

The Neuromuscular Junction

- 50 million ACh (acetylcholine) receptors
- Junctional Folds: Increase the surface area for the acetylcholine receptors

Myasthenia Gravis: Autoimmune disease of women ages 20-40

- Very few receptors available for ACh
- Diagnosed by asking someone to gaze up—after 60 seconds one eyelid will start to droop, after 90 seconds that one eyelid will completely close
 - Unable to contract muscles that open the eyes
- Symptoms: Double vision, drooping of eyelids, weakness of skeletal muscles (esp. in limbs)
- Treatments:
 - 1. Cholinesterase Inhibitors
 - Antibodies sitting on receptor, making very few available for ACh—makes sure ACh stays around longer by inhibiting enzyme that breaks down ACh to make it more likely to access the few receptors that are available
 - 2. Immunosuppressive Agents
 - Inhibit ability to produce antibodies
 - Risk for infection with decreased antibodies
 - 3. Thymus removal (Thymectomy)
 - Decreases mature T-cell production
 - Risk for contracting viruses without T-cells
 - 4. Plasmapheresis
 - Draw blood out, remove plasma, and put back albumin

Electrically Excitable Cells

- Muscle fibers and neurons
- Electrophysiology: Study of the electrical activity of cells
- Voltage—Electrical potential across plasma membrane
 - Difference in electrical charge across plasma membrane
 - In an unstimulated cells, Na and Cl tend to be in high concentration outside of cell, while K in high concentration inside of cell
 - Ions leak across membrane, causing charge

- In a stimulated cell, opening of Na channels and opening of K channels
 - Na—Fast channels that open and close quickly
 - K—Slow channels that open and close slowly
 - Na high concentration on inside, K on high concentration outside **Opposite of unstimulated
 - Depolarization: Opening of membranes in a stimulated cell
- Resting Membrane Potential: About -90 mV
 - Electrical potential of an UNSTIMULATED cell
- Action Potential: Na channels open very fast, and K channels open a little later very slowly to create a reversed electrical potential in the stimulated cell

Muscle Action Potential

- Graph—In an unstimulated cell, start at resting membrane potential (~ -90 mV, but may vary depending on type of muscle cell in a range from -100 to -70 mV)
 - 1. Membrane Depolarization: Na channels open, allowing it to rush into cell to make the membrane potential go more positive
 - Open and close almost before K channels start to open
 - 2. Membrane Repolarization: K channels open and Na channels close, allowing K out and decreased the membrane potential (more negative)
 - 3. Membrane Hyperpolarization: K channels remain open after the potential returns to resting level, allowing the electrical potential to become more negative than the resting membrane potential

Skeletal Muscle Fiber Stimulation—4 major phases of contraction and relaxation

- 1. Excitation
 - Nerve coming down with synapse on muscle cell
 - In the synaptic knob are voltage-gated Ca channels—activated by electrical signal
 - When Ca channels open, allow Ca from extracellular fluid to come into synaptic knob and bind with synaptic vesicles that contain ACh

- Cause pre-synaptic membrane to release ACh into synaptic cleft
- Sitting on post-synaptic membrane are ligand-gated ACh receptors
 - ACh receptors are channels that allow Na into cell and K out of cell
 - Activated by two molecules of ACh binding to that receptor, causing channel to open up and Na to come in/K to leave cell (similar to depolarization)
 - Causes local depolarization (end plate potential—change in membrane potential in that small area only)
 - Have to have enough local potentials to add up to threshold—point of electrical potential that causes the receptor to fire
- ****END PLATE POTENTIAL --> ACTION POTENTIAL****
- 2. Excitation-Contraction Coupling: Get signal to all of the muscle
 - Sarcolemma invaginates where terminal cisternae have voltage-gated Ca channels
 - Voltage comes down T-tubule, Ca released from sarcoplasmic reticulum into cytoplasm --> Ca that is released binds to troponin and cause tropomyosin to move out of the way
 - ****CALCIUM IS LINK BETWEEN EXCITATION (electrical) AND CONTRACTION (mechanical)****
 - Myosin must be activated by at ATP being bound to the myosin head
 - Enzyme in myosin head—Myosin ATPase: Hydrolyzes an ATP molecule
 - Allows myosin to assumed “cocked” head position
 - Uses energy from inorganic phosphate to assumed cocked position and release ADP and inorganic phosphate, creating a cross-bridge—binding of Actin and Myosin
- 3. Contraction
 - Pull actin towards M-line-->Changes overlap
 - Power Stroke: Pulling of actin by myosin
 - Every power stroke requires a molecule of ATP