Muscle Physiology

Chapter 12

Muscle Tissue

- Specially designed to contract
- Generates mechanical force
- Functions
  - locomotion and external movements
  - internal movement (circulation, digestion)
  - heat generation

Types of Muscle

- Skeletal - attached to skeleton
- Smooth - found in walls of hollow visceral organs
- Cardiac - in heart

Skeletal Muscle

- Connected to skeleton via tendons
  - attached to immobile bone at one end (origin)
  - other end attached to more moveable bone (insertion)
- Many muscles are used to bend the skeleton at joints
- Antagonistic pairs
  - Contraction of one does the opposite of its counterpart

Skeletal Muscle Organization

- Muscle fibers (cells)
  - elongate cells, parallel arrangement,
  - bundled by connective tissue
  - multiple nuclei
  - striated
  - sarcolemma - cell membrane
  - sarcoplasmic reticulum (SR)
  - Internal membranous network
  - myofibrils - intracellular contractile elements
    - thick filaments
    - thin filaments

Myofibril Structure

- Composed of sarcomeres
  - smallest functional unit of muscle
  - repeating units of thin and thick protein filaments
    - Thick Filament = Myosin
    - Thin Filament = Actin, Troponin, Tropomyosin
Thick Filament Structure

- Bundles of several hundred myosin molecules
  - intertwining tails + globular heads
- Heads contain:
  - actin binding sites
  - ATP-hydrolyzing sites
- Project outward towards actin
- Form crossbridges
  - bonds with actin
  - Important during contraction

Thin Filament Structure

- Actin
  - primary structural protein
  - spherical protein subunits connected in long, double strand
  - Contains myosin binding site
- Tropomyosin
  - threadlike proteins
  - normally cover myosin binding sites
- Troponin
  - Ca\textsuperscript{2+} Binding Protein
  - holds tropomyosin in place

Thin Filament Structure

- When Ca\textsuperscript{2+} binds to troponin
  - Shape of troponin changes
  - Shifts tropomyosin off myosin binding sites
  - Myosin binds to actin

Skeletal Muscle Contraction: Sliding Filament Mechanism

- Movement of thin filaments over thick
  - sarcomere shortening
  - thick filaments are stationary; thin are dragged across thick
  - length of the filaments do not change.

Crossbridge Cycling

- Myosin head binds to actin
- Cross bridge bends (Power Stroke)
  - thin filaments pulled toward center of sarcomere
- Cross bridge link broken
- Cross bridge ‘unbends’ and binds to next actin molecule

Muscle Contraction

- ATP required
  - ATP must bind to myosin for myosin to release actin
- Ca\textsuperscript{2+} required
  - binding of Ca\textsuperscript{2+} to troponin uncovers myosin binding sites on the actin
  - Ca\textsuperscript{2+} released inside the cell to induce contraction
Neural Activation of Muscle Contraction

- Somatic Motor Neurons stimulate AP’s in skeletal muscle cells (neurotransmitter generates EPSPs)
- Excitation-Contraction Coupling
  - Events that link muscle excitation (action potential) to muscle contraction (cross-bridge cycling)
  - Triggers release of Ca\(^{2+}\) into the cytosol of the muscle fiber

Neural Input

- Somatic motor neurons
  - under voluntary and involuntary control
  - controlled by interneurons in motor cortex and cerebellum

Neural Input

- Neuromuscular Junction (NMJ)
  - synapse between motor neuron and muscle fiber
- Presynaptic Terminal
  - enlarged axon terminal
  - contains acetylcholine (ACh)
- Motor End Plate
  - Subsynaptic membrane
  - Chemically-gated Na\(^+\) channels
  - Acetylcholinesterase enzyme
    - breaks down ACh

Sequence of Events

- AP travels down axon to terminal
- Exocytosis of ACh
- ACh diffuses across cleft
- ACh binds to ACh-gated Na\(^+\) channels
- Opens ion channels
- Graded depolarization → AP in sarcolemma of muscle fiber
- AP results in release of Ca\(^{2+}\) inside muscle fiber
- Muscle contracts and shortens

http://www.blackwellpublishing.com/matthews/nmj.html

Excitation-Contraction Coupling

- Sarcoplasmic Reticulum (SR)
  - modified ER
  - surrounds myofibrils
  - stores Ca\(^{2+}\)
- Linked to the sarcolemma by transverse tubules

http://www.blackwellpublishing.com/matthews/myosin.html
Muscle Relaxation

• $Ca^{2+}$ pumped back into the SR by active carrier-mediated transport
  – troponin releases $Ca^{2+}$
  – tropomyosin covers myosin binding sites on the actin molecules
• Membrane-bound enzyme (acetylcholinesterase)
  – breaks down ACh released at the NMJ

All or None

• Individual muscle fibers respond to a single stimulus in an *all or none* fashion
  – undergo action potential
  – action potential triggers contraction
  – stimulus $<$ threshold $=$ no contraction
  – stimulus $\geq$ threshold $=$ maximal contraction

Motor Units

• Multiple muscle fibers are enervated by a single motor neuron
• Motor Unit
  – motor neuron + all muscle fibers it innervates
  – muscle fibers in a motor unit contract as a single unit

Motor Unit Recruitment

• Individual motor units contract in an all-or-none fashion
• Differences in contractile strength are due to differences in the *number* of contracting motor units
• Motor Unit Recruitment
  – increasing the number of contracting motor units to increase the overall strength of contraction

Motor Units and Control of Movement

• Different regions of the body have different numbers and sizes of motor units
• Leg muscles
  – strong contractions, little precision of movement
  – large motor units (2000 fibers/unit)
  – few individual units
• Finger muscles
  – weaker contractions, more precise movements
  – small motor units (10 fibers/unit)
  – many individual units

Motor Units and Control of Movement

• More motor cortex area allocated to control of areas with more numerous, smaller motor units
• Precise control of the strength of muscle contractions
Energy for Muscle Activity

- Muscle contraction requires ATP
  - cross bridge cycling
  - Ca^{2+} pump activity
- Sources available
  1. cytosolic ATP
  2. creatine phosphate
  3. aerobic respiration
  4. anaerobic respiration

ATP and Creatine Phosphate

- ATP in muscle
  - limited (used up in a few contractions)
- Creatine phosphate
  - storage of high energy phosphate bonds
  - used to quickly regenerate ATP from ADP
  - limited supply in cells

Aerobic Respiration

- Occurs in mitochondria
- Requires O_2 to form ATP
  - fatty acids = primary nutrient source
  - contain lots of energy, but requires O_2 to release it
- O_2 transported in by blood (hemoglobin) and also stored in muscle tissue (myoglobin)
- Aerobic exercise
  - light to moderate exercise (walking, jogging, swimming)
- Maximum oxygen uptake
  - max rate of O_2 delivery to the muscles
  - max level of aerobic activity

Anaerobic Respiration

- Glycolysis + lactate fermentation
  - breakdown of glucose
  - stored as glycogen in muscle cells
  - Does not require O_2
  - generates ATP quickly (faster than aerobic respiration)
- Used during intense exercise
  - anaerobic exercise
  - O_2 supply cannot keep up with demand
- Lactate produced
  - muscle soreness and fatigue

Consequences of Anaerobic Respiration

- Muscle Fatigue
  - inability to maintain tension due to previous contractile activity
  - ATP stores used up
  - ion gradients across membrane disrupted
  - high lactate levels inhibit contractile protein function
- Oxygen Debt
  - increased O_2 consumption (breathing) after exercise
  - restore myoglobin and hemoglobin O_2 content, metabolize lactate, etc.

Changes with Regular Sustained Exercise

- ↑ number and size of mitochondria
- ↑ number of blood capillaries supplying muscle
  - ↑ O_2 and nutrients + more efficient waste removal
- ↑ amt. myoglobin in muscle tissue
- ↑ size of muscle fibers (weight training)
  - ↑ # of myofibrils
  - no change in # of muscle fibers
Smooth Muscle

- visceral organs
- small tapered fibers
- single nuclei
- lack striations
- poorly developed sarcoplasmic reticulum

Smooth Muscle Contraction

- No striations
  - contractile proteins not arranged in sarcomeres
  - arranged in fish-net network
  - allows for extensive contraction, even when stretched

Smooth Muscle Excitation-Contraction Coupling

- Depolarization of sarcolemma opens voltage-gated Ca²⁺ channels
  - can open in response to graded potentials
  - contraction strength is proportional to stimulus strength
- Ca²⁺ enters the cell from the extracellular fluid

Smooth Muscle Excitation-Contraction Coupling

- Ca²⁺ binds with calmodulin in cytoplasm
- Ca²⁺-calmodulin binds to myosin light chain kinase (MLCK)
  - activates MLCK
- MLCK phosphorylates myosin
  - needed for myosin to bind actin
- Cross-bridge cycling