Muscle

By
Dr. Carmen Rexach
Physiology
Mt. San Antonio College
Gross muscle structure

Contraction of muscle causes tendon to pull on bone with resulting movement at the joints
Muscle fiber = muscle cell

- Striated
- Multinucleated
- voluntary
- Myoblasts

Longitudinal section of fibers in tongue. Peripheral nuclei (N). A band (A), I band (I).
Myofibrils

- Fill the muscle cells moving organelles to the periphery
- Composed of myofilaments organized as sarcomeres
Striations

• Dark bands
  - anisotropic band
• Light bands
  - isotropic band
• Arrangement of the thick and thin filaments
• Functional unit of the muscle
Myofilaments: Thick filaments

- Composed of myosin, a protein
- Two interwoven tails polypeptide tails terminating in globular heads
- Two binding sites
**Myofilaments: Thin filaments**

- **Actin complex**
  - Actin
  - Troponin
  - Tropomyosin

- **Troponin**
  - TnI
    - binds to actin
    - inhibitory
  - TnT
    - Helps secure tropomyosin to actin
  - TnC
    - Binds Ca++

- **Actin**
  - G(globular)-actin
  - F(filamentous)-actin

- **Tropomyosin**
  - Block myosin binding sites on actin
Myofilaments: Elastic filament

- Composed of titin
- Connects thick filament to Z disc
- Functions
  - Helps keep thick filaments in position in sarcomere during contraction and relaxation
  - Generates passive tension
  - Adds to muscle elasticity
(c) Portion of a thin filament

(d) Longitudinal section of filaments within one sarcomere of a myofibril

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Sarcoplasmic reticulum and T tubules

Two terminal cisternae and a T-tubule come together forming a triad. T-tubule proteins detect voltage changes, foot proteins on SR regulate Ca\textsuperscript{++} release
Sliding filament theory of contraction

- Contractions resulting from shortening of the distance between Z lines
  - thin filaments will move closer together
  - distance decreases as filaments overlap
  - I band and H bands shorten during contraction
  - A band stays the same
Relaxed sarcomere

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Partially contracted sarcomere
3. Fully contracted sarcomere
Motor units

- **Muscle contraction** begins with motor neuron stimulation of muscle fibers

- **Motor neurons**
  - cell body in ventral horn of spinal cord
  - emerges as single axon with many collateral branches

- **Definition**
  - motor neuron plus all the muscle fibers it innervates
Motor units

Spinal cord
Motor neuron cell body
Nerve
Motor unit 1
Motor unit 2
Muscle
Axonal terminals at neuromuscular junctions
Muscle fibers
Branching axon to motor unit
Muscle fibers

(a)

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Innervation Ratio

• Fine motor control
  - 1:3 (extraocular muscles)
  - 1:180 (soleus)
  - Characteristics
    • smaller cell bodies
    • stimulated by lower levels of excitatory inputs

• Gross motor control
  - 1:1000-2000 (gastrocnemius)
    • larger cell bodies
    • descends from higher levels
Neuromuscular junction

Diagram of the neuromuscular junction, showing the axon terminal of a motor neuron, the synaptic cleft, the junctional folds of the sarcolemma at the motor end plate, and the part of a myofibril. The diagram also illustrates the role of Acetylcholine (ACh) molecules in binding to the receptor, the subsequent opening of the Na⁺/K⁺ channel, and the involvement of Acetylcholinesterase in degrading ACh.
Action potential vs. graded potential

- **Action potential**
  - A rapid change in the membrane potential of a cell from negative to positive and then back
  - All or none event
  - Positive feedback loop
  - Signal is propagated with the same strength
  - Occurs over axons of neurons and muscle fibers

- **Graded potential**
  - Varying strength
  - Fizzles out over distance
  - May lead to an action potential
  - Occurs over nerve cell bodies, at neuromuscular junctions, and other structures
Neuromuscular junction

- ACh released from the terminal end bulb of motor neuron at the neuromuscular junction
- ACh binds to receptors at motor end plate
- Receptor activation generates an End Plate Potential
- EPP leads to an action potential
Generation of A/P across sarcolemma

1) Voltage-gated Na⁺ channels in sarcolemma open due to change in current generated by EPP.
2) Na⁺ move into cell from high concentration to low initiating action potential.
3) A/P moves along muscle sarcolemma in both directions as depolarization wave spreads.
4) Na⁺ channels close.
5) Voltage-gated K⁺ channels open, sarcolemma repolarizes as K⁺ moves out of cell.
6) Refractory period prevents stimulation until repolarization complete.
7) A/P moves down t-tubules causing release of Ca²⁺ from SR.

Result: Excitation-contraction coupling.
Excitation-contraction coupling

- $Ca^{++}$ binds to troponin
- troponin changes shape
- causes tropomyosin to change shape
- myosin binding sites on the actin are exposed
- Cross-bridging can now take place
Excitation of T tubule stimulates SR to release calcium ions

Calcium binds to troponin; tropomyosin shifts and exposes active sites of actin

2. Excitation-Contraction Coupling
Role of Ca$$^{++}$$ in muscle contraction

- Initiates shape changes which makes binding sites on actin accessible
- Level of $10^{-6}$ M is sufficient to initiate contraction
- Muscle relaxes when Ca$$^{++}$$ pumped back into sarcoplasmic reticulum
  - Ca$$^{++}$$ bound to calsequestrin in SR
- Most Ca$$^{++}$$ stored in terminal cisternae
Cross bridge cycle

- Fiber is resting, access to myosin binding site on actin is blocked and myosin heads are not attached.
- Myosin head is activated; myosin + ATP = myosin × ADP + Pi
- Cross bridge formed by myosin head binding to actin
- Power stroke causes filaments to slide
- New ATP molecule binds to myosin heads to release from actin
- Myosin is activated by myosin ATPase enzyme splitting new ATP
- Cycling continues
- This results in asynchronous pulling action
Cross bridge Cycle

1. Myosin cross bridge attaches to the actin myofilament

2. Working stroke—the myosin head pivots and bends as it pulls on the actin filament, sliding it toward the M line

3. As new ATP attaches to the myosin head, the cross bridge detaches

4. As ATP is split into ADP and Pᵢ, cocking of the myosin head occurs

ADP hydrolysis

Myosin head (high-energy configuration)

ADP and Pᵢ (inorganic phosphate) released

ADP

ATP

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When action potential stops

- $\text{Ca}^{++}$ pumped back into the sarcoplasmic reticulum
- Absence of $\text{Ca}^{++}$ allows troponin to reestablish its normal shape
- Tropomyosin blocks the myosin binding sites on actin
- Cross-bridging is prevented
Summary
3 steps to muscle contraction

• $Ca^{++}$ released
  - Neurotransmitter initiates an action potential which releases $Ca^{++}$ from SR

• $Ca^{++}$ binding allows myofilaments to interact
  - Excitation-contraction coupling

• Crossbridge cycle shortens muscle
3 uses for ATP in muscle contraction

• Activation of myosin (high-energy myosin)
• release of myosin head from actin molecule
• active transport of Ca^{++} into SR from the sarcoplasm
Skeletal muscle contraction

- **Summation**: additive effects of contraction of different muscle fibers

- **Tetanus**: fusion of contractions
  - **Incomplete**: short relaxation between successive twitches
  - **Complete**: smooth, sustained contraction

- **Treppe**: demonstrates graded nature of muscle fiber contraction
  - May reflect increased presence of Ca$^{++}$
Unfused tetanus: partial dissipation of elastic tension between subsequent stimuli.

Fused tetanus: no time for dissipation of elastic tension between rapidly recurring stimuli.
Types of muscle contractions

• **Contractions**
  - *isotonic* = same strength = muscle shortens
  - *isometric* = same length
  - *lengthening*: filaments pull apart

• **Forces**
  - *tension*: force exerted on an object by a contracting muscle
  - *load*: force exerted on muscle by weight of an object

• **Series-elastic component**
  - non-contractile portions of muscle & tendon
Muscle twitch

- **Twitch**: rapid contraction of one muscle fiber, or group of muscle fibers
- Observed on myogram
- 3 phases
  - Latent period
    - Excitation contraction coupling occurs
    - Tension builds
  - Contraction
    - Cross bridges active
    - If tension greater than load, muscle will shorten
  - Relaxation
    - Ca++ pumped into SR
    - Return to baseline
Muscle twitch

Variation in length of contraction dependent upon metabolic properties of myofibrils and enzymes used.
Muscle response to increased stimuli

- **Recruitment**
  - Multiple motor unit summation
- **Threshold stimulus**
  - Stimulus producing $1^{st}$ observable contraction
- **Maximal stimulus**
  - Strongest stimulus producing increased contractile force
- **Small vs. large motor units**
  - Small stimulus = small motor units = small response
    - Usually stimulated first in muscle contraction
  - Large stimulus = large motor units = large response
  - Stimulation usually asynchronous, but may be stimulated simultaneously