Muscle Physiology

INTRODUCTION

There are three types of muscle; *skeletal muscle, cardiac muscle, and smooth muscle*. Muscle comprises the largest group of tissues in the body, accounting for approximately half of the body's weight. Skeletal muscle alone makes up about 40% of the body's weight in men and 32% in women, with smooth and cardiac muscle making up another 10% of the total weight. Although the three muscle types are structurally and functionally distinct, they can be classified in two different ways according to their common characteristics (Figure 8-1). First, muscles are categorized as striated (skeletal and cardiac muscle) or unstriated (smooth muscle), depending on whether alternating dark and light bands, or striations (stripes), can be seen when the muscle is viewed under a light microscope. Second, muscles are categorized as voluntary (skeletal muscle) or involuntary (cardiac and smooth muscle), depending respectively on whether they are innervated by the somatic nervous system and are subject to voluntary control, or are innervated by the autonomic nervous system and are not subject to voluntary control. Although skeletal muscle is categorized as voluntary, because it can be consciously controlled, much skeletal muscle activity is also subject to subconscious, involuntary regulation, such as that related to posture, balance, and stereotypical movements like walking.

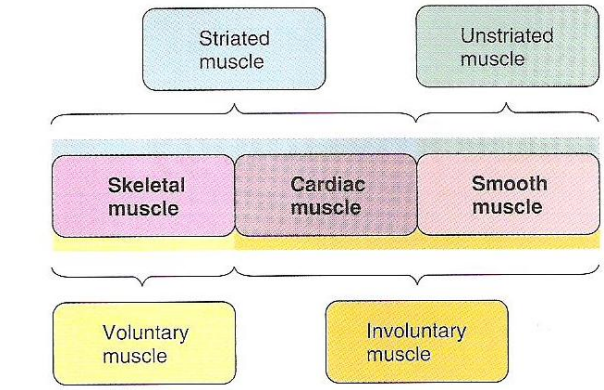


FIGURE 8-1
Categorization of muscle

STRUCTURE OF SKELETAL MUSCLE

A single skeletal muscle cell, known as a muscle fiber, is relatively large, elongated, and cylinder-shaped. A skeletal muscle consists of a number of muscle fibers lying parallel to each other and bundled together by connective tissue (Figure 8-2a). The fibers usually extend the entire length of the muscle.

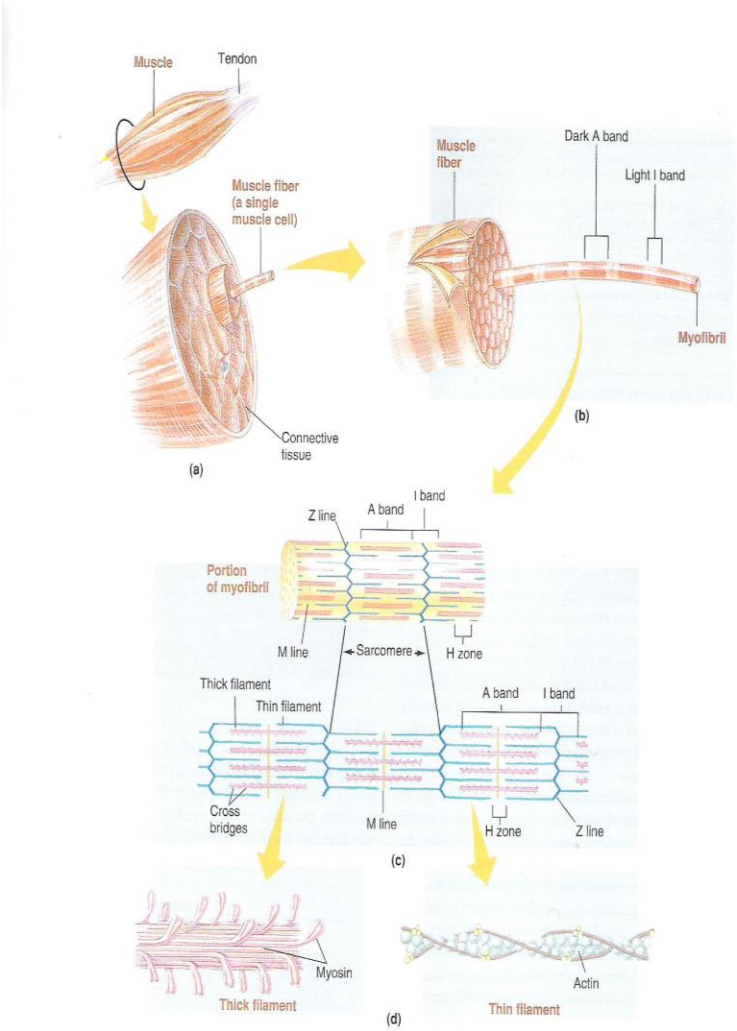


FIGURE 8-2

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 fibers are striated by a highly organized internal arrangement

The predominant structural feature of a skeletal muscle fiber is numerous **myofibrils**. These specialized contractile elements, which constitute 80% of the volume of the muscle fiber, are cylindrical intracellular structures that extend the entire length of the muscle fiber (Figure 8-2b), each myofibril consisting of a regular arrangement of highly organized cytoskeletal elements -the thick and the thin filaments (Figure 8-2c). The **thick filaments** are special assembles of the protein *myosin,* whereas the **thin filaments** are made up

primarily of the protein *actin* (Figure 8-2d). The levels of organization in a skeletal muscle can be summarized as follows:

Whole muscle	→	muscle fiber	→	myofibrils	→	thick and thin filaments	→	myosin and actin
(an organ)		*(a cell)*		*(a specialized Intracellular Structure)*		*(cytoskeletal elements)*		*(protein molecules)*

Viewed with a light microscope, a myofibril displays alternating dark bands (the **A bands**) and light bands (the **I bands**). The bands of all the myofibrils lined up parallel to each other collectively produce the striated or striped appearance of a skeletal muscle fiber. Alternate stacked sets of thick and thin filaments that slightly overlap each other are responsible for the A and I bands (Figure 8-2e). An A band is a stacked set of thick filaments along with the portions of the thin filaments that overlap on both ends of the thick filaments. The thick filaments lie only within the A band and extend its entire width; that is, the two ends of the thick filaments within a stack define the outer limits of a given A band. The lighter area within the middle of the A band, where the thin filaments do not reach, is the **H zone**. Only the central portions of the thick filaments are found in this region. A system of supporting proteins holds the thick filaments together vertically within each stack. These proteins can be seen as the **M line**, which extends vertically down the middle of the A band within the center of the H zone.

The **I band** consists of the remaining portion of the thin filaments that do not project into the A band. Visible in the middle of each I band is a dense, vertical **Z line**. The area between two Z lines is called a **sarcomere**, which is the functional unit of skeletal muscle. A functional unit of any organ is the smallest component that can perform all the functions of that organ. Accordingly, a sarcomere is the smallest component of a muscle fiber that can contract. The Z line is a flat, cytoskeletal disc that connects the thin filaments of two adjoining sarcomeres. Thus the I band contains only thin filaments from two adjacent sarcomeres but not the entire length of these filaments.

Not visible under a light microscope, single strands of a giant, highly elastic protein known as **titin** extend in both directions from the M line along the length of the thick filament to the Z lines at opposite ends of the sarcomere. Titin is the largest protein in the body, being made up of nearly 30,000 amino acids. It serves two important roles: (l) along with the M-line proteins, titin helps stabilize the position of the thick filaments in relation to the thin filaments, and (2) by acting like a spring, it greatly augments a muscle's elasticity. That is, titin helps a muscle stretched by an external force passively recoil or spring back to its resting length when the stretching force is removed, much like a stretched spring.

With an electron microscope, fine cross bridges can be seen extending from each thick filament toward the surrounding thin filaments in the areas where the thick and thin filaments overlap (Figure 8-2c). To give you an idea of the magnitude of these filaments, a single muscle fiber may contain an estimated 16 billion thick and 32 billion thin filaments, all arranged in a very precise pattern within the myofibrils

Myosin forms the thick filaments

Each thick filament has several hundred myosin molecules packed together in a specific arrangement. A myosin molecule is a protein consisting of two identical subunits, each shaped somewhat like a golf club (Figure 8-4a). The protein's tail ends are intertwined around each other like golf-club shafts twisted together, with the two globular heads projecting out at one end. The two halves of each thick filament are mirror images made up of myosin molecules lying length-wise in a regular, staggered array, with their tails oriented toward the center of the filament and their globular heads protruding outward at regular intervals (Figure 8-4b). These heads form the cross bridges between the thick and thin filaments. Each cross bridge has two important sites crucial to the contractile process: (l) an actin-binding site and (2) a myosin ATPase (ATP-splitting) site.

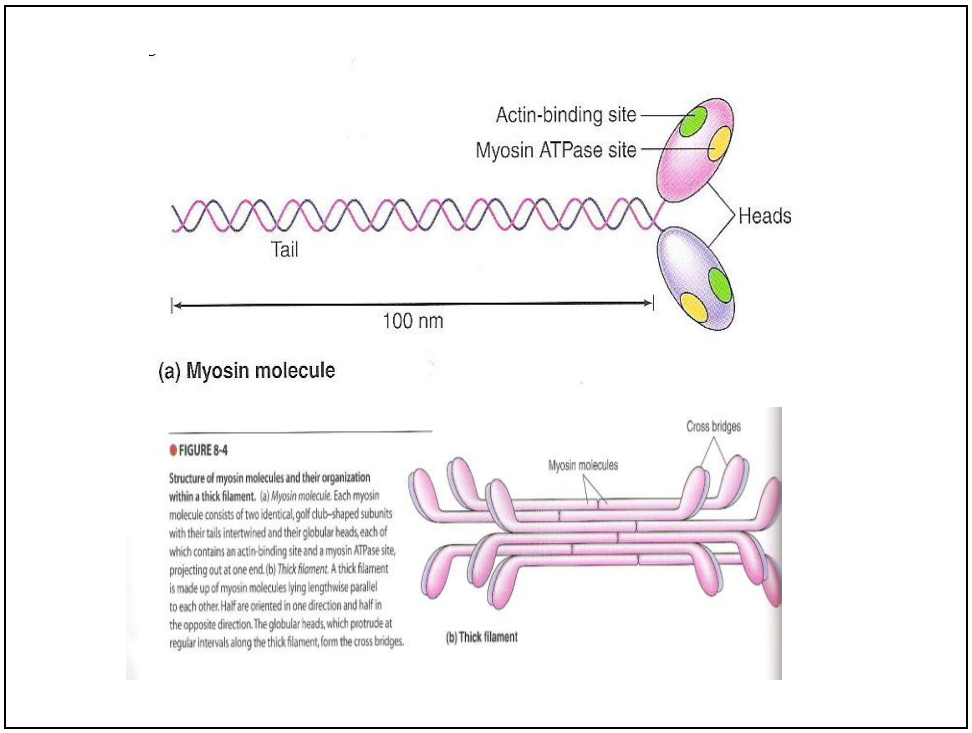


FIGURE 8-4

Structure 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 consist of three proteins: *actin, tropomyosin,* and *troponin* (Figure 8-5). Actin molecules, the primary structural proteins of the thin filament, are spherical. The backbone of a thin filament is formed by actin molecules joined into two strands and twisted together, like two intertwined strings of pearls. Each actin molecule has a special binding site for attachment with a myosin cross bridge. By a mechanism to be described shortly, binding of myosin and actin molecules at the cross bridges results in energy-consuming contraction of the muscle fiber. Accordingly, myosin and actin are often called **contractile proteins**, even though neither myosin nor actin actually contracts.

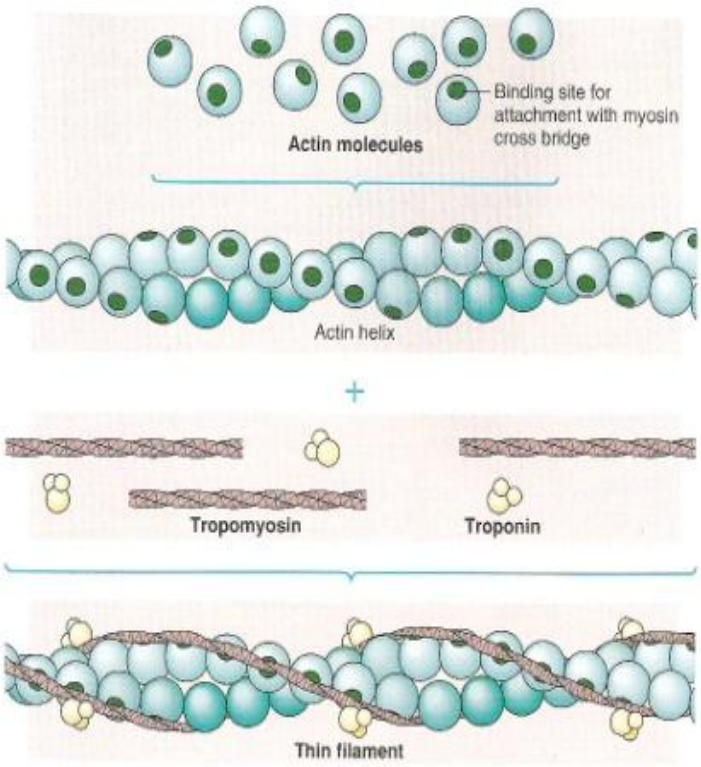


FIGURE 8-5

Composition of a thin filament. The main structural component of a thin filament is two chains of spherical actin molecules that are twisted together. Troponin molecules (which consist of three small, spherical subunits) and threadlike tropomyosin molecules are arranged to form a ribbon that lies alongside the groove of the actin helix and physically covers the binding sites on actin molecules for attachment with myosin cross bridges. (The thin filaments shown here are not drawn in proportion to the thick filaments in Figure 8-4. Thick filaments are two to three times larger in diameter than thin filaments.)

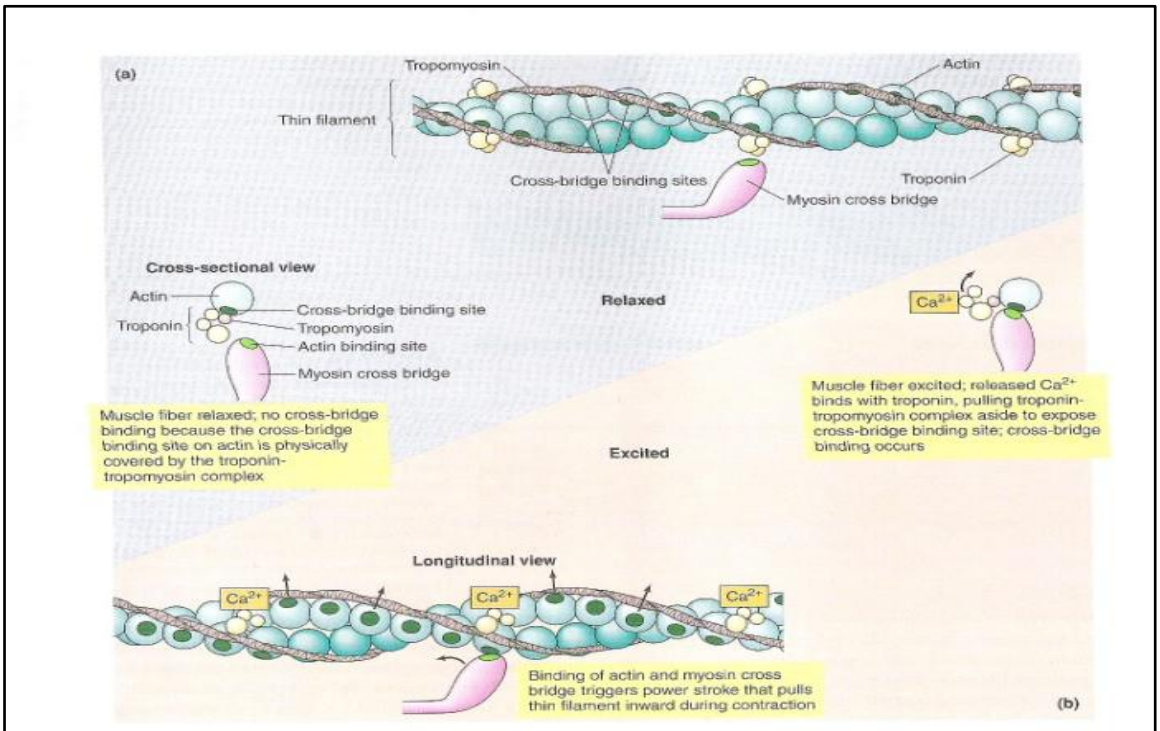


FIGURE 8-6

Role of calcium in turning on cross bridges

In a relaxed muscle fiber, contraction does not take place; actin cannot bind with cross bridges, because of the way the two other types of protein-tropomyosin and troponin-are positioned within the thin filament. **Tropomyosin** molecules are threadlike proteins that lie end-to-end alongside the groove of the actin spiral. In this position, tropomyosin covers the actin sites that bind with the cross bridges, blocking the interaction that leads to muscle contraction. The other thin filament component, **troponin**, is a protein complex made of three polypeptide units: one binds to tropomyosin, one binds to actin, and a third can bind with Ca^{2+}. When troponin is not bound to Ca^{2+}, this protein stabilizes tropomyosin in its blocking position over actin's crossbridge binding sites (Figure 8-6a). When Ca^{2+} binds to troponin, the shape of this protein is changed in such a way that tropomyosin slips away from its blocking position (Figure 8-6b). With tropomyosin out of the way, actin and myosin can bind and interact at the cross bridges, resulting in muscle contraction. Tropomyosin and troponin are often called **regulatory proteins** because of their role in covering (preventing contraction) or exposing (permitting contraction) the binding sites for cross-bridge interaction between actin and myosin.

MOLECULAR BASIS OF SKELETAL MUSCLE CONTRACTION

Cross-bridge interaction between actin and myosin brings about muscle contraction by means of the sliding filament mechanism.

SLIDING FILAMENT MECHANISM

The thin filaments on each side of a sarcomere slide inward over the stationary thick filaments toward the A band's center during contraction (Figure 8-7). As they slide inward, the thin filaments pull the Z lines to which they are attached closer together, so the sarcomere shortens. As all the sarcomeres throughout the muscle fiber's length shorten simultaneously, the entire fiber shortens. This is the **sliding filament mechanism** of muscle contraction. The H zone, in the center of the A band where the thin filaments do not reach, becomes smaller as the thin filaments approach each other when they slide more deeply inward. The I hand, which consists of the portions of the thin filaments that do not overlap with the thick filaments, narrows as the thin filaments further overlap the thick filaments during their inward slide. The thin filaments themselves do not change length during muscle fiber shortening. The width of the A band remains unchanged during contraction, because its width is determined by the length of the thick filaments, and the thick filaments do not change length during the shortening process. Note that neither the thick nor thin filaments decrease in length to shorten the sarcomere. Instead, contraction is accomplished by the thin filaments from the opposite sides of each sarcomere sliding closer together between the thick filaments.

POWER STROKE

Cross-bridge activity pulls the thin filaments inward relative to the stationary thick filaments. During contraction, with the tropomyosin and troponin "chaperones" pulled out of the way by Ca^{2+}, the myosin cross bridges from a thick filament can bind with the actin molecules in the surrounding thin filaments. Let's concentrate on a single cross-bridge interaction (figure 8-8a). 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 bridge changes shape, bending inward as if it were on a hinge, "stroking" toward

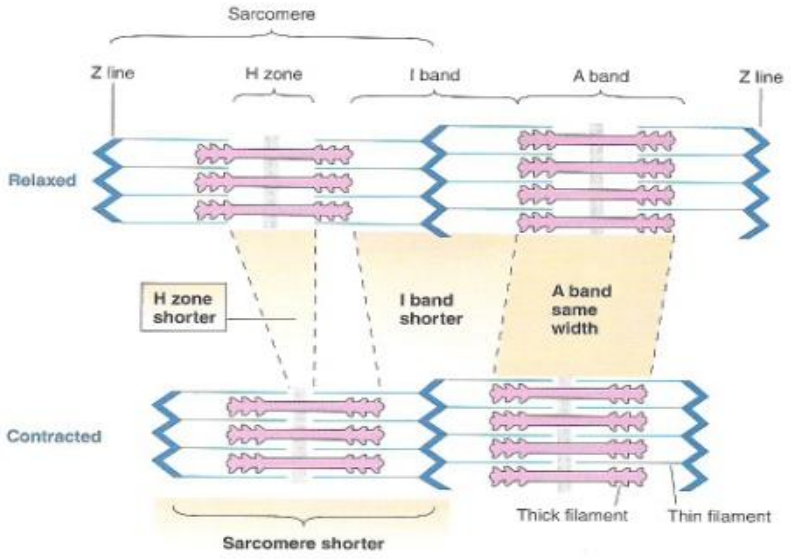
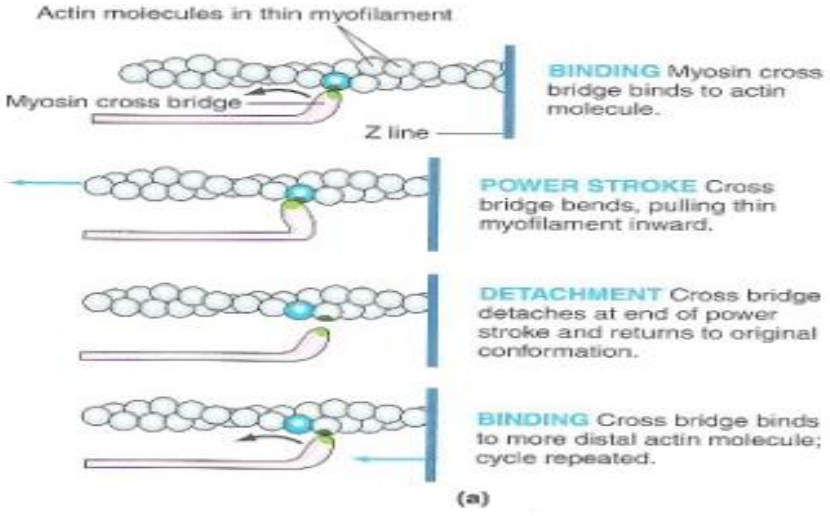


FIGURE 8-7

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.



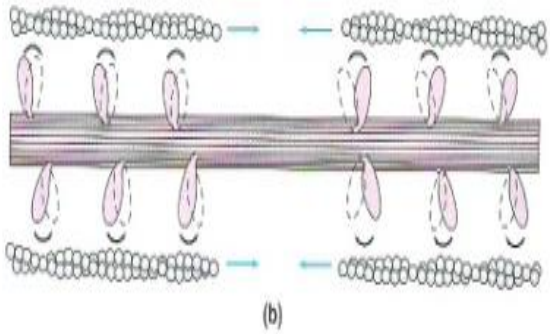


FIGURE 8-8

Cross-bridge activity. (a) During each cross-bridge cycle, the cross bridge binds with an actin molecule, bends to pull the thin filament inward during the power stroke, then detaches and returns to its resting conformation, ready to repeat the cycle. (b) The power strokes of all cross bridges extending from a thick filament are directed toward the center of the thick filament.

the center of the sarcomere, like the stroking of a boat oar. This so-called power stroke of a cross bridge pulls inward the thin filament to which it is attached. A single power stroke pulls the thin filament inward only a small percentage of the total shortening distance. Repeated cycles of cross-bridge binding and bending complete the shortening.

At the end of one cross-bridge cycle, the link between the myosin cross bridge and actin molecule breaks. The cross bridge returns to its original shape and binds to the next actin molecule behind its previous actin partner. The cross bridge bends once again to pull the thin filament in further, then detaches and repeats the cycle. Repeated cycles of cross-bridge power strokes successively pull in the thin filaments.

Because of the way myosin molecules are oriented within a thick filament (Figure 8-8b), all the cross bridges stroke toward the center of the sarcomere, so that all the surrounding thin filaments on each end of the sarcomere are pulled inward simultaneously The cross bridges aligned with given thin filaments do not all stroke in harmony, however. At any time during contraction, part of the cross bridges are attached to the thin filaments and are stroking, while others are returning to their original conformation in preparation for binding with another actin molecule. Thus some cross bridges are "holding on" to the thin filaments, whereas others "let go" to hind with new actin. Were it not for this asynchronous cycling of the cross bridges, the thin filaments would slip back toward their resting position between strokes.

How does muscle excitation switch on this cross-bridge cycling? The term **excitation-contraction coupling** refers to the series of events linking muscle excitation (the presence of an action potential in a muscle fiber) to muscle contraction (cross-bridge activity that causes the thin filaments to slide closer together to produce sarcomere shortening).

SPREAD OF THE ACTION POTENTIAL DOWN THE T TUBULES

At each junction of an A band and I band, the surface membrane dips into the muscle fiber to form a transverse tubule (T tubule), which runs perpendicularly from the surface of the muscle cell membrane into the central portions of the muscle fiber (Figure 8-9). 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, rapidly transmitting the surface electric activity into the central portions of the fiber. The presence of a local action potential in the T tubules induces permeability changes in a separate membranous network within the muscle fiber, the sarcoplasmic reticulum.

RELEASE OF CALCIUM FROM THE SARCOPLASMIC RETICULUM

The sarcoplasmic reticulum is a modified endoplasmic reticulum that consists of a fine network of interconnected compartments surrounding each myofibril (Figure 8-9). This membranous network encircles the myofibril throughout its length but is not continuous. Separate segments of sarcoplasmic reticulum are wrapped around each A band and each I band. The ends of each segment expand to form saclike regions, the lateral sacs, which are separated from the adjacent T tubules by a slight gap (Figure 8-9). The sarcoplasmic reticulum's lateral sacs store Ca^{2+}. Spread of an action potential down a T tubule triggers the opening of Ca^{2+}.