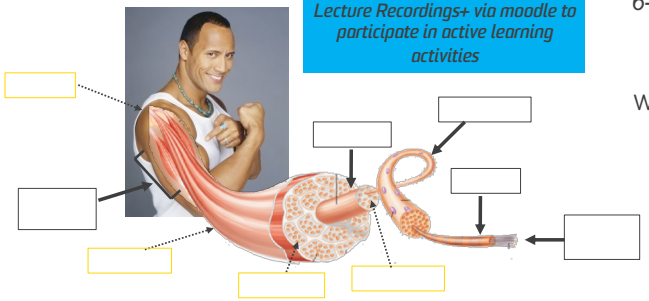
PHSL2101/PHSL2121/PHSL2501

Muscle 2

Dr. Chelsea Goulton
6-March-2018

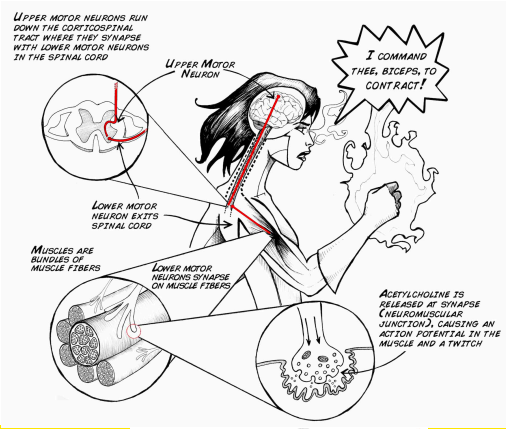
Please log in to ECHO360/ Lecture Recordings+ via moodle to participate in active learning activities



Review:
While you are waiting:
Fill the Gaps!
No cheating 😉

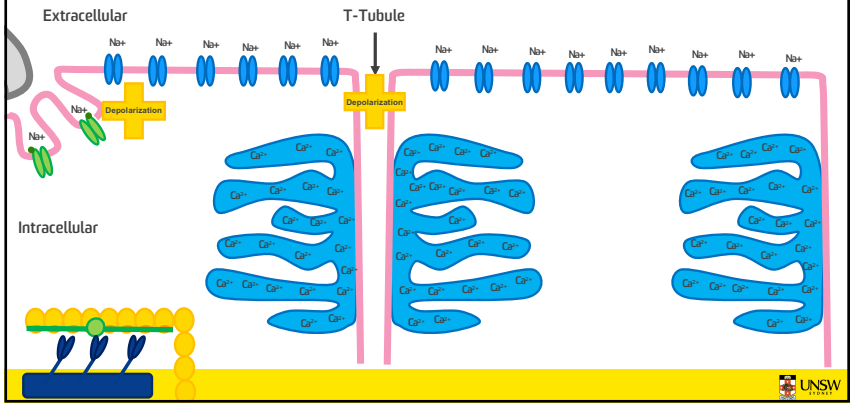
Muscle Structures
Connective Tissues

Review

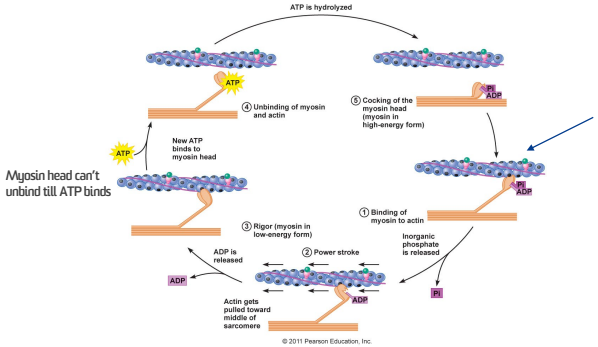


BACKYARD BRAINS

Review: Excitation-Contraction Coupling



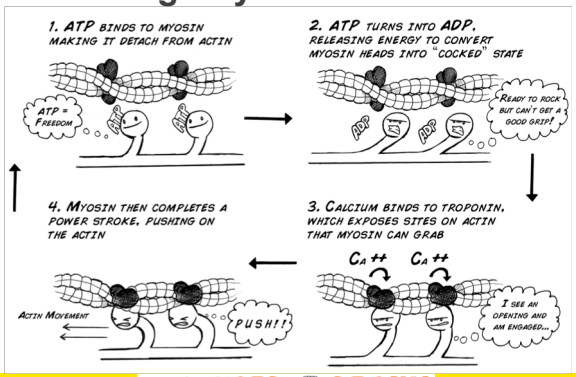
The Crossbridge Cycle



- Ca^{2+} concentration rises
- Binds to Troponin Complex
- Tropomyosin moves to expose the myosin binding sites

High energy to low energy conformation of myosin head

The Crossbridge Cycle

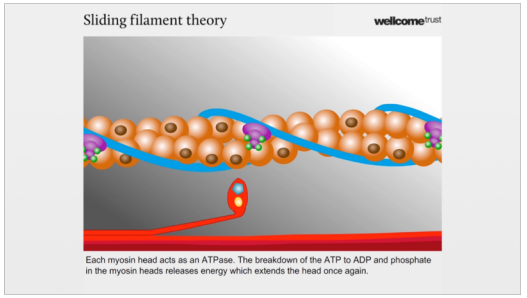


BACKYARD BRAINS

UNSW

Sliding Filament & Cross-bridge Cycle Summary

BigPicture
Bringing cutting-edge science into the classroom and beyond



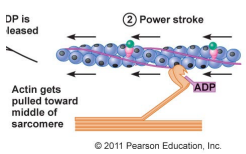
Video: www.bigpictureeducation.com/animation-sliding-filament-theory

UNSW

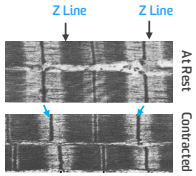
It's the little things…

Take a moment to appreciate the scale of what is going on.

Myosin heads move 10nm during a powerstroke



Each sarcomere will contract by 1-2μm during a twitch



The whole muscle can shorten a number of cm e.g. biceps 2-3cm

Multiple Choice

What two major regulatory molecules/ions could you remove to stop the cross-bridge cycle?

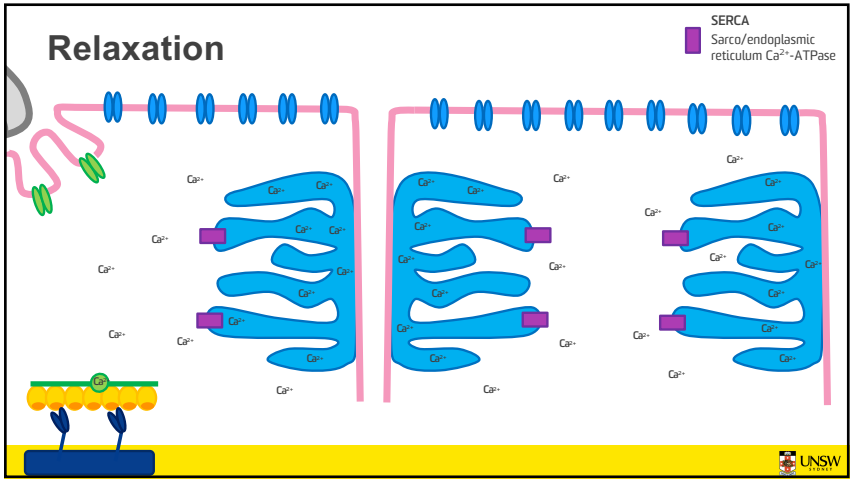
- Phosphate and ATP
- Ca2+ and ADP
- Ca2+ and ATP
- ATP and Troponin

Multiple Choice

And which actuallly gets removed to stop the cross-brdige cycle and allow muscle relaxation?

- Calcium
- ATP
- ADP
- Phosphate
- Troponin

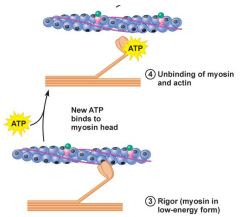
Relaxation



Rigor Mortis

When you die, your circulation stops, meaning that muscle cells are no longer provided with nutrients & oxygen

- Within a few hours, cells run out of ATP and are unable to produce more
  - ATP is required to actively pump Ca^{2+} ions out of the cytosol.
  - ATP is also required to unbind the myosin head from the actin binding site
- Once ATP levels become too low:
  - Ca^{2+} concentration gradually rises to trigger a sustained contraction
  - Myosin molecules become stuck in the cross-bridge
  - Hence all the muscles become stiff



You do not want your muscles to run out of ATP!

Factors affecting force output

The key determinant is how many cross-bridges can form

- But when a neuron activates a muscle fiber, the contraction response is all or none
- And we know some fibers/whole muscles can generate variable amounts of force

So what factors can affect how much force a muscle can develop?

1. Frequency of stimulation
2. Changes in length
3. Number of fibres stimulated
4. Fiber diameter

You will get to explore these in the prac lab

1. Frequency of Stimulation

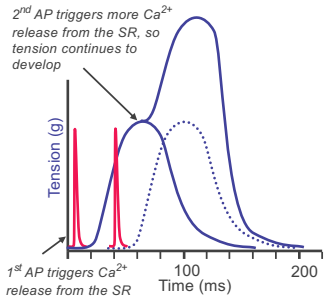
When looking at a single muscle fiber, a single twitch is not long enough for maximal force to be generated.

There are two reasons for this:

1. Ca^{2+} released from the SR is not enough to saturate troponin complex binding sites
2. *Energy goes into taking up the slack in the elastic elements of the tissue before external tension is developed.*

If a 2nd AP comes along before the fiber has completely relaxed from the first twitch, there will be an additive effect

- This is called **summation**

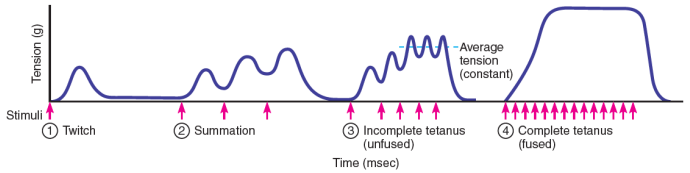


Adapted from Principles of Human Physiology (2013)

1. Frequency of Stimulation

At higher frequencies of stimulation, summation will bring the muscle to its maximal force output

- This is called a **tetanus**
- Tetanic stimulation of muscle fibres plays a key role in allowing us to perform smooth, fluid muscle movements



You will get the chance to prove this to yourself in the lab

Principles of Human Physiology (2013)

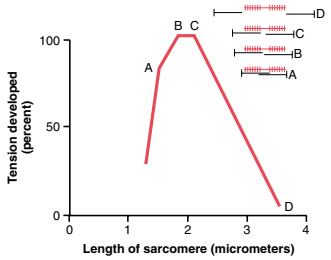
2. Changes in Fiber Length

To understand why the length is important, you need to think about the **sliding filament theory**

- Remember: Force is all about the number of cross-bridges that can form
- So if sarcomere is too stretched or too compressed less force will be developed

Remember **Titin** the molecular spring?

- Positions thick & thin filaments in the optimal position to generate force upon initiation of contraction



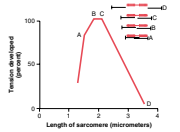
2. Changes in Fiber Length

Interestingly, you do not get quite the same relationship in whole muscle

- Muscle fibres are made up of many sarcomeres in series, so why?

The key difference here is that whole muscle also has the many layers of elastic **connective tissue**

- Remember the bungy cord?
- When the muscle is stretched, they will also create tension. This is called **passive tension.**
- So the total force output will be a combination of **active tension** from cross-bridges and **passive tension** from connective tissues.



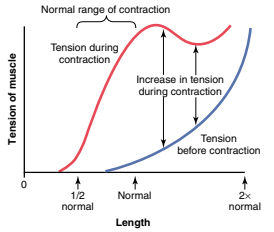


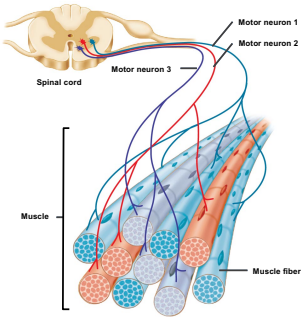
Figure 6-10 Relation of muscle length to tension in the muscle both before and during muscle contraction.

You will get the chance to replicate this result in the lab

3. Number of Muscle Fibres Stimulated

Each α-motor neuron branches to innervate a number of muscle fibers: This is called a **motor unit**

- Variable number of fibers in each motor unit
- Fibers are distributed through the muscle



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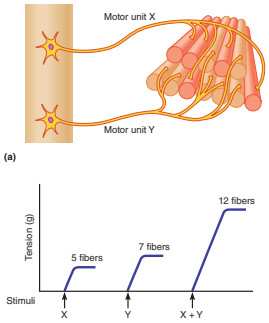
The total tension that a muscle produces can be varied a huge amount by:

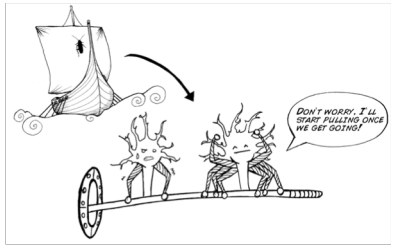
1. Selecting different sized motor units
2. Recruiting additional motor units as more force is required

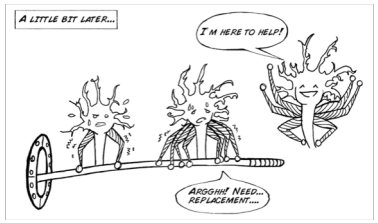


3. Number of muscle fibres stimulated

In vivo, the **recruitment** of motor units is done according to size

- Smaller motor units will be recruited first, followed by progressively larger motor units





BACKYARD BRAINS

3. Number of muscle fibres stimulated

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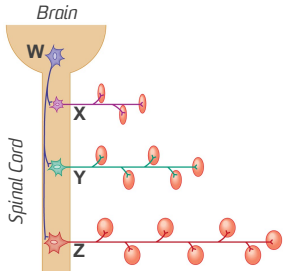
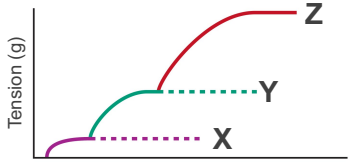




Excitation from Upper Motor Neuron
(Action Potential Frequency in W)

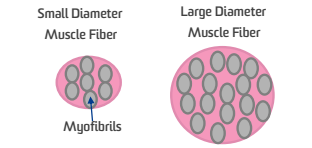
4. Fiber Diameter

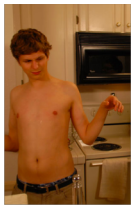
Larger diameter fibers can produce a great force upon contraction

- But there is no difference in cross-sectional density of thick & thin filaments
- Rather, there is a greater number of myofibrils within a muscle fiber

If a muscle fiber is stimulated lots it will grow in diameter

- This is called **hypertrophy**
- The number of fibers in the muscle does not change, but the diameter will increase
- This means that each fibre can produce more tension





Functional Requirements of Different Skeletal Muscles

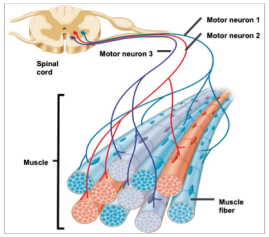
There are 650+ skeletal muscles in the human body

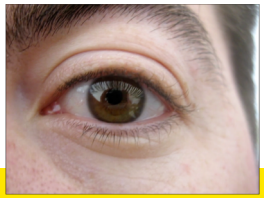
- Different muscles can have very different functional requirements.
- What varies between muscle types to allow for this?

Motor Units

Motor units can vary hugely in size between different types of muscle

- In the eye, one nerve will innervate ~12 fibres.
- While in the leg, one nerve may innervate 2000+ fibres.
- Relates to how fine finely controlled the muscle contractions need to be





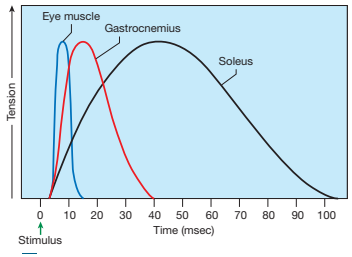
Slow-Twitch & Fast-Twitch Muscle Fibres

There are two main types of fibre in skeletal muscle

- Type I or “Slow-Twitch”
- Type II or “Fast-Twitch”

Key differences are:

- How quickly they contract & relax
- How they generate their ATP
- Rate of fatigue



Most muscles will have a mixture of the two types,
with the ratio reflecting the main functional requirement of that muscle

Muscle Fiber Types: Fast vs. Slow Twitch

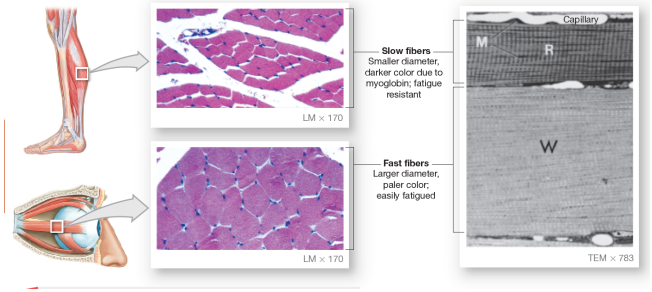
Table 10–2 Properties of Skeletal Muscle Fiber Types

Property	Fast Fibers	Slow Fibers
Cross-sectional diameter	Large	Small
Time to peak tension	Rapid	Prolonged
Contraction speed	Fast	Slow
Fatigue resistance	Low	High
Color	White	Red
Myoglobin content	Low	High
Capillary supply	Scarce	Dense
Mitochondria	Few	Many
Glycolytic enzyme concentration in sarcoplasm	High	Low
Sources of substrates for ATP generation during contraction (metabolism)	Carbohydrates (anaerobic)	Lipids (fatty acids), carbohydrates, proteins (amino acids) (aerobic)
Alternative names	Type II-B, FF (fast fatigue), white, fast-twitch glycolytic	Type I, S (slow), red, SO (slow oxidative), slow-twitch oxidative

Sarcoplasmic Reticulum — Envelops every myofibril — Envelops groups of myofibrils

Muscle Fiber Types: Fast vs. Slow Twitch

Figure 10–21 **Fast versus Slow Fibers.** The TEM on the right is a longitudinal section of skeletal muscle, showing more mitochondria (M) and a more extensive capillary supply in a slow fiber (R, for red) than in a fast fiber (W, for white).



But most muscles have roughly 50% each fiber type

Multiple Choice

If you had a greater proportion of Type I (slow twitch) fibres in your quad muscles, which of the following do you think you might be best at?

- Sprinting
- Marathon Running
- High Jumping

Are athletes born or made?

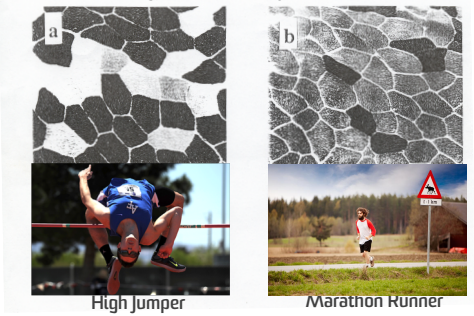
Generally accepted that the ratio of Type I to Type II fibres is determined by genetics

- The ratio you are born with is the ratio you maintain

Many studies have shown a relative difference in ratio of fibres in speed vs. endurance athletes

Cross Section of Quadriceps Muscle

(Type II/Fast twitch fibres stain dark)

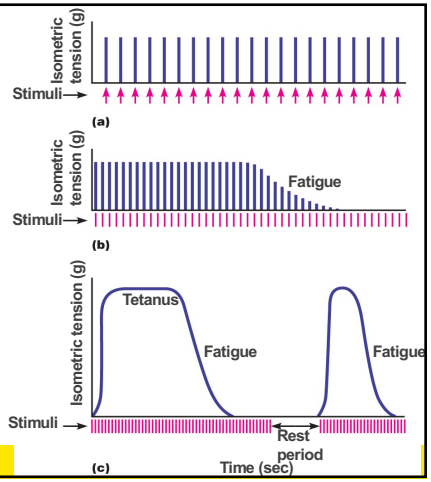


High Jumper — Marathon Runner

Fatigue

Don't have time to go into the details of fatigue (and you don't need to know them!)

- But just so you are aware, it's a "tiring out" of the muscle fibres
- Can no longer produce maximum force



Asynchronous Activation of Motor Units

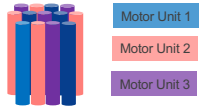
When you initate a muscle contraction, all motor units involved will not be stimulated at once

- One example demonstrating this is with **recruitment**

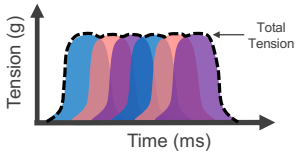
Asynchronous activation also helps to produce smooth movements over time

- Different motor units will fire on and off throughout the movement
- This reduces fatigue and helps maintain constant force over longer periods of time

E.g. carrying your shopping bags down the street



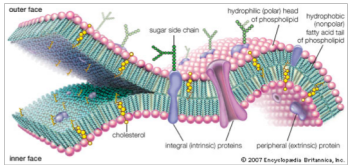
This is a cross section of muscle showing fibres from three motor units



Consider this…

We have these strings of molecular motors, moving around and generating force, bundled up inside the sarcolemma

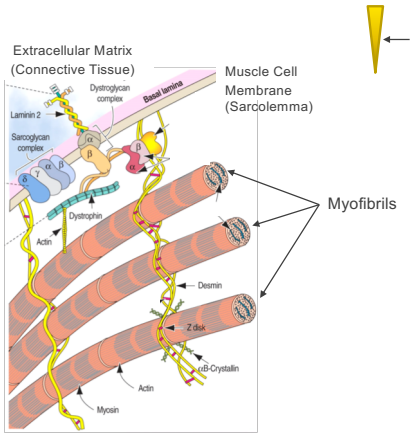
- The sarcolemma is a lipid bilayer, how does all this movement not just bust it apart?



Structural Proteins

One essential role is in protecting the muscle cell from being damaged during contraction

- Proteins involved in stabilizing the sarcolemma
  - Dystrophin & the Dystrophin Associated Complex
  - Responsible for a class of genetic disorders – Muscular Dystrophies



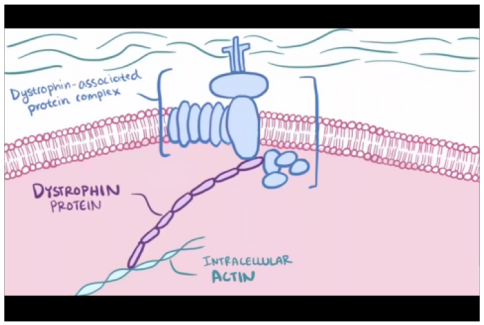
Duchenne Muscular Dystrophy

2nd most common fatal genetic disease in children.

- 1:3300 live male births
- X-linked recessive condition
- Typically wheel chair bound by age 10-12
- Generally die in 20's due to respiratory or cardiac failure

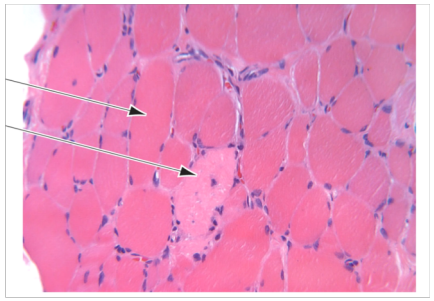
Duchenne's Muscular Dystrophy

- Genetic mutation leads to loss of functional dystrophin
- Sarcolemma is not as stable so it can get damaged
- Repeated damage leads to degeneration of the muscle fiber
- Muscles atrophy



Full Video: https://www.youtube.com/watch?v=DGOmN6rnsNk

Duchenne's Muscular Dystrophy



But the sarcolemma is still fragile…

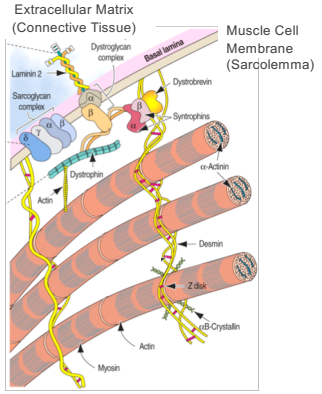
Even in healthy cells muscle damage can occur after strenuous activity

- Delayed Onset Muscle Soreness (DOMS)
  - Generally felt a few hours after exercise and can last up to a few days
- Partly due to small tears in the muscle tissue
  - Levels of creatine kinase and myoglobin are elevated in the blood
  - Suggests sarcolemma damage is involved
  - Leads to activation of pain receptors
- But what doesn't kill you makes you stronger!
  - Muscle damage in small amounts leads to hypertrophy.

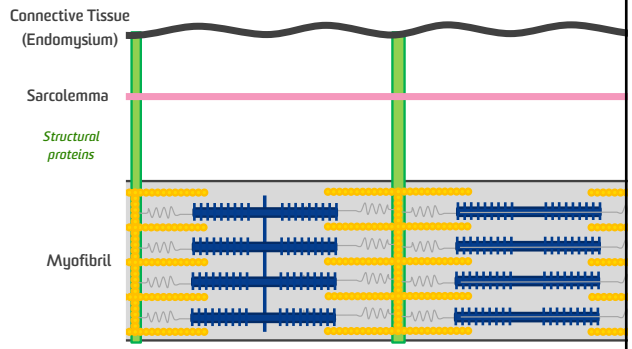
Structural Proteins

Another role is in transmitting force outside the cell to the connective tissues

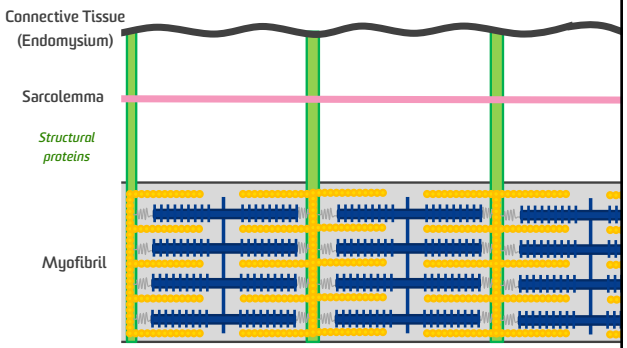
- Don't need to know specific proteins involved
- Z-lines of myofibrils are aligned by these structural proteins
- These attach to the sarcolemma and also interact with the surrounding connective tissue
- In this way, force is transmitted laterally as well as longitudinally



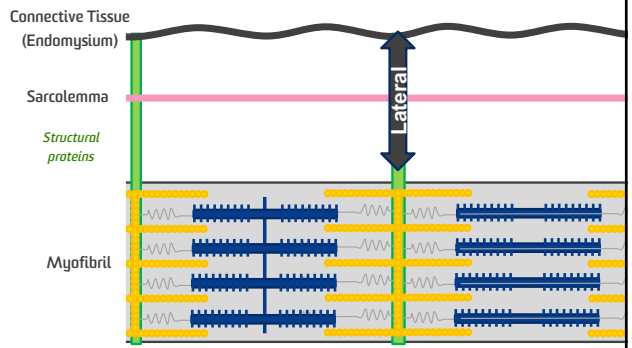
Relaxed



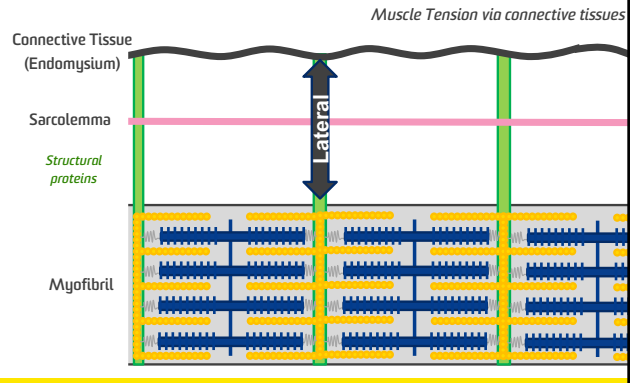
Contracted



Relaxed

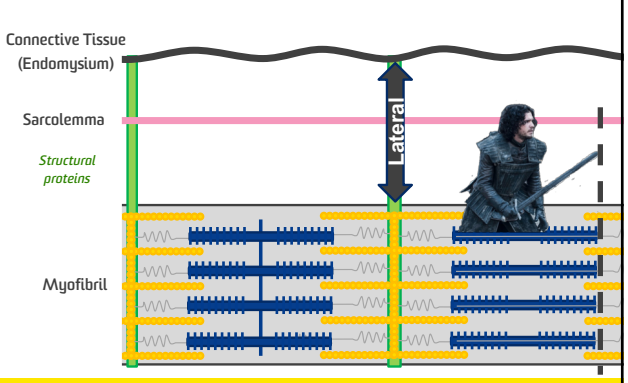


Contracted



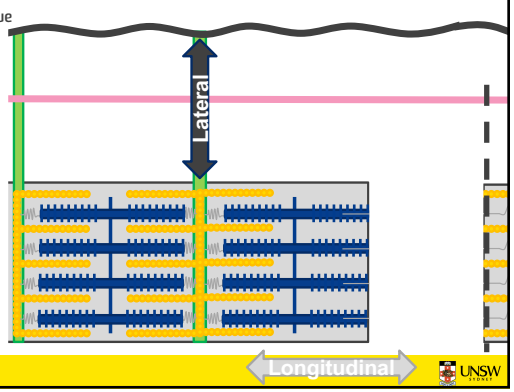
Relaxed

- But muscle fibers are very long
- What happens if it is damaged?



Contracted

- The longitudinal transmission in that fiber might be lost
- But lateral transmission maintained in intact portions of the fiber
- Interactions between muscle fibers and connective tissue layers means force output is maintained



Learning Objectives: Skeletal Muscle (Lecture 2)

1. Describe the steps involved in the cross-bridge cycle
2. Explain the mechanisms which control force output from skeletal muscle.
3. Outline the differences between slow-twitch and fast-twitch muscle fibres and how they affect skeletal muscle contractions.
4. Understand the importance of structural proteins in maintaining muscle function

Skeletal Muscle

Allows us to move within and interact with the world around us.

What are the main requirements?

- Generate movement of body structures
- Respond quickly
- Generate variable force
- Adapt to demands