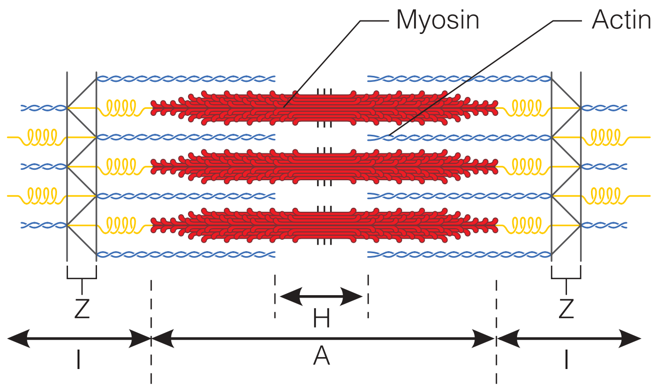
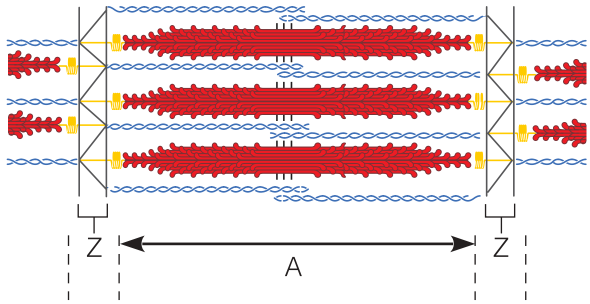
### Mechanism of Muscle Contraction: The Sliding Filament Theory

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. Energized by ATP, each cross bridge attaches and detaches several times during a contraction, acting much like a tiny oar to generate tension and pull the thin filaments toward the center of the sarcomere. As this event occurs simultaneously in sarcomeres throughout the cell, the muscle cell shortens (Figure 6.7). The attachment of the myosin cross bridges to actin requires calcium ions ($Ca^{2+}$). So where does the calcium come from? As indicated in Figure 6.5b, action potentials (black arrows) 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 precise 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 just a few thousandths of a second.




(a)




(b)

**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.

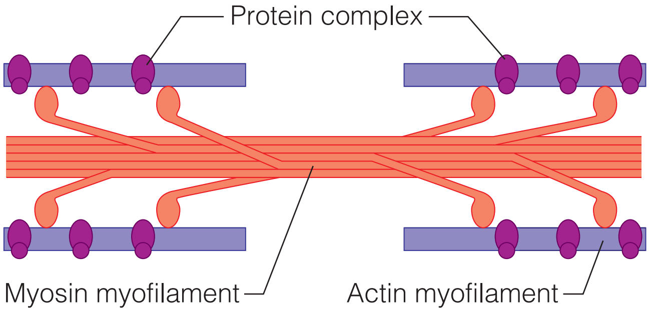
## Contraction of a Skeletal Muscle as a Whole

### 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, skeletal muscles are organs that consist of thousands of muscle cells, and they react to stimuli with **graded responses,** or different degrees of shortening. In general, graded muscle contractions can be produced two ways: (1) by changing the *frequency* of muscle stimulation, and (2) by changing the *number* of muscle cells being stimulated. A muscle's response to each of these is briefly described next.

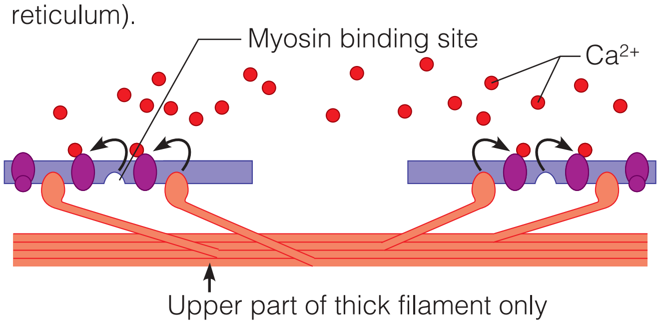
#### *Muscle Response to Increasingly Rapid Stimulation*

Although **muscle twitches** (single, brief, jerky contractions) sometimes occur as a result of 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,**



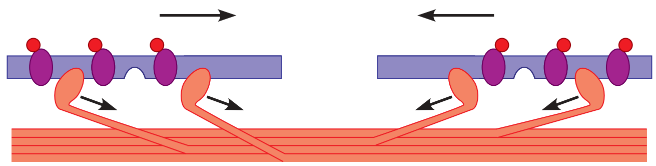

**(a)**

In a relaxed muscle cell, the regulatory proteins forming part of the actin myofilaments prevent myosin binding (see **a**). When an action potential 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, they change 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)**

Free myosin has a unique property: Its heads are "cocked," much like a set mousetrap. The physical attachment of myosin to actin "springs the trap," causing the myosin heads to snap (pivot) toward the center of the sarcomere. Since the actin and myosin are still firmly bound to each other 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 take another "step" and attach to a binding site farther along the thin filament. 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 is repeated again and again during contraction. Notice that the myofilaments themselves do not shorten during contraction; they simply slide past each other. When the action potential ends and calcium ions are reabsorbed into the SR storage areas, the regulatory proteins resume their original shape and position, and again block myosin binding to the thin filaments. Since myosin now has nothing to attach to, the muscle cell relaxes and settles back to its original length.

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

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

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

***Muscle Response to Stronger Stimuli*** Although tetanus also produces stronger muscle contractions, 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 will be slight. In the strongest contractions, when all the motor units are active and all the muscle cells are being stimulated, the muscle

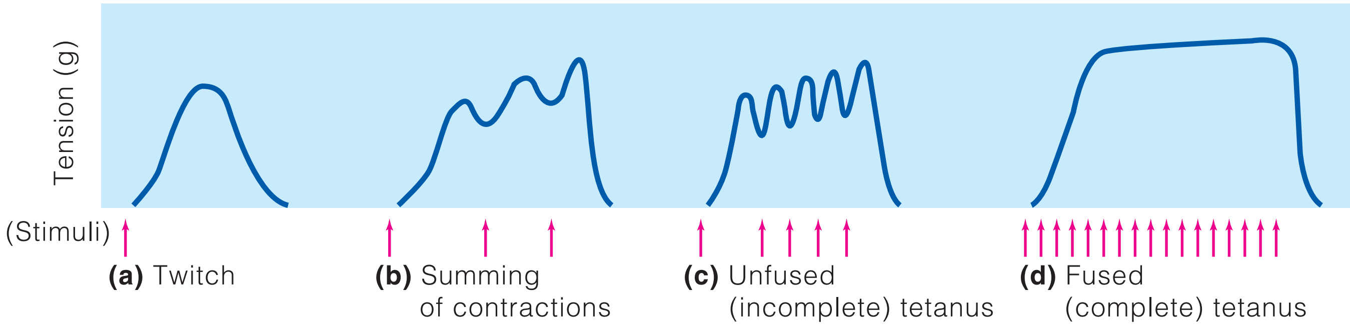



**FIGURE 6.9 A whole muscle's response to different rates of stimulation.** In **(a),** a single stimulus is delivered, and the muscle contracts and relaxes (a twitch contraction). In **(b),** stimuli are delivered more frequently, so the muscle does not have time to completely relax; contraction force increases because the 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.)

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!

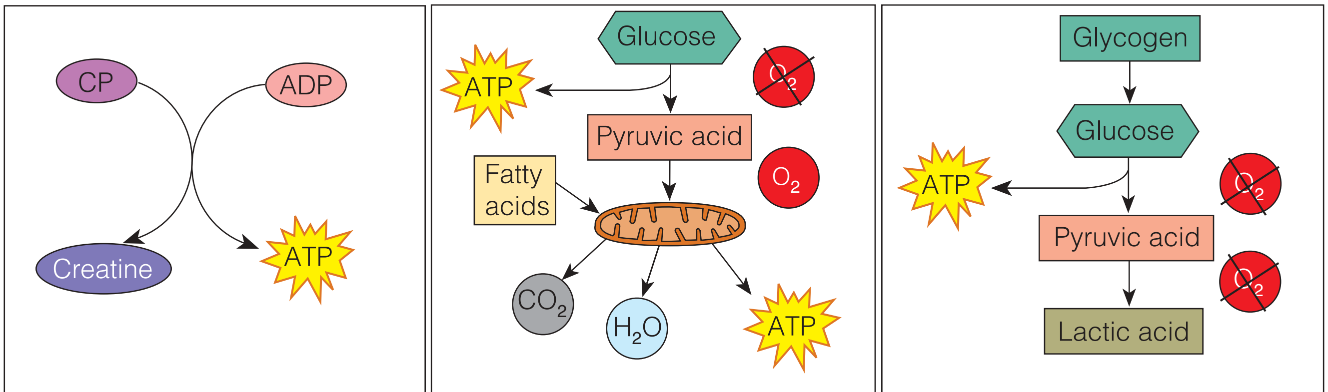
### Providing Energy for Muscle Contraction

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 4 to 6 seconds' worth, just enough to get you going. Since 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.

Essentially, 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 about 20 seconds).
2. **Aerobic respiration** (Figure 6.10b). 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 broken is captured in the bonds of ATP molecules. Although aerobic respiration provides a rich ATP harvest (36 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 6.10c). The initial steps of glucose breakdown occur via a pathway called *glycolysis,* which does not use oxygen and hence is an *anaerobic* (literally "without oxygen") part of the metabolic pathway. 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

**Q** *Which of these methods of ATP generation is commonly used by the leg muscles of a long-distance cyclist?*




| **(a)** Direct phosphorylation of ADP by reaction with creatine phosphate (CP) | **(b)** Aerobic respiration (oxidative phosphorylation) | **(c)** Anaerobic glycolysis and lactic acid formation |
|---|---|---|
| Energy source: CP | Energy sources: glucose; pyruvic acid; free fatty acids from adipose tissue; amino acids from protein catabolism | Energy source: glucose |
| Oxygen use: None<br>Products: 1 ATP per CP, creatine<br>Duration of energy provision: 15 sec | Oxygen use: Required<br>Products: 36 ATP per glucose, $CO_2$, $H_2O$<br>Duration of energy provision: Hours | Oxygen use: None<br>Products: 2 ATP per glucose, lactic acid<br>Duration of energy provision: 30–60 sec |

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

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 mechanisms 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 60 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 fatigue and muscle soreness.

**A** *The aerobic mechanism (b).*

### Muscle Fatigue and Oxygen Debt

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, an active or 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 debt** 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 mechanism described above. In addition, the muscle's ATP supply starts to run low. The increasing acidity in the muscle and the lack of ATP 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 debt, which always occurs to some extent during vigorous muscle activity, must be "paid back" whether or not fatigue occurs. 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 behavior, 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 actin-containing filaments past them within the muscle fibers.

**Isotonic contractions** (literally, "same tone" or tension) are more 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 "skidding 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

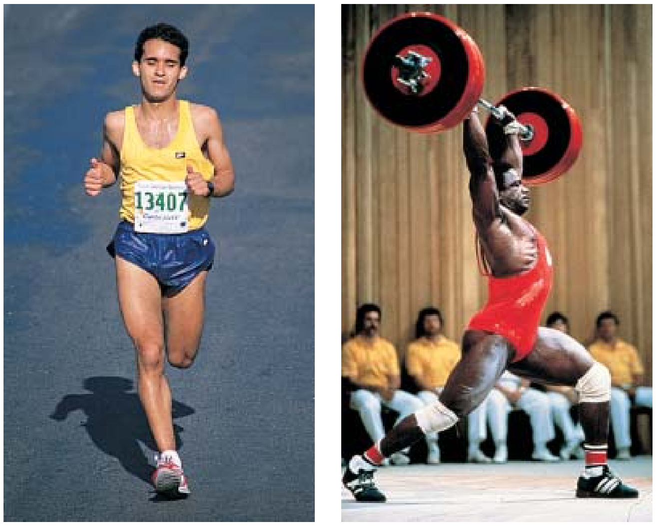
If the nerve supply to a muscle is destroyed (as in an accident), the muscle is no longer stimulated in this manner, and it loses tone and becomes paralyzed. Soon after, it becomes *flaccid* (flak′sid), or soft and flabby, and begins to *atrophy* (waste away).

### Effect of Exercise on Muscles

The amount of work done by a muscle 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




(a) (b)

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

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 one 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) in which the muscles are pitted against some immovable object (or nearly so). Resistance exercises require very little time and little or no special equipment. A few minutes every other day is usually sufficient. A wall can be pushed against, and buttock muscles can be strongly contracted 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 results is due mainly to enlargement of individual muscle cells (they make more contractile filaments), rather than 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.

## Muscle Movements, Types, and Names

This section is a bit of a hodge-podge. It includes some topics that don't really fit together, but they don't fit anywhere else any better. For example, there are five very basic understandings about gross muscle activity. I call these the *Five Golden Rules* of skeletal muscle activity because until you understand them, comprehending muscle movements and appreciating muscle interactions is nearly impossible. These golden rules are summarized for your quick review in Table 6.2.

### Types of Body Movements

Every one of our 600-odd skeletal muscles is attached to bone, or to other connective tissue structures, at no less than two points. One of these

**TABLE 6.2 The Five Golden Rules of Skeletal Muscle Activity**

1. With a few exceptions, all muscles cross at least one joint.
2. Typically, the bulk of the muscle lies proximal to the joint crossed.
3. All muscles have at least two attachments: the origin and the insertion.
4. Muscles can only pull; they never push.
5. During contraction, the muscle insertion moves toward the origin.