# Muscle Tissue Organization

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Known for its voluntary control and striated (striped) appearance, skeletal muscle plays a vital role in our ability to perform intentional movements. It comprises about 40% of our body weight alongside its connective tissues.

image by Hannah C. S13

Even though muscle fibers are comprised of many cells fused together, the resultant structure becomes one unit called the muscle cell, which we refer to as the **muscle fiber**. These muscle fibers are bound together into bundles, or **fascicles**, and are supplied with a rich network of blood vessels and nerves (see figure above number**1**). The fascicles are then bundled together to form the intact muscle. Muscle fibers are the same diameter as a hair strand (100-120um). As you look down at your bicep, visualize small strands of hair extending from your shoulder to the radius bone in your forearm. Clearly, one hair strand would be too fragile to move your arm, but hundreds of millions are very adequate! Let's dissect a skeletal muscle, beginning with the entire muscle and continuing internally down to the submicroscopic level of a single muscle cell. Please use the numbered figure above as reference as you read through this section. In an intact skeletal muscle, a rich network of nerves and blood vessels nourish and control each muscle cell. These muscle fibers are individually wrapped (endomysium;**4**) and then bound together (perimysium;**3**) by several different layers of fibrous connective tissue.

The **epimysium**(epi means “outside,” and mysium means “muscle”) is a layer of dense fibrous connective tissue that surrounds the entire muscle (labeled above). This layer is also often referred to as the **fascia**(**2**). Each skeletal muscle is formed from several bundled fascicles of skeletal muscle fibers, and each fascicle is surrounded by **perimysium**(peri means “around”;**3**). Each single muscle cell is wrapped individually with a fine layer of loose (areolar) connective tissue called **endomysium**(endo means “inside”;**4**). These connective tissue layers are continuous with each other, and they all extend beyond the ends of the muscle fibers themselves, forming the **tendons**that anchor muscles to bone (**5**), and moving the bones when the muscles contract.

Deep to the endomysium, each skeletal muscle cell is surrounded by a cell membrane known as the **sarcolemma**(you will see the prefixes sarc- and myo- quite a bit in this discussion, so you should understand that these are prefixes that refer to "muscle";**6**). Most of the space in the cytoplasm, or **sarcoplasm**is taken up by cylindrical (rod-like) **myofibril**protein structures (**7**). Each muscle fiber contains hundreds or even thousands of myofibrils that extend from one end of each muscle fiber to the other. These myofibrils take up about 80% of the intracellular space and are so densely packed inside these cells that mitochondria and other organelles get sandwiched between them while the nuclei get pushed to the outside and are located on the periphery, right under the sarcolemma.

Each myofibril is comprised of several varieties of protein molecules that form the **myofilaments**, and it is these myofilaments (actin, myosin, titin) that give muscles their contractile properties. The myofilaments are arranged in structures called **sarcomeres**(sarc- means “muscle,” and mere means “part”). The striations seen microscopically within skeletal muscle fibers are formed by the regular, organized arrangement of myofilaments—much like what we would see if we painted stripes on chopsticks and bundled them together with plastic wrap, with the plastic wrap representing the sarcolemma (see histological micrograph below).

Repeating structures like sarcomeres make anatomists like Bro. Anderson giddy with excitement because they can start putting names on things! The arrangement of the sarcomere is repeating and predictable and under a microscope we see alternating dark and light areas.

Skeletal Muscle Sarcomere: Thick and Thin Filaments, Z Line, H Zone, I & A Bands. File:Sarcomere.gif; Author: Sameerb; Site: https://commons.wikimedia.org/wiki/File:Sarcomere.gif; License: Public Domain, No restrictions

The dark areas are called **A bands**, which is easy to remember because "A" is the second letter in "dark." The light areas are called **I bands**and are also easy to remember because "i" is the second letter in "light." ("A" actually stands for anisotropic, and "I" stands for isotropic. Both of these terms refer to the light absorbing character of each band). The image below shows a micrograph of a sarcomere, along with a drawing representing the different parts of the sarcomere.

#### A Closer look at the myofibrils

image by JS F24

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Each myofibril is comprised of several varieties of protein molecules that form the myofilaments, and each myofilament contains the contractile segments that allow contraction. These contractile segments are known as sarcomeres (sarc- means “muscle,” and mere means “part”). The striations seen microscopically within skeletal muscle fibers are formed by the regular, organized arrangement of myofilaments, much like what we would see if we painted stripes on chopsticks and bundled them together with plastic wrap, with the plastic wrap representing the sarcolemma.

**Z-disc**proteins make up the Z-line that create perpendicular borders that form the repeating sarcomeres. **CapZ**and **alpha-actinin**anchor the protein **nebulin**to the Z line and extend out to the center where the length is capped off by the protein **tropomodulin**. Between molecules of nebulin is the elastic protein called **titin**. Titin is thought to play a major role in resetting the sarcomere after each contraction. Thus, each sarcomere consists of nebulin and titin proteins that set the stage for the organization of the contractile and regulatory proteins.

Each actin is composed of two strands of fibrous actin(**F-actin**) and a series of **troponin**and **tropomyosin**molecules. Each F-actin (also known as the thin filament) is formed by two strings of globular actin(**G-actin)**wound together in a double helical structure, much like twisting two strands of pearls with each other. In this analogy, each G-actin is like an individual pearl and each F-actin is like a strand of pearls. Each G-actin monomer has a binding site for ATP that it uses to polymerize to another G-actin monomer and nebulin. Following polymerization of G-actin monomers to form F-actin strands, the original ATP binding site is altered and becomes a binding site for the molecule myosin, called an **active site**. The protein **tropomyosin**extends over the entire F-actin filament and covers the newly created myosin binding sites. Each tropomyosin molecule is long enough to cover the active binding sites on seven G-actin molecules. These proteins run, end to end, along the entire length of the F-actin. Associated with each tropomyosin molecule is a third polypeptide complex known as **troponin**. Troponin complexes contain three globular polypeptides (Troponin I, Troponin T, and Troponin C) that have distinct functions. Troponin I binds to actin, troponin T binds to tropomyosin and helps position it on the F-actin strands, and troponin C binds calcium ions. Troponin C has four binding sites for calcium, two high-affinity binding sites and two low-affinity-binding sites. At low intracellular Ca2+ concentrations the high-affinity binding sites are occupied and help maintain the stability of the troponin complex. When intracellular calcium concentrations rise, then the low-affinity binding sites are occupied which causes a conformational change in the entire complex. This conformation change will result in troponin “pulling” the tropomyosin molecule away from the myosin binding sites of actin.

Image by JS F24

The final contractile myofilament (also called the thick filaments) is composed of about 300 myosin type II molecules bound together and surrounding the molecule titin which attaches near the Z-Line in each sarcomere. Each individual myosin type II protein is made up of six protein subunits, two heavy chains and four light chains. The heavy chains have a shape similar to a golf club, having a long shaft-like structure called the tail. The tails are each connected to a globular myosin head. The shafts, or tails, wrap around each other and interact with the tails of other myosin molecules, forming the shaft of the thick filament. The globular heads project out and are oriented towards the actin thin filament. It is the myosin heads that bind to the active sites on the actin. The connection between the head and the shaft of the myosin molecules is sometimes referred to as the neck region. It is in the neck region that we find the light chains of myosin. Each of the myosin heads is associated with two myosin light chains, an alkali (sometimes called essential) light chain and a regulatory light chain, that play a role in regulating the actions of the myosin heads.

Myosin has two **hinge regions.**These regions are where the myosin can rotate. We will see later how the myosin will rotate around one hinge to elevate and attach actin and then it will rotate in a region near the head to perform what will be called the power stroke. More on this later!

Additionally, each myosin head has an ATPase that binds to and hydrolyzes ATP during muscle contraction. It is the ATP that provides the energy for muscle contraction. The three-dimensional arrangement of the myosin heads is very important. Imagine that you were looking at a thick filament from the end, and there is a myosin head sticking straight up. As you moved around the circumference of the thick filament, you would see myosin heads every 30 degrees. This allows each thick filament to interact with six thin filaments. Likewise, each thin filament can interact with three thick filaments. This arrangement requires that there be two thin filaments for every thick filament in the myofibril. See the image below.

Muscle Fiber Detailed Diagram. Adapted from the following image: Title: 1022\_Muscle\_Fibers\_(small).jpg; Author: OpenStax College; Site: http://cnx.org/contents/6df8aab3-1741-4016-b5a9-ac51b52fade0@3/Skeletal-Muscle License: licensed under a Creative Commons Attribution 4.0 License;

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