Lecture 17
25 Feb 2008

Vertebrate Physiology
ECOL 437 (MCB/VetSci 437)
Univ. of Arizona, spring 2008
Kevin Bonine & Kevin Oh

1. Muscle (Ch17)

http://eebweb.arizona.edu/eeb_course_websites.htm

Vertebrate Physiology 437

Muscle
A. Sarcomere
B. Cross-bridge cycling
C. Length-tension relationship
D. Excitation-contraction coupling
E. Force-Velocity curves, Power
F. Fiber Types
G. Motor Units/Recruitment
H. Energetics
I. Fatigue
J. Repair and Regeneration

- Smooth and Cardiac introduction
- Integration of NS and Muscle Function

Housekeeping, 25 February 2008

Upcoming Readings
Today: Ch17
Wed 27 Feb: Research Question Due
Wed 27 Feb: Ch17
LAB Wed 27 Feb: muscle readings on website
Fri 29 Feb: Ch18
Monday 03 Mar: Ch18
Wed 05 Mar: Ch 19
LAB Wed 05 Mar: locomotion reading on website

Lab discussion leaders: 05 March
1pm - Julia, Matt C.
3pm - Dolziel, Nick

Lab discussion leaders: 27 Feb
1pm - Steve & Cassia
3pm - Kevin & Jennifer

Research Proposal Tips:
- Physiology and science should be subject, not researchers and experiments
- Having interesting question or problem helps give direction and focus
- More physiology
- Subheadings often helpful
- More sophisticated Future Directions, including gaps in current knowledge, flaws in current studies, proposed detailed experiments, think outside the box
- Synthesize, not serial book reports
- Abstract, role is summary of entire paper, not an intro to the intro
- Avoid Pronouns (its, these, this, ...which, there are)
- Passive voice to be avoided (e.g., Avoid passive voice)
- Leading and following zeroes (0.5, .5, .50)
- Page numbers
- Citation format (J. of Physiology, instructions to authors, [full journal names])
- Turn in old, graded work with each new version
- Peer editing (read quickly, then read for content and writing, comments helpful)

Muscle
Uses:
- most observable animal behavior
- most visceral function
- generally act by shortening

Classification:
- striated
  - skeletal or cardiac
- smooth
  - walls of hollow organs

All muscle movement based on myofilaments (actin and myosin) sliding past each other...

Utilize: ATP, Ca^{2+}, ~APs (Myc., Sarco- = muscle related)
Skeletal Muscle

Structure:
- muscle attached to bone (skeleton) via tendons
- muscle comprises elongate, multinucleate, muscle fibers
- multinucleate muscle fibers derived from combination of many myoblasts (embryonic muscle cells)
- within each muscle fiber are many parallel myofibrils
- each myofibril contains sarcomeres arranged in series (end-to-end)
- sarcomere is functional unit of muscle

Sarcomere

Sarcomeres in adjacent myofibrils are aligned leading to striated appearance

- Z-disk at each end of sarcomere
- Actin thin myofilaments attached to each Z-disk
- Myosin thick myofilaments in between actins (6,3)

Which regions change length and which remain the same as the sarcomere shortens?

- Z-disk (actin attaches)
- I-band (actin only)
- A-band (myosin length)
- M-line (midpoint of myosin)
- H-zone (myosin only)

During muscle contraction, myosin thick filaments slide past actin thin filaments toward Z-lines

Sarcomere Composition

Actin composed of:
- individual molecules of G-actin (globular)
- united into chains called F-actin (filamentous)
- which form a two-stranded helix

In the groove of the two F-actin strands is tropomyosin, which also has globular troponin molecules attached to it

Myosin composed of:
- 2 heavy chains with globular heads
- 2 essential light chains
- 2 regulatory light chains

The light chains are involved in the speed of contraction (important for different muscle fiber-types)

Myosin molecules spontaneously aggregate into complexes with the heads at the ends and the tails toward the middle
Sarcomere Function

Actin and Myosin molecules slide past each other, but don’t themselves change length.

Cross-bridges form transiently between myosin head and actin filament (actomyosin).

Sliding Filament Theory

Cross-bridge forces are additive. Same force all along myofibril.

Sarcomere shortens during contraction.

Number of Cross-bridges (and therefore contraction magnitude) increased with appropriate overlap of actin with myosin heads.

Why lose force production at short end?
What constrains muscle length in the body?

Cross Bridges and Force Production

Myosin head binds to actin (actomyosin), then pulls myosin toward Z-line thereby shortening sarcomere (= contraction).

Length-Tension Relationship

Normal muscle function at or near the plateau (1.8-2.2).

Hill et al. 2004, Fig 17.12
Myosin head has to be able to detach and bind again to actin further along in order to continue to generate force. Detachment requires ATP bind to myosin head.

Cross Bridges and Force Production

ATP required for the dissociation of actin and myosin (else rigor mortis)
Myosin acts as an ATPase, hydrolyzing ATP to ADP + Pi (Energy of ATP hydrolysis "cocks" the myosin head)

Actomyosin complex forms (= crossbridge) (1)

Myosin releases ADP and Pi (very slowly unless bound to actin) (2)

Cycle repeats until Ca++ resequestered or run out of energy

Regulation of Contraction

CALCIUM and the cross bridge

Need free Ca++ in cytosol to get contraction
Calcium binds troponin which is attached to tropomyosin on actin
This causes conformational change in tropomyosin exposing actin binding sites for myosin heads (not shown)
Without calcium, contraction is inhibited

Excitation-Contraction Coupling, from the beginning...

1. AP from CNS arrives at neuromuscular junction.
2. ACh released into synapse.
3. ACh binds to nicotinic receptors on motor endplate.
4. Ion channels for K+ and Na+ open; greater Na+ influx leads to depolarization and AP in muscle plasma membrane
EPP = Endplate Potential (~Excitatory Post-Synaptic Potential or EPSP)
**Excitation-Contraction Coupling, the middle I...**

5. Change in membrane potential (AP) reaches deep into the muscle cell via transverse tubules (T-tubules; one per Z-disk)

![Diagram of muscle cell with T-tubules](image1)

**Excitation-Contraction Coupling, the middle II...**

6. T-tubules have voltage sensitive proteins called dihydropyridine receptors

7. Dihydropyridine receptors in the T-tubules are mechanically linked with ryanodine receptors (RR) on the sarcoplasmic reticulum (SR)

The ends of the SR adjacent to the T-tubule are called terminal cisternae (w/ calsequestrin)

8. Calcium stored in the SR. Released into the cytosol via the ryanodine receptor channel when the RR is mechanically triggered by the voltage sensitive dihydropyridine receptor.

**Excitation-Contraction Coupling, the last bit...**

9. Calcium triggers release of more calcium from some ryanodine receptors that are not linked to dihydropyridine receptors

Called calcium-induced calcium release

10. Calcium binds to troponin leading to actomyosin complex...

11. After repolarization, calcium actively (requires ATP) moved back into SR where much of it is bound to calsequestrin

12. Muscle relaxes as long as ATP is present to allow actomyosin complex to dissociate

**Time course of excitation-contraction events**

- Latent period about 2ms

**Review of EC Coupling and Muscle Contraction**

**Muscle Model**

- Bone
- Parallel Elastic Component (sarcolemma, connective tissue within muscle)
- Contractile Unit (sarcomeres)
- Series Elastic Component (tendon, connective tissue linking muscle fibers to tendon, titin, Z-line material, cross-bridge links)
- Muscle & Tendon
- Bone

Randall et al., 2002
Isometric Contraction

\[ \text{iso} = \text{same} \]
\[ \text{metric} = \text{length} \]

**Isotonic Contraction**

\[ \text{iso} = \text{same} \]
\[ \text{tonic} = \text{tension} \]

**Purely isotonic contraction**

**Force-Velocity Curve**

- Greatest force during isometric contraction
- Greatest velocity when muscle is unloaded

**Muscles can produce power**

- Muscle fiber types vary in their mechanical properties
- Power = force \times velocity
- Maximum power output is found at intermediate force and velocity (~40%)

**Different Muscle Fiber-Types**

<table>
<thead>
<tr>
<th>Property</th>
<th>Slow oxidative (type I)</th>
<th>Fast oxidative (type IIa)</th>
<th>Fast glycolytic (type IIb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiber diameter</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Force per cross-sectional area</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Rate of contraction ( V_{max} )</td>
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<td>1</td>
<td>1</td>
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<tr>
<td>Mitochondrial ATPase activity</td>
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<td>1</td>
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<tr>
<td>Resistance to fatigue</td>
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<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Number of mitochondria</td>
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<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Capacity for oxidative phosphorylation</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Enzymes for anaerobic glycolysis</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Source: Adapted from Sherwood, 2003. Key: \( \downarrow \) Low \( \uparrow \) Intermediate \( \uparrow \) High
**Histochemistry**

Serial sections stained for:  
- **FOG** (fast-twitch)  
  oxidative glycolytic; dark mATPase and dark SDH  
- **SO** (slow-oxidative)  
  light mATPase, dark SDH  
- **FG** (fast-twitch)  
  glycolytic; dark mATPase, light SDH  
- **mATPase**  
- **SDH** (oxidative)

**Myosin isoform, ATPase speed**  
SR Ca-ATPase speed

IIx (=IIb) ten times faster than I

IIx default, exercise leads to I and IIa

MGF (~IGF-1) – mechanogrowth factor  
autocrine, paracrine  
made by muscle after sarcolemma damage  
loss = muscular dystrophy

Why Athletes Taper?

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**Olympic Athletes**