Muscle Function

Jie Wang, MD PhD

The Heart Failure Center
College of Physicians&Surgeons
Columbia University
New York City, NY, USA

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

	Location	Anatomy	Neural Control	Output
Skeletal	Skeleton	Striated	Voluntary	High Power
Cardiac	Heart	Striated	In-Voluntary	High Power
Smooth	Hollow Organs	Non-Striated	In-Voluntary	Low Power

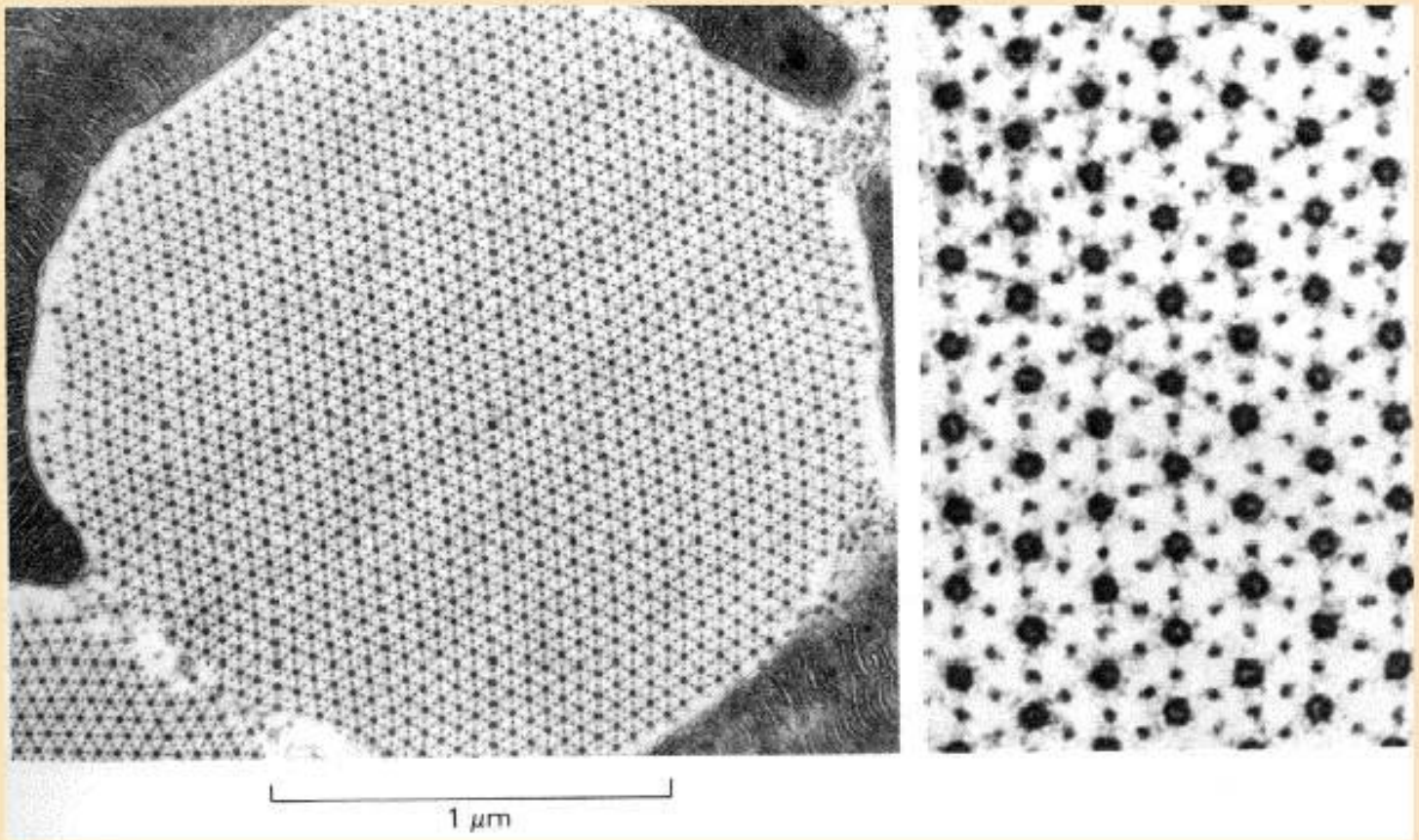
Structure of Contractile Apparatus

1. Cytoskeleton: Titin, Nebulin

2. Thin Filaments(1.5 μm): Actin, Tropomyosin, nebulin, troponin

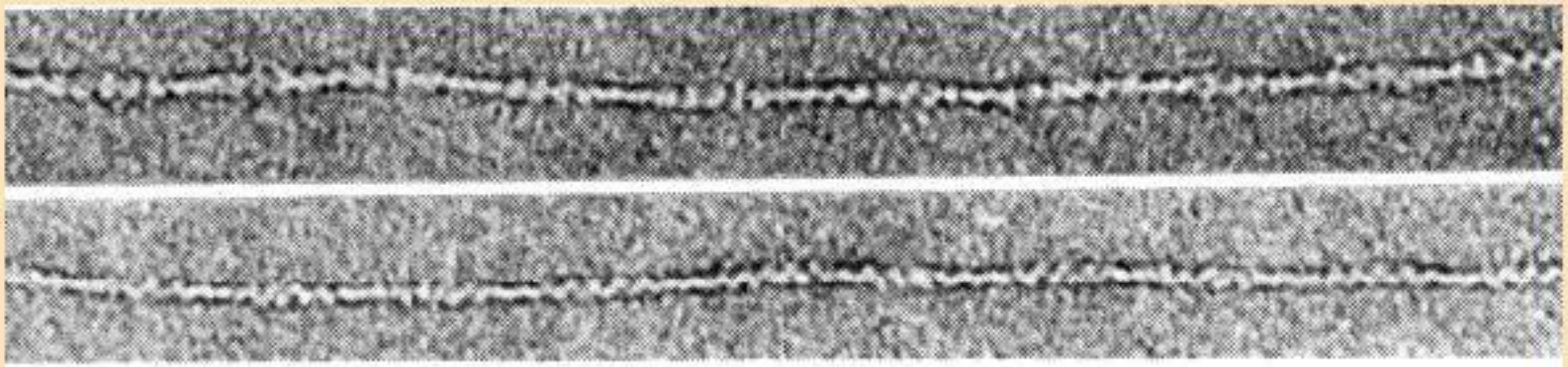
3. Thick Filaments (1.6 μm, 300-400 across-bridges): Myosin, Titin

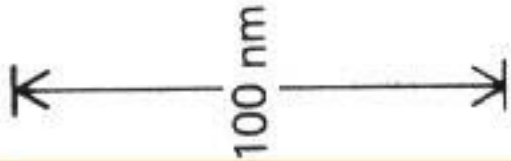
Striated Muscle

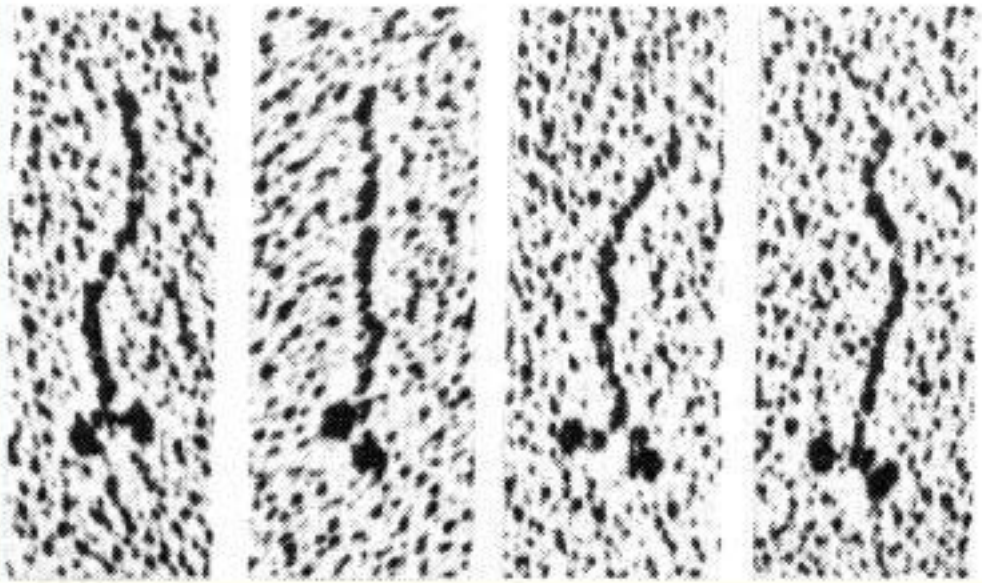


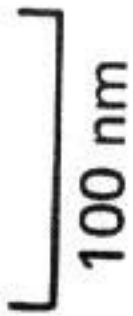
Actin & Myosin

Thin Filaments



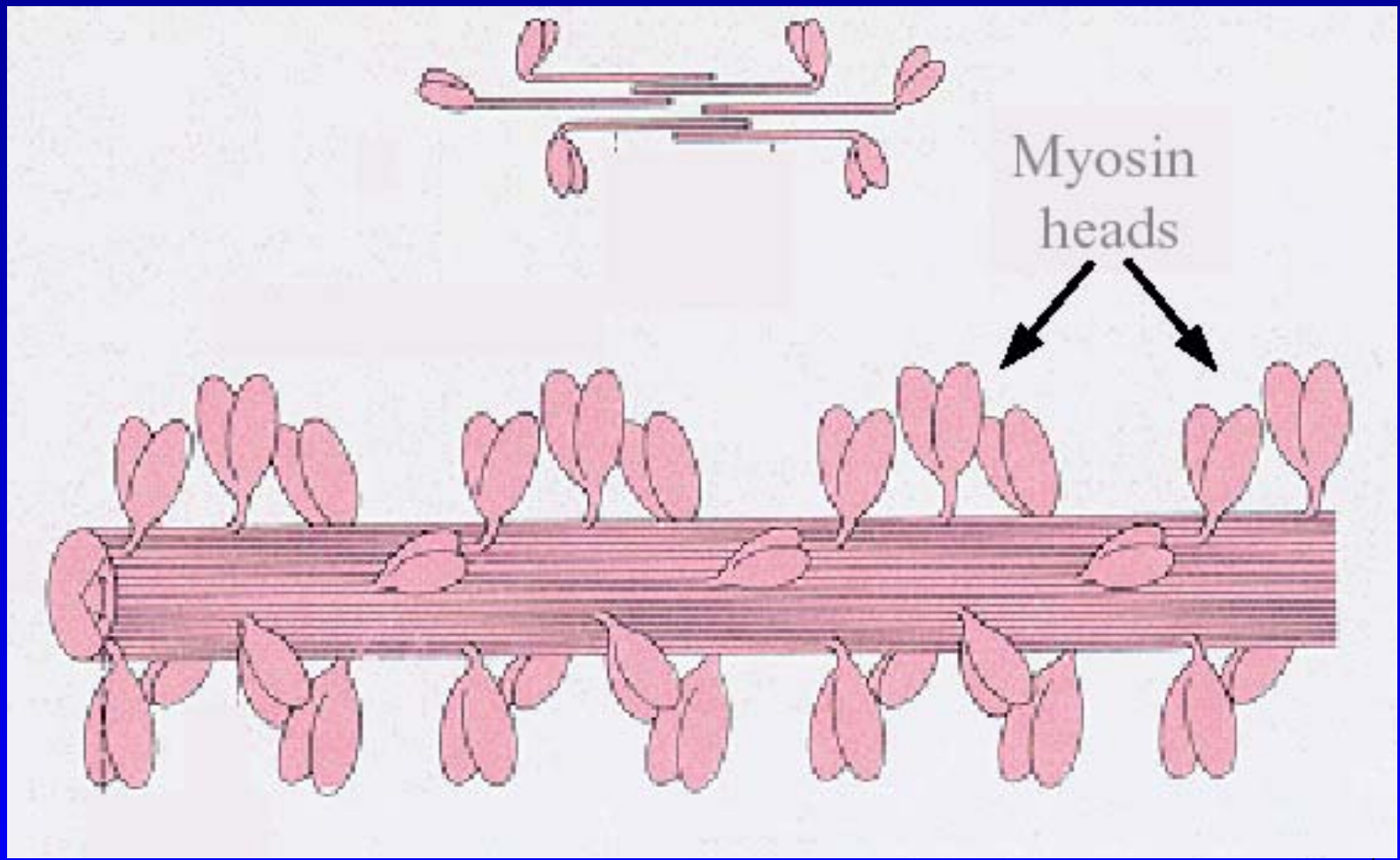






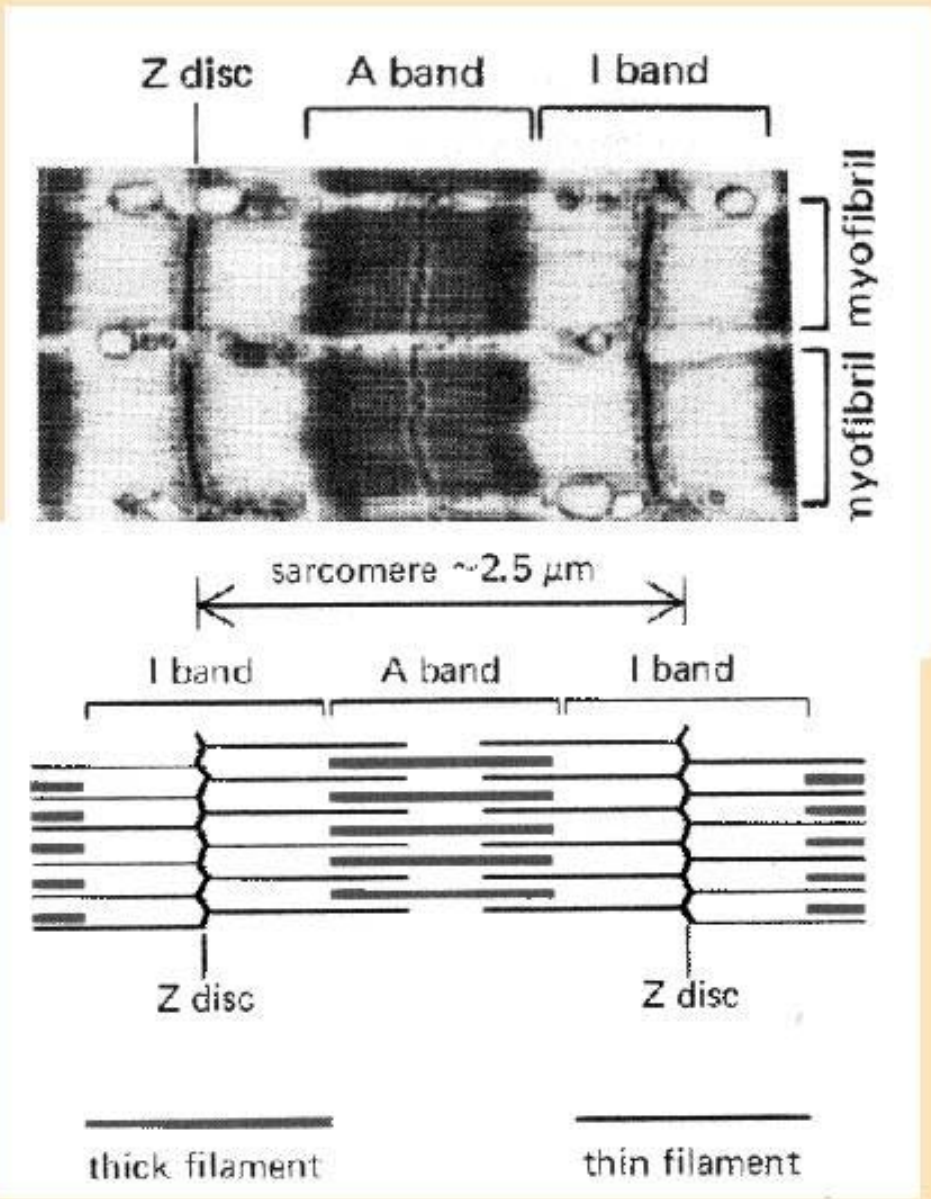
Myosin Molecules

Structure of the Thick Filament

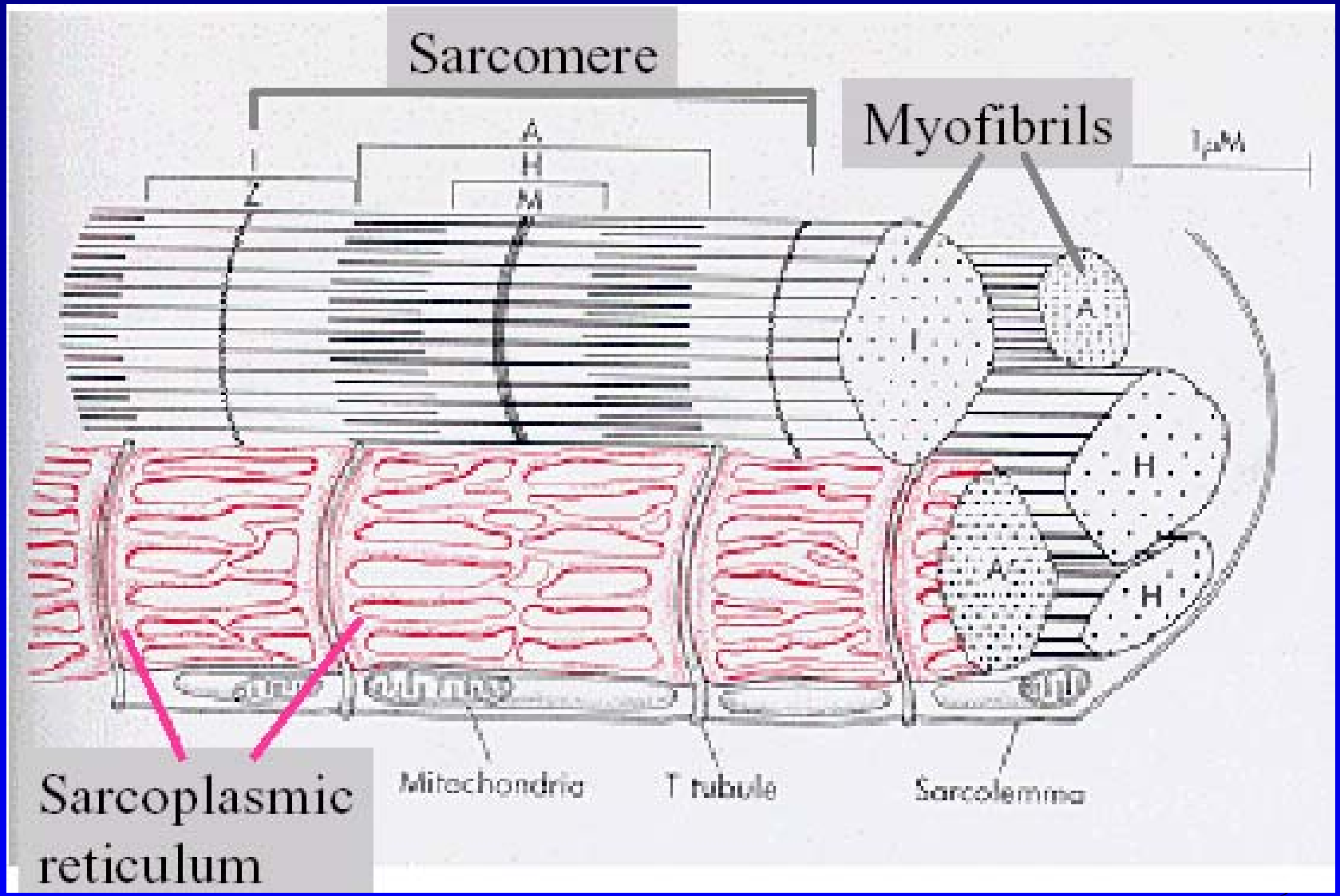


Sarcomere

Sarcomere



Structure of Myofibrils

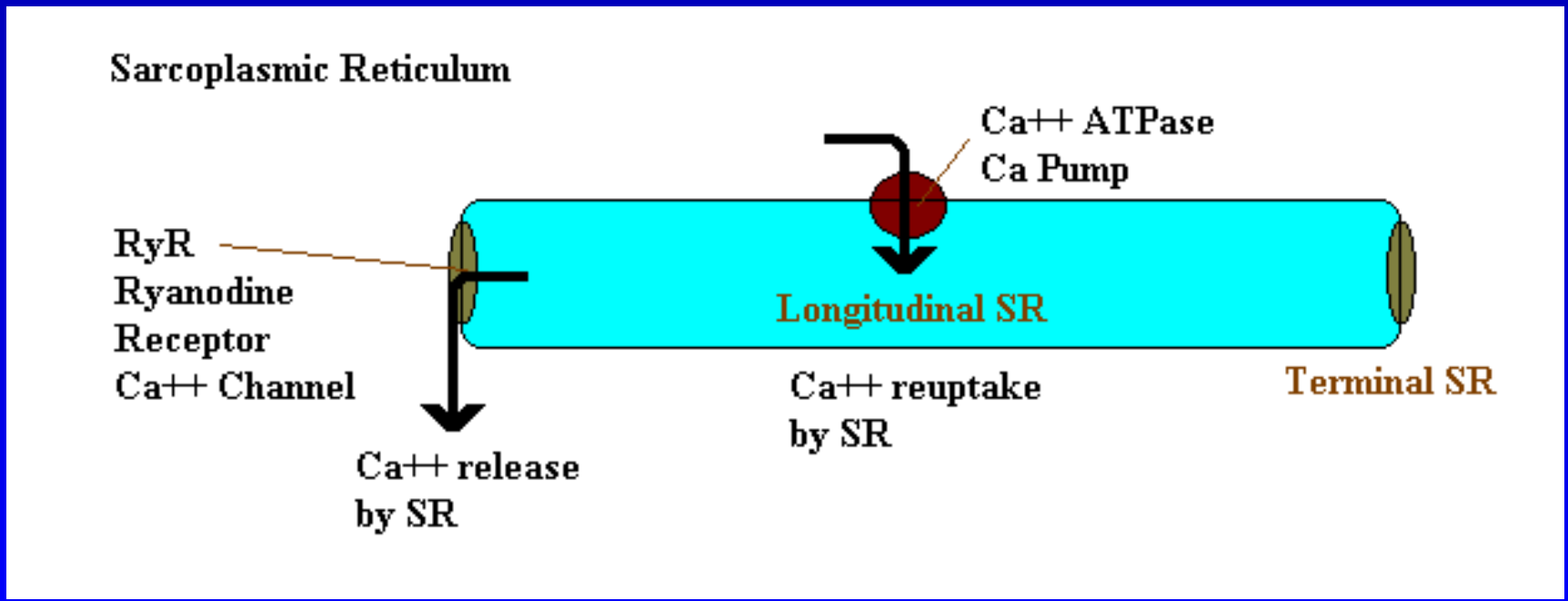


Sarcoplasmic Reticulum & Ca^{++} Regulation

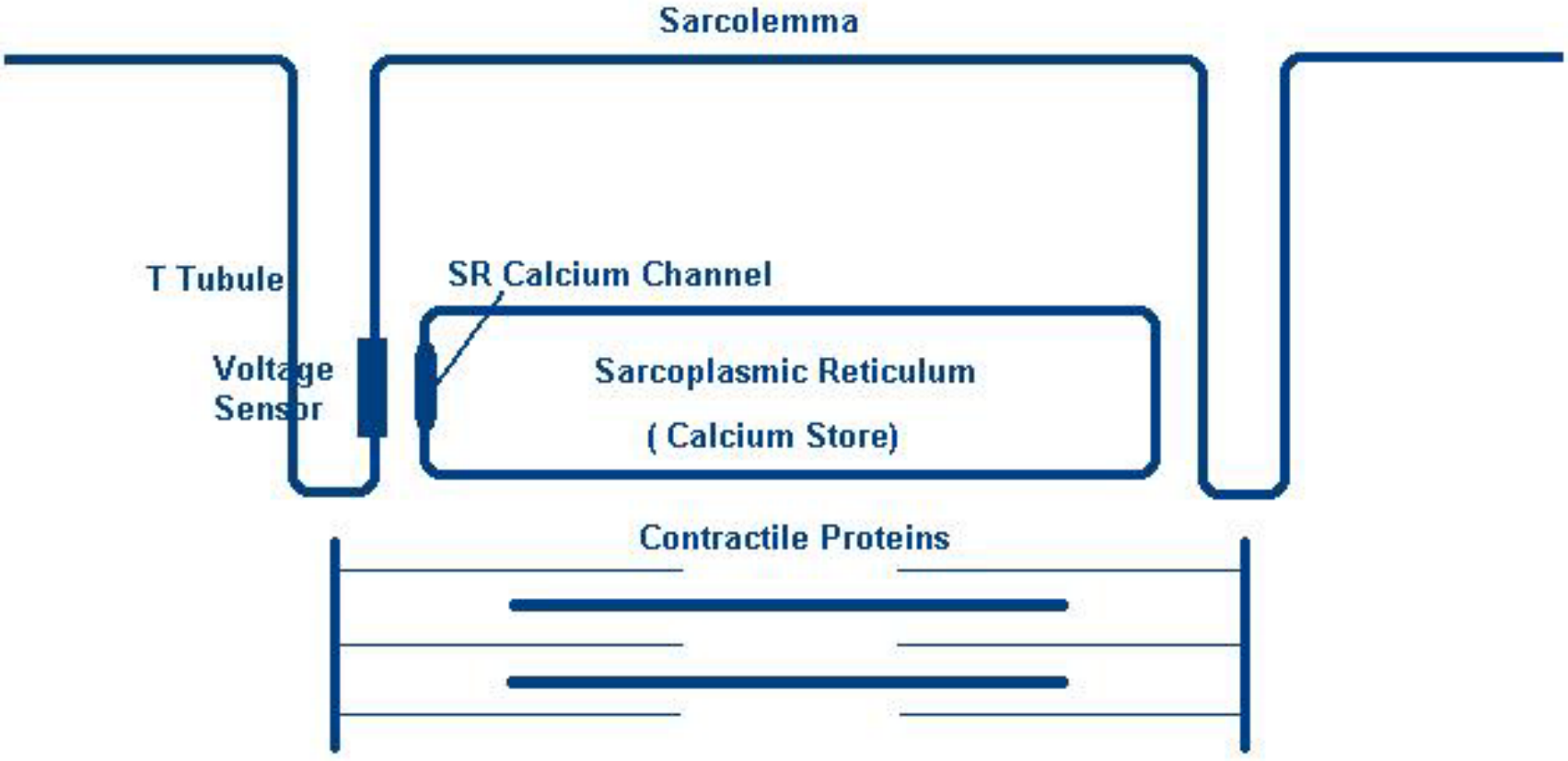
Within the SR there are structural and functional divisions:

- **Longitudinal SR**
- **Junctional SR (or Terminal SR)**

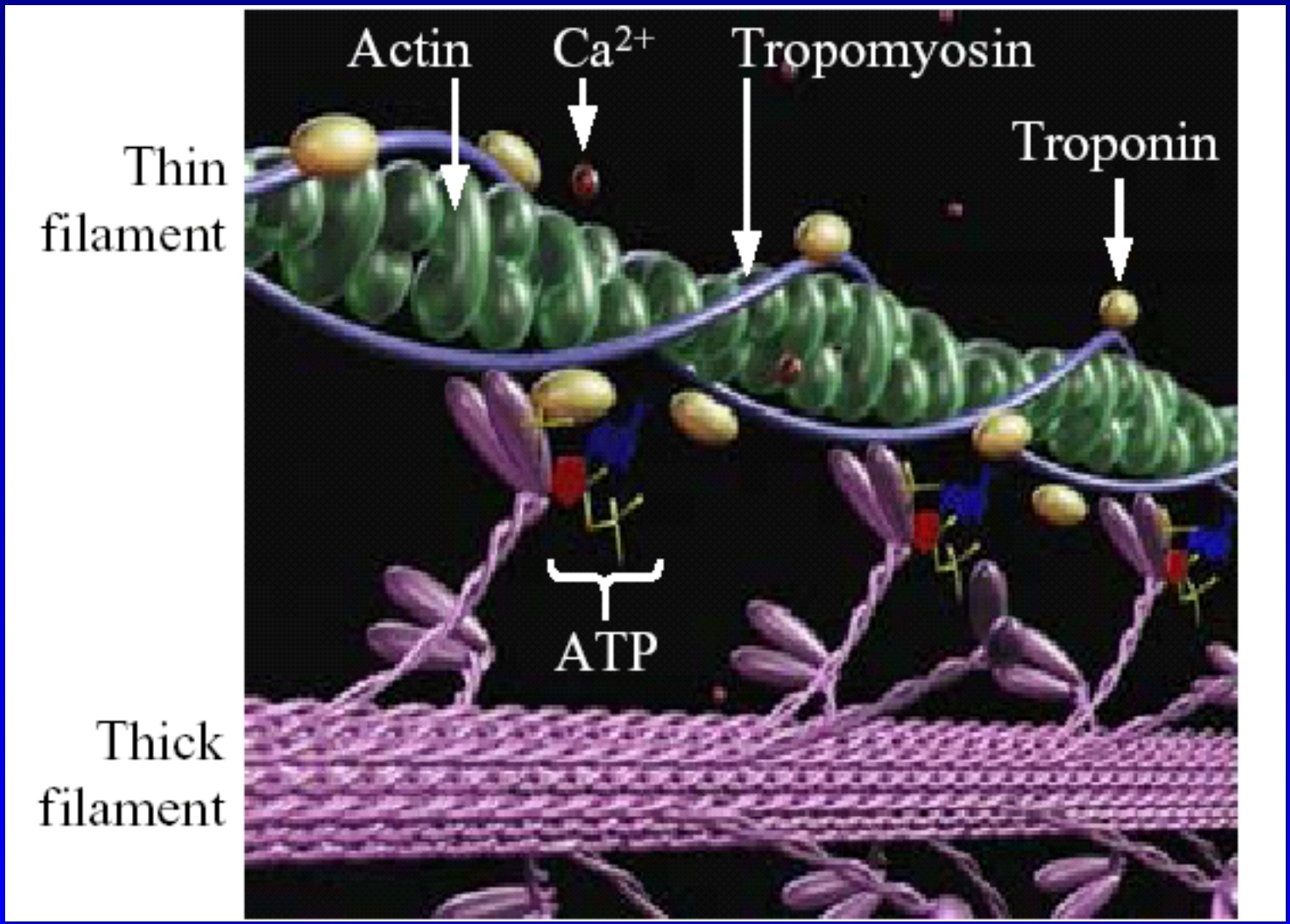
The Ryanodine Receptor is found in Junctional SR which is aligned to the DHP Receptor of the T tubules. Longitudinal SR has a Calcium Pump to remove Ca^{++} from the myofilaments at the end of a contraction.



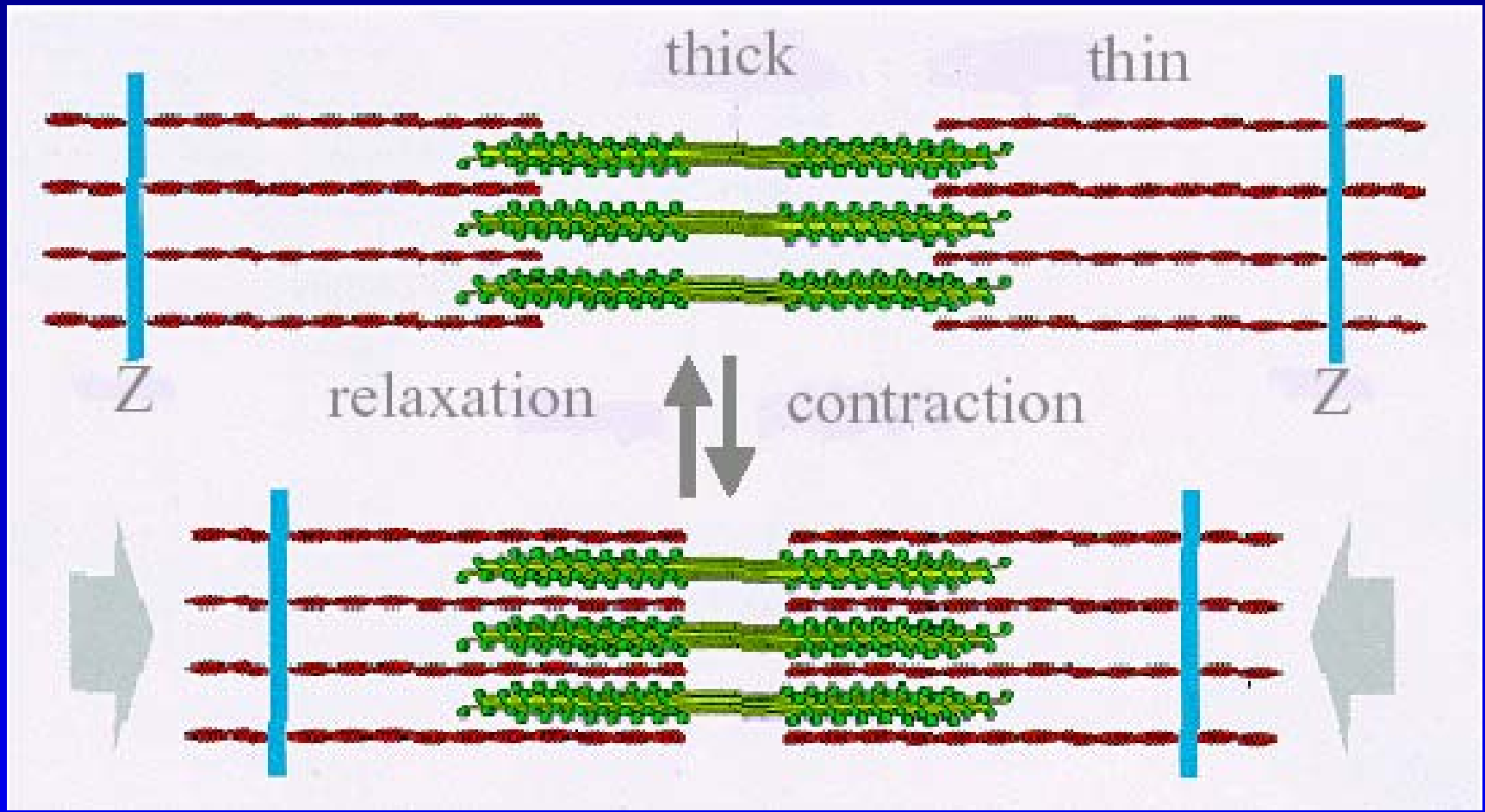
Structure of Sarcomere



Actin-Myosin Interactions



Sliding Filament Model of Contraction



Mechanical variables and Their Units

Three Primary Variables:

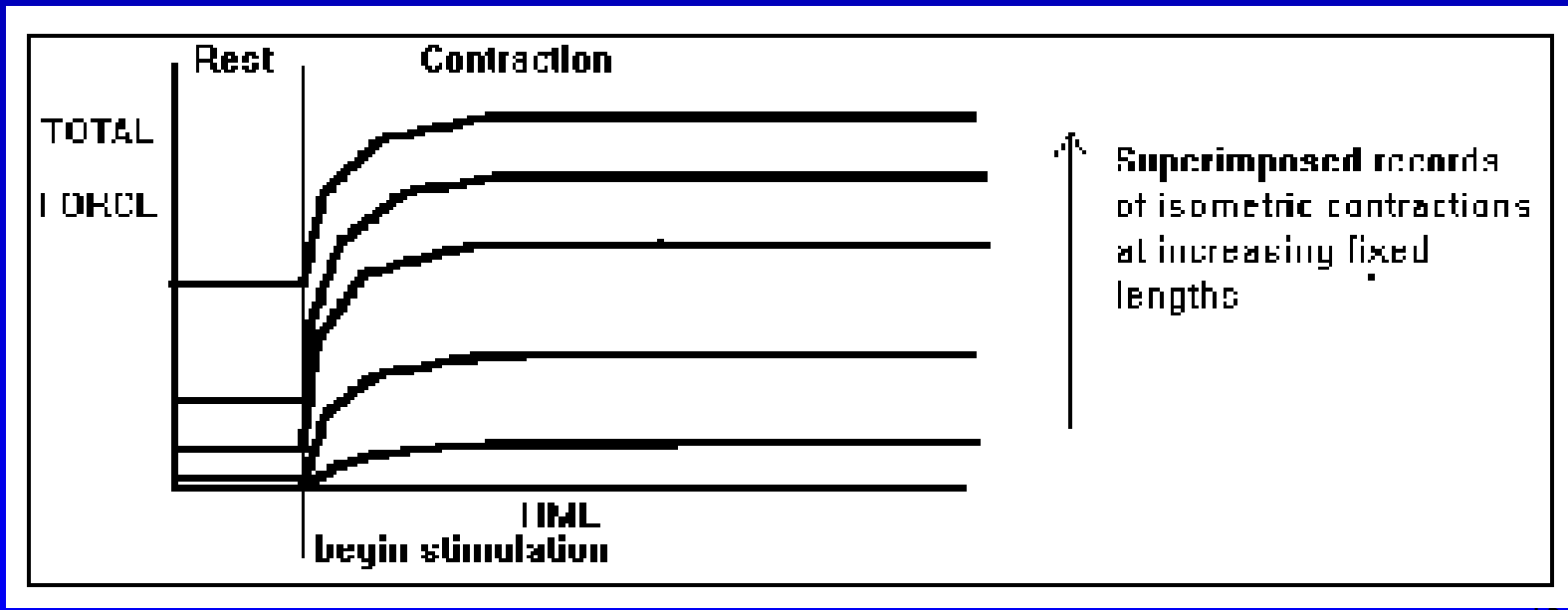
1. **Force (g or kg, newtons {=102 g})**
2. **Length (cell/sarcomere, meter, millimeters micrometers)**
3. **Time**

Parameters can be calculated:

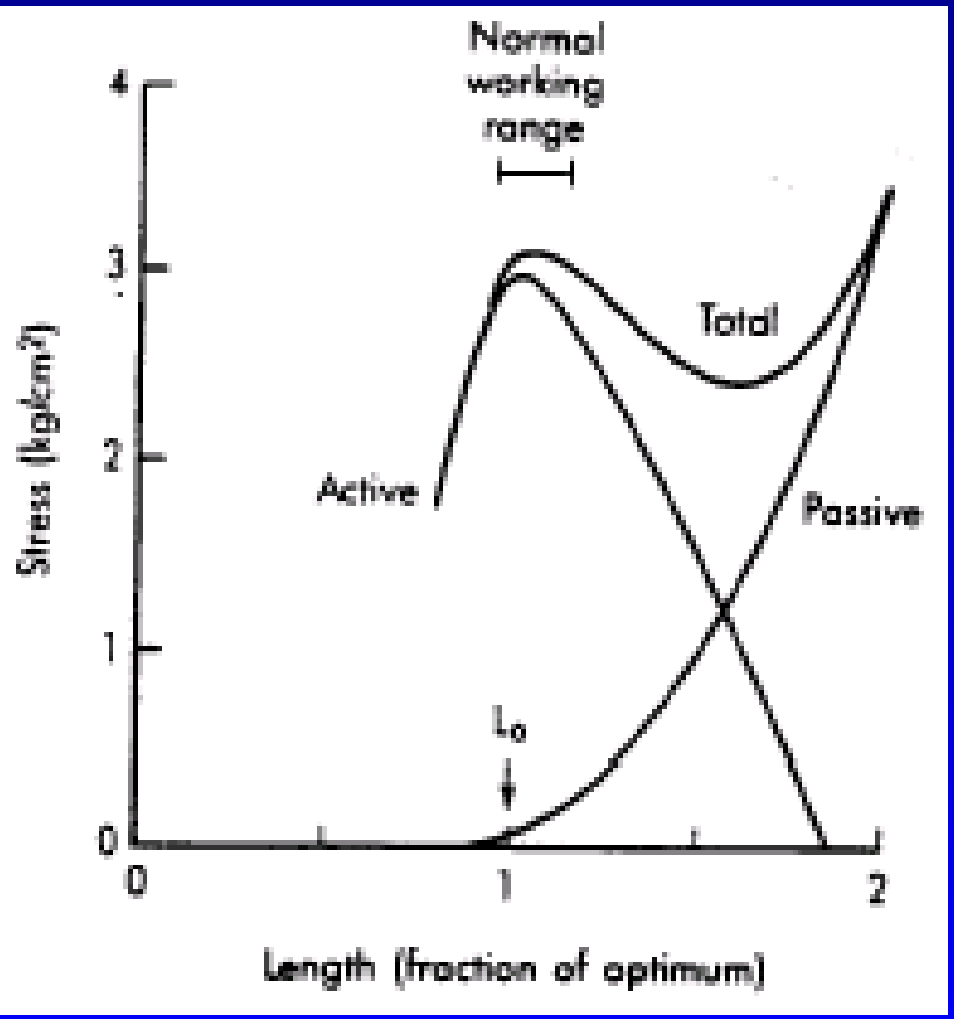
1. **Shortening velocity (m/sec)**
2. **Work (forceXdistance) (nXm=joules)**
3. **Power (work/time) (nXm/sec=watts)**
4. **Stress (force/cell cross-sectional area) (n/m^2)**

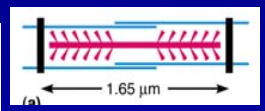
Isometric

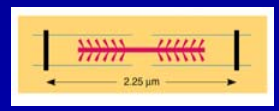
- **Where the muscle is fixed at both ends at a certain length. When the muscle is stimulated, it cannot shorten, but develops tension (fix length, measure force as a functin of time).**

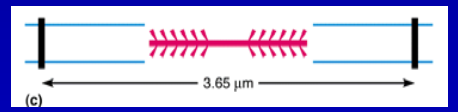


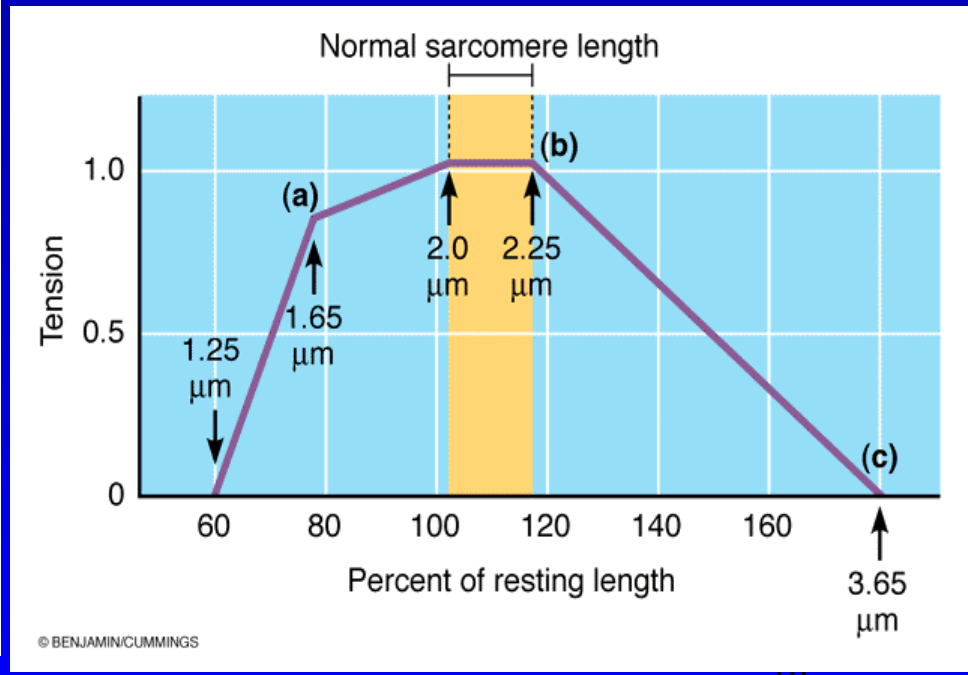
Force-Length Relationships





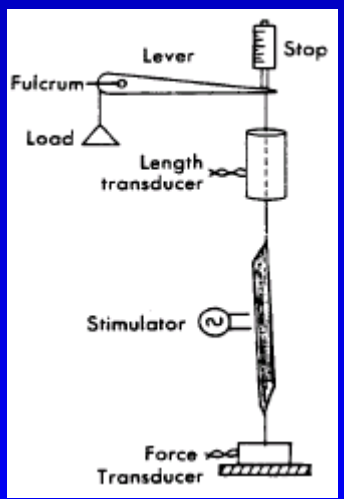


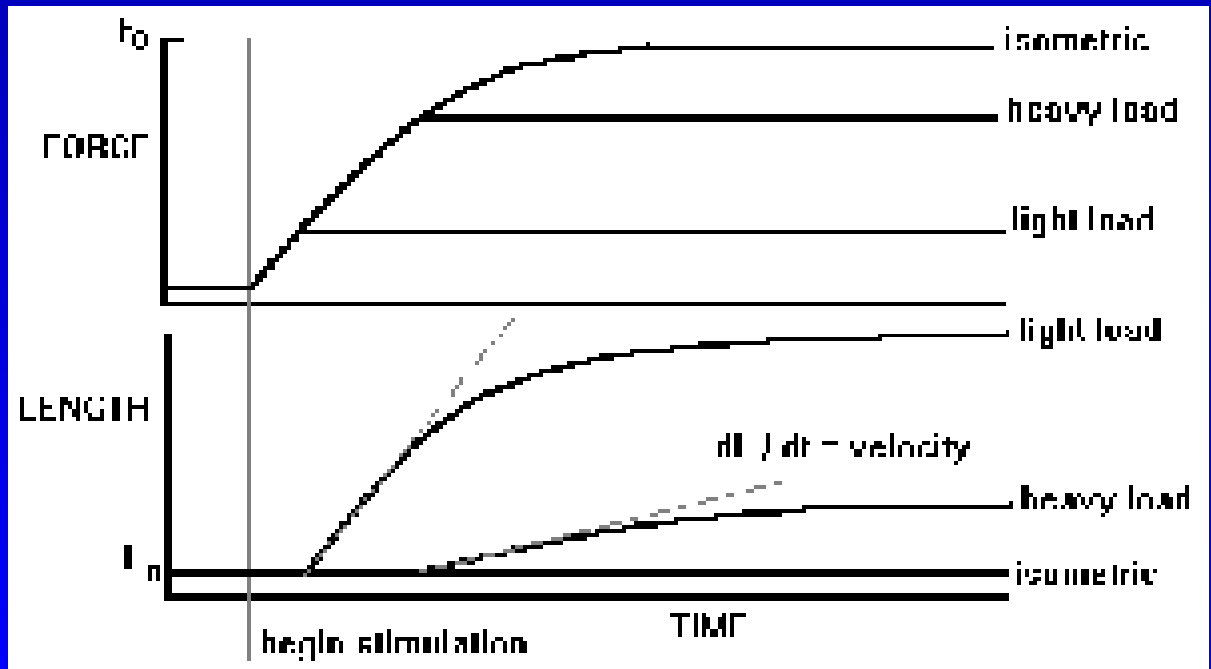




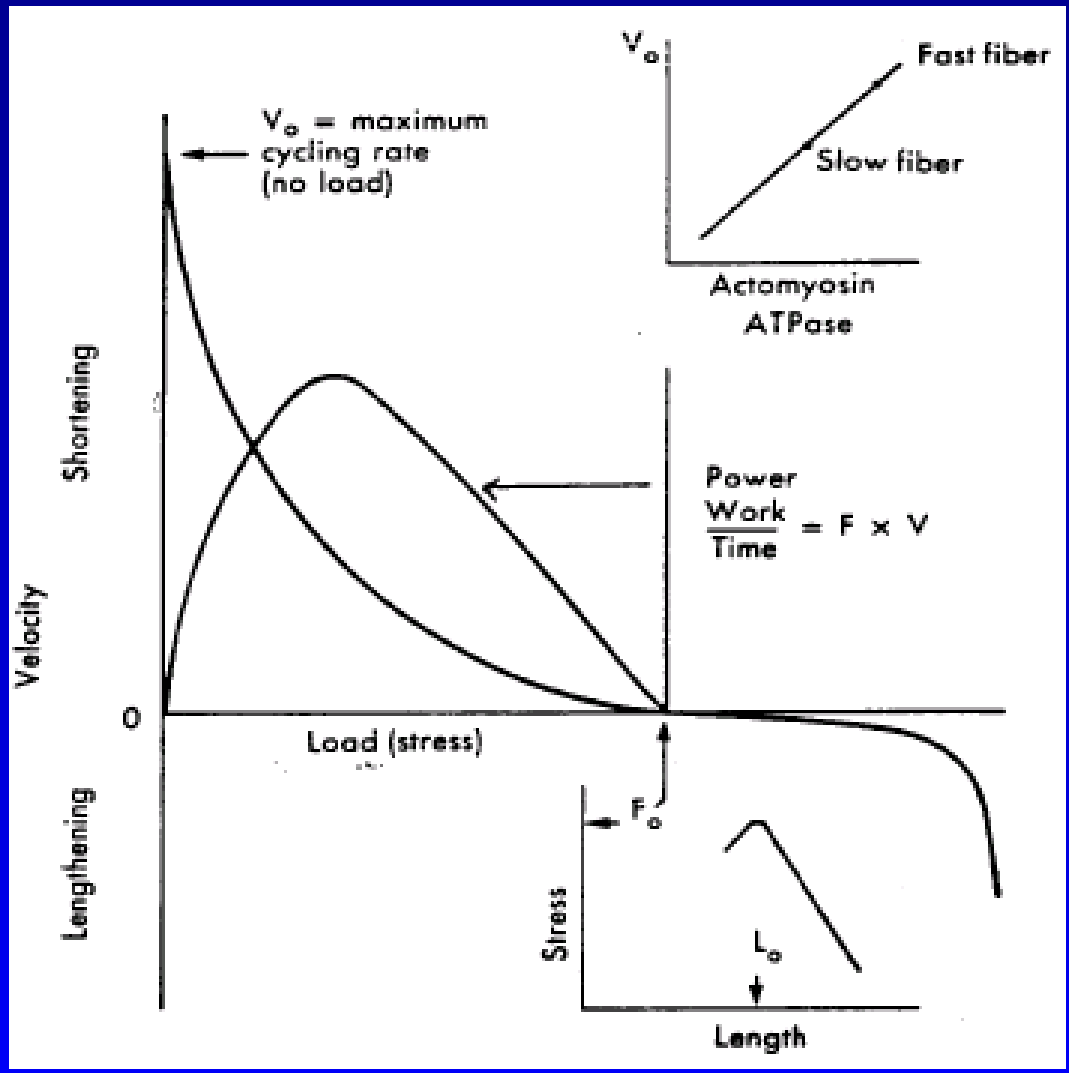
Isotonic

- 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).



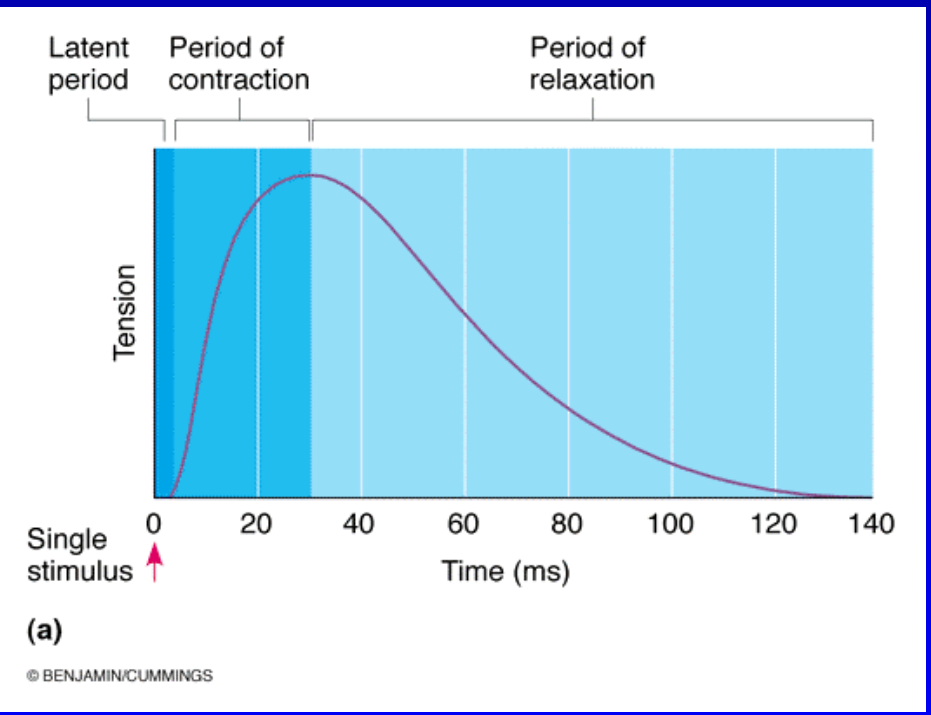


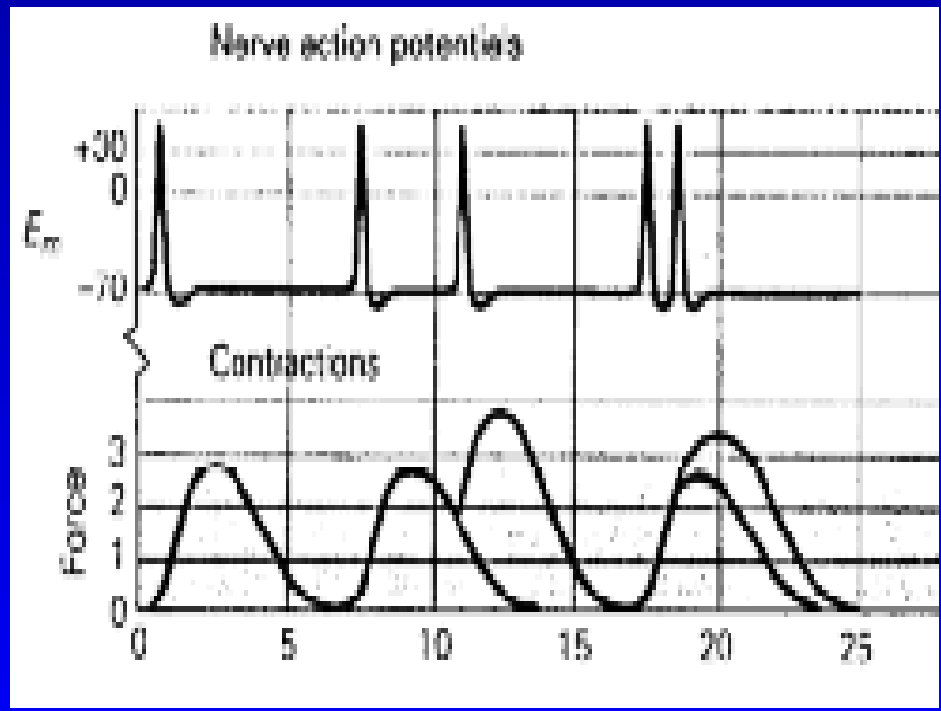
Velocity-Stress Relationships



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

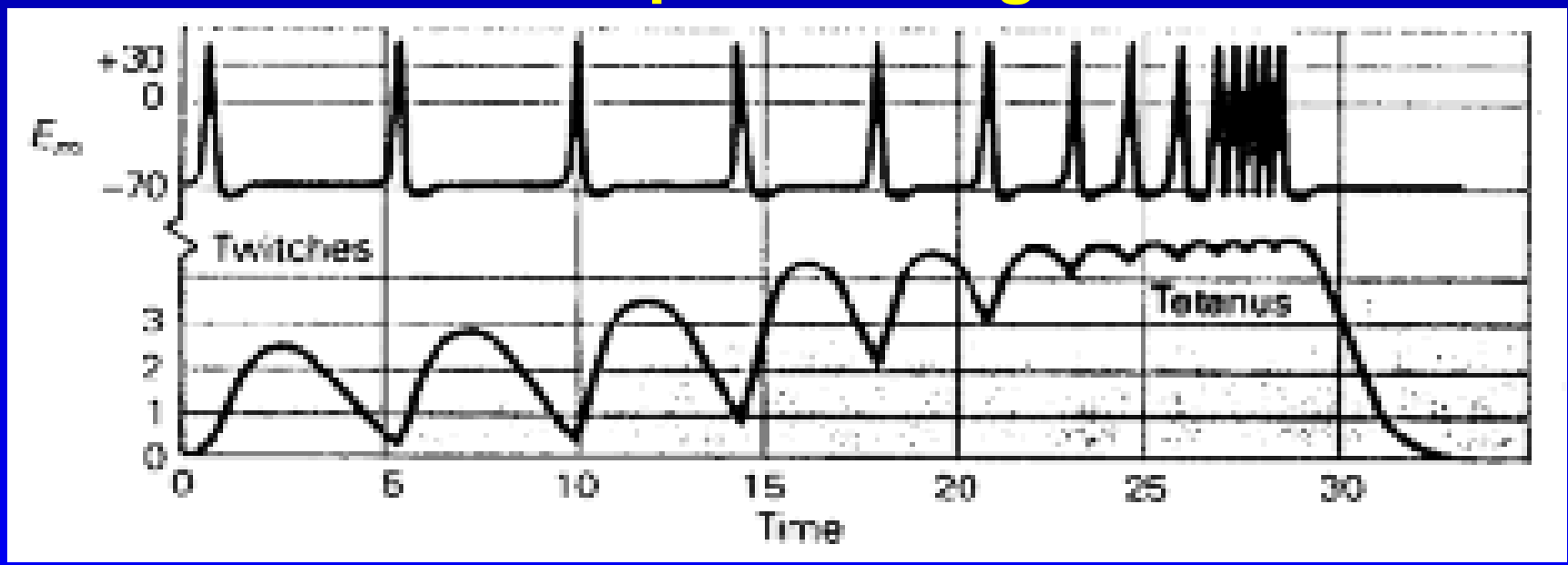
A muscle twitch may be varied by a variety of stimuli differences or manipulations of the muscle itself:

- 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 Ca2+ falls to resting level
- The mechanical response is increased as the 2nd twich sums with the first

Tetanization is summation of twitches to produce higher force



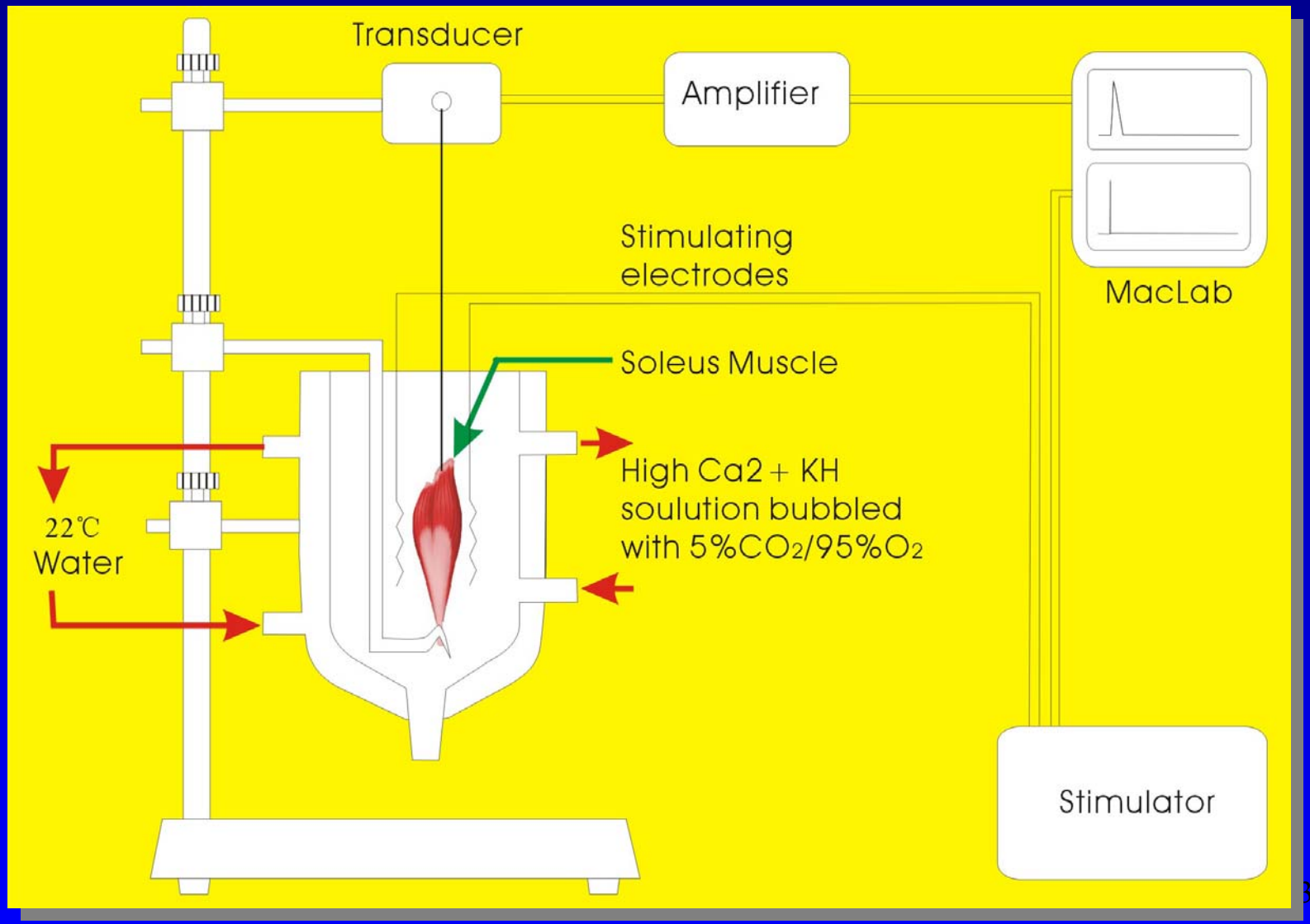
Muscle Fatigue

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

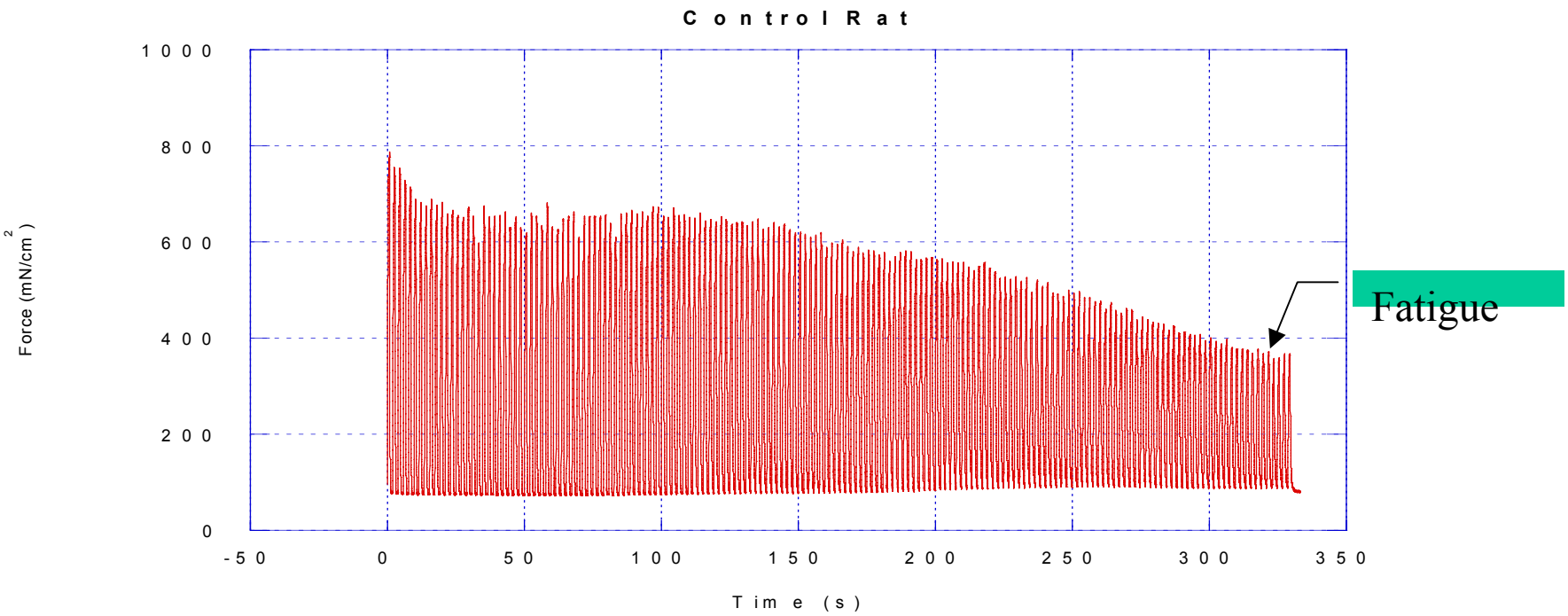


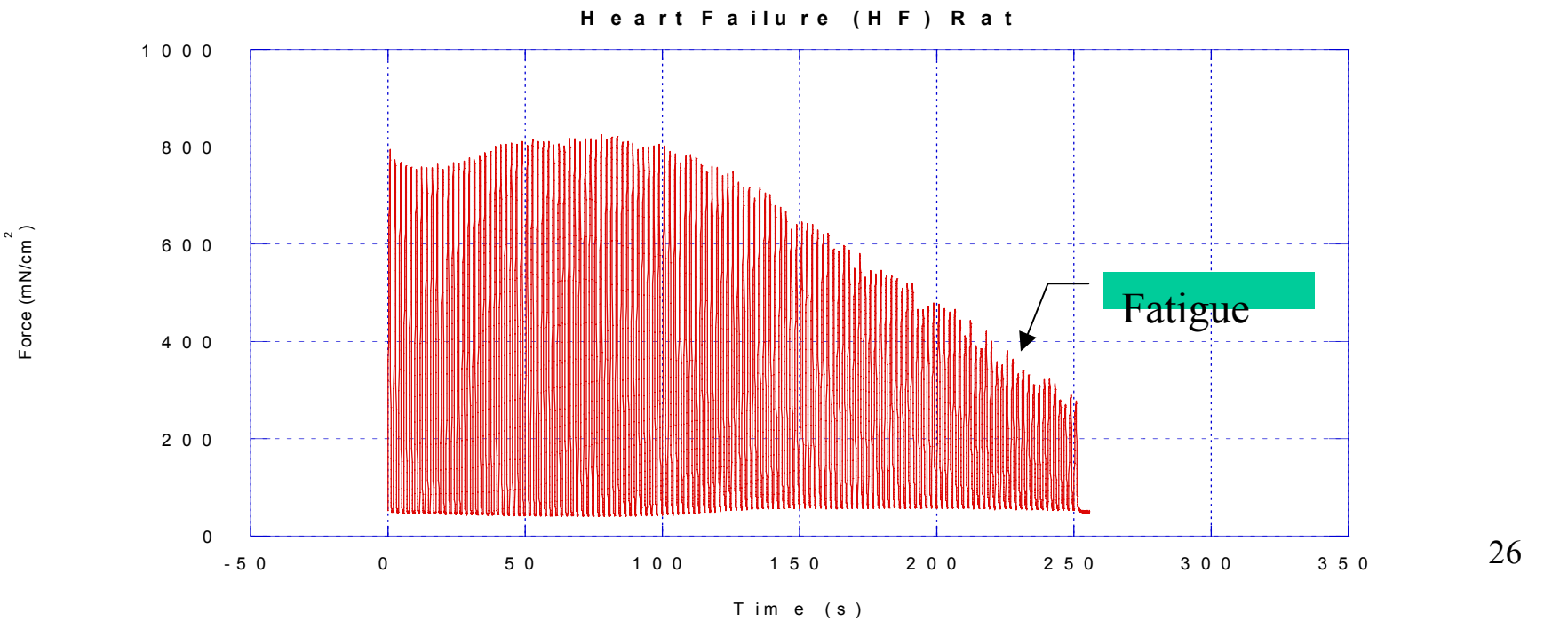
Tetanus Protocol

- 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
1000
800
600
400
200
0
Force (mN/cm 2)
-50
0
50
100
150
200
250
300
350
Time (s)
Fatigue


Heart Failure (HF) Rat
1000
800
600
400
200
0
Force (mN/cm 2)
-50
0
50
100
150
200
250
300
350
Time (s)
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 μm diameter, 200-300 μm 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

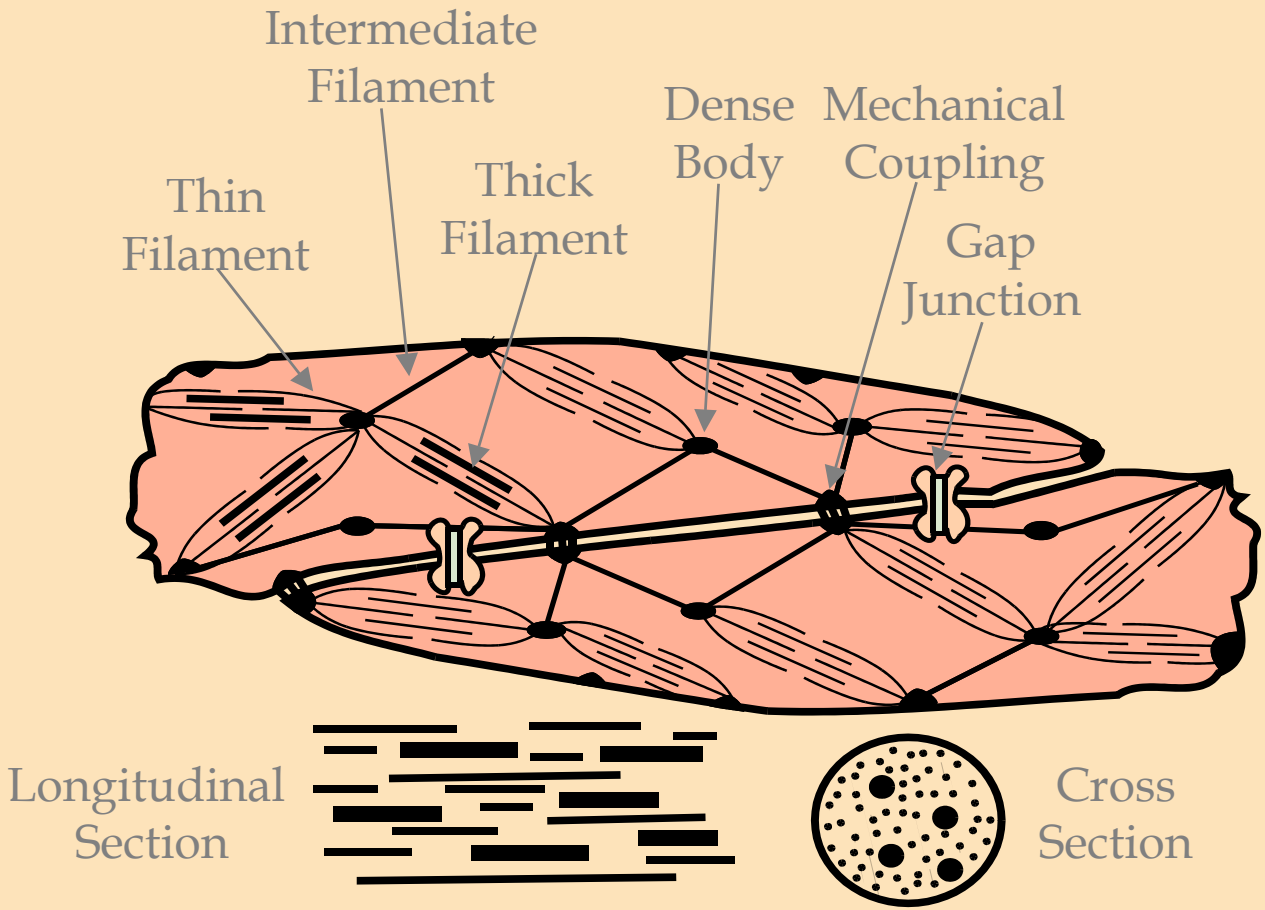
- Spindle shaped cells
- Relatively small compared to skeletal and cardiac muscle
  - 2-5 μm wide
  - 50-200 μm long.

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



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.**