Smooth muscle

Six types of smooth muscle with different functions:
Vascular
Gastrointestinal
Urinary
Respiratory
Reproductive
Ocular

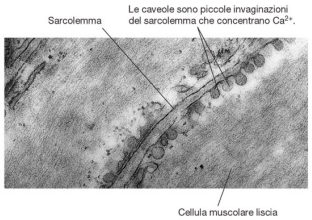
- Absence of sarcomeres: contractile fibers arranged in interwoven bundles
- Layers of smooth muscle arranged in various directions
- Contraction and relaxation controlled by paracrine signals and hormones, as well as by neurotransmitters: integration of multiple signals
- Variable electrophysiological properties: they can hyperpolarize or depolarize, even without generating action potentials

Contraction can occur: following an action potential, an electrotonic potential, or in the absence of electrical changes in the membrane

Smooth muscle

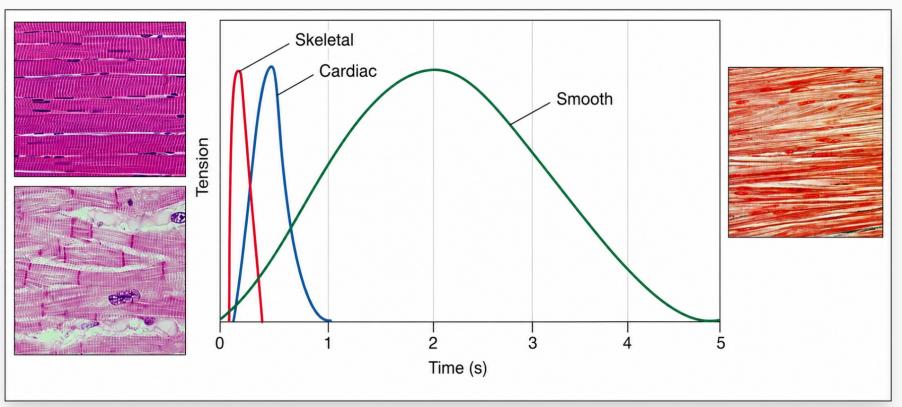
Elements in common with skeletal muscle

- Presence of cross-bridges between actin and myosin
- Presence of a sarcoplasmic reticulum with channels for Ca2+ release
- The Ca2+ signal activates the contraction process

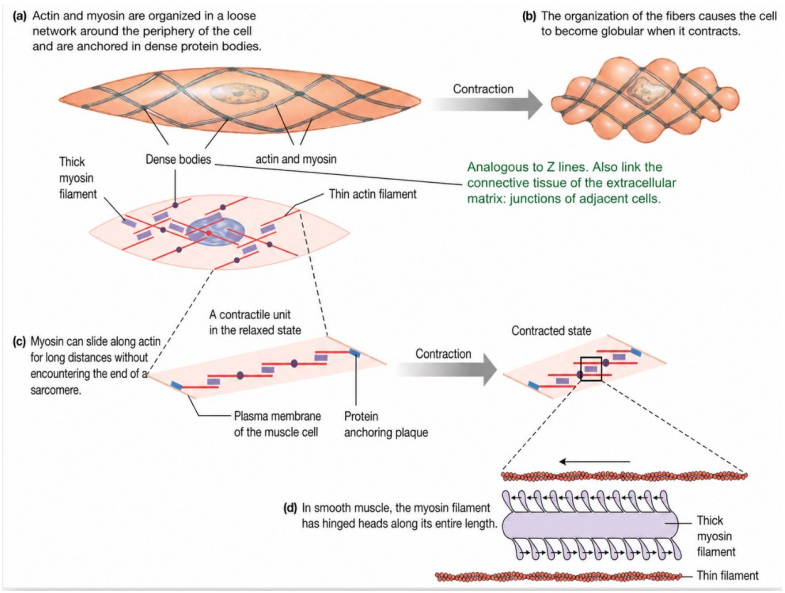


Differences compared to skeletal muscle

- Absence of sarcomeres
- Actin and myosin are longer and constituted by different isoforms
- Slower ATPase activity
- One of the light chains of the myosin head plays a regulatory role in the contraction–relaxation phases
- Actin–myosin ratio: **10–15 A : 1 M** versus **6 A : 1 M** in skeletal muscle
- Troponin is absent, but other regulatory proteins are involved such as caldesmon and calponin
- Less abundant sarcoplasmic reticulum (no T-tubules)
- The main channel for Ca2+ release from the endoplasmic reticulum is associated with IP3 (a second messenger generated by the phospholipase C pathway)
- Concentration of Ca2+ in caveolae (associated with reticulum tubules)



Muscle twitch is slower than that of skeletal and cardiac muscle during both the **contraction** and **relaxation** phases
Contraction requires less energy (and can be sustained for longer periods)



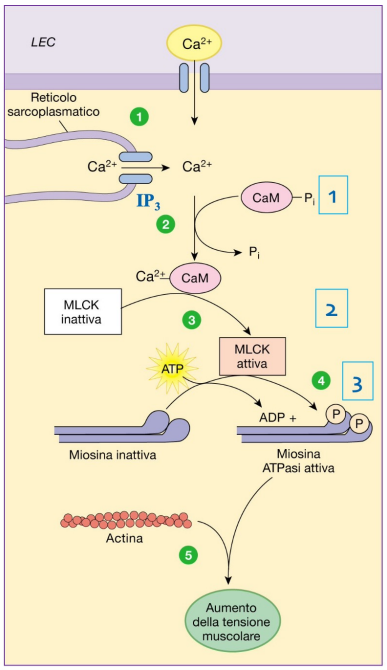
Actin and myosin are arranged **irregularly** (not in an ordered pattern).

The filaments form an **oblique network** within the cell. For this reason, the muscle is called "***smooth***" (without striations).

Myosin slides along actin without rigid limits.

It can contract extensively → resulting in greater shortening. The cell becomes globular.

Contraction



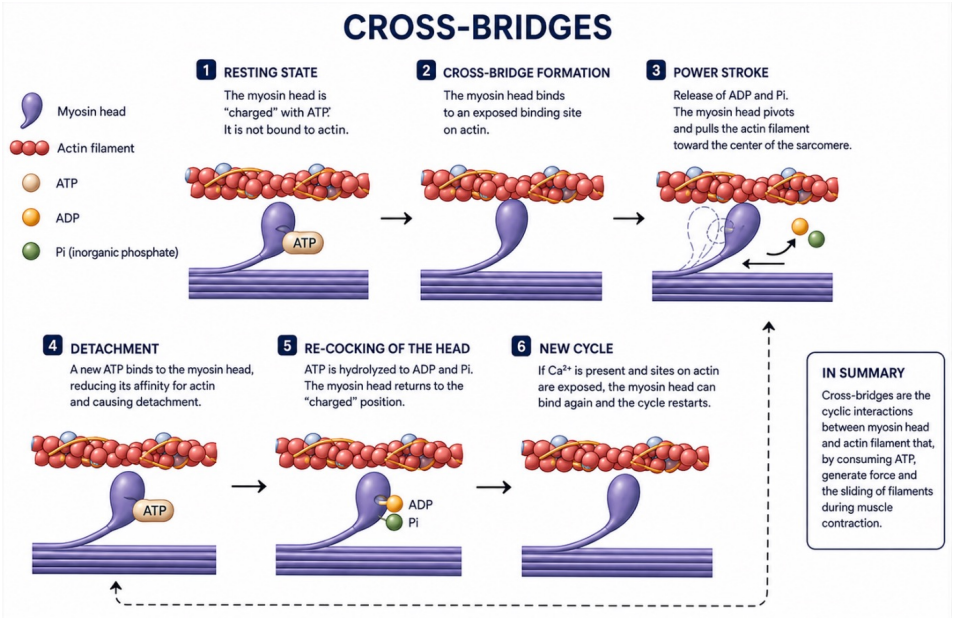
A nervous, hormonal, or mechanical stimulus causes an increase in intracellular Ca^{2+}, which may come either from outside the cell or from the sarcoplasmic reticulum (also through IP_3-mediated release).
Ca^{2+} binds to calmodulin, forming a complex that activates MLCK (Myosin Light Chain Kinase).
MLCK uses ATP to phosphorylate myosin, enabling it to bind to actin and initiate the cross-bridge cycle, resulting in tension development and contraction.
When the Ca^{2+} concentration decreases, MLCP (Myosin Light Chain Phosphatase) is activated and dephosphorylates myosin, leading to muscle relaxation.
Thus, in smooth muscle, contraction is regulated by myosin phosphorylation (unlike skeletal muscle, where regulation occurs at the level of actin).

Cross-bridges:

When myosin heads attach to actin, they form “bridges” between two different filaments.

These bridges are arranged transversely relative to the direction of the filaments, hence the name “cross-bridges.

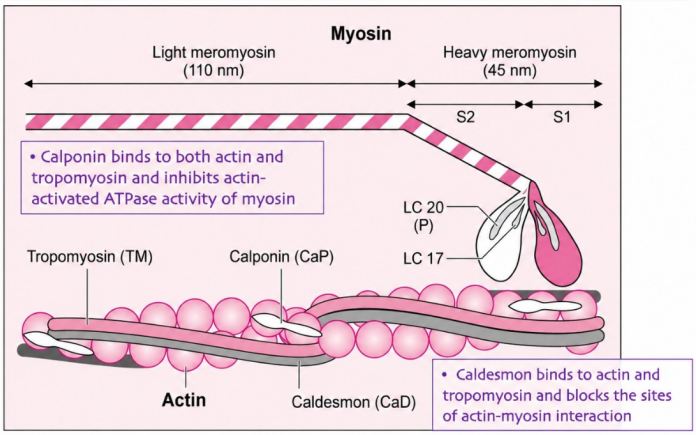
In smooth muscle, contraction is regulated by the phosphorylation of myosin (unlike skeletal muscle, where it is regulated by actin).


CROSS-BRIDGES
Myosin head
Actin filament
ATP
ADP
Pi (inorganic phosphate)
1 RESTING STATE
The myosin head is "charged" with ATP. It is not bound to actin.
2 CROSS-BRIDGE FORMATION
The myosin head binds to an exposed binding site on actin.
3 POWER STROKE
Release of ADP and Pi. The myosin head pivots and pulls the actin filament toward the center of the sarcomere.
ATP
4 DETACHMENT
A new ATP binds to the myosin head, reducing its affinity for actin and causing detachment.
5 RE-COCKING OF THE HEAD
ATP is hydrolyzed to ADP and Pi. The myosin head returns to the "charged" position.
6 NEW CYCLE
If Ca2+ is present and sites on actin are exposed, the myosin head can bind again and the cycle restarts.
ATP
ADP
Pi
IN SUMMARY
Cross-bridges are the cyclic interactions between myosin head and actin filament that, by consuming ATP, generate force and the sliding of filaments during muscle contraction.

Caldesmon
•Protein associated with actin filaments
•Inhibits actin–myosin interaction at rest
•The Ca^{2+}–calmodulin complex modify the caldesmon removing this inhibition → contraction can occur

Calpain
•Ca^{2+}-dependent protease
•Modifies/degrades regulatory proteins (including caldesmon)
•Facilitates smooth muscle contraction and structural remodeling

Caldesmon and Calponin: regulatory proteins associated with actin that have an inhibitory effect on actin-myosin interaction



Overview of smooth muscle cell excitability

Membrane potential of approximately −56/−60 mV.

Ion channels can open and close spontaneously.

Action potentials are generated by Ca^{2+} rather than by Na^{+}, as in skeletal muscle.

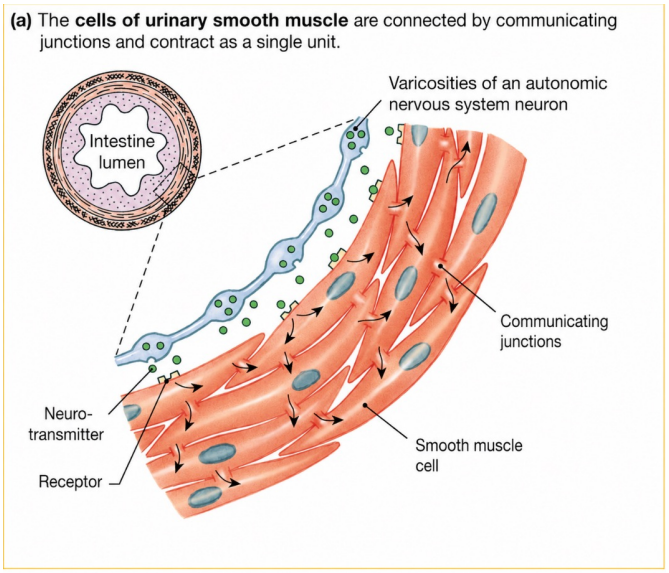
Repolarization is due to K^{+} efflux through voltage-dependent channels (as in skeletal muscle).

Contraction can also occur without an action potential, through electrotonic currents that do not reach the threshold.

Membrane potential of about −56/−60 mV
This characteristic makes them more “excitable” and capable of automatic activity (e.g., in the intestine).
Contraction can also occur without an action potential, through electrotonic currents that do not reach threshold.
This happens because even a small depolarization
→ can open some Ca^{2+} channels
→ a small amount of Ca^{2+} enters the cell
→ calmodulin and MLCK are activated
→ contraction occurs.

Types of smooth muscle

Unitary



All cells work together as a single unit.

Characteristics
Cells are connected by communicating junctions (gap junctions)
The signal passes from one cell to another
They all contract together

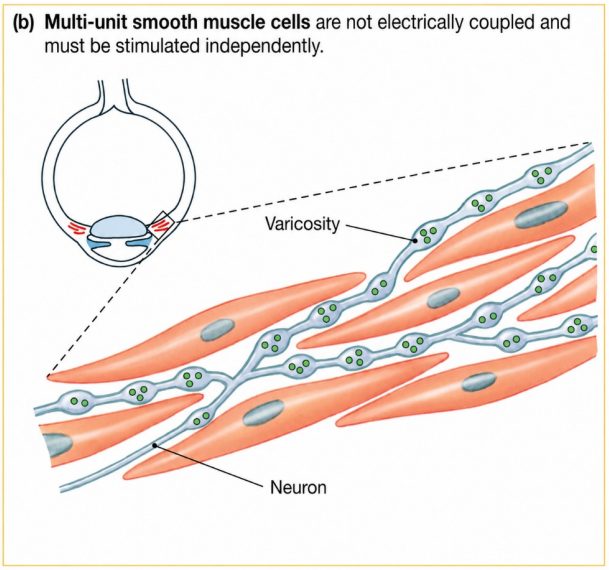
How it works
One cell becomes activated →
the signal spreads →
the entire muscle contracts

Where it is found
Intestine
Uterus
Many blood vessels

Force
Depends on how much Ca^{2+} enters.

Types of smooth muscle

Multi-Unitary



Each cell works independently.

Characteristics
Cells are NOT electrically connected
Each cell receives its own nervous stimulus
Independent contraction

How it works
The nerve stimulates individual cells → you can activate few or many of them

Where it is found
Eye (iris)
Piloerector muscles (skin)

Force
It can be increased by recruiting more cells.