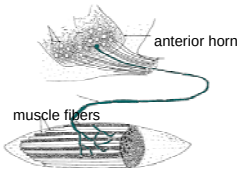
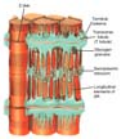
Lecture 17
25 Feb 2008

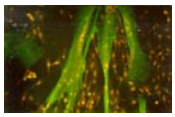
Vertebrate Physiology
ECOL 437 (MCB/VetSci 437)
Univ. of Arizona, spring 2008

Kevin Bonine & Kevin Oh



1. Muscle (Ch17)





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

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 – Dalziel, Nick

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

The Edges of Life Lecture Series

The Edges of Life – 7pm at Centennial Hall

Wednesday, March 5
Life's Technological Edge: The Singularity is Near: When Humans Transcend Biology
Ray Kurzweil, *via Teleportec Teleporter*
Founder, Chairman and Chief Executive Officer, Kurzweil Technologies
Humanity is on the edge of a vast transformation, when what it means to be human will be both enriched and challenged. Inventor and futurist Ray Kurzweil will introduce this radically optimistic singularity, an era when we break our genetic shackles to create a nonbiological intelligence trillions of times more powerful than today. In this new world, humans will transcend biological limitations to achieve entirely new levels of progress and longevity.
This lecture co-sponsored by: UA College of Engineering and UA College of Science

These do not count as physiology lectures.

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

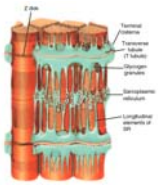
-Synthesize, not serial book reports
-Abstract, role is summary of entire paper, not an intro to the intro

-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)

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

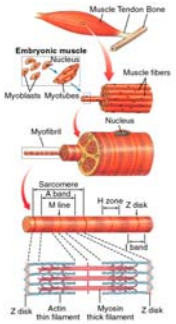
Muscle

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

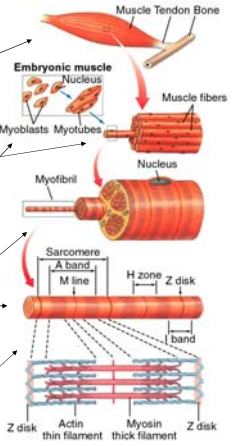


(*Myo-*, *Sarco-* = muscle related)

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

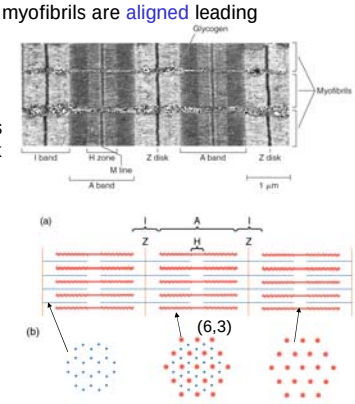
Sarcomeres in adjacent myofibrils are aligned leading to striated appearance

Z-disk at each end of sarcomere

Actin thin myofilaments attached to each Z-disk

Myosin thick myofilaments in between actins (6,3)

Actin and Myosin overlap is what allows muscle contraction



Sarcomere

Areas within sarcomere given names:

Z-disk (actin attaches)

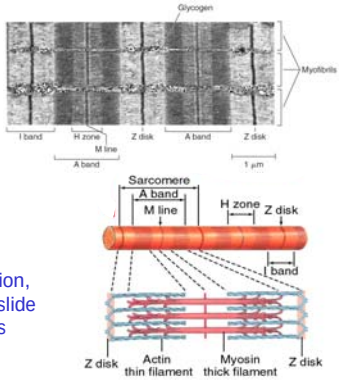
I-band (actin only)

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



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)

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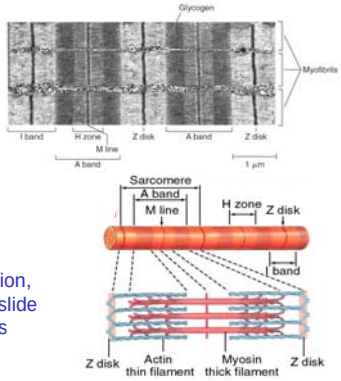
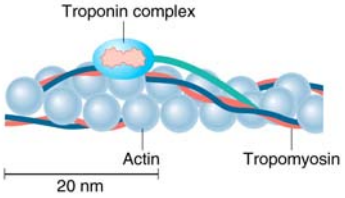


Sarcomere Composition

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

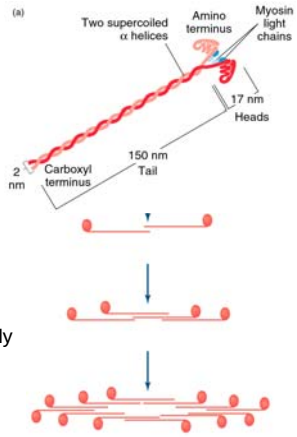


Sarcomere Composition

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

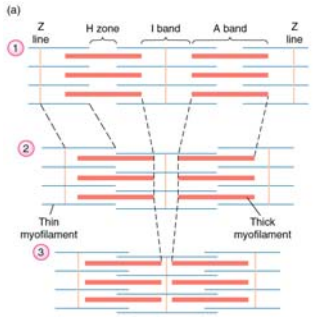


Sarcomere Function

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

Sliding Filament Theory

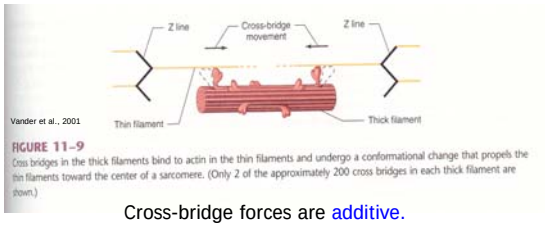
Cross-bridges form transiently between myosin head and actin filament (actomyosin)



Sarcomere shortens during contraction

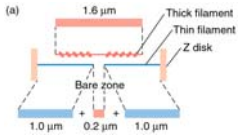
Cross Bridges and Force Production

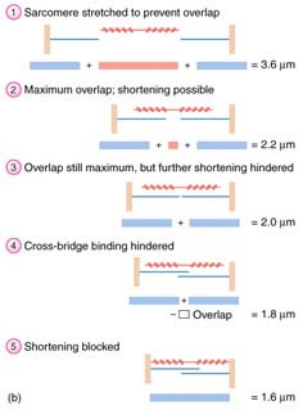
Myosin head binds to actin (actomyosin), then pulls myosin toward z-line thereby shortening sarcomere (= contraction)



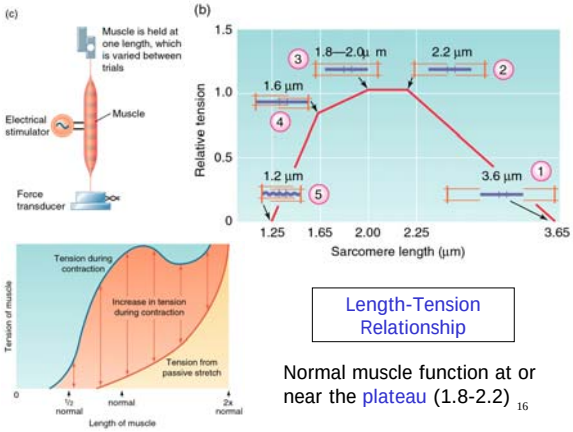
Cross-bridge forces are additive. Same force all along myofibril.

Sarcomere Function





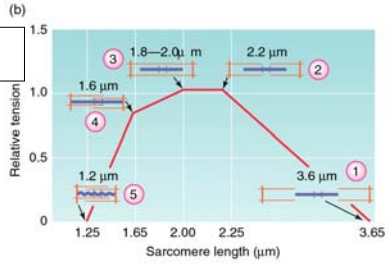
Number of Cross-bridges (and therefore contraction magnitude) increased with appropriate overlap of actin with myosin heads



Length-Tension Relationship

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

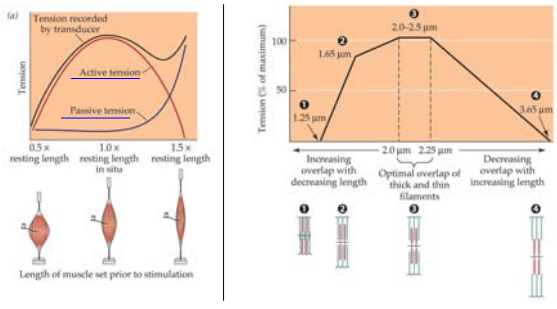
Length-Tension Relationship



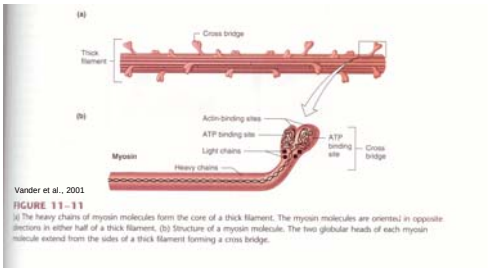
Why lose force production at short end?

What constrains muscle length in the body?

Length-Tension Relationship



Hill et al. 2004, Fig 17.12



Vander et al., 2001

FIGURE 11–11

(a) The heavy chains of myosin molecules form the core of a thick filament. The myosin molecules are oriented in opposite directions in either half of a thick filament. (b) Structure of a myosin molecule. The two globular heads of each myosin molecule extend from the sides of a thick filament forming a cross bridge.

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

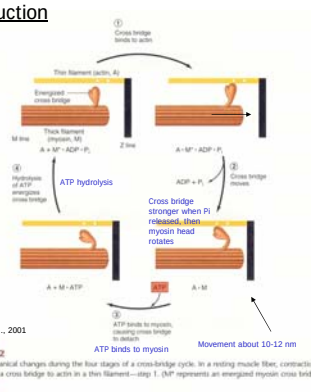
Cross Bridges and Force Production

ATP required for the (3) dissociation of actin and myosin (else *rigor mortis*)

Myosin acts as an ATPase, hydrolyzing ATP to ADP + P_i (4) (Energy of ATP hydrolysis "cocks" the myosin head)

Actomyosin complex forms (= crossbridge) (1)

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



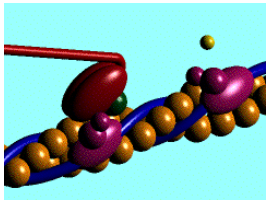
Vander et al., 2001

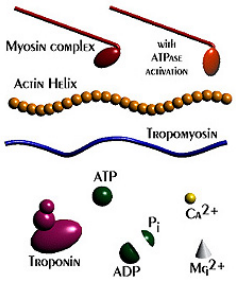
FIGURE 11–12

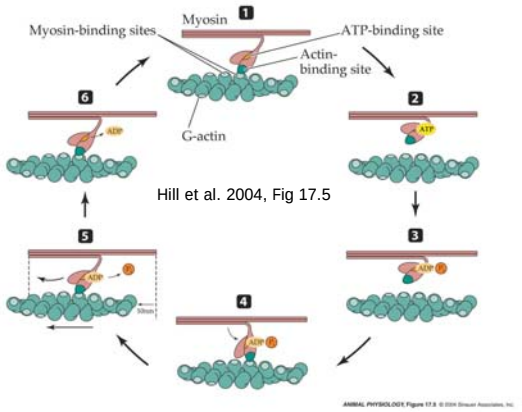
Chemical and mechanical changes during the four stages of a cross-bridge cycle. In a resting muscle fiber, contractio with the binding of a cross bridge to actin in a thin filament—step 1. (M* represents an energized myosin cross brid

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

San Diego State University College of Sciences
Biology 590 - Human Physiology
Actin Myosin Crossbridge 3D Animation*







Hill et al. 2004, Fig 17.5

Regulation of Contraction

CALCIUM and the cross bridge

Need free Ca^{2+} 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

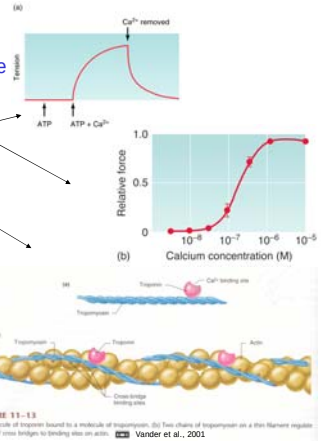


FIGURE 11–13

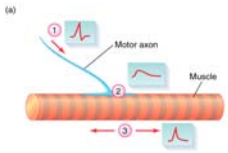
(a) Molecule of troponin bound to a molecule of tropomyosin. (b) Two chains of tropomyosin on a thin filament regulate access of cross bridges to binding sites on actin.

Vander et al., 2001

Excitation-Contraction Coupling, from the beginning…

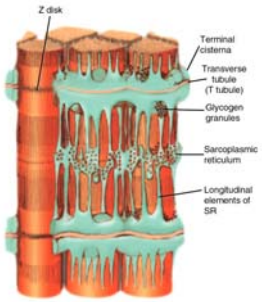
1. AP from CNS arrives at neuromuscular junction.
2. ACh released into synapse.
3. ACh binds to nicotinic receptors on motor endplate.
4. Ion channels for K+ and Na+ open; greater Na+ influx leads to depolarization and AP in muscle plasma membrane

EPP = Endplate Potential
(~Excitatory Post-Synaptic Potential or EPSP)



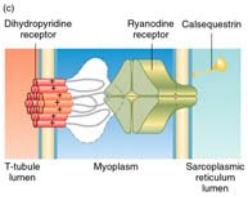
Excitation-Contraction Coupling, the middle I…

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



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

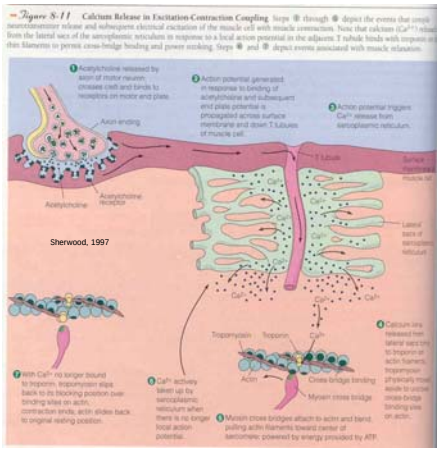
Called *calcium-induced calcium release*

10. Calcium binds to troponin leading to actomyosin complex…

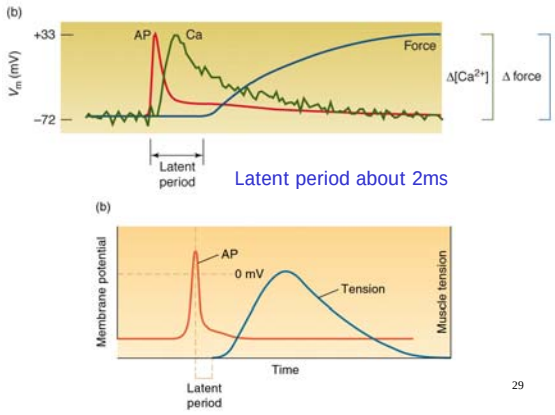
11. After repolarization, calcium actively (requires ATP) moved back into SR where much of it is bound to calsequestrin

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

Review of EC Coupling and Muscle Contraction

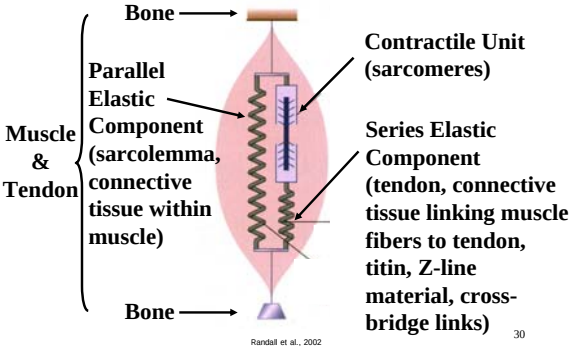


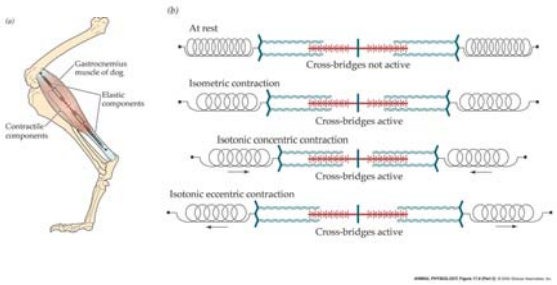
Time course of excitation-contraction events



Latent period about 2ms

Muscle Model

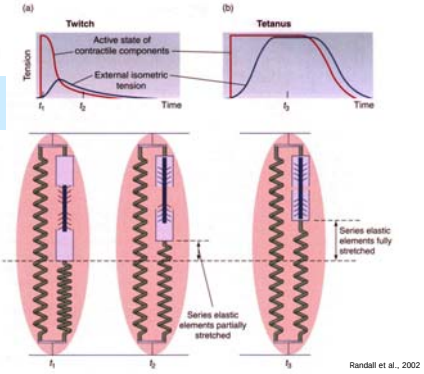




Hill et al. 2004, Fig 17.8

Isometric Contraction

iso = same
metric = length

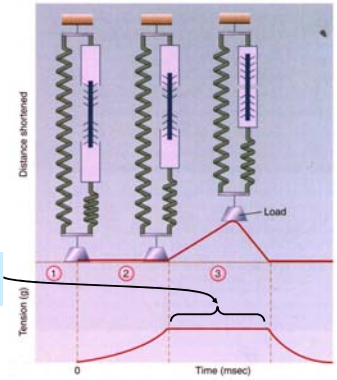


Randall et al., 2002

Isotonic Contraction

iso = same
tonic = tension

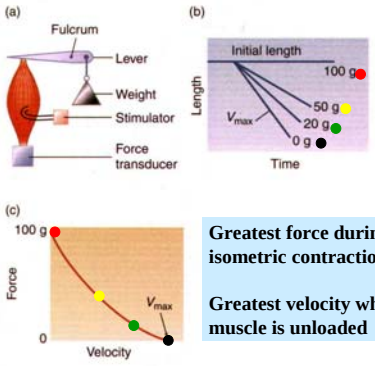
Purely isotonic contraction



Randall et al., 2002

Thanks to Randi Weinstein

Force-Velocity Curve



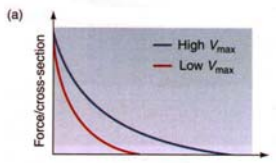
Randall et al., 2002

Greatest force during isometric contraction

Greatest velocity when muscle is unloaded

Muscles can produce power

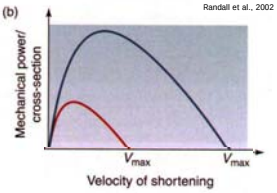
Muscle fiber types vary in their mechanical properties



Randall et al., 2002

Power = force * velocity

Maximum power output is found at intermediate force and velocity (~40%)



Different Muscle Fiber-Types

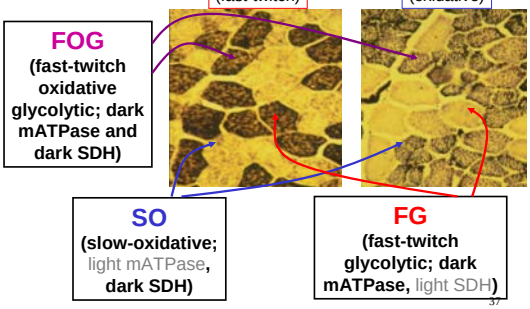
Table 10-1 Properties of twitch (phasic) fibers in mammalian skeletal muscles
Randall et al., 2002

Property	Slow oxidative (type I)	Fast oxidative (type IIa)	Fast glycolytic (type IIb)
Fiber diameter	↓	↔	↑
Force per cross-sectional area	↓	↔	↑
Rate of contraction (V_{max})	↓	↑	↑
Myosin ATPase activity	↓	↑	↑
Resistance to fatigue	↑	↔	↓
Number of mitochondria	↑	↑	↓
Capacity for oxidative phosphorylation	↑	↑	↓
Enzymes for anaerobic glycolysis	↓	↔	↑

Source: Adapted from Sherwood, 2001. Key = ↓ Low ↔ Intermediate ↑ High

Histochemistry

Serial sections stained for: **mATPase** (fast-twitch) **SDH** (oxidative)



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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

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