Section Two: Chapter 13: Muscle Tissue and Skeletal Muscle System

In the body, muscle tissue plays a variety of important role across every system. Within the body there are three different types of muscle tissue: **1) Skeletal** muscle, **2) Cardiac** muscle, and **3) Smooth** muscle.

These three types of muscle are very different in their function, structure and location, and this contributes to the versatility of muscle tissue. Despite key differences in the three muscle types, there are many fundamental commonalities that all muscle tissues share. In this chapter we will examine the basic similarities that all muscle tissues have, and then focus on how each is different and distinctly suited to its particular role.

This chapter provides an initial comparison of the three muscle types in terms of general functions and characteristics as summarized in **Table 13. 1**. The emphasis then moves to an in depth exploration of **skeletal muscle**. The chapter is closed with a presentation of the nature of **smooth muscle** physiology. The details of cardiac muscle are covered in chapter 14, with other details of smooth muscle covered in the ANS, vascular and digestive physiology in chapters 9, 16 and 20.

All Muscle Tissues share General Properties

All three muscle tissues have important general properties in common, they are:

1) *Contractility* – muscle cells typically shorten when electrically stimulated, generating force.
2) *Excitability* – muscle cells respond to electrical stimulation and exhibit action potentials.
3) *Extensibility* – muscle tissue can stretch when a force is applied to it.
4) *Elasticity* – muscle tissue can recoil to its original shape when the force stretching it is removed.

How are the three types of Muscle Different?

To paint a broad picture, we can concisely distinguish the three type of muscle and their roles this way:

1) Skeletal Muscle – attached to the skeletal system (bones) – for body movement.
2) Cardiac Muscle – found in the heart – for controlling blood flow and pressure.
3) Smooth Muscle – in walls of internal organs, in blood vessels – for actions in organs and vessels.

All muscle cells have charges across their plasma membranes that can change from being polarized (very different on either side) to being depolarized (more similar). If this language sounds familiar it is because we are talking about **cell voltage** and **action potentials**. For all muscle cells, the electrical **excitation** of the **action potential** is the precursor (signal) to initiate **muscle contraction** and **generate force**. In general this is referred to as excitation-contraction coupling. The precise mechanism each muscle type engages in varies, and will be explored separately.

Control of Muscle

The term '*control*' here means where do the signals come from that effect muscle action. In terms of **skeletal muscle**, the signals for it to contract come completely from the **nervous system**. And when skeletal muscle relaxes it is due to receiving no signal from the nerves to contract! While the nervous system can influence the excitability of cardiac and smooth muscle to some degree, both **cardiac muscle** and **smooth muscle** can respond to other stimuli, such as hormones, paracrine and other local stimuli.

Let's now take a look at each type of muscle tissue more closely in order to understand their similarities and important differences in terms of function, location, histology and control.

Skeletal Muscle

Skeletal muscle can be seen just deep to the skin and its primary role is body movement. It works together with the skeletal system (bones) and movable articulations (joints) in the body to achieve the movement of a specific body part or whole body movement.

For example, the tailor's muscle of the thigh is called the **sartorius** shown in **Fig. 13.1** to the right. It is the longest muscle in the human body. It can measure up to 600 mm in length, this is just under 24 inches, which means it's about 2 feet long!

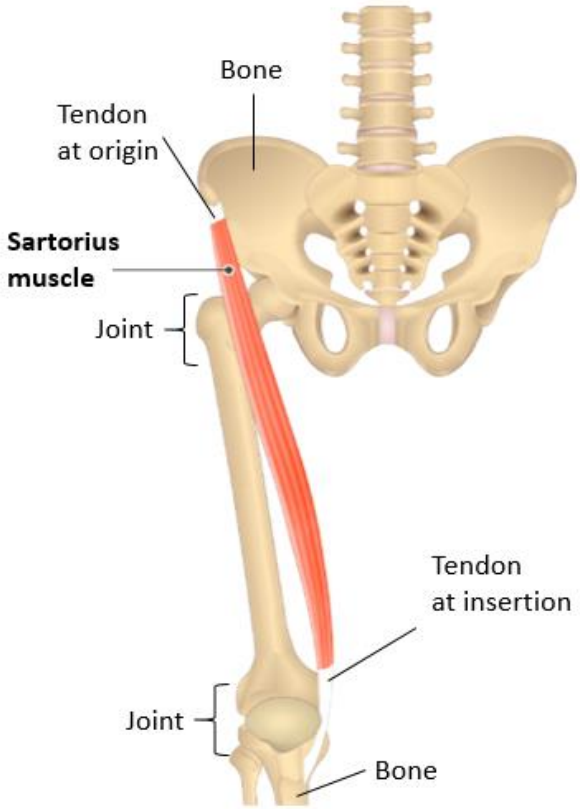


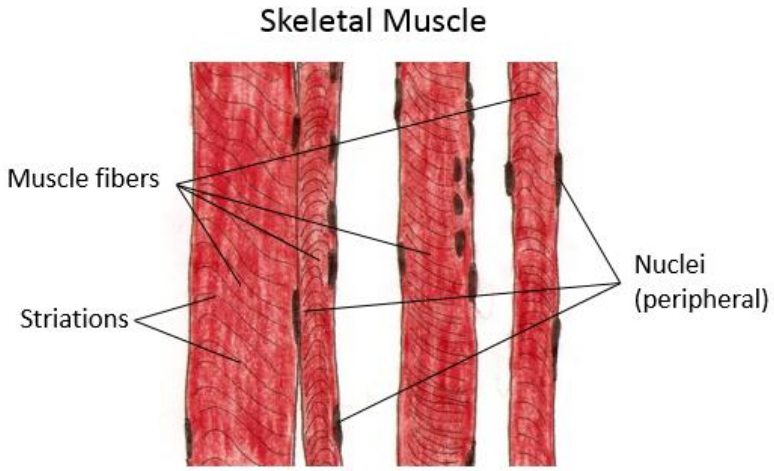
Figure 13.1 Shows the sartorius muscle of the anterior thigh and its origin (proximal site of attachment) and its insertion point (distal site of attachment). Skeletal muscle causes movement (an action) when it contracts depending on the movable (synovial) joints that the muscle crosses.

Functions

Most skeletal muscle is attached to bones by tendons to produce **body movement**, either of a body part or movement of the entire body. Skeletal muscle also provides **protection** and **support** to internal organs, nerves and blood vessels of the body, and generates significant **body heat generation** from contracting. It also acts as **sphincters** throughout the body, controlling the opening/closing of passageways.

Histology

Under the microscope, skeletal muscle cells are **elongated** and **cylindrical**, like a bunch of uncooked spaghetti noodles packed closely together (see **Fig. 13.2**.) They are **striated** (show a banding pattern) and **multinucleated** with the nuclei scattered toward the periphery. This is because the origin of skeletal muscle is actually a fusion of many **myoblast** cells, the embryonic progenitor from the mesoderm that differentiates into muscle cells. This fusion of myoblasts is specific to skeletal muscle but cardiac or smooth muscle.



Control

Skeletal muscle is controlled by the Somatic Nervous System (SNS) and predominantly is under **voluntary control**, with the important exception of reflexes, which are automated. This means that each skeletal muscle fiber is innervated (supplied with nerves) by motor somatic neurons and it is a signal from these neurons that triggers muscular contraction.

Figure 13.2 The long, cylindrical, multinucleated, striated skeletal muscle fibers (cells) under the microscope are shown is this drawing of skeletal muscle in longitudinal section.

Cardiac Muscle

Cardiac muscle is found only in the heart, where it makes up the bulk of that tissue.

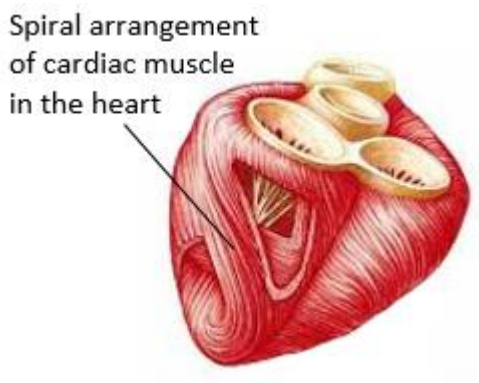


Figure 13.3 The spiral arrangement of the contractile myocardiocytes of the heart assist in generating powerful contractions.

Functions

The heart functions as a powerful rhythmic circulator in the body and the cardiac muscle cells, called **myocardiocytes**, contract to generate the force assisting in the significant pressure gradients required to circulate blood throughout the entire body. Recall myocardiocytes have lots of mitochondria as the heart is contracting all the time to deliver oxygen (O_2) and nutrient rich blood to all the body tissues and to collect and remove carbon dioxide (CO_2) and wastes from the tissues in close coordination with the lungs of the respiratory system.

As you can imagine, myocardiocytes are naturally very resistant to fatigue, since they must be able to continuously contract and relax to effectively circulate blood. The arrangement of the myocardiocytes is spiral to make for the most efficient energetic contraction as shown the drawing to the left in **Fig. 13.3**. The in-depth discussion of cardiac muscles cells is in the cardiovascular chapter 14.

Histology

Cardiac tissue is very distinct when examined under the microscope (see **Fig. 13.4** below). It has **branched** and **striated** muscle fibers and this tissue is what comprises the vast majority of the organ the heart. Each myocardiocyte, has one **centrally located nucleus**. The cells are all connected to each other by **intercalated discs** that allow for **1)** cell to cell communication (via gap junctions), and **2)** extensive cell attachments to keep the tissue together.

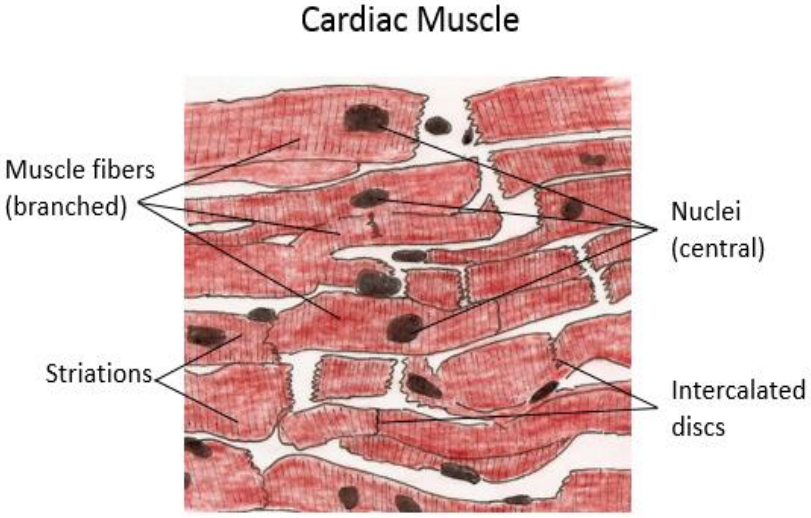


Figure 13.4 Cardiac muscle (myocardiocytes) under the microscope showing striations and intercalated discs.

Control

The activity of the heart is primarily regulated by its **intrinsic myogenic control**, literally meaning 'generated within the muscle'. This is because within the heart is the **electrical conduction system** that orchestrates the rhythm, force and frequency of the heartbeat. The sinoatrial (SA) node represents the intrinsic pacemaker that is in tune with the entire electrical conduction system.

The autonomic nervous system **(ANS)** also modulates the heart's activity. As we will see, it is the **parasympathetic** division that **slows** the heart rate down (the 'resting' division), while the **sympathetic** division **increases** the heart rate and the force of contraction (the 'fight or flight' division). Importantly, the heart's activity can also be modulated by local and hormonal and paracrine input, including hormones like epinephrine and atrial natriuretic peptide (ANP). There are also biofeedback mechanisms which involve voluntary control over the heart's activity. In general, the heart's activity is considered to be under **involuntary control**.

Smooth Muscle

Functions

Smooth muscle is found throughout the body, where it has a multitude of functions. It is located in internal organs of the body, for example, smooth muscle is an integral part of the **esophagus**, **stomach**, **small** and **large intestines** of the **digestive tract**. It is also found in the **urinary bladder**, the **ureters** and the **urethra** of the urinary system. They are also in the wall of the airways of the lungs (e.g., **bronchioles**), and in the ducts and accessory structures of the **reproductive systems** of both genders. Another vital location of smooth muscle is in the **walls of blood vessels** of the cardiovascular system. Smooth muscle cells can be arranged in many ways (see **Fig. 13.5**). When the smooth muscle in blood vessel walls contracts this will cause vasoconstriction, and when it relaxes, vasodilation results. Changing the diameter of blood vessels has a very powerful impact on both blood flow and blood pressure.

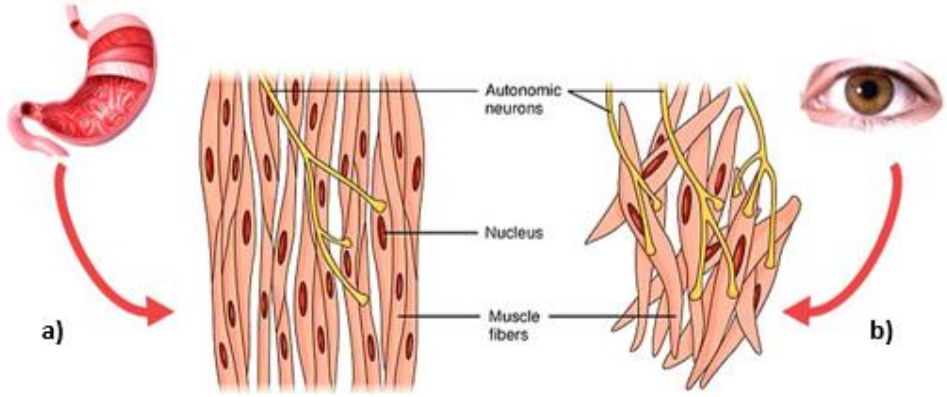


Figure 13.5 Shows the different arrangements of smooth muscle fibers (cells) depending on where they are in the body, **a)** is in the wall of the stomach and **b)** is in the iris of the eye.

Histology

Like its name implies, smooth muscle appears rather smooth under the microscope, they are **non-striated** because they lack any banding patterns and this gives them a smooth appearance compared to the other two muscles types. Their cell shape is described as **spindle shaped** (tethered at the ends, like a football or a cigar), with a singular large **centrally located nucleus**.

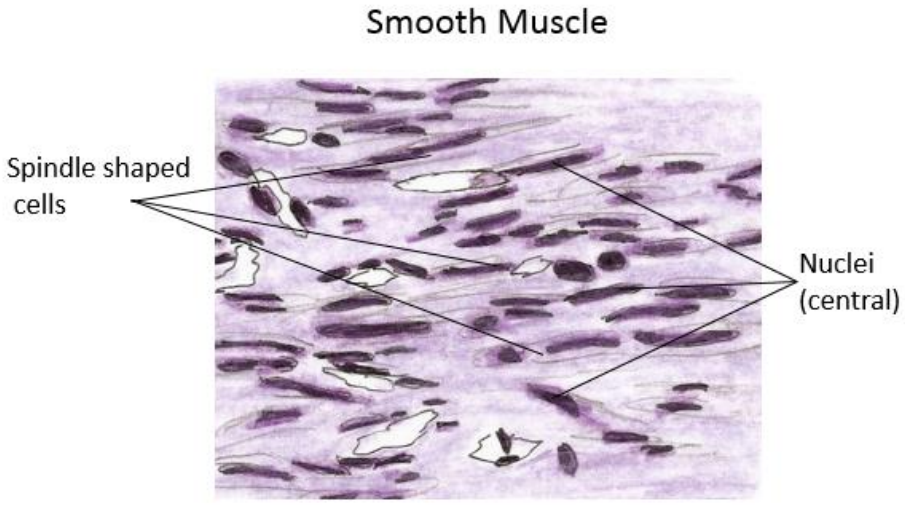


Figure 13.6 Smooth muscle cells under the microscope.

Control

In terms of how it is controlled, smooth muscle is considered to be under **involuntary control**, predominantly under the control of the autonomic nervous system (ANS). As previously mentioned in chapter 10 covering the ANS, smooth muscle is one of the three target tissues for the ANS. The **parasympathetic** and **sympathetic** divisions often have consistent effects on smooth muscle, however the underlying response will be dependent on the specific type of receptors present. Smooth muscle is also heavily influence by local **paracrine mediators**, such as nitric oxide (NO) and local levels of oxygen (O_2) and carbon dioxide (CO_2). **Hormones** circulating in the blood also exert control over smooth muscle activity. At the risk of sounding repetitive, whether the smooth muscle contracts or relaxes is largely dependent on the receptors present on that smooth muscle, and this is contingent upon the location of the tissue in the body.

Table 13.1 Table showing a comparison between the three types of muscle tissue in the body.

	Skeletal Muscle	Cardiac Muscle	Smooth Muscle
Location	Attached to bones, eyes, tongue, upper esophagus	Within the heart	Internal organs, skin, and vessels
Role	Body movement, one part or whole body moment	Beating of the heart chambers and pumping blood	Movement in viscera, altering diameters of passageways
Cell shape	Long, cylindrical, parallel and multinucleated	Shorter and branched	Spindle or fusiform shaped
Contraction mechanism	Ca^{2+} binds to troponin exposing actin's binding site	Ca^{2+} binds to troponin exposing actin's binding site	Ca^{2+}-calmodulin activation of myosin light chain kinase (MLCK) to Phosphorylate myosin
Growth Renewal and Repair	Hypertrophy with limited renewal via satellite cells. Repair of micro tears.	Hypertrophy, limited renewal. Repair of micro tears.	Hypertrophy and hyperplasia (mitosis).
T-tubules	Triads formations	Dyad formations	None
Distinctive features	Extremely organized densely packed sarcomeres	Intercalated discs with gap junctions and desmosomes	Gap junctions caveolae and dense bodies
Striations (Banding)	Yes	Yes	No
Control	Voluntary* Somatic Nervous System	Involuntary# Intrinsic myogenic control, ANS, and hormones	Involuntary ANS, paracrines and hormones
Strength	Strongest	Moderate	Weakest
Fatigue	Fastest to fatigue	Intermediate fatigue	Slowest to fatigue

** Except for reflexes.*
 # Except for biofeedback.

Summary Muscle Comparisons

There are many more comparisons to make between these three different types of muscle, but the information above in **Table 13.1** provides a nice summary of many of the points already discussed and numerous others that have not been discussed in any detail at this point. As we continue our exploration of the various types of muscle tissue, issues related to how Ca^{2+} (calcium ions) are used during contraction will become more prominent.

Now the many and varied aspects of the skeletal muscular system will be fleshed out, so to speak!

Functions of the Skeletal Muscular System

Now that we have made a basic survey of the three types of muscle in the human body and compared them to each other, at this juncture we will now set our focus on **skeletal muscle** physiology and take an in depth look at is functions and in particular, at the details of the **Neuromuscular Junction** (NMJ) to understand how skeletal muscle is stimulated and how contraction occurs.

Skeletal Muscle Represents from 30% to 40% of Total Body Mass

In the human body, skeletal muscle accounts for about 40% of body mass in males, and 30% of body mass in females. That is a significant amount and is one reason why skeletal muscle activity has such a big impact on the entire body. Contracting skeletal muscle uses a lot of energy and produces a lot of heat.

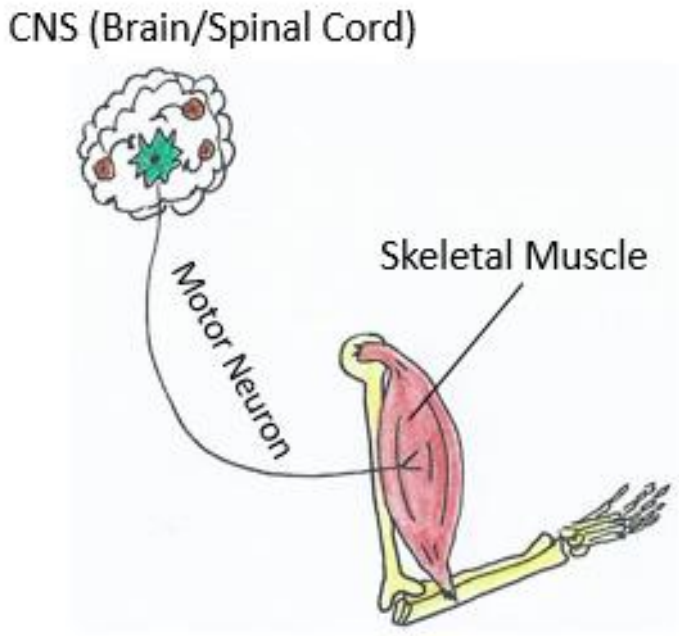


Figure 13.7 In this sketch, it shows the motor neurons originating in the brain to innervate skeletal muscle attached to the skeleton.

As previously stated, skeletal muscle is innervated (controlled) by the **somatic nervous system** (SNS), therefore it requires nervous stimulation in order to contract. As seen in **Figure 13.7** to the left, the initiation of skeletal muscle contraction (and therefore body movement) begins in the brain and spinal cord. Somatic motor neurons carrying commands from the central nervous system and go directly to the muscles fibers. The NT **ACh** is released by these somatic motor neurons and they bind to **nicotinic receptors** on the skeletal muscle membrane – then presto – contraction!

Any time there is an absence of nervous stimulation, skeletal muscle relaxes. Most skeletal muscle even when relaxed has some muscle tone, it is like having a slight muscle contraction at rest. Even when you are sitting down on a comfortable chair, postural muscles are contracting to maintain body position and balance.

Skeletal muscle is attached to bones of the skeleton, with long bones acting as levers, and the joints (articulations) acting as the movable pivot (fulcrum). The action or energy arm in this "level system" is the contraction of skeletal muscle, this is the force applied to create body movement. The vast majority of body movement is achieved by opposing lever actions from antagonistic skeletal muscle groups.

As we shall see further on in this section, there are actually **three different types of skeletal muscle fibers**.

They are called: **1) slow-twitch**, **2) intermediate-twitch**, and **3) fast-twitch** skeletal muscle fibers. Alternately, they can also be referred to as: **1) slow oxidative** (SO), **2) fast oxidative** (FO) and **3) fast glycolytic** (FG), respectively. The latter naming indicates the metabolism involved in these different skeletal muscle fibers. It is very important to appreciate the different skeletal muscle fiber types and their functions in order to understand how this impacts body movement and exercise actions. Each type of skeletal muscle fiber has a unique metabolism, strength and endurance. This is examined toward the end of this chapter.

Review of the Basic Functions of Skeletal Muscle

1. **Body Movement:** The skeletal muscular system, together with the skeletal system (bones) and the articulations (joints) allows for dynamic body movement.

2. **Protection of Deeper Tissues:** The superficial nature of skeletal muscle allows for it to cover and protect structures and internal organs deep to them. For example, the abdomen is one of the most venerable body areas of the body because there is not bony protection, but the four layers of abdominal muscles provide significant

3. **Guards Entrances and Exits:** The skeletal muscle external sphincters control and protect openings and passages in the body. For example, the orbicularis oris is the sphincter around the mouth that controls what does and does not enter the mouth.

4. **Generates Body Heat:** The active metabolic nature of skeletal muscle means that the more it is used the more body heat it generates. In a time of lower body temperature or hypothermia, shivering of skeletal muscles (which is the oscillatory twitching of antagonistic muscle groups) is a physiological response that occurs to produce heat.

The Pattern of Whole Muscle, Musc1le Fascicles, Muscle Fibers, and Myofibrils

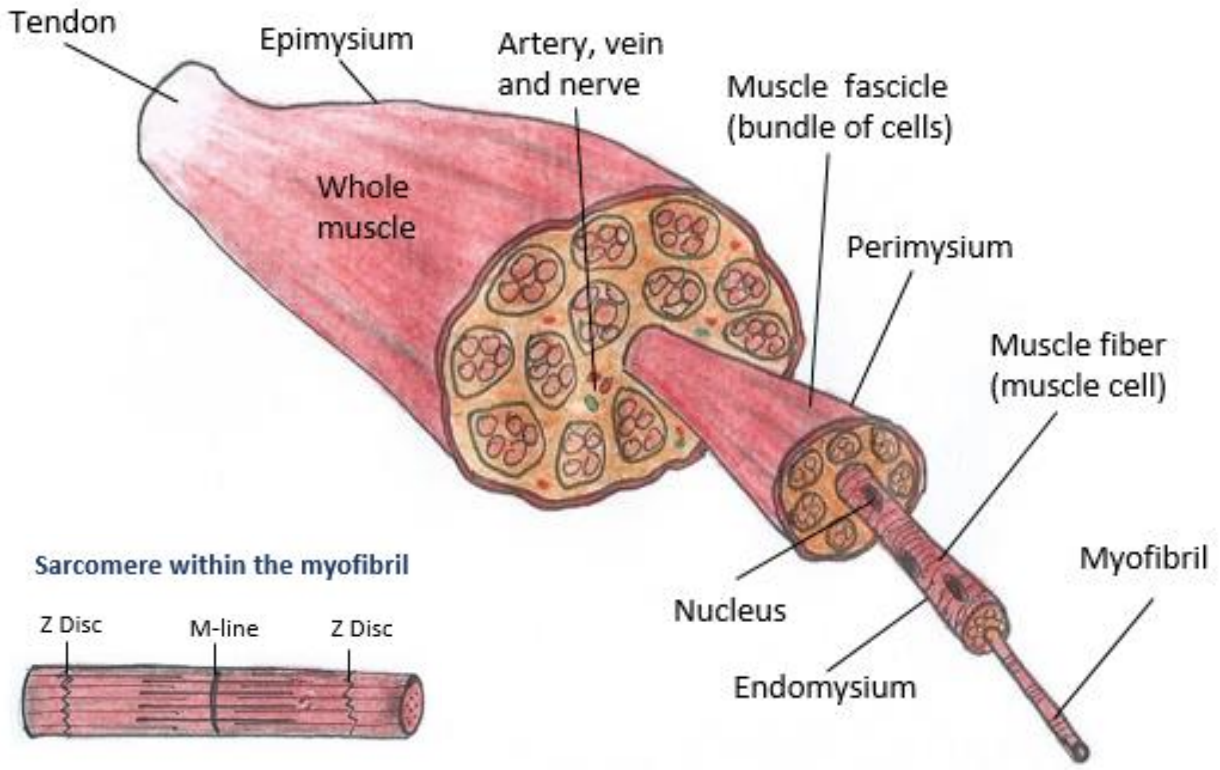


Figure 13.8 This drawing shows whole skeletal muscle and how it is composed of deeper structures within it that are very similar to the larger structure. The whole muscle is made of muscle fascicles, which are made of bundles of muscle fibers, which are made of bundles of myofibrils. Finally, deep on the microscopic level, is the sarcomere, the functional unit of skeletal where the actions of contraction can be explored.

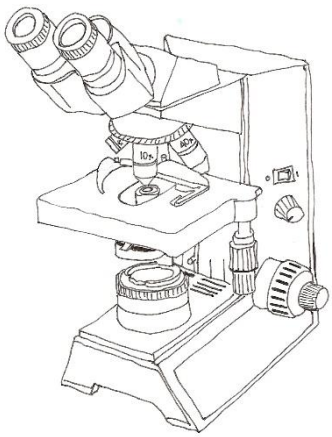
Skeletal Muscle Vocabulary

There are certain terms used when discussing muscle tissue, especially skeletal muscle. It is somewhat like a vocabulary list. Here is a brief summary of some common terms that are specialized for skeletal muscle. Many of these structures are displayed in **Figures 13.9**, **13.10** and **13.11**.

- ***Muscle fiber*** – this is what a single muscle *cell* is called, used especially with skeletal muscle.
- ***Sarcoplasm*** - is the cytoplasm of muscle cells.
- ***Sarcolemma*** - is the plasma membrane of the muscle fiber (cell).
- ***Motor end plate*** – is a specialized portion of the sarcolemma directly across from the somatic nerve end bulb. The motor end plate is usually located in the middle of the muscle fiber.
- ***Sarcoplasmic Reticulum*** (SR) is a specialized endoplasmic reticulum (ER) in muscle cells for storing intracellular Ca^{2+} ions. The release of these Ca^{2+} ions is crucial for the contraction of muscle cells.
- ***Sarcomere*** – is the functional unit of skeletal muscle (the smallest structure which does the job of the whole) in that it contracts and generate force. The sarcomere contains the contractile proteins actin and myosin, as well as the regulatory proteins troponin and tropomyosin.
- ***Transverse-tubules*** (***T-tubules***) - are invaginations of the sarcolemma deep into the cell on either side of a sarcomere. Their role is to quickly spread the action potential across the entire muscle cell.
- ***Later sacs*** (***terminal cisternae***) – these are the lateral portions of the SR located on either side of the t-tubules. Their close proximity allow for quick opening of Ca^{2+} channels on the SR.
- ***Triad*** - the grouping of one t-tubule and two lateral sacs.

Going Microscopic to Investigate the Step by Step Process of Muscle Contraction

As we start to examine skeletal muscle physiology, we need to look very closely at the skeletal muscle fiber and how the somatic motor neuron transmits its signal, how the skeletal muscle cell receives the signal, and how this results muscle contraction. We will start with the **sarcomere**, which is the functional unit for skeletal muscle, that is, it's the smallest part that does the job of the whole.



The Somatic Nervous System innervates all Skeletal Muscle

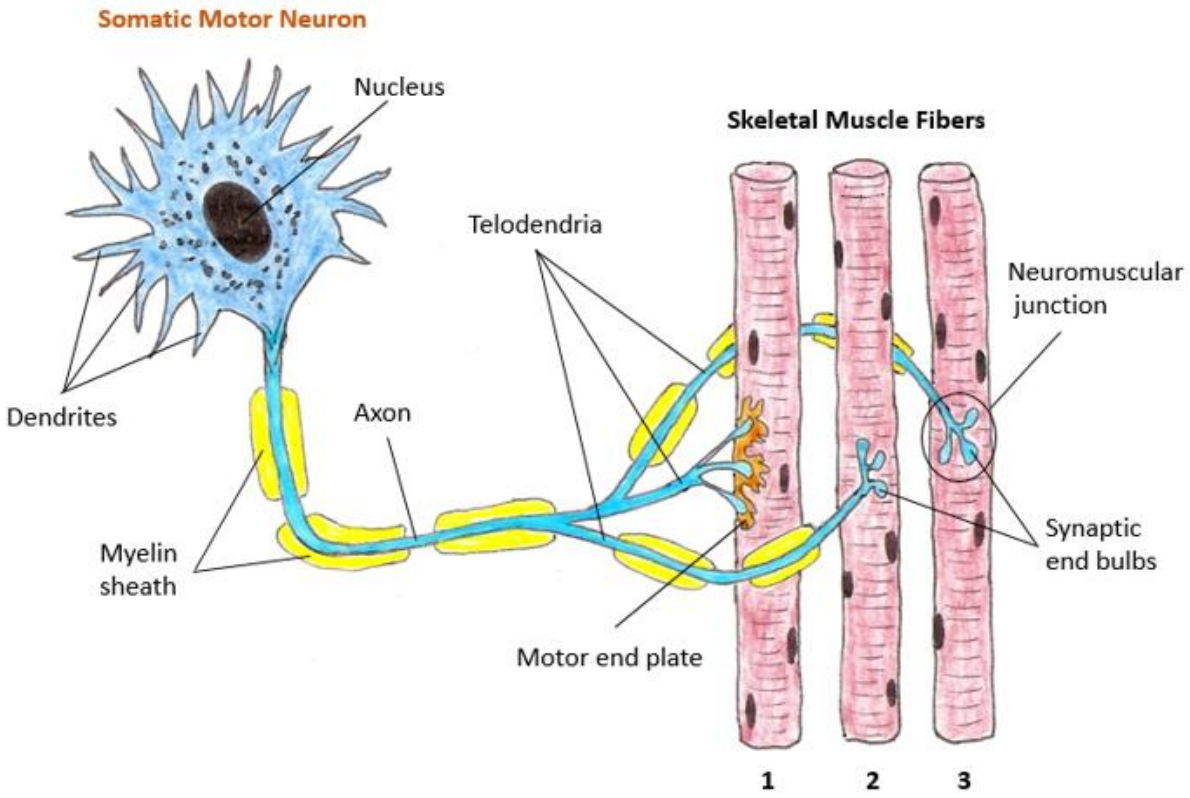


Figure 13.9 This is a diagrammatic overview of how the somatic nervous system (SNS) innervates all skeletal muscle. The myelinated motor neuron here is innervating muscle fibers number 1, 2 and 3.

The Big Picture

The overall functional arrangement of skeletal muscle is exemplified in **Fig. 13.9** above. The motor neuron radiates out into the periphery and innervates single individual muscle fibers (cells) that act as a group.

The Sarcomere

The sarcomere is the **functional unit** of skeletal muscle. A functional unit is the smallest part of the 'whole' that does the job of the entire structure. Therefore, a sarcomere is the smallest element in skeletal (and cardiac) muscle that contracts and generates force when electrically stimulated.

When viewed under a microscope, skeletal muscle fibers of varied lengths are highly organized in a stacked pattern. The myofibril strands, actin and myosin, form bundles of filament arranged parallel to one another. When a muscle in our body contracts, it is seen to do so according to '**The Sliding Filament Theory**'. This theory predicts that a muscle contracts when filaments are allowed to slide past each other. This interaction yields a contractile force. The reason the sarcomere structure is so useful to understand is that its arrangement can demonstrate how muscle physically shortens. This is the unit that is able to compensate for the lengthening or shortening of a flexing muscle.

The sliding filament theory was first posited by scientists who had used high-resolution microscopy and filament stains to observe myosin and actin filaments in action at various stages of contraction. They were able to visualize the physical lengthening of the sarcomere in its relaxed state, and the shortening in its contracted state. Their observations led to the discovery of the sarcomere '**bands**' described below.

The Functional Unit of Skeletal Muscle – The Sarcomere

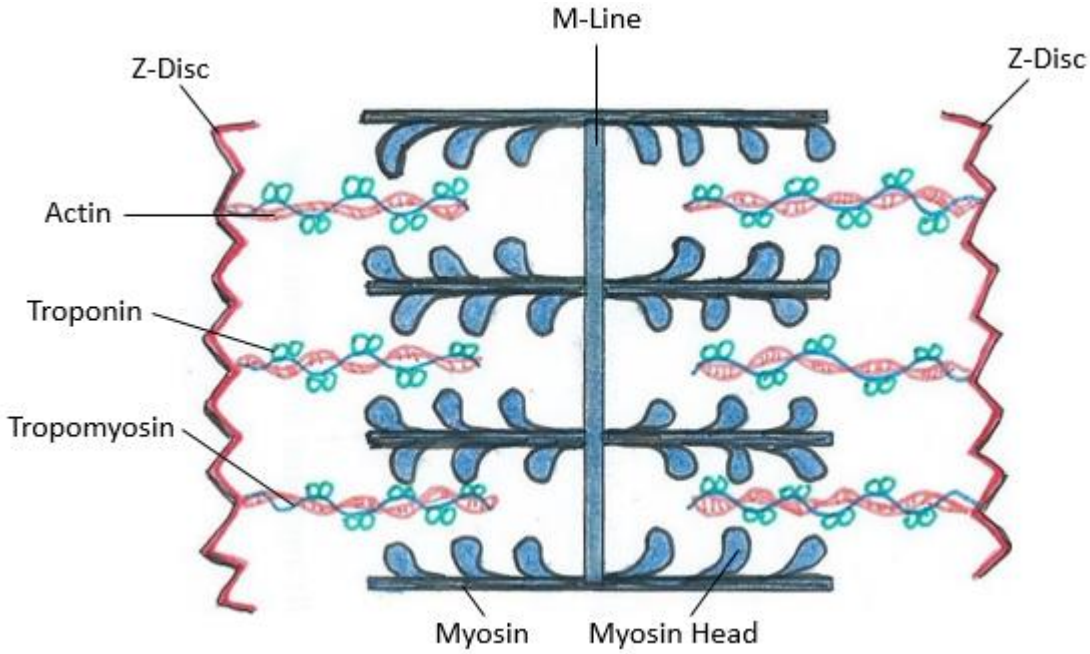


Figure 13.10 A diagrammatic drawing of the sarcomere of skeletal muscle, showing the arrangements of the myofilaments, regulatory proteins and other structures that make up one sarcomere.

Two Contractile Proteins

The muscle cell is filled with myofibrils. A myofibril is a bundle of contractile and elastic proteins that are responsible for muscle contraction. It contains the two major contractile proteins, **myosin** (thick filament) and **actin** the (thin filament). Examine the simple yet hopefully effective drawing of a 'stick figure' sarcomere above in **Figure 13.10**.

Actin – is a thin contractile protein that is attached to the **Z discs** of the sarcomere. There are active sites on actin and when these are exposed, myosin heads will bind with the active sites of actin. Actin also has two regulatory proteins, **troponin** and **tropomyosin**, both are closely associated with it (see below).

Myosin – is a thick contractile protein with many myosin heads radiating off the thick body of myosin. Each myosin head has **two binding sites** on it, one for actin (the other contractile protein) and one to bind and hydrolyze ATP. Myosin has a high affinity for actin and the bond between actin and myosin is called a **crossbridge**.

Two Regulatory Proteins

As we have already seen, the sarcomere is made mostly of actin and myosin, these two are considered the contractile proteins. There are also two regulatory proteins in the sarcomere that are associated with the contractile protein actin. They are troponin and tropomyosin.

Troponin – binds Ca^{2+} when the levels of Ca^{2+} inside the sarcoplasm increase.

Tropomyosin – covers the active site on actin. When tropomyosin is in place, actin and myosin are prevented from binding together. Therefore when there is no Ca^{2+}, free in the cell outside of the SR, crossbridges between actin and myosin cannot be formed and no contraction can occur.

Skeletal muscle fibers (cells) are composed of myofibrils, which are composed of the thick and the thin myofilaments, myosin and actin respectively. Myosin, actin, and the two regulatory proteins troponin and tropomyosin (with some elastic titan fibers) are repeated many many times in units called sarcomeres. The sarcomere is responsible for the striated appearance of skeletal muscle and forms the basic mechanisms that are necessary for muscle contraction.

As seen in the **Figure 13.10** above, the sarcomere is arranged such that the thick and thin filaments can overlap each other, and therefore can 'slide' past each other during contraction. None of the contractile proteins (actin or myosin) shorten or lengthen during contraction; rather they move past one another during contraction. The entire sarcomere changes its length but the contractile proteins do not change their lengths.

The striations of skeletal and cardiac are created by the banding pattern that exists within the sarcomere. These bands include the A band, I band and H band (or zone). Other structures of the sarcomere include the central M line and two Z disks, one at each end of the sarcomere.

If we outline what each band is comprised of and then consider how these bands change during contraction, this will give us insight into how the sarcomere shortens to generate tension.

- The **H band** - contains myosin (the thick filament) only, with no overlap of actin in this band.
- The **I band** - contains actin (the thin filament) only, with no overlap of myosin in this band.
- The **A band** - contains all of the myosin, regardless of how much actin is overlapping.

The width of some bands change during contraction, the discovery of this was what led to the notion of the sliding filament theory. In class we will analyze the structure of the sarcomere and as we discuss the way the bands are arranged, it will hopefully be clear which bands change and which do not.

The H and I bands shorten during contraction and they also lengthen when the sarcomere is stretched. The A band does not shorten during contraction or lengthen when stretched. The A band is all of the myosin, so it cannot change its length. Because myosin is very thick compared to actin, the A band (which is all of the myosin) is sometimes called the **Dark Band**. Also, the I band (made from actin only) is sometimes called the **Light Band**. These terms are based on the shades seen under the electron microscope. Think of **A** being in the word 'Dark' and **I** being in the word 'Light'.

The Neuromuscular Junction for Skeletal Muscle

The Somatic Nervous System (SNS) controls the skeletal muscle of the body. Somatic motor neurons are myelinated neurons that travel from the Central Nervous System (CNS) to the periphery and innervate skeletal muscle fibers for body movement. According to the well research biochemical theory, much has been pieced together about how the neuron and the muscle cell communication for skeletal action. The site of communication is called the Neuromuscular Junction (NMJ) see **Figure 13.11** below.

It may be noticed that there are a lot of similarities between the neuromuscular junction and the synapse (the site of two neurons communicating). The important exception is that the neuron sending the signal is now communicating with **skeletal muscle**. Hopefully this means that the first half of the story (sending the signal) is familiar, and the variation comes with the slightly modified response of the muscle cell.

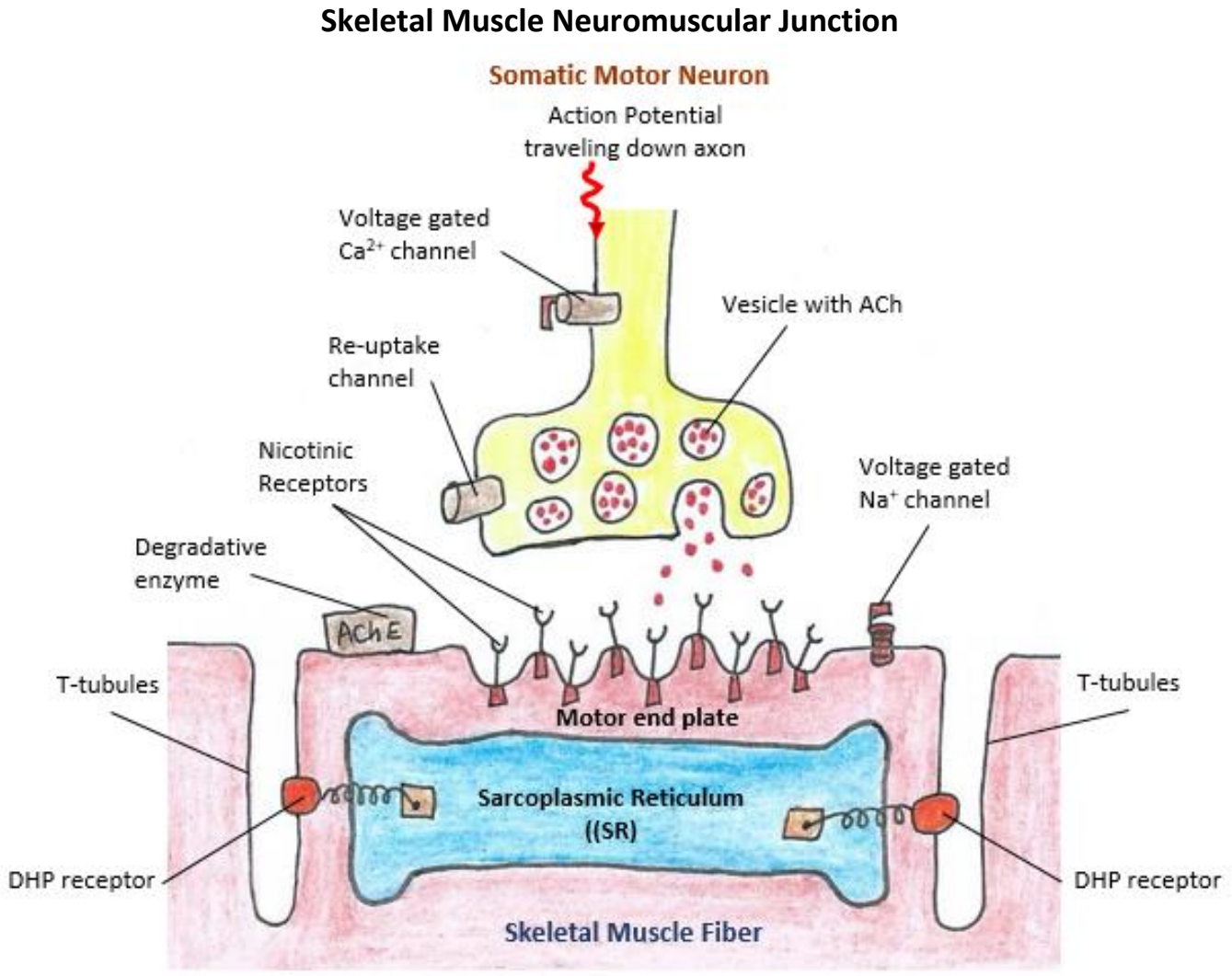


Figure 13.11 A diagrammatic drawing of the neuromuscular junction (NMJ) for skeletal muscle. The somatic motor neuron has all the same components as seen earlier in the synapse. Now instead of communicating with another neuron, it is sending signal to a skeletal muscle fiber at the NMJ. When ACh binds to nicotinic receptors on the motor end plate, it triggers the opening of voltage gated channels resulting in depolarization of muscle cell membrane, causing a motor end plate potential, which becomes an action potential in muscle cells.

Summary of Biochemical Events of Muscle Contraction

1. The nerve impulse (action potential) of the somatic motor neuron arrives at the neuromuscular junction and **voltage gated Ca^{2+} channels open**, allowing influx of Ca^{2+} into end bulb of the neuron.

2. Acetylcholine (ACh) is released from the somatic motor neuron by **exocytosis** and diffuses across the NMJ to the motor end plate of skeletal muscle.

3. ACh binds with **nicotinic receptors** at the motor end plate, these receptors are linked to ligand gated ion channels open, allowing Na^+ influx (plus a little bit of K^+ efflux), which results in the depolarization of the muscle cell membrane. This results in a **motor end plate potential**, which becomes an **action potential** (AP) in muscle cells.

4. The impulse (AP) in the muscle tissue is spread very quickly throughout the cell by the transverse ('T') tubules. Located on the **T-tubules** are the **dihydropyridine** (DHP) **receptors** that are mechanically linked to the lateral sacs (terminal cisternae) of the **sarcoplasmic reticulum** (SR). When triggered by the change in membrane potential (AP) traveling down the t-tubules, the DHP receptors change shape and mechanically open gates on the SR. This then causes the SR to release the Ca^{2+} stored there out into the cytosol (sarcoplasm) of the skeletal muscle.

5. The increase in free intracellular $[Ca^{2+}]_i$ can then bind to the regulatory protein **troponin**, causing it to change shape and move.

6. The movement of troponin then moves **tropomyosin** away from covering the active site on actin, thus exposing the myosin binding site on actin.

7. Due to the strong affinity between them, the myosin head binds to the actin to form a **crossbridge** – a bond between an actin and a myosin.

8. Crossbridge formation stimulates ATPase activity on the myosin head, and allows the **power stroke** to occur. The power stroke is the 'pulling' by myosin of actin toward the M line by the pivoting of the myosin head. The myosin head is going from a **high Energy state** to a **low Energy state** during the power stroke (Potential E converted to Kinetic E).

9. If more ATP is available, then the crossbridge is broken and myosin releases actin. This allows for the repositioning of the myosin head into the high energy state.

10. If the nerve impulse is still present, steps 7 through 9 will be repeated and the muscle will continue to contract and generate force.

This muscle contraction will continue until: **1)** the impulse stops, or **2)** fatigue occurs.

Details of ATP and Myosin-Actin Cycling in Muscle Contraction

In skeletal muscle, when Ca^{2+} is released from the SR the myosin heads are free to bind to the unguarded actin and pull actin inwards toward the M line to produce muscle contraction. This action requires energy, which is provided by ATP. Recall that the myosin head has 2 binding sites; one for **actin**, the other for **ATP**.

At rest when muscle is relaxed, ATP has *already* been bound to the myosin head and is used to cock the myosin into the **high Energy state** (see **Fig. 13.12** a below). The energy released during hydrolysis of ATP is used to move the myosin into a position of high potential energy, the ADP and Pi produced are still attached at the site.

If muscle stimulation occurs and the binding sites on actin become available, myosin immediately forms a crossbridge with actin (see **Fig. 13.12 b** below). This is when the ADP and Pi are released from the myosin head, allowing myosin to ***expend that stored energy as a conformational change***. Like a mouse trap that has been released, the myosin head forcefully springs forward toward the M-line, pulling the attached actin along with it. This is called the "**Power Stroke**" because this is the step that produces force.

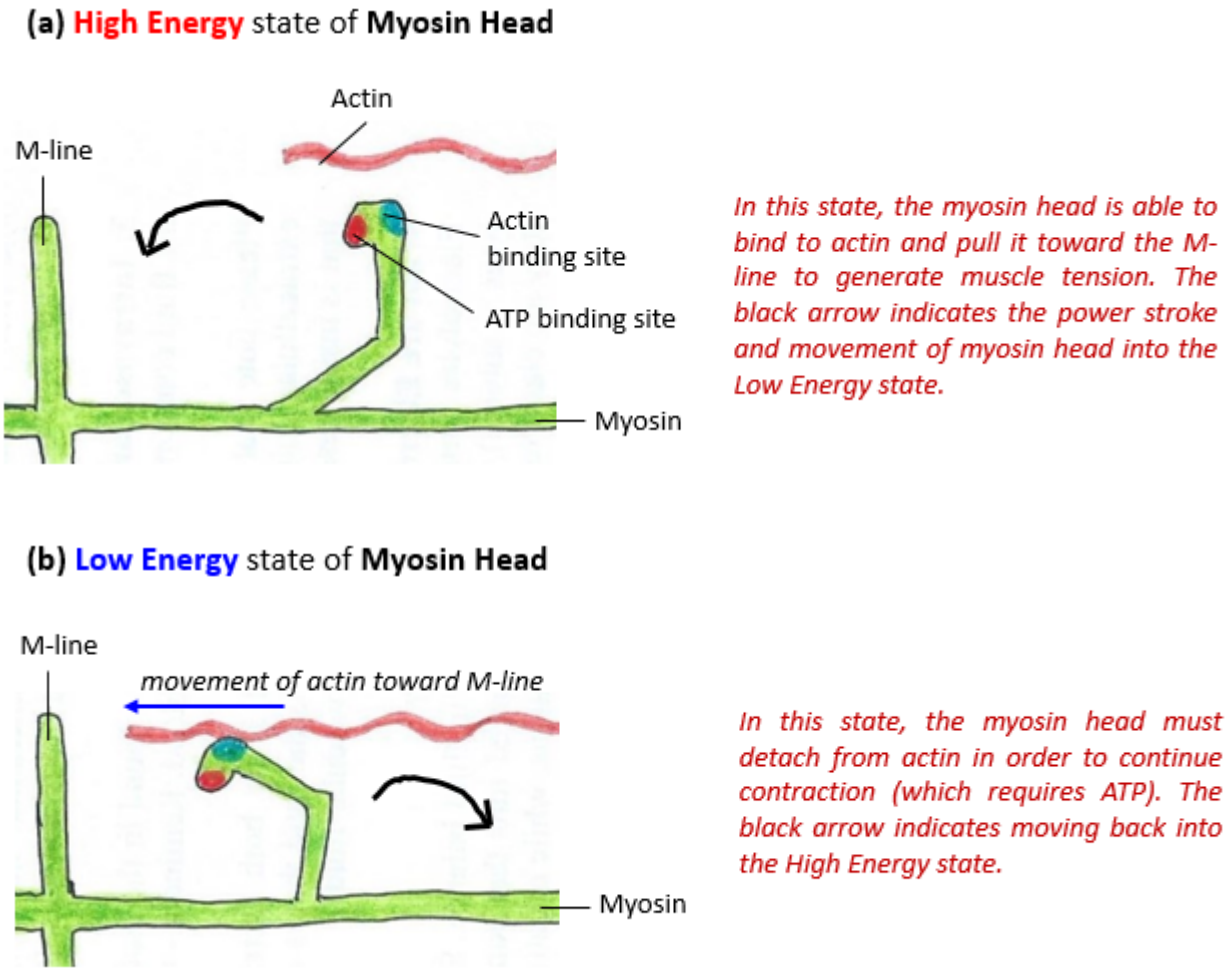


Figure 13.12 Shown are the two states of the pivoting myosin head: **a)** at rest, the pivoting myosin head is pulled or cocked back in the high energy state, like a spring invested with potential energy. In **b)** the myosin head is able to bind with the actin and this triggers the release of ADP and the P_i from the ATP binding site, transforming the potential energy into kinetic energy of motion during the power stroke, when the myosin pulls actin toward the M line generating force. At the end of the power stroke, the myosin head is now in the low energy state and will require additional ATP to release from actin and be cocked back to the high energy state for contraction to continue.

At the end of the power stroke the myosin is at its **low Energy state**, and the ATP site is vacant. The crossbridge is still in place but if ATP is present, it binds to myosin, which causes myosin to release actin - this is where we say the ATP 'breaks' the crossbridge. Now free of actin, the myosin ATPase hydrolyzes ATP to ADP + P_i and uses the E liberated to cock it back into the high energy state. If actin is still unguarded, it will bind to actin (forming a crossbridge) and repeat the entire process of discarding the ADP +P_i for the power stroke, etc.

Again, when at rest, the myosin will remain in the high energy state, as it waits for another opportunity to bind with actin and pull it toward the M-line.

The Myosin Head

- In the **High Energy State** (see **Figure 13.12 a**), the myosin head is cocked back and ready to bind with actin and pull actin toward the M-line.

- Myosin got into this High Energy state by binding ATP, and hydrolyzing it to ADP and P_i, which remains in the ATP binding site.

- The ADP and P_i are only expelled from the binding site when the myosin binds with actin, this allows myosin to spring toward the M-line pulling actin with it = the **Power Stroke**.

- After pulling to its limit, the myosin is now in its Low Energy state (see **Figure 13.12 b**). If ATP is available it binds with the myosin head and breaks the crossbridge, then cocks myosin back into the High Energy state.

How to Stop Contracting Skeletal Muscle

1. Stop the Nerve Impulse (action potential) coming from the Somatic motor neuron.

2. This will stop allowing the Ca^{2+} to be released from the SR of skeletal muscle cells.

3. The Ca^{2+} will be pumped back into SR (re-sequestered) by active transport (*Ca^{2+}ATPase). **It takes 1 ATP to pump 2 Ca^{2+} back into the SR**. *This pump is active all the time.

4. Without the free [Ca^{2+}]i, troponin is no longer bound to Ca^{2+} and the tropomyosin then moves back over to cover the binding sites on actin. Thus crossbridges formation cannot occur.

5. When all the myosin heads detach, actin slides back to its original position and the muscle relaxes.

Things that Effect Skeletal Muscle Contraction at the Neuromuscular Junction

Botulism toxin: This is an extremely potent neurotoxin, it **prevents ACh release** from somatic motor neuron from. This means that the signal to skeletal muscle from the nerve never arrives at the neuromuscular junction, there is no exocytosis of ACh, no stimulation of nicotinic receptors and no muscular contraction. If the body is exposed to this toxin systemically, i.e., in the blood stream, it can cause whole body paralysis, including paralysis of the diaphragm muscle, which is skeletal muscle. Since the diaphragm is the primary muscle of respiration, this results in a cessation of breathing. In this way it can lead to death. There are other applications of this neurotoxin though. Botox is an older brand name drug of botulinum toxin type A that doctors use to relax wrinkles without surgery. It's a method for the *temporary* elimination or reduction of fine facial lines or wrinkles. When Botox is applied locally via injections into facial muscles, it causes localized paralysis of skeletal muscles which are the muscles that control facial expression. Apparently the most commonly treated areas are frown lines, forehead creases, crow's feet near the eyes, see the Fig below for the change in the knitted brow.

Figure 13.13. A customer demonstrating sever 'glabellar frowning' before, and 14 days after Botox treatment. In both the before and after photos the client is engaging in 'maximum frown'. As seen in the after picture the skeletal muscles are not able to contract, due to the Botulism toxin.

Curare: This is a poison from a plant that is commonly applied to darts used for immobilizing pray when hunting animals. Curare binds to **nicotinic receptors** at the NMJ and does not stimulate a response from the skeletal muscle. In other words, curare is an antagonist for ACh. Since curare **blocks the nicotinic receptors**, it stops the skeletal muscle from contracting, again causing whole body paralysis, including paralysis of the diaphragm muscle, resulting in the cessation of breathing.

Organophosphates: This is a poison used in pesticides (and mustard gas), it inhibits the actions of **acetylcholinesterase** (AChE), the enzyme that breaks down ACh at the NMJ. The consequence of blocking the effects of AChE is that the NMJ is that there is an excess of ACh due to the inhibition of degrading it and this overstimulates the skeletal muscle causing a continuous or spastic contraction. Spastic skeletal muscle contraction also prevents breathing since oscillatory contraction and relaxation cycles of the diaphragm are required for breathing.

Tetanus toxin: This is a potent neurotoxin made by Clostridiim tetani, but cases of this toxin causing violent spasms or paralysis of skeletal muscle is not well documents, as it seems impossible to find case studies or scientific literature about it causing 'lock-jaw' or any other condition. Experimentally it is known that it can act by blocking **GABA** and **glycine** neurons in the CNS. These are both inhibitory neurons, so by blocking glycine release in the spinal cord, this removes the inhibition of somatic motor neurons, allowing them to fire uncontrollably.

What is Rigor Mortis?

Rigor mortis is muscle contraction (rigor) after death (mortis). For skeletal muscle this can set in from about 2 to 12 hours after death, but the onset will depend on several factors, such as body activity immediately before death, temperature of surroundings, etc. The total amount of time that rigor mortis can last is also variable. It may only last for a few hours, or it could last several days, however, there is an end to it. Rigor mortis eventually dissipates and the muscles become limp and pliable once more.

The Physiology of Rigor Mortis

So we now know that rigor mortis is that postmortem (after death) stiffness that results from chemical changes in the body's skeletal muscle tissues. Now to answer why and how it occurs.

- After death no skeletal (or other) muscle contractions can occur because there is no signal to the muscle tissue to release Ca^{2+} from its internal stores in the sarcoplasmic reticulum (SR). As time goes by and the body begins to deteriorate, the SR of skeletal muscle is a tissue that disintegrates early, and this causes the **Ca^{2+} ions stored in the SR to leak out** and spill into the sarcoplasm. For skeletal muscle, where does Ca^{2+} usually go when it gets out of the SR? **Ca^{2+} ions diffuse out and bind to troponin**. Even after death, this binding will cause a conformational change as it sits on top of tropomyosin. As occurred in life, it will still move tropomyosin, which then exposes the active site and actin. All of this occurs without the need for any ATP.

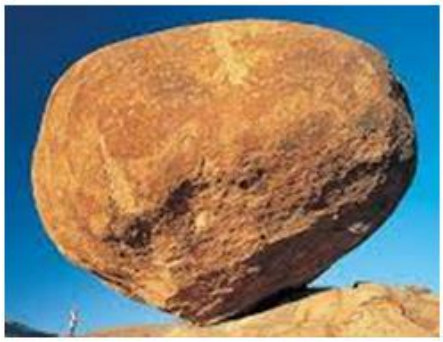
- If the myosin heads are in the high Energy state (which it is at rest), then myosin will bind to actin and pull it toward the M-line, **initiating the power stroke**! This causes an increase in muscle tension or a contraction. Is there any ATP to break this crossbridge? No, **there is no AP to break that crossbridge**. Therefore, the skeletal muscle stays contracted! This is rigor mortis.

- As more time progresses, and depending on the ambient temperature, there is further deterioration of the proteins in the body, including myosin and actin. This deterioration disengages the crossbridges, muscle tension reduces and the muscles become limp and pliable once more.

- The onset and resolution of rigor mortis helps in estimating the time since death as well as to ascertain what activity was occurring just prior to death and if the body had been moved after death.

How to Vary the Force of Skeletal Muscle Contraction

Often the stimulation of skeletal muscle is described as an '**all or none**' event, much like the action potentials of the nervous system. *However*, we all know from our daily experiences that there is not just one level of force that skeletal muscle can exert. The force one might have to apply to move that boulder (see images at right) is very different to the force required to pick up that feather. So how do we get an array of variation in force of skeletal muscle contraction?



How do we reconcile the electrical events that signal skeletal muscles to contract to the incredible variety of body movements we see all the time?

The amazing range of body actions is possible because skeletal muscle can vary the force of its contraction in multiple ways. There are three (**3**) important ways that the contraction of skeletal muscle can be varied or graded. They are:

1) Temporal Summation
2) Spatial Summation
3) Length of the Resting Sarcomere

These factors also apply to what force we *anticipate* we will have to apply to an activity. The assessment of the amount of force needed will also involve various sensory input as well.

Everyday Examples

Maybe this has happened to you. There is a beverage carton like the one seen to the right in the fridge and you think it's full because you just got it. With that anticipation you grab it, activating a large muscle contingency to get that yummy beverage, but as you are lifting it the carton springs up to your face unexpectedly! Why? Because the carton is actually almost empty (someone got there first!), and the anticipated force applied was overestimated compared to the actual load. If the beverage were in a see through glass bottle, this adjustment in muscle force activation could have been made visually and been accounted for, using less force for a lighter load. This is one aspect of varying skeletal muscle force to suit the task.

Another example is getting that jar of Kalamata olives open! To the left is seen a nice jar of delicious organic Kalamata olives and yet on your first attempt, the lid will not yield! So what are the options? Ask someone nearby with bigger hands to have a go, or get that dangerous knife out… However, if no one else is present and you show fortitude and caution by forgoing the knife, then you might try to twist the lid again, but this time with greater force! Wrench that lid with 'more intensity'. Your sensory perception has identified that more force is required and it is those three (3) elements above that can be combined in a number of ways to access a greater combined muscular force. It's amazing what you can do if you really want those olives.

The 3 different factors listed above can be integrated and combined to provide an enormous range of responses from skeletal muscle to best meet the situation at hand. Below we will look at the *details* for each of these elements and hopefully have a better appreciation for the complexities of muscle action.

Muscle Force or Tension

When skeletal muscle contracts it generates force. The force or tension generated is expressed in units of **grams** (g). For all of the graphs shown that discuss muscle force or tension, it is important to remember that we are examining muscle action and our focus is on the **tension generated** (in grams) and not on the membrane voltage of skeletal muscle.

Skeletal muscle fibers (cells) do **have action potentials**, which are sometimes called **end plate potentials**. However, we are not going to focus on the changes in voltage that occur in skeletal muscle fibers as we did for neurons, and as we will for myocardiocytes. Let's be grateful for that! The main reason is when skeletal muscle has an action potential, that is a signal for the fibers to **contract**, and we want to move right to the force that is generated by that contraction as there are many issues to examine within that.

The Skeletal Muscle Twitch

The simplest type of skeletal muscle contraction is a muscle **twitch**. Just like if your eye lid twitches for a brief moment if you maybe feel a little stressed. A twitch is a **brief single muscle contraction** that actually contains 3 distinct phases in term of muscle tension generation.

The three phases (or periods) of a muscle twitch are:

1. **The Latent phase** – this is the delay in time between the stimulus and the onset of muscle tension, shown as force in grams (g).
2. **The Contraction phase** – this is the generation of force and the graph going upwards.
3. **The Relaxation phase** – this is when the muscle is losing force and the graph is going downwards.

As seen in **Figure 13.14** below, on the graph below that shows force generated (g) over time (msec).

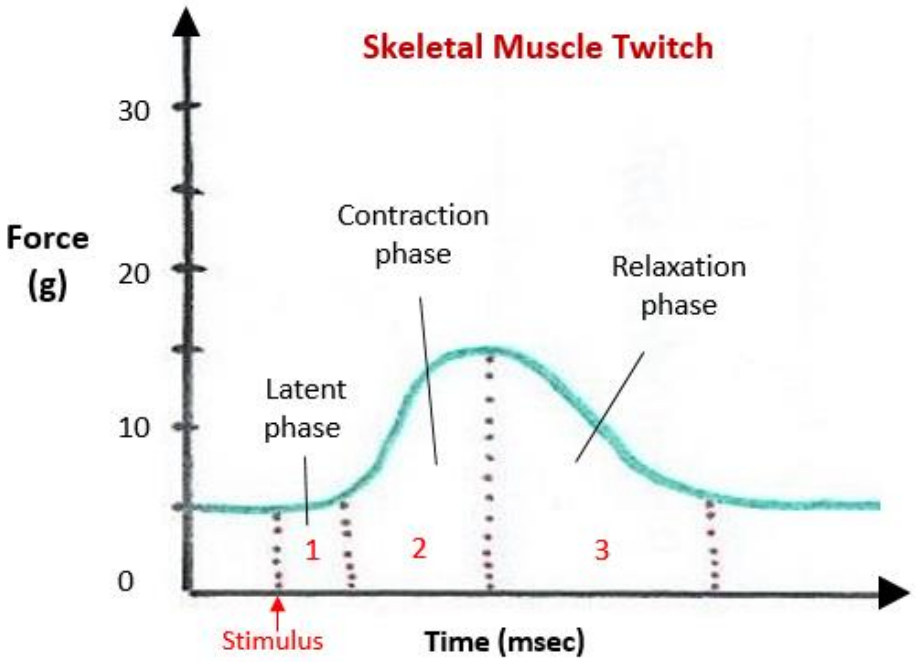


Figure 13.14 This graph shows the changes in force (g) generated during a simple muscle twitch of a single muscle fiber. The muscle twitch has three phases, which are indicated in the graph. First is the latent phase, this is the delay in time from the stimulus until the onset of contraction (shown by the increase in force). Second is the contraction phase when the muscle is generating force (and graph is going up). Third is the relaxation phase when the muscle is no longer generating tension and starts to relax, causing decrease in force.

Note that in the graph in **Fig. 13.14** above, the last phase, the relaxation phase, is the longest in duration. This comes into play as we examine temporal summation (below), because if there is another stimulation of the muscle fiber before it fully relaxes, this phase will not only shorten, but it can also disappear entirely! Not only that, but the contraction phase will have a larger height (amplitude), meaning it will have a greater amount of force.

Now for some details on the three ways that the force of skeletal muscle can be varied, or graded.

1) Temporal Summation of Skeletal Muscle

The term 'temporal' here refers to time, which in this case means the time in between the action potentials stimulating skeletal muscle, that is the frequency of stimulation.

In the simplest description, **temporal summation** can be stated as this: As the frequency of stimulation increases, there is an increase in **force** of contraction in skeletal muscle.

The key to temporal summation in skeletal muscle is that by *increasing the rate of stimulus* to one muscle fiber such that before there is sufficient time for that muscle fiber to completely relax in between stimuli, it contracts again, which increases the amount of tension generated by that muscle fiber. As shown in the graph of temporal summation in **Figure 13.15**, a muscle fiber contracts more powerfully when several stimuli arrive in **rapid succession** compared to a single stimulus, which results in a muscle twitch.

Note that during the initial period of rapid stimuli, the muscle tension increases but has a slight relaxation periods it continues to increase tension, this is called **incomplete** or **unfused tetanus**. Tetanus just means 'sustained contractions' (and is not about a toxin). In this phase there is not complete contraction, so that is why it is called incomplete or unfused. To Germans scientists, the wavy incrementally increasing tension line in the graph looked like a staircase, and the term 'treppe' is sometimes used as the name for this phase, which means staircase in German.

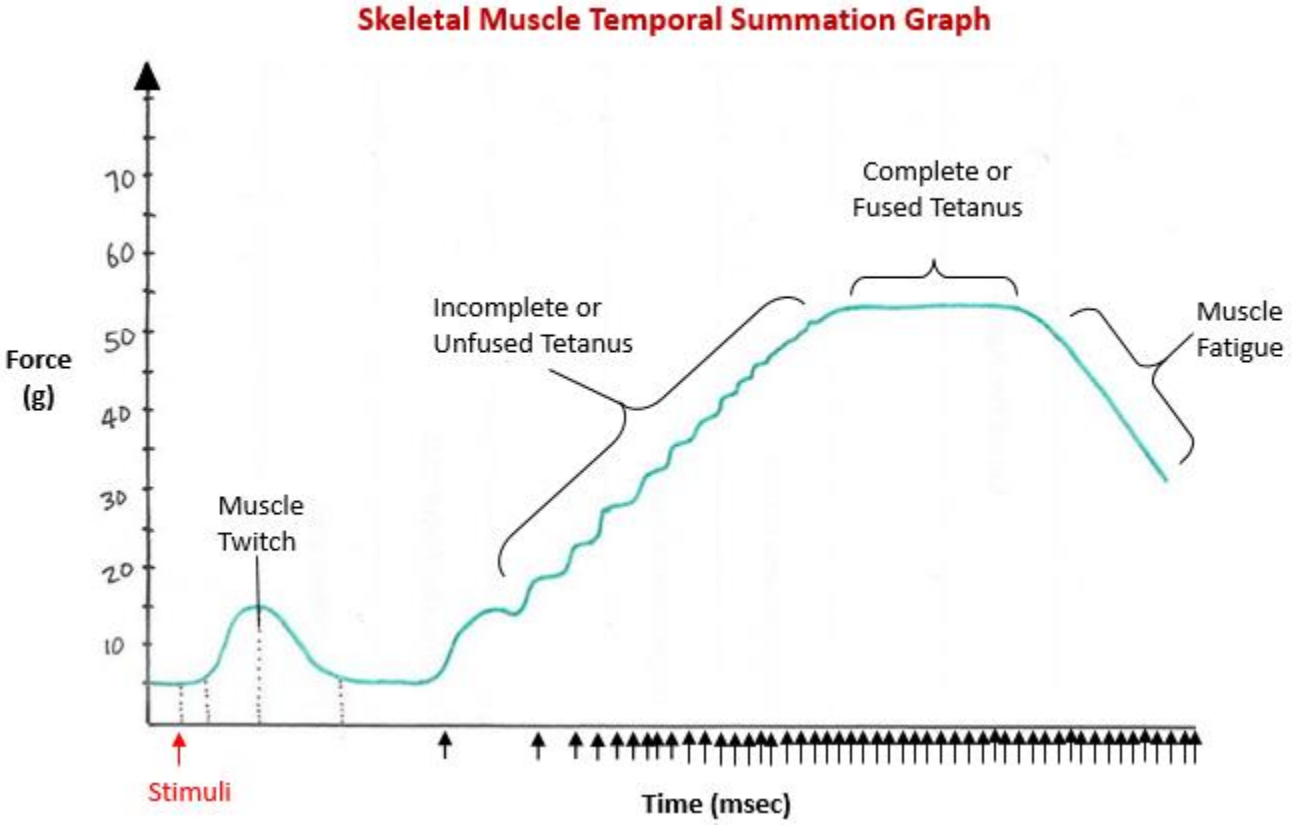


Figure 13.15 This graph shows the changes in force (g) generated during a simple muscle twitch of a single muscle fiber. It then shows how force increases as the frequency of stimulation increased, until maximum tension is reached at complete tetanus. Ultimately, skeletal muscle will fatigue and be unable to sustain tension due to overuse, regardless of stimulation.

If the frequency of stimulation is so high that there is no muscle relaxation in between successive stimuli, this is called **complete** or **fused tetanus**. Here the muscle is now in a steady state of fused (complete) muscle contraction. It is at this time in this phase that **maximum tension is generated**.

What is Occurring at the Muscle Fiber level?

The likely explanation for why there are these different phases during temporal summation is that it involves the elastic properties of muscles. The tension developed in the muscle at the onset of contraction is translated through many structures (e.g., the thick and thin filaments, Z discs, elastin, etc.). Only when all of these elastic structures are taut can an increase in tension occur. When a second stimulus occurs very close to the previous stimulus, the elastic structures are not yet slack again so less delay occurs before the onset of tension.

If the ***frequency of stimulation*** continues to increase, the muscle does not have time to relax completely before the next contraction begins. Thus, each successive contraction after the first one is stronger than a single muscle twitch and treppe or incomplete tetanus occurs. At the point when there is no 'give' in the muscles elasticity, complete tetanus can be maintained if the stimulus is frequent enough.

Skeletal Muscle Fatigue

In the physiological sense, skeletal muscle fatigue is the inability of muscle to generate adequate force due to prolonged or overuse of the muscle. As seen on the graph in **Figure 13.15**, despite continued stimulation of the muscle, after a time the muscle fiber will not be able to continue to maintain complete tetanus, and muscle fatigue is inevitable, though training can greatly extend complete tetanus. The specific factors that contribute to skeletal muscle fatigue are discussed below.

2) Spatial Summation of Skeletal Muscle

Recall that we have seen the terms temporal and spatial summation before, but in reference to neurons and graded potentials. Similar to neurons, spatial summation in skeletal muscle contraction is about a ***group of muscle fibers*** being stimulated at the same time by different neurons in 'space'.

In order to really appreciate spatial summation we need to understand what a motor unit is, since **spatial summation** involves **motor unit recruitment**. In fact spatial summation is called motor unit recruitment.

A skeletal motor unit consists of **one somatic motor neuron** and **all of the muscle fibers it innervates**.

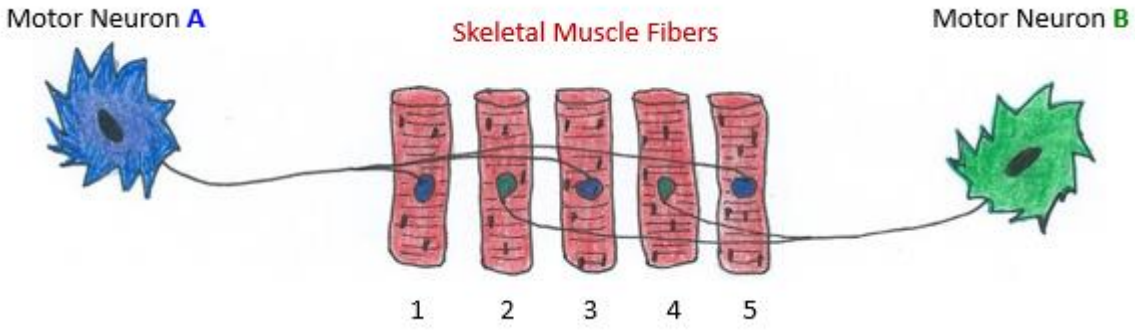


Figure 13.16 In the drawing above there are two skeletal motor units, A and B. Motor Unit A is motor neuron A and muscle fibers 1, 3 and 5. Motor unit B is motor neuron B and muscle fibers 2 and 4. Motor units can range from being very small to very large. In any one motor unit the muscles fibers must all be the same type, that is slow, intermediate or fast twitch skeletal muscle fibers.

If we consider the two motor units shown in **Figure 13.16**, and we were to graph the tension (force) generated by these muscles fiber in response to various stimulations by motor neurons A and B, we would see what spatial summation looks like in terms of varying the force of contraction.

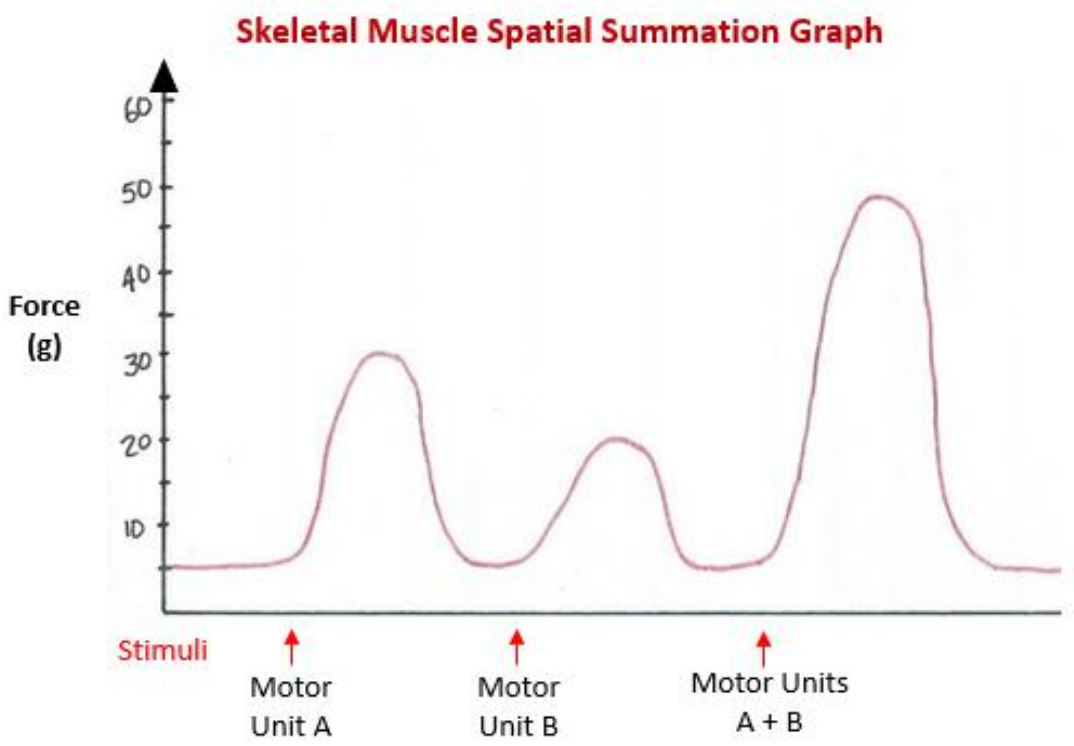


Figure 13.17 The graph shows the force (g) generated in skeletal muscle according to the two motor units A and B. From the graph, we see that stimulation of motor unit A causes a force of about 30 g, whereas stimulation of motor unit B causes a force of about 20 g. When motor units A and B are stimulated simultaneously their forces are summed, or added together. This can be seen by the actions of A and B together reaching 50 g of tension.

Spatial summation in skeletal muscle is achieved by an increase in the strength of the stimulus (e.g., the voltage in laboratory apparatus). This causes a greater number of motor neurons to fire and results in an increase in the number of motor units involved. Because they are acting at the same time, all together they generate **a more forceful muscle contraction**. This process is also called motor unit recruitment.

For the illustration in **Fig. 13.17** above, if an average stimulus causes motor unit A to fire, it generates about 30 g of force. If a weaker stimulus causes motor unit B to fire, it generates about 20 g of force. If a very large stimulus activates both motor units A and B, then the force they generate is summated and there is 50 g of force from both acting at the same time. The summation part of the name is indicating that the various forces involved can be *added* or summed up together, yielding a greater force.

Skeletal Motor Units have Different Sizes

Are there motor units of different sizes? Yes, absolutely. There are very small motor units (1 motor neuron to 10 muscle fibers) to very large motor units (1 motor neuron to 1,000's of muscle fibers) and everything in between. In **Figure 13.17** above, which motor unit is larger A or B? ____.

Typically, smaller motor units are more sensitive (or excitable) than larger motor units. What this indicates is that the smaller motor units respond to a weak stimulus, while the larger motor units require a stronger stimulus to be activated and contract.

Typically in the body motor units operate asynchronously (meaning unsynchronized or not at the same time) so that when one motor unit is contracting, another is at rest and not working, but the overall muscle

contraction is very smooth. If one motor unit begin to tire, another one can take over the task, as a way to sort of relive the muscle groups and allow them to rest intermittently. This is a way to avoid muscle fatigue.

Examples of different motor unit sizes:

- Laryngeal muscle: 2 muscle cells/motor unit.
- Rectus muscle (eye): about 10 muscle cells/motor unit
- Tensor tympani (ear): 10-125 muscle cells/motor unit.
- Gastrocnemius: about 2,000 muscle cells/motor unit.
- Quadriceps: about 3,000 muscle cells/motor unit.

3) Length of the Resting Sarcomere

We know that the sarcomere is. Did you know that the length of a sarcomere can be measured? It is a very small structure, microns (µm) in size, but the changing lengths have been calculated at rest and during contractions.

As it turns out, the length of a sarcomere when it is at rest will have an impact on the amount of force that sarcomere can generate when stimulated. The relationship between the length of the sarcomere and the force it can generate is an interesting one, and when we go back to our knowledge of the structure of sarcomeres from earlier, the graph below in **Fig. 13.18** makes a lot of sense.

A slightly stretched muscle will contract with a stronger force than an un-stretched one. Why? It's all about the overlap of the myofilaments actin and myosin! There is an optimal length of the skeletal muscle sarcomere at rest which generates the most force during contraction.

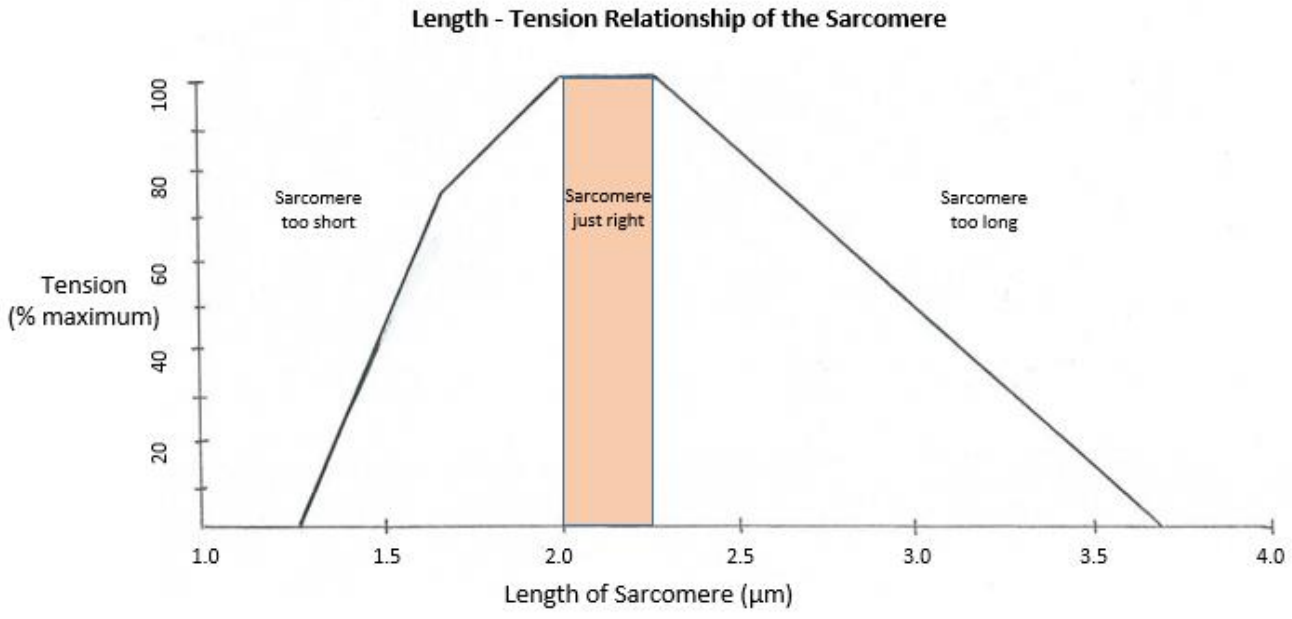


Figure 13.18 This graph shows the amount of tension generated (as a percentage of the maximum) when a sarcomere is stimulated at various 'resting' lengths in microns (µm). The shaded area is the resting sarcomere length that generates the greatest amount of tension (force) and this is called the 'optimal length'. When the sarcomere is at the length when contraction is stimulated, it generates the greatest amount of force. When the sarcomere is too short (left side of optimal length) or too long (right side of optimal length), the sarcomere cannot generate as much tension.

Too Short

If the sarcomere is too short, it means there's too much overlap of the myofilaments actin and myosin, almost like it's contracted already, so there is not much more room to get it shorter, and as a consequence the contractile fibers cannot it cannot generate substantial force. Looking at the length-tension relationship of the sarcomere **Fig. 13.18**, the shorter the sarcomeres is, the less tension it can generate. In fact, if the sarcomere is less that about 1.3 µm in length, it cannot generate any tension at all.

Too Long

If the sarcomere is too long, there is not enough overlap of actin and myosin and it also cannot generate maximum force. In this case, it is like the sarcomere is stretched, yielding fewer opportunities for the contractile filaments actin and myosin to interact enough to pull the Z-discs toward the M-line. Similarly, **Figure 13.18** show that the longer the sarcomeres is, the less tension it can generate. Ultimately, if the sarcomere is any longer than about 3.7 µm in length, it cannot generate any tension at all.

Just Right

At the optimal length, which is not too long and not too short, the resting sarcomere will generate maximum force compared to the other lengths of the sarcomere. This occurs in the length range of about 2.1 to 2.2 µm. That is a fairly small range, and the tension quickly drops off on either side of that range.

Isotonic and Isometric Skeletal Muscle Contractions

While skeletal muscle contracts and generates **tension**, it may lengthen, shorten, or remain the same. That may seem surprising, since the term 'contraction' appears synonymous with shortening or at least implies it. However, to be precise, when referring to the skeletal muscular system, contraction means muscle fibers generating **tension** stimulated by somatic motor neurons.

It turns out that several types of muscle contractions can occur, and they are defined by the changes in the length of the muscle during contraction. The two main categories covered here, they are: **1) Isotonic** (which has concentric and eccentric) and **2) Isometric**.

1. Isotonic Contractions

The prefix iso means same, and tonic means tension. Therefore, these are contractions that maintain constant tension in the muscle as the muscle changes length. This can occur only when a muscle's maximal force of contraction exceeds the total load on the muscle. Isotonic muscle contractions can be either concentric (muscle shortens) or eccentric (muscle lengthens), see **Fig 13.19**.

a) Concentric Contractions

This involves muscle shortening while generating force. Occurs throughout body and throughout the length of the muscle, generating force at the musculo-tendinous junction; such contractions alter the angle of the joints to which the muscles are attached, causing the muscle to shorten and the angle of the joint to change. For instance, a concentric contraction would be a biceps curl (at right). A concentric contraction of the triceps would change the angle of the joint in the opposite direction, straightening the arm downward.

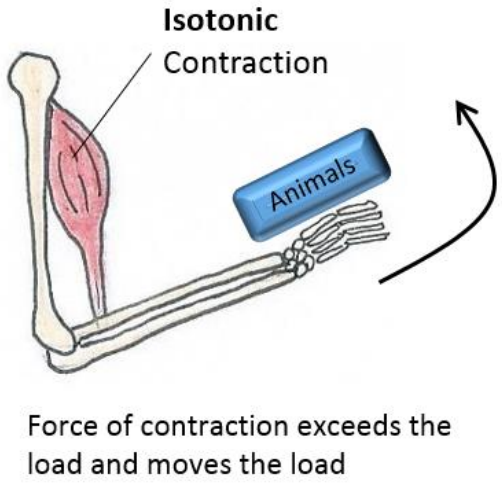


Figure 13.19 Shows isotonic contraction, which involves movement as the tone (strength) remains the same.

b) Eccentric Contractions

This involves **elongation** of a muscle while generating force. Such contractions *decelerate* the muscle joints (acting as "brakes" to concentric contractions) and can alter the position of the load force. These contractions can be both voluntary and involuntary. During an eccentric contraction, the muscle elongates while under tension due to an opposing force which is greater than the force generated by the muscle.

Rather than working to pull a joint in the direction of the muscle contraction, the muscle acts to decelerate the joint at the end of a movement or otherwise control the repositioning of a load. Imagine it's similar to lowering a heavy drawbridge, force is required to control this elongating movement. It can occur involuntarily (when attempting to move a weight too heavy for the muscle to lift) or voluntarily (when the muscle is "smoothing out" a movement). Over the short-term, strength training involving both eccentric and concentric contractions appear to increase muscular strength more than training with concentric contractions alone.

2. Isometric Contractions

The prefix iso means same, and metric means length, thus these contractions occur when muscle generates force without changing length. This is when joints are not moved by a muscle action, and even though force is generated and tension is maintained, muscles do not change length, because the force load is being met, that is, the muscle contraction is sufficient for to meet the force of the load. See **Fig 13.20**.

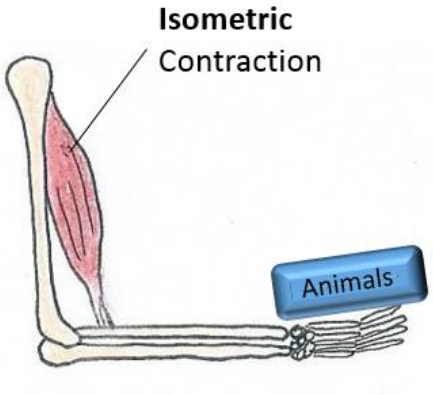


Figure 13.20 Shows isometric contraction, which involves an increase in force but no movement as the length remains the same.

This is common in muscle actions of hands and forearm. Imagine you are holding a book about how cute and adorable animals are, holding it out in front of you with your forearms without lifting it, just meeting the load (weight) of the book. When the muscle action meets the weight or force of any load, this involves muscle tension without movement of the arm or muscles. An interesting note is that isotonic contractions occur in the middle of a contraction while isometric contractions occur at the beginning and end.

What about coffee? :)

Sensory Receptors in Skeletal Muscle

Somatosensory perception has been covered already and we have seen that there are sensory receptors within skeletal muscle that provide information about the **stretch** and level of **tension** exerted by body muscles. There are also **proprioceptors** found within the tendon that attached skeletal muscle to bone, and within the collagenous fibers of the joint capsules that are moved by skeletal muscle action. It is important to know the activity of skeletal muscle in order to know where one body part is in relation to others (and the head), and in order to protect muscle tissue form injury.

Muscle Spindles

Almost all muscles in the body encompass **muscle spindles**, which are sensory receptors composed of several differentiated muscle fibers called **intrafusal fibers**, enclosed in a spindle-shaped connective tissue sac. The terminal portions (ends) of the intrafusal fibers contract and the central region is non-contractile (**Figure 13.21**). The muscle spindles sense changes in length, and the rate (speed) of muscle lengthening.

These muscle spindles reside within muscle at specific locations and send information to the CNS regarding **changes** in the **tension** and **length** of an individual muscle, as well as the rate of movement and stretch. With this information, the CNS computes the position and movement of our extremities in space, which is a required for motor control, maintaining posture and ensuring stable gait (locomotion or walking). The responses of muscle spindles to changes in length also play an important role in regulating the contraction of muscles, by **activating motor neurons** via the **stretch reflex** to resist muscle stretch.

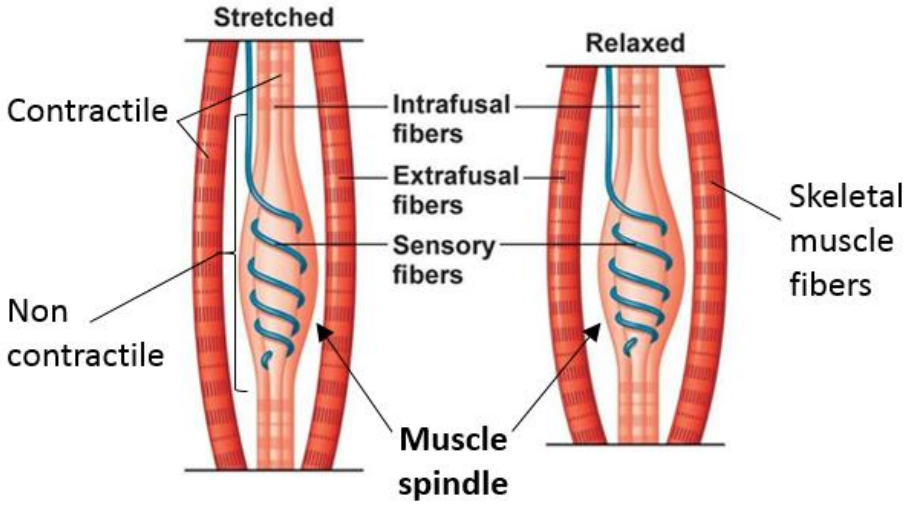


Figure 13.21 Shows the location and structure of the muscle spindle within skeletal muscle. The sensory nerve ending coils around the swollen spindle-shaped connective tissue sac, with intrafusal fibers at both ends, which can contract, but the central swollen area cannot contract. The extrafusal fibers are skeletal muscle fibers that are not a part of the muscle spindle unit.

The Motor Neurons

The **alpha (α) motor neurons** innervate the **extrafusal** fibers, and these are simply the skeletal muscle fibers that are not involved in the muscle spindle sensations. These skeletal fibers are of course highly contractile and can generate great force providing the muscle with its power. It is the **gamma (γ) motor neurons** (GMN), also called fusi-motor neurons, that innervate the intrafusal fibers, which contract only slightly, but this contraction keeps the spindle taut at all times and maintains its sensitivity to changes in the length of the muscle. Both the alpha and gamma motor neurons have their cell bodies in the **anterior grey horn** of the spinal cord. They receive input from the **reticular formation** of the **pons** in the **brainstem**.

Example of a Monosynaptic Spinal Reflex

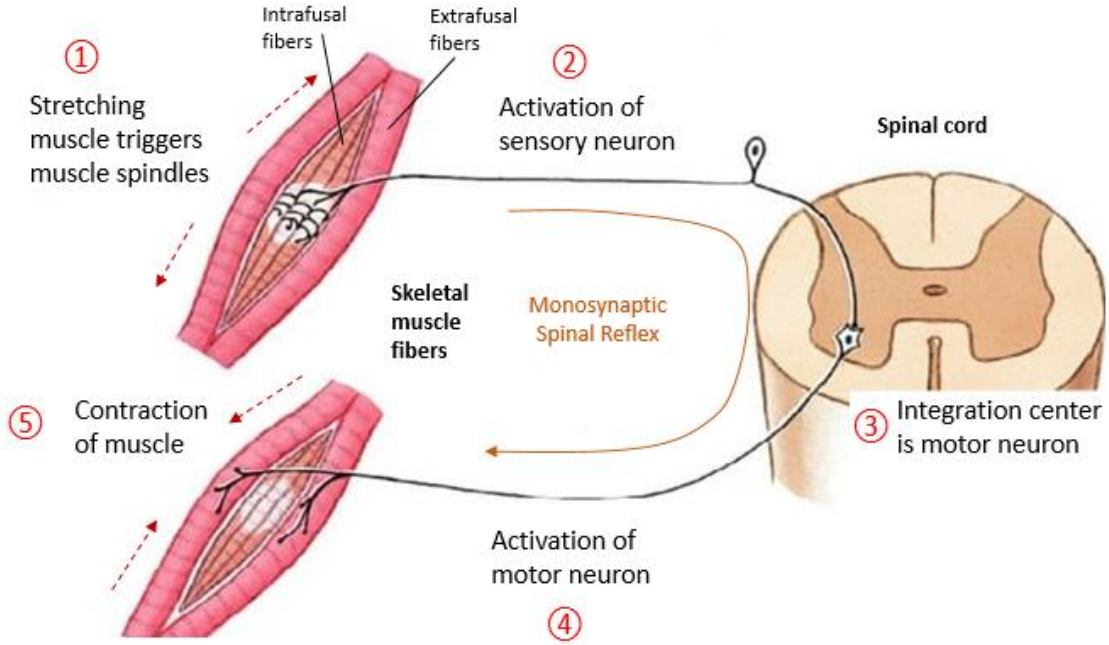
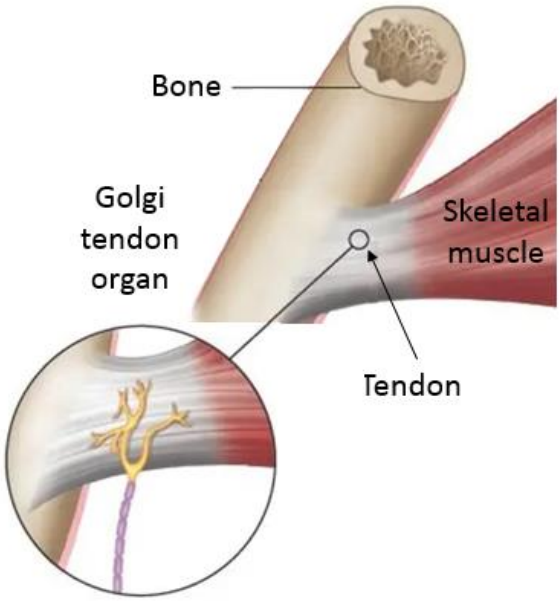


Figure 13.22 This shows the sequence of events (① through ⑤) during a simple stretch reflex instigated by a muscle spindle. The stretching of the muscle sets of the monosynaptic (one synapse) reflex arc which has its integration in the spinal cord and sends out a motor neuron to contract the muscle automatically. The 'knee jerk' or patellar reflex is an example of this arc.

Golgi Tendon Organs

Also important in body movement are **Golgi tendon organs** (GTOs). These are **proprioceptors** found in tendon near the junction of tendon and muscle fibers (**myotendinous junction**), and also found within **joint capsules**. These are sensory endings enclosed in a spindle-like connective tissue capsule that respond to the **stretch of a tendon**, or the **contraction of a muscle**.



When an excessive load or stretch is detected by the GTO, it inhibits the muscle from contracting any further and relaxes the muscle, thereby safeguarding both the tendons and muscle tissue from injury. The GTO acts by a **monosynaptic reflex** (one synapse reflex arc), which is very fast. The GTO reflex is a monosynaptic spinal reflex but is also called a **tendon reflex**, an **inverse stretch reflex**, and an **autogenic inhibition**. Since it is **inhibitory**, the result of excess muscle tension stimulates the GTO of the muscle to ***stop contracting***, and hence it is auto-regulated and self-induced. Maybe this is a familiar experience when lifting something that is or becomes too heavy, often that triggers an automatic giving out of the muscle from this reflex. In a treatment setting, the application of firm pressure to a muscle for 30 seconds, will cause it to relax and reduces muscle tone and spasm.

Figure 13.23 The point where the tendon of skeletal muscle attaches to bone is where the Golgi tendon organs are located, as well as in the collagen fibers of joint capsules. These act as sensors to protect against over contraction.

The Metabolism of Skeletal Muscle Tissue: Energy Transfer

The direct energy source for muscle work is ATP. The immediate source of energy required for muscle contraction is **ATP** and contraction can continue for a long time as long as there is adequate ATP. The supply of ATP depends on **a)** O_2 availability and **b)** organic energy sources, such as glucose, glycogen, or lipids. During the course of exercise or any physical activity, different mechanisms of ATP synthesis are used depending on the intensity and duration of activity.

There are three main sources of ATP generation for skeletal muscle contraction and they often time occur in this order:

① Immediate → ② Short Term → ③ Long Term

Creatine-Phosphate | Glycolysis | Oxidative Phosphorylation

As the three ways that skeletal muscle generates the ATP it needs to continue contracting, it can be thought of as the body shifting gears and elegantly moving from one mode to the next in order to respond to the needs of the body.

① Immediate - The Creatine-Phosphate or *Phosphogen* System

There is a molecule in muscle tissue called **creatine** and when ATP is available, the high energy phosphate from ATP is transferred over to creatine and converted into **creatine phosphate** (C-P). The ATP is then converted into ADP (see **Fig. 13.22** below). By doing this the C-P is like a type of energy storage molecule in muscle cells. Muscle is limited in how much C-P it can store, but as you will see it is readily available and can get muscle action started.

When muscle tissue is at rest it takes that opportunity to make more C-P in the cell, like preparing for future activity in 'down time'. Creatine phosphate is analogous to having some supplies in the pantry (a few cans of beans) that are there for whenever you might need them, it creates the availability of a very quick source of ATP.

As a muscle begins to contract it requires energy in the form of ATP. If creatine phosphate is present, there is a quick transfer of its high energy phosphate back to the ADP in the cell to create **ATP**. This reaction requires the enzyme **creatine kinase** (CK), which takes that phosphate group from C-P and puts it onto ADP, making a quick source of ATP available for the cell. See figure X for how the balance of creatine and creatine phosphate in the muscle cell at rest and during exercise. The phosphorylation and dephosphorization of creatine is a reversible reaction, and it turns out that this reaction is catalyzed by creatine kinases in both directions.

This 'immediate' ATP source is used when initiating in an intense activity. For example, if running 100 m back to your car because you left your homework on the back seat and need to turn in in 3 minutes, the creatine phosphate or 'phosphogen' system will be the primary energy source for the first 6 to 15 seconds. When the activity is intense, this supply will not last very long. If you start a brisk walk, it will be used for the approximately the first 1 minute of that muscle activity.

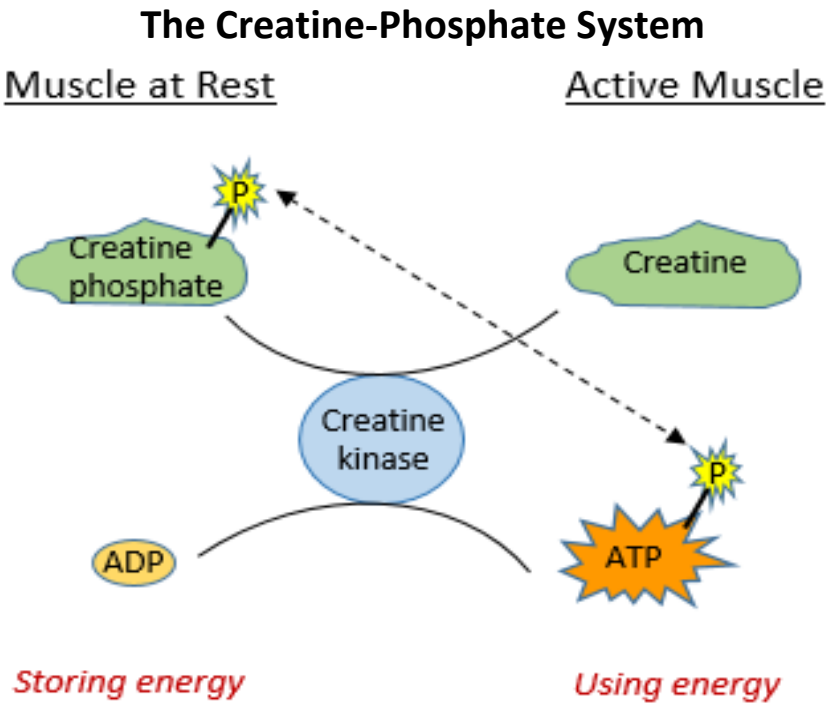


Figure 13.24 When skeletal muscle is at rest, it uses ATP to make creatine phosphate, which is catalyzed by creatine kinase. If the muscle becomes active, the same enzyme, creatine kinase, can transfer the phosphate from creatine phosphate to ADP, making ATP and creatine. This creates a source of ATP for muscle to use incredibly quickly. The source of creatine phosphate is very limited. When the muscle is a rest again it replenishes the store of creatine phosphate.

This source of ATP supplies the active muscle ***anaerobically*** (without O_2), as the cardio-respiratory system cannot deliver O_2 that fast or enough to meet the huge demands of the muscle tissue across the body. Thus, the role of creatine phosphate is to very quickly supply ATP to muscle tissue, as the body makes accommodations for other sources of ATP, should you wish to continue with muscle activity! Note in **Fig. 13.24** above that as soon as the muscle is at rest, it will re-build its limited supply of phosphorylated creatine utilizing the available ATP.

Creatine becomes Creatinine

When the **creatine** produced by muscles is ultimately broken down, it makes the nitrogenous waste product **creatinine**. It is routinely eliminated in the urine and replenished. Creatinine is an important molecule for clinical measurements because creatinine levels in blood are almost entirely filtered and cleared by the kidneys and excreted in the urine. Thus, **creatinine clearance tests** can be used as an index of kidney function. Higher levels of creatinine in blood serum may indicate that your kidneys aren't functioning optimally, though several other factors can influence blood creatinine levels, such as drugs or medications, low blood volume, dehydration, diet, etc.

Several different tissue types in the body use creatine, and for that reason the enzyme **creatine kinase** is found in skeletal muscle, heart muscle and even the brain. Increased levels of creatine kinase are released into the blood when there is muscle damage. The exact tissue that is damaged can be determined by the different **isotypes** of creatine kinase. For example, skeletal muscle has an isotype that is different to the heart tissue isotype, therefore, if creatine kinase levels are found to be high in blood, it may be skeletal muscle damage, or if it's the cardiac muscle isotype it may indicate myocardial infarction, or a heart attack.

② Short Term - Glycolysis

As the **phosphogen** system is exhausted, meaning as Creatine-P in the cell runs out, if contractions are to continue, then the muscle tissue must 'buy time' until the cardio-respiratory system can supply enough oxygen (O_2) to meet ATP generation aerobically (with O_2). This means meeting the 'short term' needs and it must be done an aerobically (without O_2).

This is what happens: The skeletal muscle cell mobilizes its glycogen stores (recall glycogen is the storage molecule of glucose in animals) so that it can get glucose molecules and then begin the process of breaking the glucose down. The terms **Glycolysis** literally means cutting glucose. As you can see in **Figure 13.25** below, the process of glycolysis is done anaerobically, no O_2 is required. There are a number of steps and enzymes involved, but the essence of glycolysis is that the 6-carbon molecule that is glucose is cut into two 3-carbon molecules called pyruvate. Snapping the glucose molecule in half liberates some of the potential energy stored in the covalent chemical bonds. In order to initiate glycolysis, the investment of 2 ATP are required, however, it generates 4 ATP, so the net gain in ATP during the glycolysis of 1 glucose molecule is 2 ATP (see diagram below).

As glycolysis is continued it generates lactic acid. When lactic acid builds up, it lowers the surrounding pH and the proteins in muscle can begin to denature the contractile proteins, resulting in muscle fatigue. That is why this system can also be called the **Glycogen-Lactic Acid System**. It can produce ATP for about 30 to 40 seconds of maximal muscular activity, for example, a run around the bases from an infield homerun (it's longer than you think). Glycolysis operates fairly fast, but is inefficient. The 1 glucose only generates a net of **2** ATP. As we will see in a moment, there is still a lot more energy to be gleaned from the 2 pyruvate molecules. This presents another drawback of having to use glycolysis for too long.

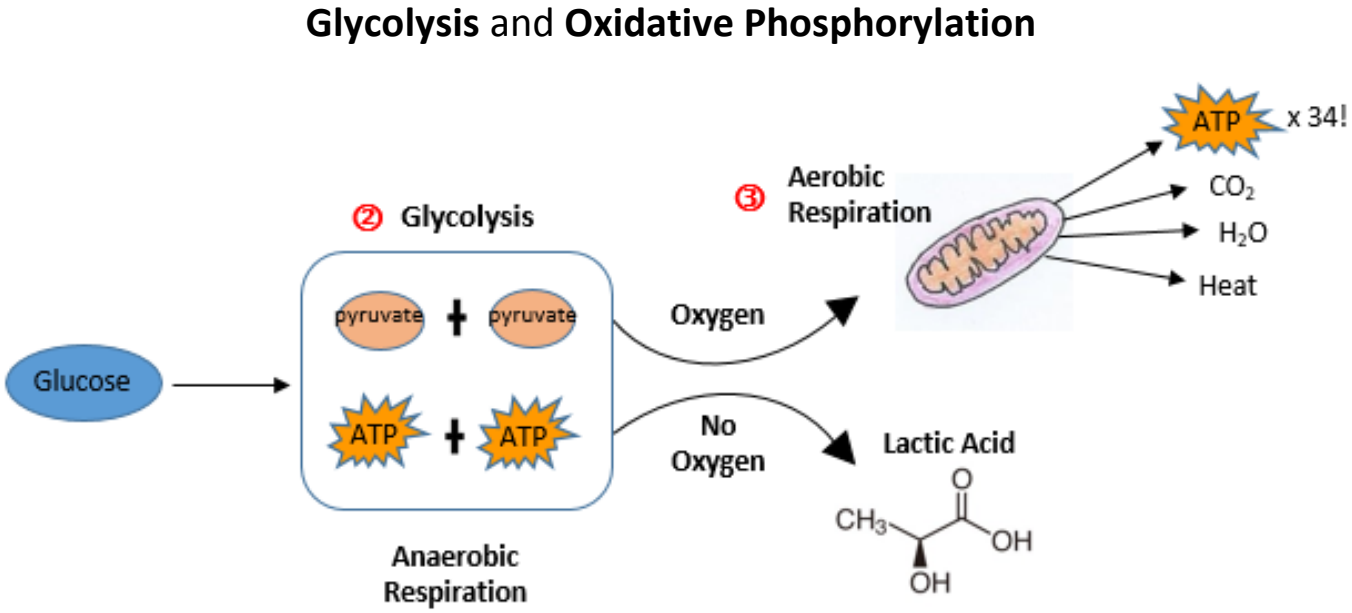


Figure 13.25 This diagram shows the pathways for glucose being used to make ATP in skeletal muscle. In anaerobic conditions (without oxygen) glycolysis can generate 2 ATP per glucose molecule. For any further breaking down of the glucose molecule to occur, oxygen (O_2) must be present. When enough O_2 is available, anaerobic respiration (with oxygen) can occur in the mitochondria, yielding and additional 34 ATP for that same glucose molecule. If one glucose molecule goes through glycolysis and aerobic respiration, then the total ATP yield is 36 (2 + 34).

③ Long Term - Oxidative Phosphorylation

After about 40 seconds of maximal activity, the cardio-respiratory system finally catches up to supply enough oxygen (O_2) to meet ATP generation ***aerobically*** (see **Figure 13.23** above). This last method (oxidative phosphorylation) requires oxygen and takes longer to generate ATP but it is much more efficient (1 glucose generates a net of **36** ATP). If exercising for more than 10 minutes, over 90% of ATP is produced aerobically.

When vigorously exercising, the consumption rate of O_2 may increase 3 to 4 times the levels at rest in order to keep ATP production up with demand. Individuals breathe heavily at first, but then the pattern of breathing stabilizes at a higher level. Fatigue (for various reasons) is a factor in how long an individual can continue the muscular activity. So what is muscle fatigue?

What is Skeletal Muscle Fatigue?

Muscle fatigue is a progressive weakness and loss of muscle contraction from prolonged use of muscle. The essence is that any muscle will tend lose the ability to maintain adequate force and become fatigued if it is overused. There are a number of causes that are related to muscle fatigue, and the most significant probable causes are listed below.

<u>Reasons for Muscle Fatigue</u>

1. **Lack of organic fuel** sources **glucose** or **glycogen**. When they are consumed, then there will be a decrease in **ATP** available to generate muscle contraction. Glucose is considered the main 'fuel' source for muscle contraction, but it must be 'burned' by either glycolysis or aerobic respiration to make ATP, as it is ATP that is directly needed to power muscle contraction. Therefore, anytime there is not enough ATP, fatigue will ensue.

2. A shortage of ATP will also cause a **slowing of the Na^+/K^+ pumps**. When they are less active, then the RMP will be altered and **decrease the excitability** of the cell. Thus even if the signals to contract continue, the cells are not as responsive due to the decrease in excitability.

3. The incessant efflux of K^+ which is rushing out of the cell during each action potential also adds to the reduction of the excitability of cell. It is equivalent to a decreased intracellular K^+ concentration ($[K^+]_i$).

4. The increase in **lactic acid** that tends to build up in muscle tissue causes a **decrease in pH**, as the sarcoplasm becomes **more acidic**. This decrease in pH can cause the protein to denature and alter shape and function. This impairs the contractile proteins actin and myosin, and weakens the mechanisms of contraction and generating force.

5. The somatic motor nerve fibers become exhausted, and **depletion of ACh** at the synapse occurs. Without enough or any ACh, skeletal muscle cannot be stimulated to contract. This is called "**junctional fatigue**".

6. The origin of these signals is the CNS and the experience of "**mental fatigue**" can occur. Even if none of the above conditions existed, fatigue is still possible. If a person thinks 'I cannot go on', this thought process can be enough to feel that it is not possible to continue with muscular action!

Other Types of Contractions

Cramps: Action potentials fire at abnormally high rate (higher than when at maximum voluntary contraction) causing sustained tetanus contraction. Thought to be to electrolyte imbalance.

Muscle knot: an area of contracted muscle fibers not able to release or relax. When a muscle is overworked or injured, it can tighten up and contract more in one area than another. Muscles around the painful area will also bunch up, tightening into a knot to protect the area from further injury -a response known as "guarding". Muscle knots are caused by several things including pain in muscle tissue, overuse, strains and even trauma.

Convulsions: Violent, involuntary contractions of groups of muscles.

Fibrillation: Rapid, irregular, uncoordinated muscle contractions (i.e. ventricular fibrillation in the heart).

Muscle Growth and Differentiation

There is no mitosis of skeletal muscle tissue in adults, in other words, muscle cells do not multiply in number in order to get larger. Muscle enlargement results from the **hypertrophy** of muscle cells, where hypertrophy of a cell means it gets larger in size, typically from being used more. For a muscle cell to become larger it requires more and more protein, as most of the sarcomere is made of proteins (actin, myosin, troponin, tropomyosin, etc.).

When the cell gets smaller in size it is called **atrophy**, typically from a reduction in use. The word trophy actually means 'to nourish', but can be taken to mean to growth; thus the prefix Hyper- means above normal, higher, and the prefix A- means without.

During **Hypertrophy** there is an increase 1 through 7. During **Atrophy** there is a decrease in 1 through 7.

1. Myofibrils (actin & myosin) in muscle cell.
2. Mitochondria.
3. Enzymes.
4. Stored organic materials (i.e., fat & glycogen).
5. Creatine-phosphate.
6. ATP
7. Efficiency of the muscle.

Skeletal Muscle Repair

Repair of injured skeletal muscle fibers usually involves dormant stem cells called **satellite cells**, which produce **myoblasts**, which in turn fuse to produce new muscle fibers spontaneously in response to minor injuries, such as micro tears and muscle strains. However, if a muscle injury is severe, it may cause tissue scaring with the formation of fibrotic tissue or incomplete healing that could result in some impairment of muscle function.

Skeletal Muscle Contractions and Blood Glucose

The contraction of skeletal muscle during exercise significantly **increases muscle uptake of glucose from the blood**. This means it decreases blood glucose levels. In a study by Richter (2021) it was shown that when skeletal muscle is used with substantial intensity and duration during exercise, it increases muscle glucose uptake from the blood **up to 100 times compared with rest**. The magnitude of the increase will depend on the exercise intensity and duration, however, just an increase of 20 times would be impressive.

As covered in the endocrine section, the actions of **insulin** increase the uptake and utilization of glucose by muscle and adipose-tissue cells by activating the translocation of GLUT 4 transporters (for glucose) from their intercellular vesicles into the plasma membrane (see **Figure 13.26** below).

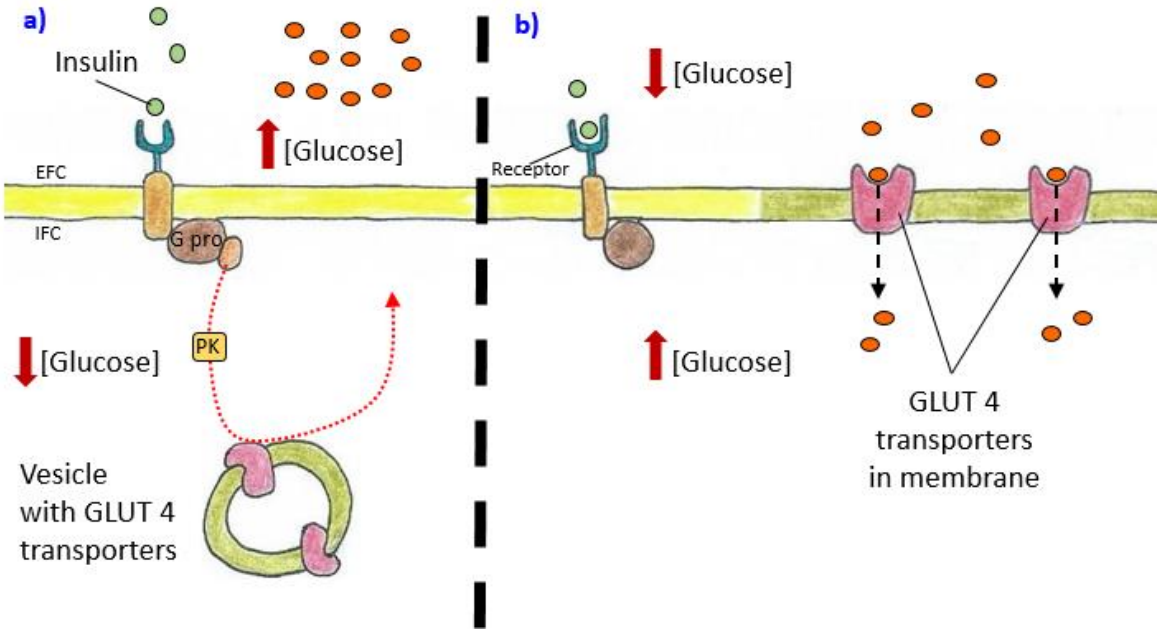


Figure 13.26 When glucose concertation is high **a)** in the extraocular fluid (ECF), insulin from the pancreas binds to surface receptors triggering a second messenger system that activates the translocation of GLUT 4 transporters from vesicles into the plasma membrane. The increase in GLUT 4 transporters **b)** causes an increase in transport of glucose into the cell. Richter (2021) suggests that exercising skeletal muscle may have a diminished need for insulin.

Exercise Decreases Blood Glucose without additional Insulin

The unique aspect of exercise-induced muscle glucose uptake, compared to the insulin-induced glucose transport, is the high **metabolic rate** in muscle during exercise which uses large amounts of glucose. Anytime skeletal muscle is active it draws more glucose from the blood that is **not dependent on insulin**, and this protects the cells from becoming desensitized to insulin, which is the hallmark of pre-diabetes which can lead to diabetes mellitus type 2 (see topic of ***diabetes mellitus*** in chapter 12).

As we know, skeletal muscle generates **heat** during contraction due to the kinetics involved and due to the **hydrolysis of ATP**, thus increasing muscle temperature. Skeletal muscle temperature at rest depends on the external temperature but is typically 3.6 to 5.4°F below core temperature of 96.8 to 99.3°F. During intense exercise however, muscle temperature may increase to **104** to **106 °F**. This is an increase of up to 10 to 12.5°F, and it's likely these increases in temperature increase transporter activity, hence having the effect of lowering blood glucose more dramatically. Also, during simple muscle contraction and relaxation and even stretching, the mechanical deformation of the muscle tissue seems to increase GLUT 4 transporter activity and increases glucose uptake.

Slow, Intermediate and Fast Twitch Skeletal Muscle Fibers

In terms of the skeletal muscles all around your body, it turns out there are actually three different types of skeletal muscle fibers. The three types of skeletal muscle fibers are: **Slow Twitch**; **Intermediate Twitch**; and **Fast Twitch**.

Recall that a muscle twitch is a brief, simple, single contraction. So part of the nomenclature for these muscle fibers is about the characteristics of the specific twitch that these fibers produce. In terms of the anatomy and physiology of these skeletal muscles fibers, there are quite a few significant differences between these types. As the name implies the 'intermediate' twitch muscle fibers have characteristics that are a combination somewhere in between the slow and fast muscle fibers. When we cover the comprehensive details of slow and fast twitch muscle fibers, even though the specific details of the intermediate fibers are not included in the comparative tables, they can be extrapolated as basically a mixture of slow and fast fibers.

Most of our skeletal muscles are a mixture of both slow and fast twitch muscle fibers, and that is mostly what we focus on.

Slow Twitch Fibers

The 'slow' part of the name is meaningful and will help to make connections about function. Slow muscle fiber has a slow onset of contraction. As you can see in **Table 13.2** below, it takes about 3 times longer than fast twitch to generate tension after the stimulus. In other words, that latent phase (the first phase of the twitch) takes much longer in slow fibers than fast fibers. Slow fibers are also much slower to fatigue. These muscles are for endurance and posture, focusing on sustained, smaller movements and postural control.

In terms of their anatomy, the slow muscle fibers have a much **smaller diameter** than fast fibers, and contain more **mitochondria** and **myoglobin** because their metabolism is aerobic and requires plenty of O_2 in order to continue to contract (see **Fig. 13.27** below). The have **many capillaries** providing a rich blood supply, and the smaller diameter is to facilitate faster diffusion of the glucose and O_2 the blood stream brings the needed to make ATP aerobically. For this reason they are also called '**slow oxidative**' muscle. Due to all of these characteristics, this tissue is more **red** in color, and is also called **dark muscle**.

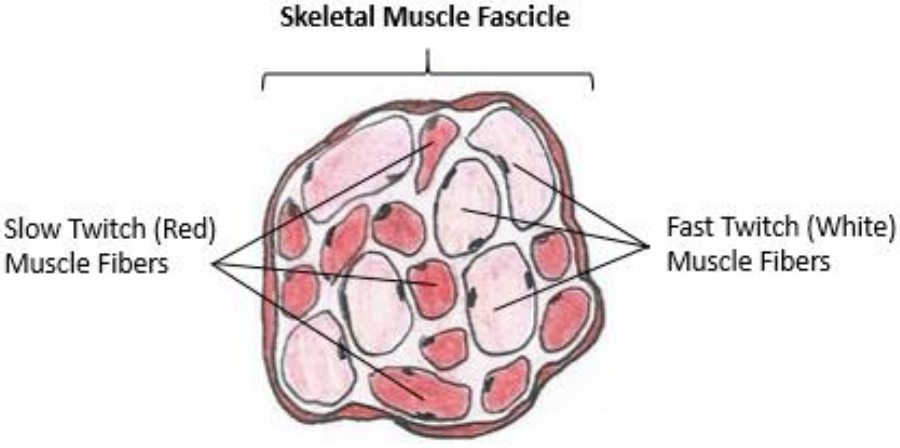


Figure 13.27 This diagram shows both slow and fast twitch muscles fiber in a skeletal muscle fascicle. Muscle fascicles will have fibers of different types, however a motor unit innervating muscle fibers will only contain one type of skeletal fiber, for example having only fast or slow fibers. Note the smaller, darker (red) muscle fibers that are slow twitch and the larger pale (white) fast twitch fibers.

Fast Twitch Fibers

The fast twitch fibers have a fast onset of contraction, this is because they depend on glycolysis for ATP and this is available more rapidly than oxidative phosphorylation. For this reason they are also called **fast-twitch glycolytic**. The fast-twitch muscle fibers give that sudden bursts of energy for very powerful and rapid movements. However, because they rely on anaerobic respiration, they are fast to fatigue.

In terms of their anatomy, the fast muscle fibers have a **large diameters** and contain more myofibrils, and contain very few mitochondria or myoglobin because their metabolism is an aerobic and does not require any O_2 when contracting. The have very few capillaries but instead have **large glycogen granules** and **enzymes for glycolysis** so that this pathway can be utilized for ATP anaerobically. For this reason they are also called '**fast glycolytic**' muscle. Due to of all these characteristics, this tissue is less red in color, often looking **pale**, and so is also called **white muscle**.

At birth all skeletal muscle fibers are slow twitch or red, and this changes later in life with activity. The vast majority of muscles contain about 50% of each slow and fast twitch, and the intermediate fibers are the types that can be converted to some degree to slow or fast, dependent on use.

Some muscle contain all red fibers, such as those for posture, which need to be fatigue resistant. However, no one skeletal muscle fascicle contains more than 50% of white fibers. Importantly, all the muscle fibers in one motor unit are always of the same type, that is, one motor unit will be composed of all red fibers or all white fibers. **Table 13.2** below summarizes the properties of slow and fast twitch muscle fibers.

Examples of Slow and Fast twitch fibers in the Body

Here is a specific example in the body for each slow and fast twitch fibers. The **soleus** muscle in the calf that is often called **the marathon runner's muscle**. It is flat and not very developed but is highly resistant to fatigue and can contract for hours non-stop. The numerous lumbar muscles that are involved in maintaining posture contain mainly slow twitch muscle fibers.

The **gastrocnemius** muscle is another muscle in the calf, it is the most superficial one, which is very large and often called **the sprinter's muscle**. They are fast and very powerful but are also fast to fatigue. The extrinsic muscles that move your eyes are also made up of fast twitch muscle fibers, for the rapid movements required for visual reflexes.

Summary of Properties of all Skeletal Muscle Fibers

Slow-twitch muscles use energy slowly and fairly evenly to make it last a long time. This enables them to continue to consistently contract for a long periods of time, maintaining constant power. This is in steep contrast to fast-twitch muscles, which use **up a lot of energy very quickly**, to produce very powerful actions, but the tradeoff is that they also fatigue very quickly. In between these two extremes are the intermediate fibers which exhibit a good combination of both slow and fast twitch muscle characteristics. The intermediate fibers are the ones that can become more like slow or fast twitch muscles with training; endurance training converts them to slow, power weight training converts them to fast.

Slow Twitch (Red Fibers) Type I	Fast Twitch (White Fibers) Type II
Tonically active much of the time.	Relaxed most of the time.
Under-go very little hypertrophy.	Under-go hypertrophy.
Important in endurance (jogging).	Important in brute strength (kicking).

Table 13.2. Properties of Slow (Red), Intermediate, and Fast (White) Twitch Skeletal Muscle Fibers.

Muscle Properties	Slow (Red) Type I	Intermediate Type IIA	Fast (White) Type II
Contraction time (onset)	75 msec (slow onset)	*Approx. 30-50 msec	25 msec (fast onset)
Contraction duration	Longer	Intermediate	Shorter
Diameter of muscle fiber	Small	Slightly larger	Large
Myosin ATPase activity	Slow	Fast	Very fast
Glycogen storage	Low	High	High
1^{o} ATP source (Metabolism)	Oxidative Phosphorylation	Oxidative-Glycolytic	Glycolysis
Mitochondrial content	High	Medium	Low
Myoglobin content	High	High	Low
Blood supply	High	Medium	Low
Color of muscle tissue	Dark or Red	More Dark than Pale	Pale or White
Fatigue	Slow to fatigue	Slower to fatigue	Fast to fatigue
Functional use of muscle	Posture, walking (constant)	Can be converted with training	Jump, sprinting (rare)
Activity	Long term aerobic	Long term anaerobic	Short term anaerobic
Force Generated (Power production)	Low	Moderate	Very High
SR Ca^{2+} ATPase activity	Slow	Fast	Fast
Fibers/Motor Unit	Less than 300	More than 300	More than 300
Major Fuel Source*	Triglycerides Glucose	Creatine Phosphate Glycogen	Creatine Phosphate Glycogen

In **Table 13.2** above is a comprehensive summary of the various differences between the three types of skeletal muscle fibers.

Smooth Muscle Contraction

Smooth Muscle Cells

The cells of smooth muscle do not have sarcomeres and that is why they do not have striations, but they do have the thin and thick filaments **actin** and **myosin** respectively. Another important structure called **dense bodies** is what these contractile proteins attach to. The dense bodies are like the z-discs of the sarcomeres for skeletal and cardiac muscle cells. Like spot-welds, the fibers are anchored to the sarcolemma by the dense bodies (see Fig X below). Just as in skeletal and cardia muscle, the $Ca^{2+}$are stored in the SR sequestration from the extracellular fluid through membrane invaginations called **calveolae** (singular caveola). Another difference is that smooth muscle do not contain **troponin**, so it is not regulated in the same way via by the troponin-tropomyosin unit, and is instead regulated by the protein **calmodulin**. Calmodulin is an acidic, Ca^{2+} binding protein that activates **crossbridge cycling** and the development of force in response to transient intracellular increases in a Ca^{2+} by the activation of **myosin light-chain kinase** (MLCK) and the phosphorylation of myosin.

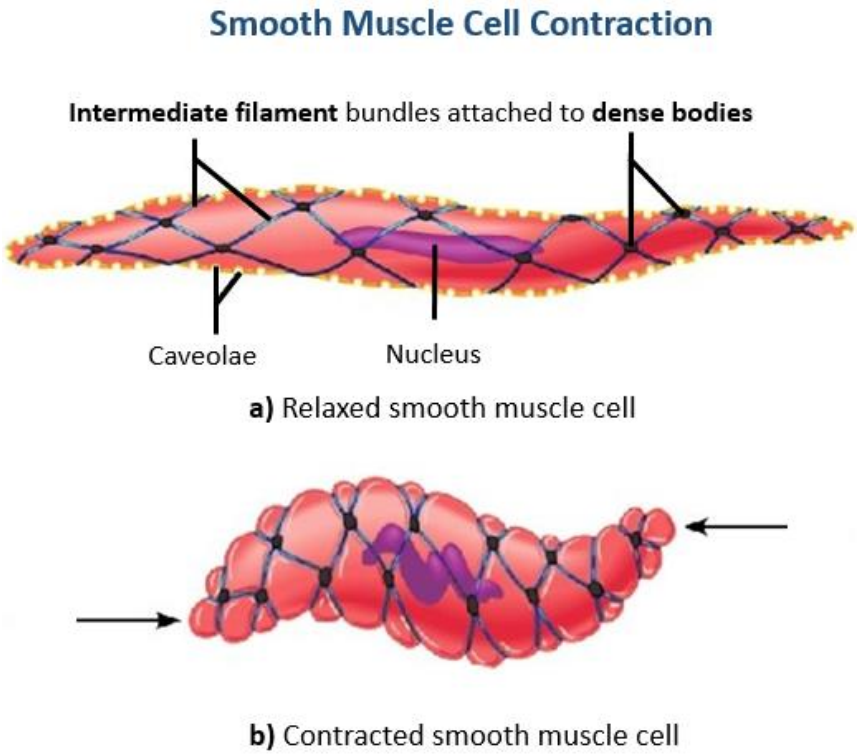


Figure 13.28 The smooth muscle cell **a)** in a relaxed state, and **b)** in a contracted state. The intermediate filaments interconnect to the dense bodies which are anchored to the cytoskeleton. The caveolae are small invaginations around the smooth muscle membrane.

The arrangement of the thin and thick filaments are not in sarcomeres, but more diagonal. During contraction, the thin filaments slide past the thick filaments and as they do they pull on the dense bodies that are stapled to the sarcolemma and in turn pulls on the network of **intermediate filaments** running throughout the sarcoplasm. This structural organization causes a type of synching of the muscle cell pulling its ends closer to its puckering middle (see **Figure 13.28** above).

Smooth muscle has sarcoplasmic reticulum (SR), but **do not have T-tubules**, there is no need for them in these smaller cells. Importantly, similar to cardiac muscle, there are Ca^{2+}channels in the sarcolemma that bring in $Ca^{2+}$from the ECF to release Ca^{2+} from the SR.

Smooth Muscle Contraction Mechanisms

When stimulates to contract, by eithers nervous innervation (ANS), hormones, local paracrines or stretching, there is an increase in intracellular Ca^{2+} concertation ($[Ca^{2+}]_i$) and that is what sets the action in motion. The increase in intracellular Ca^{2+} binds to calmodulin, and it is the **Ca^{2+}-calmodulin complex** that activates the myosin light-chain kinase (MLCK). Recall that kinases are enzymes that stick phosphates on things, in this case it is myosin that gets phosphorylated!

The activated MLCK then tells two friends… that was an old school joke but it is an amplification cascade. The MLCK **activates the myosin heads** by phosphorylating them, the Phosphate comes from hydrolyzing ATP to ADP and P_i, it is the P_i that binds to the myosin head. Now the myosin heads can bind to actin, and pull the thin filaments like a synch.

The ability of smooth muscle SR to store Ca^{2+} is limited, thus the importance of incoming Ca^{2+} from the ECF that accounts for most of the Ca^{2+} that triggers contraction. It enters via Ca^{2+} channels on the sarcolemma that open during the action potential. The influx of Ca^{2+} binds with the calmodulin and the activation of MLCK proceeds as described above and seen **Figure 13.29** to the right.

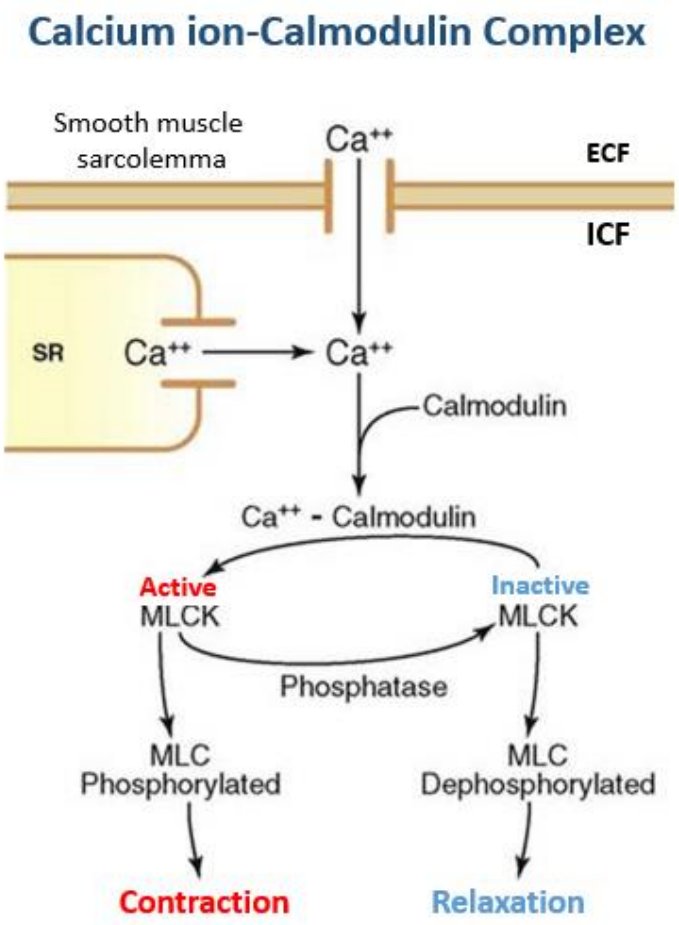


Figure 13.29 The increase of intracellular Ca^{2+} in smooth muscle forms the Ca^{2+}-calmodulin complex which then activates the myosin light-chain kinase (MLCK) promoting contraction. When intracellular Ca^{2+} levels decrease, it deactivates the MLCK and causes the smooth muscle cell to relax.

Smooth muscle contraction will continue contract until the free intracellular Ca^{2+} is actively pumped back into the SR and back out into the ECF, which requires ATP. Interestingly, there remains a low baseline level of intracellular Ca^{2+} and this enables smooth muscle to maintain its basal muscle tone, that is, it remains slightly contracted, which is critical in blood vessels and other structures.

In terms of the force generated by smooth muscle, it has the **least strength** of the three types of muscle. However, its endurance is very impressive, and the tradeoff here is that of the three types of muscle it is the **most fatigue resistant**. Smooth muscles must maintain tension for long periods without rest, and contractions are able to continue without using large amounts of energy. Also, some smooth muscle is able to maintain contractions with virtually no Ca^{2+} and the MLCK is inactivated. A subset of myosin-actin cross-bridges called **latch-bridges** can keep the thick and thin filaments linked together for a prolonged period, without requiring ATP. This is what enables smooth muscle to maintaining its tone for long periods without much expenditure of energy.

Control of Smooth Muscle

Smooth muscle is generally under involuntary control. The triggers for smooth muscle contraction include hormones, neural stimulation by the ANS, and local factors. In certain locations, such as the walls of visceral organs, stretching the muscle can trigger its contraction (the stress-relaxation response).

In smooth muscle, the innervation from the ANS is **not** like the neuromuscular junction of skeletal muscle. For smooth muscle, there is a series of neurotransmitter-filled bulges called **varicosities** (or bouton) as an axon courses throughout smooth muscle, creating motor units, as depicted in **Figure 13.30** below. The varicosity releases neurotransmitters into the neuromuscular junction for smooth muscle. There is speculation that **caveolae** modulate smooth muscle cell contraction by way of ion channels and receptors. It is postulated that they could be involved in the **serotonin** or **5-HT** (5-hydroxytryptamine) mediation of smooth muscle contraction triggered by 5-HT_{2A} receptors on the smooth muscle sarcolemma.

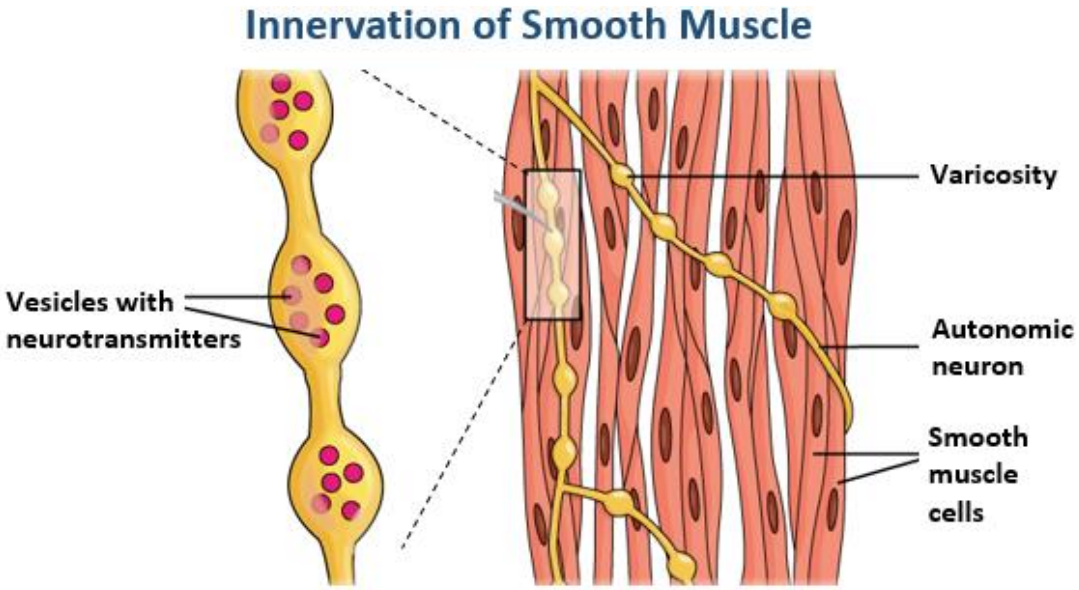


Figure 13.30 The innervation of smooth muscle is via the autonomic nervous system, both parasympathetic and sympathetic divisions are involved. The axons have varicosities which contain vesicles that contain the neurotransmitters, and the wrap around the smooth muscle tissue for comprehensive coverage.

Motor Units

The motor units are the series of varicosities from the autonomic neurons roaming smooth muscle tissue. Smooth muscle is organized in two ways: **1)** as single-unit smooth muscle (most common); and **2)** as multiunit smooth muscle.

1) Single-unit muscle cells are joined by **gap junctions**, this enables them to functionally contract as a single coordinated unit. This is common in the walls of internal viscera (organs) – but not the heart because it is composed of cardiac muscle. An important characteristic of visceral smooth muscle is its stress-relaxation response, in that when the walls of a hollow organ are stretched (e.g., when filling), this mechanical distension triggers contraction, which is then followed immediately by relaxation, to prevent premature emptying of its contents. The stomach and the bladder are good examples of this. Visceral smooth muscle produces constant yet slow contractions allowing substances (e.g., food in the GI tract), to be moved gently through the body.

2) Multi-unit muscle cells do not have gap junctions and thus are not electrically coupled so that contraction does not spread from one cell to the next, but rather is confined to the cell that was originally stimulated. The ANS and hormones can act as stimuli for these smooth muscles, but they are not activated by stretching. This smooth muscle found in large blood vessels, the respiratory airways, and in the eyes.

Hypertrophy and Hyperplasia in Smooth Muscle

All the cells in muscle tissue, skeletal, cardiac and smooth muscle, can undergo **hypertrophy** and become larger in size. However, unlike skeletal and cardiac, smooth muscle can divide to make more cells, this is a process called **hyperplasia**. The most significant example of this is the myometrium of the uterus at puberty, which is smooth muscle that experiences hyperplasia when increased levels of estrogen occur significantly increasing the size of the myometrial layer.

Review Questions for Chapter 13: Muscles

1. The type of muscle that has a striped appearance and is involuntary is:
- **a)** elastic
- **b)** cardiac
- **c)** excitable
- **d)** smooth
- **e)** striated

2. During isotonic contraction of a skeletal muscle fiber the _____.
- **a)** A bands shorten.
- **b)** I bands shorten.
- **c)** Z discs lengthen.
- **d)** b and c.

3. A "motor unit" for skeletal muscle refers to
- **a)** a single motor neuron plus all the muscle fibers it innervates.
- **b)** a single muscle fiber plus all of the motor neurons that innervate it.
- **c)** all of the motor neurons supplying a single muscle.
- **d)** a pair of antagonistic muscles.
- **e)** all of the muscles that affect the movement of any given joint.

4. In skeletal muscle, calcium facilitates contraction by binding to _____.
- **a)** tropomyosin.
- **b)** actin.
- **c)** troponin.
- **d)** myosin.
- **e)** the thick filament.

5. Rigor mortis occurs because
- **a)** The ATP required for the detachment of cross bridges is not being formed.
- **b)** The ATP required for the formation of cross bridges is not being formed.
- **c)** The ATP required for the formation of cross bridges continues after death.
- **d)** The deterioration of muscle proteins prevents detachment of cross bridges.
- **e)** None of the above.

6. Muscle relaxation would begin to occur when:

- **a)** Ca^{2+} is actively transported out of the sarcoplasmic reticulum.
- **b)** Ca^{2+} diffuses out of the sarcoplasmic reticulum.
- **c)** Ca^{2+} is actively transported into the sarcoplasmic reticulum.
- **d)** Ca^{2+} diffuses into the sarcoplasmic reticulum.

7. The end plate potential (action potential) rapidly spreads to through a muscle cell by way of the:

- **a)** Z lines.
- **b)** Sarcoplasmic reticulum.
- **c)** H zone.
- **d)** Transverse tubules.
- **e)** Pores in the plasma membrane.

8. Jill is a sprinter specializing in quick and powerful actions, then periods of rest. Joan is a marathon runner specializing in long, steady runs. Compared to Joan, Jill is likely to have

- **a)** Legs with a larger diameter.
- **b)** Legs with a smaller diameter.
- **c)** Hypertrophy of type I muscle fibers.
- **d)** a and c.
- **e)** b and c.

9. The fibers in a muscle spindle

- **a)** Are not true muscle fibers because they cannot contract.
- **b)** Are innervated by gamma motor neurons.
- **c)** Function to maintain tension on spindle receptors.
- **d)** b and c.
- **e)** a, b and c.

10. Golgi tendon organs

- **a)** Are located in the tendons joining muscle and bone.
- **b)** Monitor the strength of muscle contractions.
- **c)** Are associated with monosynaptic reflexes.
- **d)** a and b.
- **e)** a, b and c.

Answers in Appendix B