Chapter 4. Muscular system
Single-fiber contraction

Structure and Function of Human Body
Lecture 23
By Sukyung Park

Review

- Structure of skeletal muscles

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Contraction mechanisms

- myosin binds to actin, and slides it
- pulling the Z-lines closer together
- reducing the width of the I-bands
- Note that filament lengths have not changed: Shortening of sarcomere!
- As long as muscle fiber remains activated, sliding-filament mechanisms continue

Myosin

- Thick filament: polymer of myosin molecules, each of which has a flexible cross-bridge
  - Myosin molecules are oriented in opposite directions
**Actin**

- **Thin filament**: polymer of actin molecules, globular protein helical chain, that has a binding site for myosin cross bridge.

  ![Actin Diagram](image)

  - Binding site for myosin cross bridge

- In relaxed skeletal muscle, **tropomyosin** blocks the cross-bridge binding site on actin.

  ![Tropomyosin Diagram](image)

**Troponin, Tropomyosin and Calcium**

- Contraction occurs when calcium ions bind to troponin; this complex then pulls tropomyosin away from the cross-bridge binding site.

  ![Troponin Diagram](image)

  - Calcium ions pulls tropomyosin away

  - Cross-bridge Binding sites
Cross-bridge cycle requires ATP

1. Cross-bridge cycle initiated by calcium

   1. Myosin-binding site on actin becomes available, so the energized cross-bridge binds

      \[ A + M \cdot ADP \cdot P_i \xrightarrow{\text{Actin binding}} A \cdot M \cdot ADP \cdot P_i \]

   2. The full hydrolysis and

      \[ A \cdot M \cdot ADP \cdot P_i \xrightarrow{\text{Cross-bridge movement}} A \cdot M + ADP + P_i \]

   3. Binding of a “new” ATP to the cross-bridge the bridge (not the energy source at this point)

      \[ A \cdot M + ATP \xrightarrow{\text{Cross-bridge dislocation from actin}} A + M \cdot ATP \]

   4. Partial hydrolysis of the bound ATP energizes the bridge

      \[ A + M \cdot ATP \xrightarrow{\text{ATP hydrolysis}} A + M \cdot ADP \cdot P_i \]
Excitation – contraction coupling

- Latent period between excitation by AP and development of tension in a skeletal muscle includes the time needed to release Ca²⁺ from sarcoplasmic reticulum, move tropomyosin, and cycle the cross-bridges. **AP does NOT directly act upon the contractile proteins.**

![Graph showing muscle action potential and contraction](image)

Sarcoplasmic reticulum

1. **Sarcoplasmic reticulum**
2. **Lateral sacs** store and release calcium ions into cytoplasm

![Diagram of sarcoplasmic reticulum](image)
3.

- Single AP is enough to saturate all troponin binding sites on thin filament
- Contraction continues until calcium is removed by active-transport proteins, Ca\(^{2+}\)-ATPases, that pumps calcium ions back into reticulum

**Release and uptake of calcium ions**

Passage of an AP along the transverse tubule opens nearby voltage-gated Ca channels, the “ryanodine receptor,” located on the sarcoplasmic reticulum, and calcium ions released into the cytosol bind to troponin.

The calcium-troponin complex “pulls” tropomyosin off the myosin-binding site of actin, thus allowing the binding of the cross-bridge, followed by its flexing to slide the actin filament.
<table>
<thead>
<tr>
<th>Functions of ATP in Skeletal Muscle Contraction</th>
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<tbody>
<tr>
<td>1. Hydrolysis of ATP by myosin energizes the cross-bridges, providing the energy for force generation.</td>
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<tr>
<td>2. Binding of ATP to myosin dissociates cross-bridges bound to actin, allowing the bridges to repeat their cycle of activity.</td>
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<tr>
<td>3. Hydrolysis of ATP by the $\text{Ca}^{2+}$-ATPase in the sarcoplasmic reticulum provides the energy for the active transport of calcium ions into the reticulum, lowering cytosolic calcium to prerelease levels, ending the contraction, and allowing the muscle fiber to relax.</td>
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**Summary**

- List the sequence of events in a single cross-bridge cycle

1) The **influx** of **calcium**, triggering the exposure of **binding sites** on **actin**.

2) The binding of **myosin** to actin.

3) The **power stroke** of the **cross bridge** that causes the sliding of the **thin filaments**.

4) The binding of **ATP** to the cross bridge, which results in the cross bridge disconnecting from actin.

5) The **hydrolysis** of ATP, which leads to the re-energizing and repositioning of the cross bridge.

6) The **transport** of calcium ions back into the **sarcoplasmic reticulum**.
Review

- Window panning review of
  - Muscle contraction mechanism: sliding filament mechanism
  - ATP & muscle contraction
  - AP propagation in muscle construction