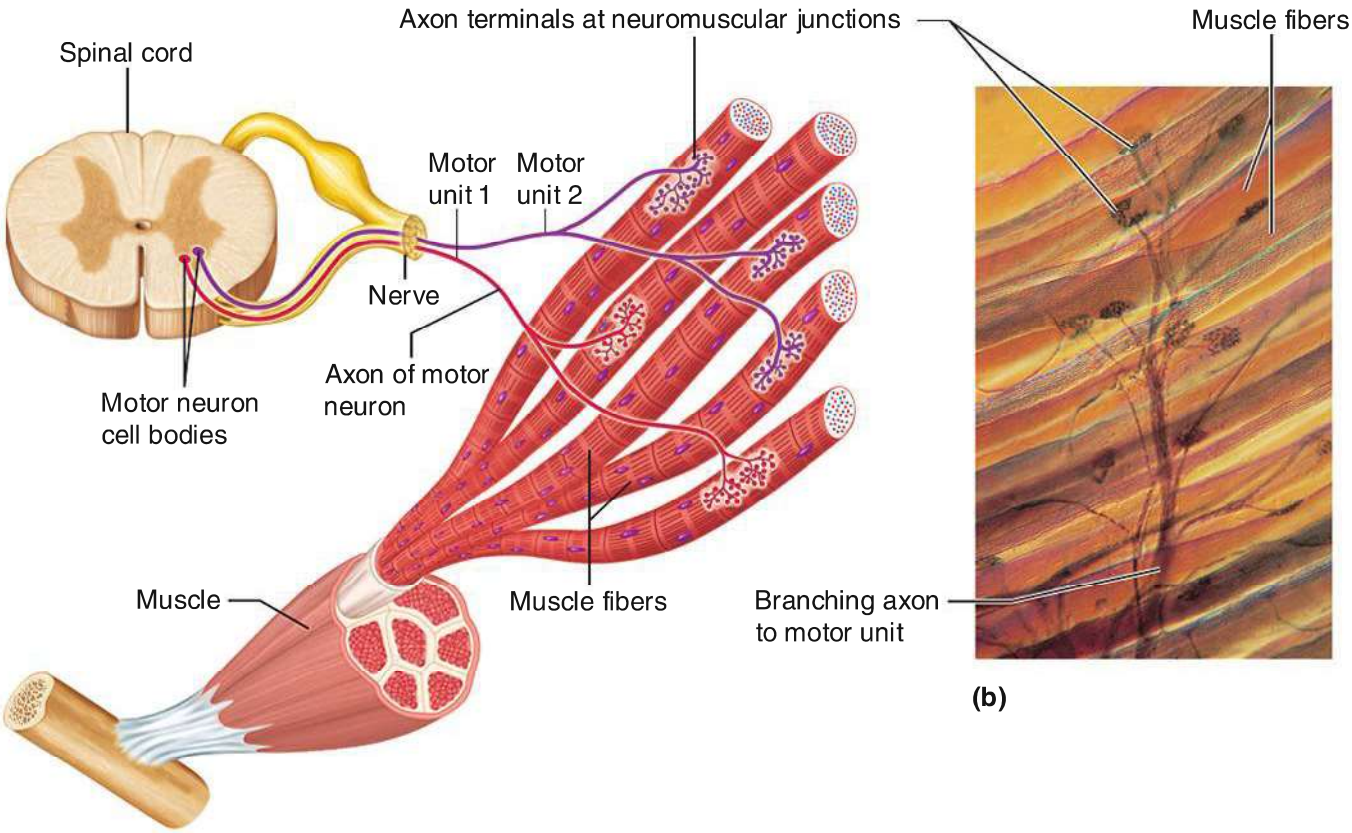


Figure 6.4 Motor units. Each motor unit consists of a motor neuron and all the muscle fibers it activates. **(a)** Portions of two motor units are shown. The motor neurons reside in the spinal cord, and their axons extend to the muscle. Within the muscle, each axon divides into a number of axon terminals, distributed to muscle fibers scattered throughout the muscle. **(b)** Photo of a portion of a motor unit (100×).

The Nerve Stimulus and the Action Potential

To contract, skeletal muscle cells must be stimulated by nerve impulses. One motor neuron (nerve cell) may stimulate a few muscle cells or hundreds of them, depending on the particular muscle and the work it does. One neuron and all the skeletal muscle cells it stimulates is called a **motor unit** (Figure 6.4). When a long, thread-like extension of the neuron, called the *nerve fiber* or **axon,** reaches the muscle, it branches into a number of **axon terminals,** each of which forms junctions with the sarcolemma of a different muscle cell (Figure 6.5). These junctions, called **neuromuscular** (literally, "nerve-muscle") **junctions,** contain vesicles filled with a chemical referred to as a **neurotransmitter.** The specific neurotransmitter that stimulates skeletal muscle cells is **acetylcholine** (as″e-til-ko′lēn), or **ACh.** Although the nerve endings and the muscle cells' membranes are very close, they never touch. The gap between them, the **synaptic cleft,** is filled with tissue (interstitial) fluid.

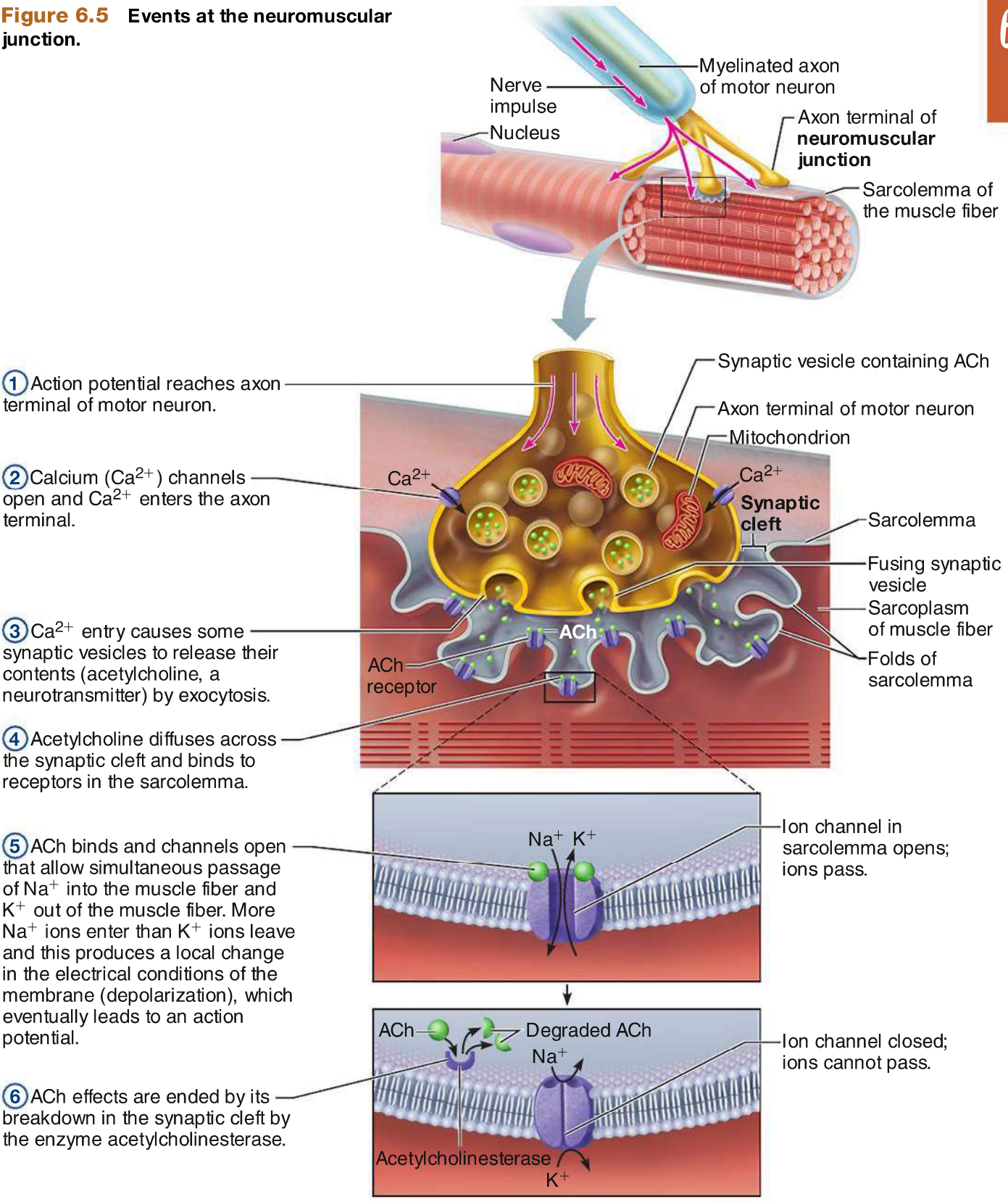
DID YOU GET IT?

6. What two structures are closely associated at a neuromuscular junction?

For the answer, see Appendix D.

Now that we have described the structure of the neuromuscular junction, we are ready to examine what happens there. As you read, refer to the numbered steps in Figure 6.5. When a nerve impulse reaches the axon terminals ①, calcium channels open and calcium (Ca^{2+}) enters the

Figure 6.5 **Events at the neuromuscular junction.**



terminal (2). Calcium entry causes some of the synaptic vesicles in the axon terminal to release acetylcholine (3), which then diffuses across the synaptic cleft and attaches to receptors (membrane proteins) that are located in highly folded regions of the sarcolemma (4). If enough acetylcholine is released, the sarcolemma at that point becomes *temporarily* even more permeable to sodium ions (Na^+), which rush into the muscle cell, and to potassium ions (K^+), which diffuse out of the cell. However, more Na^+ enters than K^+ leaves. This imbalance gives the cell interior an excess of positive ions, which reverses the electrical conditions of the sarcolemma, an event called *depolarization,* and opens more channels that allow Na^+ entry only (5). This "upset" generates an electrical current called an **action potential.** Once begun, the action potential is unstoppable; it travels over the entire surface of the sarcolemma, conducting the electrical impulse from one end of the cell to the other. The result is contraction of the muscle cell.

Note that while the action potential is occurring, acetylcholine, which began the process, is broken down to acetic acid and choline by enzymes (acetylcholinesterase, or AChE) present on the sarcolemma and in the synaptic cleft (6) (see Figure 6.5 (6)). For this reason, a single nerve impulse produces only one contraction. This prevents continued contraction of the muscle cell in the absence of additional nerve impulses. The muscle cell relaxes until stimulated by the next round of acetylcholine release.

We explain this series of events more fully on pp. 235–238 in the discussion of nerve physiology, but perhaps it would be helpful to compare this to some common event, such as lighting a match under a small dry twig (**Figure 6.6**). The charring of the twig by the flame can be compared to the change in membrane permeability that allows sodium ions into the cell. When that part of the twig becomes hot enough (when enough sodium ions have entered the cell), the twig will suddenly burst into flame, and the flame will consume the twig (the action potential will be conducted along the entire length of the sarcolemma).

The events that return the cell to its resting state include (1) diffusion of potassium ions (K^+) out of the cell and (2) operation of the sodium-potassium pump, the active transport mechanism that moves the sodium and potassium ions back to their initial positions.

DID YOU GET IT?

7. What ions enter the muscle cell during action potential generation?

For the answer, see Appendix D.

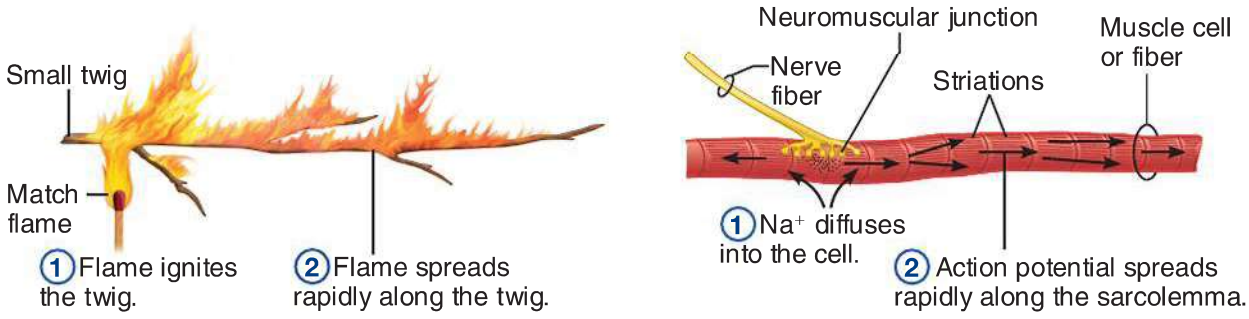


Figure 6.6 Comparison of the action potential to a flame consuming a dry twig. (a) The first event in igniting a dry twig is holding the match flame under one area of the twig. The second event is the twig's bursting into flame when it has been heated enough and spreading of the flame to burn the entire twig. **(b)** The first event in exciting a muscle cell is the rapid diffusion of sodium ions (Na^+) into the cell when the permeability of the sarcolemma changes. The second event is the spreading of the action potential along the sarcolemma when enough sodium ions have entered to upset the electrical conditions in the cell.

Mechanism of Muscle Contraction: The Sliding Filament Theory

✓ Describe the events of muscle cell contraction.

What causes the filaments to slide? This question brings us back to the myosin heads that protrude all around the ends of the thick filaments. When muscle fibers are activated by the nervous system as just described, the myosin heads attach to binding sites on the thin filaments, and the sliding begins. Each cross bridge attaches and detaches several times during a contraction, generating tension that helps to pull the thin filaments toward the center of the sarcomere. As this event occurs simultaneously in sarcomeres throughout the muscle cell, the cell shortens (**Figure 6.7**).

This "walking" of the myosin cross bridges, or heads, along the thin filaments during muscle shortening is much like a centipede's gait. Some myosin heads ("legs") are always in contact with actin ("the ground"), so that the thin filaments cannot slide backward as this cycle repeats again and again during contraction. Notice that the myofilaments themselves do not shorten during contraction; they simply slide past each other.

The attachment of the myosin cross bridges to actin requires calcium ions (Ca^{2+}). So where does the calcium come from? Action potentials pass deep into the muscle cell along membranous tubules that fold inward from the sarcolemma. Inside the cell, the action potentials stimulate the sarcoplasmic reticulum to release calcium ions into the cytoplasm. The calcium ions trigger the binding of myosin to actin, initiating filament sliding. This sliding process and the role of calcium are depicted in **Figure 6.8**. When the action potential ends, calcium ions are immediately reabsorbed into the SR storage areas, and the muscle cell relaxes and settles back to its original length. This whole series of events takes a few thousandths of a second.

DID YOU GET IT?

8. What chemical—ATP or Ca^{2+}—triggers sliding of the muscle filaments?
9. Which is a cross-bridge attachment more similar to: a precise rowing team or a person pulling a bucket on a rope out of a well?

For answers, see Appendix D.

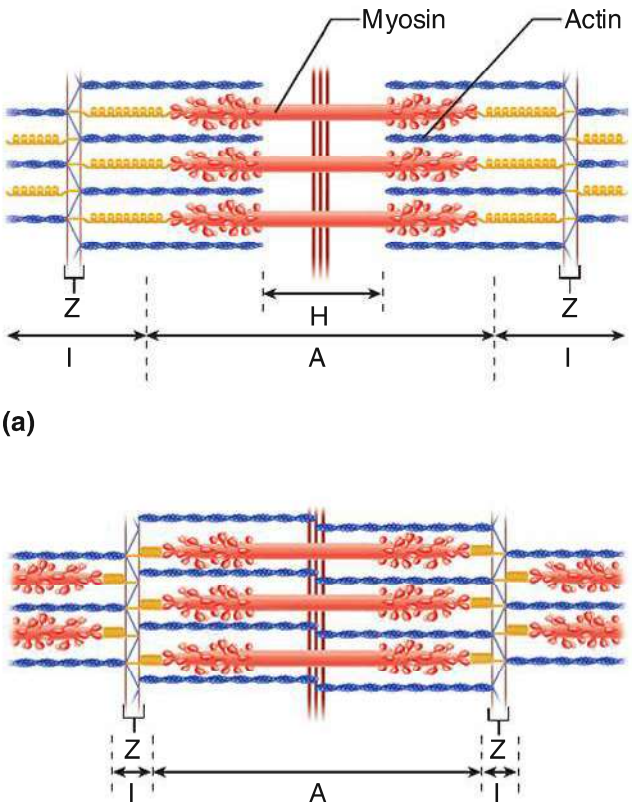


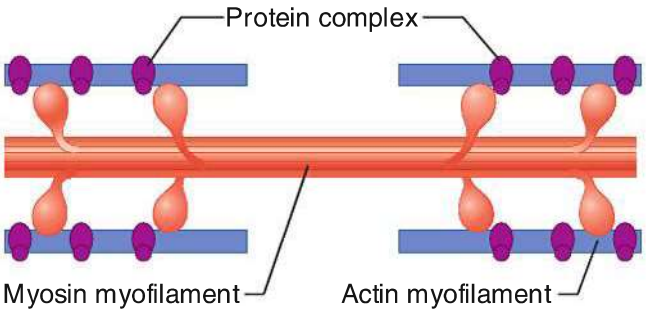
Figure 6.7 Diagrammatic views of a sarcomere. **(a)** Relaxed; **(b)** fully contracted. Notice that in the contracted sarcomere, the light H zone in the center of the A band has disappeared, the Z discs are closer to the thick filaments, and the I bands have nearly disappeared. The A bands move closer together but do not change in length.

Contraction of a Skeletal Muscle as a Whole

✓ Define *graded response, tetanus, isotonic* and *isometric contractions,* and *muscle tone* as these terms apply to a skeletal muscle.

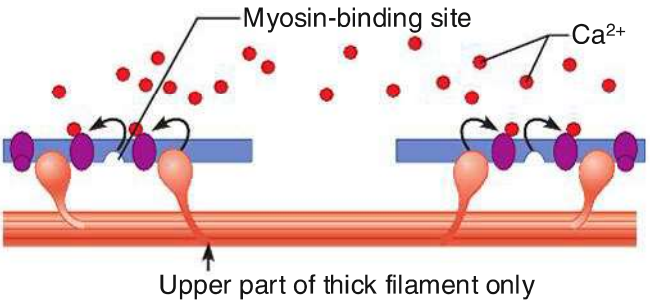
Graded Responses

In skeletal muscles, the "all-or-none" law of muscle physiology applies to the *muscle cell,* not to the whole muscle. It states that a muscle cell will contract to its fullest extent when it is stimulated adequately; it never partially contracts. However, the whole muscle reacts to stimuli with **graded responses,** or different degrees of shortening. In general, graded muscle contractions can be produced two ways: (1) by changing the



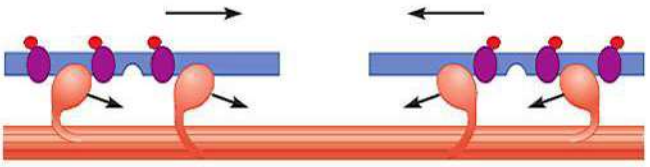
(a)

In a relaxed muscle cell, the regulatory proteins forming part of the actin myofilaments prevent myosin binding (see **a**). When an action potential (AP) sweeps along its sarcolemma and a muscle cell is excited, calcium ions (Ca^{2+}) are released from intracellular storage areas (the sacs of the sarcoplasmic reticulum).



(b)

The flood of calcium acts as the final trigger for contraction, because as calcium binds to the regulatory proteins on the actin filaments, the proteins undergo a change in both their shape and their position on the thin filaments. This action exposes myosin-binding sites on the actin, to which the myosin heads can attach (see **b**), and the myosin heads immediately begin seeking out binding sites.



(c)

The free myosin heads are "cocked," much like a set mousetrap. Myosin attachment to actin "springs the trap," causing the myosin heads to snap (pivot) toward the center of the sarcomere. When this happens, the thin filaments are slightly pulled toward the center of the sarcomere (see **c**). ATP provides the energy needed to release and recock each myosin head so that it is ready to attach to a binding site farther along the thin filament. When the AP ends and calcium ions are returned to SR storage areas, the regulatory proteins resume their original shape and position, and again block myosin binding to the thin filaments. As a result, the muscle cell relaxes and settles back to its original length.

Figure 6.8 **Schematic representation of contraction mechanism: The sliding filament theory.**

frequency of muscle stimulation and (2) by changing the *number* of muscle cells being stimulated at one time. We briefly describe a muscle's response to each of these next.

Muscle Response to Increasingly Rapid Stimulation

Although **muscle twitches** (single, brief, jerky contractions) sometimes result from certain nervous system problems, this is *not* the way our muscles normally operate. In most types of muscle activity, nerve impulses are delivered to the muscle at a very rapid rate—so rapid that the muscle does not get a chance to relax completely between stimuli. As a result, the effects of the successive contractions are "summed" (added) together, and the contractions of the muscle get stronger and smoother. When the muscle is stimulated so rapidly that no evidence of relaxation is seen and the contractions are completely smooth and sustained, the muscle is said to be in **fused,** or **complete, tetanus** (tet′ah-nus), or in

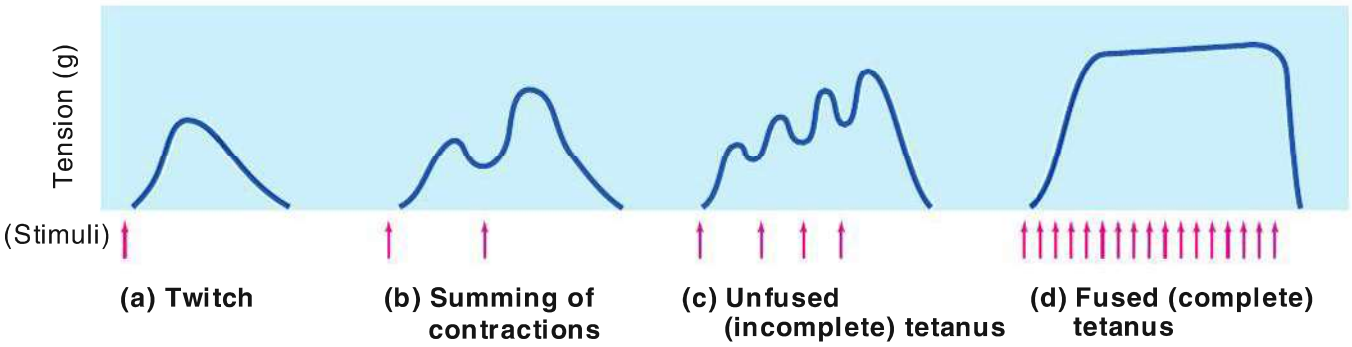


Figure 6.9 A whole muscle's response to different rates of stimulation. In **(a),** a single stimulus is delivered, and the muscle contracts and relaxes (a twitch contraction). In **(b),** stimuli are delivered more frequently, so the muscle does not have time to completely relax; contraction force increases because effects of the individual twitches are summed. In **(c),** more complete fusion of the twitches (unfused tetanus) occurs as stimuli are delivered at a still faster rate.In **(d),** fused tetanus, a smooth continuous contraction without any evidence of relaxation, results from a very rapid rate of stimulation. (Points at which stimuli are delivered are indicated by red arrows. Tension [measured in grams] on the vertical axis refers to the relative force of muscle contraction.)

tetanic contraction.* Until this point is reached, the muscle is said to be exhibiting **unfused,** or **incomplete, tetanus** (Figure 6.9).

Muscle Response to Stronger Stimuli Tetanus produces stronger muscle contractions, but its primary role is to produce smooth and prolonged muscle contractions. How forcefully a muscle contracts depends to a large extent on how many of its cells are stimulated. When only a few cells are stimulated, the contraction of the muscle as a whole is slight. When all the motor units are active and all the muscle cells are stimulated, the muscle contraction is as strong as it can get. Thus, muscle contractions can be slight or vigorous depending on what work has to be done. The same hand that gently soothes can also deliver a stinging slap!

Providing Energy for Muscle Contraction

✓ Describe three ways in which ATP is regenerated during muscle activity.

As a muscle contracts, the bonds of ATP molecules are hydrolyzed to release the needed energy. Surprisingly, muscles store very limited supplies of ATP—only a few seconds' worth, just enough to get you going. Because ATP is the *only* energy source that can be used directly to power muscle activity, ATP must be regenerated continuously if contraction is to continue.

Working muscles use three pathways for ATP regeneration:

1. **Direct phosphorylation of ADP by creatine phosphate** (Figure 6.10a). The unique high-energy molecule **creatine phosphate (CP)** is found in muscle fibers but not other cell types. As ATP is being depleted, interactions between CP and ADP result in transfers of a high-energy phosphate group from CP to ADP, thus regenerating more ATP in a fraction of a second. Although muscle cells store perhaps five times as much CP as ATP, the CP supplies are also soon exhausted (in less than 15 seconds).
2. **Aerobic respiration** (Figure 6.10c). At rest and during light to moderate exercise, some 95 percent of the ATP used for muscle activity comes from aerobic respiration. **Aerobic respiration** occurs in the mitochondria and involves a series of metabolic pathways that use oxygen. These pathways are collectively referred to as *oxidative phosphorylation*. During aerobic respiration, glucose is broken down completely to carbon dioxide and water, and some of the energy released as the bonds are

*Tetanic contraction is normal and desirable and is quite different from the pathological condition of tetanus (commonly called *lockjaw*), which is caused by a toxin made by bacteria. Lockjaw causes muscles to go into uncontrollable spasms, finally causing respiratory arrest.

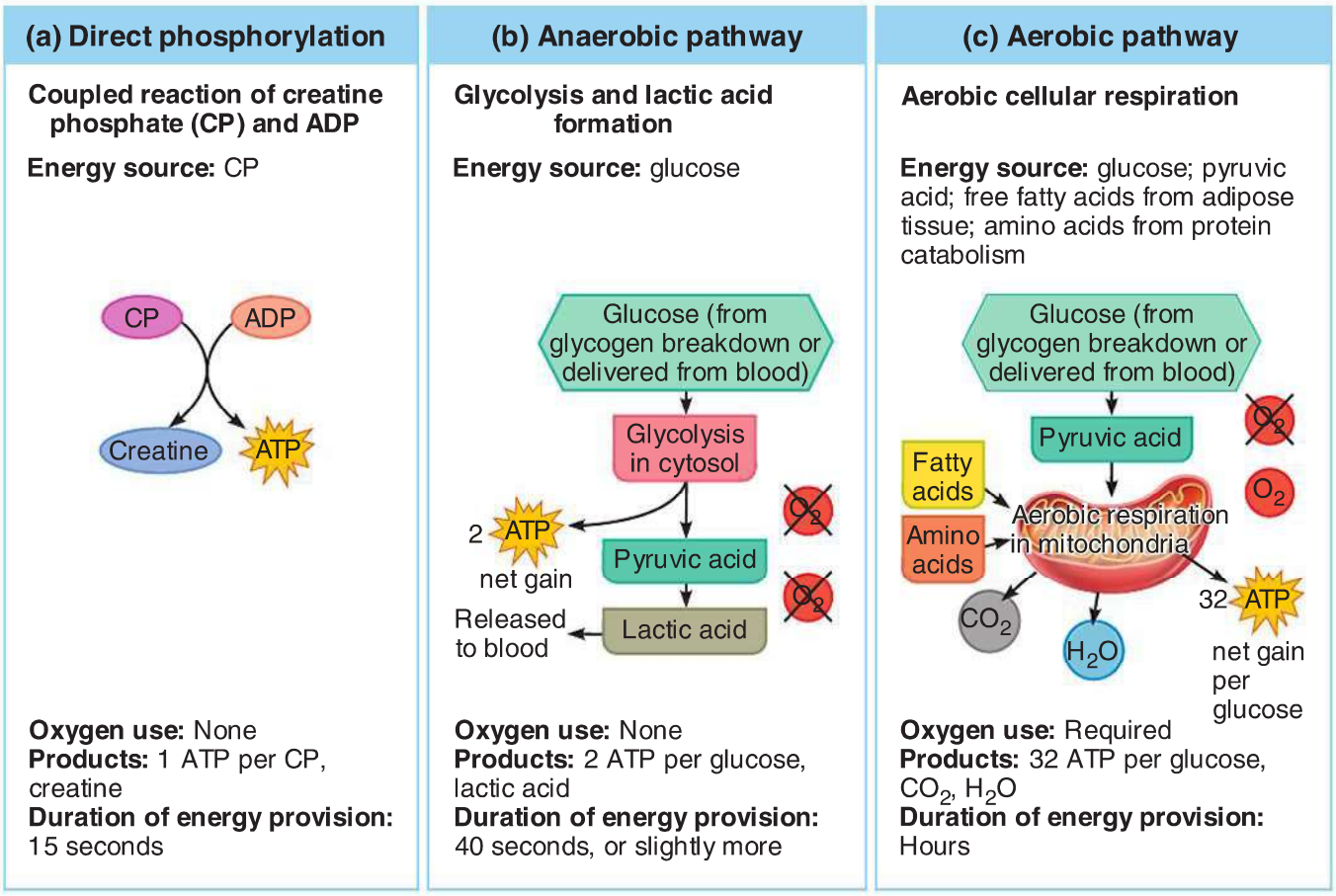


Figure 6.10 **Methods of regenerating ATP during muscle activity.** The fastest mechanism is **(a)** direct phosphorylation; the slowest is **(c)** aerobic respiration.

broken is captured in the bonds of ATP molecules. Although aerobic respiration provides a rich ATP harvest (about 32 ATP per 1 glucose), it is fairly slow and requires continuous delivery of oxygen and nutrient fuels to the muscle to keep it going.

3. **Anaerobic glycolysis and lactic acid formation** (Figure 6.10b). The initial steps of glucose breakdown occur via a pathway called *glycolysis,* which does not use oxygen and hence is *anaerobic* (literally "without oxygen"). During glycolysis, which occurs in the cytosol, glucose is broken down to pyruvic acid, and small amounts of energy are captured in ATP bonds (2 ATP per 1 glucose molecule). As long as enough oxygen is present, the pyruvic acid then enters the oxygen-requiring aerobic pathways that occur within the mitochondria to produce more ATP as described above. However, when muscle activity is intense, or oxygen and glucose delivery is temporarily inadequate to meet the needs of the working muscles, the sluggish aerobic pathways cannot keep up with the demands for ATP. Under these conditions, the pyruvic acid generated during glycolysis is converted to **lactic acid,** and the overall process is referred to as **anaerobic glycolysis.**

Anaerobic glycolysis produces only about 5 percent as much ATP from each glucose molecule as aerobic respiration. However, it is some 2½ times faster, and it can provide most of the ATP needed for 30 to 40 seconds of strenuous muscle activity. The main shortcomings of anaerobic glycolysis are that it uses huge amounts of glucose for a small ATP harvest, and accumulating lactic acid promotes muscle soreness.

DID YOU GET IT?

10. What are the three energy sources for skeletal muscle contraction?

11. What is the immediate source of energy for muscle contraction?

For answers, see Appendix D.

Muscle Fatigue and Oxygen Deficit

✓ Define *oxygen deficit* and *muscle fatigue,* and list possible causes of muscle fatigue.

If we exercise our muscles strenuously for a long time, **muscle fatigue** occurs. A muscle is fatigued when it is unable to contract even though it is still being stimulated. Without rest, a working muscle begins to tire and contracts more weakly until it finally ceases reacting and stops contracting. Muscle fatigue is believed to result from the **oxygen deficit** that occurs during prolonged muscle activity: A person is not able to take in oxygen fast enough to keep the muscles supplied with all the oxygen they need when they are working vigorously. Obviously, then, the work that a muscle can do and how long it can work without becoming fatigued depend on how good its blood supply is. When muscles lack oxygen, lactic acid begins to accumulate in the muscle via the anaerobic pathway described above. In addition, the muscle's ATP supply starts to run low and ionic imbalance occurs. Together these factors cause the muscle to contract less and less effectively and finally to stop contracting altogether.

True muscle fatigue, in which the muscle quits entirely, rarely occurs in most of us because we feel fatigued long before it happens and we simply slow down or stop our activity. It *does* happen commonly in marathon runners. Many of them have literally collapsed when their muscles became fatigued and could no longer work.

Oxygen deficit, which always occurs to some extent during vigorous muscle activity, must be "paid back" whether fatigue occurs or not. During the recovery period after activity, the individual breathes rapidly and deeply. This continues until the muscles have received the amount of oxygen needed to get rid of the accumulated lactic acid and make ATP and creatine phosphate reserves.

Types of Muscle Contractions—Isotonic and Isometric

Until now, we have been discussing contraction in terms of shortening, but muscles do not always shorten when they contract. (I can hear you saying, "What kind of double-talk is that?"—but pay attention.) The event that is common to all muscle contractions is that *tension* develops in the muscle as the actin and myosin myofilaments interact and the myosin cross bridges attempt to slide the thin actin-containing filaments past the thick myosin myofilaments.

Isotonic contractions (literally, "same tone" or tension) are familiar to most of us. In isotonic contractions, the myofilaments are successful in their sliding movements, the muscle shortens, and movement occurs. Bending the knee, rotating the arms, and smiling are all examples of isotonic contractions.

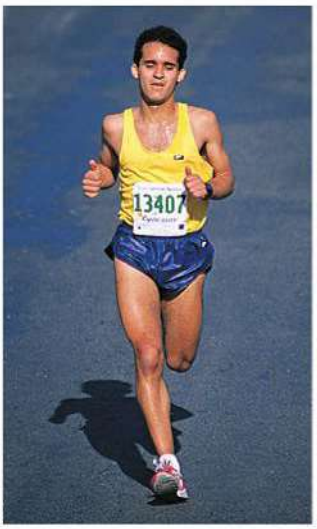
Contractions in which the muscles do not shorten are called **isometric contractions** (literally, "same measurement" or length). In isometric contractions, the myosin myofilaments are "spinning their wheels," and the tension in the muscle keeps increasing. They are trying to slide, but the muscle is pitted against some more or less immovable object. For example, muscles are contracting isometrically when you try to lift a 400-pound dresser alone. When you straighten a bent elbow, the triceps muscle is contracting isotonically. But when you push against a wall with bent elbows, the wall doesn't move, and the triceps muscles, which cannot shorten to straighten the elbows, are contracting isometrically.

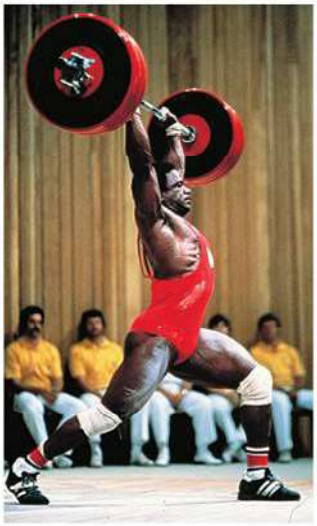
Muscle Tone

One aspect of skeletal muscle activity cannot be consciously controlled. Even when a muscle is voluntarily relaxed, some of its fibers are contracting—first one group and then another. Their contraction is not visible, but, as a result of it, the muscle remains firm, healthy, and constantly ready for action. This state of continuous partial contractions is called **muscle tone.** Muscle tone is the result of different motor units, which are scattered through the muscle, being stimulated by the nervous system in a systematic way.

HOMEOSTATIC IMBALANCE

If the nerve supply to a muscle is destroyed (as in an accident), the muscle is no longer stimulated in this manner, and it loses tone and becomes paralyzed. Soon after, it becomes **flaccid** (flak′sid), or soft and flabby, and begins to **atrophy** (waste away).





(a) (b)

Figure 6.11 The effects of aerobic training versus strength training. (a) A marathon runner. **(b)** A weight lifter.

Effect of Exercise on Muscles

✓ Describe the effects of aerobic and resistance exercise on skeletal muscles and other body organs.

The amount of work a muscle does is reflected in changes in the muscle itself. Muscle inactivity (due to a loss of nerve supply, immobilization, or whatever the cause) always leads to muscle weakness and wasting. Muscles are no exception to the saying "Use it or lose it!"

Conversely, regular exercise increases muscle size, strength, and endurance. However, not all types of exercise produce these effects—in fact, there are important differences in the benefits of exercise.

Aerobic, or **endurance,** types of exercise, such as participating in an aerobics class, jogging, or biking (**Figure 6.11a**), result in stronger, more flexible muscles with greater resistance to fatigue. These changes come about, at least partly, because the blood supply to the muscles increases, and the individual muscle cells form more mitochondria and store more oxygen. However, aerobic exercise benefits much more than the skeletal muscles. It makes overall body metabolism more efficient, improves digestion (and elimination), enhances neuromuscular coordination, and makes the skeleton stronger. The heart enlarges (*hypertrophies*) so that more blood is pumped out with each beat, fat deposits are cleared from the blood vessel walls, and the lungs become more efficient in gas exchange. These benefits may be permanent or temporary, depending on how often and how vigorously a person exercises.

Aerobic exercise does *not* cause the muscles to increase much in size, even though the exercise may go on for hours. The bulging muscles of a bodybuilder or professional weight lifter result mainly from **resistance,** or **isometric, exercises** (Figure 6.11b), which pit the muscles against some immovable object (or nearly immovable). Resistance exercises require very little time and little or no special equipment. A few minutes every other day is usually sufficient. You can push against a wall, and you can strongly contract buttock muscles even while standing in line at the grocery store. The key is forcing the muscles to contract with as much force as possible. The increased muscle size and strength that result are due mainly to enlargement of individual muscle cells (they make more contractile filaments) rather than to an increase in their number. The amount of connective tissue that reinforces the muscle also increases.

Because endurance and resistance exercises produce different patterns of muscle response, it is important to know what your exercise goals are. Lifting weights will not improve your endurance for a marathon. By the same token, jogging will do little to improve your muscle definition for competing in the Mr. or Ms. Muscle contest, nor will it make you stronger for moving furniture. Obviously, the best exercise program for most people is one that includes both types of exercise.

DID YOU GET IT?

12. Gary is trying with all his might to pull a tree stump out of the ground. It does not budge. Which type of contraction are his muscles undergoing?

13. What is meant by the term *oxygen deficit*?

14. To develop big, beautiful skeletal muscles, should your exercise focus be aerobic or resistance type exercise?

For answers, see Appendix D.

Muscle Movements, Types, and Names

✓ Define *origin, insertion, prime mover, antagonist, synergist,* and *fixator* as they relate to muscles.

✓ Demonstrate or identify the different types of body movements.