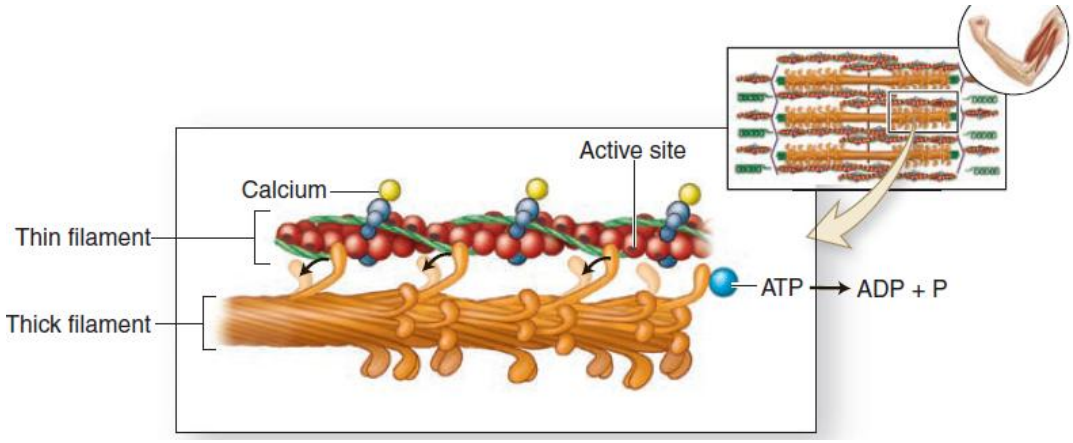


2. As the muscle impulse spreads quickly from the sarcolemma along T tubules, calcium ions are released from terminal cisternae into the sarcoplasm.

3. Calcium ions bind to troponin. Troponin changes shape, movingtropomyosin on the actin to expose active sites on actin moleculesof thin filaments. Myosin heads of thick filaments attach to exposedactive sites to form crossbridges.



4. Myosin heads pivot, moving thin filaments toward the sarcomere center. ATP binds myosin heads and is broken down into ADP and P. Myosin heads detach from thin filaments and return to their prepivot position. The repeating cycle of *attach-pivot-detach-return* slides thick and thin filaments past one another. The sarcomere shortens and the muscle contracts. The cycle continues as long as calcium ions remain bound to troponin to keep active sites



exposed.

5. When the impulse stops, calcium ions are actively transported into the sarcoplasmic reticulum, tropomyosin re-covers active sites, and filamentspassively slide back to their relaxed state.