Intro to Skeletal Muscle Physiology

•In order for contraction of skeletal muscle to occur, electrical signals (action potentials) from motor neurons must be transformed into chemical signals (neurotransmitters)
–Takes place at the neuromuscular junction
•These chemical signals then stimulate electrical signals in sarcolemma of the muscle fiber - if the chemical stimulation is strong enough.
•The electrical signal in the muscle fiber (action potential) then activate a series of events that lead to the shortening of the skeletal muscle fiber

Intro to Skeletal Muscle Physiology

•Predominant theory of skeletal muscle contraction–Well supported by research
•Sliding filament model of contraction–Interactions between the thin and thick filaments of the sarcomere produce the contraction (shortening) of a skeletal muscle cell
–In relaxed state, thin and thick filaments overlap slightly
–During contraction, thin filaments slide toward the m-line past the thick filaments actin and myosin overlap more
•Occurs when myosin heads bind to actin and pull cross bridges and power stroke

Muscle Action Potential

•Brief overview of action potential (AP)–AP dependent on voltage gated Na+ and K+ channel interactions
–Normal resting membrane voltage
•There is a difference in charges inside the cell vs outside –Inside charge is negative compared to outside (outside value is 0)
•Na+ at high concentration outside the cell vs inside•K+ at high concentration inside the cell vs outside

Events in Generation of an Action Potential

•Depolarizationphase - generation and propagation of an action potential (AP)
–End plate potential spreads to adjacent membrane areas
–Voltage-gated Na+ channels open–Na+ influx decreases membrane voltage (makes less negative) toward critical voltage called threshold
•Membrane voltage in which AP will begin
–If threshold reached, AP initiated
•Rapid increase in amount of open voltage gated sodium channels
•Rapid Na+ influx into the cell leads to fast positive change in voltage of the intracellular side of membrane
•Na+ flows into the cell, down its electrochemical gradient
–Once initiated, is unstoppable muscle fiber contraction

Excitation-Contraction (E-C) Coupling

•Events that transmit AP along sarcolemma lead to sliding of myofilaments
•AP brief; ends before contraction
–However, causes rise in intracellular Ca2+ contraction
•Latent period
–Time when E-C coupling events occur
–Time between AP initiation and beginning of contraction

Neuromuscular Junction

•Situated midway along length of muscle fiber
•Axon terminal and muscle fiber separated by gel-filled space called synaptic cleft
•Synaptic vesicles of axon terminal contain neurotransmitter acetylcholine (ACh)
•Junctional folds of sarcolemma contain ACh receptors
–nAChR (nicotinic acetylcholine receptor)
•NMJ includes axon terminals, synaptic cleft, junctional folds

Chemical and Electrical Gradients of Muscle

•Chemical gradients of skeletal muscle at rest–Comparison intracellular [X] vs. extracellular [X] (Sarcoplasmic vs. interstitial)
•Intracellular [Ca] very low•Intracellular [Na] very low
•Intracellular [K] high
•At rest, the average skeletal muscle cell internal membrane voltage (charge at the surface of the intracellular portion of the plasma membrane) is -95mV with respect to a 0 mV outside membrane voltage
–The charge at the surface of the extracellular side of the membrane is almost always 0mV

Chemical and Electrical Gradients of Muscle

•Generic graphic for a skeletal muscle cell
–Compares membrane voltage and concentrations of important ions inside vs. outside

concentrations are also applicable to most neurons

Events at the Neuromuscular Junction

•Nerve impulse arrives at axon terminal ACh released into synaptic cleft
•ACh diffuses across cleft (from high concentration to low) and binds with ACh receptors on sarcolemma
•Electrical events generation of action potential

Generation of an Action Potential

•Resting sarcolemma polarized
–Voltage across membrane different
•Action potential in sarcolemma caused by changes in electrical charges
•Occurs in three steps
–End plate potential
–Depolarization
–Repolarization

Events in Generation of an Action Potential

•AP spreads across sarcolemma •Voltage-gated Na+ channels open in adjacent sarcolemma portions causing them to depolarize to threshold
–Spreads across sarcolemma very quickly

Events of Excitation-Contraction (E-C) Coupling

•AP propagated along the sarcollema and into T-tubules
•AP travels down into the T-tubules where it activates DHP receptors
•DHP receptors
–These voltage-sensitive proteins allow a small amount of calcium to flow into the sarcoplasm but also mechanically stimulate the Ryanodine receptors on the SR
•The Ryanodine receptors are the calcium "flood gates" of the SR
–When stimulated by the DHP receptors, the ryanodine receptors allow Ca2+ release from SR into the sarcoplasm
–This increases sarcoplasmic calcium concentration supplying the majority of Ca2+ necessary for contraction of skeletal muscle

Physiology of Skeletal Muscle Fibers

•For skeletal muscle to contract
–Activation (at neuromuscular junction)
•Must be nervous system stimulation
•Must generate action potential in sarcolemma
–Excitation-contraction coupling
•Action potential propagated along sarcolemma
•Intracellular Ca2+ levels must rise briefly leading to the onset of contraction

The Nerve Stimulus and Events at the NMJ

•Skeletal muscles stimulated by somatic motor neurons
–Under voluntary control•Axons of motor neurons travel from central nervous system via nerves (bundles of mostly neuron axons) to skeletal muscle
•Each axon may form several branches as it enters whole muscle
•Each axon ending forms a neuromuscular junction with single muscle fiber

Destruction of Acetylcholine

•ACh effects quickly terminated by enzyme acetylcholinesterase in synaptic cleft
–Breaks down ACh to acetate and choline
–Prevents continued muscle fiber contraction in absence of additional stimulation

Gen of an Action Potential Across the Sarcolemma

•End plate potential (local depolarization)
–ACh binding opens chemically (ligand) gated ion channels
–Simultaneous diffusion of Na+ (inward) and K+(outward)
•More Na+ diffuses in, so interior of sarcolemma becomes less negative
–Local depolarization = end plate potential

Events in Generation of an Action Potential

•Repolarization – restoring electrical conditions of RMP
–Voltage-gated K+ channels begin to open
–K+efflux (outflow) begins to outpace Na+ influx•rapidly restores resting polarity (makes negative again)
•Na+ are closing, eventually decreasing Na+ influx
–Another muscle fiber depolarization AP cannot be stimulated
•in refractory period until repolarization complete
–Eventually, K+ channels close (lowers K+ efflux)
–Chemical and electrical conditions of resting state restored by Na+-K+pump and K+ leaking out of the cell through K+leak channels

Channels Involved in Initiating Muscle Contraction

•Nerve impulse (AP) reaches axon terminal voltage-gated calcium channels open ACh released to synaptic cleft
•ACh binds to its receptors on sarcolemma opens ligand-gated Na+ and K+ channels end plate potential
•Opens voltage-gated Na+ channels AP propagation

Channels Involved in Initiating Muscle Contraction (cont)

•Voltage-sensitive proteins in T tubules (DHP receptors) change shape and activate the Ryanodine receptors SR releases Ca2+ to cytosol