The 3 basic types of muscle tissue are: skeletal muscle, cardiac muscle, and smooth muscle.

Skeletal muscle tissue is composed of skeletal muscle cells (a.k.a. skeletal muscle fibers b/c of their length and narrowness) and is packaged into skeletal muscles, which attach to and cover the skeleton. Skeletal muscle cells are mostly voluntary and the overlap of their contractile proteins (actin and myosin) gives them a striated appearance.

Cardiac muscle tissue is found in the wall of the heart. Cardiac muscle cells are short (and are thus not referred to as fibers), involuntary, and striated. The contraction of cardiac muscle cells generates the force that propels blood through the body’s circulatory system.

Smooth muscle tissue is found in the walls of hollow visceral organs (e.g. esophagus, stomach, intestines, trachea, bronchi, ureters, urinary bladder, urethra, uterus, blood vessels, etc.). Smooth muscle cells are referred to as smooth muscle fibers and are involuntary and lack striations.

Muscle cells have 4 defining characteristics: excitability, contractility, extensibility, and elasticity. They are excitatory b/c in response to a signal (e.g. binding ACh released by a motor neuron) they will generate an action potential. Muscle cells are contractile b/c they have the capacity to forcibly shorten in response to a stimulus. Muscle cells are extensible b/c they can be stretched beyond their resting length. Muscle cells are elastic b/c they recoil and reassume their resting length in response to being stretched.

Basic functions of muscle are: movement, joint stability, heat generation, and posture maintenance. Movement is created in a variety of ways. Skeletal muscle tissue manipulates and moves the body and its major parts. Cardiac muscle is responsible for moving blood through the circulatory system. Smooth muscle helps move other bodily fluids (digestive matter, urine, semen, etc.). Skeletal muscle contraction stabilizes the joints (particularly freely moveable synovial joints). Skeletal muscle cells are rather inefficient at converting their stored chemical energy into the energy of motion. Roughly 75% of their stored energy is lost as heat. This heat helps maintain body temperature. Skeletal muscles are constantly working to maintain posture and resist gravity.

Each named skeletal muscle is an organ consisting of multiple tissues. Skeletal muscle tissue is the dominant tissue but nervous tissue, epithelial tissue, and connective tissue are found as well. Skeletal muscles are typically richly innervated and vascularized. The skeletal muscle is surrounded by a coat of dense irregular CT (the epimysium). Within the muscle there are bundles of skeletal muscle fibers known as fascicles. Each fascicle is surrounded a layer of fibrous CT (the perimysium). Each skeletal muscle fiber has a loose sheath of connective tissue (the endomysium).

The attachment of a skeletal muscle to a bone is usually classified as an origin (the bone that does not move) or an insertion (the bone that moves). The skeletal muscle is attached to an origin or insertion via an extension of the epimysium that connects to the periosteum of the bone. If the attachment is ropelike, it is a tendon. If the attachment is sheetlike, it is an aponeurosis.

A skeletal muscle cell is a long cylindrical cell (a fiber) with multiple nuclei. It is long and multinucleate b/c it is formed from the fusion of hundreds of embryonic cells called myoblasts. A large cell formed by the fusion of multiple smaller cells is known as a syncytium.

The plasma membrane of the skeletal muscle cell is the sarcolemma. The cytoplasm of the skeletal
A muscle cell is known as **sarcoplasm** and it contains structures that allow the cell to generate the ATP needed for contraction. These structures include: granules of **glycogen** (a glucose polymer), **mitochondria**, and **myoglobin** (an oxygen storing protein). The majority of the sarcoplasm is composed of rods known as **myofibrils**. Note that the sarcolemma has invaginations called **T tubules**. On each side of a single T tubule is an expanded portion of the muscle fiber’s endoplasmic reticulum. The endoplasmic reticulum of a muscle cell is known as a **sarcoplasmic reticulum**. The expanded portions of the sarcoplasmic reticulum adjacent to the T tubules are called **terminal cisternae**. A single T tubule and its flanking pair of terminal cisternae are referred to as a **triad**.

Each myofibril is composed of **myofilaments** and consists of a repeating orderly arrangement of units known as **sarcomeres**. The myofilaments are primarily composed of the proteins: **actin** and **myosin**. Actin is referred to as the **thin filament**. Myosin is referred to as the **thick filament**.

The myofibril will consist of the following pattern: a region of just thin filaments followed by a region of thin and thick filaments overlapping. This continues along the length of every myofibril and gives skeletal muscle fibers as a whole their striated appearance. The regions of thin filament appear light and are referred to as **I bands** and the regions of overlap appear dark and are referred to as **A bands**. The dark A band has a small lighter area in its midsection known as the **H zone** which is vertically bisected by a dark line called an **M line**. The H zone contains thick filament only and has no overlap. Each I band is also bisected vertically by a dark line known as a **Z disc**.

The sarcomere is a defined segment of a myofibril and is the basic contractile unit of the muscle cell. Examining the structure and the contraction of a sarcomere gives us insight into the contraction of the whole cell. This is because each myofibril consists of thousands of sarcomeres as whole and each cell contains thousands of myofibrils.

A sarcomere starts at a Z disc in the middle of an I band (the region of thin filament only). It includes an A band (the region of overlap) and it ends at the next Z disc. Proteins within the Z disc link the thin filaments of one sarcomere to the thin filaments of the next. Z disc proteins also link adjacent myofibrils to one another and links myofibrils to the sarcolemma. In a similar fashion, the M line anchors and stabilizes the thick filaments.

Thick filaments are composed of myosin proteins. Each myosin protein consists of a cylindrical rod and 2 round heads. Within the A band of each sarcomere the thin actin filaments and the thick myosin filaments overlap. During muscle contraction, the myosin heads latch onto the overlapped actin filaments. (The linkage btwn actin and myosin is known as a **cross bridge**.) The myosin heads then pull the actin filaments towards the center of the sarcomere. This shortens the sarcomere. All the sarcomeres within the muscle fiber will contract together. Since the sarcomeres are linked to the sarcolemma, the muscle fiber itself will shorten. During this act of contraction, the amount of overlap btwn thick and thin filaments will increase. Thus the following get smaller during contraction:

- The muscle fiber
- The myofibrils within the muscle fiber
- Sarcomeres
- Distance btwn Z discs
- I band
- H zone

Note that the A bands move closer together but they do not decrease in size. This description of the mechanism of contraction is known as the **sliding filament model of contraction**.
The next step is examining how the muscle fiber is stimulated and how that stimulation in turn causes cross bridge formation and sarcomere shortening. This is referred to as **excitation-contraction coupling**. The axon terminal of a somatic motor neuron is adjacent to the motor end plate of a skeletal muscle fiber. These 2 structures (plus the intervening synaptic cleft) collectively form a neuromuscular junction. The arrival of an action potential at the axon terminal will prompt the release of acetylcholine into the synaptic cleft. ACh will diffuse across the synaptic cleft and bind to the nicotinic cholinergic receptors on the motor end plate. These receptors are chemical-gated ion channels. The binding of ACh causes these channels to open. This results in the influx of Na⁺, membrane depolarization, and the formation of a graded potential at the motor end plate. This graded potential is known as an end plate potential. The end plate potential then travels away from the motor end plate and the wave of depolarization causes the opening of voltage-gated channels and the generation of an action potential.

Note that the stimulation of the motor end plate by the ACh is short-lived since the synaptic cleft contains the enzyme acetylcholinesterase which quickly breaks down ACh.

The action potential spreads along the sarcolemma. The action potential will spread down the membrane of the T tubules. The propagation of the action potential down the T tubule membrane causes a change in the shape of a voltage-sensitive integral protein in the T tubule membrane. This shape change pulls on an integral protein in the membrane of the neighboring terminal cisterna. This protein in the terminal cisterna membrane is actually an ion channel and the pulling causes it to open. The terminal cisterna stores Ca²⁺ and the opening of the channel causes the stored calcium to leave the terminal cisterna and enter the sarcoplasm. (The above events happen at multiple locations in the muscle fiber and involve millions of T tubules and terminal cisternae.)

The rise in sarcoplasmic Ca²⁺ levels will begin the process of contraction. Under resting circumstances, myosin cannot latch onto actin and form cross bridges b/c the myosin-binding sites on actin are blocked by a protein called tropomyosin. The position of tropomyosin (and thus the availability of the myosin-binding site) is determined by a protein attached to tropomyosin called troponin. The calcium that enters the sarcoplasm from the terminal cisternae will bind to troponin. The binding of calcium to troponin causes troponin to change shape. This causes tropomyosin to change shape and exposes the myosin-binding sites on the actin filaments. This allows myosin to bind to actin (i.e. to form cross bridges) and contraction occurs.

The calcium levels in the sarcoplasm do not stay elevated for long. The membrane of the sarcoplasmic reticulum contains an integral protein known as the SR-Ca²⁺-ATPase which breaks down ATP and actively transports calcium back into the sarcoplasmic reticulum. The removal of calcium from the sarcoplasm causes troponin to revert to its original shape which causes tropomyosin to revert to its original shape and recover the myosin-binding sites on actin preventing myosin from latching on any longer and allowing the sarcomere to return to its resting length.

As long as calcium levels are elevated, the myosin will pull on actin again and again causing the sarcomere to grow shorter and shorter. The series of events in which the myosin heads pull the thin filaments ever closer to the middle of the sarcomere is known as the cross bridge cycle. In order for the myosin head to bind to the actin, the myosin head must be cocked and ready. Getting cocked requires the hydrolysis of ATP into ADP (adenosine phosphate) and P₇ (inorganic phosphate). The cocked myosin will be in position to bind actin and will have the ADP and the P₇ attached to it. If the myosin-binding site
is available, the cocked myosin head will bind to it forming a cross bridge. Then the myosin head releases its bound ADP and P. This causes the myosin to perform its **power stroke** in which it pivots and pulls the actin filament towards the center of the sarcomere. The binding of a new ATP molecule allows the myosin head to detach from the actin filament. The myosin can then hydrolyze the new ATP molecule, recock, and form another cross bridge. This cycle continues until the myosin-binding site is no longer available.

A skeletal muscle is innervated by one or more **motor nerves**. Each motor nerve contains axons of hundreds of motor neurons. Each motor neuron axon will split and yield multiple telodendria, axon terminals, and neuromuscular junctions. A **motor unit** refers to the group of muscle fibers that are stimulated by a single motor neuron. The number of muscle fibers per motor unit is small in muscles responsible for fine, precise movements (e.g. the extraocular muscles). It can be large in muscles responsible for big, gross movements (e.g. the gluteus maximus). Note that the muscle fibers of a motor unit are not clustered together but are distributed throughout the muscle. All of the muscle fibers w/i a motor unit will contract together (since they are stimulated by the same motor neuron). The amount of tension generated by a muscle is proportional to the number of motor units that are activated.

The response of a motor unit to a single action potential of its motor neuron is a **muscle twitch**. The first few milliseconds of the response are called the **latent period**. During this time excitation-contraction coupling is occurring but no muscular tension can be seen. Next is the **period of contraction** in which muscle shortening occurs and contractile force is generated. Then we have the **period of relaxation** during which contractile force declines and the muscle returns to its resting length. Different muscles will have twitches of different lengths.

An increase in frequency of the motor neuron action potentials will result in increased generation of contractile force by the muscle. If 2 muscle twitches occur in succession, the second twitch will be stronger than the first. This is b/c the calcium levels in the sarcoplasm will still be elevated from the first twitch and the second twitch will prompt the sarcoplasmic reticulum to release more calcium. This is known as **wave summation**. Stimulating the muscle at a faster and faster rate will cause the relaxation periods to become shorter and shorter and the amount of tension generated to increase. This is known as **incomplete tetanus**. Eventually the stimulation frequency is so high that the muscle does not relax at all. This is known as **complete tetanus**.

There are 2 basic types of muscle contractions: **isotonic contractions** and **isometric contractions**. During an isotonic contraction the muscle changes length and tension is developed. If the muscular tension is greater than the resistance (e.g. a dumbbell) then the muscle will shorten. This is then referred to as a **concentric contraction**. The shortening is explained by the sliding filament theory previously discussed. Concentric contractions are what we typically think of as muscle contractions. However, if the muscular tension is less than the load, the muscle will lengthen rather than shorten. This is known as an **eccentric contraction**. The tension developed by the lengthening muscle helps to brake or decelerate the movement. Think about slowly lowering a heavy object. The molecular mechanism by which the lengthening muscle develops tension is not yet completely understood. In an isometric contraction, the muscle will generate tension but the muscle as a whole does not change length.

A functioning muscle cell requires ATP for the detachment of myosin from actin and for the action of the SR Ca<sup>++</sup> ATPase. However a muscle cell only has a small quantity of stored ATP– enough for about 5 seconds of muscle activity. Luckily there are mechanisms for generating the needed ATP.
Muscle cells contain a high energy molecule called **creatine phosphate**. Creatine phosphate can donate its phosphate group to ADP in order to regenerate ATP. This reaction is catalyzed by **creatine kinase** and provides ATP for about another 10 seconds of contraction.

More ATP can be produced by the breakdown of glucose. The muscle cell can acquire glucose from its glycogen stores or from the blood. The **catabolism** (breakdown) of glucose is known as **glycolysis** and occurs in the sarcoplasm. For each molecule of glucose that is broken down, the products of glycolysis are: 2 molecules of **pyruvate**, 2 molecules of ATP, and 2 molecules of **NADH** (another reserve of chemical energy). If oxygen is not available, the 2 molecules of pyruvate will be converted into 2 molecules **lactic acid**. The generation of lactic acid allows other rounds of glycolysis to occur – since it turns NADH back into NAD⁺ which is necessary for glycolysis. The evidence that this lactic acid is responsible for muscle soreness is tenuous at best. The lactic acid produced travels via the blood to the liver where it is converted back into glucose which helps replenish the body's glycogen stores. The breakdown of glucose to form pyruvate and then the conversion of pyruvate to lactate is referred to as the **anaerobic pathway** since it occurs in the absence of oxygen.

If sufficient oxygen is present, the pyruvate will enter the mitochondria. Within the mitochondria pyruvate undergoes a series of chemical reactions (known as the **citric acid cycle** or the **Krebs cycle**) that yield CO₂ and H₂O and produce more molecules of NADH as well as another reserve of chemical energy known as **FADH₂**. The NADH and FADH₂ are then utilized by mitochondrial enzymes to produce a significant amount of ATP in a set of reactions referred to as the **electron transport chain**. Oxygen is necessary for these reactions to occur and thus this pathway for glucose/pyruvate is referred to as the **aerobic pathway**. The aerobic pathway produces 32 molecules of ATP per molecule of glucose. Compare that to the anaerobic pathway.

**Muscle fatigue** primarily occurs as a result of imbalances in the ion levels of the sarcoplasm and the local interstitial fluid surrounding the muscle fiber. It can also from the depletion of motor neuron neurotransmitters. There is also the theory of **central fatigue** in which the brain inhibits the activation of motor neurons during intense/prolonged muscle activity so as to minimize the possibility of organ/tissue damage.

Post-contraction a muscle fiber must regenerate its stores of oxygen, ATP, creatine phosphate, and glycogen. The production of these molecules requires an elevated level of blood flow and oxygen delivery to the recovering muscle. This demand is referred to as **oxygen debt**.

Muscle fibers can be classified based on their speed of contraction as **slow fibers** and **fast fibers**. Fibers can also be classified based on how they form their ATP. Fibers that rely primarily on aerobic pathways are said to be **oxidative** and fibers that rely on anaerobic pathways are said to be **glycolytic**. Overall fibers are said to be **slow oxidative**, **fast oxidative**, or **fast glycolytic**. The slow oxidative fibers are fatigue resistant and involved in performing activities of endurance and maintenance of posture. The fast oxidative fibers are moderately fatigue resistant and are involved in activities like sprinting. The fast glycolytic fibers are very fatigable and are involved in powerful movements such as doing a standing broad jump.

Endurance and resistance training can have dramatic effects on skeletal muscle. Endurance training causes an increase in the capillary density of the whole muscle and an increase in the density of mitochondria and myoglobin w/i the individual muscle fibers. Resistance training can cause an increase
in the density of myofibrils as well as the size of the myofibrils.