Muscle Contractions

Control of Skeletal Muscle Contractions

1. Muscle contraction begins when an action potential reaches the synaptic terminal of a motor neuron.

   The neurotransmitter **acetylcholine (ACh)** is then released into the synaptic cleft of the **neuromuscular junction.**

   ACh binds to ACh receptors on the **motor end plate** of the skeletal muscle fiber.

2. Binding of Ach causes the muscle cell's membrane (also known as the **sarcolemma**) to become permeable to Na^+.

   These ions rush into the **sarcoplasm** (the cytoplasm of the muscle cell) causing the entire surface of the cell to **depolarize** (becomes more positively charged).   With the help of **_T tubules_** (transverse tubules which run from the surface of the muscle cell directly into the cell), the depolarization reaches into the center of the cell as well.

STEPS IN INITIATING MUSCLE CONTRACTION

Synaptic terminal   Motor end plate   T tubule   Sarcolemma

1 ACh released, binding to receptors

2 Action potential reaches T tubule

3 Sarcoplasmic reticulum releases Ca^{2+}

Ca^{2+}

Actin

4 Active site exposure, cross-bridge formation

Myosin

5 Contraction begins

3. The depolarization of T tubules causes the **sarcoplasmic reticulum** (similar to an endoplasmic reticulum) to release Ca^{2+} into the sarcoplasm.

4. When Ca^{2+} binds to **troponin**, it alters the position of the **_tropomyosin_** on the actin filament, exposing the **myosin binding sites** (*see diagram on next page).* When the binding sites are exposed, "*myosin heads*" on the myosin filament can then bind to the exposed sites on the actin filament.

5. As the myosin heads interact with actin, contraction begins. The sliding filament model is used to describe how the contraction of the muscle cell occurs.

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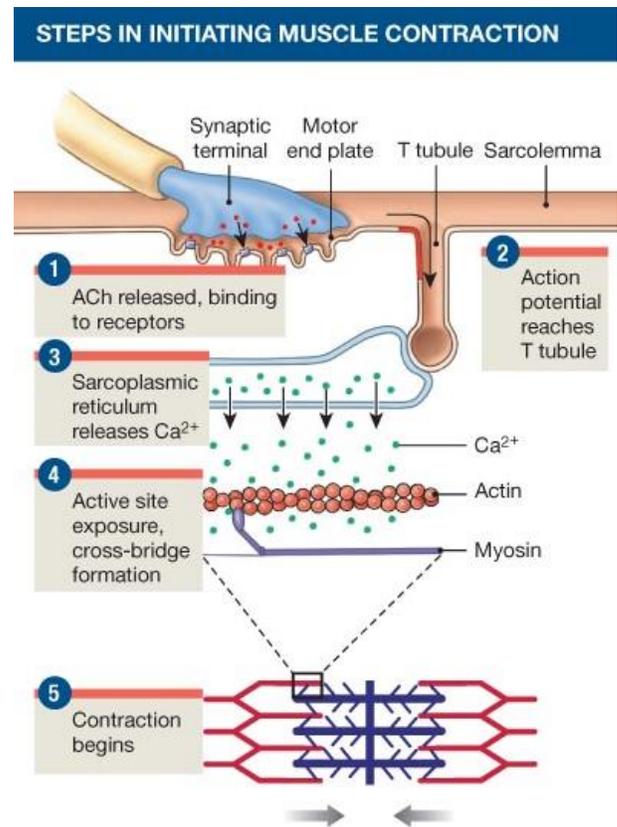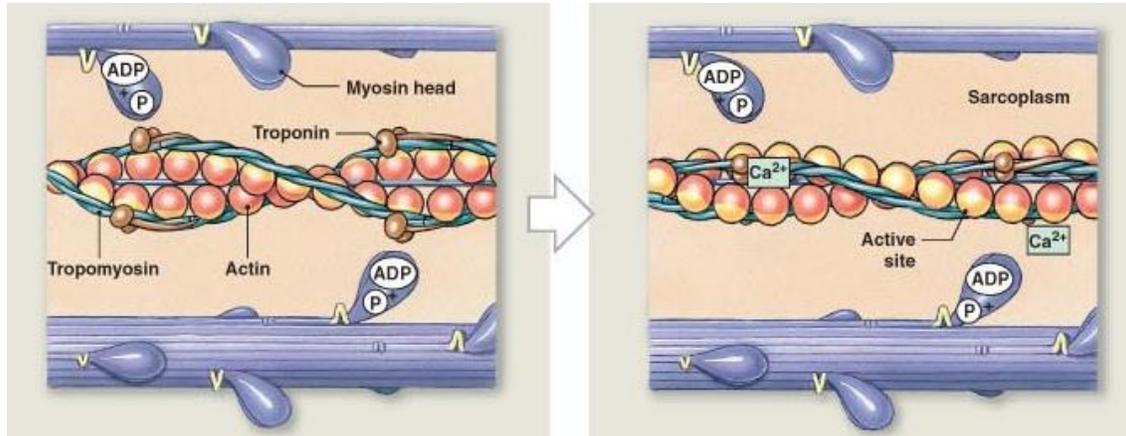
Myosin binding sites (yellow) are blocked by tropomyosin when muscle cells are resting.

Myosin binding sites (yellow) are exposed when Ca^{2+} binds to troponin.

The Sliding Filament Model

1. Myosin heads are initially in an "activated" position with ADP and P_i bound to them. When myosin heads bind to the myosin binding sites on actin, a cross-bridge is formed.

2. ADP and P_i are then released and the myosin heads pivot (pulling inward and pulling the actin filament along). This is called the power stroke and contraction occurs.

Quick Analogy: The myosin head works like a mouse trap. When the myosin heads are in an activated position, it is similar to setting a mouse trap. Energy is stored in these positions. When the myosin head contacts the actin filament, the release of ADP and P_i causes it to snap forward, like setting off the mouse trap.

3. ATP then binds to the myosin heads causing them to detach from the myosin binding sites on actin.

4. The hydrolysis of ATP (into ADP and P_i) produces energy which is used to move the myosin head back into an "activated" position.

Steps 1 to 4 are repeated as long as ATP is available and Ca^{2+} is present in the sarcoplasm.

Helpful animation: http://bcs.whfreeman.com/thelifewire/content/chp47/4702001.html

Termination of muscle contraction

Muscle contraction stops when motor neurons no longer signal for a muscle contraction. ACh is removed from the neuromuscular junction through reabsorption at the synaptic terminal and digestion by acetylcholinesterase (AChE). Without ACh at the motor end plate, there is no longer a depolarization of the sarcolemma and T-tubules, and Ca^{2+} is actively pumped back into the sarcoplasmic reticulum. Ca^{2+} releases from troponin and tropomyosin again blocks the myosin binding sites. The myosin stops binding to the actin filament and muscle contraction stops. Relaxation of the muscle occurs.

Practice questions:

1. Rigor mortis sets in a few hours after a person dies. Rigor mortis occurs when the muscles stiffen. This is due to the fact that ATP can no longer be generated by the muscle cells. How does the lack of ATP lead to rigor mortis? Hint: in which step of the sliding filament model does lack of ATP affect most?

2. The green mamba snake produces venom containing an AChE inhibitor. An AChE inhibitor prevents AChE from working. When bitten by a green mamba, what are some of the effects you might see in your skeletal muscles?

3. Dantrolene is a drug used to treat muscle spasms (involuntary contractions of skeletal muscles). It interferes with the release of Ca^{2+} from the sarcoplasmic reticulum. Explain the mechanism of how this drug works to stop muscle spasms.

Answers:

1. The lack of ATP affects step 3 of the sliding filament model. Without ATP, the myosin heads remain attached to the actin filament. The muscles will stay contracted leading to the stiffness seen in rigor mortis.

2. If AChE does not work, ACh cannot be broken down and remains attached to the receptors on the motor end plate. This will lead to continuous depolarization of the sarcolemma and Ca^{2+} remain in the sarcoplasm. This will cause extended stimulation of skeletal muscles and they will continuously contract. No relaxation occurs.

3. Without the release of Ca^{2+} from the sarcoplasmic reticulum, tropomyosin continues to block the myosin binding sites on actin. Myosin heads cannot interact with actin. This prevents muscle contractions from occurring and will help treat muscle spasms.