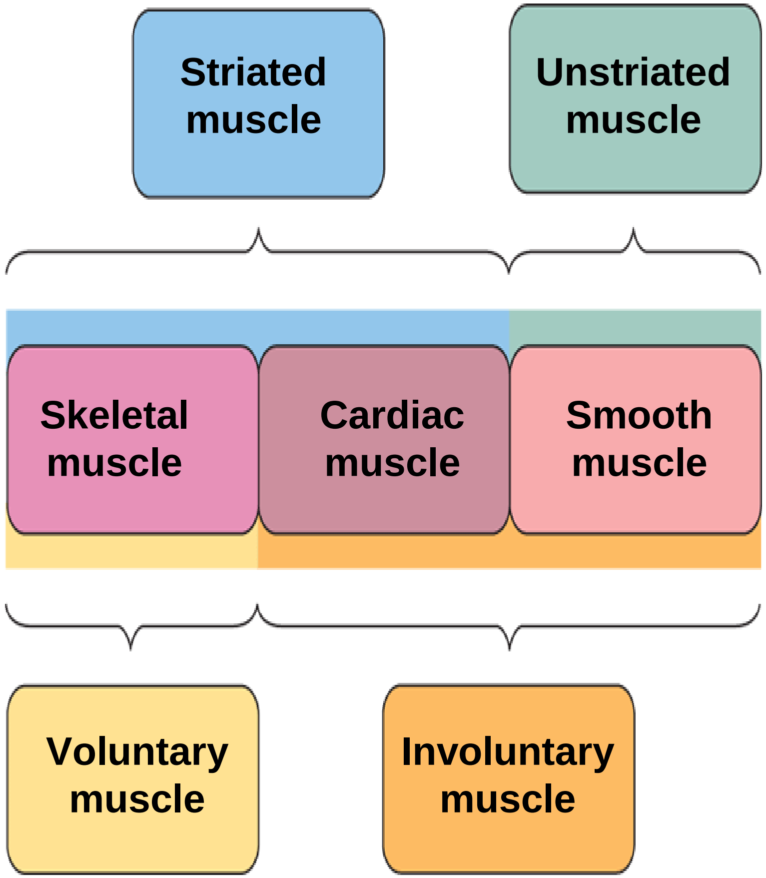
ECE 370
Introduction to Biomedical Engineering

Musculoskeletal Physiology

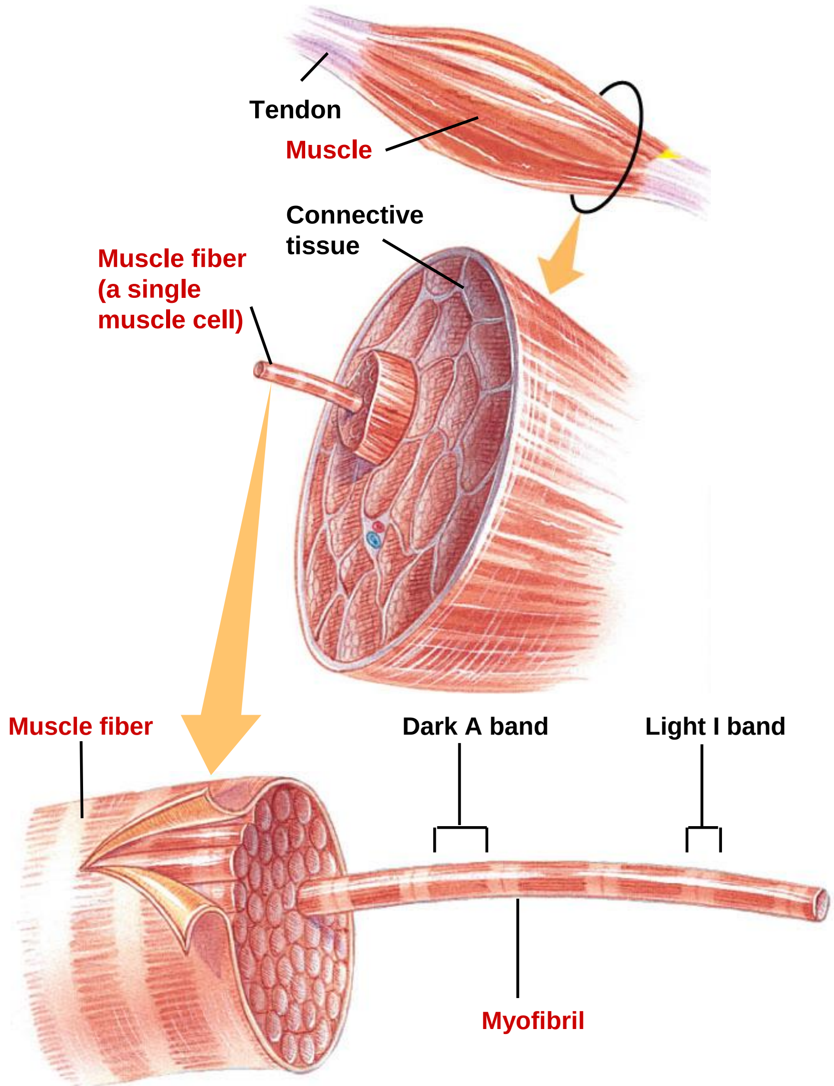
Muscle

- **Comprises largest group of tissues in body**
  - Skeletal (30-40% BW), smooth and cardiac (10% BW)
- **Controlled muscle contraction allows**
  - Purposeful movement of the whole body or parts of the body
  - Manipulation of external objects
  - Propulsion of contents through various hollow internal organs
  - Emptying of contents of certain organs to external environment
- **Three types of muscle**
  - Skeletal muscle
    - Make up muscular system
  - Cardiac muscle
    - Found only in the heart
  - Smooth muscle
    - Appears throughout the body systems as components of hollow organs and tubes
- **Classified in two different ways**
  - Striated or unstriated
  - Voluntary or involuntary



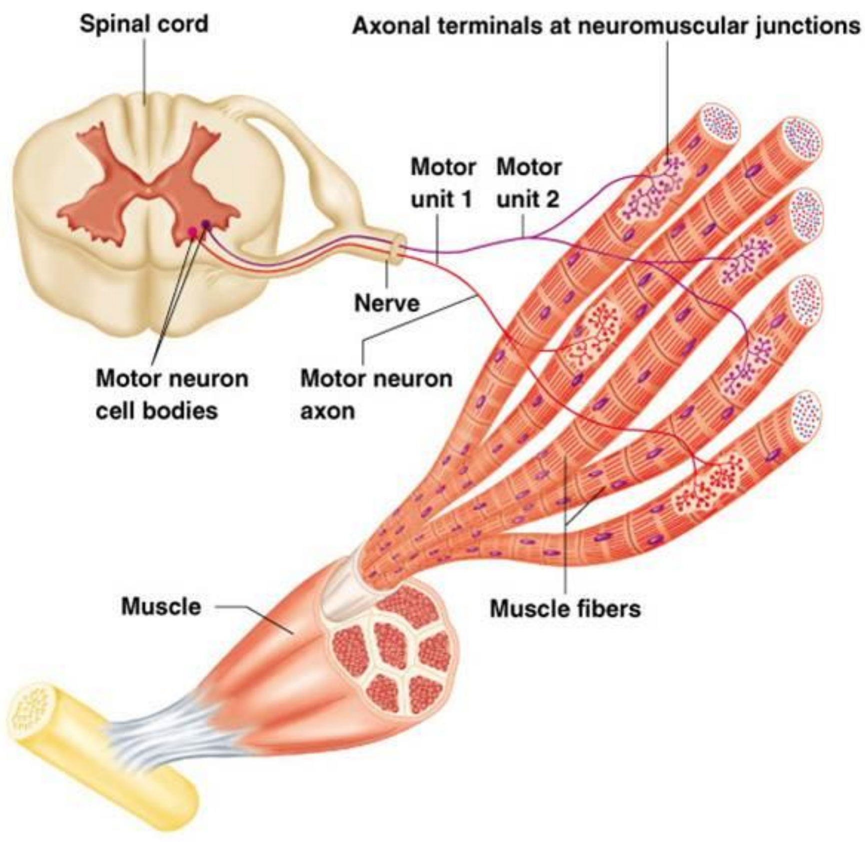
Structure of Skeletal Muscle

- **Muscle consists a number of muscle fibers lying parallel to one another and held together by connective tissue**
- **Single skeletal muscle cell is known as a muscle fiber**
  - Multinucleated
  - Large, elongated, and cylindrically shaped
  - Fibers usually extend entire length of muscle



Neuromuscular Junction

- **Axon terminal of motor neuron forms neuromuscular junction with a single muscle cell**
  - Terminal button (of neuron)
  - Motor End Plate (of muscle cell)
- **One neuron may send axons to one or more muscle fibers**



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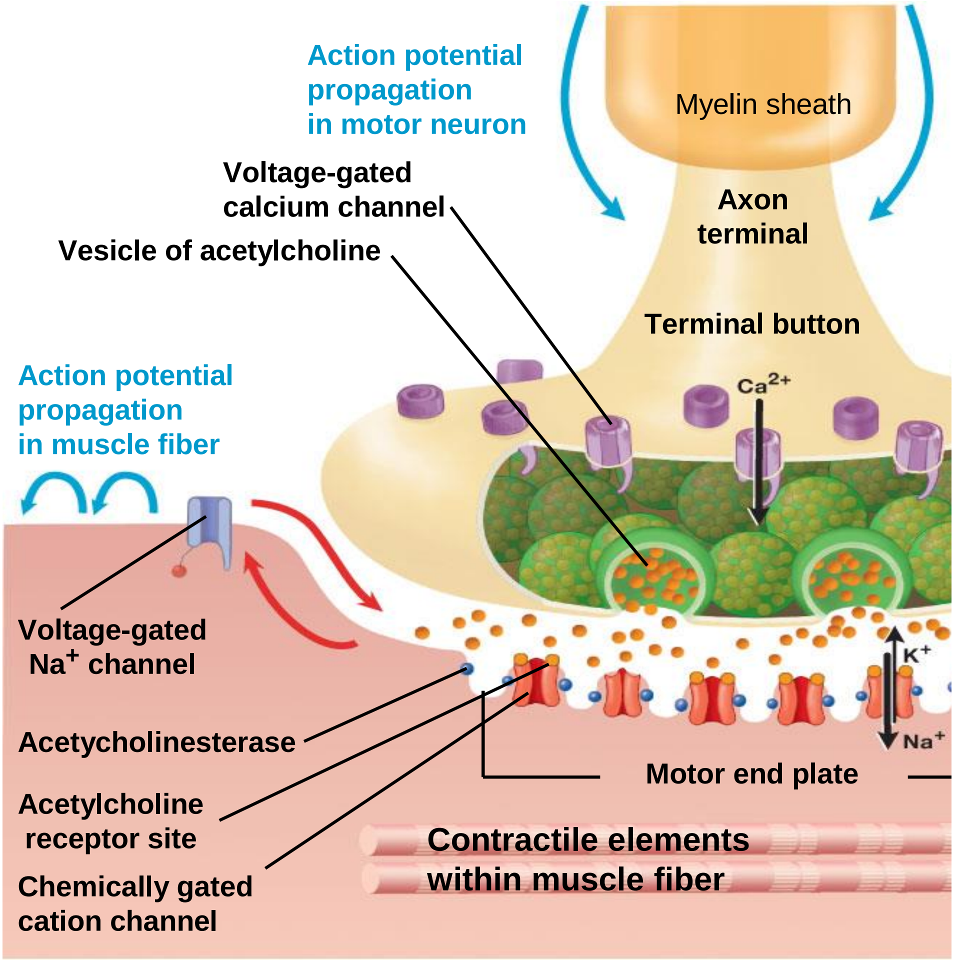
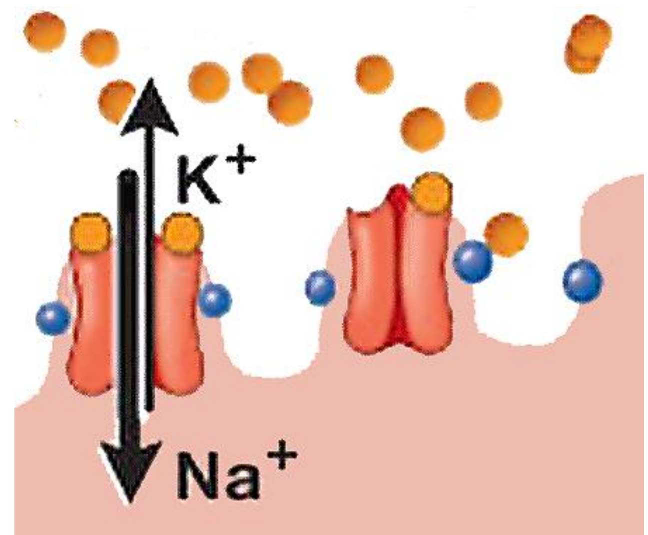
Neuromuscular Junction

- **Signals are passed between nerve terminal and muscle fiber by means of neurotransmitter ACh**
  - AP in motor neuron reaches terminal
  - Voltage-gated Ca2+ channels open
  - ACh is released by exocytosis
  - ACh diffuses across the space and binds to receptor sites on motor end plate of muscle cell membrane
  - Binding triggers opening of cation channels in motor end plate
  - Na+ movements (larger than K+ movements) depolarize motor end plate, producing end-plate potential
  - Local current flow between depolarized end plate and adjacent muscle cell membrane brings adjacent areas to threshold
  - Action potential is initiated and propagated throughout muscle fiber



Neuromuscular Junction

- **Acetylcholinesterase**
  - On the chemically-gated cation channels of the end plate
  - Inactivates ACh (as ACh molecules attaches and detaches from the receptors)
  - Ends end-plate potential and the action potential
  - Ensures prompt termination of contraction

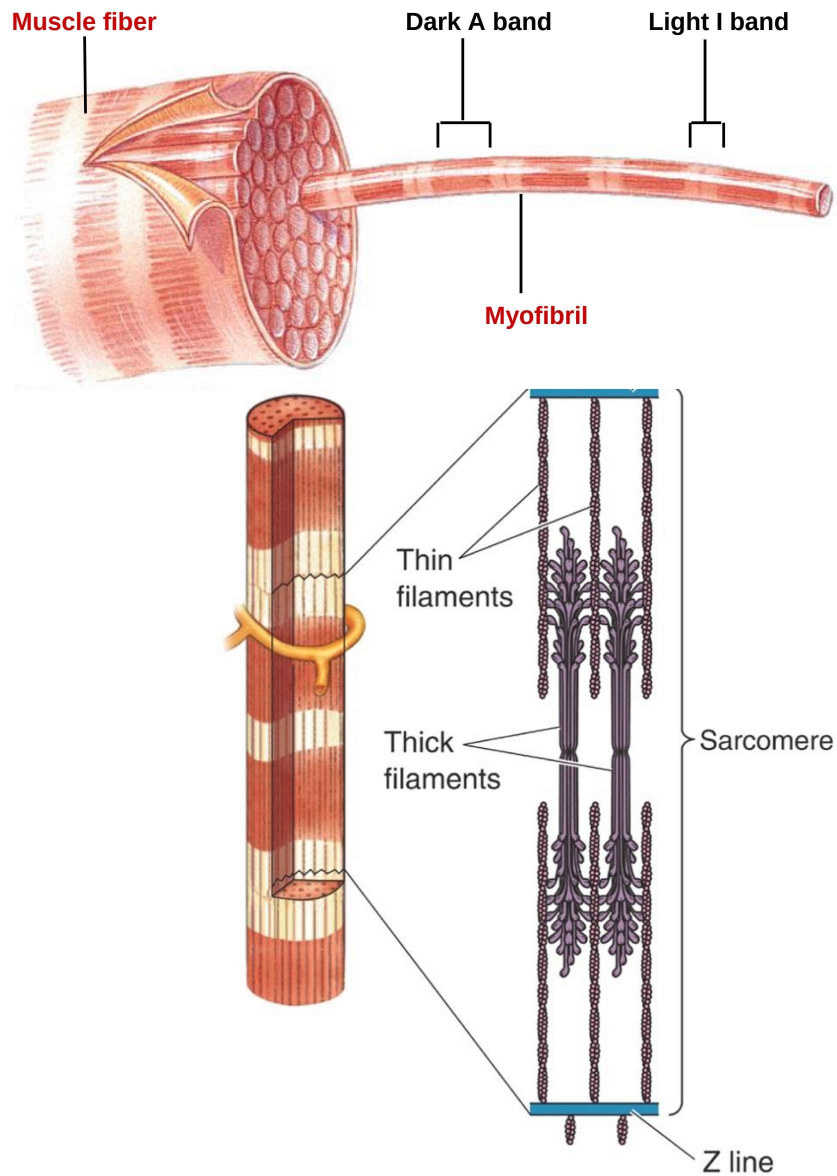


Neuromuscular Junction

- **Neuromuscular junction is vulnerable to chemical agents and diseases**
  - Black widow spider venom
    - Causes explosive release of ACh
    - Prolonged depolarization keeps Na+ channels at inactive state
    - Respiratory failure from diaphragm paralysis
  - Botulism toxin
    - From food infected with Clostridium Botulinum → Botulism
    - Blocks release of ACh
    - Respiratory failure from inability to contract diaphragm
  - Curare
    - Poisonous arrowheads
    - Binds at ACh receptor sites but has no activity and is not degrated
  - Organophosphates
    - Pesticide and military nerve gases
    - Prevent inactivation of Ach by inhibiting AChE
    - Effect similar to Black widow spider venom
  - Myasthenia gravis inactivates ACh receptor sites
    - Autoimmune condition (Antibodies against ACh receptors)
    - ACh is degraded before it can act.
    - Antidote is neostigmine (inhibits AChE and prolongs ACh action)

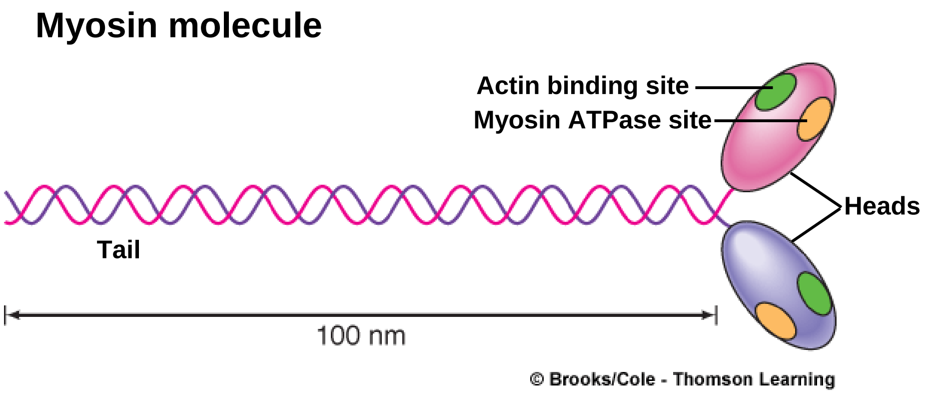
Excitation-Contraction Coupling

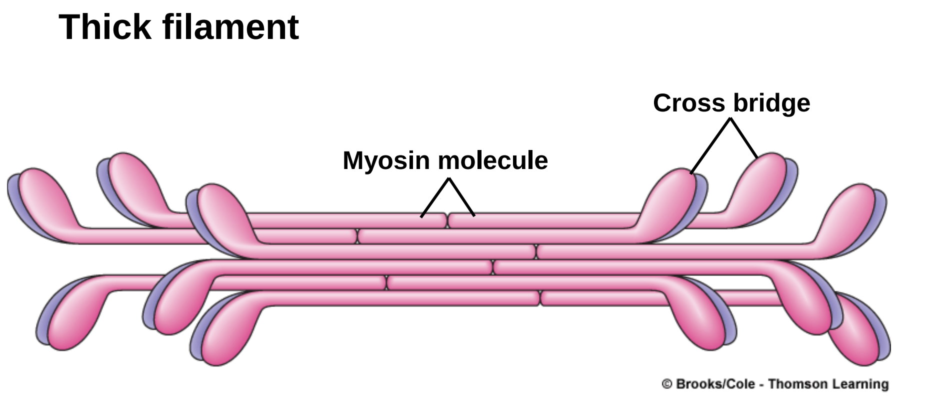
- **Muscle fiber (cell)**
  - Many myofibrils
- **Myofibrils**
  - Contractile elements of muscle fiber
  - Viewed microscopically they display alternating dark (the A bands) and light bands (the I bands) giving appearance of striations
  - Regular arrangement of thick and thin filaments
    - Thick filaments – myosin (protein)
    - Thin filaments – actin (protein)
- **Sarcomere**
  - Functional unit of skeletal muscle
  - Found between two Z lines
    - Z lines connect thin filaments of two adjoining sarcomeres



Excitation-Contraction Coupling

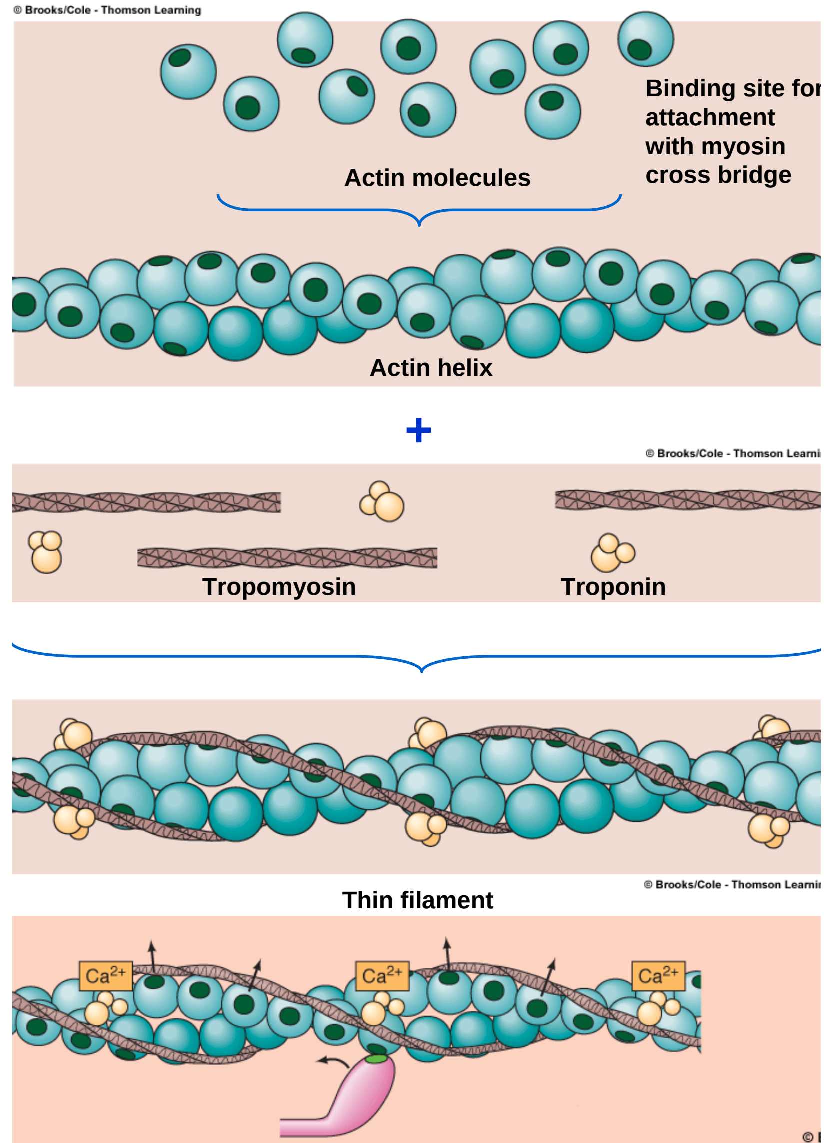
- **Thick filaments**
  - Myosin
  - Several hundred of them
  - Heads form cross bridges between thick and thin filaments
    - Cross bridge has two important sites critical to contractile process
      - An actin-binding site
      - A myosin ATPase (ATP-splitting) site





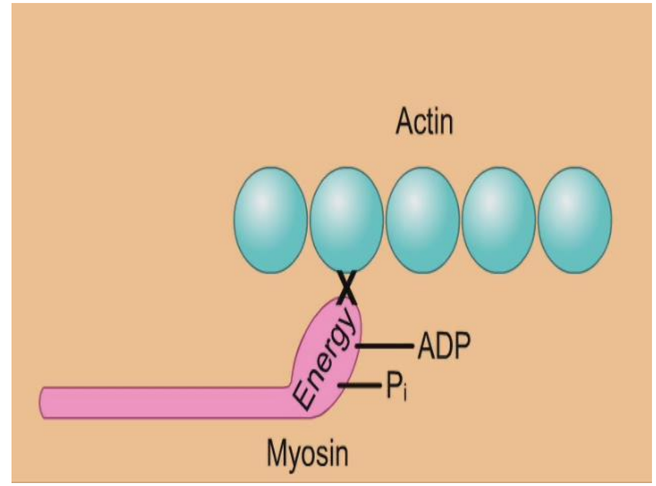
Excitation-Contraction Coupling

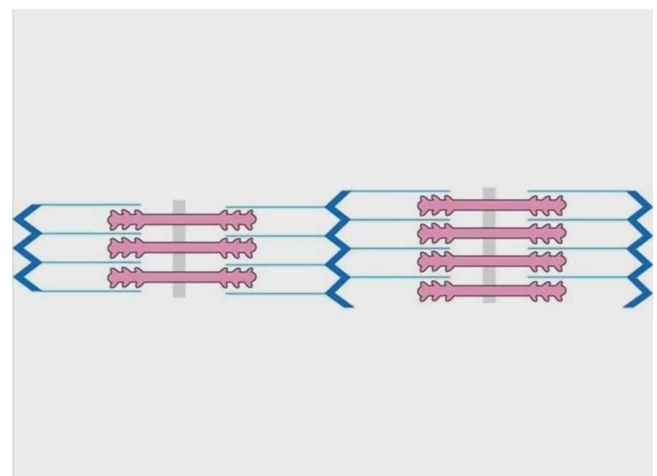
- **Thin filaments**
  - Actin
    - Primary structural component of thin filaments
    - Each actin molecule has special binding site for attachment with myosin cross bridge
  - Tropomyosin
    - Thread-like molecules that covers actin sites blocking interaction with thick filaments
  - Troponin
    - Made of three polypeptide units
      - One binds to tropomyosin
      - One binds to actin
      - One can bind with Ca2+
  - When Ca2+ binds to troponin
    - Tropomyosin moves away from blocking position
    - Cross bridges can form



Excitation-Contraction Coupling

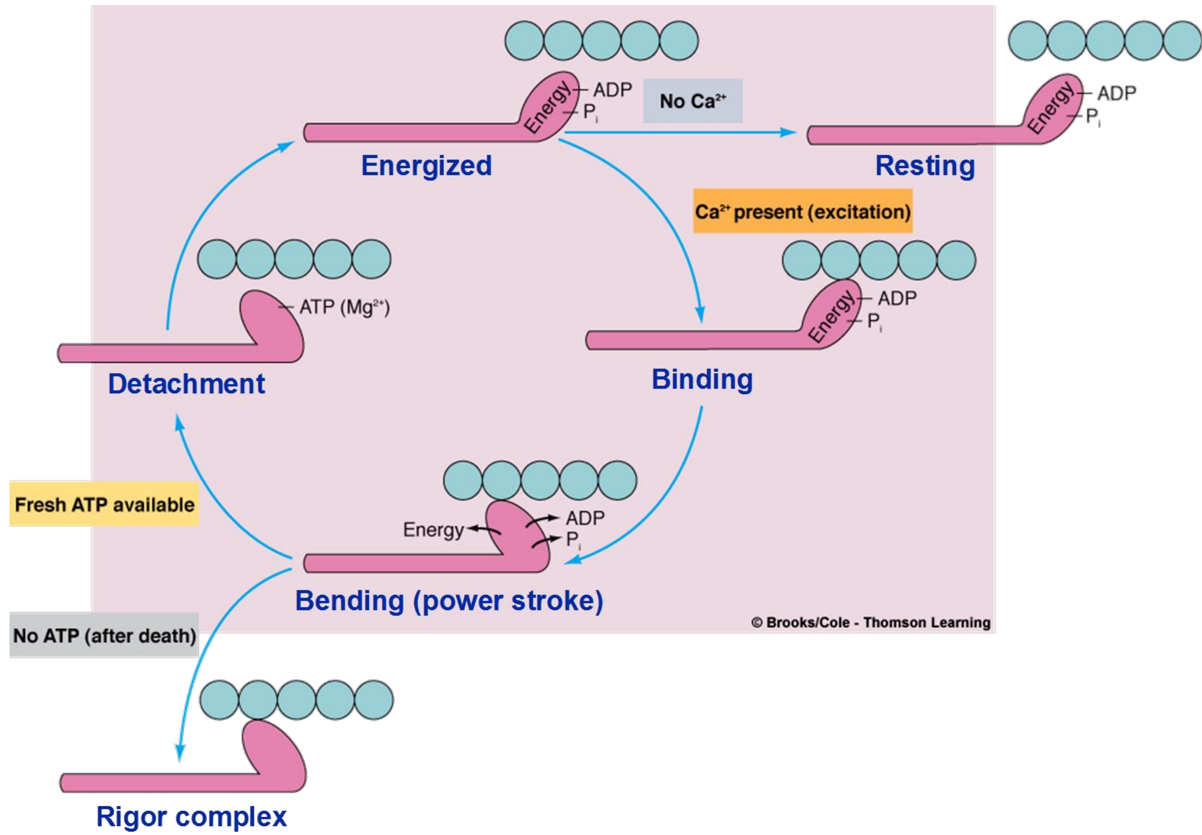
- **Power Stroke**
  - Ca2+ released into sarcoplasm
  - Myosin heads bind to actin, binding sides exposed
  - Myosin heads swivel toward center of sarcomere (power stroke)
  - ADP released
  - ATP binds to myosin head and detaches it from actin
  - Hydrolysis of ATP transfers energy to myosin head and reorients it





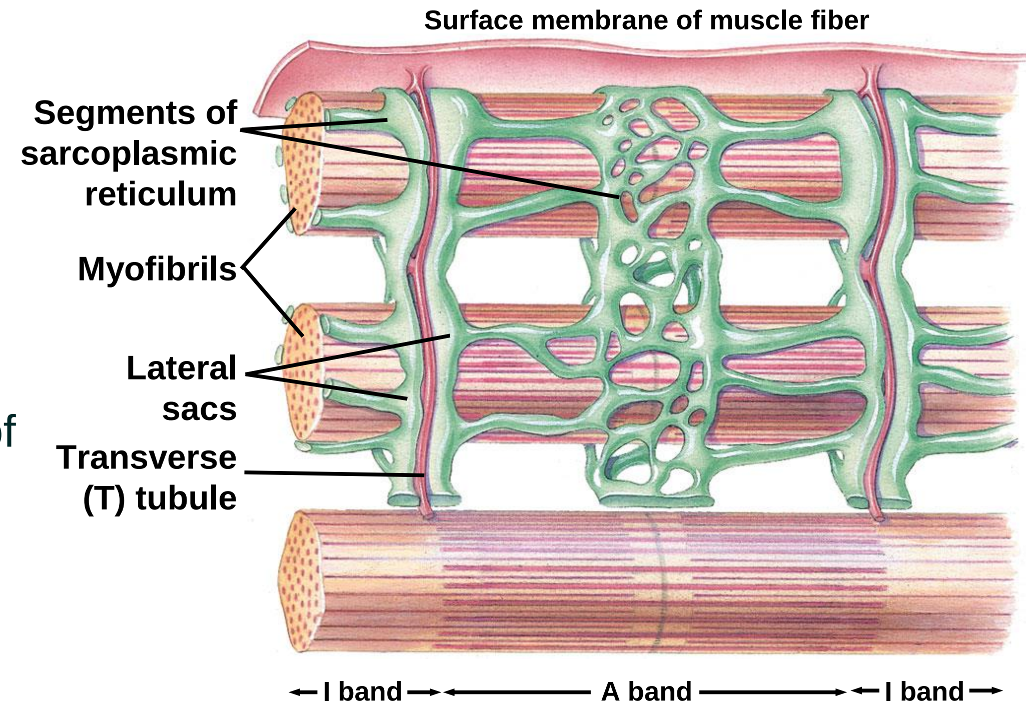
Excitation-Contraction Coupling

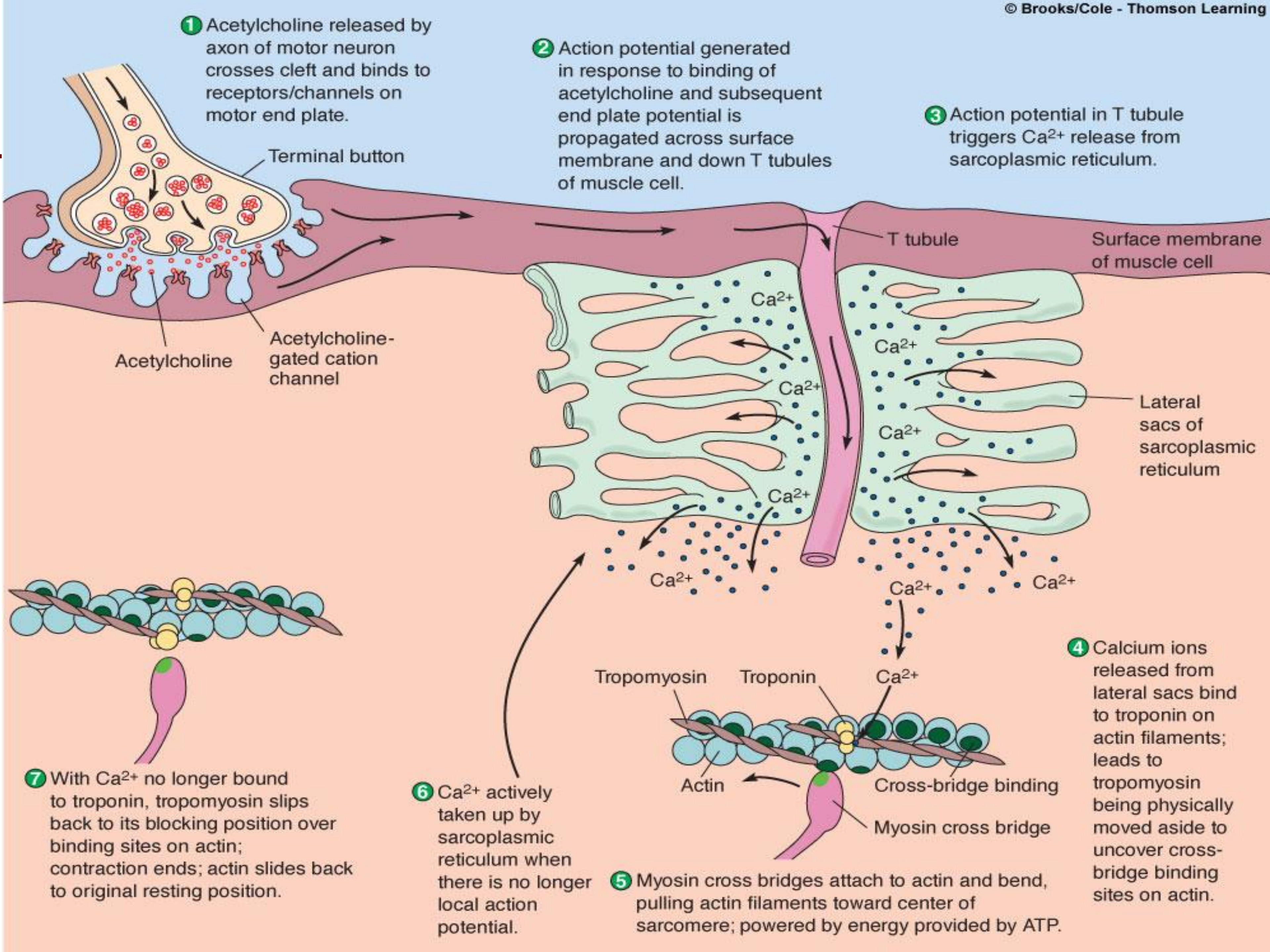
- **Contraction continues if ATP is available and Ca2+ level in sarcoplasm is high**
- **Myosin head remains attached until ATP binds → rigor mortis**
    - Ca2+ released
    - ATP quickly depleted
    - Onset in a few hours
    - Can last 1-2 days
- **Ca2+ stores are in the sarcoplasmic reticulum**



Excitation-Contraction Coupling

- **Sarcoplasmic Reticulum (SR)**
  - Modified endoplasmic reticulum
  - A fine network of interconnected compartments that surround each myofibril
  - Not continuous but encircles myofibril throughout its length
- **T tubules**
  - Run perpendicularly from surface of muscle cell membrane into central portions of the muscle fiber
  - T tubule membrane is continuous with surface membrane → action potential on surface membrane spreads down into T-tubule
  - Spread of action potential triggers release of Ca2+ from SR into cytosol

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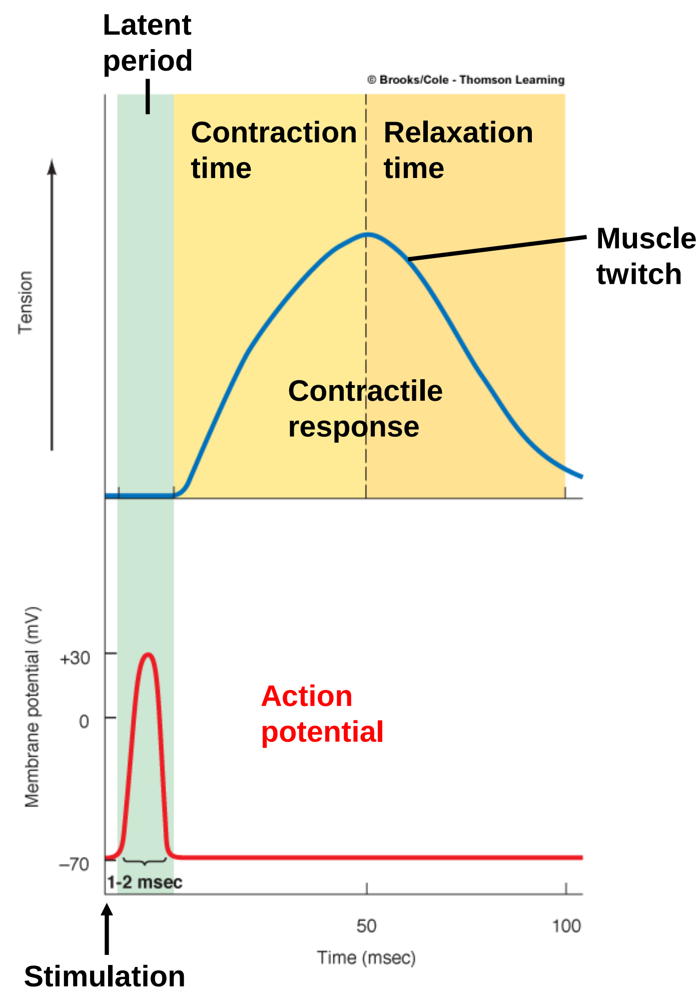
1 Acetylcholine released by axon of motor neuron crosses cleft and binds to receptors/channels on motor end plate.
Terminal button
2 Action potential generated in response to binding of acetylcholine and subsequent end plate potential is propagated across surface membrane and down T tubules of muscle cell.
3 Action potential in T tubule triggers Ca2+ release from sarcoplasmic reticulum.
T tubule
Surface membrane of muscle cell
Acetylcholine
Acetylcholine-gated cation channel
Ca2+
Lateral sacs of sarcoplasmic reticulum
Tropomyosin
Troponin
Actin
Cross-bridge binding
Myosin cross bridge
4 Calcium ions released from lateral sacs bind to troponin on actin filaments; leads to tropomyosin being physically moved aside to uncover cross-bridge binding sites on actin.
5 Myosin cross bridges attach to actin and bend, pulling actin filaments toward center of sarcomere; powered by energy provided by ATP.
6 Ca2+ actively taken up by sarcoplasmic reticulum when there is no longer local action potential.
7 With Ca2+ no longer bound to troponin, tropomyosin slips back to its blocking position over binding sites on actin; contraction ends; actin slides back to original resting position.

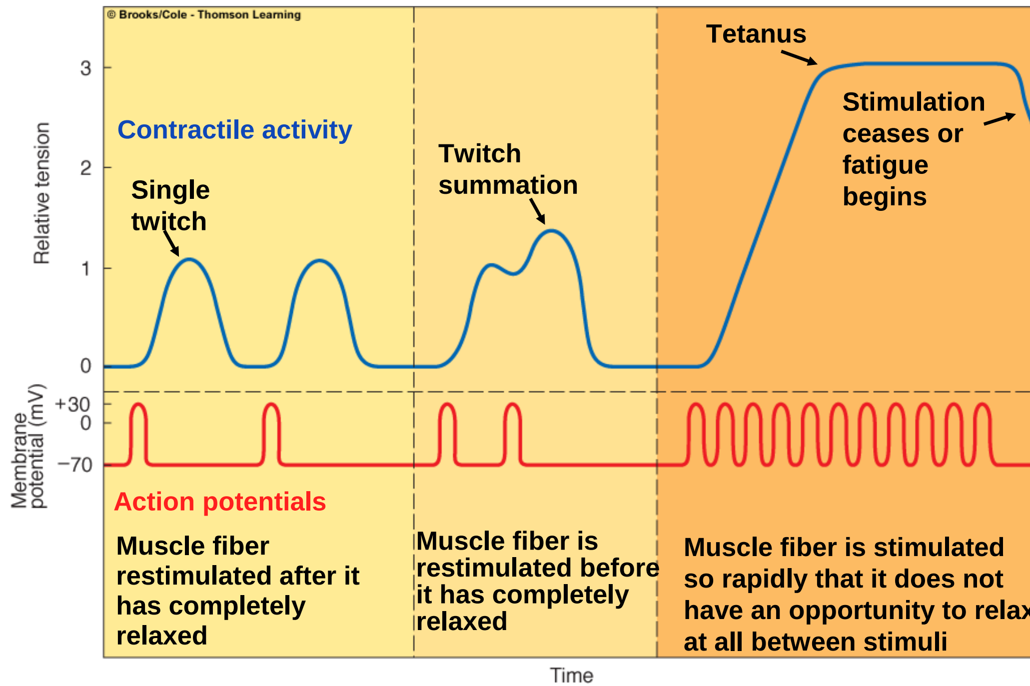
Excitation-Contraction Coupling

- **Contractile activity**
  - AP is very short (1-2 msec)
  - Contraction does not start until enough Ca2+ is released
    - Latent period
  - Contraction process requires time to complete
    - Contraction time (~50 msec)
  - Relaxation also requires time to complete
    - Relaxation time (~50 msec)
- **Twitch – Contraction of single muscle fiber from single AP**
  - Brief, weak contraction
  - Produced from single action potential
  - Too short and too weak to be useful
  - Normally does not take place in body



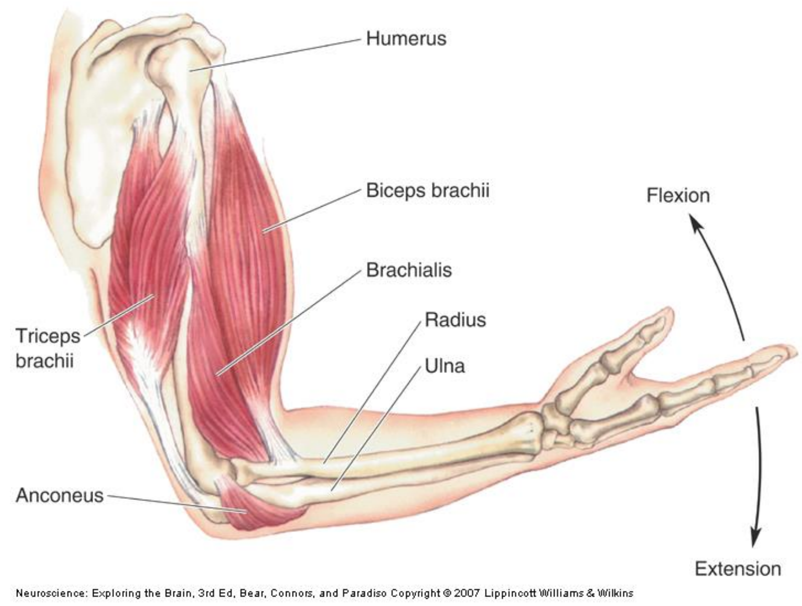
Frequency of Stimulation

- **Twitch summation**
  - Individual twitches are summed
    - AP much sorter in time than contraction → Multiple APs can be delivered
  - Results from sustained elevation of cytosolic calcium
- **Tetanus**
  - Occurs if muscle fiber is stimulated so rapidly that it does not have a chance to relax between stimuli
  - Contraction is usually three to four times stronger than a single twitch
  - Do not confuse with the disease of the same name!



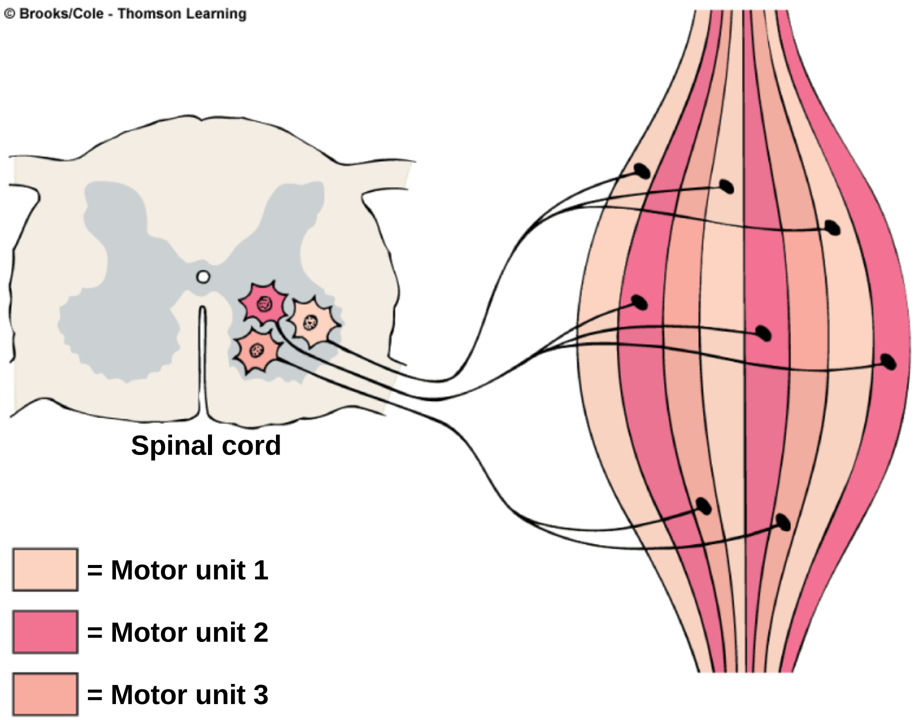
Skeletal Muscle Mechanics

- **Muscle consists of groups of muscle fibers bundled together and attached to bones**
  - Connective tissue covering muscle divides muscle internally into bundles
  - Connective tissue extends beyond ends of muscle to form tendons
    - Tendons attach muscle to bone
- **Muscle Contraction**
  - Contractions of whole muscle can be of varying strength
  - Two primary factors which can be adjusted to accomplish gradation of whole-muscle tension
    - Tension developed by each contracting fiber
    - Number of muscle fibers contracting within a muscle



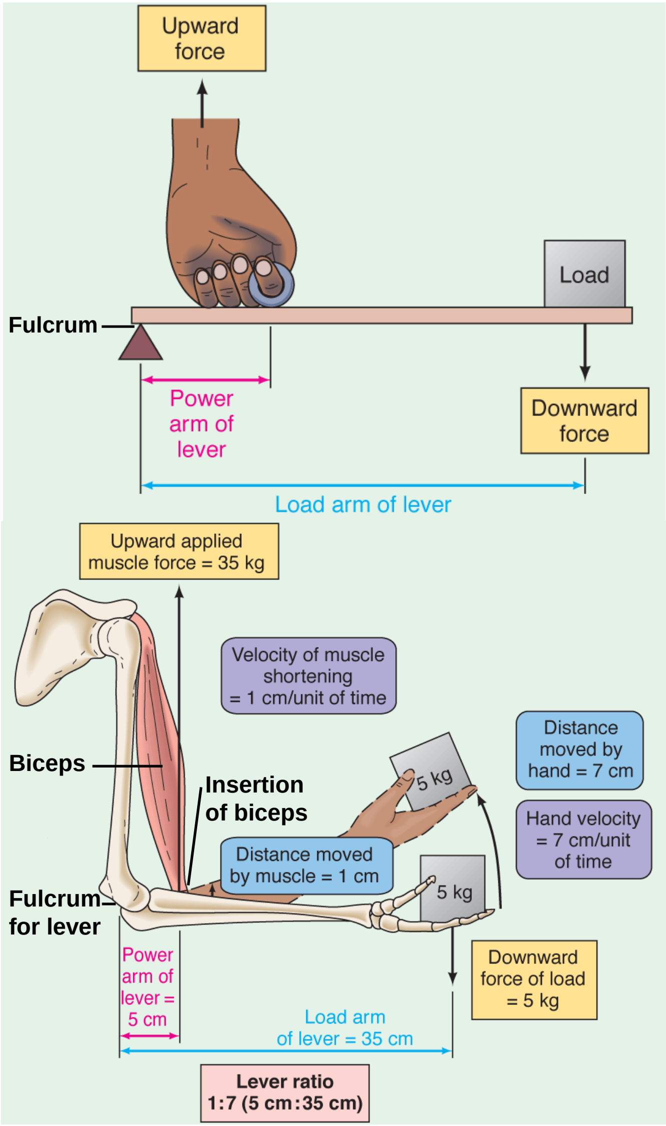
Motor Unit Recruitment

- **Motor unit**
  - One motor neuron and the muscle fibers it innervates
- **Number of muscle fibers varies among different motor units**
- **Number of muscle fibers per motor unit and number of motor units per muscle vary widely**
  - Muscles that produce precise, delicate movements contain fewer fibers per motor unit
  - Muscles performing powerful, coarsely controlled movement have larger number of fibers per motor unit
- **Asynchronous recruitment of motor units helps delay or prevent fatigue**
- **Muscle fibers which fatigue easily are recruited later**
  - Can engage in endurance activities for a long time but can only deliver full force for brief periods of time



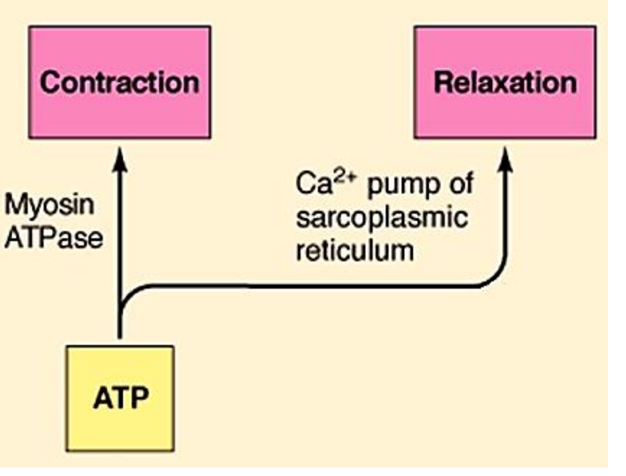
Lever Systems

- **Bones, muscles, and joints interact to form lever systems**
  - Bones function as levers
  - Joints function as fulcrums
  - Skeletal muscles provide force to move bones
- **Muscles usually exert more force than actual weight of load!**
  - Advantages: higher speed, more distance



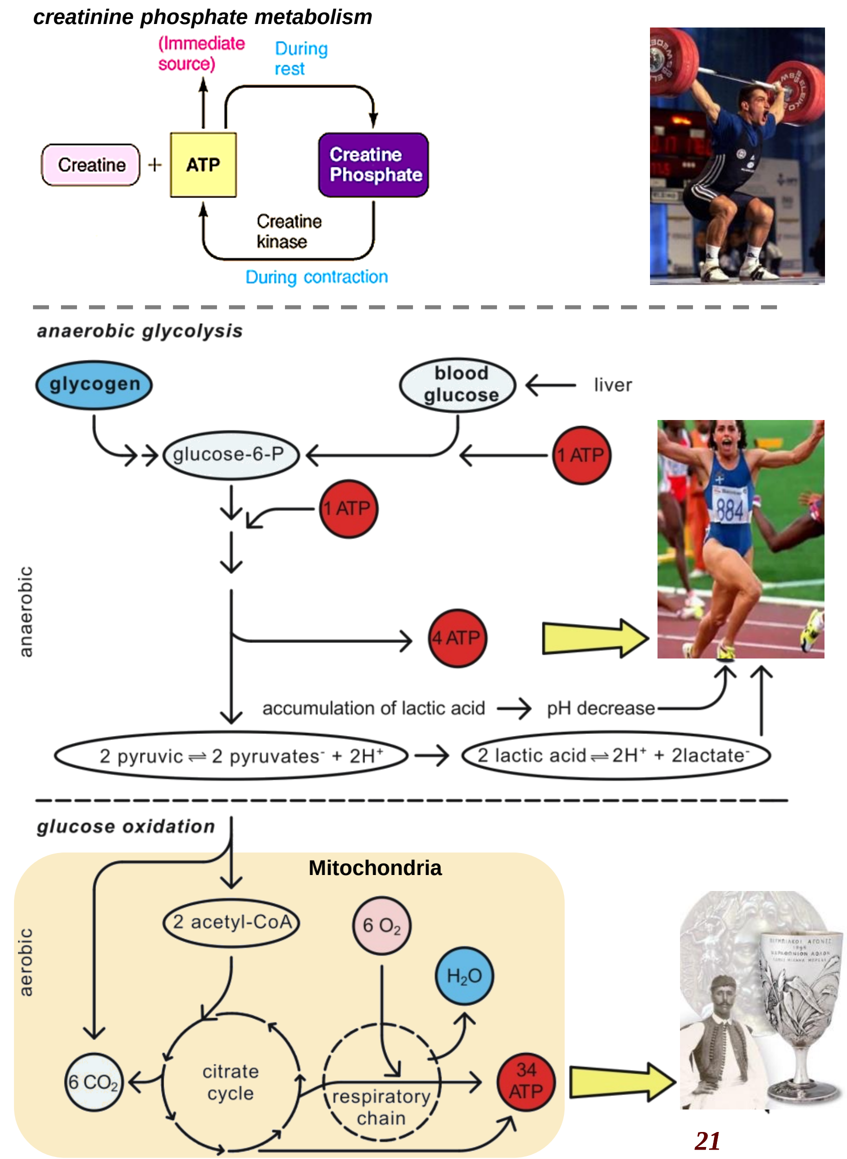
Skeletal Muscle Metabolism

- **Contraction-Relaxation Steps Requiring ATP**
  - Splitting of ATP by myosin ATPase provides energy for power stroke of cross bridge
  - Binding of fresh molecule of ATP to myosin lets bridge detach from actin filament at end of power stroke so cycle can be repeated
  - Active transport of Ca2+ back into sarcoplasmic reticulum during relaxation depends on energy derived from breakdown of ATP



Skeletal Muscle Metabolism

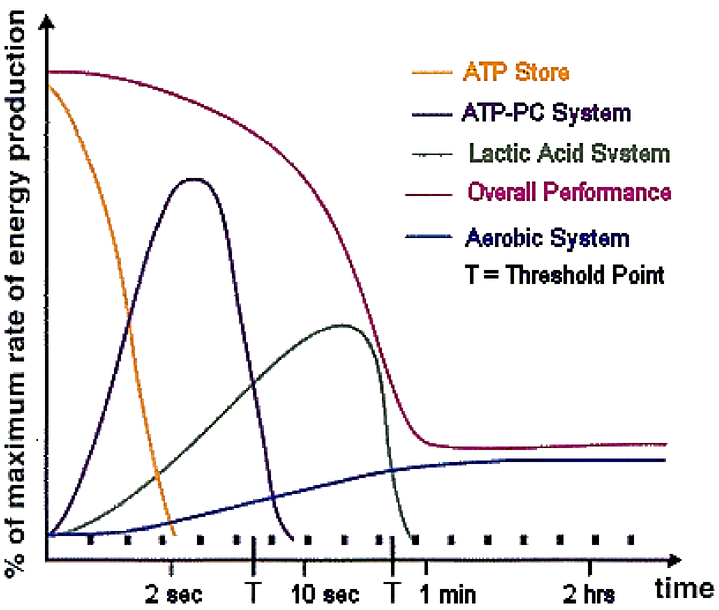
- **Energy Sources for Contraction**
  - Transfer of high-energy phosphate from creatine phosphate to ADP
    - First energy storehouse tapped at onset of contractile activity
    - Short duration or bursts of exercise
      - ~160g or 12.5 kcal
      - E.g. 100 m running
  - Glycolysis in anaerobic conditions
    - Supports anaerobic or high-intensity exercise
    - Less efficient but much faster than oxidative phosphorylation
    - Quickly depletes glycogen supplies
    - Lactic acid is produced
      - Soreness that occurs during the time (not after) intense exercise
    - Energy depletion and ↓ pH contribute to muscle fatigue
  - Oxidative phosphorylation (citric acid cycle and electron transport system)
    - Moderate exercise (Aerobic or endurance-type exercise)
    - Takes place within muscle mitochondria if sufficient O2 is present
      - Deeper & faster breathing, ↑ Heart rate and contraction, Dilation of blood vessels
      - Myoglobin (Similar to hemoglobin) → Increase the transfer and store of O_2 in muscle cells
    - Uses glucose or fatty acids
      - Glucose derived from muscle glycogen (chains of glucose) stores
        - Limited (~ 150g or 600 kcal)
        - Athletes can store more (2000 kcal for marathon runners)
      - Glucose derived from liver glycogen stores
        - Limited (~80-200g or 320-800 kcal)
      - Fatty acids derived from lipolisis
        - Plenty of these! (~15kg or 135.000 kcal)



Skeletal Muscle Metabolism

Sport	Creatine & Glycolisis	Glycolysis & Oxidative	Oxidative
Golf swing	95	5	
Sprints	90	10	
Volleyball	80	5	15
Gymnastics	80	15	5
Tennis	70	20	10
Basketball	60	20	20
Soccer	50	20	30
Skiing	33	33	33
Rowing	20	30	50
Distance running	10	20	70
Swimming 1.5km	10	20	70

Table adapted from Fox E. L. et al, The Physiological Basis for Exercise and Sport, 1993



Fatigue

- **Contractile activity can not be sustained indefinitely → Fatigue**
- **Muscle Fatigue**
  - Occurs when exercising muscle can no longer respond to stimulation with same degree of contractile activity
  - Defense mechanism that protects muscle from reaching point at which it can no longer produce ATP
  - Underlying causes of muscle fatigue are unclear. Implicated
    - ADP increase (interferes with cross-bridges and Ca^{2+} uptake in the SR)
    - Lactic acid accumulation (may interfere with key enzymes in energy-producing pathways)
    - Accumulation of extracellular K^+ (decrease in membrane potential)
    - Depletion of glycogen
- **Central Fatigue**
  - Occurs when CNS no longer adequately activates motor neurons supplying working muscles
  - Often psychologically based
    - Discomfort, boredom or tiredness
  - Mechanisms involved in central fatigue are poorly understood
- **Recovery**
  - Excess postexercise O_2 consumption (EPOC) helps
    - Restore Creatine Phosphate (few minutes)
    - Replenish ATP
    - Convert Lactic acid to pyruvate for oxidative ATP generation
    - Cover increased general O_2 demand because of higher temperature
  - Nutrient replenishment (1-2 days after a marathon)

Types of Muscle

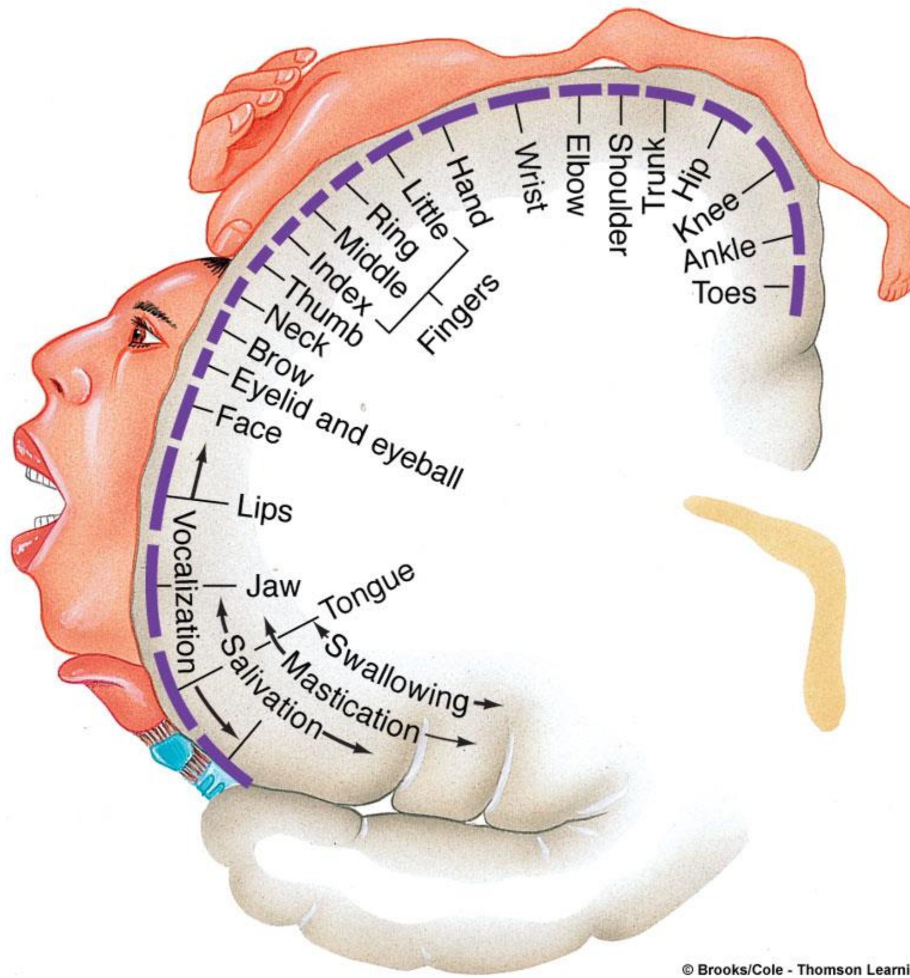
- **Types of Motor Units**
  - Red muscle fibers
    - Oxidative fibers contain more mitochondria and myoglobin and have a richer blood supply → red meat
    - Slow to contract, can sustain contraction
  - White muscle fibers
    - Few mitochondria, anaerobic metabolism
    - Contract and fatigue rapidly
  - Fast motor units
    - Larger diameter, faster conducting neurons
    - Rapidly fatiguing white fibers
  - Slow motor units
    - Smaller diameter, slower conducting neurons
    - Slowly fatiguing red fibers

Muscle Adaptation & Repair

- **Muscle has a high degree of plasticity**
  - Improvement of oxidative capacity
    - From regular aerobic exercise
    - Capillaries and mitochondria increase
  - Hypertrophy
    - From anaerobic high intensity exercise
    - Muscle fiber diameter increases (more actin and myosin)
    - Mainly fast-glycolytic fibers
- **Testosterone and other steroids increase the synthesis of actin and myosin**
  - Steroid abuse
- **Fast muscle fibers are interconvertible**
  - Oxidative ↔ glycolytic
  - But NOT fast ↔ slow
- **Muscle atrophy**
  - Disuse atrophy (e.g. space exploration)
  - Denervation atrophy (e.g. paralysis)
- **Muscle has limited repair cababilities**
  - Satellite cells can create a few myoblasts which fuse and create a few muscle fibers

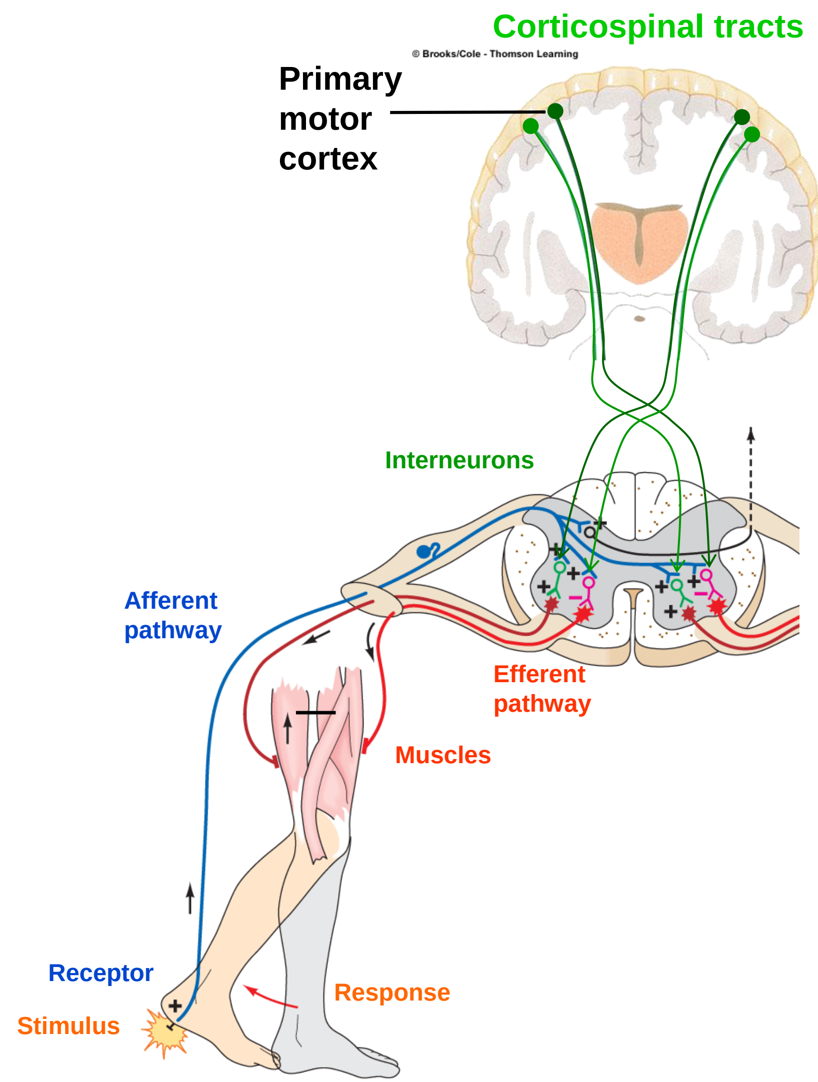
Control of Motor Movement

- **Frontal lobe – Primary Motor Cortex**
  - Voluntary control for muscle movement
  - Motor cortex on each side controls muscles on the opposite side of the body
    - Tracts originating in the cortex cross (at level of pyramids) before continuing down spinal cord to terminate muscle
  - Body regions are topographically mapped
    - Different parts of the body are not equally represented
    - Motor Homonculus
    - Proportional to precision and complexity of motor skills
  - Controls the opposite side of the body
    - Damage on right side results in motor deficit on left side



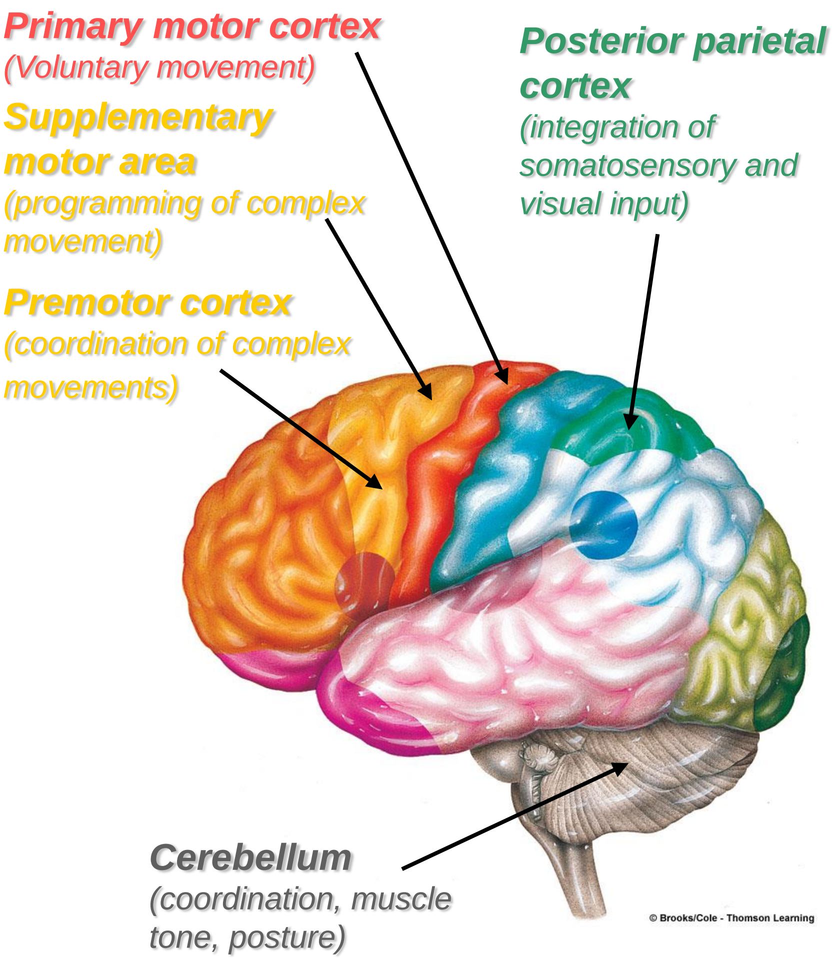
Control of Motor Movement

- **Efferent pathway**
  - Primary motor cortex → upper motor neurons → Brain stem (cross to the other side) → spinal cord → Lower motor neurons
- **Input to lower motor-neurons**
  - From upper motor neurons (primary motor cortex)
    - Responsible for fine voluntary movement
  - From afferent neurons
    - Usually through intervening interneurons
    - Responsible for spinal reflexes (e.g. withdrawal)



Control of Motor Movement

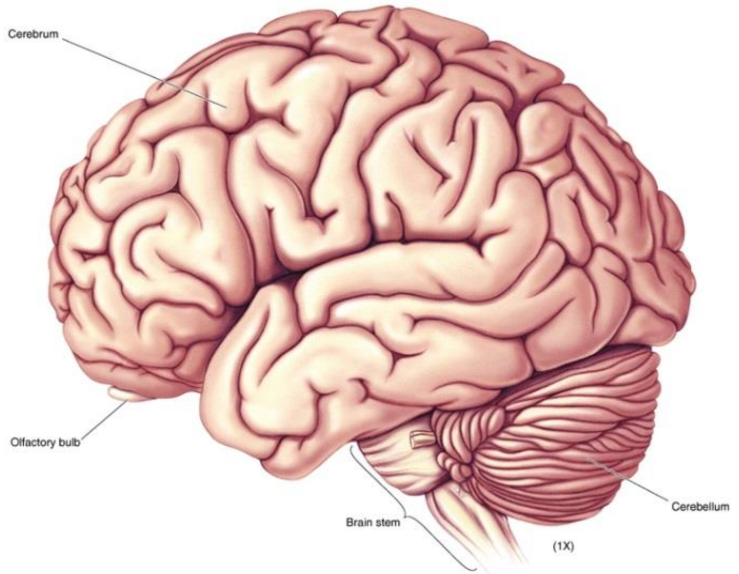
- **Movement**
  - The motor cortex itself does not initiate movement
  - Frontal lobe → Strategy
    - with inputs from the parietal lode (body and world map)
  - Premotor and Supplementary motor cortex → Planning
  - Motor Cortex → Execution
  - Cerebellum → Coordination
  - Basal Ganglia → Initiation and Correction

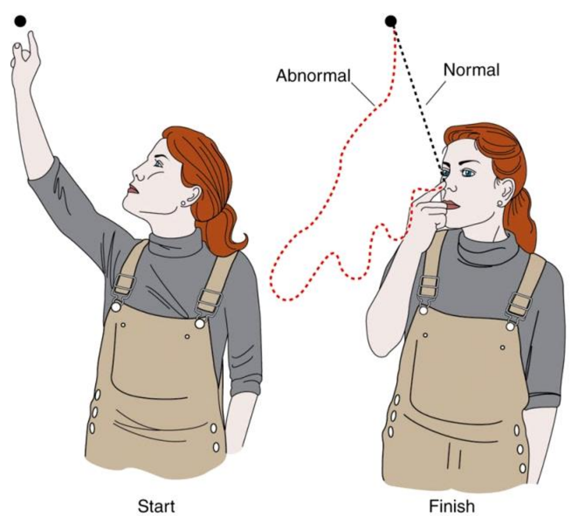


Control of Motor Movement

Cerebellum

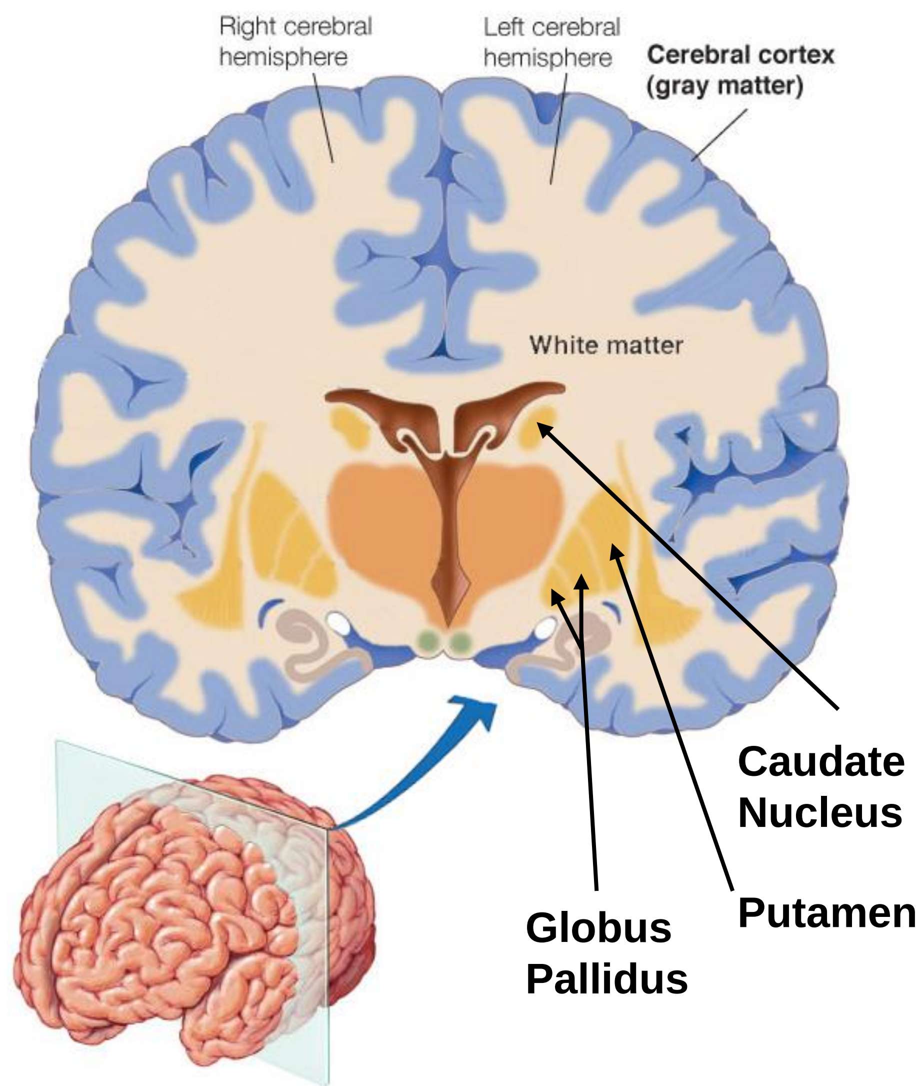
- **Highly folded, posterior, part of brain**
- **Important in**
  - Balance
  - Coordination of voluntary movement
  - Procedural memories (e.g. motor skills gained through repetitive training
- **Activities**
  - Maintenance of balance, control of eye movements
  - Regulation of muscle tone (enhancement, opposite of basal nuclei), coordination of skilled voluntary movement
  - Planning and initiation of voluntary activity
- **Cerebellar disease**
  - Intention tremor → present only during voluntary activity





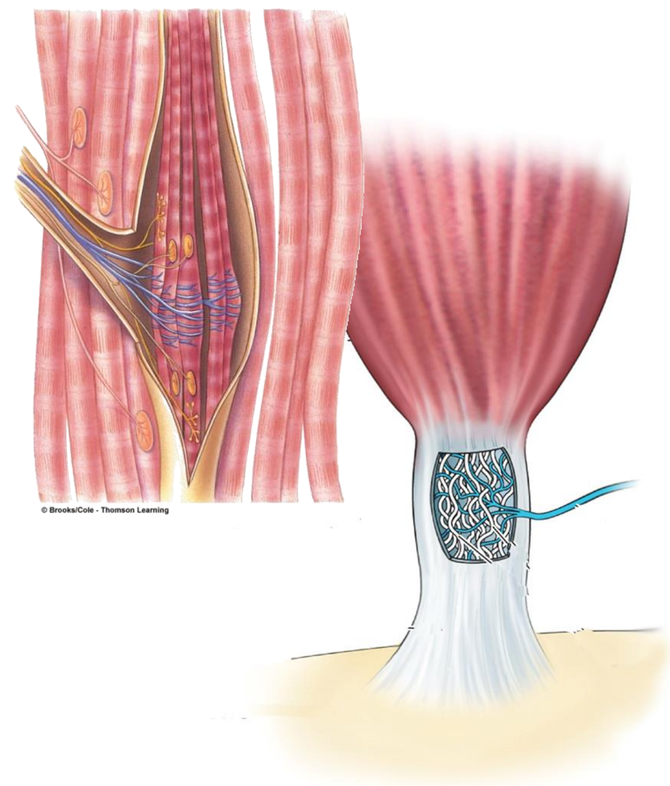
Basal Ganglia

- **Masses of grey matter deep inside the white matter**
- **Act by modifying ongoing activity in motor pathways**
    - Inhibit muscle tone
        - Proper tone - balance of excitatory and inhibitory inputs to motor neurons that innervate skeletal muscle
    - Select and maintain purposeful motor activity while suppressing unwanted patterns of movement
    - Monitor and coordinate slow and sustained contractions
        - Especially those related to posture and support
- **Parkinson’s disease**
    - Damage to basal ganglia neurons and a deficiency in dopamine
        - Increased muscle tone or rigidity
        - Resting tremors (eg unwanted movements
        - Slowness in initiating and carrying out motor behaviors



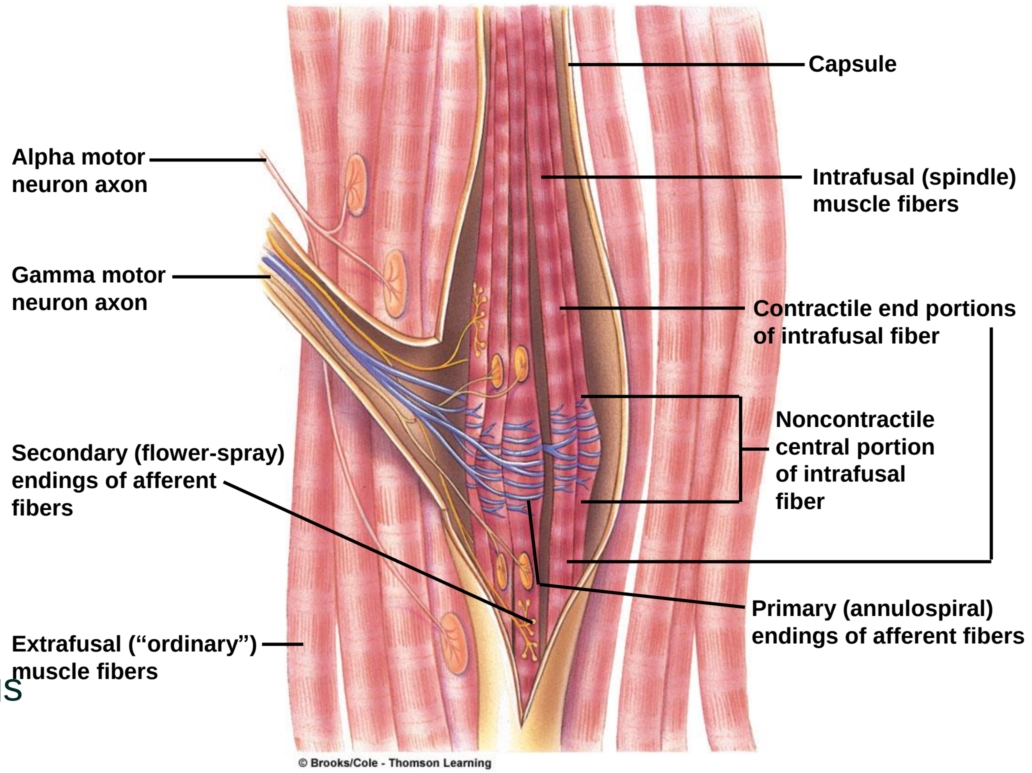
Muscle Receptors

- **Receptors are necessary to plan and control complicated movement and balance**
- **The brain receives information from all muscles and joints in the body → proprioception**
- **Two types of muscle receptors**
  - Muscle spindles
    - Monitor muscle length and tension
  - Golgi tendon organs
    - Monitor whole muscle tension



Muscle Receptors

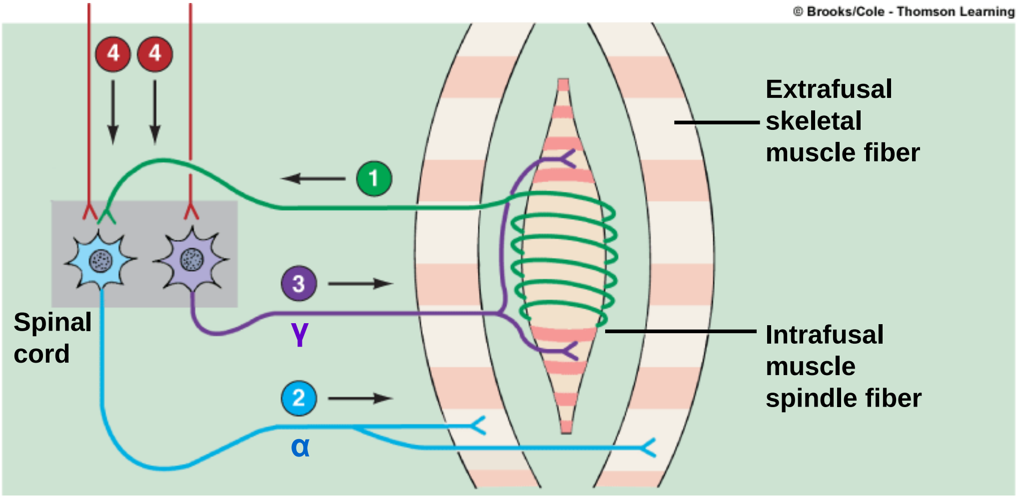
- **Muscle Spindles**
  - Consist of collections of specialized muscle fibers known as intrafusal fibers
    - Lie within spindle-shaped connective tissue capsules parallel to extrafusal fibers
    - Have contractile ends and a non-contractile central portion
  - Each spindle has its own private nerve supply
    - Plays key role in stretch reflex
    - Efferent
      - Gamma motor neurons*
    - Afferent
      - Primary (annulospiral) endings (in the central portion)
      - Secondary (flower-spray) endings (at the end segments)

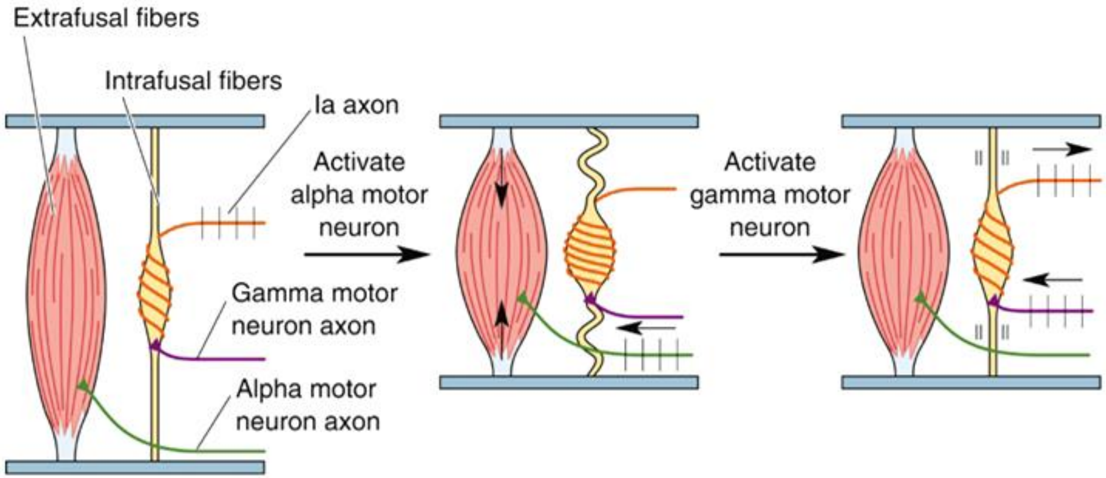


* Efferent neurons to extrafusal fibers are called alpha motor neurons

Muscle Receptors

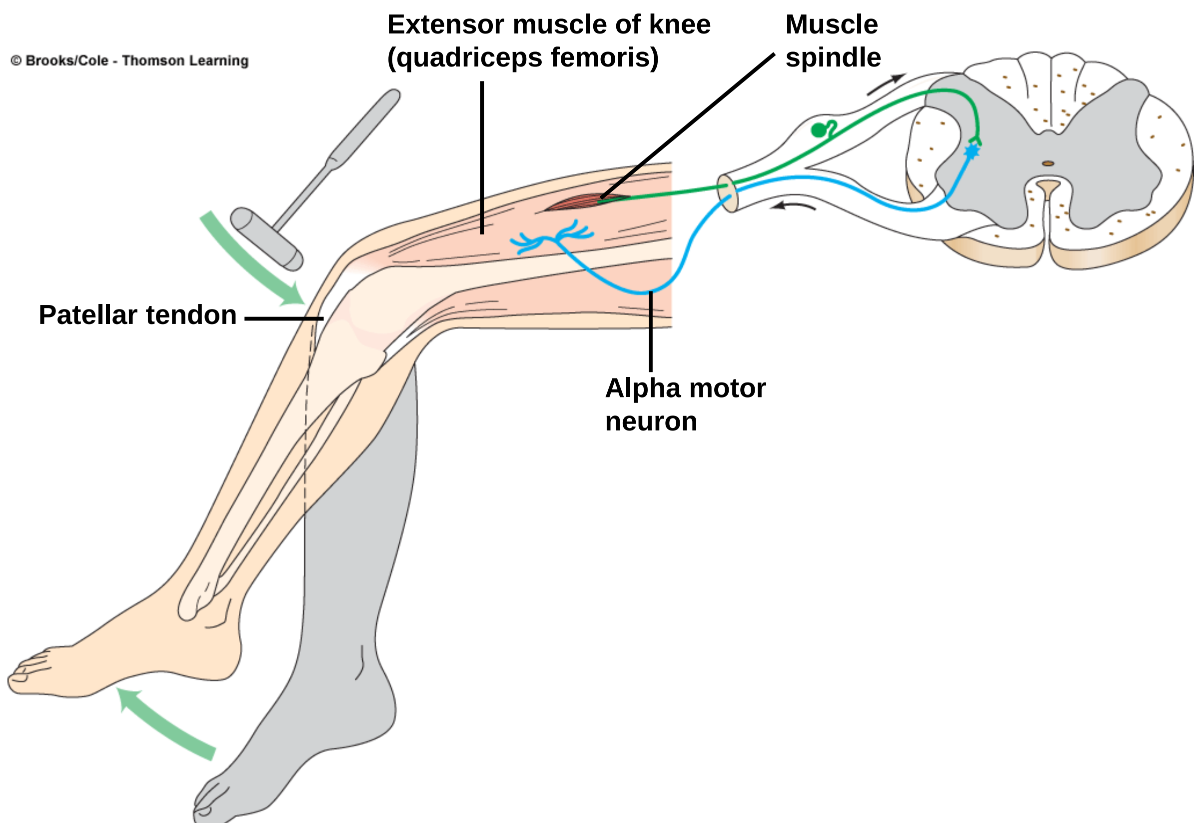
- **Coactivation of alpha and gamma motor neurons**
  - Spindle coactivation during muscle contraction
  - Spindle contracted to reduce length
    - With no coactivation
      - Slackened spindle
      - Not sensitive to stretch
  - Adjustment to keep muscle spindles sensitive to stretch





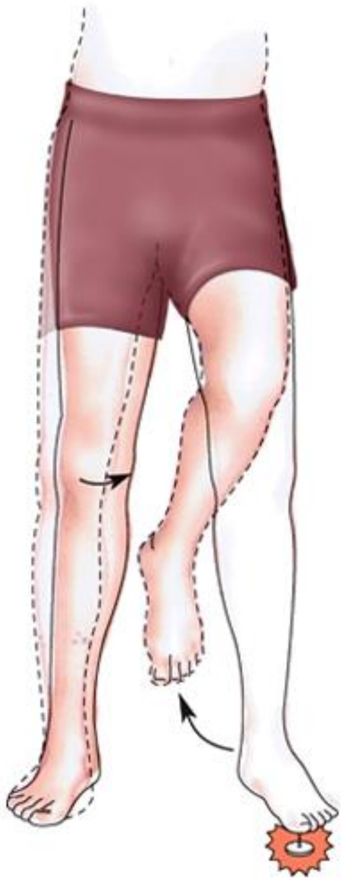
Muscle Receptors

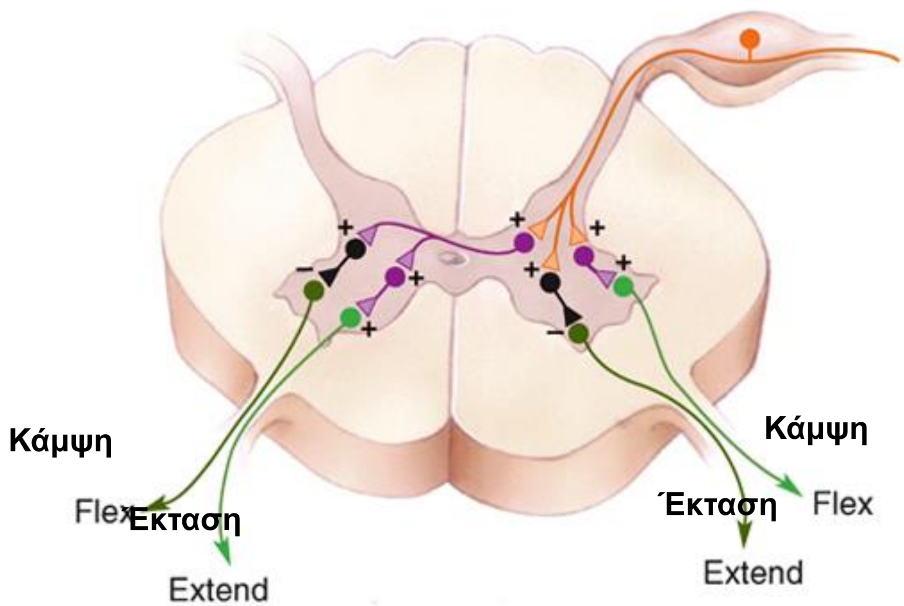
- **Stretch Reflex**
  - Primary purpose
    - Resist tendency for passive stretch of extensor muscles by gravitational forces when person is standing upright
  - Classic example is patellar tendon, or knee-jerk reflex



Muscle Receptors

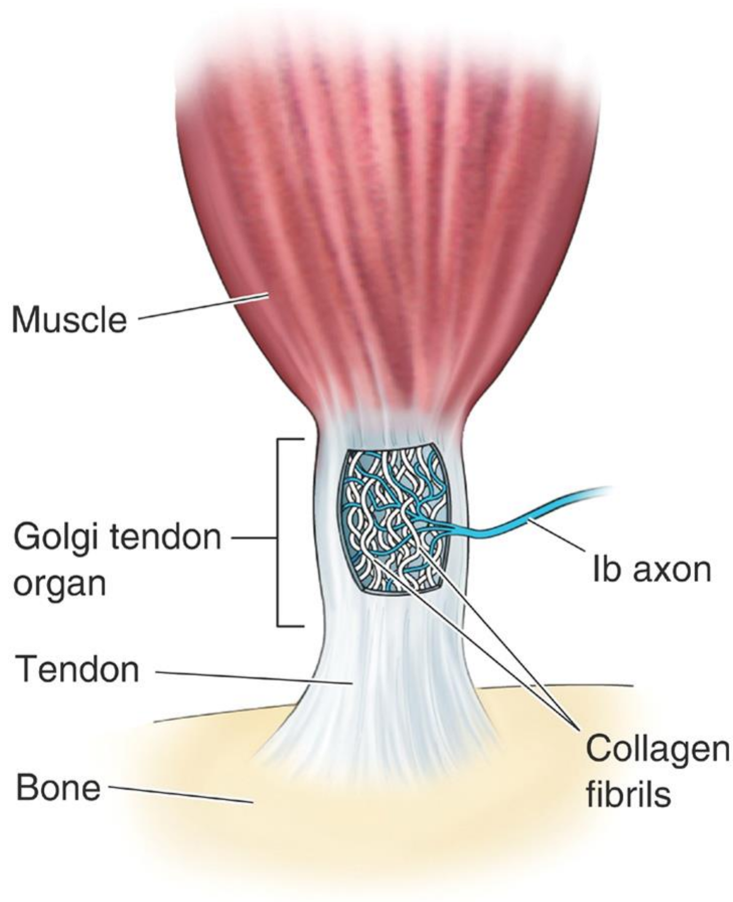
- More complicated reflexes





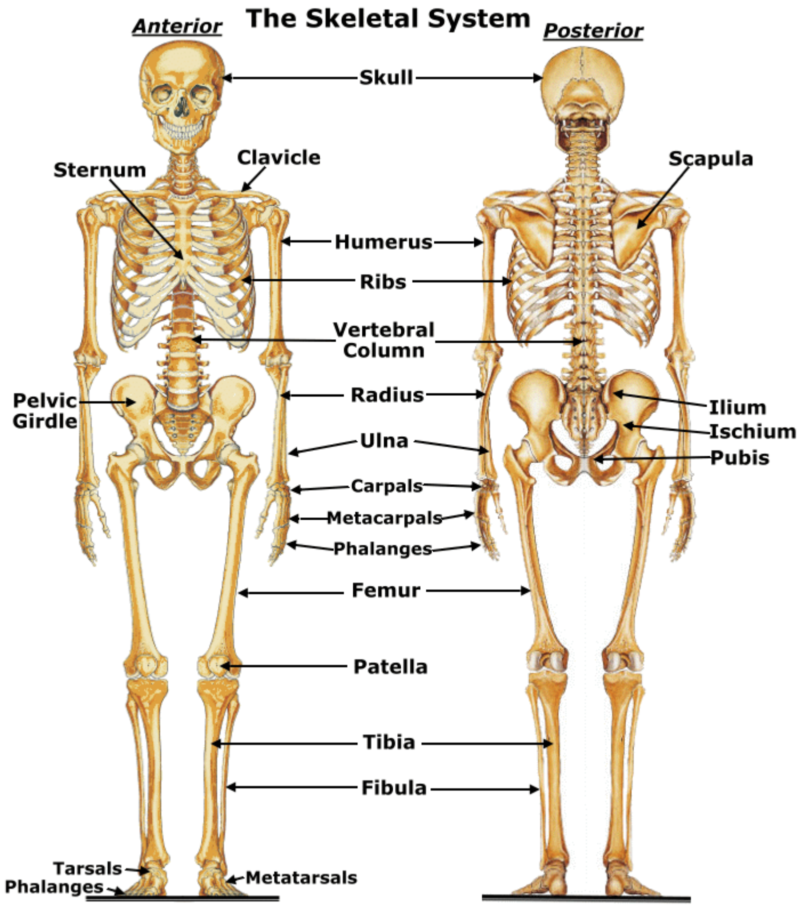
Muscle Receptors

- **Gogli Tendon Organs**
  - Provide necessary feedback for overall muscle tension
    - Integrates all factors which influence tension
  - Specialized nerve fibers embedded in the tendons
  - Stretch of tendons exerts force on nerve endings
    - Increase firing rate
  - Part of this information reaches conscious awareness
    - We are aware of tension (but not of length) of muscles



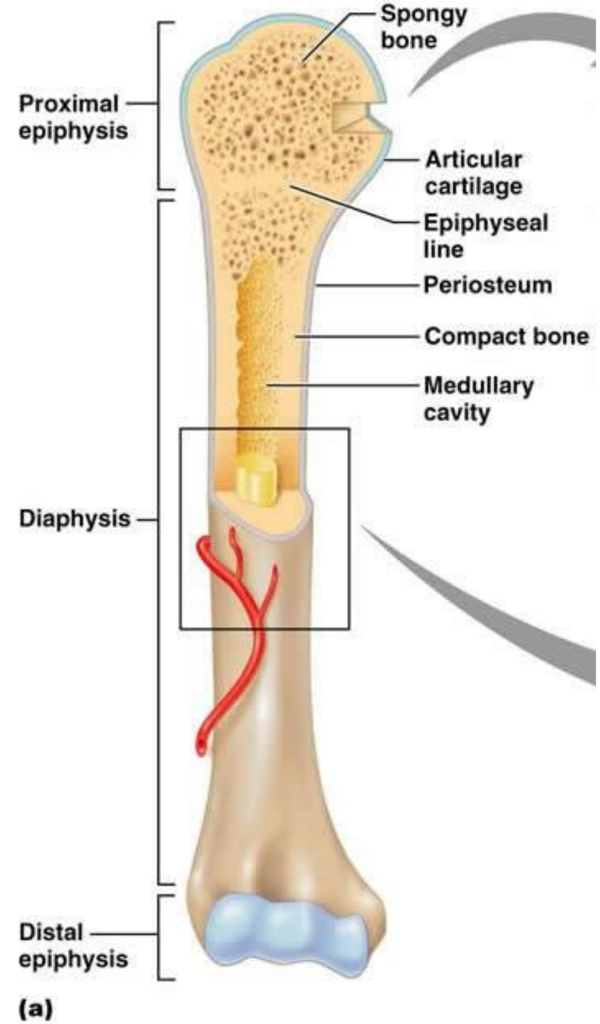
Skeletal System

- **Bones are made of several tissues**
  - Primarily made of collagen and hydroxyapatite - $Ca_{10}(PO_4)_6(OH)_2$
  - About 206 bones in the human body
- **Functions of Skeletal System**
  - SUPPORT:
    - Hard framework that supports and anchors the soft organs of the body.
  - PROTECTION:
    - Surrounds organs such as the brain and spinal cord.
  - MOVEMENT:
    - Allows for muscle attachment therefore the bones are used as levers.
  - STORAGE:
    - Minerals and lipids are stored within bone material.
  - BLOOD CELL FORMATION:
    - The bone marrow is responsible for blood cell production.



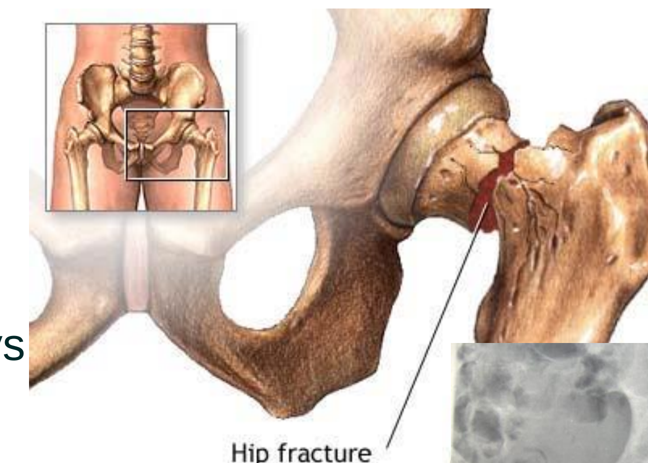
Structure of Bone and Joints

- **Features of a long bone:**
  - Epiphysis:
    - Ends of the bone.
  - Diaphysis:
    - The shaft of the bone which surrounds the medullary cavity.
  - Articular Cartilage:
    - Cushions the ends of the bones and allows for smooth movement.
- **Bone Structure**
  - Periosteum – hard outer covering
    - Cells for growth and repair
  - Compact bone – hard strong layer
    - Bone cells, blood vessels, protein with Ca and P
  - Spongy bone – at ends of long bones
    - Has small open spaces to lighten weight
  - Marrow cavity – hollow in middle of long bones
- **Bone Marrow**
  - Red marrow – produces blood cells and clotting factors
    - Found in humerus, femur, sternum, ribs, vertebrae, pelvis
    - Produces RBC 2 million per second
  - Yellow marrow – stores fat
    - Found in many bones



Structure of Bone and Joints

- **Osteoporosis**
  - Decline in Bone Density
    - Bone Resorption > Bone Deposition
  - Increase Risk for Fracture
    - compression fractures of vertebrae
    - hip fractures
  - Role of calcium, vitamin D, estrogen, exercise
- **Broken Bones**
  - Fracture is a break of the bone
  - Simple or Complex fracture
  - Regrowth of bone:
    - Spongy bone forms in first few days
    - Blood vessels regrow and spongy bone hardens
    - Full healing takes 1-2 months
    - Healing capacity diminishes with age



Structure of Bone and Joints

- **Joints**
  - Cartilage covers ends of movable bones
    - Reduces friction
  - Lubricated by fluid from capillaries
- **Arthritis:**
  - Osteoarthritis- 90% of pop. By age 40
  - chronic inflammation of articular cartilage
  - can be normal age-dependent change
  - can also be pathology due to
    - Age-related changes
    - decrease blood supply
    - trauma