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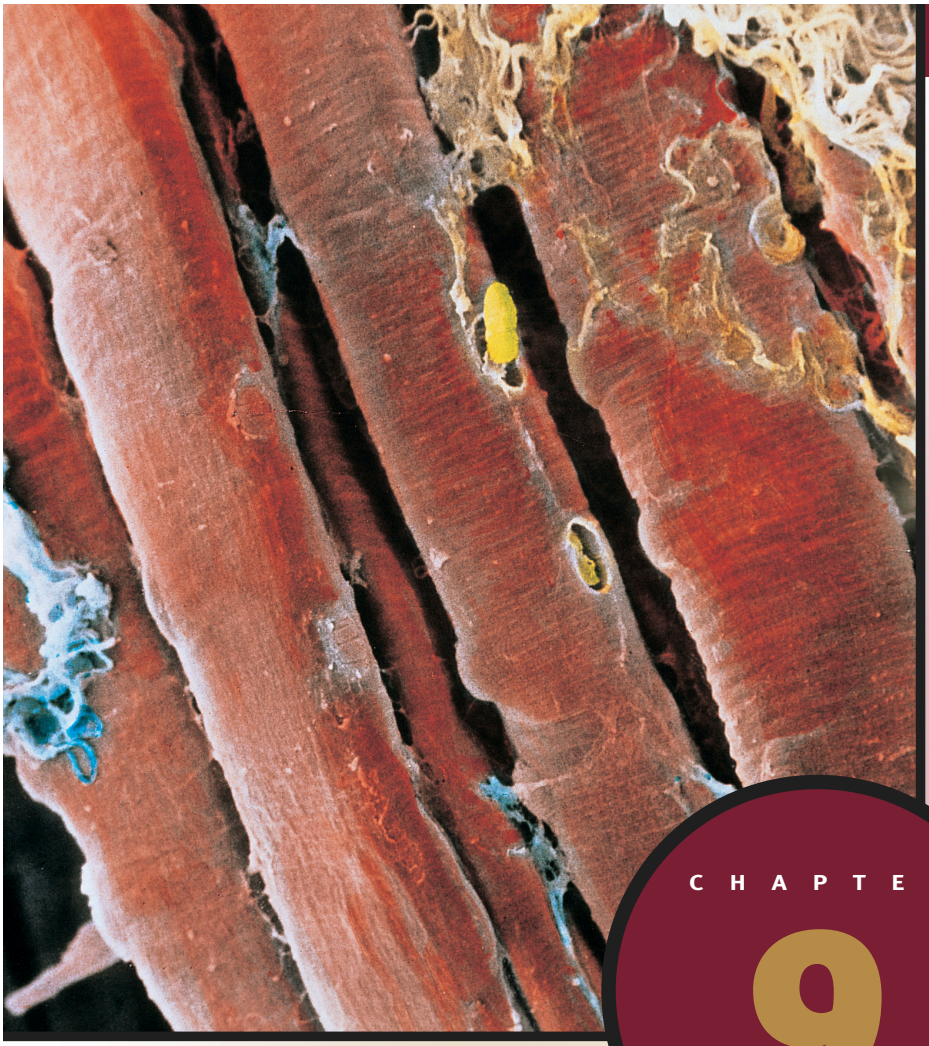


Color-enhanced scanning electron micrograph of skeletal muscle fibers.

Muscular System

Histology and Physiology

CHAPTER 9

Movements of the limbs, heart, and other parts of the body are made possible by muscle cells that function like tiny motors. Muscle cells use energy extracted from nutrient molecules much like motors use energy provided by electric current. The nervous system regulates and coordinates muscle cells so that smooth, coordinated movements are produced much like a computer regulates and coordinates several motors in robotic machines used to perform some assembly line functions.

This chapter presents the *functions of the muscular system* (272), *general functional characteristics of muscle* (272), and *skeletal muscle structure* (273). The *sliding filament model* (278) of muscle contraction is explained. The *physiology of skeletal muscle fibers* (278), the *physiology of skeletal muscle* (287), the *types of muscle contractions* (292), *fatigue* (294), *energy sources* (296), *slow and fast fibers* (297), and *heat production* (299) are presented. The structure and function of *smooth muscle* (299) and *cardiac muscle* (303) are introduced, but cardiac muscle is discussed in greater detail in chapter 20. Finally the *effects of aging on skeletal muscle* (304) are presented. Because skeletal muscle is more abundant and more is known about it, skeletal muscle is examined in the greatest detail.

Functions of the Muscular System

Objective

- ***Describe the major functions of muscle.***

Movements within the body are accomplished by cilia or flagella on the surface of some cells, by the force of gravity, or by the contraction of muscles. Most of the body's movements, from the beating of the heart to running a marathon, result from muscle contractions. As described in chapter 4, there are three types of muscle tissue: skeletal, smooth, and cardiac. The major functions of muscles are:

1. *Body movement.* Most skeletal muscles are attached to bones, are typically under conscious control, and are responsible for most body movements including walking, running, or manipulating objects with the hands.
2. *Maintenance of posture.* Skeletal muscles constantly maintain tone, which keeps us sitting or standing erect.
3. *Respiration.* Muscles of the thorax are responsible for the movements necessary for respiration.
4. *Production of body heat.* When skeletal muscles contract, heat is given off as a by-product. This released heat is critical to the maintenance of body temperature.
5. *Communication.* Skeletal muscles are involved in all aspects of communication, such as speaking, writing, typing, gesturing, and facial expression.
6. *Constriction of organs and vessels.* The contraction of smooth muscle within the walls of internal organs and vessels causes constriction of those structures. This constriction can help propel and mix food and water in the digestive tract, propel secretions from organs, and regulate blood flow through vessels.
7. *Heart beat.* The contraction of cardiac muscle causes the heart to beat, propelling blood to all parts of the body.

1. List the functions of skeletal, smooth, and cardiac muscles and explain how each is accomplished.

General Functional Characteristics of Muscle

Objectives

- ***Describe the major properties of muscle.***
- ***List the major types of muscle tissue, and describe their general characteristics.***

Muscle tissue is highly specialized to contract, or shorten, forcefully. The process of metabolism extracts energy from nutrient molecules. Part of that energy is used for muscle contraction and the remainder is used for other cell processes or is released as heat.

Properties of Muscle

Muscle has four major functional properties: contractility, excitability, extensibility, and elasticity.

1. **Contractility** is the ability of muscle to shorten with a force. When muscle contracts, it causes movement of the structures to which it is attached, or it may increase pressure inside hollow organs or vessels. Although muscle shortens forcefully during contraction, it lengthens passively; that is, gravity, contraction of an opposing muscle, or the pressure of fluid in a hollow organ or vessel produces a force that acts on the shortened muscle, causing it to lengthen.
2. **Excitability** is the capacity of muscle to respond to a stimulus. Normally skeletal muscle contracts as a result of stimulation by nerves. Smooth muscle and cardiac muscle can contract without outside stimuli, but they also respond to stimulation by nerves and hormones.
3. **Extensibility** means that muscle can be stretched to its normal resting length and beyond to a limited degree.
4. **Elasticity** is the ability of muscle to recoil to its original resting length after it has been stretched.

Types of Muscle Tissue

Table 9.1 provides a comparison of the major characteristics of skeletal, smooth, and cardiac muscle. Skeletal muscle with its associated connective tissue constitutes about 40% of the body's weight and is responsible for locomotion, facial expressions, posture, respiratory movements, and many other body movements. The nervous system voluntarily, or consciously, controls the functions of the skeletal muscles.

Smooth muscle is the most widely distributed type of muscle in the body, and it has the greatest variety of functions. It's in the walls of hollow organs and tubes, the interior of the eye, the walls of blood vessels, and other areas. Smooth muscle performs a variety of functions, including propelling urine through the urinary tract, mixing food in the stomach and intestine, dilating and constricting the pupils, and regulating the flow of blood through blood vessels.

Cardiac muscle is found only in the heart, and its contractions provide the major force for moving blood through the circulatory system. Unlike skeletal muscle, cardiac muscle and many smooth muscles are autorhythmic, that is, they contract spontaneously at somewhat regular intervals, and nervous or hormonal stimulation is not always required for them to contract. Furthermore, unlike skeletal muscle, smooth muscle and cardiac muscle are not consciously controlled by the nervous system. Rather, they are controlled involuntarily, or unconsciously by the autonomic nervous system and the endocrine system (see chapters 16 and 18).

2. Define contractility, excitability, extensibility, and elasticity of muscle tissue.

Table 9.1 Comparison of Muscle Types

Features	Skeletal Muscle	Smooth Muscle	Cardiac Muscle
Location	Attached to bones	Walls of hollow organs, blood vessels, eyes, glands, and skin	Heart
Cell shape	Very long and cylindrical (1 mm–4 cm in length and may extend the entire length of short muscles; 10–100 µm in diameter)	Spindle-shaped (15–200 µm in length and 5–8 µm in diameter)	Cylindrical and branched (100–500 µm in length; 12–20 µm in diameter)
Nucleus	Multiple, peripherally located	Single, centrally located	Single, centrally located
Special cell–cell attachments	None	Gap junctions join some visceral smooth muscle cells together	Intercalated disks join cells to one another
Striations	Yes	No	Yes
Control	Voluntary and involuntary (reflexes)	Involuntary	Involuntary
Capable of spontaneous contraction	No	Yes (some smooth muscle)	Yes
Function	Body movement	Food movement through the digestive tract, emptying of the urinary bladder, regulation of blood vessel diameter, change in pupil size, contraction of many gland ducts, movement of hair, and many other functions	Pumps blood; contractions provide the major force for propelling blood through blood vessels

3. *Compare the structure, function, location, and control of the three major muscle tissue types.*

Skeletal Muscle Structure

Objectives

- *Describe the structure of a muscle, including its connective tissue elements, blood vessels, and nerves.*
- *Diagram the arrangement of myofilaments, myofibrils, sarcomeres, and sarcoplasmic reticulum in a muscle fiber.*

Skeletal muscles are composed of skeletal **muscle fibers** associated with smaller amounts of connective tissue, blood vessels, and nerves. Skeletal muscle fibers are skeletal muscle cells. Each skeletal muscle fiber is a single cylindrical cell containing several nuclei located around the periphery of the fiber near the plasma membrane (figure 9.1). Muscle fibers develop from less mature multinucleated cells called **myoblasts** (mī′ō-blasts). Their multiple nuclei result from the fusion of myoblast precursor cells and not from the division of nuclei within myoblasts. Myoblasts are converted to muscle fibers as contractile proteins accumulate within their cytoplasm. Shortly after the myoblasts form, nerves grow into the area and innervate the developing muscle fibers.

The number of skeletal muscle fibers remains relatively constant after birth. Enlargement, or hypertrophy, of muscles after birth therefore results not from a substantial increase in the

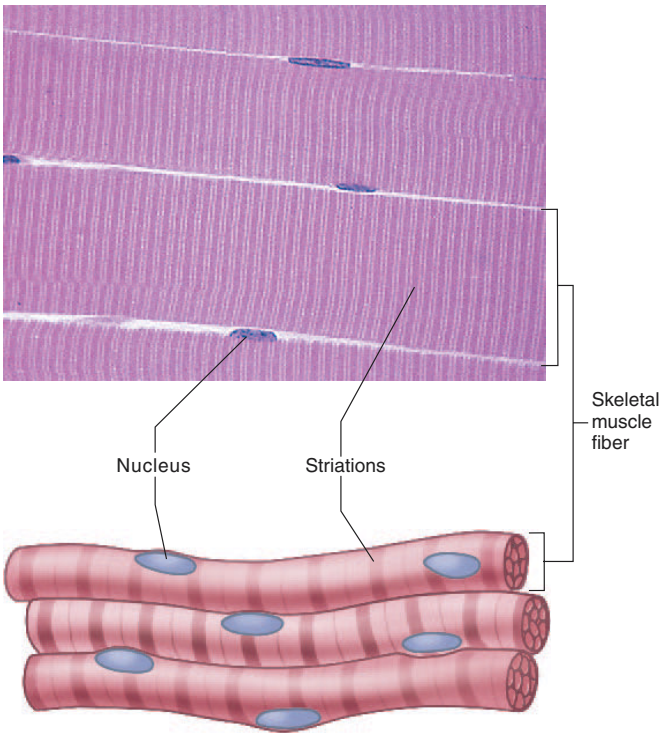


Figure 9.1 Skeletal Muscle Fibers
Skeletal muscle fibers in longitudinal section.

number of muscle fibers, but from an increase in their size. Similarly, hypertrophy of muscles in response to exercise is due mainly to an increase in muscle fiber size, rather than a substantial increase in number.

As seen in longitudinal section, alternating light and dark bands give the muscle fiber a **striated** (strī′āt-ĕd; banded), or striped, appearance (see figure 9.1). A single fiber can extend from one end of a small muscle to the other, but several muscle fibers arranged end to end are required to extend the full length of most longer muscles. Muscle fibers range from approximately 1 mm to about 4 cm in length and from 10–100 μm in diameter. Large muscles contain large-diameter fibers, whereas small, delicate muscles have small-diameter fibers. All the muscle fibers in a given muscle have similar dimensions.

Connective Tissue

Surrounding each muscle fiber is a delicate **external lamina** (lam′i-nă) composed primarily of reticular fibers. This external lamina is produced by the muscle fiber and, when observed through a light microscope, cannot be distinguished from the plasma membrane of the muscle fiber, the **sarcolemma** (sar′kō-lem′ă). The prefix *sarco-* (G. flesh) refers to muscle or resembling flesh and is used to name some structures found in muscle cells. The **endomysium** (en′dō-miz′ē-ŭm, en′dō-mis′ē-ŭm; G. mys, muscle), a delicate network of loose connective tissue with numerous reticular fibers, surrounds each muscle fiber outside the external lamina (figure 9.2). A bundle of muscle fibers with their endomysium is surrounded by another, heavier connective tissue layer called the **perimysium** (per′ĭ-mis′ē-ŭm, per′ĭ-miz′ē-ŭm). Each bundle ensheathed by perimysium is a muscle **fasciculus** (fă-sik′ū-lŭs). A muscle consists of many fasciculi grouped together and surrounded by a third and heavier layer, the **epimysium** (ep-ĭ-mis′ē-ŭm), which is composed of dense, collagenous connective tissue and covers the entire surface of the muscle.

Fascia (fash′ē-ă) is connective tissue that covers the body by forming a sheet of tissue under the skin; it also surrounds individual muscles or groups of muscles. The fascia around an individual muscle is also called epimysium. The connective tissue components of muscles are continuous with one another. At the end of muscles, the connective tissue components are continuous with the connective tissue of tendons and the periosteum of bone (see chapter 6). The connective tissue of muscle holds the muscle cells together and attaches muscles to tendons and bones.

Nerve and Blood Vessels

The nerves and blood vessels that extend to skeletal muscles are abundant. **Motor neurons** are specialized nerve cells. Their cell bodies are located in the brainstem or spinal cord and their axons extend to skeletal muscle fibers through nerves. The motor neurons stimulate muscles to contract. An artery and either one or two veins extend together with a nerve through the connective tissue layers of skeletal muscles (see figure 9.2). Numerous branches of the arteries supply the extensive capillary beds surrounding the muscle fibers, and blood is carried away from the capillary beds by branches of the veins. At the level of the perimysium, the axons of motor neurons branch repeatedly, each branch projecting toward the center of one muscle fiber. The contact between the axons and the muscle fibers, called synapses, or neuromuscular junctions, are described later in the chapter (see section on "Neuromuscular Junction" on page 282). Each motor neuron innervates more than one muscle fiber, and every muscle fiber receives a branch of an axon.

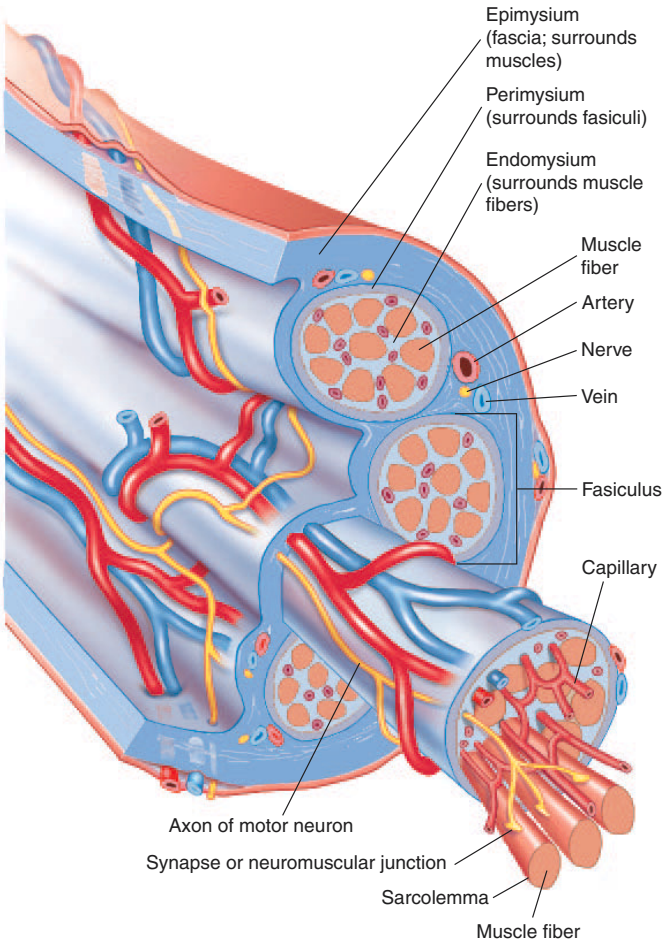


Figure 9.2 Skeletal Muscle Structure: Connective Tissue, Innervation, and Blood Supply

Relationship between muscle fibers, fasciculi, and associated connective tissue layers: the epimysium, perimysium, and endomysium. Arteries, veins, and nerves course together through the connective tissue of muscles. They branch frequently as they approach individual muscle fibers. At the level of the perimysium, axons of neurons branch and each branch extends to a muscle fiber.

Muscle Fibers

The many nuclei of each muscle fiber lie just inside the sarcolemma, whereas most of the interior of the fiber is filled with myofibrils (figure 9.3). Other organelles, such as the numerous mitochondria and glycogen granules, are packed between the myofibrils. The cytoplasm without the myofibrils is called **sarcoplasm** (sar′kō-plazm). Each **myofibril** (mī-ō-fī′bril) is a threadlike structure approximately 1–3 μm in diameter that extends from one end of the muscle fiber to the other. Myofibrils are composed of two kinds of protein filaments called **myofilaments**

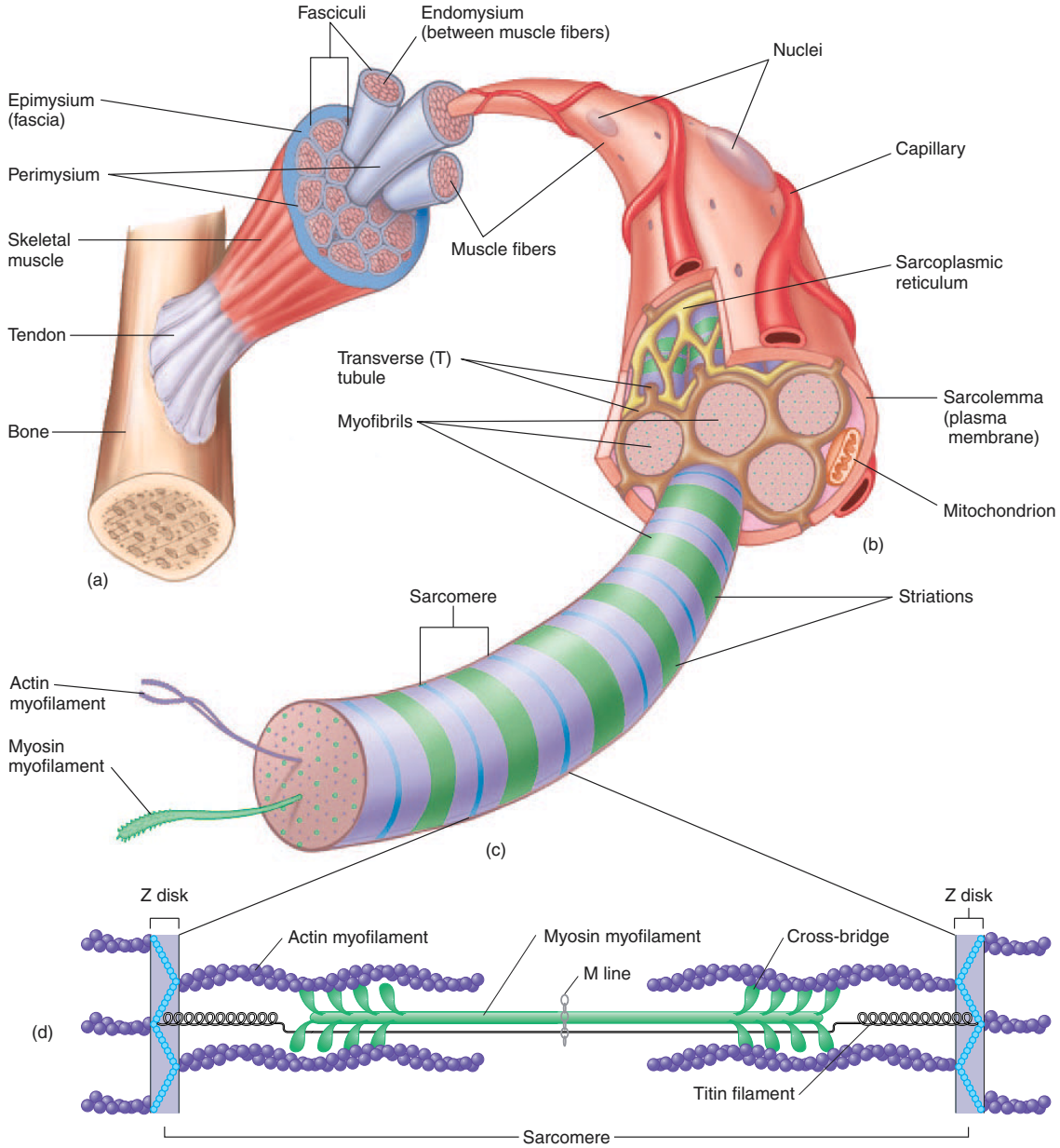


Figure 9.3 Parts of a Muscle

(*a*) Part of a muscle attached by a tendon to a bone. A muscle is composed of muscle fasciculi, each surrounded by perimysium. The fasciculi are composed of bundles of individual muscle fibers (muscle cells), each surrounded by endomysium. (*b*) Enlargement of one muscle fiber. The muscle fiber contains several myofibrils. (*c*) A myofibril extended out the end of the muscle fiber. The banding patterns of the sarcomeres are shown in the myofibril. (*d*) A single sarcomere of a myofibril is composed of actin myofilaments and myosin myofilaments. The Z disk anchors the actin myofilaments, and the myosin myofilaments are held in place by titin molecules and the M line.

(mī-ō-fil′ă-ments). **Actin** (ak′tin) **myofilaments,** or thin myofilaments, are approximately 8 nanometers (nm) in diameter and 1000 nm in length, whereas **myosin** (mī′ō-sin) **myofilaments,** or thick myofilaments, are approximately 12 nm in diameter and 1800 nm in length. The actin and myosin myofilaments are organized in highly ordered units called **sarcomeres** (sar′kō-mērz), which are joined end to end to form the myofibrils (figure 9.4*a*).

Actin and Myosin Myofilaments

Each actin myofilament is composed of two strands of **fibrous actin (F actin),** a series of **tropomyosin** (trō-pō-mī′ō-sin) **molecules,** and a series of **troponin** (trō′pō-nin) **molecules** (figure 9.4*b* and *c*). The two strands of F actin are coiled to form a double helix that extends the length of the actin myofilament. Each F actin strand is a polymer of approximately 200 small globular units called **globular actin (G actin)** monomers. Each G actin monomer has an active site to which myosin molecules can bind during muscle contraction. Tropomyosin is an elongated protein that winds along the groove of the F actin double helix. Each tropomyosin molecule is sufficiently long to cover seven G actin active sites. Troponin is composed of three subunits: one that binds to actin, a second that binds to tropomyosin, and a third that binds to calcium ions. The troponin molecules are spaced between the ends of the tropomyosin molecules in the groove between the F actin strands. The complex of tropomyosin and troponin regulates the interaction between active sites on G actin and myosin.

Myosin myofilaments are composed of many elongated **myosin molecules** shaped like golf clubs (see figure 9.4*b* and *c*). Each myosin molecule consists of two **heavy myosin molecules** wound together to form a **rod portion** lying parallel to the myosin

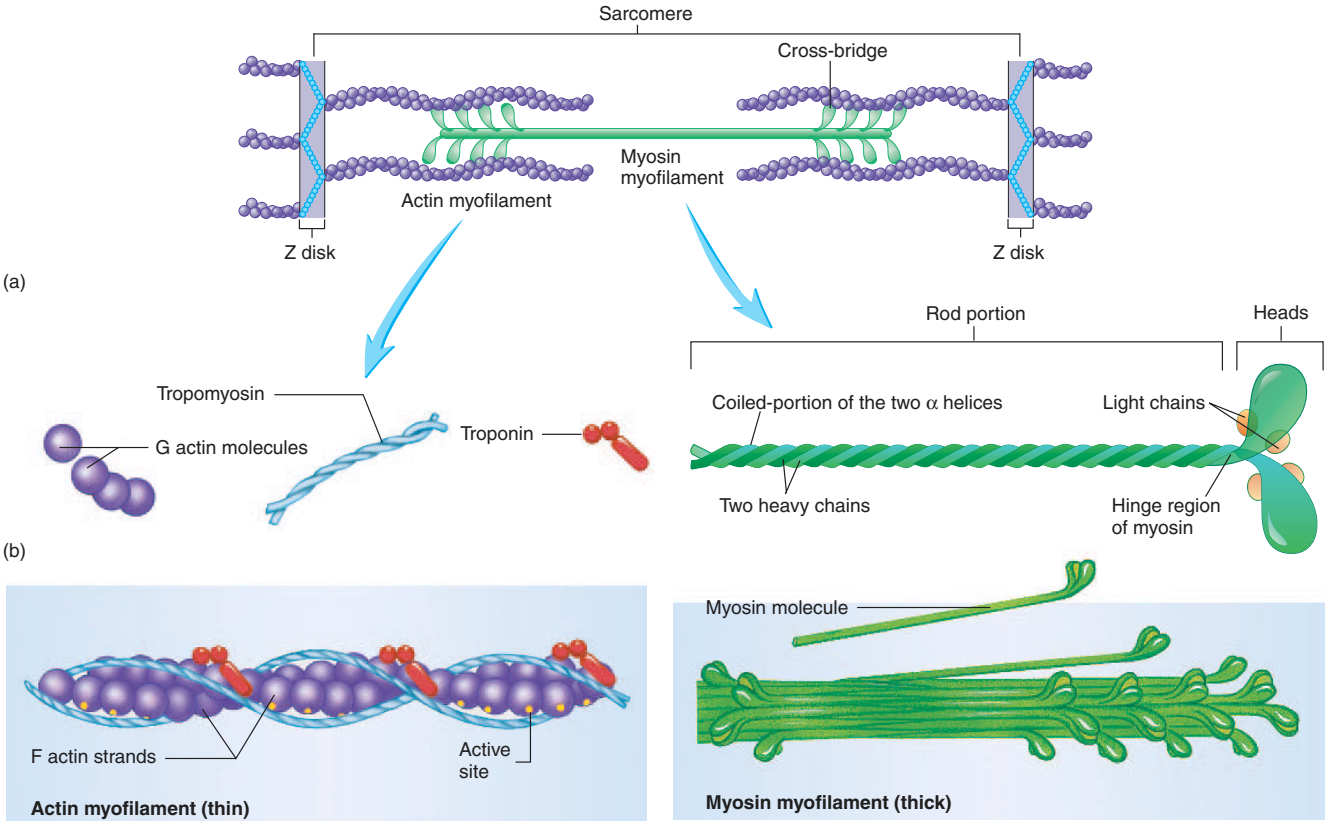


Figure 9.4 Structure of Actin and Myosin

(*a*) The sarcomere consists of actin (thin) and myosin (thick) myofilaments. The actin myofilaments are attached to Z disks and myosin myofilaments are suspended between the actin myofilaments. (*b*) Actin myofilaments are composed of individual globular actin (G actin) molecules (purple spheres), tropomyosin molecules (blue strands), and troponin (red spheres). A myosin molecule (green) is a golf-club-shaped structure composed of two molecules of heavy myosin wound together to form the rod portion and a double globular head. Four smaller light myosin molecules are located on the heads of the myosin molecule. (*c*) G actin molecules, tropomyosin molecules, and troponin molecules are assembled into a single actin myofilament. Active sites are located on the G actin molecules. Myosin myofilaments are composed of many individual golf-club-shaped myosin molecules. The rod portions are in parallel arrangement, with all the heads pointing in the same direction at one end and in the opposite direction at the other end of the myosin myofilament.

myofilament and two **heads** that extend laterally (see figure 9.4*b* and figure 9.3*d*). Four light myosin chains are attached to the heads of each myosin molecule. Each myosin myofilament consists of about 300 myosin molecules arranged so that about 150 of them have their heads projecting toward each end. The centers of the myosin myofilaments consist of only the rod portions of the myosin molecules. The myosin heads have three important properties: (1) The heads can bind to active sites on the actin molecules to form **cross-bridges.** (2) The heads are attached to the rod portion by a hinge region that can bend and straighten during contraction. (3) The heads have ATPase activity, the enzymatic activity that breaks down adenosine triphosphate (ATP), releasing energy. Part of the energy is used to bend the hinge region of the myosin molecule during contraction.

Sarcomeres

Each sarcomere extends from one Z disk to an adjacent Z disk (see figure 9.4 and figure 9.5). A **Z disk** is a filamentous network of protein forming a disklike structure for the attachment of actin myofilaments

(a) Electron micrograph of longitudinal section of a skeletal muscle fiber showing several sarcomeres, with A bands, I bands, Z disks, H zones, and M lines

(b) The arrangement of I and A bands, H zones, Z disks, and M lines in sarcomeres

(c) Cross sections through regions of the sarcomeres are indicated by gray bars

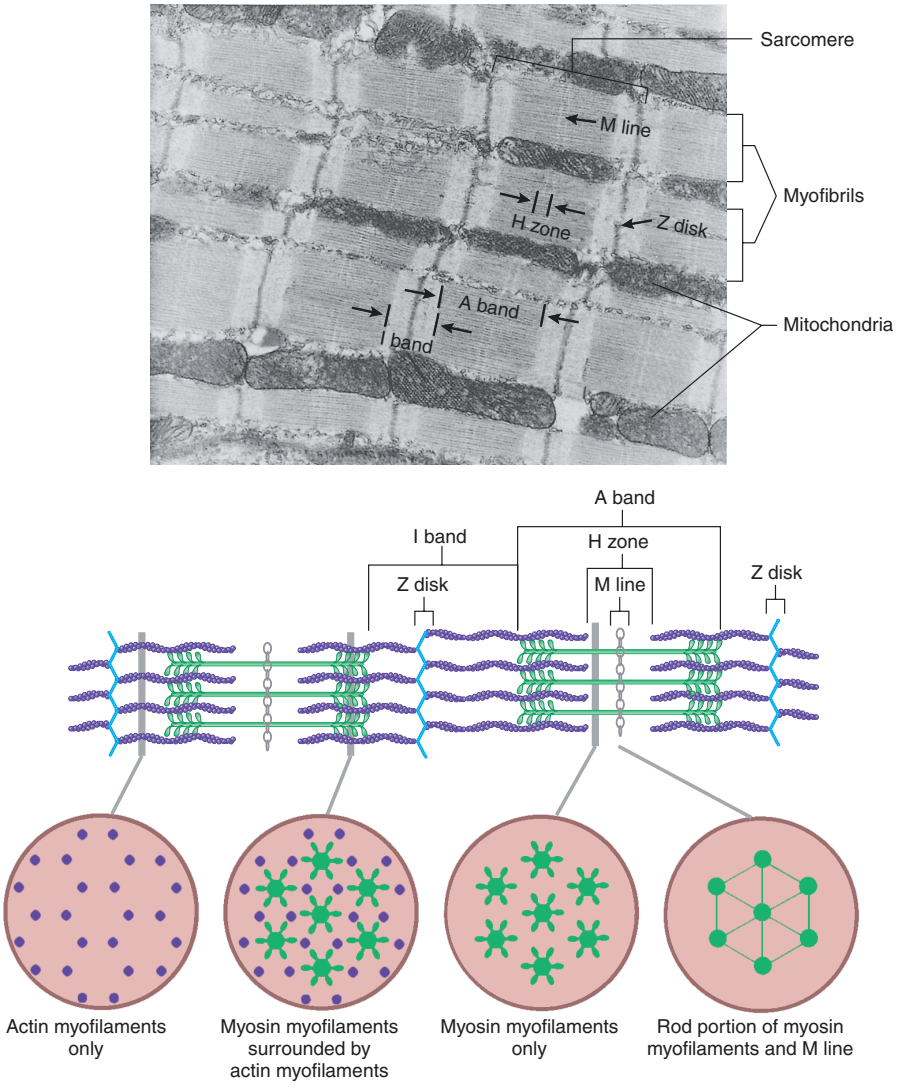


Figure 9.5 Components of Sarcomeres

(*a*) Electron micrograph of longitudinal section of a skeletal muscle fiber showing several sarcomeres, with A bands, I bands, Z disks, H zones, and M lines. (*b*) The arrangement of I and A bands, H zones, Z disks, and M lines in sarcomeres. (*c*) Cross sections through regions of the sarcomeres are indicated by gray bars.

(see figure 9.5). The arrangement of the actin myofilaments and myosin myofilaments gives the myofibril a banded, or striated, appearance when viewed longitudinally. Each **isotropic** (ī-sō-trop′ik) (light band), or **I, band** includes a Z disk and extends from either side of the Z disk to the ends of the myosin myofilaments. When seen in longitudinal and cross sections, the I band on either side of the Z disk consists only of actin myofilaments. Each **anisotropic** (an-ī-sō-trop′ik) (dark band), or **A, band** extends the length of the myosin myofilaments within a sarcomere. The actin and myosin myofilaments overlap for some distance at both ends of the A band. In a cross section of the A band in the area where actin and myosin myofilaments overlap, each myosin myofilament is visibly surrounded by six actin myofilaments. In the center of each A band is a smaller band called the **H zone,** where the actin and myosin myofilaments do not overlap and only myosin myofilaments are present. A dark band called the **M line** is in the middle of the H zone and consists of delicate filaments that attach to the center of the myosin myofilaments. The M line helps to hold the myosin myofilaments in place similar to the way the Z disk holds actin myofilaments in place (figure 9.5*b* and *c*). The numerous myofibrils are oriented within each muscle fiber so that A bands and I bands of parallel myofibrils are aligned and thus produce the striated pattern seen through a microscope.

What Makes Muscles Extensible and Elastic?

In addition to actin and myosin, there are other less visible proteins within sarcomeres. These proteins help to hold actin and myosin in place, and one of them accounts for muscle's ability to stretch (extensibility) and recoil (elasticity). **Titin** (tī′tin) (see figure 9.3) is one of the largest known proteins, consisting of a single chain of nearly 27,000 amino acids. It attaches to Z disks and extends along myosin myofilaments to the M line. The myosin myofilaments are attached to the titin molecules, which help to hold them in position. Part of the titin molecule in the I band functions like a spring, allowing the sarcomere to stretch and recoil. Another large protein, called **nebulin** (neb′ū-lin), appears to hold the thin filaments in place. These proteins extend from each side of the Z disk and along the actin myofilaments. Each nebulin molecule is as long as an actin myofilament.

4. *Define skeletal muscle fiber. Do the number of muscle fibers increase significantly after birth?*
5. *Name the connective tissue structures that surround muscle fibers, muscle fasciculi, and whole muscles. Define sarcolemma and fascia.*
6. *What are motor neurons? How do the axons of motor neurons and blood vessels extend to muscle fibers?*
7. *Define sarcoplasm, myofibril, and myofilament.*
8. *How do G actin, tropomyosin, and troponin combine to form an actin myofilament? Name the three subunits of troponin.*
9. *Describe the structure of myosin molecules and how they combine to form a myosin myofilament.*
10. *List three important properties of the myosin head. What is a cross-bridge?*
11. *How are Z disks, actin myofilaments, myosin myofilaments, and M lines arranged to form a sarcomere? Describe how this arrangement produces the I band, A band, and H zone.*

Sliding Filament Model

Objectives

- *Describe the sliding filament model of muscle contraction.*
- *Explain how sarcomeres shorten without change in the length of the myofilaments.*

The **sliding filament model** of muscle contraction includes all the events that result in actin myofilaments sliding over myosin myofilaments to shorten the sarcomeres of muscle fibers. Actin and myosin myofilaments do not change length during contraction of skeletal muscle. Instead, the actin and myosin myofilaments slide past one another in a way that causes the sarcomeres to shorten (figure 9.6). The shortening of sarcomeres is responsible for the contraction of skeletal muscles. When sarcomeres shorten the myofibrils, which consist of sarcomeres joined end to end, shorten. The myofibrils extend the length of the muscle fibers, and when they shorten, the muscle fibers shorten. Muscle bundles are made up of muscle fibers and muscles are made up of muscle bundles. Therefore, when sarcomeres shorten, myofibrils, muscle fibers, muscle bundles, and muscles shorten to produce muscle contractions.

During relaxation of muscle the sarcomeres lengthen. For this to happen, some force must be applied to a muscle to cause them to lengthen, such as forces produced by other muscles or by gravity.

12. *Why do the I bands and H zones shorten during muscle contraction, but the length of the A band is unchanged?*
13. *How does shortening of sarcomeres explain muscle contraction?*

P R E D I C T 1

Explain the events that influence the width of each band of a sarcomere when a muscle goes through the sequence of being stretched, contracted, and relaxed.

Physiology of Skeletal Muscle Fibers

Objectives

- *Describe the resting membrane potential and the production of action potentials.*
- *Explain the events responsible for the propagation of an action potential along an axon.*
- *Describe the events that result in muscle contraction and relaxation in response to an action potential in a motor neuron.*

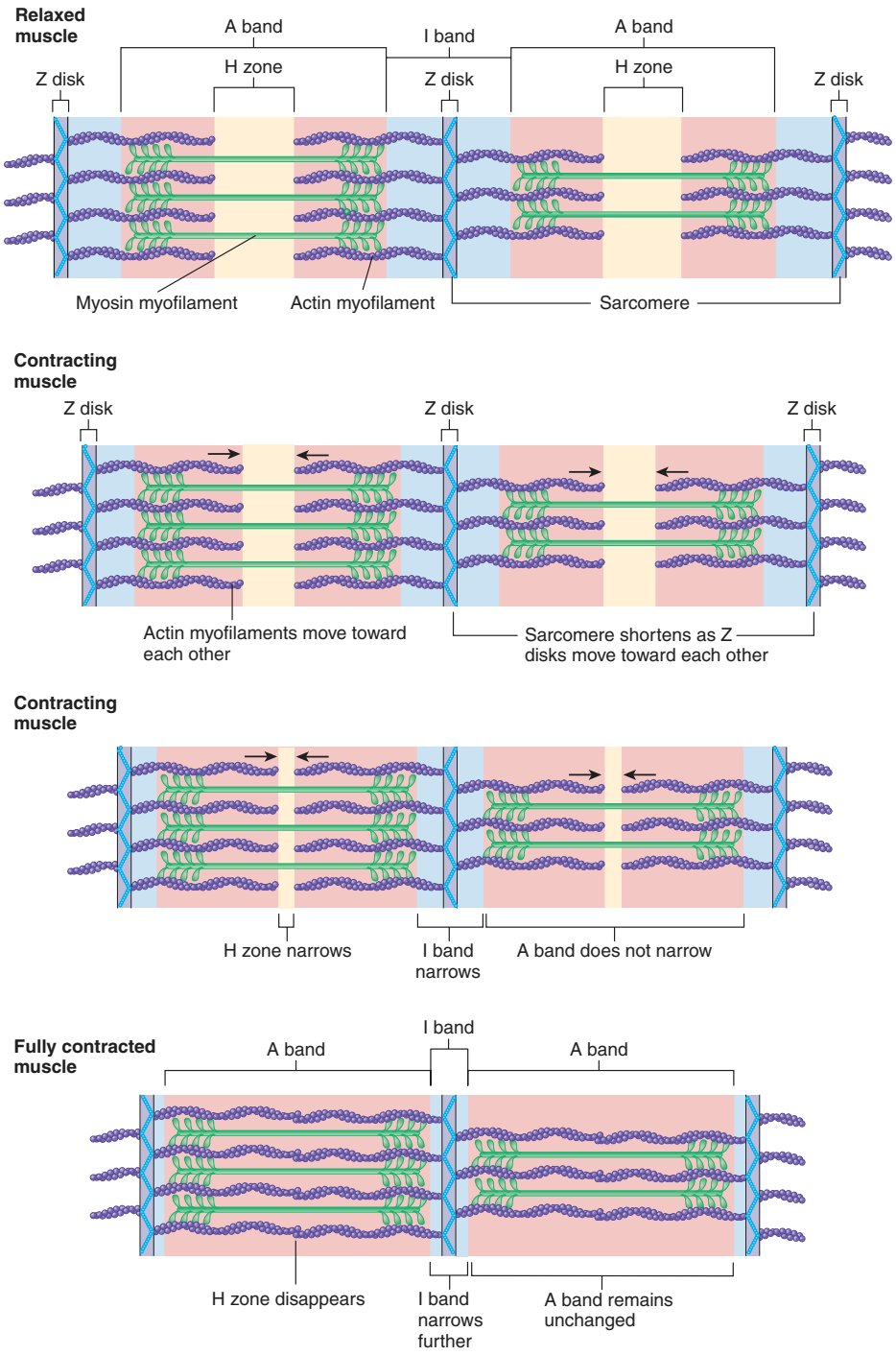
Axons of nerve cells extend from the brain and spinal cord to skeletal muscle fibers. The nervous system controls the contractions of skeletal muscles through electric signals called **action potentials,** which are transmitted along the axons to muscle fibers. The action potentials transmitted by the axons stimulate the production of action potentials in the muscle fibers, which cause them to contract.

1. Actin and myosin myofilaments in a relaxed muscle (*right*) and a contracted muscle (*#4 below*) are the same length. Myofilaments do not change length during muscle contraction.

2. During contraction, actin myofilaments at each end of the sarcomere slide past the myosin myofilaments toward each other. As a result, the Z disks are brought closer together, and the sarcomere shortens.

3. As the actin myofilaments slide over the myosin myofilaments, the H zones (*yellow*) and the I bands (*blue*) narrow. The A bands, which are equal to the length of the myosin myofilaments, do not narrow, because the length of the myosin myofilaments does not change.

4. In a fully contracted muscle, the ends of the actin myofilaments overlap and the H zone disappears.



Process Figure 9.6 Sarcomere Shortening

Membrane Potentials

Plasma membranes are **polarized,** which means there is a voltage difference, or electrical charge difference, across the membrane before action potentials can be generated. This charge difference is called the **resting membrane potential** (figure 9.7). The negative charge at the internal surface of the plasma membrane compared to its outer surface results mainly from the concentration differences of ions and charged molecules across the plasma membrane and to its permeability characteristics. The concentration of K^+ inside the cell is much higher than its concentration outside the cell. The plasma membrane is relatively permeable to K^+ and much less permeable to negatively charged molecules found inside the cell. Consequently, positively charged K^+ tends to diffuse out of the cell leaving the negatively charged molecules behind. The membrane becomes polarized when the tendency for K^+ to diffuse out of the cell is resisted by the negative charges of the molecules inside the cell. The resting membrane potential is described more fully in chapter 11.

The resting membrane potential can be measured in units called **millivolts** (mV; mV = 1/1000 Volt). The potential differences across the plasma membranes of nerve cells and muscle fibers are between −70 to −90 mV. The potential difference is reported as a negative number because the inner surface of the plasma membrane is negative compared to the outside.

Ion Channels

Once the resting membrane potential is established, action potentials can be produced. An action potential is a reversal of the resting membrane potential such that the inside of the plasma membrane becomes positively charged compared to the outside. The permeability characteristics of the plasma membrane change as a result of the opening of certain ion channels, when a cell is stimulated. The diffusion of ions through these channels changes the charge across the plasma membrane and produces an action potential. Two types of gated ion channels are responsible for producing action potentials:

1. *Ligand-gated ion channels.* A **ligand** (lī′gand) is a molecule that binds to a receptor. A **receptor** is a protein or glycoprotein that has a receptor site to which a ligand can bind. **Ligand-gated ion channels** are channels which open in response to a ligand binding to a receptor that is part of the ion channel (see figure 3.8). For example, the axons of nerve cells supplying skeletal muscle fibers release ligands, called **neurotransmitters** (noor′ō-trans-mit′er), which bind to ligand-gated Na^+ channels in the membrane of the muscle fibers. As a result, the Na^+ channels open, allowing Na^+ to enter the cell.
2. *Voltage-gated ion channels.* These channels open and close in response to small voltage (charge) changes across the plasma membrane. When a nerve or muscle cell is stimulated, the charge difference changes and that causes voltage-gated ion channels to open or close.

Ligand-gated and voltage-gated ion channels are specific for the type of ion that passes through them. The specific type of ion channels that opens determine what ions move across the plasma membrane. For example, opening ligand-gated Na^+ channels allows Na^+ to cross the plasma membrane, whereas the opening of voltage-gated K^+ channels allows K^+ to cross.

The concentration gradient for an ion determines whether that ion enters or leaves the cell after the ion channel, specific for that ion, opens (see chapter 3). For example, there is a higher concentration of Na^+ and Ca^{2+} outside the cell than inside it. Consequently, when gated Na^+ channels open, Na^+ moves through them into the cell. In a similar fashion, when gated Ca^{2+} channels open, Ca^{2+} moves into the cell.

P R E D I C T 2

There is a higher concentration of K^+ inside the cell than outside it. When gated K^+ channels open, in what direction does K^+ move?

Action Potentials

An action potential takes approximately 1 to a few milliseconds to occur, and it has two phases called depolarization and repolarization. Stimulation of a cell can cause depolarization of its plasma membrane, which is graphed in figure 9.8*a*. **Depolarization** occurs when the inside of the plasma membrane becomes less negative, which is indicated by movement of the curve upward toward zero. The depolarization phase of an action potential is triggered if the depolarization changes the membrane potential to a value called **threshold** (figure 9.8*b*). The charge difference across the plasma membrane reverses when the membrane potential becomes a positive value. **Repolarization** is the return of the membrane potential to its resting value.

Depolarization and repolarization result from the opening and closing of gated ion channels. Before a nerve or muscle cell is stimulated, these gated ion channels are closed (figure 9.9 *1*). When the cell is stimulated, gated Na^+ channels open, and Na^+ diffuses into the cell. The positively charged Na^+ makes the inside of the cell membrane less negative. If the depolarization reaches threshold, many voltage-gated Na^+ channels open rapidly and Na^+ diffuse into the cell until the inside of the membrane becomes positive for a brief time (figure 9.9 *2*). Additional permeability changes in the plasma membrane stop depolarization and start repolarization shortly after

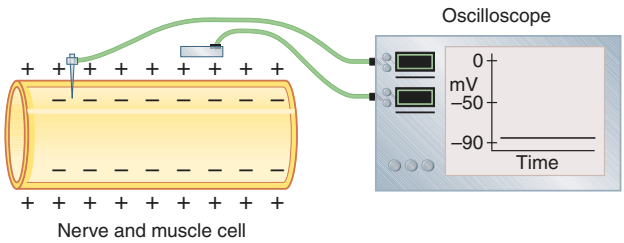
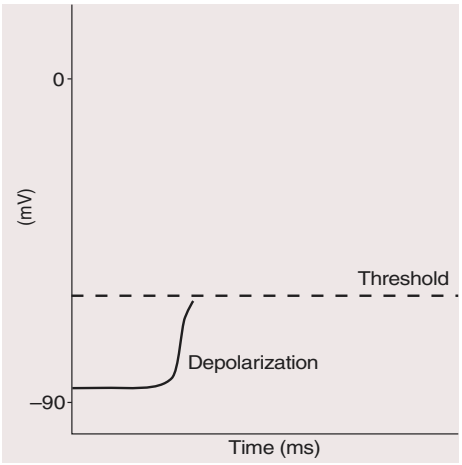
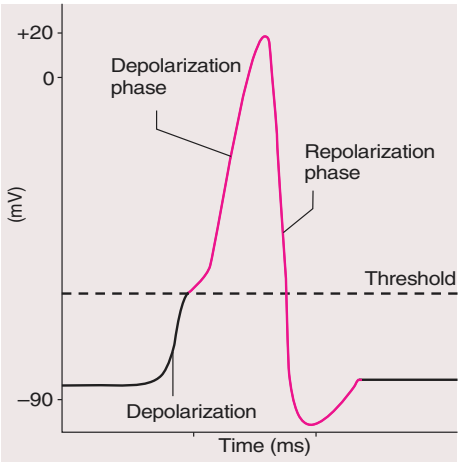


Figure 9.7 Measuring the Resting Membrane Potential

The recording electrode is inside the membrane, the reference electrode is outside, and a potential difference of about −85 mV is recorded by the recording device (oscilloscope), with the inside of the membrane negative with respect to the outside of the membrane.



(a) Depolarization is a change of the charge difference across the plasma membrane, making the charge inside of the cell less negative and the outside of the plasma membrane less positive.



(b) During the depolarization phase the membrane potential changes from approximately –85 mV to approximately +20 mV. During the repolarization phase of the resting membrane potential, the inside of the plasma membrane changes in charge from approximately +20 mV to –85 mV. This is the repolarization phase of the action potential.

Figure 9.8 Depolarization and the Action Potential

the inside of the plasma membrane becomes positive. The repolarization phase results from the closing of gated Na^+ channels and the opening of gated K^+ channels (figure 9.9 *3*). Thus, the movement of Na^+ into the cell stops and the movement of K^+ out of the cell increases. These changes cause the inside of the plasma membrane to become more negative and the outside to become more positive. The action potential ends and the resting membrane potential is reestablished when the gated K^+ channels close.

Action potentials occur according to the **all-or-none principle.** If a stimulus is strong enough to produce a depolarization that reaches threshold, or even if it exceeds threshold by a substantial amount, all of the permeability changes responsible for an action potential proceed without stopping and are constant in magnitude (the "all" part). If a stimulus is so weak that the depolarization does not reach threshold, few of the permeability changes occur. The membrane potential returns to its resting level after a brief period without producing an action potential (the "none" part). An action potential can be compared to the flash system of a camera. Once the shutter is triggered (reaches threshold), the camera flashes (an action potential is produced), and each flash is the same brightness (the "all" part) as the previous flashes. If the shutter is depressed, but not triggered (does not reach threshold), no flash results (the "none" part).

An action potential occurs in a very small area of the plasma membrane and does not affect the entire plasma membrane at one time. Action potentials can, however, **propagate** or spread across the plasma membrane because an action potential produced at one location in the plasma membrane can stimulate the production of an action potential at another location (figure 9.10). Note that an action potential does not actually move along the plasma membrane. Rather, an action potential at one location stimulates the production of another action potential in an adjacent location, which, in turn, stimulates the production of another and so on. It is much like a long row of toppling dominos in which each domino knocks down the next domino. Each domino falls, but no single domino actually travels the length of the row.

The **action potential frequency** is the number of action potentials produced per unit of time. As the strength of the stimulus applied to a nerve or muscle cell increases, once threshold is reached, the action potential frequency increases as the strength of the stimulus increases. All the action potentials are identical. The action potential frequency can affect the strength of a muscle contraction (see Stimulus Frequency and Muscle Contraction, page 291).

In summary, the resting membrane potential results from a charge difference across the plasma membrane. An action potential, which is a reversal of that charge difference, stimulates cells to respond. The nervous system controls muscle contractions by sending action potentials along axons to muscle cells and stimulating action potentials in them. An increased frequency of action potentials sent to the muscle cells can result in an increased strength of muscle contraction.

14. *Define resting membrane potential.*
15. *What types of gated ion channels are responsible for producing action potentials?*
16. *What value must depolarization reach in a cell to trigger an action potential?*
17. *Describe the changes that occur during the depolarization and repolarization phases of an action potential.*
18. *What is the all-or-none principle of action potentials and what is its significance?*
19. *Describe the propagation of an action potential.*
20. *How does the frequency of action potentials affect muscle contractions?*

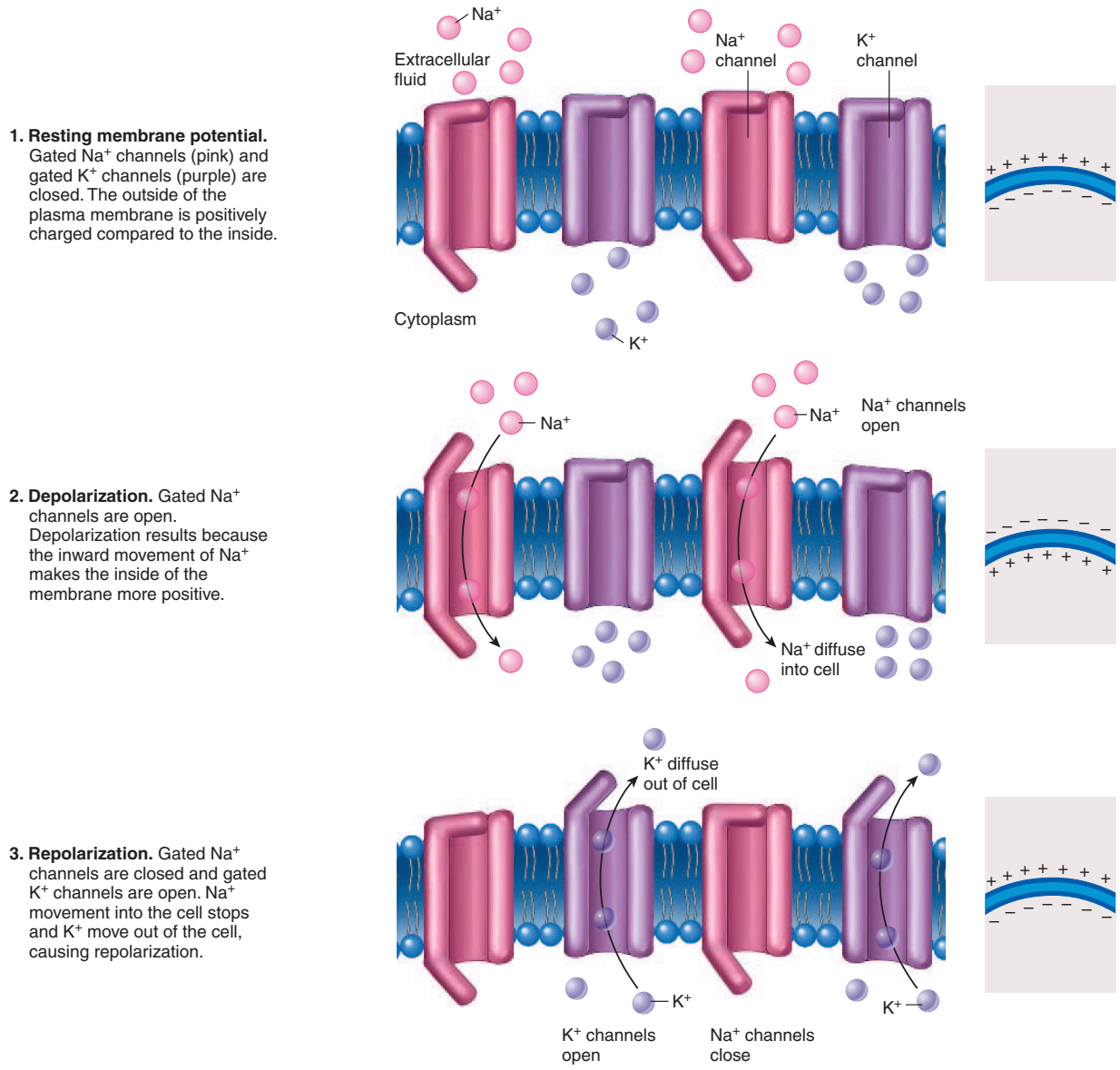


Figure 9.9 Gated Ion Channels and the Action Potential

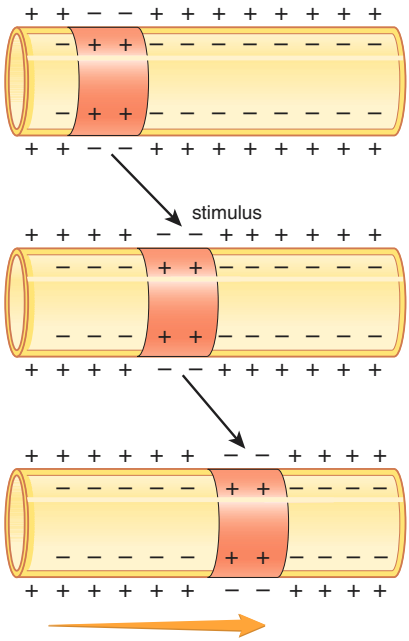
Step 1 illustrates the status of gated Na^+ and K^+ channels in a resting cell. Steps 2 and 3 show how the channels open and close to produce an action potential. Next to each step, the charge difference across the plasma membrane is illustrated.

Neuromuscular Junction

Axons of motor neurons carry action potentials at a high velocity from the brainstem and spinal cord to skeletal muscle fibers. The axons branch repeatedly, and each branch projects toward one muscle fiber to innervate it. Thus, each muscle fiber receives a branch of an axon, and each axon innervates more than one muscle fiber (see figure 9.2).

Near the muscle fiber it innervates, each axon branch forms a cluster of enlarged axon terminals that rests in an invagination of the sarcolemma to form a **synapse,** or **neuromuscular junction,** which consists of the axon terminals and the area of the muscle fiber sarcolemma they innervate. Each axon terminal is the **presynaptic** (prē′si-nap′tik) **terminal.** The space between the axon terminal and the muscle fiber is the **synaptic** (si-nap′tik) **cleft,** and the muscle plasma membrane in the area of the junction is the **postsynaptic** (pōst-si-nap′tik) **membrane,** or **motor end-plate** (figure 9.11).

Each presynaptic terminal contains numerous mitochondria and many small, spherical sacs approximately 45 μm in diameter, called **synaptic vesicles.** The vesicles contain **acetylcholine**



1. An action potential in a local area of the plasma membrane is indicated by the orange band. Note the reversal of charge across the membrane.
2. The action potential is a stimulus that causes the production of another action potential in the adjacent plasma membrane.
3. The action potential propagates along the plasma membrane (indicated by orange arrow).

Figure 9.10 Action Potential Propagation

(ACh; as-e-til-kō′1ēn), an organic molecule composed of acetic acid and choline, which functions as a neurotransmitter. A **neurotransmitter** (noor′ō-trans-mit′er) is a substance released from a presynaptic membrane that diffuses across the synaptic cleft and stimulates (or inhibits) the production of an action potential in the postsynaptic membrane.

When an action potential reaches the presynaptic terminal, it causes voltage-gated calcium ion (Ca^{2+}) channels in the plasma membrane of the axon to open, and as a result, Ca^{2+} diffuse into the cell (figure 9.12*a*). Once inside the cell, the ions cause the contents of a few synaptic vesicles to be secreted by exocytosis from the presynaptic terminal into the synaptic cleft. The acetylcholine molecules released from the synaptic vesicles then diffuse across the cleft and bind to receptor molecules located within the postsynaptic membrane. This causes ligand-gated Na^+ channels to open, increasing the permeability of the membrane to Na^+. Na^+ then diffuse into the cell causing depolarization. In skeletal muscle, each action potential in the motor neuron causes a depolarization that exceeds threshold, resulting in the production of an action potential in the muscle fiber.

P R E D I C T 3

Predict the consequence if presynaptic action potentials in an axon could not release sufficient acetylcholine to cause depolarization to threshold in a skeletal muscle fiber.

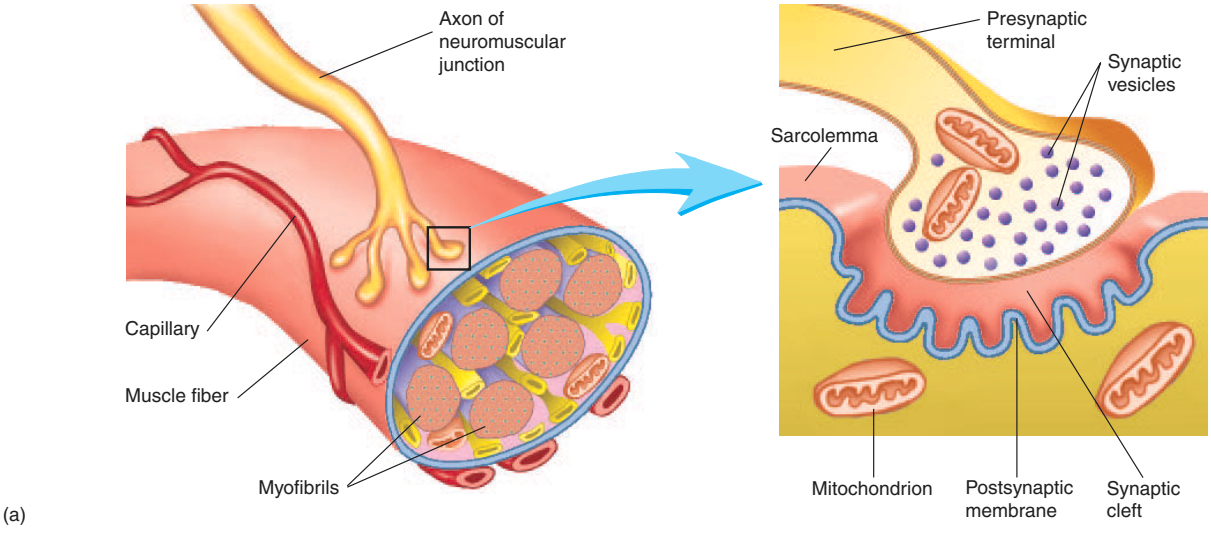
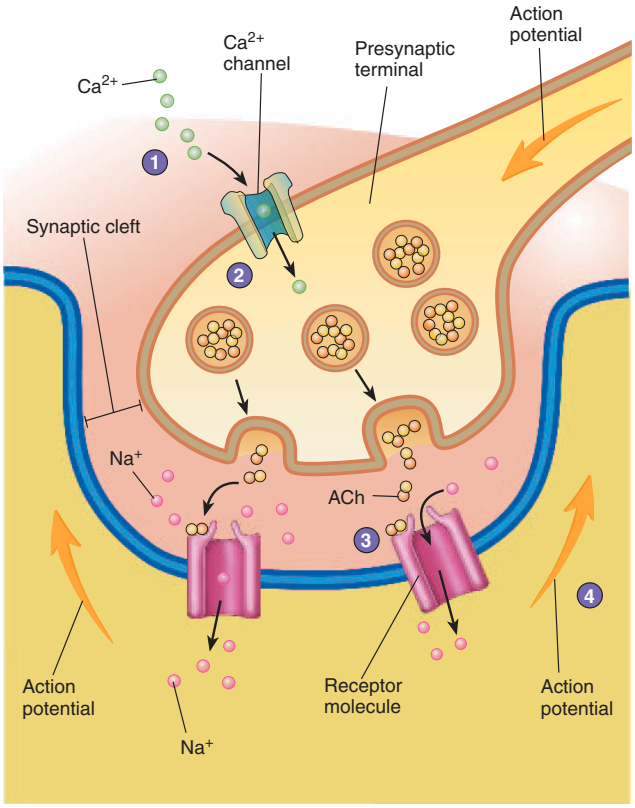


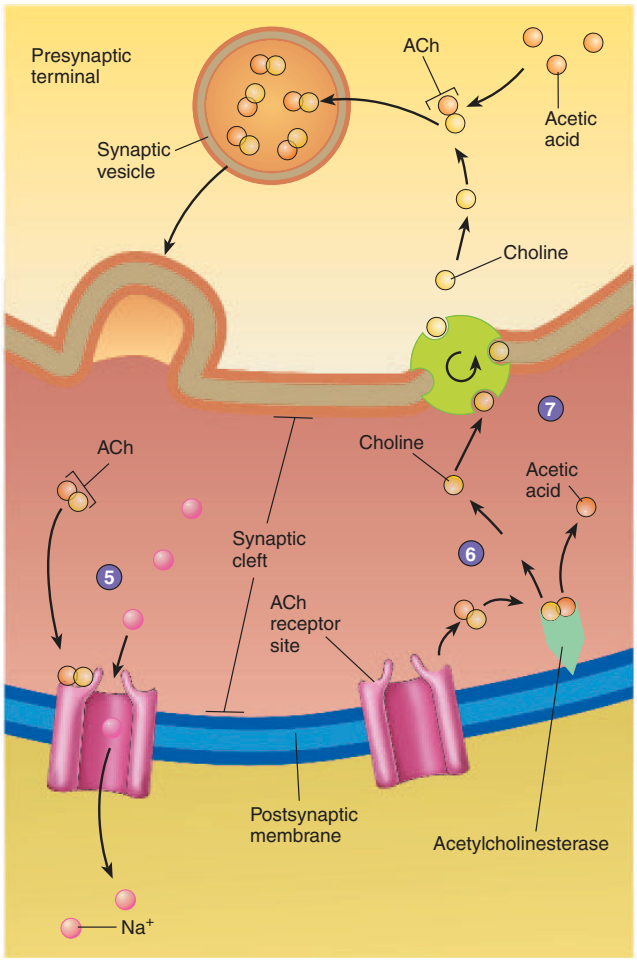
Figure 9.11 Neuromuscular Junction

(*a*) Diagram showing the neuromuscular junction. Several branches of an axon form the neuromuscular junction with a single muscle fiber. (*b*) Photomicrograph of a neuromuscular junction.



1. An action potential arrives at the presynaptic terminal causing voltage gated Ca^{2+} channels to open, increasing the Ca^{2+} permeability of the presynaptic terminal.
2. Ca^{2+} enter the presynaptic terminal and initiate the release of a neurotransmitter, acetylcholine (ACh), from synaptic vesicles into the presynaptic cleft.
3. Diffusion of ACh across the synaptic cleft and binding of ACh to ACh receptors on the postsynaptic muscle fiber membrane causes an increase in the permeability of ligand-gated Na^+ channels.
4. The increase in Na^+ permeability results in depolarization of the postsynaptic membrane; once threshold has been reached a postsynaptic action potential results.

(a)



5. Once ACh is released into the synaptic cleft it binds to the receptors for ACh on the postsynaptic membrane and causes Na^+ channels to open.
6. ACh is rapidly broken down in the synaptic cleft by acetylcholinesterase to acetic acid and choline.
7. The choline is reabsorbed by the presynaptic terminal and combined with acetic acid to form more ACh, which enters synaptic vesicles. Acetic acid is taken up by many cell types.

(b)

Process Figure 9.12 Function of the Neuromuscular Junction

(*a*) Release of ACh in response to an action potential at the neuromuscular junction. (*b*) Breakdown of ACh in the neuromuscular junction.

Acetylcholine released into the synaptic cleft is rapidly broken down to acetic acid and choline by the enzyme **acetylcholinesterase** (as′e-til-kō-lin-es′ter-ās; figure 9.12*b*). Acetylcholinesterase keeps acetylcholine from accumulating within the synaptic cleft, where it would act as a constant stimulus at the postsynaptic terminal. The release of acetylcholine and its rapid degradation in the synaptic cleft ensures that one presynaptic action potential yields only one postsynaptic action potential. Choline molecules are actively reabsorbed by the presynaptic terminal and then combined with the acetic acid produced within the cell to form acetylcholine. Recycling choline molecules requires less energy and is more rapid than completely synthesizing new acetylcholine molecules each time they are released from the presynaptic terminal. Acetic acid is an intermediate in the process of glucose metabolism

(see chapter 25). A variety of cells can take it up and use it after it diffuses from the area of the neuromuscular junction.

21. *Describe the neuromuscular junction. How does an action potential in the neuron produce an action potential in the muscle cell?*
22. *What is the importance of acetylcholinesterase in the synaptic cleft?*

Excitation–Contraction Coupling

Action potentials produced in the sarcolemma of a skeletal muscle fiber can lead to contraction of the fiber. The mechanism by which an action potential causes contraction of a muscle fiber is called **excitation–contraction coupling,** and it involves the sarcolemma, T tubules, sarcoplasmic reticulum, Ca^{2+}, and troponin. The sarcolemma has along its surface many regularly arranged tubelike invaginations called **transverse,** or **T tubules.** T tubules project into the muscle fiber and wrap around sarcomeres in the region where actin and myosin myofilaments overlap (see figures 9.3 and 9.13). The lumen of each T tubule is filled with extracellular fluid and is continuous with the exterior of the muscle fiber. Suspended in the sarcoplasm between the T tubules is a highly specialized, smooth endoplasmic reticulum called the **sarcoplasmic reticulum** (sar-kō-plaz′mik re-tik′ū-lŭm). Near the T tubules, the sarcoplasmic reticulum is enlarged to form **terminal cisternae** (sis-ter′nē). A T tubule and the two adjacent terminal cisternae together are called a **triad** (trī′ad) (see figure 9.13). The sarcoplasmic reticulum actively transports Ca^{2+} into its lumen; thus the concentration of Ca^{2+} is approximately 2000 times higher within the sarcoplasmic reticulum than in the sarcoplasm of a resting muscle.

Excitation–contraction coupling begins at the neuromuscular junction with the production of an action potential in the sarcolemma. The action potential is propagated along the entire sarcolemma of the muscle fiber. When the action potential reaches the T tubules, the membranes of the T tubules undergo depolarization, because the T tubules are invaginations of the sarcolemma. The T tubules carry the depolarizations into the interior of the muscle fiber, and the depolarizations of the T tubules of the triads cause voltage-gated Ca^{2+} channels in the sarcoplasmic reticulum to open. When the voltage-gated Ca^{2+} channels of the sarcoplasmic reticulum open, Ca^{2+} rapidly diffuse the short distance from the sarcoplasmic reticulum into the sarcoplasm surrounding the myofibrils (figure 9.14).

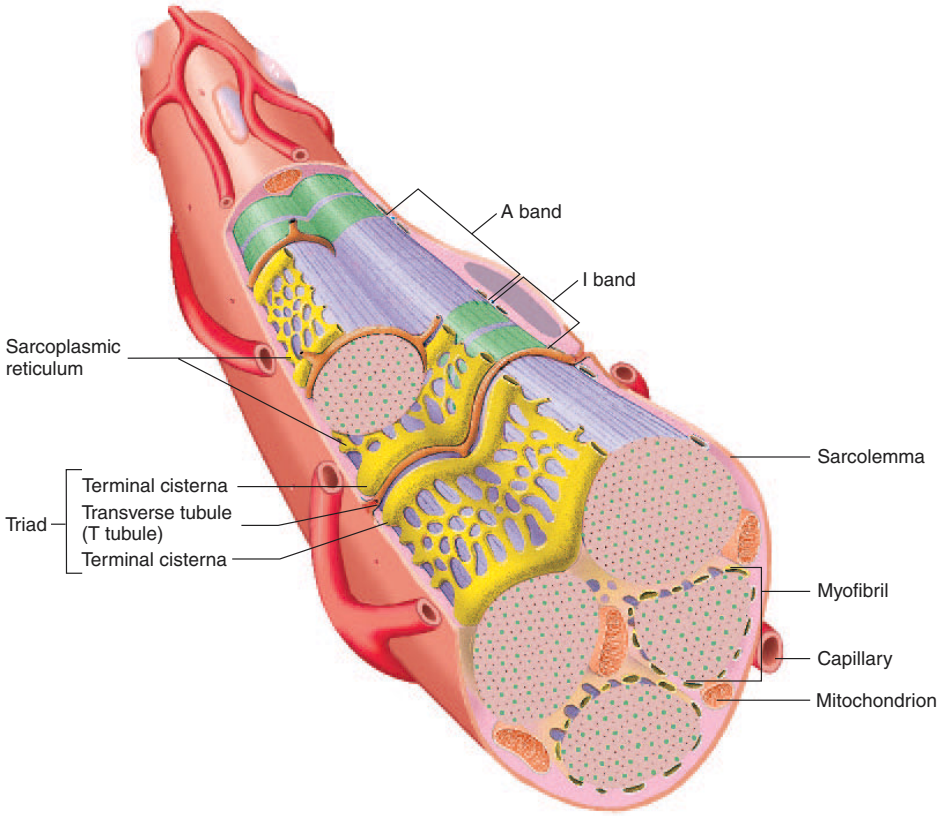


Figure 9.13 T Tubules and Sarcoplasmic Reticulum

A T tubule and the sarcoplasmic reticulum on either side of the T tubule (triad).

Ca^{2+} bind to troponin of the actin myofilaments. The combination of Ca^{2+} with troponin causes the troponin–tropomyosin complex to move deeper into the groove between the two F actin molecules and thus expose active sites on the actin myofilaments. These exposed active sites bind to the heads of the myosin molecules to form cross-bridges (see figure 9.14). Movement of the cross-bridges results in contraction.

The Effect of Blocking Acetylcholine Receptors and Acetylcholinesterase

Anything that affects the production, release, and degradation of acetylcholine or its ability to bind to its receptor molecule also affects the transmission of action potentials across the neuromuscular junction. For example, some insecticides contain organophosphates that bind to and inhibit the function of acetylcholinesterase. As a result, acetylcholine is not degraded and accumulates in the synaptic cleft, where it acts as a constant stimulus to the muscle fiber. Insects exposed to such insecticides die, partly because their muscles contract and cannot relax—a condition called **spastic paralysis** (spas′tik pă-ral′i-sis), which is followed by fatigue of the muscles.

In humans a similar response to these insecticides occurs. The skeletal muscles responsible for respiration cannot undergo their normal cycle of contraction and relaxation. Instead they remain in a state of spastic paralysis until they become fatigued. Victims die of respiratory failure. Other organic poisons such as curare bind to the acetylcholine receptors, preventing acetylcholine from binding to them. Curare does not allow activation of the receptors, and therefore the muscle is incapable of contracting in response to nervous stimulation—a condition called **flaccid** (flak′sid, flas′id) **paralysis.** Curare is not a poison to which people are commonly exposed, but it has been used to investigate the role of acetylcholine in the neuromuscular synapse and is sometimes used in small doses to relax muscles during certain kinds of surgery.

Myasthenia gravis (mī-as-thē′nē-ă grăv′is) results from the production of antibodies that bind to acetylcholine receptors, eventually causing the destruction of the receptor and thus reducing the number of receptors. As a consequence, muscles exhibit a degree of flaccid paralysis or are extremely weak. A class of drugs that includes neostigmine partially blocks the action of acetylcholinesterase and sometimes is used to treat myasthenia gravis. The drugs cause acetylcholine levels to increase in the synaptic cleft and combine more effectively with the remaining acetylcholine receptor sites.

PREDICT 4

Predict the specific cause of death resulting from a lethal dose of (a) organophosphate poison or (b) curare.

Cross-Bridge Movement

A cycle of events resulting in contraction proceeds very rapidly when the heads of the myosin molecules bind to actin (figure 9.15). The heads of myosin molecules move at their hinged region, forcing the actin myofilament, to which the heads of the myosin molecules are attached, to slide over the surface of the myosin myofilament. After movement, each myosin head releases from the actin and returns to its original position. It can then form another cross-bridge at a different site on the actin myofilament, followed by movement, release of the cross-bridge, and return to its original position. During a single contraction, each myosin molecule undergoes the cycle of cross-bridge formation, movement, release, and return to its original position many times.

The energy from one ATP molecule is required for each cycle of cross-bridge formation, movement, and release. After a cross-bridge has formed and movement has occurred, release of the myosin head from actin requires ATP to bind to the head of the myosin molecule. ATPase in the head of the myosin myofilament breaks down ATP into adenosine diphosphate (ADP) and a phosphate molecule, and energy released during this breakdown is stored in the head of the myosin molecule. Both ADP and phosphate remain bound to the myosin head. As a result of ATP being broken down, the cross-bridge is released, and the myosin head is restored to its original position (see figure 9.15). Then the myosin molecule binds to another actin active site to form another cross-bridge, and the phosphate is released from the myosin head. Much of the stored energy is used for cross-bridge formation and movement, and the ADP molecule is then released from the myosin head. Before the cross-bridge can be released for another cycle, an ATP molecule must once again bind to the head of the myosin molecule.

Movement of the myosin molecule while the cross-bridge is attached is called the **power stroke,** whereas return of the myosin head to its original position after cross-bridge release is called the **recovery stroke.** Many cycles of power and recovery strokes occur during each muscle contraction. While muscle is relaxed, energy stored in the heads of the myosin molecules is held in reserve until the next contraction. When Ca^{2+} is released from the sarcoplasmic reticulum in response to an action potential, the cycle of cross-bridge formation, movement, and release, which results in contraction, begins (see figures 9.14 and 9.15).

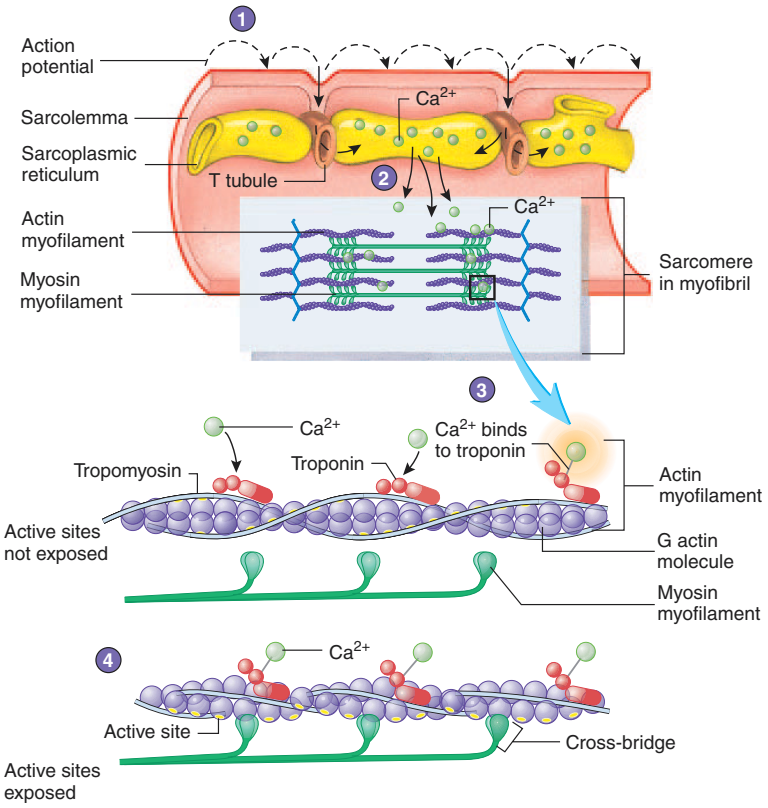
Muscle Relaxation

Relaxation occurs as a result of the active transport of Ca^{2+} back into the sarcoplasmic reticulum. As the Ca^{2+} concentration decreases in the sarcoplasm, the ions diffuse away from the troponin molecules. The troponin–tropomyosin complex then reestablishes its position, which blocks the active sites on the actin molecules. As a consequence, cross-bridges cannot re-form once they have been released, and relaxation occurs.

Energy is needed to make muscles contract, but it is also needed to make muscles relax. The active transport of Ca^{2+} into the sarcoplasmic reticulum requires ATP. The active transport processes that maintain the normal concentrations of Na^+ and K^+ across the sarcolemma also require ATP. The amount of ATP required for cross-bridge formation during contraction is much greater than the other energy requirements in a skeletal muscle.

23. *How does an action potential produced in the postsynaptic membrane of the neuromuscular junction eventually result in contraction of the muscle fiber?*
24. *What conditions are required for relaxation of the muscle fiber?*

1. An action potential produced at the neuromuscular junction is propagated along the sarcolemma of the skeletal muscle, causing a depolarization to spread along the membrane of the T tubules.
2. The depolarization of the T tubule causes voltage-gated Ca^{2+} channels to open, resulting in an increase in the permeability of the sarcoplasmic reticulum to Ca^{2+}. Ca^{2+} then diffuse from the sarcoplasmic reticulum into the sarcoplasm.
3. Ca^{2+} released from the sarcoplasmic reticulum bind to troponin molecules in the actin myofilament. Consequently, the troponin molecules bound to G actin molecules are released. This causes tropomyosin molecules to move, thereby exposing active sites on the G actin molecules.
4. Once active sites on G actin molecules are exposed, the heads of the myosin myofilaments bind to them to form cross-bridges.



Process Figure 9.14 Action Potentials and Muscle Contraction

25. Where in the contraction and relaxation processes is ATP required? Define power stroke and recovery stroke.

PREDICT 5

Predict the consequences of having the following conditions develop in a muscle in response to a stimulus: (a) Na^+ cannot enter the skeletal muscle through voltage-gated Na^+ channels, (b) very little ATP is present in the muscle fiber before a stimulus is applied, and (c) adequate ATP is present within the muscle fiber, but action potentials occur at a frequency so great that calcium is not transported back into the sarcoplasmic reticulum between individual action potentials.

Physiology of Skeletal Muscle

Objectives

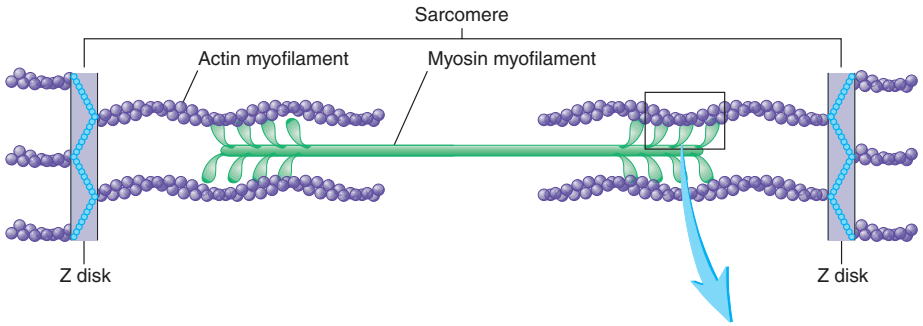
- *Describe the phases of a muscle twitch.*
- *Explain why isolated skeletal muscle fibers and motor units respond in an all-or-none fashion.*
- *Describe the effects of multiple motor unit summation, multiple-wave summation, and treppe.*

Muscle Twitch

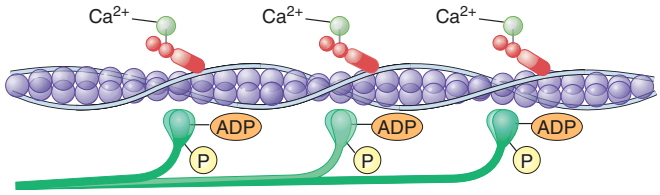
A **muscle twitch** is the contraction of a muscle in response to a stimulus that causes an action potential in one or more muscle fibers. Even though the normal function of muscles is more complex, an understanding of the muscle twitch makes the function of muscles in living organisms easier to comprehend.

A hypothetical contraction of a single muscle fiber in response to a single action potential is illustrated in figure 9.16. The time between application of the stimulus to the motor neuron and the beginning of contraction is the **lag,** or **latent, phase;** the time during which contraction occurs is the **contraction phase;** and the time during which relaxation occurs is the **relaxation phase** (table 9.2). An action potential is an electrochemical event, but contraction is a mechanical event. An action potential is measured in millivolts and is completed in less than 2 milliseconds. Muscle contraction is measured as a force, also called tension. It is reported as the number of grams lifted, or the distance the muscle shortens, and requires up to 1 second to occur.

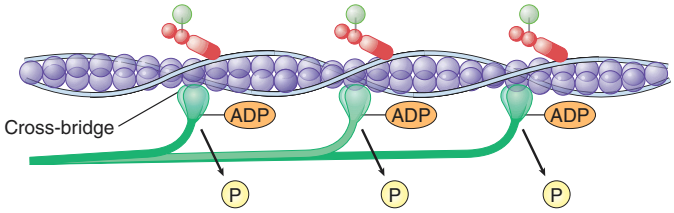
26. Define the phases of a muscle twitch and describe the events responsible for each phase.



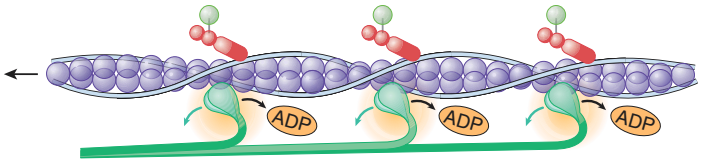
1. During contraction of a muscle, Ca^{2+} binds to troponin, causing exposure of active sites on actin myofilaments.



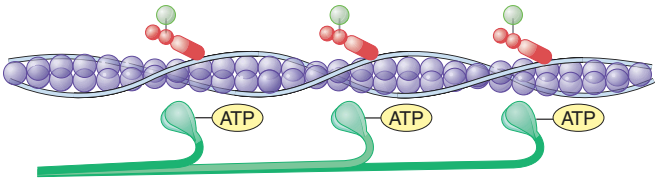
2. The myosin molecules attach to the exposed active sites on the actin myofilaments to form cross-bridges, and phosphate (P) is released from the myosin head.



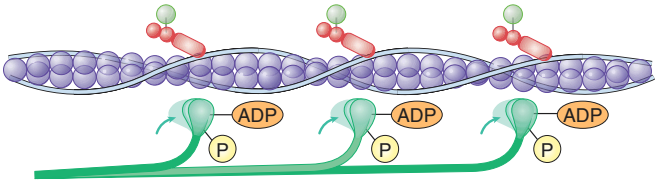
3. Energy stored in the head of the myosin myofilament is used to move the head of the myosin molecule. Movement of the head causes the actin myofilament to slide past the myosin myofilament. ADP is released from the myosin head.



4. An ATP molecule binds to the myosin head resulting in the release of actin from myosin.



5. The ATP is broken down to ADP and phosphate, which remain bound to the myosin head, the head of the myosin molecule returns to its resting position, and energy is stored in the head of the myosin molecule. If Ca^{2+} is still attached to troponin, cross-bridge formation and movement are repeated (return to step 1). This cycle occurs many times during a muscle contraction.



Process Figure 9.15 Breakdown of ATP and Cross-Bridge Movement During Muscle Contraction

Table 9.2 Events That Occur During Each Phase of a Muscle Twitch*

Lag Phase

An action potential is propagated to the presynaptic terminal of the motor neuron.

The action potential causes the permeability of the presynaptic terminal to increase.

Ca^{2+} diffuse into the presynaptic terminal, causing acetylcholine contained within several synaptic vesicles to be released by exocytosis into the synaptic cleft.

Acetylcholine released from the presynaptic terminal diffuses across the synaptic cleft and binds to acetylcholine receptor molecules in the postsynaptic membrane of the sarcolemma.

The binding of acetylcholine to its receptor site causes ligand-gated Na^+ channels to open, and the postsynaptic membrane becomes more permeable to Na^+.

Na^+ diffuse into the muscle fiber, causing a local depolarization that exceeds threshold and produces an action potential.

Acetycholine is rapidly degraded in the synaptic cleft to acetic acid and choline by acetylcholinesterase, thus limiting the length of time acetylcholine is bound to its receptor site. The result is that one presynaptic action potential produces one postsynaptic action potential in each muscle fiber.

The action potential produced in a muscle fiber is propagated from the postsynaptic membrane near the middle of the fiber toward both ends and into the T tubules.

The depolarization that occurs in the T tubule in response to the action potential causes voltage-gated Ca^{2+} channels of the membrane of the sarcoplasmic reticulum to open, and the membrane of the sarcoplasmic reticulum becomes very permeable to Ca^{2+}.

Ca^{2+} diffuse from the sarcoplasmic reticulum into the sarcoplasm.

Ca^{2+} bind to troponin; the troponin–tropomyosin complex changes its position and exposes the active site on the actin myofilaments.

Contraction Phase

Cross-bridges between actin molecules and myosin molecules form, move, release, and re-form many times, causing the sarcomeres to shorten. Energy stored in the head of the myosin molecule allows cross-bridge formation and movement. After cross-bridge movement has occurred, ATP must bind to the myosin head. The ATP is broken down to ADP, and some of the energy is used to release the cross-bridge and cause the head of the myosin molecule to move back to its resting position, where it is ready to form another cross-bridge. Some of the energy from the ATP is stored in the myosin head and is used for the next cross-bridge formation and movement (see figure 9.14). Energy is also released as heat.

Relaxation Phase

Ca^{2+} is actively transported into the sarcoplasmic reticulum.

The troponin–tropomyosin complexes inhibit cross-bridge formation.

The muscle fibers lengthen passively.

*Assuming that the process begins with a single action potential in the motor neuron.

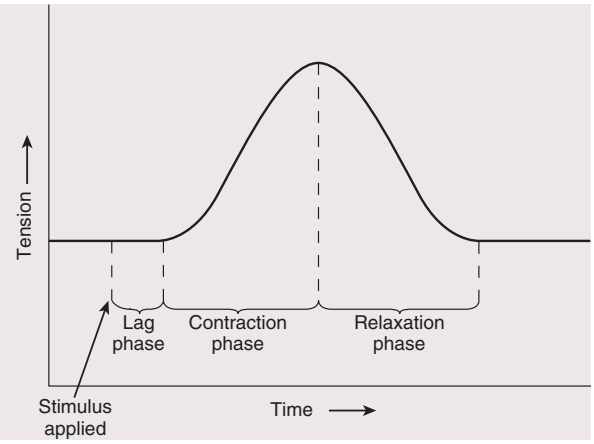


Figure 9.16 Phases of a Muscle Twitch

Hypothetical muscle twitch in a single muscle fiber. There is a short lag phase after stimulus application, followed by a contraction phase and a relaxation phase.

Stimulus Strength and Muscle Contraction

An isolated skeletal muscle fiber produces contractions of equal force in response to each action potential. This is called the **all-or-none law of skeletal muscle contraction** and can be explained on the basis of action potential production in the skeletal muscle fiber. When brief electric stimuli of increasing strength are applied to the muscle fiber sarcolemma, the following events occur: (1) a **subthreshold stimulus** does not produce an action potential, and no muscle contraction occurs; (2) a **threshold stimulus** produces an action potential and results in contraction of the muscle cell; or (3) a stronger-than-threshold stimulus produces an action potential of the same magnitude as the threshold stimulus and therefore produces an identical contraction. Thus, for a given condition, once an action potential is generated, the skeletal muscle fiber contracts to produce a constant force. If internal conditions change, it's possible for the force of contraction to change as well. For example, increasing the amount of calcium available to the muscle cell results in a stronger force of contraction; conversely, muscle fatigue can result in a weaker force of contraction.

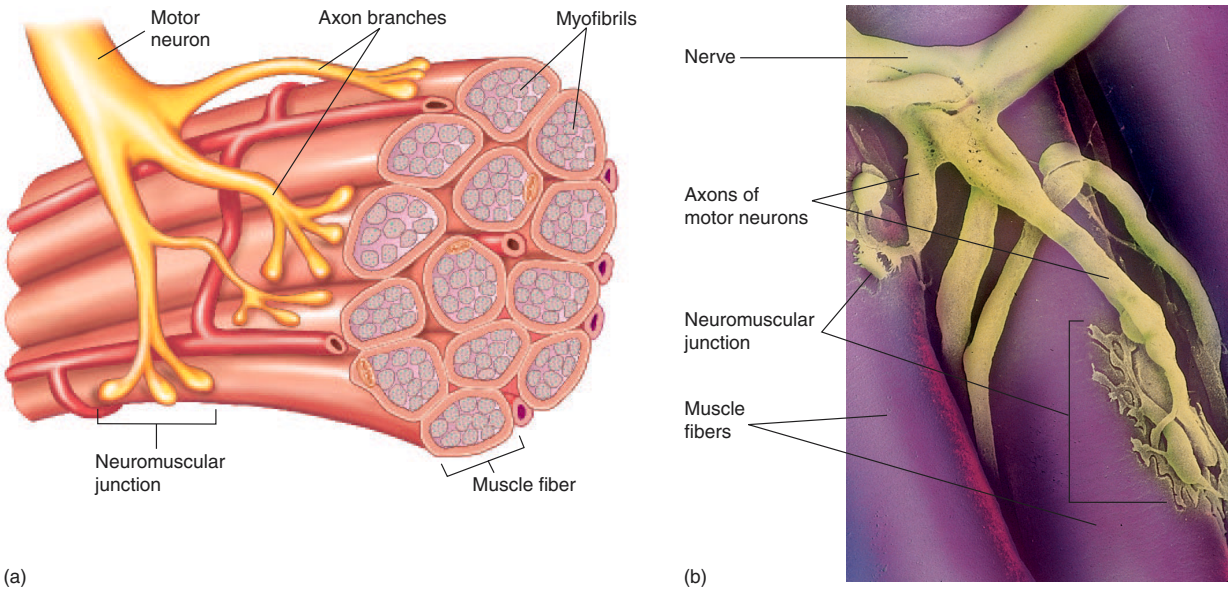


Figure 9.17 The Motor Unit

(*a*) A motor unit consists of a single motor neuron and all the muscle fibers its branches innervate. (*b*) Photomicrograph of motor units.

Within a skeletal muscle, skeletal muscle fibers form **motor units,** each of which consists of a single motor neuron and all of the muscle fibers it innervates (figure 9.17). Like individual muscle fibers, motor units respond in an all-or-none fashion. All the muscle fibers of a motor unit contract to produce a constant force in response to a threshold stimulus because an action potential in a motor neuron initiates action potentials in all the muscle fibers it innervates.

Whole muscles exhibit characteristics that are more complex than those of individual muscle fibers or motor units. Instead of responding in an all-or-none fashion, whole muscles respond to stimuli in a **graded fashion,** which means the strength of the contractions can range from weak to strong depending on the strength of the stimuli.

A muscle is composed of many motor units, and the axons of the motor units combine to form a nerve. A whole muscle contracts with either a small force or a large force, depending on the number of motor units stimulated to contract. This relationship is called **multiple motor unit summation** because the force of contraction increases as more and more motor units are stimulated. Multiple motor unit summation resulting in graded responses can be demonstrated by applying brief electric stimuli of increasing strength to the nerve supplying a muscle (figure 9.18). A subthreshold stimulus is not strong enough to cause an action potential in any of the axons in a nerve and causes no contraction. As the stimulus strength increases it eventually becomes a threshold stimulus. At threshold, the stimulus is strong enough to produce an action potential in a single motor unit axon, and all the muscle fibers of that motor unit contract. Progressively stronger stimuli called **submaximal stimuli** produce action potentials in axons of additional motor units. A **maximal stimulus** produces action potentials in the axons of all motor units. Consequently, even greater stimulus strengths, **supramaximal stimuli** have no additional effect. As the stimulus strength increases between threshold and maximum values, motor units are **recruited,** which means that the number of motor units responding to the stimuli increases and the force of contraction produced by the muscle increases in a graded fashion. Each motor unit, however, responds to every action potential by producing contractions of equal magnitude.

Motor units in different muscles do not always contain the same number of muscle fibers. Muscles performing delicate and precise movements have motor units with a small number of muscle fibers, whereas muscles performing more powerful but less precise contractions have motor units with many muscle fibers. For example, in very delicate muscles, such as those that move the eye, the number of muscle fibers per motor unit can be fewer than 10, whereas in the heavy muscles of the thigh the number can be several hundred.

27. *Why does a single muscle fiber either not contract or contract with the same force in response to stimuli of different strengths?*
28. *Why does a motor unit either not contract or contract with the same force in response to stimuli of different strengths?*
29. *How does increasing the strength of a stimulus cause a whole muscle to respond in a graded fashion? Define multiple motor unit summation.*

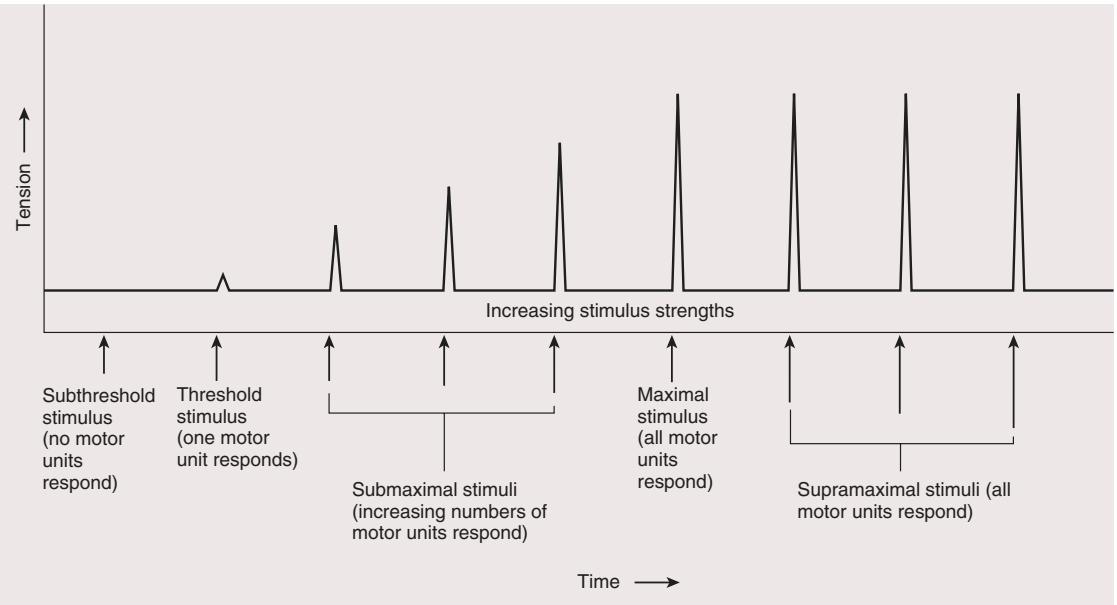


Figure 9.18 Multiple Motor Unit Summation

Multiple motor unit summation occurs as stimuli of increasing strength are applied to a nerve that innervates a muscle. The amount of tension (height of peaks) is influenced by the number of motor units responding.

P R E D I C T 6

In patients with poliomyelitis (pō′lē-ō-mī′ĕ-lī′tis), motor neurons are destroyed, causing loss of muscle function and even flaccid paralysis. Sometimes recovery occurs because of the formation of axon branches from the remaining motor neurons. These branches innervate the paralyzed muscle fibers to produce motor units with many more muscle fibers than usual, resulting in the recovery of muscle function. What effect would this reinnervation of muscle fibers have on the degree of muscle control in a person who has recovered from poliomyelitis?

Stimulus Frequency and Muscle Contraction

An action potential in a single muscle fiber causes it to contract. Although the action potential triggers contraction of the muscle fiber, the action potential is completed long before the contraction phase is completed. In addition, the contractile mechanism in a muscle fiber exhibits no refractory period. That is, relaxation of a muscle fiber is not required before a second action potential can stimulate a second contraction. As the frequency of action potentials in a skeletal muscle fiber increases, the frequency of contraction also increases (figure 9.19). In **incomplete tetanus** (tet′ă-nŭs), muscle fibers partially relax between the contractions, but in **complete tetanus** action potentials are produced so rapidly in muscle fibers that no muscle relaxation occurs between them. The tension produced by a muscle inceases as the frequency of contractions increases. This increased tension is called **multiple-wave summation.**

Tetanus of a muscle caused by stimuli of increasing frequency can be explained by the effect of the action potentials on Ca^{2+} release from the sarcoplasmic reticulum. The first action potential causes Ca^{2+} release from the sarcoplasmic reticulum, the Ca^{2+} diffuse to the myofibrils, and contraction occurs. Relaxation begins as the Ca^{2+} are pumped back into the sarcoplasmic reticulum. If the next action potential occurs before relaxation is

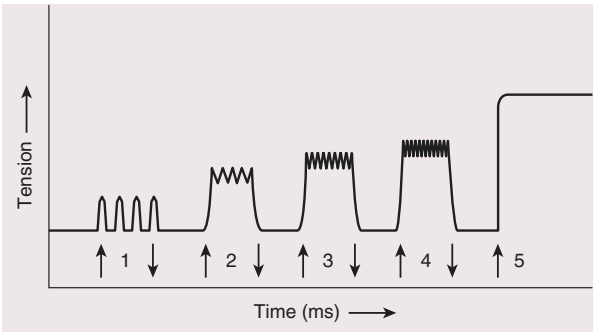


Figure 9.19 Multiple-Wave Summation

Multiple-wave summation caused by stimuli of increased frequency (1–5): complete relaxation between stimuli (1), incomplete tetanus—partial relaxation between stimuli (2–4), and complete tetanus–no relaxation between stimuli (5).

complete, however, two things happen. First, because enough time has not passed for all the Ca^{2+} to reenter the sarcoplasmic reticulum, Ca^{2+} levels around the myofibrils remain elevated. Second, the next action potential causes the release of additional Ca^{2+} from the sarcoplasmic reticulum. Thus, the elevated Ca^{2+} levels in the sarcoplasm produce continued contraction of the muscle fiber. Action potentials at a high frequency can increase Ca^{2+} concentrations in the sarcoplasm to an extent that the muscle fiber is contracted completely and does not relax at all.

At least two factors play roles in the increased tension observed during multiple-wave summation. First, as the action potential frequency increases, the concentration of Ca^{2+} around the myofibrils becomes greater than during a single muscle twitch, thereby causing a much greater degree of contraction. The additional Ca^{2+} cause the exposure of additional active sites on the actin myofilaments. Second, the sarcoplasm and the connective tissue components of muscle have some elasticity. During each separate muscle twitch, some of the tension produced by the contracting muscle fibers is used to stretch those elastic elements, and the remaining tension is applied to the load to be lifted. In a single muscle twitch, relaxation begins before the elastic components are totally stretched. The maximum tension produced during a single muscle twitch is therefore not applied to the load to be lifted. In a muscle stimulated at a high frequency, the elastic elements are stretched during the very early part of the prolonged contraction. After the elastic components are stretched, all of the tension produced by the muscle is applied to the load to be lifted, and the observed tension produced by the muscle is increased.

Another example of a graded response is **treppe** (trep′eh; staircase), which occurs in muscle that has rested for a prolonged period (figure 9.20). If the muscle is stimulated with a maximal stimulus at a low frequency, which allows complete relaxation between the stimuli, the contraction triggered by the second stimulus produces a slightly greater tension than the first. The contraction triggered by the third stimulus produces a contraction with a greater tension than the second. After only a few stimuli, the tension produced by all the contractions is equal.

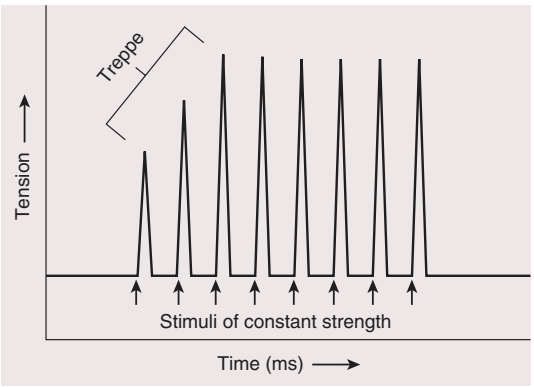


Figure 9.20 Treppe

When a rested muscle is stimulated repeatedly with maximal stimuli at a frequency that allows complete relaxation between stimuli, the second contraction produces a slightly greater tension than the first, and the third contraction produces greater tension than the second. After a few contractions, the tension produced by all contractions is equal.

A possible explanation for treppe is an increase in Ca^{2+} levels around the myofibrils. The Ca^{2+} released in response to the first stimulus is not taken up completely by the sarcoplasmic reticulum before the second stimulus causes the release of additional Ca^{2+}, even though the muscle completely relaxes between the muscle twitches. As a consequence, during the first few contractions of the muscle, the Ca^{2+} concentration in the sarcoplasm increases slightly, making contraction more efficient because of the increased number of ions available to bind to troponin. Treppe achieved during warm-up exercises can contribute to improved muscle efficiency during athletic events. Factors such as increased blood flow to the muscle and increased muscle temperature probably are involved as well. Increased muscle temperature causes the enzymes responsible for muscle contraction to function at a more rapid rate.

30. *How does the lack of a refractory period in skeletal muscle fiber contraction explain multiple-wave summation? Define incomplete tetanus and complete tetanus.*
31. *Give two reasons why rapid, repeated stimulation of a muscle fiber increases its force of contraction.*
32. *Describe treppe and explain how it occurs.*

Types of Muscle Contractions

Objectives

- *Describe the types of muscle contraction.*
- *Explain how muscle tone is maintained and how slow contraction and relaxation occur in skeletal muscle.*
- *Describe how the length of a muscle influences the force of contraction.*

Muscle contractions are classified based on the type of contraction that predominates (table 9.3). In **isometric** (ī-sō-met′rik) **contractions,** the length of the muscle doesn't change, but the amount of tension increases during the contraction process. Isometric contractions are responsible for the constant length of the postural muscles of the body such as muscles that hold the spine erect while a person is sitting or standing. In **isotonic** (ī-sō-ton′ik) **contractions,** the amount of tension produced by the muscle is constant during contraction, but the length of the muscle changes. Movements of the arms or fingers are predominantly isotonic contractions. Examples include waving or using a computer keyboard. Most muscle contractions are not strictly isometric or isotonic contractions. For example, both the length and tension of muscles change when a person walks or opens a heavy door. Although some mechanical differences do exist, both types of contractions result from the same contractile process within muscle cells.

Table 9.3 Types of Muscle Contractions

Contraction Types	Characteristics
Multiple motor unit summation	Each motor unit responds in an all-or-none fashion.
	A whole muscle is capable of producing an increasing amount of tension as the number of motor units stimulated increases.
Multiple-wave summation	Summation results when many action potentials are produced in a muscle fiber.
	Contraction occurs in response to the first action potential, but there's not enough time for relaxation to occur between action potentials.
	Because each action potential causes the release of Ca^{2+} from the sarcoplasmic reticulum, the ions remain elevated in the sarcoplasm to produce a tetanic contraction.
	The tension produced as a result of multiple-wave summation is greater than the tension produced by a single muscle twitch. The increased tension results from the greater concentration of Ca^{2+} in the sarcoplasm and the stretch of the elastic components of the muscle early in contraction.
Tetanus of muscles	Tetanus of muscles results from multiple-wave summation.
	Incomplete tetanus occurs when the action potential frequency is low enough to allow partial relaxation of the muscle fibers.
	Complete tetanus occurs when the action potential frequency is high enough that no relaxation of the muscle fibers occurs.
Treppe	Tension produced increases for the first few contractions in response to a maximal stimulus at a low frequency in a muscle that has been at rest for some time.
	Increased tension may result from the accumulation of small amounts of Ca^{2+} in the sarcoplasm for the first few contractions or from an increasing rate of enzyme activity.
Isotonic contraction	A muscle produces a constant tension during contraction.
	A muscle shortens during contraction.
	This type is characteristic of finger and hand movements.
Isometric contraction	A muscle produces an increasing tension during contraction.
	The length of a muscle remains constant during contraction.
	This type is characteristic of postural muscles that maintain a constant tension without changing their length.
Concentric contractions	A muscle produces increasing tension as it shortens.
Eccentric contractions	A muscle produces tension, but the length of the muscle is increasing.

Concentric (kon-sen′trik) **contractions** are isotonic contractions in which tension in the muscle is great enough to overcome the opposing resistance, and the muscle shortens. Concentric contractions include contractions that result in an increasing tension as the muscle shortens. A large percentage of the movements performed by muscle contractions are concentric contractions. **Eccentric** (ek-sen′trik) **contractions** are isotonic contractions in which tension is maintained in a muscle, but the opposing resistance is great enough to cause the muscle to increase in length (see table 9.3). Eccentric contractions are performed when a person slowly lowers a heavy weight. During eccentric contractions, muscles produce substantial force. Eccentric contractions are of clinical interest because repetitive eccentric contractions, such as seen in the lower limbs of people who run downhill for long distances, tend to injure muscle fibers and the connective tissue of muscles.

Muscle tone refers to the constant tension produced by muscles of the body for long periods of time. Muscle tone is responsible for keeping the back and legs straight, the head upright, and the abdomen flat. Muscle tone depends on a small percentage of all the motor units contracting out of phase with one another at any point in time. The same motor units are not contracting all the time, however. A small percentage of motor units is stimulated with a frequency of nerve impulses that causes incomplete tetanus for short periods. The motor units that are contracting are stimulated in such a way that the tension produced by the whole muscle remains constant.

P R E D I C T 7

Mary Myosin overheard an argument between two students who could not decide if a weight lifter who lifts a weight above the head and then holds it there before lowering it is using isometric, isotonic, concentric, or eccentric muscle contractions. Mary is an expert on muscle contractions, so she settles the debate. What was her explanation?

Movements of the body are usually smooth and occur at widely differing rates—some very slowly and others quite rapidly. Most movements are produced by muscle contractions, but very few of the movements resemble the rapid contractions of

individual muscle twitches. Smooth, slow contractions result from an increasing number of motor units contracting out of phase as the muscles shorten, and from a decreasing number of motor units contracting out of phase as muscles lengthen. Each individual motor unit exhibits either incomplete or complete tetanus, but because the contractions are out of phase and because the number of motor units activated varies at each point in time, a smooth contraction results. Consequently, muscles are capable of contracting either slowly or rapidly, depending on the number of motor units stimulated and the rate at which that number increases or decreases.

Length Versus Tension

Active tension is the force applied to an object to be lifted when a muscle contracts. The initial length of a muscle has a strong influence on the amount of active tension it produces. As the length of a muscle increases, its active tension also increases, to a point. If the muscle is stretched farther than that optimum length, the active tension it produces begins to decline. The muscle length plotted against the tension produced by the muscle in response to maximal stimuli is the **active tension curve** (figure 9.21).

If a muscle is stretched so that the actin and myosin myofilaments within the sarcomeres do not overlap or overlap to a very small extent, the muscle produces very little active tension when it is stimulated. Also, if the muscle is not stretched at all, the myosin myofilaments touch each of the Z disks in each sarcomere, and very little contraction of the sarcomeres can occur. If the muscle is stretched to its optimum length, optimal overlap of the actin and myosin myofilaments takes place. When the muscle is stimulated, cross-bridge formation results in maximal contraction.

Passive tension is the tension applied to the load when a muscle is stretched but not stimulated. It is similar to the tension produced if the muscle is replaced with an elastic band. Passive tension exists because the muscle and its connective tissue have some elasticity. The sum of active and passive tension is called **total tension.**

33. *Define isometric, isotonic, concentric, and eccentric contractions. What is muscle tone, and how is it maintained?*
34. *How are smooth, slow contractions produced in muscles?*
35. *Draw an active tension curve. How does the overlap of actin and myosin explain the shape of the curve?*

Weight Lifters and Muscle Length

Weight lifters and others who lift heavy objects usually assume positions so that their muscles are stretched close to their optimum length before lifting. For example, the position a weight lifter assumes before power lifting stretches the arm and leg muscles to a near-optimum length for muscle contraction, and the stance a lineman assumes in a football game stretches most muscle groups in the legs so they are near their optimum length for suddenly moving the body forward.

Fatigue

Objectives

- *Compare the mechanisms involved in the major types of fatigue.*
- *Explain the causes of physiologic contracture and rigor mortis.*

Fatigue (fă-tēg′) is the decreased capacity to do work and the reduced efficiency of performance that normally follows a period of activity. The rate at which individuals develop fatigue is highly variable, but it's a phenomenon that everyone has experienced. Fatigue can develop at three possible sites: the nervous system, the muscles, and the neuromuscular junction.

Psychologic fatigue, the most common type of fatigue, involves the central nervous system. The muscles are capable of functioning, but the individual "perceives" that additional muscular work is not possible. A burst of activity in a tired athlete in response to encouragement from spectators is an illustration of how psychologic fatigue can be overcome. The onset and duration of psychologic fatigue vary greatly and depend on the emotional state of the individual.

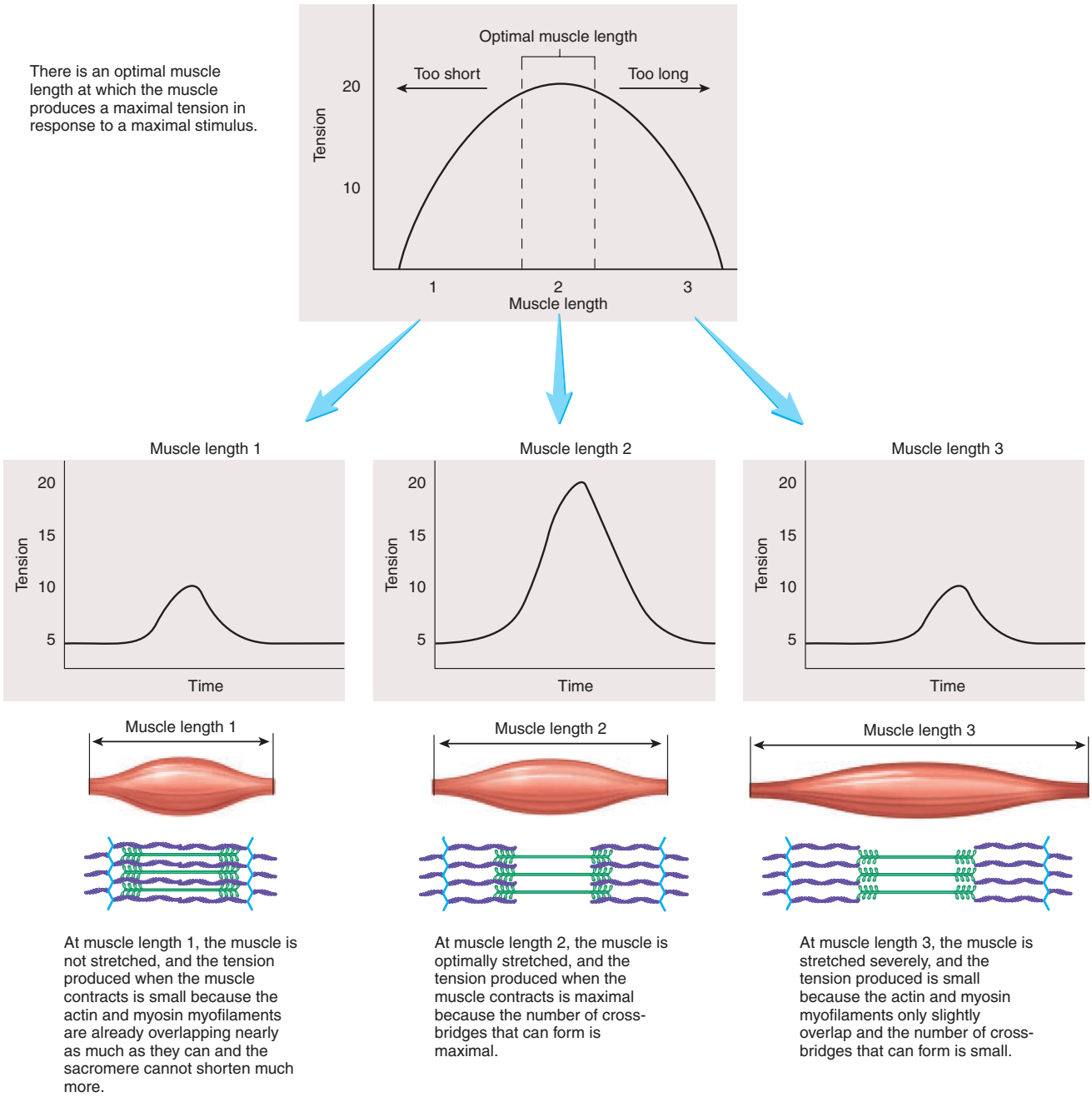
The second most common type of fatigue occurs in the muscle fiber. **Muscular fatigue** results from ATP depletion. Without adequate ATP levels in muscle fibers, cross-bridges cannot function normally. As a consequence, the tension that a muscle is capable of producing declines. Fatigue in the lower limbs of marathon runners or in the upper and lower limbs of swimmers are examples.

The least common type of fatigue, called **synaptic fatigue,** occurs in the neuromuscular junction. If the action potential frequency in motor neurons is great enough, the release of acetylcholine from the presynaptic terminals is greater than the rate of acetylcholine synthesis. As a result, the synaptic vesicles become depleted, and insufficient acetylcholine is released to stimulate the muscle fibers. Under normal physiologic conditions, fatigue of neuromuscular junctions is rare; however, it may occur under conditions of extreme exertion.

Muscle Soreness Resulting from Exercise

Pain frequently develops after 1 or 2 days in muscles that are vigorously exercised, and the pain can last for several days. The pain is more common in untrained people who exercise vigorously. In addition, highly repetitive eccentric contractions of muscles produce pain more readily than concentric contractions. The pain is associated with damage to skeletal muscle fibers and with connective tissue surrounding the skeletal muscle fibers. In people with muscle soreness induced by exercise, enzymes that are normally found inside muscle fibers can be detected in the extracellular fluid. In addition, fragments of collagen molecules can be found in the extracellular fluid of muscles. These observations indicate that injury occurs to both muscle fibers and the connective tissue of muscles. The pain produced appears to be the result of inflammation resulting from damage to muscle fibers and the connective tissue.

There is an optimal muscle length at which the muscle produces a maximal tension in response to a maximal stimulus.



At muscle length 1, the muscle is not stretched, and the tension produced when the muscle contracts is small because the actin and myosin myofilaments are already overlapping nearly as much as they can and the sacromere cannot shorten much more.

At muscle length 2, the muscle is optimally stretched, and the tension produced when the muscle contracts is maximal because the number of cross-bridges that can form is maximal.

At muscle length 3, the muscle is stretched severely, and the tension produced is small because the actin and myosin myofilaments only slightly overlap and the number of cross-bridges that can form is small.

Figure 9.21 Muscle Length and Tension

The length of a muscle, before it is stimulated, influences the force of contraction of the muscle.

Physiologic Contracture and Rigor Mortis

As a result of extreme muscular fatigue, muscles occasionally become incapable of either contracting or relaxing—a condition called **physiologic contracture** (kon-trak′choor), which is caused by a lack of ATP within the muscle fibers. ATP can decline to very low levels when a muscle is stimulated strongly, such as under conditions of extreme exercise. When ATP levels are very low, active transport of Ca^{2+} into the sarcoplasmic reticulum slows, Ca^{2+} accumulates within the sarcoplasm, and ATP is unavailable to bind to the myosin molecules that have formed cross-bridges with the actin myofilaments. As a consequence, the previously formed cross-bridges cannot release, resulting in physiologic contracture.

Rigor mortis (rig′er mōr′tĭs) is the development of rigid muscles several hours after death and is similar to physiologic contracture. ATP production stops shortly after death, and ATP levels within muscle fibers decline. Because of low ATP levels, active transport of Ca^{2+} into the sarcoplasmic reticulum stops, and Ca^{2+} leaks from the sarcoplasmic reticulum into the sarcoplasm. Ca^{2+} can also leak from the sarcoplasmic reticulum as a result of the breakdown of the sarcoplasmic reticulum membrane after cell death. As Ca^{2+} levels increase in the sarcoplasm, cross-bridges form. Too little ATP is available to bind to the myosin molecules, however, so the cross-bridges are unable to release and re-form in a cyclic fashion to produce contractions. As a consequence, the muscles remain stiff until tissue degeneration occurs.

36. *Define the term fatigue, and list three locations in which fatigue can develop.*
37. *Define and explain the cause of physiologic contracture and rigor mortis.*

Energy Sources

Objectives

- *List the energy sources used to synthesize ATP for muscle contraction.*
- *Describe the events that lead to an oxygen debt and recovery from it.*

ATP provides the immediate source of energy for muscle contractions. As long as adequate amounts of ATP are present, muscles can contract repeatedly for a long time. ATP must be synthesized continuously to sustain muscle contractions, and ATP synthesis must be equal to ATP breakdown because only small amounts of ATP are stored in the muscle fibers. The energy required to produce ATP comes from three sources: (1) creatine phosphate, (2) anaerobic respiration, and (3) aerobic respiration. Only the main points of anaerobic respiration and aerobic respiration are considered here (a more detailed discussion can be found in chapter 25).

Creatine Phosphate

During resting conditions, energy from aerobic respiration is used to synthesize **creatine** (krē′ă-tēn, krē′ă-tin) **phosphate.** Creatine phosphate accumulates in muscle cells and functions to store energy, which can be used to synthesize ATP. As ATP levels begin to fall, ADP reacts with creatine phosphate to produce ATP and creatine.

$$\text{ADP} + \text{Creatine phosphate} \rightarrow \text{Creatine} + \text{ATP}$$

The reaction occurs very rapidly and is able to maintain ATP levels as long as creatine phosphate is available in the cell. During intense muscular contraction, however, creatine phosphate levels are quickly exhausted. ATP and creatine phosphate present in the cell provide enough energy to sustain maximum contractions for about 8–10 seconds.

Anaerobic Respiration

Anaerobic (an-ār-ō′bik) **respiration** occurs in the absence of oxygen and results in the breakdown of glucose to yield ATP and lactic acid. For each molecule of glucose metabolized, a net production of two ATP molecules and two molecules of lactic acid occurs. The first part of anaerobic metabolism and aerobic metabolism are common to each other. In both cases, each glucose molecule is broken down into two molecules of pyruvic acid. Two molecules of ATP are used in this process, but four molecules of ATP are produced, resulting in a net gain of two ATP molecules for each glucose molecule metabolized. In anaerobic metabolism, the pyruvic acid is then converted to lactic acid. Unlike pyruvic acid, much of the lactic acid diffuses out of the muscle fibers into the bloodstream.

Anaerobic respiration is less efficient than aerobic respiration, but it's faster, especially when oxygen availability limits aerobic respiration. By using many glucose molecules, anaerobic respiration can rapidly produce ATP for a short time. During short periods of intense exercise, such as sprinting, anaerobic respiration combined with the breakdown of creatine phosphate provides enough ATP to support intense muscle contraction for up to 3 minutes. ATP formation from creatine phosphate and anaerobic metabolism is limited by depletion of creatine phosphate and glucose and the buildup of lactic acid within muscle fibers.

Aerobic Respiration

Aerobic (ār-ō′bik) **respiration** requires oxygen and breaks down glucose to produce ATP, carbon dioxide, and water. Compared to anaerobic respiration, aerobic respiration is much more efficient. The metabolism of a glucose molecule by anaerobic respiration produces a net gain of two ATP molecules for each glucose molecule. In contrast, aerobic respiration can produce up to 38 ATP molecules for each glucose molecule. In addition, aerobic respiration uses a greater variety of molecules as energy sources, such as fatty acids and amino acids. Some glucose is used as an energy source in skeletal muscles, but fatty acids provide a more important source of energy during sustained exercise and during resting conditions.

In aerobic respiration, pyruvic acid is metabolized by chemical reactions within mitochondria. Two closely coupled sequences of reactions in mitochondria, called the citric acid cycle and the

electron-transport chain, produce many ATP molecules. Carbon dioxide molecules are produced and, in the last step, oxygen atoms combine with hydrogen atoms to form water. Thus carbon dioxide, water, and ATP are major end products of aerobic metabolism. The following equation represents aerobic respiration of one molecule of glucose:

$$\text{Glucose} + 6\,O_2 + 38\,\text{ADP} + 38\,\text{P} \rightarrow 6\,CO_2 + 6\,H_2O + \text{About } 38\,\text{ATP}$$

Although aerobic metabolism produces many more ATP molecules for each glucose molecule metabolized than does anaerobic metabolism, the rate at which the ATP molecules are produced is slower. Resting muscles or muscles undergoing long-term exercise, such as long-distance running or other endurance exercises, depend primarily on aerobic respiration for ATP synthesis.

Oxygen Debt

After intense exercise, the rate of aerobic metabolism remains elevated for a time. The oxygen taken in by the body, above that required for resting metabolism after exercise, is called the **oxygen debt.** It represents the difference between the amount of oxygen needed for aerobic respiration during muscle activity and the amount that actually was used. ATP produced by anaerobic sources and used during muscle activity contributes to the oxygen debt. The increased aerobic metabolism after exercise reestablishes normal ATP and creatine phosphate levels in muscle fibers. It also converts excess lactic acid to pyruvic acid and then to glucose, primarily in the liver. The glucose is used to help restore glycogen levels in muscle fibers and in liver cells.

Anaerobic Exercise and Oxygen Debt

During brief but intense exercise, such as during a sprint, much of the ATP used by exercising muscles comes from the conversion of creatine phosphate to creatine and from anaerobic respiration. Glycogen is broken down to glucose in the skeletal muscle fibers and in the liver. Glucose is released from the liver into the circulatory system and can be taken up by skeletal muscle fibers. Anaerobic respiration converts the glucose molecules to ATP and lactic acid. Heavy breathing and elevated aerobic respiration after the race results from the oxygen debt. The increased aerobic respiration pays back the oxygen debt by converting creatine to creatine phosphate and converting the excess lactic acid to glucose, which is then stored as glycogen in muscles and in the liver once again. The magnitude of the oxygen debt depends on the intensity of the exercise, the length of time it was sustained, and the physical condition of the individual. Those who are in poor physical condition do not have as great a capacity as well-trained athletes do to perform aerobic metabolism.

38. *Contrast the efficiency of aerobic and anaerobic respiration. When is each type used by cells?*
39. *What is the function of creatine phosphate? When does lactic acid increase in a muscle cell?*
40. *Define oxygen debt. What does the body do to repay the oxygen debt?*

PREDICT 8

After a 10 km run with a sprint at the end, a runner continues to breathe heavily for a time. Compare the function of the elevated metabolic processes during the run, near the end, and shortly after the run.

Slow and Fast Fibers

Objectives

- *Distinguish between fast-twitch muscles and slow-twitch muscles.*
- *Predict the effects of both aerobic exercise and anaerobic exercise on the structure and function of skeletal muscle.*

Not all skeletal muscles have identical functional capabilities. They differ in several respects including having muscle fibers that contain slightly different forms of myosin. The myosin of slow-twitch muscle fibers causes these fibers to contract more slowly, and these cells are more resistant to fatigue, whereas the myosin of fast-twitch muscle fibers cause these fibers to contract quickly and these cells fatigue quickly (table 9.4). The proportion of muscle fiber types differs within individual muscles.

Slow-Twitch, or High-Oxidative, Muscle Fibers

Slow-twitch, high-oxidative, or **type I muscle fibers,** contract more slowly, are smaller in diameter, have a better developed blood supply, have more mitochondria, and are more fatigue-resistant than fast-twitch muscle fibers. Slow-twitch muscle fibers respond relatively slowly to nervous stimulation and break down ATP at a limited rate within the heads of their myosin molecules. Aerobic respiration is the primary source for ATP synthesis in slow-twitch muscles, and their capacity to perform aerobic respiration is enhanced by a plentiful blood supply and the presence of numerous mitochondria. They are sometimes called high-oxidative muscle fibers because of their enhanced capacity to carry out aerobic respiration. Slow-twitch fibers also contain large amounts of **myoglobin** (mī-ō-glō′bin), a dark pigment similar to hemoglobin, which binds oxygen and acts as a reservoir for it when the blood does not supply an adequate amount. Myoglobin thus enhances the capacity of the muscle fibers to perform aerobic respiration.

Fast-Twitch, or Low-Oxidative, Muscle Fibers

Fast-twitch, low-oxidative, or **type II muscle fibers,** respond rapidly to nervous stimulation and contain myosin molecules that break down ATP more rapidly than do slow-twitch muscle fibers. This allows their cross-bridges to form, release, and re-form more rapidly than those in slow-twitch muscle fibers. Muscles containing a high percentage of these fibers have a less well-developed blood supply than muscles containing a high percentage of slow-twitch muscle fibers. In addition, fast-twitch muscle fibers have very little myoglobin and fewer and smaller mitochondria. Fast-twitch muscle fibers have large deposits of glycogen and are well adapted to perform anaerobic respiration. The anaerobic respiration of fast-twitch muscle fibers, however, is not adapted for supplying a large amount of ATP for a prolonged period. The muscle fibers tend to contract

Table 9.4 Characteristics of Skeletal Muscle Fiber Types

Characteristics	Slow-Twitch High-Oxidative Type I	Fast-Twitch Low-Oxidative Type IIa	Low-Oxidative Type IIx
Fiber diameter	Smallest	Intermediate	Largest
Myoglobin content	High	Intermediate	Low
Mitochondria	Many	Intermediate	Few
Capillaries	Many	Intermediate	Few
Metabolism	High aerobic capacity	Intermediate aerobic capacity	Low aerobic capacity
	Low anaerobic capacity	High anaerobic capacity	Highest anaerobic capacity
Fatigue	Resistant	Resistant	Not resistant
Rate of ATP breakdown by ATPase in myosin	Slow	Fast	Fast
Glycogen concentration	Low	High	High
Location where fibers are numerous (largely genetically determined)	Generally postural muscles and more in lower than upper limbs (e.g., in endurance athletes)	Can predominate in lower limbs (e.g., in athletes who are sprinters)	Upper limbs (more in upper than lower limbs and more in legs of athletes who are sprinters)
Functions	Endurance activities and posture	Endurance activities in endurance trained muscles	Rapid, intense movements of short duration

rapidly for a shorter time and fatigue relatively quickly. Fast-twitch muscle fibers exist in two forms, type IIx and type IIa. Type IIx muscle fibers are classical fast-twitch muscle fibers. Type IIa fibers contain a different form of myosin which breaks ATP down more slowly and contracts more slowly. In addition these muscle fibers are more resistant to fatigue than type IIx fibers.

Distribution of Fast-Twitch and Slow-Twitch Muscle Fibers

The muscles of many animals are composed primarily of either fast-twitch or slow-twitch muscle fibers. The white meat of a chicken or pheasant breast, which is composed mainly of fast-twitch fibers, appears whitish because of its relatively poor blood supply and lack of myoglobin. The muscles are adapted to contract rapidly for a short time but fatigue quickly. The red, or dark, meat of a chicken leg or of a duck breast is composed of slow-twitch fibers and appears darker because of the relatively well-developed blood supply and a large amount of myoglobin. These muscles are adapted to contract slowly for a longer time and to fatigue slowly. The distribution of slow-twitch and fast-twitch muscle fibers is consistent with the behavior of these animals. For example, pheasants can fly relatively fast for short distances, and ducks fly more slowly for long distances.

Humans exhibit no clear separation of slow-twitch and fast-twitch muscle fibers in individual muscles. Most muscles have both types of fibers, although the number of each varies for each muscle. The large postural muscles contain more slow-twitch fibers, whereas muscles of the upper limbs contain more fast-twitch fibers.

The distribution of slow-twitch and fast-twitch muscle fibers in a given muscle is fairly constant for each individual and apparently is established developmentally. People who are good sprinters have a greater percentage of fast-twitch muscle fibers, whereas good long-distance runners have a higher percentage of slow-twitch muscle fibers in their leg muscles. Athletes who are able to perform a variety of anaerobic and aerobic exercises tend to have a more balanced mixture of fast-twitch and slow-twitch muscle fibers.

Effects of Exercise

Neither fast-twitch nor slow-twitch muscle fibers can be easily converted to muscle fibers of the other type. Training can increase the size and the capacity of both types of muscle fibers to perform more efficiently. Intense exercise resulting in anaerobic metabolism such as weight lifting increases muscular strength and mass and results in an increased enlargement of fast-twitch muscle fibers more than slow-twitch muscle fibers. Aerobic exercise increases the vascularity of muscle and causes enlargement of slow-twitch muscle fibers. Aerobic metabolism can convert some fast-twitch muscle fibers that fatigue readily (type IIx) to fast-twitch muscle fibers that resist fatigue (type IIa). Aerobically trained fast-twitch muscle, with more type IIa fibers, can be called **fatigue-resistant fast-twitch muscles.** In addition to changes in myosin, there is an increase in the number of mitochondria in the muscle cells, and an increase in their blood supply. Weight training followed by periods of rest can convert some muscle fibers from type IIa to type IIx. Through training, a person with more fast-twitch muscle fibers can run long distances, and a person with more slow-twitch muscle fibers can increase the speed at which he or she runs.

P R E D I C T 9

What kind of exercise regimen is appropriate for people who are training to be endurance runners? What effect will the composition of their muscles, in terms of muscle fiber type, have on their ability to perform in an endurance race?

A muscle increases in size, or **hypertrophies** (hī-per′trō-fēz), and increases in strength and endurance in response to exercise. Conversely, a muscle that is not used decreases in size, or **atrophies** (at′rō-fēz). The muscular atrophy that occurs in limbs placed in casts for several weeks is an example. Because muscle cell numbers don't change appreciably during most of a person's life, atrophy and hypertrophy of muscles result from changes in the size of individual muscle fibers. As fibers increase in size, the number of myofibrils and sarcomeres, increases within each muscle fiber. The number of nuclei in each muscle cell increases in response to exercise, but the nuclei of muscle cells cannot divide. New nuclei are added to muscle fibers because small satellite cells near skeletal muscle cells increase in number in response to exercise and then fuse with the skeletal muscle cells. Other elements, such as blood vessels, connective tissue, and mitochondria, also increase. Atrophy of muscles due to lack of exercise results from a decrease in all of these elements without a decrease in muscle cell number. Severe atrophy, such as occurs in elderly people who cannot readily move their limbs, however, does involve an irreversible decrease in the number of muscle cells and can lead to paralysis.

The increased strength of trained muscle is greater than would be expected if that strength were based only on the change in muscle size. Part of the increase in strength results from the ability of the nervous system to recruit a large number of motor units simultaneously in a trained person to perform movements with better neuromuscular coordination. In addition, trained muscles usually are restricted less by excess fat. Metabolic enzymes increase in hypertrophied muscle fibers, resulting in a greater capacity for nutrient uptake and ATP production. Improved endurance in trained muscles is in part a result of improved metabolism, increased circulation to the exercising muscles, increased numbers of capillaries, more efficient respiration, and a greater capacity for the heart to pump blood.

Anabolic Steroids and Growth Hormone

Some people take synthetic hormones called **anabolic steroids** (an-ă-bol′ik stēr′oydz, ster′oydz) to increase the size and strength of their muscles. Anabolic steroids are related to testosterone, a reproductive hormone secreted by the testes, except that they have been altered so that the reproductive effects of these compounds are minimized, but their effect on skeletal muscles is maintained. Testosterone and anabolic steroids cause skeletal muscle tissue to hypertrophy. People who take large doses of an anabolic steroid exhibit an increase in body weight and total skeletal muscle mass, and many athletes believe that anabolic steroids improve performance that depends on strength. Unfortunately, evidence indicates that harmful side effects are associated with taking anabolic steroids, including periods of irritability, testicular atrophy and sterility, cardiovascular diseases such as heart attack or stroke, and abnormal liver function. Most athletic organizations prohibit the use of anabolic steroids, and some even analyze urine samples either randomly or periodically for evidence of their use. Penalties exist for athletes who have evidence of anabolic steroid metabolites in their urine.

Growth hormone is also used inappropriately to increase muscle size by some individuals. Growth hormone increases protein synthesis in muscle tissue although it doesn't produce the same kinds of side effects as those produced by anabolic steroids. The large doses of growth hormone used by athletes, however, can cause harmful side effects if taken over a long period (see chapter 18).

41. Contrast the structural and functional differences between slow-twitch and fast-twitch muscle fibers, and explain the functions for which each type is best adapted.

42. What factors contribute to an increase in muscle strength and endurance? How does anaerobic versus aerobic exercise affect muscles?

Heat Production

Objective

- *Explain the events responsible for the generation of heat produced by muscle before, during, and after exercise and when shivering.*

The rate of metabolism in skeletal muscle differs before, during, and after exercise. As chemical reactions occur within cells, some energy is released in the form of heat. Normal body temperature results in large part from this heat. Because the rate of chemical reactions increases in muscle fibers during contraction, the rate of heat production also increases, causing an increase in body temperature. After exercise, elevated metabolism resulting from the oxygen debt helps keep the body temperature elevated. If the body temperature increases as a result of increased contraction of skeletal muscle, vasodilation of blood vessels in the skin and sweating function to speed heat loss and keep the body temperature within its normal range (see chapter 25).

When the body temperature declines below a certain level, the nervous system responds by inducing **shivering,** which involves rapid skeletal muscle contractions that produce shaking rather than coordinated movements. The muscle movement increases heat production up to 18 times that of resting levels, and the heat produced during shivering can exceed that produced during moderate exercise. The elevated heat production during shivering helps raise the body temperature to its normal range.

43. How do muscles contribute to the heat responsible for body temperature before, during, and after exercise? What is accomplished by shivering?

Smooth Muscle

Objectives

- *Compare the structure and contraction processes of smooth muscle and skeletal muscle.*
- *List the types of smooth muscle, and describe the characteristics of each.*
- *Describe the relationship between the resting membrane potential, action potentials, and contraction in smooth muscle.*

Smooth muscle is distributed widely throughout the body and is more variable in function than other muscle types. Smooth muscle cells (figure 9.22) are smaller than skeletal muscle cells, ranging from 15 to 200 μm in length and from 5 to 10 mm in diameter. They are spindle-shaped, with a single nucleus located in the middle of the cell. Compared to skeletal muscle, fewer actin and myosin myofilaments are present, and there are more actin than myosin myofilaments. The actin and myosin myofilaments

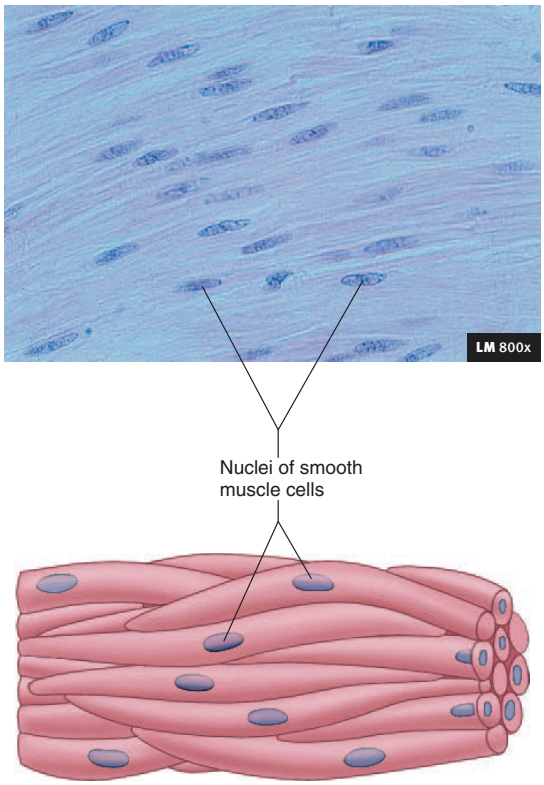


Figure 9.22 Smooth Muscle Histology

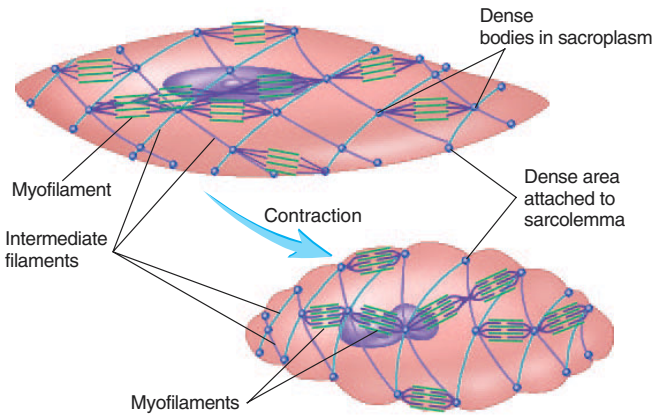


Figure 9.23 Contractile Proteins in a Smooth Muscle Cell

Bundles of contractile myofilaments containing actin and myosin are anchored at one end to dense areas in the plasma membrane and at the other end, through dense bodies, to intermediate filament. The contractile myofilaments are oriented with the long axis of the cell, and when actin and myosin slide over one another during contraction, the cell shortens.

overlap, but they are organized as loose bundles. Consequently, smooth muscle doesn't have a striated appearance. Actin myofilaments are attached to **dense bodies,** which are scattered through the cell cytoplasm, and to **dense areas,** which are in the plasma membrane. Dense bodies and dense areas are considered to be equivalent to the Z disks in skeletal muscle. Noncontractile **intermediate filaments** also attach to the dense bodies. The intermediate filaments and dense bodies form an intracellular cytoskeleton that has a longitudinal or spiral organization. The smooth muscle cells shorten when the actin and myosin slide over one another during contraction (figure 9.23).

Sarcoplasmic reticulum is not as well developed in smooth muscle cells as it is in skeletal muscle fibers, and no T tubule system exists in smooth muscle. Some shallow invaginated areas called **caveolae** (kav-ē-ō′lē) are along the surface of the plasma membrane. The function of caveolae is not well known, but it may be similar to that of both the T tubules and the sarcoplasmic reticulum of skeletal muscle.

The Ca^{2+} required to initiate contractions in smooth muscle enters the cell from the extracellular fluid and from the smooth endoplasmic reticulum. The greater distance Ca^{2+} must diffuse, the rate at which action potentials are propagated between smooth muscle cells, and the slower rate of cross-bridge formation between actin and myosin myofilaments are responsible for the slower contraction of smooth muscle compared to skeletal muscle.

Ca^{2+} regulates contraction in smooth muscle cells. The role of Ca^{2+} in smooth muscle differs from that in skeletal muscle cells, because there are no troponin molecules associated with actin fibers of smooth muscle cells. Ca^{2+} that enters the cytoplasm binds to a protein called **calmodulin** (kal-mod′ū-lin). Calmodulin molecules with Ca^{2+} bound to them activate an enzyme called **myosin kinase** (kī′nās), which transfers a phosphate group from ATP to light myosin molecules on the heads of myosin molecules. Cross-bridge formation occurs when myosin myofilaments have phosphate groups bound to them. The enzymes responsible for cross-bridge cycling are slower than the enzymes in skeletal muscle resulting in slower cross-bridge formation. Once activated, cross-bridge formation has energy requirements very similar to those for cross-bridge formation in skeletal muscle fibers.

Relaxation of smooth muscle results because of the activity of another enzyme called **myosin phosphatase** (fos′fă-tās). This enzyme removes the phosphate group from the myosin molecules (figure 9.24). If the phosphate is removed from myosin while the cross-bridges are attached to actin, the cross-bridges release very slowly. This explains how smooth muscle is able to sustain tension for long periods and without extensive energy expenditure. This is often called the "latch state" of smooth muscle contraction. If myosin phosphatase removes the phosphate from myosin molecules while the cross-bridges are not attached, relaxation occurs much more rapidly.

Elevated Ca^{2+} levels in the sarcoplasm of smooth muscle cells result in the activation of myosin molecules and cross-bridge formation. Also, the action of myosin phosphatase results in a high percentage of myosin molecules having their phosphates removed while bound to actin. This process favors sustained contractions, or the "latch state," and a low rate of energy consumption because of the slow release of cross-bridges. As long as Ca^{2+} is present, cross-bridges re-form quickly after they are released.

1. A hormone combines with a hormone receptor and activates a G protein mechanism, or depolarization of the plasma membrane occurs.

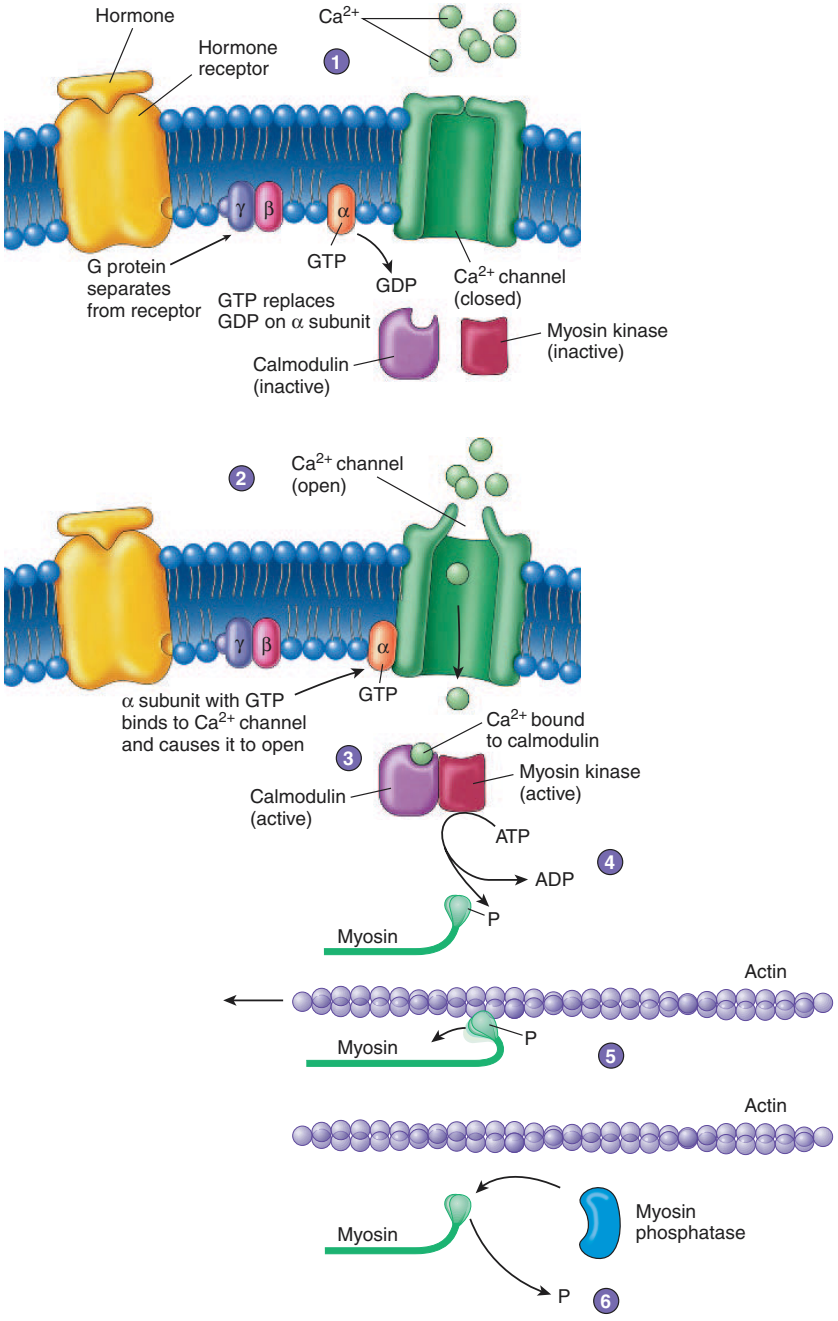
2. An α subunit opens the Ca^{2+} channel in the plasma membrane, or depolarization opens Ca^{2+} channels. Ca^{2+} diffuse through the Ca^{2+} channels and combine with calmodulin.

3. Calmodulin with a Ca^{2+} bound to it binds with myosin kinase and activates it.

4. Activated myosin kinase attaches phosphate from ATP to myosin heads to activate the contractile process.

5. A cycle of cross-bridge formation, movement, detachment, and cross-bridge formation occurs.

6. Relaxation occurs when myosin phosphatase removes phosphate from myosin.



Process Figure 9.24 Smooth Muscle Contraction

Consequently, many cross-bridges are intact at any given time in contracted smooth muscle.

Ca^{2+} levels in the sarcoplasm of smooth muscle are reduced as Ca^{2+} is actively transported across the plasma membrane, including the plasma membrane of caveolae, and into the sarcoplasmic reticulum. Relaxation occurs in response to lower blood levels of Ca^{2+}.

Types of Smooth Muscle

Smooth muscle can be either visceral or multiunit. **Visceral** (vis′er-ăl), or **unitary, smooth muscle** is more common than multiunit smooth muscle. It occurs in sheets and includes smooth muscle of the digestive, reproductive, and urinary tracts. Visceral smooth muscle has numerous gap junctions (see chapter 4), which allow action potentials to pass directly from one cell to another. As a consequence, sheets of smooth muscle cells function as a unit, and a wave of contraction traverses the entire smooth muscle sheet. Visceral smooth muscle is often autorhythmic, but some contracts only when stimulated. For example, visceral smooth muscles of the digestive tract contract spontaneously and at relatively regular intervals, whereas the visceral smooth muscle of the urinary bladder contracts when stimulated by the nervous system.

Multiunit smooth muscle occurs as sheets, such as in the walls of blood vessels; as small bundles such as in the arrector pili muscles and the iris of the eye, or as single cells such as in the capsule of the spleen. Multiunit smooth muscle has fewer gap junctions than visceral smooth muscle cells, and cells or groups of cells act as independent units. It normally contracts only when stimulated by nerves or hormones.

Elaborate synapses between neurons and smooth muscle fibers similar to those in skeletal muscle are not present in smooth muscle. Axons of nerve cells terminate in a series of dilations in the axons located within the connective tissue among the smooth muscle cells. These dilations have vesicles containing neurotransmitter molecules. Once released, the neurotransmitter molecules diffuse among the smooth muscle cells and bind to receptors on their surfaces.

44. Describe a typical smooth muscle cell. How does its structure and its contraction process differ from a skeletal muscle cell?

45. Compare visceral smooth muscle and multiunit smooth muscle. Explain why visceral smooth muscle contracts as a single unit.

Electrical Properties of Smooth Muscle

The resting membrane potential of smooth muscle cells is not as negative as that of skeletal muscle fibers. It ranges from −55 to −60 mV compared with approximately −85 mV in skeletal muscle fibers. Furthermore, the resting membrane potential fluctuates, with slow depolarization and repolarization phases occurring in many visceral smooth muscle cells. These slow waves of depolarization and repolarization are propagated from cell to cell for short distances and cause contractions (figure 9.25*a*). More "classic" action potentials can be triggered by the slow waves of depolarization and usually are propagated for longer distances (figure 9.25*b*). The slow waves in the resting membrane potential result from a spontaneous and progressive increase in the permeability of the plasma membrane to Na^+ and Ca^{2+}. Both types of ions diffuse into the cell through their respective channels and produce the depolarization.

Smooth muscle does not respond in an all-or-none fashion to action potentials. A series of action potentials in smooth muscle can result in a single, slow contraction followed by slow relaxation instead of individual contractions in response to each action potential, as occurs in skeletal muscle. A slow wave of depolarization that has one to several more classic-appearing action potentials superimposed on it is common in many types of smooth muscle. After the wave of depolarization, the smooth muscle undergoes contraction.

Spontaneously generated action potentials that lead to contractions are characteristic of visceral smooth muscle in the uterus, the ureter, and the digestive tract. Certain smooth muscle cells in these organs function as **pacemaker cells,** which tend to develop action potentials more rapidly than other cells.

The nervous system can regulate smooth muscle contractions by increasing or decreasing action potentials carried by nerve cell axons to smooth muscle. Responses of smooth muscle cells

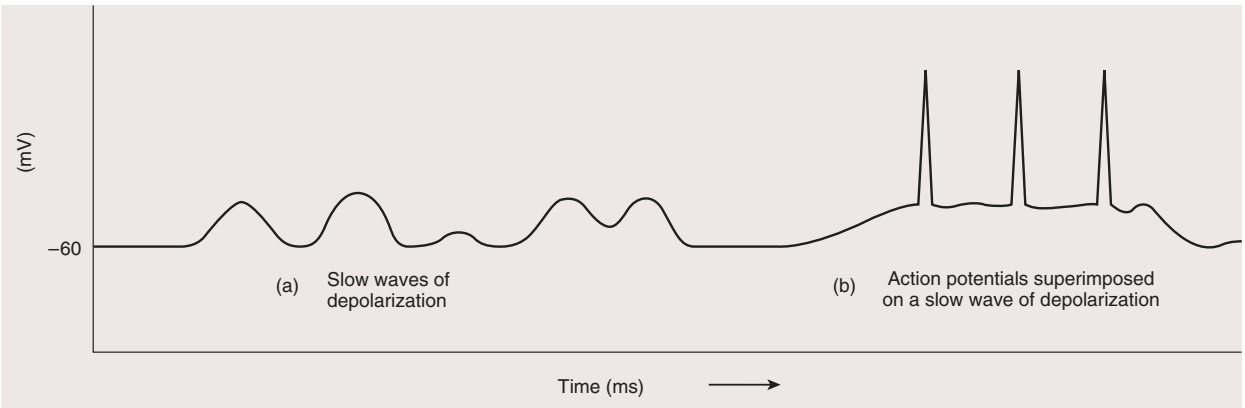


Figure 9.25 Membrane Potential from a Smooth Muscle Preparation

(*a*) Slow waves of depolarization. (*b*) Action potentials in smooth muscle superimposed on a slow wave of depolarization.

result in depolarization and increased contraction or hyperpolarization and decreased contraction.

Hormones can bind to hormone receptors on some smooth muscle plasma membranes. The combination of the hormone with the receptor causes ligand-gated Ca^{2+} channels in the plasma membrane to open (see figure 9.24). Ca^{2+} then enters the cell and causes smooth muscle contractions to occur without a major change in the membrane potential. For example, some smooth muscles contract when exposed to the hormone epinephrine because epinephrine combines with epinephrine receptors. Epinephrine combined with its receptors activates G proteins in the plasma membrane (see chapter 3 or 17). The G protein molecules can produce intracellular mediator molecules, which open the ligand-gated Ca^{2+} channels in the plasma membrane or sarcoplasmic reticulum.

PREDICT 10

Explain how a ligand could bind to a membrane-bound receptor in a smooth muscle cell and cause a sustained contraction of the smooth muscle cell for a prolonged period without a large increase in ATP breakdown.

Functional Properties of Smooth Muscle

Smooth muscle has four functional properties not seen in skeletal muscle: (1) some visceral smooth muscle exhibits autorhythmic contractions; (2) smooth muscle tends to contract in response to a sudden stretch but not to a slow increase in length; (3) smooth muscle exhibits a relatively constant tension, called **smooth muscle tone,** over a long period and maintains that same tension in response to a gradual increase in the smooth muscle length; (4) the amplitude of contraction produced by smooth muscle also remains constant, although the muscle length varies. Smooth muscle is therefore well adapted for lining the walls of hollow organs such as the stomach and the urinary bladder. As the volume of the stomach or urinary bladder increases, only a small increase develops in the tension applied to their contents. Also, as the volume of the large and small intestines increases, the contractions that move food through them do not change dramatically in amplitude.

The metabolism of smooth muscle cells is similar to that of skeletal muscle fibers. They are poorly adapted to perform anaerobic metabolism, however. An oxygen debt does not develop in smooth muscle, and fatigue occurs quickly in the absence of an adequate oxygen supply.

Regulation of Smooth Muscle

Nerves that innervate smooth muscle are part of the autonomic division of the nervous system, whereas skeletal muscle is innervated by the somatic motor nervous system (see chapter 11). The regulation of smooth muscle is therefore involuntary, and the regulation of skeletal muscle is voluntary.

The most important neurotransmitters released from nerves that innervate smooth muscle cells are acetylcholine and norepinephrine. Acetylcholine stimulates some smooth muscle types to contract and inhibits others.

Hormones are also important in regulating smooth muscle. Epinephrine, a hormone from the adrenal medulla, stimulates some smooth muscles, such as those in the blood vessels of the intestine, and inhibits other smooth muscles, such as those in the intestinal wall. Oxytocin stimulates contractions of uterine smooth muscle, especially during delivery of a baby. These and other hormones are discussed more thoroughly in chapters 17 and 18. Other chemical substances, such as histamine and prostaglandins, also influence smooth muscle function.

The type of receptors present on the plasma membrane to which the neurotransmitters or hormones bind determines the response of the smooth muscle. Some smooth muscle types have receptors to which acetylcholine binds, and the response of the receptor is to stimulate contractions; other smooth muscle types have receptors to which acetylcholine binds, and the response of the receptor is to inhibit contractions. A similar relationship exists for smooth muscle receptors for norepinephrine and certain hormones.

The receptor molecules that result in stimulation of smooth muscle contractions often open either Na^+ or Ca^{2+} channels. When these channels open, Na^+ and Ca^{2+} pass through their respective channels into the cell and cause depolarization of the plasma membrane. It's also possible for the receptor to open Ca^{2+} channels in the plasma membrane and sarcoplasmic reticulum. As a result, Ca^{2+} can diffuse into the cytoplasm of the smooth muscle cells without depolarization of the membrane potential to its threshold level, and therefore not produce action potentials.

The receptor molecules that result in inhibition of smooth muscle contractions often close Na^+ and Ca^{2+} channels or open K^+ channels. The result is hyperpolarization of the smooth muscle cells and inhibition. It's also possible for the receptors to increase the activity of the Ca^{2+} pump that transports Ca^{2+} out of the cell or into the sarcoplasmic reticulum. As a result, relaxation may occur without a change in the resting membrane potential.

The response of specific smooth muscle types to either neurotransmitters or hormones is presented in chapters dealing with the smooth muscle types.

46. *How are spontaneous contractions produced in smooth muscle?*
47. *List four functional properties of smooth muscle that are not seen in skeletal muscle. Can smooth muscle develop an oxygen debt?*
48. *How do the nervous system and hormones regulate smooth muscle contraction? How are ion channels affected by receptors that stimulate smooth muscle contractions? How are ion channels affected by receptors that inhibit smooth muscle contractions?*

Cardiac Muscle

Objective

- *Compare the structural and functional characteristics of cardiac muscle to those of skeletal muscle.*

Cardiac muscle is found only in the heart and is discussed in detail in chapter 20. Cardiac muscle tissue is striated like skeletal muscle, but each cell usually contains one nucleus located near the center. Adjacent cells join together to form branching fibers by specialized cell-to-cell attachments called **intercalated** (in-ter′kă-lā-ted) **disks,** which have gap junctions that allow action potentials to

Clinical Focus Disorders of Muscle Tissue

Muscle disorders are caused by disruption of normal innervation, degeneration and replacement of muscle cells, injury, lack of use, or disease.

Atrophy

Muscular atrophy is a decrease in the size of muscles. Individual muscle fibers decrease in size, and a progressive loss of myofibrils occurs.

Disuse atrophy is muscular atrophy that results from a lack of muscle use. Bedridden people, people with limbs in casts, or those who are inactive for other reasons experience disuse atrophy in the unused muscles. Disuse atrophy is temporary if a muscle is exercised after it is taken out of a cast, for example. Extreme disuse of a muscle, however, results in muscular atrophy in which skeletal muscle fibers are permanently lost and replaced by connective tissue. Immobility that occurs in bedridden elderly people can lead to permanent and severe muscular atrophy.

Denervation (dē-ner-vā′shŭn) **atrophy** results when nerves that supply skeletal muscles are severed. When motor neurons innervating skeletal muscle fibers are severed, the result is flaccid paralysis. If the muscle is reinnervated, muscle function is restored, and atrophy is stopped. If skeletal muscle is permanently denervated, however, it atrophies and exhibits permanent flaccid paralysis. Eventually muscle fibers are replaced by connective tissue, and the condition cannot be reversed.

Transcutaneous stimulators are used to supply electric stimuli to muscles that have had their nerves temporarily damaged or to muscles that are put in casts for a prolonged period. The electric stimuli keep the muscles functioning and prevent them from permanently atrophying while the nerves resupply the muscles or until the cast is removed.

Muscular Dystrophy

Muscular dystrophy (dis′trō-fē) is one of a group of diseases called **myopathies** (mī-op′ă-thēz) that destroy skeletal muscle tissue. Usually the diseases are inherited and are characterized by degeneration of muscle cells, leading to atrophy and eventual replacement by connective tissue.

Duchenne's muscular dystrophy is an inherited sex-linked (X-linked) recessive disorder that almost exclusively affects males. As muscles atrophy and are replaced by connective tissue, they shorten, causing immobility of joints and postural abnormalities such as scoliosis. By early adolescence, affected individuals are usually confined to wheelchairs (see Systems Pathology). Facioscapulohumoral (fa′sī-ō-skap-ū-lo-hū′mor-al) muscular dystrophy is generally less severe, and it affects both sexes later in life. The muscles of the face and shoulder girdle are primarily involved. Facioscapulohumoral muscular dystrophy appears to be inherited as an autosomal-dominant condition.

Both types of muscular dystrophy are inherited and progressive, and no drugs can prevent the progression of the disease. Therapy primarily involves exercises. Braces and corrective surgery sometimes help correct abnormal posture caused by the advanced disease. Research is directed at identifying the genes responsible for all types of muscular dystrophy, exploring the mechanism that leads to the disease condition, and finding an effective treatment once the mechanism for the disease is known.

Fibrosis

Fibrosis (fī-brō′sis), or scarring, is the replacement of damaged cardiac muscle or skeletal muscle by connective tissue. Fibrosis is associated with severe trauma to skeletal muscle and with heart attack (myocardial infarction) in cardiac muscle.

Fibrositis

Fibrositis (fī-brō-sī′tis) is an inflammation of fibrous connective tissue, resulting in stiffness, pain, or soreness. It is not progressive, nor does it lead to tissue destruction. Fibrositis can be caused by repeated muscular strain or prolonged muscular tension.

Cramps

Cramps are painful, spastic contractions of muscles that usually result from an irritation within a muscle that causes a reflex contraction (see chapter 12). Local inflammation resulting from a buildup of lactic acid and fibrositis causes reflex contraction of muscle fibers surrounding the irritated region.

Fibromyalgia (fī-brō-mī-al′ja), or chronic muscle pain syndrome, has muscle pain as its main symptom. Fibromyalgia has no known cure, but it is not progressive, crippling, or life-threatening. The pain occurs in muscles or where muscles join their tendons, but not in joints. The pain is chronic and widespread, and is distinguished from other causes of chronic pain by the identification of tender points in muscles, by the length of time the pain persists, and by failure to identify any other cause of the condition.

pass from cell to cell. Cardiac muscle cells are autorhythmic, and one part of the heart normally acts as the pacemaker. The action potentials of cardiac muscle are similar to those in nerve and skeletal muscle but have a much longer duration and refractory period. The depolarization of cardiac muscle results from the influx of both Na^+ and Ca^{2+} across the plasma membrane. Regulation of contraction in cardiac muscle by Ca^{2+} is similar to that of skeletal muscle.

49. Compare the structural and functional characteristics of cardiac muscle to those of skeletal muscle.

Effects of Aging on Skeletal Muscle

Objective

- ***Describe the effects of aging on skeletal muscle.***

Several changes occur in aging skeletal muscle that reduce muscle mass, increase the time that muscle takes to contract in response to nervous stimuli, reduce stamina, and increase recovery time. There is a loss of muscle fibers as aging occurs, and the loss

Systems Pathology

Duchenne's Muscular Dystrophy

A couple became concerned about their 3-year-old son when they noticed that he was much weaker than other boys his age and the differences appeared to become more pronounced as time passed. The boy had difficulty sitting, standing, and walking. He seemed clumsy and fell often. He had difficulty climbing stairs, and he often got from a sitting position on the floor to a standing position by using his hands and arms to climb up his legs. His muscles appeared to be poorly developed. The couple took their son to a physician to have him examined. After several kinds of tests, they were informed that their son had Duchenne's muscular dystrophy.

Background Information

Duchenne's muscular dystrophy (DMD) is usually identified in children at around 3 years of age when the parents notice slow motor development with progressive weakness and muscle wasting (figure A). Typically, muscular weakness begins in the pelvic girdle and causes a waddling gait. Temporary enlargement of the calf muscles is apparent in 80% of cases. Rising from the floor by climbing up the legs is characteristic and is caused by weakness of the lumbar and gluteal muscles. Within 3–5 years, muscles of the shoulder girdle become involved. Wasting of the muscles contributes to muscular atrophy and deformity of the skeleton. People with DMD are usually unable to walk by 10–12 years of age, and few live beyond age 20. No effective treatment exists to prevent the progressive deterioration of muscles in DMD.



Figure A Young Children with Duchenne's Muscular Dystrophy

begins as early as 25 years of age. By 80 years of age 50% of the muscle mass is gone, and this is due mainly to the loss of muscle fibers. Weight-lifting exercises help slow the loss of muscle mass, but it doesn't prevent the loss of muscle fibers. In addition, fast-twitch muscle fibers decrease in number more rapidly than slow-twitch fibers. Most of the loss of strength and speed is due to the loss of muscle fibers and the loss of fast-twitch muscle fibers. Also, at the synapses the surface area of the synapse decreases. Consequently, action potentials in neurons stimulate action potential production in muscle cells more slowly, and action potentials may not be produced in muscle cells consistently. The number of motor neurons also decreases. Some of the muscle fibers that lose their innervation when a neuron dies are reinnervated by a branch of another motor neuron. This makes motor units in skeletal muscle fewer in number, with a greater number of muscle fibers for each neuron. This may result in less precise control of muscles. Aging is associated with a decrease in the density of capillaries in skeletal muscles, and after exercise a longer period of time is required to recover.

Many of the age-related changes in skeletal muscle can be dramatically slowed if people remain physically active. As people age, they often assume a sedentary life style. Age-related changes develop more rapidly in these people. It has been demonstrated that elderly people who are sedentary can become stronger and more mobile in response to exercise.

50. Describe the changes in muscle mass and response time that occur in aging skeletal muscle.

System Interactions

System	Interaction
Skeletal	Replacement of muscles by connective tissue results in shortened inflexible muscles, causing severe deformities of the skeletal system. The shortened muscles are referred to as contractures. Kyphoscoliosis, severe curvature of the spinal column laterally and anteriorly, can be so severe that normal respiratory movements are impaired. Deformities of the limbs result from the contractures. Surgery is sometimes required to prevent contractures from making it impossible for the individual to sit in a wheelchair.
Nervous	Some degree of mental retardation occurs in a large percentage of people with DMD.
Cardiovascular	Cardiac muscle is affected by DMD. Consequently, heart failure occurs in a large number of people with advanced DMD. Heart and respiratory muscles are affected, and death caused by respiratory or cardiac failure usually occurs before age 20. Cardiac involvement becomes serious in as many as 95% of cases.
Lymphatic and immune	No obvious direct effects occur to the lymphatic system, but phagocytosis of muscle fibers is accomplished mainly by macrophages.
Respiratory	Deformity of the thorax and increasing weakness of the respiratory muscles result in inadequate respiratory movements and an increase in respiratory infections such as pneumonia. Inadequate respiratory movements due to weak respiratory muscles is a major factor in many deaths.
Digestive	Smooth muscle tissue is influenced by muscular dystrophy. The reduced ability of smooth muscle to contract can result in abnormalities of the digestive system, such as an enlarged colon diameter, a twisting of the intestine resulting in increased intestinal obstruction, cramping, and reduced absorption of nutrients.
Urinary	Reduced smooth muscle function and being wheelchair-dependent increase the frequency of urinary tract infections.

DMD results from an abnormal gene located on the X chromosome, at a position called Xp21, and is therefore a sex-linked (X-linked) condition. Although the gene is carried by females, DMD affects males almost exclusively. This chromosome position, or gene locus, is responsible for producing a protein called dystrophin, which plays a role in attaching myofibrils to and regulating the activity of other proteins in the plasma membrane. Dystrophin is thought to protect muscle cells against mechanical stress in the normal individual. In DMD, part of the gene at Xp21 is missing, and the protein it produces malfunctions, resulting in abnormal contractions and progressive muscular weakness.

PREDICT 11

A boy with Duchenne's muscular dystrophy developed pulmonary edema and then pneumonia. His physician diagnosed the condition in the following way: the pulmonary edema was the result of heart failure and the increased fluid in the lungs acted as a site where bacteria invaded and grew. The fact that the boy could not breathe deeply or cough effectively made the condition worse. Explain how a boy with DMD might develop heart failure and ineffective respiratory movements.

SUMMARY

Functions of the Muscular System (p. 272)

Muscle is responsible for movement of the arms, legs, heart, and other parts of the body, maintenance of posture, respiration, production of body heat, communication, contraction of organs and vessels, and the heart beat.

General Functional Characteristics of Muscle (p. 272)

Properties of Muscle

1. Muscle exhibits contractility (shortens forcefully), excitability (responds to stimuli), extensibility (can be stretched), and elasticity (recoils to resting length).
2. Muscle tissue shortens forcefully but lengthens passively.

Types of Muscle Tissue

1. The three types of muscle are skeletal, smooth, and cardiac.
2. Skeletal muscle is responsible for most body movements, smooth muscle is found in the wall of hollow organs and tubes and moves substances through them, and cardiac muscle is found in the heart and pumps blood.

Skeletal Muscle: Structure (p. 273)

Skeletal muscle fibers are multinucleated and appear striated.

Connective Tissue

1. Endomysium surrounds each muscle fiber.
2. Muscle fibers are covered by the external lamina and the endomysium.
3. Muscle fasciculi, bundles of muscle fibers, are covered by the perimysium.
4. Muscle consisting of fasciculi is covered by the epimysium, or fascia.
5. The connective tissue of muscle is bound firmly to the connective tissue of tendons and bone.

Nerve and Blood Vessels

1. Motor neurons extend together with arteries and veins through the connective tissue of skeletal muscles.
2. At the level of the perimysium, axons of motor neurons branch and each branch projects to a muscle fiber to form a synapse.

Muscle Fibers

1. A muscle fiber is a single cell consisting of a plasma membrane (sarcolemma), cytoplasm (sarcoplasm), several nuclei, and myofibrils.
2. Myofibrils are composed of two major protein fibers: actin and myosin.
   - Actin myofilaments consist of a double helix of F actin (composed of G actin monomers), tropomyosin, and troponin.
   - Myosin molecules, consisting of two globular heads and a rodlike portion, constitute myosin myofilaments.
   - A cross-bridge is formed when the myosin binds to the actin.
3. Actin and myosin are organized to form sarcomeres.
   - Sarcomeres are bound by Z disks that hold actin myofilaments.
   - Six actin myofilaments (thin filaments) surround a myosin myofilament (thick filament).
   - Myofibrils appear striated because of A bands and I bands.

Sliding Filament Model (p. 278)

1. Actin and myosin myofilaments do not change in length during contraction.
2. Actin and myosin myofilaments slide past one another in a way that causes sarcomeres to shorten.
3. The I band and H zones become narrower during contraction, and the A band remains constant in length.

Physiology of Skeletal Muscle Fibers (p. 278)

Membrane Potentials

1. Plasma membranes are polarized, which means there is a charge difference called the resting membrane potential, across the plasma membrane. The membrane becomes polarized when the tendency for K^+ to diffuse out of the cell is resisted by the negative charges of molecules inside of the cell.

Ion Channels

1. An action potential is a reversal of the resting membrane potential so the inside of the plasma membrane becomes positive.
2. Ion channels are responsible for producing action potentials.
3. Two types of membrane channels produce action potentials, ligand-gated and voltage-gated ion channels.

Action Potentials

1. The charge difference across the plasma membrane of cells is the resting membrane potential.
2. Depolarization results from an increase in the permeability of the plasma membrane to Na^+.
3. An all-or-none action potential is produced if depolarization reaches threshold.
4. The depolarization phase of the action potential results from many Na^+ channels opening in an all-or-none fashion.
5. The repolarization phase of the action potential occurs when the Na^+ channels close and K^+ channels open briefly.
6. Propagation of action potentials along the plasma membrane of neurons and skeletal muscle fibers occurs in an all-or-none fashion.

Neuromuscular Junction

1. The presynaptic terminal of the axon is separated from the postsynaptic membrane of the muscle fiber by the synaptic cleft.
2. Acetylcholine released from the presynaptic terminal binds to receptors of the postsynaptic membrane, thereby changing membrane permeability and producing an action potential.
3. After an action potential occurs, acetylcholinesterase splits acetylcholine into acetic acid and choline. Choline is reabsorbed into the presynaptic terminal to re-form acetylcholine.

Excitation–Contraction Coupling

1. Invaginations of the sarcolemma form T tubules that wrap around the sarcomeres.
2. A triad is a T tubule and two terminal cisternae (an enlarged area of sarcoplasmic reticulum).
3. Action potentials move into the T tubule system, causing voltage-gated Ca^{2+} channels to open to release Ca^{2+} from the sarcoplasmic reticulum.
4. Ca^{2+} diffuses from the sarcoplasmic reticulum to the myofilaments and binds to troponin, causing tropomyosin to move and expose actin to myosin.
5. Contraction occurs when actin and myosin bind, myosin changes shape, and actin is pulled past the myosin.
6. Relaxation occurs when calcium is taken up by the sarcoplasmic reticulum, ATP binds to myosin, and tropomyosin moves back so actin is no longer exposed to myosin.

Cross Bridge Movement

1. One ATP molecule is required for each cycle of cross-bridge formation, movement, and release.
2. ATP is also required to transport Ca^{2+} into the sarcoplasmic reticulum and to maintain normal concentration gradients across the plasma membrane.

Muscle Relaxation

1. Ca^{2+} is transported into the sarcoplasmic reticulum.
2. Ca^{2+} diffuses away from troponin, preventing further cross-bridge formation.

Physiology of Skeletal Muscle (p. 287)

Muscle Twitch

1. A muscle twitch is the contraction of a single muscle fiber or a whole muscle in response to a stimulus.
2. A muscle twitch has lag, contraction, and relaxation phases.

Stimulus Strength and Muscle Contraction

1. For a given condition, a muscle fiber or motor unit contracts with a consistent force in response to each action potential, which is called the all-or-none law of skeletal muscle contraction.
2. For a whole muscle, a stimulus of increasing magnitude results in graded contractions of increased force as more motor units are recruited (multiple motor unit summation).

Stimulus Frequency and Muscle Contraction

1. A stimulus of increasing frequency increases the force of contraction (multiple-wave summation).
2. Incomplete tetanus is partial relaxation between contractions, and complete tetanus is no relaxation between contractions.
3. The force of contraction of a whole muscle increases with increased frequency of stimulation because of an increasing concentration of Ca^{2+} around the myofibrils and because of complete stretching of muscle elastic elements.
4. Treppe is an increase in the force of contraction during the first few contractions of a rested muscle.

Types of Muscle Contractions (p. 292)

1. Isometric contractions cause a change in muscle tension but no change in muscle length.
2. Isotonic contractions cause a change in muscle length but no change in muscle tension.
3. Concentric contractions cause muscles to shorten and tension to increase.

4. Eccentric contractions cause muscles to increase in length and the tension to gradually decrease.
5. Muscle tone is maintenance of a steady tension for long periods.
6. Asynchronous contractions of motor units produce smooth, steady muscle contractions.

Length Versus Tension

Muscle contracts with less-than-maximum force if its initial length is shorter or longer than optimum.

Fatigue (p. 294)

Fatigue is the decreased ability to do work and can be caused by the central nervous system, depletion of ATP in muscles, or depletion of acetylcholine in the neuromuscular synapse.

Physiologic Contracture and Rigor Mortis

Physiologic contracture (inability of muscles to contract or relax) and rigor mortis (stiff muscles after death) result from inadequate amounts of ATP.

Energy Sources (p. 296)

Energy for muscle contraction comes from ATP.

Creatine Phosphate

ATP can be synthesized when ADP reacts with creatine phosphate to form creatine and ATP. ATP from this source provides energy for a short time during intense exercise.

Anaerobic Respiration

ATP is synthesized by anaerobic respiration and is used to provide energy for a short time during intense exercise. Anaerobic respiration produces ATP less efficiently but more rapidly than aerobic respiration. Lactic acid levels increase because of anaerobic respiration.

Aerobic Respiration

ATP is synthesized by aerobic respiration. Although ATP is produced more efficiently, it is produced more slowly. Aerobic respiration produces energy for muscle contractions under resting conditions or during exercises such as long-distance running.

Oxygen Debt

After anaerobic respiration, aerobic respiration is higher than normal, thereby restoring creatine phosphate levels and converting lactic acid to glucose.

Slow and Fast Fibers (p. 297)

Slow-Twitch, or High-Oxidative, Muscle Fibers

Slow-twitch muscle fibers split ATP slowly and have a well-developed blood supply, many mitochondria, and myoglobin.

Fast-Twitch, or Low-Oxidative, Muscle Fibers

Fast-twitch muscle fibers split ATP rapidly.

1. Fatigable fast-twitch fibers have large amounts of glycogen, a poor blood supply, fewer mitochondria, and little myoglobin.
2. Fatigue-resistant fast-twitch fibers have a well-developed blood supply, more mitochondria, and more myoglobin.

Distribution of Fast-Twitch and Slow-Twitch Muscle Fibers

People who are good sprinters have a greater percentage of fast-twitch muscle fibers, and people who are good long-distance runners have a higher percentage of slow-twitch muscle fibers in their leg muscles.

Effects of Exercise

1. Muscles increase (hypertrophy) or decrease (atrophy) in size because of a change in the size of muscle fibers.
2. Anaerobic exercise develops fatigable fast-twitch fibers. Aerobic exercise develops slow-twitch fibers and changes fatigable fast-twitch fibers into fatigue-resistant fast-twitch fibers.

Heat Production (p. 299)

1. Heat is produced as a by-product of chemical reactions in muscles.
2. Shivering produces heat to maintain body temperature.

Smooth Muscle (p. 299)

1. Smooth muscle cells are spindle-shaped with a single nucleus. They have actin myofilaments and myosin myofilaments but are not striated.
2. The sarcoplasmic reticulum is poorly developed, and caveolae may function as a T tubule system.
3. Ca^{2+} enters the cell to initiate contraction; calmodulin binds to Ca^{2+} and activates an enzyme that transfers a phosphate group from ATP to myosin. When phosphate groups are attached to myosin, cross-bridges form.
4. Relaxation results when myosin phosphatase removes a phosphate group from the myosin molecule.
   - If phosphate is removed while the cross-bridges are attached, relaxation occurs very slowly, and this is referred to as the catch phase.
   - If phosphate is removed while the cross-bridges are not attached, relaxation occurs rapidly.

Types of Smooth Muscle

1. Visceral smooth muscle fibers contract slowly, have gap junctions (and thus function as a single unit), and can be autorhythmic.
2. Multiunit smooth muscle fibers contract rapidly in response to stimulation by neurons and function independently.

Electrical Properties of Smooth Muscle

1. Spontaneous contractions result from Na^{+} and Ca^{2+} leakage into cells. Na^{+} and Ca^{2+} movement into the cell is involved in depolarization.
2. The autonomic nervous system and hormones can inhibit or stimulate action potentials (and thus contractions). Hormones can also stimulate or inhibit contractions without affecting membrane potentials.

Functional Properties of Smooth Muscle

1. Smooth muscle can contract autorhythmically in response to stretch or when stimulated by the autonomic nervous system or hormones.
2. Smooth muscle maintains a steady tension for long periods.
3. The force of smooth muscle contraction remains nearly constant, despite changes in muscle length.
4. Smooth muscle does not develop an oxygen debt.

Regulation of Smooth Muscle

1. Smooth muscle is innervated by the autonomic nervous system and is involuntary.
2. Hormones are important in regulating smooth muscle. Some hormones can increase the Ca^{2+} permeability of some smooth muscle membranes and, therefore, cause contraction without a change in the resting membrane potential.

Cardiac Muscle (p. 303)

Cardiac muscle fibers are striated, have a single nucleus, are connected by intercalated disks (thus function as a single unit), and are capable of autorhythmicity.

Effects of Aging on Skeletal Muscle (p. 304)

1. Aging skeletal muscle is associated with reduced muscle mass, increased response time, and increased time that muscle takes to contract in response to nervous stimuli.
2. Muscle fibers decrease in number, motor units decrease in number, and recovery time increases.

REVIEW AND COMPREHENSION

1. Which of these is true of skeletal muscle?
   a. spindle-shaped cells
   b. under involuntary control
   c. many peripherally located nuclei per muscle cell
   d. forms the walls of hollow internal organs
   e. may be autorhythmic
2. Which of these is *not* a major functional characteristic of muscle?
   a. contractility
   b. elasticity
   c. excitability
   d. extensibility
   e. secretability
3. The connective tissue sheath that surrounds a muscle fasciculus is the
   a. perimysium.
   b. endomysium.
   c. epimysium (fascia).
   d. hypomysium.
   e. external lamina.
4. Given these structures:
   1. whole muscle
   2. muscle fiber (cell)
   3. myofilament
   4. myofibril
   5. muscle fasciculus

   Choose the arrangement that lists the structures in the correct order from the largest to the smallest structure.
   a. 1,2,5,3,4
   b. 1,2,5,4,3
   c. 1,5,2,3,4
   d. 1,5,2,4,3
   e. 1,5,4,2,3
5. Each myofibril
   a. is made up of many muscle fibers.
   b. contains sarcoplasmic reticulum.
   c. is made up of many sarcomeres.
   d. contains T tubules.
   e. is the same thing as a muscle fiber.
6. Myosin myofilaments are
   a. attached to the Z disk.
   b. found primarily in the I band.
   c. thinner than actin myofilaments.
   d. absent from the H zone.
   e. attached to filaments that form the M line.
7. Which of these statements about the molecular structure of myofilaments is true?
   a. Tropomyosin has a binding site for Ca^{2+}.
   b. The head of the myosin molecule binds to an active site on G actin.
   c. ATPase is found on troponin.
   d. Troponin binds to the rodlike portion of myosin.
   e. Actin molecules have a hingelike portion that bends and straightens during contraction.
8. The part of the sarcolemma that invaginates into the interior of the skeletal muscle cells is the
   a. T tubule system.
   b. sarcoplasmic reticulum.
   c. myofibrils.
   d. terminal cisternae.
   e. mitochondria.
9. During the depolarization phase of an action potential, the permeability of the plasma membrane to
   a. Ca^{2+} increases.
   b. Na^{+} increases.
   c. K^{+} increases.
   d. Ca^{2+} decreases.
   e. Na^{+} decreases.
10. During depolarization, the inside of the membrane
    a. becomes more negative than the outside of the membrane.
    b. becomes more positive than the outside of the membrane.
    c. is unchanged.
11. During repolarization of the plasma membrane,
    a. Na^{+} moves to the inside of the cell.
    b. Na^{+} moves to the outside of the cell.
    c. K^{+} moves to the inside of the cell.
    d. K^{+} moves to the outside of the cell.
12. Given these events:
    1. acetylcholine broken down into acetic acid and choline
    2. acetylcholine moves across the synaptic cleft
    3. action potential reaches the terminal branch of the motor neuron
    4. acetylcholine combines with a receptor molecule
    5. action potential is produced on the muscle fiber's plasma membrane

    Choose the arrangement that lists the events in the order they occur at a neuromuscular junction.
    a. 2,3,4,1,5
    b. 3,2,4,5,1
    c. 3,4,2,1,5
    d. 4,5,2,1,3
    e. 5,1,2,4,3
13. Acetylcholinesterase is an important molecule in the neuromuscular junction because it
    a. stimulates receptors on the presynaptic terminal.
    b. synthesizes acetylcholine from acetic acid and choline.
    c. stimulates receptors within the postsynaptic membrane.
    d. breaks down acetylcholine.
    e. causes the release of Ca^{2+} from the sarcoplasmic reticulum.

14. Given these events:
    1. sarcoplasmic reticulum releases Ca^{2+}
    2. sarcoplasmic reticulum takes up Ca^{2+}
    3. Ca^{2+} diffuses into myofibrils
    4. action potential moves down the T tubule
    5. sarcomere shortens
    6. muscle relaxes

    Choose the arrangement that lists the events in the order they occur following a single stimulation of a skeletal muscle cell.
    a. 1,3,4,5,2,6
    b. 2,3,5,4,6,1
    c. 4,1,3,5,2,6
    d. 4,2,3,5,1,6
    e. 5,1,4,3,2,6
15. Given these events:
    1. Ca^{2+} combines with tropomyosin
    2. Ca^{2+} combines with troponin
    3. tropomyosin pulls away from actin
    4. troponin pulls away from actin
    5. tropomyosin pulls away from myosin
    6. troponin pulls away from myosin
    7. myosin binds to actin

    Choose the arrangement that lists the events in the order they occur during muscle contraction.
    a. 1,4,7
    b. 2,5,6
    c. 1,3,7
    d. 2,4,7
    e. 2,3,7
16. Which of these regions shortens during skeletal muscle contraction?
    a. A band
    b. I band
    c. H zone
    d. both a and b
    e. both b and c
17. With stimuli of increasing strength, which of these is capable of a graded response?
    a. nerve axon
    b. muscle fiber
    c. motor unit
    d. whole muscle
18. Considering the force of contraction of a skeletal muscle cell, multiple-wave summation occurs because of
    a. increased strength of action potentials on the plasma membrane.
    b. a decreased number of cross-bridges formed.
    c. an increase in Ca^{2+} concentration around the myofibrils.
    d. an increased number of motor units recruited.
    e. increased permeability of the sarcolemma to Ca^{2+}.
19. Which of these events occurs during the lag (latent) phase of muscle contraction?
    a. cross-bridge movement
    b. active transport of Ca^{2+} into the sarcoplasmic reticulum
    c. Ca^{2+} binds to troponin
    d. the sarcomere shortens
    e. ATP is broken down to ADP
20. A weight lifter attempts to lift a weight from the floor, but the weight is so heavy he is unable to move it. The type of muscle contraction the weight lifter used was mostly
    a. isometric.
    b. isotonic.
    c. isokinetic.
    d. concentric.
    e. eccentric.
21. An active tension curve illustrates
    a. how isometric contractions occur.
    b. that the greatest force of contraction occurs if a muscle is not stretched at all.
    c. that passive tension can create active tension.
    d. that optimal overlap of actin and myosin produces the greatest force of contraction.
    e. that the greatest force of contraction occurs with little or no overlap of actin and myosin.
22. Which of these types of fatigue is the most common?
    a. muscular fatigue
    b. psychologic fatigue
    c. synaptic fatigue
    d. army fatigue
23. Given these conditions:
    1. low ATP levels
    2. little or no transport of Ca^{2+} into the sarcoplasmic reticulum
    3. cross-bridges release
    4. Na^{+} accumulates in the sarcoplasm
    5. cross-bridges form

    Choose the conditions that occur in both physiologic contracture and rigor mortis.
    a. 1,2,3
    b. 1,2,5
    c. 1,2,3,4
    d. 1,2,4,5
    e. 1,2,3,4,5
24. Jerry Jogger's 3 mile run every morning takes about 30 minutes. Which of these sources provides most of the energy for his run?
    a. aerobic respiration
    b. anaerobic respiration
    c. creatine phosphate
    d. stored ATP
25. Which of these conditions would one expect to find within the leg muscle cells of a world-class marathon runner?
    a. myoglobin-poor
    b. contract very quickly
    c. primarily anaerobic
    d. numerous mitochondria
    e. large deposits of glycogen
26. Which of these does *not* occur as a result of muscle hypertrophy?
    a. increase in number of sarcomeres
    b. increase in number of myofibrils
    c. increase in number of fibers
    d. increase in blood vessels and mitochondria
    e. increase in connective tissue
27. Relaxation in smooth muscle occurs when
    a. myosin kinase attaches phosphate to the myosin head.
    b. Ca^{2+} binds to calmodulin.
    c. myosin phosphatase removes phosphate from myosin.
    d. Ca^{2+} channels open.
    e. Ca^{2+} is released from the sarcoplasmic reticulum.
28. Compared to skeletal muscle, visceral smooth muscle
    a. has the same ability to be stretched.
    b. when stretched, loses the ability to contract forcefully.
    c. maintains about the same tension, even when stretched.
    d. cannot maintain long, steady contractions.
    e. can accumulate a substantial oxygen debt.

29. Which of these often have spontaneous contractions?
    a. multiunit smooth muscle
    b. visceral smooth muscle
    c. skeletal muscle
    d. both a and b
    e. both b and c

30. Which of these statements concerning aging and skeletal muscle is correct?
    a. There is a loss of muscle fibers with aging.
    b. Slow-twitch fibers decrease in number faster than fast-twitch fibers.
    c. Loss of strength and speed is mainly due to loss of neuromuscular junctions.
    d. There is an increase in density of capillaries in skeletal muscle.
    e. The number of motor neurons remains constant.

Answers in Appendix F

CRITICAL THINKING

1. Bob Canner improperly canned some homegrown vegetables. As a result, he contracted botulism poisoning after eating the vegetables. Symptoms included difficulty in swallowing and breathing. Eventually he died of respiratory failure (his respiratory muscles relaxed and would not contract). Assuming that botulism toxin affects the neuromuscular synapse, propose the ways that the toxin could produce the observed symptoms.
2. A patient is thought to be suffering from either muscular dystrophy or myasthenia gravis. How would you distinguish between the two conditions?
3. Under certain circumstances, the actin and myosin myofilaments can be extracted from muscle cells and placed in a beaker. They subsequently bind together to form long filaments of actin and myosin. Addition of what cell organelle or molecule to the beaker would make the actin and myosin myofilaments unbind?
4. Explain the effect of a lower-than-normal temperature on each of the processes that occur in the lag (latent) phase of muscle contraction.
5. Design an experiment to test the following hypothesis: Muscle A has the same number of motor units as muscle B. Assume you could stimulate the nerves that innervate skeletal muscles with an electronic stimulator and monitor the tension produced by the muscles.
6. Compare the differences that occur when a muscle such as the biceps slowly lifts and lowers a weight and when a muscle twitches.
7. Predict the shape of an active tension curve for visceral smooth muscle. How does it differ from the active tension curve for skeletal muscle?
8. A researcher is investigating the composition of muscle tissue in the gastrocnemius muscles (in the calf of the leg) of athletes. A needle biopsy is taken from the muscle, and the concentration (or enzyme activity) of several substances is determined. Describe the major differences this researcher sees when comparing the muscles from athletes who perform in the following events: 100 m dash, weight lifting, and 10,000 m run.
9. Harvey Leche milked cows by hand each morning before school. One morning he slept later than usual and had to hurry to get to school on time. As he was milking the cows as fast as he could, his hands became very tired, and for a short time he could neither release his grip nor squeeze harder. Explain what happened.
10. Blood vessels that supply oxygen to smooth muscle undergo constriction. Explain how this phenomenon affects the ability of smooth muscle to contract.
11. Shorty McFleet noticed that his rate of respiration was elevated after running a 100 m race but was not as elevated after running slowly for a much longer distance. Because you studied muscle physiology, he asked you for an explanation. What would you say?
12. It's known that high blood K^+ concentrations cause depolarization of the resting membrane potential. Predict the effect of high blood K^+ levels on smooth muscle function. Explain.
13. Predict and explain the response if the ATP concentration in a muscle that was exhibiting rigor mortis could be instantly increased.
14. A hormone stimulates smooth muscle from a blood vessel to contract. The hormone only causes a small change in the membrane potential, however, even though the smooth muscle tissue contracts substantially. Explain.
15. These experiments were performed in an anatomy and physiology laboratory. The rate and depth of respiration for a resting student were determined. In experiment A, students ran in place for 30 seconds and then immediately sat down and relaxed, and respiration rate and depth were again determined. Experiment B was just like experiment A, except that the students held their breath while running in place. What differences in respiration would you expect for the two different experiments? Explain the basis for your predictions.

Answers in Appendix G

ANSWERS TO PREDICT QUESTIONS

1. When a muscle changes length, the I bands and the H zones change in width, but the A band does not. When a muscle is stretched, the I bands and the H zones increase in width as the length of the sarcomere increases. When a muscle contracts, cross-bridges form and cause the actin myofilaments to slide over the myosin myofilaments. The result is that the I bands and H zones decrease in width as the sarcomeres shorten. When a muscle relaxes, cross-bridges release, and actin myofilaments slide past myosin myofilaments as the sarcomeres lengthen. The I bands and H zones increase in width.
2. When gated K^+ channels open, K^+ diffuse from an area of higher concentration inside of the cell to an area of lower concentration outside of the cell.
3. If insufficient acetylcholine is released from the presynaptic terminal of an axon, an action potential is not produced in the muscle fiber and the muscle cannot contract. An action potential must be produced in the muscle fiber for contraction to occur. If inadequate acetylcholine is released from the presynaptic terminal of an axon, several action potentials in the axons would have to occur to cause the presynaptic terminal neurons to release enough acetylcholine to produce an action potential in the muscle fibers. Each action potential would release some acetylcholine, and, in response, a local potential may be produced in the postsynaptic membrane. If the local potentials were produced over a short period, they could summate (see chapter 11) and reach threshold. If threshold is reached, an action potential is produced.

4. a. Organophosphate poisons inhibit the activity of acetylcholinesterase, which breaks down acetylcholine at the neuromuscular junction and limits the length of time the acetylcholine stimulates the postsynaptic terminal of the muscle fiber. Consequently, acetylcholine accumulates in the synaptic cleft and continuously stimulates the muscle fiber. As a result, the muscle remains contracted until it fatigues. Death is caused by the inability of the victim to breathe. Either the respiratory muscles are in spastic paralysis, or they are so depleted of ATP that they cannot contract at all.
   b. Curare binds to acetylcholine receptors and thus prevents acetylcholine from binding to them. Because curare does not activate the receptors, the muscles don't respond to nervous stimulation. The person suffers from flaccid paralysis and dies from suffocation because the respiratory muscles are not able to contract.
5. a. If Na^+ cannot enter the muscle fiber, no action potentials are produced in the muscle fiber because the influx of Na^+ causes the depolarization phase of the action potential. Without action potentials, the muscle fiber cannot contract at all. The result is flaccid paralysis.
   b. If ATP levels are low in a muscle fiber before stimulation, the following events occur. Energy from the breakdown of ATP already is stored in the heads of the myosin molecules. After stimulation, cross-bridges form. If not enough additional ATP molecules are in the muscle cells to bind to the myosin molecules to allow for cross-bridge release, however, the muscle becomes stiff without contracting or relaxing.
   c. If ATP levels in the muscle fiber are adequate but the action potential frequency is so high that Ca^{2+} accumulates around the myofilaments, the muscle contracts continuously without relaxing. As long as the ions are numerous within the sarcoplasm in the area of the myofilaments, cross-bridge formation is possible. If ATP levels are adequate, cross-bridge formation, release, and formation can proceed again, resulting in a continuously contracting muscle.
6. A decrease occurs in muscle control when reinnervation of muscle fibers occurs after poliomyelitis because the number of motor units in the muscle is decreased. Reinnervation results in a greater number of muscle fibers per motor unit. Control is reduced because the number of motor units that can be recruited is decreased. The greater the number of motor units in a muscle, the greater is the ability to have fine gradations of muscle contraction as motor units are recruited. A smaller number of motor units means that gradations of muscle contraction are not as fine.
7. As a weight is lifted, the muscle contractions are concentric contractions. When a weight lifter lifts a heavy weight above the head, most of the muscle groups contract with a force while the muscle is shortening. Concentric contractions are a category of isotonic contractions in which tension in the muscle increases or remains about the same while the muscle shortens. While the weight is held above Mary's head, the contractions are isometric contractions, because the length of the muscles doesn't change. While the weight is lowered, unless the weight lifter simply drops the weight, the length of the muscles increases as the weight is lowered for most of the muscle groups. Eccentric contractions are contractions in which tension is maintained in a muscle while the muscle increases in length. The major muscle groups are therefore contracting eccentrically while the weight is lowered.
8. During a 10 km run, aerobic metabolism is the primary source of ATP production for muscle contraction. Anaerobic metabolism provides enough ATP for up to 3 minutes during vigorous anaerobic exercise, but running a 10 km race takes much longer. If the runner sprints at the end of the 10 km run, however, anaerobic metabolism accounts for some of the energy production. After the run, aerobic metabolism is elevated for a time to pay back the oxygen debt. Anaerobic metabolism near the end of the run produces lactic acid, which is converted back to glucose after the run, a process that requires ATP. ATP is also required to restore the normal creatine phosphate levels in the muscle fibers and is produced through aerobic metabolism, which uses oxygen. The amount of oxygen used to produce the necessary ATP is the oxygen debt.
9. Long-distance runners should concentrate on running long distances. Slow-twitch muscles function very well for long-distance running. In addition, exercise that causes the muscles to perform aerobic metabolism improves the ability to carry on aerobic exercise and is more effective than exercise done under anaerobic conditions. Aerobic exercise combined with a large percentage of slow-twitch muscle fibers is the best combination for long-distance runners. Aerobic exercise, however, increases the ability of even fast-twitch muscles to resist fatigue.
10. A ligand that binds to its receptor and results in a sustained increase in the permeability of the plasma membrane to Ca^{2+} results in a sustained contraction without a large increase in ATP breakdown. The increased intracellular concentration of Ca^{2+} increases the number of phosphate groups removed from the myosin molecules while cross-bridges are attached. Because these cross-bridges release slowly, the result is a sustained contraction.
11. Muscular dystrophy affects the muscles of respiration and causes deformity of the thoracic cavity. The reduced capacity of muscle tissue to contract is one factor that reduces the ability to breath deeply or cough effectively. In addition, the thoracic cavity can become severely deformed because of the replacement of skeletal muscle with connective tissue. The deformity can result in severe kyphoscoliosis, which also reduces the ability to breath deeply. In addition, muscular dystrophy can affect the muscle of the heart and cause heart failure. The persistent edema in the lung increases the chance of bacteria multiplying in the lung tissue.

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