

BIO 301

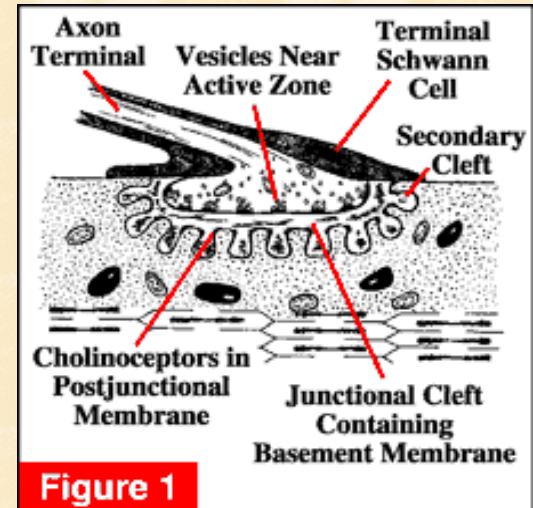
Human Physiology

Muscle

The nervous system 'communicates' with muscle via neuromuscular (also called myoneural) junctions. These junctions (Figure 1) work very much like a synapse between neurons. In other words:

- the impulse arrives at the end bulb,
- chemical transmitter is released and diffuses across the neuromuscular cleft,
- the transmitter molecules fill receptor sites in the membrane of the muscle & increase membrane permeability to sodium,
- sodium then diffuses in & the membrane potential becomes less negative,
- and, if the threshold potential is reached, an action potential occurs, an impulse travels along the muscle cell membrane, and the muscle contracts.

Some muscles (skeletal muscles) will not contract unless stimulated by neurons; other muscles (smooth & cardiac) will contract without nervous stimulation but their contraction can be influenced by the nervous system. Thus, the nervous and muscle systems are closely interconnected. Let's now focus on muscle - what is its structure & how does it work.



Characteristics of muscle:

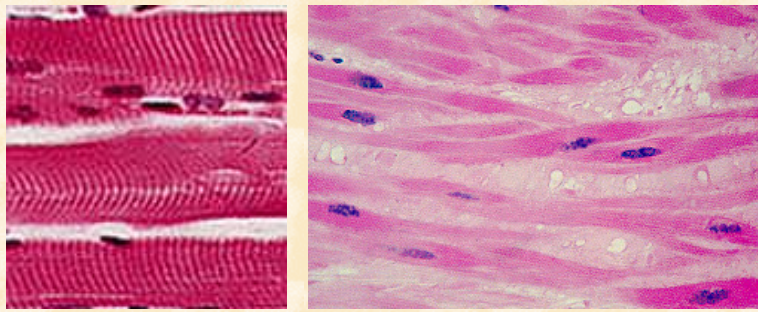
- excitability - responds to stimuli (e.g., nervous impulses)
- contractility - able to shorten in length
- extensibility - stretches when pulled
- elasticity - tends to return to original shape & length after contraction or extension

Functions of muscle:

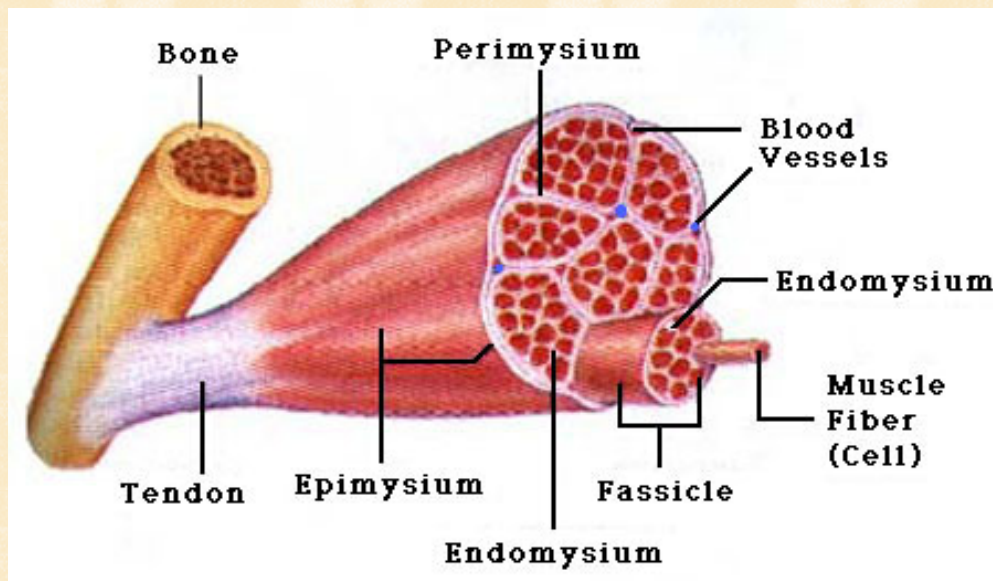
- motion
- maintenance of posture
- heat production

Types of muscle:

- skeletal:
 - attached to bones & moves skeleton
 - also called striated muscle (because of its appearance under the microscope, as shown in the photo to the left)
 - voluntary muscle

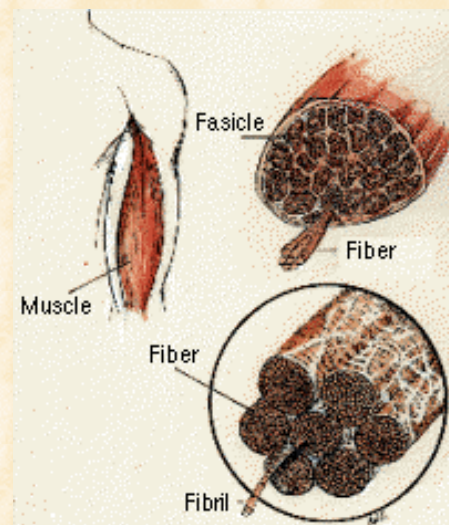


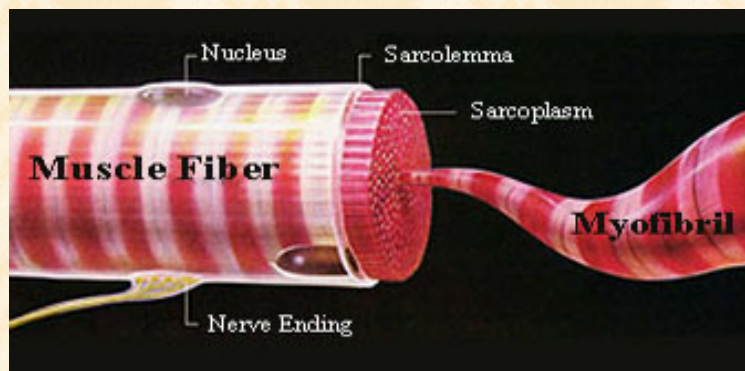
- smooth (photo on the right)
 - involuntary muscle
 - muscle of the viscera (e.g., in walls of blood vessels, intestine, & other 'hollow' structures and organs in the body)
- cardiac:
 - muscle of the heart
 - involuntary



Structure of Skeletal Muscle:

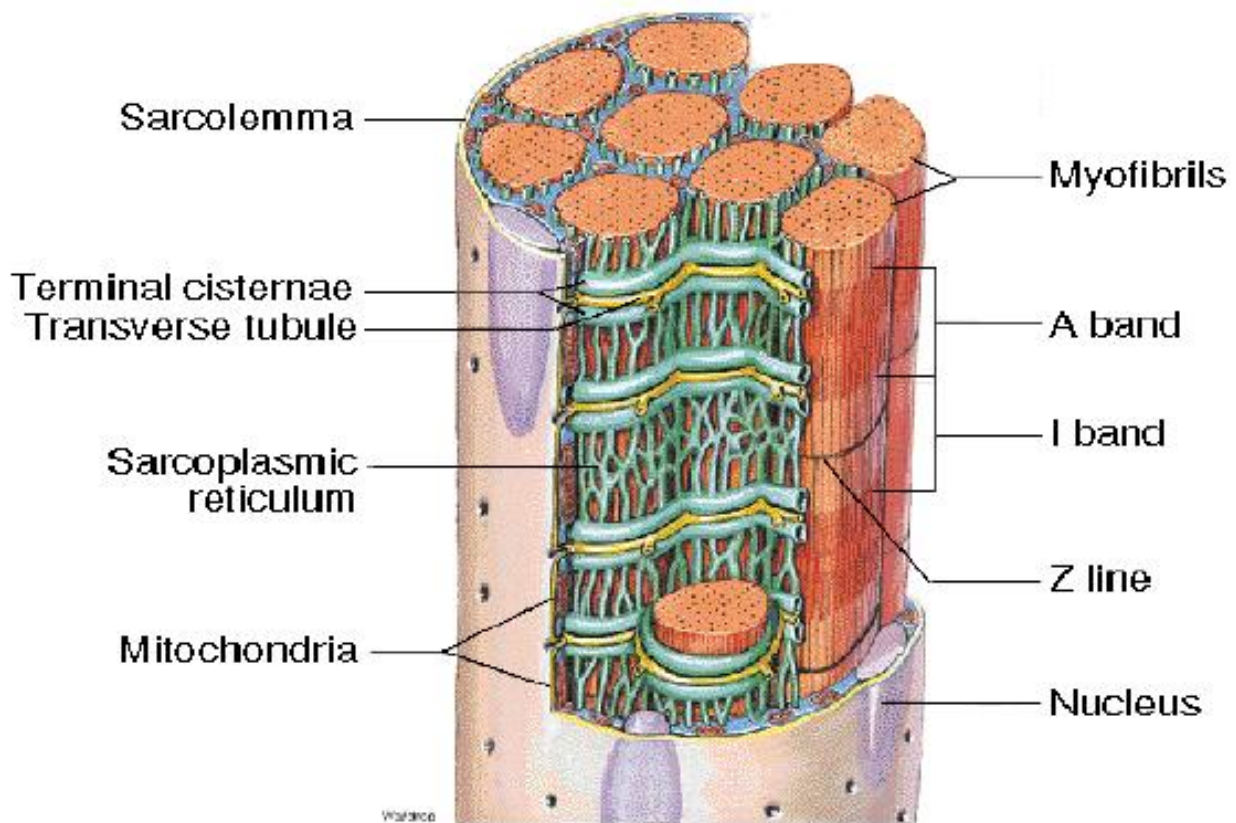
Skeletal muscles are usually attached to bone by tendons composed of connective tissue. This connective tissue also ensheaths the entire muscle & is called epimysium. Skeletal muscles consist of numerous subunits or bundles called fascicles (or fascicles). Fascicles are also surrounded by connective tissue (called the perimysium) and each fascicle is composed of numerous muscle fibers (or muscle cells). Muscle cells, ensheathed by endomysium, consist of many fibrils (or myofibrils), and these myofibrils are made up of long protein molecules called myofilaments. There are two types of myofilaments in myofibrils: thick myofilaments and thin myofilaments.





The cell membrane of a muscle cell is called the sarcolemma, and this membrane, like that of neurons, maintains a membrane potential. So, impulses travel along muscle cell membranes just as they do along nerve cell membranes. However, the 'function' of impulses in muscle cells is to bring about contraction. To understand how a muscle contracts, you need to know a bit about the structure of muscle cells.

Sarcoplasmic Reticulum

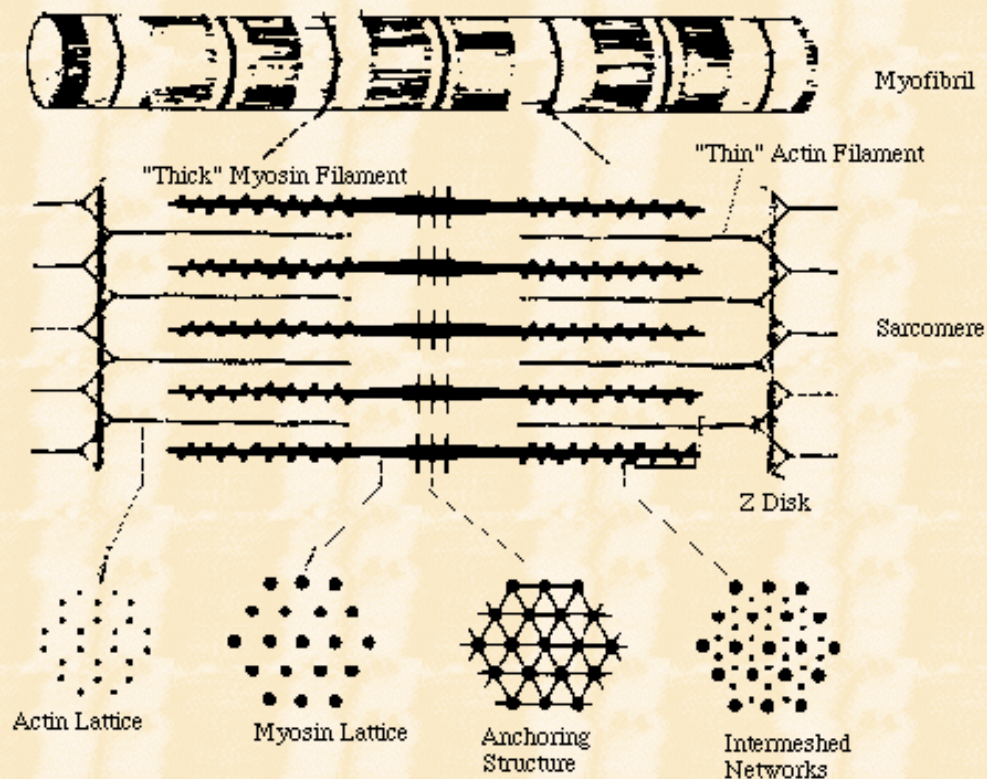


The SARCOLEMMA has a unique feature: it has holes in it. These "holes" lead into tubes called TRANSVERSE TUBULES (or T-TUBULES for short). These tubules pass down into the muscle cell and go around the MYOFIBRILS. However, these tubules DO NOT open into the interior of the muscle cell; they pass completely through and open somewhere else on the

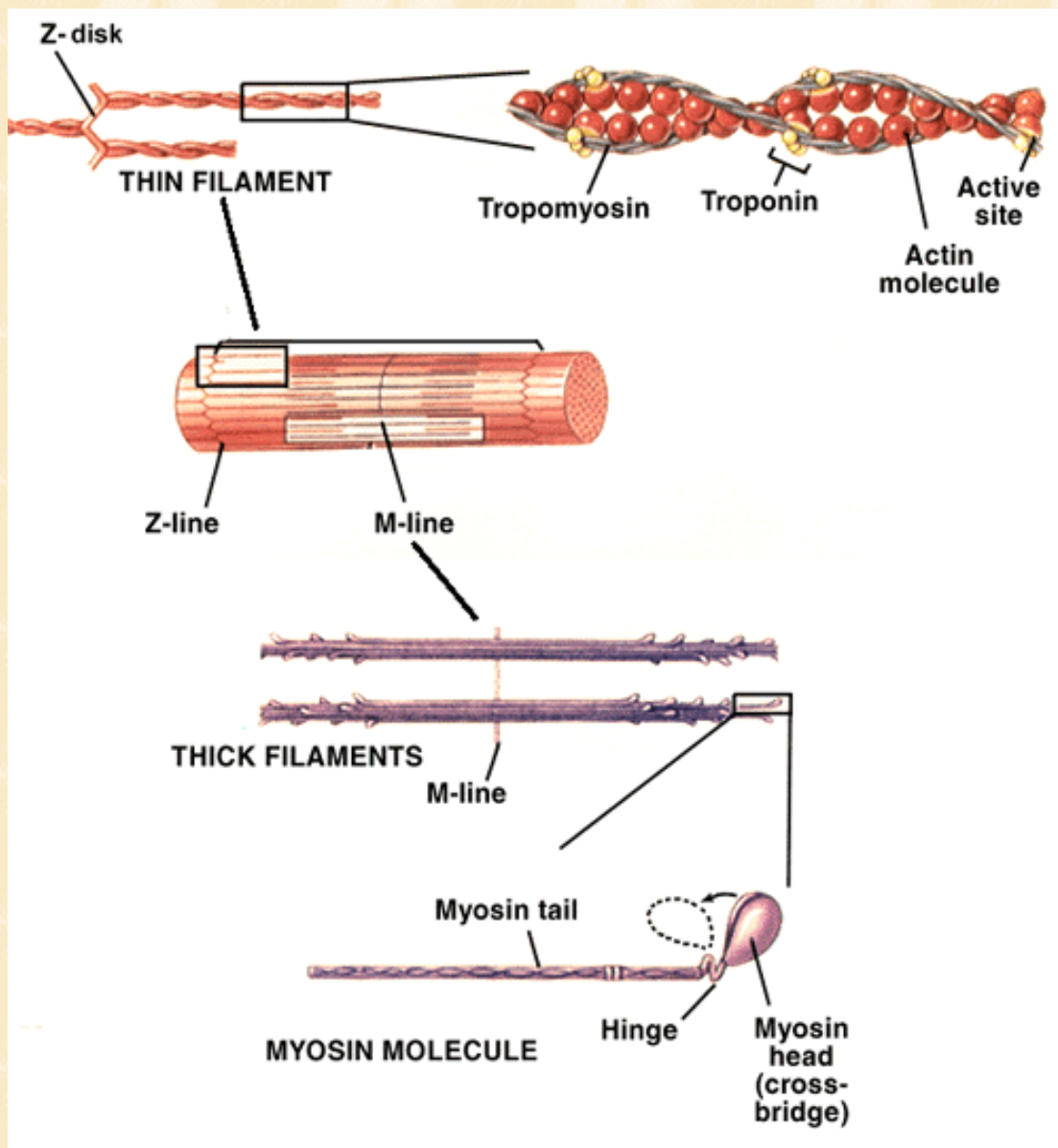
sarcolemma (i.e., these tubules are not used to get things into and out of the muscle cell). The function of T-TUBULES is to conduct impulses from the surface of the cell (SARCOLEMMMA) down into the cell and, specifically, to another structure in the cell called the SARCOPLASMIC RETICULUM.

The SARCOPLASMIC RETICULUM (SR) is a bit like the endoplasmic reticulum of other cells, e.g., it's hollow. But the primary function of the SARCOPLASMIC RETICULUM is to STORE CALCIUM IONS. Sarcoplasmic reticulum is very abundant in skeletal muscle cells and is closely associated with the MYOFIBRILS (and, therefore, the MYOFILAMENTS). The membrane of the SR is well-equipped to handle calcium: there are "pumps" (active transport) for calcium so that calcium is constantly being "pumped" into the SR from the cytoplasm of the muscle cell (called the SARCOPLASM). As a result, in a relaxed muscle, there is a very high concentration of calcium in the SR and a very low concentration in the sarcoplasm (and, therefore, among the myofibrils & myofilaments). In addition, the membrane has special openings, or "gates", for calcium. In a relaxed muscle, these gates are closed and calcium cannot pass through the membrane. So, the calcium remains in the SR. However, if an impulse travels along the membrane of the SR, the calcium "gates" open &, therefore, calcium diffuses rapidly out of the SR & into the sarcoplasm where the myofibrils & myofilaments are located. This, as you will see, is a key step in muscle contraction.

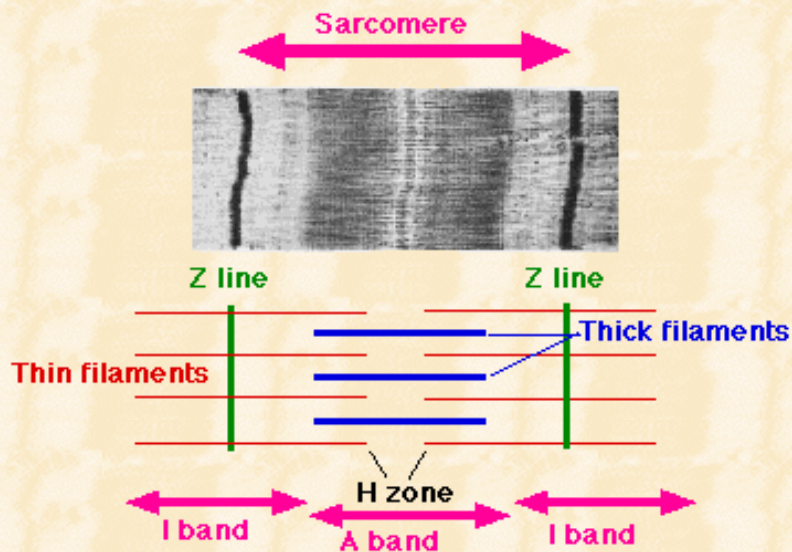
Myofibrils are composed of 2 types of myofilaments: thick and thin. In skeletal muscle, these myofilaments are arranged in a very regular, precise pattern: thick myofilaments are always surrounded by 6 thin myofilaments. In a side view, thin myofilaments can be seen above and below each thick myofilament.



Each myofibril is composed of many subunits lined up end-to-end. These subunits are, of course, composed of myofilaments and are called SARCOMERES. The drawings above & below show just a very small section of the entire length of a myofibril and so you can only see one complete SARCOMERE.



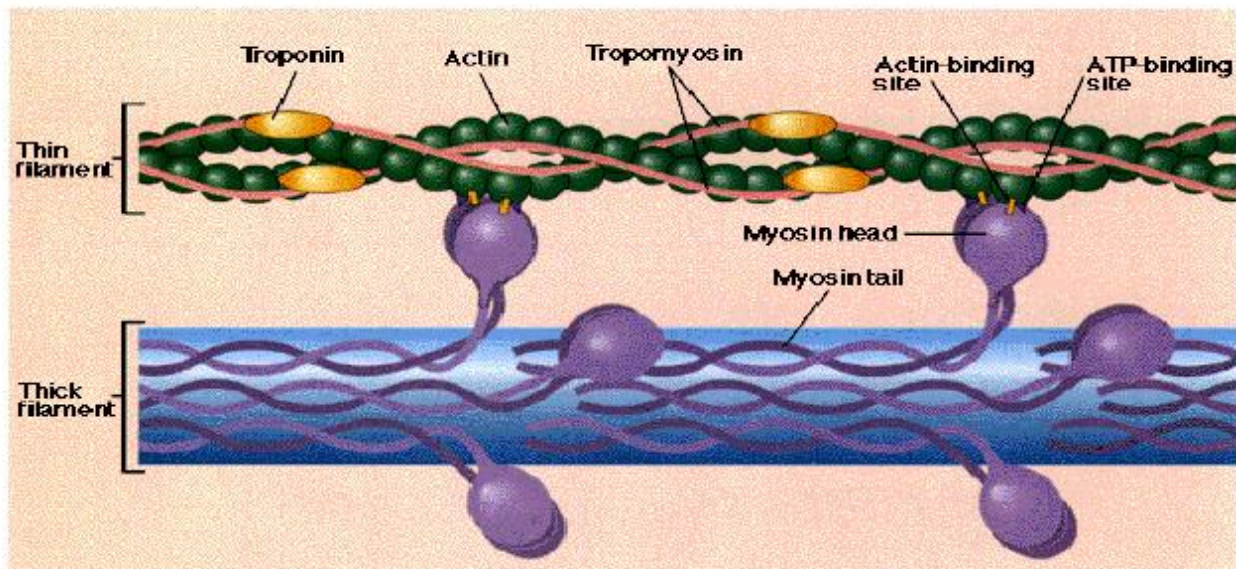
In each sarcomere, thin myofilaments extend in from each end. Thick myofilaments are found in the middle of the sarcomere and do not extend to the ends. Because of this arrangement, when skeletal muscle is viewed with a microscope, the ends of a sarcomere (where only thin myofilaments are found) appear lighter than the central section (which is dark because of the presence of the thick myofilaments). Thus, a myofibril has alternating light and dark areas because each consists of many sarcomeres lined up end-to-end. This is why skeletal muscle is called **STRIATED MUSCLE** (i.e., the alternating light and dark areas look like stripes or striations). The light areas are called the **I-BANDS** and the darker areas the **A-BANDS**. Near the center of each I-BAND is a thin dark line called the **Z-LINE** (or Z-membrane in the drawing below). The Z-LINE is where adjacent sarcomeres come together and the thin myofilaments of adjacent sarcomeres overlap slightly. Thus, a sarcomere can be defined as the area between Z-lines.



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Thick myofilaments are composed of a protein called MYOSIN. Each MYOSIN molecule has a tail which forms the core of the thick myofilament plus a head that projects out from the core of the filament. These MYOSIN heads are also commonly referred to as CROSS-BRIDGES.

Myosin & the Thick Filament

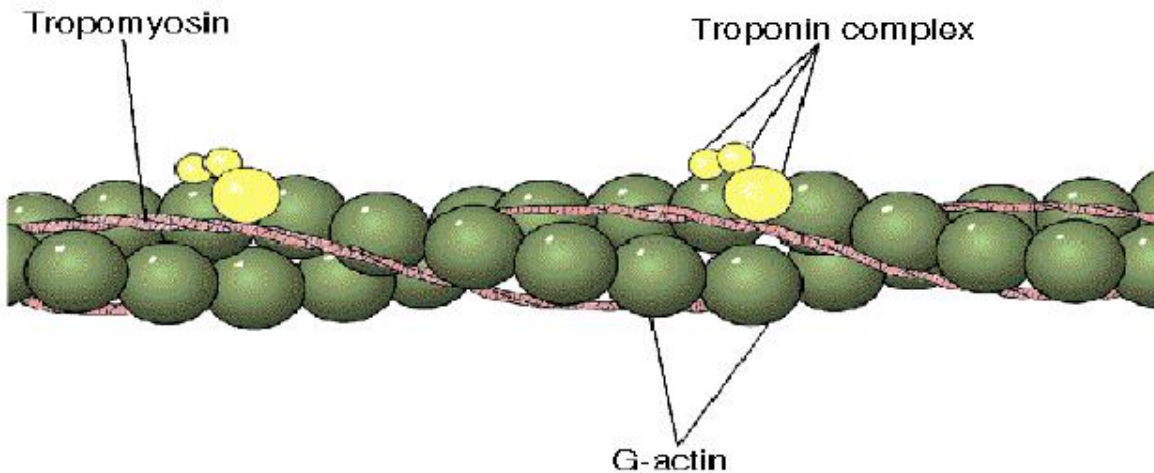


The MYOSIN HEAD has several important characteristics:

- it has ATP-binding sites into which fit molecules of ATP. ATP represents potential energy.
- it has ACTIN-binding sites into which fit molecules of ACTIN. Actin is part of the thin myofilament and will be discussed in more detail shortly.
- it has a "hinge" at the point where it leaves the core of the thick myofilament. This allows the head to swivel back and forth, and the "swivelling" is, as will be described shortly, what actually causes muscle contraction.

Thin myofilaments are composed of 3 types of protein: ACTIN, TROPONIN, and TROPOMYOSIN.

Thin Filament Structure



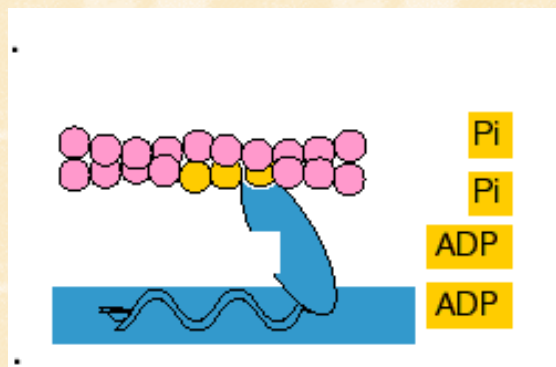
The actin molecules (or G-actin as above) are spherical and form long chains. Each thin myofilament contains two such chains that coil around each other. TROPOMYOSIN molecules are long, thin molecules that wrap around the chain of ACTIN. At the end of each tropomyosin is a TROPONIN molecule. The TROPOMYOSIN and TROPONIN molecules are connected to each other. Each of these 3 proteins plays a key role in muscle contraction:

- **ACTIN** - when actin combines with MYOSIN HEAD the ATP associated with the head breaks down into ADP. This reaction released energy that causes the MYOSIN HEAD to SWIVEL.
- **TROPOMYOSIN** - In a relaxed muscle, the MYOSIN HEADS of the thick myofilament lie against TROPOMYOSIN molecules of the thin myofilament. As long as the MYOSIN HEADS remain in contact with TROPOMYOSIN nothing happens (i.e., a muscle remains relaxed).
- **TROPONIN** - Troponin molecules have binding sites for calcium ions. When a calcium ion fills this site it causes a change in the shape and position of TROPONIN. And, when TROPONIN shifts, it pulls the TROPOMYOSIN to which

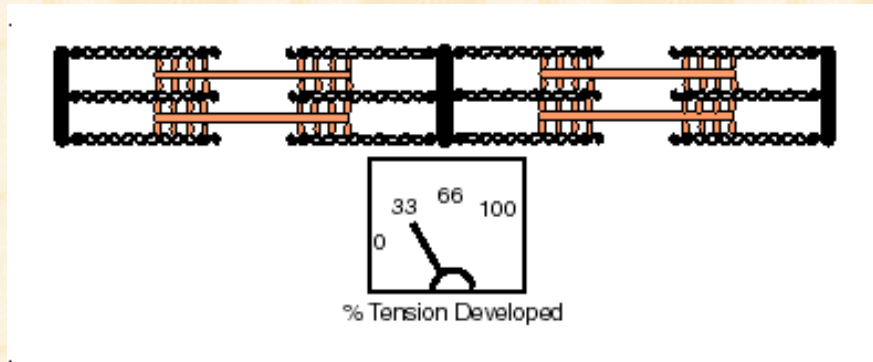
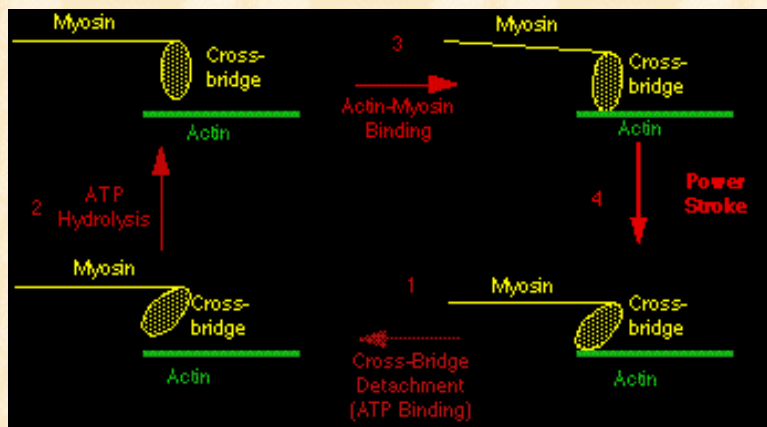
it is attached. When TROPOMYOSIN is moved, the MYOSIN HEAD that was touching the tropomyosin now comes in contact with an underlying ACTIN molecule.

Muscle contraction

- 1 - Because skeletal muscle is voluntary muscle, contraction requires a nervous impulse. So, step 1 in contraction is when the impulse is transferred from a neuron to the SARCOLEMMA of a muscle cell.
- 2 - The impulse travels along the SARCOLEMMA and down the T-TUBULES. From the T-TUBULES, the impulse passes to the SARCOPLASMIC RETICULUM.
- 3 - As the impulse travels along the Sarcoplasmic Reticulum (SR), the calcium gates in the membrane of the SR open. As a result, CALCIUM diffuses out of the SR and among the myofilaments.
- 4 - Calcium fills the binding sites in the TROPONIN molecules. As noted previously, this alters the shape and position of the TROPONIN which in turn causes movement of the attached TROPOMYOSIN molecule.
- 5 - Movement of TROPOMYOSIN permits the MYOSIN HEAD to contact ACTIN.
- 6 - Contact with ACTIN causes the MYOSIN HEAD to swivel.



- 7 - During the swivel, the MYOSIN HEAD is firmly attached to ACTIN. So, when the HEAD swivels it pulls the ACTIN (and, therefore, the entire thin myofilament) forward. (Obviously, one MYOSIN HEAD cannot pull the entire thin myofilament. Many MYOSIN HEADS are swivelling simultaneously, or nearly so, and their collective efforts are enough to pull the entire thin myofilament).



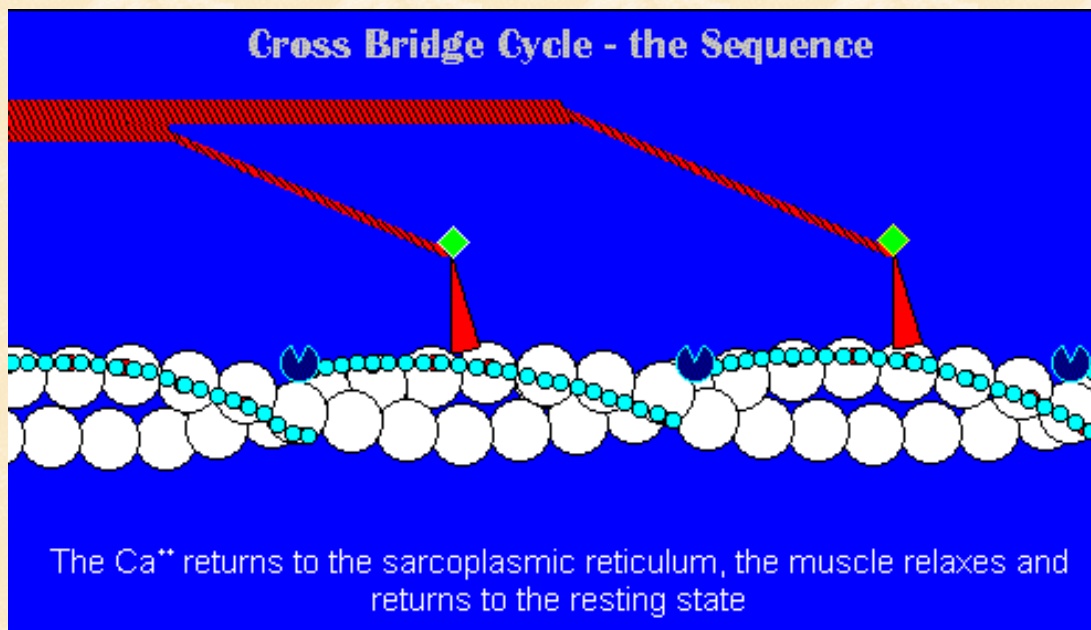
8 - At the end of the swivel, ATP fits into the binding site on the cross-bridge & this breaks the bond between the cross-bridge (myosin) and actin. The MYOSIN HEAD then swivels back. As it swivels back, the ATP breaks down to ADP & P and the cross-bridge again binds to an actin molecule.

9 - As a result, the HEAD is once again bound firmly to ACTIN. However, because the HEAD was not attached to actin when it swivelled back, the HEAD will bind to a different ACTIN molecule (i.e., one further back on the thin myofilament). Once the HEAD is attached to ACTIN, the cross-bridge again swivels, SO STEP 7 IS REPEATED.

As long as calcium is present (attached to TROPONIN), steps 7 through 9 will continue. And, as they do, the thin myofilament is being "pulled" by the MYOSIN HEADS of the thick myofilament. Thus, the THICK & THIN myofilaments are actually sliding past each other. As this occurs, the distance between the Z-lines of the sarcomere decreases. As sarcomeres get shorter, the myofibril, of course, gets shorter. And, obviously, the muscle fibers (and entire muscle) get shorter.

Skeletal muscle relaxes when the nervous impulse stops. No impulse means that the membrane of the SARCOPLASMIC RETICULUM is no longer permeable to calcium (i.e., no impulse means that the CALCIUM GATES close). So, calcium no longer diffuses out. The CALCIUM PUMP in the membrane will now transport the calcium back into the SR. As this occurs, calcium ions leave the binding sites on the TOPONIN MOLECULES. Without calcium, TROPONIN returns to its original shape and position as does the attached TROPOMYOSIN. This means that TROPOMYOSIN is now back in position, in contact with the MYOSIN HEAD. So, the MYOSIN head is no longer in contact with ACTIN and, therefore, the muscle stops contracting (i.e., relaxes).

So, under most circumstances, calcium is the "switch" that turns muscle "on and off" (contracting and relaxing). When a muscle is used for an extended period, ATP supplies can diminish. As ATP concentration in a muscle declines, the MYOSIN HEADS remain bound to actin and can no longer swivel. This decline in ATP levels in a muscle causes MUSCLE FATIGUE. Even though calcium is still present (and a nervous impulse is being transmitted to the muscle), contraction (or at least a strong contraction) is not possible.



- 1 - Calcium released from sarcoplasmic reticulum
- 2 - Myosin head energized via myosin-ATPase activity which converts the bound ATP to ADP + Pi
- 3 - Calcium binds to troponin
- 4 - Tropomyosin translocates to uncover the cross-bridge binding sites
- 5 - The energized myosin binding sites approach the binding sites
- 6 - The first myosin head binds to actin
- 7 - The bound myosin head releases ADP + Pi, flips and the muscle shortens
- 8 - The second myosin head binds to actin
- 9 - The first myosin head binds ATP to allow the actin and myosin to unbind
- 10 - The second myosin head releases its ADP + Pi, flips & the muscle shortens further
- 11 - The second myosin head binds to ATP to allow the actin and myosin to unbind
- 12 - The second myosin head unbinds from the actin, flips back and is ready for the next cycle
- 13 - The cross-bridge cycle is terminated by the loss of calcium from the troponin
- 14 - Tropomyosin translocates to cover the cross-bridge binding sites
- 15 - The calcium returns to the sarcoplasmic reticulum, the muscle relaxes & returns to the resting state

Also check out: www.blackwellpublishing.com/matthews/myosin.html

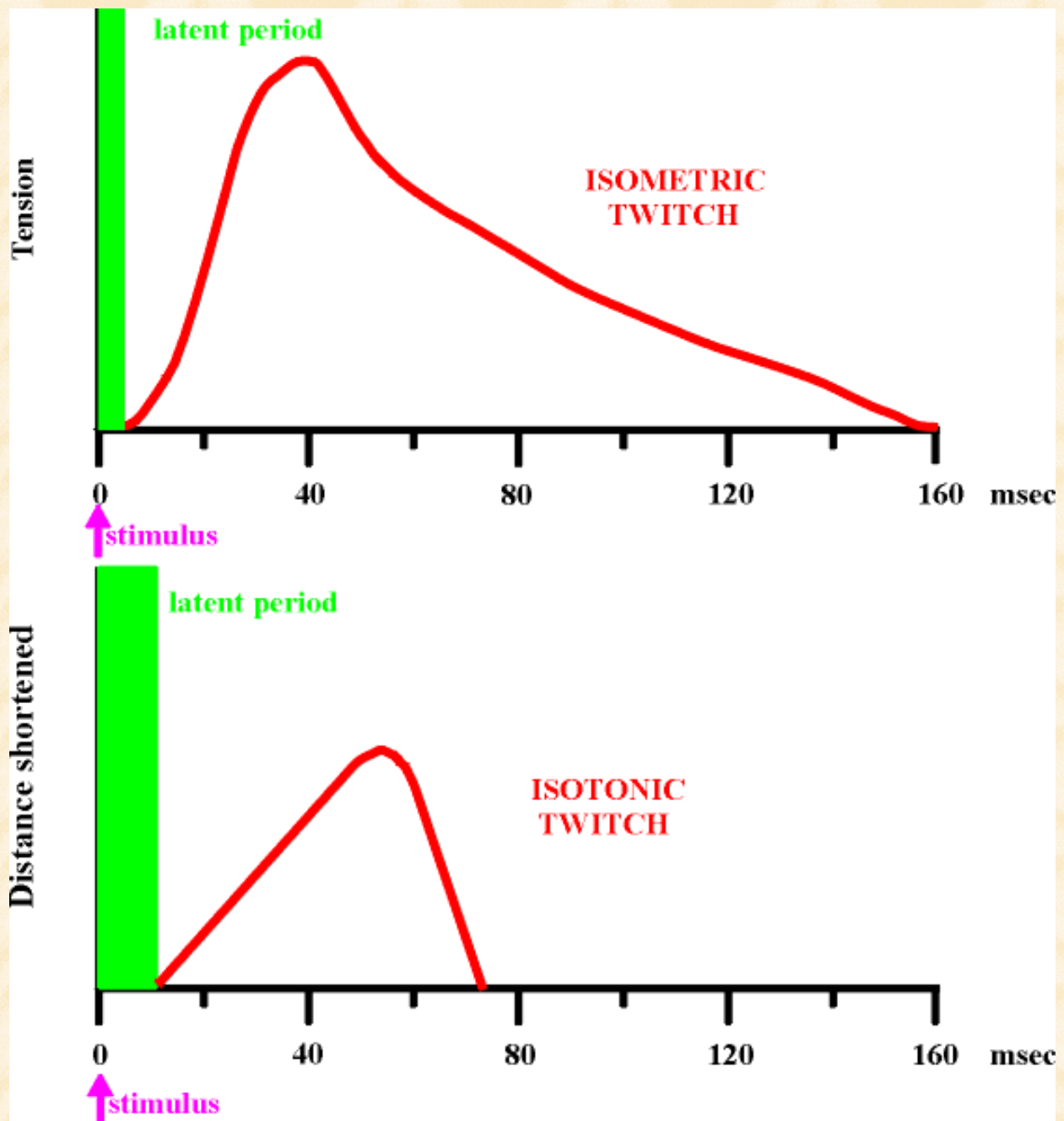
Types of contractions:

- 1 - isotonic - tension or force generated by the muscle is greater than the load & the muscle shortens
- 2 - isometric - load is greater than the tension or force generated by the muscle & the muscle does not shorten

Twitch - the response of a skeletal muscle to a single stimulation (or action potential):

- latent period - no change in length; time during which impulse is traveling along sarcolemma & down t-tubules to sarcoplasmic reticulum, calcium is being released, and so on (in other words, muscle cannot contract instantaneously!)
- contraction period - tension increases (cross-bridges are swivelling)

- relaxation period - muscle relaxes (tension decreases) & tends to return to its original length

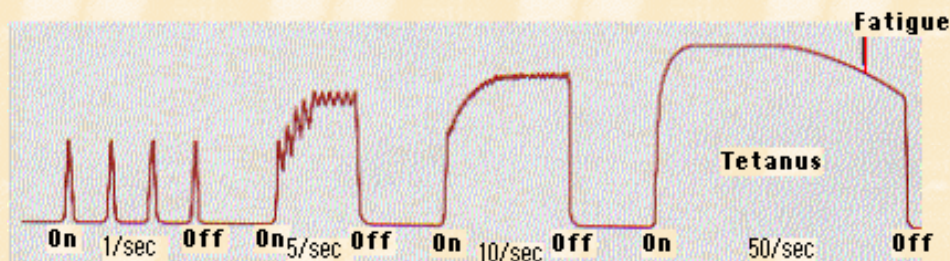
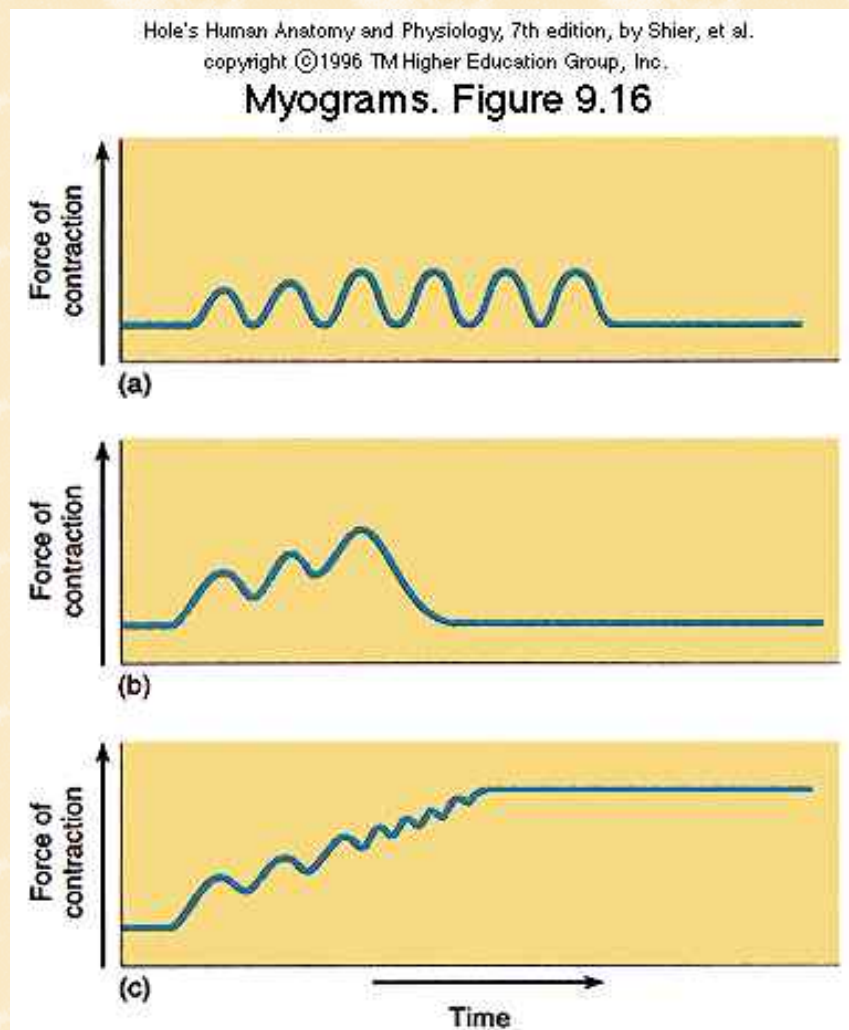


An important characteristic of skeletal muscle is its ability to contract to varying degrees. A muscle, like the biceps, contracts with varying degrees of force depending on the circumstance (this is also referred to as a graded response). Muscles do this by a process called summation, specifically by motor unit summation and wave summation.

Motor Unit Summation - the degree of contraction of a skeletal muscle is influenced by the number of motor units being stimulated (with a motor unit being a motor neuron plus all of the muscle fibers it innervates; see diagram below). Skeletal muscles consist of numerous motor units and, therefore, stimulating more motor units creates a stronger contraction.

Wave Summation - an increase in the frequency with which a muscle is stimulated increases the strength of contraction. This is illustrated in (b). With rapid stimulation (so rapid that a muscle does not completely relax between successive stimulations), a muscle fiber is re-stimulated while there is still some contractile activity. As a result, there is a 'summation' of the contractile force. In addition, with rapid stimulation there isn't enough time between successive stimulations to remove all the calcium from the sarcoplasm. So, with several stimulations in rapid succession, calcium levels in the sarcoplasm increase. More calcium means more active cross-bridges and, therefore, a stronger contraction.

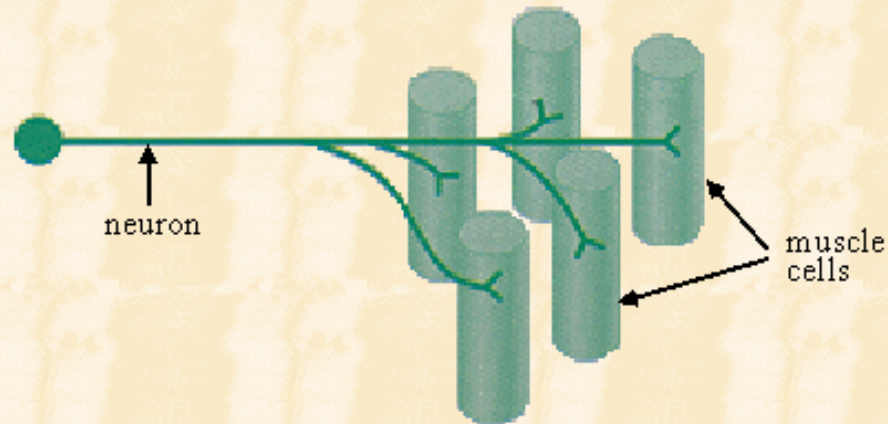
If a muscle fiber is stimulated so rapidly that it does not relax at all between stimuli, a smooth, sustained contraction called **tetanus** occurs (illustrated by the straight line in c above & in the diagram below).



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MOTOR UNITS

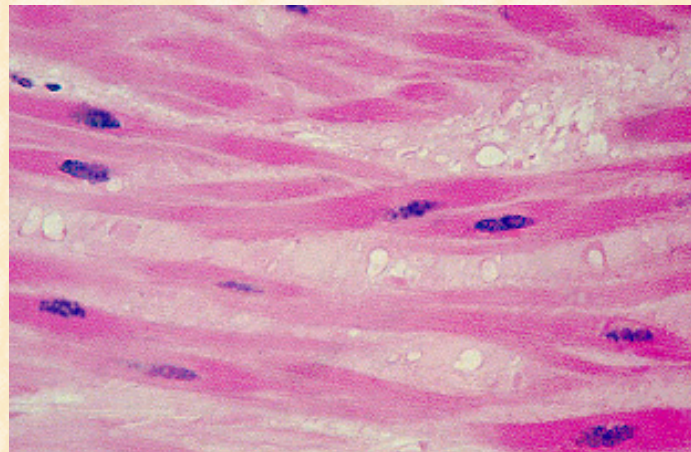
The combination of the motor nerve cell (neuron) and all the muscle cells it innervates is known as a motor unit



When an electrical impulse travels down the axon, all muscle cells attached to the motor unit contract simultaneously

SMOOTH MUSCLE:

- involuntary muscle; innervated by the Autonomic Nervous System (visceral efferent fibers)
- found primarily in the walls of hollow organs & tubes
- spindle-shaped cells typically arranged in sheets
- cells do not have t-tubules & have very little sarcoplasmic reticulum
- cells do not contain sarcomeres (so are not striated) but are made up of thick & thin myofilaments. Thin filaments in smooth muscle do not contain troponin.
- calcium does not bind to troponin but, rather, to a protein called calmodulin. The calcium-calmodulin complex 'activates' myosin which then binds to actin & contraction (swivelling of cross-bridges) begins.



Two types of smooth muscle:

1 - visceral, or unitary, smooth muscle

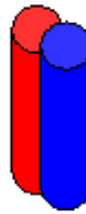
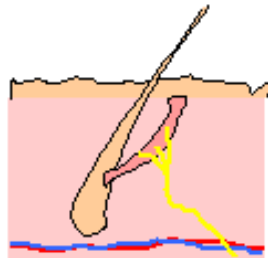
- found in the walls of hollow organs (e.g., small blood vessels, digestive tract, urinary system, & reproductive system)
- multiple fibers contract as a unit (because impulses travel easily across gap junctions from cell to cell) &, in some cases, are self-excitable (generate spontaneous action potentials & contractions)

2 - multiunit smooth muscle

- consists of motor units that are activated by nervous stimulation
- found in the walls of large blood vessels, in the eye (adjusting the shape of the lens to permit accommodation & the size of the pupil to adjust the amount of light entering the eye), & at the base of hair follicle (the 'goose bump' muscles)

2. MULTIUNIT

- a. Individual Fibers
- b. Motor units w/ ANS neurons



Useful links:

[Actin Myosin animation](#)

[Introduction to Muscle Physiology and Design](#)

[McGraw-Hill: Musculoskeletal system](#)

[Muscle Function](#)

[Properties of Skeletal Muscle](#)

[Summary of Muscle Physiology](#)

[Back to BIO 301 syllabus](#)

[Lecture Notes 1 - Cell Structure & Metabolism](#)

Lecture Notes 2 - Neurons & the Nervous System I

Lecture Notes 2b - Neurons & the Nervous System II

Lecture Notes 4 - Blood & Body Defenses

Lecture Notes 5 - Cardiovascular System

Lecture Notes 6 - Respiratory System
