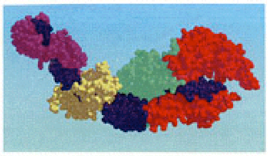
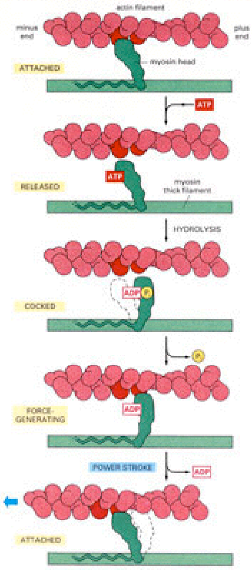
Muscles

Muscle Contraction



Space-filling model of the head of muscle myosin. The model is oriented so that the actin-binding surface is located at the lower right-hand corner. Three domains of the myosin heavy chain are colored *green*, *red*, and *blue*, respectively, whereas the two light chains are shown in *yellow* and *purple*. (From I. Rayment et al., *Science*, 261:50–58, 1993. © 1993 the AAAS.)



ATTACHED—At the start of the cycle shown in this figure, a myosin head lacking a bound nucleotide is locked tightly onto an actin filament in a *rigor* configuration (so named because it is responsible for rigor mortis, the rigidity of death). In an actively contracting muscle this state is very short-lived, being rapidly terminated by the binding of a molecule of ATP.

RELEASED—A molecule of ATP binds to the large cleft on the "back" of the head (that is, on the side farthest from the actin filament) and immediately causes a slight change in the conformation of the domains that make up the actin-binding site (see Figure 16-90). This reduces the affinity of the head for actin and allows it to move along the filament. (The space drawn here between the head and actin emphasizes this change, although in reality the head probably remains very close to the actin.)

COCKED—The cleft closes like a clam shell around the ATP molecule, triggering a large shape change that causes the head to be displaced along the filament by a distance of about 5 nm. Hydrolysis of ATP occurs, but the ADP and P_i produced remain tightly bound to the protein

FORCE-GENERATING—The weak binding of the myosin head to a new site on the actin filament causes release of the inorganic phosphate produced by ATP hydrolysis, concomitantly with the tight binding of the head to actin. This release triggers the power stroke—the force-generating change in shape during which the head regains its original conformation. In the course of the power stroke, the head loses its bound ADP, thereby returning to the start of a new cycle.

ATTACHED—At the end of the cycle, the myosin head is again locked tightly to the actin filament in a rigor configuration. Note that the head has moved to a new position on the actin filament.

The cycle of changes by which a myosin molecule walks along an actin filament. (Based on I. Rayment et al., *Science* 261:50–58, 1993. © 1993 the AAAS.)

Muscle Contraction and ATP

Muscle Contraction Requires Large Amounts of ATP Energy

The energy for muscle contraction comes from ATP, which in turn comes from the metabolism of glucose and fatty acids. But so little ATP is actually stored in the muscles that just a few twitches could quickly exhaust the supply. How do muscles overcome this limitation? Although there is little ATP, there is another phosphate compound stored in the muscles, **creatine phosphate**, which is formed by linkage of a phosphate group to the substance creatine. Creatine phosphate cannot be used directly to power muscle contraction, but it can transfer its phosphate group to ADP to form ATP:

$$\text{Creatine phosphate} + \text{ADP} + H^+ \text{ ---> Creatine} + \text{ATP}$$

The newly formed ATP then acts as the direct energy source for contraction. The muscle stores enough creatine phosphate to enable it to contract strongly during the several seconds it takes before the machinery of glycolysis and cellular respiration can produce additional ATP.

If the demands on the muscles are not great, much of the energy used to replenish the supply of creatine phosphate and ATP may come from the complete oxidation of glucose and/or fatty acids to carbon dioxide and water, which requires oxygen. During the unavoidable delay before adjustments of the gas-exchange and circulatory systems increase the oxygen supply to the active muscles, some of the oxygen necessary for aerobic respiration in red muscles may come from oxygenated **myoglobin**. Myoglobin is a special oxygen-storage protein in muscle. Like hemoglobin, it forms a loose combination with oxygen while the oxygen supply is plentiful, and stores it until the demand for oxygen increases. Consequently, muscle has its own built-in oxygen supply.

But during rigorous muscular activity, such as strenuous exercise or the lifting of a very heavy object, the energy demands of the muscles (especially white muscles) are great (see Table below) and the oxygen from myoglobin is quickly used up. Because sufficient oxygen cannot be gotten to the tissues fast enough, the muscles obtain the extra energy they need from anaerobic processes. This is accomplished by producing lactic acid through fermentation, and incurring what physiologists call an **oxygen debt**. Some of the lactic acid accumulates in the muscles, but much of it diffuses into the muscle capillaries and is transported in the blood to the liver. When the rigorous activity is over, a period of hard breathing or panting helps supply the liver with the large quantities of oxygen it requires for aerobic respiration (see figure below), thereby paying back the oxygen debt. In the liver, the lactic acid is converted back into pyruvic acid, most of which is oxidized to carbon dioxide and water. The ATP energy thus obtained is used to replace the ATP and creatine phosphate stores, and to synthesize glucose and glycogen from the remaining lactic acid. Note that it is the liver cells, not the muscle cells, where lactic acid is reconverted into pyruvic acid.

Lactic acid, precisely because it is an acid, can damage the muscle fibers if it is not removed promptly. This is why a “cool down” period is so important after strenuous exercise. The continued circulation of blood through the muscle aids in lactic acid removal. “Sore” muscles are the result of damage to the muscle proteins due to lactic acid accumulation. Endurance-training programs for athletes are designed to increase the oxygen availability in muscles and thereby encourage aerobic metabolism. During such training, the number of mitochondria within the muscle fibers increases, the stores of myoglobin enlarge, and the growth of new blood capillaries within the muscle is stimulated, thereby increasing blood flow through the muscle. As a result, trained athletes are capable of carrying out more strenuous activity without greatly increasing their lactic acid production and accumulation.

Muscle spasms and cramps result from involuntary strong contractions of a muscle. The cramp or spasm is accompanied by sudden pain, which probably results from mechanically stimulating pain receptors within the muscle or from compressing the blood vessels and interfering with the delivery of oxygen to the fibers. Most cramps and spasms will clear up of their own accord within a few minutes. Muscle cramps are sometimes associated with a calcium deficiency, especially in pregnant women, but this does not appear to be true in all cases. The mechanism of cramping is still not understood.

Muscle Fatigue

WHAT CAUSES MUSCLE FATIGUE?

Prolonged and strong contractions of a muscle leads to the well-known state of muscle fatigue. Fatigue during moderate exercise occurs as the muscle fibers deplete their reserve glycogen stores and the oxygen supply is insufficient. The muscle fibers then turn to anaerobic metabolism and pyruvic acid is converted into lactic acid rather than being metabolized aerobically in the mitochondrion. This is important because **the build up of lactic acid causes extreme fatigue**. Why is this so?

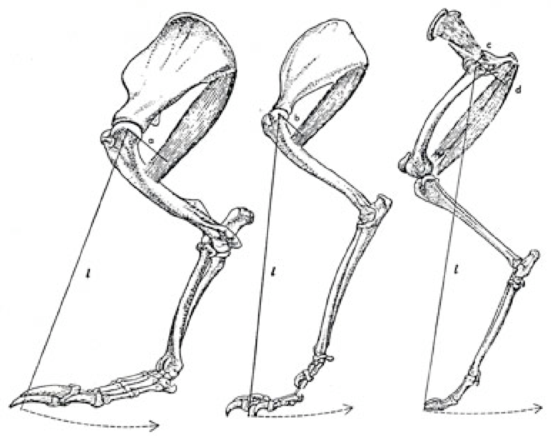
The production of lactic arid within the muscle fibers results in a rise in intracellular H^+ ions and a fall in pH within the fibers. The decrease in muscle pH, in turn, inhibits the activity of key glycolytic enzymes so that the rate of ATP production is reduced. Although ATP is needed for muscle contraction (to bind to the myosin head to detach them from the actin and to power the recocking (energizing) of the myosin head, the more direct effect of the depletion of ATP is thought to involve the excitation-contraction system. ATP is needed for the active transport of Ca^{2+} ions into the sarcoplasmic reticulum, so a decrease in ATP results in a loss of Ca^{2+} ions to the extracellular environment. With inadequate stores of Ca^{2+} ions in the sarcoplasmic reticulum, excitation-coupling is hindered in muscle fibers. Thus there appears to be two factors involved in fatigue; the **build up of lactic acid and, following, a decrease in the amount of ATP that slows excitation of the muscle**.

Energy Systems Used in Various Sports

100 meter dash

Phosphagen system almost entirely	jumping weight lifting diving football dashes
Phosphagen and glycogen lactic acid systems	200 meter dash basketball baseball home run ice hockey dashes
Glycogen lactic acid system, mainly	400 meter dash 100 meter swim tennis soccer
Glycogen lactic acid and aerobic systems	800 meter dash 200 meter swim 1500 meter skating boxing 2000 meter rowing 1500 meter run 1 mile run 400 meter swim
Aerobic system	10,000 meter skating cross-country skiing marathon run (26.2 miles, 42.2 km) jogging

Points of Insertion Determine Power and Speed of Musculoskeletal Systems



POWER AND SPEED are alternatively achieved in the badger (left) and the cheetah (middle) by placement of the teres major muscle. In the cheetah the small distance (b) between the muscle insertion and the joint it moves yields a higher rate of oscillation than in the badger, in which the distance (a) is greater. The higher oscillation rate, coupled with a longer leg (l), yields a faster stride. In the vicuna (right) the gluteus muscle (c) develops about five times the velocity but only a fifth the force of the larger semimembranosus muscle (d). The animal may use the latter to overcome inertia; the former, for high speed. Legs are not the same scale.

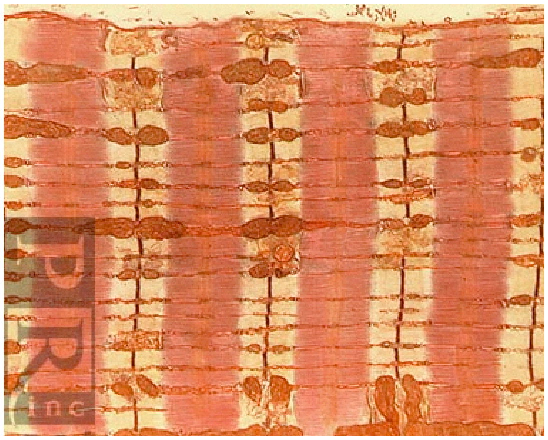
Types of Skeletal Muscle: Red and White Muscle

Two types of skeletal muscle are often recognized: red muscle (or slow twitch muscle) and the white muscle (or fast twitch muscle). **Red muscle** has a rich blood supply, numerous mitochondria, and much myoglobin, a compound similar to hemoglobin that forms a loose combination with oxygen and stores it in the muscle. Red muscle, which derives its color from the myoglobin it contains, oxidizes fatty acids as its primary source of energy. Although it contracts rather slowly, it is capable of long-term activity without appreciable fatigue. By contrast, **white muscle** has a more limited blood supply, few mitochondria, and a low myoglobin content. It depends almost entirely on anaerobic breakdown of glycogen for its energy supply and is capable of very strong, rapid contractions for a short period of time. Because these fibers have fewer mitochondria and capillaries than red fibers, their ability to resynthesize ATP through oxidative phosphorylation is limited and thus they fatigue rapidly. Most skeletal muscles are a combination of the two types, but one type usually predominates. A familiar example is the “white meat” and “dark meat” of a chicken or turkey.

Clearly, the two types of muscle fibers are adapted for different purposes and perform different functions. In humans, the leg and back muscles that support the weight of the body and maintain posture must be able to contract for long periods of time without fatigue. These muscles tend to have a high proportion of red fibers. Other, more intermittently used muscles, such as those of the arms, must be able to produce strong, rapid muscular contractions for a short period (as in lifting a heavy weight). Here white fibers may predominate.

Although everyone has varying percentages of these muscle types, microscopic examination of the muscle fibers of highly proficient athletes has shown some interesting correlations. The leg muscles of male marathon runners tend to have more red fibers than do those of untrained individuals or sprinters and high – jumpers. Muscles with a high percentage of red fibers, with a capacity for sustained contractions and resistance to fatigue, seem to be associated with endurance activities such as long distance running or swimming. A higher proportion of white fibers give a muscle the ability to generate high peak forces; such muscles are better suited for sports where explosive speed, power, and quickness are required.

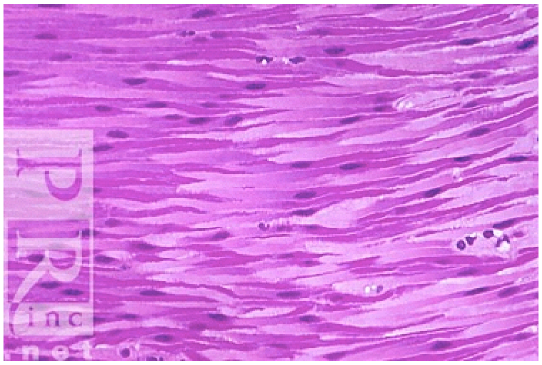
Muscle fibers types also differ between the sexes. Women usually have fewer white fibers than men do. Thus a female athlete may perhaps lack the explosive strength of the male, but will have more endurance because of the high proportion of red fibers. Correlated with this is a difference in total body fat; women have an average of 20% body fat compared to 15% for men. During endurance activities, women’s red fibers can use this fat for fuel. Men, whose muscles contain more white fibers, depend more on stored carbohydrate for fuel, and therefore may have less endurance. It is clear that the gap between male and female athletes in some areas is narrowing. In distance swimming, for example, where body size differences are reduced by the water, women are beginning to compete favorably with men. The same is true for marathon running. Some physicians have suggested that in the future, with improved training, women will be superior to men in running or swimming races of thirty or more miles.



Striated muscle. Colored transmission electron micrograph (TEM) of a longitudinal section through striated skeletal muscle. The striated banding-pattern of the muscle fibrils is seen. The fibrils run in parallel (from left to right) and between them runs sarcoplasmic reticulum (SR) that transmits nerve impulses to the fibrils. Here, the SR contains many mitochondria (brown). Within each fibril are contractile units called sarcomeres separated by red lines. A sarcomere has protein filaments of myosin (pink) and actin (yellow) that slide over each other, thereby causing the whole muscle to contract. Skeletal muscle is responsible for voluntary muscle movement in the body. Credit: Quest / Photo Researchers, Inc.

SMOOTH MUSCLE

The name “smooth muscle” is used because this type of muscle lacks striations. Smooth muscle tissue is formed of spindle-shaped cells, each containing a single, large, centrally-located nucleus. Notice how the cells are arranged to form a sheet.



Histology of smooth muscle. Smooth muscle is found in the walls of blood vessels, tubular organs such as the stomach and uterus, the iris, or associated with hair follicles. It is not under voluntary control, each cell has one nucleus and it displays automaticity in the visceral form. In multiunit smooth muscle each cell exists as a discreet independent unit that is innervated by a single nerve ending. Magnification:100X. Credit: M. I. Walker / Photo Researchers, Inc

Smooth muscle cells are not nearly as long as striated muscle cells and, generally speaking, not as strong. Skeletal muscle contractions can be explosive, while those of smooth muscle are applied slowly and smoothly. There are exceptions of course - contractions of an offended digestive system can occasionally be rapid, and their power is often quite impressive when expelling food from either end. Noteworthy also is the power of the smooth muscle of the uterus; it rivals the strongest skeletal muscles in our bodies, and its stamina surpasses them all.

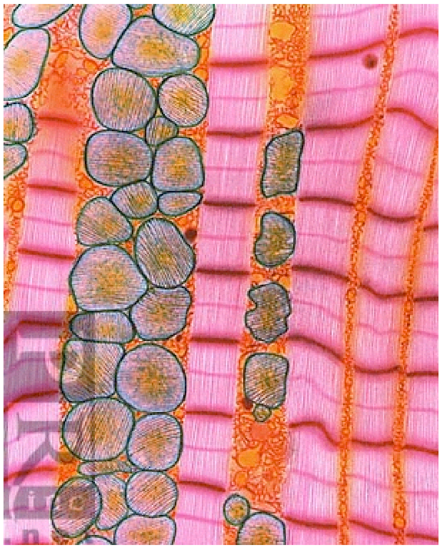
HOW DOES SMOOTH MUSCLE CONTRACT?

The description of muscle contraction outlined in your text applies only to vertebrate skeletal muscle. Smooth muscle, though similar, displays some interesting differences. In skeletal muscle ATP activates the myosin heads and Ca^{++} ions trigger movement by binding to the troponin complex of the actin filaments. In smooth muscle, Ca^{++} ions activate the myosin, through two intermediate enzymes, before the ATP becomes involved. This helps explain why smooth muscle contracts so slowly compared to skeletal muscle.

Although smooth muscle contraction is slow, it is efficient; it uses only about 10% of the ATP required by skeletal muscle to produce the same strength of contraction.

CARDIAC MUSCLE

Each cardiac muscle cell has a single nucleus. At the end of one cell, where it joins another, is a dark band, the intercalated disk — places where the plasma membranes of two cardiac fibers abut.



Heart muscle. Colored transmission electron micrograph (TEM) of a longitudinal section through healthy heart (cardiac) muscle. Large oval mitochondria lie between the muscle fibers (pink). The thick transverse bands on the fibers are Z lines regions with a more dense arrangement of actin, one of the two types of muscle filament. In order to beat, the heart produces regular electrical impulses causing the muscle filaments to slide over one another and contract the cardiac muscle. The high concentration of mitochondria reflects the large respirational demands of the heart. Magnification unknown. Credit: Quest / Photo Researchers, Inc.

Cardiac muscle is unique to the vertebrate heart. It is able to beat incessantly because it never maintains a contraction. It contracts, and promptly relaxes, and its periods of relaxation are twice as long as it contraction periods, so it actually gets plenty of rest. Its rest periods and contraction periods are strictly programmed; the muscle rests, then it must contract before it can rest again. Cardiac muscle is unlike smooth or skeletal muscle in that it cannot rely on anaerobic metabolic pathways to provide its energy; hence it must never – ever – fail to get all the oxygen it needs. Cardiac muscle is the only muscle in our bodies that is unable, except in disease states, to achieve a state of sustained contraction.

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