Muscle Contraction
The sliding filament theory

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Muscles are comprised of multiple fibres. These fibres are similarly composed of multiple sarcomeres. Sarcomeres are the functional units of muscle. Each sarcomere contains many parallel, overlapping thin (actin) and thick (myosin) filaments. The muscle contracts when these filaments slide past each other, resulting in a shortening of the sarcomere and thus the muscle. This is known as the **sliding filament theory**. Cross-bridge cycling forms the molecular basis for this sliding movement.

Introduction

There are three major muscle types found in the human body: skeletal, cardiac, and smooth muscle.

Function of muscle tissue

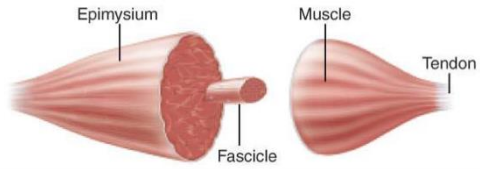
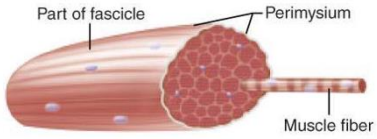
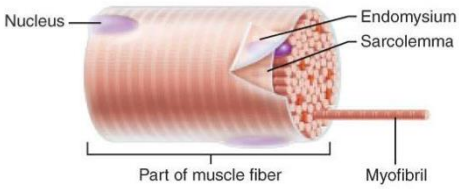
1. *Locomotion*
2. *Vasoconstriction and vasodilatation* - of blood vessel walls are the results of smooth muscle contraction.
3. *Peristalsis* - wavelike motion along the digestive tract is produced by the smooth muscle.
4. *Cardiac motion*
5. *Posture maintenance* - skeletal muscle maintains body posture and muscle tone.
6. *Heat generation* - about 75% of ATP energy used in muscle contraction is released as heat.

In order to achieve all the above functions, the three muscle tissue types have to repeat the processes of contraction (shortening) and relaxation (lengthening).

Burt first let’s zoom in and take a look at the anatomy of muscle.

Microanatomy of muscle cells

TABLE 1. MACROANATOMY OF SKELETAL MUSCLE

STRUCTURE AND ORGANIZATIONAL LEVEL	DESCRIPTION	CONNECTIVE TISSUE WRAPPINGS
Muscle *(organ)* 	A muscle consists of hundreds to thousands of muscle cells, plus connective tissue wrappings, blood vessels, and nerve fibers.	Covered externally by the epimysium
Fascicle (a portion of the muscle) 	A fascicle is a discrete bundle of muscle cells, segregated from the rest of the muscle by a connective tissue sheath.	Surrounded by a perimysium
Muscle Fiber (cell) 	A muscle fiber is an elongated multinucleate cell; it has a banded (striated) appearance.	Surrounded by endomysium

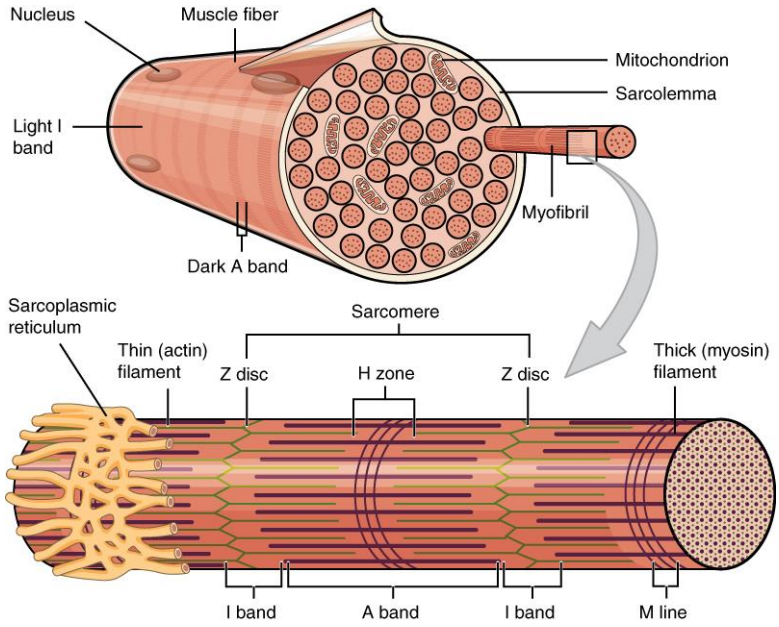


FIG 1. MICROANATOMY OF THE MYOFIBRILS

Myocytes have specialised cellular features in addition to the usual complement of Golgi apparatus, mitochondria and ribosomes:

1. **The Sarcoplasmic reticulum** (SR): A modified endoplasmic reticulum that acts as an intracellular store of calcium (Ca^{2+}), which can rapidly release and sequester Ca^{2+}.

2. **The transverse (T)-tubules:** Invaginations of the muscle surface membrane, or sarcolemma, capable of relaying action potentials deep into the myocyte.

3. **Myofibrils:** The contractile apparatus of the cell. These are fibrils arranged in parallel with one another spanning the entire length of the myocyte.

What is a sarcomere?

A sarcomere (Fig 2.) is the functional unit of skeletal muscle. The overlapping actin and myosin filaments form the scaffolding for the cross-bridging mechanism of muscle shortening.
Striation pattern of muscle

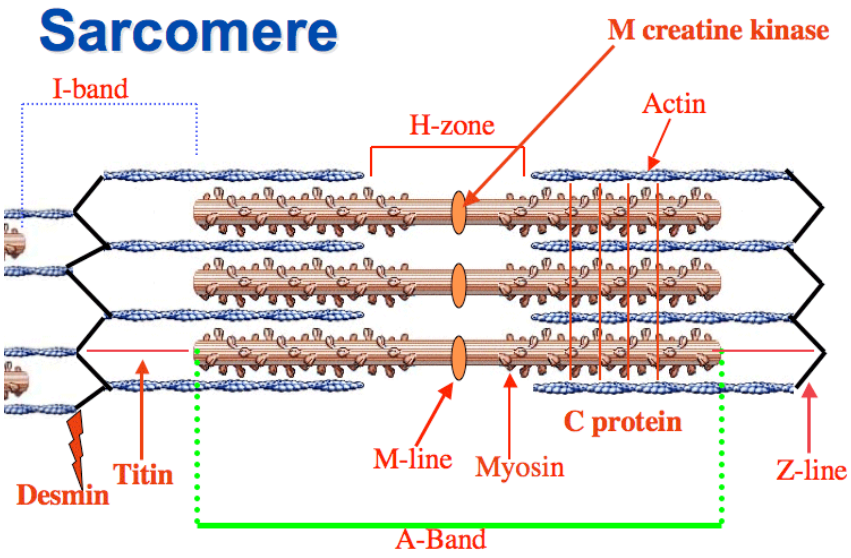


FIG 2. SARCOMERE STRUCTURE WHICH CONSISTS OF OVERLAPPING ACTIN AND MYOSIN FILAMENTS

Multiple sarcomeres are arranged in parallel within a myofibril which creates the muscle's striated appearance, as well as the dark and lighter 'bands'. Exactly which structural components make up these colour bands, are crucial in understanding how the sarcomere performs the important task of contraction. **(Fig 1)**

Table 2 Major histological differences between the 3 muscle types

Skeletal	Cardiac	Smooth
Striated	Striated	Non-striated
Actin & mysosin form sarcomeres	Actin & mysosin form sarcomeres	Actin & mysosin not organised into sarcomeres
Sacrolemma lacks junctional complexes between fibres	Junctional complexes between fibres including gap junctions	Gap junctions
Each fiber innervated	Electrical syncytium	Electrical syncytium
Troponin to bind calcium	Troponin to bind calcium	Calmodulin to bind calcium
High ATPase activity (fast muscle)	Intermediate ATPase activity	Low ATPase activity (slow muscle)
Extensive sarcoplasmic reticulum	Intermediate sarcoplasmic reticulum	Limited sarcoplasmic reticulum
T Tubules	T Tubules	Lack T Tubules, SR controlled by second messengers
Surface membrane lacks calcium channels	Voltage-gated calcium channels	Voltage-gated calcium channels

I band: (Light bands). Comprised of the thin Actin filaments. Outer edge of the adjacent sarcomeres.
Z line: Marks the junction of actin filaments in adjacent sarcomeres. Also anchors the actin filaments.
A band: (Dark bands). Thick myosin filaments, which overlap thin actin filaments.
H band: Central region zone. Consists of thick filaments.
M band: (Dark band). In the centre of the A band.

What are Myosin, Actin, Troponin and Tropomyosin?

1. Myosin - the "thick" filaments

Each thick filament contains myosin, a large protein that has two globular 'heads 'and a long 'tail'. The myosin heads have distinct binding sites for actin and ATP **(Fig 3).**

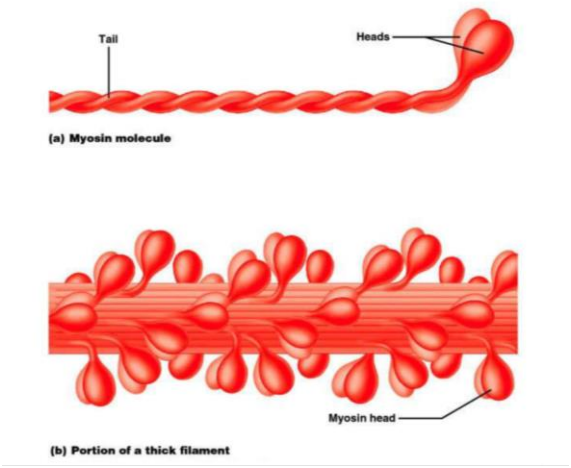


FIG 2. ULTRASTRUCTURE OF THICK MYOSIN FILAMENTS

2. Actin, tropomyosin and troponin - "thin" filament components

Each thick filament is surrounded by six thin filaments, in an approximately hexagonal arrangement. Each thin filament is composed of three proteins: the contractile protein actin, and the regulatory proteins tropomyosin and troponin.

Tropomyosin is a fibrous protein chain that lies in the groove between the two strands of actin. *Tropomyosin* covers the myosin binding site, preventing cross-bridges forming between actin and myosin.

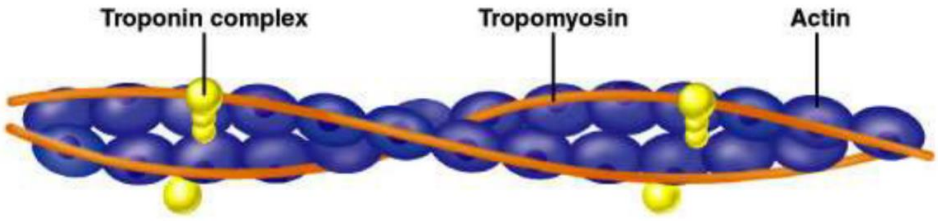


FIG 3. STRUCTURE OF THIN FILAMENTS

- **Troponin** is the protein complex located at regularly spaced intervals along the tropomyosin protein chain. The troponin complex is made up of three subunits.
- **Troponin T** binds the troponin complex to tropomyosin (hence 'T').
- **Troponin I** has an uncertain role.

- **Troponin C** contains the Ca2+ binding site (hence ‘C ’for Ca2+). Binding of Ca2+ to troponin C causes tropomyosin to roll deeper into the actin groove, which uncovers the myosin binding site, allowing cross-bridges to form between actin and myosin

Muscle contraction / myofibril shortening

Four Key steps:

1. Depolarisation and Calcium Ion Release

- An action potential from a motor neuron triggers the release of acetylcholine into the motor end plate
- Acetylcholine initiates depolarisation within the sarcolemma, which is spread through the muscle fibre via T tubules
- Depolarisation causes the sarcoplasmic reticulum to release stores of calcium ions (Ca2+)
- Calcium ions play a pivotal role in initiating muscular contractions

2. Actin and Myosin Cross-Bridge Formation

- On actin, the binding sites for the myosin heads are covered by a blocking complex (troponin and tropomyosin)
- Calcium ions bind to troponin and reconfigure the complex, exposing the binding sites for the myosin heads
- The myosin heads then form a cross-bridge with the actin filaments

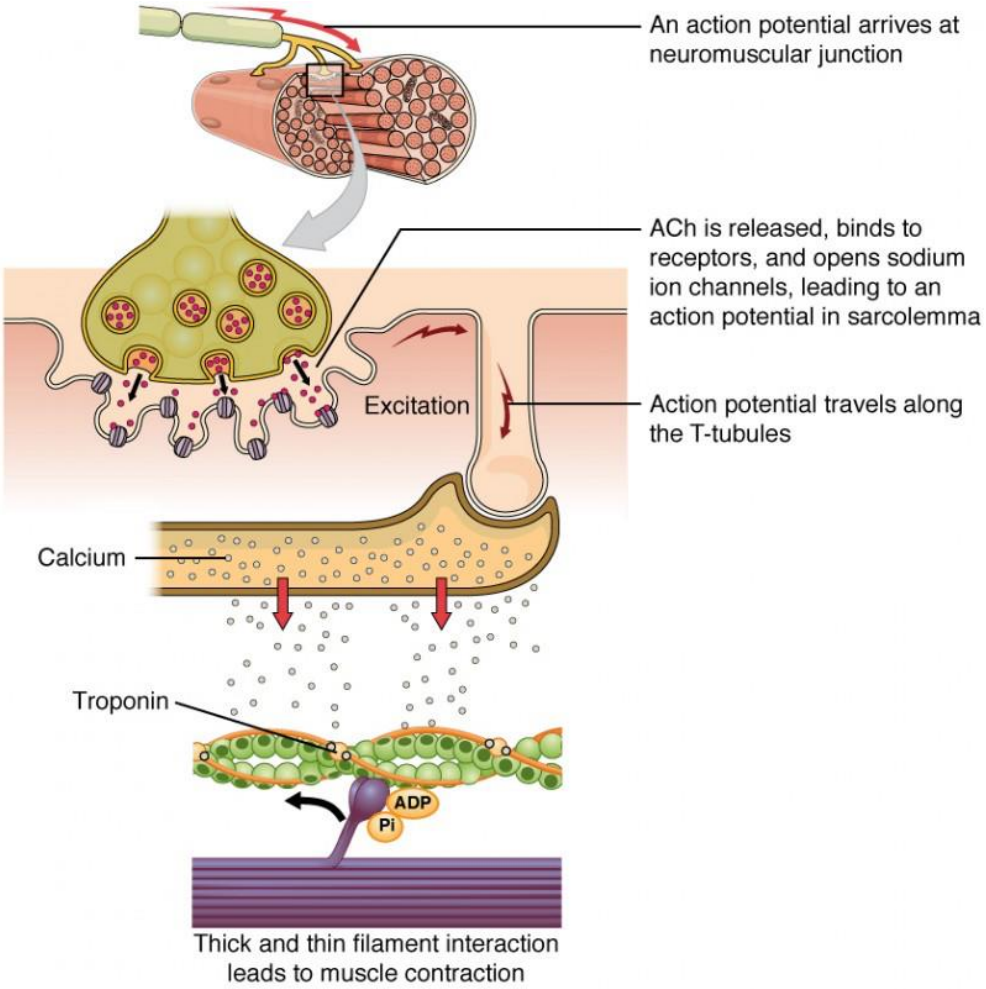
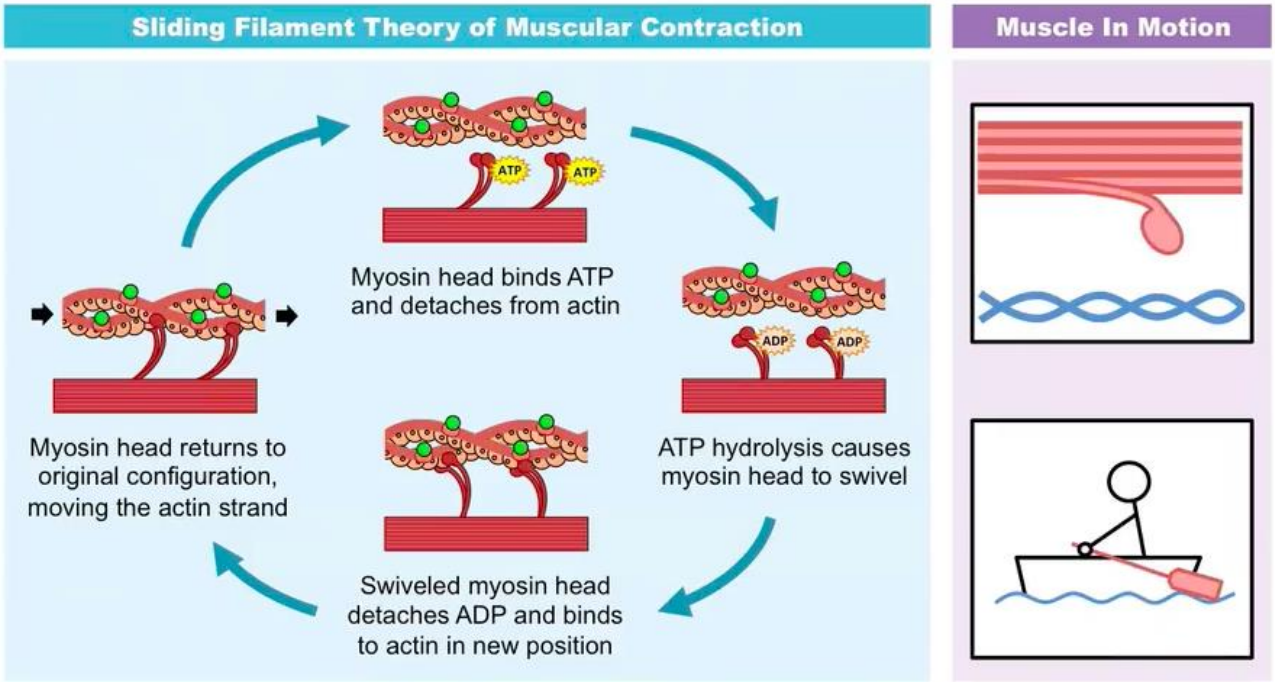


Fig 4. Muscle Contraction

3. Sliding Mechanism of Actin and Myosin

- ATP binds to the myosin head, breaking the cross-bridge between actin and myosin
- ATP hydrolysis causes the myosin heads to change position and swivel, moving them towards the next actin binding site
- The myosin heads bind to the new actin sites and return to their original conformation
- This reorientation drags the actin along the myosin in a sliding mechanism
- The myosin heads move the actin filaments in a similar fashion to the way in which an oar propels a rowboat.

Sliding Filaments Mechanism



4. Sarcomere Shortening

- The repeated reorientation of the myosin heads drags the actin filaments along the length of the myosin
- As actin filaments are anchored to Z lines, the dragging of actin pulls the Z lines closer together, shortening the sarcomere
- As the individual sarcomeres become shorter in length, the muscle fibre as a whole contracts
- Resulting in the Z discs moving closer to one-another.

What is meant by excitation-contraction coupling?

Excitation-contraction coupling refers to the processes linking depolarization of the muscle cell membrane to the initiation of myocyte contraction.

Summary of Muscle Contraction

- Action potential in a motor neuron triggers the release of Ca2+ ions from the sarcoplasmic reticulum
- Calcium ions bind to troponin (on actin) and cause tropomyosin to move, exposing binding sites for the myosin heads
- The actin filaments and myosin heads form a cross-bridge that is broken by ATP
- ATP hydrolysis causes the myosin heads to swivel and change orientation
- Swivelled myosin heads bind to the actin filament before returning to their original conformation (releasing ADP + Pi)
- The repositioning of the myosin heads move the actin filaments towards the centre of the sarcomere
- The sliding of actin along myosin therefore shortens the sarcomere, causing muscle contraction

References

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