# Chapter 7 Muscle

Muscle tissue is the most abundant tissue of the body and one of the most adaptable. The Muscular System has a unique feature in that it consists of cells that contract. There are 600 named muscles in the body and 3 types of muscle – ***skeletal, cardiac, and smooth***.

I. **Functions**
   A. **Body Movement** – skeletal muscle is responsible for the overall movements of the body
   B. **Maintenance of Posture** – skeletal muscles maintain tone
   C. **Respiration** – skeletal muscles of the thorax are responsible for the movements for respiration
   D. **Production of Body Heat** – skeletal muscle contraction has the byproduct of heat – useful in maintaining body temperature
   E. **Communication** – skeletal muscle is involved in *all* aspects of communication, both verbal and nonverbal
   F. **Constriction of organs and Vessels** – smooth muscle contractions with in the walls of organs and vessels aid in many body functions (propels and mixes food, propels secretions from organs, and regulates blood flow)
   G. **Heart Beat** – cardiac muscle contractions propel blood through out the body

II. **Skeletal Muscle** – also called voluntary or striated muscle – rod shaped cells with many peripheral nuclei – quick contracting – ***not*** capable of mitotic division – most capable of developing an oxygen dept
   A. **Characteristics** – skeletal muscle and its associated connective tissue constitutes approx. 40% of body's weight. Most skeletal muscles are attached to the Skeletal System (hence the name); however it is also called **striated muscle** because of the transverse bands that can be seen in the muscle under the microscope – **4 major functional characteristics**
      1. **Contractility** – the ability to shorted with force – skeletal muscle shortens actively (with force) but lengthens passively
      2. **Excitability** – the capacity to respond to a stimulus – contraction is a result of nerve stimulation
      3. **Extensibility** – stretch ability – skeletal muscle can be stretched beyond its normal resting length to a limited degree
      4. **Elasticity** – the ability to recoil to its original length after being stretched
   B. **Structure**
      1. **Epimysium** – loose connective tissue sheath surrounding each skeletal muscle
      2. **Muscle Fasciculi** – visible bundles that compose the muscle – these bundles are composed of multiple muscle fibers (cells)
      3. **Perimysium** – loose connective tissue surrounding the muscle fasciculi
      4. **Muscle Fiber** – a single cylindrical cell that contains several nuclei located at the periphery (edge) of the cell – largest are up to 30cm long, .15mm in diameter, and containing several thousand nuclei
      5. **Endomysium** – loose connective tissue surrounding each muscle fiber – functions to separate and electrically isolate each cell
      6. **Sarcoplasm** – cytoplasm of the muscle fiber
      7. **Myofibril** – thread like structure extending through the muscle fiber from one end to the other in the sarcoplasm – composed of two ***myofilaments*** *(protein fibers)-actin and myosin*

8. **Sarcomere** – the basic structural and functional unit of skeletal muscle – the smallest portion of skeletal muscle capable of contraction – one ordered unit of a myofibril
    a. **Z disk** – a network of protein fibers (titin – a protein responsible for elastic recoil) forming attachment sites for actin myofilaments
    *b.* **Actin myofilaments** – *thin* filaments resembling two strands of pearls twisted together
    *c.* **Myosin myofilaments** – *thick* filaments resembling bundles of miniature golf clubs
9. **Sarcolemma** – cell membrane of a muscle fiber
10. **T tubules (transverse tubules)** – tube like invaginations of the sarcolemma located at regular intervals and connecting the sarcolemma with the sarcoplasmic reticulum (ER)
11. **Sarcoplasmic reticulum** – endoplasmic reticulum (ER) of the muscle cell – stores calcium ions used in contraction of the muscle
12. **Terminal cisterna** – an enlarged end part of the sarcoplasmic reticulum
13. **Triad** – 2 terminal cisterna and a T tubule

C. **Functions in the Sarcomere**
1. **Z disk** – provide attachment sites for actin and elastic recoil for the Sarcomere
2. **Actin Myofilament** – consist of troponin, and tropomyosin – provides attachment sights for myosin heads – works in conjunction with the myosin in the *sliding filament theory.*
    a. **Troponin** – molecule on the actin that contains a calcium binding site which alters the shape of the troponin moving it aside to expose the tropomyosin
    b. **Tropomyosin** – filament covering the troponin sites, runs along the grove between the twisted pearl structure of the actin
3. **Myosin Myofilament** – centered between the sets of actin filaments and having golf club like heads that attach to the troponin sites when activated to work in a ratchet like fashion producing contraction – see *sliding filament theory* – myosin heads contain 2 binding sites
    a. **ATP site** – binds ATP used to make power strokes producing contraction – enzyme ***myosinatpase*** servers the ATP into ADP + P
    b. **Tropomyosin site** – binds to the tropomyosin after calcium binds to the troponin moving it aside to expose the tropomyosin

D. **Membrane Potentials** – muscle fibers, like other cells, have electrical properties with the outside of the cell being more electropositive and the inside being more electronegative – providing an opportunity for action
1. **Resting Membrane Potential** – when a cell is about -70mv inside it at (RMP) – this develops for 2 reasons
    a. **Potassium ($K^+$) diffusion** – continuous diffusion of $K^+$ down the concentration gradient to the outside of the cell
    b. **Cell membrane Permeability** – potassium diffuses easily across the cell membrane
        - Essentially, because $K^+$ are positively charged and the only ion with channels open for diffusion they will diffuse down the concentration gradient to the outside of the cell until the outside of the cell becomes more positive than the inside of the cell. However, when the inside of the cell reaches about minus 70 millivolts (-70mv) diffusion stops because of the law of opposite attraction – meaning that the overall

negative charge of the inside of the cell will no longer allow for more positively charged potassium to diffuse out.

- Lonnie Term: Resting membrane potential (RMP) is an equilibrium in which the tendency for $K^+$ to diffuse out of the cell is opposed by the negative charges inside the cell which hold on to, by attraction, the positively charged $K^+$.

2. **Depolarization** – electric reversal – when a muscle or nerve cell is stimulated Na+ (sodium) channels open and $Na^+$ quickly diffuses down the concentration gradient and ***into*** the cell causing the inside to become more positive (about 35mv) than the outside – near the end of depolarization $Na^+$ channels close and additional $K^+$ channels open
3. **Repolarization** – the change back to RMP - the process by which the cell's inside again becomes more electronegative than the outside – $Na^+$ channels all close and $K^+$ channels are open and $K^+$ is diffusing down its concentration gradient (out of the cell)
4. **Action Potential** – the rapid depolarization and repolarization (about 1-2 milliseconds) of the cell membrane – resulting in contraction for a muscle fiber

*****The *sodium-potassium exchange pump* transports $K^+$ (from outside the cell) into the cell and $Na^+$ (from inside the cell) to the outside of the cell – this active transport system maintains resting concentrations of ions on either side of the cell membrane.

E. **Nerve Supply** – skeletal muscle does not contract unless stimulated by *motor neurons.*

1. **Somatic Motor Neurons** – nerve cells along which action potentials travel to skeletal muscle fibers - axons of motor neurons branch (teladendron) to innervate several muscle fibers – located in the anterior horn of the grey matter in the spinal cord
2. **Neuromuscular junction/synapse** – junction between the axon branch (teladendron) and the muscle fiber it innervates – located near the center of the muscle fiber – is formed by a cluster of enlarged axon terminals (ends of the teladendron) resting in indentations of the muscle fiber's membrane (sarcolemma)
   a. **presynaptic terminal** – an enlarged area at the end of the axon branch (teladendron)
   b. **synaptic cleft** – space between the presynaptic terminal and the sarcolemma
   c. **postsynaptic membrane** – the sarcolemma at the site of the presynaptic terminal and synaptic cleft
   d. **synaptic vesicles** – small packages of protein enzymes located in the presynaptic terminal (made by the golgi apparatus)
   e. **neurotransmitter** – a substance packaged in a synaptic vesicle that when released by the presynaptic terminal into the synaptic cleft stimulates or inhibits the postsynaptic cell
      - ***acetylcholine*** – is the neurotransmitter used to stimulate skeletal muscle – is a ligand that opens ligand-gated sodium channels

***** There are 3 types of gated channels that allow specific ions to pass through a cell membrane – ligand gated, voltage gated, mechanically gated – sodium ($Na^+$) has only 2 types of channels to use ligand gated and voltage gated

3. **Motor Unit** – a motor neuron and ***all*** the muscle fibers it innervates

F. **Sliding Filament Model & Zones** (see p. XXX)
    1. **Zones** – areas of measurement that make up the sarcomere to show contraction in the sliding filament model
        a. **M line** – center line of a sarcomere and attachment site for myosin filaments
        b. **H zone** – area of the sarcomere extending out from the M line on either side - composed of myosin only (no actin)
        c. **A band** – area of the sarcomere extending from one end of the myosin to the other end, includes the M line, the H zone, and the area where actin and myosin overlap
        d. **Z disk** – the area of the sarcomere indicating the ends of the sarcomere and the attachment site for actin filaments.
        e. **I band** – area that includes the Z disk , made out of 2 ends of adjoining sarcomeres, and composed of actin only (no myosin)
    2. **Sliding filament model** – used to show/explain muscle contraction with one sarcomere – in this model myosin and actin filaments slide past one another shortening or narrowing the H zone and I band, the filaments themselves ***do not*** shorten.

G. **Skeletal Muscle Contraction** (step-by-step starting with depolarization of motor neuron) – Brain triggers an action potential which travels down the spine to the motor neuron which depolarizes carrying the action potential to the presynaptic terminal causing $Ca^{2+}$ voltage gated channels to open - $Ca^{2+}$ from the extra cellular fluid rushes into the terminal and stimulates the release (exocytosis of the synaptic vesicles) of acetylcholine (a neurotransmitter) into the synaptic cleft – acetylcholine then binds to the ligand gated $Na^{+}$ channels of the postsynaptic membrane opening them to allow passage of $Na^{+}$ to enter the cell – this stimulates voltage gated $Na^{+}$ channels to open along the rest of the muscle fiber and down the T tubules allowing even more $Na^{+}$ to enter the cell – $Na^{+}$ entering the muscle fiber stimulate the sarcoplasmic reticulum to depolarize (which stores calcium, $Ca^{2+}$) releasing $Ca^{2+}$ into the sarcoplasm where it attaches to binding sites on the troponin – the troponin then undergoes a shape change that moves it out of the way exposing the tropomyosin binding sites of the actin – exposure of these sites cause the myosin heads to bind to them forming <u>*cross bridges*</u> – the myosin then uses ATP (which also has a binding site on the myosin head) and myosinatpase (which severs ATP bonds) to perform the power strokes that ratchet the actin along the myosin toward the M line. ***Remember this takes all of about 1 to 2 milliseconds!***
    1. **Rigor mortis** – is caused by cross bridges that have not been released because of a lack of ATP after death – after 7 to 8 hour this condition subsides due to decomposition (the process of natural denaturing of proteins, which make up the actin and myosin, releasing the cross bridges)
    2. **2nd Law of Thermodynamics** – all systems in the universe go from a state of order to a state of disorder – corollary: any time you convert from one type of energy to another type of energy there will be a loss – in muscle contraction, where we go from chemical energy to mechanical energy, the *loss* of energy is given up by heat

H. **Muscle Twitch, Summation, Tetanus, & Recruitment**
    1. **Muscle Twitch** – the contraction of a muscle fiber in response to a stimulus – muscles contract in an <u>*all*</u> or <u>*nothing*</u> fashion – has 3 phases taking 1 to 2 ms
        a. **lag phase** – the time between stimulus application and the beginning of contraction – from the time the action potential is produced in the motor

neuron to the time the $Ca^{2+}$ binds to the troponin causing exposure of the tropomyosin binding sites

b. **contraction phase** – the time it takes the muscle fiber to contract all the way – results from cross bridge formation, movement, and cycling

c. **relaxation phase** – the time during which the muscle relaxes – when $Ca^{2+}$ is actively transported back into the sarcoplasmic reticulum (via the calcium pump) causing the troponin too shape change back to where it blocks (covers) the tropomyosin binding sites

2. **Strength of Contraction/Muscle Force** – graded contraction of a muscle – achieved one of two ways

a. **summation** – increasing the force of contraction by rapid and repeated stimulation of *specific* muscle fibers within a muscle – when the *stimulus frequency* is such that a specific muscle fiber has reached *tetanus*

- stimulus frequency – the number of times per second that a motor neuron is stimulated
- tetanus – stimulus frequency is so rapid that there is no relaxation phase - achieving full contraction force as a result of the $Ca^{2+}$ being repeatedly released from the sarcoplasmic reticulum (SR) faster than it can be transported back into the SR there by keeping the tropomyosin binding sites exposed

b. **recruitment** – the strength of contraction of a muscle is increased by increasing the number of motor neurons stimulated (which increases the number of muscle fibers depolarized) – maximum force of contraction in a muscle happens when ***all*** the motor units innervating ***all*** the muscle fibers of that muscle are stimulated

*****Because motor units are recruited gradually some motor units are stimulated and held in tetanus as other units are added to produce slow, smooth, sustained contraction (movement).

I. **Muscle's Energy Requirements** – during periods of activity muscles obtain ATP (adenosine triphosphate) from 4 sources

1. **Free ATP** – already existing in the cell – produced by the mitochondria to maintain certain cellular activity (active transport, protein production, etc…) – *this is used first*

2. **Phosphagen System** – enzymes that can convert different molecules to extra ATP for muscle contraction during activity for a short period of time, extending initial muscle activity – *this is used second*

a. **creatinekinase** (creatinephosphokinase) - is an enzyme that can take 1 creatinephosphate + 1 ADP (adenosine diphospate) and convert them to 1 creatine (an energy storing molecule) and 1 ATP

b. **myokinase** - is another enzyme that can take 2 ADP and convert them into 1 ATP and 1 AMP (adenosine monophosphate)

3. **Anaerobic Respiration** – this process ***occurs in the sarcoplasm*** of muscle fiber, ***does not require oxygen***, ***uses only glucose*** - this process is *glycolysis* in which 1 glucose ($C_6H_{12}O_6$) is acted on by glycolitic enzymes that break the glucose down into 2 pyruvic acids and 4 ATP however this process uses 2 ATP so the muscle has a net gain of only 2 ATP – unfortunately the end product of this process is lactic acid (created by the pyruvic acid) which interferes with the glycolitic enzyme's ability to perform glycolysis, it also irritates the muscle fibers causing pain so the process can continue for only a short time as a *stop-gap measure* – lactic acid diffuses

into the blood lowering the pH which causes respiration to increase – ***used third***

4. **Aerobic Respiration** – is a continuation from anaerobic respiration – ***requires oxygen, performed in the mitochondria, and can use glucose, lipids, or amino acids*** (proteins) – starts with glycolysis which produces 2 pyruvic acids that in the presence of oxygen are converted into acetyl coenzyme A which enters the mitochondria to run in two processes, the *Krebs cycle* & *Electron transport chain*, where the glucose in the presence of oxygen is disassembled and reassembled into carbon dioxide and water – producing 36 ATP – a total of 38 ATP are produced (2 ATP by glycolysis + 36 ATP by Krebs cycle and Electron transport chain)
    - $C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + Ⓔ$
      $\downarrow$
      $36 \times ADP + Pi \rightarrow ATP$

*****When you exercise – causing physiological changes to occur – your respiratory system always runs a little behind. Hence you don't start breathing hard when you first start to exercise but soon after and when you've completed exercise your respiration rate and volume remain elevated for a short time in order to catch up with the changes that occurred. This is called ***paying the oxygen dept*** because oxygen is required to restore the following chemical levels: conversion of lactic acid build-up to glucose; replenish depleted ATP and creatinephosphate stores in the muscle fibers; replenish $O_2$ stores in the lungs, blood, and muscle.

J. **Fatigue**
    1. **Psychological Fatigue** – is the most common type of fatigue – involving the central nervous system (CNS) rather than the muscles – individual perceives that muscle contraction can not continue – can be overcome
    2. **Muscle Fatigue** – results when ATP is used for muscle contraction faster than can be produced by muscle fibers and lactic acid builds up faster than can be removed – muscle contractions become weaker and weaker
    3. **Muscle Contracture** – under extreme muscular fatigue muscles may become incapable of either contracting or relaxing – this occurs when there is too little ATP to bind to myosin filaments
K. **Types of Muscle Contractions**
    1. **Isometric Contractions** – the amount of tension increases but the length of muscle does not change
    2. **Isotonic Contractions** – the amount of tension is constant and the muscle length decreases
        a. **Concentric Contractions** – isotonic contractions in which muscle tension increases as the length decreases
        b. **Eccentric Contractions** – isotonic contractions in which muscle tension is maintained as the muscle length increases
L. **Muscle Tone** – the constant tension produced by muscle over a long period of time – keeps our back and legs straight and our heads in an upright position also keeps our abdomens from bulging – depends on a small amount of ***all*** motor units in certain muscles being stimulated to contract tectonically but out of phase with one another
M. **Slow and Fast Fibers** – classification based on differences in the rod portion of the myosin filament – both are found through out human skeletal muscle with no clear separations

1. **Slow-twitch Fibers** – contain type I myosin as the predominant or exclusive type – they are darker in appearance due to richer blood supply and the presence ***myoglobin*** (is an oxygen binding protein which stores oxygen in muscle) – they contract more slowly but are more fatigue resistant – they have more mitochondria making them better suited for aerobic metabolism – generally more are found in large postural muscles - Marathoner
2. **Fast-twitch Fibers** – contain type II or IIx myosin – contract quickly and fatigue quickly – they are whitish in appearance - contain large stores of glycogen making them well adapted for anaerobic metabolism – generally found more in upper limbs – Sprinter

III. **Smooth and Cardiac Muscle**

A. **Smooth Muscle** – small spindle shape with one centrally located nucleus – capable of mitotic division – contract more slowly than skeletal muscle and ***do not*** develop an oxygen dept – are autorhythmic, involuntary, and sometimes stimulated by hormones (regulation in the digestive system) – found in the walls of the hollow organs of the body (stomach, intestines, blood vessels, eye's iris, bladder) – ***non-striated*** but thick and thin filaments are present – ***no*** Z disks instead thin filaments are attached by way of cytoskeleton to ***dense bodies*** (little masses of protein on the inner face of the sarcolemma – scant sarcoplasmic reticulum and ***no*** T-tubules – calcium needed for contraction comes from extra cellular fluid (ECF) by way of calcium channels (pumped back out by the calcium pump during relaxation) – nerve supply (when present) is autonomic – 2 types

1. **Multi Unit** – located in some of the largest arteries, air passages, erector pili muscles, and the iris – terminal branches of nerve axons synapse with individual myocytes forming motor units, however, they are autonomic with each motor unit contracting separately
2. **Single Unit** (visceral muscle) – located in most blood vessels as well as digestive, respiratory, urinary, and reproductive tracts – myocytes are arranged in two layers (inner circular and outer longitudinal) and are connected by gap junctions (which allow specific molecules and ions to pass between cells; communication) – an autonomic neuron passes between the two layers and has thousands of ***varicosities*** (bead like swellings containing mitochondria (ATP production) and synaptic vesicles (neurotransmitters) which wash over the myocytes when released and attach to receptor sites in the sarcolemma called ***diffusion junctions***) – when stimulated these myocytes act as one contracting all together
3. **Stimulation, Contraction, and Relaxation**
    a. **Contraction** – in response to hormones, carbon dioxide, low pH, oxygen deficiency and stretch – *triggered* by $Ca^{2+}$ , *energized* by ATP, *achieved* by the sliding of filaments – little $Ca^{2+}$ comes from the SR (sarcoplasmic reticulum) most comes from the ECF (extracellular fluid) and enters the cell by calcium channels in the sarcolemma, some voltage-gated & some ligand-gated (in the response to hormones and neurotransmitters) and some mechanically-gated (in response to stretch) – ***has no troponin*** instead it has a protein **calmodulin** (which is associated with the myosin instead of the actin) – activates an enzyme, **myosin light-chain kinase** (which transfers a phosphate group (P) from ATP to the myosin head – this in turn activates ***myosin ATPase*** enabling it to bind to actin – however the myosin must bind and hydrolyze another ATP to make the power stroke) – thick filaments pull on the thin filaments which pull on the intermediate filaments that

pull on the dense bodies of the plasma membrane shortening the ***entire*** cell in a twisting like motion (like wringing a towel). Contraction phases (*latent* about 0.1 sec, *contraction* about 0.5 sec, and *relaxation* about 1-2 sec) take 2-3 sec because of the **myosin latch-bridge mechanism** which allows the myosin to stay attached to the actin for a prolonged period of time ***without*** ATP consumption – this makes smooth muscle much more efficient in ATP usage than skeletal muscle (smooth muscle uses about $1/10^{th}$ the amount of ATP than skeletal muscle for the same amount of contraction) – making smooth muscle ***very fatigue resistant*** and enabling maintenance of smooth muscle tone (tonic contraction)

b. **Stress relaxation Responses**
   - **Receptive** relaxation - smooth muscle, when briefly stretched, will contract and resist then relax (urinary bladder)
   - **Peristalsis** – contractions that propel contents along the organ (esophagus and colon)

B. **Cardiac Muscle** – long, striated, and branching with usually only one nucleus per cell – containing actin and myosin organized into sarcomeres but distribution is not as uniform as skeletal muscle – contractions are *autorythmic* and *aerobic* (does not fatigue) – contraction time is 300-500 msec – is rich in myoglobin and glycogen – contains large amount of mitochondria – is vulnerable to oxygen loss – has a sarcoplasmic reticulum that is less developed than skeletal muscle however its T-tubules are larger to allow for more $Ca^{2+}$ from the ECF – has both sympathetic and parasympathetic stimulation

1. **Cardiac Conduction** – autorythmic – start at the SA node (group of cells that leak sodium, $Na^+$) – *pacemaker potential* myocytes in the SA node sit at about $^-$60mv (at repolarization with no true RMP) but because they leak $Na^+$ (into the cell) that number tends to drift up toward 0mv and with no compensating out flow of potassium ($K^+$) at $^-$40mv $Ca^{2+}$ channels open and $Ca^{2+}$ rushes into the cell finishing depolarization – when the cell reaches about 0mv (or a little above) it causes voltage-gated $Na^+$ channels to open on the rest of the myocytes – intercalated disks pass the electrical action potential along – myocytes outside the SA node have a RMP (resting membrane potential) of about $^-$90mv - as $Na^+$ channels open depolarizing the cells until they $^+$30mv – when they hit 0mv (on the way up to $^+$30mv) voltage-gated $Ca^{2+}$ channels open ($Ca^{2+}$ into the cell) causing a plateau effect – at $^+$30mv $Na^+$ and $Ca^{2+}$ channels close and as efflux (out of cell) of $K^+$ occurs repolarizing the myocytes back to $^-$90mv and the *sodium-potassium pumps* and *calcium pumps* restore ionic levels in the cell
2. **Sympathetic stimulation** – of the SA node by an autonomic neuron (by neurotransmitters) causes $Na^+$ channels to open increasing the rate at which the pacemaker potential occurs
3. **Parasympathetic stimulation** – will inhibit $Na^+$ channel

C. **Hypertrophy & Hyperplasia**

1. **hypertrophy** – increased muscle size due to increased myofibril content (per transcription and translation) – skeletal muscles – ***no mitotic division***
2. **hyperplasia** – increased muscle size due to increased cell numbers – smooth muscle (uterus during pregnancy)
3. **atrophy** – decreased muscle size due to decrease in myofibril content
4. **flaccid** – no muscle tone due to lack of intervation by motor neuron

IV. **General Anatomical Terms/Skeletal Muscle**

A. **Tendon** – extension of the epimysium – connects muscle to bone
B. **Aponeuroses** – sheet like tendons
C. **Origin** – the head or most stationary end of the muscle
D. **Insertion** – the end of the muscle attached to the bone undergoing the greatest movement
E. **Belly** – largest part of the muscle between origin and insertion
F. **Agonist** – a muscle that accomplishes a certain movement
G. **Antagonist** – a muscle acting in opposition to the agonist
H. **Synergist** – members of a group of muscles working together to produce a movement (Quads)
I. **Prime mover** – the muscle, in a group of synergists, that is responsible for the majority of that movement
J. **Flexors** – muscles that decrease angle across a joint
K. **Extensors** – muscles that increase angle across a joint