Nerve and Muscle Physiology Overview

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EID424
Bioengineering Applications in Sports Medicine
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Overview

- Basic cell physiology intro
- The nerve cell
- The action potential
- Nerve to muscle
- Muscle contraction
- AL Hodgkin and AF Huxley received the 1963 Nobel Prize for working out many of the details here
  - Work with squid axon
    - Very large (0.5mm dia), easy to manipulate

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Overview

- Note:
  - We'll be dealing mostly with the physiology of active tissue
    - Nerve
    - Muscle
  - More general physiology later
    - Sources of energy

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Basic Cell Structure

- High school Bio 101 redux

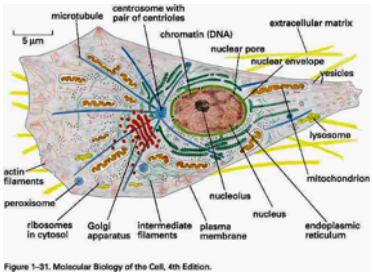

Figure 1–31. Molecular Biology of the Cell, 4th Edition.

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Basic Cell Structure

- Structures of interest:
  - Nucleus
    - Genetic material
  - Mitochondria
    - Store energy
      - ATP!
        - Used to provide energy for *all* active processes
  - Microtubules
    - Transport
  - Endo(sarco-)plasmic reticulum
    - Endo-: protein synthesis
    - Sarco-: in muscle cells, store Ca++

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Basic Cell Structure

- More structures of interest:
  - Cytoplasm/cytosol
    - Negative relative to outside the cell
      - ~ -10 mV in red blood cells
      - ~ -70 mV in nerve cells
      - ~ -90 mV in muscle cells
        - Field strength 12,000 V/mm [Deutsch and Deutsch, 1992]
  - Cell membrane
    - Selectively permeable to certain ions
    - Specialized *protein channels* control access
    - Very good insulator

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What's This -90 mV?

- Cells maintain a *resting potential*
  - Also called *membrane potential*
  - Keep some salt out
    - Otherwise, draw in too much water
  - Aids in transport of other molecules
  - Provides proper environment for other cellular processes (e.g., protein synthesis)
  - Necessary for nerve/muscle cell function

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Sources of Membrane Potential

- Cell membrane is permeable to various ions
  - Na+ constantly leaks in from extracellular fluid
  - K+ constantly leaks out

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Sodium-Potassium Pump

- Present in all animal cells
- *Actively* pushes Na+ out of the cell, pulls K+ into the cell
  - Works against concentration gradients
  - Requires energy (ATP)
    - More than one-third of resting energy consumption!

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Sodium-Potassium Pump

- Concentration gradients cause:
  - Na+ to leak into cell
  - K+ to leak out of cell
- Na+-K+ pump offsets this diffusion

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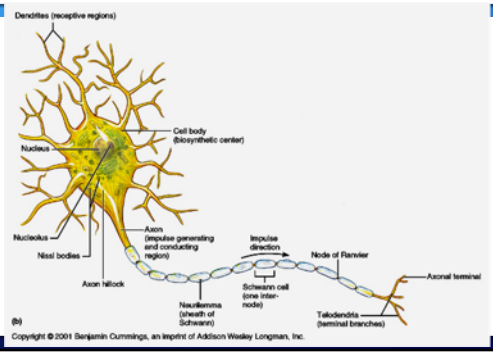
The Neuron



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Types of Neurons

- Motor neuron
  - Innervates muscle tissue
- Sensory neuron
  - Picks up stimuli from special receptors
  - Transmits information to spinal cord/brain
- Interneuron
  - Sits between other neurons

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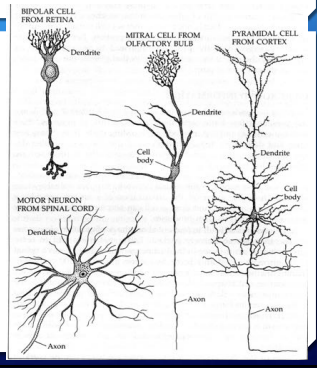
The Neuron

- Cell body (soma)
- Dendrites
- Axon hillock
- Axon
  - (un)myelinated
- Axon terminals
  - Synapse



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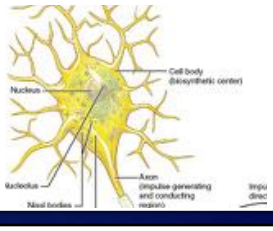
The Neuron: Cell Body

- Contains the usual cell organelles
- Most normal cell functions occur here



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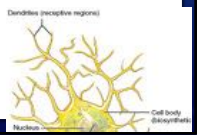
The Neuron: Dendrites

- Projections from cell body
- Accept inputs from outside the cell
  - Other neurons
  - Sensory receptors
- Increase surface area over which stimuli may be received



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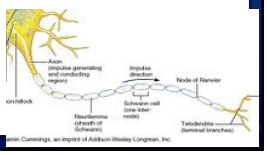
The Neuron: Axon

- Long fiber extending from cell body
- This is what is referred to as a "nerve"
  - i.e., "femoral nerve," "median nerve"
  - Really bundles of axons
  - Can be several feet long (spinal cord to hand/foot)
- Carries electrical impulses
  - Action potential
  - The crux of the biscuit



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The Action Potential

- A sudden change in voltage
- Quick return to resting potential
- Either happens or does not
  - Action potentials are all the same size
  - Strength of stimulus/contraction indicated by frequency of action potentials, not amplitude
- Also referred to as the nerve "firing"

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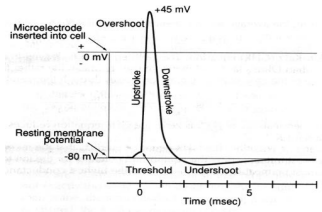
The Action Potential: What's It Look Like?



- "We have to get into it sideways"
  - Prof. S. Ben-Avi, many times in the 1980s-1990s

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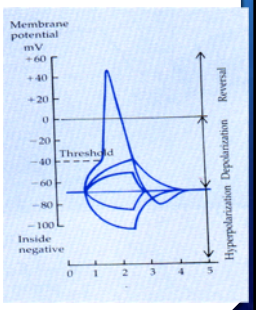
The Action Potential Explained

- Changing voltages in the axon hillock in response to stimuli
  - *Graded potentials*
- Nothing happens until these graded potentials exceed a threshold potential
  - 20-30 mV above baseline
  - Unless threshold reached, potential returns to baseline
- Then…



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The Action Potential Explained

- Voltage-sensitive Na+ channels in the cell membrane start to open causing…
- The voltage to become more positive causing…
- Even more voltage-sensitive Na+ channels to open
- Rare example of naturally-occurring positive feedback
- Membrane potential grows to +25-35 mV

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The Action Potential Explained

- Na+ stops flooding in
  - Some gates close
  - High concentration inside cell limits diffusion
  - Positive voltage inhibits entry of positively-charged ions
- K+ gates open
- K+ leaves the cell
  - More slowly than Na+ entered

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Action Potential Explained

- As K+ leaves, cell returns to resting state
- But…
  - Membrane potential overshoots resting potential
    - Membrane is hyperpolarized
  - *Refractory period*
    - Na+ channels inactive
    - No action potential can occur
- After several msec, cell returns to normal state

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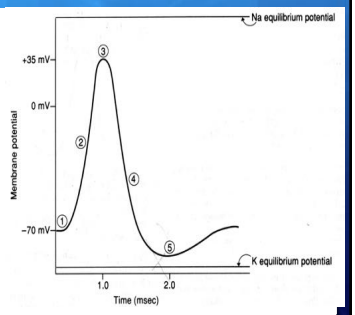
Action Potential Schematic

1. Resting potential
2. Influx of Na+
3. K+ gates open
4. Outflow of K+
5. Hyperpolarization/ refractory period



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Action Potential Propagation

- Action potentials are not stationary
  - Depolarization causes diffusion of neighboring ions until neighboring area reaches threshold potential
    - Fire!
  - *Refractory period* prevents action potential from traveling backward
- Travel along length of axon to axon terminals
- Ends at axon terminals

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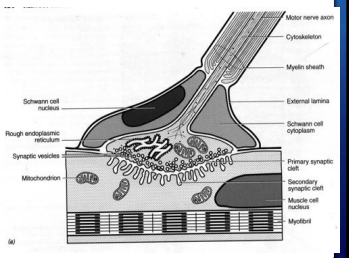
Cell-Cell Transmission of Information: The Synapse

- Action potential ends at end of axon
- At end of axon there is either
  - Another nerve cell (dendrites)
  - A muscle
- Small gap in between
  - Synapse



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Synaptic Transmission

- Action potential triggers release of Ca++
- Presence of Ca++ triggers release of special chemicals stored in *synaptic vesicles*
  - Neurotransmitters
  - Acetylcholine (ACh) most important for nerve-muscle transmission
  - Excitatory
  - Inhibitory
- Neurotransmitters diffuse across synapse

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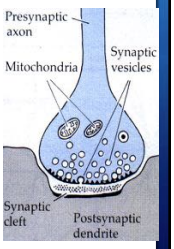
Synaptic Transmission

- Special proteins (*receptors*) on other end of synapse pick up neurotransmitters
- If enough excitatory neurotransmitters are received, depolarization will occur
  - And not too many inhibitory
- New action potential
- More action potentials received → more neurotransmitters released



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Action Potential Summary

- All-or-nothing electrical response
  - Stronger stimulus → more action potentials
- Fast, positive change from influx of Na+
- Slower (but still fast!) negative change from outgoing K+
- Chemical transmission to next neuron/muscle though synapse via neurotransmitters
  - Graded chemical response
  - Excitatory or inhibitory

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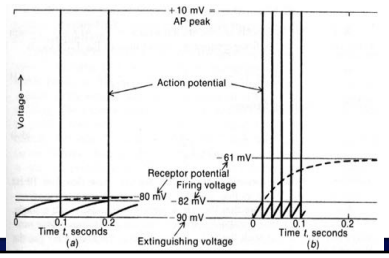
Action Potential is All-or Nothing!

- Muy importante!
- Intensity of stimulus is related to frequency of action potentials



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Speed of AP Propagation

- Larger diameter axons → faster AP propagation
  - Wider pipe
  - Thicker wire
  - Pick your analogy
- In a complex organism, nerves practically can only be so big before they take up too much space

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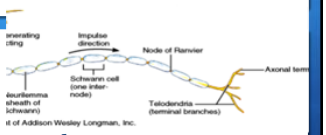
Myelinated Nerves



- Myelin
  - Insulating layer grows around axon
    - Schwann cells
    - Basically, layers of fat wrapped around
  - Axon not exposed to extracellular fluid except at periodic points
    - *Nodes of Ranvier*
    - Highly-concentrated Na+ gates

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So Why Does Myelin Help?

- AP "jumps" from node to node
  - *Saltatory conduction*
- AP does not have to be regenerated along entire length of axon
  - Only at nodes
  - Saves energy as well as speeding things up
- Nodes typically 1-2 mm apart
  - Diameter-dependent

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How Much Faster?

- Conduction velocity of unmyelinated nerves very slow
  - Up to 1.5 m/sec
- Myelinated nerves can be up to 120 m/sec
  - Depends on size
  - Would have to have 38x greater diameter if unmyelinated

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Myelinated and Unmyelinated Nerves

- Not all nerves myelinated
  - Only about one-third
- Slower signaling often sufficient
  - e.g., perception of pain
- Reflexes (motor) controlled by myelinated nerves
- Consequences of de-myelination severe
  - Demyelinating disease called _____?
  - Slower conduction velocity
  - Greater energy consumption

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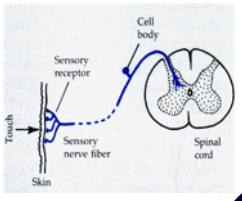
Speaking of Reflexes

- Reflex arc
  - Impulse goes from sensory nerve…
  - To interneuron in spinal cord…
  - To motor nerve…
  - To muscle
- Brain is not involved



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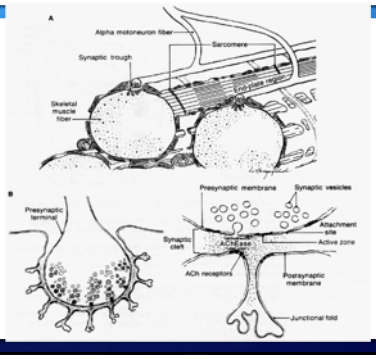
Nerve to Muscle



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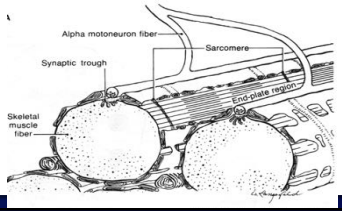
Neuromuscular Junction

- Axon branches at end
- Each branch terminates at a muscle fiber
- Also called *motor endplate*
  - *Innervation zone* of muscle



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The Motor Unit

- The quantum of the neuromuscular system
- Consists of:
  - Motor neuron
  - All muscle fibers innervated by it
- Motor unit either fires or does not
  - *All* muscle fibers contract or *none* do
  - Consequence of innervation by a single neuron

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Muscle Fiber

- Similar electrically to neurons
- Action potential propagates across the surface of the fiber
  - All or nothing!
  - Slower propagation than nerve
  - Action potential causes muscle contraction
    - Allows physical interaction of proteins in muscle fibers

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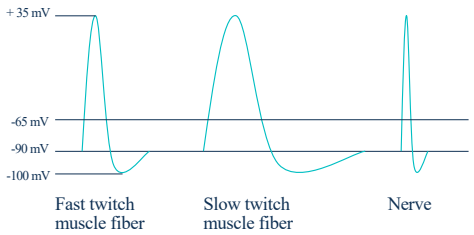
Comparison of Muscle and Nerve Action Potentials



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Types of Muscle

- Smooth muscle
- Cardiac muscle
- Skeletal (striated) muscle

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Smooth Muscle

- Found in the viscera of the body
  - Regulates blood vessels, airways, digestive tract
- Different animal from skeletal muscle
  - Smooth, not striated appearance
  - No sarcomeres, different excitation
  - Almost always in a partially-contracted state
  - Does not fatigue
- Involuntary

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Cardiac Muscle

- Found in the heart (duh)
- More like skeletal muscle
  - Striated
- Important differences
  - Entire heart contracts at once
  - Contracts on its own
    - Innervation influences *rate* of contraction only
  - Long action potential
  - Always relaxes after contracting
- TBD in more detail with EKG at a later date

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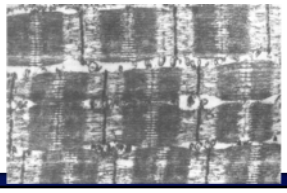
Skeletal Muscle

- Attached to bone via tough, fibrous tissue
  - Called _____?
- Also called striated muscle because of its appearance
- What we will primarily be discussing



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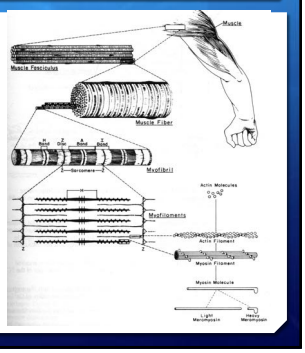
Muscle Anatomy

- Muscle organized in progressively smaller bundles of fibers
- Individual muscle cells called *sarcomeres*



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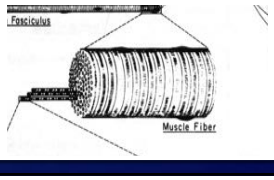
Muscle Fiber

- Composed of many *myofibrils*
- Each myofibril composed of multiple sarcomeres
- Groups of muscle fibers (and a motor neuron) comprise a motor unit



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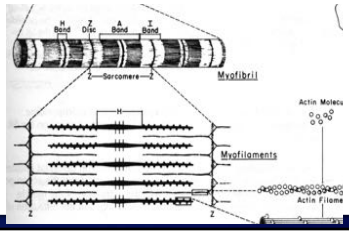
Myofibrils

- Individual sarcomeres bounded by fibrous *z-lines*
- *A-bands* composed of overlapping *myofilaments*
  - These are the contractile elements of muscle tissue



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Mechanism of Muscle Contraction

- Thick filaments
  - Myosin (heavy chains, light chains)
- Thin filaments
  - Actin
- These filaments bond to each other when given the chance

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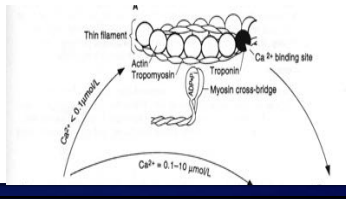
Filament Resting State

- Troponin and tropomyosin block attachment of mysoin head to actin
  - Regulatory proteins



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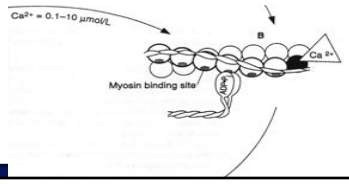
Filaments in Presence of AP

- AP causes sarcoplasmic reticulum to release Ca++ into the cell
- Ca++ binds to troponin and moves tropomyosin out of the way
- Myosin head can now bind to actin
  - Forms a *cross bridge*



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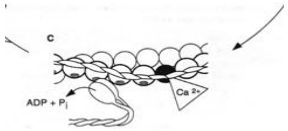
Sliding Filaments

- Using energy from ATP, myosin head ratchets and pulls the thin filament
  - *Sliding filament theory* of muscle contraction
  - By using more ATP, this process can be repeated as long as calcium is present



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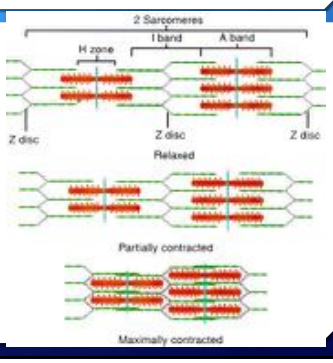
Sliding Filaments

- *I-band* decreases
- *A-band* remains the same
  - Length of thick filaments fixed
- Maximal contraction
  - Complete overlap of thick and thin filaments



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Relaxation

- In the absence of an AP, Ca++ is gathered back into the sarcoplasmic reticulum
  - Myosin and actin are no longer free to bind
  - Muscle returns to resting length
  - Requires energy
    - No ATP → myosin head stuck to actin
      - Rigor mortis
- It takes time, effort to relax!
  - With fatigue rate of force development *and* relaxation grow longer

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Types of Muscle Fiber

- Type I
  - Slow twitch
- Type II
  - Fast twitch
  - IIa
  - IIb

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Type I Muscle Fiber

- Slow twitch
  - Less sarcoplasmic reticulum
  - Slower to reclaim Ca^{++}
- Slow conduction velocity
- Small fibers
- Few fibers per motor unit
- Responsible for fine movements

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Type I Muscle Fiber

- Able to extract oxygen from blood
  - Aerobic metabolism
  - Many mitochondria, myoglobin
  - Many capillaries
  - Huge (virtually infinite) supply of energy
  - Relatively slow, but efficient ATP production
- Resistant to fatigue

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Type II Muscle Fiber

- Fast twitch
- High conduction velocity
  - Relative to Type I; still slow compared to nerve
- Large fibers
- Many fibers per motor unit
- Responsible for gross movements

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Type II Muscle Fiber

- Primary energy supply is sugar stored in muscle
  - Glycogen
  - Anaerobic
  - Fastest way to derive energy
    - Glycolysis
    - Not very efficient
  - Only a small supply
  - Produces lactic acid
- Fatigues easily

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The Two Type IIs

- Type IIa
  - What we've been talking about
- Type IIb
  - Hybrid
  - Fast-twitch, fatigue-resistant
  - Aerobic
- Type IIc? IIx?

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Motor Unit Recruitment

- Size principal
  - Smaller motor units recruited first
    - Type I
    - Can work longer
  - Greater force required → more motor units recruited
  - As greater force is required, Type II motor units recruited

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Modes of Muscle Contraction

- Concentric
- Isometric
- Eccentric
- More helpful to use "action" instead of "contraction"

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Concentric Muscle Action

- Length of muscle shortens while doing work
- What people most commonly think of
  - Biceps brachii in arm while lifting an object
  - Quadriceps in leg when kicking a ball

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Isometric Muscle Action

- Muscle remains the same length while doing work
- Push against an object that does not move
- Often used as a standard activity for normalization

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Eccentric Muscle Action

- Muscle lengthens while doing work
  - *Lengthens* while *contracting*?
- Quadriceps when landing from a jump
- Partially, cross bridges being pulled apart
  - Mostly, muscle acting isometrically and tendon stretching
- Able to generate more force eccentrically than concentrically
  - Muscle damage/reformation

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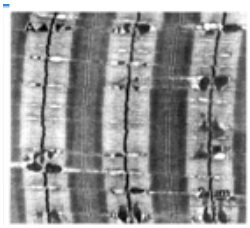
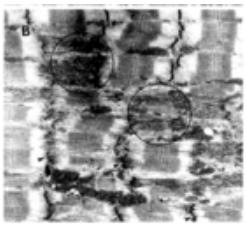
Aside: Muscle Damage



Normal



Damaged

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Aside: Muscle Damage

- Normal physiology, not injury
  - Not a muscle tear
- Eccentric action
  - Sarcomeres pulled apart
  - Delayed-onset muscle soreness [DOMS]
  - Protective effect
    - Do bout of eccentric work to cause damage, causes soreness
    - Subsequent bouts do not cause soreness

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Muscle Force Generation

- AP produces a muscle *twitch*
  - Twitch force
- Successive twitches, sufficiently fast can increase force
  - Force summation
  - Increase in force because second twitch starts before muscle completely relaxed
- Fast-enough twitches cause smooth force generation
  - Tetanus, tetanic contraction
  - Not the one you get from a cut!

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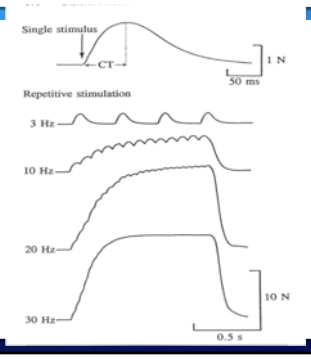
Tetanic Contractions



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Agonist-Antagonist Muscles

- Agonist
  - Responsible for motion in one direction about joint
- Antagonist
  - Responsible for other direction
- Theoretically, while one is active, the other is silent
  - In reality, co-contraction

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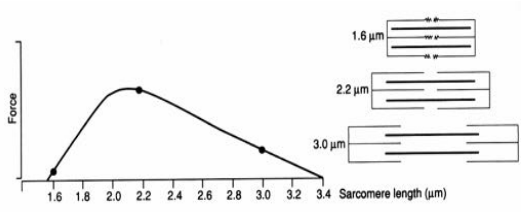
Muscle Length-Tension Relationship

- Force generating capacity of muscles depends on length of fibers



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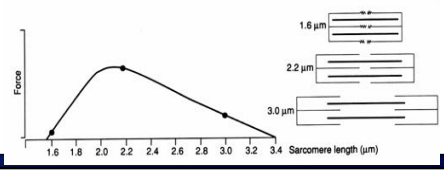
Muscle Length-Tension Relationship

- Sarcomeres very long
  - Little overlap between thick and thin filaments
  - Few cross bridges
  - Low force generation



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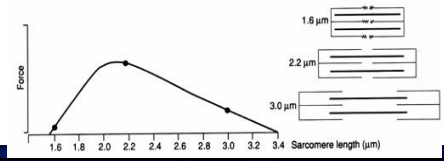
Muscle Length-Tension Relationship

- Sarcomeres very short
  - Thin filaments start to interfere with each other
  - Force generation impaired
  - When maximally contracted, no force generating capacity
    - Thick filaments hit z-lines



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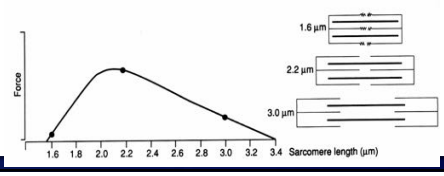
Muscle Length-Tension Relationship

- Sarcomere at optimal length
  - Maximum thick and thin filament overlap
  - Maximum number of cross bridges form
  - Max force generation



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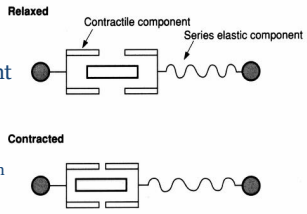
Muscle Model

- Hill muscle model
  - Contractile element
  - Series elastic component
  - Some also use parallel elastic component
    - Connective tissue between fibers



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Muscle Model: Contractile Element

- Models contractile properties
  - Muscle fiber
- Accounts for all force generation
- Must take into account all contractile properties
  - Length-tension relationship
  - Load-velocity relationship
    - Greater load, slower velocity of shortening

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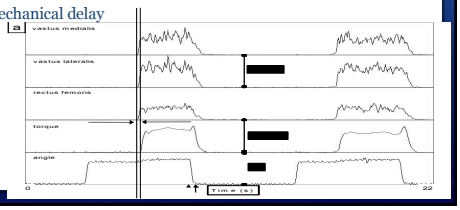
Muscle Model: Series Elastic Component

- Tissue between muscle fibers and bone
  - Tendon
  - Aponeurosis
    - Junction of muscle and tendon
- Must stretch out before any force transmitted from muscle to bone
  - Electromechanical delay



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Measurements Based on This

- EKG
  - Electrocardiography
  - Electrical activity of heart
- EMG
  - Electromyography
  - Electrical activity of skeletal muscle

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Lots More Measurements…

- EEG
  - Electroencephelogram (brain)
- EOG
  - Electrooculogram (eye)
- MMG
  - Mechanomyogram (sliding muscle filament *sounds*)
  - Sometimes called AMG (acoustomyography)
- EGG
  - Electrogastogram (stomach)
- …

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