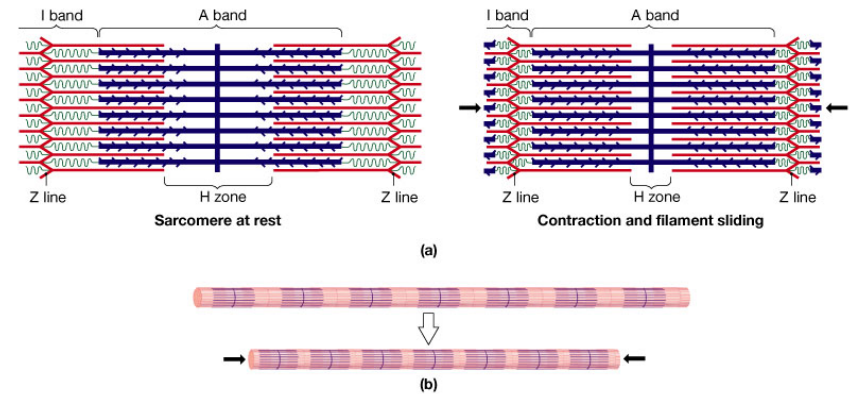


# BI204 CHAP 10A

## Muscle Physiology

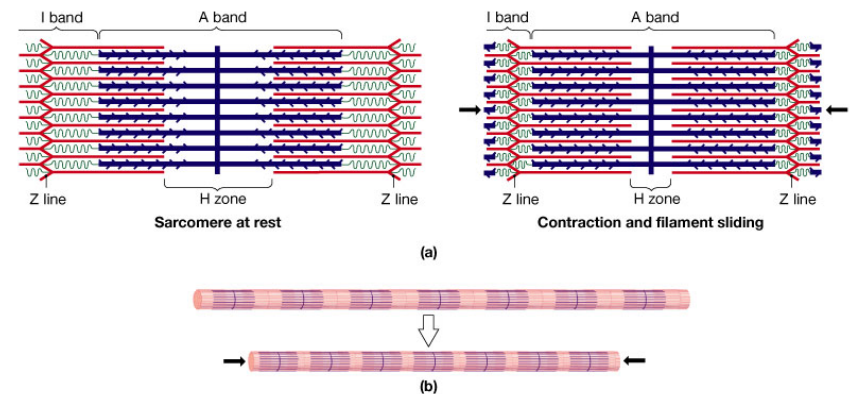
# Sliding Filament Theory

- During muscle contraction 1) H zones & I bands get smaller 2) zones of overlap get larger 3) Z lines move closer together 4) width of A band remains constant
- Thin filaments must be sliding toward center of each sarcomere along side of thick filaments
- Contraction ends with disappearance of I bands & Z lines in contact with ends of thick filaments



# Sliding Filament Theory

- During contraction sliding occurs in every sarcomere along myofibril so myofibril gets shorter & since myofibrils are attached to sarcolemma at each Z line & at either end of muscle fiber when myofibril shortens then muscle fiber shortens
- Called sliding filament theory of muscle contraction

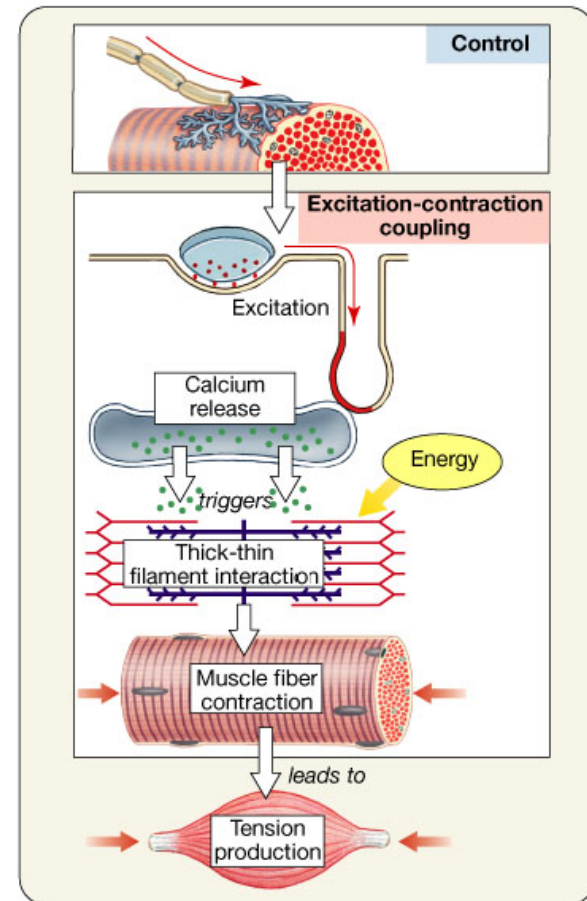


# Skeletal Muscle Contraction

- Individual cells in muscle tissue are tied together mainly by collagen fibers so when muscle cells contract they pull on the fibers & generate tension & the object is pulled toward the source of the tension
- Tension must overcome resistance which opposes movement
- Many factors affect resistance – shape, size, etc.
- Compression or push away from source of push must still overcome resistance but muscle cells can only generate tension or pull but not push or compression

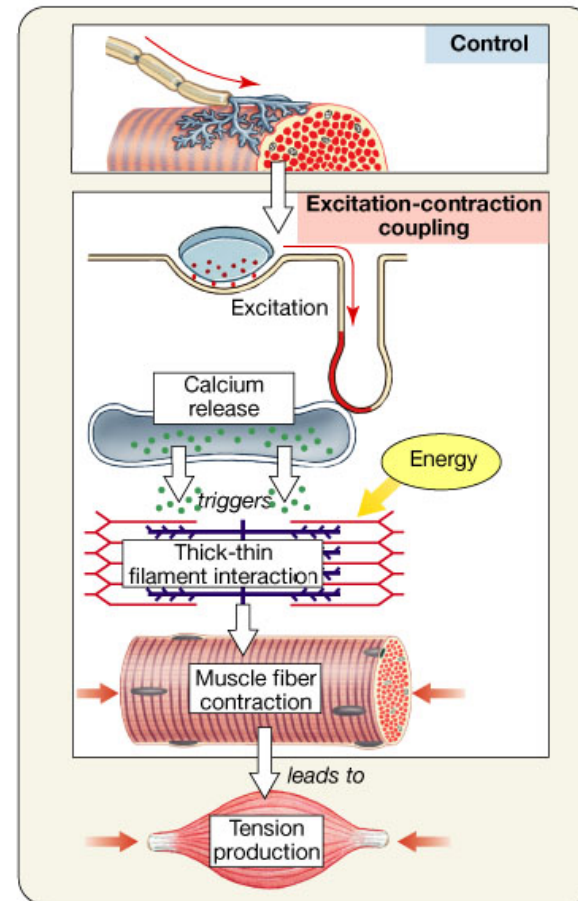
# Skeletal Muscle Contraction cont.

- Skeletal muscle contracts only when fibers activated by neurons whose cell bodies are in CNS
- Neuron activates muscle fiber through stimulation of the sarcolemma



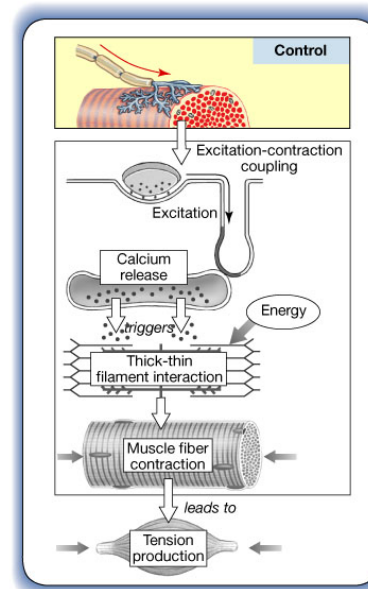
# Skeletal Muscle Contraction cont.

- Excitation – contraction coupling follows activation of sarcolemma
- 1<sup>st</sup> step is release of calcium ions from cisternae of SR
- Calcium ions trigger interactions between thick & thin filaments resulting in muscle fiber contraction
- Filament interactions produce tension & use energy

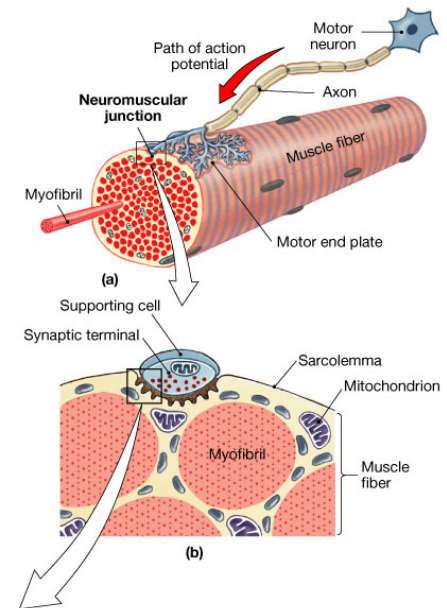


# Skeletal Muscle Contraction cont.

- Skeletal muscle contraction controlled by nervous system at specialized junction called neuromuscular junction which is present midway along each muscle fiber
- Single axon branches in perimysium to form many fine branches which end in synaptic terminals which contain vesicles containing acetylcholine the neurotransmitter which changes the permeability or other properties of sarcolemma

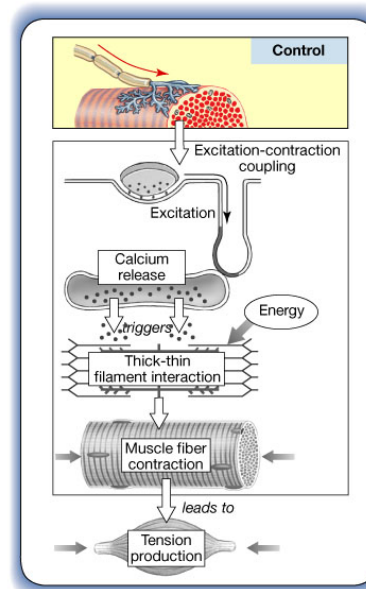


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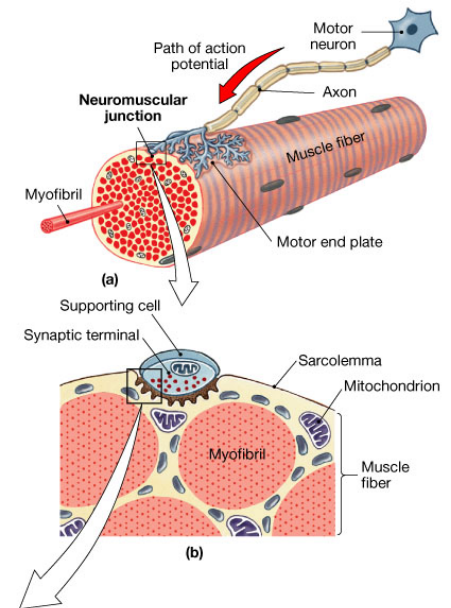


# Skeletal Muscle Contraction cont.

- Synaptic cleft - a narrow space – separates the synaptic terminal from the sarcolemma whose surface contains receptors that bind Ach at the motor end plate
- Motor end plate has many folds called junctional folds which increase surface area & contain many more Ach receptors & also have the enzyme acetylcholinesterase which breaks down ACh

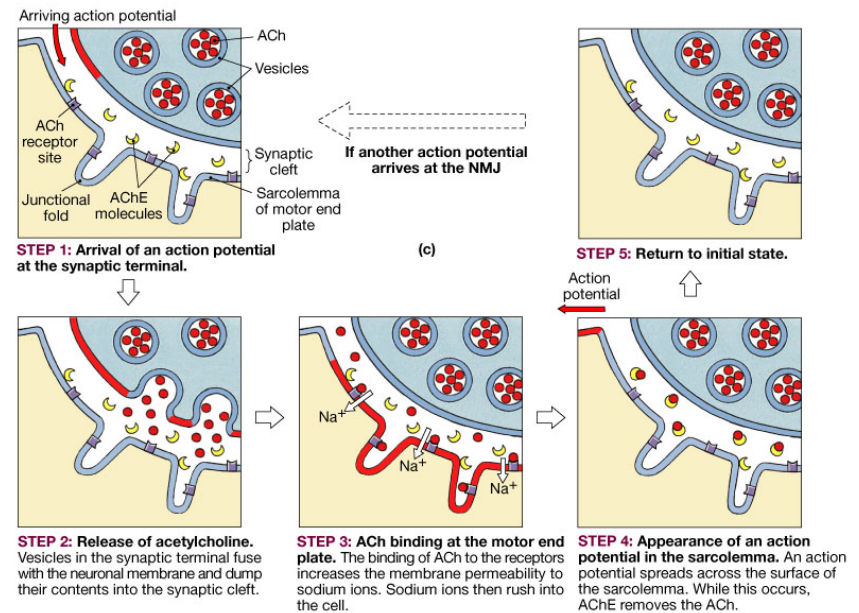


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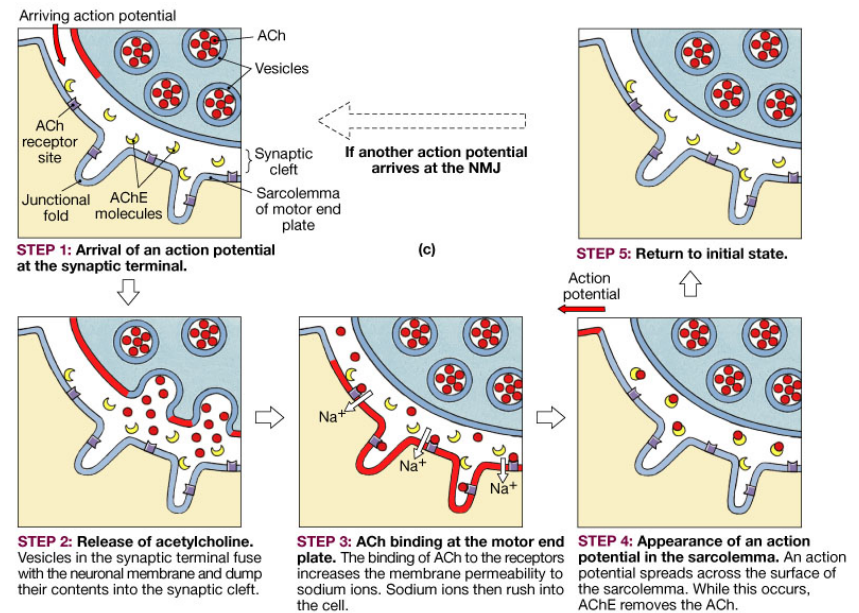
# Skeletal Muscle Contraction cont.

- Step 1 – arrival of action potential – electrical impulse or sudden change in transmembrane potential that travels along length of axon to its end
- Step 2 – release of Ach – when action potential arrives at synaptic terminal permeability changes in membrane trigger exocytosis of Ach into synaptic cleft as vesicles in ending fuse with membrane



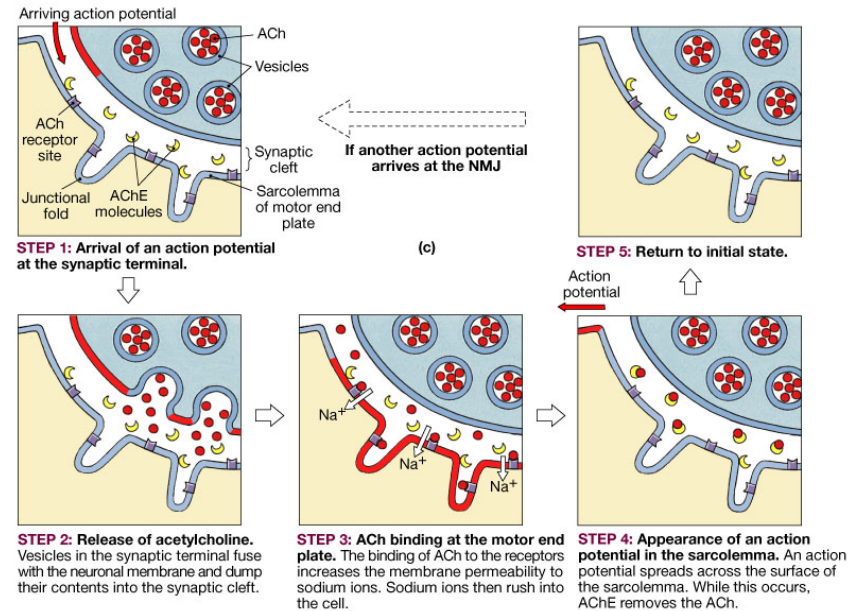
# Skeletal Muscle Contraction cont.

- Step 3 – Ach binding at motor end plate – released Ach molecules diffuse across cleft to sarcolemma containing Ach synaptic receptors
- Ach binds to receptors & changes permeability to sodium ion which move down their concentration gradient into the sarcoplasm & influx continues until AChE degrades ACh



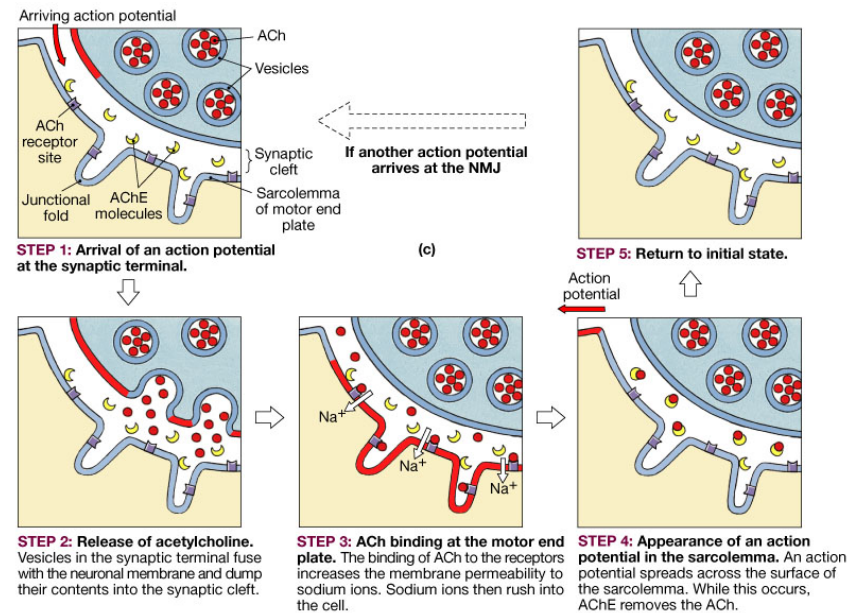
# Skeletal Muscle Contraction cont.

- Step 4 – appearance of action potential in sarcolemma – sudden rush of sodium ions results in generation of action potential in sarcolemma which starts at motor end plate & travels along sarcolemma to both ends of muscle cell & also travels down transverse tubules to cell interior
- Arrival of action potential at nerve ending leads to action potential in sarcolemma



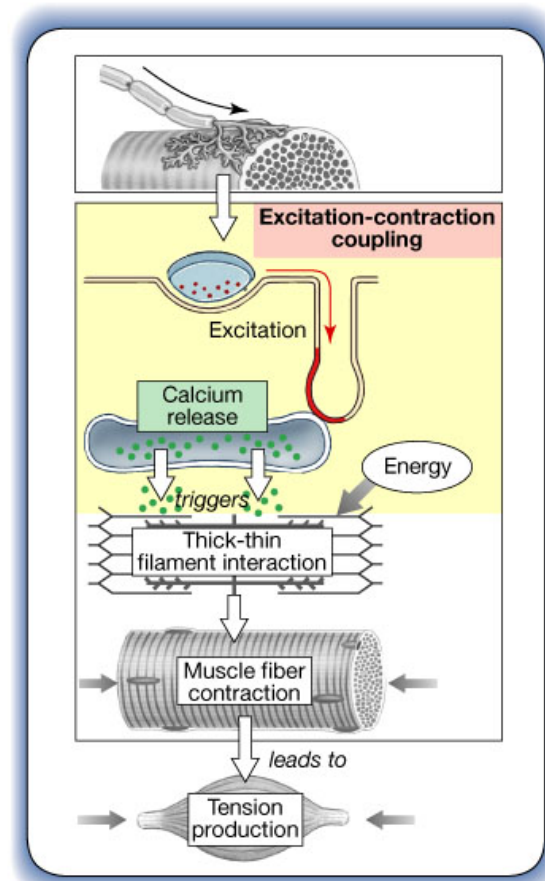
# Skeletal Muscle Contraction cont.

- Step 5 – return to initial state – as action potential spreads across sarcolemma the ACh is broken down by the enzyme AChE products are taken up by nerve ending & reused to make ACh



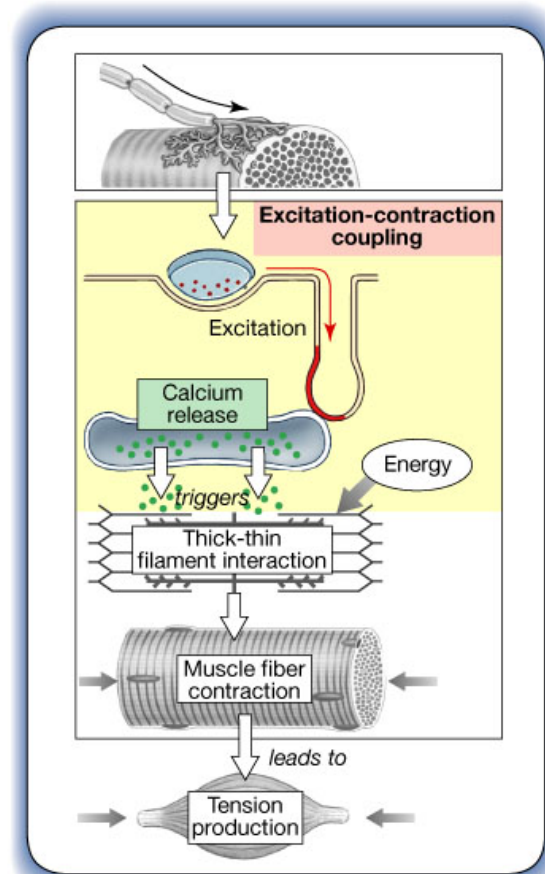
# Excitation-Contraction Coupling

- Excitation – contraction coupling is the link between generation of action potential in sarcolemma & start of muscle contraction
- Coupling occurs at triads which is structure of T tubule contacting terminal cisternae of SR on each side & function of SR is to sequester calcium ions



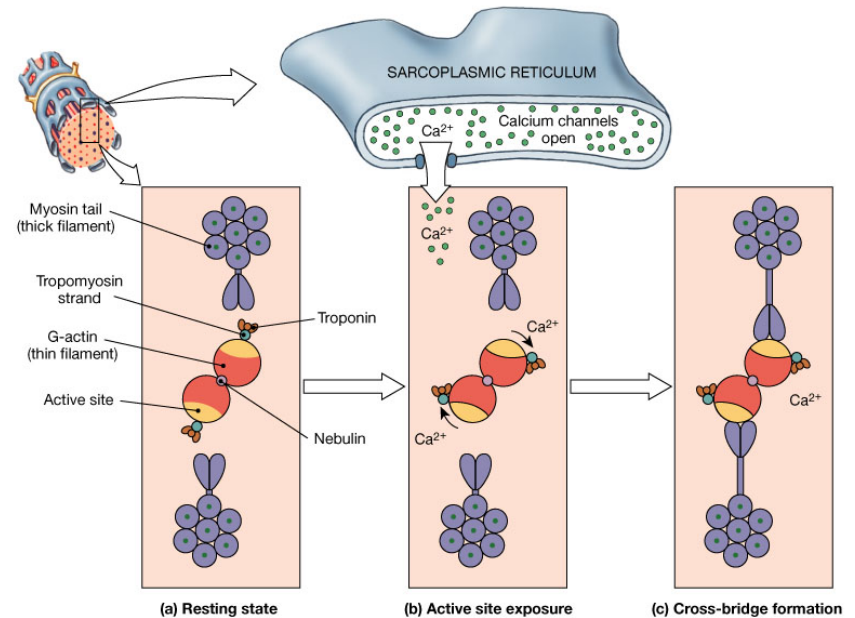
# Excitation-Contraction Coupling cont.

- When action potential reaches triad it triggers release of calcium ion from cisternae of SR with change in permeability lasting 30 msec but in 1 msec calcium ion conc is 100x resting levels



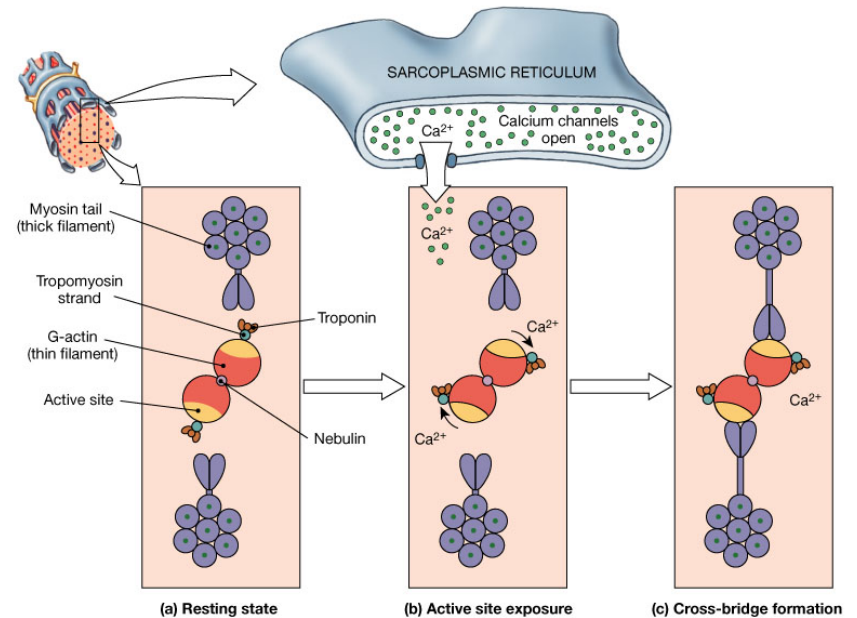
# Excitation-Contraction Coupling cont.

- Terminal cisternae circle the zone of overlap where thick & thin filaments interact & effect of calcium release is instantaneous
- Troponin keeps active sites inaccessible & calcium ion can remove this block



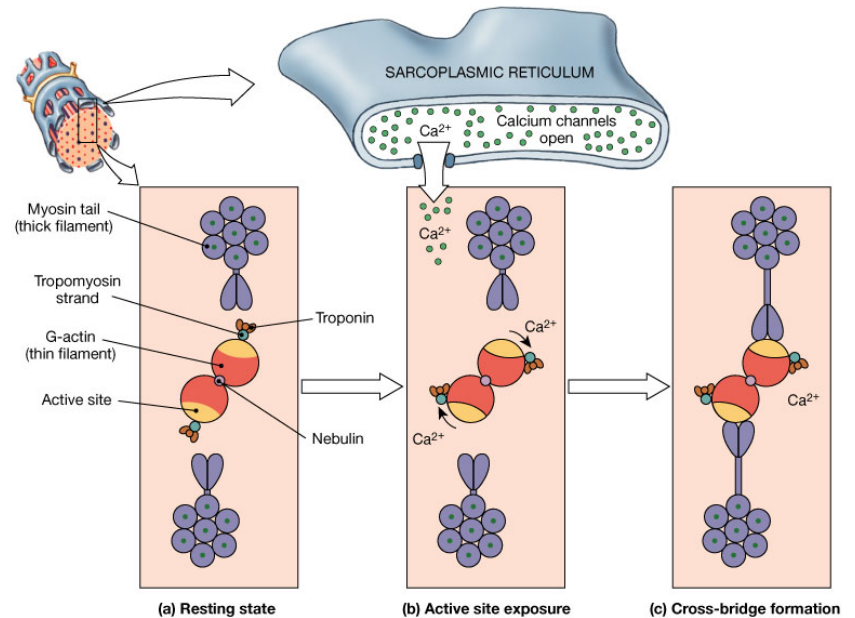
# Excitation-Contraction Coupling

- Troponin binds to actin & to tropomyosin & also has a binding site for calcium ion
- At rest tropomyosin covers the active site & prevents interaction between thick & thin filaments



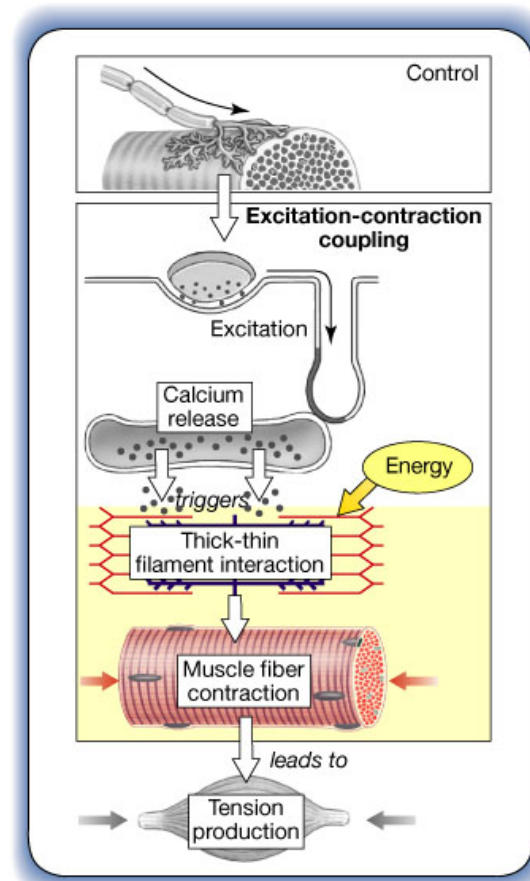
# Excitation-Contraction Coupling cont.

- Calcium binding site on troponin is empty when skeletal muscle is at rest
- When calcium ion is released from SR & binds to troponin 1st troponin changes shape weakening bond between troponin & actin and 2<sup>nd</sup> troponin changes position swinging tropomyosin away from active site so **contraction cycle** can begin



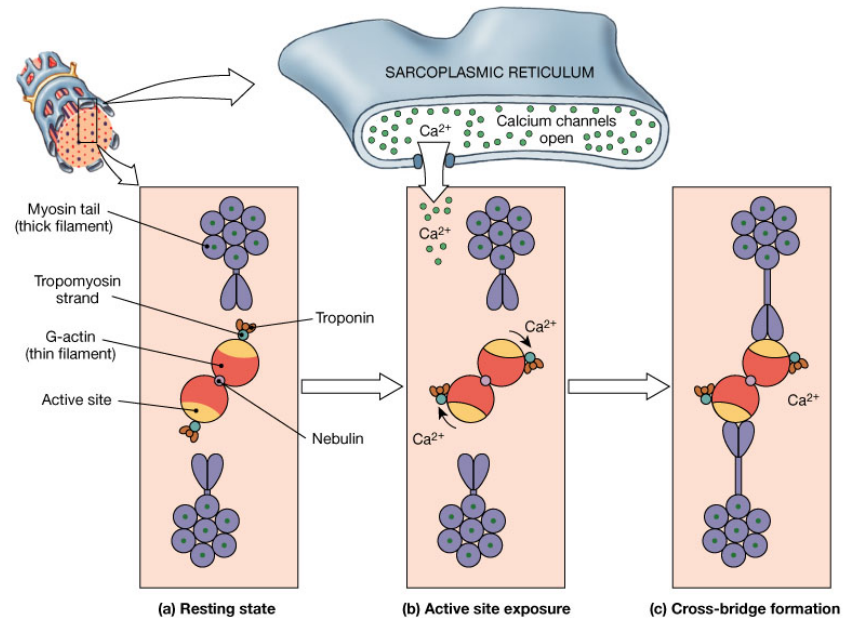
# Contraction Cycle

- Cycle details molecular events of contraction
- In resting sarcomere myosin heads are energized – ready to contract
- Myosin head functions as ATPase so can break down ATP & at start of cycle ATP is already degraded & released energy stored
- ADP & phosphate still bound to myosin head



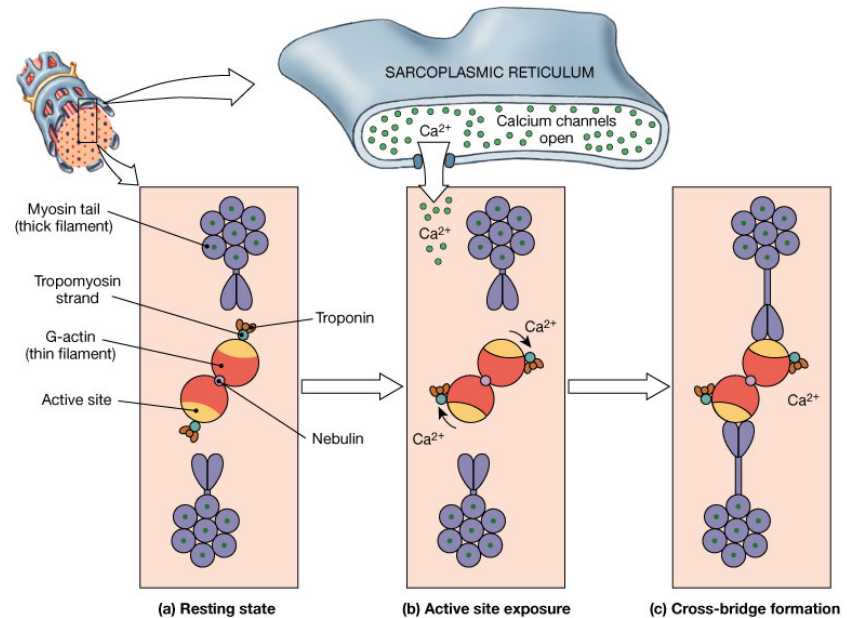
# Contraction Cycle cont.

- Step 1 – exposure of active sites – calcium ion enters sarcoplasm & binds to troponin which 1) changes shape then 2) changes position pulling tropomyosin away from active sites & allowing interaction with energized myosin heads



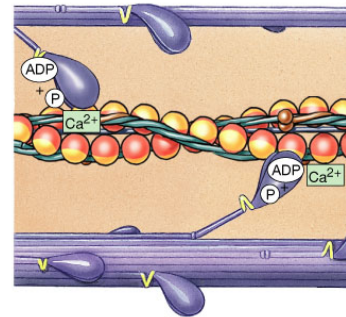
# Excitation-Contraction Coupling cont.

- Step 2 – cross bridge formation – when active sites are exposed energized myosin heads bind to active sites on G actin forming cross bridges
- Step 3 – pivoting – in resting sarcomere myosin heads point away from M line in ‘cocked’ position which requires energy to achieve & energy comes from ATP breakdown

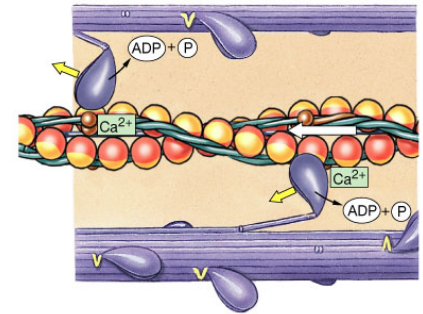


# Excitation-Contraction Coupling cont.

- After cross bridge formation stored energy is released as myosin heads pivot toward M line called power stroke & ADP and phosphate released when it occurs
- Step 4 – detachment of cross bridges – after ADP & phosphate group get released a new ATP binds to myosin head & link between active site on actin molecule & myosin head is broken & active site can now form another cross bridge



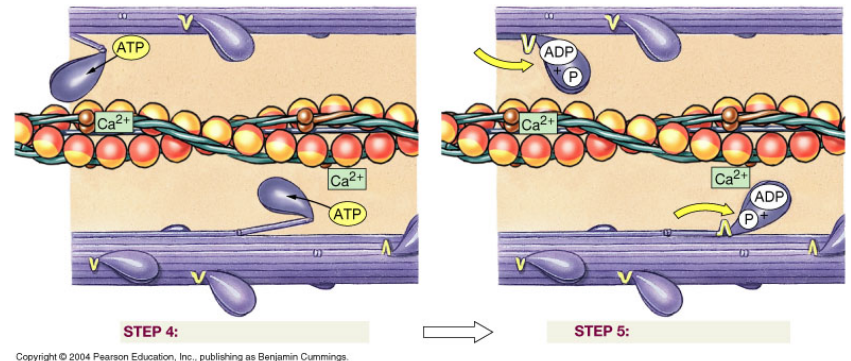
STEP 2: Cross-bridge attachment  
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STEP 3: Pivoting of myosin head

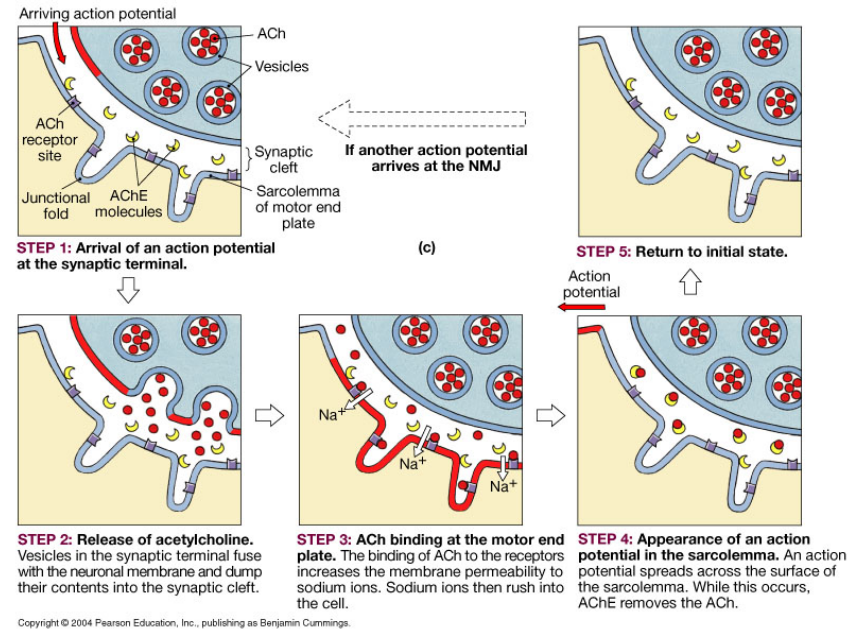
# Excitation-Contraction Coupling cont.

- Step 5 – reactivation of myosin – occurs when free myosin head splits ATP into ADP & phosphate group & energy released is used to ‘cock’ the myosin head
- Cycle can be repeated



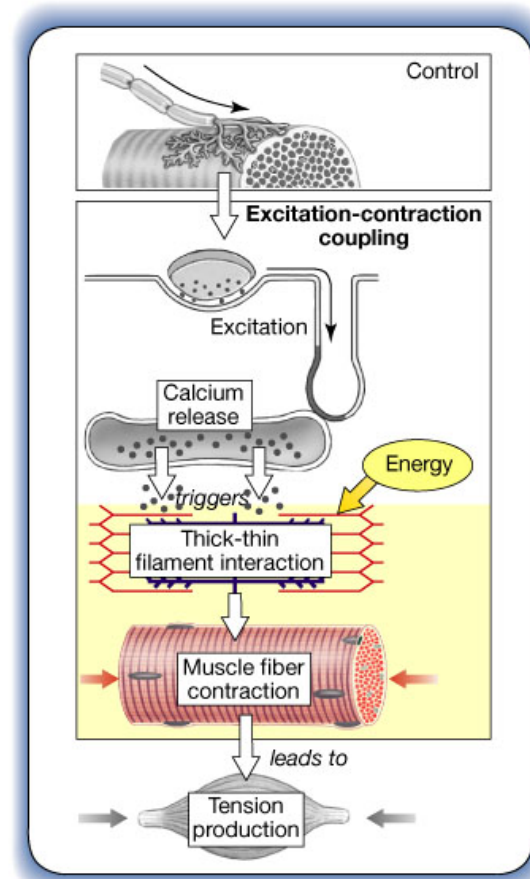
# Excitation-Contraction Coupling cont.

- Botulism – contaminated canned or smoked food containing a toxin which prevents release of Ach at synaptic endings leading to muscle paralysis which can be fatal
- Myasthenia gravis due to loss of Ach receptors at neuromuscular junction caused by immune system attack due to genetic factors predisposing individuals to the condition



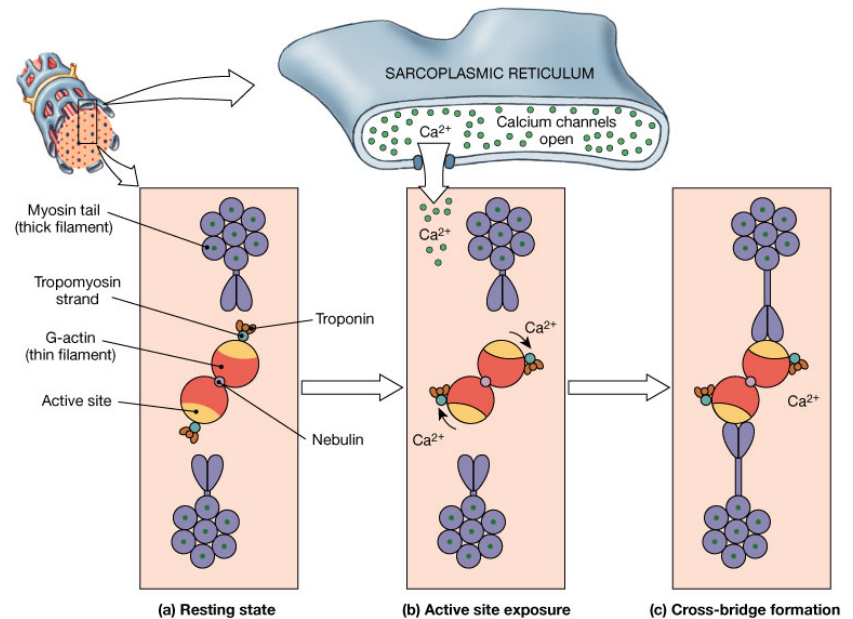
# Relaxation

- Duration of contraction depends on 1) duration of stimulation at NMJ 2) presence of free calcium in sarcoplasm 3) availability of ATP
- Need repeated action potentials at NMJ to increase level of Ach at sarcolemma since Ach starts to be degraded as soon as it is released



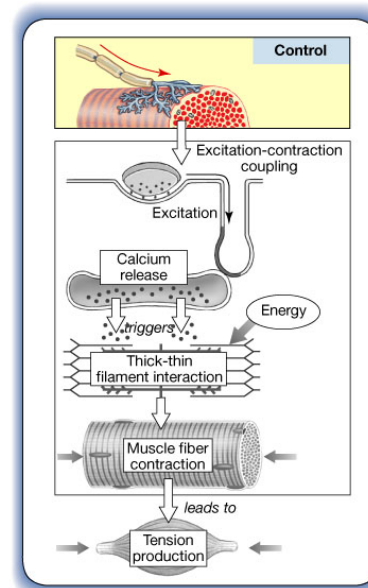
# Relaxation cont.

- If have only 1 action potential then calcium ion concentration returns to normal quickly because 1) active transport out of cell 2) reuptake by SR which is more important mechanism
- As calcium ion returns to normal levels 1) calcium ion detaches from troponin 2) troponin returns to original position 3) active sites re-covered by tropomyosin

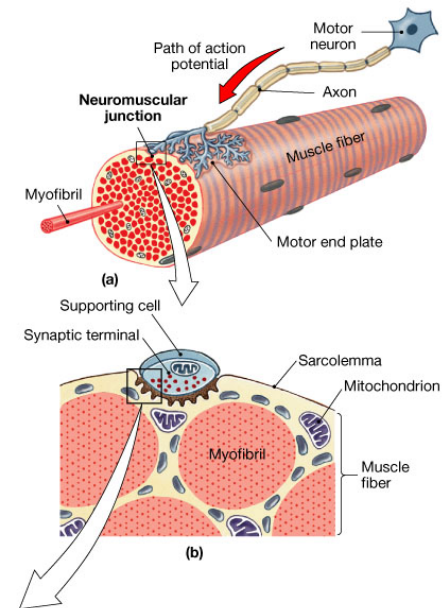


# Tension Production in Muscle Fiber or Cell

- When sarcomeres shorten in contraction then muscle fiber shortens & exerts tension on CT fibers attached to muscle fiber but tension produced can vary
- Amount of tension produced by single muscle fiber depends on number of pivoting cross bridges & no way to control number of contracting sarcomeres – all or none principle

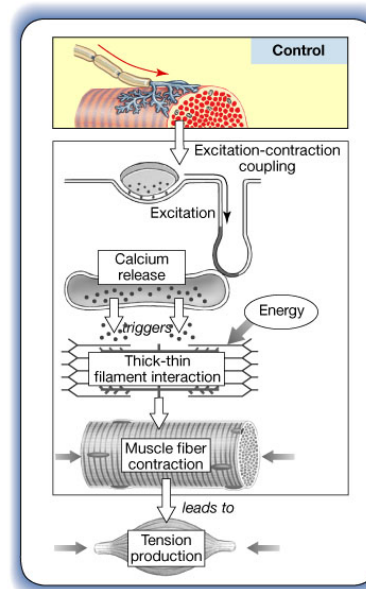


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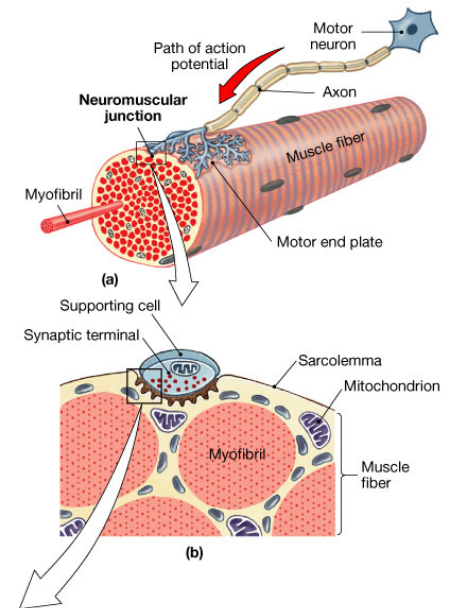


# Tension Production in Muscle Fiber or Cell cont.

- Tension can vary in single muscle fiber depending on 1) resting length of muscle fiber at time of stimulation which determines degree of overlap of thick & thin filaments 2) frequency of stimulation which affects internal calcium ion concentration

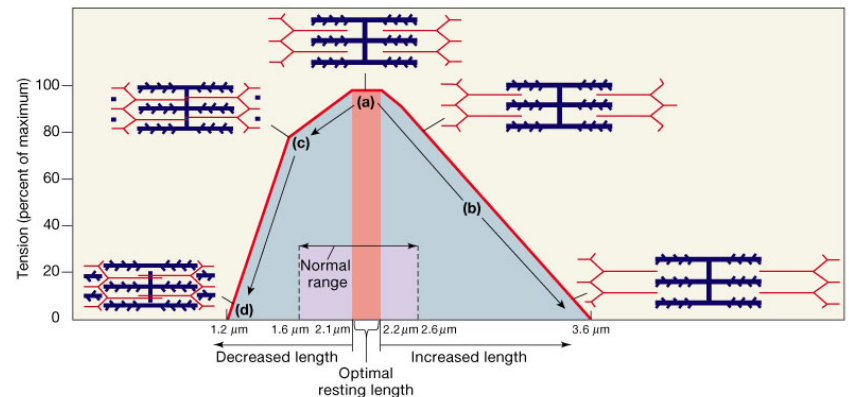


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# Tension Production in Muscle Fiber or Cell cont.

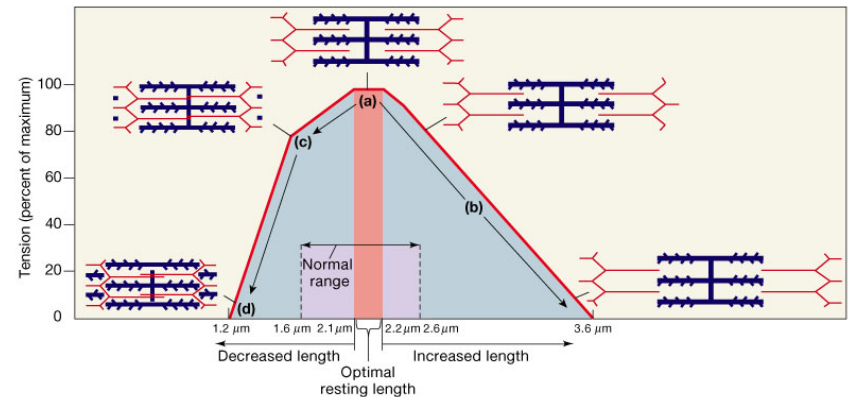
- Length-tension relation – skeletal muscle fibers contract most forcefully over narrow range of resting lengths
- Normal range of resting sarcomere lengths is 75-130% of optimal sarcomere length with muscles & CT & bones preventing excess compression or stretching



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# Tension Production in Muscle Fiber or Cell cont.

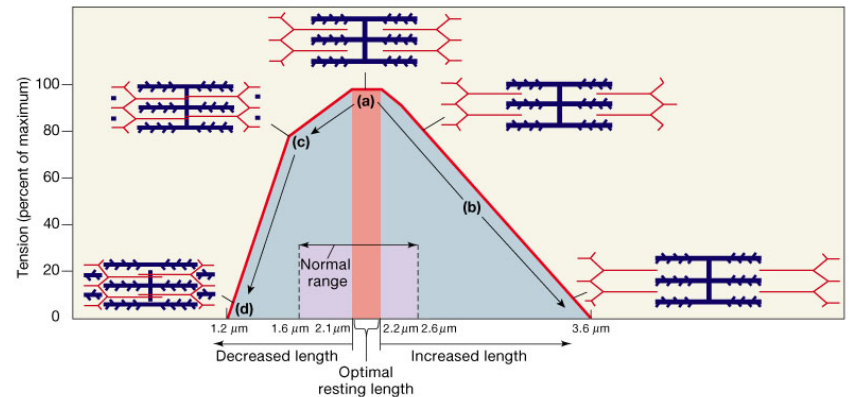
- Sarcomere works best in optimal range of lengths where maximum number of cross bridges can form so tension produced is maximal
- When sarcomere is outside this range either too long or too short tension production is reduced



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# Tension Production in Muscle Fiber or Cell cont.

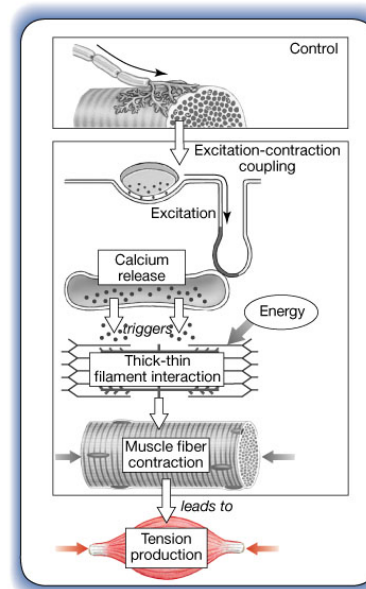
- Frequency of stimulation – single stimulation produces single contraction or twitch lasting 7-100 msec which is too brief for normal activity (can generate heat when shivering)
- Duration of contraction extended by repeated stimulation & sustained contraction produces more tension



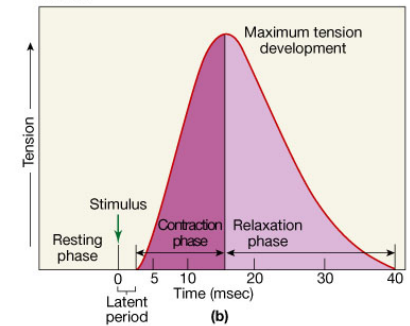
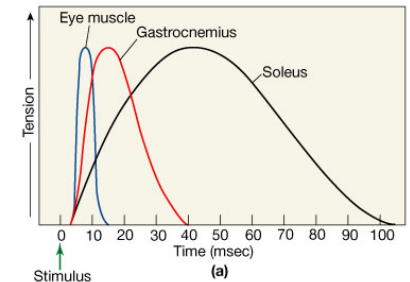
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# Tension Production in Muscle Fiber or Cell cont.

- Twitch – single stimulus-contraction – relaxation sequence in a muscle fiber
- Vary in duration due to many factors like type & location of muscle, temperature
- Myogram is graph of twitch tension development in muscle fiber

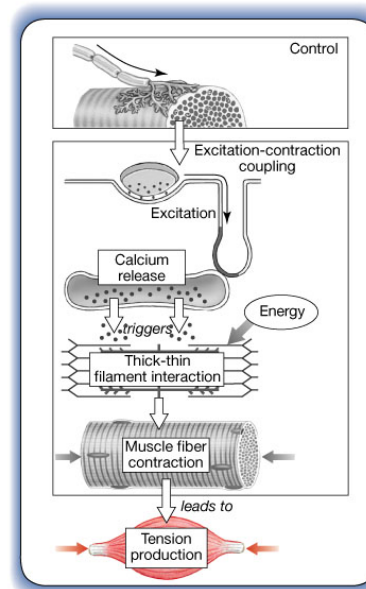


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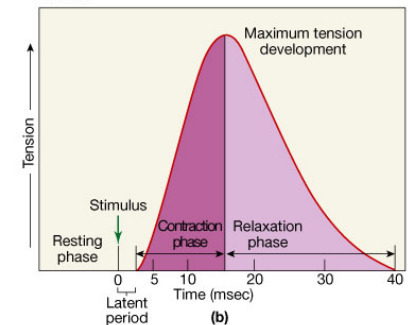
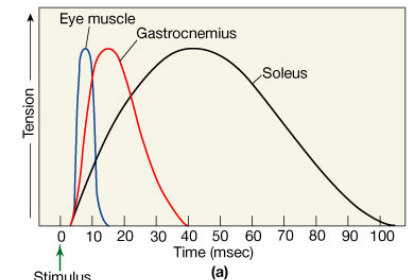


# Tension Production in Muscle Fiber or Cell cont.

- Single twitch divided into latent period, contraction phase, relaxation phase
- Latent period – begins at stimulation – where action potential sweeps over sarcolemma & SR releases calcium ion

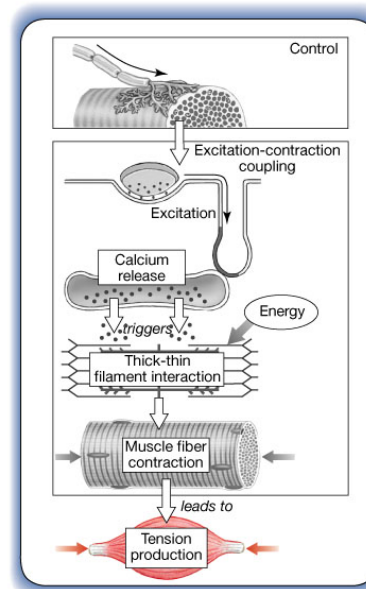


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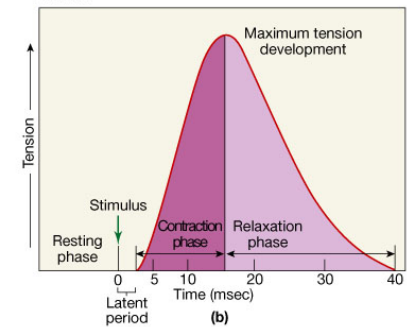
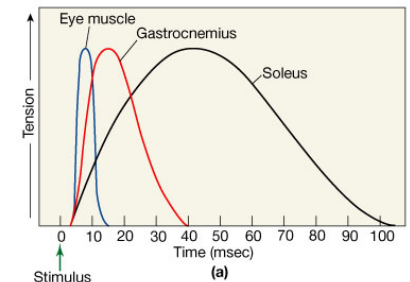


# Tension Production in Muscle Fiber or Cell cont.

- Latent period cont. – no tension produced since no contraction cycle has started
- Contraction phase – tension rises & peaks due to calcium ion binding to troponin & active sites are exposed & cross bridge formation is occurring

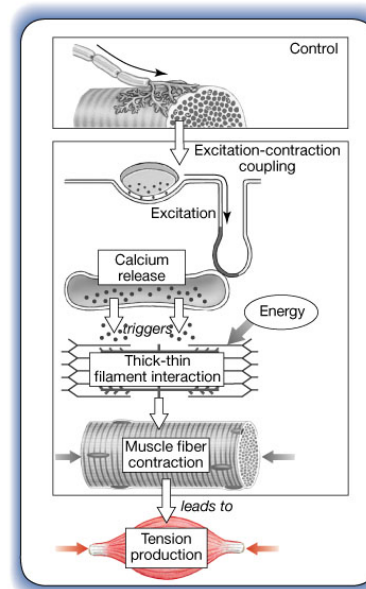


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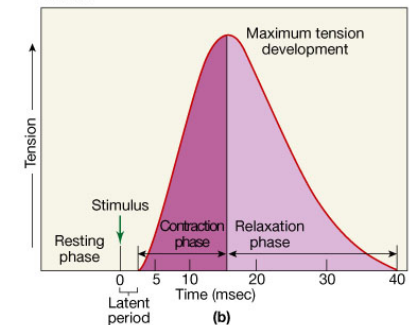
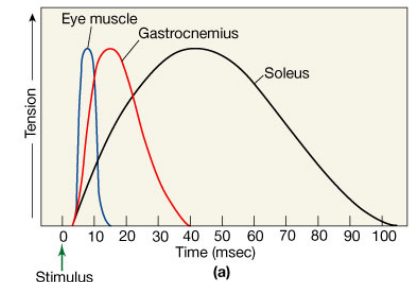


# Tension Production in Muscle Fiber or Cell cont.

- Relaxation phase – calcium levels falling, active sites being covered by tropomyosin, number of active cross bridges declining

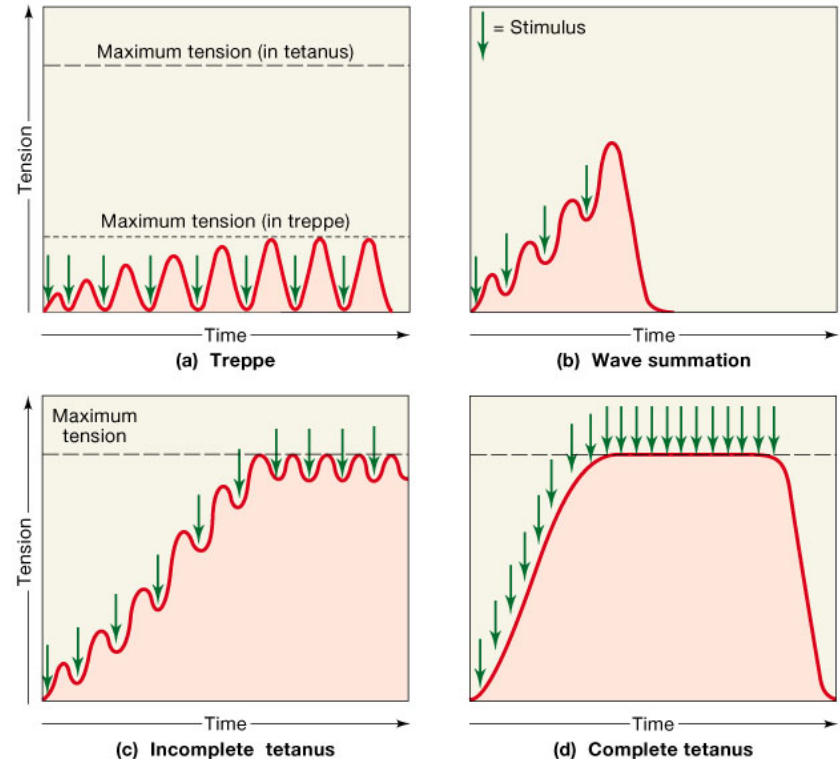


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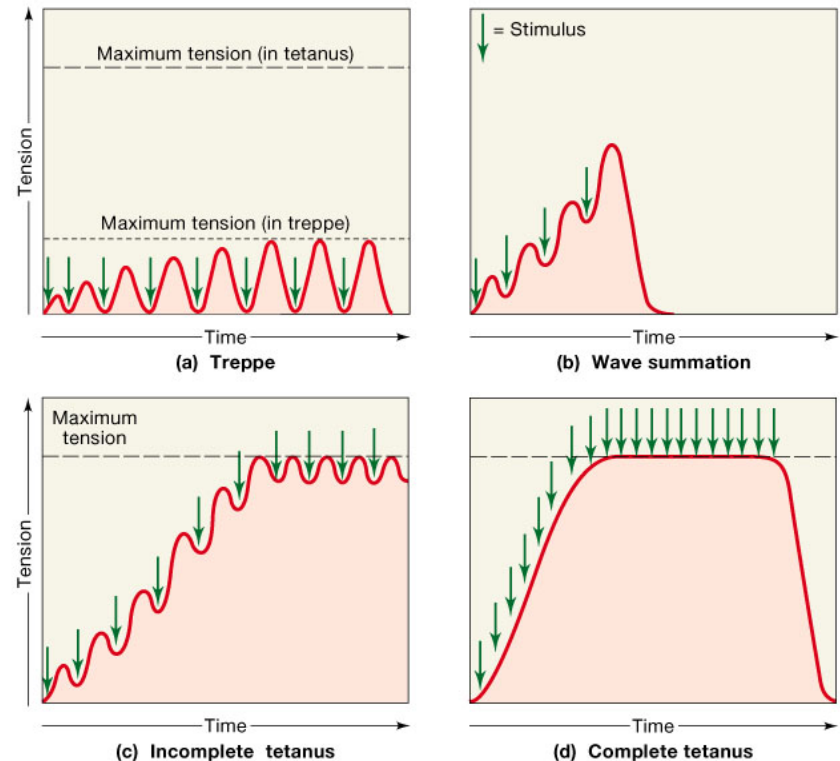
# Tension Production in Muscle Fiber or Cell cont.

- Treppe – 2<sup>nd</sup> stimulation immediately after 1<sup>st</sup> relaxation phase leads to higher maximum tension in 2<sup>nd</sup> contraction
- Due to increased concentration of calcium ions in sarcoplasm



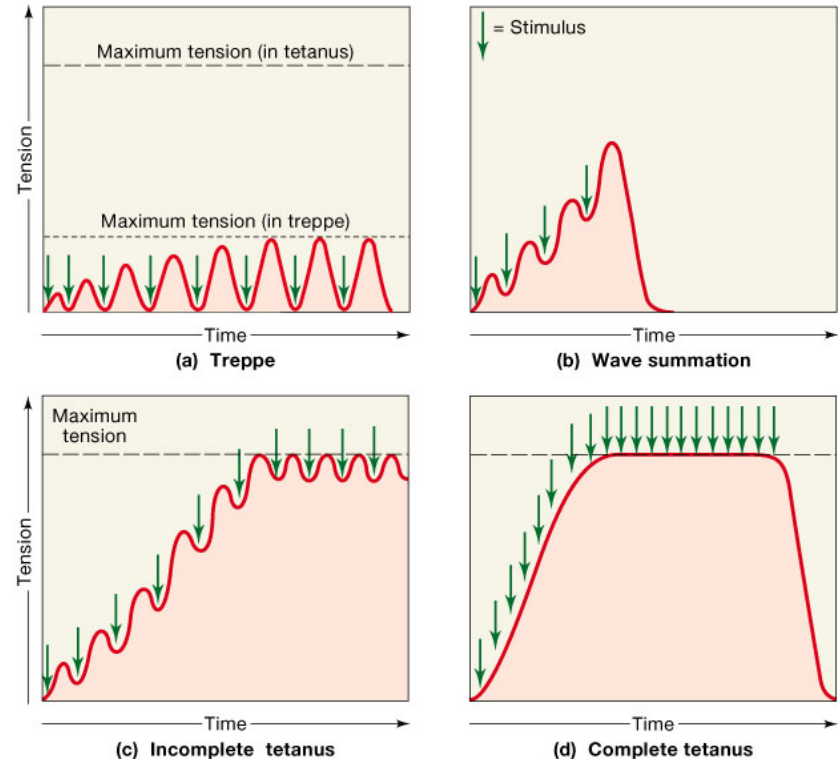
# Tension Production in Muscle Fiber or Cell cont.

- Wave summation – if 2<sup>nd</sup> stimulation occurs before relaxation phase ends then 2<sup>nd</sup> more powerful contraction occurs
- Rate of stimulation called frequency or stimulation over time
- Frequency at which see wave summation depends on duration of twitch



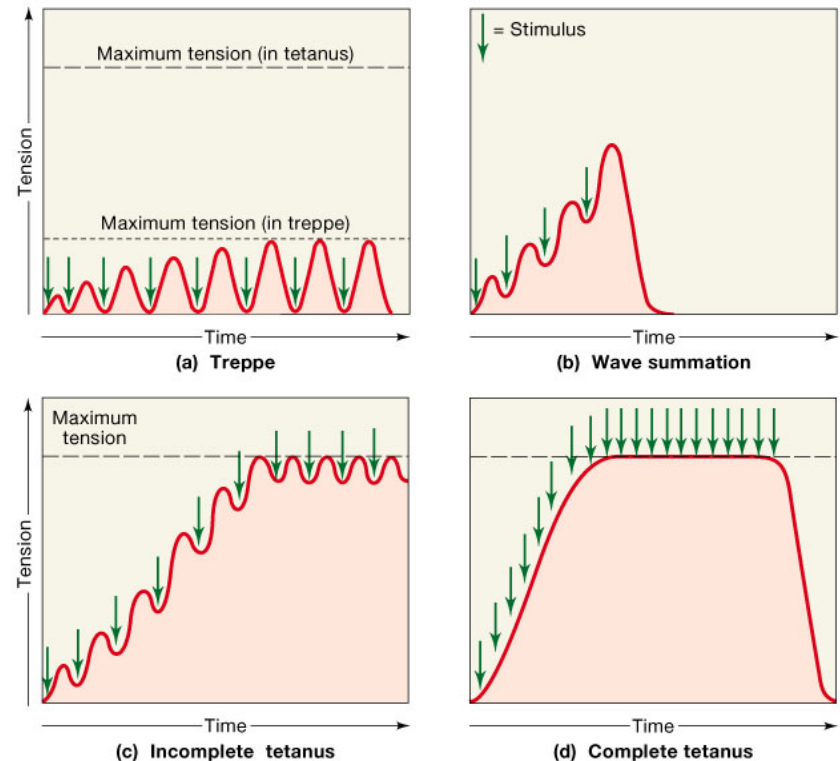
# Tension Production in Muscle Fiber or Cell cont.

- When stimulation continues & muscle cell never relaxes completely then tension peaks at 4x maximum tension seen in treppe
- When peak tension produced in muscle during rapid cycles of contraction & relaxation called incomplete tetanus



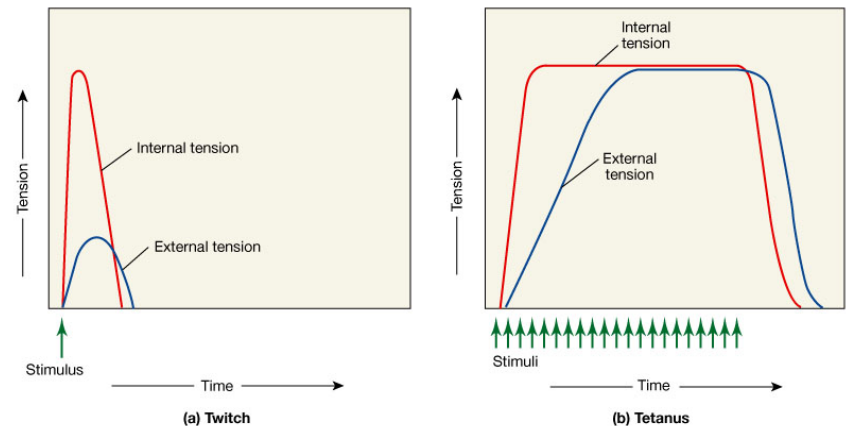
# Tension Production in Muscle Fiber or Cell cont.

- Complete tetanus obtained by increasing stimulation rate until relaxation phase eliminated
- Action potentials arrive so fast that calcium ions cannot return to SR so contraction state prolonged making it continuous – normal muscle contractions involve complete tetanus



# Tension Production in skeletal muscles

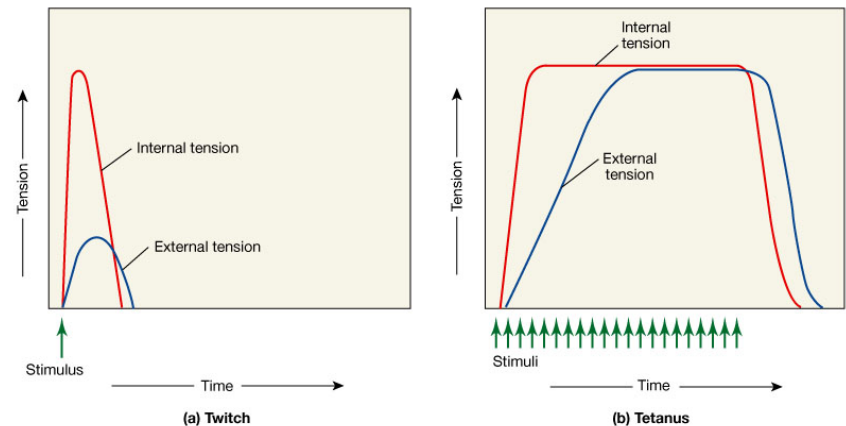
- Amount of tension produced by whole muscle depends on  
1) internal & external tension produced by stimulated muscle fibers  
2) total number of muscle fibers stimulated



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# Tension Production in Skeletal Muscles cont.

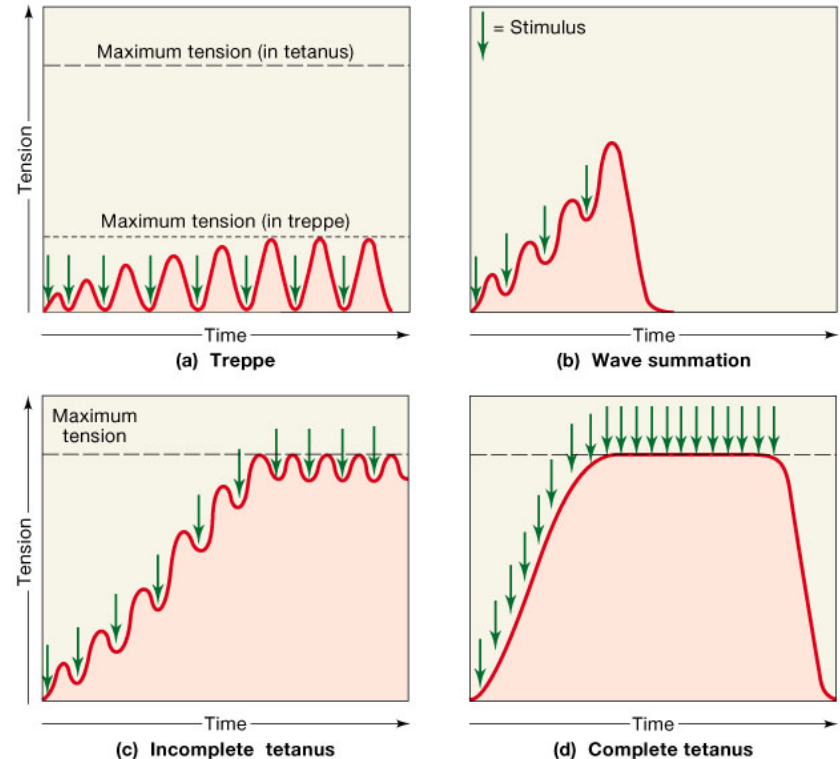
- Muscle fibers not directly connected to structures they pull against but connected to extracellular fibers (collagen) of epi-, peri-, & endomysium which are flexible & elastic
- When muscle contracts myofibrils in muscle cells generate internal tension & internal tension applied to extracellular fibers generating external tension in extracellular fibers



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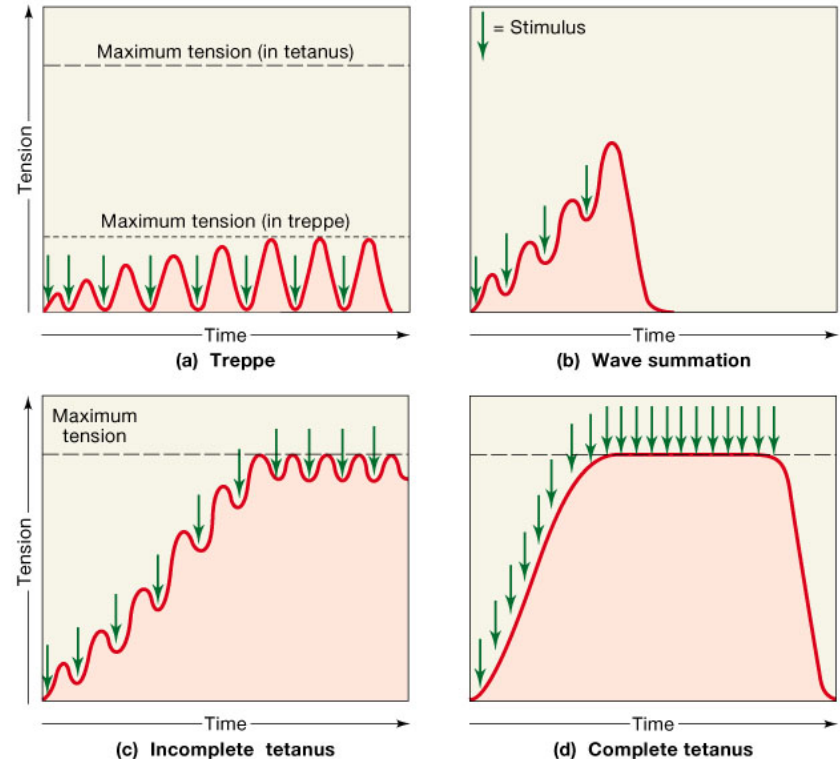
# Tension Production in Skeletal Muscles cont.

- As external tension increases extracellular fibers stretch (called series elastic elements) at 1<sup>st</sup> then tension builds so external tension does not build as rapidly as internal tension



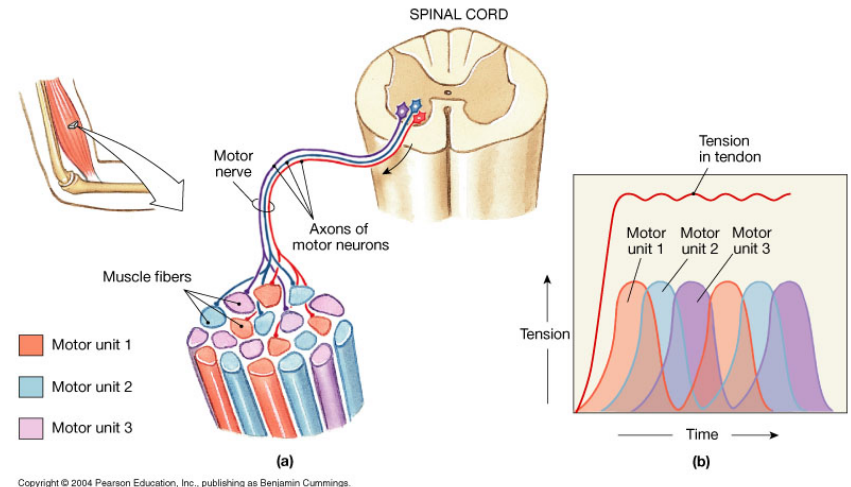
# Tension Production in Skeletal Muscle cont.

- During relaxation of the muscle the series elastic elements recoil & pull on the muscle
- Myogram measures external tension – for a twitch not enough time for the external to reach peak but for sustained contraction external equals internal tension



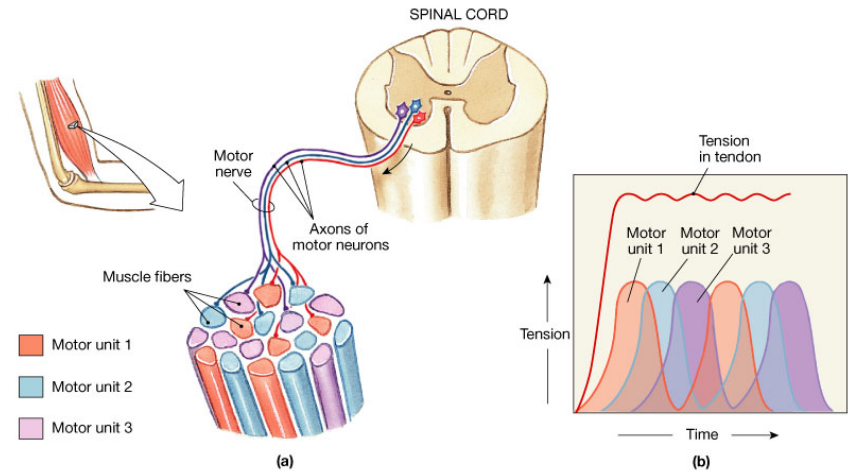
# Tension Production in Skeletal Muscle cont.

- Motor units consists of all the muscle fibers controlled by a single motor neuron
- Amount of tension produced by a whole muscle is the sum of the tension produced by single muscle fibers so controlling the number of activated muscle fibers controls the amount of tension generated



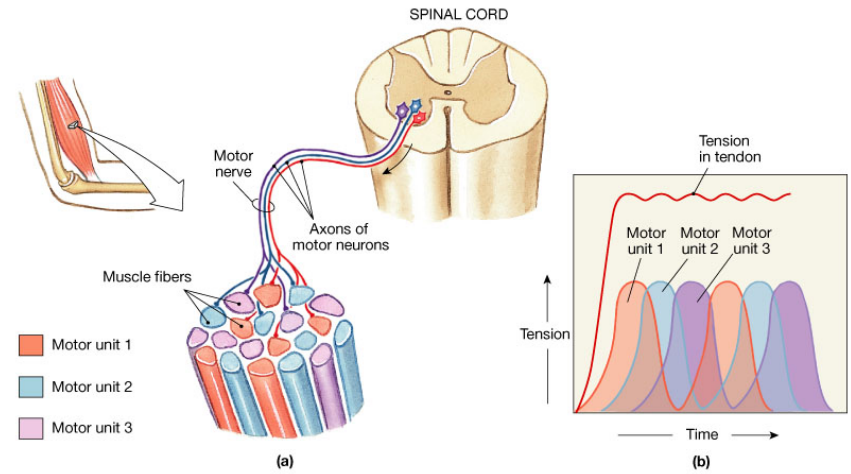
# Tension Production in Skeletal Muscle cont.

- Muscles used for very fine motor control have very few muscle fibers per motor neuron and muscles used for bulk movement have several thousand fibers per motor neuron the fibers of different types of motor neurons are intermingled in the muscle



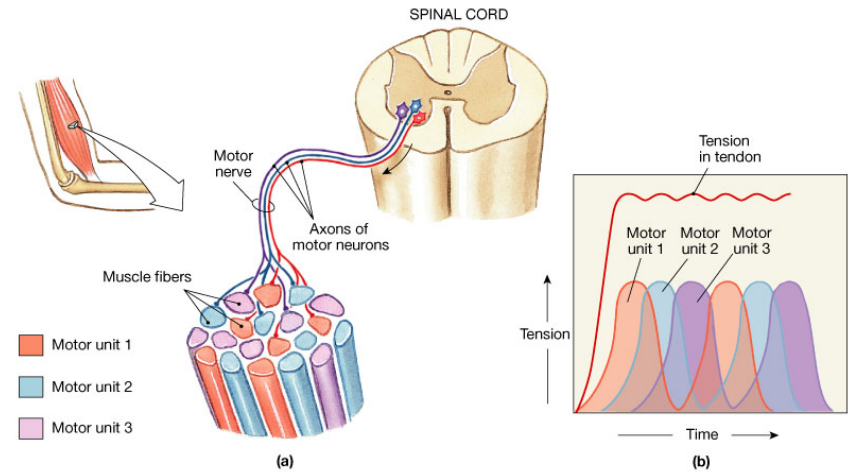
# Tension Production in Skeletal Muscle cont.

- During arm movement 1<sup>st</sup> activate smallest motor units in the muscle (react the slowest) then activate increasingly larger units so tension increase is smooth & steady process called recruitment



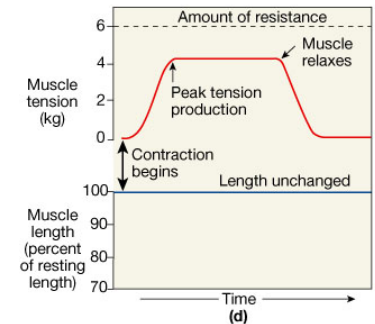
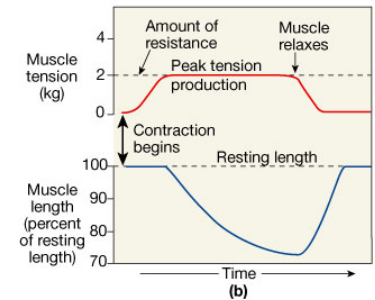
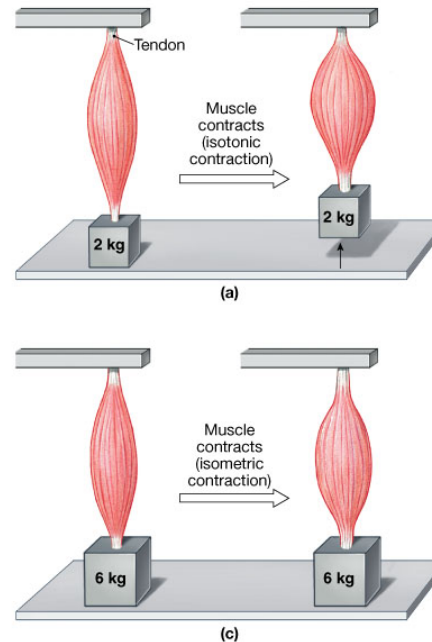
# Tension Production in Skeletal Muscle cont.

- Peak tension occurs when all motor units contract in state of complete tetanus
- Muscle tone – some motor units in a relaxed muscle are contracting & the units contracting keeps changing but joints are stabilized



# Tension Production in Skeletal Muscle cont.

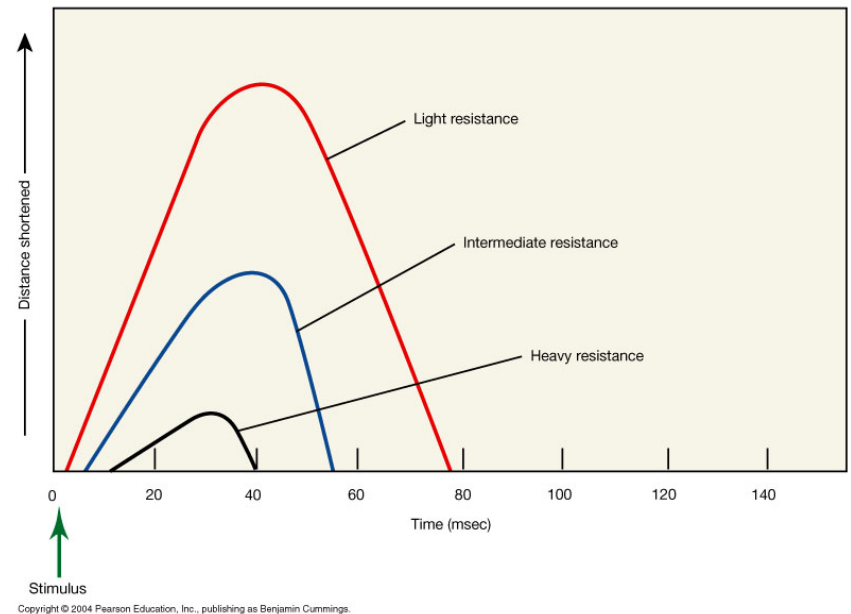
- Isotonic contractions – tension rises & skeletal muscle shortens 2 types – concentric & eccentric – in concentric the muscle tension exceeds the resistance & muscle shortens but in eccentric peak tension is less than resistance & muscle elongates due to action of another muscle or pull of gravity



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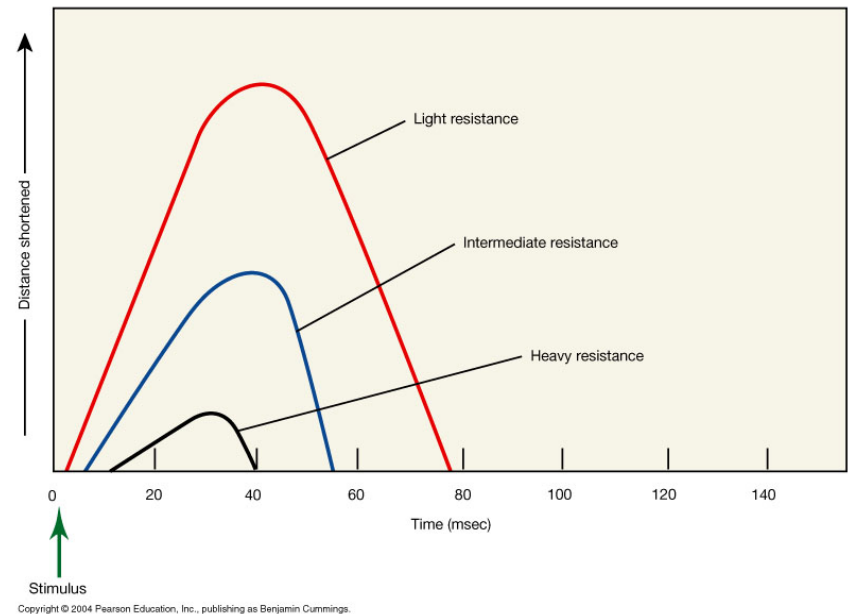
# Tension Production in Skeletal Muscle cont.

- In isometric contraction whole muscle does not change in length & tension produced never exceeds resistance
- Light object lifted more rapidly than heavy object because resistance & speed of contraction inversely related



# Tension Production in Skeletal Muscle cont.

- After a contraction muscle returns to original length due to combination of elastic forces, opposing muscle contractions & gravity

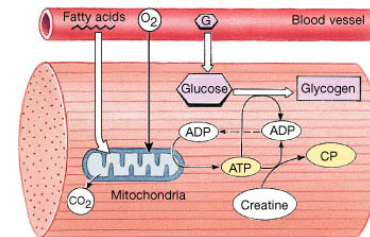


# Muscular Activity & Energy Use

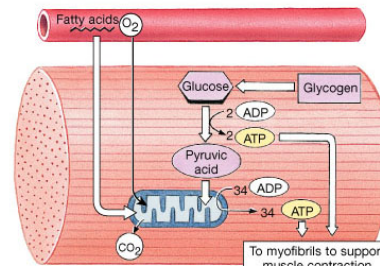
- Single muscle fiber has 15 billion thick filaments & in contracting muscle each thick filament breaks 2500 ATP/sec
- Not possible to store that much ATP so muscle fiber must generate it as it uses the ATP
- Muscle cells contain creatine & creatine phosphate which are used as an initial energy reservoir – 15 sec
- $\text{ATP} + \text{creatine} \rightarrow \text{ADP} + \text{creatine phosphate}$
- $\text{ADP} + \text{creatine phosphate} \rightarrow \text{ATP} + \text{creatine}$

# Muscle & Energy

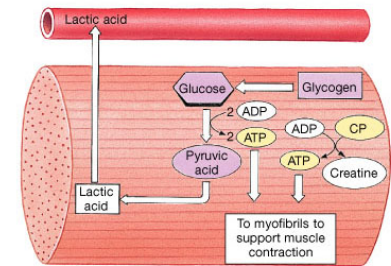
- ATP generated by aerobic metabolism in mitochondria & glycolysis in cytoplasm
- Resting muscle – need for ATP low so reserves built up – CP, glycogen, ATP, fatty acids, glucose



(a) Resting muscle: Fatty acids are catabolized; the ATP produced is used to build energy reserves of ATP, CP, and glycogen.



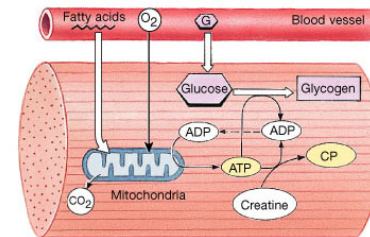
(b) Moderate activity: Glucose and fatty acids are catabolized; the ATP produced is used to power contraction.



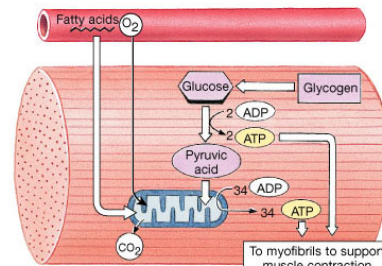
(c) Peak activity: Most ATP is produced through glycolysis, with lactic acid as a by-product. Mitochondrial activity (not shown) now provides only about one-third of the ATP consumed.

# Muscle & Energy

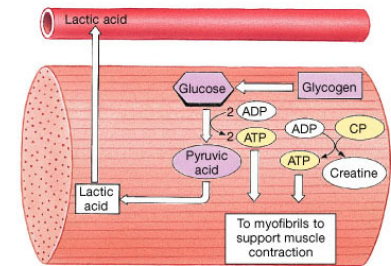
- At moderate activity ATP demand increases & is met by mitochondria
- At peak activity levels ATP demand is maximal & oxygen levels are limiting so 1/3 of demand met by mitochondria & rest by glycolysis



(a) Resting muscle: Fatty acids are catabolized; the ATP produced is used to build energy reserves of ATP, CP, and glycogen.



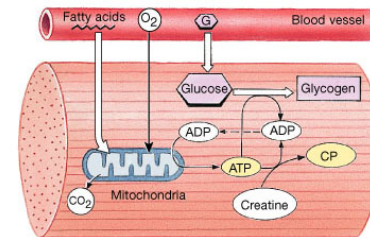
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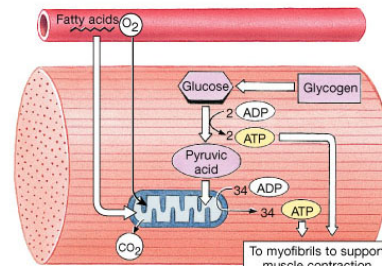
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# Muscle & Energy

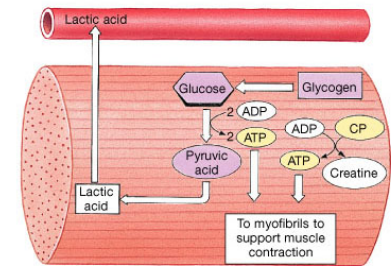
- Glycolysis produces pyruvic acid which, if not able to enter mitochondria due to low oxygen levels, is turned into lactic acid which can lower intracellular pH which affects function



(a) Resting muscle: Fatty acids are catabolized; the ATP produced is used to build energy reserves of ATP, CP, and glycogen.



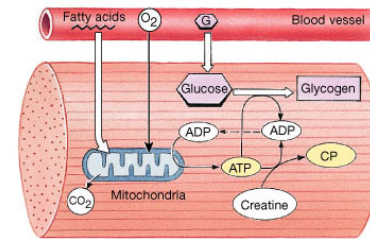
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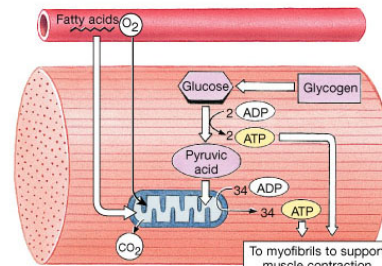
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# Muscle & Energy

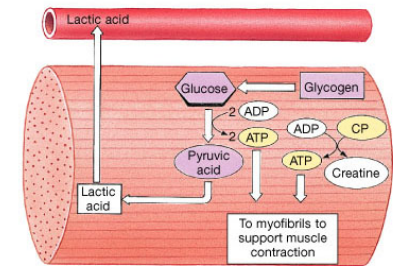
- Normal muscle function requires 1) lots of intracellular energy reserves 2) normal circulatory supply 3) normal blood oxygen levels 4) blood pH within normal limits(7.35-7.45) any factors which interfere with these will promote muscle fatigue



(a) Resting muscle: Fatty acids are catabolized; the ATP produced is used to build energy reserves of ATP, CP, and glycogen.



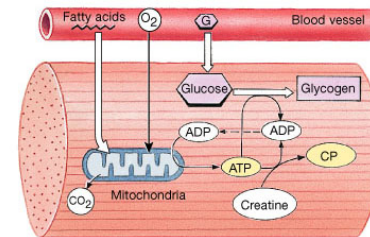
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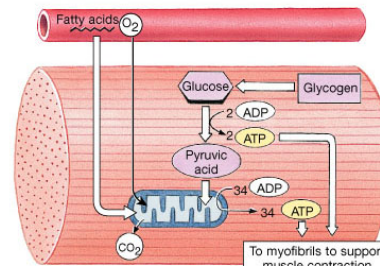
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# Muscle & Energy

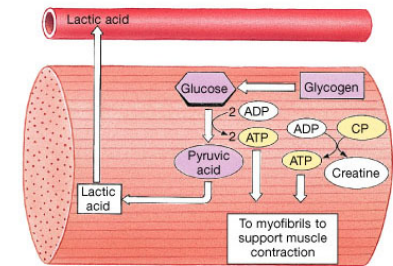
- Recovery Period – conditions return to normal pre-exercise conditions
- Sustained activity can require a week of recovery
- Lactic acid converted to pyruvic acid which is used in aerobic respiration
- Oxygen debt is amount of oxygen required to restore normal pre-exercise conditions
- Heat loss – resting muscle uses 42% of energy available in food but very active muscle uses about 30% so generates more heat



(a) Resting muscle: Fatty acids are catabolized; the ATP produced is used to build energy reserves of ATP, CP, and glycogen.



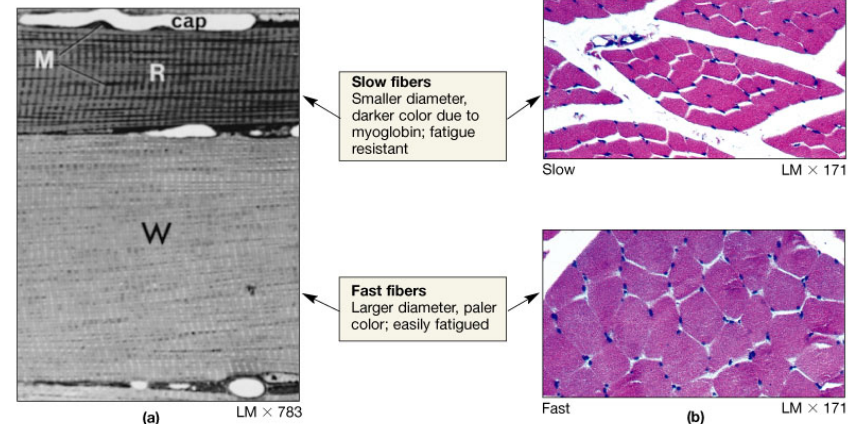
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# Muscle & Energy

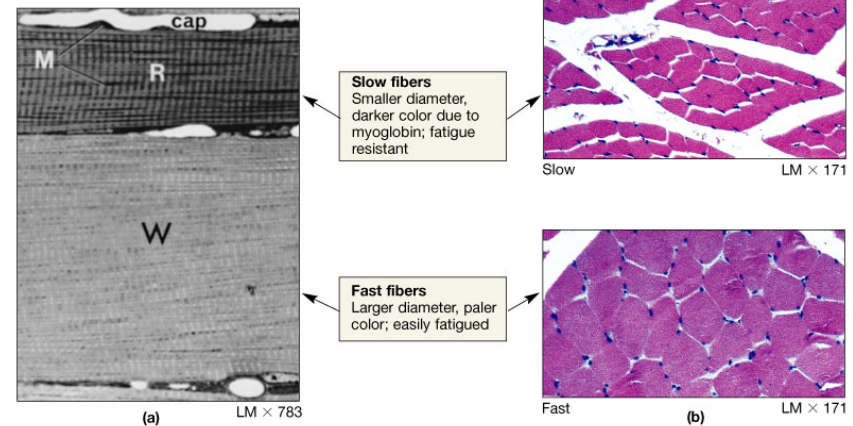
- Muscle performance divided into power & endurance
- 2 factors that determine performance of muscle are 1) types of fibers in muscle 2) physical conditioning
- 3 types of fibers in human muscle – fast, slow, intermediate fibers



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# Muscle & Energy

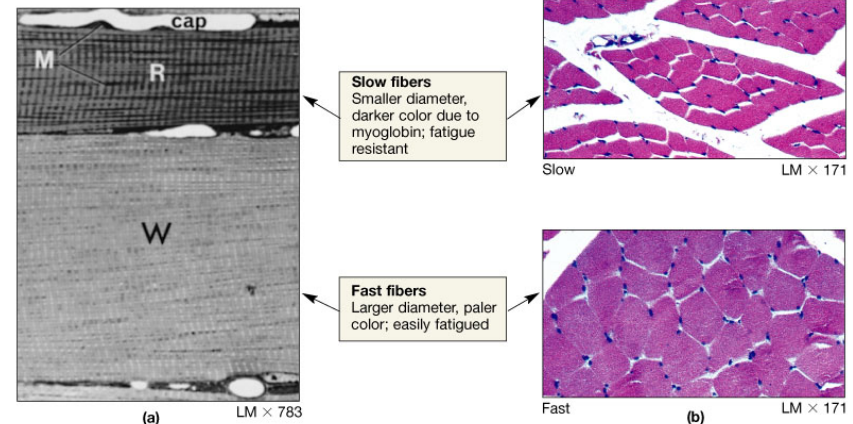
- Slow fibers are small & have slow contraction speed, are fatigue resistant, have lots of myoglobin & capillaries & mitochondria
- Fast fibers have large diameter & fast contraction speed but are not fatigue resistant and have little myoglobin, capillaries, mitochondria



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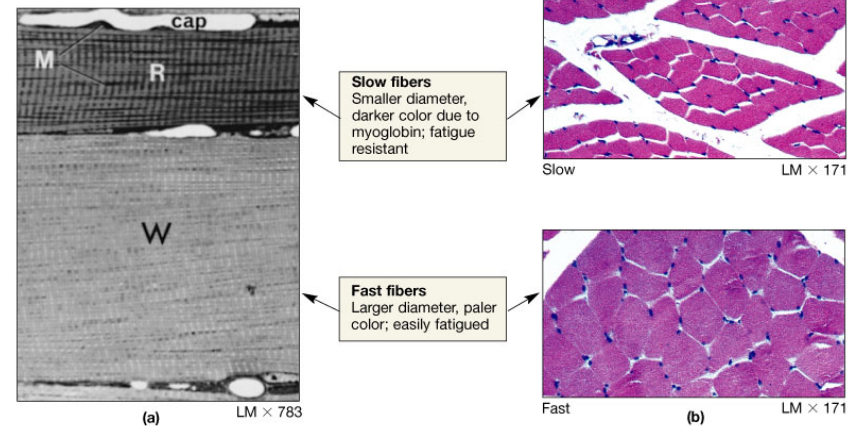
# Muscle & Energy

- Fast fibers are 'white' & slow fibers are 'red' or dark & intermediate is 'pink'
- Human muscles contain a mix of fiber types & appear pink
- Muscle hypertrophy – due to repeated exhaustive use get more myofibrils per muscle cell



# Muscle & Energy

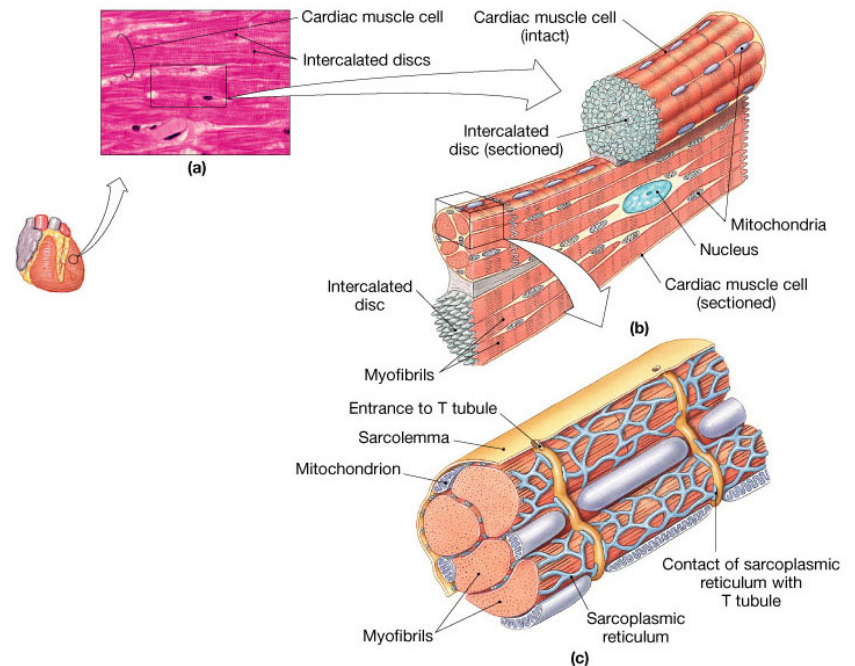
- Repeated exhaustive stimulation leads to muscle hypertrophy – more myofibrils containing more thin & thick filaments
- Physical conditioning – anaerobic & aerobic endurance – fast fibers – anaerobic & aerobic – slow fibers



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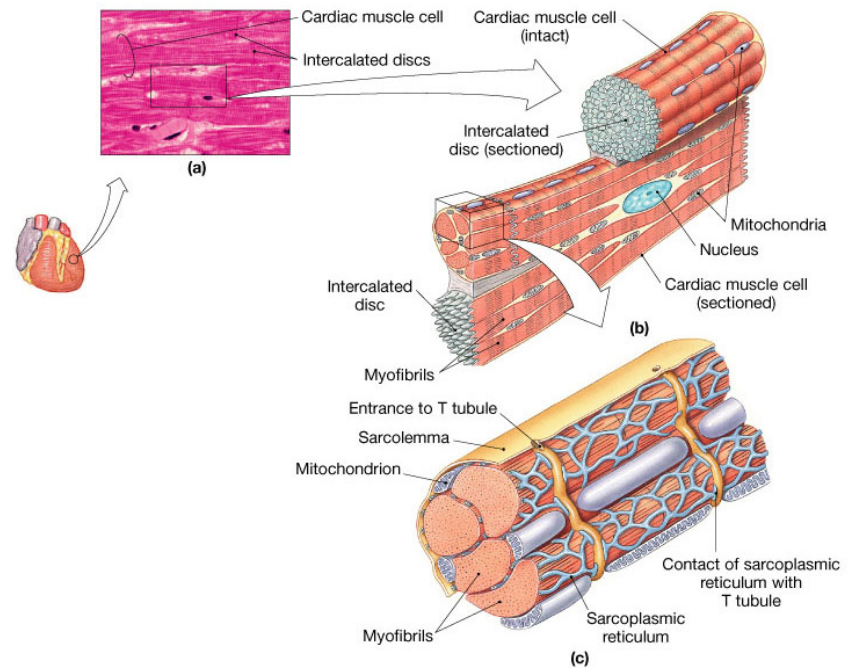
# Cardiac Muscle

- Only in the heart & contains organized myofibrils & so is striated
- Structural differences – smaller cells, single nucleus, no triads but has T tubules circling Z line, SR has no terminal cisternae, cells use aerobic respiration so have many mitochondria, contact points with other cardiac cells called intercalated discs



# Cardiac Muscle

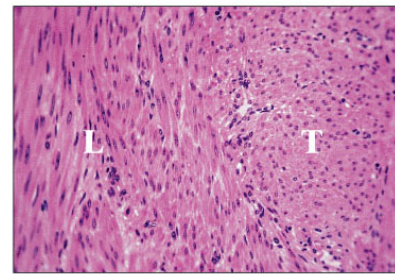
- Functional characteristics
  - pacemaker cells determine timing of contraction, NS alters pace & amt of tension during contraction, contraction lasts 10x as long as in skeletal muscle, twitches cannot undergo wave summation & cardiac cells cannot produce tetanic contraction



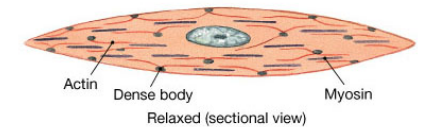
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# Smooth Muscle

- Present in most organs but differs in structure & function
- Structural differences – long & slender, one nucleus, no T tubules, myofibrils, sarcomeres, no striations, thick filaments scattered & myosin proteins arranged differently, thin filaments attached to dense bodies – network of intermediate filaments composed of desmin & dense bodies attached to sarcolemma so cell shortens



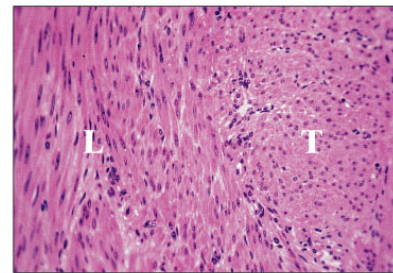
(a)



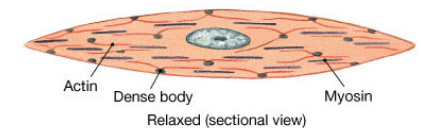
(b)

# Smooth Muscle

- Trigger for contraction is appearance of calcium in cytoplasm
- Calcium interacts with calmodulin which activates myosin light chain kinase which breaks down ATP & initiates contraction
- Smooth muscle can have pacesetter cells which undergo spontaneous depolarization & trigger contraction



(a)



Relaxed (sectional view)



Relaxed (superficial view)



Contracted (superficial view)

(b)