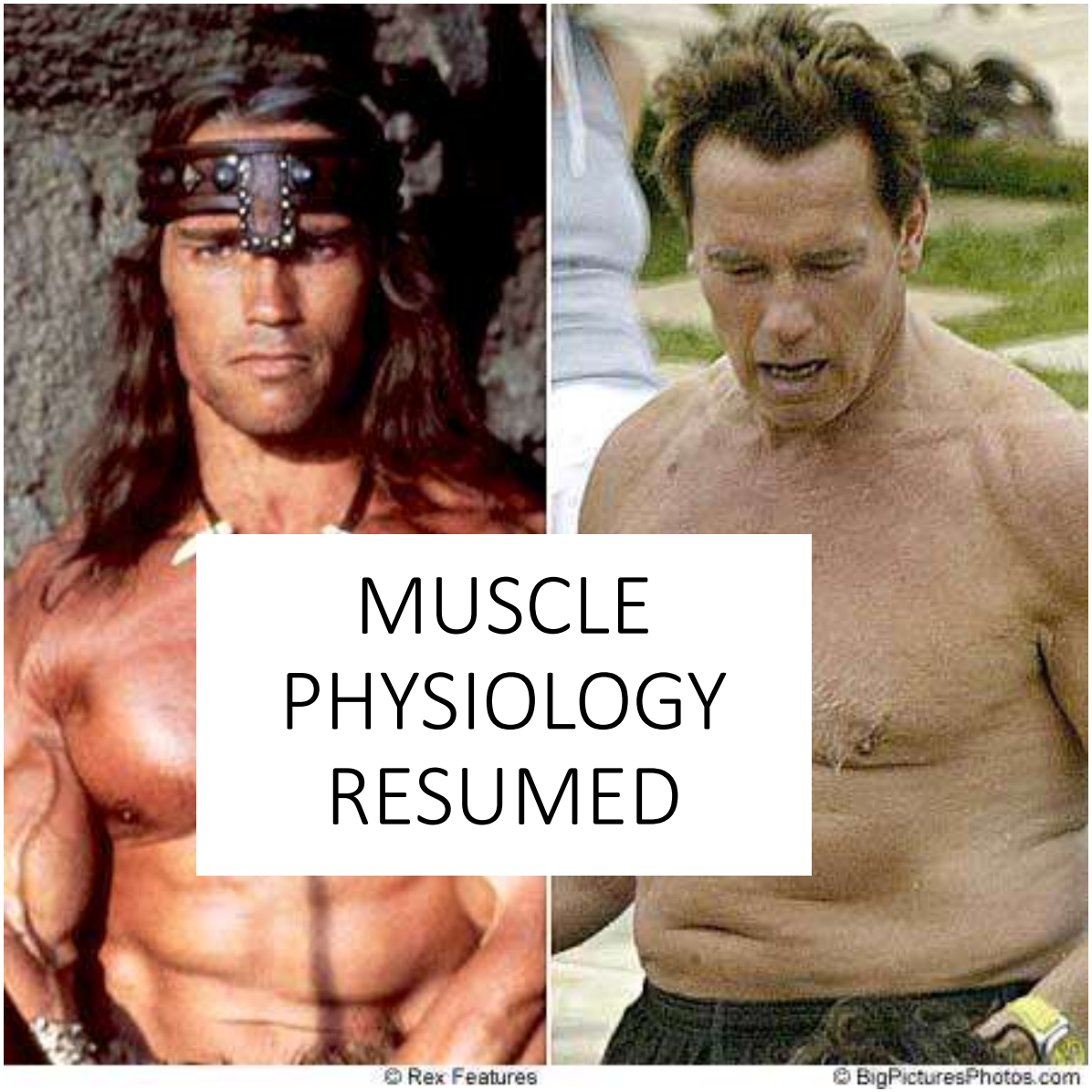
MUSCLE PHYSIOLOGY RESUMED

D.HAMMOUDI.
MD



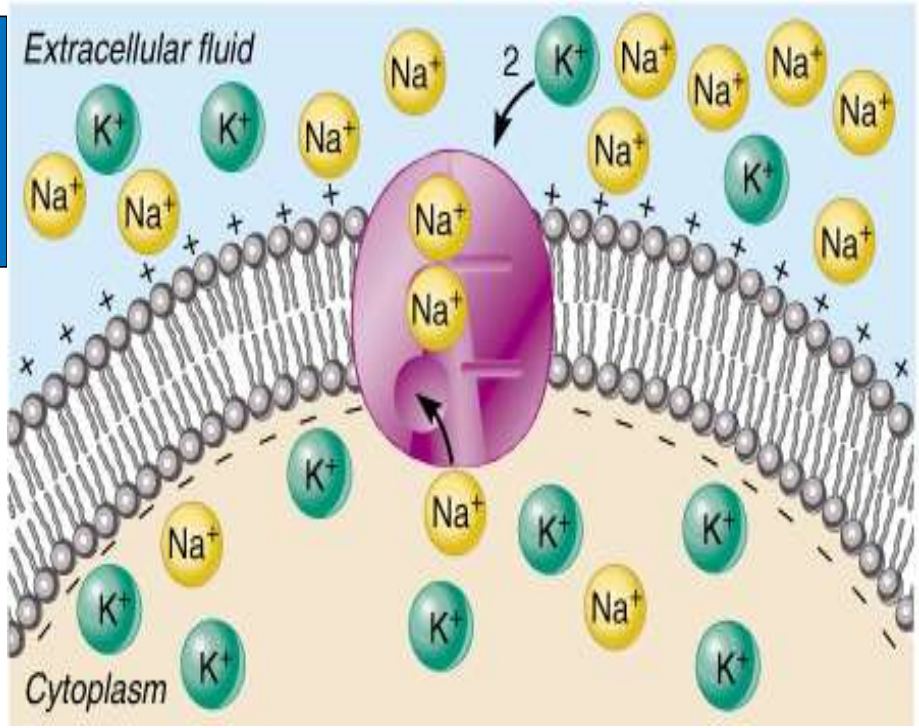
We can actually divide the whole process of muscle contraction into 4 steps:

- **Excitation**
- **Excitation-contraction coupling**
- **Contraction**
- **Relaxation**

Excitation

2. The Na^+/K^+ pump is constantly pumping 3 Na^+ ions out and 2 K^+ ions in for every ATP used. Thus more positive charge is leaving than entering.
3. There are protein anions (i.e., negatively charged proteins) within the ICF that cannot travel through the PM.

- What this adds up to is the fact that the inside of the cell is negative with respect to the outside. *The interior has less positive charge than the exterior*.



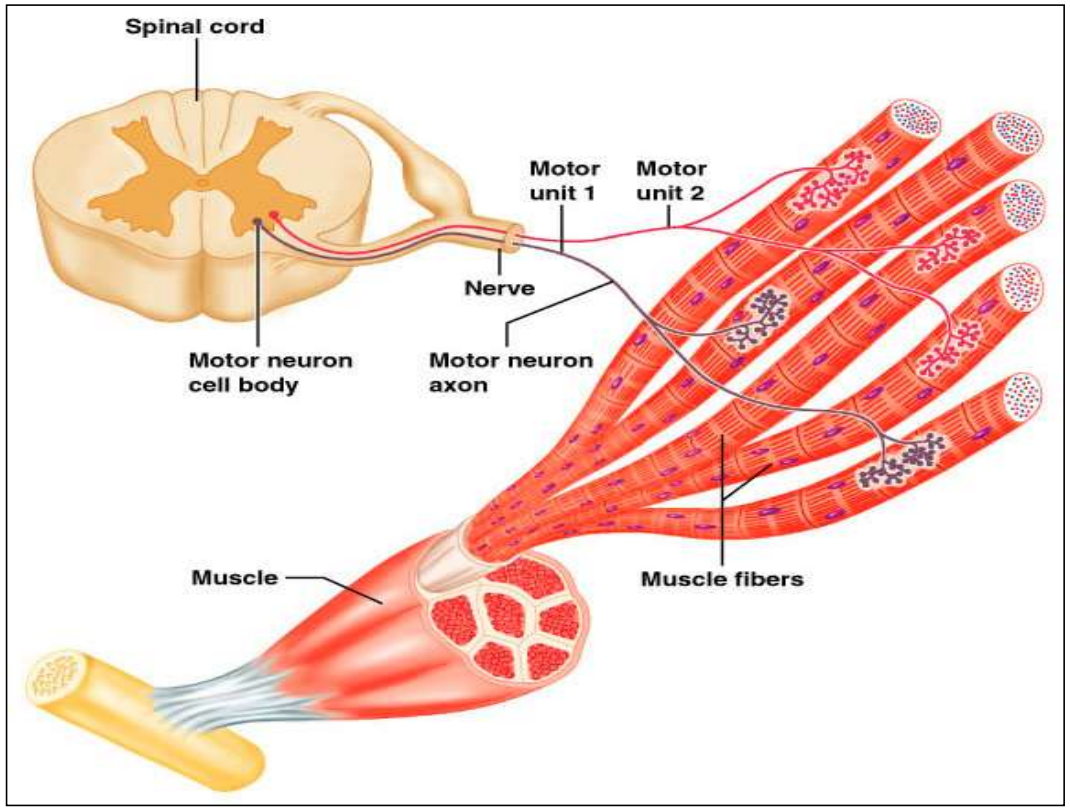
- This charge separation is known as a membrane potential (abbreviated V_m).
- The value for V_m in inactive muscle cells is typically btwn –80 and –90 millivolts.
- Cells that exhibit a V_m are said to be *polarized*.
  - Why do you suppose that is?
- V_m can be changed by influx or efflux of charge.

Excitation

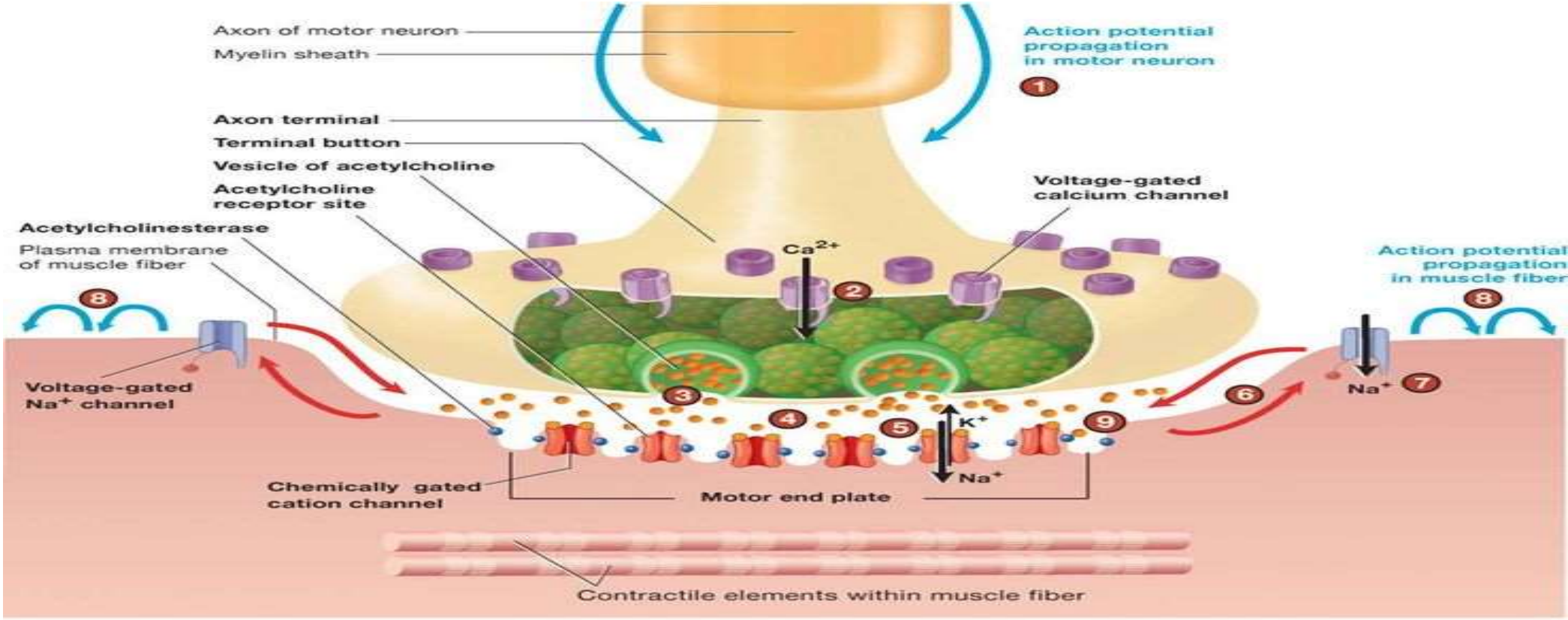
- The PM has integral proteins that act as gated ion channels. These are channels that are normally closed, but in response to a certain signal, they will open and allow specific ions to pass through them.
- Ion channels may be:
  - **Ligand-gated → the binding of an extracellular molecule (e.g., hormone, neurotransmitter) causes these channels to open.**
  - **Voltage-gated → ΔV_m causes these channels to open.**
  - **Mechanically-gated → stretch or mechanical pressure opens these channels.**
- When a channel is open, its specific ion(s) will enter or exit depending on their electrochemical gradient.

Motor Unit: The Nerve-Muscle Functional Unit

Each muscle has at least one motor nerve that may contain hundreds of motor neuron axons. Axons branch into terminals, each forming a neuromuscular junction with a single muscle fiber



A motor neuron and all the muscle fibers it supplies is called a Motor Unit



1. An action potential in a motor neuron is propagated to the terminal button.
2. The presence of an action potential in the terminal button triggers the opening of voltage-gated Ca^{2+} channels and the subsequent entry of Ca^{2+} into the terminal button.
3. Ca^{2+} triggers the release of acetylcholine by exocytosis from a portion of the vesicles.
4. Acetylcholine diffuses across the space separating the nerve and muscle cells and binds with receptor sites specific for it on the motor end plate of the muscle cell membrane.
5. This binding brings about the opening of cation channels, leading to a relatively large movement of Na^{+} into the muscle cell compared to a smaller movement of K^{+} outward.
6. The result is an end-plate potential. Local current flow occurs between the depolarized end plate and adjacent membrane.
7. This local current flow opens voltage-gated Na^{2+} channels in the adjacent membrane.
8. The resultant Na^{2+} entry reduces the potential to threshold, initiating an action potential, which is propagated throughout the muscle fiber
9. Acetylcholine is subsequently destroyed by acetylcholinesterase, an enzyme located on the motor end-plate membrane, terminating the muscle cell's response.

Sarcomere Structure -

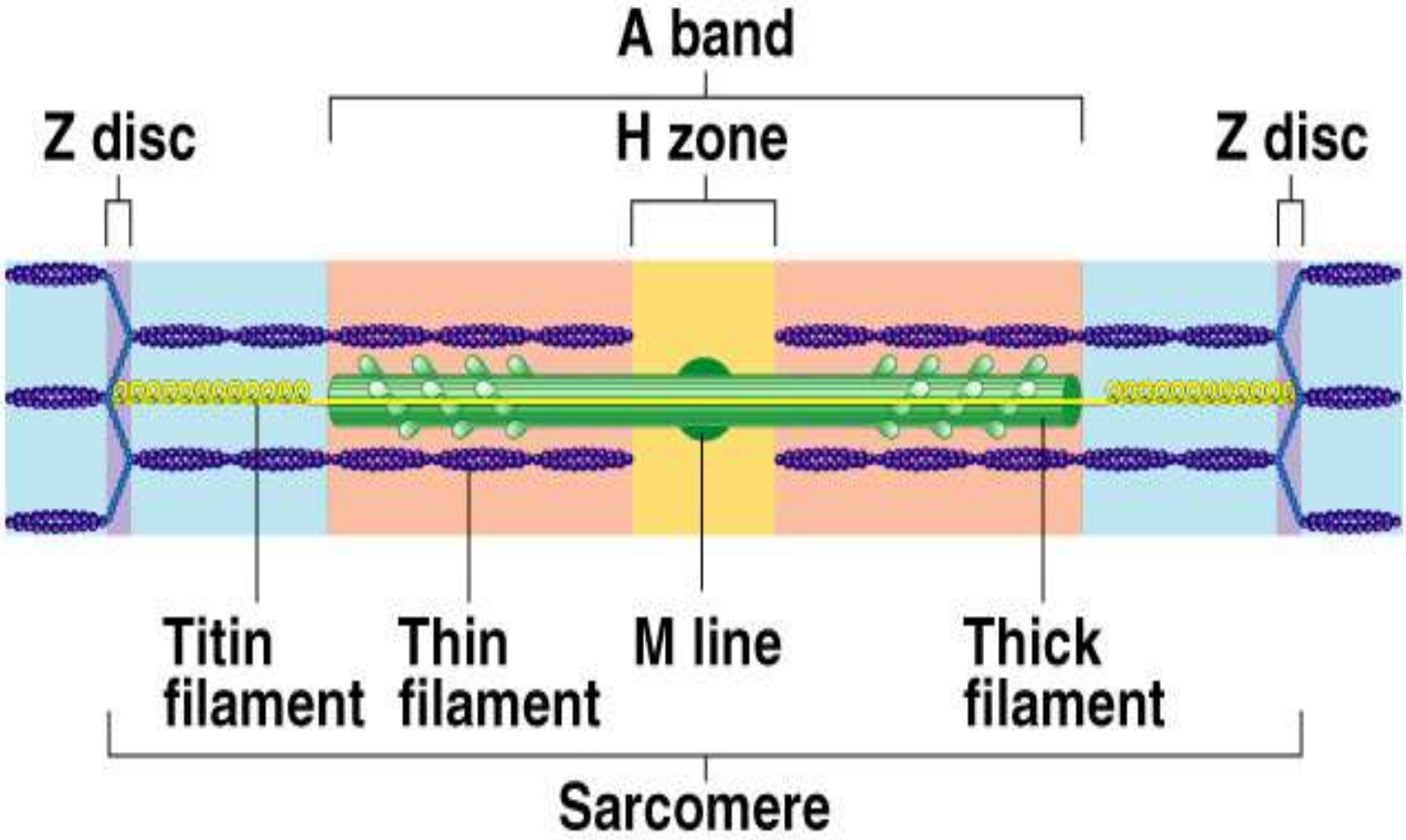
A) Thick filaments
   1) mostly myosin protein
      a) ~200 twisted myosin proteins form thick filament ("golf clubs")
      b) held in place by elastic filament (titin protein)
      c) can bind ATP
      d) splits ATP to ADP
      e) can bind actin proteins

B) Thin filaments
   1) Actin protein
      a) "bean-shaped" protein in strands
      b) has myosin-binding site
   2) Tropomyosin
      a) covers myosin-binding site
   3) Troponin
      a) **can bind calcium**
      b) regulates action of tropomyosin

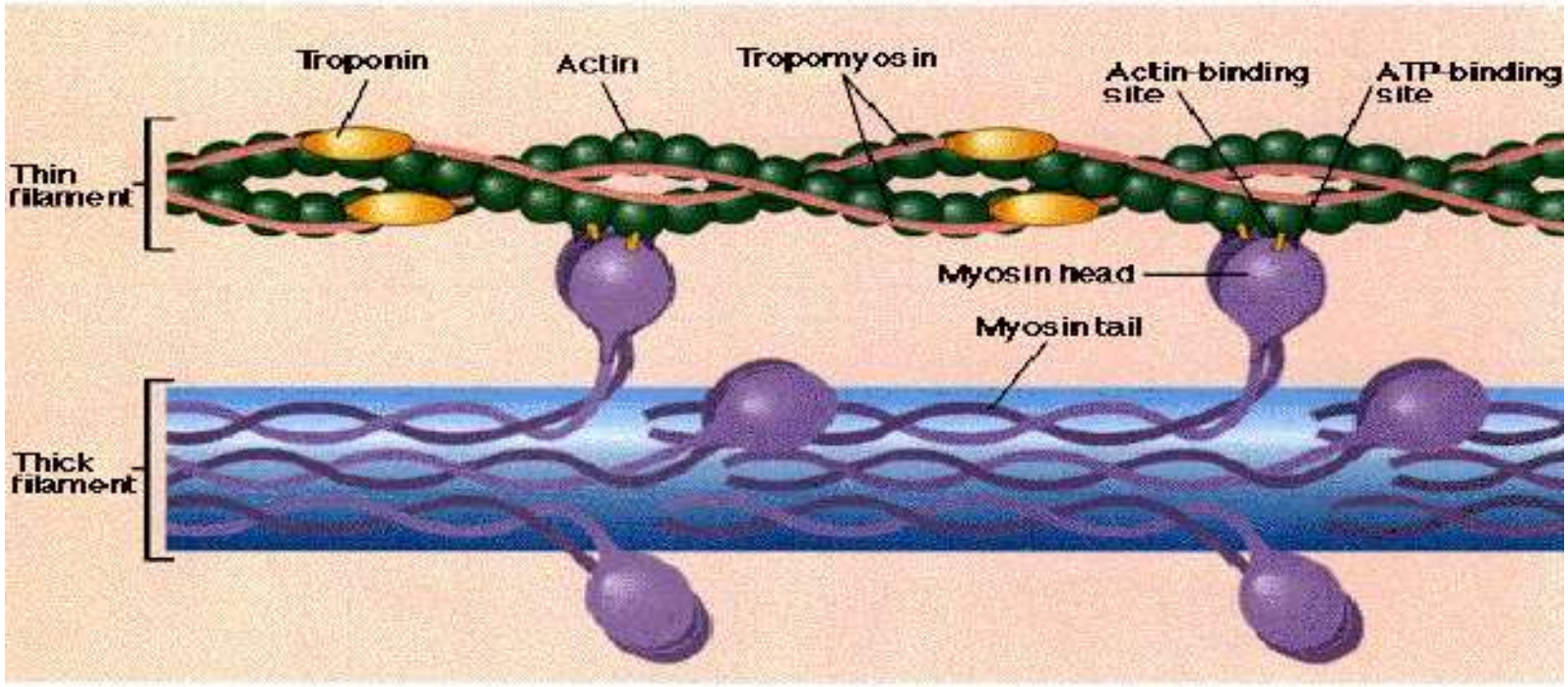
C) Contractile proteins
   1) actin & myosin

D) Regulatory proteins
   1) troponin & tropomyosin

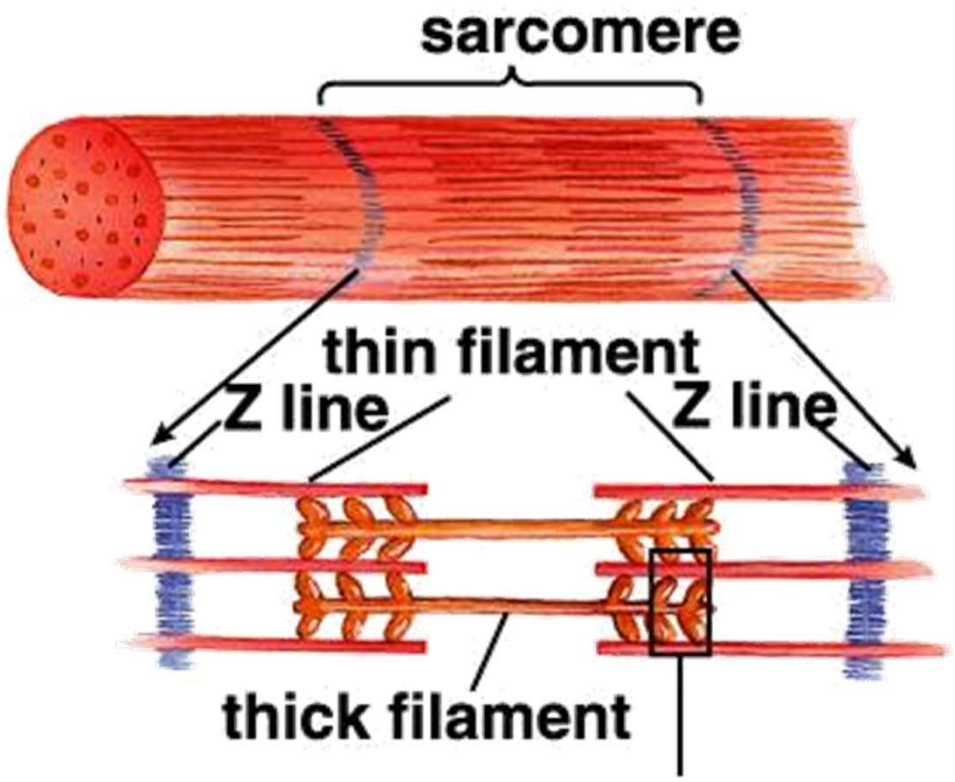
SARCOMERE


A band
Z disc
H zone
Z disc
Titin filament
Thin filament
M line
Thick filament
Sarcomere

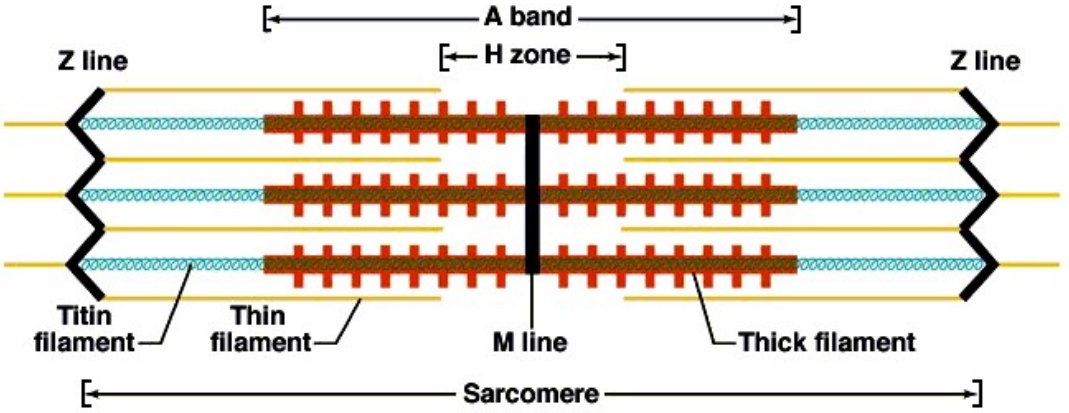
Myosin & the Thick Filament



MYOFIBRIL AND SARCOMERE

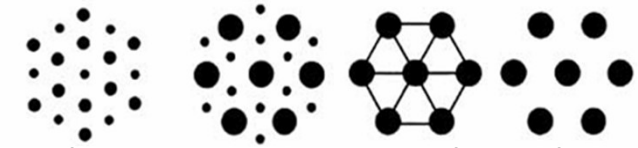


Sarcomere: functional unit of striated muscle

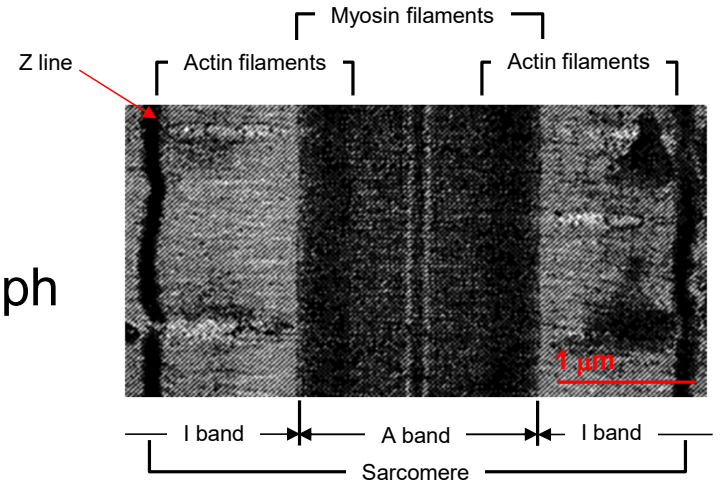


Modified from Vander, Sherman, Luciano *Human Physiology,* McGraw-Hill.

Cross-sectional views of:

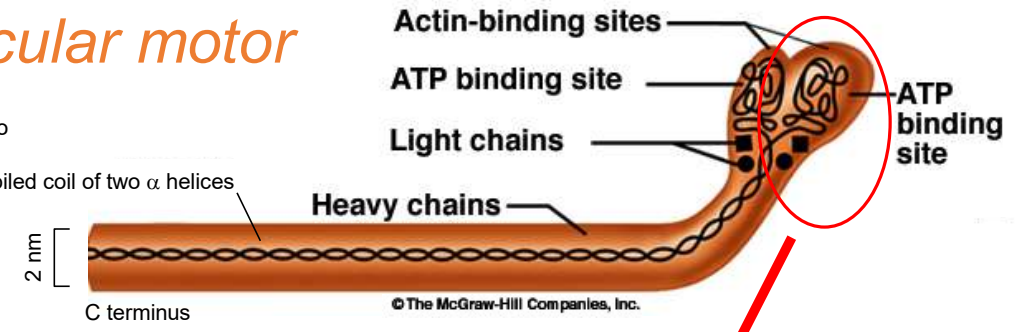


Electron micrograph

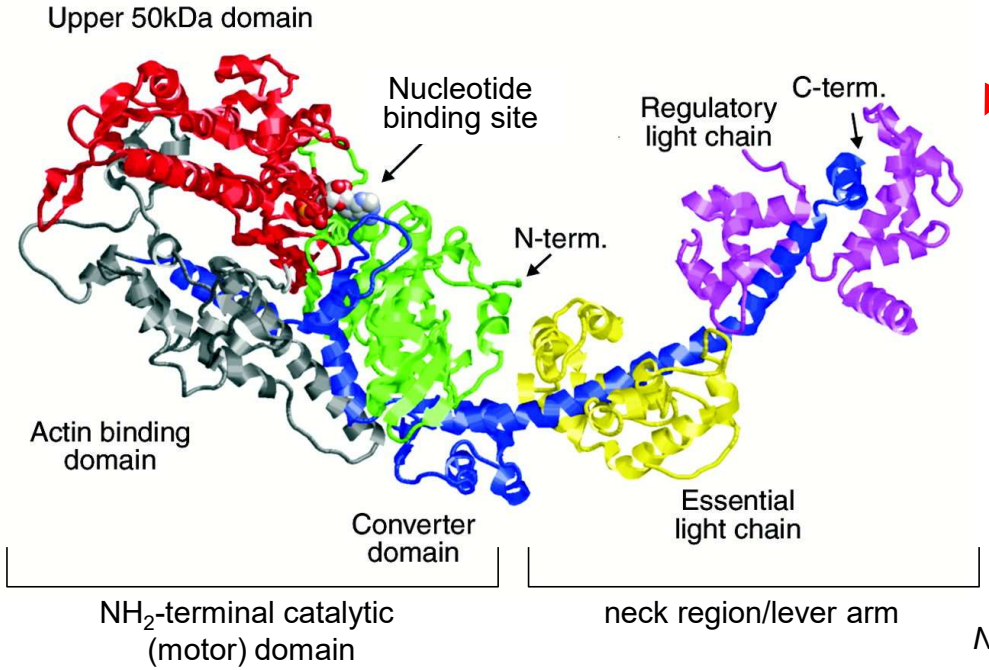


Myosin is a molecular motor

Modified from Vander, Sherman, Luciano
Human Physiology, McGraw-Hill.



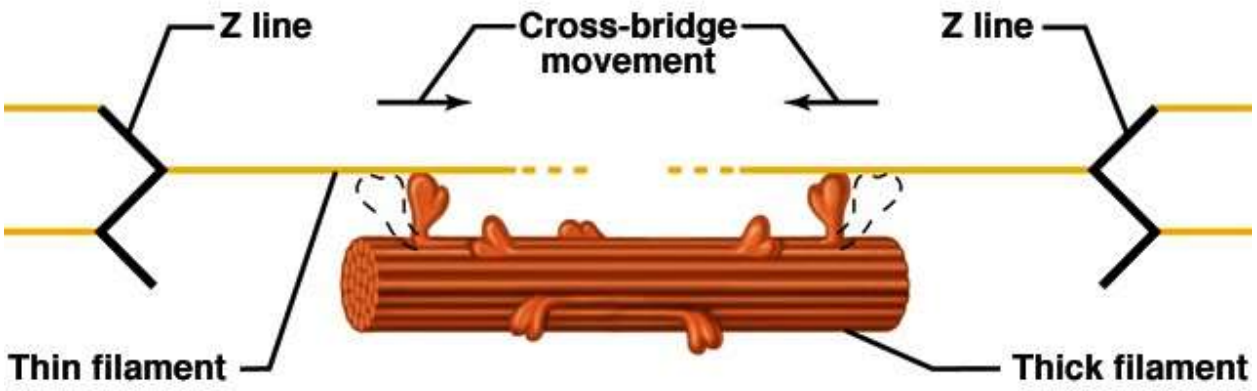
Myosin head: retains all of the motor functions of myosin, i.e. the ability to produce movement and force.



Myosin S1 fragment crystal structure

Ruegg et al., (2002)
News Physiol Sci 17:213-218.

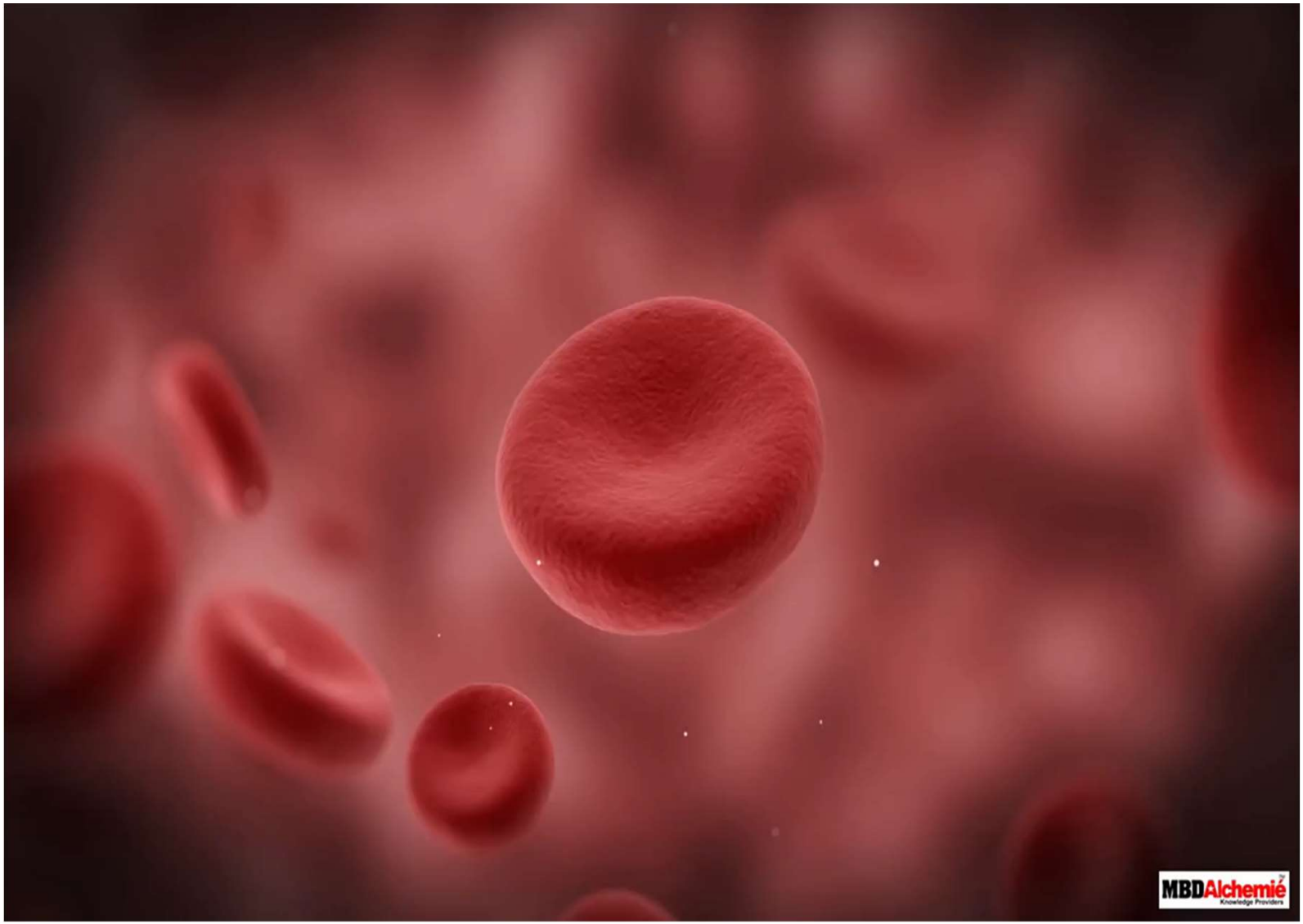
How striated muscle works: The Sliding Filament Model



From Vander, Sherman, Luciano
Human Physiology, McGraw-Hill.

The lever movement drives displacement of the actin filament relative to the myosin head (~5 nm), and by deforming internal elastic structures, produces force (~5 pN).

Thick and thin filaments interdigitate and “slide” relative to each other.


MBDAlchemie
Knowledge Providers

Events of Muscle Contraction

1) arrival of neuronal action potential at neuromuscular junction

2) release and diffusion of acetylcholine into synaptic cleft

3) binding of acetylcholine to receptor at motor end plate

4) activation of action potential on muscle surface (sarcolemma)

5) release of calcium from sarcoplasmic reticulum inside muscle fiber

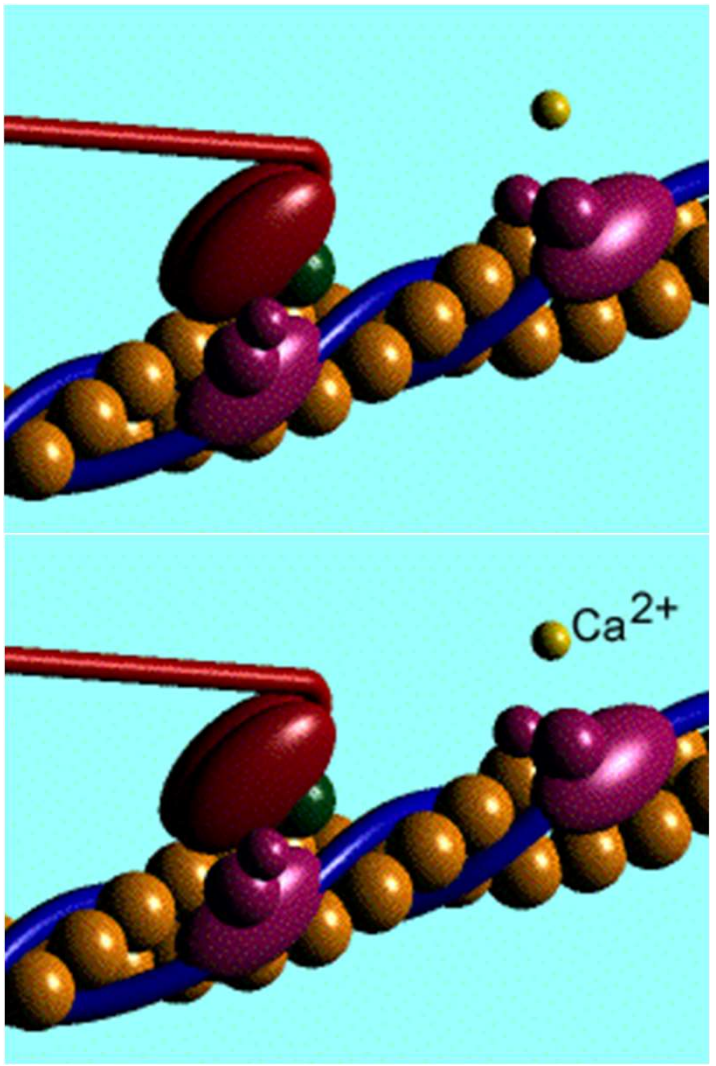
6) binding of calcium to troponin/tropomyosin complex

7) exposure of myosin-binding site on actin

8) binding of actin and myosin and "Power stroke" single ratchet of myosin to pull actin and release ADP

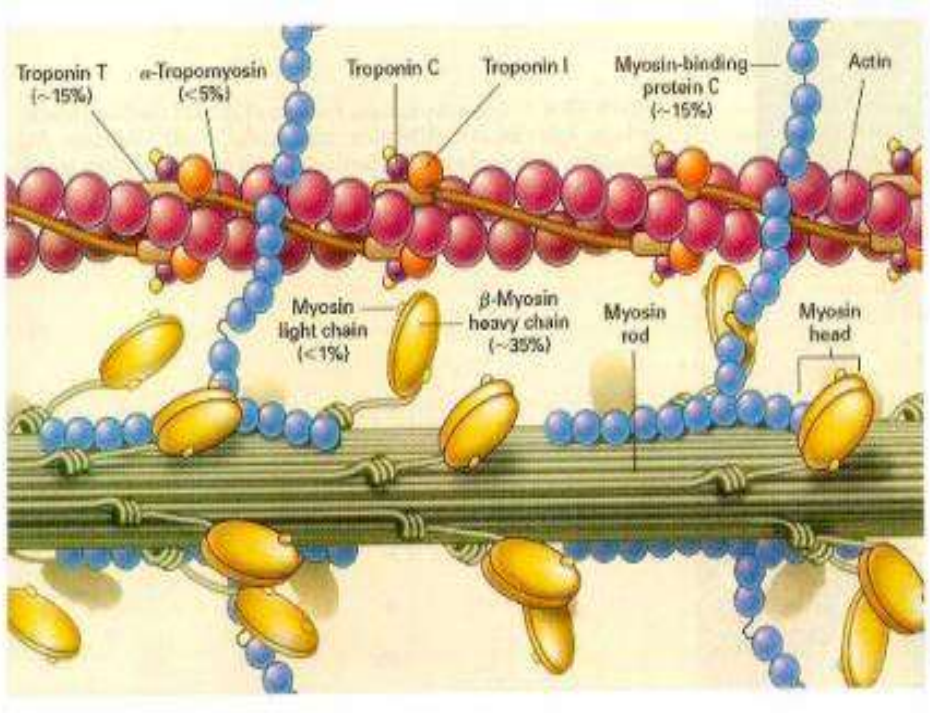
9) myosin releases actin, swivels back, binds and splits ATP ("reset")

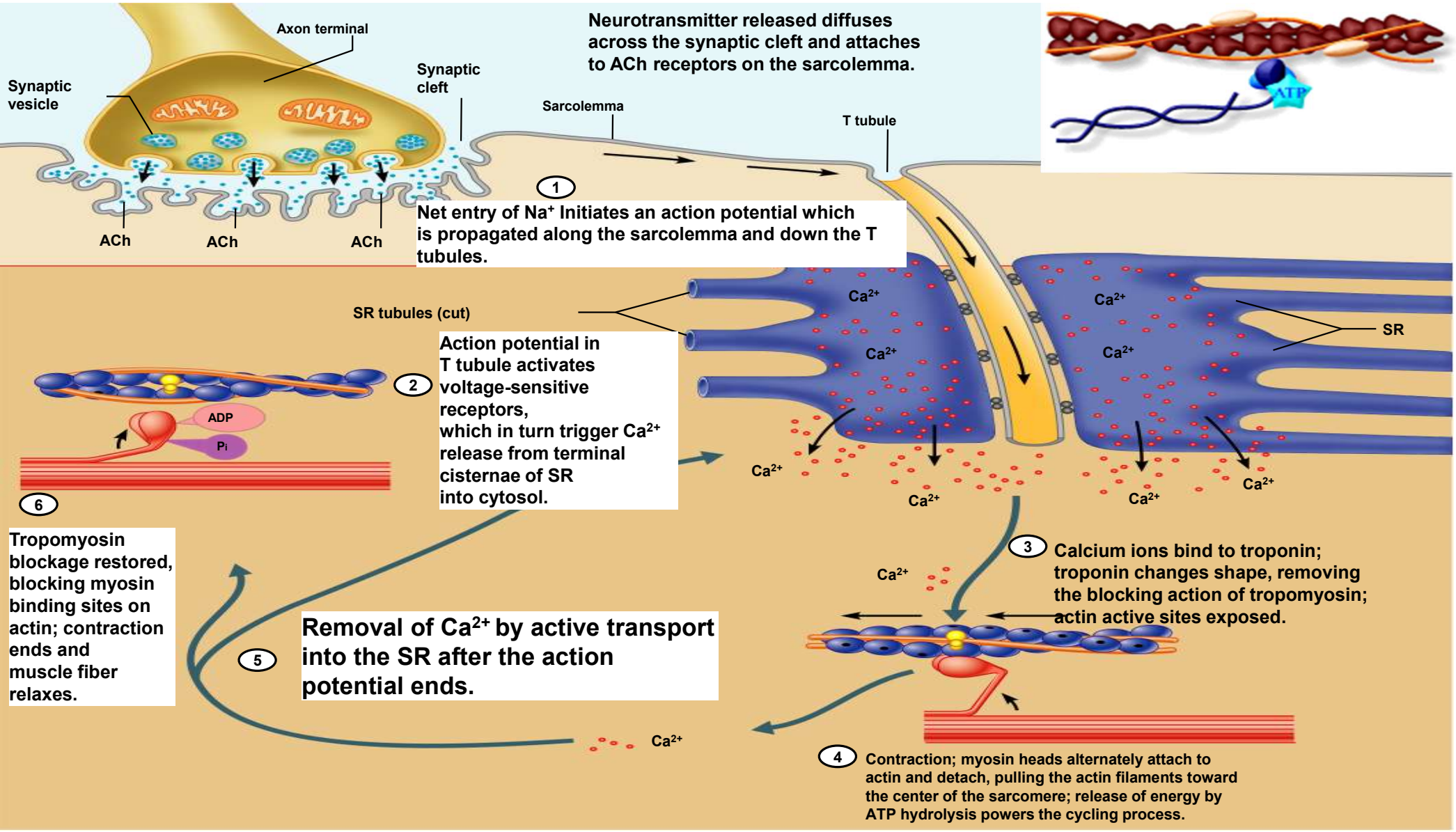
10) repeat binding myosin to actin (Repeat step 8-10)

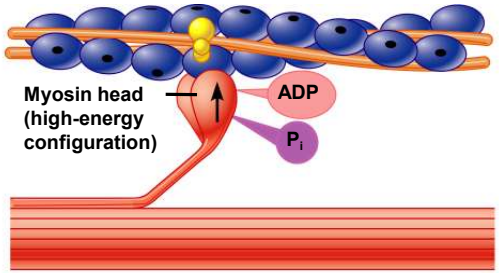


Exitation-contraction Coupling Role of Ca^{++}

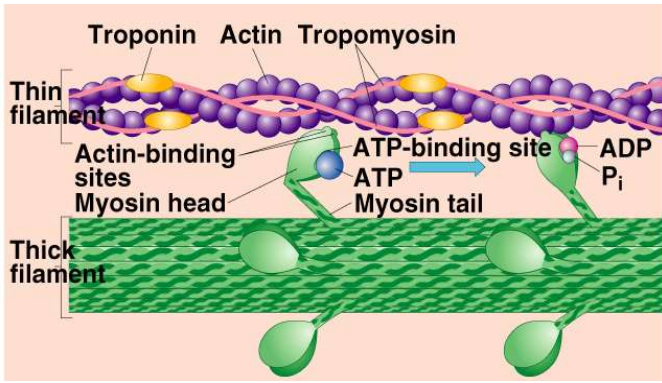
- Ca^{++} combines with Troponin-C
- Complex inhibits Troponin-I (has strong affinity for Actin)
- Inhibition of Tn-1 reveals active sites on Actin
- M heads combine, detach and recombine
- Binding causes conformational change in the head
- Binding of actin and myosin activates ATPase
- ATPase splits ATP
- MH + ATP → ADP + Pi + energy released
- Head tilts backwards toward the arm
- The process repeated using more ATP and Ca^{++}
- In fast twitch muscle fibers, the ATPase activity is high

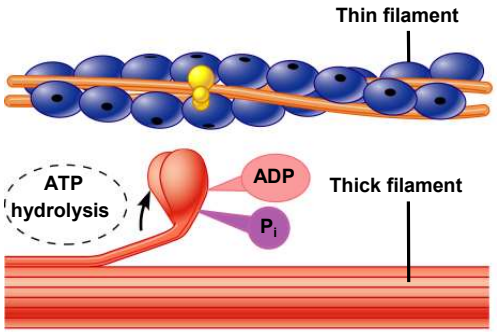



Axon terminal
Synaptic vesicle
Synaptic cleft
Sarcolemma
T tubule
Neurotransmitter released diffuses across the synaptic cleft and attaches to ACh receptors on the sarcolemma.
ATP
ACh
ACh
ACh
1
Net entry of Na+ Initiates an action potential which is propagated along the sarcolemma and down the T tubules.
SR tubules (cut)
SR
Ca2+
2
Action potential in T tubule activates voltage-sensitive receptors, which in turn trigger Ca2+ release from terminal cisternae of SR into cytosol.
ADP
Pi
6
Tropomyosin blockage restored, blocking myosin binding sites on actin; contraction ends and muscle fiber relaxes.
5
Removal of Ca2+ by active transport into the SR after the action potential ends.
3
Calcium ions bind to troponin; troponin changes shape, removing the blocking action of tropomyosin; actin active sites exposed.
4
Contraction; myosin heads alternately attach to actin and detach, pulling the actin filaments toward the center of the sarcomere; release of energy by ATP hydrolysis powers the cycling process.

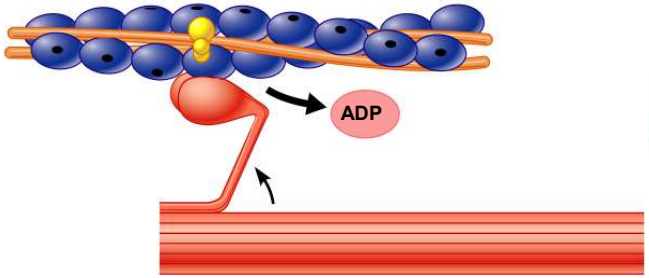


1 Myosin head attaches to the actin myofilament, forming a cross bridge.

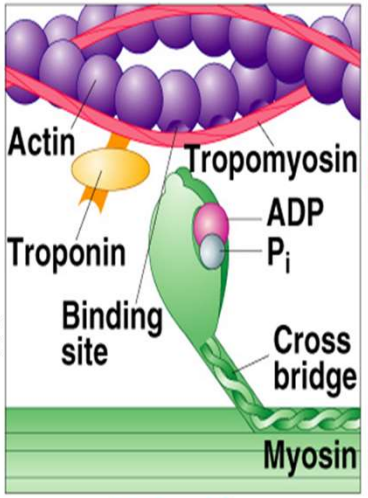




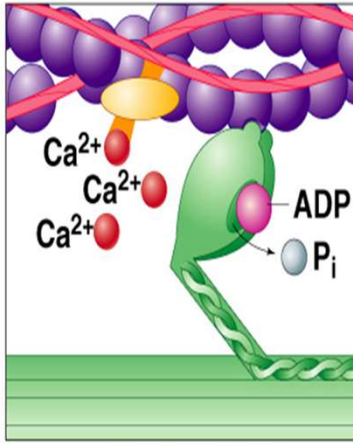
4 As ATP is split into ADP and P_i, the myosin head is energized (cocked into the high-energy conformation).



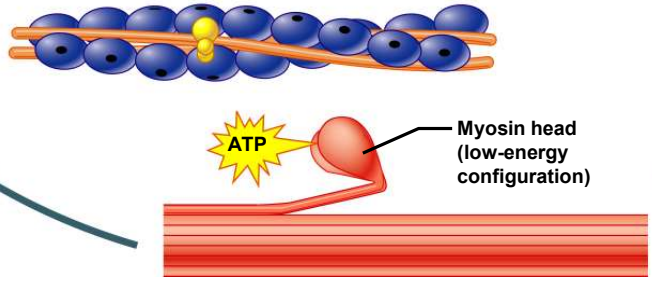
2 Inorganic phosphate (P_i) generated in the previous contraction cycle is released, initiating the power (working) stroke. The myosin head pivots and bends as it pulls on the actin filament sliding it toward the M line. Then ADP is release



Relaxed muscle



Contracting muscle



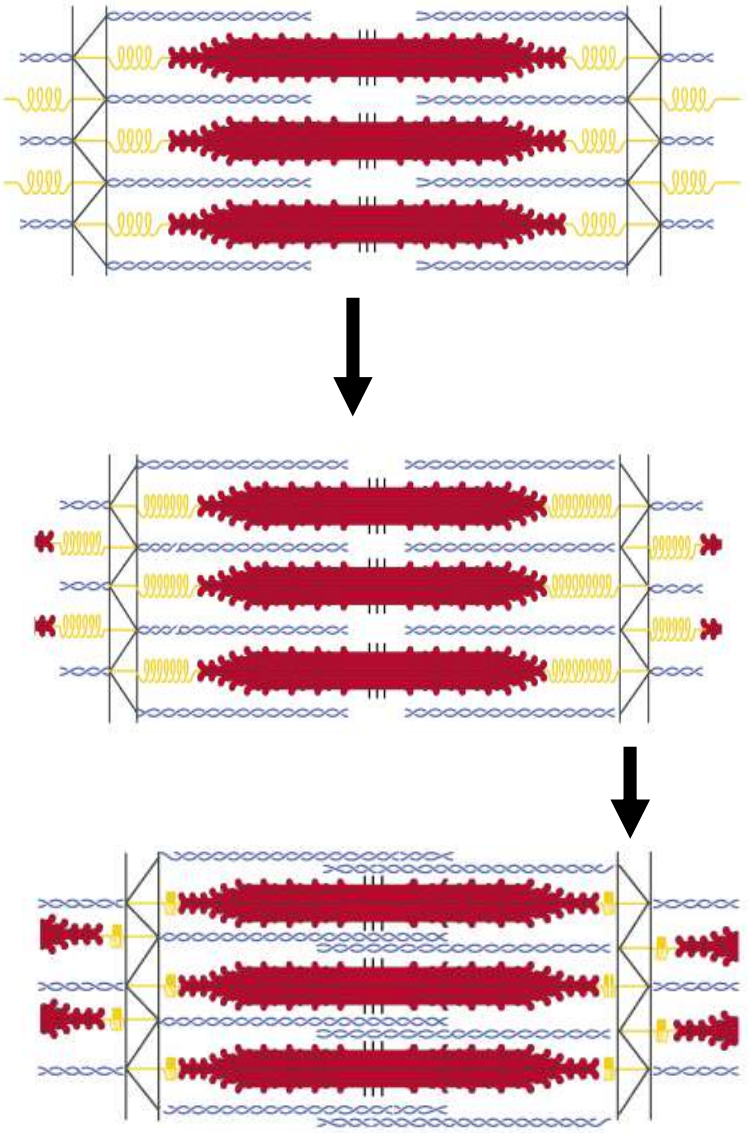
3 As new ATP attaches to the myosin head, the link between myosin and actin weakens, and the cross bridge detaches.

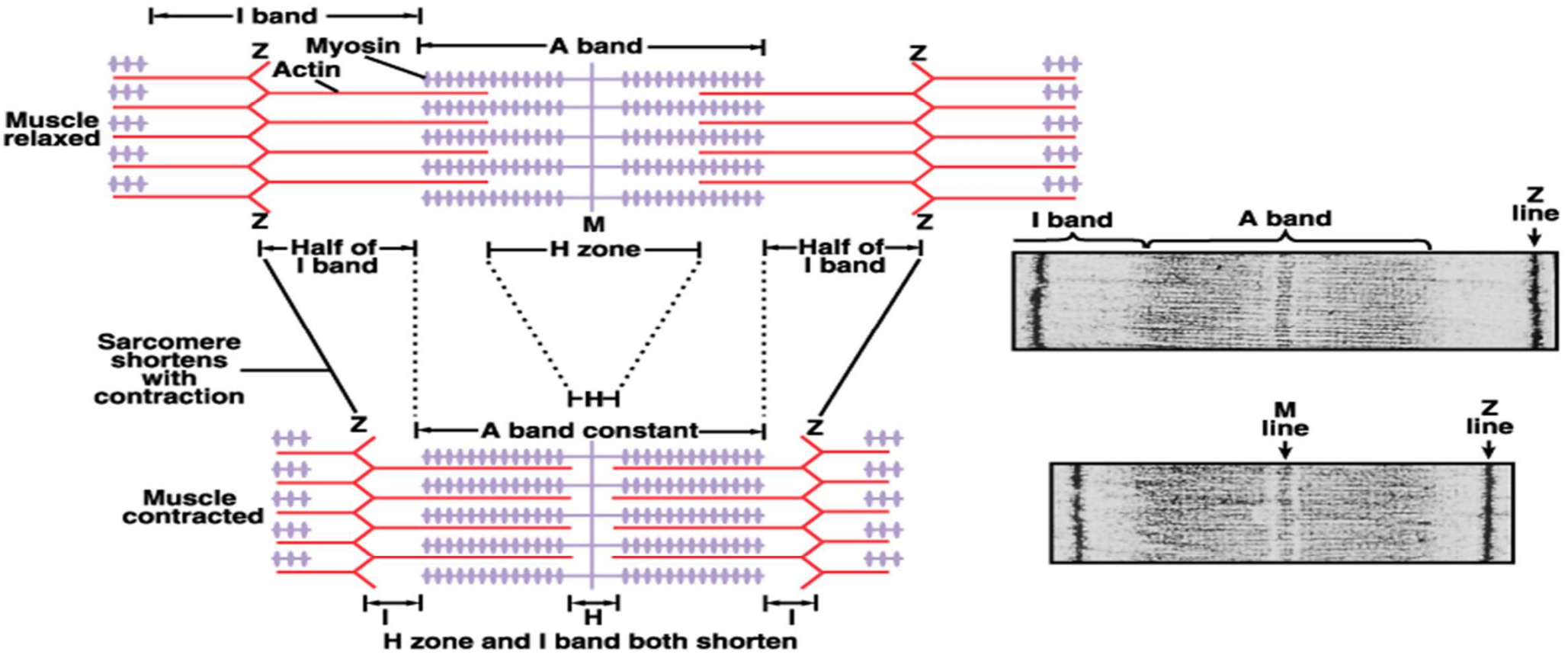
ATP

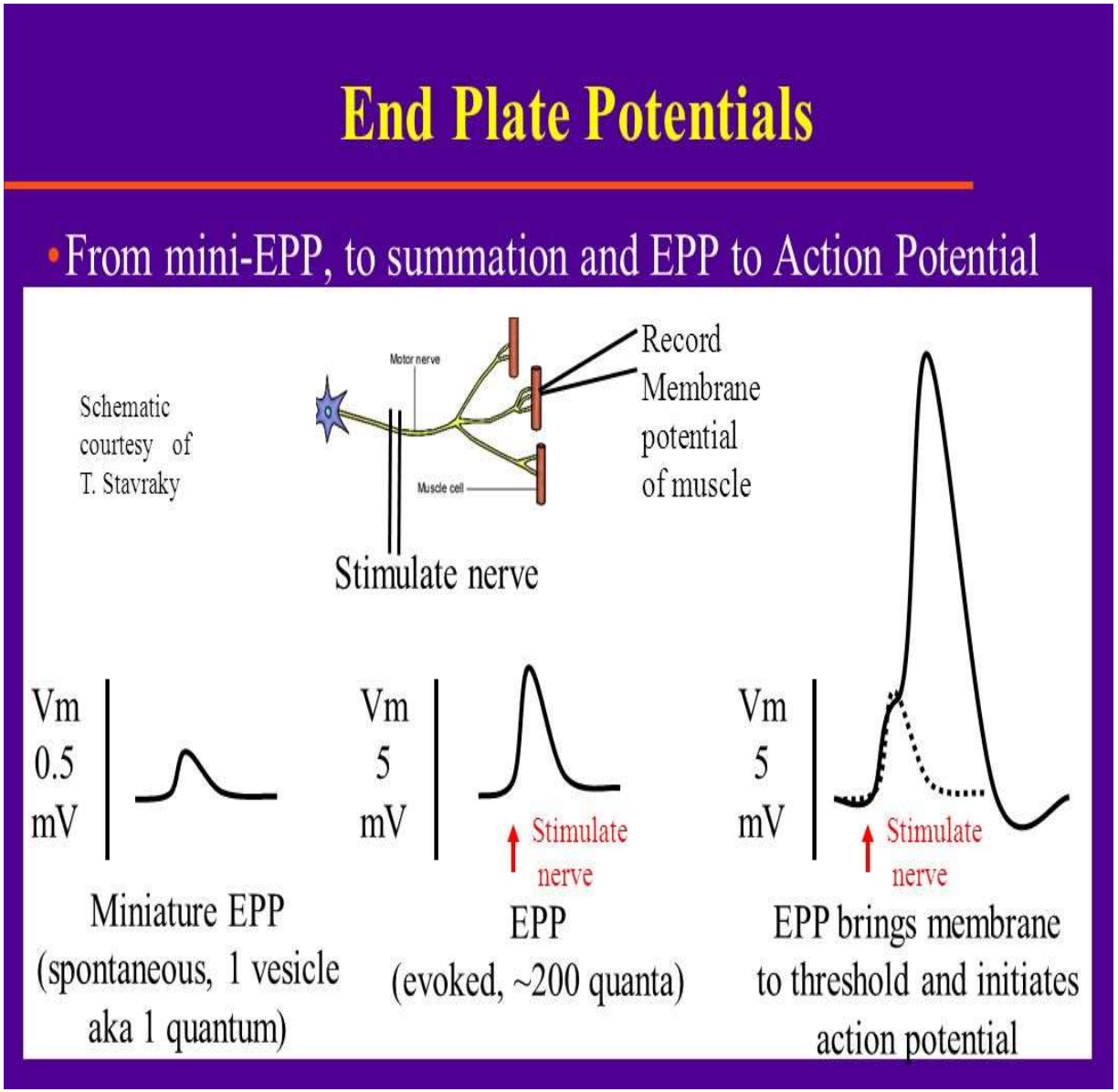
Here is what happensas the filaments slide and the sarcomere and the muscle fiber shortens.
In the process of contraction,

what happens to the:

1. **Distance btwn Z discs**
2. **Length of the A band**
3. **Length of the H zone**
4. **Length of the I band**



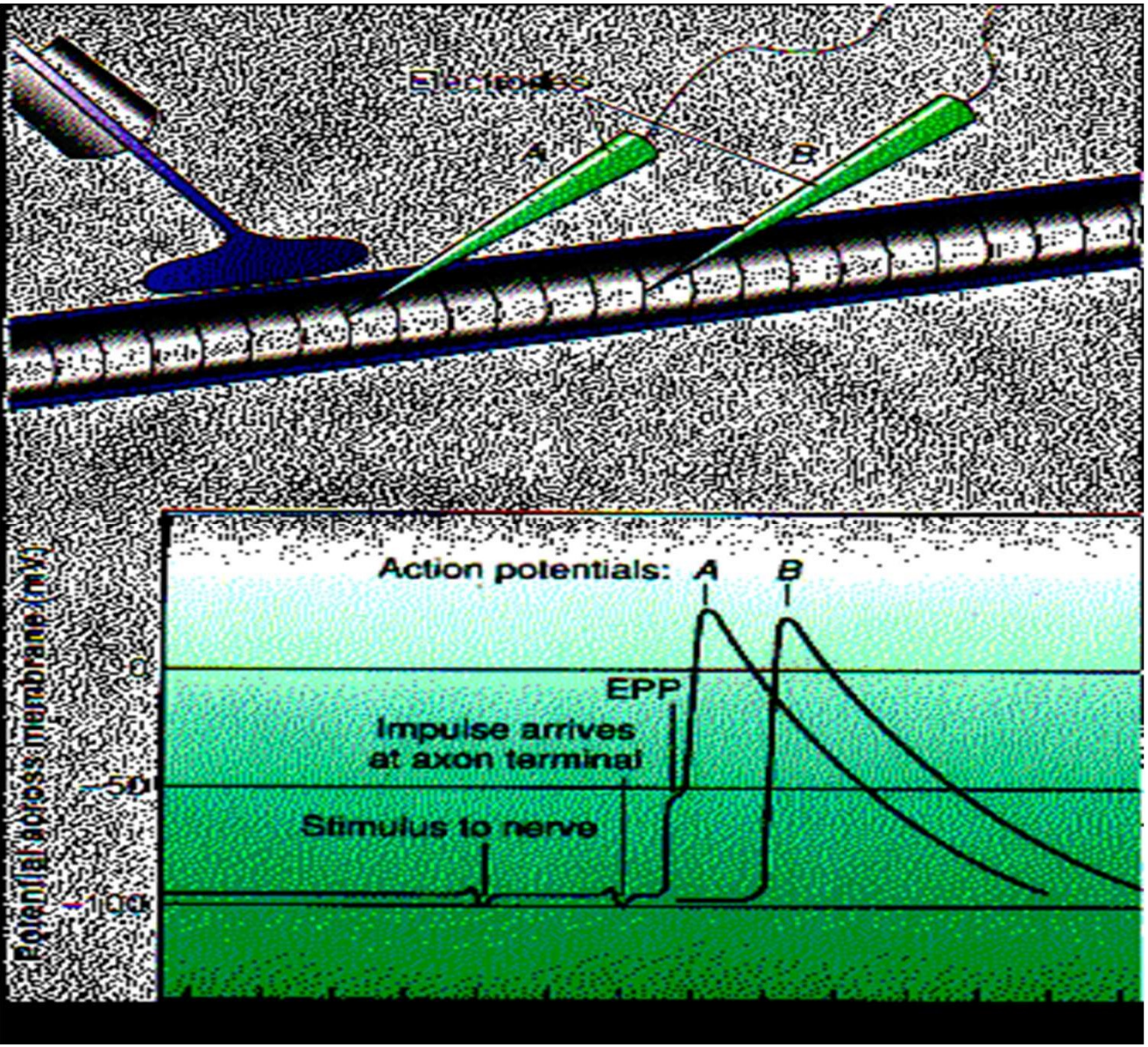

I band
A band
Myosin
Actin
Z
M
Muscle relaxed
Half of I band
H zone
Sarcomere shortens with contraction
A band constant
Muscle contracted
H
I
H zone and I band both shorten
I band
A band
Z line
M line



End plate potentials (EPPs):

- **depolarizations of skeletal muscle fibers caused by neurotransmitters binding to the postsynaptic membrane in the neuromuscular junction**.

- They are called "**end plates**" because:
  - **the postsynaptic terminals of muscle fibers have a large, saucer-like appearance.**

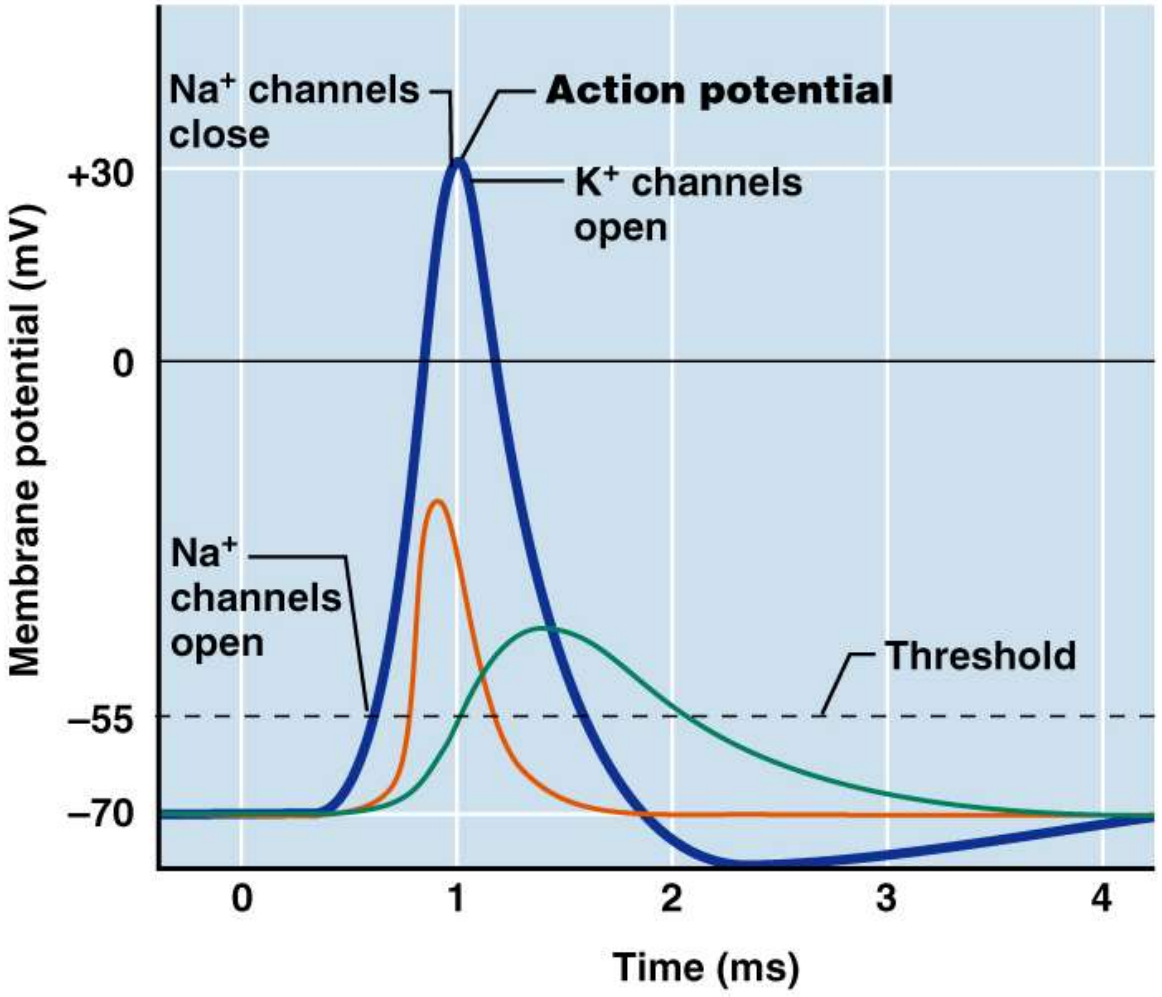


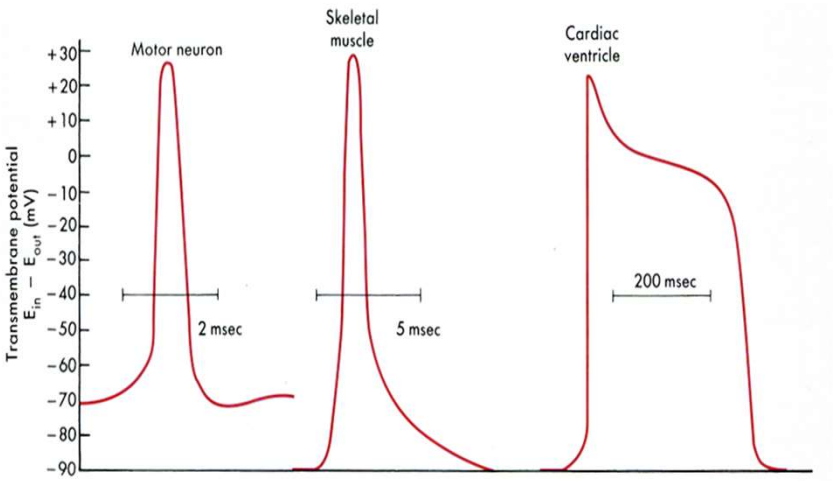
Arrival of a nerve impulse at the axon terminal of the motor neuron

=➔ acetylcholine to be released into the neuromuscular junction which creates an **end plate potential** (**EPP**) in the membrane beneath it (**A**) but not farther away (**B**).

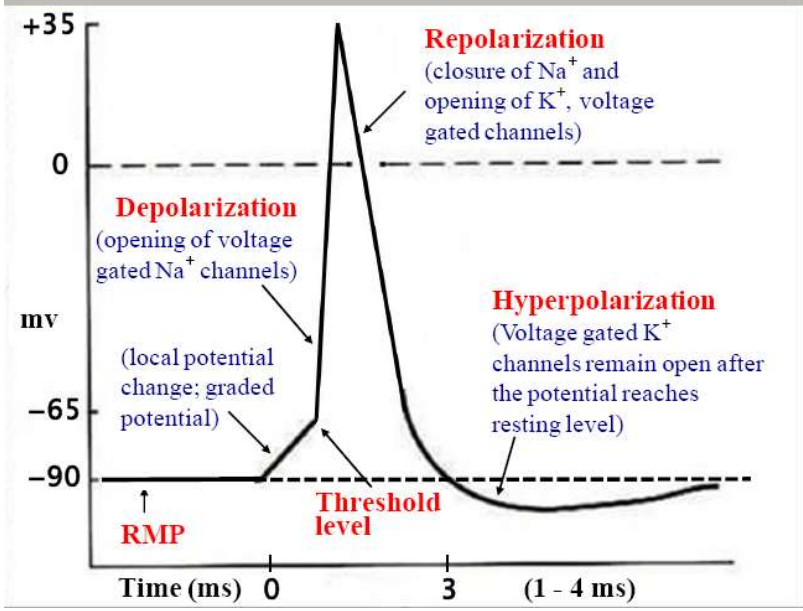
When the EPP reaches the threshold of the fiber (about -50 mv), an **action potential is generated that sweeps along the fiber** (**B**)

Action Potential Scan





Action potential

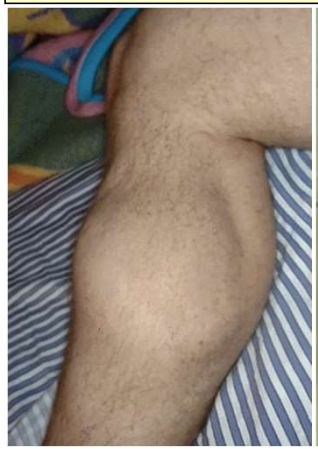


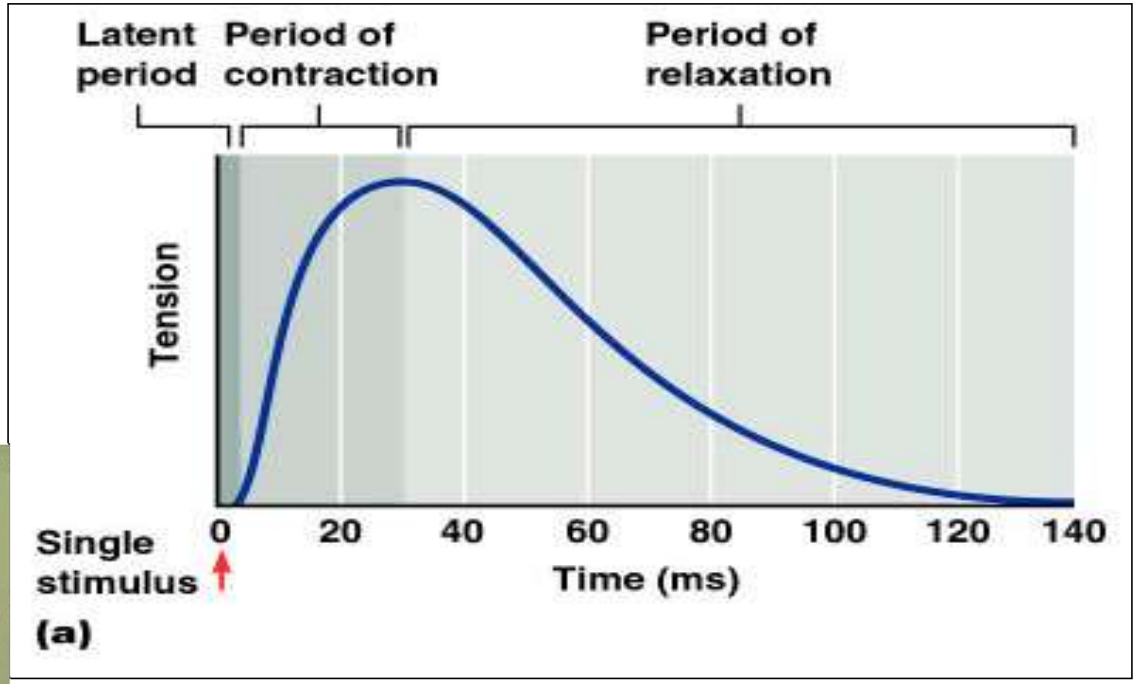
Muscle Twitch

- **A muscle twitch is the response of a muscle to a single action potential of its motor neuron.**
- **The fibers contract quickly and then relax.**

Three phases:

- **Latent Period**
- **Period of Contraction**
- **Period of Relaxation**





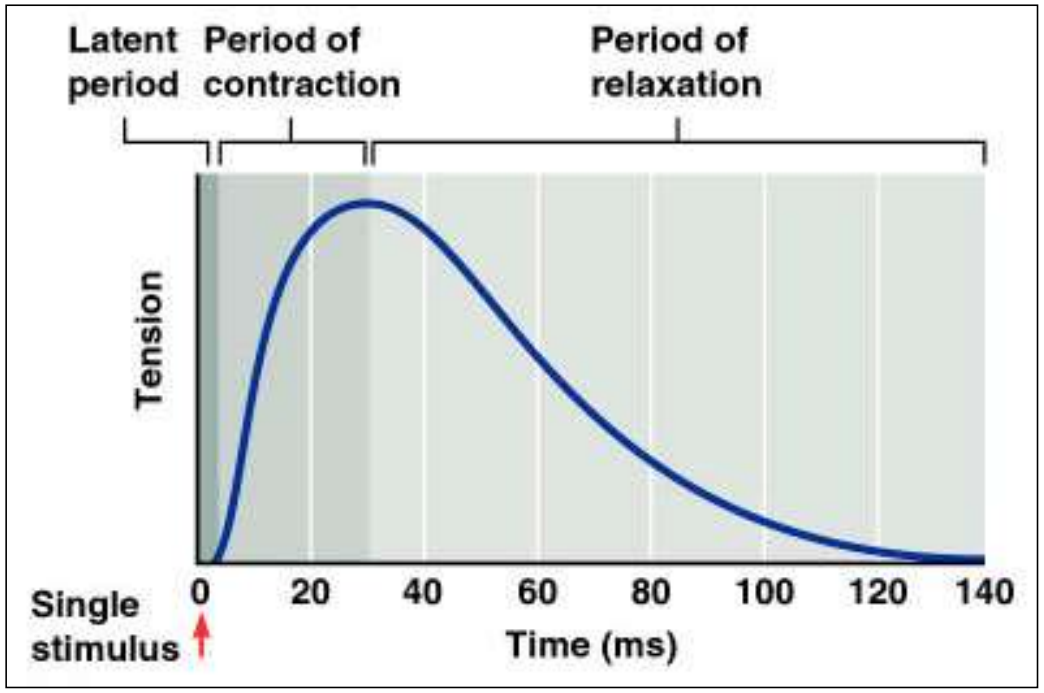
Myogram – graphic recording of contractile activity

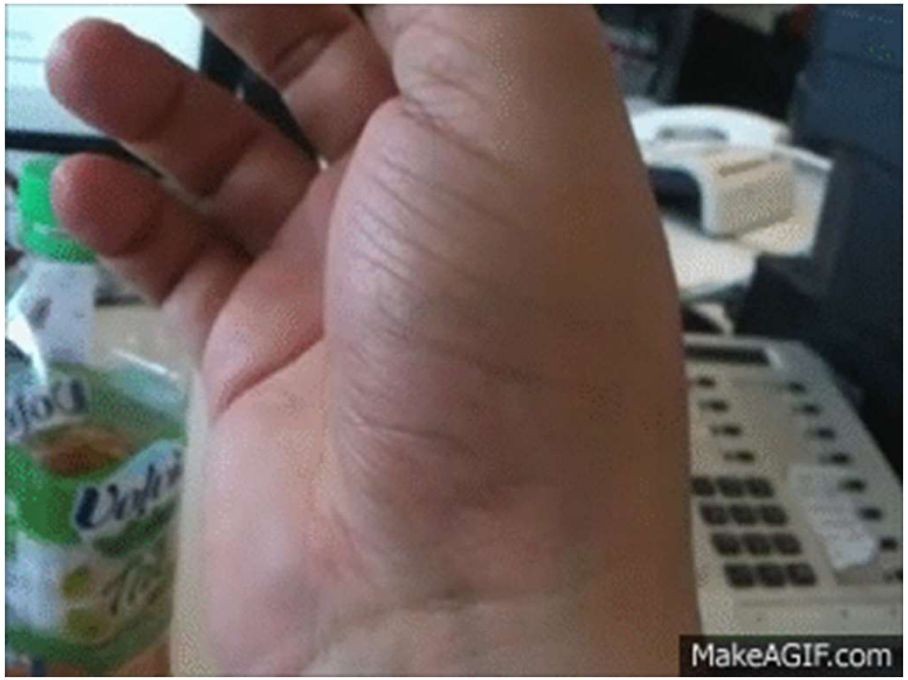
Muscle Twitch

Latent Period – the first few ms after stimulation when excitation-contraction is occurring

Period of Contraction – cross bridges are active and the muscle shortens if the tension is great enough to overcome the load

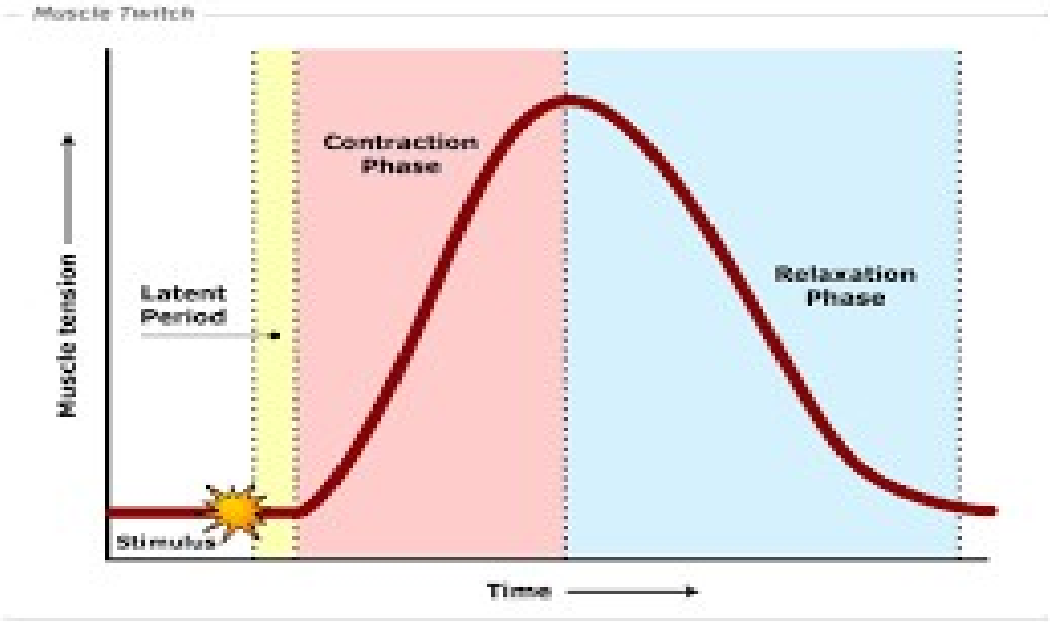
Period of Relaxation – Ca^{2+} is pumped back into SR and muscle tension decreases to baseline level

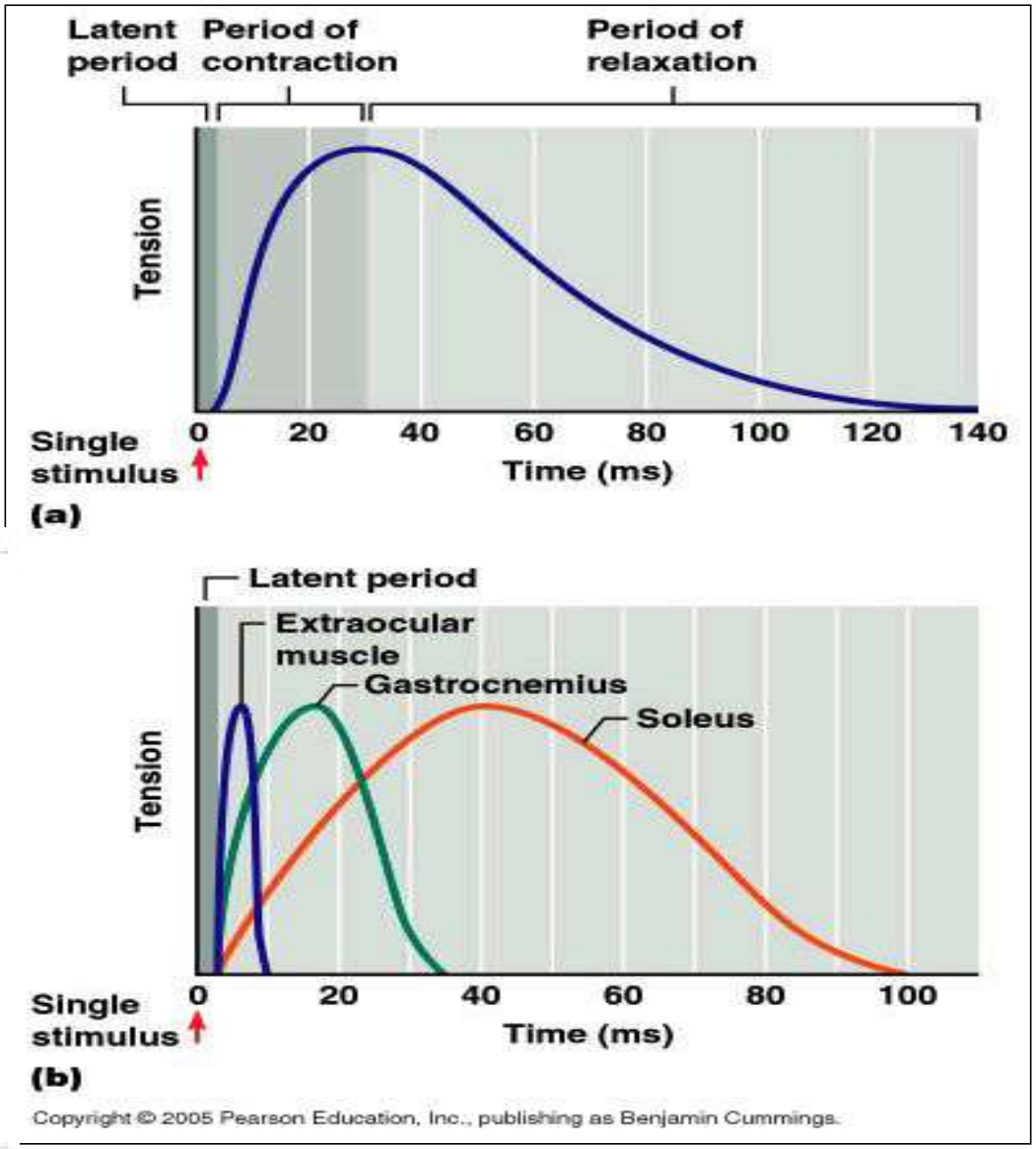


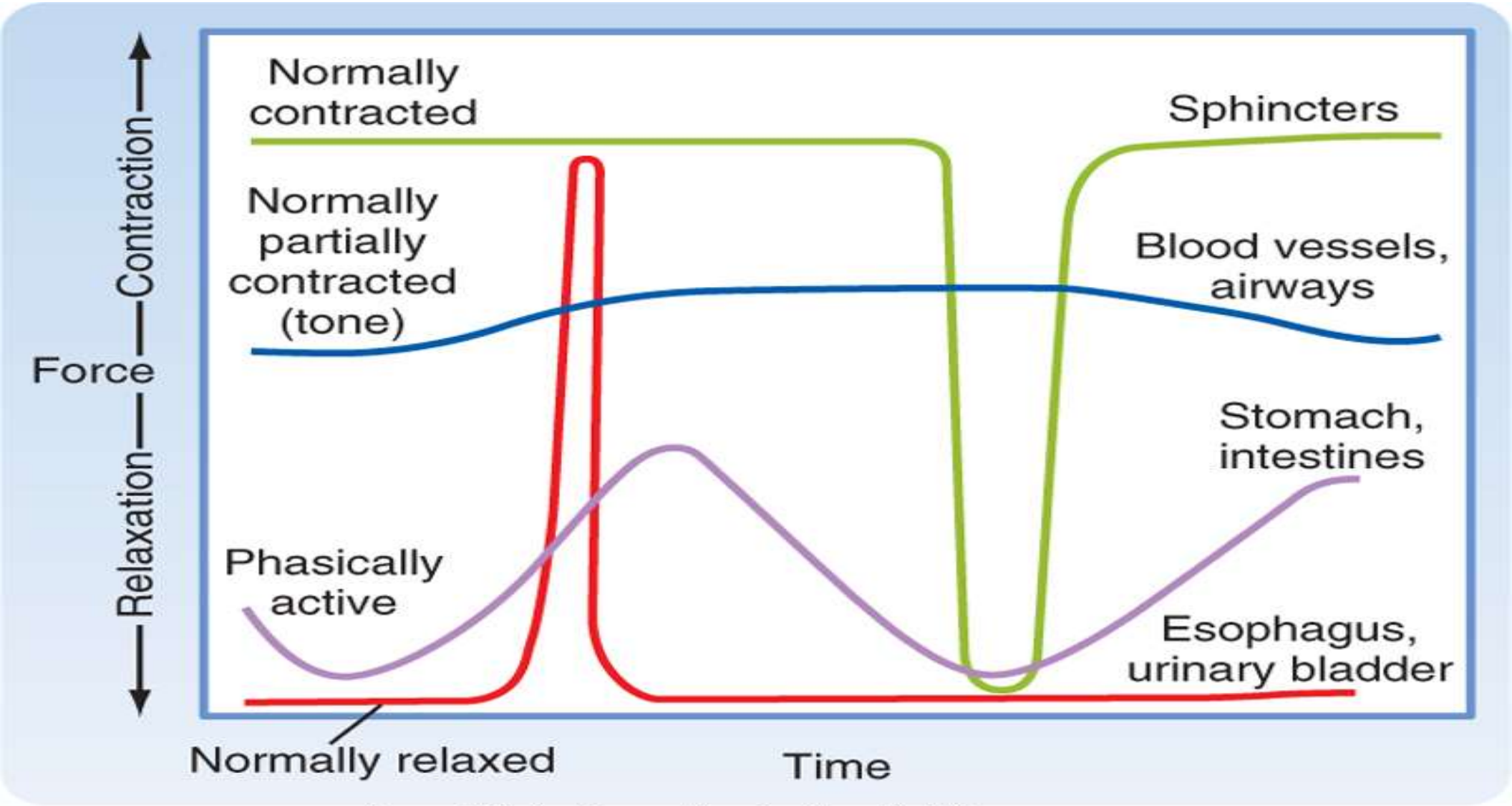


Muscle Twitch

- Twitch contraction of some muscles (extraocular) are rapid and brief.
- others (gastrocnemius, soleus) are slower and longer





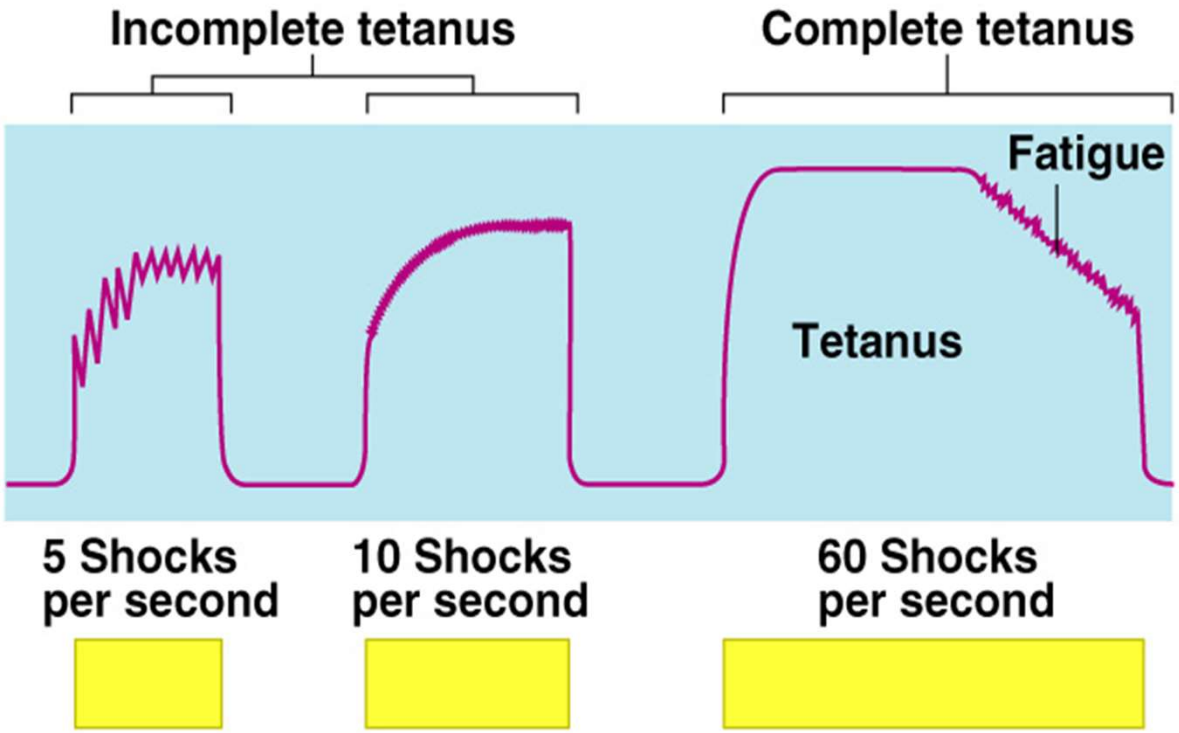


- **Twitch** = muscle contraction

- **Summation:**
  - If second stimulus is administered before complete relaxation of muscle.

- **Complete tetanus**:
  - Fusion frequency of stimulation.
  - No visible relaxation between twitches.
    - Smooth sustained contraction.

- **Tendons:**
  - **Have elasticity.**
  - **Display recoil.**
    - **Spring back to resting length.**



The three primary fiber types in human skeletal muscle

- **Slow twitch oxidative (SO)**
- **Fast twitch oxidative glycolytic (FOG)**
- **Fast twitch glycolytic (FG)**

Muscle at rest

ATP from metabolism + creatine ⟶ ADP + phosphocreatine

Working muscle

Phosphocreatine + ADP $\xrightarrow{\text{creatine kinase}}$ Creatine + ATP

Creatine + ATP → needed for →

- Myosin ATPase (contraction)
- Ca^{2+}-ATPase (relaxation)
- Na^{+}-K^{+}-ATPase (restores ions that cross cell membrane during action potential to their original compartments)

Individual Fiber Types

Fast fibers

- **Type IIb**
  - Fast Fast-twitch fibers twitch fibers
  - Fast Fast-glycolytic glycolytic fibers fibers

- **Type IIa**
  - Intermediate fibers Intermediate fibers
  - Fast Fast-oxidative oxidative glycolytic glycolytic fibers

Slow fibers

- **Type I fibers**
  - Slow Slow-twitch fibers twitch fibers
  - Slow Slow-oxidative oxidative fibers

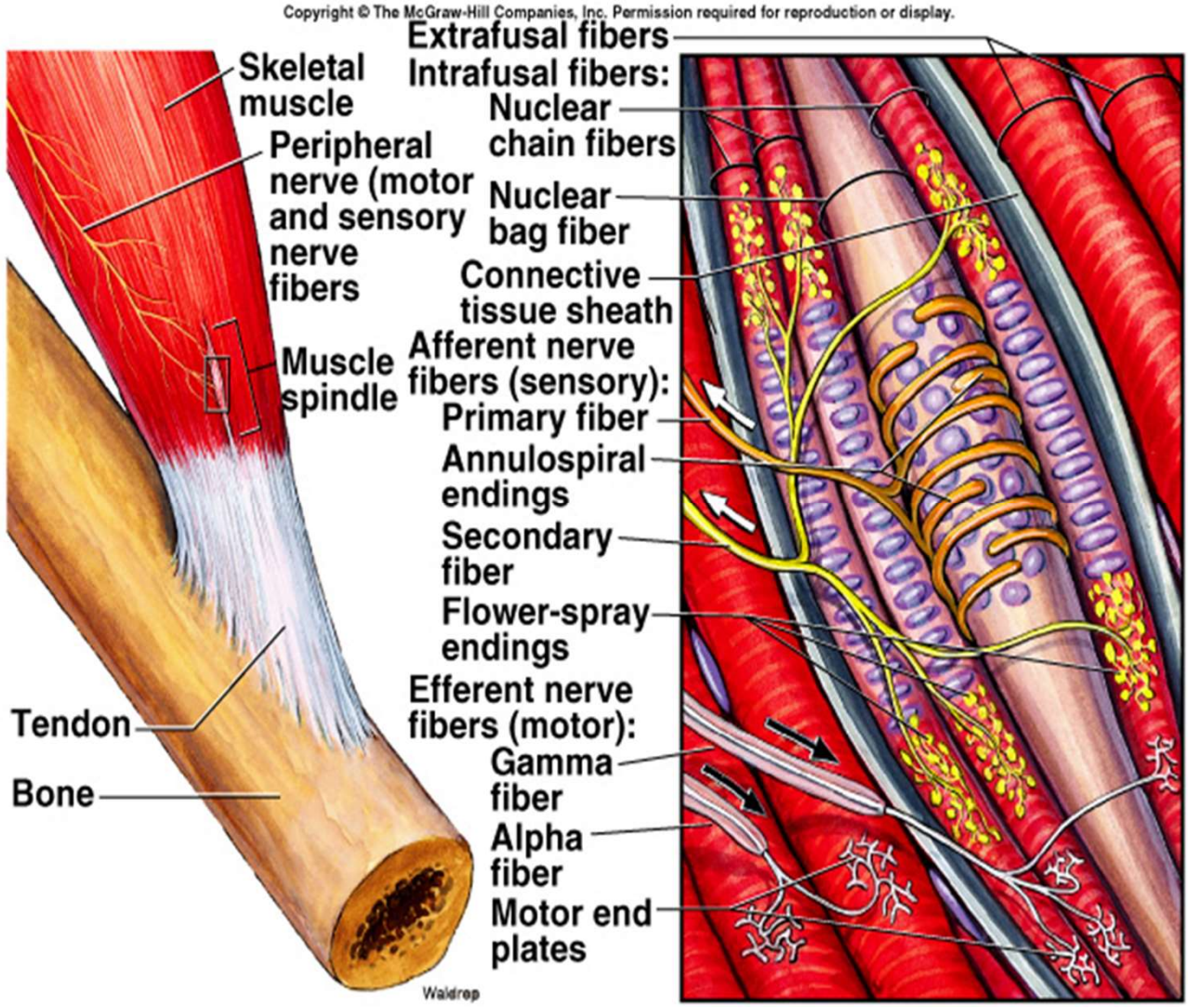
- **Slow-twitch:**
  - Red fibers.
  - High oxidative capacity for aerobic respiration.
  - **Many: mitochondria, capillaries**
  - Myoglobin (like hemoglobin) for oxygen.
  - Postural muscles
- **Fast-twitch (type II fibers):**
  - **White fibers.**
  - **respire anaerobically.**
  - **much glycogen.**
- **Fast-twitch oxidative (type IIA fibers):**
  - **Also white fibers.**
- **People vary genetically in proportion of fast- and slow-twitch fibers in their muscles.**

- **Weight lifting: hypertrophy.**
- **Endurance training: more mitochondria.**

Muscle Spindle Apparatus

- **Muscle spindle apparatus**
  - Length detector.
  - Contains thin muscle cells called intrafusal fibers.
  - Reflex contraction in response to rapid stretch.
  - **Stimulated by γ motor neurons from spinal cord.**
  - Helps maintain muscle tone (resting muscle length and state of tension).

- **Extrafusal fibers (rest of muscle!)**: stimulated by α **motor neurons** from spinal cord.

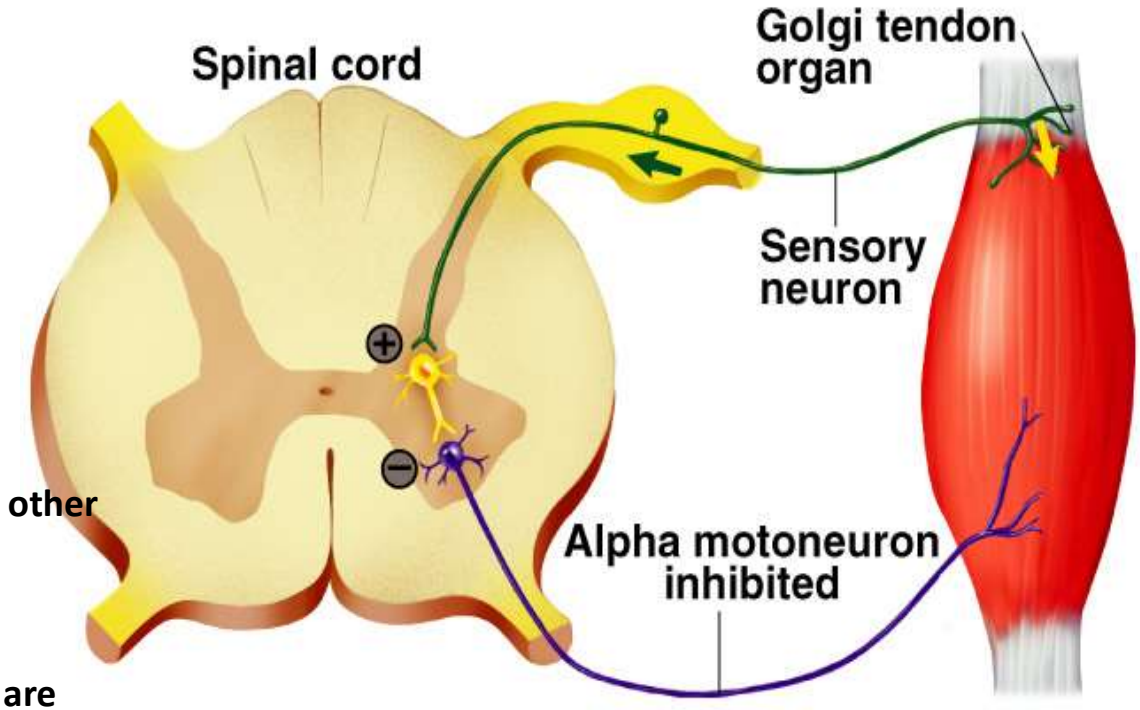


Golgi Tendon Organ

•**Golgi tendon organ**

•Helps prevent excessive muscle contraction or excessive passive muscle stretching.

•A reflex.



Reciprocal Innervation

- **motor neurons of antagonistic muscles inhibit each other (through interneurons) so they don't both contract simultaneously.**
- **When limb is flexed, antagonistic extensor muscles are passively stretched.**

Graded Muscle Responses

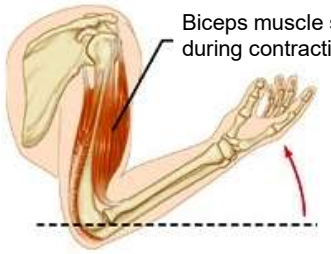
Graded muscle responses are:

- Variations in the degree or strength of muscle contraction in response to demand
- Required for proper control of skeletal movement

- Muscle contraction can be graded (varied) in two ways:
  By changing the Frequency of the stimulus
  - By changing the Strength of the stimulus

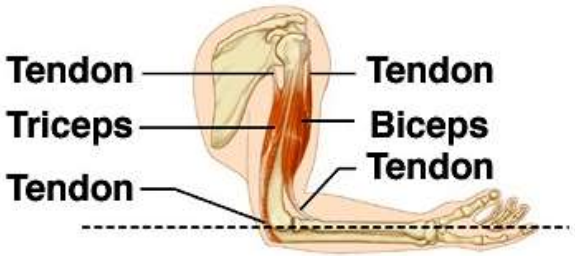
Three potential actions during muscle contraction:

- shortening



(Isotonic: shortening against fixed load, speed dependent on M·ATPase activity and load)

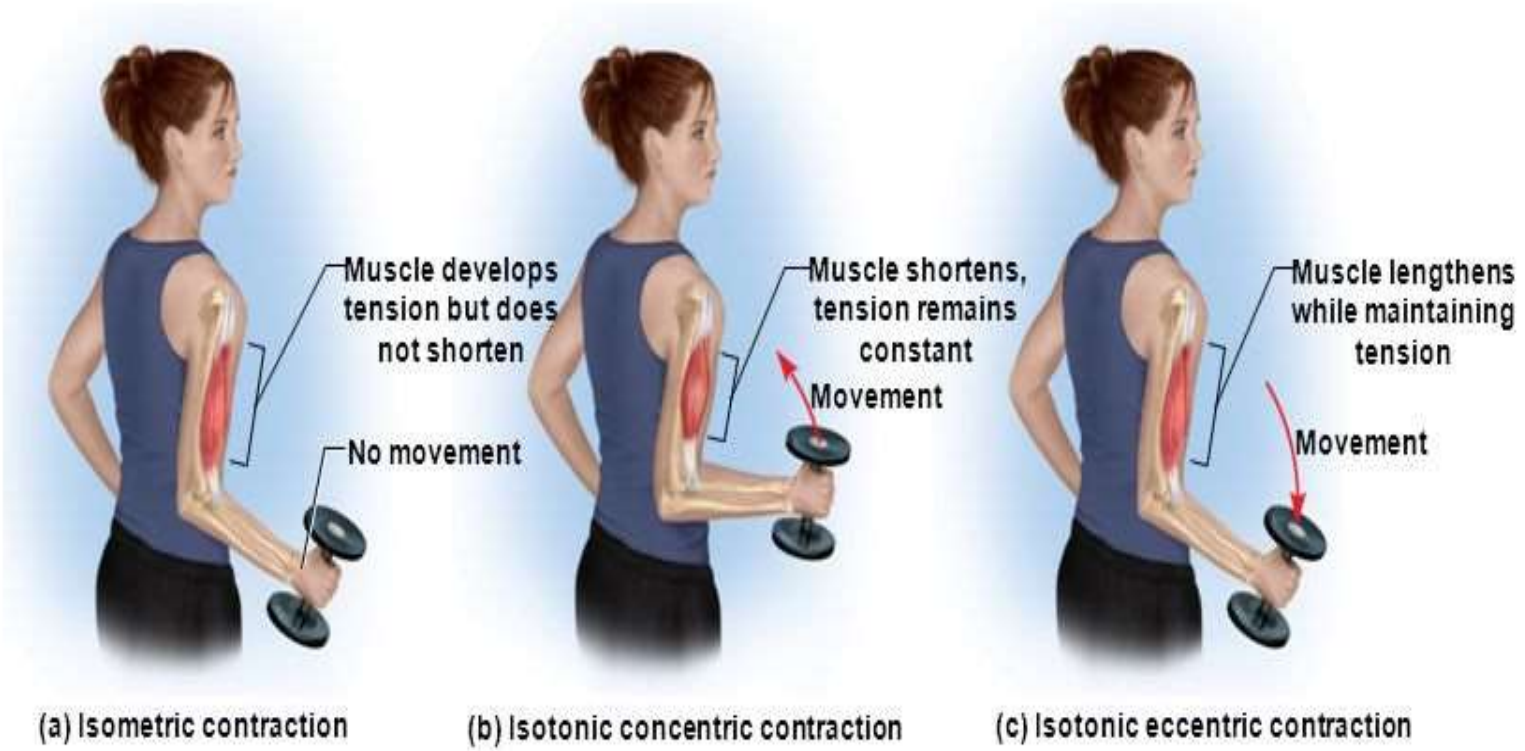
- isometric



- lengthening

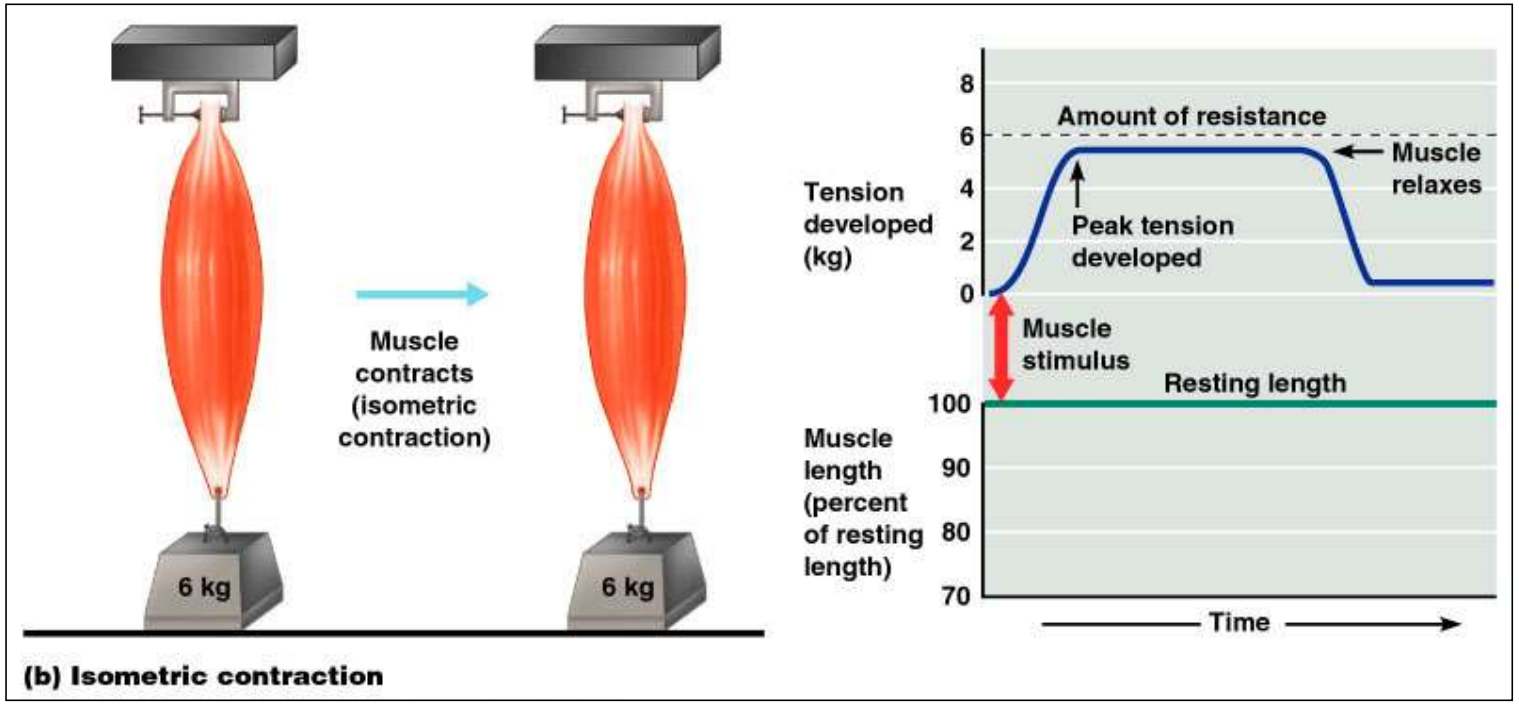
Most likely to cause muscle injury

Modified from Vander, Sherman, Luciano *Human Physiology,* McGraw-Hill.


Muscle develops tension but does not shorten
No movement
Muscle shortens, tension remains constant
Movement
Muscle lengthens while maintaining tension
Movement
(a) Isometric contraction
(b) Isotonic concentric contraction
(c) Isotonic eccentric contraction

Isometric Contractions

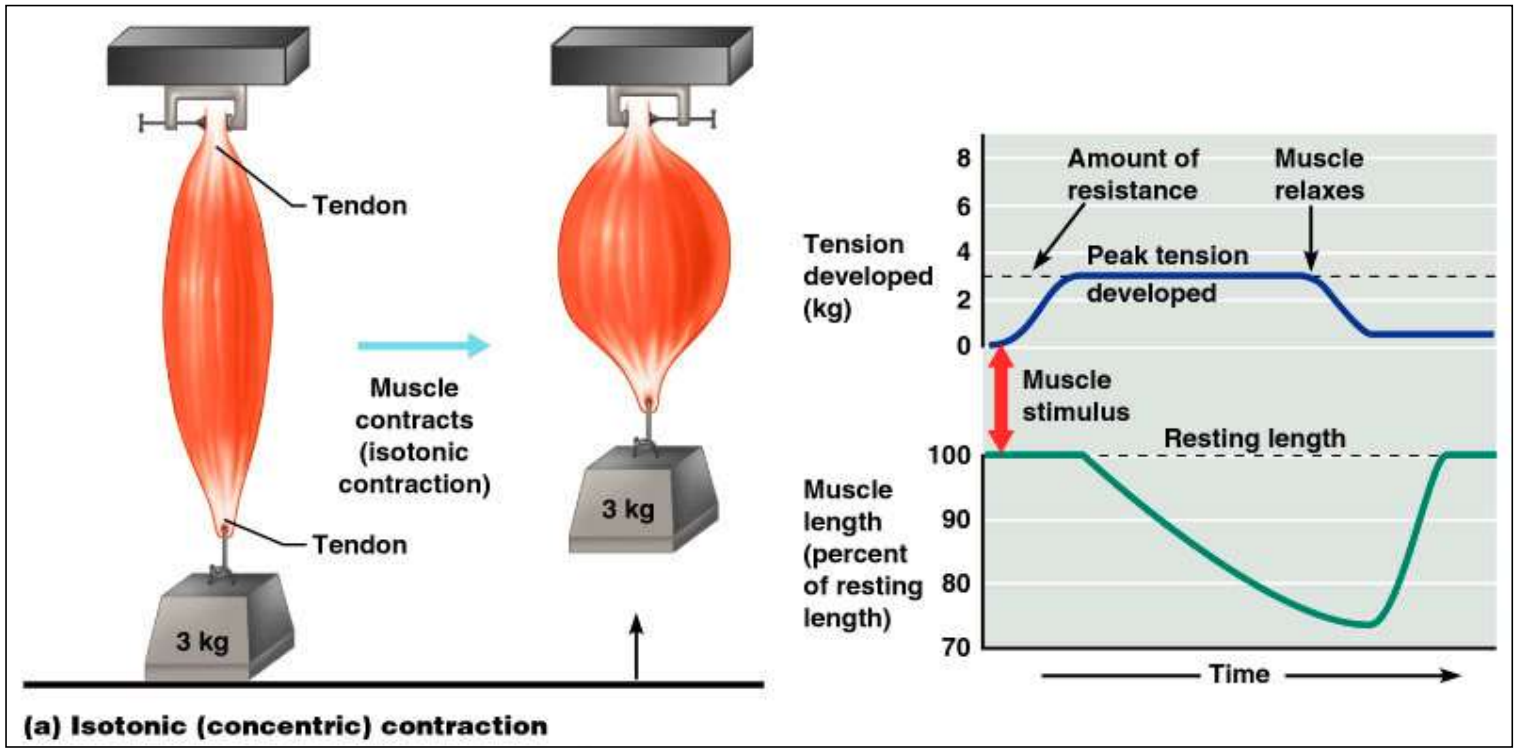
No change in overall muscle length



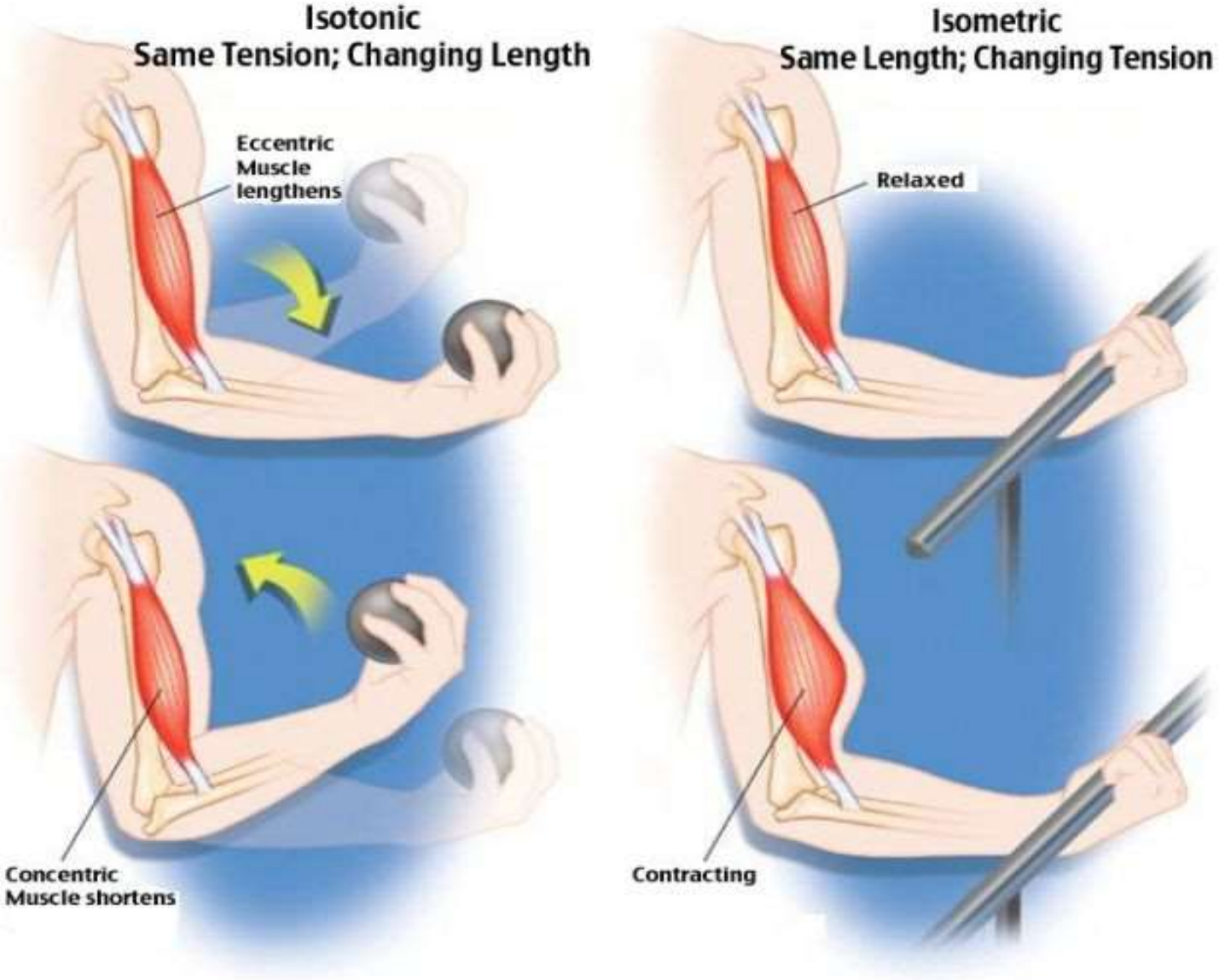
In isometric contractions, increasing muscle tension (force) is measured

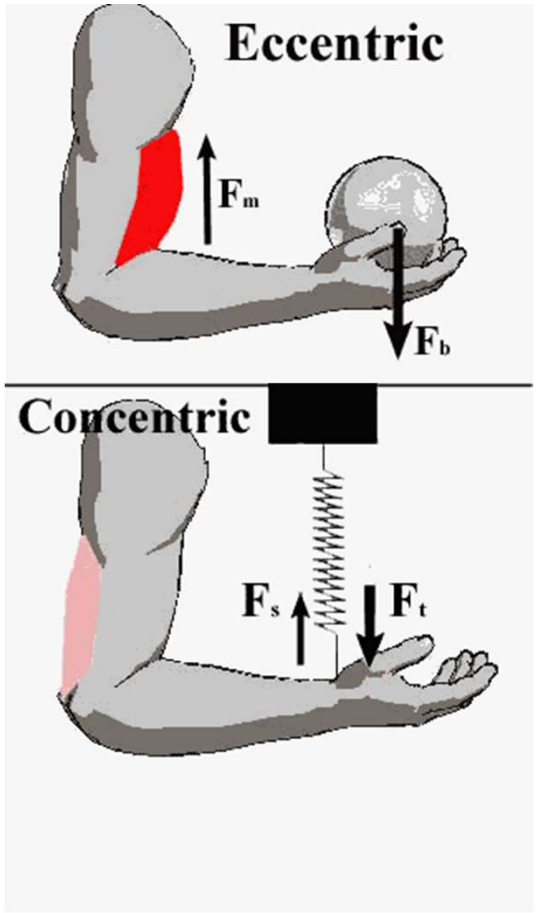
This illustrates a concentric isotonic contraction

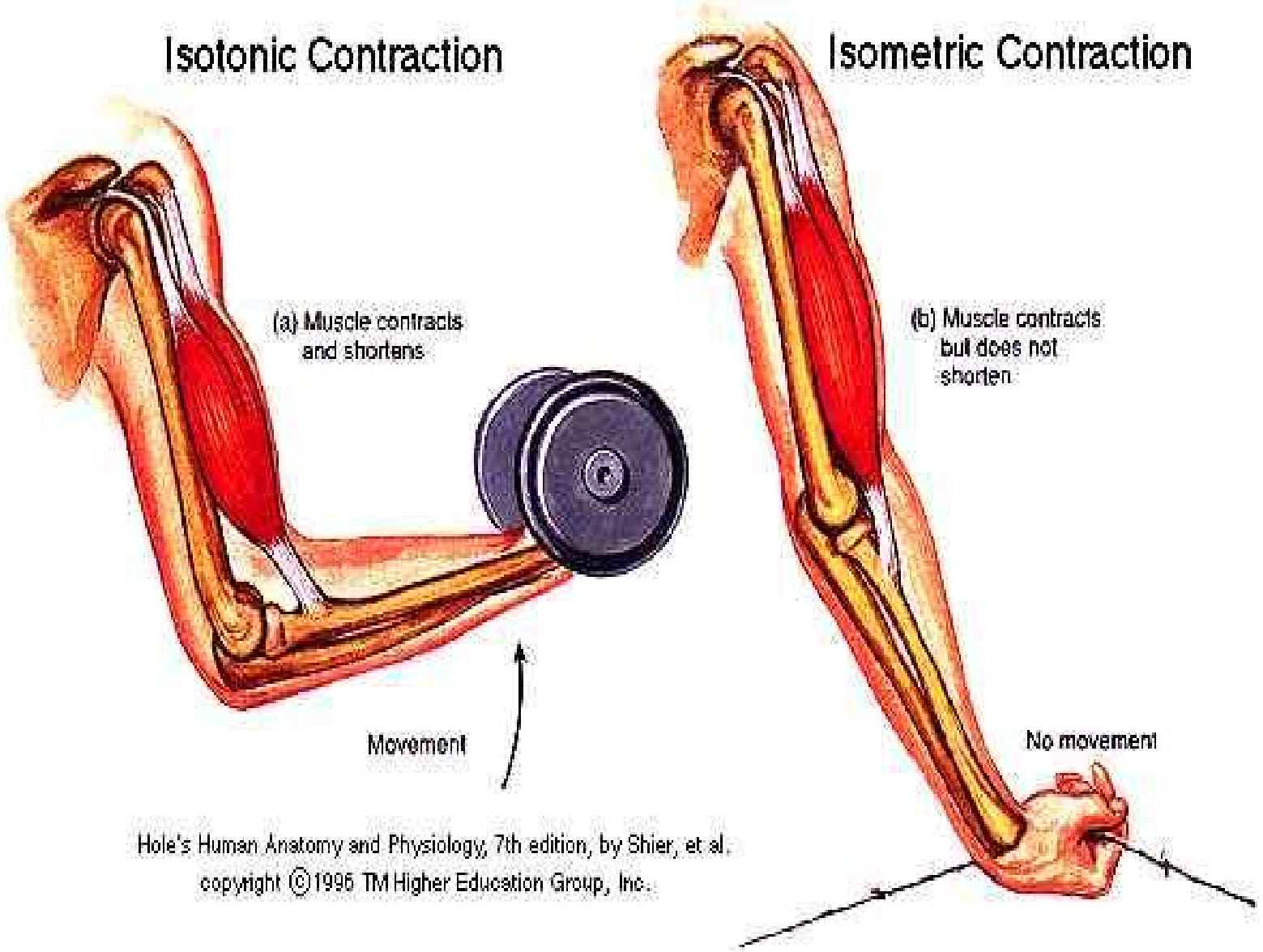
Isotonic Contraction



In isotonic contractions, the amount of shortening (distance in mm) is measured


Isotonic
Same Tension; Changing Length
Eccentric
Muscle
lengthens
Concentric
Muscle shortens
Isometric
Same Length; Changing Tension
Relaxed
Contracting


Eccentric
F_m
F_b
Concentric
F_s
F_t

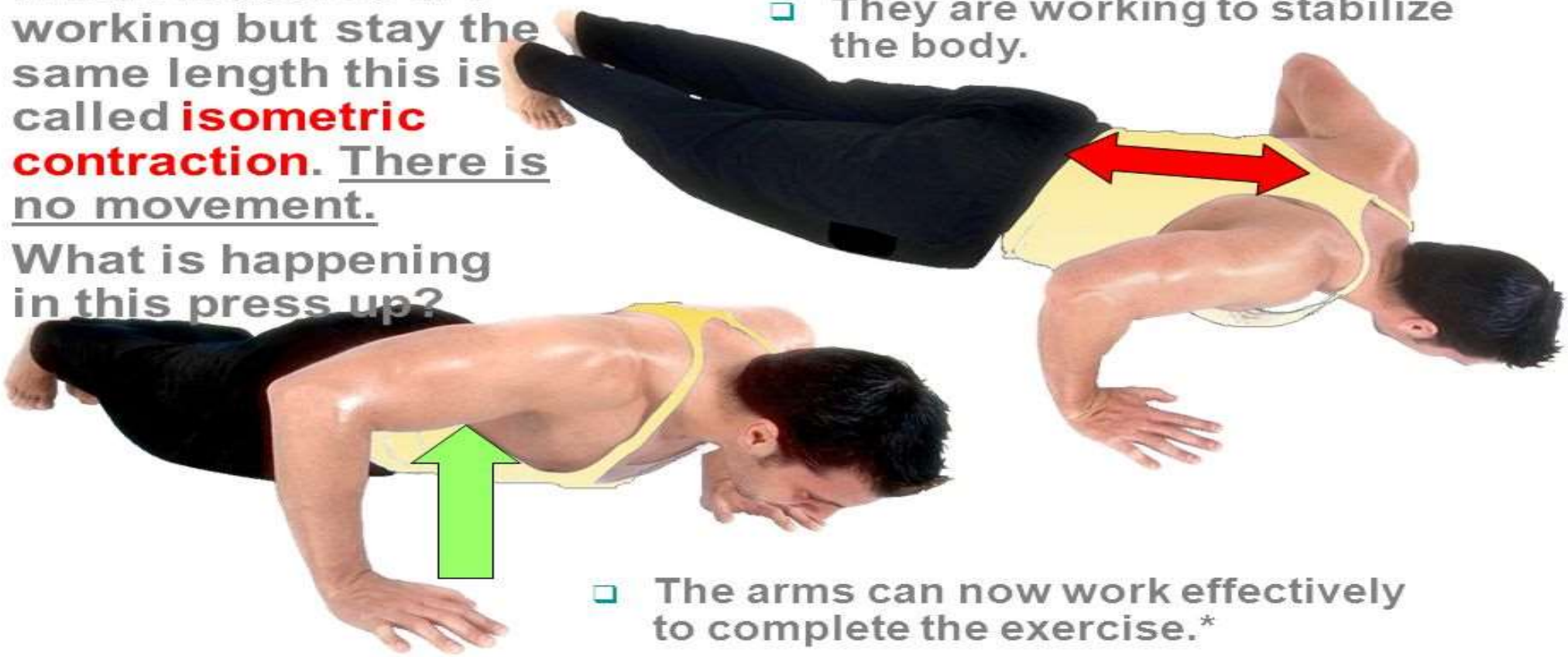


Hole's Human Anatomy and Physiology, 7th edition, by Shier, et al.

Isometric contraction

Muscle Contraction (Isometric)

- When muscles are working but stay the same length this is called **isometric contraction**. <u>There is no movement.</u>
- What is happening in this press up?



- There is isometric contraction of the back muscles.
- They are working to stabilize the body.
- The arms can now work effectively to complete the exercise.*

Muscle Response to Stronger Stimuli

- Threshold stimulus – the stimulus strength at which the first observable muscle contraction occurs

- Beyond threshold, muscle contracts more vigorously as stimulus strength is increased

- Force of contraction is precisely controlled by multiple motor unit summation

- This phenomenon, called recruitment, brings more and more muscle fibers into play

Energy Metabolism in Skeletal Muscle –

A) **Creatine-phosphagen system**
1) uses creatine phosphokinase (CPK or CK)
a) CPK-MM in skeletal muscle
b) CPK-MB in cardiac muscle
2) delivers ~ 30 sec max. activity

B) **Lactic acid pathway (glycolytic pathway)**
1) anaerobic use of glucose (glycolysis mainly)
2) 2ATP/glucose
3) lactic acid waste product
4) can be "recycled" by liver

C) **Aerobic respiration (oxidative) pathway**
1) most efficient use of glucose
2) 36ATP/glucose
3) requires oxygen
4) occurs in mitochondria

D) **Sources of glucose**
1) blood glucose
2) stored glycogen

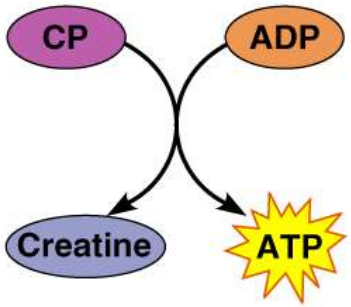
E) **Sources/carriers of oxygen**
1) hemoglobin
2) myoglobin

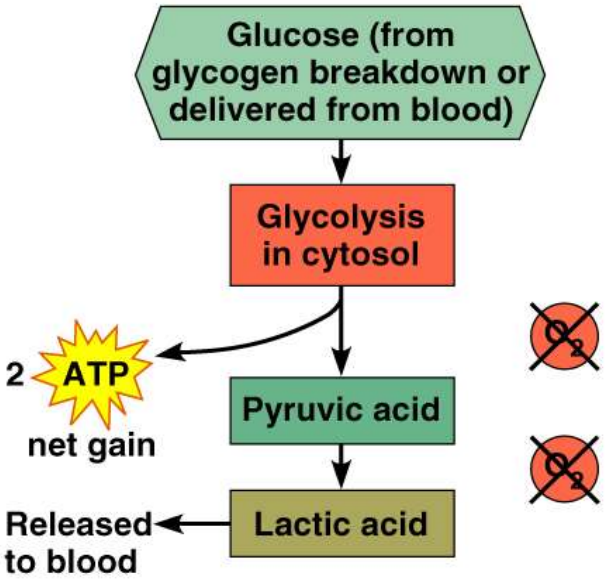
F) **Recovery oxygen** consumption

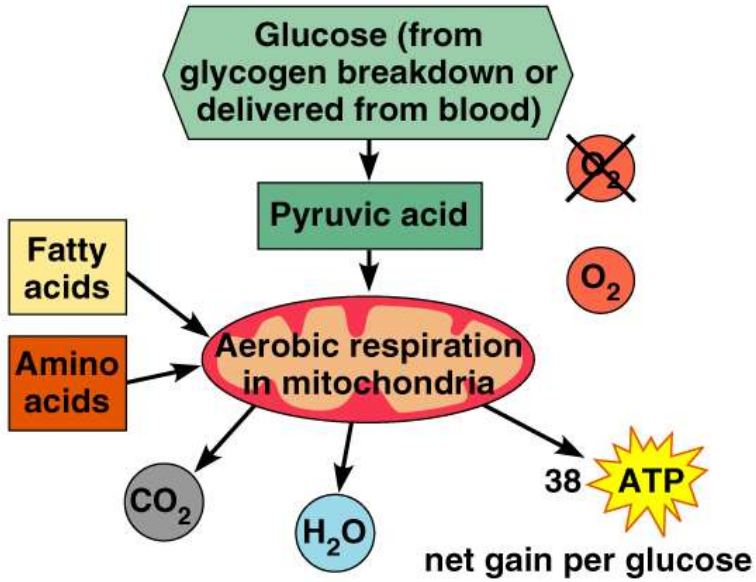
1) due to increased metabolic rate and continued use

2) lactic acid can be recycled in liver

➔4 lactic acid converted to glucose, 1 converted to carbon dioxide







(a) Direct phosphorylation [coupled reaction of creatine phosphate (CP) and ADP]	(b) Anaerobic mechanism (glycolysis and lactic acid formation)	(c) Aerobic mechanism (aerobic cellular respiration)
Energy source: CP	Energy source: glucose	Energy source: glucose; pyruvic acid; free fatty acids from adipose tissue; amino acids from protein catabolism
Oxygen use: None Products: 1 ATP per CP, creatine Duration of energy provision: 15 s.	Oxygen use: None Products: 2 ATP per glucose, lactic acid Duration of energy provision: 30–60 s.	Oxygen use: Required Products: 38 ATP per glucose, CO_2, H_2O Duration of energy provision: Hours

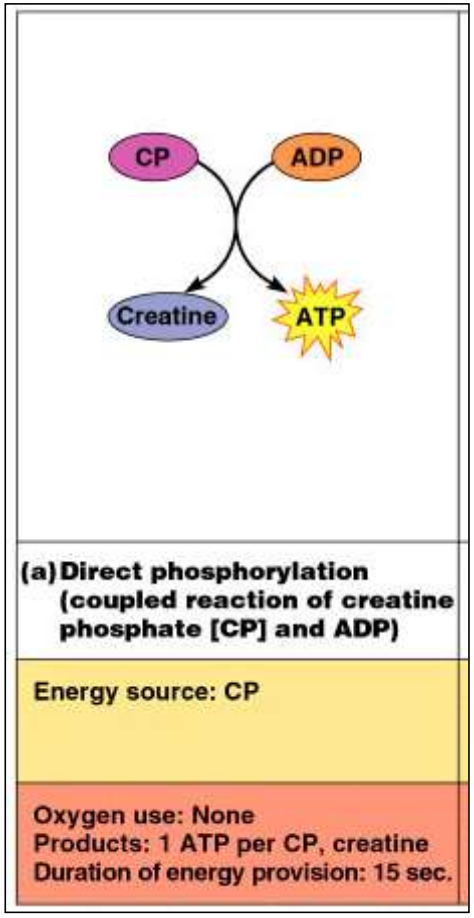
Muscle Metabolism: Energy

ATP is the only energy source that is used directly for contractile activity

As soon as available ATP is hydrolyzed (4-6 seconds), it is regenerated by three pathways:

- **Interaction of ADP with Creatine Phosphate (CP)**
- **From stored glycogen via Anaerobic Glycolysis**
- **From Aerobic Respiration**

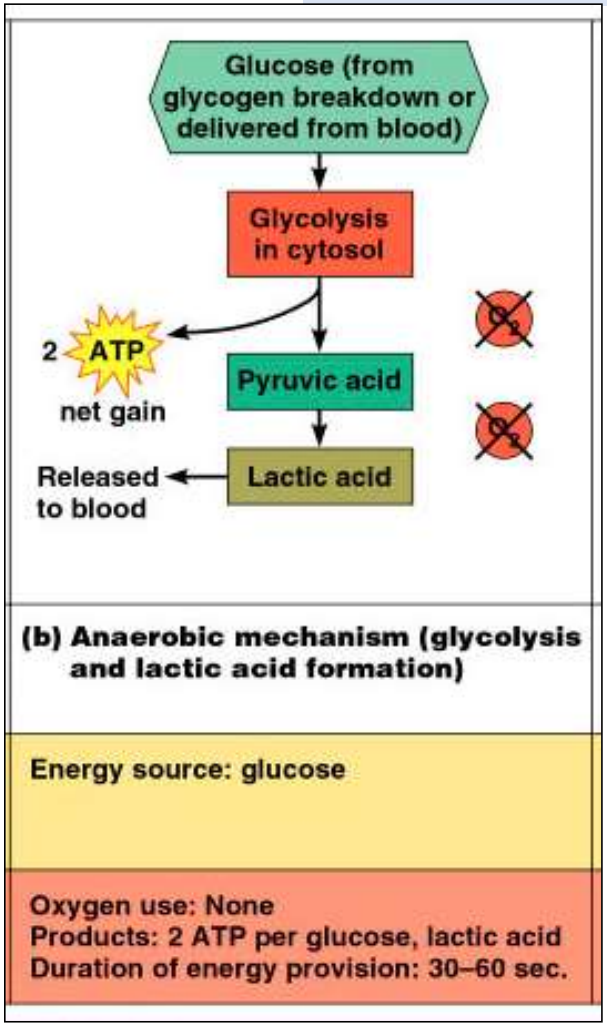
CP-ADP Reaction



Creatine phosphate + ADP → creatine + ATP

- **Transfer of energy as a phosphate group is moved from CP to ADP – the reaction is catalyzed by the enzyme creatine kinase**
- **Stored ATP and CP provide energy for maximum muscle power for 10-15 seconds**

Anaerobic Glycolysis

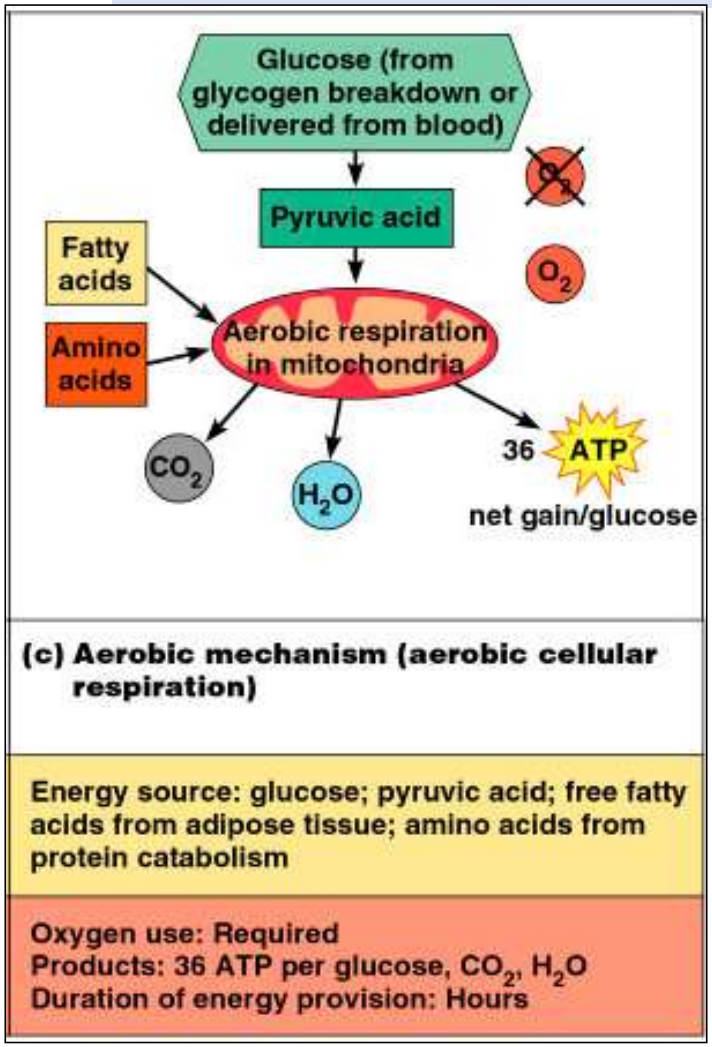


When muscle contractile activity reaches 70% of maximum:

- **Muscles compress blood vessels and O_2 delivery is impaired (anaerobic conditions)**
- **Pyruvic acid is converted into lactic acid**
- **Lactic acid diffuses into the bloodstream – can be used as energy source by the liver, kidneys, and heart**

Can be converted back into pyruvic acid, glucose, or glycogen by the liver

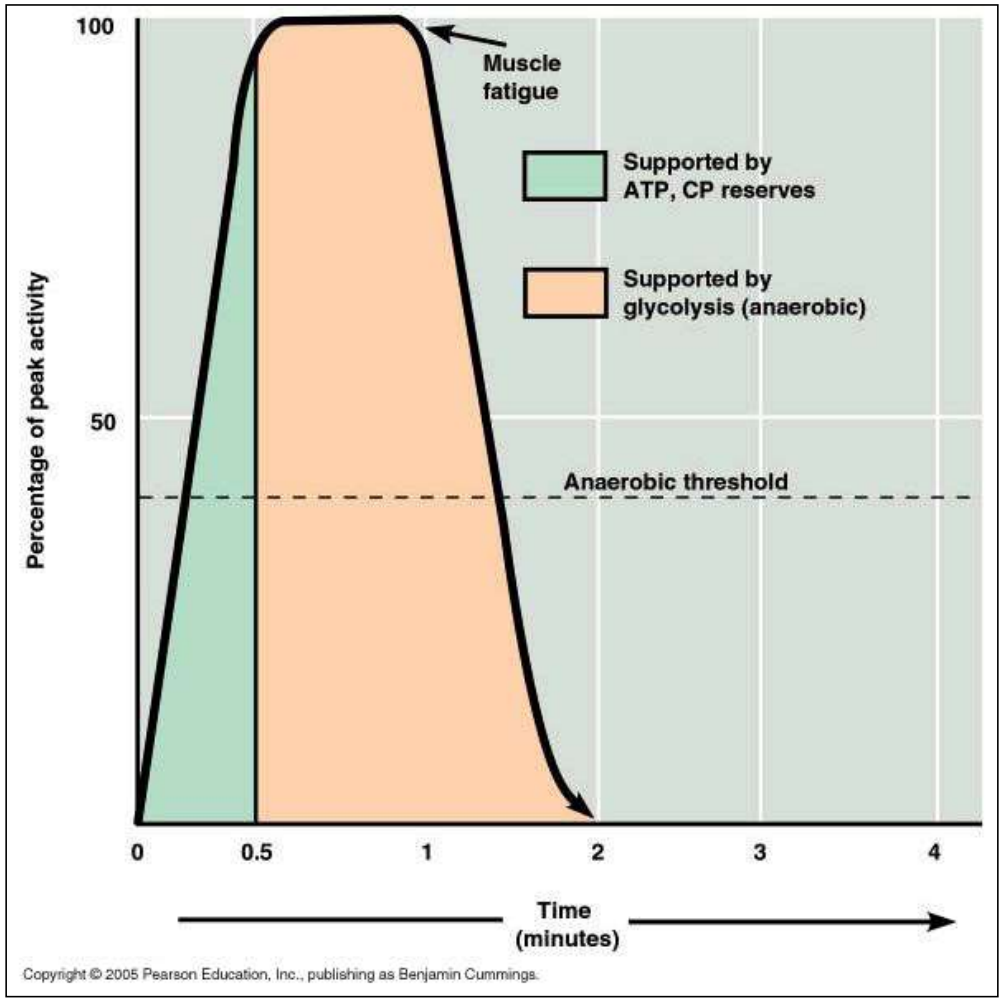
Glycolysis and Aerobic Respiration



$Glucose + O_2 \rightarrow CO_2 + H_2O + ATP$

- **Aerobic respiration occurs in mitochondria - requires O_2**
- **A series of reactions where glucose is fully broken down with a high yield of ATP**

Energy System or Source during peak activity



Muscle Fatigue

- **Muscle fatigue** – the muscle is physiologically not able to contract
- **Occurs when oxygen is limited and ATP production fails to keep pace with ATP use**
  - Lactic acid accumulation and ionic imbalances may also contribute to muscle fatigue

When no ATP is available, contractures (continuous contraction) may result because cross bridges are unable to detach

- **Intense exercise produces rapid muscle fatigue (with rapid recovery)**
- **Na^+-K^+ pumps cannot restore ionic balances quickly enough**

- **Low-intensity exercise produces slow-developing fatigue (with longer recovery period)**
- **SR may be damaged, interfering with Ca^{2+} regulation**

Oxygen Debt

- Vigorous exercise can cause dramatic changes in muscle chemistry

- **For a muscle to return to its pre-exercise state:**
- **Oxygen reserves must be replenished**
  - **(Lactic acid must be converted to pyruvic acid?)**
  - **Glycogen stores must be replaced**
  - **ATP and CP reserves must be resynthesized**

- **Oxygen debt – the extra amount of O_2 needed for the above restorative processes**

Heat Production During Muscle Activity

- Only 40% of the energy released in muscle activity is useful as work
- The remaining 60% is given off as heat
- Heat is dissipated by radiation of heat from the skin and sweating

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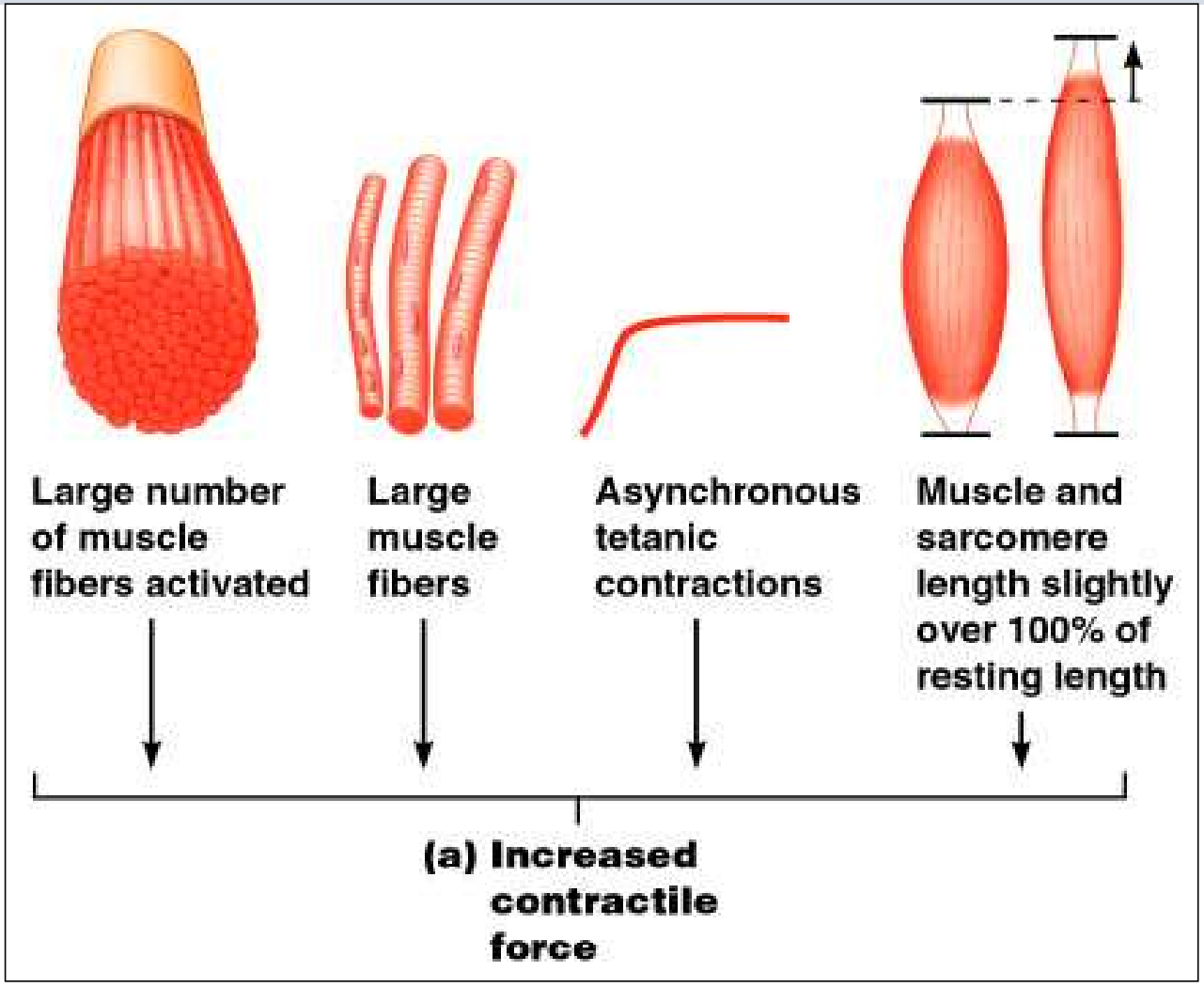
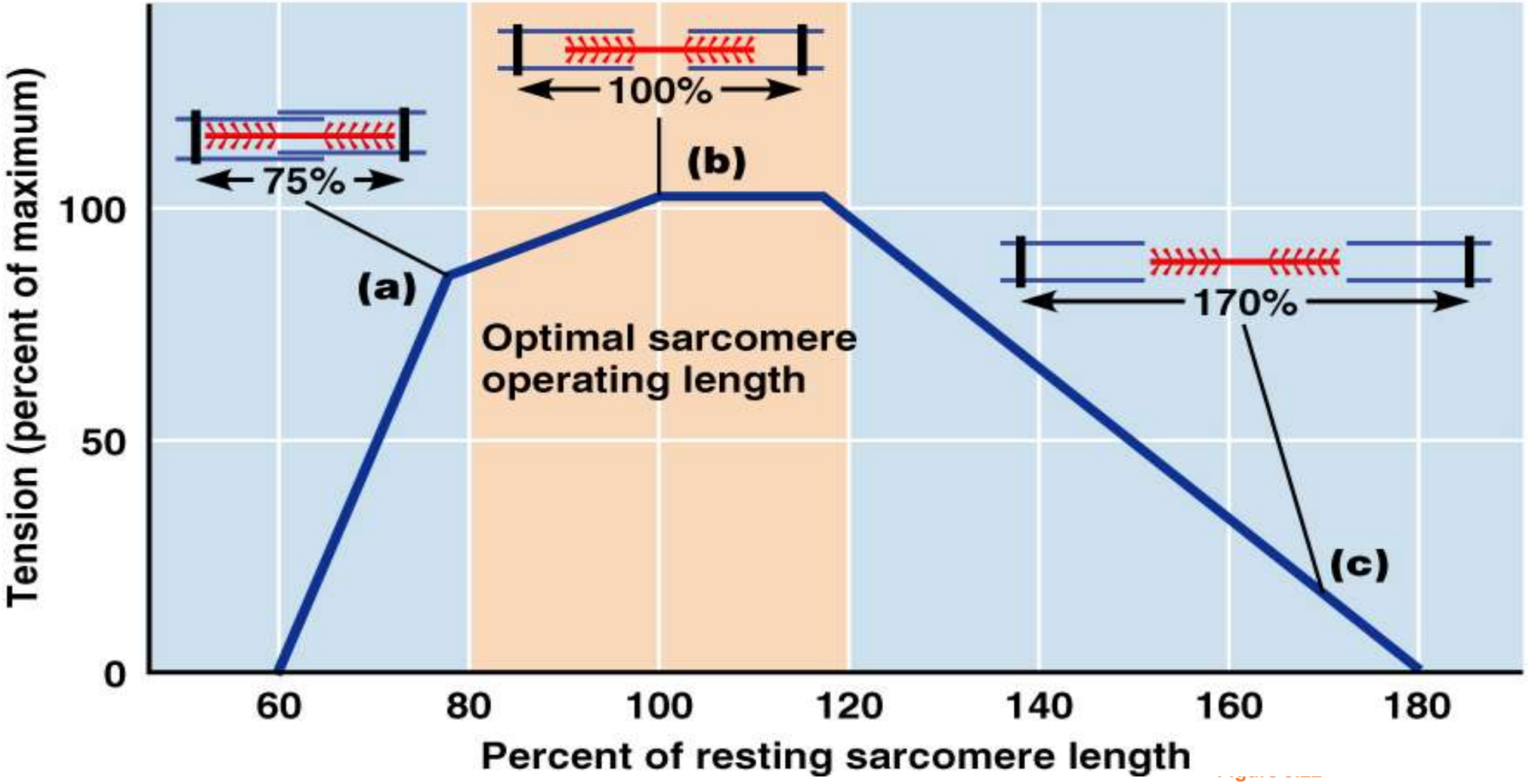
Force of Muscle Contraction



Length Tension Relationships

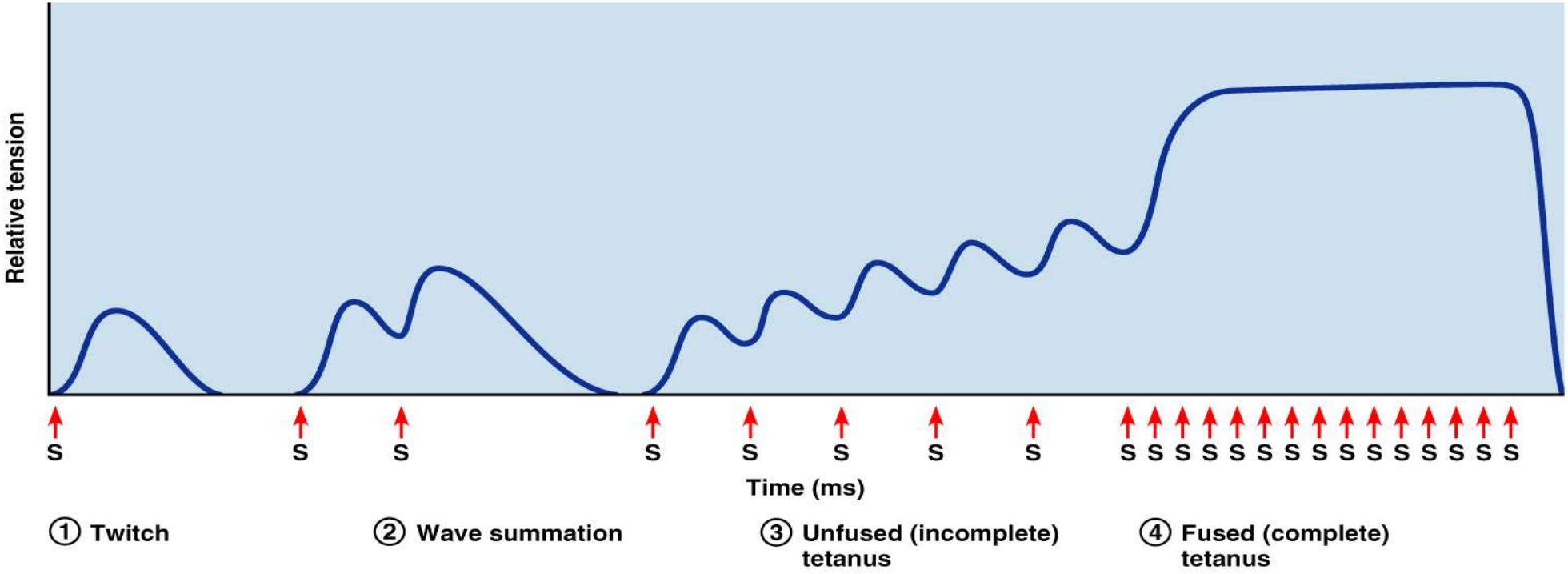


Structural and Functional Characteristics of the Three Types of Skeletal Muscle Fibers

	SLOW OXIDATIVE FIBERS	FAST OXIDATIVE FIBERS	FAST GLYCOLYTIC FIBERS
METABOLIC CHARACTERISTICS			
Speed of contraction	Slow	Fast	Fast
Myosin ATPase activity	Slow	Fast	Fast
Primary pathway for ATP synthesis	Aerobic	Aerobic (some anaerobic glycolysis)	Anaerobic glycolysis
Myoglobin content	High	High	Low
Glycogen stores	Low	Intermediate	High
Recruitment order	First	Second	Third
Rate of fatigue	Slow (fatigue-resistant)	Intermediate (moderately fatigue-resistant)	Fast (fatigable)
ACTIVITIES BEST SUITED FOR			
	Endurance-type activities—e.g., running a marathon; maintaining posture (antigravity muscles)	Sprinting, walking	Short-term intense or powerful movements, e.g., hitting a baseball
STRUCTURAL CHARACTERISTICS			
Color	Red	Red to pink	White (pale)
Fiber diameter	Small	Intermediate	Large
Mitochondria	Many	Many	Few
Capillaries	Many	Many	Few

Muscle Response to Varying Stimuli

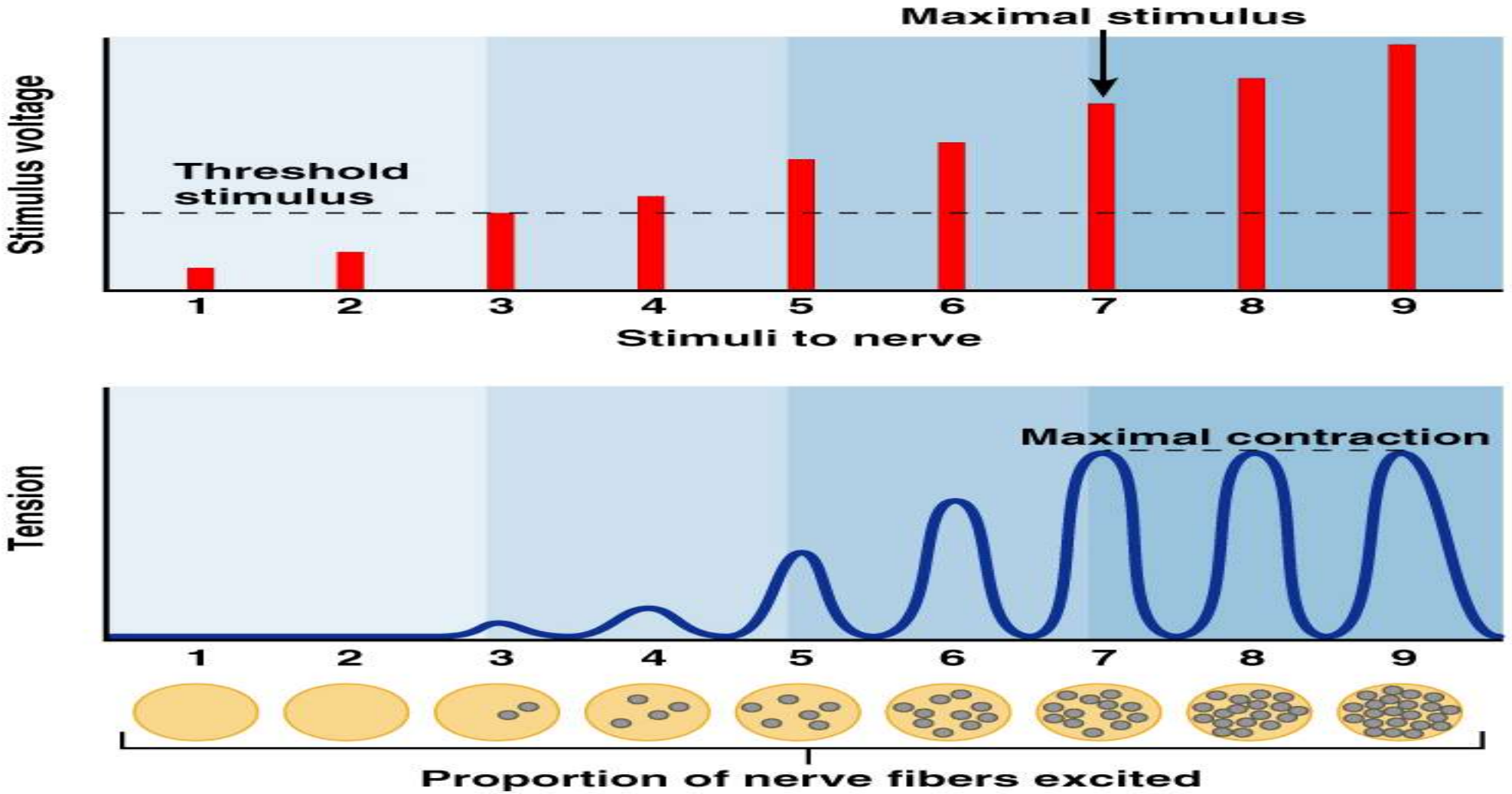
- **A single stimulus results in a single contractile response – a muscle twitch**
- **Frequently delivered stimuli (muscle does not have time to completely relax) increases contractile force – wave summation**
- **More rapidly delivered stimuli result in incomplete tetanus**
- **If stimuli are given quickly enough, complete tetanus results**



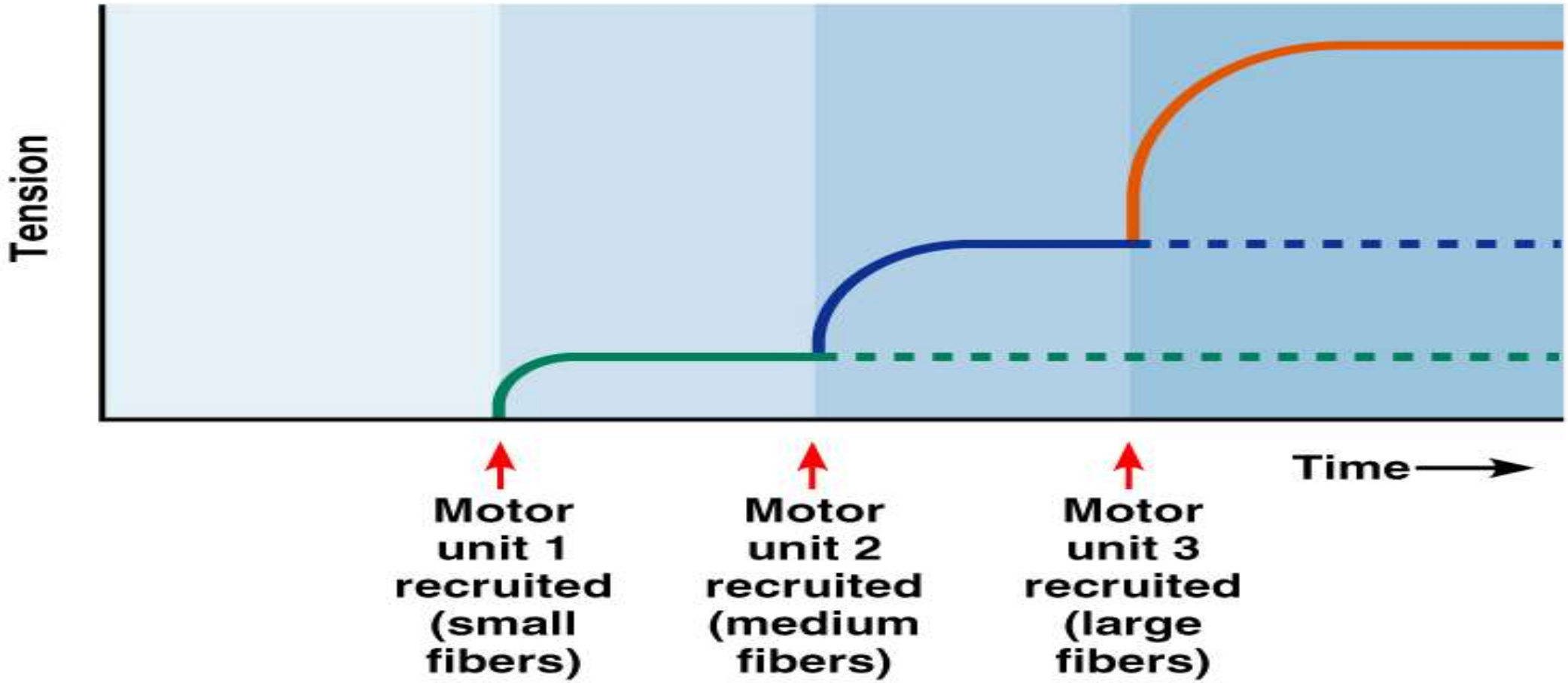
Muscle Response: Stimulation Strength

- **Threshold stimulus – the stimulus strength at which the first observable muscle contraction occurs**
- **Beyond threshold, muscle contracts more vigorously as stimulus strength is increased**
- **Force of contraction is precisely controlled by multiple motor unit summation**
- **This phenomenon, called recruitment, brings more and more muscle fibers into play**

Stimulus Intensity and Muscle Tension

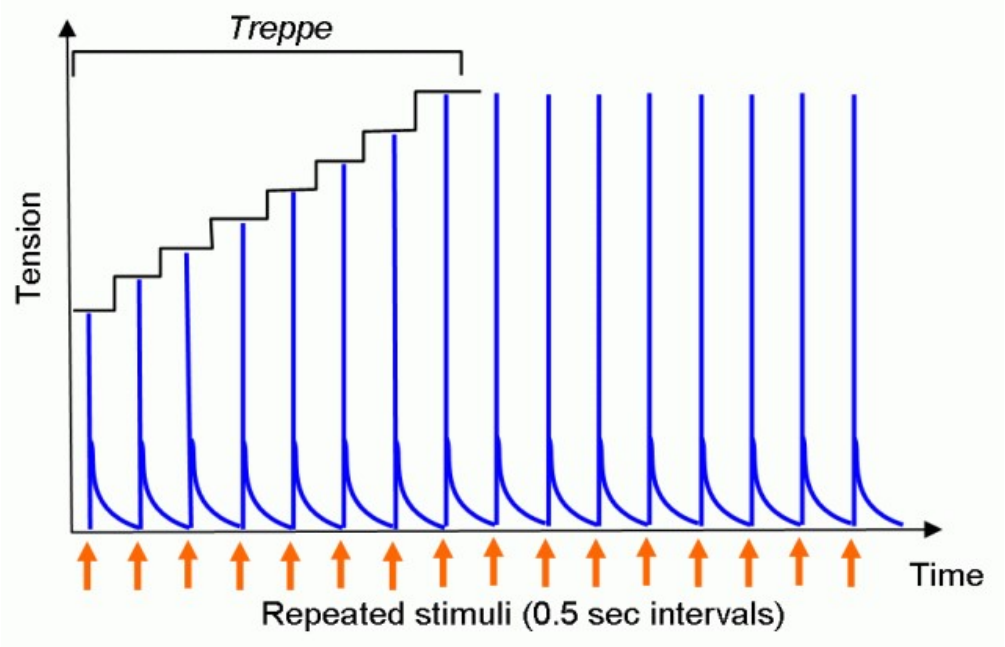


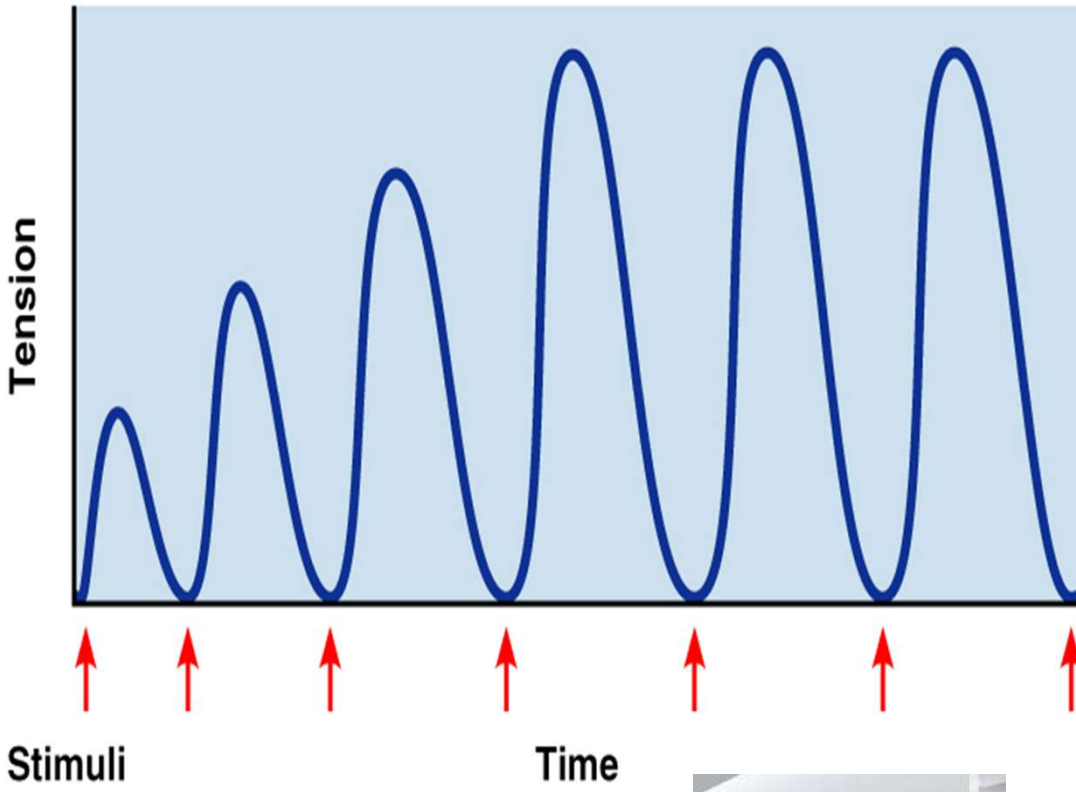
Size Principle



Treppe: The Staircase Effect

- **Staircase – increased contraction in response to multiple stimuli of the same strength**
- **Contractions increase because:**
  - There is increasing availability of Ca^{2+} in the sarcoplasm
  - **Muscle enzyme systems become more efficient because heat is increased as muscle contracts**

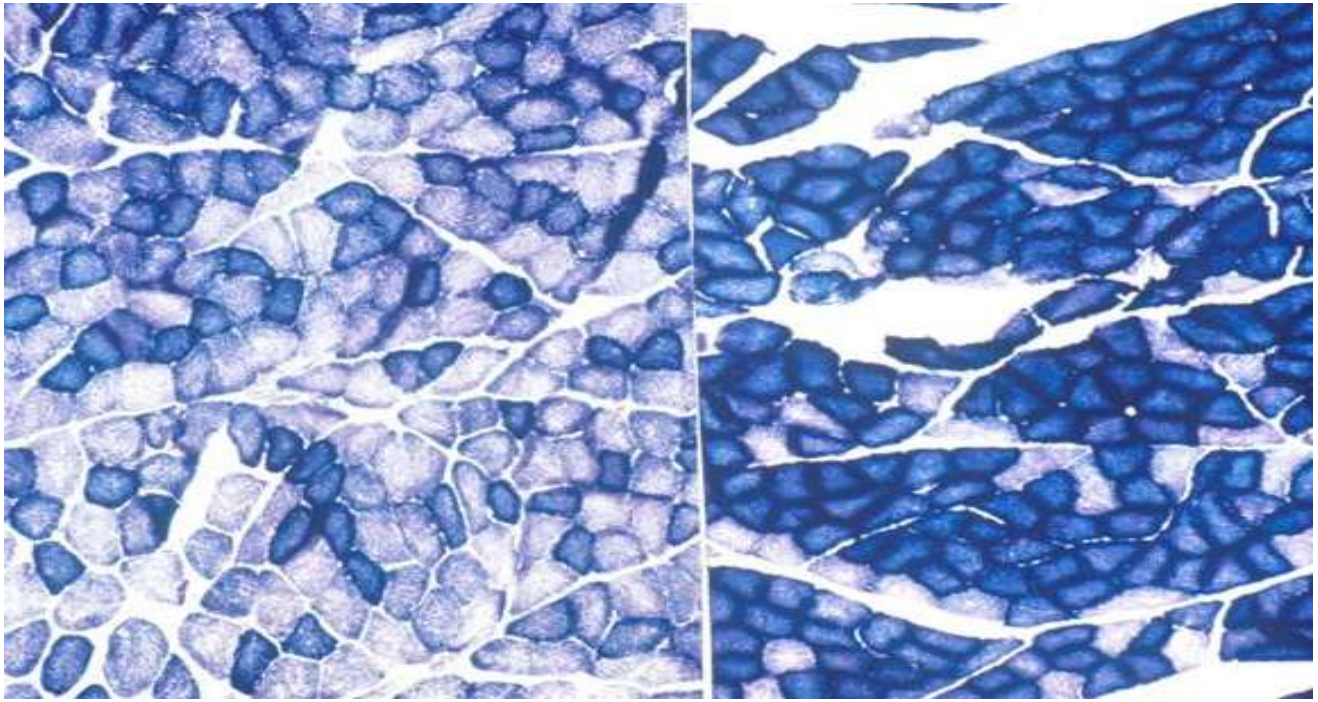




- ***Endurance training***

- **Little hypertrophy but major biochemical adaptations within muscle fibers.**

- **Increased numbers of mitochondria; concentration and activities of oxidative**
- **enzymes (e.g. succinate dehydrogenase).**



Control

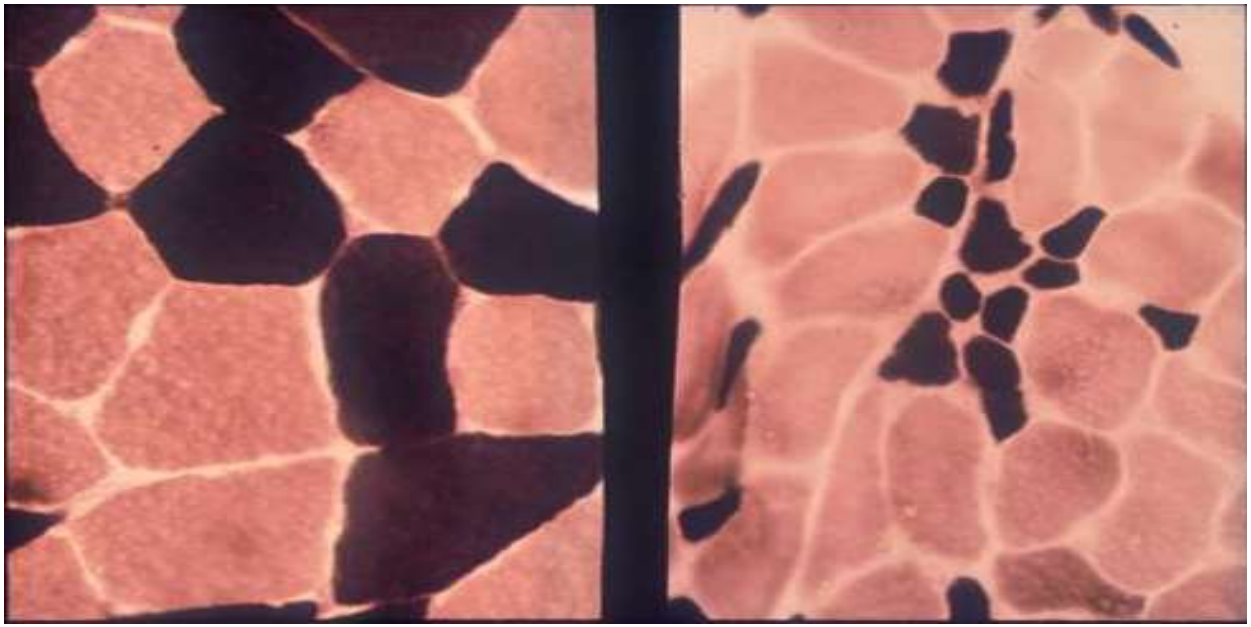
12-weeks
treadmill running

Images courtesy of John Faulkner and Timothy White

Succinate dehydrogenase (SDH) activity:

- **Low activity light**
- **High activity dark**

- *Disuse causes atrophy -- USE IT OR LOSE IT!*
- **Individual fiber atrophy (loss of myofibrils) with no loss in fibers.**
- **Effect more pronounced in Type II fibers.**
- **"Completely reversible" (in young healthy individuals).**



ATPase activity:
Type I fibers light
Type II fibers dark

Control

Prolonged bed rest

Images courtesy of John Faulkner

Smooth muscles

- **It is divided into two subgroups;**
- **the single-unit (unitary) and multiunit smooth muscle.**
- **Within single-unit cells, the whole bundle or sheet contracts as a syncytium.**

•Not striated.

•NO sarcomeres.

•Lots of actin, some myosin

•Can contract even when very stretched.

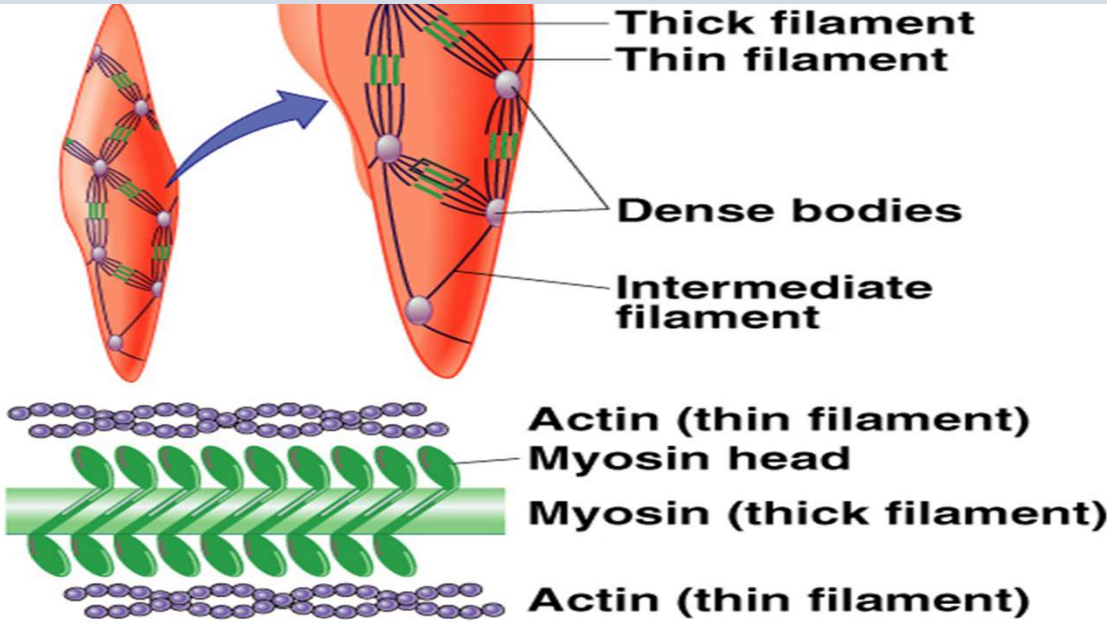
- **T tubules are absent**
- **Plasma membranes have pouchlike infoldings called caveoli**

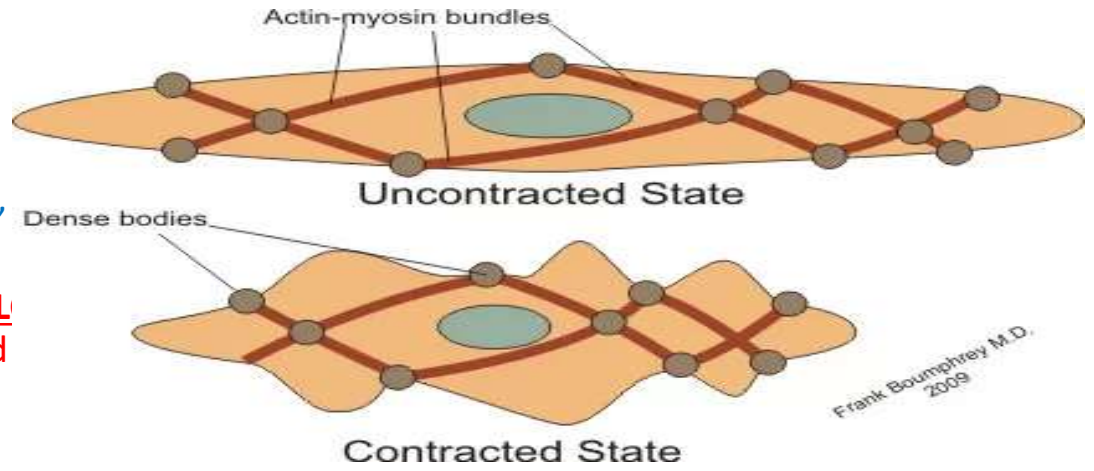
•Graded contractions

•does not contain the protein troponin; instead calmodulin

•caldesmon and calponin are significant proteins expressed within smooth muscle.

- **Actin all over the cell,** linked by myosin (web-like pattern, striations).
- **Rise in Ca^{2+}** -> Ca^{2+} binds with **calmodulin** -> activates **ML** kinase) -> Myosin heads are phosphorylated and can bind actin.

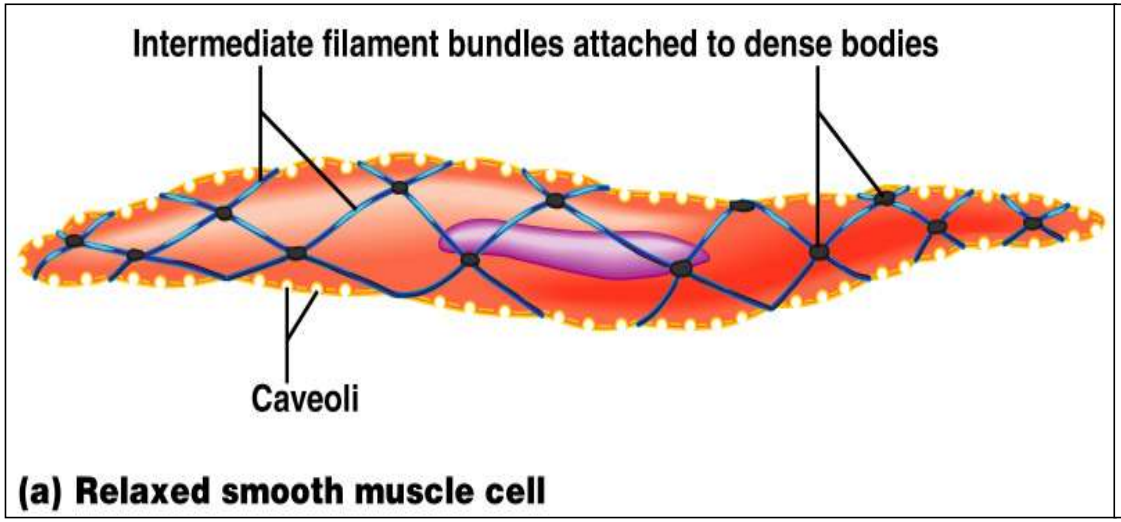


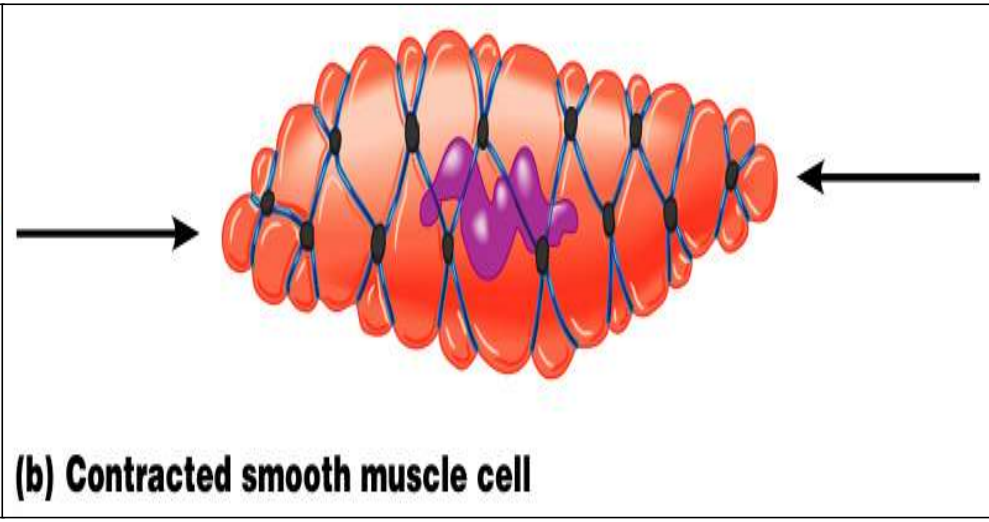


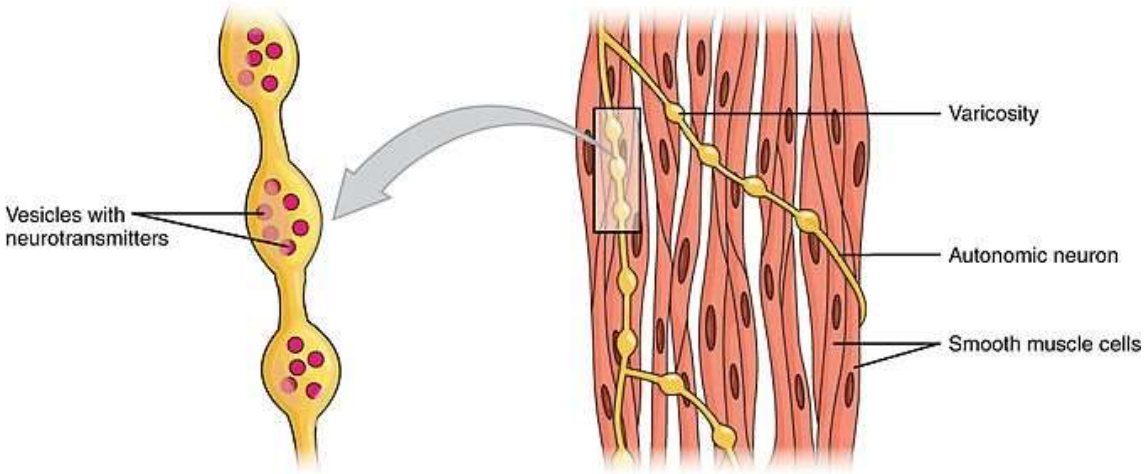
Myofilaments in Smooth Muscle

- Ratio of thick to thin filaments is much lower than in skeletal muscle
- Thick filaments have heads along their entire length
- **There is no troponin complex**
- **Thick and thin filaments are arranged diagonally**➔ causing smooth muscle to contract in a corkscrew manner
- Noncontractile intermediate filament bundles attach to dense bodies (analogous to Z discs) at regular intervals

- **Whole sheets of smooth muscle exhibit slow, synchronized contraction**
- They contract in unison, reflecting their electrical coupling with gap junctions
- Action potentials are transmitted from cell to cell
- Some smooth muscle cells:
  - **Act as pacemakers and set the contractile pace for whole sheets of muscle**
  - **Are self-excitatory and depolarize without external stimuli**

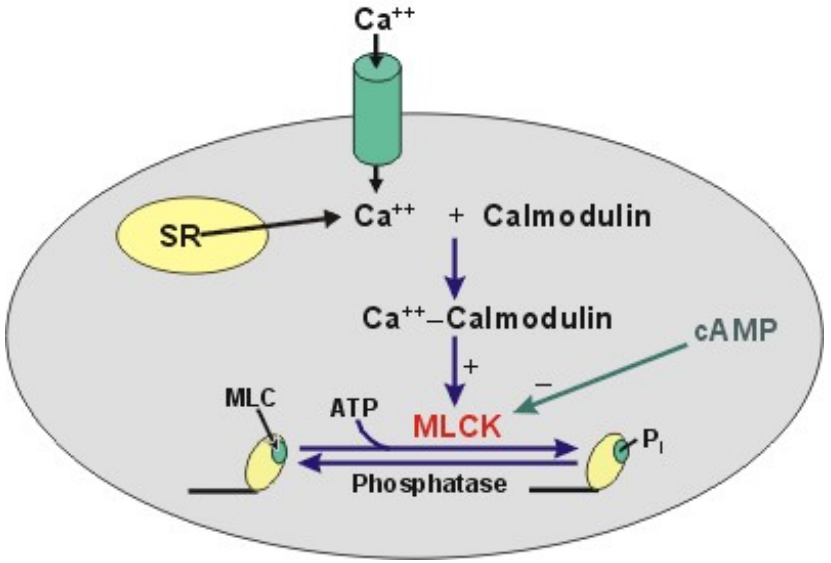






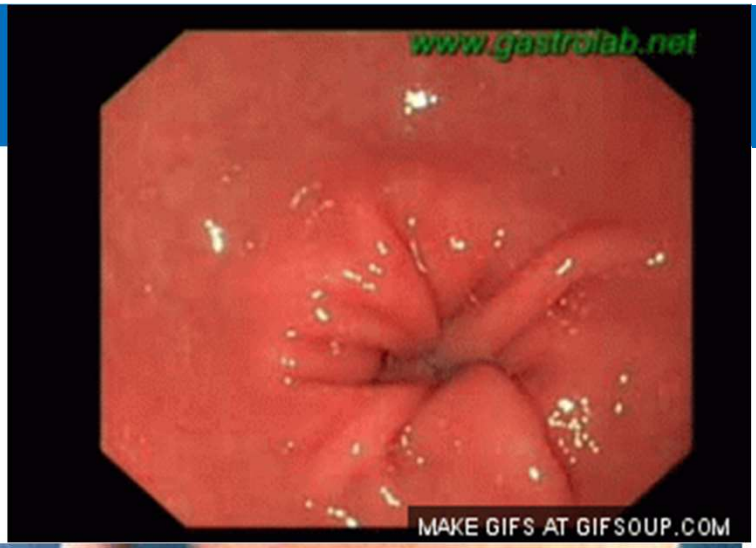
A series of axon-like swelling, called varicosities or "boutons", from autonomic neurons form motor units through the smooth muscle.

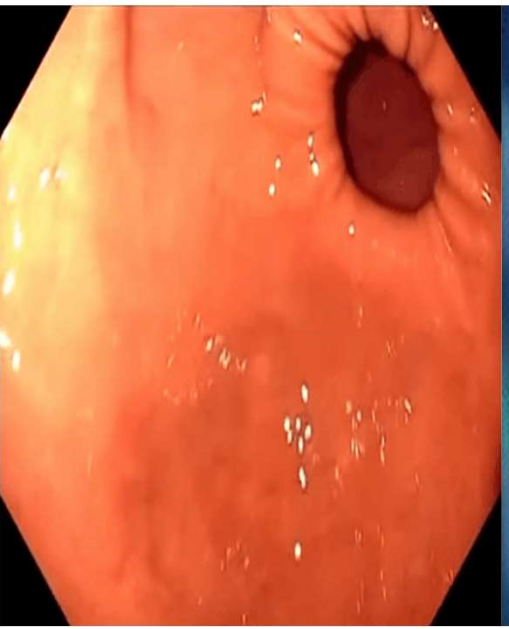
- **Smooth muscle lacks neuromuscular junctions**
- **Innervating nerves have bulbous swellings called varicosities**
- **Varicosities release neurotransmitters into wide synaptic clefts called diffuse junctions**

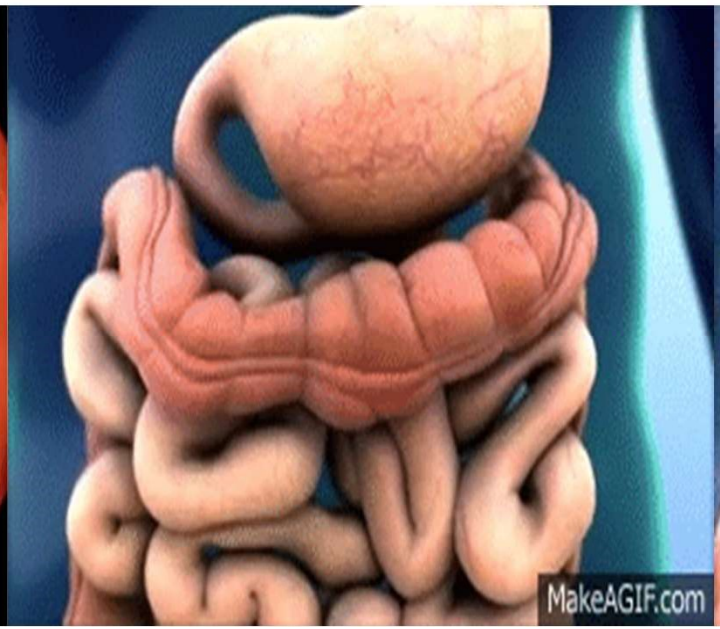


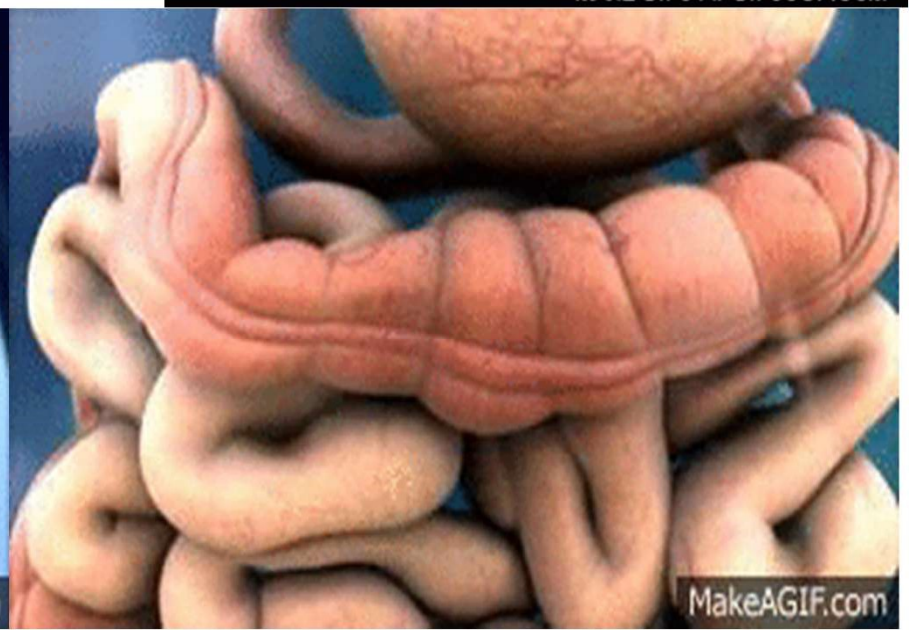
Peristalsis

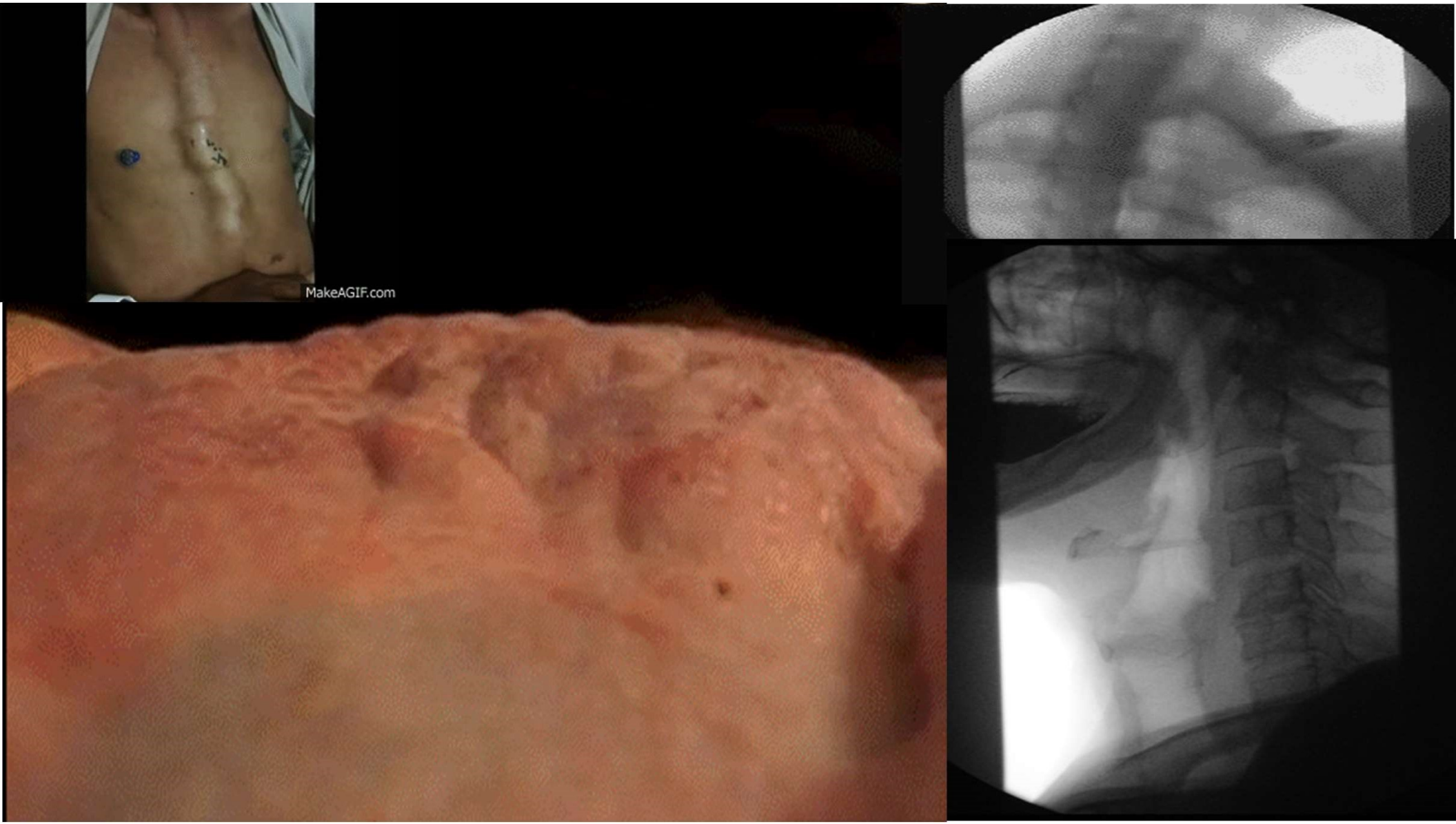
- When the longitudinal layer contracts, the organ dilates and contracts
- When the circular layer contracts, the organ elongates
- **Peristalsis** – alternating contractions and relaxations of smooth muscles that mix and squeeze substances through the lumen of hollow organs



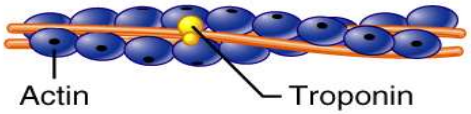
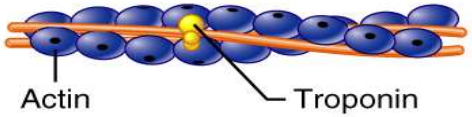
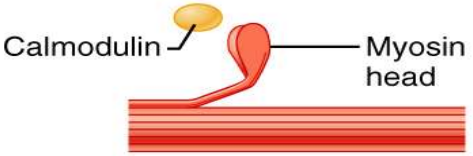
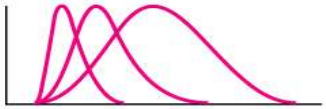
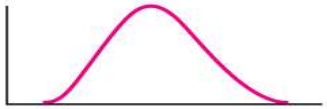
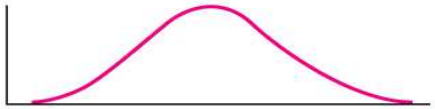







MakeAGIF.com

Comparison of Skeletal, Cardiac, and Smooth Muscle

CHARACTERISTIC	SKELETAL	CARDIAC	SMOOTH
Site of calcium regulation	Troponin on actin-containing thin filaments	Troponin on actin-containing thin filaments	Calmodulin in the sarcoplasm
			
Presence of pacemaker(s)	No	Yes	Yes (in single-unit muscle only)
Effect of nervous system stimulation	Excitation	Excitation or inhibition	Excitation or inhibition
Speed of contraction	Slow to fast	Slow	Very slow
			
Rhythmic contraction	No	Yes	Yes in single-unit muscle
Response to stretch	Contractile strength increases with degree of stretch (to a point)	Contractile strength increases with degree of stretch	Stress-relaxation response
Respiration	Aerobic and anaerobic	Aerobic	Mainly aerobic

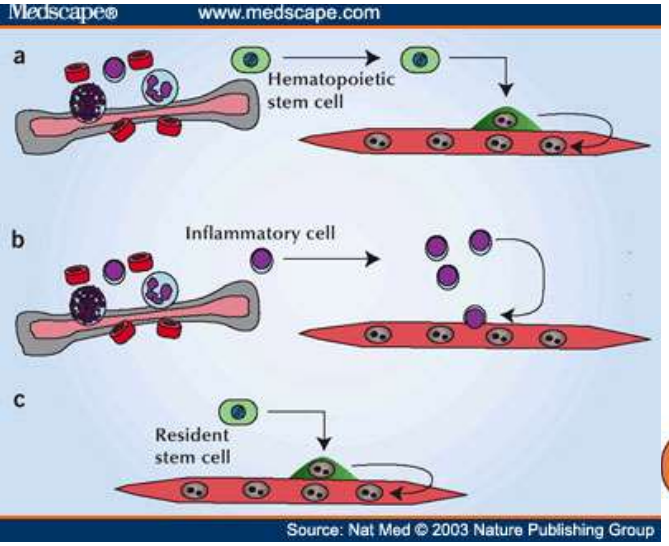
Developmental Aspects: Regeneration

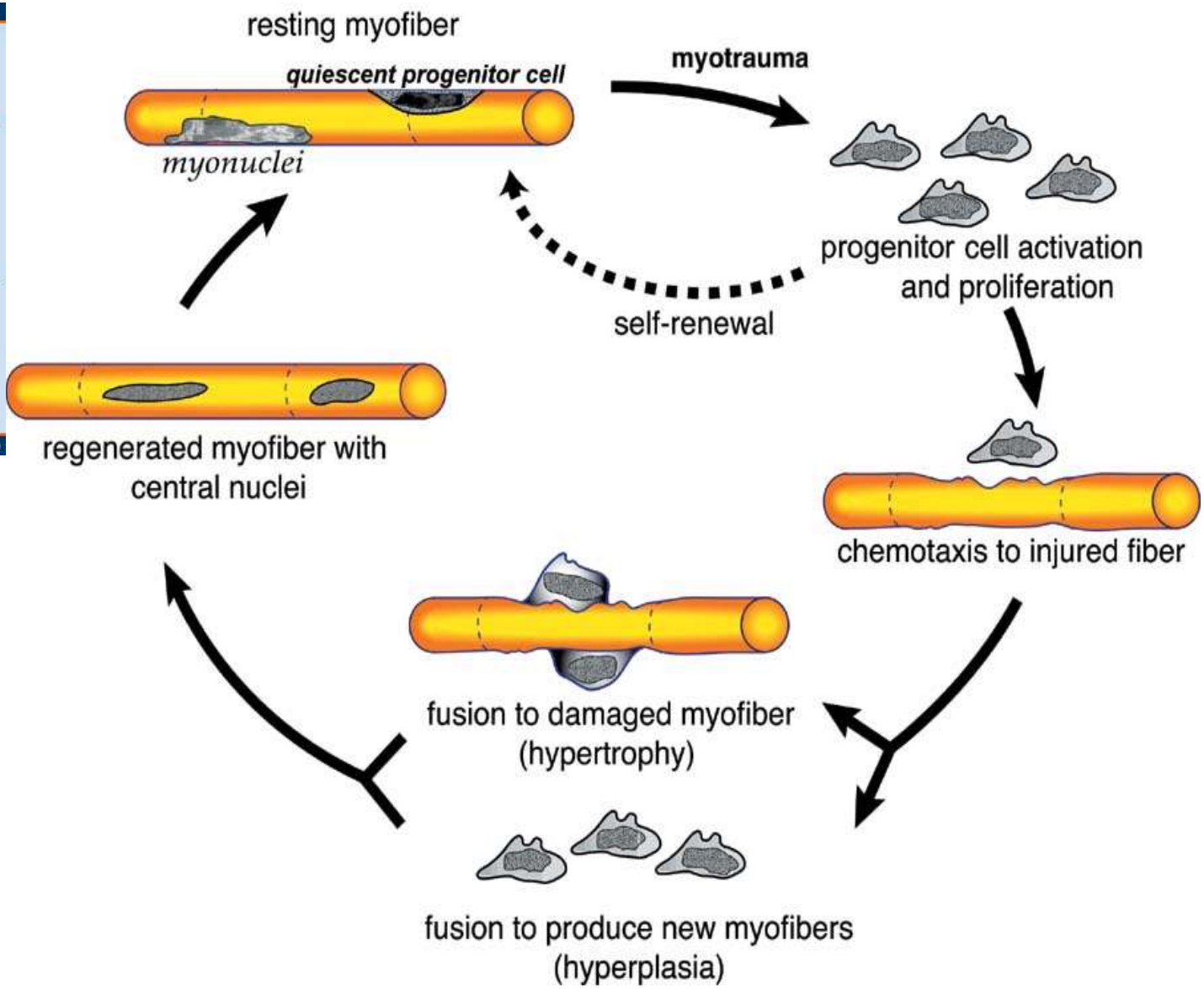
- Cardiac and skeletal muscle become amitotic, but can lengthen and thicken
- Myoblastlike satellite cells show very limited regenerative ability
- **Cardiac cells lack satellite cells**
- Smooth muscle has good regenerative ability

Satellite cells

- **Satellite cells** are mononuclear progenitor cells found in mature muscle between the basal lamina and sarcolemma.
- Satellite cells are able to differentiate and fuse to augment existing muscle fibres and to form new fibres.
- These cells are involved in the normal growth of muscle, as well as regeneration following injury or disease.

- In undamaged muscle, the majority of satellite cells are *quiescent*; they neither differentiate nor undergo cell division.
- In response to mechanical strain, satellite cells become *activated*.
- Activated satellite cells initially proliferate as skeletal myoblasts before undergoing myogenic differentiation.


Medscape®
www.medscape.com
a
Hematopoietic stem cell
b
Inflammatory cell
c
Resident stem cell
Source: Nat Med © 2003 Nature Publishing Group


resting myofiber
quiescent progenitor cell
myonuclei
myotrauma
progenitor cell activation and proliferation
self-renewal
chemotaxis to injured fiber
fusion to damaged myofiber (hypertrophy)
fusion to produce new myofibers (hyperplasia)
regenerated myofiber with central nuclei

Developmental Aspects: After Birth

- **Muscular development reflects neuromuscular coordination**
- **Development occurs head-to-toe, and proximal-to-distal**
- **Peak natural neural control of muscles is achieved by midadolescence**
- **Athletics and training can improve neuromuscular control**

- **Muscle tissue develops from embryonic mesoderm called myoblasts**
- **Multinucleated skeletal muscles form by fusion of myoblasts**
- **The growth factor *agrin* stimulates the clustering of ACh receptors at newly forming motor end plates**

Developmental Aspects: Male and Female

- There is a biological basis for greater strength in men than in women
- Women's skeletal muscle makes up 36% of their body mass
- Men's skeletal muscle makes up 42% of their body mass

- These differences are due primarily to the male sex hormone testosterone
- With more muscle mass, men are generally stronger than women
- Body strength per unit muscle mass, however, is the same in both sexes

What are the Differences Between Men and Women:

- The average male is stronger than women;
- Men are more enduring because of the volume of the heart and higher hemoglobin concentrations.
-Maximum oxygen consumption is more significant in case of men;
- On average women are more flexible than men;
- Women tend to have a higher pain threshold than men;
- Relatively males are stronger in the upper body;
- Women relatively stronger in the lower body.

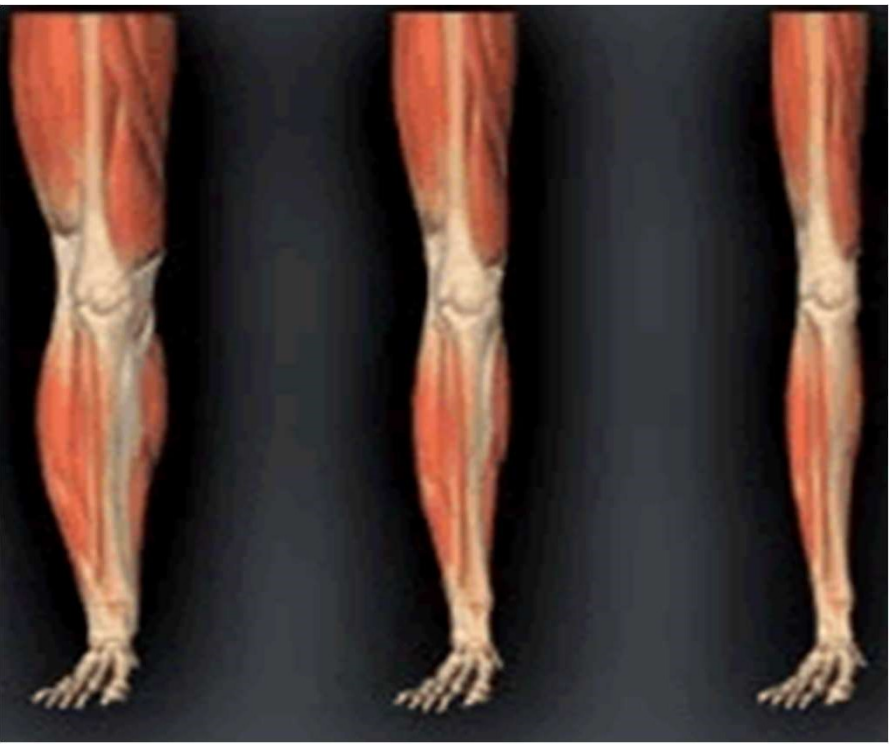


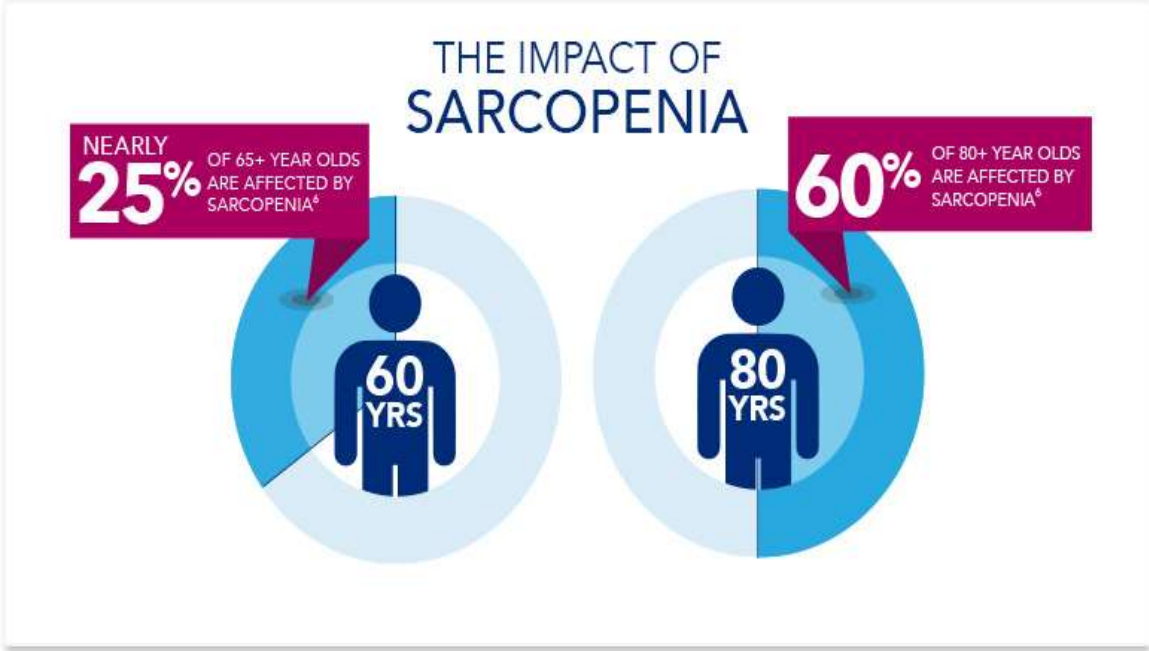


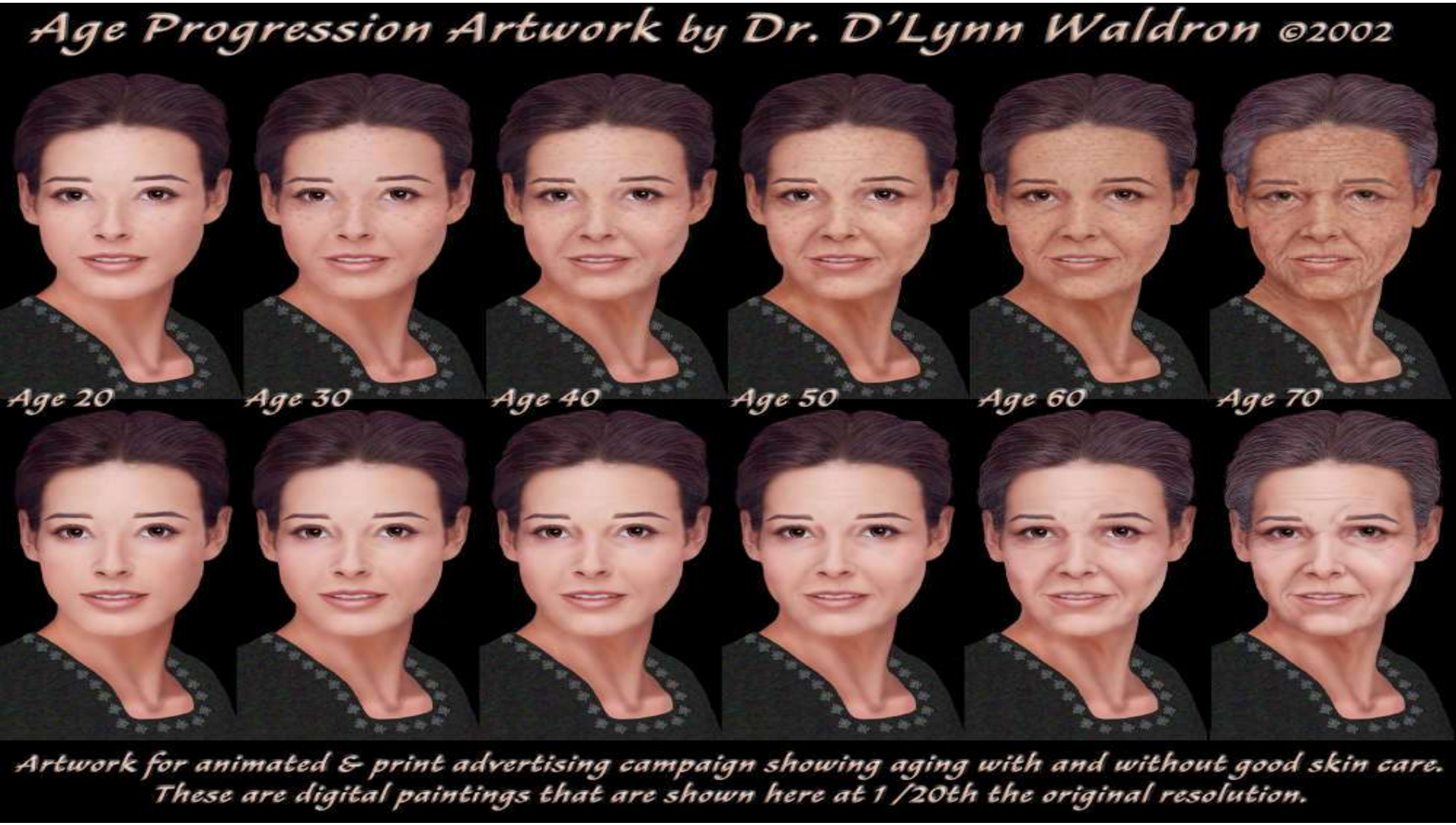



Developmental Aspects: Age Related

- **With age, connective tissue increases and muscle fibers decrease**
- **Muscles become stringier and more sinewy**
- **By age 80, 50% of muscle mass is lost (sarcopenia)**

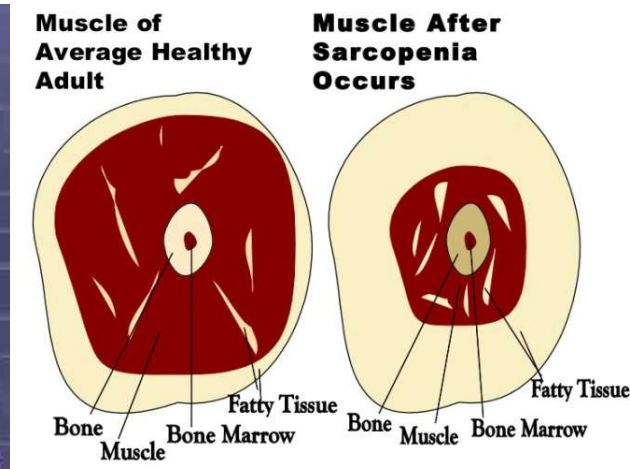


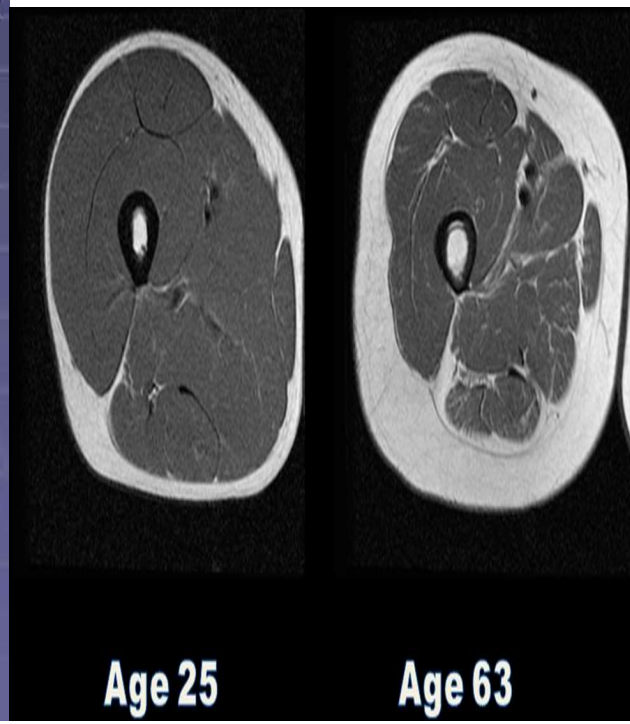



Age Progression Artwork by Dr. D'Lynn Waldron ©2002
Age 20
Age 30
Age 40
Age 50
Age 60
Age 70
Artwork for animated & print advertising campaign showing aging with and without good skin care.
These are digital paintings that are shown here at 1 /20th the original resolution.

Consequences of Sarcopenia

- Decreased resting energy expenditure
- Decreased insulin sensitivity
- Diminished muscle strength
- Increased risk of physical disability
- Increased risk of falls
- Increased risk of mortality



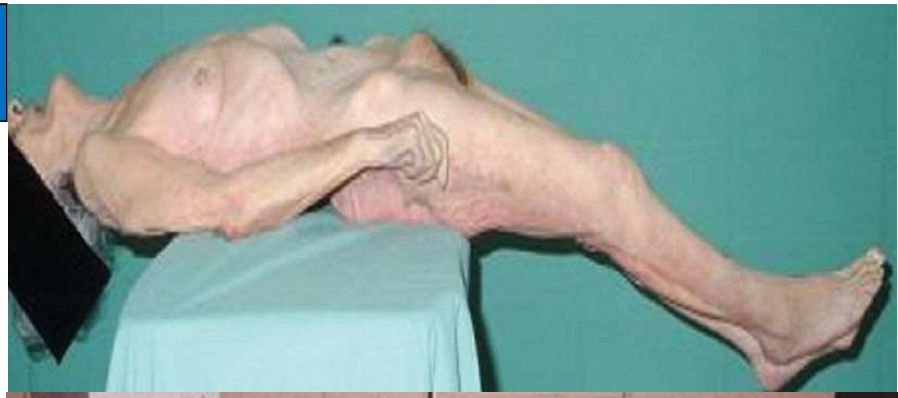


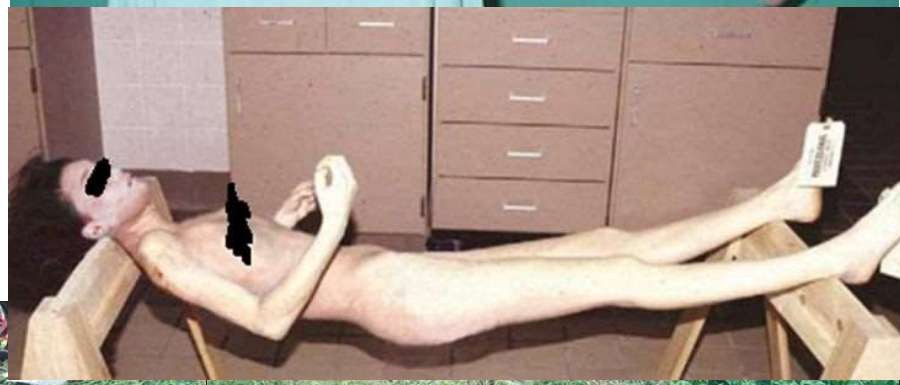
Developmental Aspects: Age Related

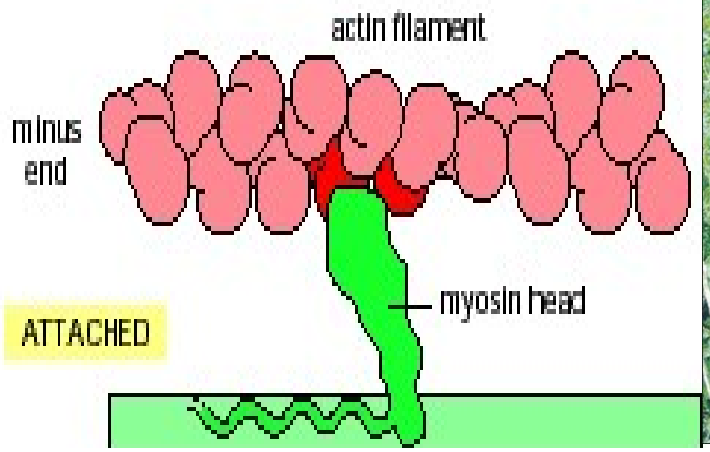
- **Regular exercise reverses sarcopenia**
- **Aging of the cardiovascular system affects every organ in the body**
- **Atherosclerosis may block distal arteries, leading to intermittent claudication and causing severe pain in leg muscles**

Rigor Mortis

- **Upon death, muscle cells are unable to prevent calcium entry.**
- **This allows myosin to bind to actin.**
- **Since there is no ATP made postmortem, the myosin cannot unbind and the body remains in a state of muscular rigidity for almost the next couple days.**







Toxins affecting NMJ

1) cobra toxin and curare
   a) block Ach receptors
   b) cause flaccid paralysis, potentially fatal respiratory arrest

2) nerve gas and insecticides
   a) inhibit AchE
   b) cause potentially fatal paralytic convulsions

3) botulism toxin
   a) block Ach release
   b) cause flaccid paralysis; potentially fatal respiratory arrest

4) tetanus toxin
   a) cause excessive Ach release from motor neurons
   b) cause potentially fatal paralytic convulsions ("lockjaw")

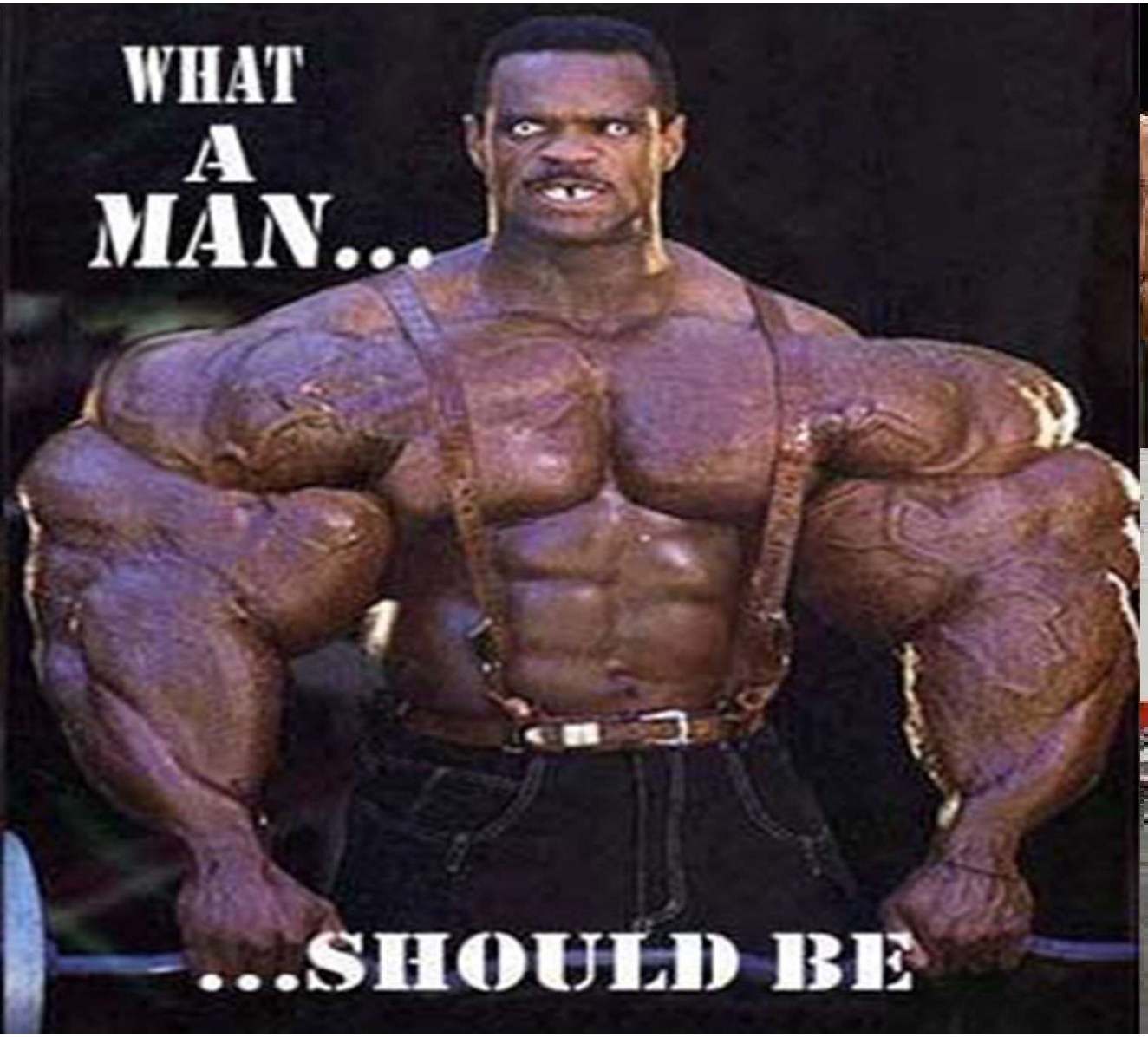
- Flaccid paralysis
  - Weakness or loss of muscle tone typically due to injury or disease of motor neurons
- Spastic paralysis
  - Sustained involuntary contraction of muscle(s) with associated loss of function
    - *How do flaccid and spastic paralysis differ?*
- Spasm
  - A sudden, involuntary smooth or skeletal muscle twitch. Can be painful. Often caused by chemical imbalances.

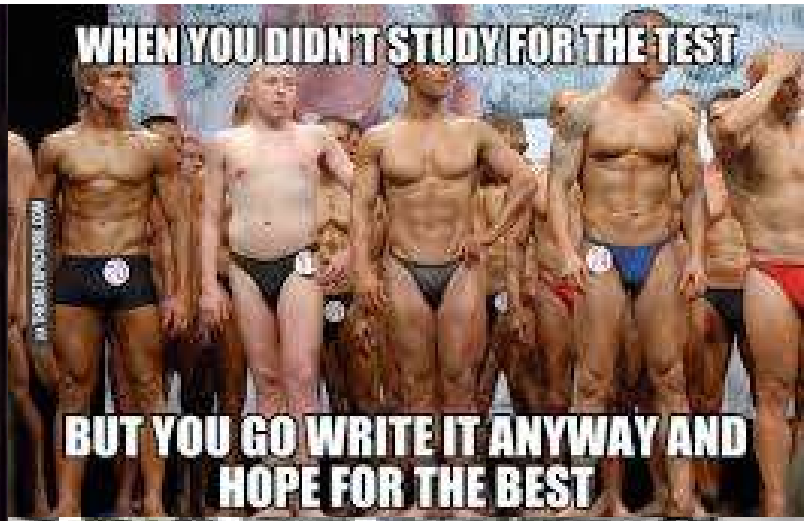
- Cramp
  - A prolonged spasm that causes the muscle to become taut and painful.
- Hypertrophy
  - Increase in size of a cell, tissue or an organ.
    - In muscles, hypertrophy of the organ is always due to cellular hypertrophy (increase in cell size) rather than cellular hyperplasia (increase in cell number)
    - Muscle hypertrophy occurs due to the synthesis of more myofibrils and synthesis of larger myofibrils.
- Atrophy
  - Reduction in size of a cell, tissue, or organ
    - In muscles, its often caused by disuse. Could a nerve injury result in disuse? Why might astronauts suffer muscle atrophy?
- Fibrosis
  - Replacement of normal tissue with heavy fibrous connective tissue (scar tissue). How would fibrosis of skeletal muscles affect muscular strength? How would it affect muscle flexibility?

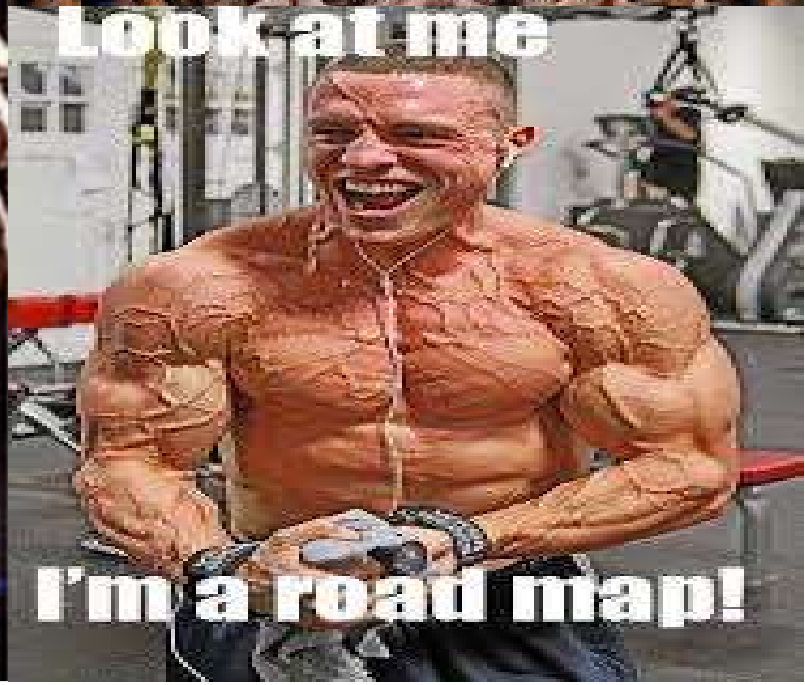
Developmental Aspects

- Muscle tissue develops from embryonic mesoderm called myoblasts
- Multinucleated skeletal muscles form by fusion of myoblasts
- The growth factor *agrin* stimulates the clustering of ACh receptors at newly forming motor end plates
- As muscles are brought under the control of the somatic nervous system, the numbers of fast and slow fibers are also determined
- Cardiac and smooth muscle myoblasts do not fuse but develop gap junctions at an early embryonic stage

- Cardiac and skeletal muscle become amitotic, but can lengthen and thicken
- Myoblastlike satellite cells show very limited regenerative ability
- Cardiac cells lack satellite cells
- Smooth muscle has good regenerative ability


WHAT
A
MAN...
...SHOULD BE


WHEN YOU DIDN'T STUDY FOR THE TEST
BUT YOU GO WRITE IT ANYWAY AND
HOPE FOR THE BEST


Look at me
I'm a road map!