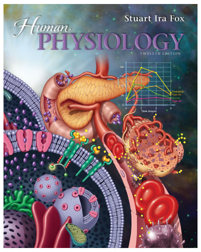
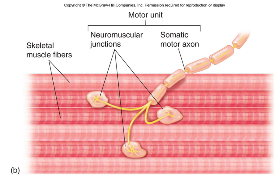


Chapter 12

Muscle: Mechanisms of Contraction and Neural Control

Lecture PowerPoint

I. Skeletal Muscles



Skeletal Muscle Action

- When a muscle contracts, it shortens.
  - This places tension on tendons connecting it to a bone.
  - This moves the bone at a joint.
  - The bone that moves is attached at the muscle insertion.
  - The muscle is attached to a bone that does not move at the muscle origin.

Skeletal Muscles

- Flexor muscles decrease the angle between two bones at a joint.
- Extensor muscles increase the angle between two bones at a joint.
  - The main muscle responsible for movement in a given direction is the agonist.
  - Flexors and extensors that work together are antagonists.

Skeletal Muscle Actions

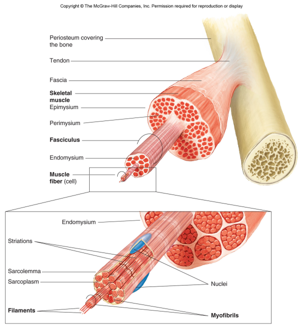
Table 12.1 | Skeletal Muscle Actions

Category	Action
Extensor	Increases the angle at a joint
Flexor	Decreases the angle at a joint
Abductor	Moves limb away from the midline of the body
Adductor	Moves limb toward the midline of the body
Levator	Moves insertion upward
Depressor	Moves insertion downward
Rotator	Rotates a bone along its axis
Sphincter	Constricts an opening

Structure of Skeletal Muscles

- Skeletal muscles are surrounded by a fibrous epimysium.
- Connective tissue called perimysium subdivides the muscle into fascicles.
- Each fascicle is subdivided into muscle fibers surrounded by endomysium.

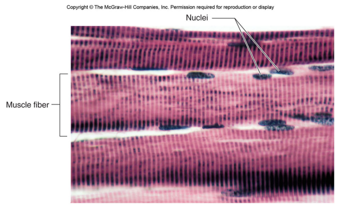
Structure of Skeletal Muscle



Muscle Fibers

- Have plasma membranes called sarcolemma
- Are multinucleated
- Are striated
  - I bands: light bands
  - A bands: dark bands

Muscle Fibers



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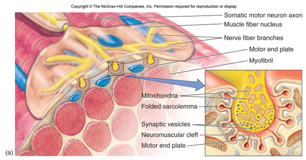
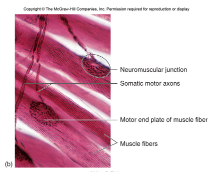
Neuromuscular Junctions and Motor End Plates

- Neuromuscular junction: site where a motor neuron stimulates a muscle fiber
- Motor end plate: area of the muscle fiber sarcolemma where a motor neuron stimulates it

Neuromuscular Junctions and Motor End Plates





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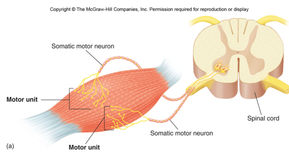
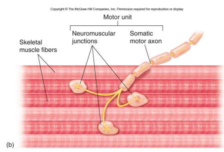
Motor Unit

- A single motor neuron and all the muscle fibers it innervates
  - All the muscle fibers in a motor unit contract at once.

Motor Unit





Motor Unit

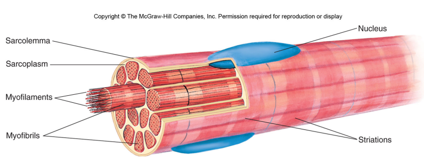
- Contraction strength comes from motor unit recruitment.
- Finer muscle control requires smaller motor units (fewer muscle fibers).
  - The eye muscles may have ~20 muscle fibers/motor units.
  - Larger, stronger muscles may have motor units with thousands of muscle fibers.
  - Control and strength are trade-offs.

II. Mechanisms of Contraction

Muscle Fibers

- Have densely packed subunits called myofibrils that run the length of the muscle fiber
  - Composed of thick and thin myofilaments

Muscle Fibers



Striations

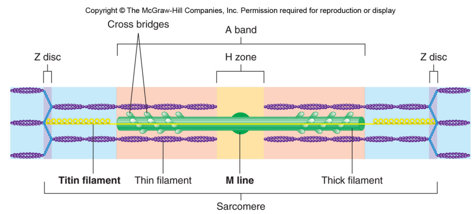
- Produced by thick and thin filaments
  - I bands contain only thin filaments.
  - A bands contain all of the thick filament with some thin filament overlap.
  - H bands are the center of the A band with no thin filament overlap.
  - Z lines are found in the center of each I band.
  - M lines are found in the center of each A band and help hold down thick filaments.

Striations

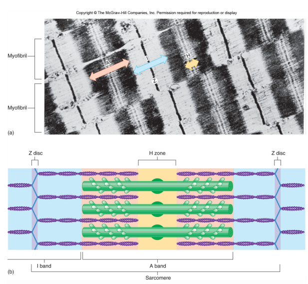
– Sarcomere: area from one Z line to the next

– Titin: protein that anchors in the thick filaments and allows elastic recoil

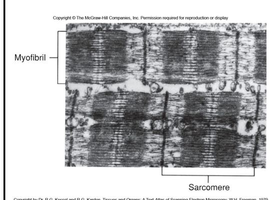
Striations

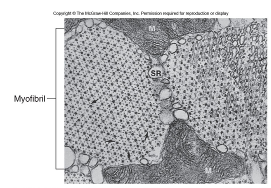


Striations



Arrangement of Thick and Thin Filaments

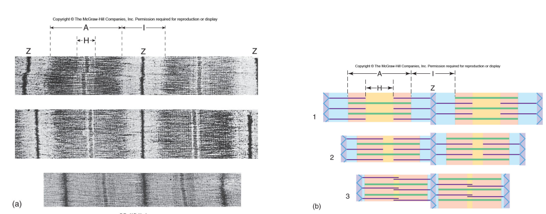




Sliding Filament Theory

- When a muscle contracts, sarcomeres shorten.
  - A bands do not shorten.
  - I bands do shorten, but thin filaments do not.
  - Thin filaments *slide* toward the H zone.

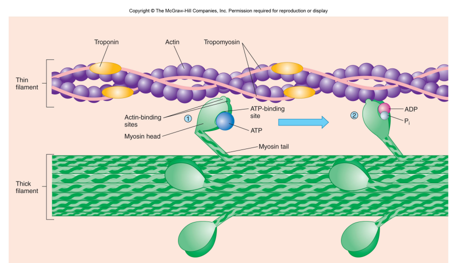
Sliding Filament Theory



More About Myofilaments

- Thick: composed of the protein myosin
  - Each protein has two globular heads with actin-binding sites and ATP-binding sites.
- Thin: composed of the protein actin
  - Have proteins called tropomyosin and troponin that prevent myosin binding at rest.

Myofilament Structure

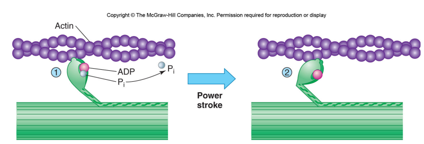


Cross Bridges

- Sliding is produced by several cross bridges that form between myosin and actin.
  - The myosin head serves as a myosin ATPase enzyme, splitting ATP into ADP + P_i.
  - This allows the head to bind to actin when the muscle is stimulated.

Cross Bridges

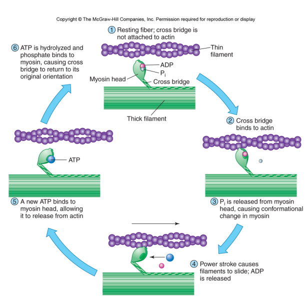
- Release of P_i upon binding cocks the myosin head, producing a power stroke that pulls the thin filament toward the center.



Cross Bridges

- After the power stroke, ADP is released and a new ATP binds.
- This makes myosin release actin.
- ATP is split.
- The myosin head straightens out and rebinds to actin farther back.

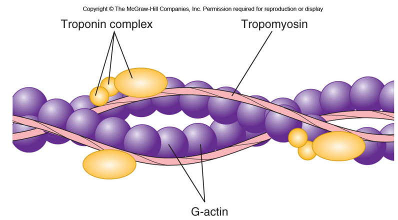
Cross Bridges



Regulation of Contraction

- Tropomyosin physically blocks cross bridges.
- Troponin complex:
  - Troponin I inhibits binding of myosin.
  - Troponin T binds to tropomyosin.
  - Troponin C binds to calcium.

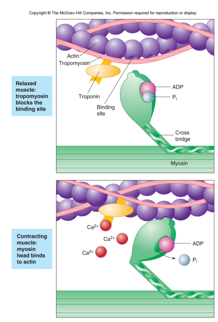
Regulation of Contraction



Role of Calcium

- When muscle cells are stimulated, Ca^{2+} is released inside the muscle fiber.
- Some attaches to troponin C, causing a conformational change in troponin and tropomyosin.
- Myosin is allowed access to form cross bridges.

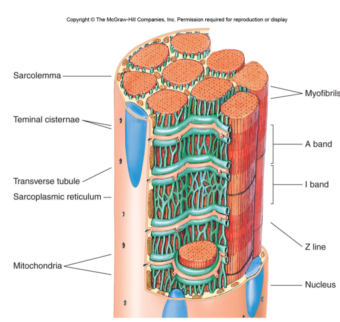
Role of Calcium



Sarcoplasmic Reticulum (SR)

- SR is modified endoplasmic reticulum that stores Ca^{2+} when muscle is at rest.
- Most is stored in terminal cisternae.

Sarcoplasmic Reticulum (SR)



Sarcoplasmic Reticulum (SR)

- When a muscle fiber is stimulated, Ca^{2+} diffuses out of calcium release channels.
- At the end of a contraction, Ca^{2+} is actively pumped back into the SR.

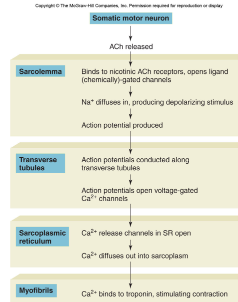
Transverse Tubules

- Narrow membranous tunnels formed from the sarcolemma
- Open to the extracellular environment
- Able to conduct action potentials
- Closely situated next to terminal cisternae

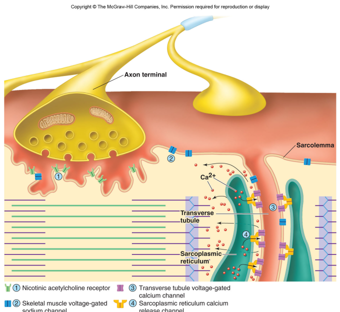
Stimulating a Muscle Fiber

1. Acetylcholine is released from the motor neuron.
2. End plate potentials are produced.
3. Action potentials are generated.
4. Voltage-gated calcium channels in transverse tubules change shape and cause calcium channels in SR to open.
5. Calcium is released and can bind to troponin C.

Excitation Contraction Coupling Summary



Stimulating a Muscle Fiber



Muscle Relaxation

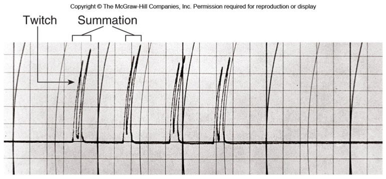
- Action potentials cease.
- Ca^{2+}-ATPase pumps move Ca^{2+} back into SR.
- No more Ca^{2+} is available to bind to troponin C, so no more cross bridges are formed.

III. Contractions of Skeletal Muscles

Studying Muscle Behavior

- Study is done in vitro where one end of the muscle is fixed and the other is movable.
- Electrical stimulations are applied, and contractions are recorded and displayed as currents.

Studying Muscle Behavior



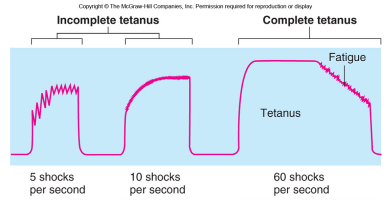
Twitch and Summation

- Twitch: when a muscle quickly contracts and relaxes after a single electrical shock of sufficient voltage
  - Increasing the voltage increases the strength of the twitch up to a maximum.
  - When a second shock is applied immediately after the first, a second twitch will partially piggyback the first. This is called summation.

Tetanus

- Increasing the frequency of electrical shocks decreases the relaxation time between twitches. This is called incomplete tetanus.
- At a certain frequency, there will be no relaxation. This is called complete tetanus.

Tetanus



Tetanus In Vivo

- Asynchronous activation of motor units
  - Some motor units start to twitch when others start to relax.
  - This produces continuous contraction of the whole muscle.
  - Recruitment makes contractions stronger.

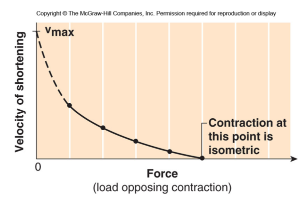
Treppe

- As the voltage is increased, the number of muscle fibers used in vitro increases.
  - This will reach a maximum value when all muscle fibers are stimulated.
  - If a fresh muscle is stimulated with several shocks at maximum voltage, each twitch will be progressively stronger.
  - When recorded, this will produce a staircase effect called treppe.

Force Velocity Curve

- For muscles to contract, they must generate force that is greater than the opposing forces.
  - The greater the force, the slower the contraction.

Force Velocity Curve



Isotonic and Isometric Contractions

- Isotonic contraction: Muscle fibers shorten when the tension produced is just greater than the load.
- Isometric contraction: Muscles can't shorten because the load is too great.
  - Can be voluntary

Concentric and Eccentric Contractions

- Concentric contraction: A muscle fiber shortens when force is greater than load.
- Eccentric contraction: A muscle may actually lengthen, despite contraction, if the load is too great.
  - Allows you to lower a weight gently after a full concentric contraction

Series Elastic Component

- Noncontractile parts of the muscle and tendons must be pulled tight when muscles contract.
- Tendons are elastic, resist distension, and snap back to resting length.
- Tendons absorb some of the tension as muscles contract.

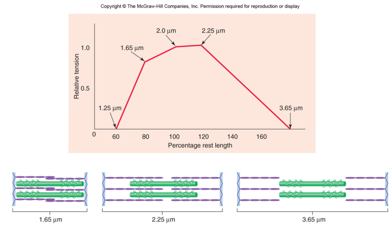
Muscle Strength

- Determined by:
  - Number of fibers recruited to contract
  - Frequency of stimulation
  - Thickness of each muscle fiber (thicker is stronger)
  - Initial length of the fiber at rest

Length-Tension Relationship

- Tension is maximal when sarcomeres are at normal resting length.
- Increasing sarcomere length decreases muscle tension.
  - There are fewer interactions between myosin and actin.
  - At a certain point, no tension can be generated.
- Decreasing sarcomere length decreases muscle tension too.

Length-Tension Relationship

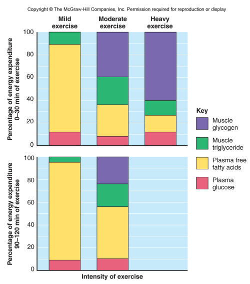


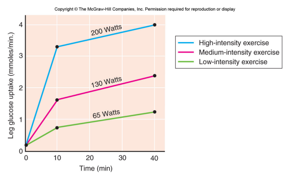
IV. Energy Requirements of Skeletal Muscles

Where Muscles Get Their Energy

- At rest and for mild exercise: from fatty acids
- For moderate exercise: from glycogen stores
- For heavy exercise: from blood glucose
  - As exercise intensity and duration increase, GLUT4 channels are inserted into the sarcolemma to allow more glucose into cells.

Where Muscles Get Their Energy





Maximal Oxygen Uptake

- Also called aerobic capacity, or V_{O_2} max
- Determines whether a given exercise is light, moderate, or heavy for a given person
- Determined by a person's age, sex, size, and athletic training
  - Greater for males and younger people
  - Ranges from 12 ml O_2/minute/kg body weight to 84 ml O_2/minute/kg body weight

Lactate Threshold

- Also called anaerobic threshold
- Another way to determine exercise intensity for a given person
- % of maximal oxygen uptake at which a rise in blood lactate levels occurs
- Occurs at about 50−70% V_{O_2} max

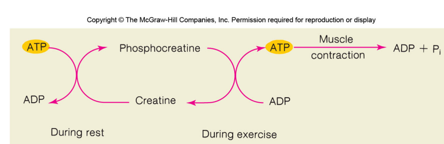
Oxygen Debt

- When a person exercises, oxygen is withdrawn from reserves in hemoglobin and myoglobin.
  - To create cross bridges in muscle contraction and pump calcium back into SR at rest
  - To metabolize lactic acid
- Breathing rate continues to be elevated after exercise to repay this debt.

Phosphocreatine

- ATP may be used faster than it can be created through cellular respiration.
- ADP is combined with P_i from phosphocreatine.
  - Creatine is produced by the liver and kidneys or obtained in the diet.
  - Phosphocreatine stores are replenished at rest.

Phosphocreatine



Slow- and Fast-Twitch Fibers

- Slow (type I): slower contraction speed; can sustain contraction for long periods without fatigue; rich capillary supply; more mitochondria; more respiratory enzymes; more myoglobin
  - Said to have high oxidative capacity, so are called slow oxidative fibers
  - Due to myoglobin content (which has a red pigment), these are also called red fibers
  - Found in postural muscles

Slow- and Fast-Twitch Fibers

- Fast (type II): faster contraction speed, fatigue fast, fewer capillaries, mitochondria, respiratory enzymes, and less myoglobin
  - Also called white fibers
  - Have more glycogen stores and are called fast glycolytic fibers
  - Found in stronger muscles

Slow- and Fast-Twitch Fibers

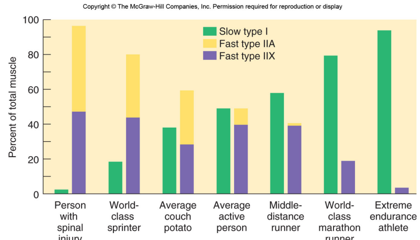
- Intermediate (type IIA): fast-twitch but with high oxidative capacity
  - Called fast oxidative fibers
- People vary greatly in the percentage of fast- or slow-twitch fibers in their muscles.
  - Result of genetics and training

Slow- and Fast-Twitch Fibers

Table 12.3 | Characteristics of Muscle Fiber Types

Feature	Slow Oxidative/Type I (Red)	Fast Oxidative/Type IIA (Red)	Fast Glycolytic/Type IIX (White)
Diameter	Small	Intermediate	Large
Z-line thickness	Wide	Intermediate	Narrow
Glycogen content	Low	Intermediate	High
Resistance to fatigue	High	Intermediate	Low
Capillaries	Many	Many	Few
Myoglobin content	High	High	Low
Respiration	Aerobic	Aerobic	Anaerobic
Oxidative capacity	High	High	Low
Glycolytic ability	Low	High	High
Twitch rate	Slow	Fast	Fast
Myosin ATPase content	Low	High	High

Slow- and Fast-Twitch Fibers



Muscle Fatigue

- Reduced ability to generate force
- Due to:
  - Accumulation of extracellular K^+, reducing membrane potential
    - Short duration
  - Depletion of stored glycogen
  - Reduced SR calcium release

Muscle Fatigue

- Lactic acid accumulation and lower pH
- Increased concentration of PO_4 due to phosphocreatine breakdown
- Lack of ATP
- Buildup of ADP
- Fatigue of upper motor neurons, called central fatigue

Adaptation to Endurance Exercise Training

- Increased ability to use fatty acids as fuel and increased intracellular triglyceride storage
- Decrease in type II and increase in type IIa muscle fibers
- Increase in number of mitochondria

Adaptation to Endurance Exercise Training

Table 12.4 | Effects of Endurance Training on Skeletal Muscles

1.	Improved ability to obtain ATP from oxidative phosphorylation
2.	Increased size and number of mitochondria
3.	Less lactic acid produced per given amount of exercise
4.	Increased myoglobin content
5.	Increased intramuscular triglyceride content
6.	Increased lipoprotein lipase (enzyme needed to utilize lipids from blood)
7.	Increased proportion of energy derived from fat; less from carbohydrates
8.	Lower rate of glycogen depletion during exercise
9.	Improved efficiency in extracting oxygen from blood
10.	Decreased number of type IIX (fast glycolytic) fibers; increased number of type IIA (fast oxidative) fibers

Adaptation to Strength Training

- Hypertrophy: Type II muscle fibers become thicker due to increased amount of actin and myosin (more sarcomeres).
  - Thicker fibers can split into two fibers, which can also increase in size.
  - Requires the addition of three more proteins that serve as muscle fiber scaffolding:
    - Titin
    - Nebulin
    - Obscurin

Muscle Repair

- Skeletal muscles have stem cells called satellite cells located near muscle fibers.
  - These can fuse to damaged muscle cells and repair them or fuse to each other to form new muscle fibers.
  - Myostatin is a paracrine regulator that inhibits satellite cells.

Muscle Decline with Aging

- Reduced muscle mass (usually type II fibers)
  - Can be helped with strength training
- Reduction in capillary blood supply
  - Can be helped with endurance training
- Fewer satellite cells, increased myostatin production

V. Neural Control of Skeletal Muscles

Lower Motor Neurons

- Cell bodies in ventral horn of spinal cord
- Influenced by:
  - Sensory feedback from muscles and tendons
  - Stimulation or inhibition from higher motor neurons from brain

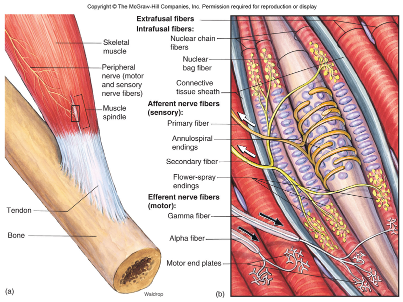
Muscle Sensory Organs

- Golgi tendon organs: respond to tension a muscle puts on a tendon
- Muscle spindle apparatus: respond to muscle length
  - Muscles that require more control have more spindles.
  - Stretching a muscle causes spindles to stretch.

Muscle Spindle Apparatus

- Contains thin muscle cells called intrafusal fibers
- Two types:
  - Nuclear bag fibers
  - Nuclear chain fibers
- Two types of sensory cells wrap around the fibers:
  - Primary (annulospiral)
  - Secondary (flower-spray)

Muscle Spindle Apparatus



Types of Lower Motor Neurons

- Alpha: innervate extrafusal (contracting) muscle fibers
- Gamma: innervate intrafusal (stretch) muscle fibers
  - Contraction of these fibers does not shorten the muscle, but does increase sensitivity to stretch.
- These are stimulated by upper motor neurons at the same time = coactivation

Skeletal Muscle Reflexes

- Skeletal muscles are usually referred to as voluntary and are controlled by higher brain regions.
- They can also contract unconsciously in response to certain stimuli.

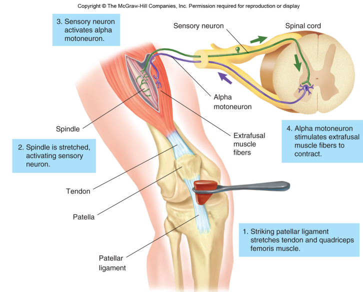
Monosynaptic Stretch Reflex

- Simplest reflex
- Only involves a sensory neuron synapsing on a motor neuron in the spinal cord
  - One synapse = monosynaptic
- Maintains optimal resting length of skeletal muscles
- Can be stimulated by striking the patellar ligament in the "knee-jerk reflex"

Monosynaptic Stretch Reflex

1. Stretch on a muscle stretches spindle fibers.
2. This activates sensory neuron.
3. Sensory neuron activates alpha motor neuron.
4. Motor neuron stimulates extrafusal muscle fiber to contract.
5. Stretch on spindle is reduced.

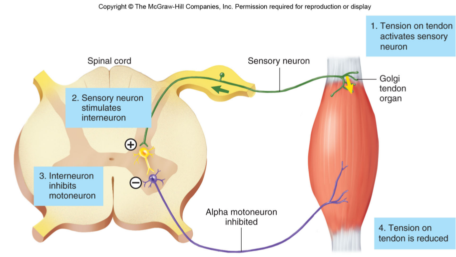
Knee-Jerk Reflex



Golgi Tendon Organs

- Constantly monitor tension in tendons
  - Sensory neuron stimulates interneuron in spinal cord.
  - Interneuron inhibits motor neuron.
  - Tension in tendon is reduced.
- Disynaptic reflex involving two synapses

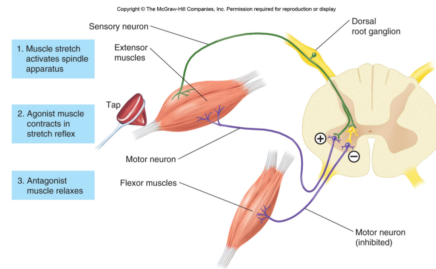
Golgi Tendon Organs



Reciprocal Innervation

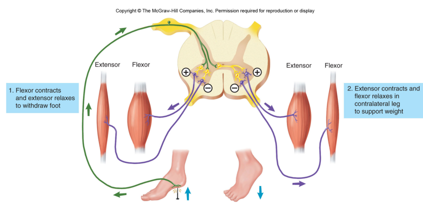
- In the knee-jerk reflex, interneurons are also stimulated in the spinal cord to inhibit antagonistic muscles on that limb.
- More complex reflexes require control of muscles on the contralateral limb. This is called double reciprocal innervation.

Reciprocal Innervation



Crossed Extensor Reflex

- Type of double reciprocal innervation seen when you step on a tack



Upper Motor Neuron Control

- Precentral gyrus: sends neurons through pyramidal tracts
- Cerebellum: receives information from muscle spindles and Golgi tendon organs as well as other senses
  - Inhibits regions of the basal nuclei, red nuclei, and vestibular nuclei
- Basal nuclei: also act to inhibit motor activity through the rubrospinal tract

VI. Cardiac and Smooth Muscles

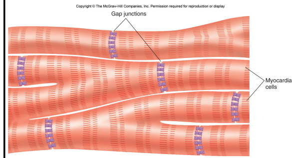
Cardiac and Smooth Muscle

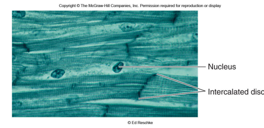
- Involuntary
- Regulated by autonomic nervous system
- Like skeletal muscle, contraction is due to myosin/actin cross bridges stimulated by calcium

Cardiac Muscle

- Striated
- Myosin and actin filaments form sarcomeres.
- Contraction occurs by means of sliding thin filaments.
- Unlike skeletal muscle fibers, these fibers are short, branched, and connected via gap junctions called intercalated discs.

Cardiac Muscle





Myocardium

- A myocardium is a mass of cardiac muscle cells connected to each other via gap junctions.
- Action potentials that occur at any cell in a myocardium can stimulate all the cells in the myocardium.
- It behaves as a single functional unit.
- The atria of the heart compose one myocardium, and the ventricles of the heart compose another myocardium.

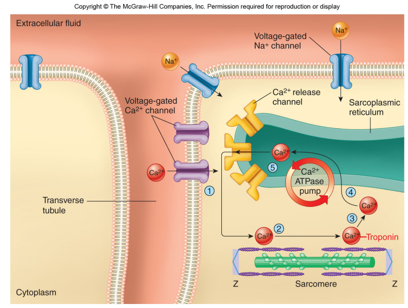
Pacemaker Potential

- Cardiac muscle can produce action potentials automatically (without innervation).
  - Begin in a region called the pacemaker
- Heart rate is influenced by autonomic innervation and hormones.

Calcium Channels

- Unlike skeletal muscle, the voltage-gated calcium channels are not directly connected to calcium channels in the SR.
  - Instead, calcium acts as a second messenger to open SR channels.
  - Called calcium-induced calcium release
  - Excitation-contraction coupling is slower.

Role of Calcium in Cardiac Muscle



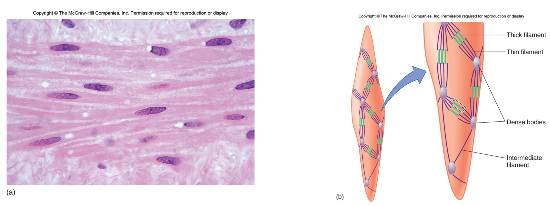
Smooth Muscle

- Found in blood vessel walls, bronchioles, digestive organs, urinary and reproductive tracts
  - Produce peristaltic waves to propel contents of these organs

Smooth Muscle

- No sarcomeres
- Long actin filaments attached to dense bodies
- Some myosin filaments
- Arrangement allows contraction even when greatly stretched

Smooth Muscle



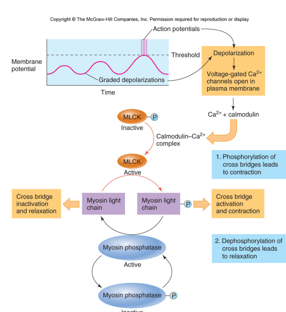
Excitation-Contraction Coupling in Smooth Muscle

- Begins with rise in intracellular calcium concentrations
  - Only some comes from SR.
  - Most comes across plasma membrane after voltage-gated calcium channels are opened.
- Calcium binds to calmodulin (no troponin in smooth muscle).
  - Activates myosin light chain kinase

Excitation-Contraction Coupling in Smooth Muscle

- Myosin light chain kinase phosphorylates myosin light chains.
  - This allows myosin to form cross bridges with actin to initiate contraction.
- Stimulation is graded. More stimulation allows in more calcium, which allows stronger contractions.
- Contractions are slow and sustained.
  - May enter a "latch state"

Excitation-Contraction Coupling in Smooth Muscle



Smooth Muscle Relaxation

- Calcium is pumped out using calcium ATPase active transport pumps.
- Calmodulin dissociates from myosin light chain kinase.
- Phosphate groups are stripped from the myosin by myosin phosphatase.

Single-unit and Multi-unit Smooth Muscles

- Single-unit: multiple gap junctions that make neighboring cells behave as a unit
  - Most smooth muscles are single-unit.
  - They display pacemaker activity moderated by stretch or autonomic innervation.
  - Only a few cells in a single-unit receive acetylcholine stimulation.
  - Muscarinic ACh receptors respond by closing K^+ channels.

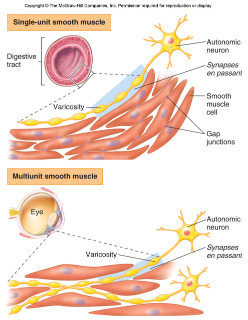
Single-unit and Multi-unit Smooth Muscles

- Multi-unit: require individual nerve innervation (no pacemaker activity)
  - Few or no gap junctions
  - Arrector pili muscles in skin and ciliary muscles in eyes are multi-unit

Autonomic Innervation

- Neurotransmitter is released along the length of an autonomic neuron from varicosities.
  - A number of smooth muscle cells are stimulated at once.
  - Form *synapses en passant*

Autonomic Innervation



Comparison of Skeletal, Cardiac, and Smooth Muscle

Table 12.8 | Comparison of Skeletal, Cardiac, and Smooth Muscle

Skeletal Muscle	Cardiac Muscle	Smooth Muscle
Striated; actin and myosin arranged in sarcomeres	Striated; actin and myosin arranged in sarcomeres	Not striated; more actin than myosin; actin inserts into dense bodies and cell membrane
Well-developed sarcoplasmic reticulum and transverse tubules	Moderately developed sarcoplasmic reticulum and transverse tubules	Poorly developed sarcoplasmic reticulum; no transverse tubules
Contains troponin in the thin filaments	Contains troponin in the thin filaments	Contains calmodulin, a protein that, when bound to Ca^{2+}, activates the enzyme myosin light-chain kinase
Ca^{2+} released into cytoplasm from sarcoplasmic reticulum	Ca^{2+} enters cytoplasm from sarcoplasmic reticulum and extracellular fluid	Ca^{2+} enters cytoplasm from extracellular fluid, sarcoplasmic reticulum, and perhaps mitochondria
Cannot contract without nerve stimulation; denervation results in muscle atrophy	Can contract without nerve stimulation; action potentials originate in pacemaker cells of heart	Maintains tone in absence of nerve stimulation; visceral smooth muscle produces pacemaker potentials; denervation results in hypersensitivity to stimulation
Muscle fibers stimulated independently; no gap junctions	Gap junctions present as intercalated discs	Gap junctions generally present