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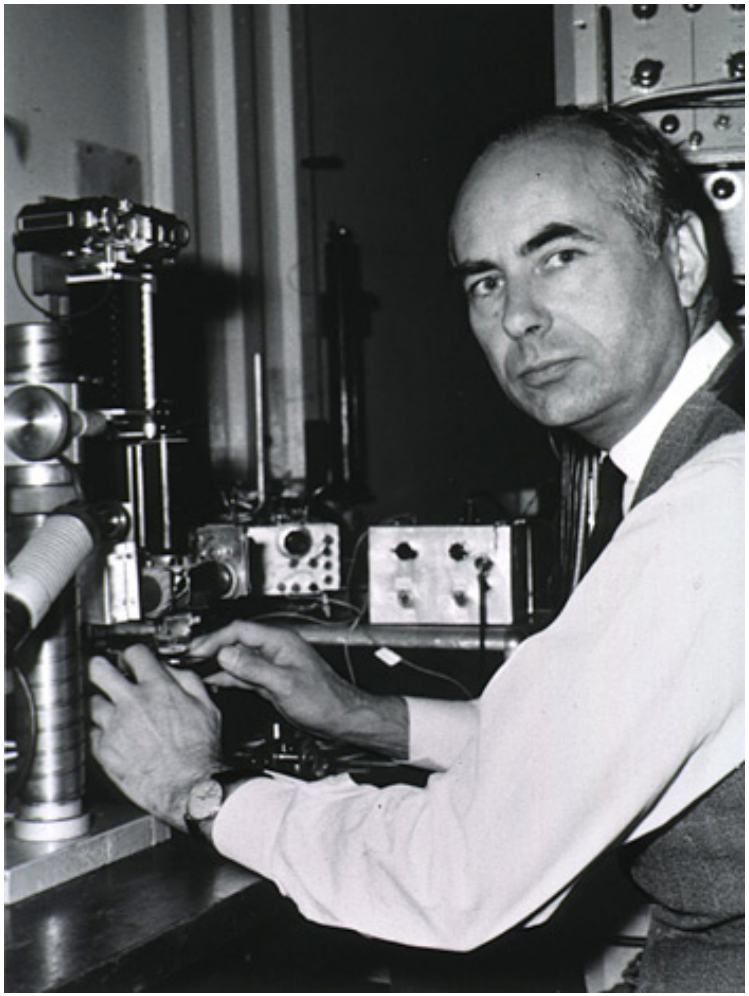
BIOL21332 Motor Systems

Sliding filaments theory

Huxley AF (1917-2012)



http://www.nobelprize.org/nobel_prizes/medicine/laureates/1963/huxley-photo.html

Brave New World

- The Doors of Perception

Sliding Filament Mechanism of Contraction

- Myosin (thick) and actin (thin) filaments = contractile proteins

- Contractile force is produced by cross bridges between thick and thin filaments

Sliding Filament Mechanism of Contraction

5 steps

Step 1: Rest.

Step 2: Activation.

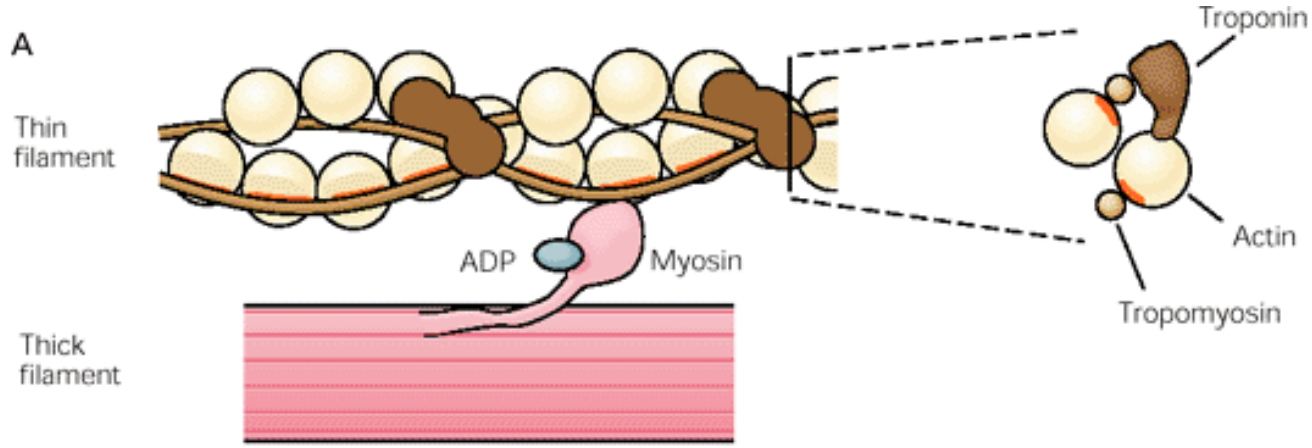
Step 3: Sliding of filaments.

Step 4: Myosin detachment.

Step 5: Reactivation of myosin.

Step 1: Rest.

Troponin-tropomyosin complexes on thin filaments block the binding sites on the actin.



Myosin heads are ADP-bound → "cocked" position

[Ca^{2+}] in sarcoplasm: low (~10^{-7} - 10^{-8} M).

There are no cross-bridges between thin and thick filaments

Sliding Filament Mechanism of Contraction

5 steps

Step 1: Rest.

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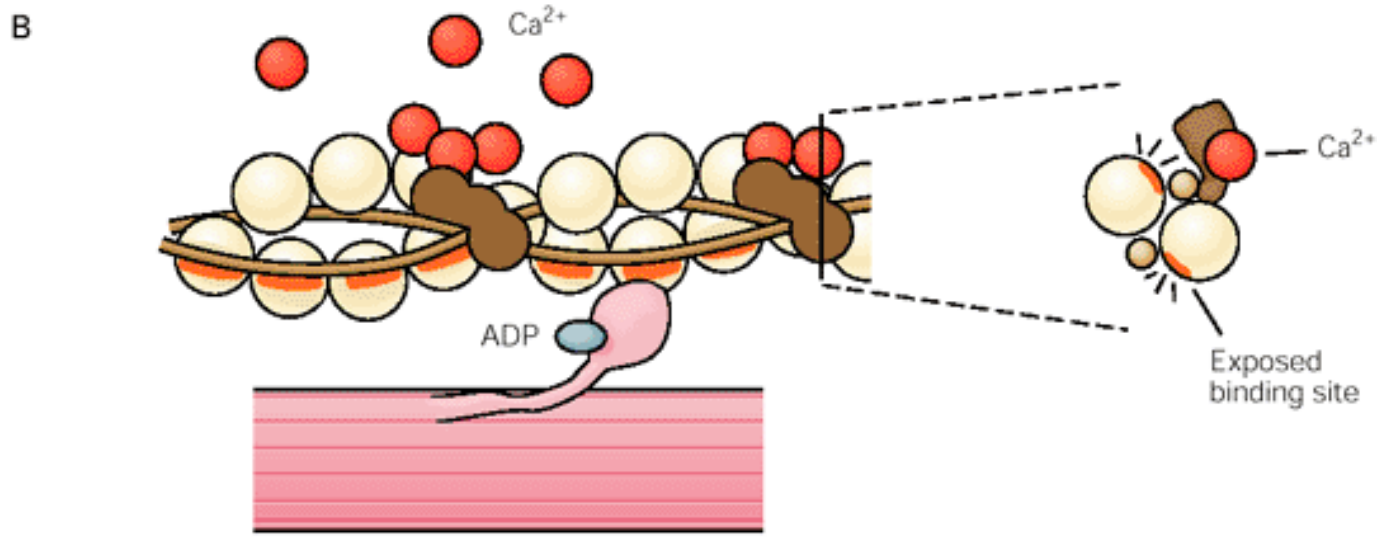
Step 3: Sliding of filaments.

Step 4: Myosin detachment.

Step 5: Reactivation of myosin.

Step 2: Activation.

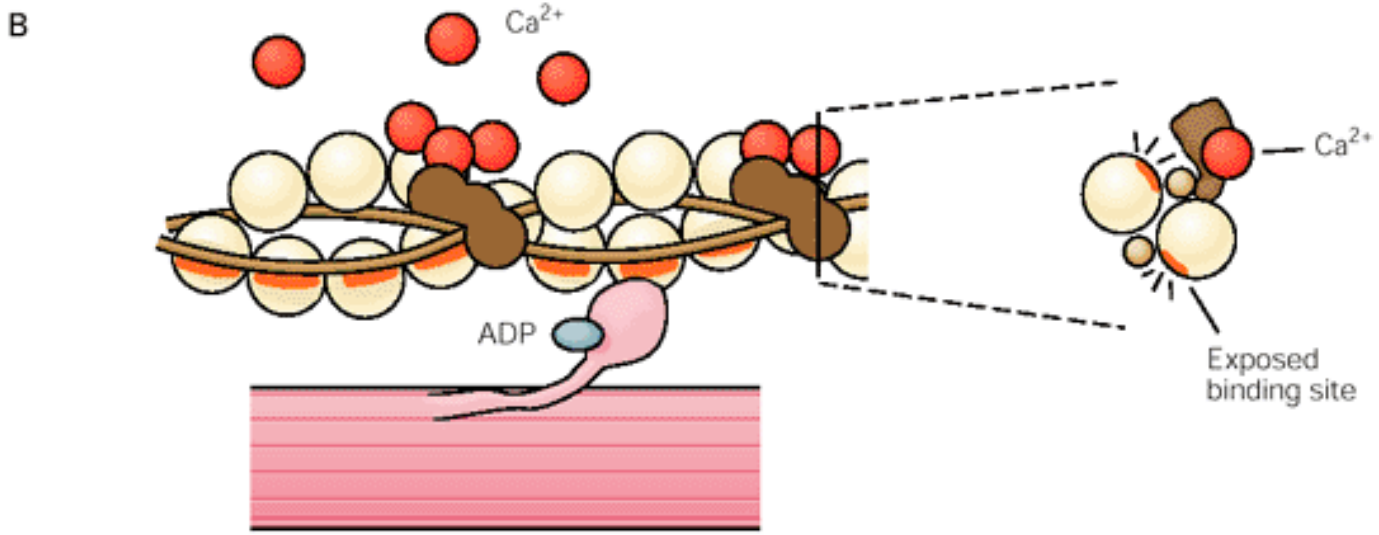
Muscle fibre is activated (action potential travels down T-tubules).



Ca^{2+} is released from the cisternae of the sarcoplasmic reticulum (SPR)

Step 2: Activation.

Ca^{2+} binds to troponin.



Conformational change in thin filament exposes actin binding sites.

Attachment of cocked myosin heads = cross-bridge formation.

Sliding Filament Mechanism of Contraction

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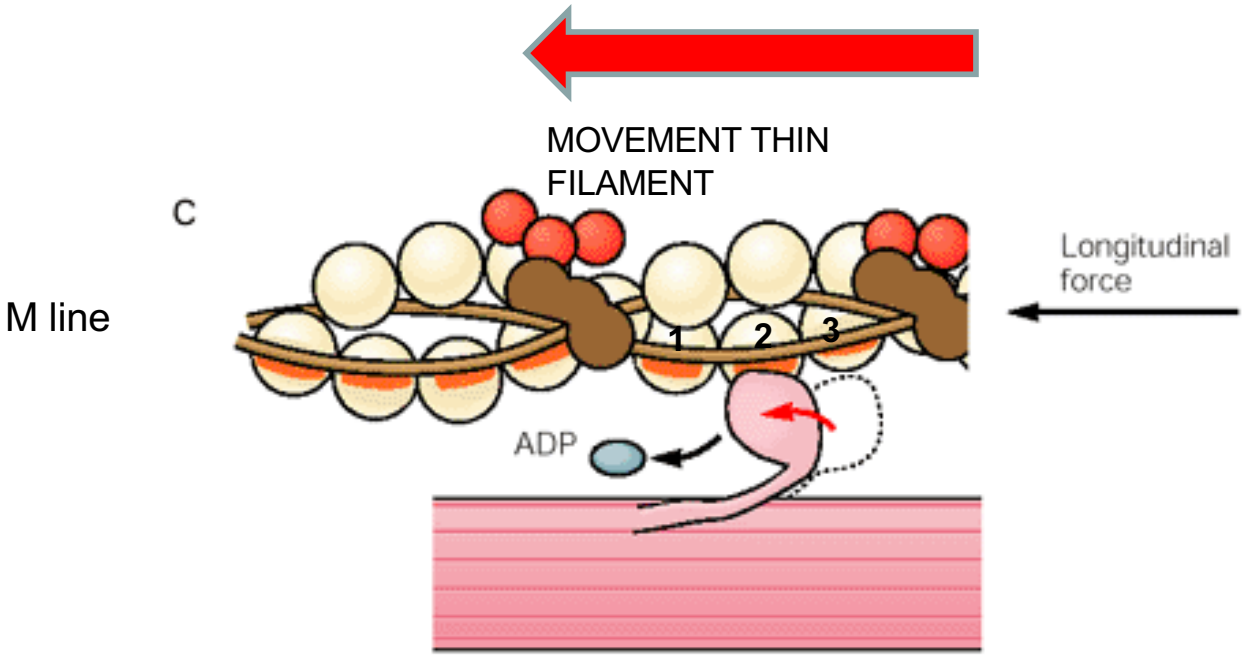
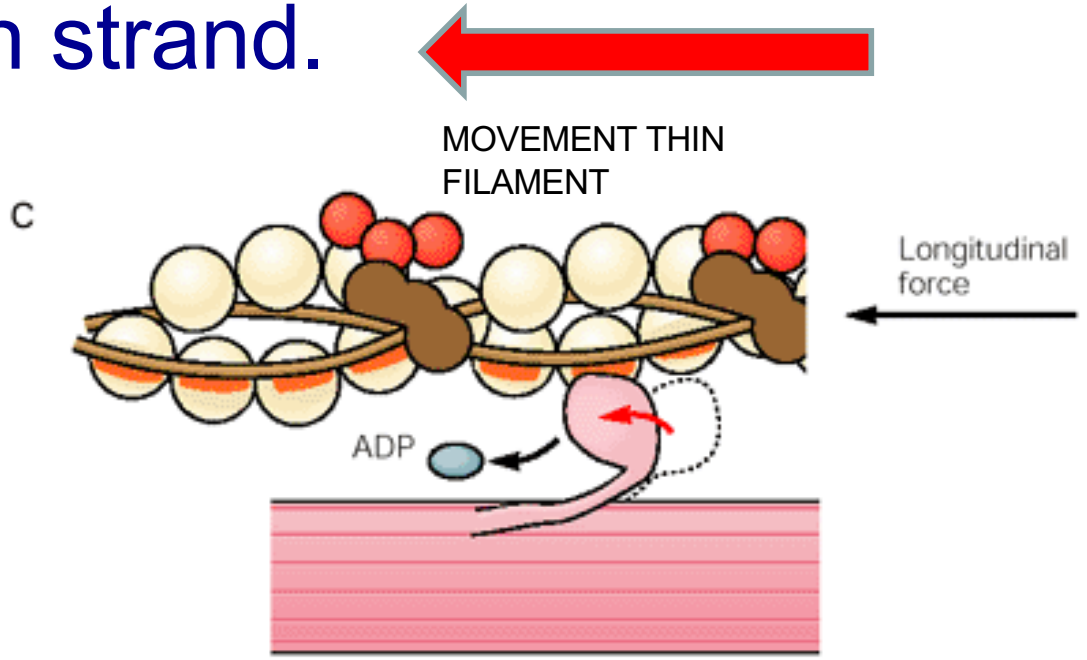


Upon formation of cross-bridges, mechanical energy (from ATP dephosphorylation) stored in “cocked” myosin heads is released → POWER STROKE.

Step 3: Sliding of filaments.

- Myosin heads have shed bound ADP: resume relaxed / native state while remaining cross-linked to thin strand.



- Longitudinal force pulls the thin and thick filaments into greater overlap **(~0.06 µm)** → shortens the muscle fibre.

Sliding Filament Mechanism of Contraction

5 steps

Step 1: Rest.

Step 2: Activation.

Step 3: Sliding of filaments.

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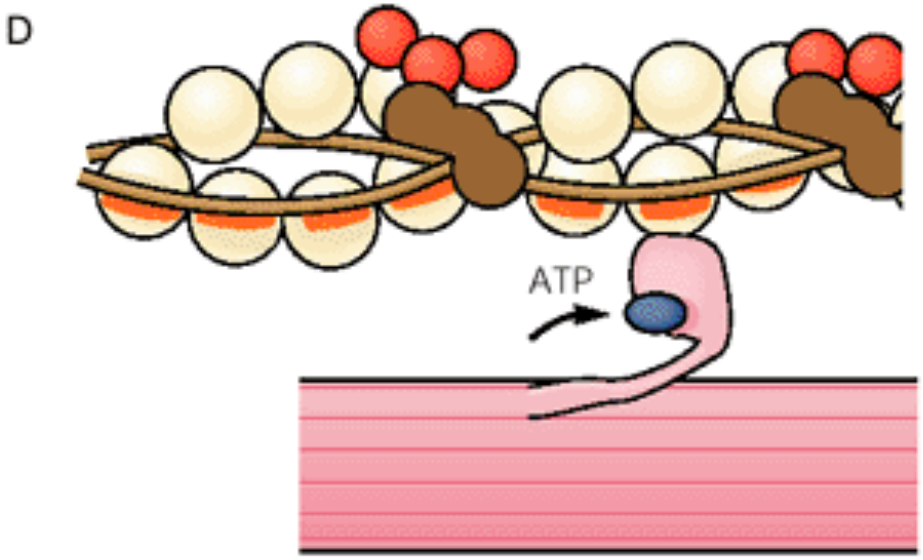
Step 5: Reactivation of myosin.

Step 4: Myosin detachment.

ATP binds to Myosin heads which then detaches from its actin binding site.



Actin-binding site is released and can form another cross-bridge to sustain muscle contraction.

Sliding Filament Mechanism of Contraction

5 steps

Step 1: Rest.

Step 2: Activation.

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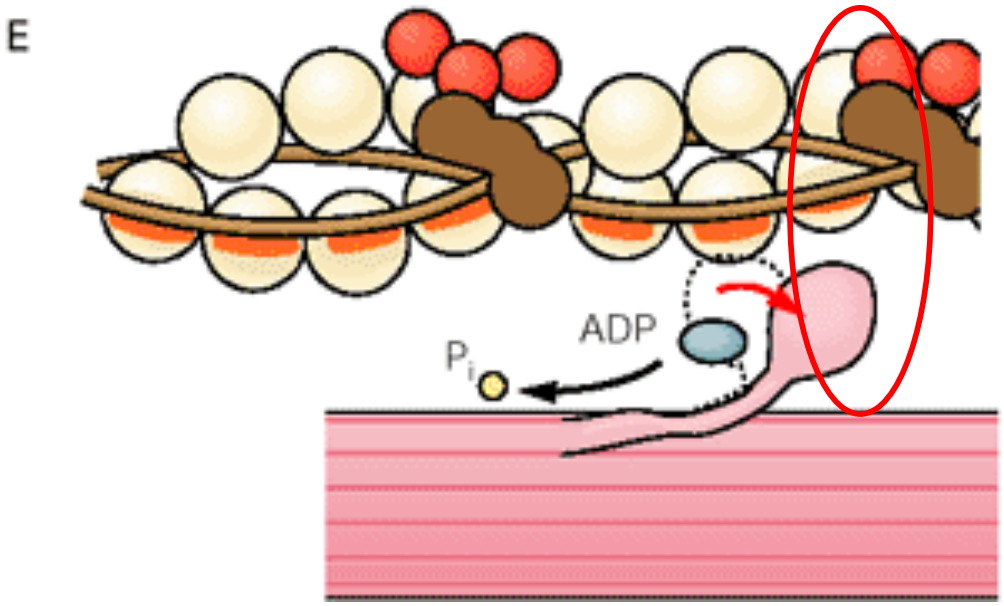
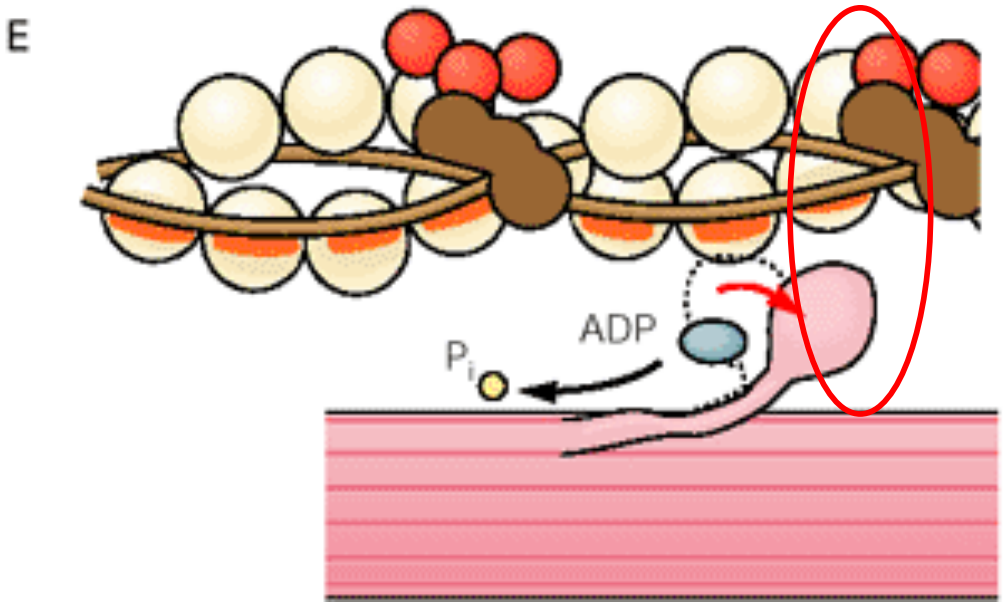
Step 5: Reactivation of myosin.

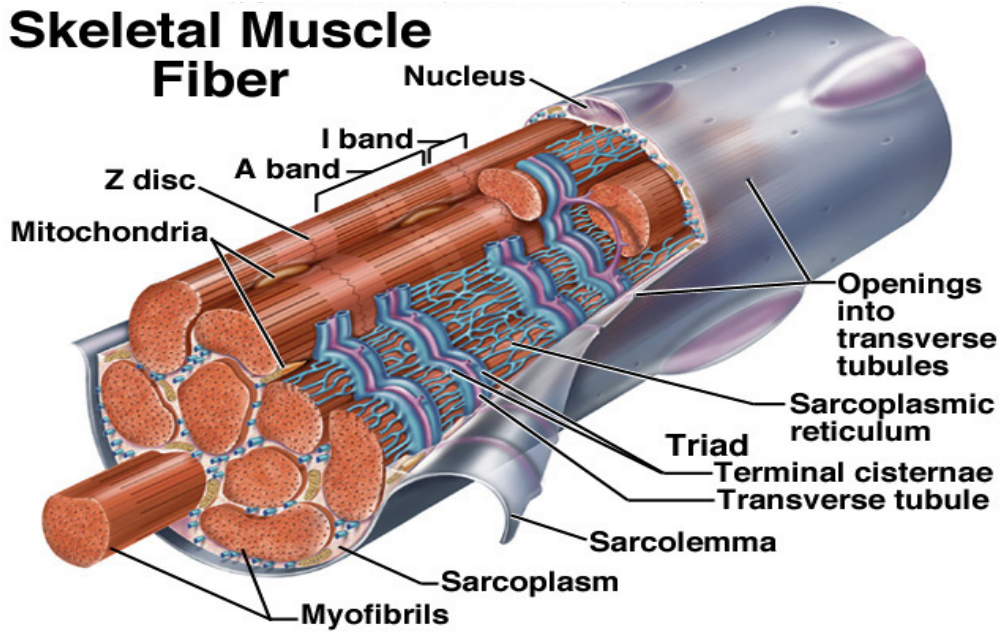


Thick filament: Energy released by dephosphorylation of ATP to bound ADP is stored in myosin heads → myosin heads are "re-cocked".

Step 5: Reactivation of myosin.



Thin filament: High [Ca^{2+}]: system remains activated (step 2), muscle contraction persists. Low [Ca^{2+}]: return to resting state (step 1): myosin heads are cocked but unable to form cross-bridge.



Muscle fibres contain network of longitudinal tubules and chambers (sarcoplasmic reticulum, SPR)

Sequester, store and release Ca^{2+}

At rest intracellular [Ca^{2+}] low, actively pumped into SPR.

Role of Ca^{2+} in excitation-contraction coupling

- Action potential initiated at the NMJ
- Travels across surface of the muscle fibre
- Depolarisation of transverse tubules within the muscle fibre

- Ca^{2+} is released from cisternae of SPR
- Ca^{2+} diffuses along myofibrials
- Ca^{2+} binds to troponin enabling cross-bridges to form

- Release of Ca^{2+} is very rapid (20-50ms to activate the thin filaments fully)
- Reuptake of Ca^{2+} is also rapid → decrease in cross-bridges (80-200 ms)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