Objectives

1. To understand the concept of sarcomere
2. To understand the contractile mechanism of muscle cells
3. To understand the concepts of Force-Length relationships and Velocity-Stress relationships
4. To understand the concepts of twitch, tetanus, and fatigue
5. To understand the differences between skeletal, cardiac, and smooth muscle
# Muscle Classification

<table>
<thead>
<tr>
<th>Location</th>
<th>Anatomy</th>
<th>Neural Control</th>
<th>Output</th>
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<tr>
<td>Skeletal</td>
<td>Skeleton</td>
<td>Striated</td>
<td>Voluntary</td>
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<tr>
<td>Cardiac</td>
<td>Heart</td>
<td>Striated</td>
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<td>Smooth</td>
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</table>
Structure of Contractile Apparatus

1. Cytoskeleton: Titin, Nebulin

2. Thin Filaments (1.5 \( \mu \text{m} \)): Actin, Tropomyosin, nebulin, troponin

3. Thick Filaments (1.6 \( \mu \text{m}, 300-400 \) across-bridges): Myosin, Titin
Striated Muscle
Actin & Myosin

Thin Filaments

Myosin Molecules
Structure of the Thick Filament
Sarcomere
Structure of Myofibrils
Sarcoplasmic Reticulum & Ca^{++} Regulation

Within the SR there are structural and functional divisions:

- Longitudinal SR
- Junctional SR (or Terminal SR)

The Ryanodine Receptor is found in Junctional SR which is aligned to the DHP Receptor of the T tubules. Longitudinal SR has a Calcium Pump to remove Ca^{++} from the myofilaments at the end of a contraction.
Structure of Sarcomere

- Sarcolemma
- T Tubule
- Voltage Sensor
- SR Calcium Channel
- Sarcoplasmic Reticulum (Calcium Store)
- Contractile Proteins
Actin-Myosin Interactions

- Thin filament
  - Actin
  - Ca$^{2+}$
  - Tropomyosin
  - Troponin

- Thick filament
  - ATP
Sliding Filament Model of Contraction
Mechanical variables and Their Units

Three Primary Variables:

1. Force (g or kg, newtons \(\approx 102 \text{ g}\))
2. Length (cell/sarcomere, meter, millimeters micrometers)
3. Time

Parameters can be calculated:

1. Shortening velocity (m/sec)
2. Work (force\times distance) (n\times m=joules)
3. Power (work/time) (n\times m/sec=watts)
4. Stress (force/cell cross-sectional area) (n/m^2)
Isometric

- Where the muscle is fixed at both ends at a certain length. When the muscle is stimulated, it cannot shorten, but develops tension (fix length, measure force as a function of time).
Force-Length Relationships

![Diagram showing force-length relationships in muscles.](image-url)

- **Active** and **Passive** components of force are depicted.
- **Normal working range** is shown on the graph.
- **Percent of resting length** is indicated along the x-axis.
- **Tension** is measured on the y-axis.

The diagram illustrates the relationship between muscle length and tension, highlighting the optimal length for maximum tension and the effects of active and passive forces.
Isotonic

- Where the muscle is fixed at one end only. When the muscle is stimulated it can shorten freely and force is developed (fix force, measure shortening as function of time).
Velocity-Stress Relationships

$V_0 = \text{maximum cycling rate (no load)}$

$\text{Power} = \frac{\text{Work}}{\text{Time}} = F \times V$

$F_0$, $L_0$
Muscle Twitch

When a single electrical stimulus is applied to a muscle or its motorneuron, it elicits a single contraction called a TWITCH.
Features of a Muscle Twitch

There is always a delay between stimulus and onset of contraction

• The rate of rise of force is always faster than the rate of decline
• The force always spontaneously declines after reaching a peak
• Twitch force is approximately 10-20% of the maximum force

A muscle twitch may be varied by a variety of stimuli differences or manipulations of the muscle itself:

• Frequency of stimulation (Hz, cycles per second)
• Duration of the stimulus pulse (msec)
• Strength of the stimulus (V or mV)
• Sarcomere length of the muscle (µm)
• Different ionic concentrations (Ca++, Mg++, ATP etc)
• Presence of pharmacological agents
Tetanus

- A second action potential can be elicited before Ca$^{2+}$ falls to resting level
- The mechanical response is increased as the 2$^{nd}$ twitch sums with the first

Tetanization is summation of twitches to produce higher force
Muscle Fatigue

Prolonged strong contractions leads to fatigue of the muscle caused by the inability of the contractile and metabolic processes to supply adequately to maintain the work load. The nerve continues to function properly passing the action potential onto the muscle fibers but the contractions become weaker and weaker due to the lack of ATP.

Cellular Fatigue

General Fatigue
Measure Soleus Contractile Function

Transducer

Amplifier

Stimulating electrodes

Soleus Muscle

High Ca2 + KH solution bubbled with 5%CO2/95%O2

22°C Water

Stimulator

MacLab
Tetanus Protocol

• Adjust soleus muscle to optimal length
• Stimulate soleus muscle 2s with 0.2 ms duration, 7 volts, and 30Hz pulses
Fatigue Protocol

• Adjust soleus muscle to optimal length
• Stimulate soleus muscle with 0.2 ms duration, 10 volts, and 30Hz pulses at 2s interval till developed tetani force decreasing to 40% of first tetani force
Control Rat

Heart Failure (HF) Rat

Fatigue
Smooth Muscle

• To describe the unique features of smooth muscle in comparison to striated muscle.

• Special emphasis on control of contractile activation.
Comparison of Skeletal Muscle with Smooth Muscle

Smooth muscle is very different to both cardiac and skeletal muscle.

Smooth Muscle has the following main properties:

- Cells not striated
- tapered cells
- single central nucleus
- size ranges from 5-15 $\mu$m diameter, 200-300 $\mu$m length
- Gap Junctions between cells
- considerable connective tissue sheaths for strength

The contractile properties of smooth muscle differ also from those of both skeletal and cardiac muscle.

These include much slower contractions that are sustained for prolonged periods of time.
Smooth Muscle Size and Shape

- Spindle shaped cells
- Relatively small compared to skeletal and cardiac muscle
  - 2-5 µm wide
  - 50-200 µm long.
Contractile Apparatus

• No sarcomeres (hence the name smooth)
  ➤ Lack neat hexagonal arrangement of actin and myosin

• Actin/myosin ratio: greater in smooth muscle (10:1) than in skeletal muscle (2:1).
Smooth Muscle Architecture

- Intermediate Filament
- Thick Filament
- Thin Filament
- Dense Body
- Mechanical Coupling
- Gap Junction

Longitudinal Section

Cross Section
Gap Junction

Allow direct electrical communications between adjacent smooth muscle cells

No T-tubules and no terminal cistern system
Smooth muscle does not require action potential to contract

Poorly developed sarcoplasmic reticulum
Needs extracellular Ca^{++} source for contraction

Tropomyosin-Tropomyosin Complex
No troponin present
Comparison of Skeletal Muscle with Cardiac Muscle

There are many similarities between skeletal and cardiac muscle but also some distinct differences.

Cardiac cells
- quite small (15-30 µm diameter, 50 µm long)
- not elongated like skeletal fibres
- short wider T tubules
- branch and connect to adjacent cells (anastomose)
- are connected by Gap Junctions and Intercalated Disks
- nuclei are central rather than peripheral
- contain many mitochondria (exclusively oxidative)
- T tubule - SR junctions are in Dyads not Triads.