9 - Muscular System

Microanatomy of Skeletal Muscle
Taft College Human Physiology
Review

(a) Myofibril

Z disc  M line  Thick filament  Thin filament  Z disc

Sarcomere

Thin filament  Thick filament  Titin filament

(b) Details of filaments and Z discs

Zone of overlap  H zone  Zone of overlap
Review
Microanatomy of Skeletal Muscle

Contracted or Relaxed Muscle?
Review

Relaxed muscle

2 Sarcomeres

H zone  I band  A band

Thick filament

Z disc  Thin filament  Z disc  M line  Z disc

Z disc  M line  Z disc

I band  A band  I band

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Contracted or Relaxed Muscle?
Where is H zone?
Microanatomy of Skeletal Muscle

- **Exercise induced muscle damage (DOMS)**
- Extensive exercise can cause damage to muscle cells. Electron micrographs show torn sarcolemmas, damaged myofibrils, and disrupted Z discs.
- Muscle soreness occurs 12 to 48 hours after strenuous exercise, called **delayed onset muscle soreness (DOMS)** accompanied by stiffness, tenderness, and swelling.
Other Structural Components of Skeletal Muscle

- All structures mentioned so far have been located within the sarcoplasm.
- Other structures within the sarcoplasm include:
  - a. Many mitochondria - provide energy for contraction.
  - b. Sarcoplasmic reticulum (SR) - similar to endoplasmic reticulum.
  - It forms a network around each myofibril and functions as a reservoir for Ca2+ ions.
  - The Ca2+ provides is the final ‘go’ signal for contraction.
  - c. T (transverse) Tubules - tube or tunnel-like invaginations of the sarcolemma that penetrate inside the muscle fiber.
  - The tubules are open to the outside of the cell and contain ECF.
  - These tubules allow a chemical message for contraction (from a neuron) to penetrate the interior of the myofiber so that all myofibrils within it can contract simultaneously.
(a) Relaxation

Troponin holds tropomyosin in position to block myosin-binding sites on actin.

(b) Contraction

Ca\textsuperscript{2+} binds to troponin, which changes the shape of the troponin–tropomyosin complex and uncovers the myosin-binding sites on actin.
Excitation of Skeletal Muscle

• How is the skeletal muscle stimulated to contract?
• Earlier we mentioned that stimulation of skeletal muscle contraction is primarily by nerve stimulation.
• Nerve impulses travel from one part of the body through nerve cells called neurons.
• The connection between 1 neuron and a 2nd neuron (or neuron to a muscle) is called a synapse.
• When we look closer at nervous system messages we will see messages to be:
• **Electrical in nature along the neurons**, but are **chemical in nature when crossing a synapse**. = **electrochemical message**
Electrochemical Message

Motor Unit

Electrical

Chemical = Neurotransmitter

ACh = Acetylcholine

Synapse

Neuron

“Presynaptic”

Neuron

“Postsynaptic”

Chemical

ACh

Synapse

Or NMJ

Muscle Cells

10 – 2000

Ave = 150
Axon collateral of somatic motor neuron
Axon terminal
Synaptic end bulb
Neuromuscular junction (NMJ)
Sarcolemma
Myofibril

Neuromuscular junction
Enlarged view of the neuromuscular junction

Sarcolemma

Motor end plate

Axon terminal
Nerve impulse
Synaptic vesicle containing acetylcholine (ACh)
Synaptic end bulb
Synaptic cleft (space)
Motor End Plate

- ACh released from synaptic vesicle
- Synaptic cleft (space)
- Binding of ACh to ACh receptors opens cation channel
- Na⁺
- Synaptic end bulb
- ACh broken down
- Motor end plate
- Muscle action potential produced

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Binding of acetylcholine to ACh receptors in the motor end plate
Neuromuscular junction

= Myoneural junction
Motor neuron- Motor neurons send information out away from brain.

Sensory neuron- Sensory neurons take information in toward brain.

Each motor neuron branches profusely near the muscle tissue to as many as 2000 separate skeletal muscle cells.

Each neuron and it’s associated muscle cells = a motor unit.
Motor Unit = single motor neuron + all of the muscle cells it innervates

Note: 2 motor units are shown here!
Motor Unit

- The number of muscle fibers controlled by a motor unit will depend on the function of the muscle. Examples:
  - A power muscle such as the gluteus maximus or gastrocnemius will have a motor unit that controls many muscle fibers (about 2000 cells = Large motor unit).
  - A finesse muscle such as the eye, larynx, or finger muscles, will have a motor unit that controls only a few muscle fibers (about 10 cells = Small motor unit).
  - The average motor unit controls 150 muscle fibers.
  - The strength of a contraction depends in part on how many motor units are stimulated.
  - More motor units = stronger force of contraction.
Excitation of Skeletal Muscle

- A synapse is a gap between 2 neurons that can only be crossed by chemical messengers. The chemical messengers are called neurotransmitters.
- Neurotransmitters are stored in the membrane-bound vesicles of the nerve ending (axon terminal).
- When an impulse moves along the axon to the axon terminal, these vesicles migrate to the gap and release their neurotransmitter (exocytosis) into the synaptic cleft.
- The neurotransmitter then diffuses across the synapse and joins to the membrane of the nerve or muscle cell.
- The neurotransmitter may cause depolarization and therefore contraction of the muscle cell.
- Various neurotransmitters found throughout the body are affected by drugs and examples will be discussed soon.
Excitation of Skeletal Muscle

1. Vesicle w/ Neurotransmitter = ACh
2. Sarcolemma = Polarized at Rest
- Resting Potential
- Ach changes permeability of Sarcolemma
  (opens Na+ channels)
3. Depolarization
  = Action Potential
  Triggers Ca++ release from S-R + Muscle Contracts
Excitation of Skeletal Muscle

1. At rest, the axon terminal is ready to release neurotransmitter when an impulse arrives.
2. When an impulse arrives the vesicles move to the axon terminal and release their neurotransmitter into the neural muscular junction where it diffuses towards the **motor end plate** located in the sarcolemma of a muscle fiber.
3. The neurotransmitter binds to the motor end plate. This initiates the continuation of the impulse in the 2nd cell.
4. In the case of a neuromuscular junction, the neurotransmitter = acetylcholine (ACh). Each motor end plate typically contains 30-40 million ACh receptors.
5. Each molecule of acetylcholine (ACh) works to change the permeability of the muscle membrane (sarcolemma). ACh opens Na+ chemical gates (facilitated diffusion).
Excitation of Skeletal Muscle

- Each molecule of acetylcholine (ACh) works to change the permeability of the muscle membrane (sarcolemma).
- ACh opens Na+ chemical gates ( = facilitated diffusion).
- Certain ion concentrations exist on both sides of the membrane at rest. Therefore, it is said to be polarized = resting potential. The outside being positive (+) and the inside negative (-), like a tiny battery.
- If enough molecules of ACh bind to receptors sites in high enough concentration, a depolarization will take place.
- (This is an example of a graded potential = a small area of the membrane deviates from the resting potential.)
- The rapid depolarization is called an action potential. The ACh receptor is a (chemically gated) channel protein that passes small cations (Na+).
- When Na ions rush in, this changes the resting potential into an action potential that travels locally along the muscle cell sarcolemma.
- The action potential propagates (moves along) on the muscle cell surface by triggering other (voltage gated) Na+ channels to open which causes the entire muscle cell to contract simultaneously.
ACh Opens Chemically Gated Protein Channel

- **Ligand** = a chemical substance that binds to a specific receptor

- **Resting Potential**
  - **Polarized** (Gates Closed)

- **ACh Opens Gate**
  - **Depolarized**

**Chemical stimulus**
- **Opens the channel**

**Channel Protein**

**Extracellular fluid**

**Plasma membrane**

**Cytoplasm**

**Acetylcholine**

**ACh**
Change in Voltage Opens Voltage Gated Channel

This diagram is a voltage-gated K+ channel.
A voltage-gated Na+ channel would operate in similar fashion.
Side Note:
Types of Protein Ion Channels

1. **Leakage** channels = open most of the time.
2. **Voltage gated** channels = open due to change in voltage.
3. **Chemically gated** channels = open due to presence of specific chemical (ligand).
4. **Mechanically gated** channels = open due to physical change (vibration, pressure, stretching). These are important in your sense of hearing, balance, and touch.

Who Cares??? What happens when these ion channels don’t work????

Goat Video   Also neuron video
Resetting the Membrane Potential

• One problem is left to be solved! Need to reset the membrane for the next impulse.
• We need to get ACh away from receptors sites. If ACh stays, we would get a continual contraction of the muscle cell = tetanus.
• To get rid of ACh, nature has an enzyme called acetylcholinesterase = (AChE).
• AChE interacts with ACh and breaks it down. Therefore removing the ACh trigger that keeps the Na+ channels open.
• After the ACh is gone, the permeability of the sarcolemma returns to normal and therefore, goes back to resting potential, a process called repolarization.
Muscular Disorders or Diseases of the Skeletal Muscle Excitation Mechanism

- **Myasthenia gravis** - a progressive neural muscular disorder characterized by abnormal fatigability (weakness and atrophy) of the muscles. Muscles are weak, and contract with little force or speed.


- Today we know:
  - It is an autoimmune disorder that produces antibodies directed against ACh receptors in the motor end plate. The antibodies bind to the ACh receptors and hinder the action of ACh.
  - The disease advances as more receptors are affected and the muscles are weaker and may cease to function.
  - Anticholinesterase drugs (neostigmine) help by making more ACh available in the synapse to bind to remaining functional receptors.
Muscular Disorders or Diseases of the Skeletal Muscle Excitation Mechanism

- **Paralysis** - Inability to voluntarily control skeletal muscle. A general term.
- Usually due to nerve damage (denervation - severed nerves), as muscle will still respond to direct (external) stimulation.
Muscular Disorders or Diseases of the Skeletal Muscle Excitation Mechanism

- **Muscle Fatigue** - If muscle is over stimulated the strength of contractions becomes progressively weaker. **Muscle fatigue** = The inability of a muscle to maintain force of contraction after prolonged activity.

- Factors that contribute to fatigue are:
  - 1. **Reduced ACh** = safety valve – NMJ quits before muscle damage is done
  - 2. **Reduced ATP production** - can lead to cramping if active transport of Ca++ quits.
  - 3. **Reduced oxygen**
  - 4. **Reduced glycogen** = fuel
  - 5. **Increased lactic acid** = waste product of anaerobic respiration.

Important fitness question – Can your mitochondria keep up with level of muscle activity?
Muscular Disorders or Diseases of the Skeletal Muscle Excitation Mechanism

- **Muscular Dystrophies** - inherited muscle destroying diseases, where muscle cells degenerate and may be replaced with fibrous C.T. or fat.
- Wheel chair use may be the result in teen years, followed by death at 20-30 years of age as diaphragm and heart muscle are affected.
- A protein in the sarcolemma (dystrophin), is missing and seems to lead to muscle fiber degeneration.
- No treatment is currently available, however gene therapy (myoblast transfer and plasmid injection) is being investigated.
Drug Effects on Muscular Excitation – Cholinesterase Inhibitors

- **Cholinesterase inhibitors** = Substances that are anti-cholinesterases and bind to AChE and **prevent AChE from breaking down Ach**. If Ach remains, muscles remain in contracted state.
- 1. **DFP** = pesticide that acts on nervous system.
- 2. **parathion** = pesticide that acts on nervous system. DFP and parathion kills insects as their nervous system sends continuous senseless messages. Totally disrupts nervous system message.
- 3. **sarin** = nerve gas used illegally in war and by terrorists in Japan.
- 4. **neostigmine** (chemical drug used in treating myasthenia gravis).
- The **inhibition of AChE** causes spastic paralysis of the muscles, a **state of continual contraction**. There is an immediate danger of suffocation if laryngeal and respiratory muscles are affected.
- The poisoned person should remain still and quiet to **avoid a startle response** that could escalate into dangerous muscle spasms.
- **Atropine (muscle relaxant)** is given as an **antidote treatment** for cholinesterase inhibitors. Soldiers in Gulf War were given syringes of atropine “just in case”. Atropine is used in eye exams to dilate pupils.
Drug Effects on Muscular Excitation – Muscle Relaxants

1. **Atropine** is given as an antidote treatment for cholinesterase inhibitors. You may have been given atropine in an eye examination. Atropine relaxes the eyes muscles of the iris and therefore dilates the pupil.

2. **Curare** - Causes flaccid paralysis by binding to ACh receptors without causing stimulation, and blocking ACh action. Therefore it blocks the neuromuscular junction and prevents muscular contraction.
   - Respiratory failure can result.
   - Used by South America Indians to poison arrows.
   - Has been used historically to relax muscles in abdominal surgery (abdominal and diaphragm muscles) so they can be moved aside. Now replaced by newer drugs.

3. **Flexeril** – used in surgery and has replaced curare.
Drug Effects on Muscular Excitation

- **Blackwidow spider venom** - contains many toxins of which one promotes constant release of neurotransmitter.
- Results in tetanus. When diaphragm is affected, breathing action is ceased.
- **Botulism** - In botulism, a toxin called botulinum is produced by the bacteria, *Clostridium botulinum*.
- The toxin is ingested with contaminated food.
- Botulinum toxin prevents the release of synaptic vesicles containing ACh, and therefore blocks nerve transmission. A type of flaccid paralysis.
- It is the most potent toxin known: 0.0001 mg will kill a person. 1/2 lb. could kill all humans.
- We use this toxin to prevent wrinkles! Botox injections keep the muscle from contracting so wrinkles do not appear.