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PHSL2101/PHSL2121/PHSL2501

Muscle 1

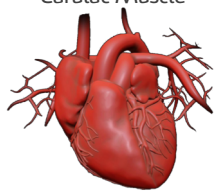
Dr. Chelsea Goulton

4-March-2019

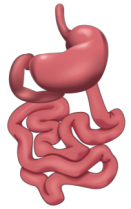
The Big Picture

Skeletal Muscle

Cardiac Muscle



Smooth Muscle



Overall learning objectives:

- To describe the three types of muscle in the body in terms of structure and mechanisms of contraction
- To compare and contrast between the different muscle types

Learning Objectives: Skeletal Muscle (Lecture 1)

1. Describe the different levels of skeletal muscle structure, naming structures and tissues from macroscopic to microscopic.
2. Explain how skeletal muscle contraction is initiated at the neuromuscular junction
3. Describe the sliding filament hypothesis
4. Describe the process of excitation-contraction coupling in skeletal muscle.
5. Understand the different roles of contractile proteins, structural proteins and connective tissues during muscle contractions.

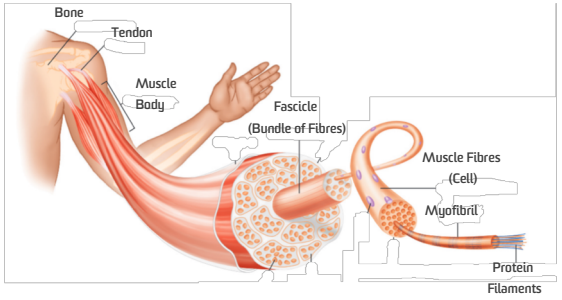
Skeletal Muscle

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

Skeletal Muscle Structure: An Overview



Macroscopic

Muscle Body

Fascicles

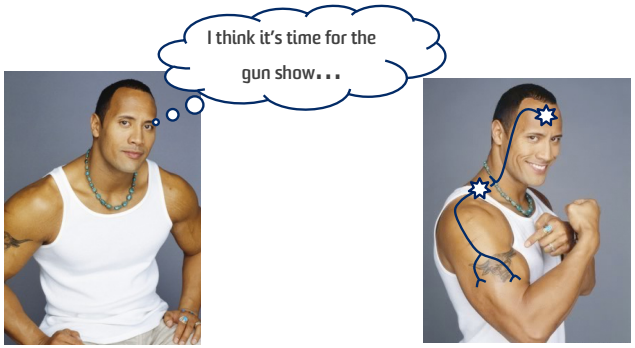
Muscle Fibre

Myofibrils

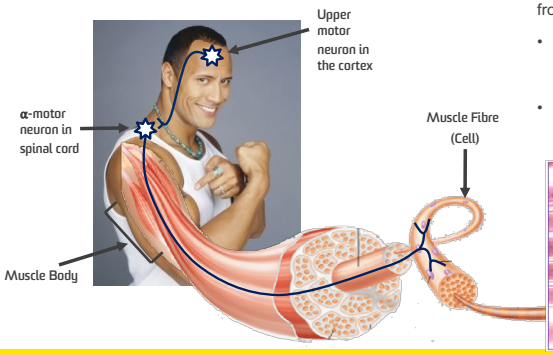
Protein Filaments

Microscopic

From thoughts to actions



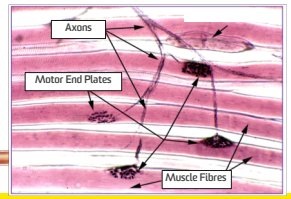
Innervation by Motor Neurons



Each **muscle fibre** will receive input from only **one α-motor** neuron

- But that neuron will form many **neuromuscular junctions** along its length
- This means the signal to contract is quickly spread throughout the fibre

**requirement: respond quickly*

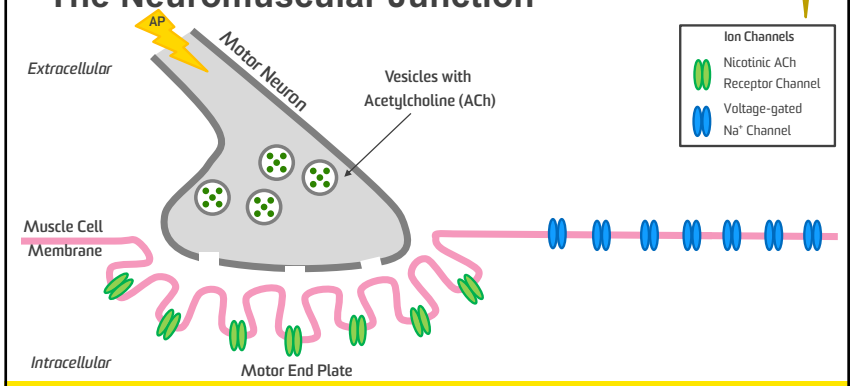


Multiple Choice

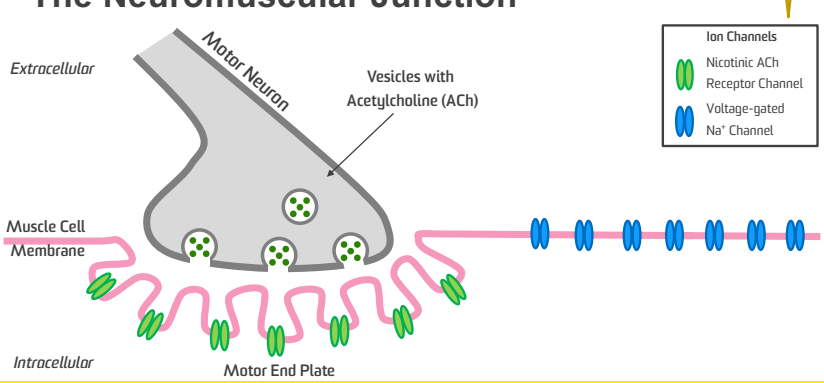
Which of the following neurotransmitters is released at the neuromuscular junction?

- Dopamine
- Glutamate
- Acetylcholine
- GABA

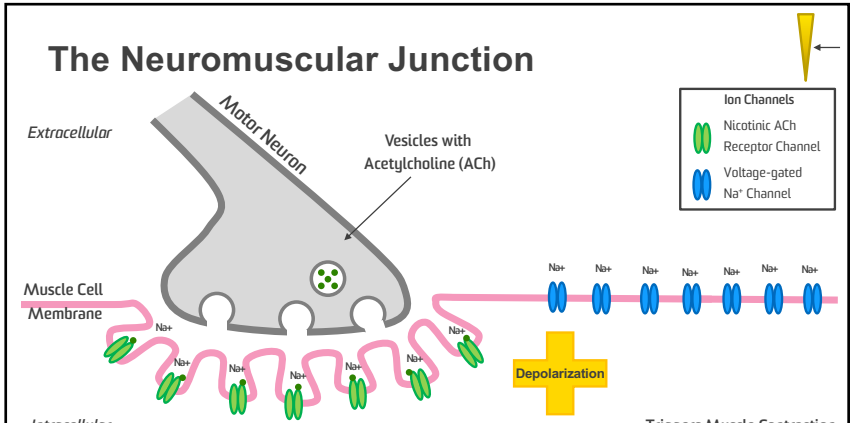
The Neuromuscular Junction



The Neuromuscular Junction



The Neuromuscular Junction

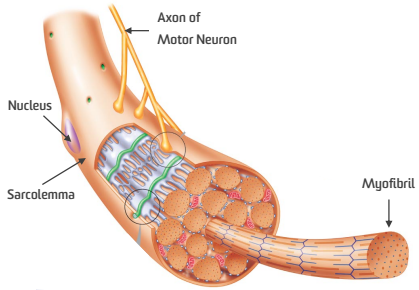


High density of ACh receptors = if the motor neuron fires the muscle fibre will almost always contract

Muscle Fibres/Fibers

Also known as muscle cells or myocytes

- Very long cell (runs full length of the muscle)
- Innervated by a single motor neuron
- **Sarcolemma** – plasma membrane of a muscle cell
- Contains hundreds of **myofibrils**
- Has many nuclei



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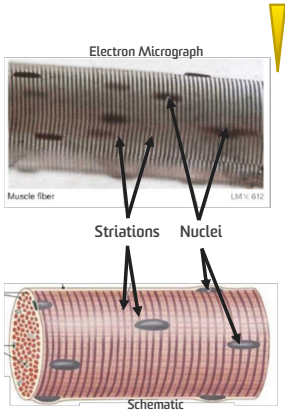
- Very long cell (runs full length of the muscle)
- Innervated by a single motor neuron
- **Sarcolemma** – plasma membrane of a muscle cell
- Contains hundreds of **myofibrils**
- Has many nuclei
- **Striated** appearance under the microscope
  - Comes from very organised structure within the myofibrils

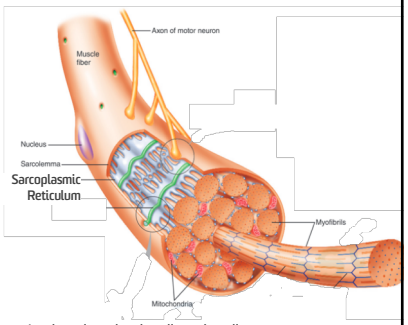


More on Muscle Fibres

Myofibrils are surrounded by a network of **sarcoplasmic reticulum (SR)**

- The SR is an essential store of Ca^{2+}
- Ca^{2+} is a tightly controlled signaling molecule in the cytoplasm of cells
  - In muscle cells it is a signal which initiates contraction
- A healthy resting muscle cell has a cytoplasmic Ca^{2+} concentration in the nanomolar range ($x10^{-9}$)
- Compare this to the SR, which has a Ca^{2+} concentration in the millimolar range ($x10^{-3}$)

= Big driving force!



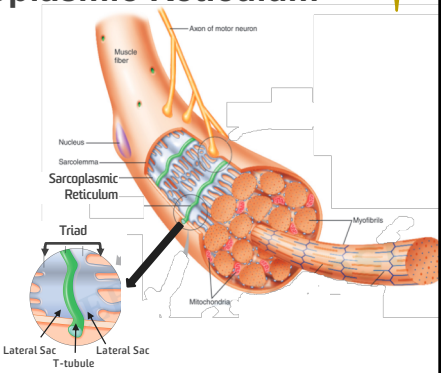
Another adaptation that allows the cell to respond quickly to stimulus

Principles of Human Physiology (2013)

T-Tubules & the Sarcoplasmic Reticulum

SR networks are closely associated with **transverse tubules (T-tubules)**

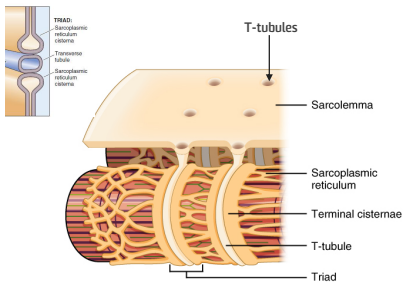
- T-tubules are continuous with the sarcolemma and go down into the cell interior
- Near the T-tubule, the SR has enlargements called **lateral sacs** or **terminal cisternae** that store calcium
- Each T-tubule is associated with two lateral sacs forming a **triad**
- This arrangement allows myofibrils even in the centre of the myocyte to *respond quickly*



Principles of Human Physiology (2013)

T-Tubules & Sarcoplasmic Reticulum

Always remember, this is a 3D structure…



OpenStax Anatomy and Physiology

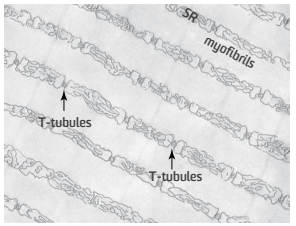
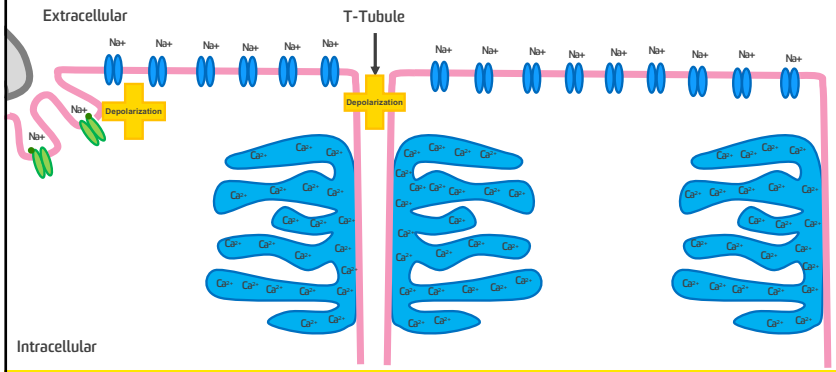


Figure 6-4 Sarcoplasmic reticulum in the extracellular spaces between the myofibrils, showing a longitudinal system paralleling the myofibrils. Also shown in cross section are T tubules (*arrows*) that lead to the exterior of the fiber membrane and are important for conducting the electrical signal into the center of the muscle fiber. (From Fawcett DW: The Cell. Philadelphia: WB Saunders, 1981.)

Guyton & Hall (2010)

Excitation-Contraction Coupling



Then Ca^{2+} interacts with the protein filaments in the myofibrils to initiate the contraction

Action Potential Triggers Ca^{2+} Release

The membrane of the T-tubule and the SR are physically linked by a complex of two proteins

Quicker response

- The **dihydropyridine receptor (DHP)**
- The **ryanodine receptor** – a calcium channel

When the AP travels down the T-tubule

- The voltage-sensitive DHP receptor changes conformation
- This allows the ryanodine receptor to open
- Ca^{2+} ions are released into the cell
  - Huge driving force and large number of channels opening means this is an "all or none" response
  - i.e. the extent of Ca^{2+} release is not graded to regulate strength or duration of contraction

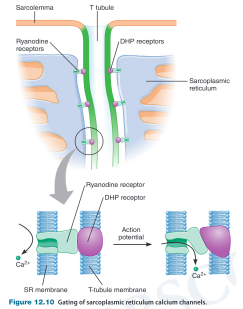


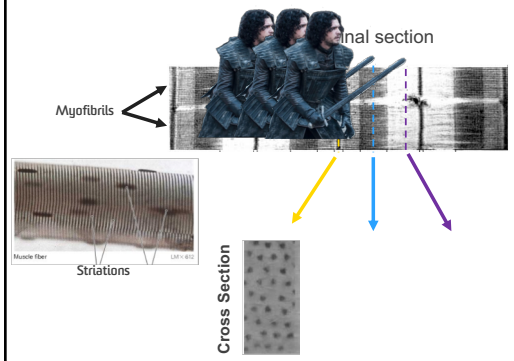
Figure 12.10 Gating of sarcoplasmic reticulum calcium channels.

Multiple Choice

What ion is released inside the myocyte to trigger a muscle contraction?

- Na+
- Ca2+
- K+
- Cl-

Protein Filaments



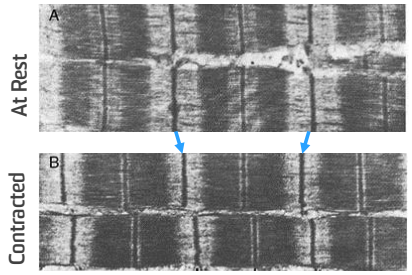
Developing a theory of how muscles contract…

What did they know?

1. There appear to be two types of proteins in a regular arrangement

H.E Huxley. *Fifty years of muscle and the sliding filament hypothesis.* Eur J. Biochem (2004)

Protein Filaments



Developing a theory of how muscles contract…

What did they know?

1. There appear to be two types of proteins in a regular arrangement
2. This structure must be able to shorten/contract

Sliding Filament Hypothesis of Contraction

H.E Huxley. *Fifty years of muscle and the sliding filament hypothesis.* Eur J. Biochem (2004)

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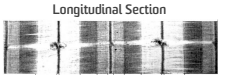
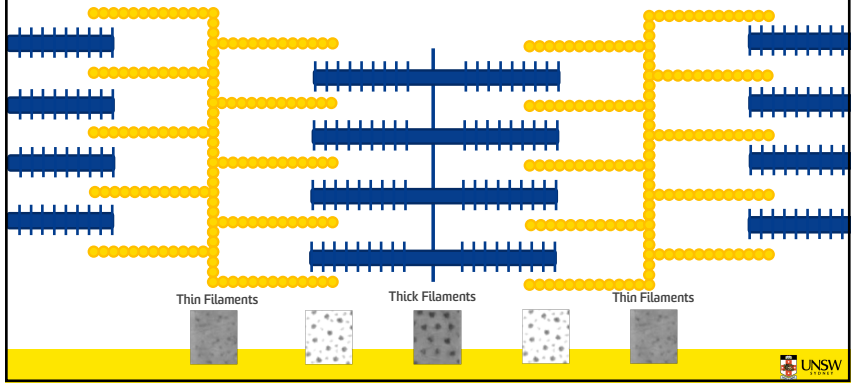
Sliding Filament Hypothesis





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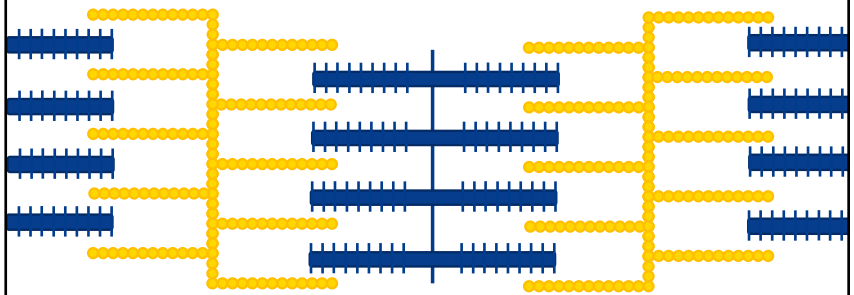
Sliding Filament Hypothesis



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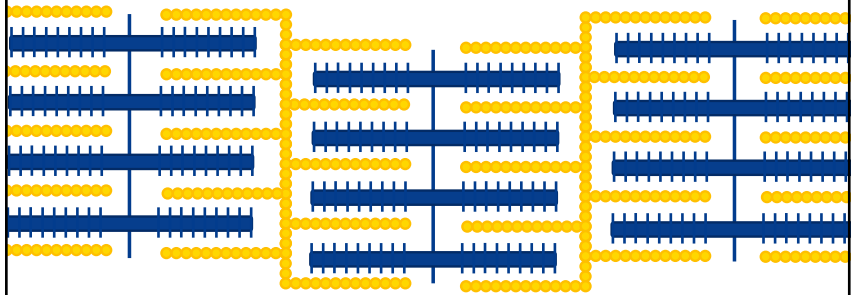
Sliding Filament Hypothesis



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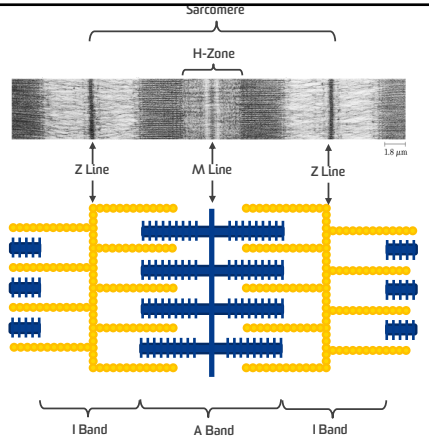
The Sarcomere

Myofibrils are made up of sarcomeres

- Smallest functional unit of contraction

Need to know the terminology used to describe sarcomere structure

- M Line (***M**iddle of sarcomere)*
- Z Line / Z disc *(end of alphabet, end of sarcomere)*
- I Band *(thin letter, only thin filaments)*
- A Band *(thick **A**nd thin filaments)*
  - Same length as thick filament so will not change in size
- H Zone *(thick letter, only thick filaments)*



Or even better, get creative and come up with your own ways to remember!

Multiple Choice

What happens to the width A Band (dark band in centre of sarcomere) during a muscle contraction?

- It gets smaller
- It gets bigger
- No change

Multiple Choice

What happens to the width of the I band (light band at edges of sarcomere) during a muscle contraction?

- It gets smaller
- It gets bigger
- No change

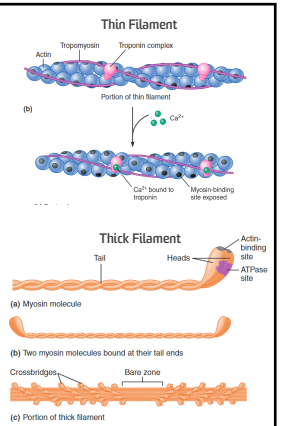
The Contractile Proteins

The **thin filament** is made of **actin** molecules and regulatory proteins

- In the presence of **Ca^{2+}**, the **troponin complex** changes conformation
- This causes **tropomyosin** to move, exposing a binding site

The **thick filament** is made of **myosin** molecules

- Each molecule is a dimer, with a twisted tail and two heads
- The **myosin heads** are the key to generating force.
  - Have an actin-binding site (forms a **cross-bridge**)
  - Have an ATPase site (generates the energy for movement)
  - Pull the thin filaments towards the centre of the sarcomere (**sliding filaments**)

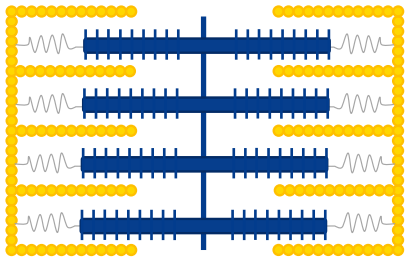


More on the "Cross-bridge Cycle" in Lecture 2

It's not all about the contractile proteins…

Titin

- Giant protein!
- Extends from the Z-line to the thick filament
- Keeps thick and thin filaments in alignment so that cross-bridges can form
- Molecular spring
  - Restores optimal sarcomere length after contraction or stretching



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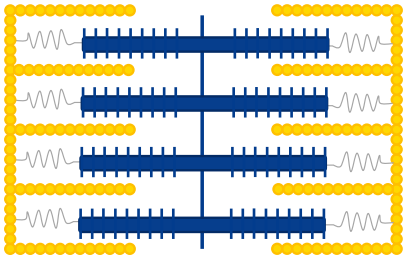
At Rest



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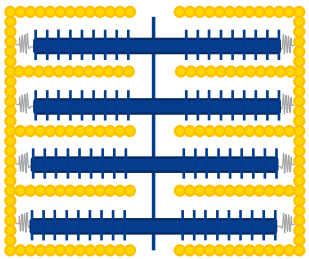
Contracted



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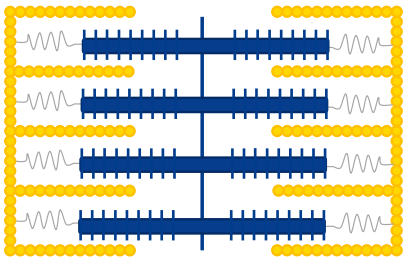
At Rest



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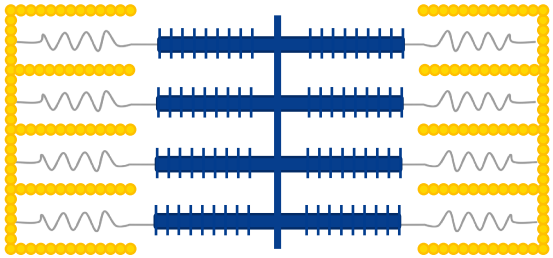
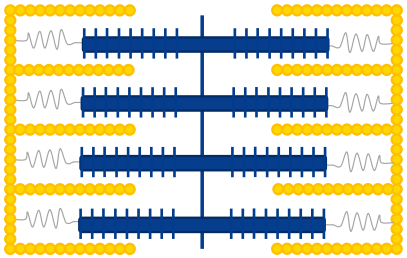
Stretching

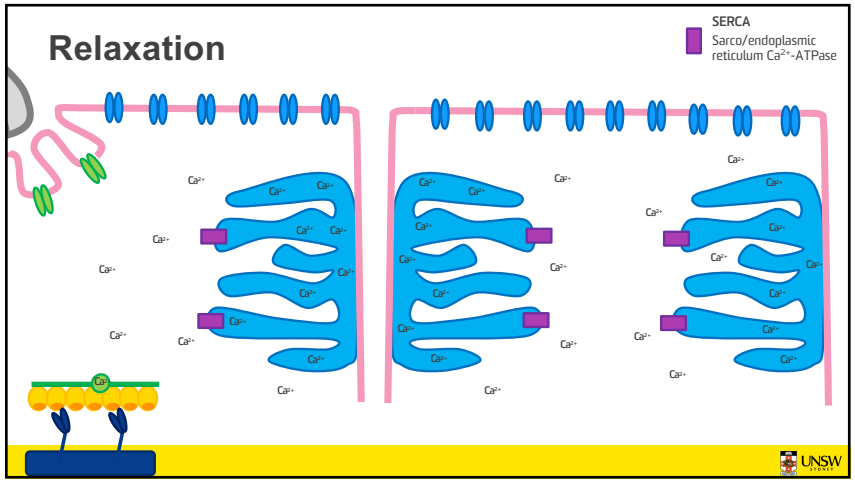


At Rest

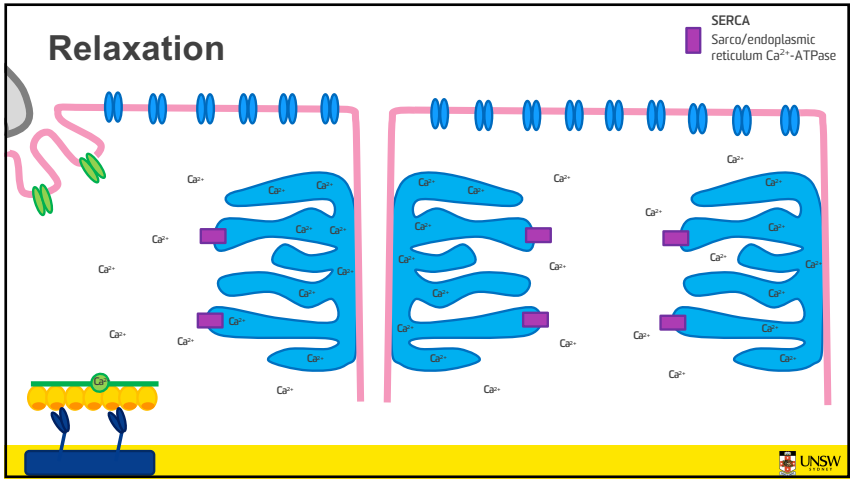


Relaxation

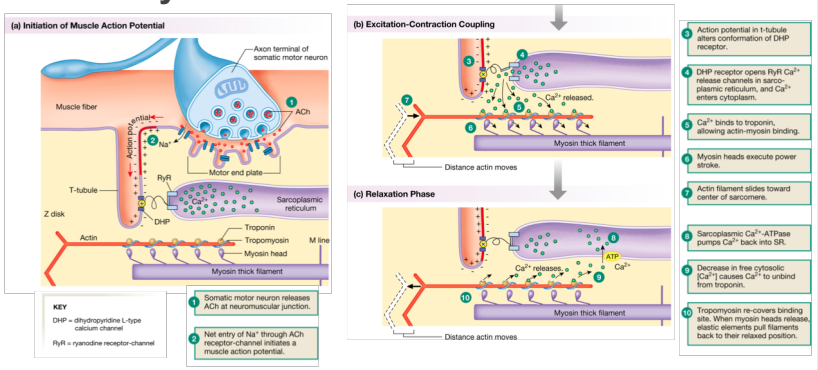
Relaxation



Relaxation



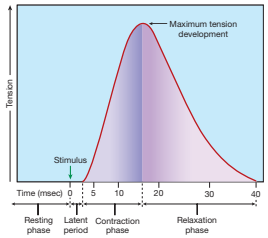
Summary: Excitation-Contraction-Relaxation

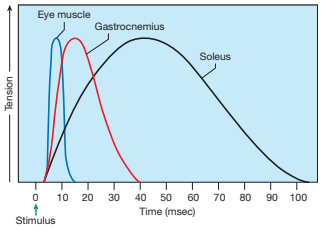


The Muscle Twitch

A **twitch** is a single stimulus-contraction-relaxation sequence in a muscle fiber or muscle

- This muscle twitch is **all-or-none** and is **reproducible**
- However different muscle fibers or muscles will have different twitch responses





Fundamentals of Anatomy & Physiology (2018)

All skeletal muscle contractions are built on this simple muscle twitch response

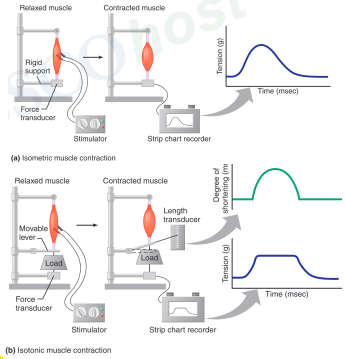
Descriptions of Muscle Contraction

Isometric (*Iso=same, Metric =length*)

- Load is greater than the force generated
- So muscle length does not change but force is generated

Isotonic (*Iso=same, Tonic =tension)*

- Load is less than the force generated
- Muscle shortens under a constant tension

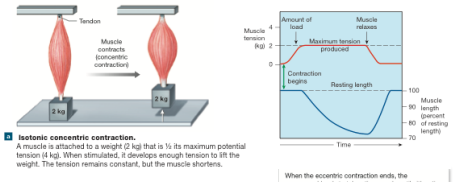


Principles of Human Physiology (2013)

Descriptions of Muscle Contraction

Concentric contraction

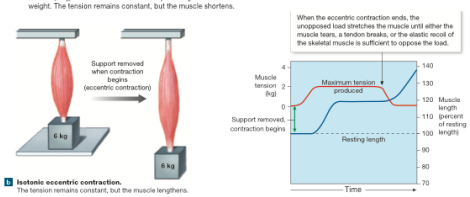
Muscle shortens while force is produced



Isotonic concentric contraction. A muscle is attached to a weight (2 kg) that is ½ its maximum potential tension (4 kg). When stimulated, it develops enough tension to lift the weight. The tension remains constant, but the muscle shortens.

Eccentric contraction

Muscle lengthens while force is produced

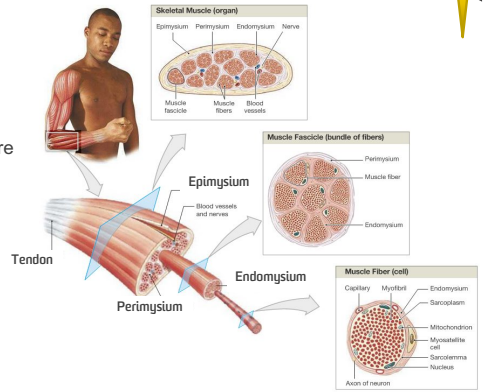


Isotonic eccentric contraction. The tension remains constant, but the muscle lengthens.

Connective Tissues

Connective tissues are found at multiple levels in the muscle

- Help maintain a regular structure – this is essential for effective transmission of force
- Elastic
  - Prevent damage due to over extension
  - Like a bungy cord



Connective Tissues

Connective tissues are found at multiple levels in the muscle

- Help maintain a regular structure – this is essential for effective transmission of force
- Elastic
  - Prevent damage due to over extension
  - Like a bungy cord

Skeletal Muscle Practical

Will be experimenting with factors that are important for regulating how much force can be generated in a muscle contraction

- Make sure you do the pre-lab activity!