Skeletal muscle is a superb example of structure aiding function. In order to comprehend this, and aid your learning of muscle contraction, it is imperative that you apply what you have learned in human anatomy and physiology of skeletal muscle to exercise. It is also important that you expand on your superficial study of muscle anatomy and become aware of additional proteins and structures that give specific contractile proteins added functionality.

The sarcomere is a useful component of the myofibril within a skeletal muscle fiber from which to investigate the molecular events of muscle contractions. However, prior to learning muscle contraction, the molecular biology of the sarcomere is required to be studied to ensure a complete understanding of the role of specific proteins, cations, excitable membranes and membranous networks in the process of muscle contraction.

Figure 1 presents a close illustration of the alignment between molecular structures of G-actin, tropomyosin, troponin and meromyosin, myosin and myosin heavy chain and light chains. Tropomyosin is a rod-shaped protein that spirals within the double stranded folds of F-actin. Multiple tropomyosin molecules are arranged end-to-end along the F-actin filament. Troponin (Tn) is a three component or domain protein, where one domain binds to actin (troponin-I, TnI), another to tropomyosin (troponin-T, TnT) and the third to calcium ions (troponin-C, TnC). As will be discussed later for muscle contraction, the interactions between the TnI, TnT and TnC domains and tropoyosin are very important, as the binding of Ca$^{2+}$ to TnC causes structural changes in these interactions that expose a binding site between F-actin and the S1 unit globular heads of the myosin heavy chains.

For the depolarization of the neuromuscular junction to trigger muscle contraction, there has to be a mechanism for connecting this depolarization to the intracellular contractile proteins. This connection is facilitated by the propagated depolarization across the sarcolemma to the transverse tubules (t-tubules) that direct the wave of depolarization inwards within the muscle fiber. Between the myofibrils is a network of membranous connective tissue called the sarcoplasmic reticulum (Figure 2). The t-tubules connect
to the terminal cisterna of the sarcoplasmic reticulum, and this junction is called a triad.

Figure 3 is an image of a thin section of skeletal muscle viewed under an electron microscope, revealing the membranous sarcoplasmic reticulum extending from z-line to z-line. Note the special arrangement and consistent association between the t-tubules and z-lines of the sarcomere. After the Ca\(^{2+}\) is released from the sarcoplasmic reticulum membranes within the sarcomere, it is immediately in the proximity of the troponin to which it binds to set in motion the molecular events of muscle contraction.

Regions of the sarcomere have been given specific names (Figure 4). In the relaxed state, the central region of each sarcomere where there are only meromyosin molecules is termed the H zone. The end and beginning of each neighboring sarcomere is called the z-line. In the middle of this zone M-proteins anchor the meromyosin molecules in place, forming a visually thicker central vertical line called the M-line. The A-band is the region of the sarcomere spanned by meromyosin. The I-band is the region of two neighboring sarcomeres, divided in two by the z-line, where there is no meromyosin.

The contractile proteins, and the sarcomere structure itself, are held in place by added small proteins. Thus, although we refer to and recognize the contractile proteins to be F-actin, meromyosin, troponin and tropomyosin, the orderly structure of the sarcomere and the contractile function that ensues, would not be possible without the proteins of the matrix. For example, in addition to the M-protein involvement, the proteins desmin and \(\alpha\)-actinin comprise the z-line, titin helps to stabilize the meromyosin molecules during contraction, and nebulin stabilizes the F-actin double stranded structure. Table 1 presents the proteins known to be important for the structure and function of the sarcomere.
### Table 1. The function of the main proteins involved in muscle contraction.

<table>
<thead>
<tr>
<th>Protein</th>
<th>Function</th>
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<tbody>
<tr>
<td>F-Actin</td>
<td>Interacts with myosin during muscle contraction.</td>
</tr>
<tr>
<td>Tropomyosin</td>
<td>Combines with troponin to cover or expose the actin binding sites depending on the presence of calcium.</td>
</tr>
<tr>
<td>Troponin</td>
<td>Binds calcium to move the troponin-tropomyosin complex to expose the actin binding sites.</td>
</tr>
<tr>
<td>Meromyosin</td>
<td>Contains ATPase activity to break down ATP, bind to actin and induce the “power stroke” of muscle contraction.</td>
</tr>
<tr>
<td>α-actinin</td>
<td>Connects actin to the proteins of the z-lines.</td>
</tr>
<tr>
<td>Desmin</td>
<td>Connects z-line from adjacent sarcomeres to aid the structural integrity of the myofibril.</td>
</tr>
<tr>
<td>M-protein</td>
<td>Holds the myosin filaments in their organized array, forming the M-line.</td>
</tr>
<tr>
<td>Nebulin</td>
<td>Holds the actin double filament together to form F-actin</td>
</tr>
<tr>
<td>Titin</td>
<td>Assists M protein to anchor the meromyosin in the middle of the sarcomere. Contributes to elastic recoil of muscle relaxation.</td>
</tr>
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</table>

**Figure 4. The regions of the sarcomere.**

**Glossary Words**

**sarcomere** is an anatomical unit of muscle contractile proteins where the proteins are arranged in a specialized configuration, framed by z-lines on each end, and gives skeletal muscle its striated appearance.

**G-actin** refers to globular actin molecules.

**tropomyosin** is a rod shaped protein that spirals around the F-actin filament in repeated segments.

**troponin** is a three peptide domain protein that binds calcium and induces a conformation change in its association with tropomyosin and actin, exposing the actin-myosin binding sites.
**Contractile Proteins and Support Matrix of Skeletal Muscle**

**meromyosin** is the thick filament containing approximately 200 myosin molecules.

**myosin** is a structurally complex protein consisting of a rod arm, hinge region and globular end region (S1 unit) that binds to actin and has ATPase activity.

**myosin heavy chain** is the portion of myosin from the hinge to the S1 units.

**light chains** are small proteins that are associated with each S1 unit (2 per unit).

**F-actin** is the protein resulting from the double strand of G-actin filaments.

**troponin** is the smaller contractile protein of skeletal muscle involved in the regulation of muscle contraction through its capability to bind calcium and expose the actin-myosin binding site.

**troponin-I** is the domain of troponin that binds to actin.

**troponin-T** is the domain of troponin that binds to tropomyosin.

**troponin-C** is the domain of troponin that binds to calcium.

**S1 unit** is the globular protein region of myosin heavy chain.

**t-tubules** are the tubules that invaginate from the sarcolemma into the skeletal muscle fiber and connect to the sarcoplasmic reticulum within the I-band of the sarcomere.

**sarcoplasmic reticulum** is an extensive system of smooth endoplasmic reticulum within skeletal muscle fibers that stores calcium and releases calcium during depolarization.

**terminal cisterna** is the region of the sarcoplasmic reticulum within the I-band and that connects to the t-tubules.

**triad** is the junction between the terminal cisterna of the sarcoplasmic reticulum and the t-tubule.

**z-line** is the protein structures that form each end of the sarcomere.

**H zone** is the central region of the sarcomere containing the M-line and only 1 contractile protein - meromyosin.

**M-proteins** are the proteins that form the central M-line and assist in anchoring the meromyosin in the central region of the sarcomere.

**M-line** is the central vertical line of the sarcomere formed by the M-proteins.
**A-band** is the region of the sarcomere spanned by meromyosin.

**I-band** refers to the regions of the sarcomere (each lateral end) where there is only the actin contractile protein.

**desmin** is the protein that assists the structural connections between adjacent sarcomeres at the z-lines.

**α-actinin** is the protein that anchors actin in place with the z-lines.

**titin** is the protein that assists in anchoring the meromyosin molecules in the center of the sarcomere.

**nebulin** is the protein that assists in the structural stability of the F-actin molecules.