SECTION 4 : MUSCLE CONTRACTION AND MOTION IN ANIMALS

LECTURE 9 : MUSCLE CONTRACTION

Roop Mallik,
BSBE – IIT Bombay

TOPIC OF LECTURES

Lec1 - Proteins as Machines
Lec2 - Rotary Motors
Lec3 - Linear Motors
Lec4 - Artificial Nanomachines

Lec5 - The Cytoskeleton (Microtubules and Cell Division)
Lec6 - The Cytoskeleton (Actin and Cell Crawling)

Lec7 - Chemotaxis
Lec8 - Beating of Cilia

Lec9 - Muscle Contraction
Lec10 - Heartbeats
Lec11 - To Sing or to Fly

Jun 2 (Fri)	Lec9 (D3)	Lec9 (D4)
Jun 6 (Tue)		Lec10 (D4)
Jun 7 (Wed)	Lec10 (D3)	
Jun 8 (Thu)	Lec11 (D3)	Lec11 (D4)

Next week :- Lecture is on Thursday Jun 8 (Not Friday Jun 9)

14 June Wed 9:30-12:30 - BB101 Endsem Exam

Resources

Lodish, Berk… Molecular Cell Biology

Jim Spudich Ibiology Talks

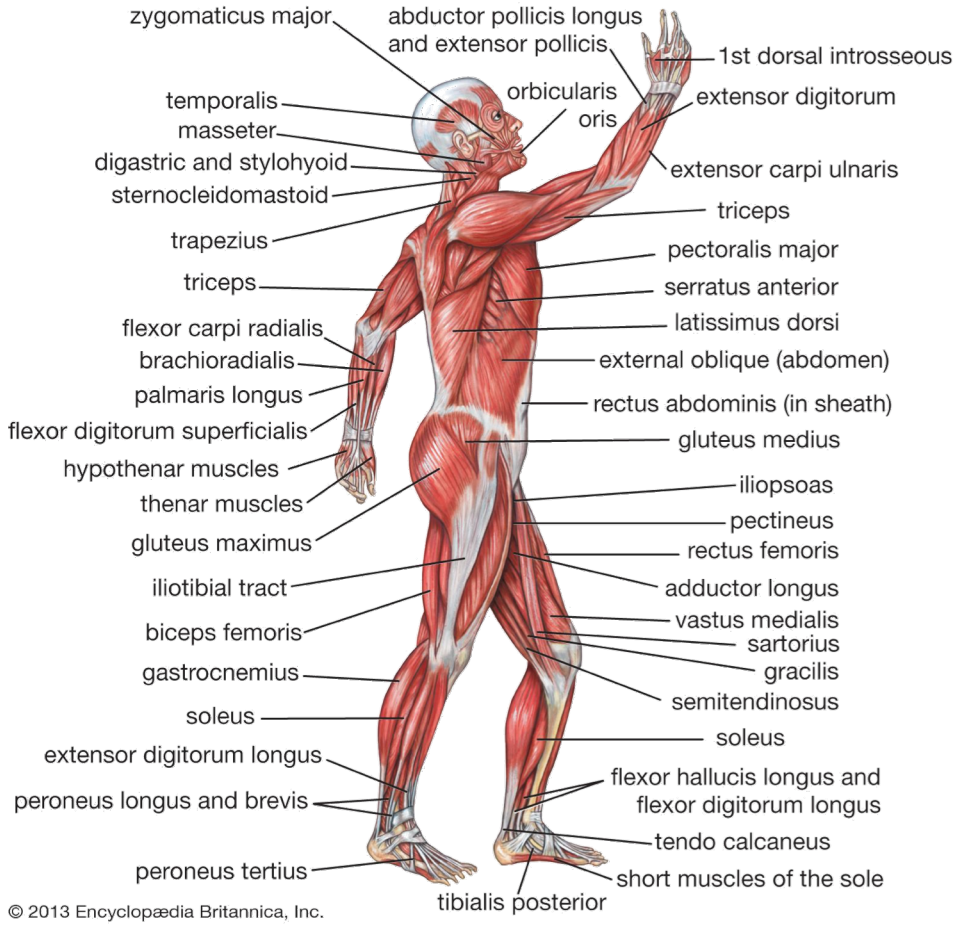
Approximately 600 different Muscles in the body
We will obviously not discuss all of this

We will discuss …

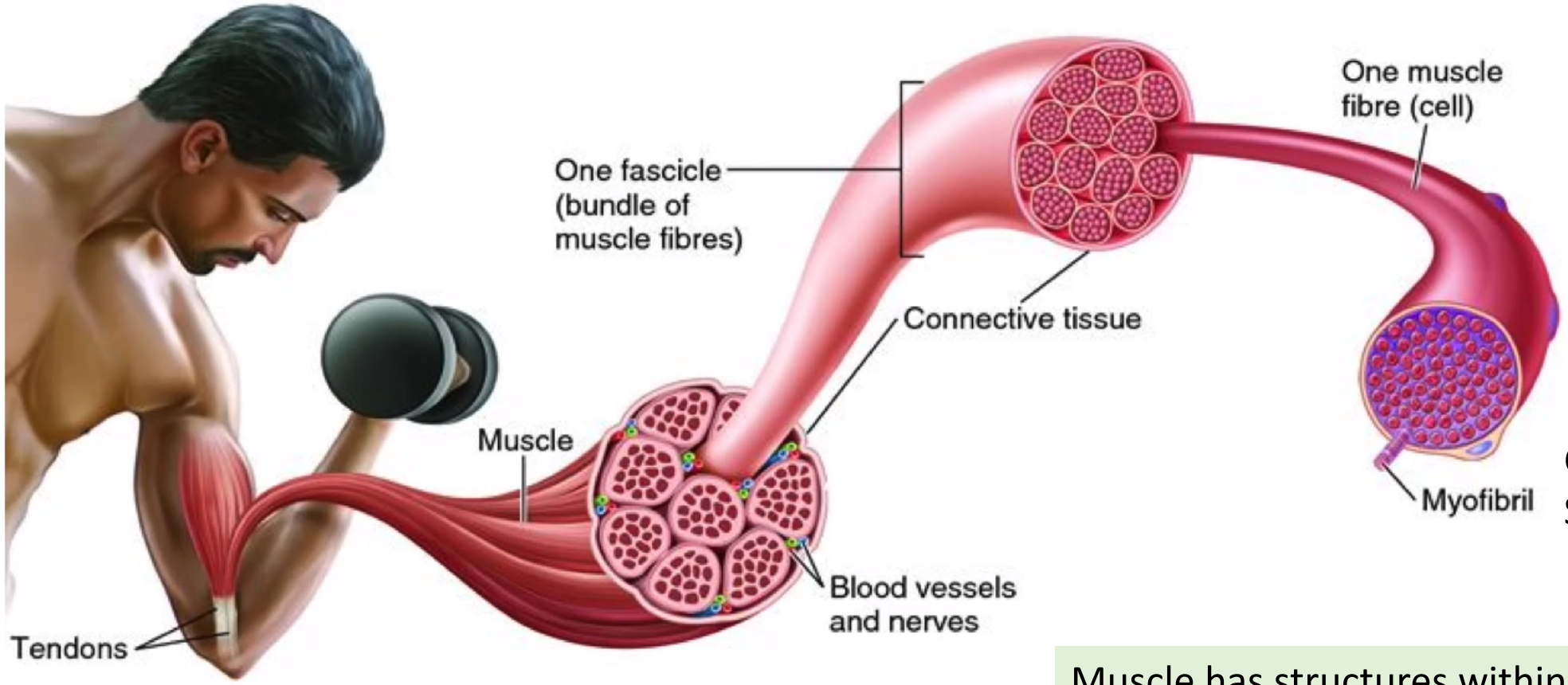
- Basic structure and properties of Muscles
- How Muscles are Controlled by the Brain
- How Myosin motors cause Muscle contraction

Properties of muscles :-

- Respond to stimulation by brain
- Contract (Shorten) after Stimulation
- Get Stretched by the application of Force
- Return to original Shape/Length after Contraction or Stretching (Elasticity)



Overview of skeletal muscle architecture



Contains Sarcomeres

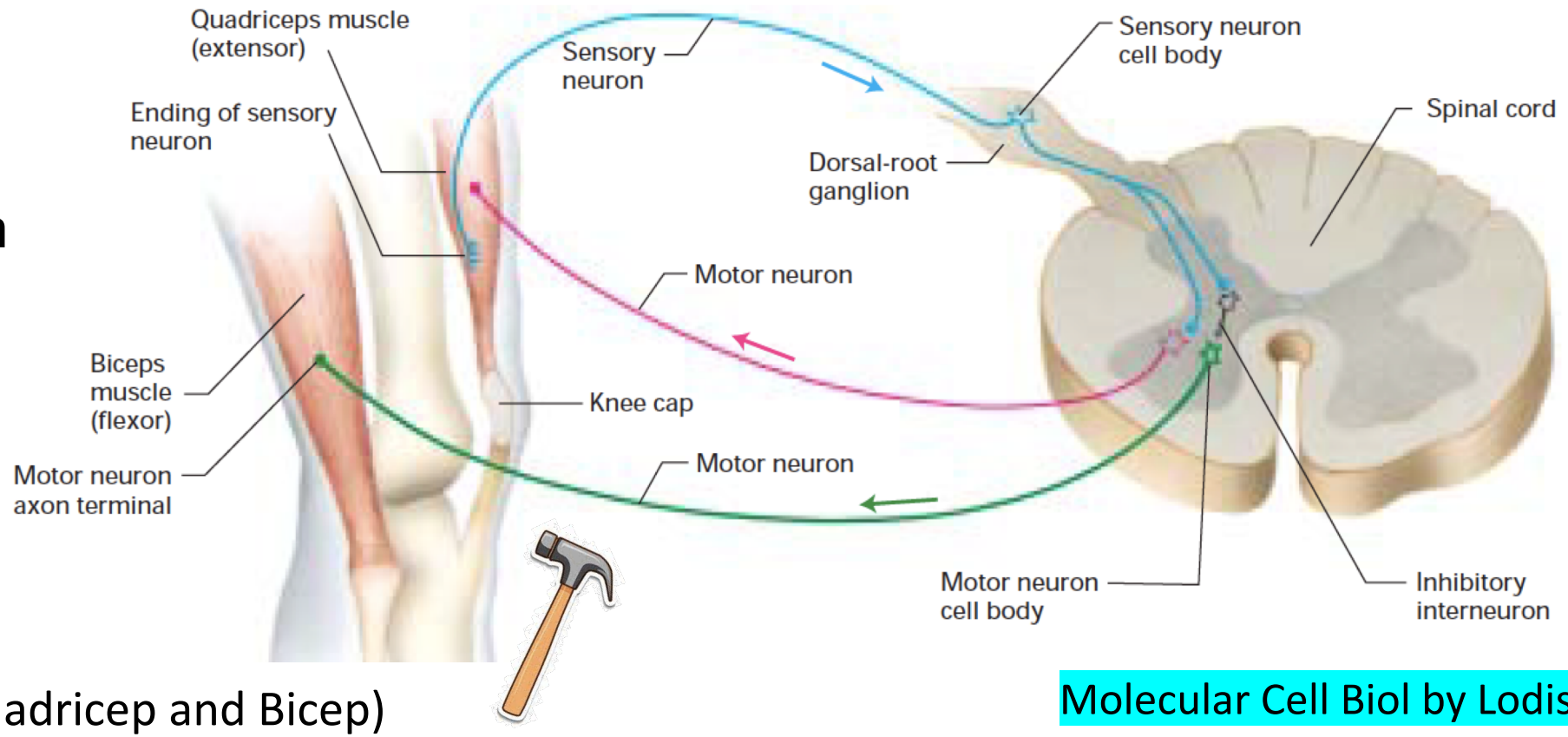
Muscle has structures within structures

… Allows you to amplify force generated at the Nanometer scale to Force at much larger scales

MUSCLE CONTRACTION

Example:-
Knee-Jerk reaction
Hammer tap below Knee-cap. Used by doctors to check abnormalities with Nerve signals

Neuromuscular Junction

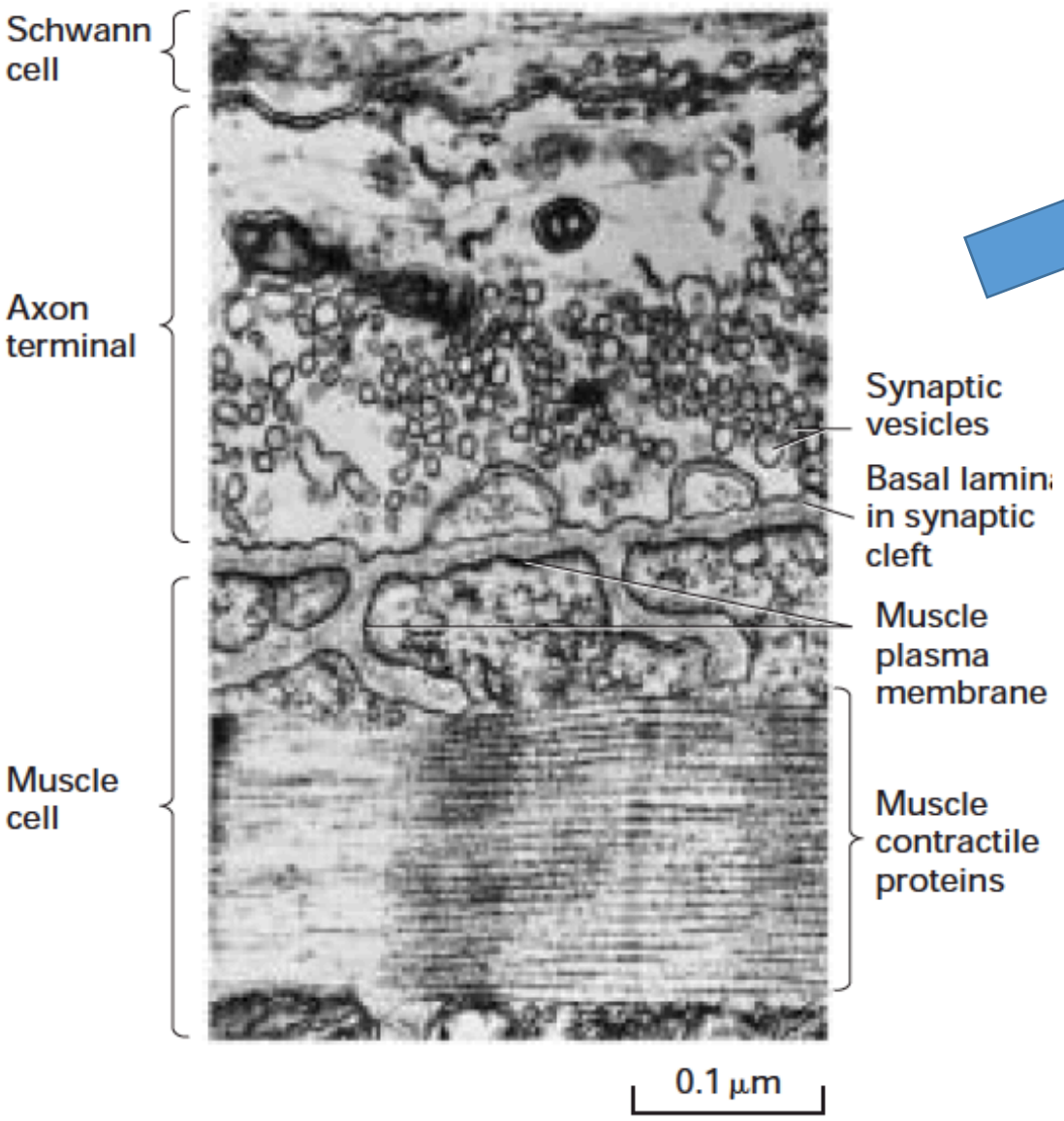


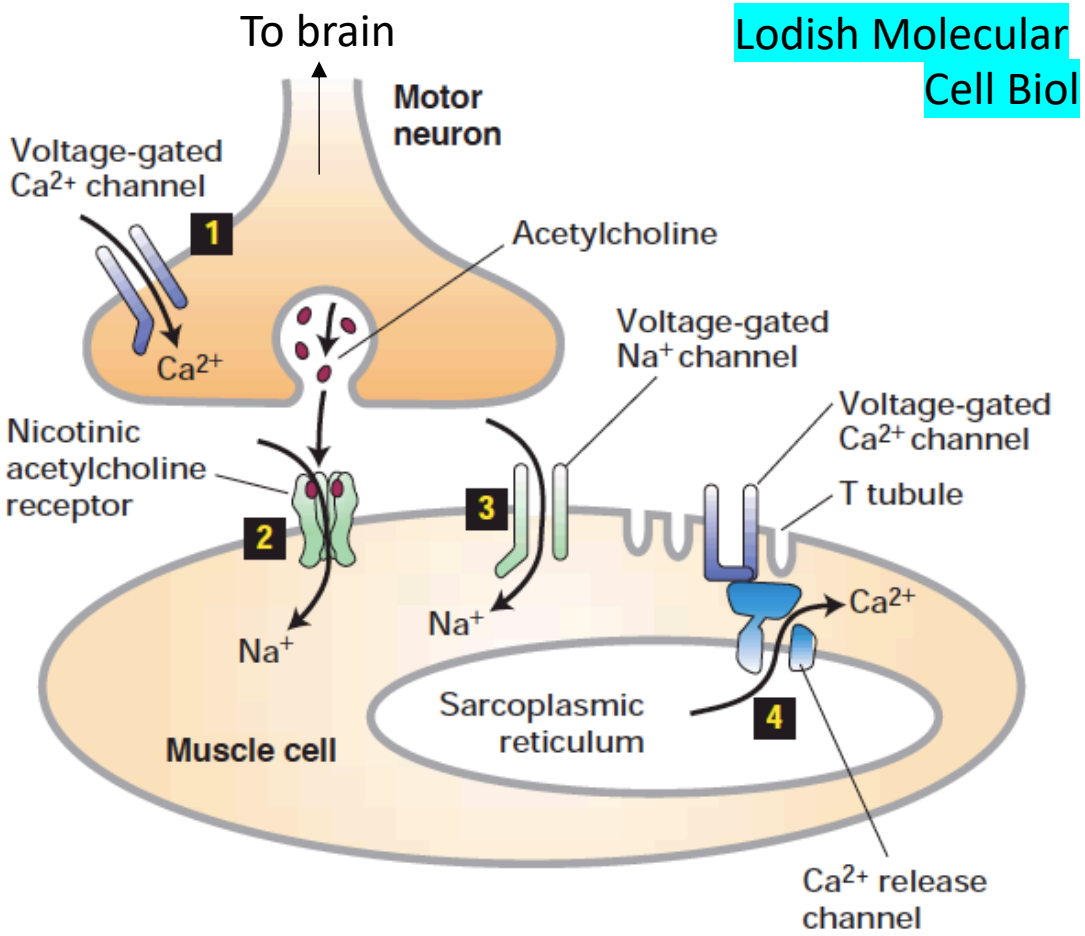
Molecular Cell Biol by Lodish

- PAIR of Muscles (Quadricep and Bicep)
- Quadricep will contract, but Bicep is prevented from Contracting
- Tap is Sensed by **Sensory Neurons** → Reaches the Spinal Cord (and brain)
- **Sensory Neuron** from Quadricep is coupled to
  - ❑ **Motor Neuron of Quadricep** (will cause Quadricep contraction)
  - ❑ **Motor Neuron of Bicep** (Via Inhibitory Neuron to prevent Bicep contraction)
- Net result is (Quadricep Contraction + Bicep Strecthing) → Extension of leg at the knee joint

What happens at the Neuromuscular Junction ?

Lodish Molecular Cell Biol





Brain impulses cause Release of acetylcholine

→ Acetylcholine binds to receptor on Muscle Cell

→ Causes entry of Na+ into Muscle Cell

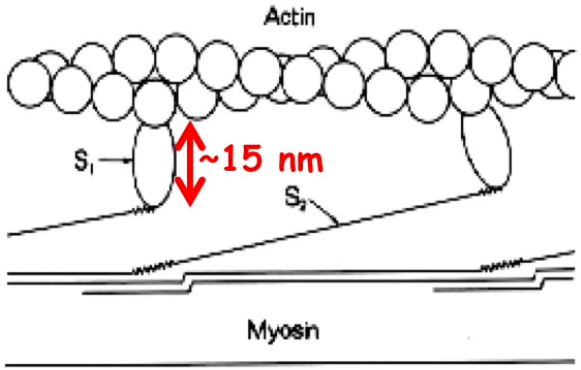
→ Ca++ stored in Sarcoplasmic Reticulum of muscle cell is released into Cytosol

→ This activates Myosin to generate force in the Sarcomere

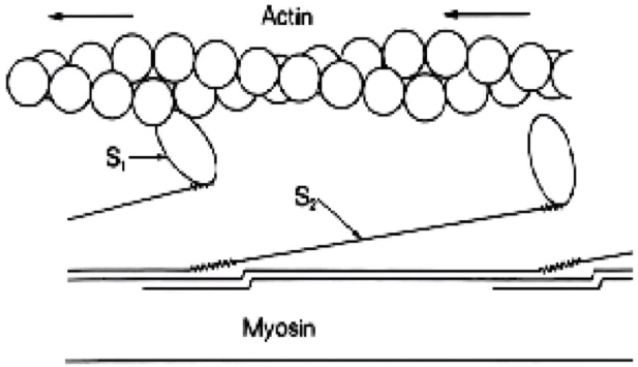
→ Muscle Contracts

Now, lets move inside the Muscle …

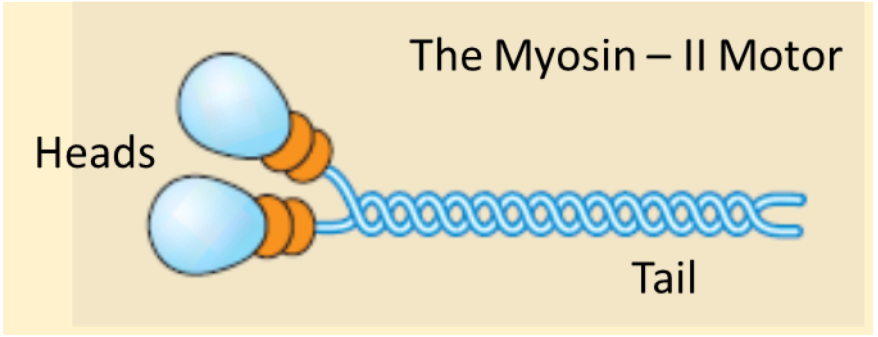
Hugh Huxley: 1969 Swinging Crossbridge Hypothesis for Force Production



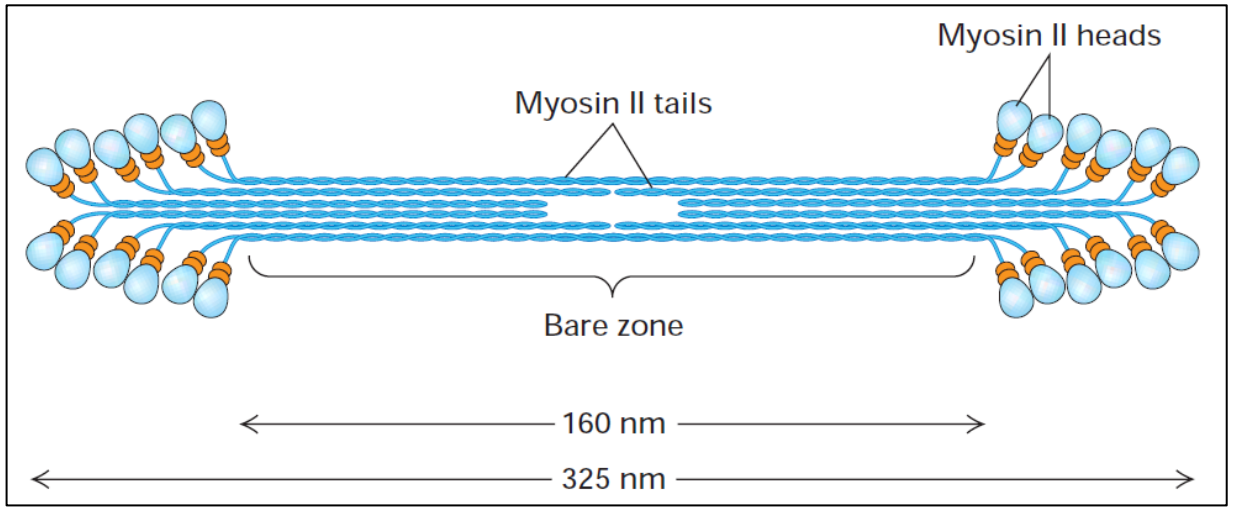
5-10nm motion



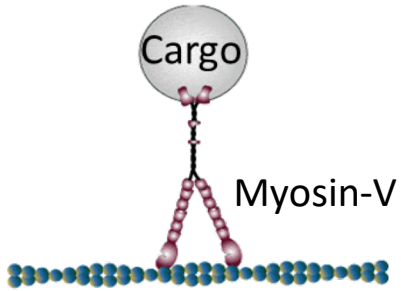
https://www.ibiology.org/cell-biology/muscle-biology/#part-1



Myosin-II generates muscle contraction by assembling into BIPOLAR filaments :-



Formation of such Myosin-II Assemblies is very different from Cargo-carrying motors
(e.g. Myosin-V, Kinesin, Dynein)



Myosin, Actin and Muscle

Lodish Molecular Cell Biol

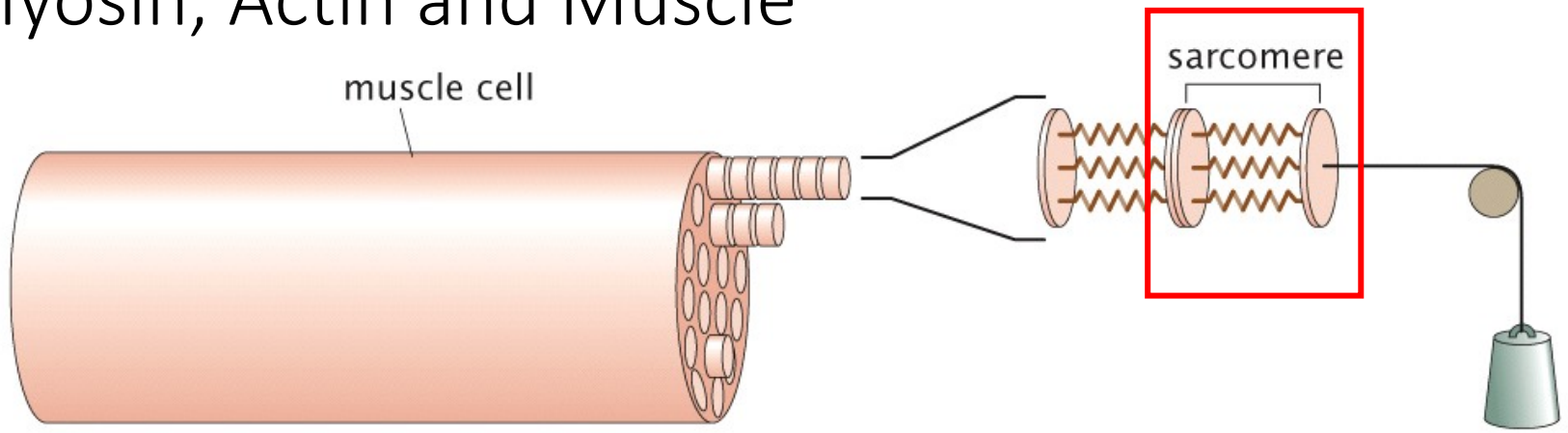
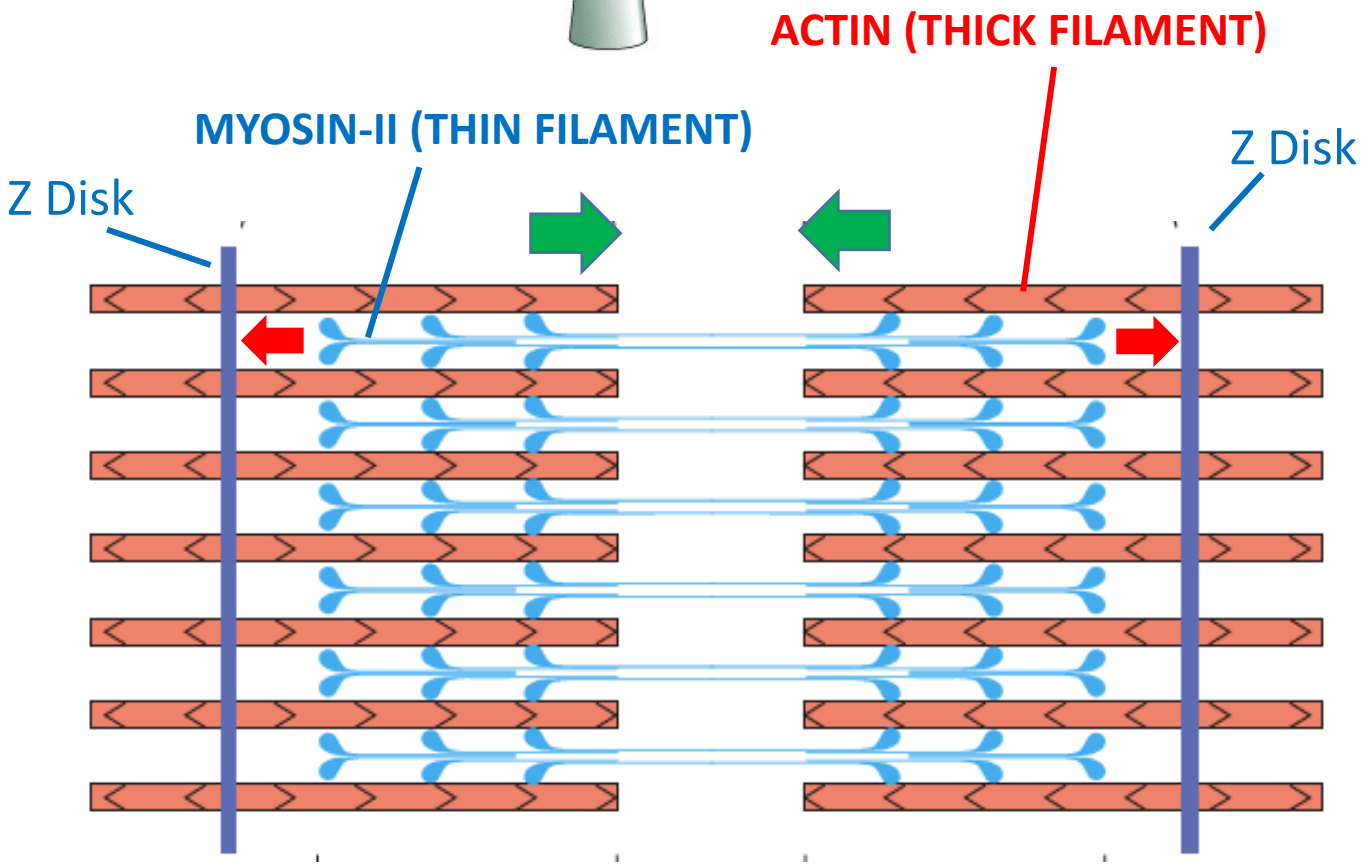


Figure 16.8 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Sarcomere can contract like a spring to lift load



Recall from Section-2

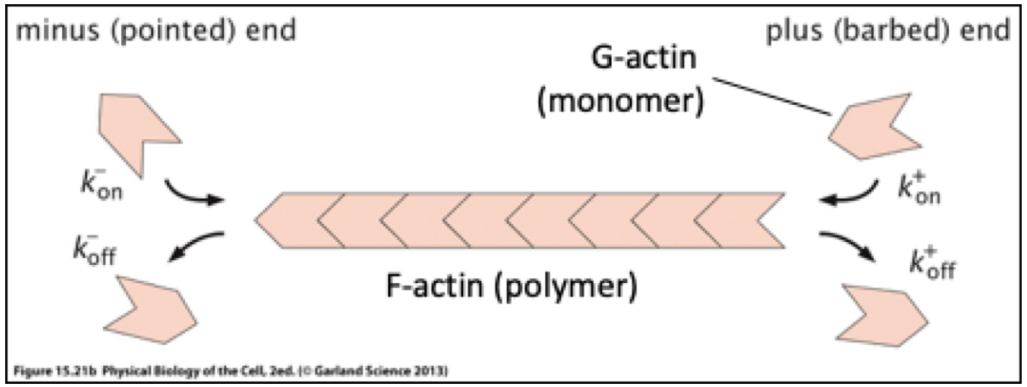
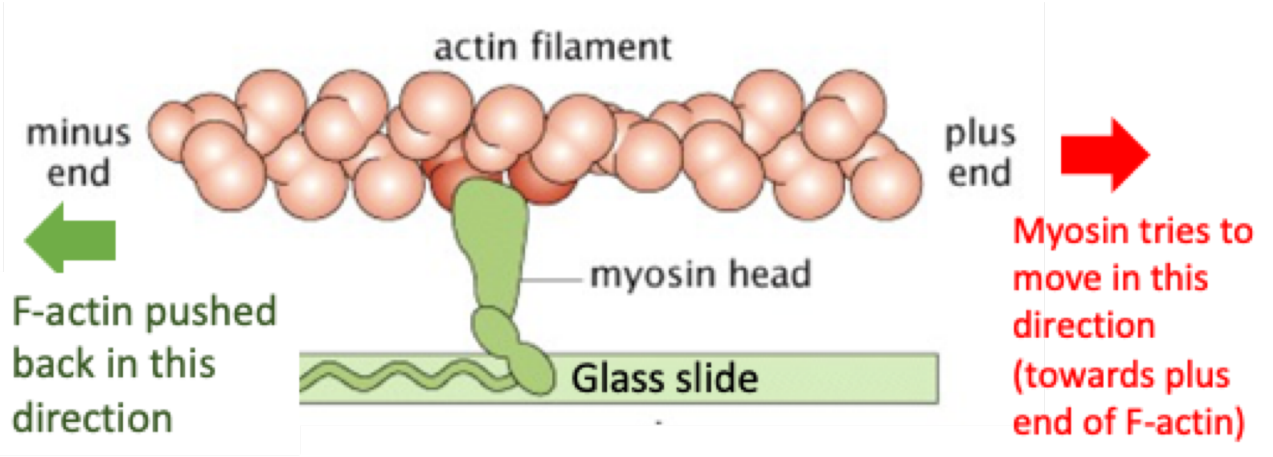


Figure 15.21b Physical Biology of the Cell, 2ed. (© Garland Science 2013)



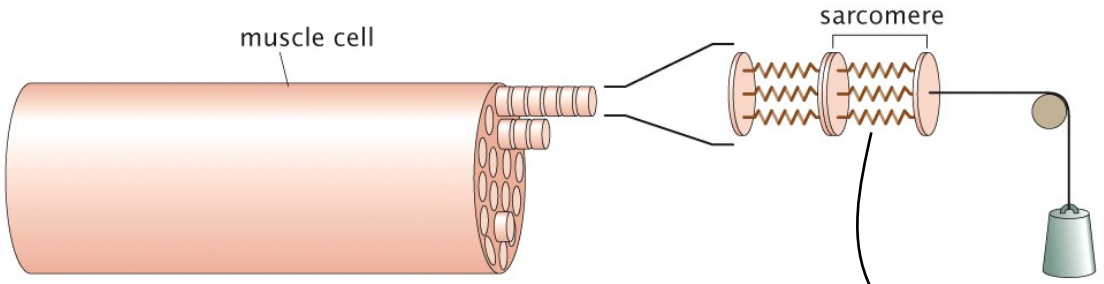
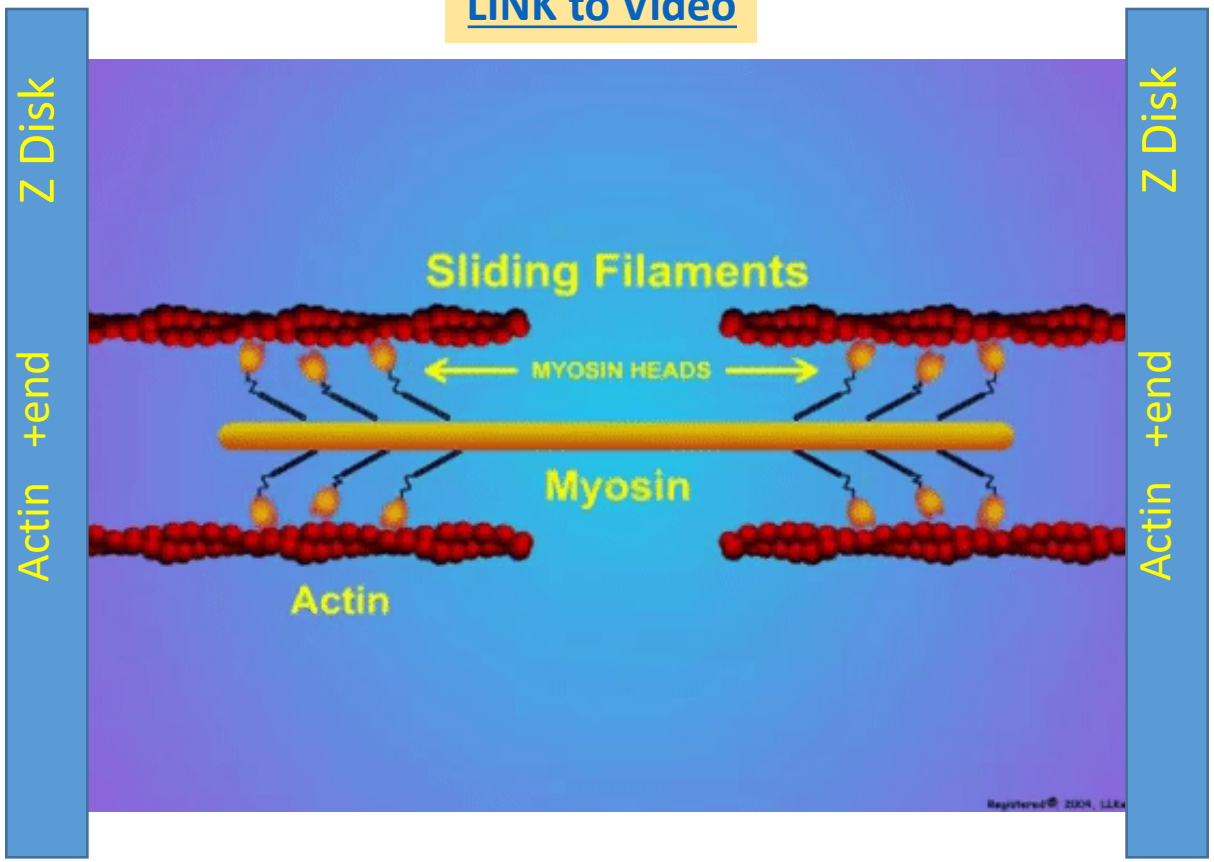


Figure 16.8 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Sarcomere Animation

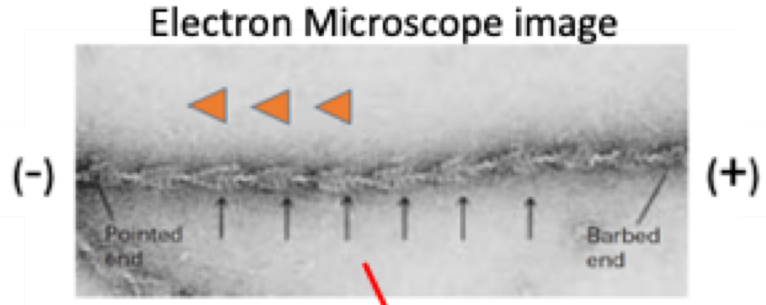
LINK to Video

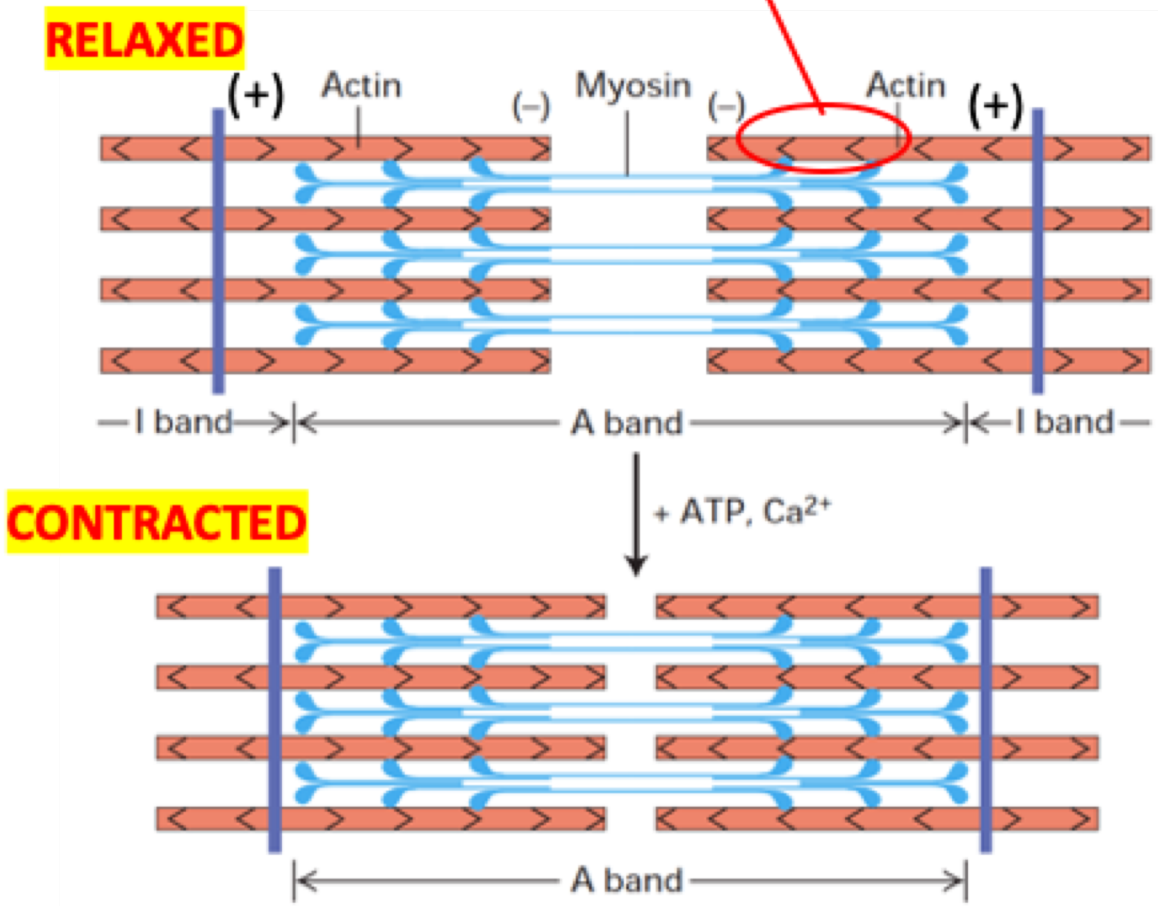


Muscle Contraction - Summary

- Muscle Cell is packed with repeating *Sarcomeres* (region between two Z-disks)
- Sarcomere contains two inter-digitating structures
  - ❑ **Thick filaments,** containing myosin
  - ❑ **Thin filaments**, containing F-actin
- F-actin & Myosin within Sarcomere are **Bipolar**
- Nerve Impulse at Motor Neuron increases Ca^{2+} in muscle cell
  - ❑ Certain proteins (Tropomyosin) that otherwise block Actin-binding site of Myosin now release those sites
  - ❑ Myosin can then bind Actin and hydrolyses ATP to generate Force and move
- Myosin in each half of a Sarcomere moves towards the +end of Actin (the Z-disk)
  - ❑ Actin filaments come closer in the middle
  - ❑ Therefore the Z disks come closer
  - ❑ Causes Contraction of Sarcomere (upto 70% of its resting length) → Contraction of Muscle

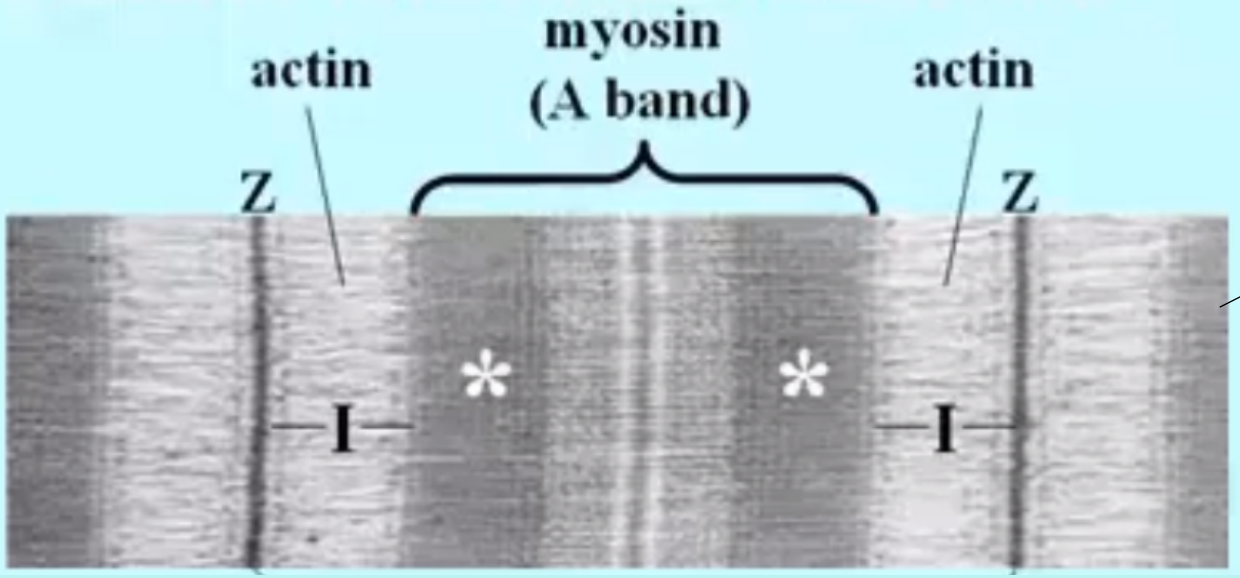
Polarity of actin. "Arrows" are pointing to the –end (pointed end) of F-actin





Electron microscope images of Relaxed and Contracted Muscle

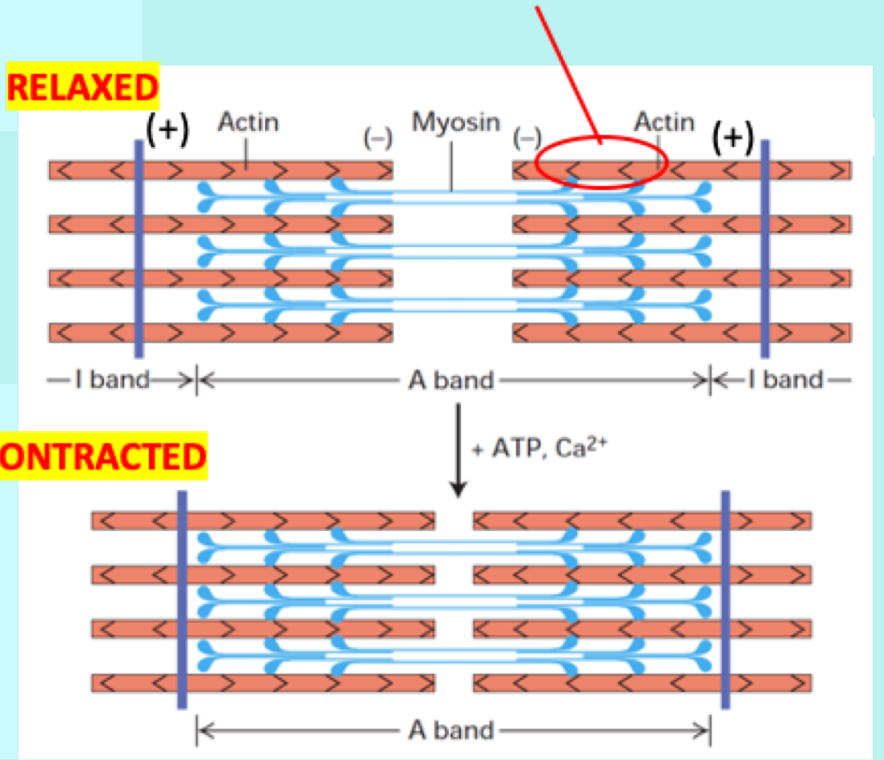
relaxed



Actin | Actin + Myosin | Myosin | Actin + Myosin | Actin

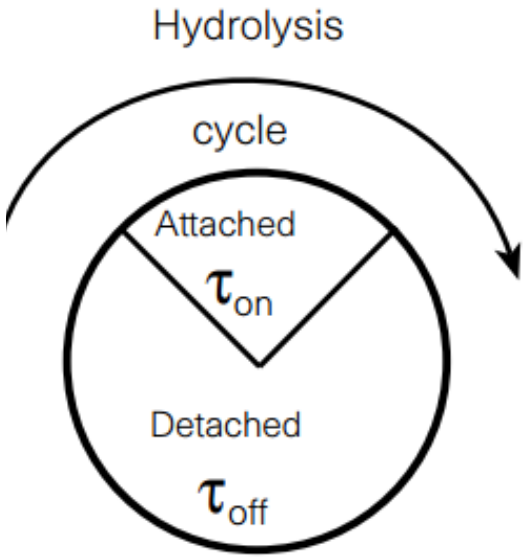
contracted

Only Myosin region is almost gone



From CMB5e Video

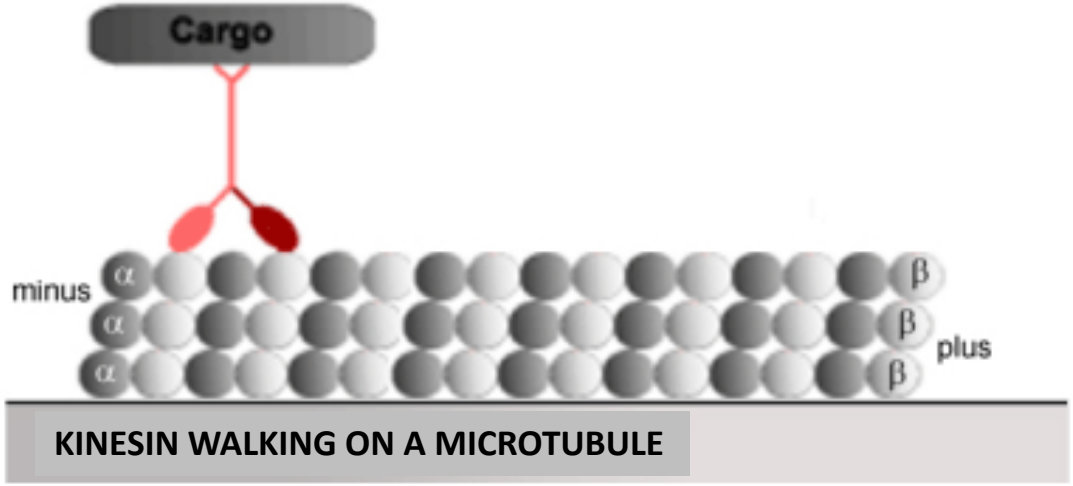
* regions where thick & thin filaments overlap



$$Duty\ Ratio\ (= r)$$

$$r = \frac{\tau_{on}}{\tau_{on} + \tau_{off}} = \frac{\tau_{on}}{\tau_{total}}$$

http://www.imb-jena.de/~kboehm



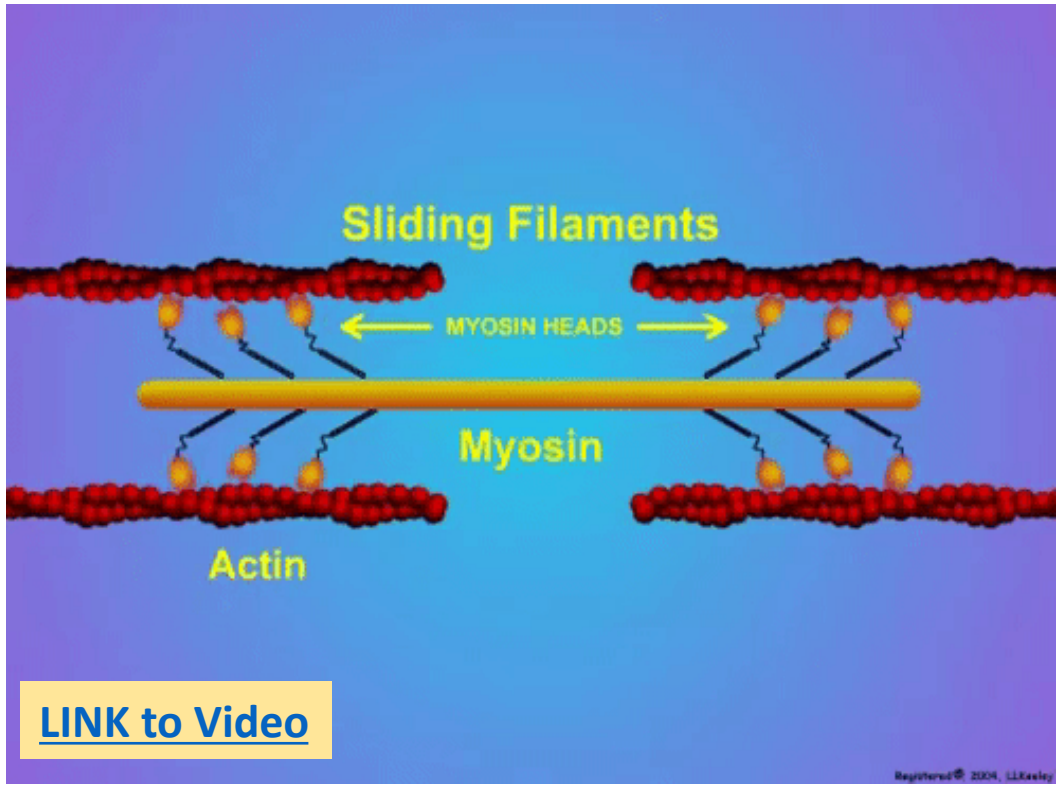
KINESIN WALKING ON A MICROTUBULE

Kinesin is a Processive Motor. It has a high Duty Ratio.
r = 0.5 for each Leg, $r \approx 1$ for the two-legged Kinesin
→ A Single Kinesin can take many Successive Steps.

Not all Motors are Processive. Duty Ratio can be Smaller.
Example : Muscle Myosin pulling on Actin filaments

Each Myosin head attaches to Actin for a short time (=τ_{ON}) and generates force. Then, myosin needs a long time to recover (=τ_{OFF}).

r for Muscle myosin = 0.2



How do we know that Myosin Generates Force towards plus end of Actin?
ACTIN GLIDING ASSAY

Actin glides with Minus-end leading

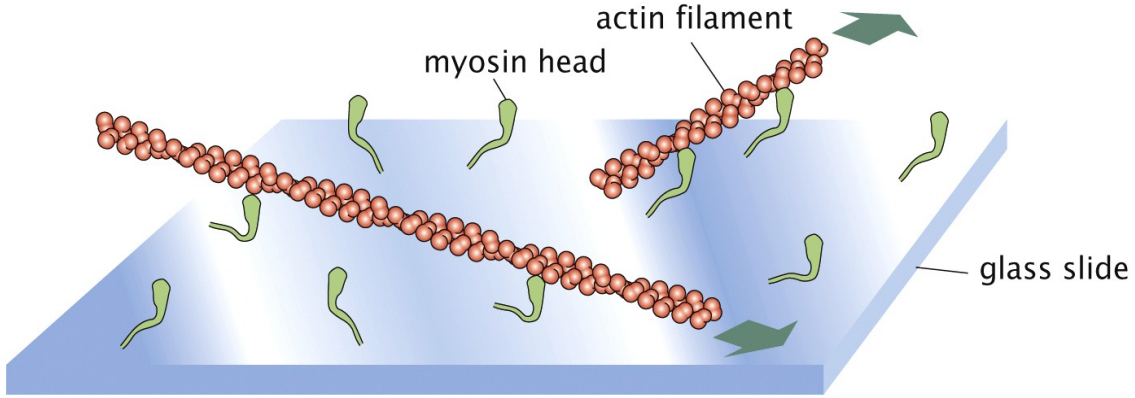


Figure 16.9a Physical Biology of the Cell, 2ed. (© Garland Science 2013)

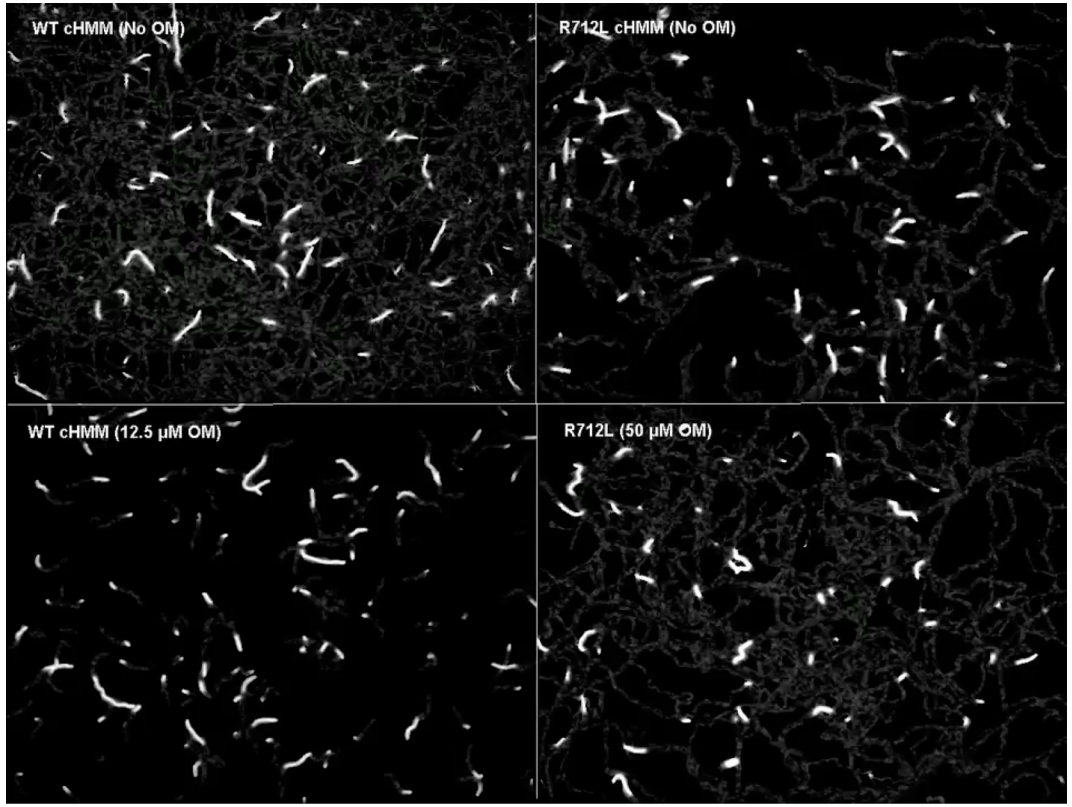
[Snoberger et al, ELife]

Myosin with hypertrophic cardiac mutation R712L has a decreased working stroke which is rescued by a Drug Called Omecamtiv Mecarbil (OM). OM is a cardiac-specific myosin activator.

Actin Gliding with Cardiac Myosin :-

1. Normal Myosin. No OM (Works well)
2. R712L Myosin. No OM (Problem)
3. Normal Myosin. With OM (Problem – WHY?)
4. R712L Myosin. With OM (Works well)

1



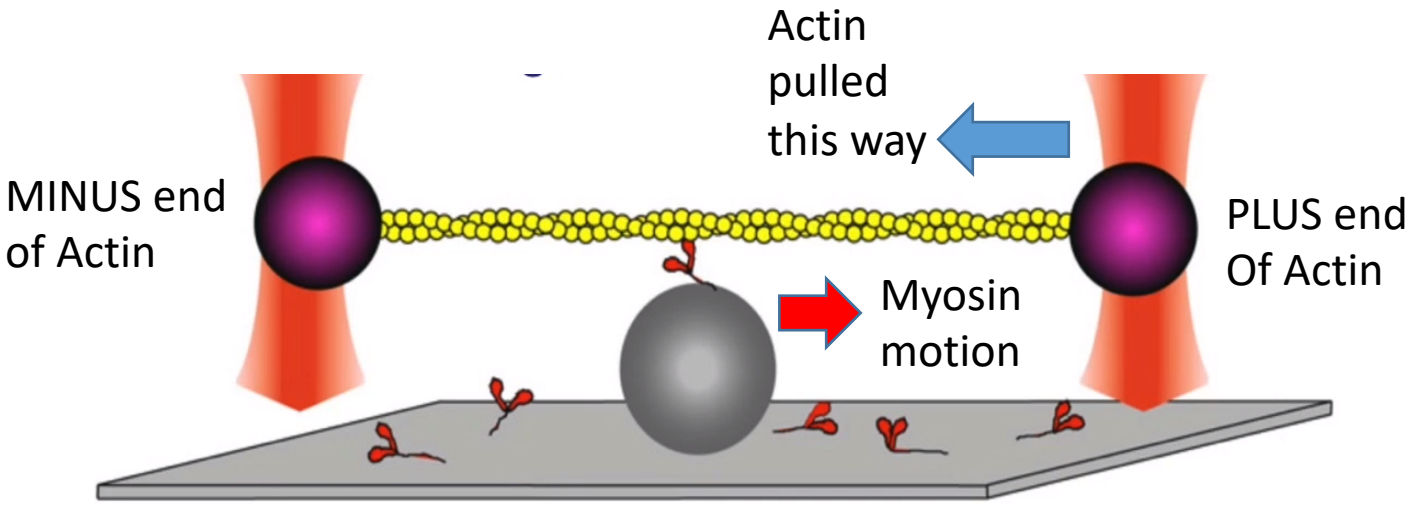
2

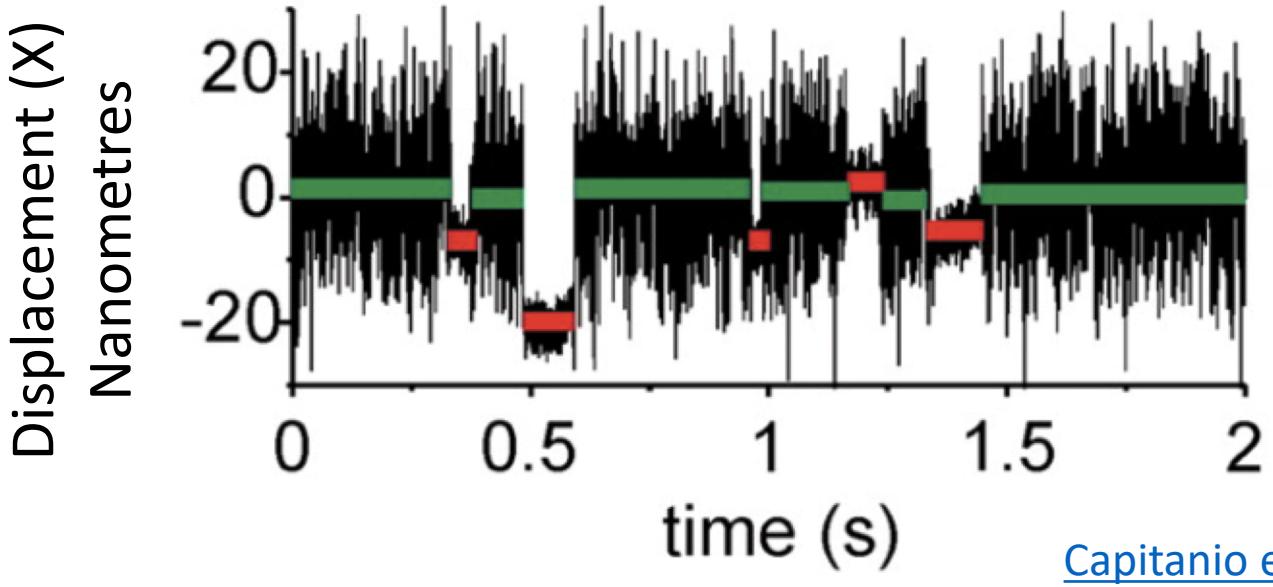
3

4

https://www.ibiology.org/cell-biology/muscle-biology/#part-1

Muscle Myosin in Dual beam laser trap



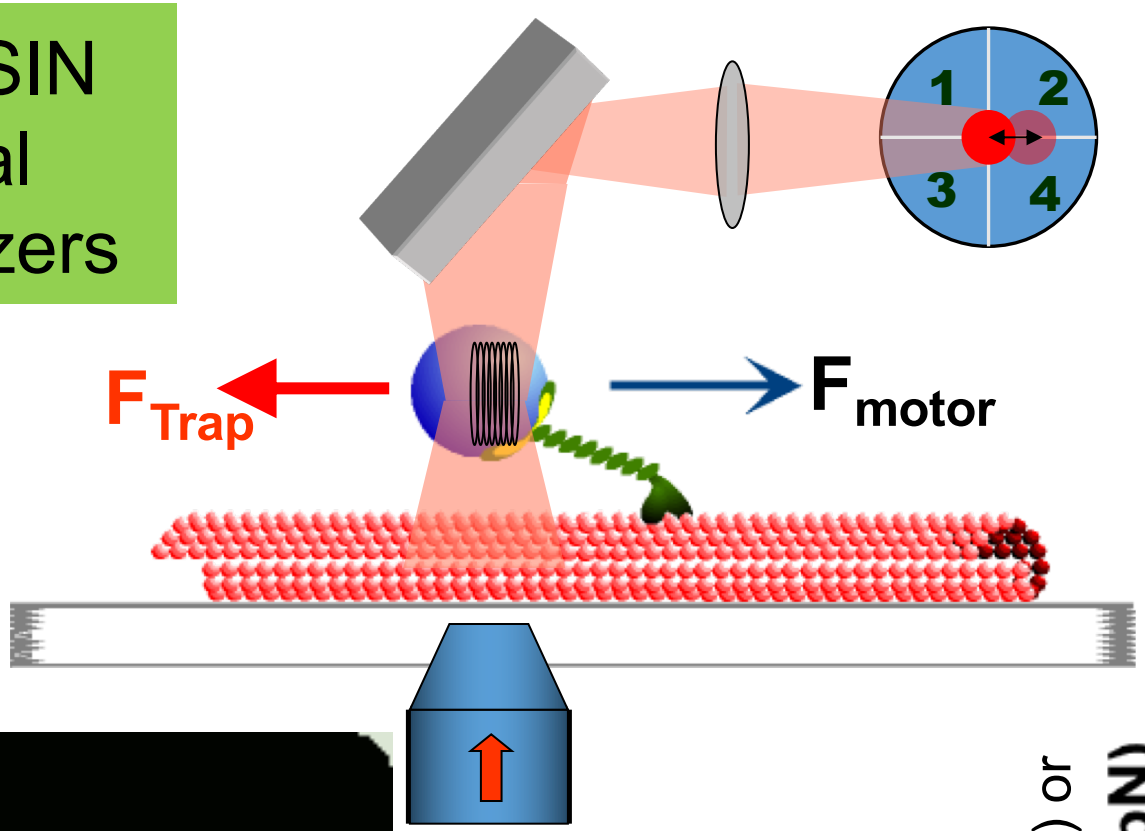


Not active
Active

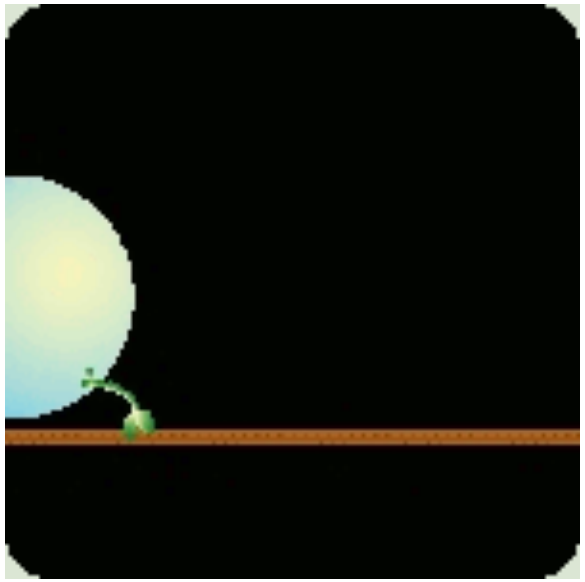
How does this experiment compare to Kinesin in Single beam Optical Trap ?

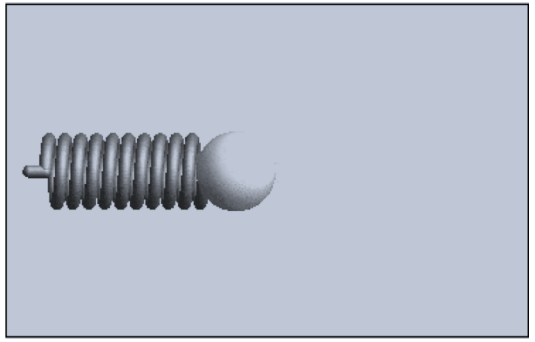
Capitanio et al, PNAS 2005

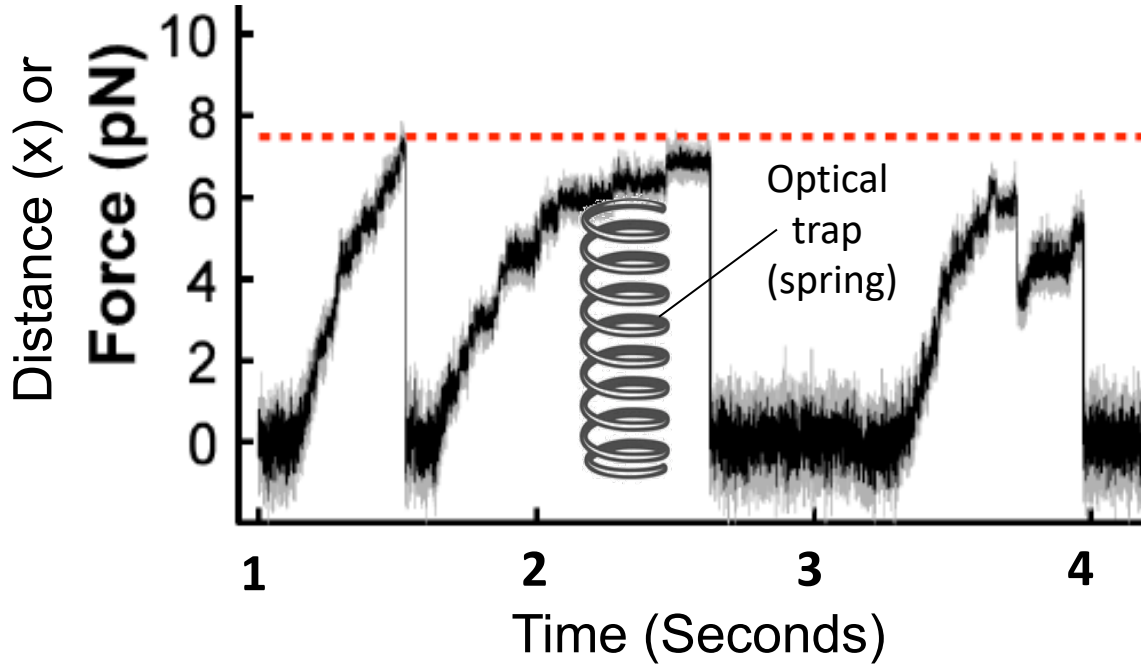
KINESIN Optical Tweezers



Force = Distance * K_{TRAP}



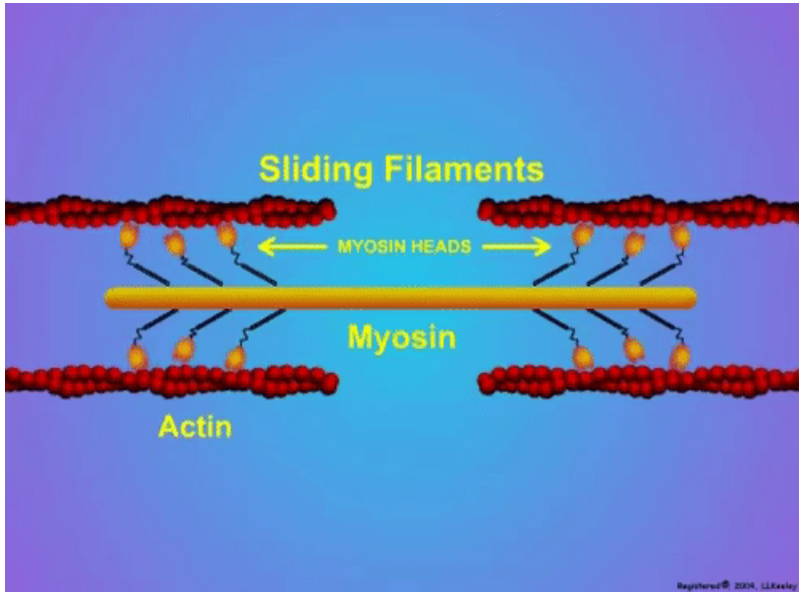




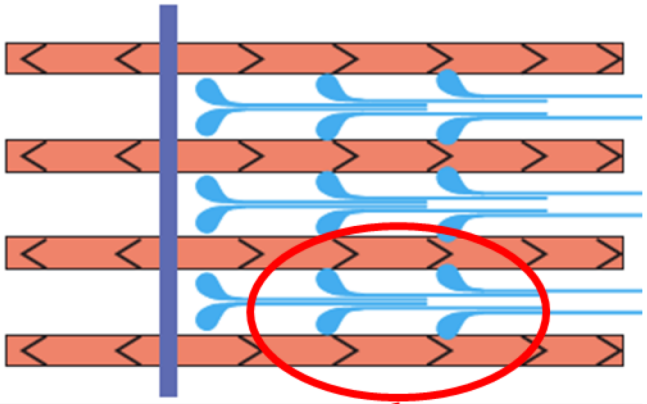
Credit : George Shubeita

PORTERS (High Duty Ratio)

ROWERS (Low Duty Ratio)



Muscle is actually much more complicated and we don't understand most of it …



ZOOM IN