SMOOTH MUSCLE: STRUCTURE, FUNCTION, AND PHYSIOLOGICAL REGULATION

[a]Maxammadrasulov Ismoyiljon
[a]doctoral student at Fergana State University

Abstract: *Smooth muscle is an involuntary, non-striated muscle type that constitutes a critical component of numerous visceral organs and vascular structures throughout the body. Unlike skeletal and cardiac muscle, smooth muscle cells lack the sarcomeric organization characteristic of striated muscle. Instead, they employ a cytoskeletal lattice of dense bodies, intermediate filaments, and interdigitating thin and thick filaments to generate force through a corkscrew-like contractile mechanism. Two principal subtypes have been characterized: unitary (visceral) smooth muscle, which exhibits electrical coupling via gap junctions enabling rhythmic, simultaneous contraction; and multi-unit smooth muscle, which operates through discrete, individually innervated cells capable of fine motor control. Regulation is primarily mediated by the autonomic nervous system, with additional modulation by circulating hormones and local chemical factors.*

Key words: *smooth muscle, sarcomeric organization, blood vessels, and respiratory airways, thin filaments, cardiac myocytes.*

Microscopic Anatomy and Structural Organization

Smooth muscle cells are typically fusiform (spindle-shaped) cells, 20–500 μm in length, and are generally uninucleated, with a single, centrally located nucleus. This contrasts with skeletal muscle fibres, which are syncytial and multinucleated as a result of myoblast fusion during development, and with cardiac myocytes, which are also predominantly uninucleated but occasionally binucleated. The plasma membrane of smooth muscle cells - referred to as the sarcolemma - is integral to both force transmission and signal transduction.

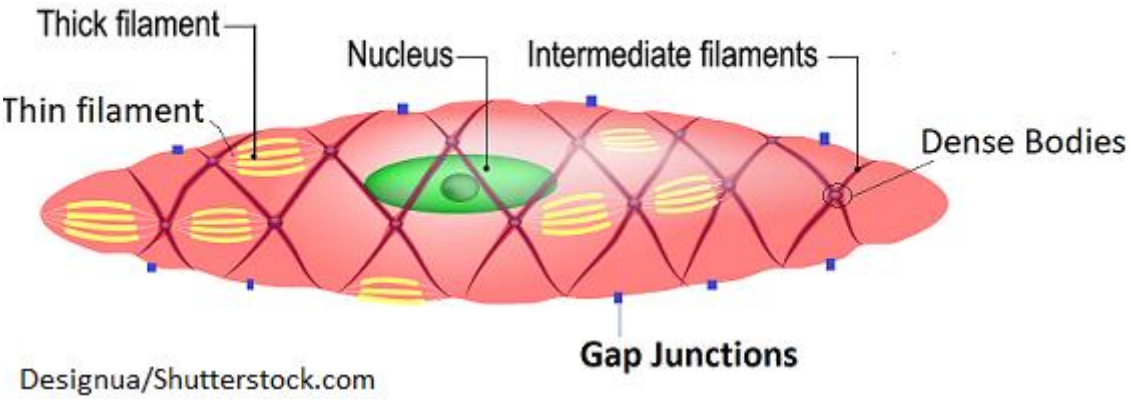


Figure 1: smooth muscle structure

Smooth muscle lacks the sarcomere - the repeating structural unit of Z-discs, thick (myosin) filaments, and thin (actin) filaments organized in a parallel array that gives skeletal and cardiac muscle its striated appearance. The absence of this organized architecture is both the basis for the 'smooth' designation and the explanation for its distinct contractile properties, including a greater range of length-tension adaptation and slower, more sustained contraction.

Dense Bodies and the Cytoskeletal Lattice: In lieu of sarcomeres, smooth muscle cells contain electron-dense structures known as dense bodies, which serve as functional analogues of the Z-discs found in striated muscle. Dense bodies are distributed throughout the cytoplasm and are also anchored to the inner leaflet of the sarcolemma via attachment plaques composed primarily of integrin proteins. The primary structural protein of dense bodies is α-actinin, which cross-links actin filaments and anchors them in position.

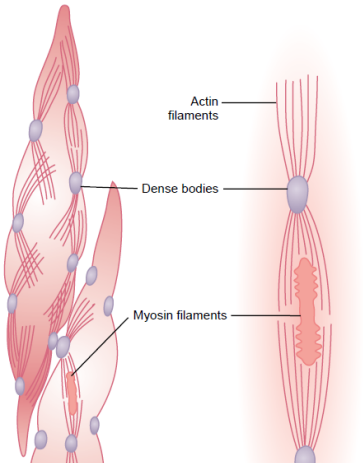


Figure 2: the structure of Dense bodies

Dense bodies are interconnected to one another by a network of intermediate filaments composed principally of two proteins: vimentin and desmin. This intermediate filament network imparts structural integrity to the cell and ensures that contractile forces generated at multiple sites within the cytoplasm are transmitted coherently to the cell membrane and, ultimately, to the extracellular matrix and surrounding tissue.

Contractile Filaments: Anchored to the dense bodies are thin filaments and thick filaments, which are the direct mediators of force generation. The thin filaments are composed principally of filamentous actin (F-actin) and tropomyosin. Notably, smooth muscle thin filaments lack troponin - the calcium-sensing regulatory complex present on skeletal and cardiac thin filaments - which has important implications for the mechanism of contraction (discussed in Section 3).

The thick filaments are composed of smooth muscle myosin II, a motor protein with ATPase activity. These thick filaments interdigitate with the surrounding thin filaments in a geometry analogous to, but less rigidly ordered than, the sarcomeric arrangement. The ratio of thin to thick filaments in smooth muscle is approximately 15:1, substantially higher than the 2:1 ratio in skeletal muscle, enabling efficient force generation across a wide range of cell lengths.

Mechanism of Contraction

The molecular basis of smooth muscle contraction involves the sliding of thin filaments relative to thick filaments, analogous in principle to the sliding filament theory of striated muscle. However, because the contractile proteins are not organized into discrete sarcomeres, the mechanical output is qualitatively different. When smooth

muscle contracts, the dense bodies - acting as force-transduction anchors - are drawn toward one another along multiple axes. This multi-directional shortening produces a characteristic corkscrew or helical deformation of the cell, which maximizes volumetric compression of the lumen it surrounds.

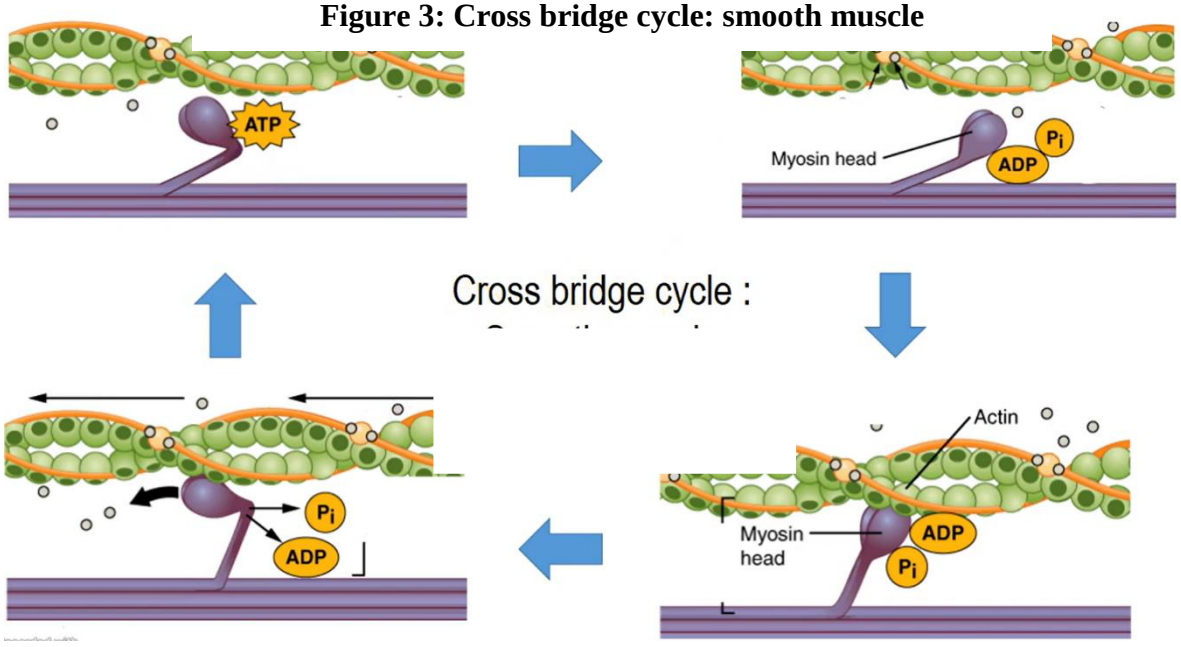
Calcium-Dependent Activation The Calmodulin–MLCK pathway

Smooth muscle contraction is initiated by an increase in intracellular free calcium concentration ($[Ca^{2+}]_i$), which can arise from calcium influx through voltage-gated or receptor-operated plasma membrane channels, or from release of calcium from the sarcoplasmic reticulum via IP_3 receptors or ryanodine receptors.

Unlike skeletal muscle, in which calcium acts via the troponin–tropomyosin complex on the thin filament, smooth muscle calcium exerts its primary effect on the thick filament regulatory pathway. Calcium (Ca^{2+}) binds to calmodulin, a ubiquitous calcium-sensing protein, forming a Ca^{2+}–calmodulin complex. This complex activates myosin light chain kinase (MLCK), which phosphorylates the regulatory light chain of myosin II (MLC_{20}) at Ser^{19}. Phosphorylation of MLC_{20} activates the myosin ATPase, enabling cross-bridge cycling between myosin and actin and, consequently, force generation and cell shortening.

Relaxation and the Latch Mechanism: Relaxation of smooth muscle occurs when $[Ca^{2+}]_i$ falls, calmodulin dissociates from MLCK, and myosin light chain phosphatase (MLCP) dephosphorylates MLC_{20}, thereby inactivating myosin ATPase activity and terminating cross-bridge cycling.

Figure 3: Cross bridge cycle: smooth muscle



Smooth muscle is also notable for exhibiting the latch state - a condition in which force is maintained at reduced energy expenditure after cross-bridges become dephosphorylated yet remain attached to actin. This property enables smooth muscle to sustain tonic contraction (e.g., in blood vessel walls) with minimal ATP consumption, a critical adaptation for tissues that must maintain prolonged states of tone.

Classification of Smooth Muscle

Smooth muscle is broadly categorized into two functional subtypes based on their cellular connectivity, innervation pattern, and physiological role: unitary (visceral) smooth muscle and multi-unit smooth muscle.

PROPERTY	UNITARY (VISCERAL)	MULTI-UNIT
Location	GI tract, urogenital tract, uterus	Iris, bronchi, large arteries, ciliary muscle, arrector pili
Gap Junctions	Present - electrically coupled	Absent - structurally independent
Innervation	Sparse; diffuse ANS varicosities	Dense; individual nerve endings per cell
Contraction type	Rhythmic, simultaneous (gross)	Graded, precise (fine control)

Unitary (Visceral) Smooth Muscle: Unitary smooth muscle, also termed single-unit or visceral smooth muscle, is the predominant smooth muscle type in the body. It is found throughout the gastrointestinal (GI) tract from the oesophagus to the rectum, the urogenital tract (including the ureters, bladder, and uterus), and portions of small blood vessels. Individual cells within this category are interconnected by gap junctions - intercellular channels formed by connexin proteins - which permit the direct transfer of ions and small molecules between adjacent cells, rendering the entire cell population electrically coupled.

This electrical coupling enables a single depolarization event, triggered either by a pacemaker cell or by neurotransmitter release from an autonomic varicosity, to propagate as a wave of excitation across many cells simultaneously. The result is a coordinated, rhythmic contraction of the muscle mass - behaviour that is essential for peristalsis in the gut and for the propulsive contractions of the ureter. This type of contraction is classified as gross, powerful movement, suitable for propelling luminal contents through tubular organs.

Additionally, unitary smooth muscle exhibits intrinsic pacemaker activity (automaticity) the capacity to generate spontaneous action potentials in the absence of extrinsic neural input - a property shared with cardiac muscle and arising from slow wave depolarizations driven by specialized interstitial cells of Cajal in the GI tract.

Multi-Unit Smooth Muscle: Multi-unit smooth muscle is characterized by the structural and functional independence of individual cells. Gap junctions are absent or sparse between cells, and each smooth muscle cell receives its own discrete autonomic nerve ending. This architecture permits graded, precise control of contraction - activating any number of individual cells independently - and is therefore suited to fine motor functions.

Multi-unit smooth muscle is found in the iris of the eye (sphincter and dilator pupillae muscles, which control pupil diameter), the ciliary muscle (which governs lens

accommodation for near vision), bronchial smooth muscle (which regulates airway diameter and thus resistance to airflow), the tunica media of large elastic and muscular arteries, and the arrector pili muscles of the skin (responsible for piloerection, or 'goosebumps'). The high density of individual nerve endings in multi-unit smooth muscle confers precise, graded responses that would be incompatible with electrical coupling.

REFERENCES

1. Hall, J.E. & Hall, M.E. Guyton and Hall Textbook of Medical Physiology (14th ed.). 2021
2. Bhimji, S.S. & Bhimji, S. Smooth Muscle. In: StatPearls. StatPearls Publishing. 2023
3. Boron, W.F. & Boulpaep, E.L. Medical Physiology (3rd ed.). Elsevier. 2017.
4. Alberts, B., et al. Molecular Biology of the Cell (7th ed.). W.W. Norton. 2022.
5. Katzung, B.G., Masters, S.B., & Trevor, A.J. Basic and Clinical Pharmacology (14th ed.). McGraw-Hill. 2018.
6. Sherwood, L. Human Physiology: From Cells to Systems (10th ed.). Cengage. 2019.
7. Somlyo, A.P. & Somlyo, A.V. Ca^{2+} sensitivity of smooth muscle and nonmuscle myosin II: modulated by G proteins, kinases, and myosin phosphatase. Physiological Reviews, 83(4), 2003.
8. Kamm, K.E. & Stull, J.T. Dedicated myosin light chain kinases with diverse cellular functions. Journal of Biological Chemistry. 2001.
9. Sanders, K.M., Koh, S.D., & Ward, S.M. Interstitial cells of Cajal as pacemakers in the gastrointestinal tract. 2006.
10. Burnstock, G. Non-synaptic transmission at autonomic neuroeffector junctions. Neurochemistry International, 2008.
11. Dillon, P.F., Aksoy, M.O., Driska, S.P., & Murphy, R.A. Myosin phosphorylation and the cross-bridge cycle in arterial smooth muscle. 1981.