9 Muscles and Muscle Tissue

In this chapter, you will learn that

Muscles use actin and myosin molecules to convert the energy of ATP into force

beginning with

9.1 Overview of muscle types, special characteristics, and functions

next exploring

Skeletal muscle

and investigating

9.2 Gross anatomy

and

9.3 Microscopic anatomy and sliding filament model

then asking

9.4 How does a nerve impulse cause a muscle fiber to contract?

and

9.5 What are the properties of whole muscle contraction?

and

9.6 How do muscles generate ATP?

and

9.7 What determines the force, velocity, and duration of contraction?

and

9.8 How does skeletal muscle respond to exercise?

then exploring

Smooth muscle

and asking

9.9 How does smooth muscle differ from skeletal muscle?

and finally, exploring

Developmental Aspects of Muscles

CAREER CONNECTION

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Because flexing muscles look like mice scurrying beneath the skin, some scientist long ago dubbed them *muscles*, from the Latin *mus* meaning "little mouse." Indeed, we tend to think of the rippling muscles of professional boxers or weight lifters when we hear the word *muscle*. But muscle is also the dominant tissue in the heart and in the walls of other hollow organs. In all its forms, muscle tissue makes up nearly half the body's mass.

Muscles are distinguished by their ability to transform chemical energy (ATP) into directed mechanical energy. In so doing, they become capable of exerting force.

9.1 There are three types of muscle tissue

Learning Outcomes

- **Compare and contrast the three basic types of muscle tissue.**
- **List four important functions of muscle tissue.**

9

Types of Muscle Tissue

Chapter 4 introduced the three types of muscle tissue—*skeletal*, *cardiac*, and *smooth* (◀ pp. 138–140). In this chapter, we first examine the structure and function of skeletal muscle. Then we consider smooth muscle more briefly, largely by comparing it with skeletal muscle. We describe cardiac muscle in detail in Chapter 18, but for easy comparison, Table 9.3 on pp. 312–313 summarizes the characteristics of all three muscle types.

Let's introduce some terminology before we describe each type of muscle.

- Skeletal and smooth muscle cells (but not cardiac muscle cells) are elongated, and are called **muscle fibers**.
- Whenever you see the prefixes **myo** or **mys** (both are word roots meaning "muscle") or **sarco** (flesh), the reference is to muscle. For example, the plasma membrane of muscle cells is called the *sarcolemma* (sar″ko-lem′ah), literally, "muscle" (sarco) "husk" (lemma), and muscle cell cytoplasm is called *sarcoplasm*.

Okay, let's get to it.

Skeletal Muscle

Skeletal muscle tissue is packaged into the *skeletal muscles*, organs that attach to and cover the skeleton. Skeletal muscle fibers are the longest muscle cells and have obvious stripes called *striations*. Although it is often activated by reflexes, skeletal muscle is called *voluntary muscle* because it is the only type subject to conscious control.

- When you think of skeletal muscle tissue, the key words to keep in mind are *skeletal*, *striated*, and *voluntary*.

Skeletal muscle is responsible for overall body mobility. It can contract rapidly, but it tires easily and must rest after short periods of activity. Nevertheless, it can exert tremendous power. Skeletal muscle is also remarkably adaptable. For example, your forearm muscles can exert a force of a fraction of an ounce to pick up a paper clip—or a force of about 6 pounds to pick up this book!

Cardiac Muscle

Cardiac muscle tissue occurs only in the heart, where it constitutes the bulk of the heart walls. Like skeletal muscle cells, cardiac muscle cells are striated, but cardiac muscle is not voluntary. Indeed, it can and does contract without being stimulated by the nervous system. Most of us have no conscious control over how fast our heart beats.

- Key words to remember for cardiac muscle are *cardiac*, *striated*, and *involuntary*.

Cardiac muscle usually contracts at a fairly steady rate set by the heart's pacemaker, but neural controls allow the heart to speed up for brief periods, as when you race across the tennis court to make that overhead smash.

Smooth Muscle

Smooth muscle tissue is found in the walls of hollow visceral organs, such as the stomach, urinary bladder, and respiratory passages. Its role is to force fluids and other substances through internal body channels. Smooth muscle also forms valves to regulate the passage of substances through internal body openings, dilates and constricts the pupils of your eyes, and forms the arrector pili muscles attached to hair follicles.

Like skeletal muscle, smooth muscle consists of elongated cells, but smooth muscle has no striations. Like cardiac muscle, smooth muscle is not subject to voluntary control. Its contractions are slow and sustained.

- We can describe smooth muscle tissue as *visceral*, *nonstriated*, and *involuntary*.

Characteristics of Muscle Tissue

What enables muscle tissue to perform its duties? Four special characteristics are key.

- **Excitability**, also termed **responsiveness**, is the ability of a cell to receive and respond to a stimulus by changing its membrane potential. In the case of muscle, the stimulus is usually a chemical—for example, a neurotransmitter released by a nerve cell.
- **Contractility** is the ability to shorten forcibly when adequately stimulated. This ability sets muscle apart from all other tissue types.
- **Extensibility** is the ability to extend or stretch. Muscle cells shorten when contracting, but they can be stretched, even beyond their resting length, when relaxed.
- **Elasticity** is the ability of a muscle cell to recoil and resume its resting length after stretching.

Muscle Functions

Muscles perform at least four important functions for the body:

- **Produce movement.** Skeletal muscles are responsible for all locomotion and manipulation. They enable you to respond quickly to jump out of the way of a car, direct your eyes, and smile or frown.

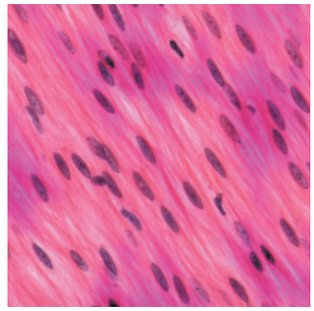
Blood courses through your body because of the rhythmically beating cardiac muscle of your heart and the smooth muscle in the walls of your blood vessels, which helps maintain blood pressure. Smooth muscle in organs of the digestive, urinary, and reproductive tracts propels substances (foodstuffs, urine, semen) through the organs and along the tract.

- **Maintain posture and body position.** We are rarely aware of the skeletal muscles that maintain body posture. Yet these muscles function almost continuously, making one tiny adjustment after another to counteract the never-ending downward pull of gravity.
- **Stabilize joints.** Even as they pull on bones to cause movement, they strengthen and stabilize the joints of the skeleton.
- **Generate heat.** Muscles generate heat as they contract, which plays a role in maintaining normal body temperature.

Check Your Understanding

1. When describing muscle, what does "striated" mean?
2. MAKE CONNECTIONS At right are photomicrographs of three types of muscle tissue (introduced in Chapter 4). For each, identify the type of muscle, state whether it is striated, whether it is voluntary, and its major location. Create a short table that summarizes this information.

For answers, see Answers Appendix.



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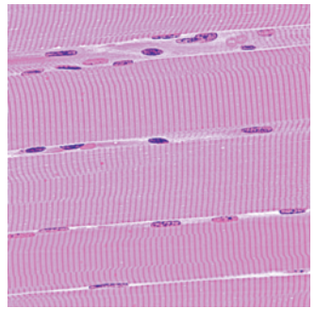

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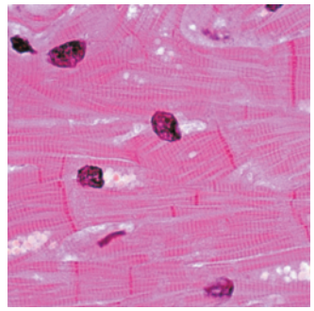

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9.2 A skeletal muscle is made up of muscle fibers, nerves, blood vessels, and connective tissues

Learning Outcome

▶ **Describe the gross structure of a skeletal muscle.**

Each **skeletal muscle** is a discrete organ, made up of several kinds of tissues. Skeletal muscle fibers predominate, but blood vessels, nerve fibers, and substantial amounts of connective tissue are also present. We can easily examine a skeletal muscle's shape and its attachments in the body without a microscope.

Nerve and Blood Supply

In general, one nerve, one artery, and one or more veins serve each muscle. These structures all enter or exit near the central part of the muscle and branch profusely through its connective tissue sheaths (described below). Unlike cells of cardiac and smooth muscle tissues, which can contract without nerve stimulation, every skeletal muscle fiber is supplied with a nerve ending that controls its activity.

Skeletal muscle has a rich blood supply. This is understandable because contracting muscle fibers use huge amounts of energy and require almost continuous delivery of oxygen and nutrients via the arteries. Muscle cells also give off large amounts of metabolic wastes that must be removed through veins if contraction is to remain efficient. Capillaries, the smallest of the body's blood vessels, take a long and winding path through muscle, and have numerous cross-links, features that accommodate changes in muscle length. They straighten when the muscle stretches and contort when the muscle contracts.

Connective Tissue Sheaths

In an intact muscle, there are several different connective tissue sheaths. Together these sheaths support each cell and reinforce and hold together the muscle, preventing the bulging muscles from bursting during exceptionally strong contractions.

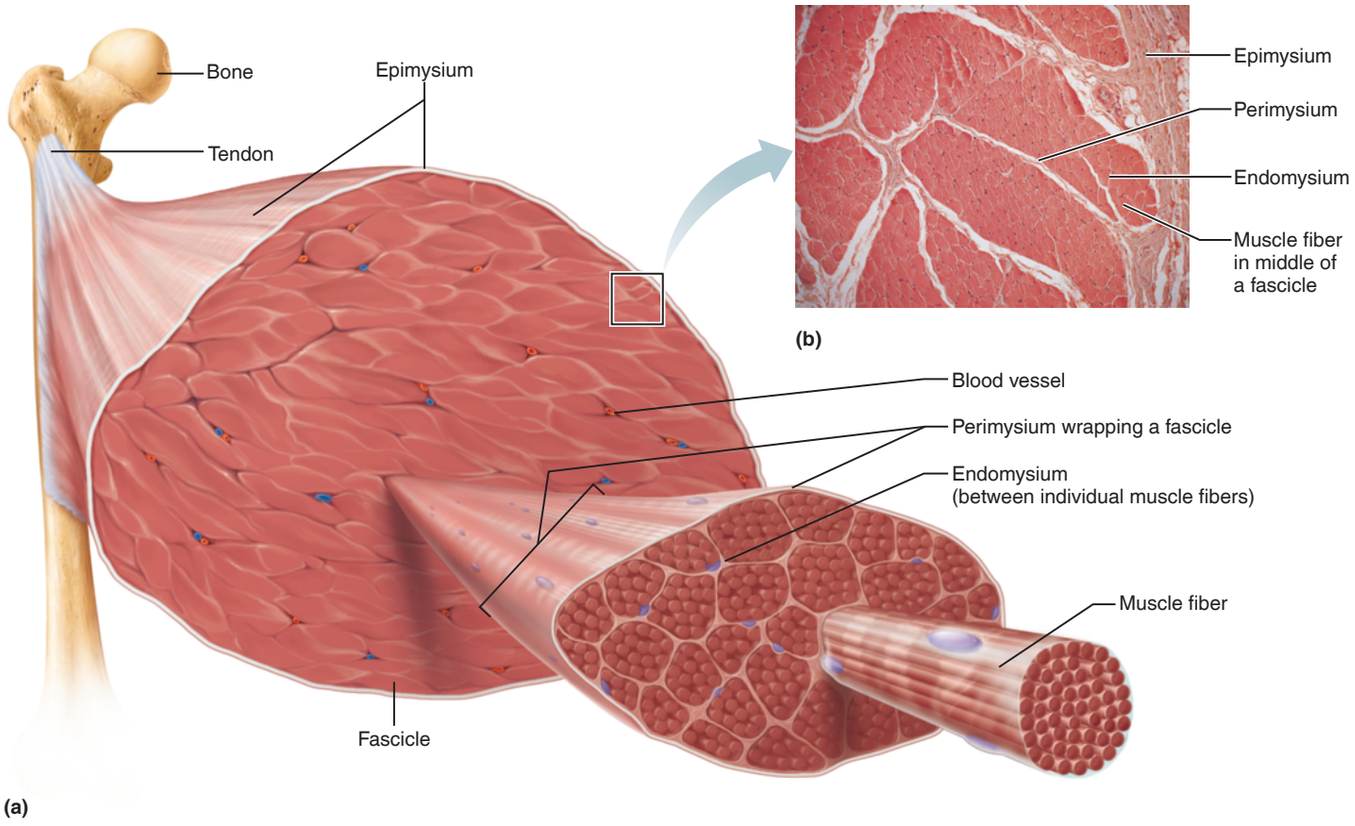


Figure 9.1 Connective tissue sheaths of skeletal muscle: epimysium, perimysium, and endomysium. (b) Photomicrograph of a cross section of part of a skeletal muscle (30×).

Let's consider these connective tissue sheaths from external to internal (see **Figure 9.1** and the top three rows of **Table 9.1**).

- **Epimysium.** The **epimysium** (ep″ĭ-mis′e-um; "outside the muscle") is an "overcoat" of dense irregular connective tissue that surrounds the whole muscle. Sometimes it blends with the deep fascia that lies between neighboring muscles or the superficial fascia deep to the skin (◀ p. 151).
- **Perimysium and fascicles.** Within each skeletal muscle, the muscle fibers are grouped into **fascicles** (fas′ĭ-klz; "bundles") that resemble bundles of sticks. Surrounding each fascicle is a layer of dense irregular connective tissue called **perimysium** (per″ĭ-mis′e-um; "around the muscle").
- **Endomysium.** The **endomysium** (en″do-mis′e-um; "within the muscle") is a wispy sheath of connective tissue that surrounds each individual muscle fiber. It consists of fine areolar connective tissue.

As shown in Figure 9.1, all of these connective tissue sheaths are continuous with one another as well as with the tendons that join muscles to bones. When muscle fibers contract, they pull on these sheaths, which transmit the pulling force to the bone to be moved. The sheaths contribute somewhat to the natural elasticity of muscle tissue, and also provide routes for the entry and exit of the blood vessels and nerve fibers that serve the muscle.

Attachments

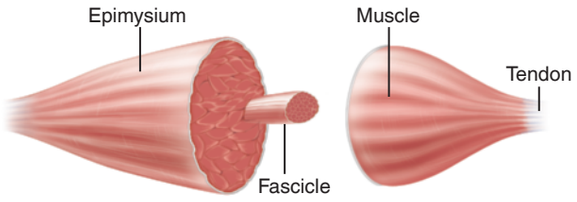
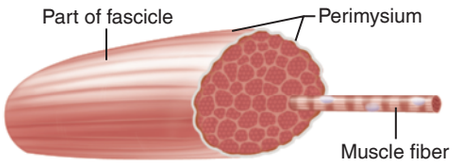
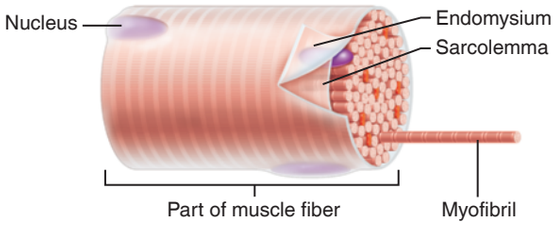
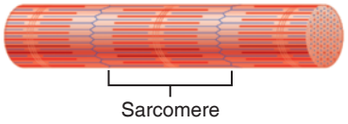
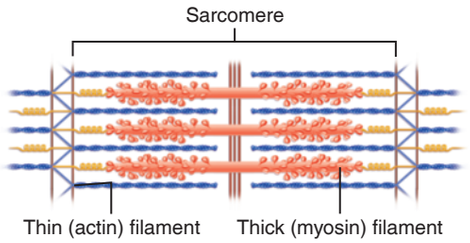
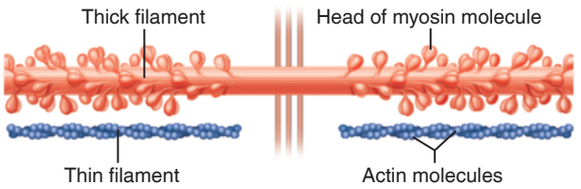
Recall from Chapter 8 that most skeletal muscles span joints and attach to bones (or other structures) in at least two places. When a muscle contracts, the movable bone, the muscle's **insertion**, moves toward the immovable or less movable bone, the muscle's **origin**. In the muscles of the limbs, the origin typically lies proximal to the insertion.

Muscle attachments, whether origin or insertion, may be direct or indirect.

- In **direct**, or **fleshy**, **attachments**, the epimysium of the muscle is fused to the periosteum of a bone or perichondrium of a cartilage.
- In **indirect attachments**, the muscle's connective tissue wrappings extend beyond the muscle either as a ropelike **tendon** (Figure 9.1a) or as a sheetlike **aponeurosis** (ap″o-nu-ro′sis) (see Figure 10.12a on p. 347). The tendon or aponeurosis anchors the muscle to the connective tissue covering of a skeletal element (bone or cartilage) or to the fascia of other muscles.

Indirect attachments are much more common because of their durability and small size. Tendons are mostly tough collagen fibers, which can withstand the abrasion of rough bony projections that would tear apart the more delicate muscle tissues. Because of their relatively small size, more tendons than

Table 9.1 Structure and Organizational Levels of Skeletal Muscle

STRUCTURE AND ORGANIZATIONAL LEVEL	DESCRIPTION	CONNECTIVE TISSUE WRAPPINGS
Muscle (organ)  	A muscle consists of hundreds to thousands of muscle cells, plus connective tissue wrappings, blood vessels, and nerve fibers.	Covered externally by the epimysium
Fascicle (a portion of the muscle)  	A fascicle is a discrete bundle of muscle cells, segregated from the rest of the muscle by a connective tissue sheath.	Surrounded by perimysium
Muscle fiber (cell)  	A muscle fiber is an elongated multinucleate cell; it has a banded (striated) appearance.	Surrounded by endomysium
Myofibril (complex organelle composed of bundles of myofilaments)  	Myofibrils are rodlike contractile elements that occupy most of the muscle cell volume. Composed of sarcomeres arranged end to end, they appear banded, and bands of adjacent myofibrils are aligned.	—
Sarcomere (a segment of a myofibril)  	A sarcomere is the contractile unit, composed of myofilaments made up of contractile proteins.	—
Myofilament, or filament (extended macromolecular structure)  	Contractile myofilaments are of two types—thick and thin. Thick filaments contain bundled myosin molecules; thin filaments contain actin molecules (plus other proteins). The sliding of the thin filaments past the thick filaments produces muscle shortening. Elastic filaments (not shown here) provide elastic recoil when tension is released and help maintain myofilament organization.	—

fleshy muscles can pass over a joint—so tendons also conserve space.

Check Your Understanding

3. How does the term epimysium relate to the role and position of this connective tissue sheath?
4. MAKE CONNECTIONS What is the difference between a tendon and a ligament? (Hint: See Chapter 4, p. 133.)

For answers, see Answers Appendix.

9.3 Skeletal muscle fibers contain calcium-regulated molecular motors

Learning Outcomes

- **Describe the microscopic structure and functional roles of the myofibrils, sarcoplasmic reticulum, and T tubules of skeletal muscle fibers.**
- **Describe the sliding filament model of muscle contraction.**

Each skeletal muscle fiber is a long cylindrical cell with multiple oval nuclei just beneath its **sarcolemma** or plasma membrane (**Figure 9.2b**). Skeletal muscle fibers are huge cells. Their diameter typically ranges from 10 to 100 µm—up to ten times that of an average body cell—and their length is phenomenal, some up to 30 cm long. Their large size and multiple nuclei are not surprising once you learn that hundreds of embryonic cells fuse to produce each fiber.

Sarcoplasm, the cytoplasm of a muscle cell, is similar to the cytoplasm of other cells, but it contains unusually large amounts of **glycosomes** (granules of stored glycogen that provide glucose during muscle cell activity for ATP production) and **myoglobin**, a red pigment that stores oxygen. Myoglobin is similar to hemoglobin, the pigment that transports oxygen in blood.

In addition to the usual organelles, a muscle cell contains three specialized structures: myofibrils, sarcoplasmic reticulum, and T tubules. Let's look at these structures more closely because they play important roles in muscle contraction.

Myofibrils

A single muscle fiber contains hundreds to thousands of rodlike **myofibrils** that run parallel to its length (Figure 9.2b). The myofibrils, each 1–2 µm in diameter, are so densely packed in the fiber that mitochondria and other organelles appear to be squeezed between them. They account for about 80% of cellular volume.

Myofibrils are made up of a chain of sarcomeres linked end to end. *Sarcomeres* (shown in Figure 9.2c and decribed shortly) contain even smaller rodlike structures called *myofilaments*. Table 9.1 (bottom three rows; p. 283) summarizes these structures.

Striations

Striations, a repeating series of dark and light bands, are evident along the length of each myofibril. In an intact muscle fiber, the dark **A bands** and light **I bands** are nearly perfectly aligned, giving the cell its striated appearance.

As illustrated in Figure 9.2c:

- Each dark A band has a lighter region in its midsection called the **H zone** (*H* for *helle*; "bright").
- Each H zone is bisected vertically by a dark line called the **M line** (*M* for middle) formed by molecules of the protein myomesin.
- Each light I band also has a midline interruption, a darker area called the **Z disc** (or Z line).

Sarcomeres

The region of a myofibril between two successive Z discs is a **sarcomere** (sar′ko-mĕr; "muscle segment"). Averaging 2 µm long, a sarcomere is the smallest contractile unit of a muscle fiber—the *functional unit* of skeletal muscle. It contains an A band flanked by half an I band at each end. Within each myofibril, the sarcomeres align end to end like boxcars in a train.

Myofilaments

If we examine the banding pattern of a myofibril at the molecular level, we see that it arises from orderly arrangement of even smaller structures within the sarcomeres. These smaller structures, the **myofilaments** or *filaments*, are the muscle equivalents of the actin-containing microfilaments and myosin motor proteins described in Chapter 3 (◀ p. 88). As you will recall, the proteins actin and myosin play a role in motility and shape change in virtually every cell in the body. This property reaches its highest development in the contractile muscle fibers. There are two types of contractile myofilaments in a sarcomere:

- The central **thick filaments** containing myosin (red) extend the entire length of the A band (Figure 9.2c and d). They are connected in the middle of the sarcomere at the M line.
- The more lateral **thin filaments** containing actin (blue) extend across the I band and partway into the A band. The Z disc, a protein sheet, anchors the thin filaments. We describe the third type of myofilament, the *elastic filament*, in the next section.

A close look at myofibril arrangement and banding patterns reveals that:

- A hexagonal arrangement of six thin filaments surrounds each thick filament, and three thick filaments enclose each thin filament. This is shown in Figure 9.2e (far right), which shows a cross section of a sarcomere in an area where thick and thin filaments overlap.
- The H zone of the A band appears less dense because the thin filaments do not extend into this region.
- The M line in the center of the H zone is slightly darker because of the fine protein strands there that hold adjacent thick filaments together.
- The myofilaments are held in alignment at the Z discs and the M lines, and are anchored to the sarcolemma at the Z discs.

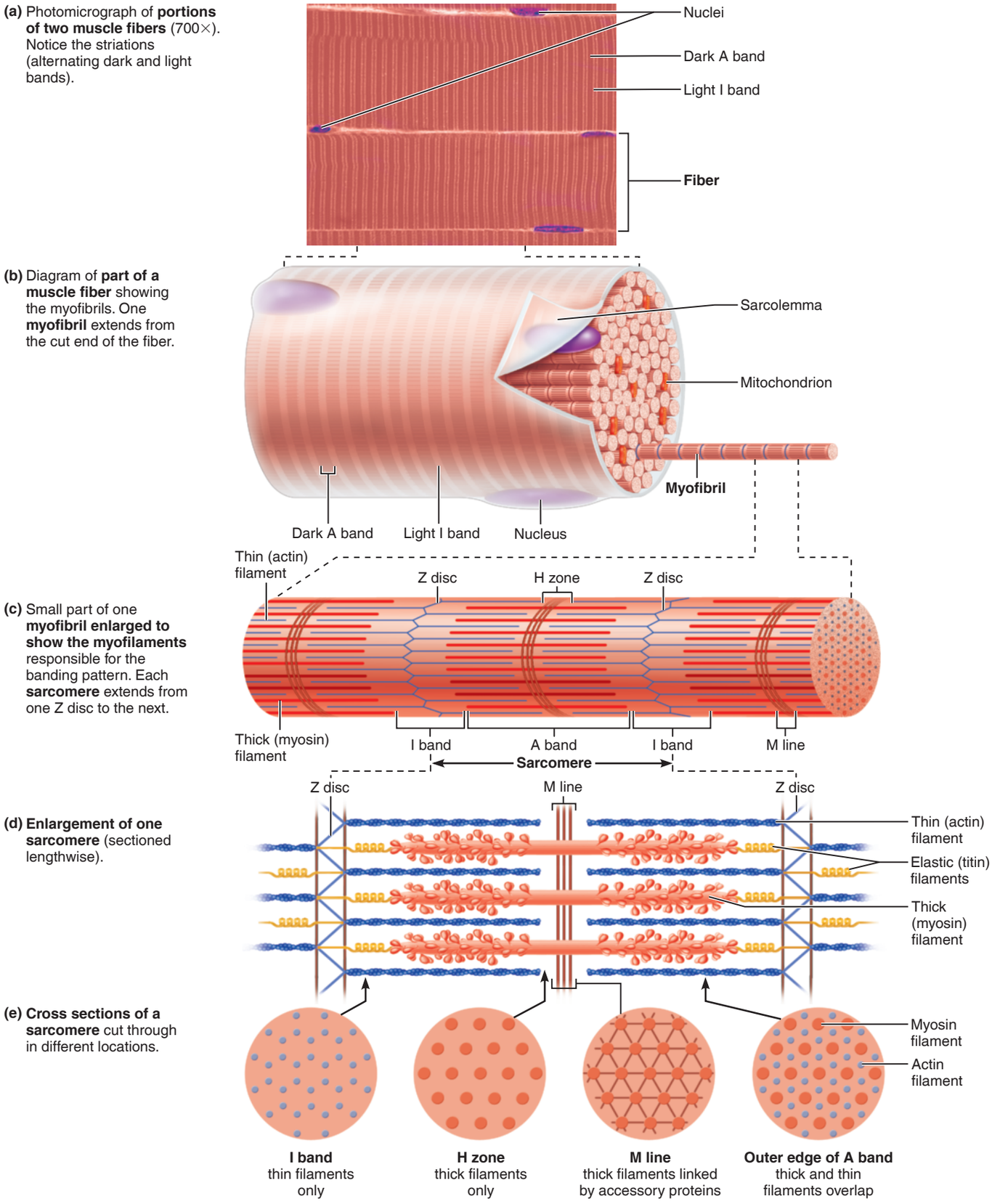


Figure 9.2 Microscopic anatomy of a skeletal muscle fiber.

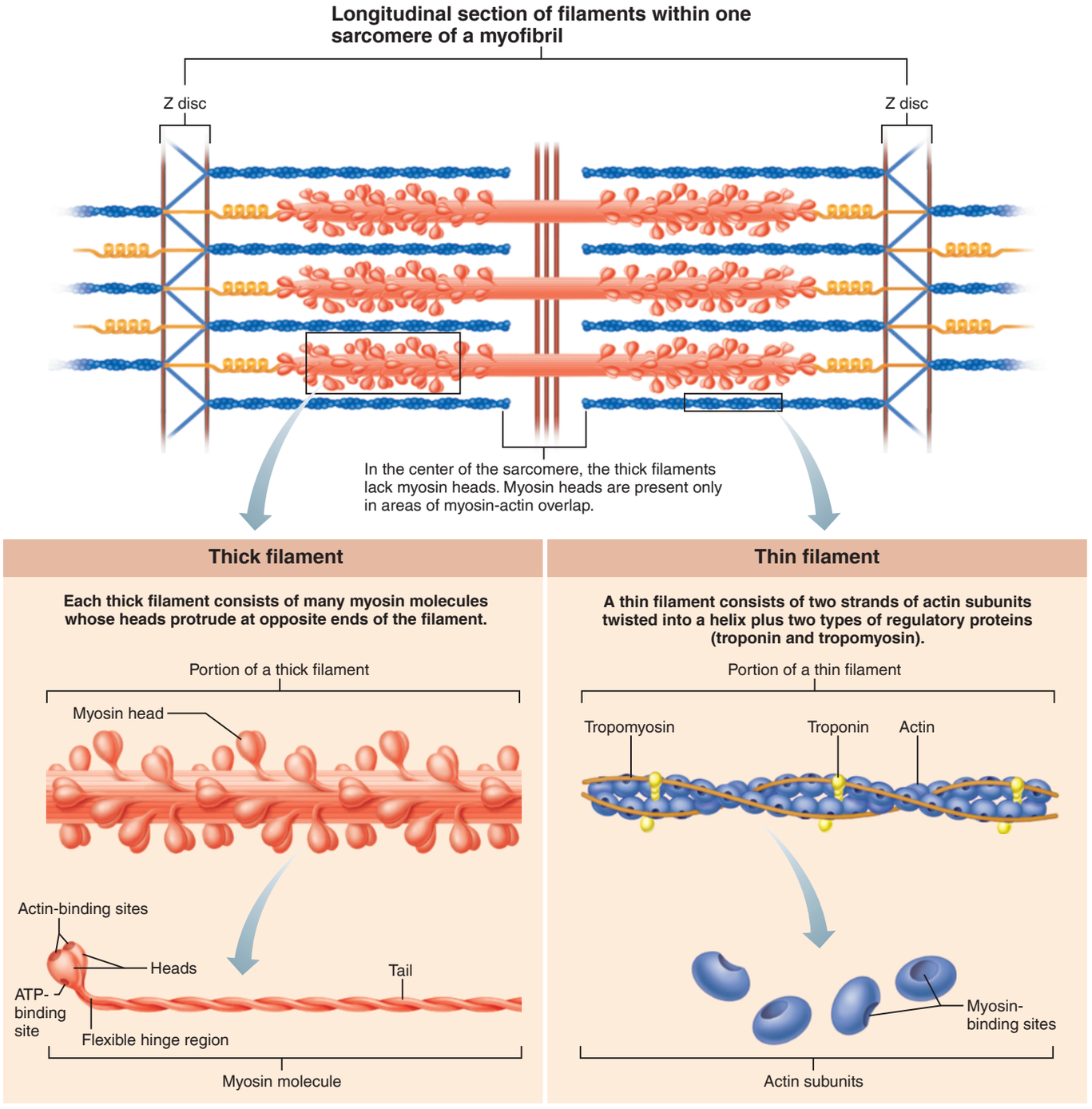


Figure 9.3 **Composition of thick and thin filaments.**

Molecular Composition of Myofilaments

Muscle contraction depends on the myosin- and actin-containing myofilaments. As noted earlier, thick filaments are composed primarily of the protein **myosin**. Each myosin molecule consists of six polypeptide chains: two heavy (high-molecular-weight) chains and four light chains. The heavy chains twist together to form myosin's rodlike tail, and each heavy chain ends in a globular *head* that is attached to the tail via a flexible hinge (**Figure 9.3**).

The globular heads, each associated with two light chains, are the "business end" of myosin. During contraction, they link the

thick and thin filaments together, forming **cross bridges**, and swivel around their point of attachment, acting as motors to generate force. Myosin itself splits ATP (acts as an ATPase) and uses the released energy to drive movement.

Each thick filament contains about 300 myosin molecules bundled together, with their tails forming the central part of the thick filament and their heads facing outward at the end of each molecule (Figure 9.3). As a result, the central portion of a thick filament (in the H zone) is smooth, but its ends are studded with a staggered array of myosin heads.

The thin filaments are composed chiefly of the protein **actin** (blue in Figure 9.3). Actin has kidney-shaped polypeptide subunits, called *globular actin* or *G actin*. Each G actin has a *myosin-binding site* (or *active site*) to which the myosin heads attach during contraction. G actin subunits polymerize into long actin filaments called *filamentous*, or *F*, *actin*. Two intertwined actin filaments, resembling a twisted double strand of pearls, form the backbone of each thin filament (Figure 9.3).

Thin filaments also contain several regulatory proteins.

- Polypeptide strands of **tropomyosin** (tro″po-mi′o-sin), a rod-shaped protein, spiral about the actin core and help stiffen and stabilize it. Successive tropomyosin molecules are arranged end to end along the actin filaments, and in a relaxed muscle fiber, they block myosin-binding sites on actin so that myosin heads on the thick filaments cannot bind to the thin filaments.
- **Troponin** (tro′po-nin), the other major protein in thin filaments, is a globular protein with three polypeptide subunits (Figure 9.3). One subunit attaches troponin to actin. Another subunit binds tropomyosin and helps position it on actin. The third subunit binds calcium ions.

Both troponin and tropomyosin help control the myosin-actin interactions involved in contraction. Several other proteins help form the structure of the myofibril.

- The **elastic filament** we referred to earlier is composed of the giant protein **titin** (Figure 9.2d). Titin extends from the Z disc to the thick filament, and then runs within the thick filament (forming its core) to attach to the M line. It holds the thick filaments in place, maintaining the organization of the A band, and helps the muscle cell spring back into shape after stretching. (The part of the titin that spans the I bands is extensible, unfolding when the muscle stretches and recoiling when the tension is released.) Titin does not resist stretching in the ordinary range of extension, but it stiffens as it uncoils, helping the muscle resist excessive stretching, which might pull the sarcomeres apart.
- Another important structural protein is **dystrophin**, which links the thin filaments to the integral proteins of the sarcolemma (which in turn are anchored to the extracellular matrix).
- Other proteins that bind filaments or sarcomeres together and maintain their alignment include *nebulin*, *myomesin*, and *C proteins*. Intermediate (desmin) filaments extend from the Z disc and connect each myofibril to the next throughout the width of the muscle cell.

HOMEOSTATIC IMBALANCE 9.1 — CLINICAL

The term **muscular dystrophy** refers to a group of inherited muscle-destroying diseases that generally appear during childhood. The affected muscles initially enlarge due to deposits of fat and connective tissue, but the muscle fibers atrophy and degenerate.

The most common and serious form is **Duchenne muscular dystrophy (DMD)**, which is inherited as a sex-linked recessive disease. It is expressed almost exclusively in males (one in every 3600 male births) and is diagnosed when the boy is between 2 and 7 years old (**Figure 9.4**). Active, normal-appearing boys become clumsy and fall frequently as their skeletal muscles weaken. The disease progresses relentlessly from the extremities upward, finally affecting the head and chest muscles, and cardiac muscle. The weakness continues to progress, but with supportive care, DMD patients are living into their 30s and beyond.

Figure 9.4 A boy with Duchenne muscular dystrophy (DMD). Physiotherapy can help maintain mobility.

DMD is caused by a defective gene for *dystrophin*, the cytoplasmic protein described above. Dystrophin links the cytoskeleton to the extracellular matrix and, like a girder, helps stabilize the sarcolemma. The fragile sarcolemma of DMD patients tears during contraction, allowing entry of excess Ca^{2+}, which damages the contractile fibers. Inflammatory cells (macrophages and lymphocytes) accumulate in the surrounding connective tissue. As the regenerative capacity of the muscle is lost, damaged cells undergo apoptosis, and muscle mass drops.

There is still no cure for DMD. Current treatments are aimed at preventing or reducing spine and joint deformities and helping those with DMD remain mobile as long as possible. Two newly-approved drugs may broaden the treatment options for certain patients.

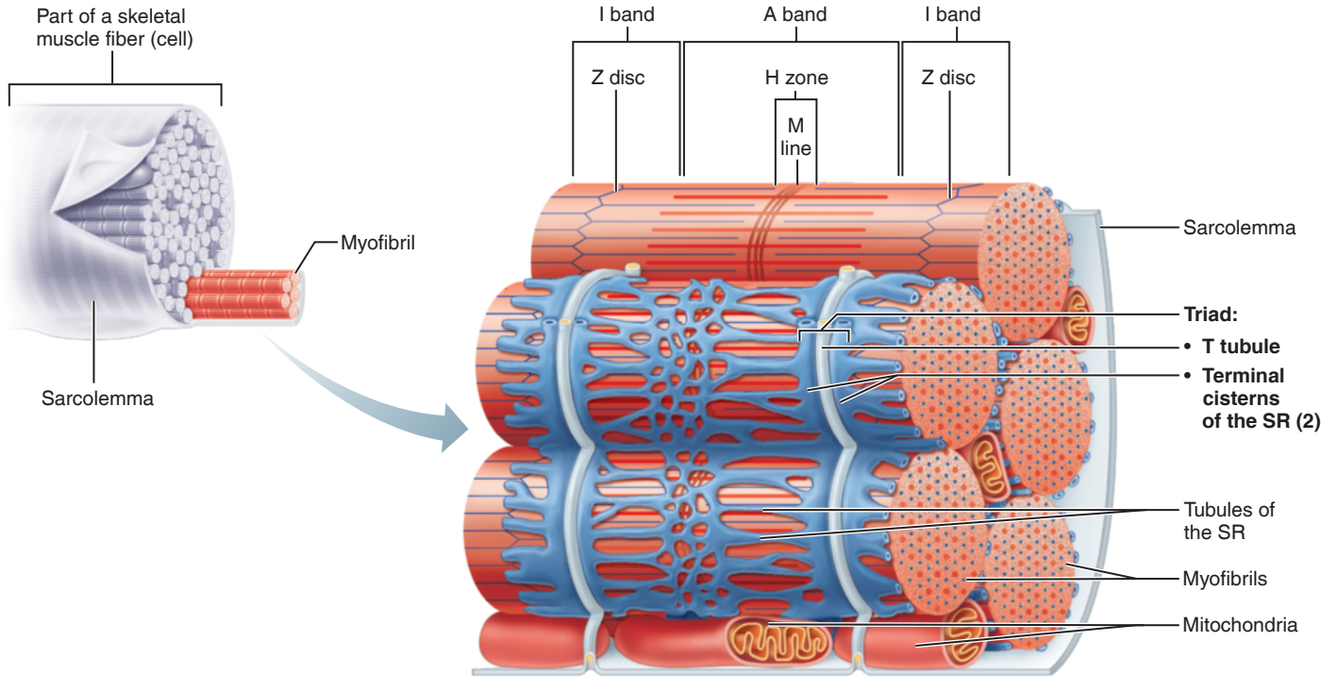


Figure 9.5 Relationship of the sarcoplasmic reticulum and T tubules to myofibrils of skeletal muscle. The tubules of the SR (blue) fuse to form the saclike terminal cisterns next to the A-I junctions. The T tubules (gray) are inward invaginations of the sarcolemma that run deep into the cell between the terminal cisterns. (See detailed view in Focus Figure 9.2, pp. 294–295.) Sites of close contact of these three elements (terminal cistern, T tubule, and terminal cistern) are called triads.

Sarcoplasmic Reticulum and T Tubules

Skeletal muscle fibers contain two sets of intracellular tubules that help regulate muscle contraction: (1) the sarcoplasmic reticulum and (2) T tubules.

Sarcoplasmic Reticulum

Shown in blue in **Figure 9.5**, the **sarcoplasmic reticulum (SR)** is an elaborate smooth endoplasmic reticulum. The SR regulates intracellular levels of ionic calcium. It stores calcium and releases it on demand when the muscle fiber is stimulated to contract. As you will see, calcium provides the final "go" signal for contraction.

Interconnecting tubules of SR surround each myofibril the way the sleeve of a loosely knitted sweater surrounds your arm. Most SR tubules run longitudinally along the myofibril, communicating with each other at the H zone. Others called **terminal cisterns** ("end sacs") form larger, perpendicular cross channels at the A band–I band junctions, and they always occur in pairs. Closely associated with the SR are large numbers of mitochondria and glycogen granules, both involved in producing the energy used during contraction.

T Tubules

At each A band–I band junction, the sarcolemma of the muscle cell protrudes deep into the cell interior, forming an elongated tube called the **T tubule** (T for "transverse"), shown in gray in Figure 9.5. The *lumen* (cavity) of the T tubule is continuous with the extracellular space. As a result, T tubules tremendously increase the muscle fiber's surface area. This allows changes in the membrane potential to rapidly penetrate deep into the muscle fiber.

Along its length, each T tubule runs between the paired terminal cisterns of the SR, forming **triads** (Figure 9.5), successive groupings of the three membranous structures (terminal cistern, T tubule, and terminal cistern). As they pass from one myofibril to the next, the T tubules also encircle each sarcomere.

Muscle contraction is ultimately controlled by nerve-initiated electrical impulses that travel along the sarcolemma. Because T tubules are continuations of the sarcolemma, they conduct impulses to the deepest regions of the muscle cell and every sarcomere. These impulses trigger the release of calcium from the adjacent terminal cisterns. Think of the T tubules as a rapid communication or messaging system that ensures that every myofibril in the muscle fiber contracts at virtually the same time.

Triad Relationships

The roles of the T tubules and SR in providing signals for contraction are tightly linked. At the triads, membrane-spanning proteins from the T tubules and SR link together across the gap between the two membranes.

- The protruding integral proteins of the T tubule act as voltage sensors.

- The integral proteins of the SR form gated channels through which the terminal cisterns release Ca^{2+} (see top right of Focus Figure 9.2 on p. 295).

Sliding Filament Model of Contraction

We almost always think "shortening" when we hear the word **contraction**, but to physiologists contraction refers only to the activation of myosin's cross bridges, which are the force-generating sites. Shortening only occurs if the cross bridges generate enough tension on the thin filaments to exceed the forces that oppose shortening, such as when you lift a bowling ball. Contraction ends when the cross bridges become inactive, the tension declines, and the muscle fiber relaxes.

In a relaxed muscle fiber, the thin and thick filaments overlap only at the ends of the A band (**Figure 9.6** ①). The **sliding filament model of contraction** states that during contraction, the thin filaments slide past the thick ones so that the actin and myosin filaments overlap to a greater degree. Neither the thick nor the thin filaments change length during contraction. Here's how it works:

- When the nervous system stimulates muscle fibers, the myosin heads on the thick filaments latch onto myosin-binding sites on actin in the thin filaments, and the sliding begins.
- These cross bridge attachments form and break several times during a contraction, acting like tiny ratchets to generate tension and propel the thin filaments toward the center of the sarcomere.
- As this event occurs simultaneously in sarcomeres throughout the cell, the muscle cell shortens.

At the microscopic level, the following things occur as a muscle cell shortens:

- The I bands shorten.
- The distance between successive Z discs shortens. As the thin filaments slide centrally, the Z discs to which they attach are pulled *toward* the M line (Figure 9.6 ②).
- The H zones disappear.
- The contiguous A bands move closer together, but their length does not change.

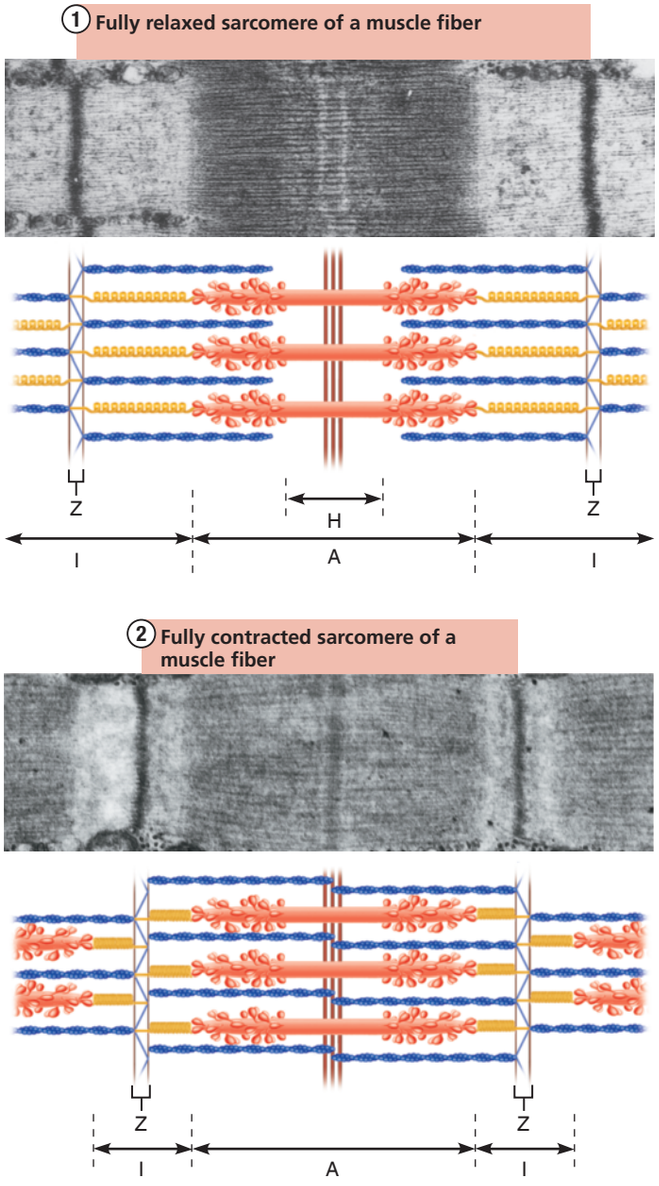
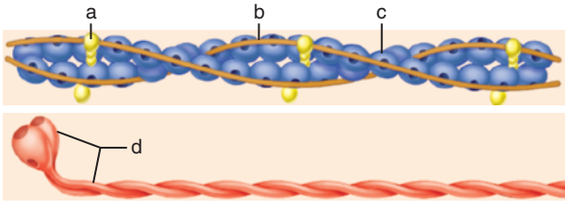


Figure 9.6 Sliding filament model of contraction. At full contraction, the Z discs approach the thick filaments and the thin filaments overlap each other. The photomicrographs (top view in ① and ②) show enlargements of 33,000×.

Check Your Understanding

5. Name proteins a, b, c, and d. Which protein can act as an enzyme to hydrolyze (split) ATP? Which binds Ca^{2+}? Which must move out of the way in order for cross bridges to form?



6. Which region or organelle—cytosol, mitochondrion, or SR—contains the highest concentration of calcium ions in a resting muscle fiber? Which structure provides the ATP needed for muscle activity?

7. DRAW Draw four thick filaments in each of two columns. Add a column of four thin filaments between the thick filaments, as they would appear in a relaxed myofibril. Then add two more columns, each with four thin filaments, on the left and right sides of the original drawing. Label an A band, an I band, and an H zone. Draw and label an M line and a Z disc.

8. MAKE CONNECTIONS Consider a phosphorus atom that is part of the membrane of the sarcoplasmic reticulum in the biceps muscle of your arm. Using the levels of structural organization (described in Chapter 1), name in order the structure that corresponds to each level of organization. Begin at the atomic level (the phosphorus atom) and end at the organ system level.

For answers, see Answers Appendix.

9.4 Motor neurons stimulate skeletal muscle fibers to contract

Learning Outcomes

- **Explain how muscle fibers are stimulated to contract by describing events that occur at the neuromuscular junction.**
- **Follow the events of excitation-contraction coupling that lead to cross bridge activity.**
- **Describe the steps of a cross bridge cycle.**

The sliding filament model tells us that myofilaments slide past each other as the sarcomeres contract. In this module, we will see exactly how this happens. But before we begin, let's fill in some background information that will help you understand this topic, and then look at the big picture of how muscle contraction works.

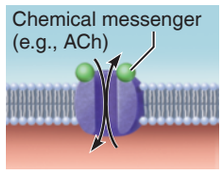
Background and Overview

Remember that skeletal muscle contractions are voluntary. For example, you *decide* when you want to contract your biceps muscle to pick up your cell phone. Making that decision involves many neurons in your brain, but the contraction of a skeletal muscle ultimately comes down to activating a few *motor neurons* in the spinal cord. Motor neurons are the way that the nervous system connects with skeletal muscles and "tells" them to contract.

Both neurons and muscles are *excitable cells*. That is, they respond to external stimuli by changing their resting membrane potential. (Remember that all cells have a resting membrane potential, which is a voltage across the plasma membrane; ◀ pp. 79–80.) These changes in membrane potential act as signals. One type of electrical signal is called an **action potential** (**AP**; sometimes called a *nerve impulse*). An AP is a large change in membrane potential that spreads rapidly over long distances within a cell. Generally, APs don't spread from cell to cell. For this reason, the signal has to be converted to a chemical signal—a chemical messenger called a *neurotransmitter* (◀ p. 81) that diffuses across the small gap between excitable cells to start the signal again. The neurotransmitter that motor neurons use to "tell" skeletal muscle to contract is **acetylcholine** (as″ĕ-til-ko′lēn), or **ACh**.

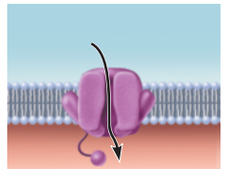
Ion Channels

Rapidly changing the membrane potential in neurons and muscle cells requires the opening and closing of membrane channel proteins that allow certain ions to pass across the membrane (◀ p. 70). The movement of ions through these ion channels changes the membrane voltage. Two classes of ion channels are important for excitation and contraction of skeletal muscle:



Chemically gated ion channel

- **Chemically gated ion channels** are opened by chemical messengers (e.g., neurotransmitters). This class of ion channel creates small local changes in the membrane potential (as we will see shortly). Receptors for acetylcholine are an example of this class. An **ACh receptor** is a single protein in the plasma membrane that is both a receptor and an ion channel.
- **Voltage-gated ion channels** open or close in response to changes in membrane potential. They underlie all action potentials. In skeletal muscle fibers, the initial change in membrane potential is created by chemically gated channels. In other words, chemically gated ion channels cause a small local *depolarization* (a decrease in the membrane potential) that then triggers the voltage-gated ion channels to create an action potential.


Voltage-gated ion channel

(We will describe ion channels in more detail in Chapter 11.)

Anatomy of Motor Neurons and the Neuromuscular Junction

Motor neurons that activate skeletal muscle fibers are called *somatic motor neurons*, or *motor neurons of the somatic* (*voluntary*) *nervous system* (**Figure 9.7**). These neurons reside in the spinal cord (except for those that supply the muscles of the head and neck). Each neuron has a long threadlike extension called an *axon* that extends from the *cell body* in the spinal cord to the muscle fiber it serves (◀ see Chapter 4, p. 140, to review the parts of a neuron). These axons exit the spinal cord and pass throughout the body bundled together as nerves.

The axon of each motor neuron branches profusely as it enters the muscle so that it can innervate multiple muscle fibers. When it reaches a muscle fiber, each axon divides again, giving off several short, curling branches that collectively form an oval **neuromuscular junction**, or **motor end plate**, with a single muscle fiber.

Each muscle fiber has only one neuromuscular junction, located approximately midway along its length. The end of the axon, called the **axon terminal**, and the muscle fiber are exceedingly close (50–80 nm apart), but they remain separated by a space, the **synaptic cleft** (Figure 9.7), which is filled with a gel-like extracellular substance rich in glycoproteins and collagen fibers.

Within the moundlike axon terminal are **synaptic vesicles**, small membranous sacs containing the neurotransmitter acetylcholine. The trough-like part of the muscle fiber's sarcolemma that helps form the neuromuscular junction is highly folded. These **junctional folds** provide a large surface area for the thousands of ACh receptors located there.

To summarize, the neuromuscular junction is like a sandwich: It is made up of part of a neuron (the axon terminals), part of a muscle cell (the junctional folds), and the "filler" between them (the synaptic cleft).

The Big Picture

Figure 9.7 presents an overview of skeletal muscle contraction and divides this process into four groups of steps. We will

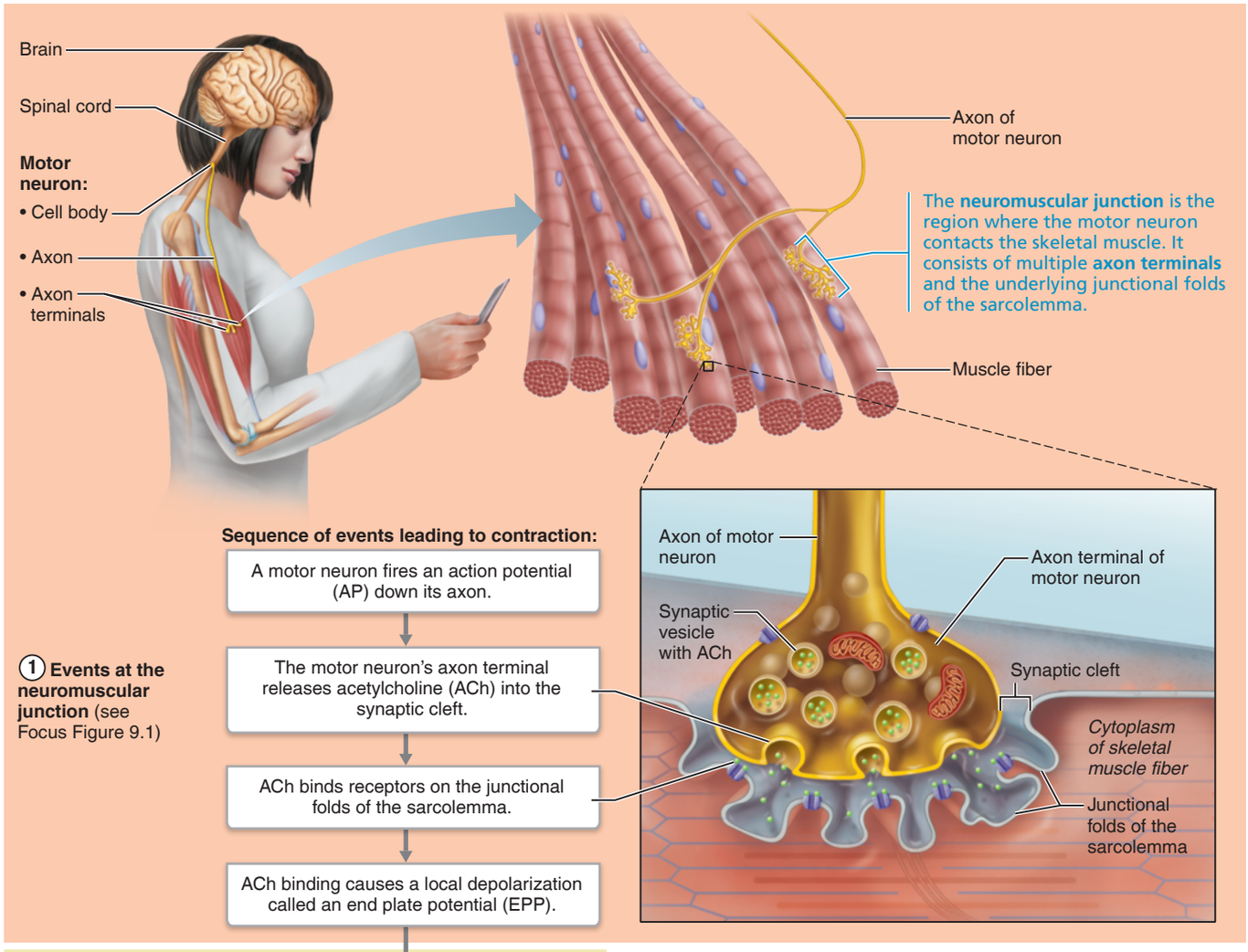


Figure 9.7 **Overview of skeletal muscle contraction.**

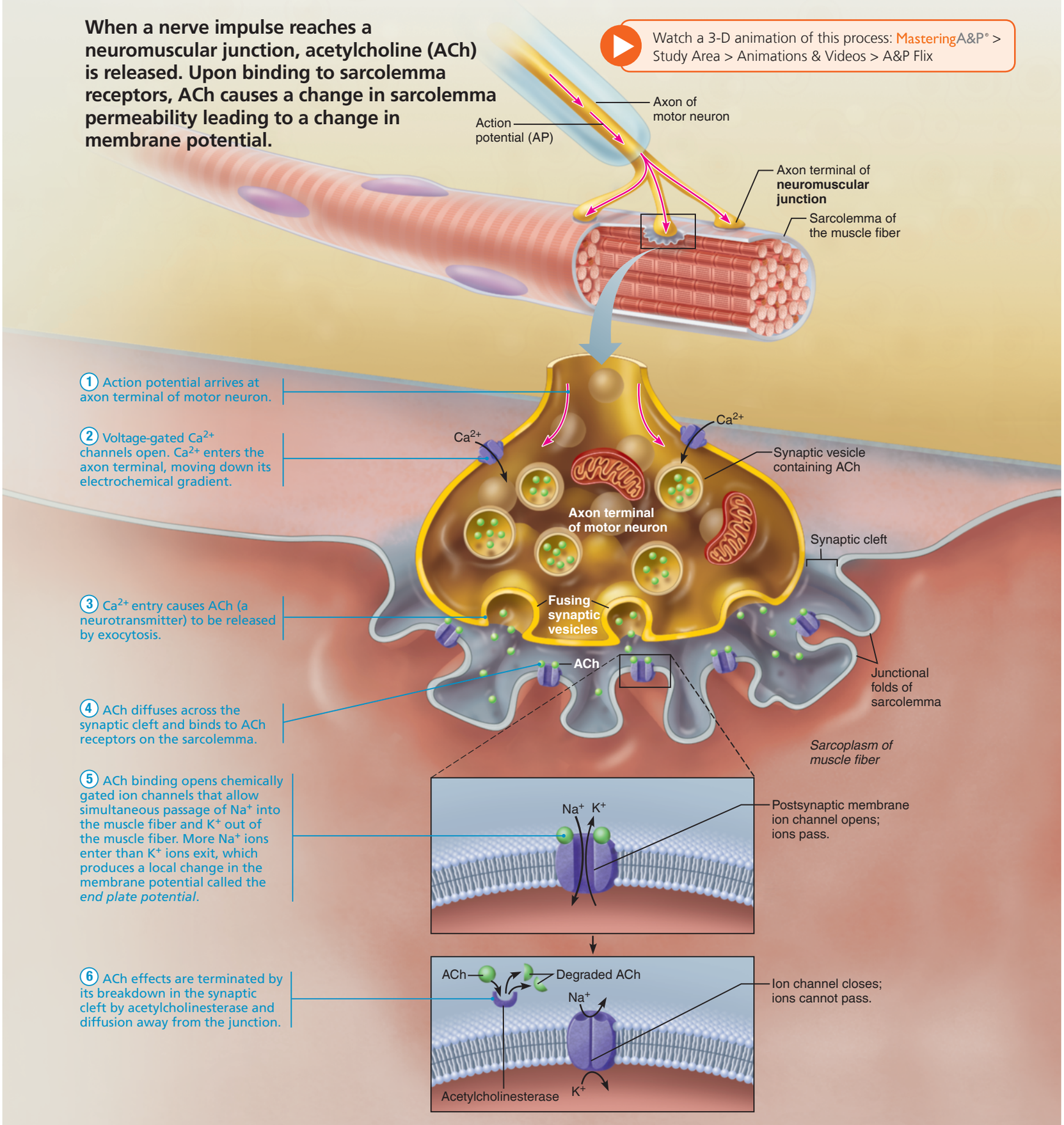
explore each group of steps in more detail in the rest of this module:

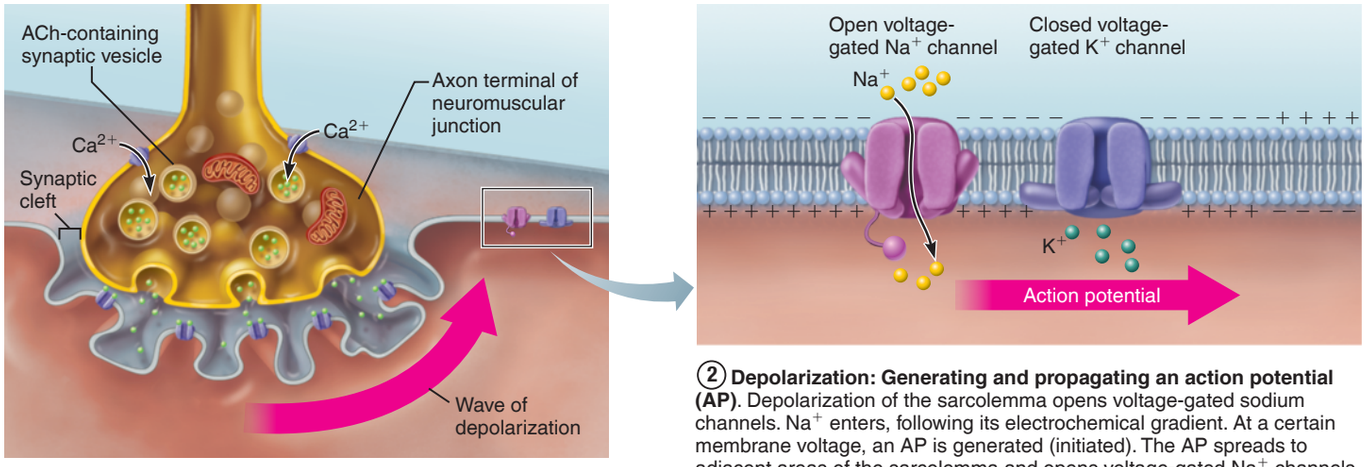
1. **Events at the neuromuscular junction** (see Focus Figure 9.1 on p. 292). The motor neuron releases ACh that stimulates the skeletal muscle fiber, causing a local depolarization (decrease in membrane potential) called an *end plate potential* (*EPP*).
2. **Muscle fiber excitation.** The EPP triggers an action potential that travels across the entire sarcolemma (see Figure 9.8 on p. 293).
3. **Excitation-contraction coupling** (see Focus Figure 9.2 on pp. 294–295). The AP in the sarcolemma propagates along the T tubules and causes release of Ca^{2+} from the terminal cisterns of the SR. Ca^{2+} is the final trigger for contraction. It is the internal messenger that links the AP to contraction. Ca^{2+} binds to troponin and this causes the myosin-binding sites on actin to be exposed so that myosin heads can bind to actin.
4. **Cross bridge cycling** (see Focus Figure 9.3 on p. 297). The muscle contracts as a result of a repeating cycle of steps that cause myofilaments to slide relative to each other.

FOCUS FIGURE 9.1 Events at the Neuromuscular Junction

When a nerve impulse reaches a neuromuscular junction, acetylcholine (ACh) is released. Upon binding to sarcolemma receptors, ACh causes a change in sarcolemma permeability leading to a change in membrane potential.

Watch a 3-D animation of this process: MasteringA&P® > Study Area > Animations & Videos > A&P Flix





① **An end plate potential (EPP) is generated at the neuromuscular junction (see Focus Figure 9.1).** The EPP causes a wave of depolarization that spreads to the adjacent sarcolemma.

② **Depolarization: Generating and propagating an action potential (AP).** Depolarization of the sarcolemma opens voltage-gated sodium channels. Na^+ enters, following its electrochemical gradient. At a certain membrane voltage, an AP is generated (initiated). The AP spreads to adjacent areas of the sarcolemma and opens voltage-gated Na^+ channels there, propagating the AP. The AP propagates along the sarcolemma in all directions, just like ripples from a pebble dropped in a pond.

③ **Repolarization: Restoring the sarcolemma to its initial polarized state (negative inside, positive outside).** The repolarization wave is also a consequence of opening and closing ion channels—voltage-gated Na^+ channels close and voltage-gated K^+ channels open. The potassium ion concentration is substantially higher inside the cell than in the extracellular fluid, so K^+ diffuses out of the muscle fiber. This restores the negatively charged conditions inside that are characteristic of a sarcolemma at rest.

Figure 9.8 Summary of events in the generation and propagation of an action potential in a skeletal muscle fiber.

Events at the Neuromuscular Junction

How does a motor neuron stimulate a skeletal muscle fiber? *Focus on Events at the Neuromuscular Junction* (**Focus Figure 9.1**) covers this process step by step. Study this figure before continuing.

The result of the events at the neuromuscular junction is a transient change in membrane potential that causes the interior of the sarcolemma to become less negative (a depolarization). This local depolarization is called an **end plate potential** (EPP). The EPP spreads to the adjacent sarcolemma and triggers an AP there.

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After ACh binds to the ACh receptors, its effects are quickly terminated by **acetylcholinesterase** (as″ĕ-til-ko″lin-es′ter-ās), an enzyme located in the synaptic cleft. Acetylcholinesterase breaks down ACh to its building blocks, acetic acid and choline. Removing ACh prevents continued muscle fiber contraction in the absence of additional nervous system stimulation.

HOMEOSTATIC IMBALANCE 9.2 — CLINICAL

Many toxins, drugs, and diseases interfere with events at the neuromuscular junction. For example, *myasthenia gravis* (*asthen* = weakness; *gravi* = heavy), a disease characterized by drooping upper eyelids, difficulty swallowing and talking, and generalized muscle weakness, involves a shortage of ACh receptors. Myasthenia gravis is an autoimmune disease in which the immune system destroys ACh receptors.

Generation of an Action Potential across the Sarcolemma

Now let's consider the electrical events that trigger an action potential along the sarcolemma. An action potential is the result of a predictable sequence of electrical changes. Once initiated, an action potential sweeps along the entire surface of the sarcolemma. Three steps are involved in triggering and then propagating an action potential. These three steps—generation of an end plate potential followed by action potential depolarization and repolarization—are shown in **Figure 9.8**. A tracing of the

(Text continues on p. 296.)

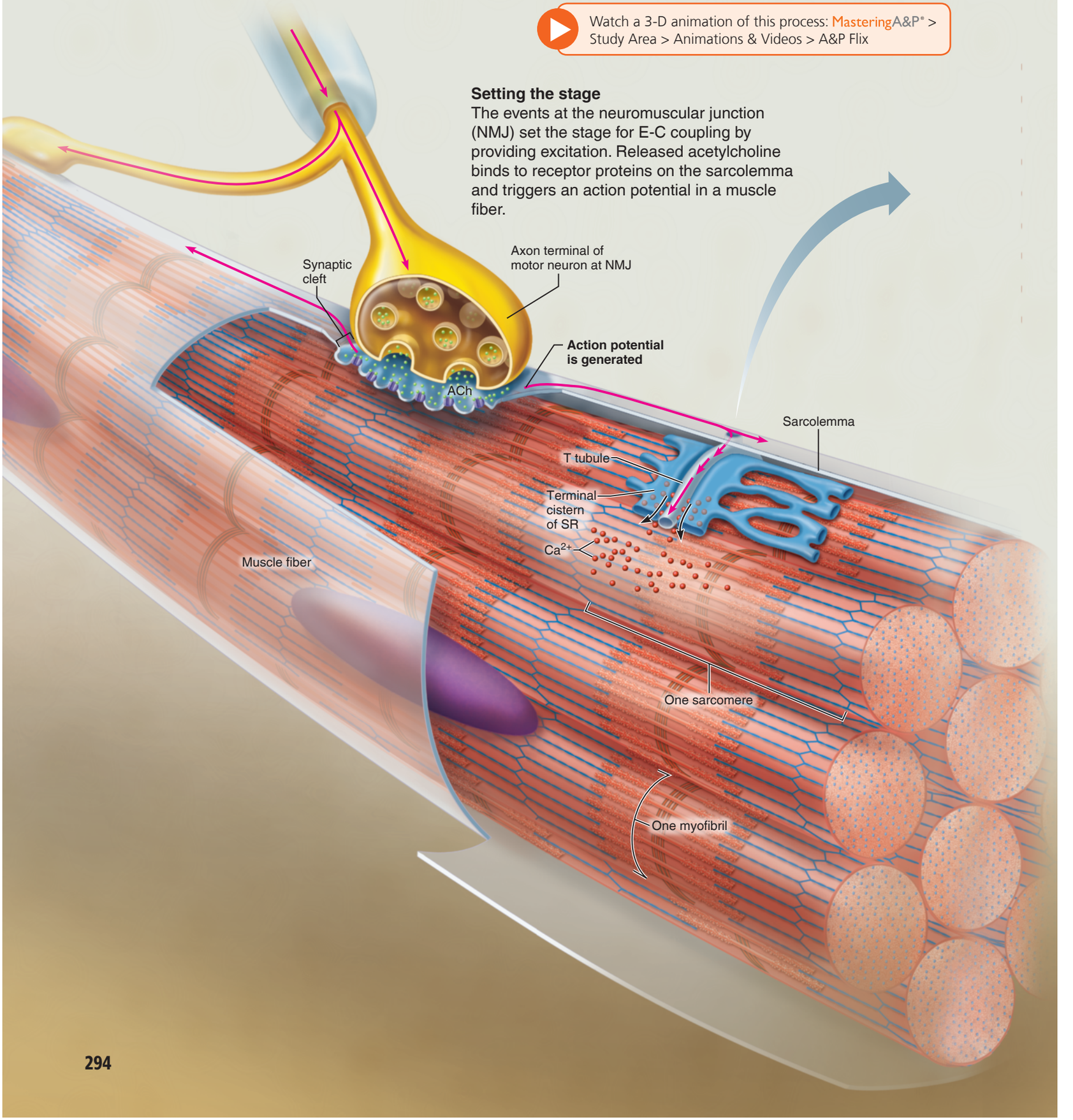
FOCUS FIGURE 9.2

Excitation-Contraction Coupling

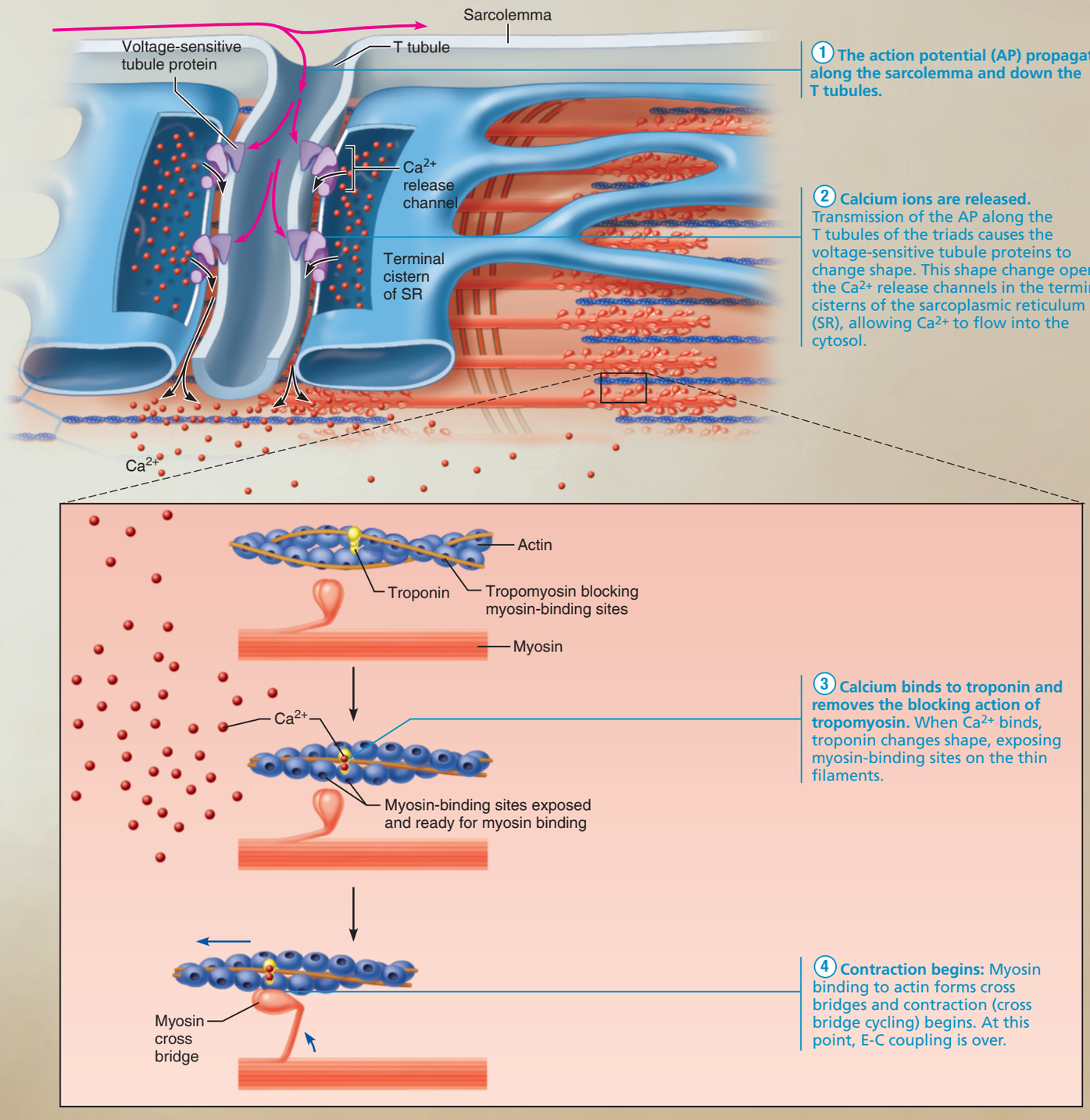
Excitation-contraction (E-C) coupling is the sequence of events by which transmission of an action potential along the sarcolemma leads to the sliding of myofilaments.

Watch a 3-D animation of this process: MasteringA&P® > Study Area > Animations & Videos > A&P Flix

Setting the stage
The events at the neuromuscular junction (NMJ) set the stage for E-C coupling by providing excitation. Released acetylcholine binds to receptor proteins on the sarcolemma and triggers an action potential in a muscle fiber.



Steps in E-C Coupling:



1 The action potential (AP) propagates along the sarcolemma and down the T tubules.

2 Calcium ions are released. Transmission of the AP along the T tubules of the triads causes the voltage-sensitive tubule proteins to change shape. This shape change opens the Ca^{2+} release channels in the terminal cisterns of the sarcoplasmic reticulum (SR), allowing Ca^{2+} to flow into the cytosol.

3 Calcium binds to troponin and removes the blocking action of tropomyosin. When Ca^{2+} binds, troponin changes shape, exposing myosin-binding sites on the thin filaments.

4 Contraction begins: Myosin binding to actin forms cross bridges and contraction (cross bridge cycling) begins. At this point, E-C coupling is over.

The aftermath

When the muscle AP ceases, the voltage-sensitive tubule proteins return to their original shape, closing the Ca^{2+} release channels of the SR. Ca^{2+} levels in the sarcoplasm fall as Ca^{2+} is continually pumped back into the SR by active transport. Without Ca^{2+}, the blocking action of tropomyosin is restored, myosin-actin interaction is inhibited, and relaxation occurs. Each time an AP arrives at the neuromuscular junction, the sequence of E-C coupling is repeated.

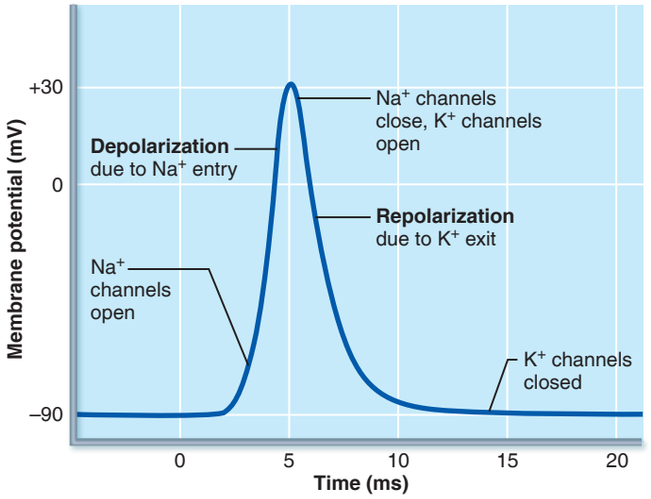


Figure 9.9 Recording of an action potential (AP) in a muscle fiber. An AP is a brief change in membrane potential.

resulting membrane potential changes is shown in **Figure 9.9**. We will describe action potentials in more detail in Chapter 11.

During repolarization, a muscle fiber is said to be in a **refractory period**, because the cell cannot be stimulated again until repolarization is complete. Note that repolarization restores only the *electrical conditions* of the resting (polarized) state. The ATP-dependent Na^+-K^+ pump restores the *ionic conditions* of the resting state, but thousands of action potentials can occur before ionic imbalances interfere with contractile activity.

Once initiated, the action potential is unstoppable. It ultimately results in contraction of the muscle fiber. Although the action potential itself lasts only a few milliseconds (ms), the contraction phase of a muscle fiber may persist for 100 ms or more and far outlasts the electrical event that triggers it.

Excitation-Contraction Coupling

Excitation-contraction (E-C) coupling is the sequence of events by which transmission of an action potential along the sarcolemma causes myofilaments to slide. The action potential is brief and ends well before any signs of contraction are obvious.

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As you will see, the electrical signal does not act directly on the myofilaments. Instead, it causes the rise in intracellular levels of calcium ions, which triggers a sequence of events that ultimately leads to sliding of the filaments.

Focus on Excitation-Contraction Coupling (**Focus Figure 9.2**) on pp. 294–295 illustrates the steps in this process. It also reveals how the integral proteins of the T tubules and terminal cisterns in the triads interact to provide the Ca^{2+} necessary for contraction to occur.

Muscle Fiber Contraction: Cross Bridge Cycling

As we have noted, cross bridge formation requires Ca^{2+}. Let's look more closely at how calcium ions promote muscle cell contraction.

When intracellular calcium levels are low, the muscle cell is relaxed because tropomyosin molecules physically block the myosin-binding sites on actin. As Ca^{2+} levels rise, the ions bind to regulatory sites on troponin. Two calcium ions must bind to a troponin, causing it to change shape and roll tropomyosin into the groove of the actin helix, away from the myosin-binding sites. In short, the tropomyosin blockade is removed when sufficient calcium is present. Once binding sites on actin are exposed, the events of the cross bridge cycle occur in rapid succession, as depicted in *Focus on the Cross Bridge Cycle* (**Focus Figure 9.3**). The cycle repeats and with each cycle, the myosin head takes another "step" by attaching to an actin site further along the thin filament. The thin filaments continue to slide as long as calcium and adequate ATP are present.

Watch a 3-D animation of this process: MasteringA&P® > Study Area > Animations & Videos > A&P Flix

Myosin walks along the adjacent thin filaments during muscle shortening like a centipede. The thin filaments cannot slide backward as the cycle repeats again and again because some myosin heads (the "legs") are always in contact with actin (the "ground"). Contracting muscles routinely shorten by 30–35% of their total resting length, so each myosin cross bridge attaches and detaches many times during a single contraction. It is likely that only half of the myosin heads of a thick filament are pulling at the same instant. The others are randomly seeking their next binding site.

As soon as Ca^{2+} is released from the SR, the Ca^{2+} pumps of the SR begin to reclaim it from the cytosol. As Ca^{2+} levels drop, Ca^{2+} comes off of troponin, which again changes shape and pulls tropomyosin up to block actin's myosin-binding sites. The contraction ends, and the muscle fiber relaxes. When cross bridge cycling ends, the myosin heads remain in their upright high-energy configuration (Focus Figure 9.3 (4)), ready to bind actin when the muscle is stimulated to contract again.

Except for the brief period following muscle cell excitation, calcium ion concentrations in the cytosol are kept almost undetectably low. When nerve impulses arrive in quick succession, intracellular Ca^{2+} levels soar due to successive "puffs" or bursts of Ca^{2+} released from the SR. In such cases, the muscle cells do not completely relax between successive stimuli and contraction is stronger and more sustained (within limits) until nervous stimulation ceases.

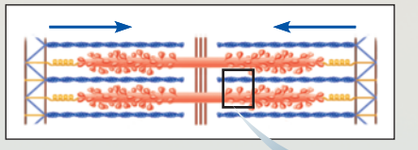
HOMEOSTATIC IMBALANCE 9.3 CLINICAL

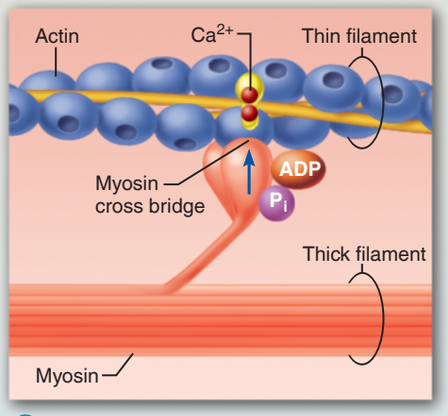
Rigor mortis (death rigor) illustrates the fact that cross bridge detachment is ATP driven. Most muscles begin to stiffen 3 to

FOCUS FIGURE 9.3 Cross Bridge Cycle

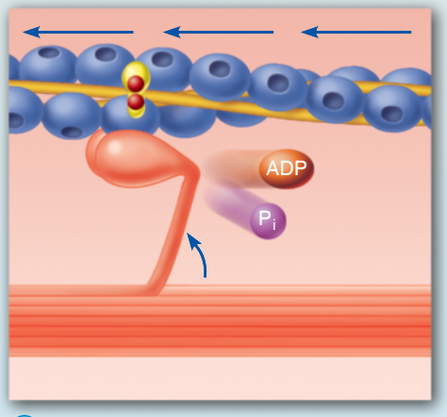
The cross bridge cycle is the series of events during which myosin heads pull thin filaments toward the center of the sarcomere.

Watch a 3-D animation of this process: MasteringA&P® > Study Area > Animations & Videos > A&P Flix

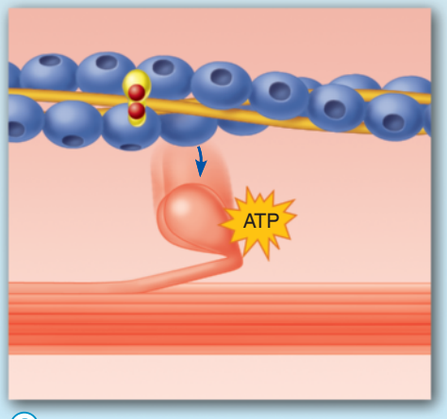




1 Cross bridge formation. Energized myosin head attaches to an actin myofilament, forming a cross bridge.



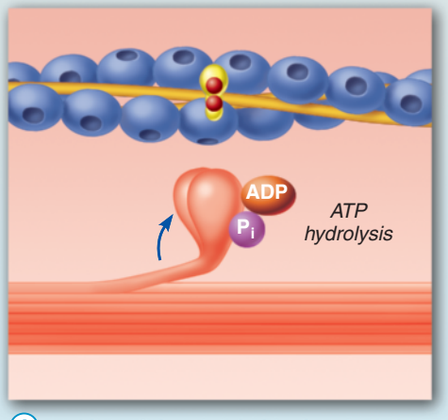
2 The power (working) stroke. ADP and P_i are released and the myosin head pivots and bends, changing to its bent low-energy state. As a result it pulls the actin filament toward the M line.



3 Cross bridge detachment. After ATP attaches to myosin, the link between myosin and actin weakens, and the myosin head detaches (the cross bridge "breaks").

In the absence of ATP, myosin heads will not detach, causing rigor mortis.

ATP



4 Cocking of the myosin head. As myosin hydrolyzes ATP to ADP and P_i, the myosin head returns to its prestroke high-energy, or "cocked," position.*

*This cycle will continue as long as ATP is available and Ca^{2+} is bound to troponin. If ATP is not available, the cycle stops between steps ② and ③.

4 hours after death. Peak rigidity occurs at 12 hours and then gradually dissipates over the next 48 to 60 hours. Dying cells are unable to exclude calcium (which is in higher concentration in the extracellular fluid), and the calcium influx into muscle cells promotes formation of myosin cross bridges. Shortly after breathing stops, ATP synthesis ceases, but ATP continues to be consumed and cross bridge detachment is impossible once all of the ATP is gone. Actin and myosin become irreversibly cross-linked, producing the stiffness of rigor mortis, which gradually disappears as muscle proteins break down after death.

Check Your Understanding

9. From the time an action potential reaches the axon terminal of a motor neuron until cross bridge cycling begins, several sets of ion channels are activated. List these channels in the order that they are activated and state what causes each to open.
10. What is the final trigger for contraction? What is the initial trigger?
11. What prevents the filaments from sliding back to their original position each time a myosin cross bridge detaches from actin?
12. WHAT IF? What would happen if a muscle fiber suddenly ran out of ATP when sarcomeres had only partially contracted?

For answers, see Answers Appendix.

9

9.5 Temporal summation and motor unit recruitment allow smooth, graded skeletal muscle contractions

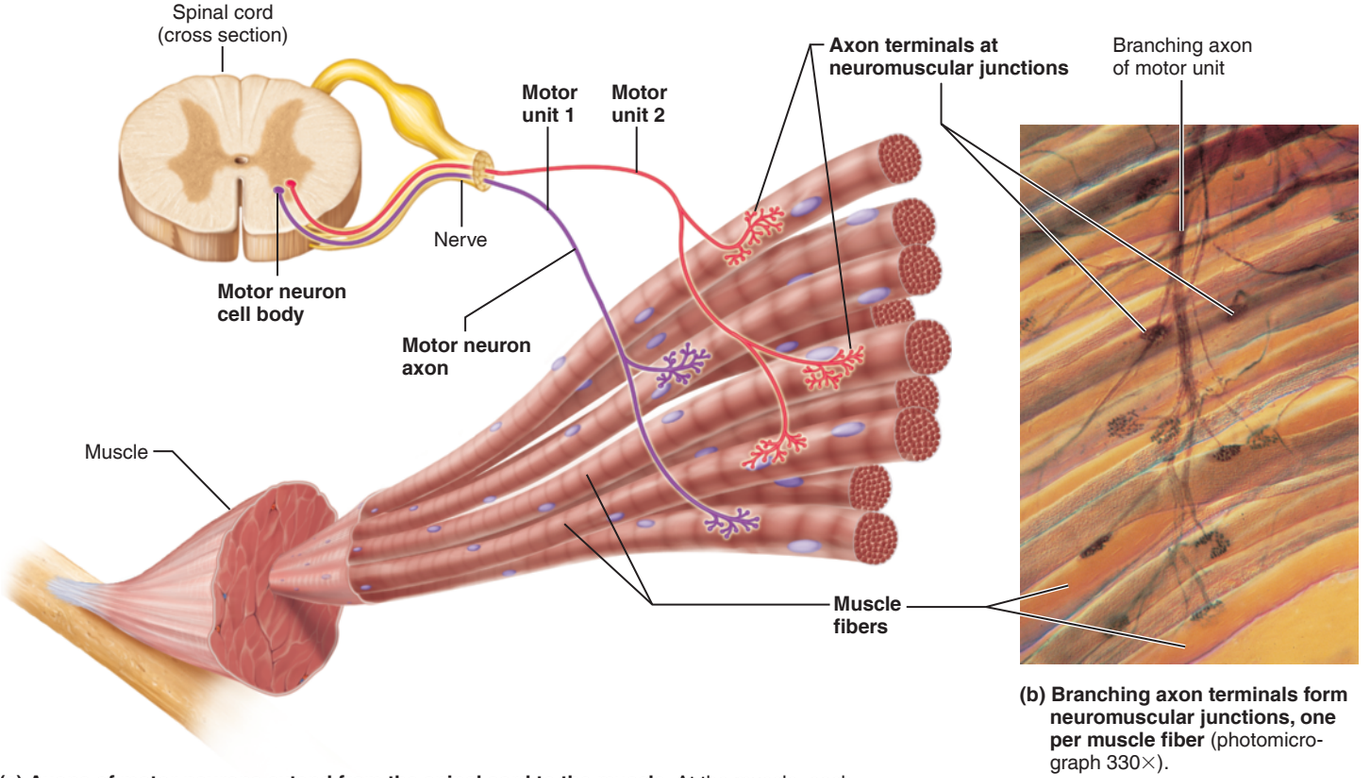
Learning Outcomes

- **Define motor unit and muscle twitch, and describe the events occurring during the three phases of a muscle twitch.**
- **Explain how smooth, graded contractions of a skeletal muscle are produced.**
- **Differentiate between isometric and isotonic contractions.**

In its relaxed state, a muscle is soft and unimpressive, not what you would expect of a prime mover of the body. However, within a few milliseconds, it can contract to become a hard elastic structure with dynamic characteristics that intrigue not only biologists but engineers and physicists as well.

Before we consider muscle contraction on the organ level, let's note two facts about muscle mechanics.

- The principles governing contraction of a single muscle fiber and of a skeletal muscle consisting of a large number of fibers are pretty much the same.



(a) Axons of motor neurons extend from the spinal cord to the muscle. At the muscle, each axon divides into a number of axon terminals that form neuromuscular junctions with muscle fibers scattered throughout the muscle.

(b) Branching axon terminals form neuromuscular junctions, one per muscle fiber (photomicrograph 330×).

Figure 9.10 A motor unit consists of one motor neuron and all the muscle fibers it innervates.

Practice Histology questions:
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- The force exerted by a contracting muscle on an object is called **muscle tension**. The opposing force exerted on the muscle by the weight of the object to be moved is called the **load**.

A skeletal muscle contracts with varying force and for different periods of time in response to our need at the time. To understand how this occurs, we must look at the nerve-muscle functional unit called a *motor unit*.

The Motor Unit

Each muscle is served by at least one *motor nerve*, and each motor nerve contains axons (fibrous extensions) of up to hundreds of motor neurons. As an axon enters a muscle, it branches into a number of endings, each of which forms a neuromuscular junction with a single muscle fiber. A **motor unit** consists of one motor neuron and all the muscle fibers it innervates, or supplies (**Figure 9.10**). When a motor neuron fires (transmits an action potential), all the muscle fibers it innervates contract.

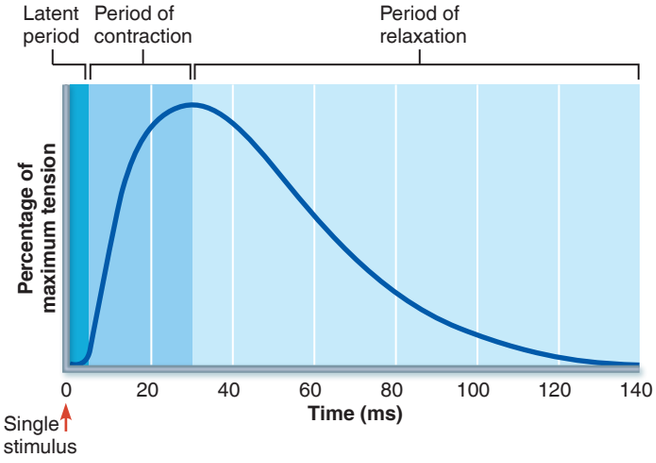
The number of muscle fibers per motor unit may be as high as several hundred or as few as four. Muscles that exert fine control (such as those controlling the fingers and eyes) have small motor units. By contrast, large, weight-bearing muscles, whose movements are less precise (such as the hip muscles), have large motor units. The muscle fibers in a single motor unit are not clustered together but are spread throughout the muscle. As a result, stimulation of a single motor unit causes a weak but uniform contraction of the muscle.

The Muscle Twitch

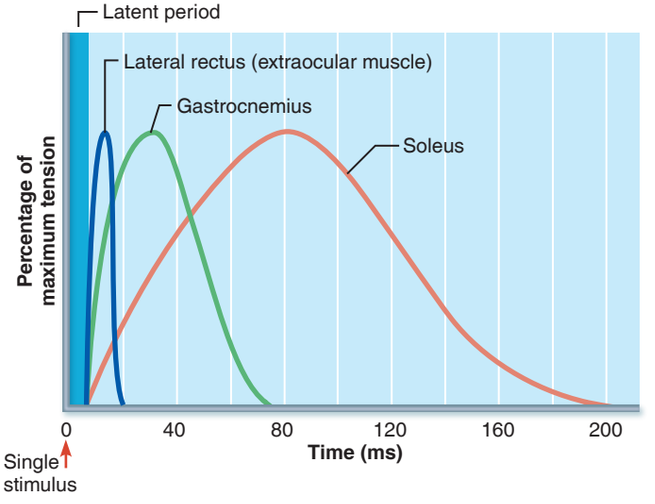
Muscle contraction is investigated in the laboratory using an isolated muscle. The muscle is attached to an apparatus that produces a **myogram**, a recording of contractile activity consisting of one or more recorded lines called *tracings*. Remember that muscles can contract without shortening (an *isometric contraction*, which we will discuss further on pp. 302–303). The myograms (graphs) in Figures 9.11–9.14 show the amount of *tension* a muscle develops when its length is held constant as it contracts.

In the laboratory, a **muscle twitch** is the response of a muscle to a single stimulation. The muscle fibers contract quickly and then relax. Every twitch myogram has three distinct phases (**Figure 9.11a**).

1. **Latent period.** The **latent period** is the first few milliseconds (ms) following stimulation when excitation-contraction coupling is occurring. During this period, cross bridges begin to cycle but muscle tension is not yet measurable so the myogram does not show a response.
2. **Period of contraction.** During the period of contraction, cross bridges are active, from the onset to the peak of tension development, and the myogram tracing rises to a peak. This period lasts 10–100 ms.
3. **Period of relaxation.** This final phase, lasting 10–100 ms, is due to pumping of Ca^{2+} back into the SR. Because the number of active cross bridges is declining, contractile force is declining. Muscle tension decreases to zero and the tracing returns to the baseline. Notice that a muscle contracts faster than it relaxes, as shown by the asymmetric shape of the curve in Figure 9.11a.



(a) Myogram showing the three phases of an isometric twitch



(b) Comparison of the relative duration of twitch responses of three muscles

Figure 9.11 The muscle twitch.

As you can see in Figure 9.11b, twitch contractions of some muscles are rapid and brief, as with the extraocular muscles controlling eye movements. In contrast, the fibers of fleshy calf muscles (gastrocnemius and soleus) contract more slowly and remain contracted for much longer periods. These differences between muscles reflect variations in enzymes and metabolic properties of the myofibrils.

Graded Muscle Contractions

Muscle twitches—like those single, jerky contractions provoked in a laboratory—may result from certain neuromuscular problems, but this is *not* the way our muscles normally operate. Instead, healthy muscle contractions are relatively smooth and

vary in strength as different demands are placed on them. These variations, needed for proper control of skeletal movement, are referred to as **graded muscle contractions**.

In general, muscle contraction can be graded in two ways:

- An increase in the *frequency* of stimulation causes *temporal summation*. The higher the frequency, the greater the strength of contraction of a given motor unit.
- An increase in the *strength* of stimulation causes *recruitment*. The stronger the stimulation, the more motor units are activated, and the stronger the contraction.

In the laboratory, it is easy to adjust the settings used to artificially stimulate a muscle. In the body, the brain determines the strength of a muscle's contraction by changing (1) the rate of firing of action potentials along the axon of its motor neuron (frequency) and (2) the number of its motor neurons that are activated (strength). In this way, we automatically and continuously adjust the strength of our muscle contractions. We are only aware of this process when it doesn't work right. For example, if you lift what you expect to be a heavy box that is in fact empty, you will use more muscle power than you should and the box will go flying!

9

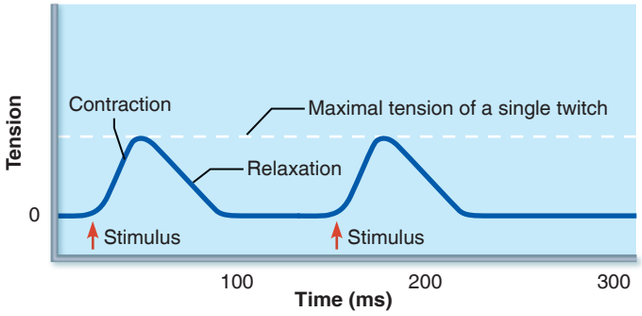
Muscle Response to Changes in Stimulus Frequency

The nervous system can achieve greater muscular force by increasing the firing rate of motor neurons. For example, if two identical stimuli (electrical shocks or nerve impulses) are delivered to a muscle in rapid succession, the second twitch will be stronger than the first. On a myogram the second twitch will appear to ride on the shoulders of the first (**Figure 9.12a**, **b**).

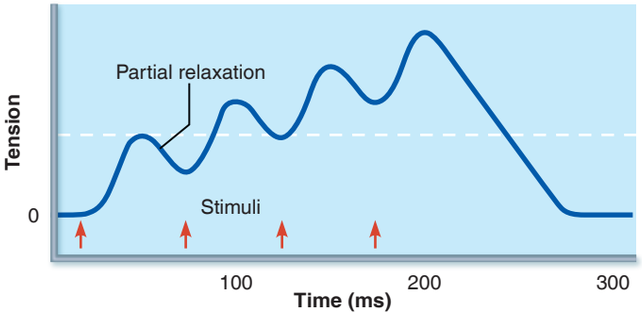
This phenomenon is called **temporal**, or **wave**, **summation**. It occurs because the second contraction begins before the muscle has completely relaxed. The second contraction is greater than the first because the muscle is already partially contracted and because even more calcium is squirted into the cytosol. In other words, the contractions are added together. (However, the refractory period is always honored. So if a second stimulus arrives before repolarization is complete, no wave summation occurs.)

If the muscle is stimulated at an increasingly faster rate:

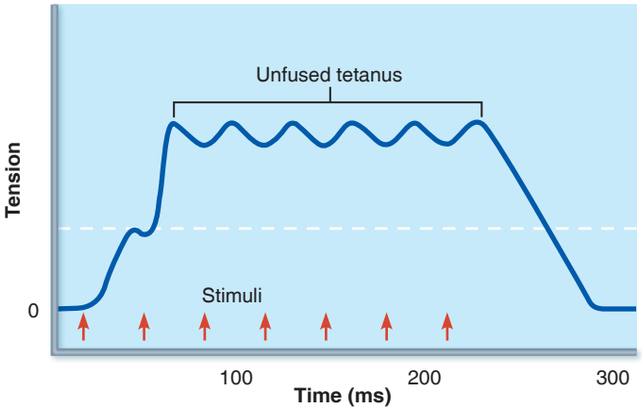
- The relaxation time between twitches becomes shorter and shorter.
- The concentration of Ca^{2+} in the cytosol rises higher and higher.
- The degree of wave summation becomes greater and greater, progressing to a sustained but quivering contraction referred



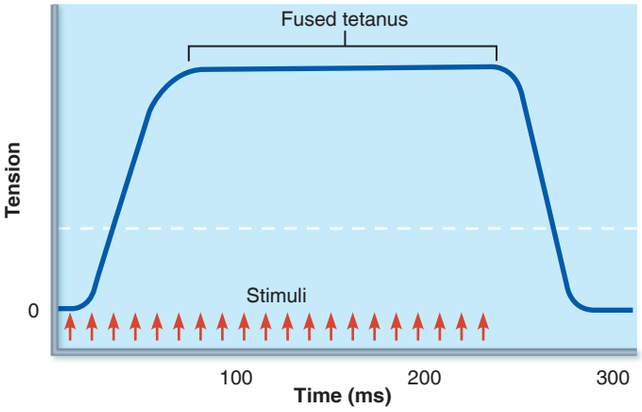
(a) Individual twitches. A second stimulus delivered after relaxation is complete does not produce summation.



(b) Temporal summation. Additional stimuli delivered before relaxation is complete produce temporal (wave) summation.



(c) Unfused tetanus. Higher stimulation frequency results in unfused tetanus.



(d) Fused tetanus. At even higher stimulus frequencies, there is no relaxation at all between stimuli. This is fused (complete) tetanus.

Figure 9.12 Temporal summation. A muscle's response to changes in stimulation frequency.

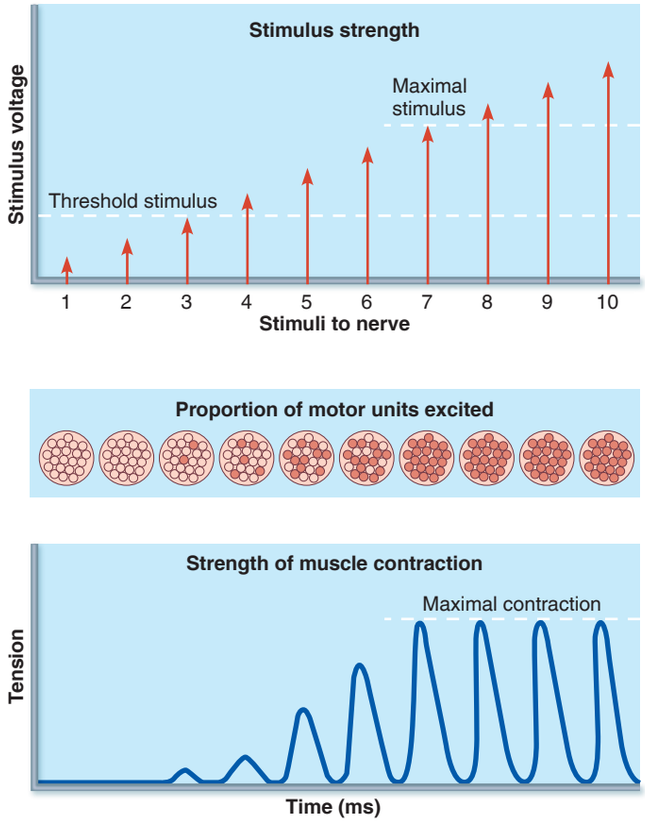


Figure 9.13 Recruitment. Relationship between stimulus intensity (graph at top) and muscle tension (myogram below). Below threshold voltage, the myogram shows no muscle response (stimuli 1 and 2). Once threshold (3) is reached, increases in voltage excite (recruit) more and more motor units until the maximal stimulus is reached (7). Further increases in stimulus voltage produce no further increase in contractile strength.

to as **unfused** or **incomplete tetanus*** (tet′ah-nus; *tetan* = rigid, tense) (Figure 9.12c).

- Finally, as the stimulation frequency continues to increase, muscle tension increases until it reaches maximal tension. At this point all evidence of muscle relaxation disappears and the contractions fuse into a smooth, sustained contraction plateau called **fused** or **complete tetanus** (Figure 9.12d). In the real world, physiological mechanisms prevent fused tetanus, so it rarely if ever occurs.

Temporal summation contributes to contractile force, but its primary function is to produce smooth, continuous muscle contractions by rapidly stimulating a specific number of muscle cells.

Muscle Response to Changes in Stimulus Strength

Recruitment, also called **multiple motor unit summation**, controls the force of contraction more precisely. In the laboratory, recruitment is achieved by delivering stimuli of increasing voltage, calling more and more muscle fibers into play.

- Stimuli that produce no observable contractions are **subthreshold stimuli**.
- The stimulus at which the first observable contraction occurs is called the **threshold stimulus** (**Figure 9.13**). Beyond this point, the muscle contracts more vigorously as the stimulus strength increases.
- The **maximal stimulus** is the strongest stimulus that increases contractile force. It represents the point at which all the muscle's motor units are recruited. In the laboratory, increasing the stimulus intensity beyond the maximal stimulus does not produce a stronger contraction.

The recruitment process is not random. Instead it is dictated by the *size principle* (**Figure 9.14**). In any muscle:

- The motor units with the smallest muscle fibers are activated first because they are controlled by the smallest, most highly excitable motor neurons.
- As motor units with larger and larger muscle fibers begin to be excited, contractile strength increases.
- The largest motor units, containing large, coarse muscle fibers, are controlled by the largest, least excitable (highest-threshold) neurons and are activated only when the most powerful contraction is necessary.

Why is the size principle important? It allows the increases in force during weak contractions (for example, those that maintain posture or slow movements) to occur in small steps, whereas gradations in muscle force are progressively greater when large amounts of force are needed for vigorous activities such as jumping or running. The size principle explains how the same hand that lightly pats your cheek can deliver a stinging slap at the volleyball during a match.

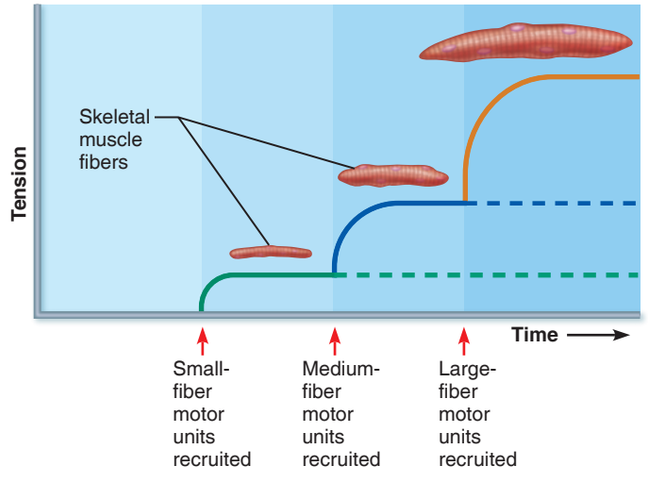


Figure 9.14 The size principle of recruitment. Motor units with the smallest fibers are recruited first, allowing fine control of contraction.

* The term *tetanus* also describes a bacterial disease (see Related Clinical Terms at the end of the chapter).

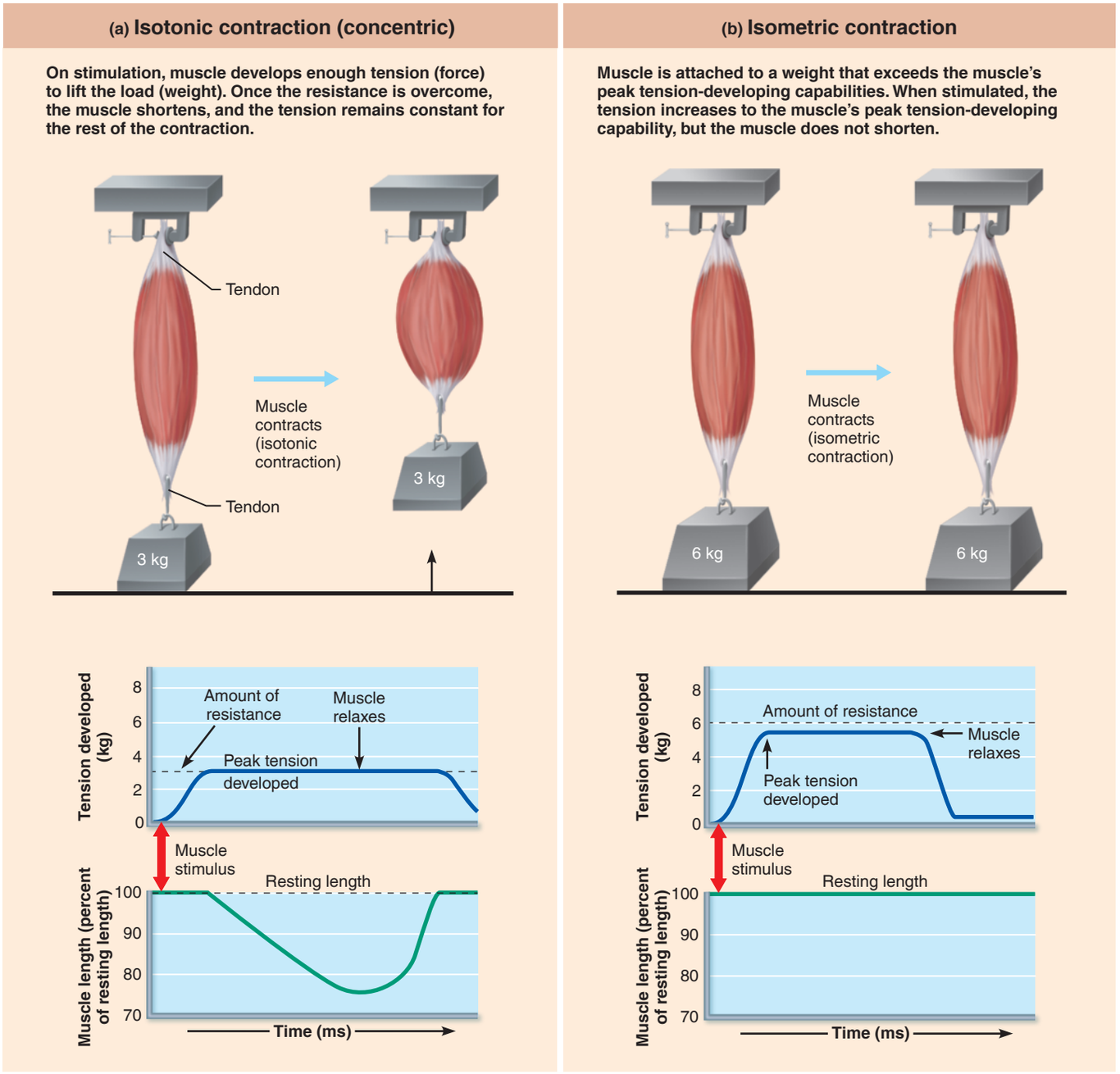


Figure 9.15 **Isotonic (concentric) and isometric contractions.**

Although *all* the motor units of a muscle may be recruited simultaneously to produce an exceptionally strong contraction, motor units are more commonly activated asynchronously. At a given instant, some are contracting while others are resting and recovering. This technique helps prolong a strong contraction by preventing or delaying fatigue. It also explains how weak contractions promoted by infrequent stimuli can remain smooth.

Muscle Tone

Skeletal muscles are described as voluntary, but even relaxed muscles are almost always slightly contracted, a phenomenon

called **muscle tone**. Muscle tone is due to spinal reflexes that activate first one group of motor units and then another in response to activated stretch receptors in the muscles. Muscle tone does not produce active movements, but it keeps the muscles firm, healthy, and ready to respond to stimulation. Skeletal muscle tone also helps stabilize joints and maintain posture.

Isotonic and Isometric Contractions

There are two main categories of contractions—*isotonic* and *isometric*, depending on whether a muscle changes length or not. Muscles change length in isotonic, but not isometric, contractions. When studying isotonic contractions in a laboratory, the *amount of muscle shortening* is measured as shown in the bottom part of **Figure 9.15a**. More commonly, isometric contractions are studied, and what is measured is *increasing muscle tension* (Figure 9.15b, top graph).

Isotonic Contractions

If the muscle tension developed overcomes the load and muscle shortening occurs, the contraction is an **isotonic contraction** (*iso* = same; *ton* = tension), as when you lift a 5-lb bag of sugar. Once sufficient tension has developed to move the load, the tension remains relatively constant through the rest of the contractile period (Figure 9.15a).

Isotonic contractions come in two "flavors"—*concentric* and *eccentric*. **Concentric contractions** are those in which the muscle shortens and does work, such as picking up a book or kicking a ball. Concentric contractions are probably more familiar, but **eccentric contractions**, in which the muscle generates force as it lengthens, are equally important for coordination and purposeful movements.

Eccentric contractions occur in your anterior thigh muscles, for example, as you walk down a steep hill. Eccentric contractions are about 50% more forceful than concentric ones at the same load and more often cause delayed-onset muscle soreness. (Consider how your thigh muscles *feel* the day after hiking that hill.) The muscle stretching that occurs during eccentric contractions causes microtrauma in the muscles that results in soreness.

Biceps curls provide a simple example of how concentric and eccentric contractions work together in our everyday activities. When you flex your elbow to draw a weight toward your shoulder, the biceps muscle in your arm is contracting concentrically. When you straighten your arm to return the weight to the bench, the isotonic contraction of your biceps is eccentric. Basically, eccentric contractions put the body in position to contract concentrically. All jumping and throwing activities involve both types of contraction.

Isometric Contractions

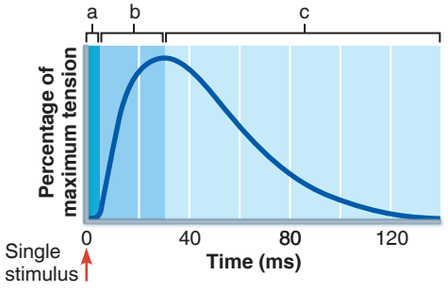
A contracting muscle does not always shorten and move a load. If muscle tension develops but the load is not moved, the contraction is an **isometric contraction** (*metric* = measure). In isometric contractions, tension may build to the muscle's peak tension-producing capacity, but the muscle *neither shortens nor lengthens* (Figure 9.15b) because the load is greater than the force (tension) the muscle is able to develop—think of trying to lift a piano single-handedly. Muscles contract isometrically when they act primarily to maintain upright posture or to hold joints stationary while movements occur at other joints.

Electrochemical and mechanical events occurring within a muscle are identical in both isotonic and isometric contractions. However, the results are different. In isotonic contractions, the thin filaments slide. In isometric contractions, the cross bridges generate force but do *not* move the thin filaments, so there is no change in the banding pattern from that of the resting state. (You could say that they are "spinning their wheels" on the same actin binding sites.)

Check Your Understanding

13. What is a motor unit?

14. Identify each phase of the muscle twitch labeled a–c in the figure below. What is happening in the muscle during phase a?



15. APPLY Jacob is competing in a chin-up competition. What type of muscle contractions are occurring in his biceps muscles immediately after he grabs the bar? As his body begins to move upward toward the bar? When his body begins to approach the mat?

For answers, see Answers Appendix.

9.6 ATP for muscle contraction is produced aerobically or anaerobically

Learning Outcomes

- **Describe three ways in which ATP is regenerated during skeletal muscle contraction.**
- **Define EPOC and muscle fatigue. List possible causes of muscle fatigue.**

Providing Energy for Contraction

As a muscle contracts, ATP supplies the energy to move and detach cross bridges, operate the calcium pump in the SR, and operate the Na^+-K^+ pump in the plasma membrane. Surprisingly, muscles store very limited reserves of ATP—4 to 6 seconds' worth at most, just enough to get you going. Because ATP is the *only* energy source used directly for contractile activities, it must be regenerated as fast as it is broken down if contraction is to continue.

Fortunately, after ATP is hydrolyzed to ADP and inorganic phosphate in muscle fibers, it is regenerated within a fraction of a second by one or more of the three pathways summarized in **Figure 9.16**: (a) direct phosphorylation of ADP by creatine phosphate, (b) anaerobic glycolysis, which converts glucose to lactic acid, and (c) aerobic respiration. All body cells use glycolysis and aerobic respiration to produce ATP, so we touch on them here but describe them in detail later, in Chapter 24.

Direct Phosphorylation of ADP by Creatine Phosphate (Figure 9.16a)

As we begin to exercise vigorously, the demand for ATP soars and the ATP stored in working muscles is consumed within a few twitches. Then **creatine phosphate (CP)** (kre′ah-tin), a unique high-energy molecule stored in muscles, is tapped to regenerate ATP while other metabolic pathways adjust to the sudden high demand for ATP.

Coupling CP with ADP transfers energy and a phosphate group from CP to ADP to form ATP almost instantly:

$$\text{Creatine phosphate} + \text{ADP} \xrightarrow{\text{creatine kinase}} \text{creatine} + \text{ATP}$$

Muscle cells store two to three times more CP than ATP. The CP reaction with ADP, catalyzed by the enzyme **creatine kinase**, is so efficient that the amount of ATP in muscle cells changes very little during the initial period of contraction.

Together, stored ATP and CP provide for maximum muscle power for about 15 seconds—long enough to energize a 100-meter dash (slightly longer if the activity is less vigorous). The coupled reaction is readily reversible, and to keep CP available, CP reserves are replenished during periods of rest or inactivity.

Anaerobic Pathway: Glycolysis and Lactic Acid Formation (Figure 9.16b)

As stored ATP and CP are exhausted, more ATP is generated by breaking down (catabolizing) glucose obtained from the blood or glycogen stored in the muscle. The initial phase of glucose breakdown is **glycolysis** (gli-kol′ĭ-sis; "sugar splitting"). This pathway occurs in both the presence and the absence of oxygen, but because it does not use oxygen, it is an anaerobic (an-a′er-ōb-ik; "without oxygen") pathway. During glycolysis, glucose is broken down to two *pyruvic acid* molecules, releasing enough energy to form small amounts of ATP (2 ATP per glucose).

When sufficient oxygen is present, the pyruvic acid produced during glycolysis enters the mitochondria, producing still more ATP in the oxygen-using pathway called aerobic respiration, described shortly. When blood flow and oxygen delivery are impaired during vigorous muscle contraction, most of the pyruvic acid is converted into **lactic acid**, and the overall process is referred to as **anaerobic glycolysis**. Oxygen delivery is impaired because bulging muscles compress the blood vessels within them. This happens when contractile activity reaches

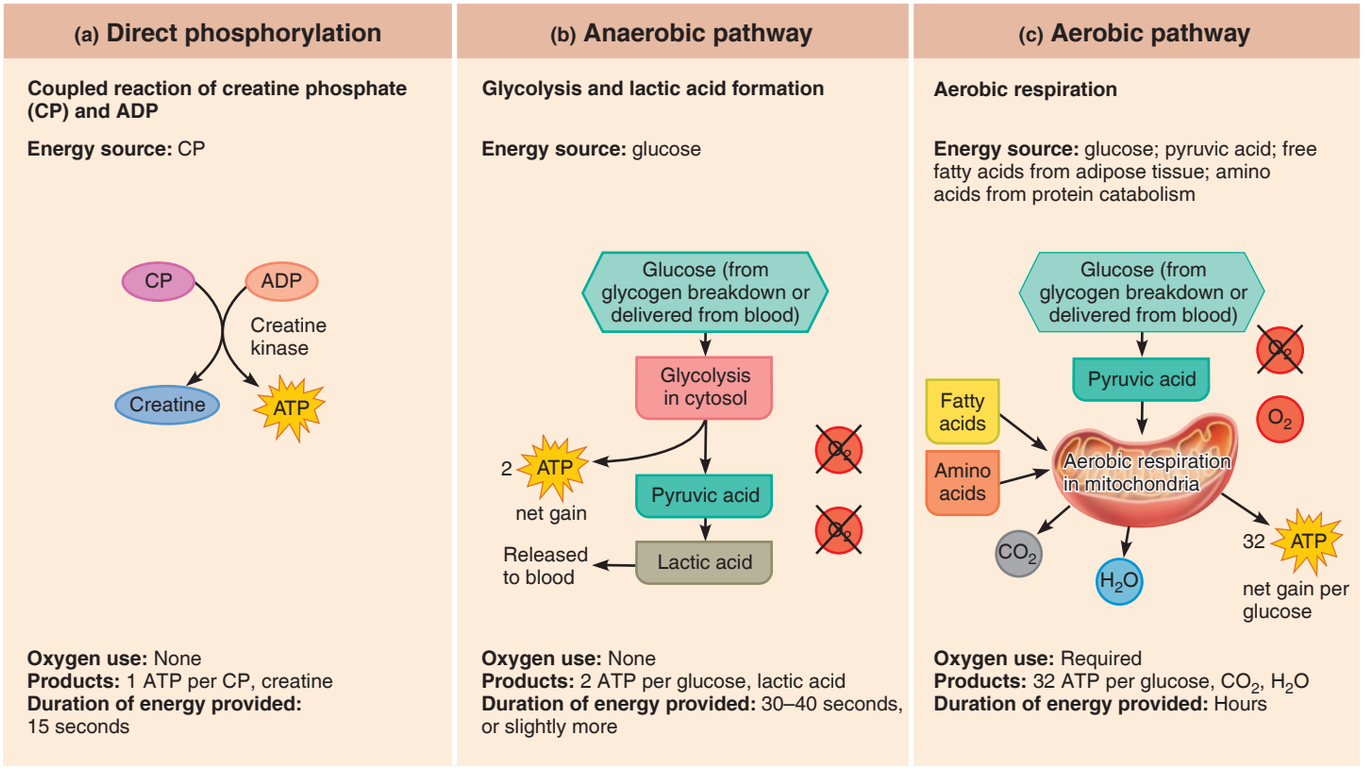


Figure 9.16 Pathways for regenerating ATP during muscle activity. The fastest pathway is direct phosphorylation **(a)**, and the slowest is aerobic respiration **(c)**.

about 70% of the maximum possible (for example, when you run 600 meters with maximal effort).

Lactic acid is the end product of glucose metabolism during anaerobic glycolysis. Most of the lactic acid diffuses out of the muscles into the bloodstream. Subsequently, the liver, heart, or kidney cells pick up the lactic acid and use it as an energy source. Additionally, liver cells can reconvert it to pyruvic acid or glucose and release it back into the bloodstream for muscle use or convert it to glycogen for storage.

The anaerobic pathway is inefficient but fast. It harvests only about 5% as much ATP from each glucose molecule as the aerobic pathway, but it produces ATP about 2½ times faster. For this reason, even when large amounts of ATP are needed for moderate periods (30–40 seconds) of strenuous muscle activity, glycolysis can provide most of this ATP. Together, stored ATP and CP and the glycolysis–lactic acid pathway can support strenuous muscle activity for nearly a minute.

Although anaerobic glycolysis readily fuels spurts of vigorous exercise, it has shortcomings. Huge amounts of glucose are used to produce relatively small harvests of ATP, and the accumulating lactic acid is partially responsible for muscle soreness during intense exercise.

Aerobic Respiration (Figure 9.16c)

During rest and light to moderate exercise, even if prolonged, 95% of the ATP used for muscle activity comes from **aerobic respiration**. Aerobic respiration requires oxygen and mitochondria, and involves a sequence of chemical reactions that break the bonds of fuel molecules and release energy to make ATP.

Aerobic respiration begins with glycolysis and is followed by reactions that take place in the mitochondria. It breaks down glucose entirely to water and carbon dioxide, and generates large amounts of ATP.

$$\text{Glucose} + \text{oxygen} \rightarrow \text{carbon dioxide} + \text{water} + \text{ATP}$$

The carbon dioxide released diffuses out of the muscle tissue into the blood, to be removed from the body by the lungs.

As exercise begins, muscle glycogen provides most of the fuel. Shortly thereafter, bloodborne glucose, pyruvic acid from glycolysis, and free fatty acids are the major sources of fuels. After about 30 minutes, fatty acids become the major energy fuels. Aerobic respiration provides a high yield of ATP (about 32 ATP per glucose), but it is slow because of its many steps and it requires continuous delivery of oxygen and nutrient fuels to keep it going.

Energy Systems Used during Exercise

Which pathways predominate during exercise? As long as a muscle cell has enough oxygen, it will form ATP by the aerobic pathway. When ATP demands are within the capacity of the aerobic pathway, light to moderate muscular activity can continue for several hours in well-conditioned individuals (**Figure 9.17**). However, when exercise demands begin to exceed the ability of the muscle cells to carry out the necessary reactions quickly enough, anaerobic pathways begin to contribute more and more of the total ATP generated. The length of time a muscle can continue to contract using aerobic pathways is called **aerobic endurance**, and the point at which muscle metabolism converts to anaerobic glycolysis is called **anaerobic threshold**.

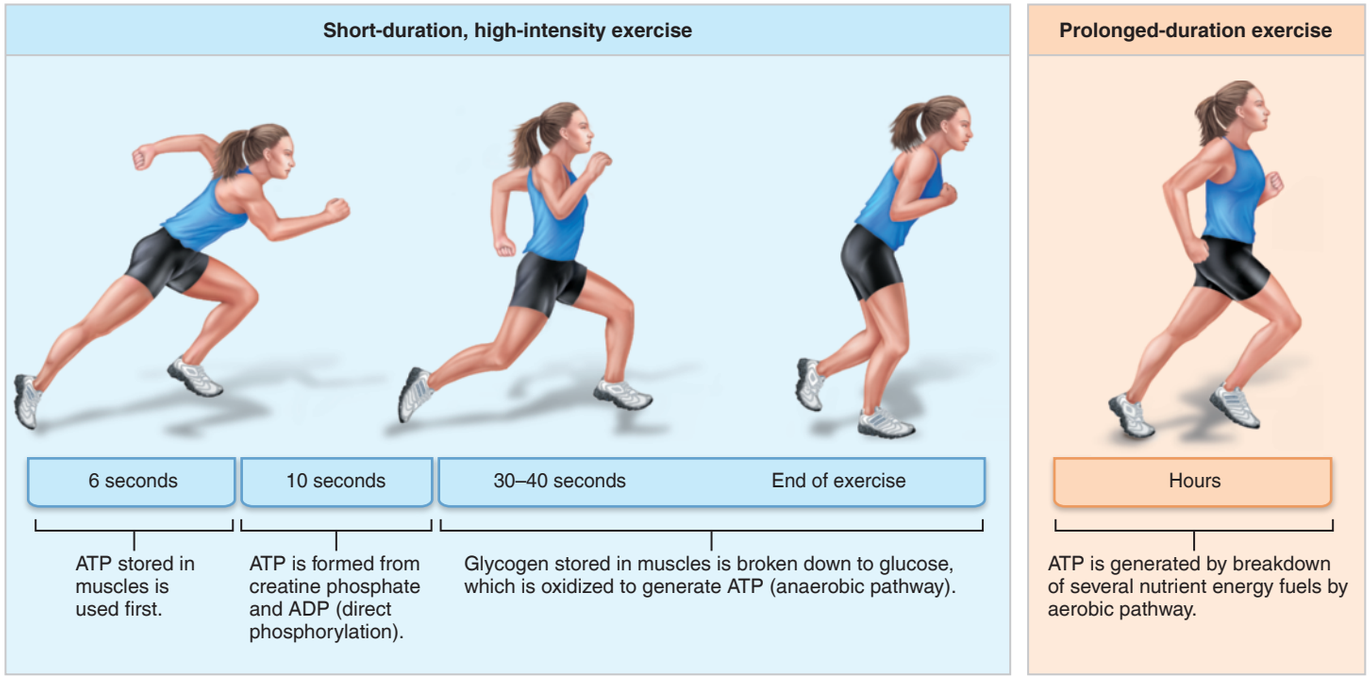


Figure 9.17 Comparison of energy sources used during short-duration exercise and prolonged-duration exercise.

Activities that require a surge of power but last only a few seconds, such as weight lifting, diving, and sprinting, rely entirely on ATP and CP stores. The slightly longer bursts of activity in tennis, soccer, and a 100-meter swim appear to be fueled almost entirely by anaerobic glycolysis (Figure 9.17). Prolonged activities such as marathon runs and bicycle touring, where endurance rather than power is the goal, depend mainly on aerobic respiration using both glucose and fatty acids as fuels. Levels of CP and ATP don't change much during prolonged exercise because ATP is generated at the same rate as it is used—a "pay as you go" system. Compared to anaerobic energy production, aerobic generation of ATP is relatively slow, but the ATP harvest is enormous.

Muscle Fatigue

Vigorous muscle activity cannot continue indefinitely. **Muscle fatigue** is a state of *physiological inability to contract* even though the muscle is still receiving stimuli. You might think that running out of ATP is the critical event that causes muscle fatigue. In fact, ATP levels inside muscle cells do drop, but muscle fatigue serves to prevent *complete* depletion of ATP in muscle, which would result in death of muscle cells and rigor mortis. (Not good!) The mechanism of muscle fatigue is complex. Although it is not fully understood, it involves alterations in excitation-contraction coupling. The following chemical changes may be involved:

- *Ionic imbalances.* Several ionic imbalances contribute to muscle fatigue. As action potentials are transmitted, potassium is lost from the muscle cells to the fluids of the T tubules and Na^+ is gained. These ionic changes disturb the membrane potential of the muscle cells. They also reduce the size of the action potential, which reduces the movement of the voltage-sensitive proteins in the T tubules and so reduces the amount of Ca^{2+} released from the SR.
- *Increased inorganic phosphate (P_i).* P_i from CP and ATP breakdown may interfere with calcium release from the SR. It may also interfere with the release of P_i from myosin and thus hamper myosin's power strokes.
- *Decreased ATP and increased magnesium (Mg^{2+}).* ATP normally binds Mg^{2+} in the cell, so as ATP levels drop, Mg^{2+} levels rise. Both low ATP and high Mg^{2+} act on the voltage-sensitive proteins in the T tubule to decrease Ca^{2+} release from the SR.
- *Decreased glycogen.* A decrease in glycogen is highly correlated with muscle fatigue.

Lactic acid has long been assumed to be a major cause of fatigue, and excessive intracellular accumulation of lactic acid raises the concentration of H^+ and alters contractile proteins. Although lactic acid and pH both contribute to the sensation of pain during intense exercise, neither seem to be directly involved in muscle fatigue.

In general, intense exercise of short duration produces fatigue rapidly, but recovery is also rapid. In contrast, the slow-developing fatigue of prolonged low-intensity exercise may require hours to days for complete recovery.

Excess Postexercise Oxygen Consumption (EPOC)

Whether or not fatigue occurs, vigorous exercise alters a muscle's chemistry dramatically. For a muscle to return to its pre-exercise state, the following must occur:

- Its oxygen reserves (stored in myoglobin) must be replenished.
- The accumulated lactic acid must be reconverted to pyruvic acid.
- Glycogen stores must be replaced.
- ATP and creatine phosphate reserves must be resynthesized.

The use of these muscle stores during anaerobic exercise simply defers when the oxygen is consumed, because replacing them requires oxygen uptake and aerobic metabolism after exercise ends. Additionally, the liver must convert any lactic acid persisting in blood to glucose or glycogen. Once exercise stops, the repayment process begins.

The extra amount of oxygen that the body must take in for these restorative processes is called the **excess postexercise oxygen consumption (EPOC)**, formerly called the oxygen debt. EPOC represents the difference between the amount of oxygen needed for totally aerobic muscle activity and the amount actually used. All anaerobic sources of ATP used during muscle activity contribute to EPOC.

Check Your Understanding

16. Chris joined the cross-country team partway through the season, and has just completed another grueling session of trying to keep up with her teammates. After the run, she is breathing heavily, her legs feel weak, and she is sweating profusely. Why is Chris breathing heavily? Which ATP-generating pathway have her working muscles been using that makes her breathless? What metabolic products might account for her muscle weakness?

For answers, see Answers Appendix.

9.7 The force, velocity, and duration of skeletal muscle contractions are determined by a variety of factors

Learning Outcomes

- **Describe factors that influence the force, velocity, and duration of skeletal muscle contraction.**
- **Describe three types of skeletal muscle fibers and explain the relative value of each type.**

Force of Muscle Contraction

The force of muscle contraction depends on the number of myosin cross bridges that are attached to actin. This in turn is affected by four factors (**Figure 9.18**), the first two of which we have already discussed:

- **Frequency of stimulation.** When a muscle is stimulated more frequently, contractions are summed (temporal summation and

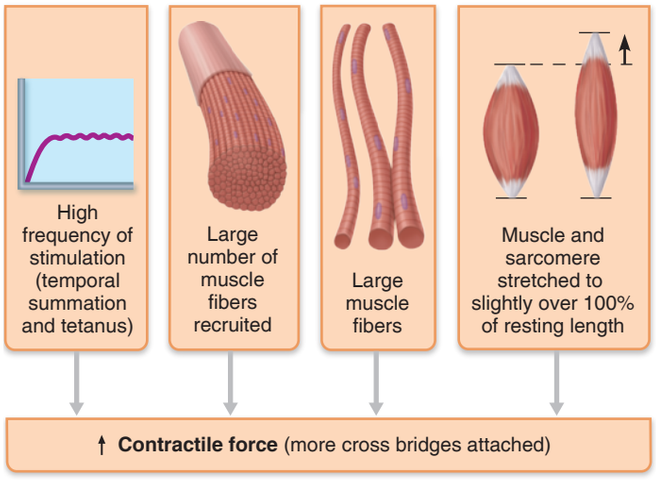


Figure 9.18 Factors that increase the force of skeletal muscle contraction.

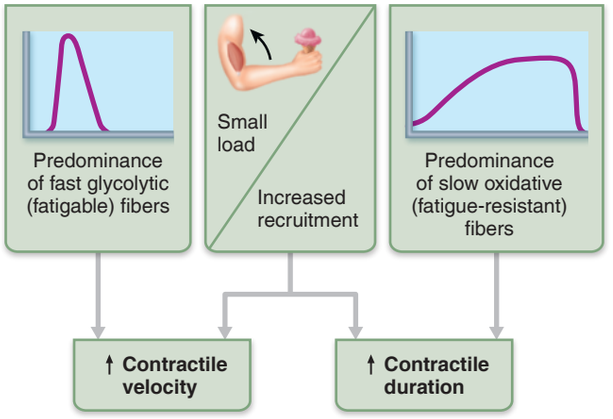


Figure 9.20 Factors influencing velocity and duration of skeletal muscle contraction.

tetany, see Figure 9.12 on p. 300). The higher the frequency of muscle stimulation, the greater the force the muscle exerts.

- **Number of muscle fibers recruited.** The more motor units recruited, the greater the force (Figure 9.13 on p. 301).
- **Size of muscle fibers.** The bulkier the muscle and the greater the cross-sectional area, the more tension it can develop. The large fibers of large motor units produce the most powerful movements. Regular resistance exercise increases muscle force by causing muscle cells to *hypertrophy* (increase in size).
- **Degree of muscle stretch.** If a muscle is stretched to various lengths and maximally stimulated, the tension the muscle can generate varies with length. The amount of tension a muscle can generate during an isometric contraction at various lengths—its **length-tension relationship**—can be shown graphically as in **Figure 9.19**. The ideal length on this curve occurs when the muscle is close to its resting length and the thin and thick filaments overlap optimally, because this permits sliding along nearly the entire length of the thin filaments. If a muscle is stretched so much that the filaments do not overlap, the myosin heads have nothing to attach to and cannot generate tension. On the other hand, if the sarcomeres are so compressed that the thin filaments interfere with one another, little or no further shortening can occur. In the body, skeletal muscles are maintained near their optimal length at rest. Our joints normally prevent bone movements that would stretch attached muscles beyond their optimal range.

Velocity and Duration of Contraction

Muscles vary in how fast they can contract and how long they can continue to contract before they fatigue. These characteristics are influenced by muscle fiber type, load, and recruitment (**Figure 9.20**).

Muscle Fiber Type

There are several ways of classifying muscle fibers, but learning about these classes will be easier if you pay attention to just two functional characteristics:

- **Speed of contraction.** On the basis of speed (velocity) of fiber shortening, there are **slow fibers** and **fast fibers**. The difference reflects how fast their myosin ATPases split ATP, and the pattern of electrical activity of their motor neurons. Contraction duration also varies with fiber type and depends on how quickly Ca^{2+} moves from the cytosol into the SR.

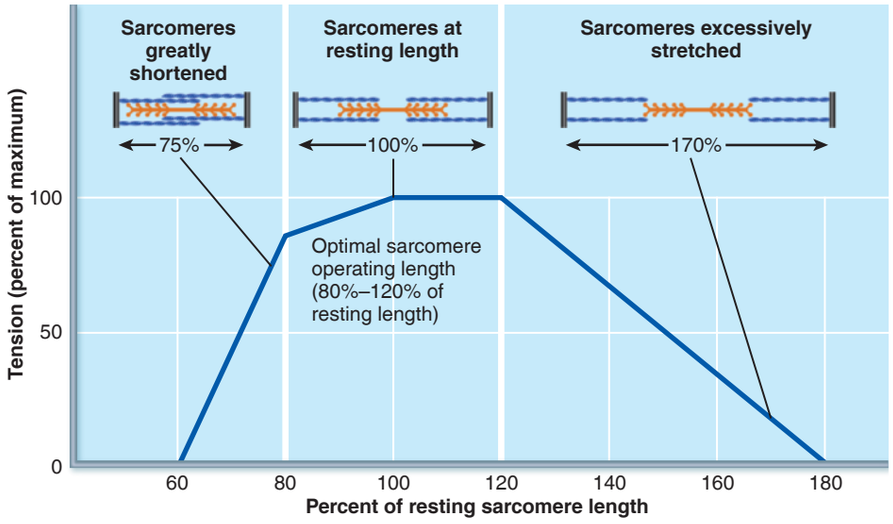


Figure 9.19 **Length-tension relationships of sarcomeres in skeletal muscles.** A muscle generates maximum force between 80 and 120% of its optimal (resting) length. Increases and decreases beyond this optimal range reduce its ability to generate tension.

- **Major pathways for forming ATP.** The cells that rely mostly on the oxygen-using aerobic pathways for ATP generation are **oxidative fibers**. Those that rely more on anaerobic glycolysis and creatine phosphate are **glycolytic fibers**.

Using these two criteria, we can classify skeletal muscle cells as: **slow oxidative fibers**, **fast oxidative fibers**, or **fast glycolytic fibers**.

Table 9.2 gives details about each group, but a word to the wise: Do not approach this information by rote memorization—you'll just get frustrated. Instead, start with what you know for any category and see how the characteristics listed support that.

For example, think about a *slow oxidative fiber* (Table 9.2, first column, and Figure 9.20, right side). We can see that it:

- Contracts *slowly* because its myosin ATPases are slow (a criterion)
- Depends on *oxygen* delivery and aerobic pathways (its major pathways for forming ATP give it *high oxidative capacity*—a criterion)
- Resists fatigue and has high endurance (typical of fibers that depend on aerobic metabolism)
- Is thin (a large amount of cytoplasm impedes diffusion of O_2 and nutrients from the blood)
- Has relatively little power (a thin cell can contain only a limited number of myofibrils)
- Has many mitochondria (actual sites of oxygen use)
- Has a rich capillary supply (the better to deliver bloodborne O_2)
- Is red (its color stems from an abundant supply of myoglobin, muscle's oxygen-binding pigment)

Add these features together and you have a muscle fiber best suited to endurance-type activities.

Now think about a *fast glycolytic fiber* (Table 9.2, third column, and Figure 9.20, left side). In contrast, it:

- Contracts *rapidly* due to the activity of fast myosin ATPases
- Uses little oxygen
- Depends on plentiful *glycogen* reserves for fuel rather than on blood-delivered nutrients
- Tires quickly because glycogen reserves are short-lived, making it a fatigable fiber
- Has a relatively large diameter, indicating both the plentiful myofilaments that allow it to contract powerfully before it "tires out" and its lack of dependence on continuous oxygen and nutrient diffusion from the blood
- Has few mitochondria, little myoglobin, and few capillaries (making it white)

For these reasons, a fast glycolytic fiber is best suited for short-term, rapid, intense movements (moving furniture across the room, for example).

Finally, consider the less common intermediate muscle fiber types, called *fast oxidative fibers* (Table 9.2, middle column).

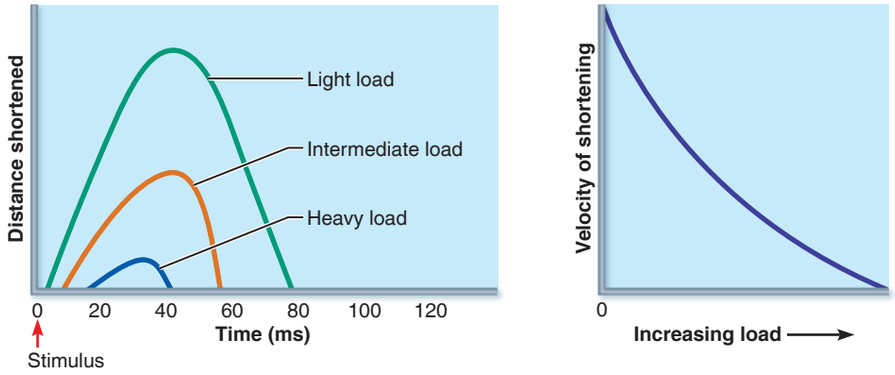
Table 9.2 Structural and Functional Characteristics of the Three Types of Skeletal Muscle Fibers

	SLOW OXIDATIVE FIBERS	FAST OXIDATIVE FIBERS	FAST GLYCOLYTIC FIBERS
Metabolic Characteristics			
Speed of contraction	Slow	Fast	Fast
Myosin ATPase activity	Slow	Fast	Fast
Primary pathway for ATP synthesis	Aerobic	Aerobic (some anaerobic glycolysis)	Anaerobic glycolysis
Myoglobin content	High	High	Low
Glycogen stores	Low	Intermediate	High
Recruitment order	First	Second	Third
Rate of fatigue	Slow (fatigue-resistant)	Intermediate (moderately fatigue-resistant)	Fast (fatigable)
Activities Best Suited For			
	Endurance-type activities—e.g., running a marathon; maintaining posture (antigravity muscles)	Sprinting, walking	Short-term intense or powerful movements, e.g., hitting a baseball
Structural Characteristics			
Fiber diameter	Small	Large*	Intermediate
Mitochondria	Many	Many	Few
Capillaries	Many	Many	Few
Color	Red	Red to pink	White (pale)

*In animal studies, fast glycolytic fibers were found to be the largest, but this is not true in humans.

They have many characteristics intermediate between the other two types (glycogen stores and power, for example). Like fast glycolytic fibers, they contract quickly, but like slow oxidative fibers, they are oxygen dependent and have a rich supply of myoglobin and capillaries.

Some muscles have a predominance of one fiber type, but most contain a mixture of fiber types, which gives them a range of contractile speeds and fatigue resistance. But, as might be expected, all muscle fibers in a particular *motor unit* are of the same type.



(a) The greater the load, the briefer the duration of muscle shortening.

(b) The greater the load, the slower the muscle shortening.

Figure 9.21 Influence of load on duration and velocity of muscle shortening.

Although everyone's muscles contain mixtures of the three fiber types, some people have relatively more of one kind. These differences are genetically initiated, but can be modified by exercise and no doubt determine athletic capabilities, such as endurance versus strength, to a large extent. For example, muscles of marathon runners have a high percentage of slow oxidative fibers (about 80%), while those of sprinters contain a higher percentage (about 60%) of fast oxidative and glycolytic fibers. Interconversion between the "fast" fiber types occurs as a result of specific exercise regimes, as we'll describe below.

Load and Recruitment

Because muscles are attached to bones, they are always pitted against some resistance, or load, when they contract. As you might expect, they contract fastest when there is no added load on them. A greater load results in a longer latent period, slower shortening, and a briefer duration of shortening (**Figure 9.21**).

In the same way that many hands on a project can get a job done more quickly and can keep working longer, the more motor units that are contracting, the faster and more prolonged the contraction.

Check Your Understanding

17. List two factors that influence contractile force and two that influence velocity of contraction.

18. APPLY Jordan called several friends to help him move. Would he prefer to have those with more slow oxidative muscle fibers or those with more fast glycolytic fibers as his helpers? Why?

19. APPLY There are no slow glycolytic fibers. Explain why it would not make sense to have these kinds of fibers.

For answers, see Answers Appendix.

9.8 How does skeletal muscle respond to exercise?

Learning Outcome

Compare and contrast the effects of aerobic and resistance exercise on skeletal muscles.

The amount of work a muscle does is reflected in changes in the muscle itself. When used actively or strenuously, muscles may become larger or stronger, or more efficient and fatigue resistant. Exercise gains are based on the overload principle. Forcing a muscle to work hard increases its strength and endurance. As muscles adapt to greater demand, they must be overloaded to produce further gains. Inactivity, on the other hand, *always* leads to muscle weakness and atrophy.

Aerobic (Endurance) Exercise

Aerobic, or **endurance**, **exercise** such as swimming, running, fast walking, and biking results in several recognizable changes in skeletal muscles:

- The number of capillaries surrounding the muscle fibers increases.
- The number of mitochondria within the muscle fibers also increases.
- The fibers synthesize more myoglobin.

These changes occur in all fiber types, but are most dramatic in slow oxidative fibers, which depend primarily on aerobic pathways. The changes result in more efficient muscle metabolism and in greater endurance, strength, and resistance to fatigue. Regular endurance exercise may convert fast glycolytic fibers into fast oxidative fibers.

Resistance Exercise

The moderately weak but sustained muscle activity required for endurance exercise does not promote significant skeletal muscle hypertrophy, even though the exercise may go on for hours. Muscle hypertrophy—think of the bulging biceps of a professional weight lifter—results mainly from high-intensity **resistance exercise** (typically under anaerobic conditions) such as weight lifting or isometric exercise, which pits muscles against high-resistance or immovable forces. Here strength, not stamina, is important, and a few minutes every other day is sufficient to allow a proverbial weakling to put on 50% more muscle within a year.

The additional muscle bulk largely reflects the increased size of individual muscle fibers (particularly the fast glycolytic variety) rather than an increased number of muscle fibers. [However, some of the bulk may result from longitudinal splitting of the fibers and subsequent growth of these "split" cells, or from the proliferation and fusion of satellite cells (see Figure 9.27).] Vigorously stressed muscle fibers also contain more mitochondria, form more myofilaments and myofibrils, store more glycogen, and develop more connective tissue between muscle cells.

Collectively these changes promote significant increases in muscle strength and size. Resistance activities can also convert fast oxidative fibers to fast glycolytic fibers. However, if the specific exercise routine is discontinued, the converted fibers revert to their original metabolic properties.

HOMEOSTATIC IMBALANCE 9.4 CLINICAL

To remain healthy, muscles must be active. Immobilization due to enforced bed rest or loss of neural stimulation results in *disuse atrophy* (degeneration and loss of mass), which begins almost as soon as the muscles are immobilized. Under such conditions, muscle strength can decline at the rate of 5% per day!

Even at rest, muscles continually receive weak stimuli (recall that they have *muscle tone*; ◀ pp. 302–303). When totally deprived of neural stimulation, a paralyzed muscle may atrophy to one-quarter of its initial size. Fibrous connective tissue replaces the lost muscle tissue, and complete recovery usually takes longer than the period of immobilization.

Check Your Understanding

20. How do aerobic and resistance exercise differ in their effects on muscle size and function?

For answers, see Answers Appendix.

9.9 Smooth muscle is nonstriated involuntary muscle

Learning Outcomes

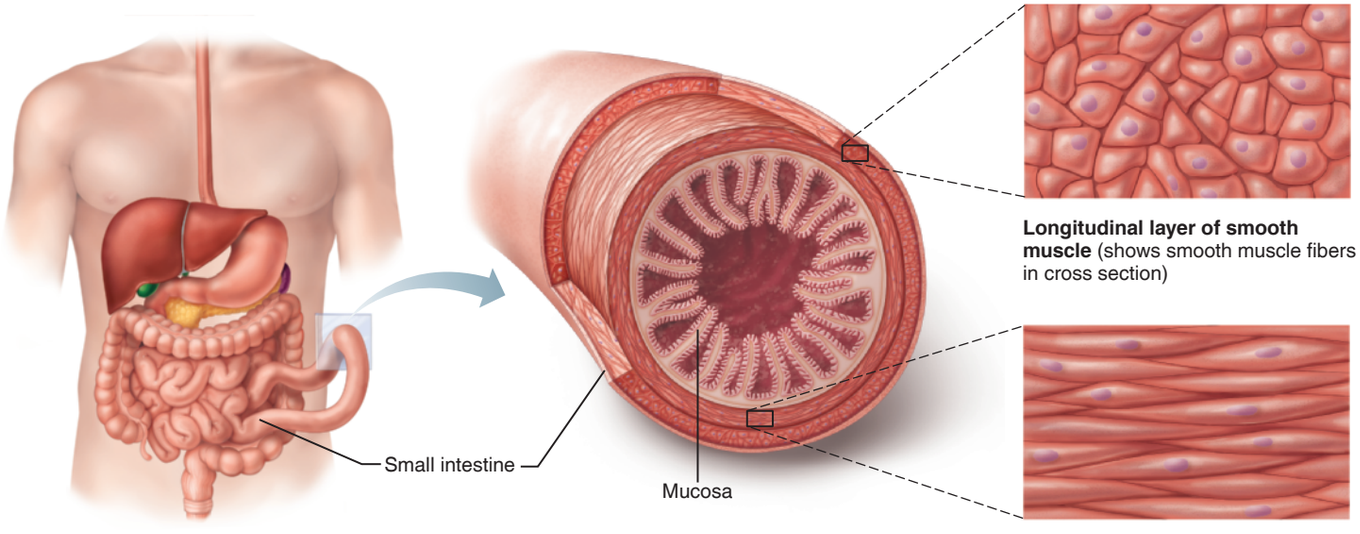
- **Compare the gross and microscopic anatomy of smooth muscle cells to that of skeletal muscle cells.**
- **Compare and contrast the contractile mechanisms and the means of activation of skeletal and smooth muscles.**
- **Distinguish between unitary and multi unit smooth muscle structurally and functionally.**

Except for the heart, which is made of cardiac muscle, the muscle in the walls of all the body's hollow organs is almost entirely smooth muscle.

Most smooth muscle is organized into sheets of tightly packed fibers. These sheets are found in the walls of all but the smallest blood vessels and in the walls of hollow organs of the respiratory, digestive, urinary, and reproductive tracts. In most cases, there are two sheets of smooth muscle with their fibers oriented at right angles to each other, as in the intestine (**Figure 9.22**).

- In the *longitudinal layer*, the muscle fibers run parallel to the long axis of the organ. Consequently, when these fibers contract, the organ shortens.
- In the *circular layer*, the fibers run around the circumference of the organ. Contraction of this layer constricts the lumen (cavity inside) of the organ.

The alternating contraction and relaxation of these layers mixes substances in the lumen and squeezes them through the organ's internal pathway. Contraction of smooth muscle in the rectum, urinary bladder, and uterus helps those organs to expel their



(a)

(b) Cross section of the intestine showing the smooth muscle layers running at right angles to each other.

Figure 9.22 Arrangement of smooth muscle in the walls of hollow organs.

contents. Smooth muscle contraction also accounts for the constricted breathing of asthma and for stomach cramps.

The chemical and mechanical events of contraction are essentially the same in all muscle tissues, but smooth muscle is distinctive in several ways, as summarized in **Table 9.3** on pp. 312–313.

Differences between Smooth and Skeletal Muscle Fibers

There are several structural differences between skeletal and smooth muscle. In contrast to skeletal muscle:

- **Smooth muscle fibers are small spindle-shaped cells.** Each cell has one centrally located nucleus (Figure 9.22b). Typically, smooth muscle fibers have a diameter of 5–10 μm and are 30–200 μm long. Skeletal muscle fibers are up to 10 times wider and thousands of times longer.
- **Smooth muscle lacks the coarse connective tissue sheaths found in skeletal muscle.** A small amount of fine connective tissue (endomysium) is secreted by the smooth muscles themselves. It is found between smooth muscle fibers and contains blood vessels and nerves. Epimysium and perimysium are not present.
- **Smooth muscle has varicosities instead of neuromuscular junctions.** The innervating nerve fibers of the autonomic (involuntary) nervous system have numerous bulbous swellings, called **varicosities** (**Figure 9.23**). Unlike the highly structured neuromuscular junctions of skeletal muscle, varicosities form **diffuse junctions** that have wide synaptic clefts. The varicosities simply "sprinkle" neurotransmitter in the general area of the smooth muscle cells. Comparing the neural input to skeletal and smooth muscles, you could say that skeletal muscle gets high-speed internet while smooth muscle gets slow-speed dial-up.

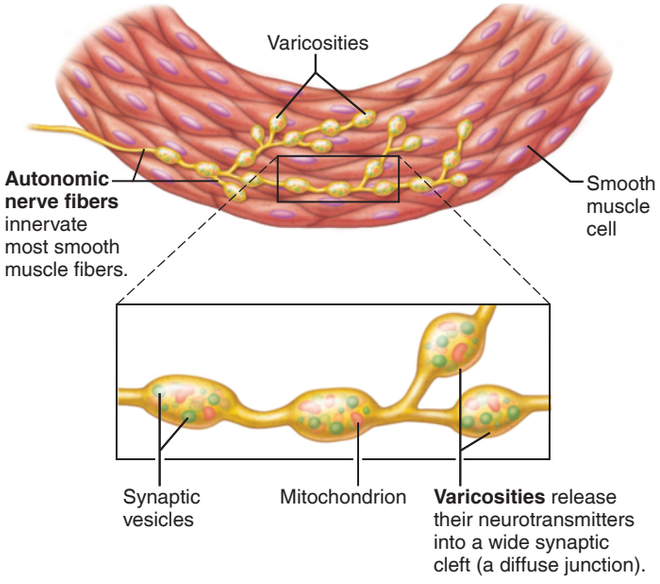


Figure 9.23 Innervation of smooth muscle.

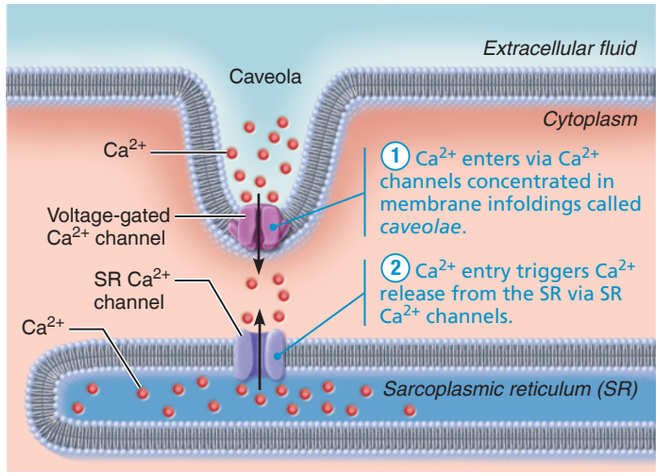


Figure 9.24 Sources of Ca^{2+} for smooth muscle contraction.

- **Smooth muscle fibers have less elaborate SR and no T tubules.** The sarcoplasmic reticulum of smooth muscle fibers has no terminal cisterns and lacks a specific pattern relative to the myofilaments. Although the SR *does* release some of the Ca^{2+} that triggers contraction, most Ca^{2+} enters through calcium channels directly from the extracellular space. The sarcolemma has multiple **caveolae** (ka″ve-o′le; "little caves"), pouchlike infoldings containing large numbers of Ca^{2+} channels (**Figure 9.24**). These calcium channels are the major source of Ca^{2+} for smooth muscle contraction. This situation is quite different from what we see in skeletal muscle, which does not depend on extracellular Ca^{2+} for excitation-contraction coupling.
- **Smooth muscle fibers are usually electrically connected by gap junctions.** Gap junctions are specialized cell connections (◀ p. 68) that allow depolarization to spread from cell to cell. In contrast, skeletal muscle fibers are electrically isolated from one another.

There are no striations in smooth muscle, as its name indicates, and therefore no sarcomeres. Smooth muscle fibers do contain overlapping thick and thin filaments, but the myosin filaments are a lot shorter than the actin filaments and the type of myosin contained differs from skeletal muscle. The proportion and organization of smooth muscle myofilaments differ from skeletal muscle in the following ways:

- **Thick filaments are fewer but have myosin heads along their entire length.** The ratio of thick to thin filaments is much lower in smooth muscle than in skeletal muscle (1:13 compared to 1:2). However, thick filaments of smooth muscle contain actin-gripping myosin heads along their *entire length*, a feature that makes smooth muscle as powerful as a skeletal muscle of the same size. Also, in smooth muscle the myosin heads are oriented in one direction on one side of the filament and in the opposite direction on the other side.

(Text continues on p. 314.)

Table 9.3 Comparison of Skeletal, Cardiac, and Smooth Muscle

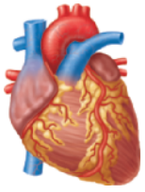
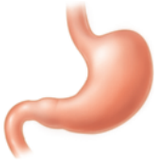
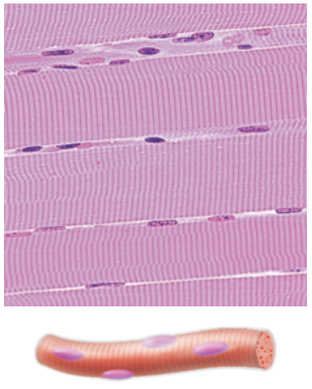
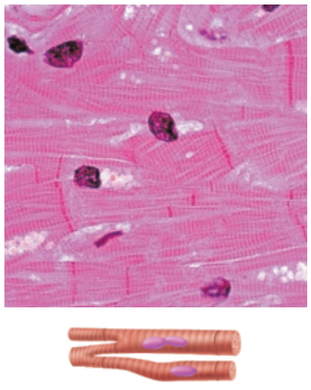
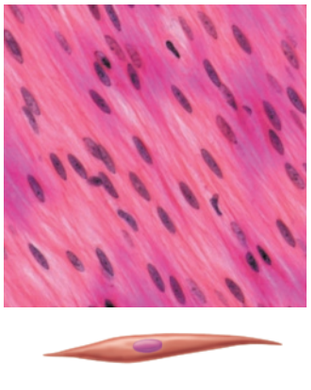
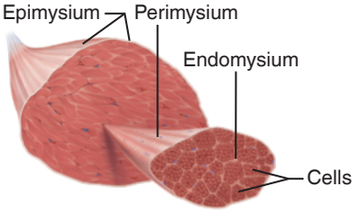
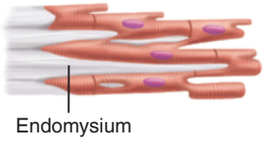
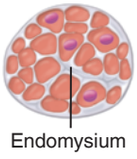
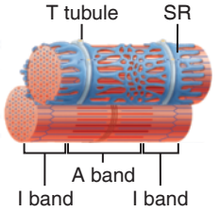
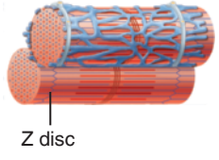
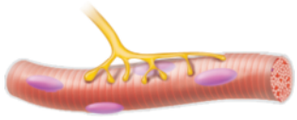
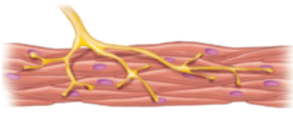
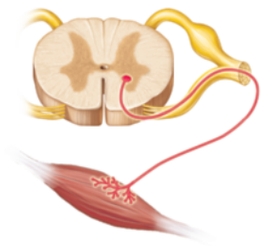
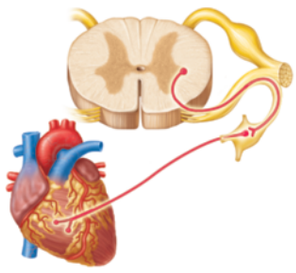
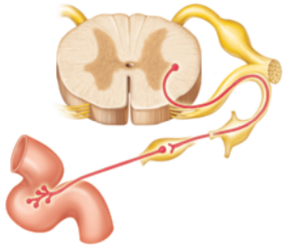
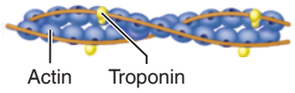
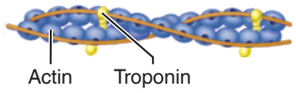
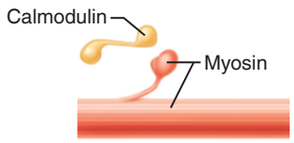
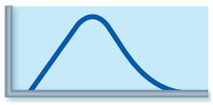
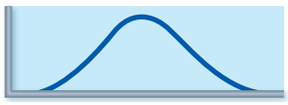
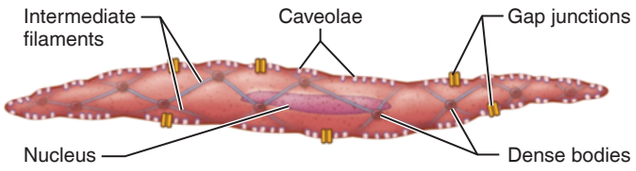
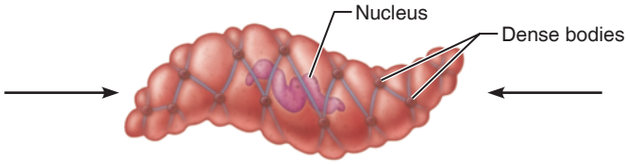
CHARACTERISTIC	SKELETAL	CARDIAC	SMOOTH
Body location	Attached to bones or (some facial muscles) to skin 	Walls of the heart 	Unitary muscle in walls of hollow visceral organs (other than the heart); multi unit muscle in intrinsic eye muscles, airways, large arteries 
Cell shape and appearance	Single, very long, cylindrical, multinucleate cells with obvious striations 	Branching chains of cells; uni- or binucleate; striations 	Single, spindle shaped, uninucleate; no striations 
Connective tissue components	Epimysium, perimysium, and endomysium 	Endomysium attached to fibrous skeleton of heart 	Endomysium 
Presence of myofibrils composed of sarcomeres	Yes	Yes, but myofibrils are of irregular thickness	No, but actin and myosin filaments are present throughout; dense bodies anchor actin filaments
Presence and location of T tubules	Yes; two per sarcomere at A-I junctions 	Yes; one per sarcomere at Z disc; larger diameter than those of skeletal muscle 	No; only caveolae

Table 9.3 (*continued*)

CHARACTERISTIC	SKELETAL	CARDIAC	SMOOTH
Elaborate sarcoplasmic reticulum	Yes; large terminal cisterns	Less than skeletal muscle (1–8% of cell volume); small terminal cisterns	Equivalent to cardiac muscle (1–8% of cell volume); some SR contacts the sarcolemma
Presence of gap junctions	No	Yes; at intercalated discs	Yes; in unitary muscle
Cells exhibit individual neuromuscular junctions	Yes 	No	Not in unitary muscle; yes in multi unit muscle 
Regulation of contraction	Voluntary via axon terminals of the somatic nervous system 	Involuntary; contraction initiated by intrinsic pacemaker cells; regulated by autonomic nervous system, hormones, and stretch 	Involuntary; initiated by intrinsic pacemaker cells (in unitary muscle) or autonomic nerves (in multi unit muscle); regulated by local chemicals, hormones, and stretch 
Source of Ca^{2+} for contraction	Sarcoplasmic reticulum (SR)	SR and from extracellular fluid	Extracellular fluid and from SR
Site of calcium regulation	Troponin on actin-containing thin filaments 	Troponin on actin-containing thin filaments 	Calmodulin in the cytosol 
Presence of pacemaker(s)	No	Yes	Yes (in unitary muscle only)
Effect of nervous system stimulation	Excitation	Excitation or inhibition	Excitation or inhibition
Speed of contraction	Slow to fast 	Slow 	Very slow 
Rhythmic contraction	No	Yes	Yes in unitary muscle
Response to stretch	Contractile strength increases with degree of stretch (to a point)	Contractile strength increases with degree of stretch	Stress-relaxation response
Metabolism	Aerobic and anaerobic	Aerobic	Mainly aerobic



(a) Relaxed smooth muscle fiber (note that gap junctions connect adjacent fibers)



(b) Contracted smooth muscle fiber

Figure 9.25 Intermediate filaments and dense bodies of smooth muscle fibers harness the pull generated by myosin cross bridges. Intermediate filaments attach to dense bodies throughout the sarcoplasm.

- **No troponin complex in thin filaments.** As in skeletal muscle, tropomyosin mechanically stabilizes the thin filaments, but smooth muscle has no calcium-binding troponin complex. Instead, a protein called *calmodulin* acts as the calcium-binding site.
- **Intermediate filament–dense body network.** Smooth muscle fibers contain a lattice-like arrangement of noncontractile *intermediate filaments* that resist tension. They attach at regular intervals to cytoplasmic structures called dense bodies (**Figure 9.25**). The **dense bodies**, which are also tethered to the sarcolemma, act as anchoring points for thin filaments and therefore correspond to Z discs of skeletal muscle.

  The intermediate filament–dense body network forms a strong, cable-like intracellular cytoskeleton that harnesses the pull generated by the sliding of the thick and thin filaments. During contraction, areas of the sarcolemma between the dense bodies bulge outward, making the cell look puffy (Figure 9.25b). Dense bodies at the sarcolemma surface also bind the muscle cell to the connective tissue fibers outside the cell and to adjacent cells. This arrangement transmits the pulling force to the surrounding connective tissue and partly accounts for the synchronous contractions of most smooth muscle.
- **Thick and thin filaments arranged diagonally.** Bundles of contractile proteins crisscross within the smooth muscle cell so they spiral down the long axis of the cell like the stripes on a candy cane). Because of this diagonal arrangement, the smooth muscle cells contract in a twisting way so that they look like tiny corkscrews (Figure 9.25b).

Contraction of Smooth Muscle

Mechanism of Contraction

In most cases, adjacent smooth muscle fibers exhibit slow, synchronized contractions, the whole sheet responding to a stimulus in unison. This synchronization reflects electrical coupling of smooth muscle cells by *gap junctions* that transmit depolarization from fiber to fiber.

Some smooth muscle fibers in the stomach and small intestine are *pacemaker cells*: Once excited, they act as "drummers" to set the pace of contraction for the entire muscle sheet. These pacemakers depolarize spontaneously in the absence of external stimuli. However, neural and chemical stimuli can modify both the rate and the intensity of smooth muscle contraction.

Contraction in smooth muscle is like contraction in skeletal muscle in the following ways:

- The final trigger for contraction is a rise in the intracellular calcium ion level.
- Actin and myosin interact by the sliding filament mechanism.
- ATP energizes the sliding process.

During excitation-contraction coupling, the SR releases Ca^{2+}, but Ca^{2+} also moves into the cell from the extracellular space via membrane channels. In all striated muscle types, calcium ions activate myosin by binding to troponin. In smooth muscle, calcium activates myosin by interacting with a regulatory molecule called **calmodulin**, a cytoplasmic calcium-binding protein. Calmodulin, in turn, interacts with a kinase enzyme called **myosin light chain kinase** or **myosin kinase**, which phosphorylates the myosin, activating it (**Figure 9.26**).

As in skeletal muscle, smooth muscle relaxes when intracellular Ca^{2+} levels drop—but getting smooth muscle to stop contracting is more complex. Events known to be involved include calcium detachment from calmodulin, active transport of Ca^{2+} into the SR and extracellular fluid, and dephosphorylation of myosin by a phosphatase enzyme, which reduces the activity of the myosin ATPases.

Energy Efficiency of Smooth Muscle Contraction

Smooth muscle takes 30 times longer to contract and relax than does skeletal muscle, but it can maintain the same contractile tension for prolonged periods at less than 1% of the energy cost. If skeletal muscle is like a speedy windup car that quickly runs down, then smooth muscle is like a steady locomotive engine that lumbers along tirelessly.

Part of the striking energy economy of smooth muscle is the sluggishness of its ATPases compared to those in skeletal muscle. Moreover, smooth muscle myofilaments may latch together during prolonged contractions. This latching also saves energy.

The smooth muscle in arterioles (small arteries) and other visceral organs routinely maintains a moderate degree of contraction, called *smooth muscle tone*, day in and day out without fatiguing. Smooth muscle has low energy requirements, and as a rule, it makes enough ATP via aerobic pathways to keep up with the demand.

Regulation of Contraction

The contraction of smooth muscle can be regulated by nerves, hormones, or local chemical changes. Let's briefly consider each of these methods.

Neural Regulation In some cases, the activation of smooth muscle by a neural stimulus is identical to that in skeletal muscle:

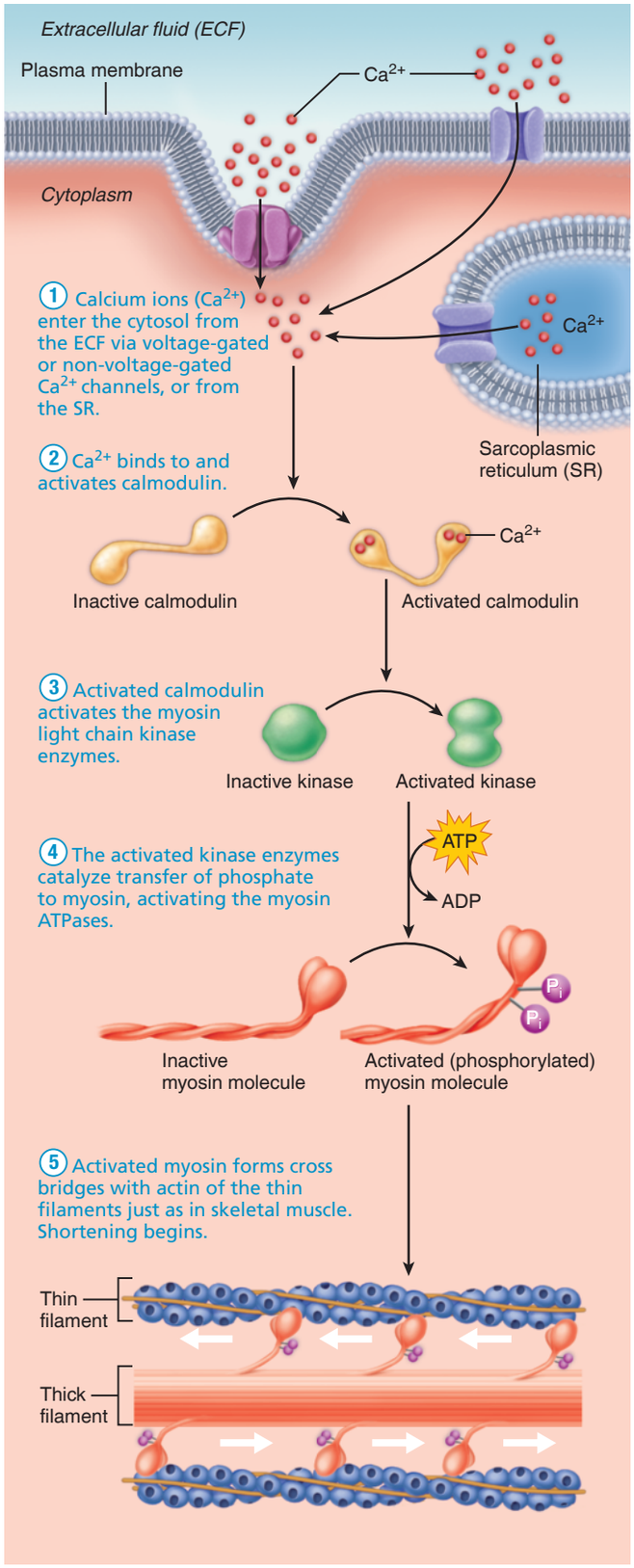


Figure 9.26 Sequence of events in excitation-contraction coupling of smooth muscle.

Neurotransmitter binding generates an action potential, which is coupled to a rise in calcium ions in the cytosol. However, some types of smooth muscle respond to neural stimulation with graded potentials (local electrical signals) only.

Recall that all somatic nerve endings, that is, nerve endings that excite skeletal muscle, release the neurotransmitter acetylcholine. However, different autonomic nerves serving the smooth muscle of visceral organs release different neurotransmitters, each of which may excite or inhibit a particular group of smooth muscle cells.

The effect of a specific neurotransmitter on a smooth muscle cell depends on the type of receptor molecules on the cell's sarcolemma. For example, when acetylcholine binds to ACh receptors on smooth muscle in the bronchioles (small air passageways of the lungs), the response is strong contraction that narrows the bronchioles. When norepinephrine, released by a different type of autonomic nerve fiber, binds to norepinephrine receptors on the *same* smooth muscle cells, the effect is inhibitory—the muscle relaxes, which dilates the bronchioles. However, when norepinephrine binds to smooth muscle in the walls of most blood vessels, it stimulates the smooth muscle cells to contract and constrict the vessel.

Hormones and Local Chemical Factors Some smooth muscle layers have no nerve supply at all. Instead, they depolarize spontaneously or in response to chemical stimuli that bind to G protein–linked receptors (◀ pp. 81–82). Other smooth muscle cells respond to both neural and chemical stimuli.

Several chemical factors cause smooth muscle to contract or relax without an action potential by enhancing or inhibiting Ca^{2+} entry into the sarcoplasm. They include certain hormones, histamine, excess carbon dioxide, low pH, and lack of oxygen. The direct response to these chemical stimuli alters smooth muscle activity according to local tissue needs and probably is most responsible for smooth muscle tone. For example, the hormone gastrin stimulates stomach smooth muscle to contract so it can churn foodstuffs more efficiently. We will consider activation of smooth muscle in specific organs as we discuss each organ in subsequent chapters.

Special Features of Smooth Muscle Contraction

Smooth muscle is intimately involved in the functioning of most hollow organs and has a number of unique characteristics. We have already considered some of these—smooth muscle tone, slow prolonged contractions, and low energy requirements. But smooth muscle also responds differently to stretch and can lengthen and shorten more than other muscle types. Let's take a look.

Response to Stretch Unlike skeletal muscle, smooth muscle spontaneously contracts when it is stretched. This is useful because it can move substances along an internal tract. However, the increased tension persists only briefly, and soon the muscle adapts to its new length and relaxes, while still retaining the ability to contract on demand.

This **stress-relaxation response** allows a hollow organ to fill or expand slowly to accommodate a greater volume without causing strong contractions that would expel its contents. This is an important attribute, because organs such as the stomach and intestines

must store their contents long enough to digest and absorb the nutrients. Likewise, your urinary bladder must be able to store the continuously made urine until it is convenient to empty your bladder, or you would spend all your time in the bathroom.

Length and Tension Changes Smooth muscle stretches much more and generates more tension than skeletal muscles stretched to a comparable extent. The irregular, overlapping arrangement of smooth muscle filaments and the lack of sarcomeres allow them to generate considerable force, even when they are substantially stretched. The total length change that skeletal muscles can undergo and still function efficiently is about 60% (from 30% shorter to 30% longer than resting length; see Figure 9.19 on p. 307), but smooth muscle can contract when it is anywhere from half to twice its resting length—a total range of 150%. This capability allows hollow organs to tolerate tremendous changes in volume without becoming flabby when they empty.

Types of Smooth Muscle

The smooth muscle in different body organs varies substantially in its (1) fiber arrangement and organization, (2) innervation, and (3) responsiveness to various stimuli. For simplicity, however, smooth muscle is usually categorized into two major types: *unitary* and *multi unit*.

Unitary Smooth Muscle

Unitary smooth muscle, sometimes called **visceral muscle** because it is in the walls of all hollow organs except the heart, is far more common. All the smooth muscle characteristics described so far pertain to unitary smooth muscle.

For example, the cells of unitary smooth muscle:

- Are arranged in opposing (longitudinal and circular) sheets
- Are innervated by varicosities of autonomic nerve fibers and often exhibit rhythmic spontaneous action potentials
- Are electrically coupled by gap junctions and so contract as a unit (for this reason recruitment does not occur in unitary smooth muscle)
- Respond to various chemical stimuli

Multi Unit Smooth Muscle

Examples of **multi unit smooth muscle** are: the smooth muscles in the large airways to the lungs and in large arteries, the arrector pili muscles attached to hair follicles, and the internal eye muscles that adjust pupil size and allow the eye to focus.

In contrast to unitary muscle, gap junctions and spontaneous depolarizations are absent. Like skeletal muscle, multi unit smooth muscle:

- Consists of muscle fibers that are structurally independent of one another
- Is richly supplied with nerve endings, each of which forms a motor unit with a number of muscle fibers
- Responds to neural stimulation with graded contractions that involve recruitment

However, skeletal muscle is served by the somatic (voluntary) division of the nervous system. Multi unit smooth muscle, like unitary smooth muscle, is innervated by the autonomic (involuntary) division and also responds to hormones.

Check Your Understanding

21. Compare the structures of skeletal and smooth muscle fibers.

22. Calcium is the trigger for contraction of all muscle types. How does its binding site differ in skeletal and smooth muscle fibers?

23. How does the stress-relaxation response suit the role of smooth muscle in hollow organs?

24. MAKE CONNECTIONS Intracellular calcium performs other important roles in the body in addition to triggering muscle contraction. Give one example. (Hint: See Chapter 3.)

For answers, see Answers Appendix.

Developmental Aspects of Muscles

With rare exceptions, all three types of muscle tissue develop from cells called **myoblasts** that arise from the embryonic mesoderm (◀ Figure 4.16, p. 146). In forming skeletal muscle tissue, several myoblasts fuse to form multinuclear *myotubes* (**Figure 9.27**). Soon functional sarcomeres appear, and skeletal muscle fibers are contracting by week 7 when the embryo is only about 2.5 cm (1 inch) long.

Initially, ACh receptors "sprout" over the entire surface of the developing myoblasts. As spinal nerves invade the muscle masses, the nerve endings target individual myoblasts and release a growth factor that stimulates clustering of ACh receptors at the newly forming neuromuscular junction in each muscle fiber. Then, the nerve endings release a different chemical that eliminates the receptor sites not innervated or stabilized by the growth factor. As the somatic nervous system assumes control of muscle fibers, the number of fast and slow contractile fiber types is determined by the nerves that innervate them.

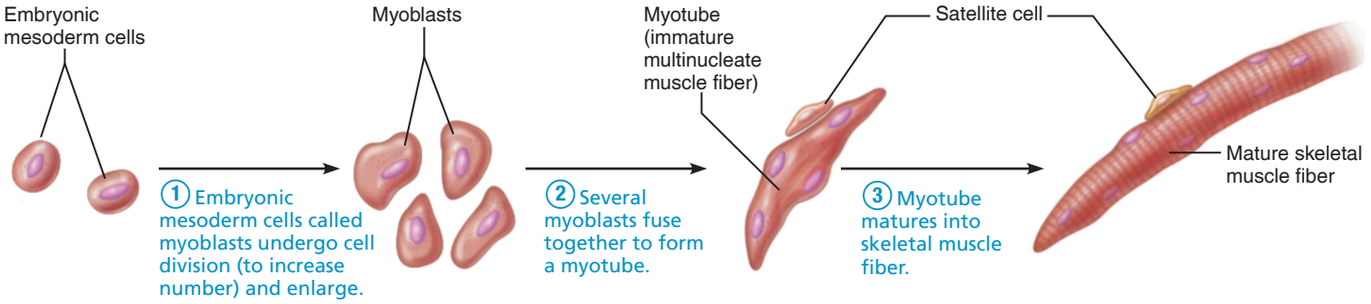


Figure 9.27 **Myoblasts fuse to form a multinucleate skeletal muscle fiber.**

Athletes Looking Good and Doing Better with Anabolic Steroids?

Society loves a winner and top athletes reap large social and monetary rewards. It is not surprising that some will grasp at anything that might increase their performance—including performance-enhancing drugs such as anabolic steroids.

These drugs are variants of the male sex hormone testosterone. They were introduced in the 1950s to treat anemia and certain muscle-wasting diseases and to prevent muscle atrophy in patients immobilized after surgery. Testosterone is responsible for the increase in muscle and bone mass and other physical changes that occur during puberty in males.

Athletes and bodybuilders were using megadoses of steroids by the early 1960s, a practice that is still going on despite drug testing programs. Investigations have stunned sports fans with revelations of steroid use by many elite athletes including Barry Bonds, Mark McGwire, Marion Jones, and Lance Armstrong.

However, steroid use is not confined to professional athletes. It is estimated that nearly one in every 10 young men has tried them, and their use has spread among young women.

It is difficult to determine the extent of anabolic steroid use because users stop doping before the event, aware that evidence of drug use is hard to find a week after they stop. "Underground" suppliers keep producing new versions of designer steroids that evade standard antidoping tests.

There is little question that many professional bodybuilders and athletes competing in events that require muscle strength are heavy users, claiming that anabolic steroids enhance muscle mass and strength, and raise oxygen-carrying capability owing to a greater volume of red blood cells.

Do the drugs do all that is claimed? Studies report increased isometric strength and body weight in steroid users. While these are results weight lifters dream about, for runners and others requiring fine muscle coordination and endurance, these changes may not translate into better performance. The jury is still out on this question.

Do the alleged advantages of steroids outweigh their risks? Absolutely not. Anabolic steroids cause: bloated faces (Cushingoid sign of steroid excess), acne and hair loss, shriveled testes and infertility, liver damage that promotes liver cancer, and changes in blood cholesterol levels that may predispose users to heart disease.

In addition, females can develop masculine characteristics such as smaller breasts, enlarged clitoris, excess body hair, and thinning scalp hair. The psychiatric hazards of anabolic steroid use may be equally threatening: One-third of users suffer serious mental problems. Depression, delusions, and manic behavior—in which users undergo Jekyll-and-Hyde personality swings and become extremely violent (termed '*roid rage*)—are all common.

Some people seem willing to try almost anything to win, short of killing themselves. Are they unwittingly doing this as well?

Myoblasts producing cardiac and smooth muscle cells do not fuse but develop gap junctions at a very early embryonic stage. Cardiac muscle is pumping blood just 3 weeks after fertilization.

Regarding muscle regeneration:

- Skeletal muscles stop dividing early on. However, *satellite cells,* myoblast-like cells associated with skeletal muscle, help repair injured fibers and allow limited regeneration of dead skeletal muscle, a capability that declines with age.
- Cardiac muscle was thought to have no regenerative capability whatsoever, but recent studies suggest that cardiac cells do divide, but only at about 1% per year. As a result, injured heart muscle is repaired mostly by scar tissue.
- Smooth muscles have a good regenerative capacity, and smooth muscle cells of blood vessels divide regularly throughout life.

Both skeletal muscle and cardiac muscle retain the ability to lengthen and thicken in a growing child and to hypertrophy in response to increased load in adults.

At birth, a baby's movements are uncoordinated and largely reflexive. Muscular development reflects the level of neuromuscular coordination, which develops in a head-to-toe and proximal-to-distal direction. A baby can lift its head before it can walk, and gross movements precede fine ones.

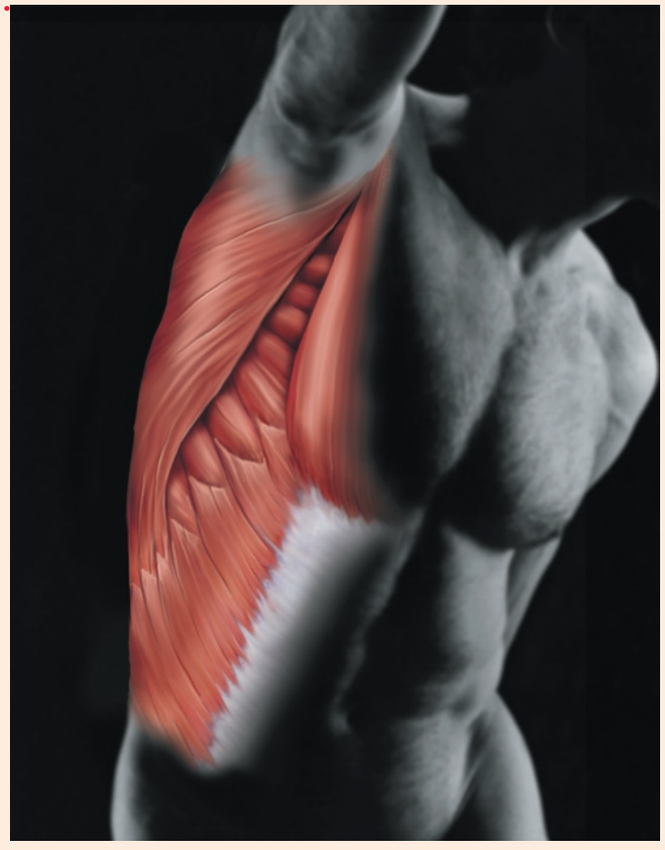
All through childhood, our control of our skeletal muscles becomes more and more sophisticated. By midadolescence, we reach the peak of our natural neural control of muscles, but can improve it by athletic or other types of training.

A frequently asked question is whether the strength difference between women and men has a biological basis. It does. Individuals vary, but on average, women's skeletal muscles make up approximately 36% of body mass, whereas men's account for about 42%. Men's greater muscular development is due primarily to the effects of testosterone on skeletal muscle, not to the effects of exercise. Body strength per unit muscle mass, however, is the same in both sexes. Strenuous muscle exercise causes more muscle enlargement in males than in females, again because of the influence of testosterone. Some athletes take large doses of synthetic male sex hormones ("steroids") to increase their muscle mass. **A Closer Look** on p. 317 discusses this illegal and physiologically dangerous practice.

Because of its rich blood supply, skeletal muscle is amazingly resistant to infection. Given good nutrition and moderate exercise, relatively few problems afflict skeletal muscles. However, muscular dystrophy (described on p. 287) is a serious congenital condition that affects skeletal muscle.

As we age, the amount of connective tissue in our skeletal muscles increases, the number of muscle fibers decreases, and the muscles become stringier, or more sinewy. By age 30, even in healthy people, a gradual loss of muscle mass, called *sarcopenia* (sar-co-pe′ne-ah), begins. Because skeletal muscles

Homeostatic Interrelationships between the Muscular System and Other Body Systems



Integumentary System Chapter 5

- Muscular exercise enhances circulation to skin and improves skin health
- Skin protects the muscles by external enclosure; helps dissipate heat generated by the muscles

Skeletal System Chapters 6–8

- Skeletal muscle activity maintains bone health and strength
- Bones provide levers for muscle activity

Nervous System Chapters 11–15

- Facial muscle activity allows emotions to be expressed
- Nervous system stimulates and regulates muscle activity
- Nervous system activity maintains muscle mass

Endocrine System Chapter 16

- Growth hormone and androgens influence skeletal muscle strength and mass; other hormones help regulate cardiac and smooth muscle activity

Cardiovascular System Chapters 17–19

- Skeletal muscle activity increases efficiency of cardiovascular functioning; helps prevent atherosclerosis and causes cardiac hypertrophy
- Cardiovascular system delivers needed oxygen and nutrients to muscles

Lymphatic System/Immunity Chapters 20–21

- Physical exercise may enhance or depress immunity depending on its intensity
- Lymphatic vessels drain leaked tissue fluids; immune system protects muscles from disease

Respiratory System Chapter 22

- Muscular exercise increases respiratory capacity and efficiency of gas exchange
- Respiratory system provides oxygen and disposes of carbon dioxide

Digestive System Chapter 23

- Physical activity increases gastrointestinal motility; skeletal muscle forms the voluntary sphincter of the anus
- Digestive system provides nutrients needed for muscle health; liver metabolizes lactic acid

Urinary System Chapters 25–26

- Skeletal muscle forms the voluntary sphincter of the urethra
- Urinary system disposes of nitrogenous wastes

Reproductive System Chapter 27

- Skeletal muscle helps support pelvic organs (e.g., uterus); assists erection of penis and clitoris
- Testicular androgen promotes increased skeletal muscle

form so much of the body mass, body weight and muscle strength decline in tandem. By age 80, muscle strength usually decreases by about 50%. This "flesh wasting" condition has serious health implications for the elderly, particularly because falling becomes a common event.

Muscles can also suffer indirectly. Aging of the cardiovascular system affects nearly every organ in the body, and muscles are no exception. As atherosclerosis ("hardening of the arteries") takes its toll and begins to block distal arteries, a circulatory condition called *intermittent claudication* (klaw″dĭ-ka′shun; "limping") occurs in some individuals. This condition restricts blood delivery to the legs, leading to excruciating pains in the leg muscles during walking, which forces the person to stop and rest.

But we don't have to slow down during old age. Regular exercise helps reverse sarcopenia, and frail elders who begin to "pump iron" (lift leg and hand weights) can rebuild muscle mass and dramatically increase their strength. Performing those lifting exercises rapidly can improve our ability to carry out the "explosive" movements needed to rise from a chair. Even moderate activity, like taking a walk daily, improves neuromuscular function and enhances independent living.

Smooth muscle is remarkably trouble free. However, smooth muscle is involved in forming the plaques of atherosclerosis that can lead to strokes and heart attacks. The involvement of smooth muscle cells in this process is described in *A Closer Look* on p. 760.

RELATED CLINICAL TERMS

Fibromyalgia A group of conditions involving chronic inflammation of muscles, their connective tissue coverings and tendons, and capsules of nearby joints. Symptoms are nonspecific and involve varying degrees of tenderness associated with specific trigger points, as well as fatigue and frequent awakening from sleep.

Hernia Protrusion of an organ through its body cavity wall. May be congenital (owing to failure of muscle fusion during development), but most often is caused by heavy lifting or obesity and subsequent muscle weakening.

Myalgia (mi-al′je-ah; *algia* = pain) Muscle pain resulting from any muscle disorder.

Myofascial pain syndrome Pain caused by a tightened band of muscle fibers, which twitch when the skin over them is touched. Mostly associated with overused or strained postural muscles.

Myopathy (mi-op′ah-the; *path* = disease, suffering) Any disease of muscle.

Myotonic dystrophy A form of muscular dystrophy that is less common than DMD; in the U.S. it affects about 14 of 100,000 people. Symptoms include a gradual reduction in muscle mass and control of the skeletal muscles, abnormal heart rhythm, and diabetes mellitus. May appear at any time; not sex-linked. Underlying genetic defect is multiple repeats of a particular gene on chromosome 19. Because the number of repeats tends to increase from generation to generation, subsequent generations develop more severe symptoms. No effective treatment.

RICE Acronym for rest, ice, compression, and elevation. The standard treatment for a pulled muscle, or excessively stretched tendons or ligaments.

Spasm A sudden, involuntary twitch in smooth or skeletal muscle ranging from merely irritating to very painful; may be due to chemical imbalances. In spasms of the eyelid or facial muscles, called tics, psychological factors may be involved. Stretching and massaging the affected area may help end the spasm. A cramp is a prolonged spasm; usually occurs at night or after exercise.

Strain Commonly called a "pulled muscle," a strain is excessive stretching and possible tearing of a muscle due to muscle overuse or abuse. The injured muscle becomes painfully inflamed (myositis), and adjacent joints are usually immobilized.

Tetanus (1) A state of sustained contraction of a muscle that is a normal aspect of skeletal muscle functioning. (2) An acute infectious disease caused by the anaerobic bacterium *Clostridium tetani* and resulting in persistent painful spasms of some skeletal muscles. Progresses to fixed rigidity of the jaws (lockjaw) and spasms of trunk and limb muscles. Usually fatal due to respiratory failure.

CHAPTER SUMMARY

9.1 There are three types of muscle tissue (pp. 280–281)

Types of Muscle Tissue (p. 280)

1. Skeletal muscle is attached to the skeleton, is striated, and can be controlled voluntarily.
2. Cardiac muscle forms the heart, is striated, and is controlled involuntarily.
3. Smooth muscle, located chiefly in the walls of hollow organs, is controlled involuntarily. Its fibers are not striated.

Characteristics of Muscle Tissue (p. 280)

4. Special functional characteristics of muscle include excitability, contractility, extensibility, and elasticity.

Muscle Functions (pp. 280–281)

5. Muscles move internal and external body parts, maintain posture, stabilize joints, and generate heat.

9.2 A skeletal muscle is made up of muscle fibers, nerves, blood vessels, and connective tissues (pp. 281–284)

1. Connective tissue coverings protect and strengthen skeletal muscle fibers (cells). Superficial to deep, these are epimysium, perimysium, and endomysium.
2. Skeletal muscle attachments (origins/insertions) may be direct or indirect via tendons or aponeuroses. Indirect attachments withstand friction better.

9.3 Skeletal muscle fibers contain calcium-regulated molecular motors (pp. 284–289)

1. Skeletal muscle fibers are long, striated, and multinucleate.
2. Myofibrils are contractile elements that occupy most of the cell volume. Their banded appearance results from a regular alternation of dark (A) and light (I) bands. Myofibrils are chains of sarcomeres; each sarcomere contains thick (myosin) and thin (actin) myofilaments arranged in a regular array. The heads of myosin molecules form cross bridges that interact with the thin filaments.
3. The sarcoplasmic reticulum (SR) is a system of membranous tubules surrounding each myofibril. Its function is to release and then sequester calcium ions.
4. T tubules are invaginations of the sarcolemma that run between the terminal cisterns of the SR. They allow an electrical stimulus to be delivered quickly deep into the cell.
5. According to the sliding filament model, cross bridge (myosin head) activity of the thick filaments pulls the thin filaments toward the sarcomere centers.

9.4 Motor neurons stimulate skeletal muscle fibers to contract (pp. 290–298)

1. Regulation of skeletal muscle cell contraction involves (a) generating and transmitting an action potential along the sarcolemma and (b) excitation-contraction coupling.
2. An end plate potential occurs when acetylcholine released by the axon terminal of a motor neuron binds to ACh receptors on the sarcolemma, causing local changes in membrane permeability, which allow ion flows that depolarize the membrane at that site.

Complete an interactive tutorial: MasteringA&P® > Study Area > Interactive Physiology > Muscular System: The Neuromuscular Junction

3. The flow of current from the locally depolarized area spreads to the adjacent area of the sarcolemma, opening voltage-gated Na^+ channels, which allows Na^+ influx. These events generate the action potential. Once initiated, the action potential is self-propagating and unstoppable.
4. As the action potential travels away from a region, Na^+ channels close and voltage-gated K^+ channels open, repolarizing the membrane.
5. In excitation-contraction coupling the action potential is propagated down the T tubules, causing calcium to be released from the SR into the cytosol.
6. Sliding of the filaments is triggered by a rise in intracellular calcium ion levels. Troponin binding of calcium moves tropomyosin away from myosin-binding sites on actin, allowing cross bridge binding. Myosin ATPases split ATP, which energizes the power strokes. ATP binding to the myosin head is necessary for cross bridge detachment. Cross bridge activity ends when calcium is pumped back into the SR.

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9.5 Temporal summation and motor unit recruitment allow smooth, graded skeletal muscle contractions (pp. 298–303)

1. A motor unit is one motor neuron and all the muscle cells it innervates. The neuron's axon has several branches, each of which forms a neuromuscular junction with one muscle cell.
2. A motor unit's response to a single brief threshold stimulus is a twitch. A twitch has three phases: latent (preparatory events occur), contraction (the muscle tenses and may shorten), and relaxation (muscle tension declines and the muscle returns to its resting length).
3. Graded responses of muscles to rapid stimuli are temporal summation and unfused and fused tetanus. A graded response to increasingly strong stimuli is multiple motor unit summation, or recruitment. The order of motor unit recruitment follows the size principle.
4. Isotonic contractions occur when the muscle shortens (concentric contraction) or lengthens (eccentric contraction) as the load is moved. Isometric contractions occur when muscle tension produces neither shortening nor lengthening.

9.6 ATP for muscle contraction is produced aerobically or anaerobically (pp. 303–306)

1. The energy source for muscle contraction is ATP, obtained from a coupled reaction of creatine phosphate with ADP and from aerobic and anaerobic metabolism of glucose.
2. When ATP is produced by anaerobic pathways, lactic acid accumulates and ionic imbalances disturb the membrane potential. To return the muscles to their pre-exercise state, ATP must be produced aerobically and used to regenerate creatine phosphate, glycogen reserves must be restored, and accumulated lactic acid must be metabolized. Oxygen used to accomplish this repayment is called excess postexercise oxygen consumption (EPOC).

9.7 The force, velocity, and duration of skeletal muscle contractions are determined by a variety of factors (pp. 306–309)

1. The force of muscle contraction is affected by the number and size of contracting muscle cells (the more and the larger the cells, the greater the force), the frequency of stimulation, and the degree of muscle stretch.
2. When the thick and thin filaments are optimally overlapping, the muscle can generate maximum force. With excessive increase or decrease in muscle length, force declines.
3. Factors determining the velocity and duration of muscle contraction are muscle fiber types, the load (the greater the load, the slower the contraction), and how many motor units are recruited.
4. The three types of muscle fibers are: (1) fast glycolytic (fatigable) fibers, (2) slow oxidative (fatigue-resistant) fibers, and (3) fast oxidative (fatigue-resistant) fibers. Most muscles contain a mixture of fiber types. The fast muscle fiber types can interconvert with certain exercise regimens.

9.8 How does skeletal muscle respond to exercise? (pp. 309–310)

1. Regular aerobic exercise gives skeletal muscles increased efficiency, endurance, strength, and resistance to fatigue.
2. In skeletal muscle, resistance exercises cause hypertrophy and large gains in strength.
3. Immobilizing muscles leads to muscle weakness and severe atrophy.

9.9 Smooth muscle is nonstriated involuntary muscle (pp. 310–316)

1. Smooth muscle cells are most often arranged in sheets. They lack elaborate connective tissue coverings.

Differences between Smooth and Skeletal Muscle Fibers (pp. 311–314)

2. A smooth muscle fiber is spindle shaped and uninucleate, and has no striations.
3. The SR is poorly developed and T tubules are absent. Actin and myosin filaments are present, but sarcomeres are not. Intermediate filaments and dense bodies form an intracellular network that harnesses the pull generated during cross bridge activity and transfers it to the surrounding connective tissue.

Contraction of Smooth Muscle (pp. 314–316)

4. Smooth muscle fibers may be electrically coupled by gap junctions.
5. ATP energizes smooth muscle contraction, which is activated by a calcium pulse. However, calcium binds to calmodulin rather than to troponin (which is not present in smooth muscle fibers), and myosin must be phosphorylated to become active in contraction.
6. Smooth muscle contracts for extended periods at low energy cost and without fatigue.
7. Neurotransmitters of the autonomic nervous system may inhibit or stimulate smooth muscle fibers. Smooth muscle contraction may also be initiated by pacemaker cells, hormones, or local chemical factors that influence intracellular calcium levels, and by mechanical stretch.
8. Special features of smooth muscle contraction include the stress-relaxation response and the ability to generate large amounts of force when extensively stretched.

Types of Smooth Muscle (p. 316)

9. Unitary smooth muscle has electrically coupled fibers that contract synchronously and often spontaneously.
10. Multi unit smooth muscle has independent, well-innervated fibers that lack gap junctions and pacemaker cells. Stimulation occurs via autonomic nerves (or hormones). Multi unit muscle contractions are rarely synchronous.

Developmental Aspects of Muscles (pp. 316, 317, 319)

1. Muscle tissue develops from embryonic mesoderm cells called myoblasts. Several myoblasts fuse to form a skeletal muscle fiber. Smooth and cardiac muscle cells develop from single myoblasts and display gap junctions.
2. For the most part, specialized skeletal and cardiac muscle cells lose their ability to divide but retain the ability to hypertrophy. Smooth muscle regenerates well and its cells are able to divide throughout life.
3. Skeletal muscle development reflects maturation of the nervous system and occurs in head-to-toe and proximal-to-distal directions. Natural neuromuscular control reaches its peak in midadolescence.
4. Women's muscles account for about 36% of their total body weight and men's for about 42%, a difference due chiefly to the effects of male sex hormones on skeletal muscle growth.
5. Skeletal muscle is richly vascularized and quite resistant to infection, but in old age, skeletal muscles become fibrous, decline in strength, and atrophy. Regular exercise can offset some of these changes.

REVIEW QUESTIONS

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Level 1 Remember/Understand

(Some questions have more than one correct answer. Select the best answer or answers from the choices given.)

1. The connective tissue covering that encloses the sarcolemma of an individual muscle fiber is called the **(a)** epimysium, **(b)** perimysium, **(c)** endomysium, **(d)** periosteum.
2. A fascicle is a **(a)** muscle, **(b)** bundle of muscle fibers enclosed by a connective tissue sheath, **(c)** bundle of myofibrils, **(d)** group of myofilaments.
3. Thick and thin myofilaments have different compositions. For each descriptive phrase, indicate whether the filament is **(a)** thick or **(b)** thin.

   ___**(1)** contains actin
   ___**(2)** contains ATPases
   ___**(3)** attaches to the Z disc
   ___**(4)** contains myosin
   ___**(5)** contains troponin
   ___**(6)** does not lie in the I band
4. The function of the T tubules in muscle contraction is to **(a)** make and store glycogen, **(b)** release Ca^{2+} into the cell interior and then pick it up again, **(c)** transmit the action potential deep into the muscle cells, **(d)** form proteins.
5. The sites where the motor nerve impulse is transmitted from the nerve endings to the skeletal muscle cell membranes are the **(a)** neuromuscular junctions, **(b)** sarcomeres, **(c)** myofilaments, **(d)** Z discs.
6. Contraction elicited by a single brief stimulus is called **(a)** a twitch, **(b)** temporal summation, **(c)** multiple motor unit summation, **(d)** fused tetanus.
7. A smooth, sustained contraction resulting from very rapid stimulation of the muscle, in which no evidence of relaxation is seen, is called **(a)** a twitch, **(b)** temporal summation, **(c)** multiple motor unit summation, **(d)** fused tetanus.
8. Characteristics of isometric contractions include all but **(a)** shortening, **(b)** increased muscle tension throughout the contraction phase, **(c)** absence of shortening, **(d)** used in resistance training.
9. During muscle contraction, ATP is provided by **(a)** a coupled reaction of creatine phosphate with ADP, **(b)** aerobic respiration of glucose, and **(c)** anaerobic glycolysis.

   ___**(1)** Which provides ATP fastest?
   ___**(2)** Which does (do) not require that oxygen be available?
   ___**(3)** Which provides the highest yield of ATP per glucose molecule?
   ___**(4)** Which results in the formation of lactic acid?
   ___**(5)** Which has carbon dioxide and water products?
   ___**(6)** Which is most important in endurance sports?
10. The neurotransmitter released by somatic motor neurons is **(a)** acetylcholine, **(b)** acetylcholinesterase, **(c)** norepinephrine.
11. The ions that enter the skeletal muscle cell during the generation of an action potential are **(a)** calcium ions, **(b)** chloride ions, **(c)** sodium ions, **(d)** potassium ions.
12. Myoglobin has a special function in muscle tissue. It **(a)** breaks down glycogen, **(b)** is a contractile protein, **(c)** holds a reserve supply of oxygen in the muscle.

13. Aerobic exercise results in all of the following except **(a)** more capillaries surrounding muscle fibers, **(b)** more mitochondria in muscle cells, **(c)** increased size and strength of existing muscle cells, **(d)** more myoglobin.
14. The smooth muscle type found in the walls of digestive and urinary system organs and that exhibits gap junctions and pacemaker cells is **(a)** multi unit, **(b)** unitary.

Level 2 Apply/Analyze

15. Name and describe the four special functional abilities of muscle that are the basis for muscle response.
16. Distinguish between **(a)** direct and indirect muscle attachments and **(b)** a tendon and an aponeurosis.
17. What is the importance of acetylcholinesterase in muscle cell contraction?
18. Explain what is meant by the term excitation-contraction coupling.
19. Define and draw a motor unit.
20. True or false: Most muscles contain a predominance of one skeletal muscle fiber type. Explain the reasoning behind your choice.
21. Describe some cause(s) of muscle fatigue and define this term clearly.
22. When a suicide victim was found, the coroner was unable to remove the drug vial clutched in his hand. Explain the reasons for this. If the victim had been discovered three days later, would the coroner have had the same difficulty? Explain.

Level 3 Evaluate/Synthesize

23. **(a)** Describe the structure of a sarcomere and indicate the relationship of the sarcomere to myofilaments. **(b)** Explain the sliding filament model of contraction using appropriately labeled diagrams of a relaxed and a contracted sarcomere.
24. Explain how a slight (but smooth) contraction differs from a vigorous contraction of the same muscle. Use the concepts of multiple motor unit summation.
25. Smooth muscle has some unique properties, such as low energy usage, and the ability to maintain contraction over long periods. Tie these properties to the function of smooth muscle in the body.
26. Muscle-relaxing drugs are administered to a patient during major surgery. Which of the two chemicals described next would be a good skeletal muscle relaxant and why?
    - Chemical A binds to and blocks ACh receptors of muscle cells.
    - Chemical B floods the muscle cells' cytoplasm with Ca^{2+}.

CLINICAL CASE STUDY

Children with Muscular Disorders

You're doing a clinical rotation with Dr. Barr, a world-renowned specialist in children's muscle disorders. On your first day, you meet three patients with the same probable diagnosis—nemaline myopathy. Jodi, age 2, has a waddling walk and difficulty standing; Linda, 6 months, has pneumonia associated with problems swallowing; and Tom, 12, has progressive weakness with foot drop and difficulty walking.

"This kind of variation is not surprising," says Dr. Barr. "A mutation in one of 11 different genes related to thin filaments can cause nemaline myopathy, so you'd expect to see it present in different ways."

Dr. Barr has scheduled all three children for a muscle biopsy (surgical removal of a small piece of muscle tissue for examination). He explains to you, "We're going to use these biopsies for two things. First, we're going to look for the characteristic histology of nemaline myopathy. Second, we're going to test for malignant hyperthermia. It's not associated with nemaline myopathy but is associated with a different myopathy that has a similar presentation."

1. What does actin do? What consequences would you expect from an abnormality in actin?
2. What does troponin do?
3. All types of nemaline myopathy cause weakness, including the ones with abnormal troponin. How could abnormal troponin cause weakness?

Malignant hyperthermia is caused by a mutation in a gene related to calcium storage and release in skeletal muscle cells. In individuals with malignant hyperthermia, certain anesthetics can trigger a massive release of calcium into the cytoplasm. This leads to the generation of enough heat to substantially raise body temperature—a life-threatening reaction.

4. NCLEX-STYLE Which statement best describes the importance of calcium in skeletal muscle contraction?
   a. Extracellular calcium entering through ion channels binds to troponin to initiate muscle contraction.
   b. Extracellular calcium entering through ion channels binds to tropomyosin to initiate muscle contraction.
   c. Calcium released from the sarcoplasmic reticulum binds to tropomyosin to initiate muscle contraction.
   d. Calcium released from the sarcoplasmic reticulum binds to troponin to initiate muscle contraction.
5. What is the function of the sarcoplasmic reticulum?
6. NCLEX-STYLE Which statement best describes what might happen if a child with malignant hyperthermia is given the wrong anesthetic and the sarcoplasmic reticulum releases all its calcium?
   a. The muscles become weak and the child is unable to breathe.
   b. The blood calcium levels rise and the bones become weak.
   c. Continuous cross bridge cycling causes the muscle to contract too much.
   d. The troponin and tropomyosin stop moving off the myosin-binding sites of actin and the muscles become paralyzed.
7. Histology confirms nemaline myopathy in all three children. They are prescribed resistance training to strengthen their respiratory muscles. How will this affect their muscle cells?