Muscle Physiology

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Functions of the muscular system

1. **Locomotion** – body movements are due to skeletal muscle contraction.

2. **Vasoconstriction and vasodilatation** - constriction and dilation of blood vessel walls are the results of smooth muscle contraction.

3. **Peristalsis** – wavelike motion along the digestive tract is produced by the smooth muscle.

4. **Cardiac motion** – heart chambers pump blood to the lungs and to the body because of cardiac muscle contraction.

5. **Posture maintenance** - contraction of skeletal muscles maintains body posture and muscle tone.

6. **Heat generation** – about 75% of ATP energy used in muscle contraction is released as heat.
Comparison of the three types of muscle

- **Striation**: only present in skeletal and cardiac muscles. Absent in smooth muscle.

- **Nucleus**: smooth and cardiac muscles are uninucleated (one nucleus per cell) skeletal muscle is multinucleated (several nuclei per cell).

- **Transverse tubule (T tubule)**: well developed in skeletal and cardiac muscles to transport calcium. Absent in smooth muscle.

- **Intercalated disk**: specialized intercellular junction that only occurs in cardiac muscle.

- **Control**: skeletal muscle is always under voluntary control, with some exceptions (the tongue and pili arrector muscles in the dermis). Smooth and cardiac muscles are under involuntary control.
Innervation: motor unit

- a) a motor nerve and a myofibril from a **neuromuscular junction** where gap (called **synapse**) occurs between the two structures. At the end of motor nerve, neurotransmitter (i.e. acetylcholine) is stored in **synaptic vesicles** which will release the neurotransmitter using exocytosis upon the stimulation of a nerve impulse. Across the synapse the surface the of myofibril contains **receptors** that can bind with the neurotransmitter.
1. Action potential arrives at axon terminal of motor neuron.
2. Voltage-gated Ca$^{2+}$ channels open. Ca$^{2+}$ enters the axon terminal, moving down its electrochemical gradient.
3. Ca$^{2+}$ entry causes ACh (a neurotransmitter) to be released by exocytosis.
4. ACh diffuses across the synaptic cleft and binds to its receptors on the sarcolemma.
1. Each skeletal muscle fiber is a single muscle cell which is the unit of contraction.

2. Muscle fibers are cylindrical cells with many nuclei.

3. The cell membrane is called sarcolemma the cytoplasm is called sarcoplasm.

4. The sarcoplasm contains abundant parallel thread like myofibrils that run in parallel fashion.
5. The myofibrils contain 2 kinds of protein filaments.

a. Thick filaments – composed of **myosin**.

b. Thin filaments – composed of **Actin**, troponin, and tropomyosin.

c. Striations are produced by alternating light and dark filaments.
Arrangement of the Filaments in a Sarcomere

- Longitudinal section within one sarcomere

(d) Enlargement of one sarcomere (sectioned lengthwise). Notice the myosin heads on the thick filaments.
Ultrastructure of Myofilaments: Thick Filaments

Each thick filament consists of many myosin molecules whose heads protrude at opposite ends of the filament.

Portion of a thick filament

- Myosin head
- Actin-binding sites
- ATP-binding site
- Heads
- Flexible hinge region
- Tail
- Myosin molecule

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Ultrastructure of Myofilaments: Thin Filaments

A thin filament consists of two strands of actin subunits twisted into a helix plus two types of regulatory proteins (troponin and tropomyosin).

Portion of a thin filament

Tropomyosin
Troponin
Actin

Active sites for myosin attachment

Actin subunits
Striation pattern of skeletal muscles: 2 parts

1. The I bands (The light bands) -

- Extends from the edge of one stack of thick filaments to the edge of next stack of thick filaments.

- The I band is composed of thin actin filaments.

2. The A bands (The dark bands) – composed of thick myosin filaments overlapping thin filaments (actin).

(c) Small part of one myofibril enlarged to show the myofilaments responsible for the banding pattern. Each sarcomere extends from one Z disc to the next.
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(d) Enlargement of one sarcomere (sectioned lengthwise). Notice the myosin heads on the thick filaments.
- Myosin filaments are held together by Z lines (not attached).

- A band consists of a region where the thick and thin filaments overlap and a region called central region (H zone) consisting of only thick filaments. In the center of A band is a dark band called the M line.

- **Sarcomere**: The segment of myofibrils that extends from one Z line to the next Z line.

(c) Small part of one myofibril enlarged to show the myofilaments responsible for the banding pattern. Each sarcomere extends from one Z disc to the next.
- **Cross bridge Attachment:** The activated myosin heads are attracted to the exposed binding sites on actin and cross bridge attachment occurs.

- **Power stroke:** The sliding action which occurs at the same time for thousands of actin and myosin molecules is referred to as the power stroke.
Muscle Response:

- All – or – none response.
  
  a. if a muscle fiber contracts at all it will contract completely.
  
  b. motor units respond in an all – or – none manner.
  
- Threshold stimulus: is the minimal stimulus needed to elicit a muscular contraction.
  
- Twitch: single short contraction reflecting stimulation of some motor units in a muscle.
  
- Latent period: is the time between stimulus and responding muscle contraction.
  
- Refractory period: During his period immediately following contraction a muscle can not respond.
The muscle twitch

(a) Myogram showing the three phases of an isometric twitch

Latent period

Extraocular muscle (lateral rectus)

Gastrocnemius

Soleus

(b) Comparison of the relative duration of twitch responses of three muscles

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**Summation**

**Summation:** A rapid series of stimuli may produce summation of twitches and a sustained contraction.
- Forceful sustained contraction without relaxation is a **tetanic contraction**.
- Tetany is the result of low $\text{Ca}^{2+}$ concentrations.

(b) Low stimulation frequency: unfused (incomplete) tetanus.
If another stimulus is applied before the muscle relaxes completely, then more tension results. This is wave (or temporal) summation and results in unfused (or incomplete) tetanus.

(c) High stimulation frequency: fused (complete) tetanus.
At higher stimulus frequencies, there is no relaxation at all between stimuli. This is fused (complete) tetanus.
Types of Contractions:

- **Isotonic**: when a muscle contracts and its ends are pulled closer together.
- **Isometric**: when a muscle contracts but attachments do not move.
- **Isokinetic**: when the force a muscle generates is less than that required to move or lift an object, the contraction is called isokinetic.

![Diagram of isotonic contraction](image)

**Diagram Explanation**

On stimulation, muscle develops enough tension (force) to lift the load (weight). Once the resistance is overcome, the muscle shortens, and the tension remains constant for the rest of the contraction.
Fast & Slow Muscles

- a. White or fast skeletal muscle fibers have few mitochondria, reduced ability to carry on aerobic respiration and tend to fatigue rapidly (ex. extra ocular muscles). Designed for speed & fatigue easily.

- b. Red or slow skeletal muscle fibers have many mitochondria, are designed for endurance and can contract for long periods of time (ex. Solues).

**Muscle Fatigue:**

- A fatigued muscle loses its ability to contract.

- Muscle fatigue is due to accumulation of lactic acid and ATP exhaustion.
Oxygen debt:

- a. During rest or moderate exercise $O_2$ is sufficient to support aerobic respiration (using may ATP molecules).

- b. During strenuous exercise $O_2$ deficiency may develop and lactic acid may accumulate as a result of anaerobic respiration.

- c. The amount of $O_2$ needed to convert accumulated lactic acid to glucose and restore supplies of ATP and creatine phosphate is called oxygen dept.
Role of Ca+ in muscle contraction:

1. promotes neurotransmitter release.
2. Triggers Ca\(^+\) release from SR.
3. Triggers sliding of myofilaments and ATPase activity.
4. promotes glycogen breakdown & ATP synthesis.
Sliding Filament Theory

1. A myofiber together with all of its myofibrils shortens by movement of the insertion towards the origin of the muscle.

2. Shortening of the myofibrils is caused by shortening of the sarcomere (The distance between Z lines is reduced).

3. Shortening of the sarcomere is accomplished by each filament remains the same during contraction.
4. Sliding is produced by power strokes of myosin cross bridges which pull the thin actin over the thick myosin.

5. The A band remains the same length during contraction but are pulled toward the origin of the muscle.

6. Adjacent A bands are pulled closer together as the I bands between them shorten.

7. The H band shorten during contraction as the thin filaments on the sides of the sarcomeres are pulled towards the middle.
1. The distal end of a motor neuron releases **Acetylcholine**.
2. Acetylcholine diffuse across the gap at the **neuromuscular junction**.
3. The **sarcolemma** is stimulated and a muscle impulse travels over the surface of the muscle fiber and deep into the fiber through the transverse tubules and reaches the sarcoplasmic reticulum.
4. **Ca\(^{2+}\)** ions diffuse from the sarcoplasmic reticulum into the sarcoplasm bind to **troponin** molecules.
Neuromuscular Junction:

Setting the stage
The events at the neuromuscular junction (NMJ) set the stage for E-C coupling by providing excitation. Released acetylcholine binds to receptor proteins on the sarcolemma and triggers an action potential in a muscle fiber.
5. **Tropomyosin** molecules move and expose specific sites on actin filament.
6. Actin and myosin filaments form linkages.
7. Actin filaments are pulled inward by myosin cross – bridges.
8. Muscle fiber shortens as a contraction occurs.
Muscle contraction: Role of Ca+

1. Calcium binds to troponin and removes the blocking action of tropomyosin. When Ca$^{2+}$ binds, troponin changes shape, exposing binding sites for myosin (active sites) on the thin filaments.

2. Active sites exposed and ready for myosin binding.

3. Contraction begins: Myosin binding to actin forms cross bridges and contraction (cross bridge cycling) begins. At this point, E-C coupling is over.
Sliding of actin filament over myosin

1. Cross bridge formation. Energized myosin head attaches to an actin myofilament, forming a cross bridge.

2. The power (working) stroke. ADP and P_i are released and the myosin head pivots and bends, changing to its bent low-energy state. As a result it pulls the actin filament toward the M line.

3. Cross bridge detachment. After ATP attaches to myosin, the link between myosin and actin weakens, and the myosin head detaches (the cross bridge "breaks").

4. Cocking of the myosin head. As ATP is hydrolyzed to ADP and P_i, the myosin head returns to its prestroke high-energy, or "cocked," position.

*This cycle will continue as long as ATP is available and Ca^{2+} is bound to troponin. If ATP is not available, the cycle stops between steps 2 and 3.*
Major events of muscle relaxation

1. Acetylcholinesterase decomposes acetylcholine and the muscle fiber membrane is no longer stimulated.
2. Ca\(^{2+}\) ions are actively transported into the sarcoplasmic reticulum.
3. ATP causes linkage between actin and myosin filaments to break.
5. Troponin & tropomysin molecules inhibit the interaction between myosin and actin filaments.
6. Muscle fiber remain relaxed yet ready until stimulated again.
Smooth Muscle Contraction

1. Smooth muscles contain filaments of actin and myosin.
2. Lack transverse tubules and S.R. is not well developed.
3. Display rhythmicity (spontaneous repeated contractions) responsible for **peristalsis** (alternate contraction and relaxation).
4. Lack troponin (protein that binds to Ca\(^{2+}\)) instead **calmodulin** binds to Ca\(^{2+}\).
5. Both Acetylcholine & Norepinephrine are neurotransmitters for smooth muscles.
6. Hormones and stretching affect smooth muscle contractions.
7. Can contract for a long period of time.
Cardiac muscle

- a) unique arrangement of actin and myosin filaments produces the cross-striations (an optical illusion under the microscope), and rapid contraction with powerful forces involved.

- b) muscle cells are joined by **intercalated disks**, and allow muscle groups to form branching networks - both features are necessary for cardiac muscle to function as a unit ("syncytium").

- c) **SR** and **T** tubules are well developed, so a large amount of **calcium** can be released rapidly through the T tubules.

- d) contains more mitochondria in each muscle cell than skeletal and smooth muscles, providing more **ATP** energy for continuous contraction.
Cardiac Muscle

- self-excitng muscle fibers form "pacemakers" which initiate spontaneous nerve impulses for autorthymic contraction. These pacemakers can be influenced by the autonomic nervous system and hormones.
Cardiac Muscle:

1. Contracts for a longer time than skeletal muscle because transverse tubules supply extra $\text{Ca}^{+2}$ ions.
2. Intercalated disc connects the ends of adjacent muscles and hold cells together as a unit (syncytium).
3. Fibers contracts as a unit.
4. Muscle fibers are self–exiting, rhythmic, and remain refractory until a contraction is completed.
5. No Tetanic contractions.
Electromyogram (EMG)

- **a) Latent period** – chemical reactions and physical changes that occur preceding the actual contraction of a skeletal muscle.

- **b) Period of contraction** – actin causing the shortening of sarcomere and the contraction of muscle.

- **c) Period of relaxation** – actin returns to its original position causing the lengthening of sarcomeres and the relaxation of muscle.
Clinical Terms:

- **Convulsion**: series of involuntary contractions of various voluntary muscles.

- **Fibrosis**: Degenerative disease in which connective tissue replaces skeletal muscle tissue.

- **Myalgia**: pain resulting from any muscular disorder.

- **Myasthenia gravis**: an autoimmune chronic disease characterized by muscles that are weak and easily fatigue. It results from the immune system's attack on neuromuscular junctions.

- **Paresis**: partial or slight paralysis of the muscle.

- **Muscular dystrophy**: progressive muscle weakness and atrophy caused by deficient dystrophin protein.
Clinical Terms

- **Myopathy**: Any muscular disease.
- **Paralysis**: Loss of ability to move a body part.
- **Myotonia**: Prolonged muscular spasm.
- **Myositis**: Inflammation of skeletal muscle tissue.
- **Spasm**: A sudden involuntary smooth or skeletal muscle twitch can range from mild to very painful irritation.
- **Tics**: Spasm of eye–lid or facial muscles.
- **Cramp**: A prolonged spasm that cause a muscle to become taut and painful.