Muscle Tissue

Introduction to Muscle Tissue

• Alternating contraction & relaxation of muscles (sometimes in conjunction with skeleton) provide motion
• Converts chemical energy to mechanical energy plus heat
• 40-50% of body mass is muscle
• Muscle types: skeletal, cardiac, smooth

Muscle Function

• Motion
• Movement of fluids
  – Blood (supply & return), digestate, secretions, reproductive fluids, urine
• Stabilizing body position or regulating organ volume
  – Postural muscles, sphincters
• Thermogenesis
  – Produce 85% of body heat as by-product
  – Shivering is involuntary & purposeful

Muscle Tissue Characteristics

• Excitability (irritability)
  – Action potentials created by neurotransmitters or hormones
• Conductivity
  – Propagation of action potentials
• Contractility
  – Generate force by shortening or not
• Extensibility
  – Stretched without damage by antagonist
• Elasticity
  – Return to original shape

Connective Tissue Structure

• Fascia - fibrous connective tissue
  – Superficial (under skin) or deep (around muscles or organs)
  – Functions include: storage of water and fat, insulation, mechanical protection, provides separation of muscles & holds nerve and vessel supply (deep)
• Three layers of integrated connective tissue connecting to tendon
  – Epimysium - covers each muscle, dense irregular connective tissue
  – Perimysium - covers each fascicle, dense irregular connective tissue
    • “Grain” of meat
  – Endomysium - covers individual fibers, areolar connective tissue
• Tendons and aponeuroses
– Tendons to bones
– Aponeuroses to bone, other muscles, or skin

• Tendon sheaths
  – Reduce friction in wrist & ankles
  – Tenosynovitis - inflammation of tendon sheaths and synovial membranes due to trauma, strain, or excessive exercise

Innervation
• Motor neurons (somatic) from CNS
  – Motor unit includes neuron and all muscles cells it innervates
    • Size varies 10-3000 muscle fibers, avg is 150
    • Force developed controlled by which units and how many
  – Eye has small units, leg has large units

• Neuromuscular junction (NMJ)
  – Site of transmission of excitation from nerve to muscle, also site for drug effects
  – Synapse - Axon terminal, motor end plate, synaptic cleft, synaptic vesicles, acetylcholine, ACh receptors

• Electromyogram

Muscle Fiber Ultrastructure
• Dimensions: 10-100 microns across, up to 30 cm long
• Sarcolemma, sarcoplasm (including myoglobin & glycogen), multiple nuclei (fusion of ~100 myoblasts), myofibrils

• Myofibrils
  – Aligned to provide striations
  – Composed of thin, thick and elastic filaments (and other protein structures)

Myofibril
• Sarcomere - racks of overlapping thick and thin filaments
  – Z disc to Z disc
• M line (supporting protein), I band, A band, H zone, zone of overlap
• Thick - myosin
  – About 300 per filament, shaft and 2 heads, actin & ATP binding sites
• Thin - actin along with tropomyosin & troponin
  – Actin has myosin binding site covered by tropomyosin
  – Troponin controls position of tropomyosin
• Structural proteins (titin, myomesin, nebulin, dystrophin and others)
  – Stabilize position of thick filaments by connecting to Z disc - myomesin at M line and titin
  – Attach myofibrils to sarcolemma - dystrophin attaching thin filaments to cell surface
  – Returns sarcomere to resting length after stretch - probably titin acting as elastic filament
Accessory Structures

- Transverse tubules (T-tubules)
  - Invaginations of sarcolemma - two per sarcomere at A-I band junction
  - Carry action potential to inside
- Sarcoplasmic reticulum
  - Terminal cisterns or sacs (triad - 2 cisterns & t-tubule)
  - Release and take up Ca\(^{2+}\)

Sliding Filament Mechanism

- General concept: myosin filament heads alternate forming cross bridges with actin, changing shape, and releasing actin; pulls Z discs together; each head 5 times per sec.
- Shortening of each sarcomere (to 1/2 resting length), shortens muscle fiber, and shortens muscle
- Presence of Ca\(^{2+}\) and ATP activated myosin important for contraction
- Removal of Ca\(^{2+}\) important for relaxation

Muscle Fiber Contraction

- Action potential reaches NMJ
- ACh released from synaptic vesicles
- ACh receptors increase permeability of Na\(^{+}\) ultimately causing muscle action potential
- AP carried throughout cell via sarcolemma and t-tubules to triad
- Effect on SR is release of Ca\(^{2+}\) (up to 10X resting) which interacts with troponin
- Activation of myosin head by ATP
- Ca\(^{2+}\) combines with troponin, moving tropomyosin off actin active site
- Myosin forms cross-bridge with actin, and changes conformation
- Myosin head is again activated with ATP, releasing actin, and returning to normal shape
- Process continues while Ca\(^{2+}\) and ATP are present

Muscle Fiber Relaxation

- ACh is broken down by acetylcholinesterase in NMJ
- Permeability of Na\(^{+}\) returns to normal
- SR stops releasing Ca\(^{2+}\) and begins pumping it back inside
- Calsequestrin (Ca\(^{2+}\) binding protein molecule) increases ability to concentrate calcium (10,000X)
- Tropomyosin recovers actin binding site
- Sarcomere length returns to normal
- Reason for *rigor mortis*

Whole Muscle Contraction
• Amount of force or shortening related to # of fibers, frequency of stimulation and length of muscle
• Brief contraction - twitch
  – Latent, contraction and relaxation periods
  – Time period varies (eye muscle - fast twitch)
  – Refractory period (skeletal short - 5 msec, cardiac long - 300 msec

**Enhanced Contraction**
• Wave summation dependent on frequency of stimulation
  – 20-30/sec - incomplete (unfused) tetanus
  – 80-100/sec - complete (fused) tetanus
  – $\text{Ca}^{2+}$ effect
• Staircase effect (treppe)
  – Increase force even though interval between twitches
  – $\text{Ca}^{2+}$ and increased temperature effects
• Normal contraction is asynchronous, unfused tetanus of multiple motor units

**Other Concepts**
• Muscle length - overlap of filaments
• Alternation of contracting fibers
  – Minimizes fatigue
  – Smoothes contraction
• Muscle tone - continual alternating contraction of some fibers
  – Hypotonia vs. hypertonia
• Isotonic contraction
  – Concentric (shortening) vs eccentric (lengthening - causes greatest damage)
• Isometric contraction (as in postural muscles)

**Muscle Size**
• Atrophy
  – disuse - reduced myofibrils
  – denervation - reduced muscle fibers
• Hypertrophy
  – Increased fiber diameter due to increased myofibrils, SR, etc.

**Body Temperature Control**
• Temperature sensors in skin and brain
• Negative feedback control from hypothalamus
  – Regulates smooth muscle around vessels for vasodilation or constriction in skin
  – Shivering

**Muscle Energy Sources**
• ATP only sufficient for a few seconds of contraction without continuing source
• Phosphagen system
  – Creatine phosphate transfers high energy phosphate to ADP forming ATP
  – 3-6 times the number of ATP
  – Sufficient supply for about 15 sec (100 m dash)
  – Creatine as a supplement - long-term effects unknown
    • 2 grams lost per day normal

• Glycogen-Lactic Acid System
  – Anaerobic use of pyruvic acid (product of glycolysis) supplies 2 ATP
  – Glucose from blood (facilitated diffusion) or glycogen stored in muscle
  – Forms lactic acid which diffuses into blood (utilized by heart, kidney & liver)
  – Sufficient supply for 30-40 secs (300 meter race)
  – Carbohydrate loading to build glycogen supply

• Aerobic System
  – Complete oxidation of pyruvic acid in mitochondria
  – Produces 36 ATP
  – Supplies energy beyond 30 sec
  – Other molecules (fatty acids & amino acids) can also be metabolized and are major source beyond 10 minutes
  – O\textsubscript{2} supplied by diffusion from blood or myoglobin in muscle cells
  – Aerobic vs. weight training

Exercise Recovery
• Recovery Oxygen consumption or O\textsubscript{2} debt
  – Lactic acid conversion to glycogen in liver
  – Resupply of ATP and creatine phosphate
  – Oxygenate myoglobin
  – Increased body temperature increases MR
  – Increased activity of respiratory muscles

• Muscle fatigue
  – Reduced quantities in sarcoplasm of Ca\textsuperscript{2+}, creatine phosphate, ATP (to a limited extent), O\textsubscript{2} 
  – Excess lactic acid & ADP
  – Inadequate ACh at NMJ

Types of Skeletal Muscle Fibers
• Slow oxidative (SO - type I) fibers
  – Slow-twitch (100-200 msec), fatigue resistant
  – Myoglobin, mitochondria and capillaries, smallest diameter
  – High aerobic capacity, slow ATP use
  – Important type in postural muscle and aerobic/endurance activity

• Fast oxidative - glycolytic (FOG - type IIA) fibers
  – Fast-twitch A (<100 msec - ATPase activity is 3-5 times faster), fatigue resistant
– Myoglobin, mitochondria and capillaries, intermediate diameter
– High aerobic capacity, rapid ATP use
– Walking and sprinting

• Fast glycolytic (FG -type IIb) fibers
  – Fast-twitch B, fatigable
  – Little myoglobin, mitochondria and capillaries, largest diameter
  – Low aerobic capacity, rapid ATP use
  – Weightlifter’s arms (strength)

• Red vs. White
  • Proportions of fibers change depending on types of exercise - usually 50% SO
    – Muscle fibers transition between types

**Structure of Cardiac Muscle**

• Fibers quadrangular in shape, branched, and single nucleus
• Diameter 14 microns; length 50-100 microns
• More sarcoplasm & mitochondria (larger too)
• Less SR, Ca^{2+} also enters through plasma membrane
• One T-tubule per sarcomere at Z-disc
• Intercalated discs anchor fibers (desmosomes) and conduct excitability (gap junctions) - enables synchronized contraction

**Physiology of Cardiac Muscle**

• Autorythmicity
• Normal continuous contraction at 75 contractions/min
• Aerobic production of ATP from glucose, fatty acids, & lactic acid
• Long refractory period - prevents tetanus and allows heart to fill
  • Period of contraction 10-15 times longer due to prolonged entry of Ca^{2+}

**Structure of Smooth Muscle**

• Two types
  – Visceral (single unit) cells connected by gap junctions and contract together
    • Around walls of hollow viscera, small blood vessels
    • May be autorhythmic
  – Multiunit cells that contract separately
    • Around large blood vessels, large airways, arrector pili, iris of eye

• Diameter 3-8 microns, length about 30-200 microns
• Tapered ends, single nucleus
• Less SR, no T-tubules, Ca^{2+} also enters through plasma membrane
• Myofilaments not orderly (in sarcomeres)
• Intermediate filaments attach myofilaments to dense bodies (analogous to Z-discs)

**Physiology of Smooth Muscle**
• Slow onset of contraction and longer duration
• Greater ability to extend and shorten
• Actin active site regulation different
  – Calmodulin in the presence of Ca$^{2+}$, activates myosin light chain kinase, which in turn phosphorylates myosin head, causing contraction
• Excited by various stimuli: APs, hormones, stretch, pH changes, O$_2$ and CO$_2$ levels, temperature, ionic concentrations
• Stress-relaxation response

Regeneration of Muscle Tissue
• Cardiac: no division or regeneration
• Skeletal: no division (after first year) and limited regeneration from satellite cells
• Smooth: limited capacity to divide (hyperplasia) and thus regenerate
• All types can increase in size (hypertrophy)