7 Muscles Physiology:

MUSCLE STRUCTURE

SLIDING FILAMENT THEORY
(or, 6[ish] easy steps to contraction)

3 TESTS OF THE SLIDING FILAMENT MODEL
BONE FUNCTION

1. STIFFNESS: Resisting deformation

- Protection
- Transmission of muscular power (= movement)
- Oppose gravity

Q: Other than imparting stiffness, what other functions do bones provide?
BONE FUNCTION

2. HEMATOPOESIS: Produce blood cells (later)

3. MINERAL (Ca++) HOMEOSTASIS (next lecture)

**Storage and Mobilization**

- Osteoblasts (deposition)
- Osteoclasts (resorption)

Bone remodeling

90% Ca

CALCIUM

PHOSPHORUS

MAGNESIUM
BONE HOMEOSTASIS (remaining stiff and storing/mobilizing Ca++)
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Q: Is the same amount of bone always desirable? How much bone should there be?
BONE HOMEOSTASIS (remaining stiff and storing/mobilizing Ca++)

**Q:** What factors might enhance or constrain osteoblast activity or cell life span? osteoclast activity or cell life span?

Harada and Rodin 2003
Review of bone remodeling

Q: Predict what happens to bone when it is subject to increased stress.

Rik Huiskes, Ronald Ruimerman, G. Harry van Lenthe and Jan D. Janssen
Q: How does loading (i.e., stress) produce a remodeling response?

Rik Huiskes, Ronald Ruimerman, G. Harry van Lenthe and Jan D. Janssen
Nature 405, 704-706 (8 June 2000)
MECHANOTRANSDUCTION
Low estrogen levels are associated with increased bone turnover and decreased bone mass.

Rate of hip fractures among Hong Kong women between 1966 and 1995.

Q: Why might medications that increase inorganic composition of bone not always be clinically beneficial?
Q: Disuse osteopenia / osteoporosis. What are some situations / conditions when bone is subject to decreased stress?
Q: What unusual traits were observed in the clinical case reported by Smith?

Q: Why was estrogen administered? Why was it ineffective?
FROM NERVE TO MUSCLE . . .

Muscle tissue represents about 40% of body weight

Q. How do motor neuron action potentials make muscles contract?

Need to understand the structure of muscle
MUSCLE STRUCTURE AND CONTRACTION

Striated
skeletal
cardiac

Smooth (unstriated)
A single motor unit consists of a **motor neuron** and all of the muscle fibers it innervates.

Muscle contraction is initiated at the neuromuscular junction.
Striated muscle fibrils

fiber

sarcoplasmic reticulum in x-section

fibril

Myofibril

Sarcomere

M line

Z disc

H zone

I band

A band
Myofilament organization dictates the macroscopic appearance of muscle.

Q: through which parts of the fiber were these sections made?
The **Sliding Filament Theory** of muscle contraction

![Diagram of the Sliding Filament Theory](image-url)
The neuromuscular junction is the point of synaptic contact between the axon terminal of a motor neuron and the muscle fiber it controls.

Action potentials in the motor neuron cause acetylcholine release into the neuromuscular junction.
1. Acetylcholine (ACh) is released from the axon terminal of a motor neuron and binds to receptors in the motor end plate. This binding elicits an end-plate potential, which triggers an action potential in the muscle cell.

2. Action potential propagates along the sarcolemma and down T tubules.

3. The action potential triggers Ca²⁺ release from SR.

4. Ca²⁺ binds to troponin, exposing myosin-binding sites.

5. Crossbridge cycle begins (muscle fiber contracts).

6. Ca²⁺ is actively transported back into lumen of SR following the action potential.

7. Tropomyosin blocks myosin-binding sites (muscle fiber relaxes).
Q: Where in the muscle contraction cycle do ligand-gated channels occur? Voltage-gated?

DHP “receptor” senses t-tubule voltage-> ryanodine receptor

ryanodine receptor releases Ca2+ into cytosol.
Relaxed: **tropomyosin** blocks the cross-bridge binding site on actin.

Ready: Ca$^{2+}$ **binds to troponin:**
- tropomyosin “moves”
- myosin binding sites exposed.
another 6 substeps involving ATP hydrolyzation

A-M binding, ready

ADP released, binding site clear

“power stroke” powered by P release

ATP binds to actin, release A-M bond

ATP partially hydrolysis

Actin head “cocked”
Q: Do sarcomeres change in length and structure when they contract? If so, which regions contract?
THREE TESTS OF THE SLIDING FILAMENT MODEL

Q: Do sarcomeres change in length and structure when they contract? If so, which regions contract?
Q: Does concentration of myoplasmic free calcium change during contraction?

Furaptra = a fluorescent calcium indicator
Furaptra = a fluorescent calcium indicator

Q: What is happening between the time of the action potential and the peak of myoplasmic calcium?

Q: Why is the contractile force generated AFTER the spike in myoplasmic free calcium?
Q: Does the force generated by muscles differ in muscles of different resting length?

HINT: ARE FILAMENTS INFINITELY LONG?
Length of muscle set prior to stimulation

(b)

- **Increasing overlap with decreasing length**
- **Optimal overlap of thick and thin filaments**
- **Decreasing overlap with increasing length**

1. 1.25 μm
2. 1.65 μm
3. 2.0–2.5 μm
4. 3.65 μm