

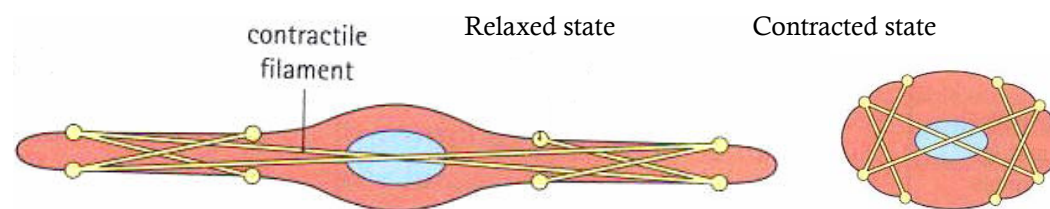
## Smooth Muscle.

### Learning Objectives.

At the end of this course, you should be able to :

1. describe the structure of smooth muscle
2. describe where smooth muscle occurs within the body
3. discuss the structural differences between smooth muscle, skeletal muscle, and cardiac muscle
4. discuss the functional differences between smooth muscle, skeletal muscle, and cardiac muscle
5. understand the control mechanisms of smooth muscle.

Smooth muscle is made of single, spindle-shaped cells. They range from 5 to 10  $\mu\text{m}$  in diameter and from 30 to 200  $\mu\text{m}$  in length. Each cell is spindle-shaped and has a single, centrally located nucleus. It gets its name because no striations are visible in them, although the cells still contain thick (myosin) and thin (actin) filaments that slide against each other to produce contraction of the cell. The thick and thin filaments are anchored near the plasma membrane.



Smooth muscle (like cardiac muscle) does not depend on motor neurons to be stimulated. However, motor neurons of the autonomic system reach smooth muscle and can stimulate or relax it, depending on the neurotransmitter they release (e.g. noradrenaline or nitric oxide).

Smooth muscle can also be made to contract by other substances released in the vicinity (paracrine stimulation), e.g. release of histamine causes contraction of the smooth muscle lining air passages (triggering an attack of asthma), or by hormones circulating in the blood, e.g. oxytocin reaching the uterus stimulates it to contract to begin childbirth.

The contraction of smooth muscle tends to be slower than that of striated muscle. It also is often sustained for long periods. This is called tonus but the mechanism is not like that in skeletal muscle.

Smooth muscle occurs within almost every organ, forming sheets, bundles, or sheaths around other tissues. Smooth muscles around blood vessels regulate blood flow through vital organs. In the digestive and urinary systems, rings of smooth muscle, called sphincters, regulate the movement of materials along internal passageways. Smooth muscles in bundles, layers, or sheets play a variety of other roles:

- Integumentary system - smooth muscles around blood vessels regulate the flow of blood to the superficial dermis; smooth muscles of the arrector pili elevate hairs.
- Cardiovascular system - smooth muscles encircling blood vessels control the distribution of blood and help regulate blood pressure.
- Respiratory system - smooth muscle contraction or relaxation alters the diameters of the respiratory passageways and changes the resistance to airflow.
- Digestive system - extensive layers of smooth muscle in the walls of the digestive tract play an essential role in moving materials along the tract. Smooth muscle in the walls of the gallbladder contract to eject bile into the digestive tract.
- Urinary system - smooth muscle tissue in the walls of small blood vessels alters the rate of filtration at the kidneys. Layers of smooth muscle in the walls of the ureter transport urine to the urinary bladder; the contraction of the smooth muscle in the wall of the urinary bladder forces urine out of the body.
- Reproductive system - layers of smooth muscle help move sperm along the reproductive tract in males and cause the ejection of glandular secretions from the accessory glands into the reproductive tract. In females, layers of smooth muscle help move oocytes (and perhaps sperm) along the reproductive tract, and contraction of the smooth muscle in the walls of the uterus expels the fetus at delivery.

## **KEY LEARNING POINTS.**



- 1. Smooth muscle cells have no visible striations, but still contain actin and myosin filaments.**
- 2. Smooth muscle cells can be controlled both autonomically and chemically, eg, by catecholamines.**
- 3. Smooth muscle contraction tends to be slower, but can be sustained for longer periods.**
- 4. Smooth muscle is found in a wide range of tissue systems throughout the body.**

## Structural Differences

Actin and myosin are present in all three muscle types. In skeletal and cardiac muscle cells, these proteins are organized in sarcomeres, with thin and thick filaments. The internal organization of a smooth muscle cell is very different:

- A smooth muscle fibre has no T tubules, and the sarcoplasmic reticulum (SR) forms a loose network throughout the sarcoplasm. Smooth muscle tissue has no myofibrils or sarcomeres. As a result, this tissue also has no striations and is called nonstriated muscle.
- Thick filaments are scattered throughout the sarcoplasm of a smooth muscle cell. The myosin proteins are organized differently than in skeletal or cardiac muscle cells, and smooth muscle cells have more cross-bridges per thick filament.
- The thin filaments in a smooth muscle cell are attached to dense bodies, structures distributed throughout the sarcoplasm in a network of intermediate filaments composed of the protein desmin. Some of the dense bodies are firmly attached to the sarcolemma. The dense bodies and intermediate filaments anchor the thin filaments such that, when sliding occurs between thin and thick filaments, the cell shortens. Dense bodies are not arranged in straight lines, so when a contraction occurs, the muscle cell twists like a corkscrew.
- Adjacent smooth muscle cells are bound together at dense bodies, transmitting the contractile forces from cell to cell throughout the tissue.
- Although smooth muscle cells are surrounded by connective tissue, the collagen fibres never unite to form tendons or aponeuroses as they do in skeletal muscles.

### KEY LEARNING POINTS.



- 1. Smooth muscle cells are not organised in sarcomeres.**
- 2. Myosin is organised differently.**
- 3. Adjacent cells are bound together, with firm attachment at the sarcolemma.**

## Functional Differences

Smooth muscle tissue differs from other muscle types in terms of

1. excitation–contraction coupling
2. length–tension relationships
3. control of contractions
4. smooth muscle tone.

***Excitation–Contraction Coupling*** - the trigger for smooth muscle contraction is the appearance of free calcium ions in the cytoplasm. Most of these calcium ions enter the cell from the extracellular fluid. Once in the sarcoplasm, the calcium ions interact with calmodulin, a calcium-binding protein. Calmodulin then activates the enzyme myosin light chain kinase, which breaks down ATP and initiates the contraction. This situation is quite different from the one in skeletal and cardiac muscles, in which the trigger for contraction is the binding of calcium ions to troponin.

***Length–Tension Relationships*** - because the thick and thin filaments are scattered and are not organized into sarcomeres, tension development and resting length in smooth muscle are not directly related. A stretched smooth muscle soon adapts to its new length and retains the ability to contract on demand. This ability to function over a wide range of lengths is called plasticity. Smooth muscle can contract over a range of lengths four times greater than that of skeletal muscle. This ability is especially important for digestive organs that undergo great changes in volume, such as the stomach. Despite the lack of sarcomere organization, smooth muscle contractions can be just as powerful as those of skeletal muscles. Like skeletal muscle fibres, smooth muscle cells often undergo sustained tetanic contractions.

***Control of Contractions*** - many smooth muscle cells are not innervated by motor neurons, and the neurons that do innervate smooth muscles are not under voluntary control. The nature of the connection with the nervous system provides a means of categorizing smooth muscle cells as either multiunit or visceral. Multiunit smooth muscle cells are innervated in motor units comparable to those

of skeletal muscles, but each smooth muscle cell may be connected to several motor neurons rather than to just one. In contrast, many visceral smooth muscle cells lack a direct contact with any motor neuron. Multiunit smooth muscle cells resemble skeletal muscle fibres and cardiac muscle cells, in that neural activity produces an action potential that is propagated over the sarcolemma. However, the contractions of these smooth muscle cells are more leisurely than are those of skeletal or cardiac muscle cells. Multiunit smooth muscle cells are located in the iris of the eye, where they regulate the diameter of the pupil; along portions of the male reproductive tract; within the walls of large arteries; and in the arrector pili muscles of the skin. Multiunit muscle cells do not typically occur in the digestive tract.

Visceral smooth muscle cells are arranged in sheets or layers. Within each layer, adjacent muscle cells are connected by gap junctions. Because they are connected in this way, whenever one muscle cell contracts, the electrical impulse that triggered the contraction can travel to adjacent smooth muscle cells. The contraction therefore spreads in a wave that soon involves every smooth muscle cell in the layer. The initial stimulus may be the activation of a motor neuron that contacts one of the muscle cells in the region. But smooth muscle cells will also contract or relax in response to chemicals, hormones, local concentrations of oxygen or carbon dioxide, or physical factors such as extreme stretching or irritation.

***Smooth Muscle Tone*** - both multiunit and visceral smooth muscle tissues show a normal background level of activity, or smooth muscle tone. The regulatory mechanisms detailed above stimulate contraction and increase muscle tone. Neural, hormonal, or chemical factors can also stimulate smooth muscle relaxation, producing a decrease in muscle tone. For example, smooth muscle cells at the entrances to capillaries regulate the amount of blood flow into each vessel. If the tissue becomes oxygen-starved, the smooth muscle cells relax. Blood flow increases, delivering additional oxygen. As conditions return to normal, the smooth muscle regains its normal muscle tone.

## **Control of smooth muscle.**

Smooth muscle has only about half the myosin found in striated muscles, and, as previously mentioned, lacks the sarcomere organization. Smooth muscle contraction speeds are very slow when compared with voluntary muscle, but it can achieve a much greater degree of shortening, and it is very economical to operate.

In contrast to the "all or none" reactions associated with nerves and striated muscles, smooth muscles often show a graded response to membrane depolarisation. Cell to cell transmission via communicating gap junctions may be very important in smooth muscles, as in the heart. The resting potential in smooth muscles is generally lower than in striated muscles, and fast voltage-gated sodium channels are not significant. Spike depolarisations associated with calcium ion entry are seen in some types of smooth muscle, but the fast action potentials associated with nerves and striated muscles are not observed. Receptors are distributed fairly evenly over the surface of smooth muscle cells, and are not organised in synapses or motor end plates seen in nerves and voluntary muscles. Many types of smooth muscle require external calcium in order to contract, and have nifedipine-sensitive calcium channels very similar to the dihydropyridine receptors observed in cardiac muscle.

Troponin is absent from smooth muscles, and their actin regulatory system (where present) differs considerably from the thin filament regulatory system found in striated muscles. Caldesmon is a smooth muscle protein that binds reversibly to the actin / tropomyosin filaments and blocks the actomyosin ATPase activity. Caldesmon can be separated from the actin, whereas troponin is a permanent feature of striated muscle thin filaments, and never dissociates from the actin.

The myosin regulatory system is much more important in smooth muscles than in striated muscle. The enzyme myosin light chain kinase is activated by calcium + calmodulin, and phosphorylates the "regulatory" light chains in the myosin head groups. This increases the inherent myosin calcium sensitivity, allowing contraction to proceed. This system also operates in striated muscle, where it

seems to play a subordinate role. Phosphorylation of myosin light chains on a second site by protein kinase C interferes with this process and leads to smooth muscle relaxation.

Isolated vascular smooth muscle contracts in response to acetyl choline, but this compound relaxes intact blood vessels as a result of nitric oxide generated by endothelial cells. Nitric oxide relaxes vascular smooth muscle via cyclic GMP. Both vascular and airway smooth muscles relax in response to beta adrenergic agonists via cyclic AMP. These effects are of considerable medical significance in the treatment of hypertension and asthma.

### **KEY LEARNING POINTS.**



- 1. The trigger for smooth muscle contraction is the appearance of free calcium ions in the cytoplasm.**
- 2. Because the thick and thin filaments are scattered and are not organised into sarcomeres, tension development and resting length in smooth muscle are not directly related.**
- 3. Neural, hormonal, or chemical factors can stimulate smooth muscle relaxation, producing a decrease in muscle tone.**
- 4. Smooth muscle contraction speeds are very slow when compared with voluntary muscle, but it can achieve a much greater degree of shortening, and it is very economical to operate.**
- 5. Troponin is absent from smooth muscles, and their actin regulatory system (where present) differs considerably from the thin filament regulatory system found in striated muscles.**
- 6. Caldesmon is a smooth muscle protein that binds reversibly to the actin / tropomyosin filaments and blocks the actomyosin ATPase activity.**