Muscle Tissue

- Alternating contraction and relaxation of cells

- Chemical energy changed into mechanical energy

3 Types of Muscle Tissue

- Skeletal muscle
  - attaches to bone, skin or fascia
  - striated with light & dark bands visible with scope
  - voluntary control of contraction & relaxation
  - multinucleated

- Cardiac muscle
  - striated in appearance
  - involuntary control
  - autorhythmic because of built in pacemaker

- Smooth muscle
  - attached to hair follicles in skin
  - in walls of hollow organs -- blood vessels & GI
  - nonstriated in appearance
  - involuntary

Functions of Muscle Tissue

- Producing body movements
- Stabilizing body positions
- Regulating organ volumes
  - bands of smooth muscle called sphincters
- Movement of substances within the body
  - blood, lymph, urine, air, food and fluids, sperm
- Producing heat
  - involuntary contractions of skeletal muscle (shivering)

Properties of Muscle Tissue

- Excitability
  - respond to chemicals released from nerve cells
- Conductivity
  - ability to propagate electrical signals over membrane
- Contractility
  - ability to shorten and generate force
- Extensibility
  - ability to be stretched without damaging the tissue

- Elasticity
  - ability to return to original shape after being stretched

Skeletal Muscle -- Connective Tissue

- Superficial fascia is loose connective tissue & fat underlying the skin
- Deep fascia = dense irregular connective tissue around muscle
- Connective tissue components of the muscle include
  - epimysium = surrounds the whole muscle
  - perimysium = surrounds bundles (fascicles) of 10-100 muscle cells
  - endomysium = separates individual muscle cells
- All these connective tissue layers extend beyond the muscle belly to form the tendon

Nerve and Blood Supply

- Each skeletal muscle is supplied by a nerve, artery and two veins.
- Each motor neuron supplies multiple muscle cells (neuromuscular junction)
- Each muscle cell is supplied by one motor neuron terminal branch and is in contact with one or two capillaries.
  - nerve fibers & capillaries are found in the endomysium between individual cells

Fusion of Myoblasts into Muscle Fibers

- Every mature muscle cell developed from 100 myoblasts that fuse together in the fetus. (multinucleated)
- Mature muscle cells can not divide
- Muscle growth is a result of cellular enlargement & not cell division
- Satellite cells retain the ability to regenerate new cells.

Muscle Fiber or Myofibers

- Muscle cells are long, cylindrical & multinucleated
- Sarcolemma = muscle cell membrane
- Sarcoplasm filled with tiny threads called myofibrils & myoglobin (red-colored, oxygen-binding protein)

Transverse Tubules

- T (transverse) tubules are invaginations of the sarcolemma into the center of the cell
  - filled with extracellular fluid
  - carry muscle action potentials down into cell
- Mitochondria lie in rows throughout the cell
  - near the muscle proteins that use ATP during contraction

Myofibrils & Myofilaments

- Muscle fibers are filled with threads called myofibrils separated by SR (sarcoplasmic reticulum)
- Myofilaments (thick & thin filaments) are the contractile proteins of muscle

Sarcoplasmic Reticulum (SR)

- System of tubular sacs similar to smooth ER in nonmuscle cells
- Stores Ca^{+2} in a relaxed muscle
- Release of Ca^{+2} triggers muscle contraction

Filaments and the Sarcomere

- Thick and thin filaments overlap each other in a pattern that creates striations (light I bands and dark A bands)
- The I band region contains only thin filaments.
- They are arranged in compartments called sarcomeres, separated by Z discs.
- In the overlap region, six thin filaments surround each thick filament

Thick & Thin Myofilaments

- Supporting proteins (M line, titin and Z disc help anchor the thick and thin filaments in place)

Overlap of Thick & Thin Myofilaments within a Myofibril

The Proteins of Muscle

- Myofibrils are built of 3 kinds of protein
  - contractile proteins
    - myosin and actin
  - regulatory proteins which turn contraction on & off
    - troponin and tropomyosin
  - structural proteins which provide proper alignment, elasticity and extensibility
    - titin, myomesin, nebulin and dystrophin

Myosin

- Thick filaments are composed of myosin
  - each molecule resembles two golf clubs twisted together
  - myosin heads (cross bridges) extend toward the thin filaments
- Held in place by the M line proteins.

Actin

- Thin filaments are made of actin, troponin, & tropomyosin
- The myosin-binding site on each actin molecule is covered by tropomyosin in relaxed muscle
- The thin filaments are held in place by Z lines. From one Z line to the next is a sarcomere.

Titin

- Titan anchors thick filament to the M line and the Z disc.
- The portion of the molecule between the Z disc and the end of the thick filament can stretch to 4 times its resting length and spring back unharmed.
- Role in recovery of the muscle from being stretched.

Other Structural Proteins

- The M line (myomesin) connects to titin and adjacent thick filaments.
- Nebulin, an inelastic protein helps align the thin filaments.
- Dystrophin links thin filaments to sarcolemma and transmits the tension generated to the tendon.

Sliding Filament Mechanism Of Contraction

- Myosin cross bridges pull on thin filaments
- Thin filaments slide inward
- Z Discs come toward each other
- Sarcomeres shorten.The muscle fiber shortens. The muscle shortens
- Notice :Thick & thin filaments do not change in length

How Does Contraction Begin?

- Nerve impulse reaches an axon terminal & synaptic vesicles release acetylcholine (ACh)
- ACh diffuses to receptors on the sarcolemma & Na+ channels open and Na+ rushes into the cell
- A muscle action potential spreads over sarcolemma and down into the transverse tubules
- SR releases Ca+2 into the sarcoplasm
- Ca+2 binds to troponin & causes troponin-tropomyosin complex to move & reveal myosin binding sites on actin--the contraction cycle begins

Excitation - Contraction Coupling

- All the steps that occur from the muscle action potential reaching the T tubule to contraction of the muscle fiber.

Contraction Cycle

- Repeating sequence of events that cause the thick & thin filaments to move past each other.
- 4 steps to contraction cycle
  - ATP hydrolysis
  - attachment of myosin to actin to form crossbridges
  - power stroke
  - detachment of myosin from actin
- Cycle keeps repeating as long as there is ATP available & high Ca+2 level near thin filament

Steps in the Contraction Cycle

- Notice how the myosin head attaches and pulls on the thin filament with the energy released from ATP

ATP and Myosin

- Myosin heads are activated by ATP
- Activated heads attach to actin & pull (power stroke)
- ADP is released. (ATP released P & ADP & energy)

- Thin filaments slide past the thick filaments
- ATP binds to myosin head & detaches it from actin
- All of these steps repeat over and over
  - if ATP is available &
  - Ca+ level near the troponin-tropomyosin complex is high

Overview: From Start to Finish

- Nerve ending
- Neurotransmittor
- Muscle membrane
- Stored Ca+2
- ATP
- Muscle proteins

Relaxation

- Acetylcholinesterase (AChE) breaks down ACh within the synaptic cleft
- Muscle action potential ceases
- Ca+2 release channels close
- Active transport pumps Ca2+ back into storage in the sarcoplasmic reticulum
- Calcium-binding protein (calsequestrin) helps hold Ca+2 in SR (Ca+2 concentration 10,000 times higher than in cytosol)
- Tropomyosin-troponin complex recovers binding site on the actin

Length of Muscle Fibers

- Optimal overlap of thick & thin filaments
  - produces greatest number of crossbridges and the greatest amount of tension
- As stretch muscle (past optimal length)
  - fewer cross bridges exist & less force is produced
- If muscle is overly shortened (less than optimal)
  - fewer cross bridges exist & less force is produced
  - thick filaments crumpled by Z discs
- Normally
  - resting muscle length remains between 70 to 130% of the optimum

Neuromuscular Junction (NMJ) or Synapse

- NMJ = myoneural junction
  - **end of axon nears the surface of a muscle fiber at its motor end plate region (remain separated by synaptic cleft or gap)**

Structures of NMJ Region

- Synaptic end bulbs are swellings of axon terminals
- End bulbs contain synaptic vesicles filled with acetylcholine (ACh)
- Motor end plate membrane contains 30 million ACh receptors.

Events Occurring After a Nerve Signal

- Arrival of nerve impulse at nerve terminal causes release of ACh from synaptic vesicles
- ACh binds to receptors on muscle motor end plate opening the gated ion channels so that Na+ can rush into the muscle cell
- Inside of muscle cell becomes more positive, triggering a muscle action potential that travels over the cell and down the T tubules
- The release of Ca+2 from the SR is triggered and the muscle cell will shorten & generate force
- Acetylcholinesterase breaks down the ACh attached to the receptors on the motor end plate so the muscle action potential will cease and the muscle cell will relax.

Muscle Metabolism

Production of ATP in Muscle Fibers

- Muscle uses ATP at a great rate when active
- Sarcoplasmic ATP only lasts for few seconds
- 3 sources of ATP production within muscle
  - creatine phosphate
  - aerobic cellular respiration
  - anaerobic cellular respiration

Creatine Phosphate

- Excess ATP within resting muscle used to form creatine phosphate
- Creatine phosphate 3-6 times more plentiful than ATP within muscle
- Its quick breakdown provides energy for creation of ATP
- Sustains maximal contraction for 15 sec (used for 100 meter dash).
- Athletes tried creatine supplementation
  - gain muscle mass but shut down bodies own synthesis (safety?)

Anaerobic Cellular Respiration

- ATP produced from glucose breakdown into pyruvic acid during glycolysis
  - if no O2 present
    - **pyruvic converted to lactic acid which diffuses into the blood**
- Glycolysis can continue anaerobically to provide ATP for 30 to 40 seconds of maximal activity (200 meter race)

Aerobic Cellular Respiration

- ATP for any activity lasting over 30 seconds
  - if sufficient oxygen is available, pyruvic acid enters the mitochondria to generate ATP, water and heat
  - fatty acids and amino acids can also be used by the mitochondria
- Provides 90% of ATP energy if activity lasts more than 10 minutes

Muscle Fatigue

- Inability to contract after prolonged activity
  - central fatigue is feeling of tiredness and a desire to stop (protective mechanism)
  - depletion of creatine phosphate
  - decline of Ca^{+2} within the sarcoplasm
- Factors that contribute to muscle fatigue
  - insufficient oxygen or glycogen
  - buildup of lactic acid and ADP
  - insufficient release of acetylcholine from motor neurons

Oxygen Consumption after Exercise

- Muscle tissue has two sources of oxygen.
  - diffuses in from the blood
  - released by myoglobin inside muscle fibers
- Aerobic system requires O_2 to produce ATP needed for prolonged activity
  - increased breathing effort during exercise
- Recovery oxygen uptake
  - elevated oxygen use after exercise (oxygen debt)
  - lactic acid is converted back to pyruvic acid
  - elevated body temperature means all reactions faster

The Motor Unit

- Motor unit = one somatic motor neuron & all the skeletal muscle cells (fibers) it stimulates
  - muscle fibers normally scattered throughout belly of muscle
  - One nerve cell supplies on average 150 muscle cells that all contract in unison.
- Total strength of a contraction depends on how many motor units are activated & how large the motor units are

Twitch Contraction

- Brief contraction of all fibers in a motor unit in response to
  - single action potential in its motor neuron
  - electrical stimulation of the neuron or muscle fibers
- Myogram = graph of a twitch contraction
  - the action potential lasts 1-2 msec
  - the twitch contraction lasts from 20 to 200 msec

Parts of a Twitch Contraction

- Latent Period--2msec
  - Ca+2 is being released from SR
  - slack is being removed from elastic components
- Contraction Period
  - 10 to 100 msec
  - filaments slide past each other
- Relaxation Period
  - 10 to 100 msec
  - active transport of Ca+2 into SR
- Refractory Period
  - muscle can not respond and has lost its excitability
  - 5 msec for skeletal & 300 msec for cardiac muscle

Wave Summation

- If second stimulation applied after the refractory period but before complete muscle relaxation---second contraction is stronger than first

Complete and Incomplete Tetanus

- Unfused tetanus
  - if stimulate at 20-30 times/second, there will be only partial relaxation between stimuli
- Fused tetanus
  - if stimulate at 80-100 times/second, a sustained contraction with no relaxation between stimuli will result

Explanation of Summation & Tetanus

- Wave summation & both types of tetanus result from Ca+2 remaining in the sarcoplasm
- Force of 2nd contraction is easily added to the first, because the elastic elements remain partially contracted and do not delay the beginning of the next contraction

Motor Unit Recruitment

- Motor units in a whole muscle fire asynchronously
  - some fibers are active others are relaxed
  - delays muscle fatigue so contraction can be sustained
- Produces smooth muscular contraction
  - not series of jerky movements
- Precise movements require smaller contractions
  - motor units must be smaller (less fibers/nerve)
- Large motor units are active when large tension is needed

Muscle Tone

- Involuntary contraction of a small number of motor units (alternately active and inactive in a constantly shifting pattern)
  - keeps muscles firm even though relaxed
  - does not produce movement

- Essential for maintaining posture (head upright)
- Important in maintaining blood pressure
  - tone of smooth muscles in walls of blood vessels

Isotonic and Isometric Contraction

- Isotonic contractions = a load is moved
  - concentric contraction = a muscle shortens to produce force and movement
  - eccentric contractions = a muscle lengthens while maintaining force and movement
- Isometric contraction = no movement occurs
  - tension is generated without muscle shortening
  - maintaining posture & supports objects in a fixed position

Classification of Muscle Fibers

- Slow oxidative (slow-twitch)
  - red in color (lots of mitochondria, myoglobin & blood vessels)
  - prolonged, sustained contractions for maintaining posture
- Fast oxidative-glycolytic (fast-twitch A)
  - red in color (lots of mitochondria, myoglobin & blood vessels)
  - split ATP at very fast rate; used for walking and sprinting
- Fast glycolytic (fast-twitch B)
  - white in color (few mitochondria & BV, low myoglobin)
  - anaerobic movements for short duration; used for weight-lifting

Fiber Types within a Whole Muscle

- Most muscles contain a mixture of all three fiber types
- Proportions vary with the usual action of the muscle
  - neck, back and leg muscles have a higher proportion of postural, slow oxidative fibers
  - shoulder and arm muscles have a higher proportion of fast glycolytic fibers
- All fibers of any one motor unit are same.
- Different fibers are recruited as needed.

Anatomy of Cardiac Muscle

- Striated , short, quadrangular-shaped, branching fibers
- Single centrally located nucleus
- Cells connected by intercalated discs with gap junctions
- Same arrangement of thick & thin filaments as skeletal

Cardiac versus Skeletal Muscle

- More sarcoplasm and mitochondria
- Larger transverse tubules located at Z discs, rather than at A-l band junctions
- Less well-developed SR
- Limited intracellular Ca^{+2} reserves
  - more Ca^{+2} enters cell from extracellular fluid during contraction

- Prolonged delivery of Ca^{+2} to sarcoplasm, produces a contraction that last 10 -15 times longer than in skeletal muscle

Appearance of Cardiac Muscle

- Striated muscle containing thick & thin filaments
- T tubules located at Z discs & less SR

Physiology of Cardiac Muscle

- Autorhythmic cells
  - contract without stimulation
- Contracts 75 times per min & needs lots O_2
- Larger mitochondria generate ATP aerobically
- Sustained contraction possible due to slow Ca^{+2} delivery
  - Ca^{+2} channels to the extracellular fluid stay open

Two Types of Smooth Muscle

- Visceral (single-unit)
  - **in the walls of hollow viscera & small BV**
  - **autorhythmic**
  - **gap junctions cause fibers to contract in unison**
- Multiunit
  - **individual fibers with own motor neuron ending**
  - **found in large arteries, large airways, arrector pili muscles,iris & ciliary body**

Microscopic Anatomy of Smooth Muscle

- Small, involuntary muscle cell -- tapering at ends
- Single, oval, centrally located nucleus
- Lack T tubules & have little SR for Ca^{+2} storage

Microscopic Anatomy of Smooth Muscle

- Thick & thin myofilaments
  not orderly arranged so lacks sarcomeres
- Sliding of thick & thin filaments generates tension
- Transferred to intermediate filaments & dense bodies attached to sarcolemma
- Muscle fiber contracts and twists into a helix as it shortens -- relaxes by untwisting

Physiology of Smooth Muscle

- Contraction starts slowly & lasts longer
  - no transverse tubules & very little SR
  - Ca^{+2} must flows in from outside
- Calmodulin replaces troponin
  - Ca^{+2} binds to calmodulin turning on an enzyme (myosin light chain kinase) that phosphorylates the myosin head so that contraction can occur
  - enzyme works slowly, slowing contraction

Smooth Muscle Tone

- Ca+2 moves slowly out of the cell
  - delaying relaxation and providing for state of continued partial contraction
  - sustained long-term
- Useful for maintaining blood pressure or a steady pressure on the contents of GI tract

Regulation of Contraction

- Regulation of contraction due to
  - nerve signals from autonomic nervous system
  - changes in local conditions (pH, O2, CO2, temperature & ionic concentrations)
  - hormones (epinephrine -- relaxes muscle in airways & some blood vessels)
- Stress-relaxation response
  - when stretched, initially contracts & then tension decreases to what is needed
  - stretch hollow organs as they fill & yet pressure remains fairly constant
  - when empties, muscle rebounds & walls firm up

Regeneration of Muscle

- Skeletal muscle fibers cannot divide after 1st year
  - growth is enlargement of existing cells
  - repair
    - **satellite cells & bone marrow produce some new cells**
    - **if not enough numbers---fibrosis occurs most often**
- Cardiac muscle fibers cannot divide or regenerate
  - all healing is done by fibrosis (scar formation)
- Smooth muscle fibers (regeneration is possible)
  - cells can grow in size (hypertrophy)
  - some cells (uterus) can divide (hyperplasia)
  - new fibers can form from stem cells in BV walls