Now that we've looked at the anatomy of the skeletal muscle, let's examine the physiology of skeletal muscle contraction.

The first step is we have to look at is the neuromuscular junction and nerve stimulation. Skeletal muscle cells are stimulated by a motor neuron. The axon of each motor neuron branches extensively to form numerous cellular extensions called synaptic terminals. The synaptic terminals then interact with the sarcolemma of the muscle fiber at a specialized site called the neuromuscular junction.

When the electrical impulse – or action potential – reaches the synaptic terminals, calcium channels within the synaptic terminal begin to open, causing calcium to rush into the axon terminal. As a result of the influx of calcium, synaptic vesicles – containing the neurotransmitter acetylcholine – will fuse with the axon membrane, releasing the neurotransmitter into the synaptic cleft by exocytosis.

Acetylcholine then diffuses across the synaptic cleft and attaches to receptors – also known as ion channels – on a highly-folded region of the sarcolemma called the motor end plate. The binding of acetylcholine to the channels causes the channel to open an influx of sodium ions into the muscle cell, resulting in depolarization of the sarcolemma – and eventually leading to an action potential and contraction.

As the action potential spreads away from the motor endplate and across the sarcolemma, acetylcholine is swiftly broken down by acetylcholinesterase. The destruction of acetylcholine prevents continued muscle contraction in the absence of nervous stimulation – and the next few slides will demonstrate those steps in more detail – in the steps from the action potential to acetylcholine being released across the synaptic cleft.

Generating the action potential of the muscle causes a depolarization of the membrane. The electrical conditions of a resting sarcolemma – also called the resting membrane potential – is said to be polarized – that is, the extracellular environment is more positive with respect to the inside of the membrane. The predominant extracellular ion is sodium, while the predominant intracellular ion is potassium. The sarcolemma is relatively impermeable to both ions while at rest, but more so to the sodium ions.

To get the muscle to contract, the membrane potential must depolarize. In the first step, known as depolarization, the binding of acetylcholine to the sodium ion channels on the motor endplate causes the channels to open. Sodium then rushes rapidly across the sarcolemma into the cytoplasm. As sodium begins to accumulate on the inside of the muscle cell, the resting potential is decreased and localized depolarization occurs – that is, the patch of sarcolemma immediately around the sodium channel becomes more positive inside with respect to the outside.

Propagation of the action potential then occurs. The positive charge inside the initial patch of sarcolemma changes the permeability of an adjacent patch, opening sodium channels there. Consequently, the sodium begins to rush into the membrane there, causing the membrane potential in that region to decrease – and depolarization occurs in that area.
Thus, the action potential begins to travel rapidly away from the motor end plate, across the entire sarcolemma, and down into the T-tubules – and you can see the propagation of the action potential here.

Next, repolarization of the sarcolemma occurs. Immediately after the depolarization wave passes, the sarcolemma’s permeability changes once again. Acetylcholine is removed from the synaptic cleft – by acetylcholinesterase – causing the sodium ion channels to close, while the potassium channels finally open in a delayed response. The influx of sodium now stops, but potassium begins to leak out, so that the outside of the membrane switches back to positive and the inside of the membrane becomes more negative. This restores the charge across the membrane, known as repolarization. However, because more potassium ions eventually leave than is necessary, the membrane becomes hyper-polarized.

The sodium potassium pump will restore the ion concentrations in the hyperpolarized membrane to reach the polarized conditions of the resting membrane potential. For each ATP, 3 sodium ions are pumped out and 2 potassium ions are pumped in. Because the ion exchange is so close to equal, there is no change in the charge across the membrane as the ions are being redistributed.

During repolarization, muscle fibers are in a refractory period when they are insensitive to further stimulation and action potentials are considered to be an all-or-none response because once initiated, they are unstoppable. And here you can see the steps that we just went through – the action potential arriving at the neuromuscular junction, signaling the release of acetylcholine, down to the calcium signals, signaling muscle contraction. This is known as the excitation-contraction coupling.

As the action potential propagates along the sarcolemma, it moves down the T-tubules. Transmission of the action potential past the triads causes the terminal cisternae of the sarcoplasmic reticulum to release calcium into the sarcoplasm, where it now becomes available to the myofilaments of the sarcomere.

The presence of calcium on the sarcomere causes myosin to bind to actin, in a process commonly referred to as the sliding-filament mechanism.

And here is the repolarization, where the effects of ACH are terminated by acetylcholinesterase and the potassium channels are opening. The repolarization will continue along the length of the sarcolemma.

Now the sliding filament mechanism is where the attachment of myosin cross-bridges within a resting muscle, inhibited by the presence of tropomyosin, which covers the active sites on the G actin. If calcium ions are released from the terminal cisternae by the action potential, they bind to troponin, changing its shape.

The troponin then pulls on the tropomyosin, so that the binding sites on actin are exposed. Once the active site is exposed, the high-energy myosin heads attach to the actin for the cross bridge formation. The release of ADP, plus phosphate from the high-energy myosin head causes the
head to pivot and bend as it pulls on the actin filament, sliding it towards the midline. This is called the power stroke and is equivalent to the contraction of the muscle.

As a new ATP attaches to the now low-energy myosin head, the myosin head detaches from the actin. ATP is split to form adenosine diphosphate, plus phosphate and the bond energy is transferred to the myosin head, causing it to move in the high-energy position, which is generally referred to as cocked – or reactivated, so that it's ready to bind to the actin binding sites once again.

When the action potential dissipates, the calcium is reabsorbed back into the terminal cisternae. When this occurs, tropomyosin moves back over the active sites on the G actin so that the cross bridge formation can no longer occur and the muscle relaxes.

And here you can see, the contraction cycle begin, when the increase occurs in cytoplasmic calcium. The active sites exposed, where calcium interacts with troponin, causing that conformational change in tropomyosin. Cross bridge formation occurs as the myosin head attaches to actin at the active site – and this causes the myosin head to pivot, resulting in the movement of the actin filaments towards the Z disk of the sarcomere, and the cross bridge detaches. A new molecule of ATP attaches to the myosin head, causing the cross bridge to detach, and the myosin head hydrolyzes ATP to adenosine diphosphate and phosphate, which returns the myosin to the cocked position.

And here is an overview of the steps that we just covered.