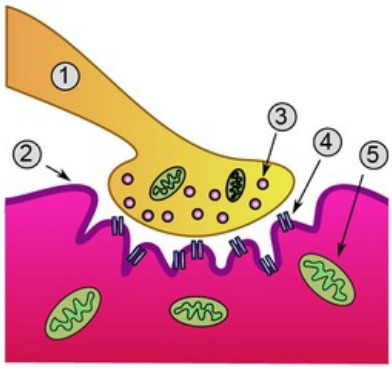
Excitation-contraction coupling in skeletal muscle

Excitation - contraction coupling in the skeletal muscle is the sequence of events through which the nerve fiber stimulates the skeletal muscle fiber causing its contraction. The cholinergic nerve fibers innervate the skeletal muscle fibers through the neuromuscular junctions, they release their neurotransmitters that cause activation of the muscle cell plasma membrane ligand gated ion channel-coupled receptors causing ion transport that in turn will activate the contractile mechanism of the muscle fiber.

Neuromuscular junction

The neuromuscular junction is the site where the neuronal axon terminals (synaptic terminal) of a motor neuron come in contact with the plasma membrane of the skeletal muscle fiber (motor end plate). In reality there is no physical contact between the two membranes, but rather a small gap exists, being similarly functional to the synaptic cleft of a chemical synapse. The synaptic terminal of the neuron is of a sausage-like shape being embedded within the muscle fiber rather than lying over the the cell. The area of the muscle plasma membrane comes in relative contact with the synaptic neuronal terminal, presents a highly folded membrane forming a wavy pattern when it is cut perpendicularly to the longitudinal axis of the neuromuscular junction indicating many features of the excitation-contraction coupling of the skeletal muscle fibers.

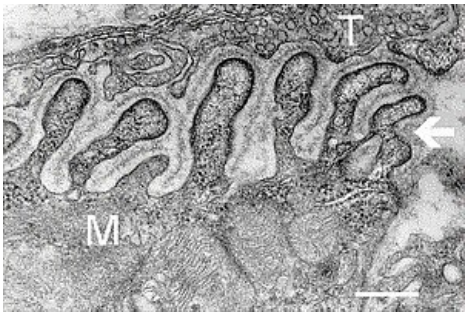


Neuromuscular junction 1. Presynaptic terminal 2. Sarcolemma 3. Synaptic vesicles 4. Acetylcholine receptors 5. Mitchondrion

- increase of the muscle fiber postsynaptic terminal surface area indicates increased number of ligand-gated ion-channel-coupled receptors on which the neurotransmitter released by the neuron can act on.
- since the folds extend inside the muscle fiber it is presumed that it promotes contraction of the deeper sarcomeres when stimulation of the motor end plate occurs.

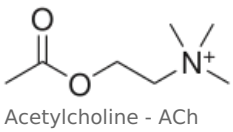
The neuromuscular junction usually refers to the interaction of an α motor neuron with a skeletal muscle fiber. The neuronal synaptic terminal are cholinergic and secrete acetylcholine (ACh) a neurotransmitter that promotes contraction of the skeletal muscle fibers. ACh introduces different effects over smooth muscle and striated muscle acting through different types of receptors. Skeletal muscle fibers contain nicotinic cholinergic receptors whereas the smooth muscle cells consist of muscarinic cholinergic receptors that are both excitatory and inhibitory.

Excitation sequence of skeletal muscle

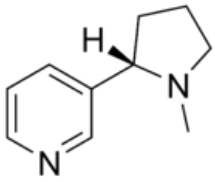


Neuromuscular junction electron micrograph

1. An action potential travels through the axon terminal and eventually reaches the synaptic terminal
2. The depolarization of the synaptic terminal from the action potential induces opening of the Ca^{2+} voltage gated channels
3. Opening of these channels allows flux of Ca^{2+} ions inside the neuron
4. Increase of the intracellular Ca^{2+} concentration introduces conformational changes of the microtubular component of the neuronal synaptic terminal cytoskeleton
5. These cytoskeletal changes lead the exocytotic process concerning the synaptic vesicles containing acetylcholine (ACh) neurotransmitter
6. Through exocytosis secretion of ACh occurs that diffuses from the synaptic terminal membrane towards the motor end plate membrane
7. As soon as the neurotransmitter reaches the plasma membrane of the skeletal musce fiber, it binds with ligand gated ion channel coupled receptors specific for ACh. These receptors are called nicotinic receptors and are sensitive to nicotine besides ACh
8. As soon as the neurotransmitter-receptors complex occurs it activates an integral protein coupled with the nicotinic receptor, undergoing conformational changes
9. These conformational changes allow the opening of the channel which in turn cause the flux of Na+ ions inside the muscle fiber
10. Accumulation of Na^{+} within the cell commence the depolarization of the membrane giving rise to the end plate potential that keeps rising towards an action potential threshold
11. The action potential spreads throughout the membrane of the fiber and especially within the T tubules of the muscle fiber deep inside the fiber
12. The thorough spreading of depolarization promotes activation of the Ca^{2+} voltage gated channels located on the plasma membrane and in the T tubules
13. Opening of the Ca^{2+} channels cause influx of Ca^{2+} ions inside the cell increases the intracellular calcium concentration which in turn open Ca^{2+} voltage gated channels of the sarcoplasmic reticuli near the T tubules allowing even greater increase of intracellular Ca^{2+}



Acetylcholine - ACh



Nicotine

Contraction sequence of skeletal muscle

1. The Ca^{2+} that accumulates after a skeletal muscle cell depolarization is the reason for the initiation and the maintenance of the contraction of the sarcomere, thus increasing the Ca^{2+} inside the cell, will also increase the contractile force produced by the fibers.
2. The free Ca^{2+} binds with the troponin C protein component of the thin actin filaments introducing the active calcium-troponin complex
3. This binding causes the conformational change of the troponin C
4. The conformational change of the troponin C induces the alteration of the conformation of the tropomyosin protein component of the thin actin filaments
5. These changes, all together, promote the exposure of the actin binding sites in order to provide anchoring of the myosin filament heads in order to induce interaction between the thick and thin filaments and elicit contraction
6. Myosin binds to the newly uncovered binding sites on the thin filament
7. The release of ADP and phosphate are tightly coupled to the power stroke. This will pull the Z bands towards each other, thus shortening the sarcomere and the I band.
8. ATP binds myosin, allowing it to release actin and be in the weak binding state
9. The myosin then hydrolyzes the ATP and uses the energy to move into the "cocked back" conformation.

Removal of Ca^{2+} from the smooth muscle cell

- **Na+/Ca^{2+} antiporter:** located in the plasma membrane, through which 3 Na^{+} ions are exchanged for a single Ca^{2+} ion. This type of Ca^{2+} transport occurs not directly through ATP cleavage but indirectly through a concentration gradient introduced by the Na^{+}/K^{+} ATPase pump also located in the plasma membrane. This kind of transport is referred as secondary active transport of Ca^{2+} ions.
- **Ca^{2+} ATPase pump:** located in the membrane of the sarcoplasmic reticulum that transports Ca^{2+} from the cytosol into the reticulum using ATP. This type of Ca^{2+} transport is referred to as the primary active transport of Ca^{2+} ions.

Links

Bibliography

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