Physiology

Muscle: Mechanisms of Contraction and Neural Control

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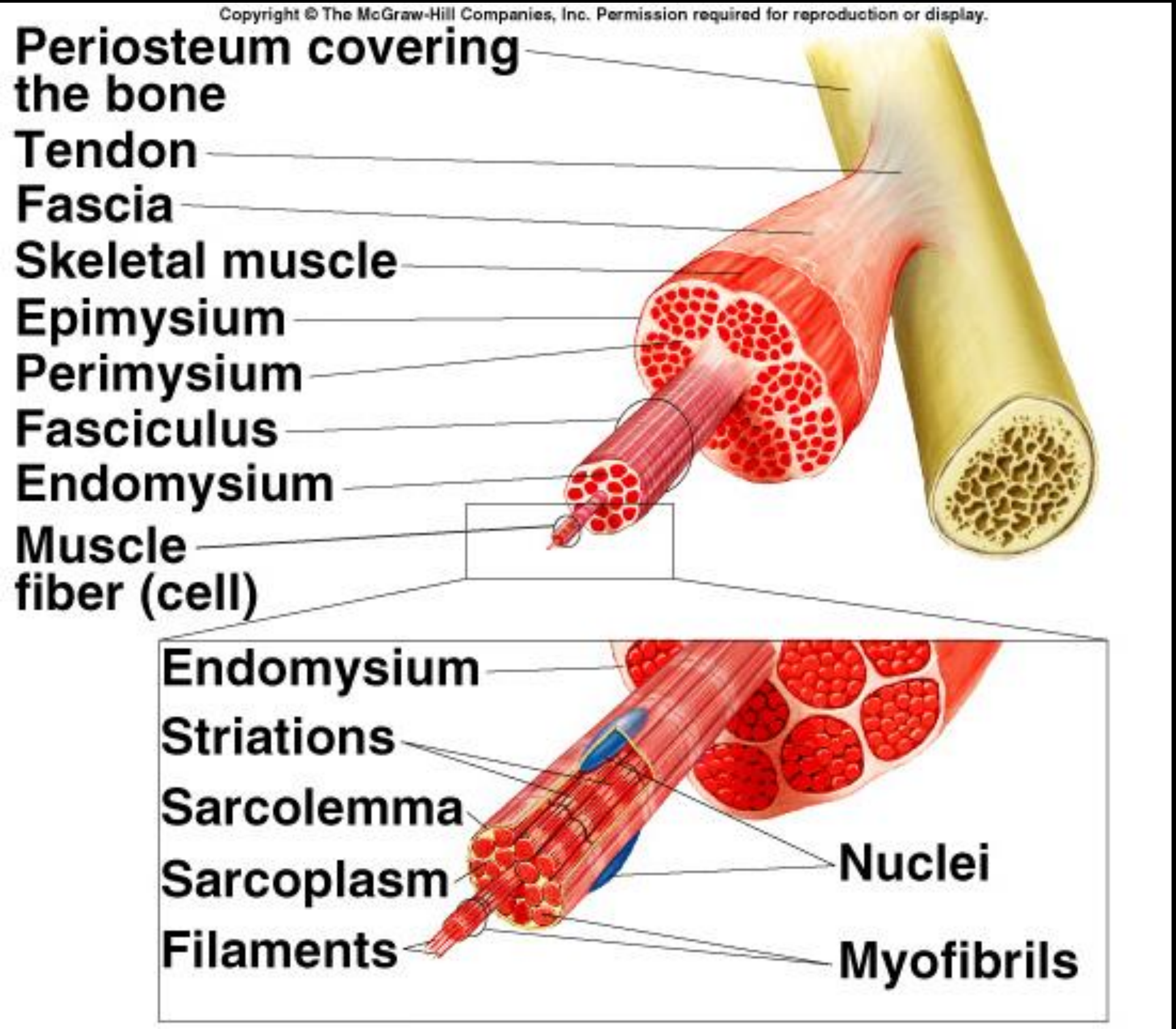
Skeletal Muscles

- Skeletal muscle attached to bone on each end by tendons.
  - Insertion:
    - More movable attachment.
      - Pulled toward origin.
  - Origin:
    - Less movable attachment.
  - Muscle tension on tendons by contracting muscles cause movement of the bones at a joint.
- Agonist muscle:
  - Prime mover of any skeletal muscle movement.
- Antagonist muscle:
  - Flexors and extensors that act on the same joint to produce opposite actions.

Structure of Skeletal Muscle

- Epimysium:
  - Tendon connective tissue extends to form fibrous sheath.
- Fascicles:
  - Connective tissue extends into the body of the muscle.
    - Composed of columns of muscle fibers.
  - Each fascicle surrounded by perimysium.
- Striated in appearance:
  - Striations produced by alternating A and I bands.

Structure of Skeletal Muscle (continued)



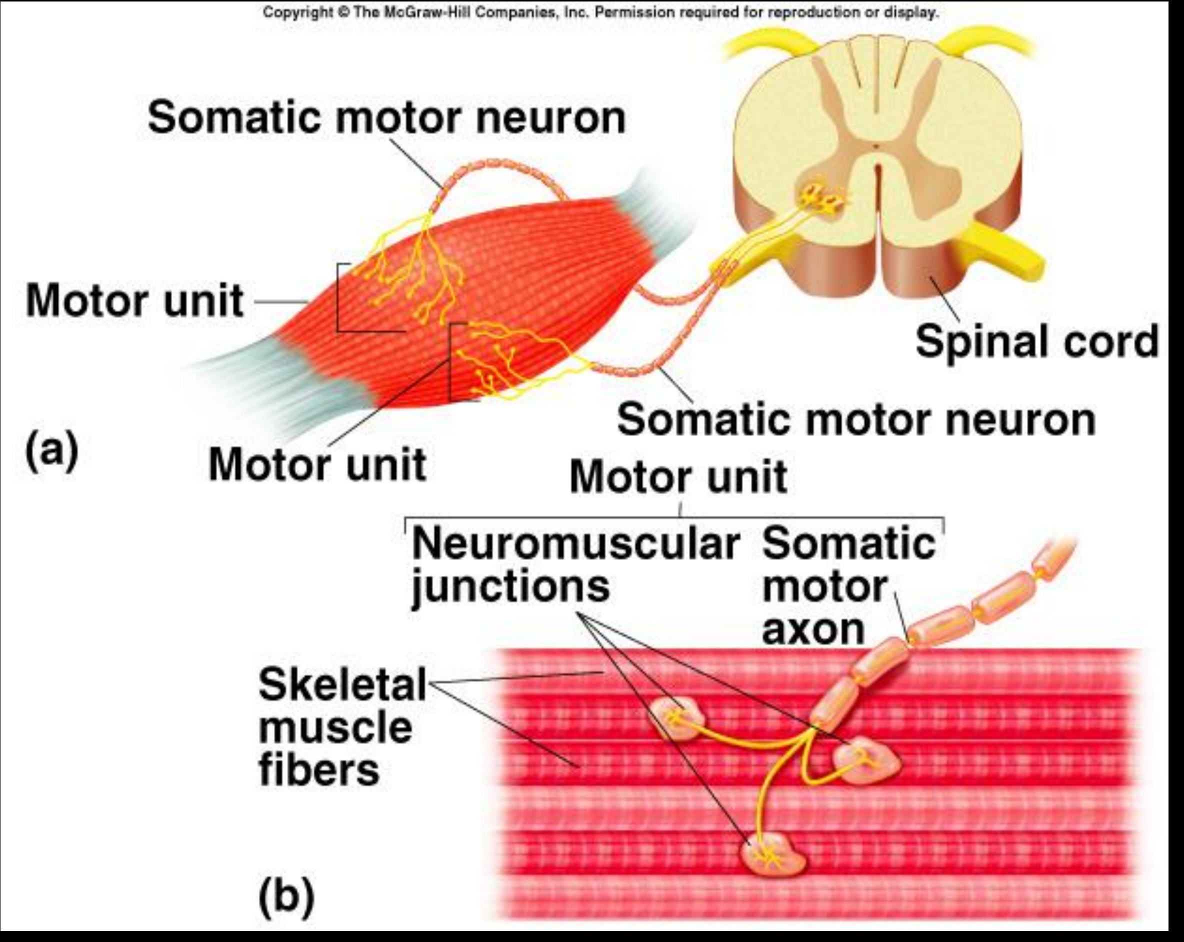
Motor Unit

When somatic neuron is activated, all the muscle fibers it innervates contract with all or none contractions.

- Innervation ratio:
  - Ratio of motor neuron: muscle fibers.
    - Fine neural control over the strength occurs when many small motor units are involved.
- Recruitment:
  - Larger and larger motor units are activated to produce greater strength.

Motor Unit (continued)

- Each somatic neuron together with all the muscle fibers it innervates.
- Each muscle fiber receives a single axon terminal from a somatic neuron.
- Each axon can have collateral branches to innervate an equal # of fibers.

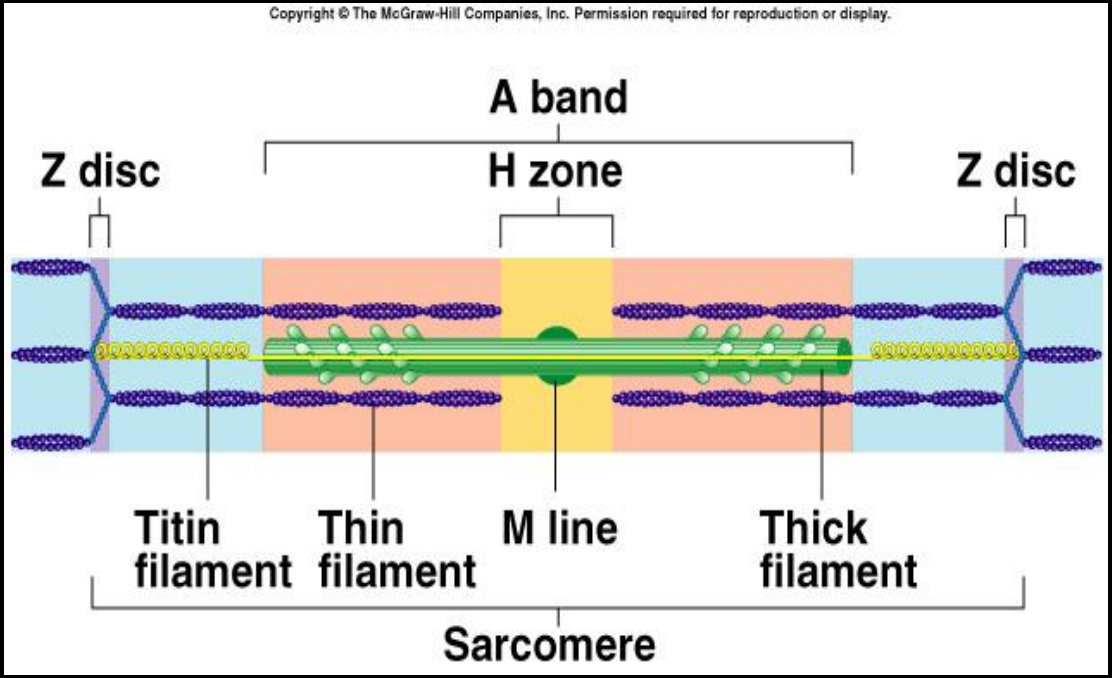


Mechanisms of Contraction

- Each myofibril contains myofilaments.
  - Thick filaments:
    - A bands contain thick filaments (primarily composed of myosin).
  - Thin filaments:
    - I bands contain thin filaments (primarily composed of actin).
      - Center of each I band is Z disc.

Mechanisms of Contraction (continued)

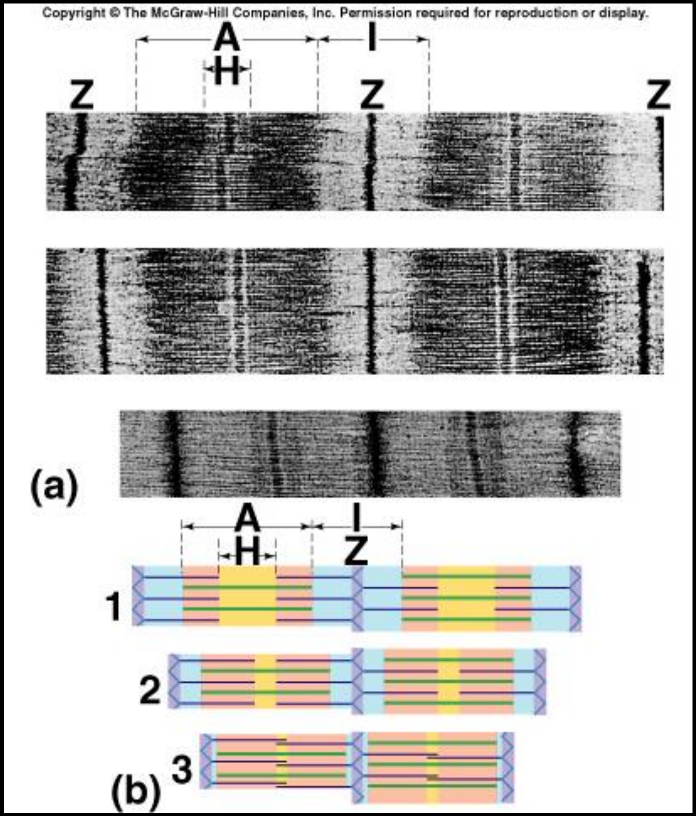
- Sarcomere:
  - Z disc to Z disc.
  - M lines:
    - Produced by protein filaments in a sarcomere.
      - Anchor myosin during contraction.
- Titin:
  - Elastic protein that runs through the myosin from M line to Z disc.
    - Contributes to elastic recoil of muscle.

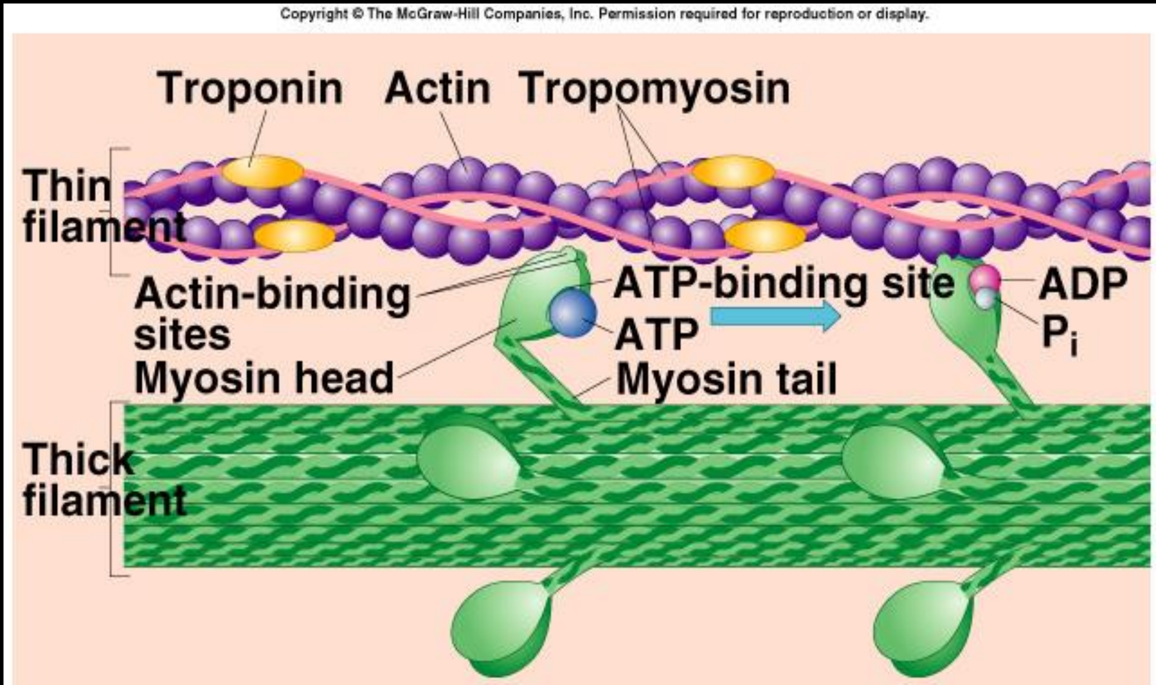


Sliding Filament Theory of Contraction

- Sliding of filaments is produced by the actions of cross bridges.
  - Cross bridges are part of the myosin proteins that extend out toward actin.
    - Form arms that terminate in heads.
  - Each myosin head contains an ATP-binding site.
    - The myosin head functions as a myosin ATPase.

Sliding Filament Theory of Contraction
(continued)





Sliding Filament Theory of Contraction
(continued)

- Muscle contracts:
  - Occurs because of sliding of thin filaments over and between thick filaments towards center.
    - Shortening the distance from Z disc to Z disc.
- A bands:
  - Contain actin.
    - Move closer together.
  - Do not shorten.
- I bands:
  - Distance between A bands of successive sarcomeres.
  - Decrease in length.
- H bands shorten.
  - Contain only myosin.
  - Shorten during contraction.

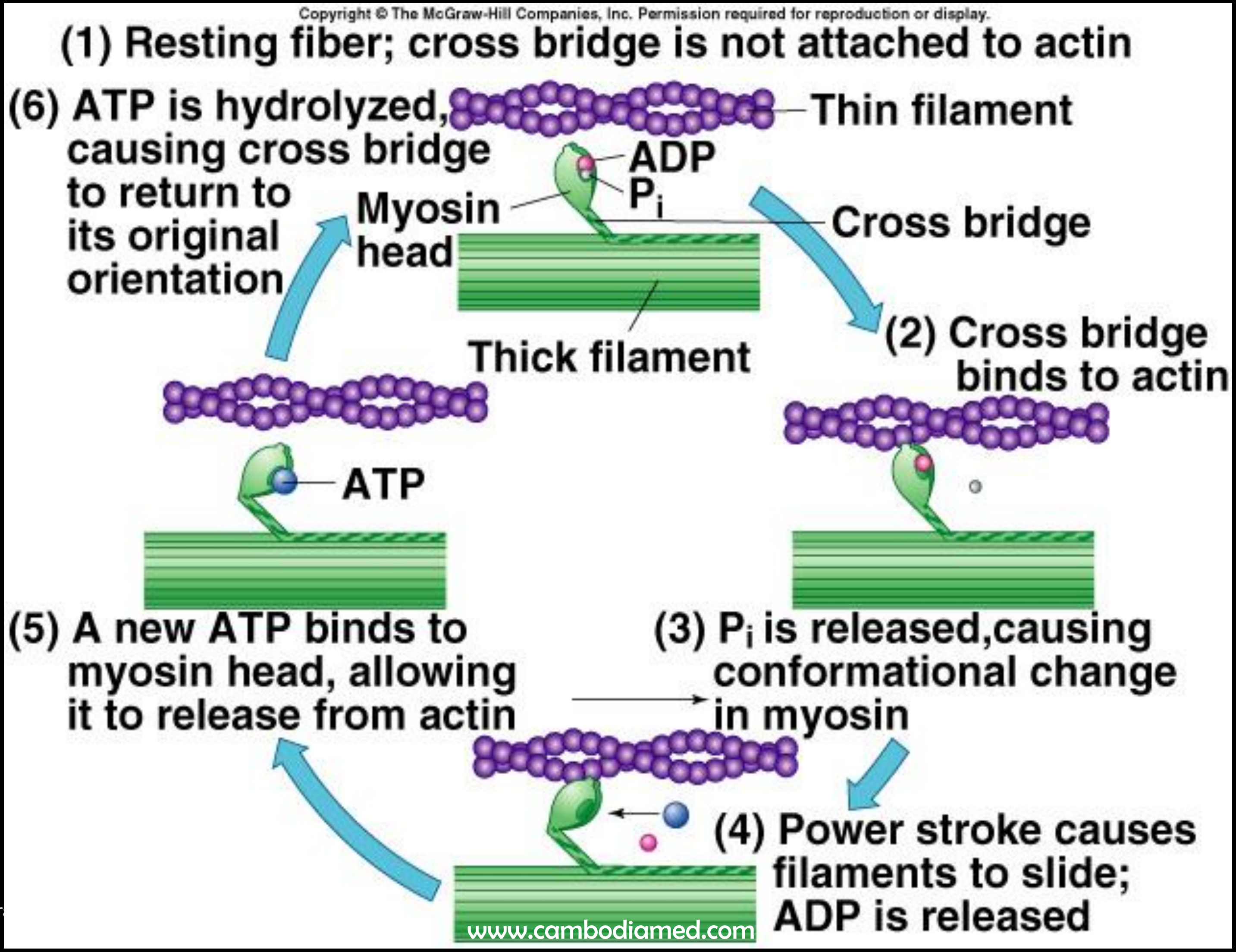
Contraction

- Myosin binding site splits ATP to ADP and P_i.
- ADP and P_i remain bound to myosin until myosin heads attach to actin.
- P_i is released, causing the power stroke to occur.
- Power stroke pulls actin toward the center of the A band.
- ADP is released, when myosin binds to a fresh ATP at the end of the power stroke.

Contraction (continued)

- Release of ADP upon binding to another ATP, causes the cross bridge bond to break.
- Cross bridges detach, ready to bind again.
- Synchronous action:
  - Only 50% of the cross bridges are attached at any given time.

Contraction (continued)



Regulation of Contraction

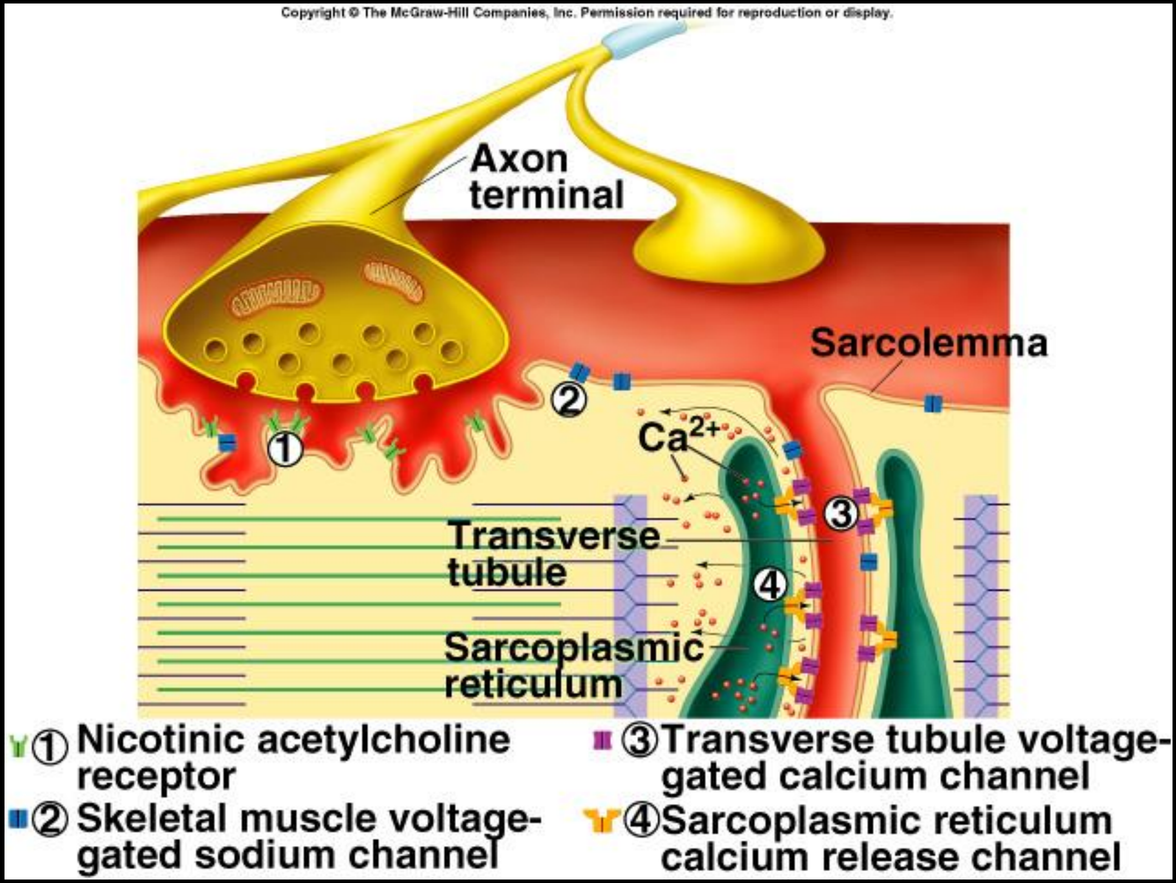
- Regulation of cross bridge attachment to actin due to:
  - Tropomyosin:.
    - Lies within grove between double row of G-actin.
  - Troponin:
    - Attached to tropomyosin.
- Serves as a switch for muscle contraction and relaxation.
  - In relaxed muscle:
    - Tropomyosin blocks binding sites on actin.

Role of Ca^{2+} in Muscle Contraction

- Muscle Relaxation:
  - $[Ca^{2+}]$ in sarcoplasm low when tropomyosin blocks attachment.
    - Prevents muscle contraction.
    - Ca^{2+} is pumped back into the SR in the terminal cisternae.
  - Muscle relaxes.

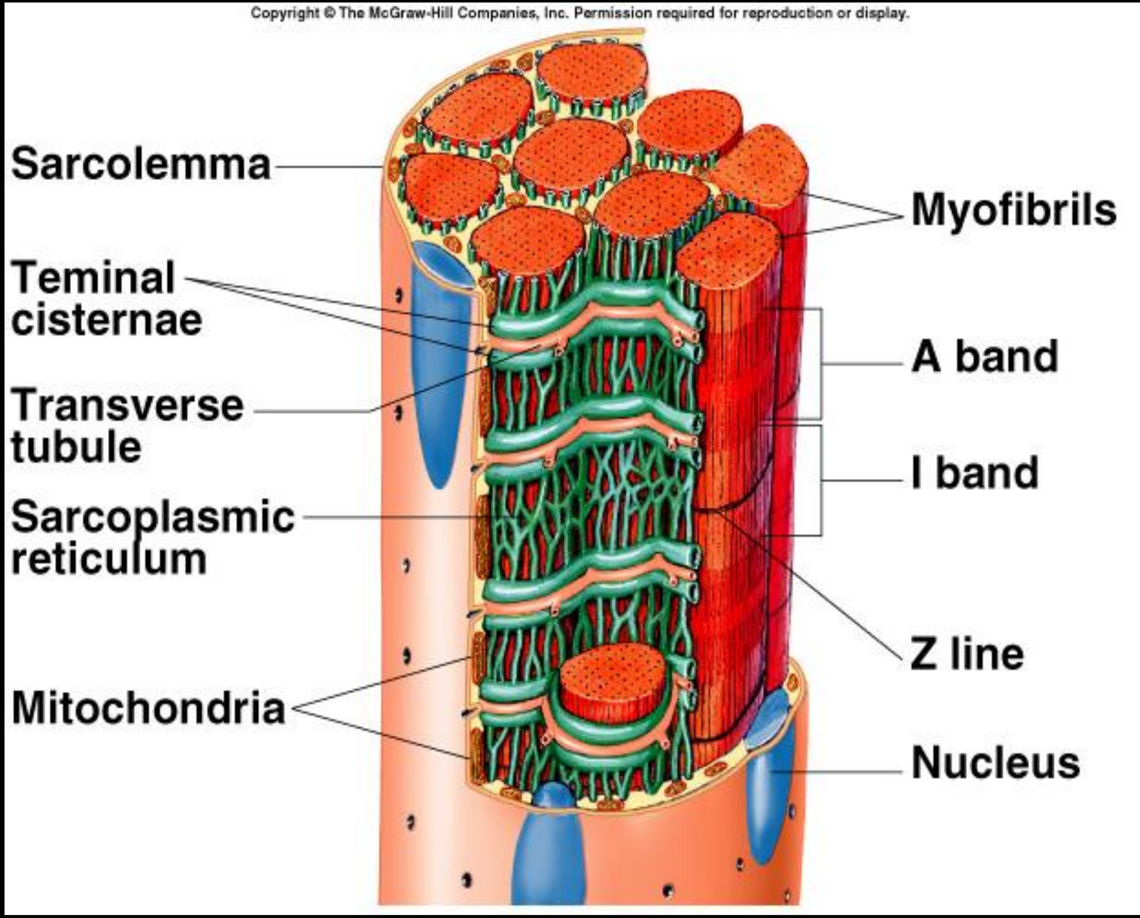
Excitation-Contraction Coupling

- Na^+ diffusion produces end-plate potential (depolarization).
- + ions are attracted to negative plasma membrane.
- If depolarization sufficient, threshold occurs, producing APs.



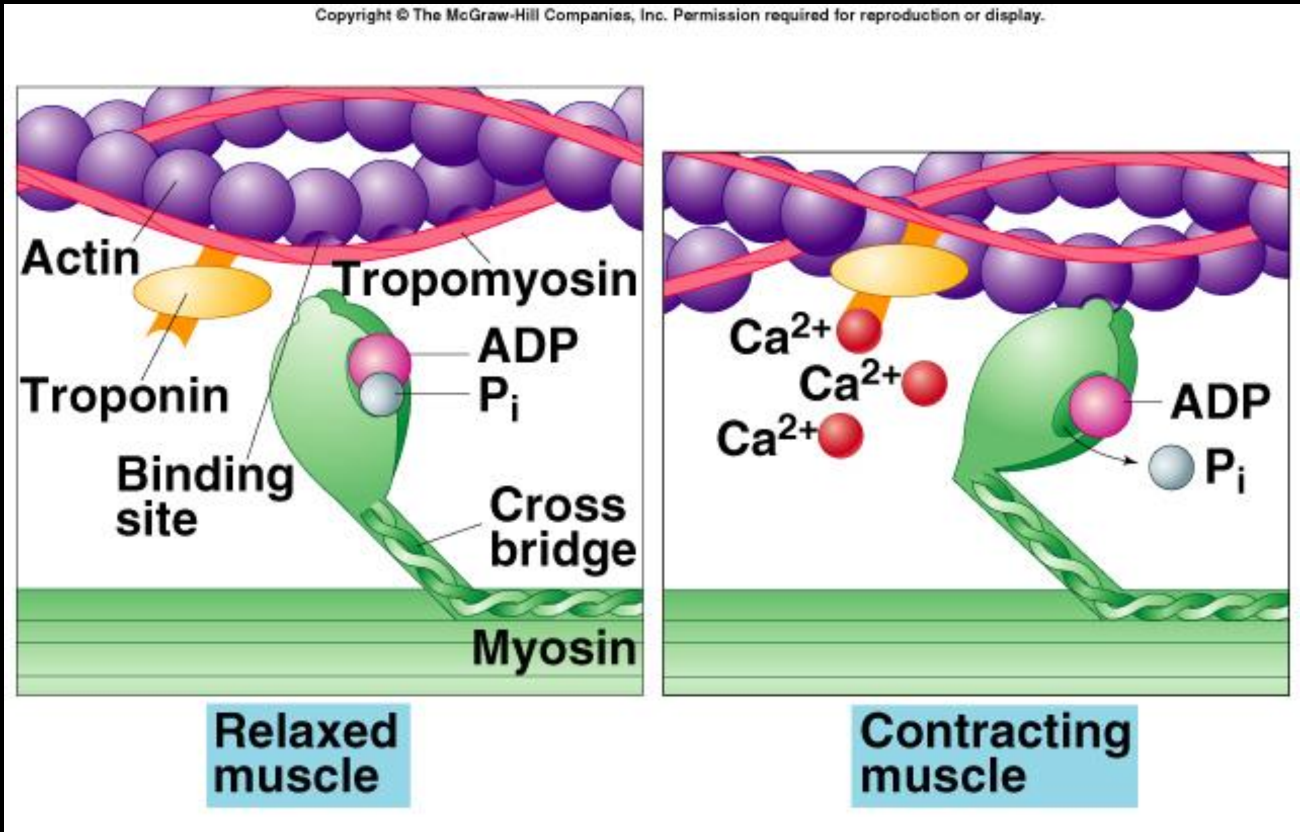
Excitation-Contraction Coupling (continued)

- APs travel down sarcolema and T tubules.
- SR terminal cisternae releases Ca^{2+} from chemical release channels:
  - Electromechanical release mechanism.
- Ca^{2+} is also released through a Ca^{2+}-induced Ca^{2+} release.



Excitation-Contraction Coupling (continued)

- Ca^{2+} attaches to troponin.
- Tropomyosin-troponin complex configuration change occurs.
- Cross bridges attach to actin.



Muscle Relaxation

- APs must cease for the muscle to relax.
- ACh-esterase degrades ACh.
- Ca^{2+} release channels close.
- Ca^{2+} pumped back into SR through Ca^{2+}-ATPase pumps.
- Choline recycled to make more ACh.

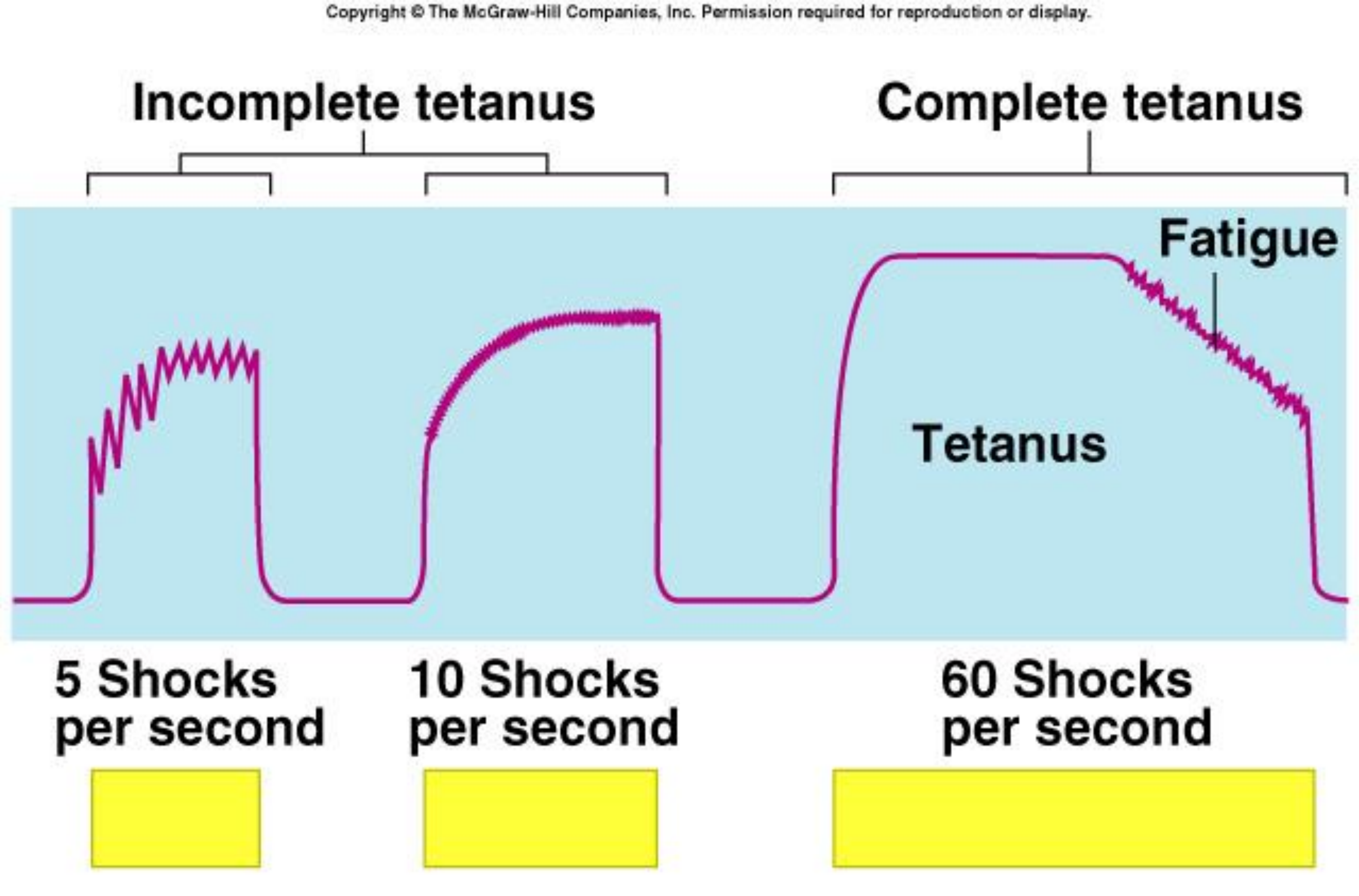
Twitch, Summation, and Tetanus

- Twitch:
  - Muscle is stimulated with a single electrical shock (above threshold).
    - Quickly contracts and then relaxes.
  - Increasing stimulus increases the strength of the twitch (up to maximum).
- Summation:
  - If second electrical shock is administered before complete relaxation of muscle.
- Incomplete tetanus:
  - Stimulator delivers an increasing frequency of electrical shocks.
    - Relaxation period shortens between twitches.
      - Strength of contraction increases.

Twitch, Summation, and Tetanus (continued)

- Complete tetanus:
  - Fusion frequency of stimulation.
  - No visible relaxation between twitches.
    - Smooth sustained contraction.
- Treppe:
  - Staircase effect.
  - Electrical shocks are delivered at maximum voltage.
    - Each shock produces a separate, stronger twitch (up to maximum).
  - Due to increase in intracellular Ca^{2+}.
    - Represents "warm-up."

Twitch, Summation, and Tetanus (continued)

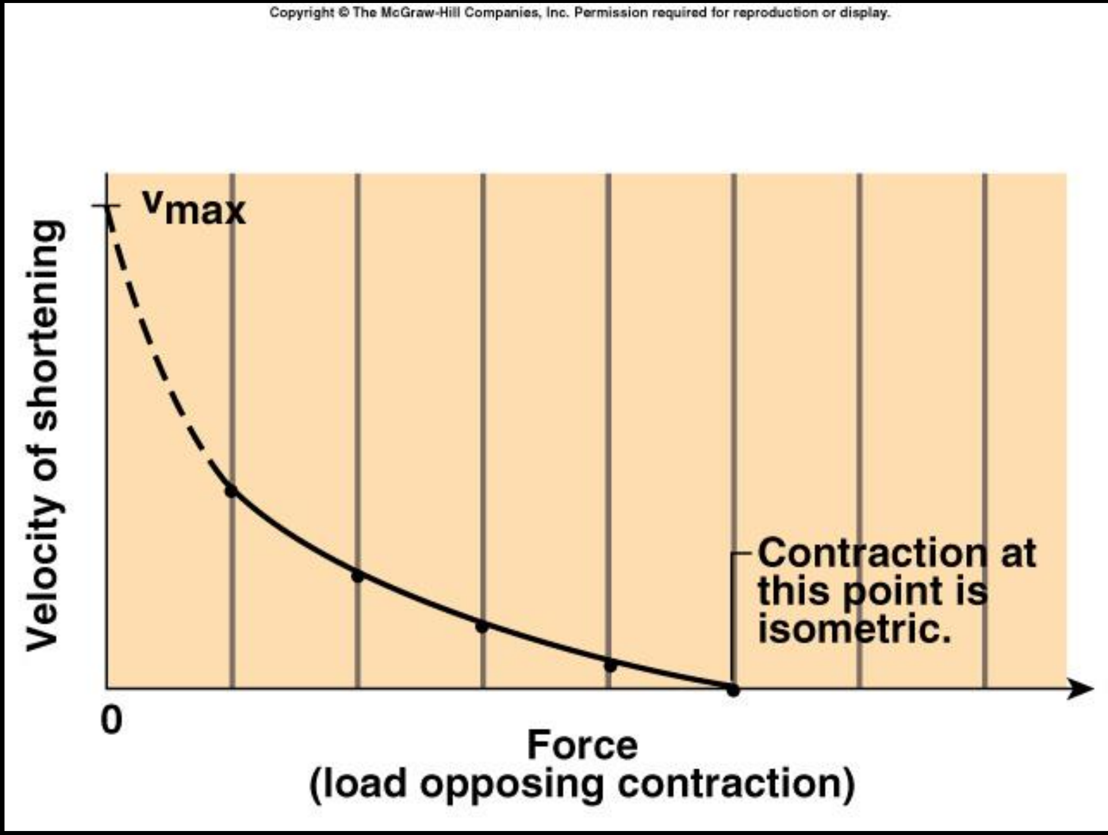


Isotonic, Isometric, and Eccentric Contractions

- In order for a muscle fiber to shorten, they must generate a force greater than the opposing forces that act to prevent movement of that muscle insertion.
- Isotonic contractions:
  - Force of contraction remains constant throughout the shortening process.
    - Velocity of muscle shortening decreases as load increases.
- Isometric contractions:
  - Length of muscle fibers remain constant, if the number of muscle fibers activated is too few to shorten the muscle.
    - Velocity of shortening is 0.

Isotonic, Isometric, and Eccentric Contractions (continued)

- Force-velocity curve:
  - Inverse relationship between force opposing muscle contraction and velocity of muscle shortening.
- Eccentric contractions:
  - Force exerted on a muscle to stretch, it is greater than the force of muscle contraction.
    - Muscle will lengthen as it contracts.



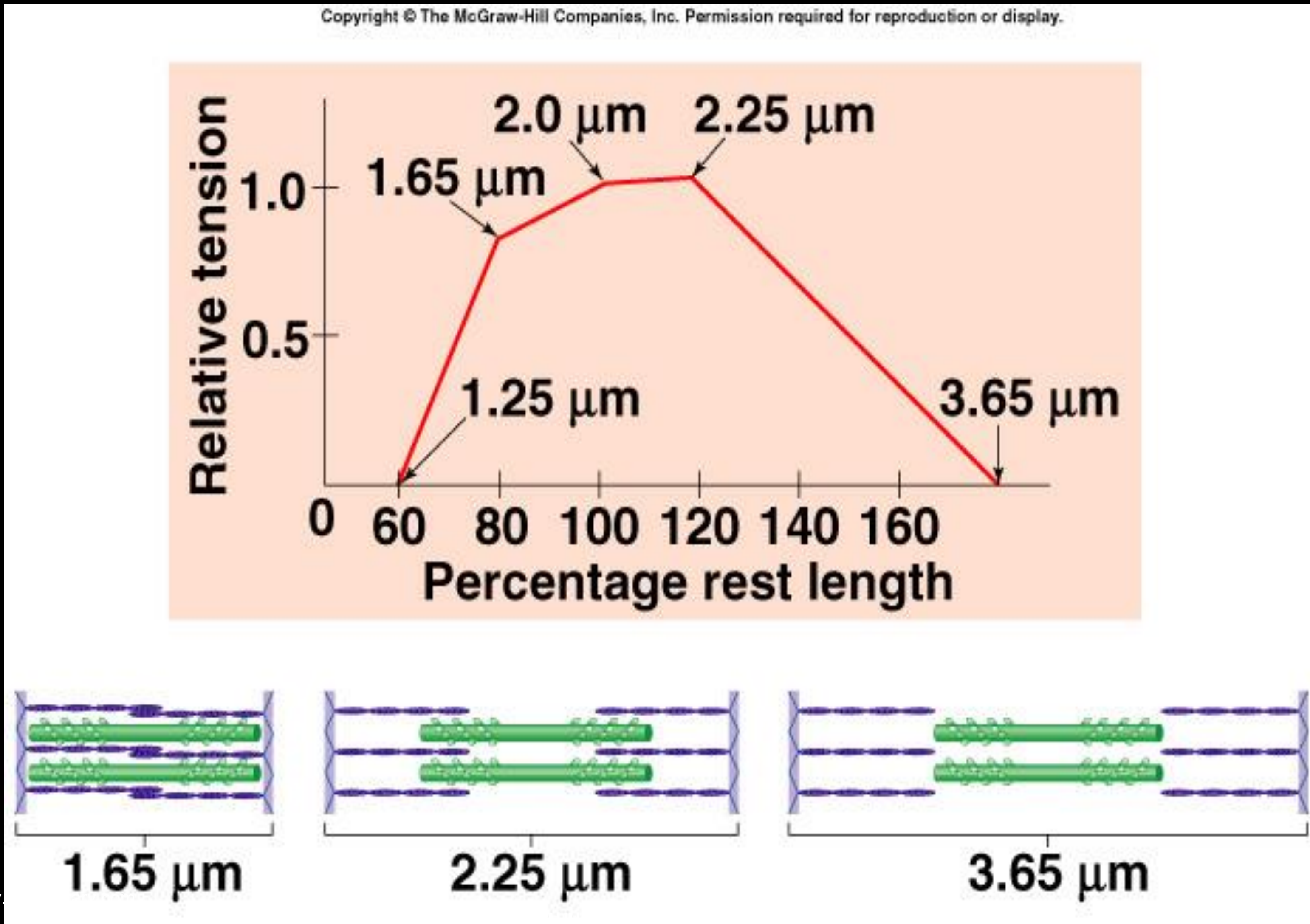
Series-Elastic Component

- Non-contractile tendons and connective tissue absorb tension as the muscle contracts.
- Tendons first must be pulled tight, before the muscle contraction results in shortening.
- Tendons:
  - Have elasticity (resist distension).
  - Display recoil.
    - Spring back to resting length.

Length-Tension Relationship

- Strength of muscle contraction influenced by:
  - Frequency of stimulation.
  - Thickness of each muscle fiber.
  - Initial length of muscle fiber.
    - Ideal resting length:
      - Length which can generate maximum force.
    - Overlap too small:
      - Few cross bridges can attach.
    - No overlap:
      - No cross bridges can attach to actin.

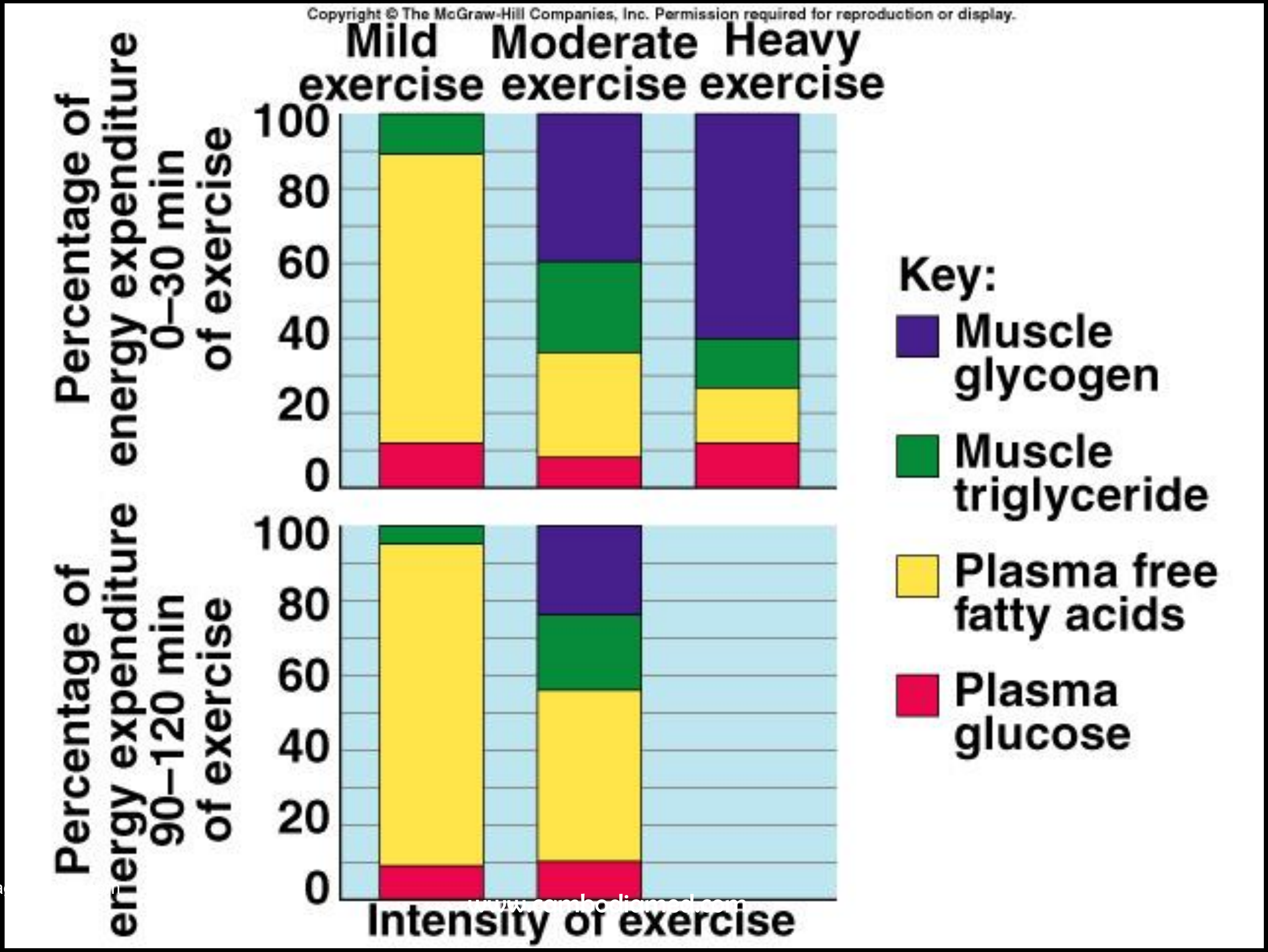
Length-Tension Relationship (continued)



Metabolism of Skeletal Muscles

- Skeletal muscles respire anaerobically first 45 - 90 sec of moderate to heavy exercise.
  - Cardiopulmonary system requires this amount of time to increase O_2 supply to exercising muscles.
  - If exercise is moderate, aerobic respiration contributes the majority of skeletal muscle requirements following the first 2 min. of exercise.
- Maximum oxygen uptake (aerobic capacity):
  - Maximum rate of oxygen consumption (V_{O_2} max) determined by age, gender, and size.

Muscle Fuel Consumption During Exercise



Metabolism of Skeletal Muscles

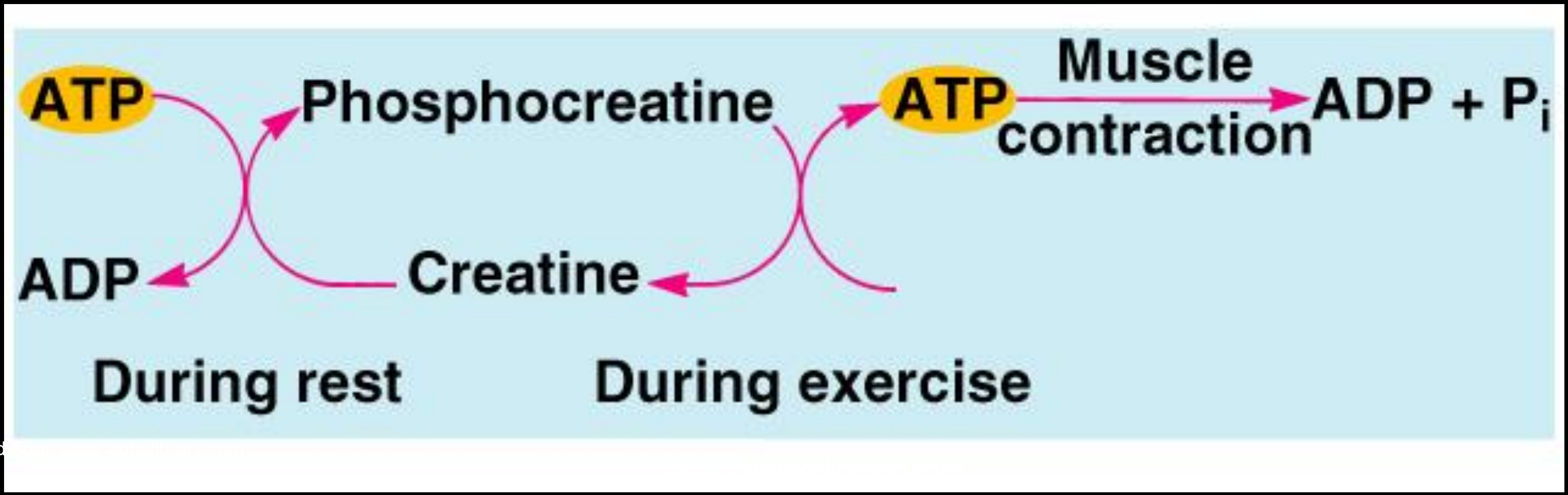
- Lactate threshold:
  - % of max. O_2 uptake at which there is a significant rise in blood [lactate].
    - Healthy individual, significant blood [lactate] appears at 50–70% V_{O2} max.
- During light exercise:
  - Most energy is derived from aerobic respiration of fatty acids.
- During moderate exercise:
  - Energy is derived equally from fatty acids and glucose.
- During heavy exercise:
  - Glucose supplies 2/3 of the energy for muscles.
    - Liver increases glycogenolysis.
- During exercise, the GLUT-4 carrier protein is moved to the muscle cell's plasma membrane.

Metabolism of Skeletal Muscles (continued)

- Oxygen debt:
  - Oxygen that was withdrawn from hemoglobin and myoglobin during exercise.
  - Extra O_2 required for metabolism tissue warmed during exercise.
  - O_2 needed for metabolism of lactic acid produced during anaerobic respiration.
- When person stops exercising, rate of oxygen uptake does not immediately return to pre-exercise levels.
  - Returns slowly.

Metabolism of Skeletal Muscles (continued)

- Phosphocreatine (creatine phosphate):
  - Rapid source of renewal of ATP.
  - ADP combines with creatine phosphate.
- [Phosphocreatine] is 3 times [ATP].
  - Ready source of high-energy phosphate.



Slow- and Fast-Twitch Fibers

- Skeletal muscle fibers can be divided on basis of contraction speed:
  - Slow-twitch (type I fibers).
  - Fast-twitch (type II fibers).
- Differences due to different myosin ATPase isoenzymes that are slow or fast.

Slow- and Fast-Twitch Fibers (continued)

- Slow-twitch (type I fibers):
  - Red fibers.
  - High oxidative capacity for aerobic respiration.
  - Resistant to fatigue.
  - Have rich capillary supply.
  - Numerous mitochondria and aerobic enzymes.
  - High [myoglobin].
    - Soleus muscle in the leg.

Slow- and Fast-Twitch Fibers (continued)

- Fast-twitch (type IIX fibers):
  - White fibers.
  - Adapted to respire anaerobically.
  - Have large stores of glycogen.
  - Have few capillaries.
  - Have few mitochondria.
    - Extraocular muscles that position the eye.
- Intermediate (type II A) fibers:
  - Great aerobic ability.
  - Resistant to fatigue.
- People vary genetically in proportion of fast- and slow-twitch fibers in their muscles.

Characteristics of Muscle Fiber Types

Table 12.4 Characteristics of Muscle Fiber Types

Feature	S low Oxidative/Red (Type I)	Fast Oxidative/White (Type IIA)	Fast Glycolytic/White (Type IIX)
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

Muscle Fatigue

- Any exercise induced reduction in the ability to maintain muscle to generate force or power.
  - Sustained muscle contraction fatigue is due to an accumulation of ECF K^+.
    - Repolarization phase of AP.
- During moderate exercise fatigue occurs when slow-twitch fibers deplete their glycogen reserve.
- Fast twitch fibers are recruited, converting glucose to lactic acid.
  - Interferes with Ca^{2+} transport.
- Central fatigue:
  - Muscle fatigue caused by changes in CNS rather than fatigue of muscles themselves.

Adaptations of Muscles to Exercise Training

- Maximum O_2 uptake during strenuous exercise:
  - In adult aged 20-25, averages 50 ml of O_2/min.
- In trained endurance athlete increases up to 86 ml of O_2/min.
  - Increases lactate threshold.
      - Produces less lactic acid.
    - Increases proportion of energy derived from aerobic respiration of fatty acids.
    - Lowers depletion of glycogen stores.

Adaptations of Muscles to Exercise Training (continued)

- All fibers adapt to endurance training:
  - Increase # of mitochondria.
- Endurance training produces an increase in type IIA fibers and a decrease in type IIX fibers.
  - Does not increase size of muscles.
- Muscle enlargement produced by:
  - Frequent periods of high-intensity exercise in which muscles work against high-resistance.
    - Type II fibers become thicker.
      - May split into 2 myofibrils.

Neural Control of Skeletal Muscles

- Lower motor neuron activity influenced by:
  - Sensory feedback from the muscles and tendons.
  - Facilitory and inhibitory effects of upper motor neurons.
    - Cell bodies in spinal cord and axons within neurons that stimulate muscle contractions.
      - Final common pathway by which sensory stimuli and higher brain centers exert control over skeletal movements.

Muscle Spindle Apparatus

- To control skeletal muscle movements, it must receive continuous sensory feedback.
- Sensory feedback includes information from:
  - Golgi tendon organs:
    - Sense tension that the muscle exerts on the tendons.
  - Muscle spindle apparatus:
    - Measures muscle length.
    - Contains thin muscle cells called intrafusal fibers.
      - Insert into tendons at each end of the muscle.
      - Contractile apparatus absent from central regions.
  - 2 types of intrafusal fibers:
    - Nuclear bag fibers:
      - Nuclei arranged in loose aggregate.
    - Nuclear chain fibers:
      - Nuclei arranged in rows.

Muscle Spindle Apparatus (continued)

- Sensory neurons:
  - Primary, annulospiral sensory endings:
    - Wrap around the central regions of both nuclear bag and chain fibers.
      - Most stimulated at onset of stretch.
  - Secondary, flower-spray endings:
    - Located over the contracting poles of nuclear chain fibers.
      - Respond to tonic (sustained) stretch.
  - Sudden, rapid stretching of a muscle causes spindles to stretch, stimulating both primary and secondary endings
    - Produces more forceful muscle contraction.

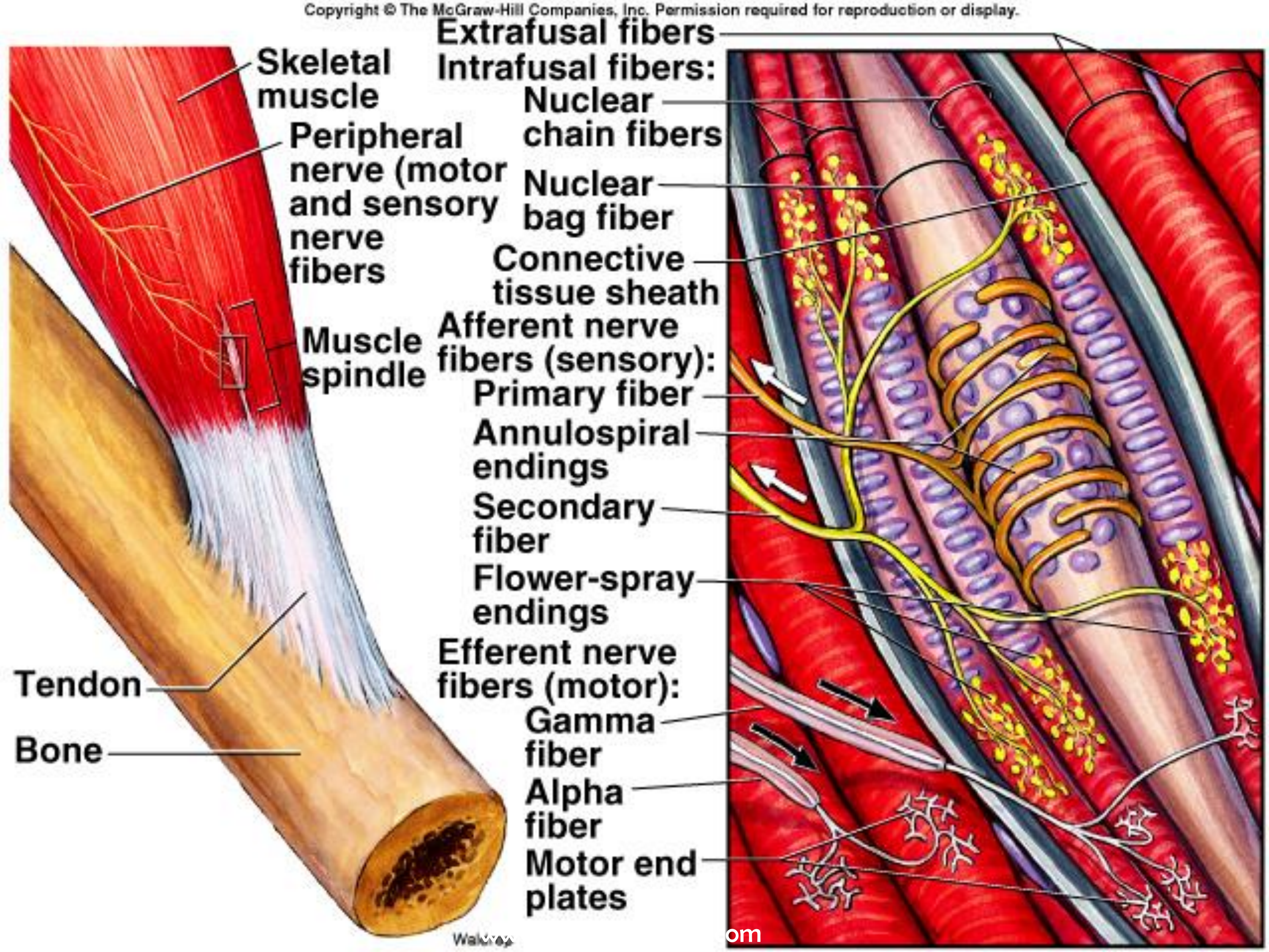
Muscle Spindle Apparatus (continued)

- Extrafusal fibers:
  - Ordinary muscle fibers outside the spindles.
  - Contain myofibrils along entire length.
  - Spindles are arranged in parallel with the extrafusal muscle fibers.
- Only extrafusal muscle fibers are strong and numerous enough to cause muscle contraction.

Alpha and Gamma Motor Neurons

- 2 types of lower motor neurons in the spinal cord:
  - α motor neurons:
    - Neurons that innervate extrafusal fibers.
    - Fast conducting fibers.
  - γ motor neurons:
    - Neurons that innervate the intrafusal fibers.
    - Cause isometric muscle contraction.
    - Too few in # to cause muscle to shorten.
- Stimulation by α motor neurons only, can cause skeletal muscle movements.

Alpha and Gamma Motor Neurons (continued)

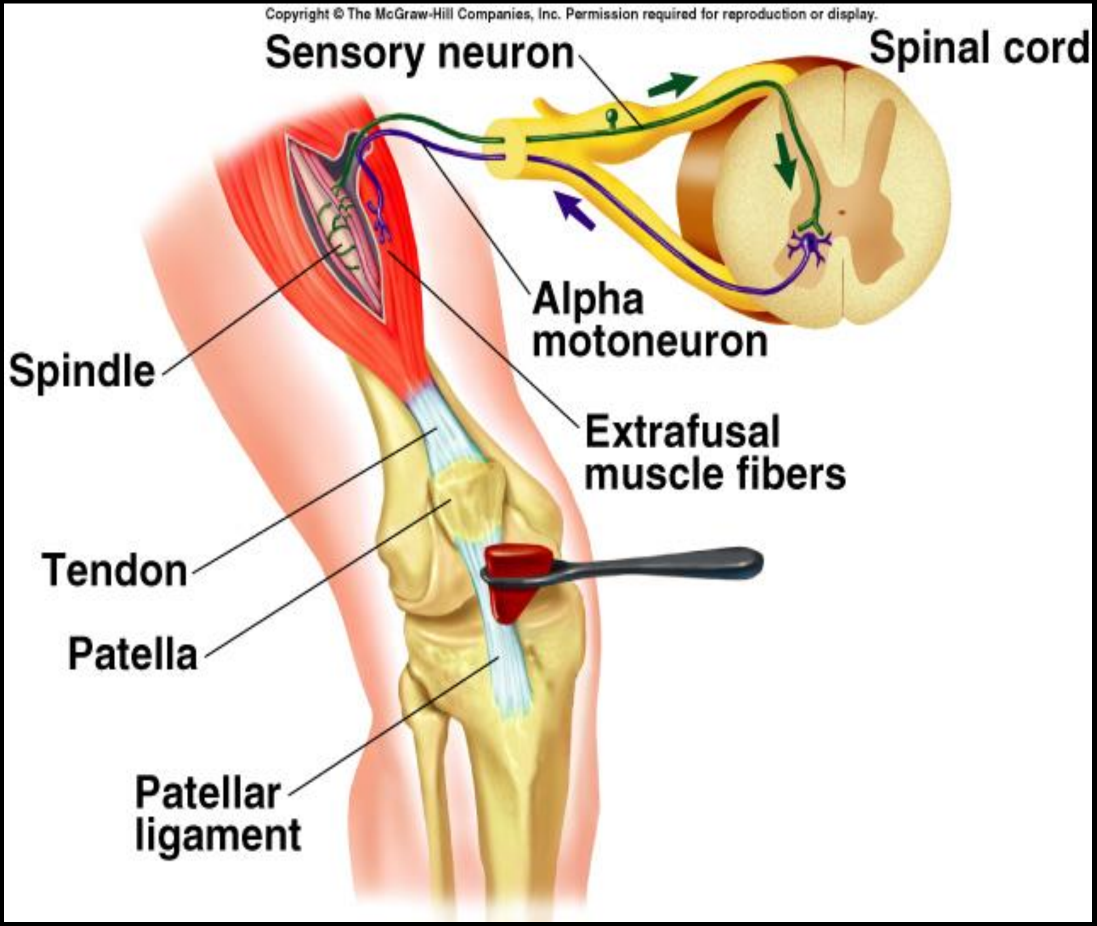


Coactivation of Alpha and Gamma Motor Neurons

- Coactivation:
  - Upper motor neurons usually stimulate α and γ motor neurons simultaneously.
  - Stimulation of α motor neurons results in muscle contraction and shortening.
  - Stimulation of γ motor neurons stimulate intrafusal fibers and take out the slack.
- Activity of γ motor neurons is maintained to keep muscle spindles under proper tension while muscles are relaxed.

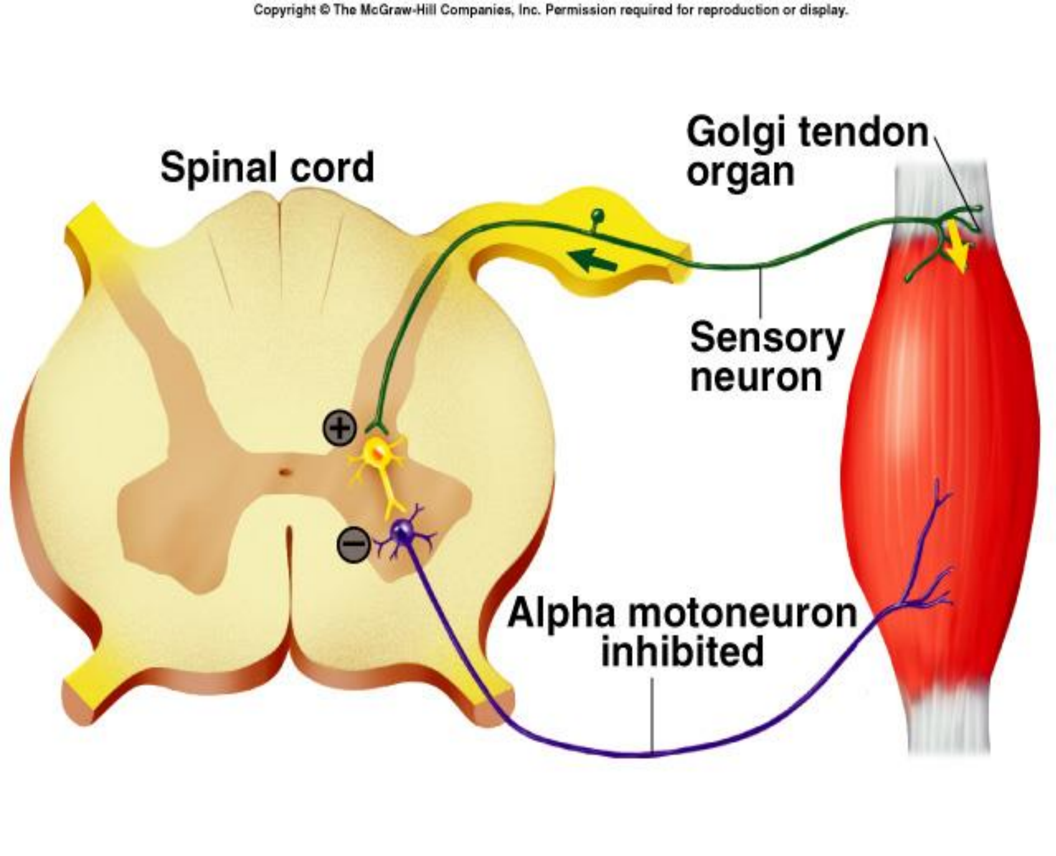
Monosynaptic-Stretch Reflex

- Consists of only one synapse within the CNS.
  - Sensory neuron synapses directly with the motor neuron.
- Striking the patellar ligament, passively stretches the spindles.
  - Stimulates primary endings in spindles, activating sensory neurons.
  - Synapse with α motor neurons stimulating extrafusal fibers.
    - Produces isotonic contraction, (knee jerk).



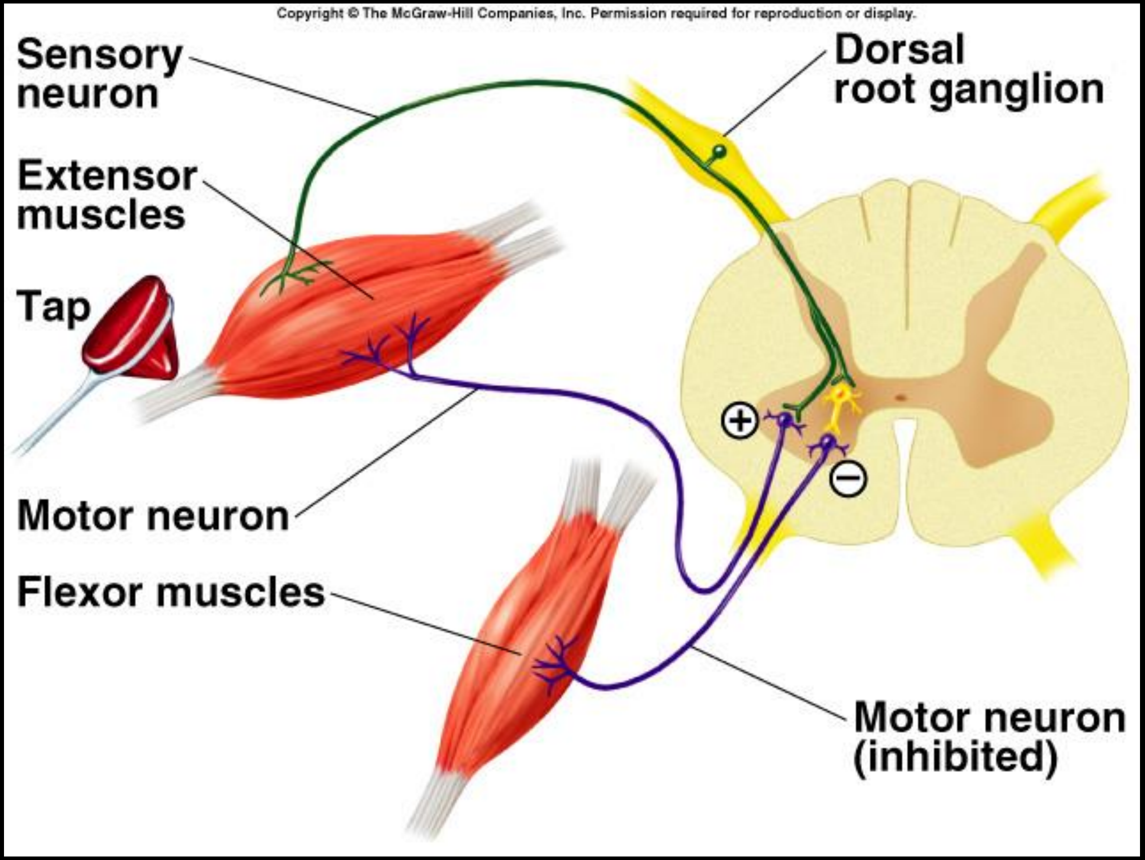
Golgi Tendon Organ Reflex

- Disynaptic reflex.
  - 2 synapses are crossed in the CNS.
- Sensory neurons synapse with interneurons.
  - These interneurons have inhibitory synapses with motor neurons.
- Helps prevent excessive muscle contraction or passive muscle stretching.



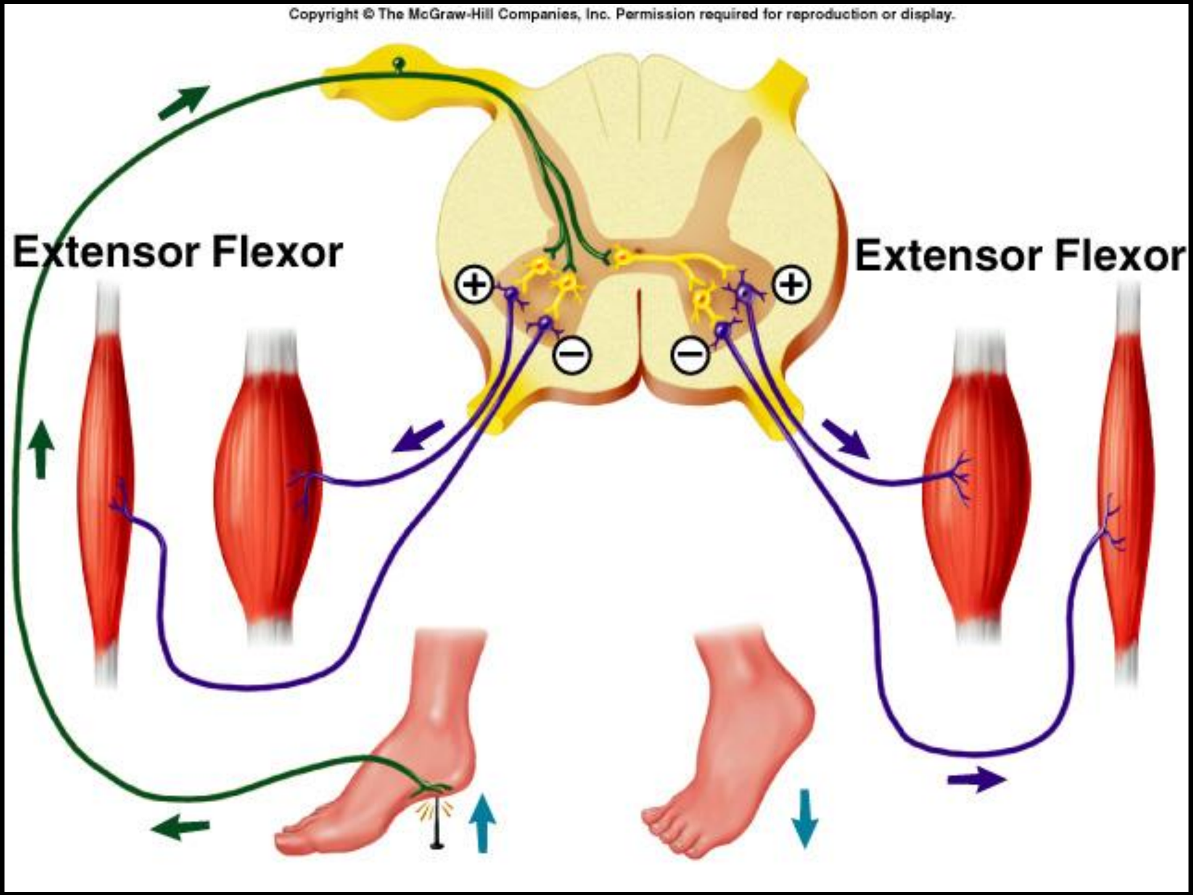
Reciprocal Innervation

- Sensory neuron stimulates motor neuron and interneuron.
- Interneurons inhibit motor neurons of antagonistic muscles.
- When limb is flexed, antagonistic extensor muscles are passively stretched.



Crossed-Extensor Reflex

- Double reciprocal innervation.
- Affects muscles on the contralateral side of the cord.
- Step on tack:
  - Foot is withdrawn by contraction of flexors and relaxation of extensors.
- Contralateral leg extends to support body.



Upper Motor Neuron Control of Skeletal Muscles

- Influence lower motor neurons.
- Pyramidal tracts:
  - Neurons in precentral gyrus contribute axons that cross to contralateral sides in the pyramids of medulla.
- Extrapyramidal tracts:
  - Neurons in the other areas of the brain.

Upper Motor Neuron Control of Skeletal Muscles (continued)

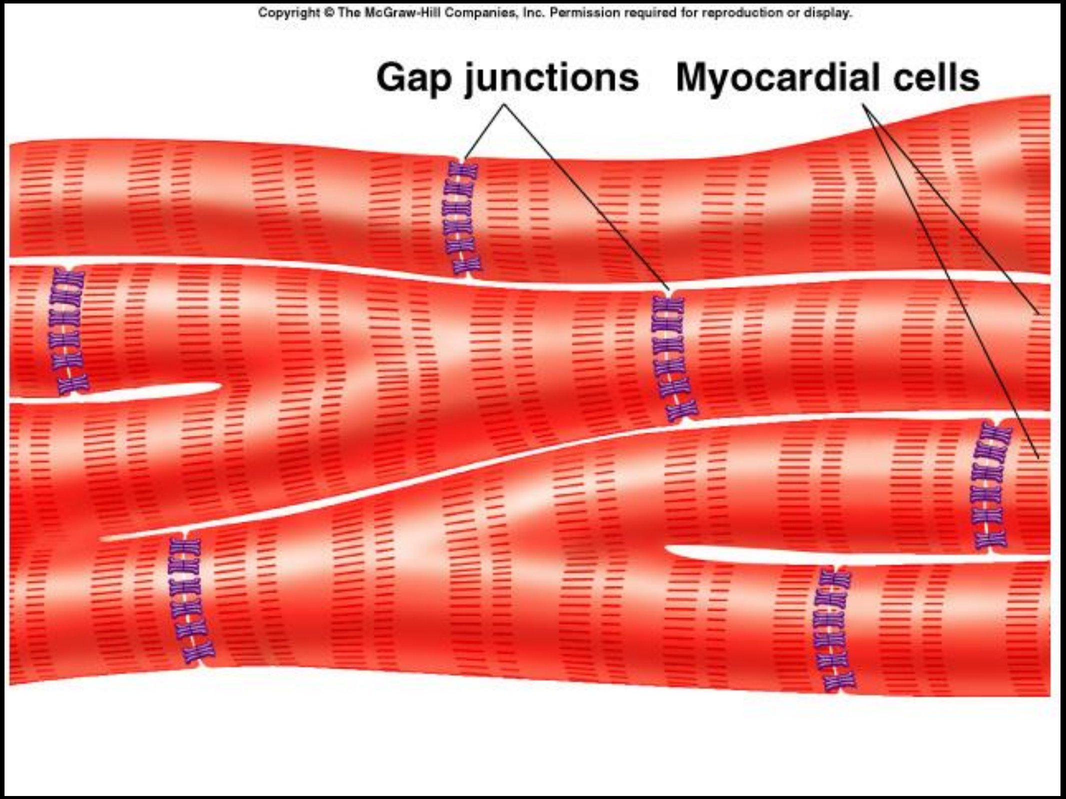
- Cerebellum:
  - Receives sensory input from muscle spindles, Golgi tendon organs, and areas of cerebral cortex devoted to vision, hearing and equilibrium.
- No descending tracts from the cerebellum.
  - Influences motor activity indirectly.
- All output from cerebellum is inhibitory.
  - Aids motor coordination.

Upper Motor Neuron Control of Skeletal Muscles (continued)

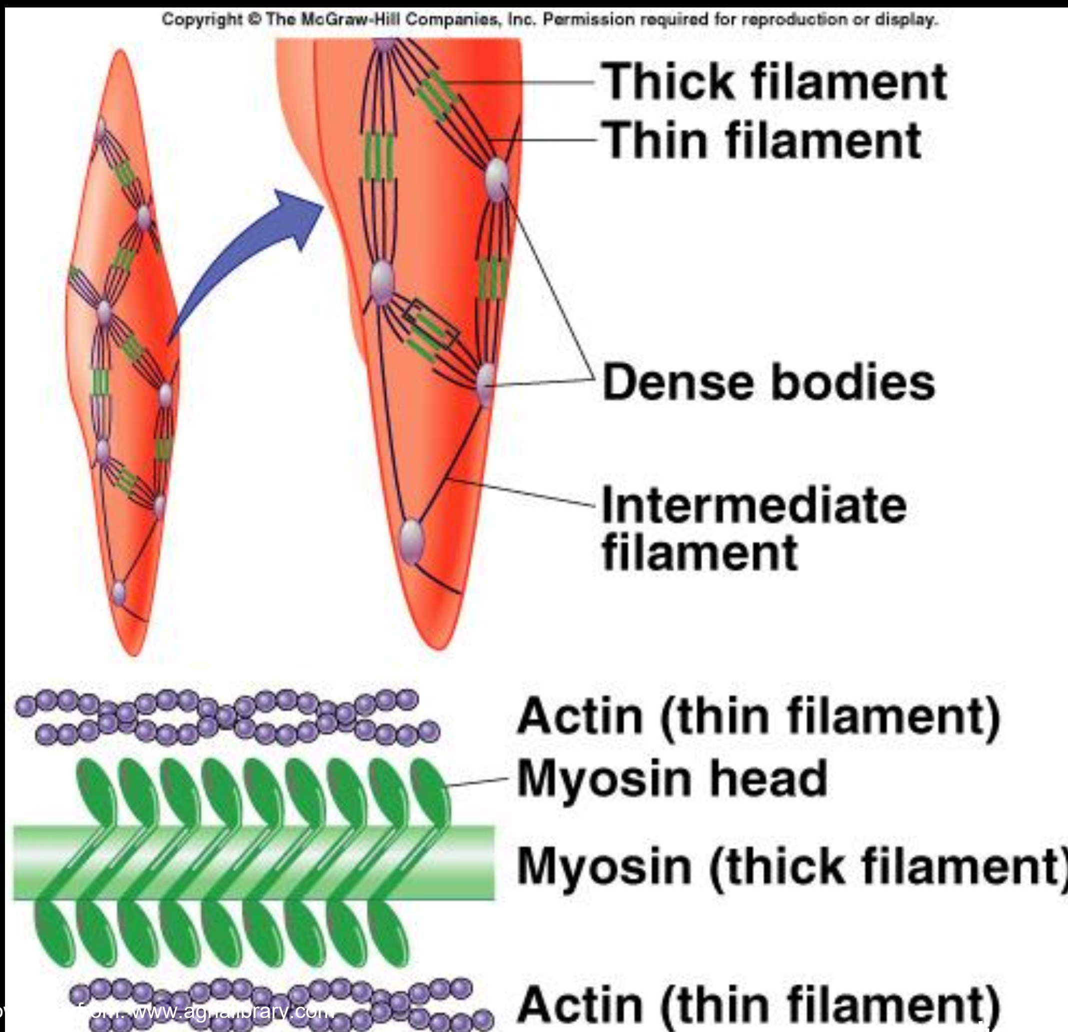
- Basal nuclei:
  - Include caudate nucleus, putamen, globus pallidus, and nuclei of thalamus, substantia nigra and red nucleus.
- Profound inhibitory effects on the activity of lower motor neurons.
  - Damage to basal nuclei result in increased muscle tone.

Cardiac Muscle

- Contain actin and myosin arranged in sarcomeres.
- Contract via sliding-filament mechanism.
- Adjacent myocardial cells joined by gap junctions.
  - APs spread through cardiac muscle through gap junctions.
    - Behaves as one unit.
  - All cells contribute to contraction.



Smooth Muscle



- Does not contain sarcomeres.
- Contains > content of actin than myosin (ratio of 16:1).
- Myosin filaments attached at ends of the cell to dense bodies.
- Contains gap junctions.

Smooth Muscle Contraction

- Depends on rise in free intracellular Ca^{2+}.
- Ca^{2+} binds with calmodulin.
  - Ca^{2+} calmodulin complex joins with and activates myosin light chain kinase.
- Myosin heads are phosphorylated.
  - Myosin heads binds with actin.
- Relaxation occurs when Ca^{2+} concentration decreases.

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