UNIT-I

Types & Classification of muscles

Course No. – VPY- 608

Credit Hrs. – 2+1=3

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Types of muscle tissue:

- There are 3 types of muscle tissue found in an animal body.
- However, they are the Biological motors that convert chemical energy into mechanical & translate the signals from the CNS into movements.

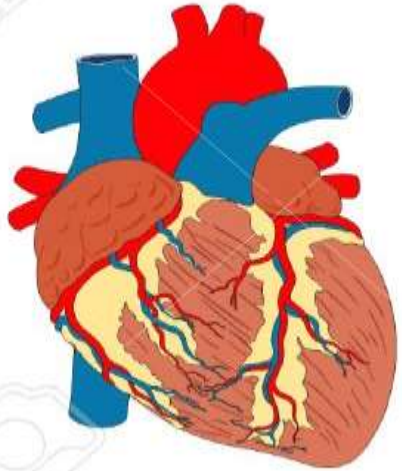
Smooth muscle (involuntary or striated) –

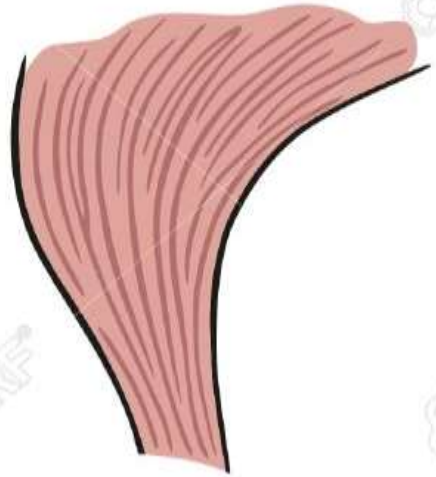
- These muscle cells have no visible striations with a microscope & found in systems of the body that are automatic in their function
- Thus, smooth muscles are major components of the digestive & uro-genital systems as well as of most blood vessels & respiratory system

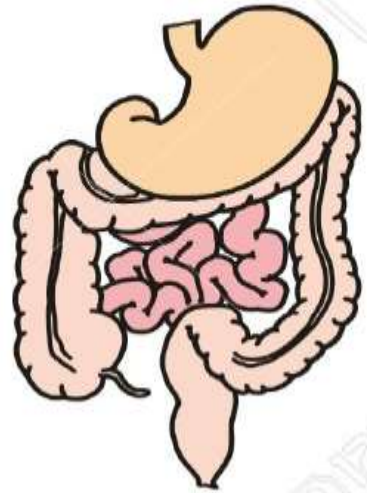
Contraction of smooth muscle-

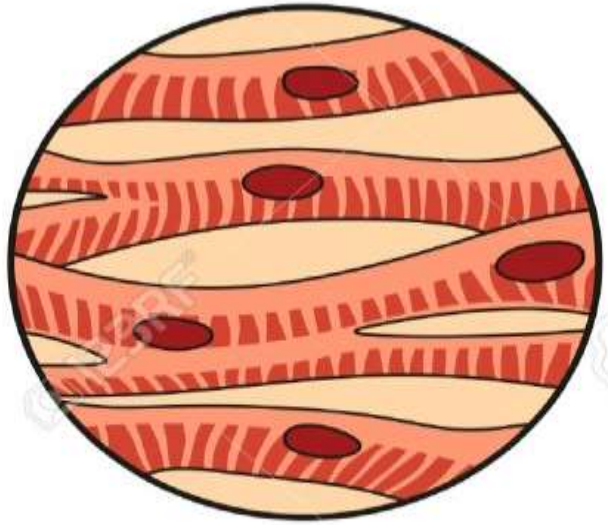
- It is an intrinsic property of the fibres themselves
- The contraction does not generally require stimulation by a nerve
- The contractile activity is regulated by ANS which may be influenced by certain drugs

Types of Muscle Tissue

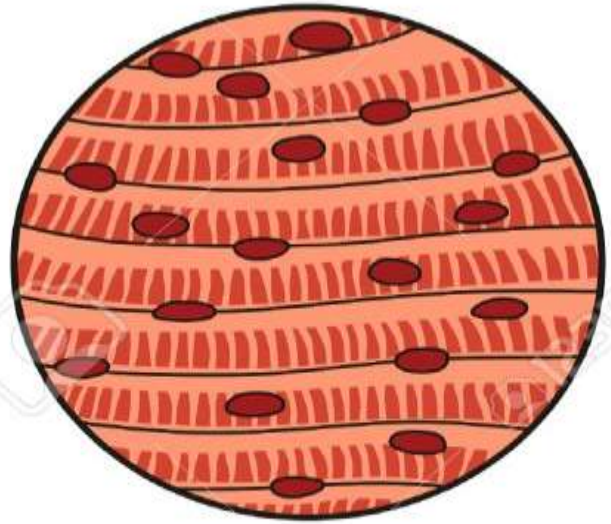




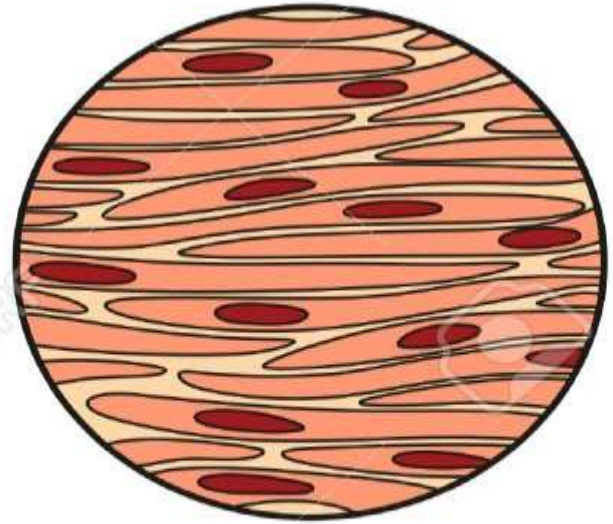




Cardiac Muscle Tissue
(Involuntary Control)



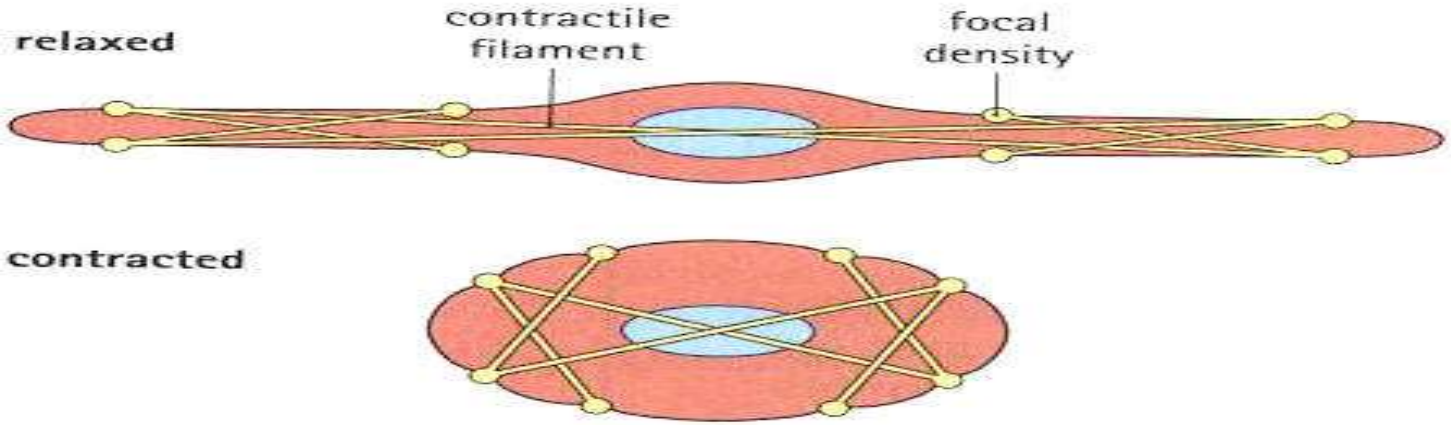
Skeletal Muscle Tissue
(Voluntary Control)



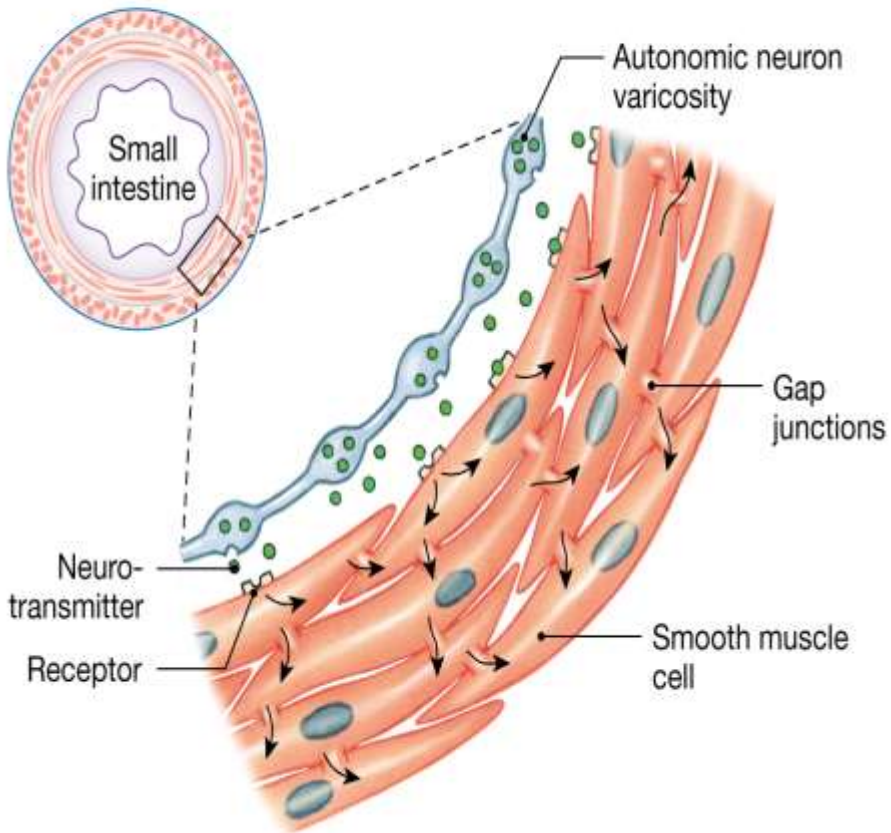
Smooth Muscle Tissue
(Involuntary Control)

Structure of smooth muscle:

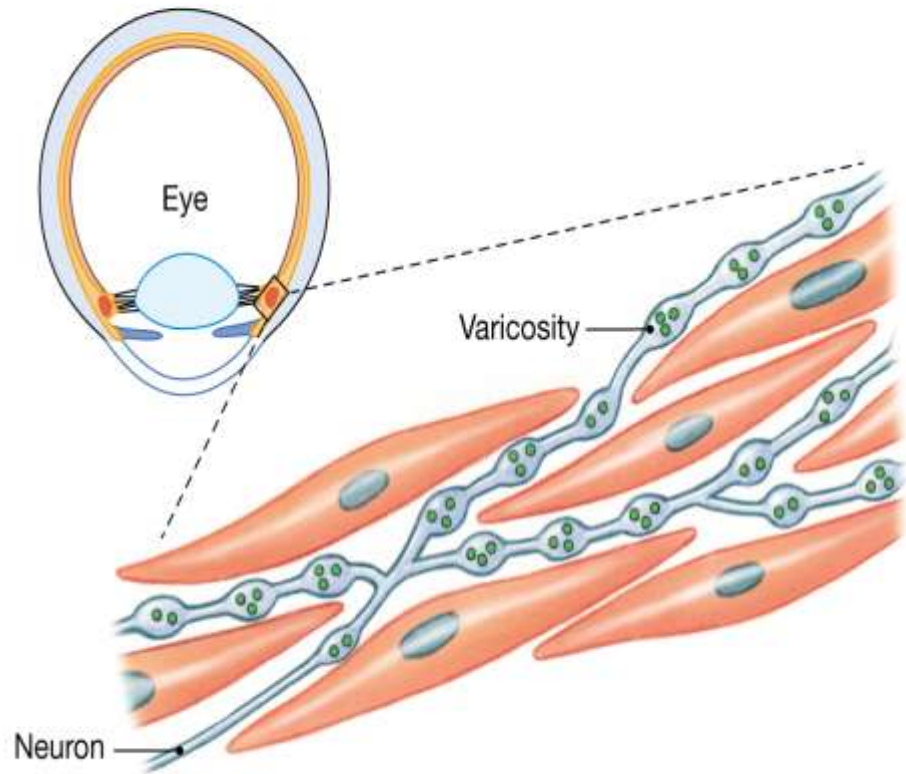
- These are made up of narrow (<10µm) elongated (up to 500 µm) cells, tapering towards their ends
- Each cell has a single centrally placed nucleus
- These cells are arranged in bundles in the same direction
- Although the cells are distinct to each other in that there is no protoplasmic continuity between them
- Membrane of the adjacent cells are fused together into are k/a tight junction
- These muscle cells contain actin & myosin filaments
- However myosin is not arranged in thick filaments although the basic mechanism of contraction in smooth muscle will be found to be similar to that of skeletal muscle



(a) Single-unit smooth muscle cells are connected by gap junctions, and the cells contract as a single unit.



(b) Multi-unit smooth muscle cells are not electrically linked, and each cell must be stimulated independently.



Cardiac muscle (in-voluantry and striated)-

- These muscles characterized by fibres with visible striations
- They contracts intrinsically & is not under voluntary control
- These muscles are restricted to heart constituting myocardium & its rhythmic contraction for circulation of blood
- They are also found in blood & lymphatic vessels in plenty

Skeletal muscle (voluntary and striated)-

- The visible striated muscles tissue are grouped into distinct organs of variable size called muscles
- They are attached to the bones of skeleton under voluntary control
- The interior of the fibre is packed with elongated protein strands (myofibrils) & filling the clefts & spaces between these strands
- It is an extensive network of smooth endoplasmic reticulum & associated tubular invaginations of surface plasma membrane (transverse or T-tubules)

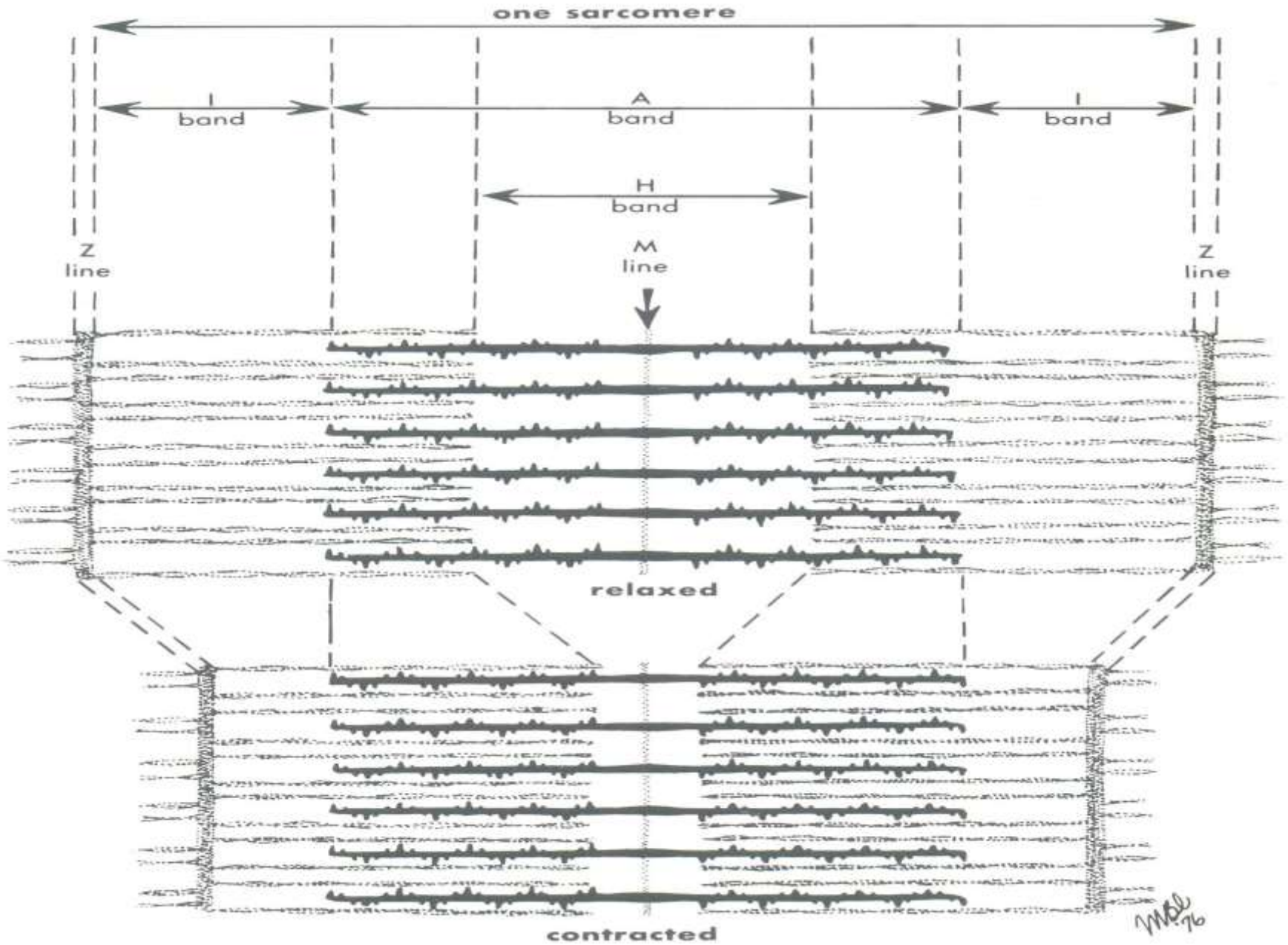
- A golgi apparatus & large no. of mitochondria as well as glycogen & fat inclusions are also found in muscle fibers
- It has multinucleated cell made up of numerous muscle fibres ranging between 10 & 100 microns in diameter

Structures of skeletal muscle-

- Muscle fibres are arranged in bundles surrounded by the fibrous CT
- The CT between individual muscle fibres are called as endomysium
- The sheath surrounding bundles of muscle fibres are called perimysium
- CT around an entire muscle is k/a epimysium
- Each muscle fibre contains several hundred myofibrils consists about 1500 myosin filaments & two times more actin filaments
- These are polymerized protein molecules responsible for muscle contraction
- Whereas thick filaments are myosin and thin filaments are actin filaments

- These filaments interdigitate and thus the myofibril have alternate light & dark bends
- The light bands contain only actin filaments called I bands and are isotropic to polarized light
- The dark bands contain the myosin filaments as well as the end of actin filaments where they overlap the myosin are called A bands because they are anisotropic to polarized light
- The combination of an A & I band is called a sarcomere
- The actin filaments are attached to each other & so called Z line or Z membrane
- It passes from one myofibril to another thus attaching them to each other and causing the respective sarcomeres

Contracted & relaxed sarcomere of skeletal muscle:



Structure of cardiac muscle:

- It consists largely of sarcoplasm, myofibrils, a sarcoplasmic reticulum, transverse tubules, nuclei & a sarcolemma
- The most striking difference is the tendency for CM fibers to join forming a network
- Unique structures found in CM are inter-calated disk
- These disks are interposed between segments of muscle & may cross the fiber in an irregular manner containing only one nucleus
- These disks represent apposed cell membranes where gap junction occur (nexi)
- Gap junctions are laterally oriented cell interfaces where two CM cells are within 10 nm of each other & permit electrical transmission from one to next
- Action potentials can readily spread from cell to cell causing the atria & the ventricles to each act electrically & mechanically as a functional syncytium as if it were as single cell mass

Mechanism & process of Relaxation, Contraction & Excitation of muscles:

Smooth muscle-

- It exhibits a special property called plasticity also referred to as stress relaxation
- SM has the ability to adjust to being stretched without ↑^{ing} the final tension (pain) or the pressure exerted on the contents within a hollow viscous surrounded by SM even though it is still elongated
- Plasticity allows expansion of stretch within physiologic limits without an ↑ in pressure & pain
- The SM doesn't lose its contractile ability & is believed due to changes in the arrangement of the myosin & actin molecules upon stretching or shortening
- These are believed to be surrounded always by CT even though it may be only as small amount of reticular tissue (collagenous + elastic fibres) which makes the major part of the CT associated with SM

- SM cells in the walls of hollow organs are arranged so that only a fraction of the cells is supplied by autonomic nerves
- These can bring about contraction, but nerve stimulation is not required, since it has various pacemaker cell points for its own depolarization and contraction resulting from stimuli such as distention, chemical or hormonal influences or myogenic self excitation without any extrinsic stimulus
- The contraction impulse (action potential) spreads across the tissue because of syncytial connections between the fibres
- Thus SM cells can be linked electrically while remaining independent chemically
- This direct transmission is called ephaptic conduction & current flows across readily & the membrane resistance is low
- Hence SM contraction can be initiated by stretch, neural, hormones, chemical and mechanical stimuli

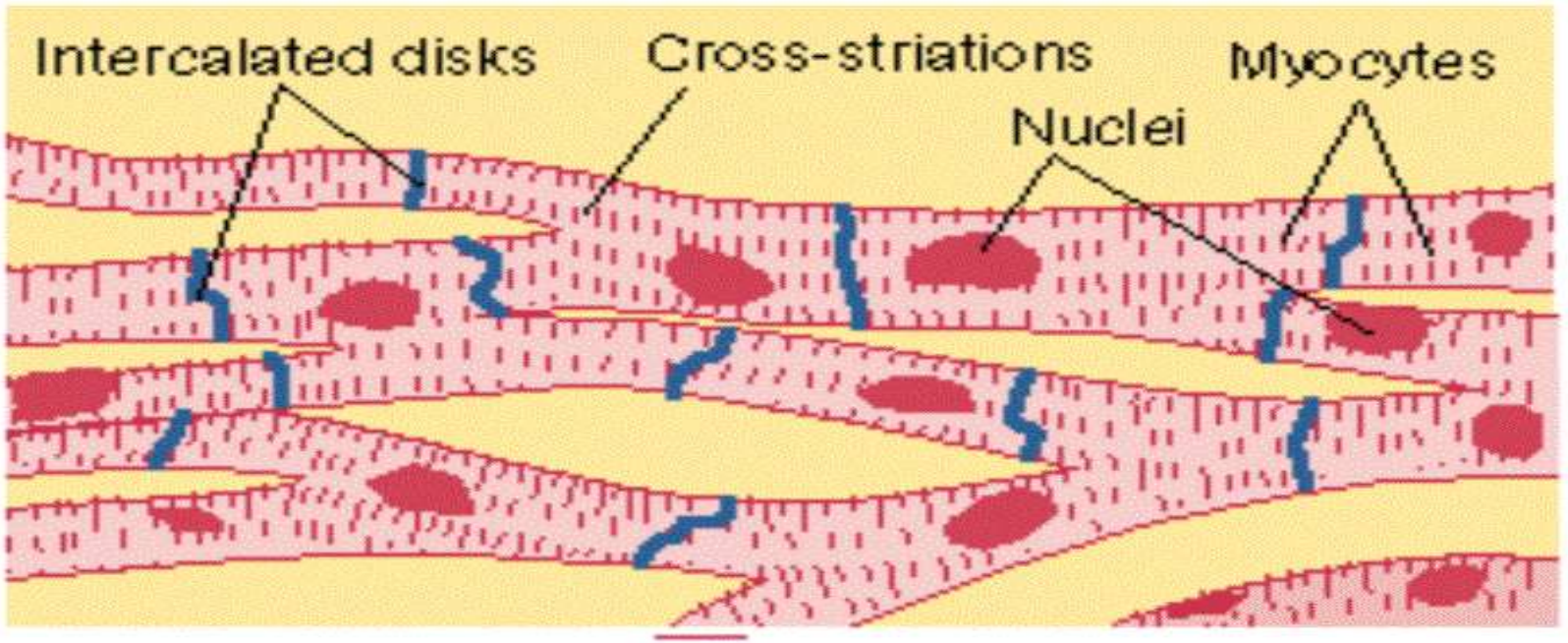
- SM cells respond to nor-epinephrine released by sympathetic nerves and to acetylcholine released by parasympathetic nerves, the one being antagonistic to the other
- Few SM consists of distinctly separated fibres that require nerve stimulation to contract called multiunit sm & includes pilomotor sm cells in the skin (iris & ciliary body of the eye)
- Myogenic or self excitation is apparently the result of Na & Ca both leaking into the fiber, causes the resting potential to decay down toward threshold as a action potential is about -35mV while the resting potential is only -55 to -50 mV
- However, the Na & Ca are pumped back out before threshold is reached, so the membrane resting potential is restored
- This cycle is repeated continuously in a sinusoidal pattern (constantly oscillation forming pacemaker)

- Ca^{2+} diffuses through the cytoplasm in 200 to 300 msecs & is an latent period (slower response) between the initial excitation & the beginning of contraction
- Ca is responsible for delaying the sequence because of slow process being consumes only 25% of O_2 as compare to skeletal muscle
- When action potentials depolarize the threshold, the transmitter substance is released & diffuses to the SM cell membranes where stimulation occurs
- This innervation is usually conducted dual i.e., in both divisions of the ANS
- In skin, the pilomotor fibres, sweat glands & cutaneous vessels receive only sympathetic innervation
- Ach is released from the parasympathetic nerve fibers & nor-epinephrine from the sympathetic fibers. For eg. Ach enhances intestinal peristalsis, whereas NE inhibits peristalsis

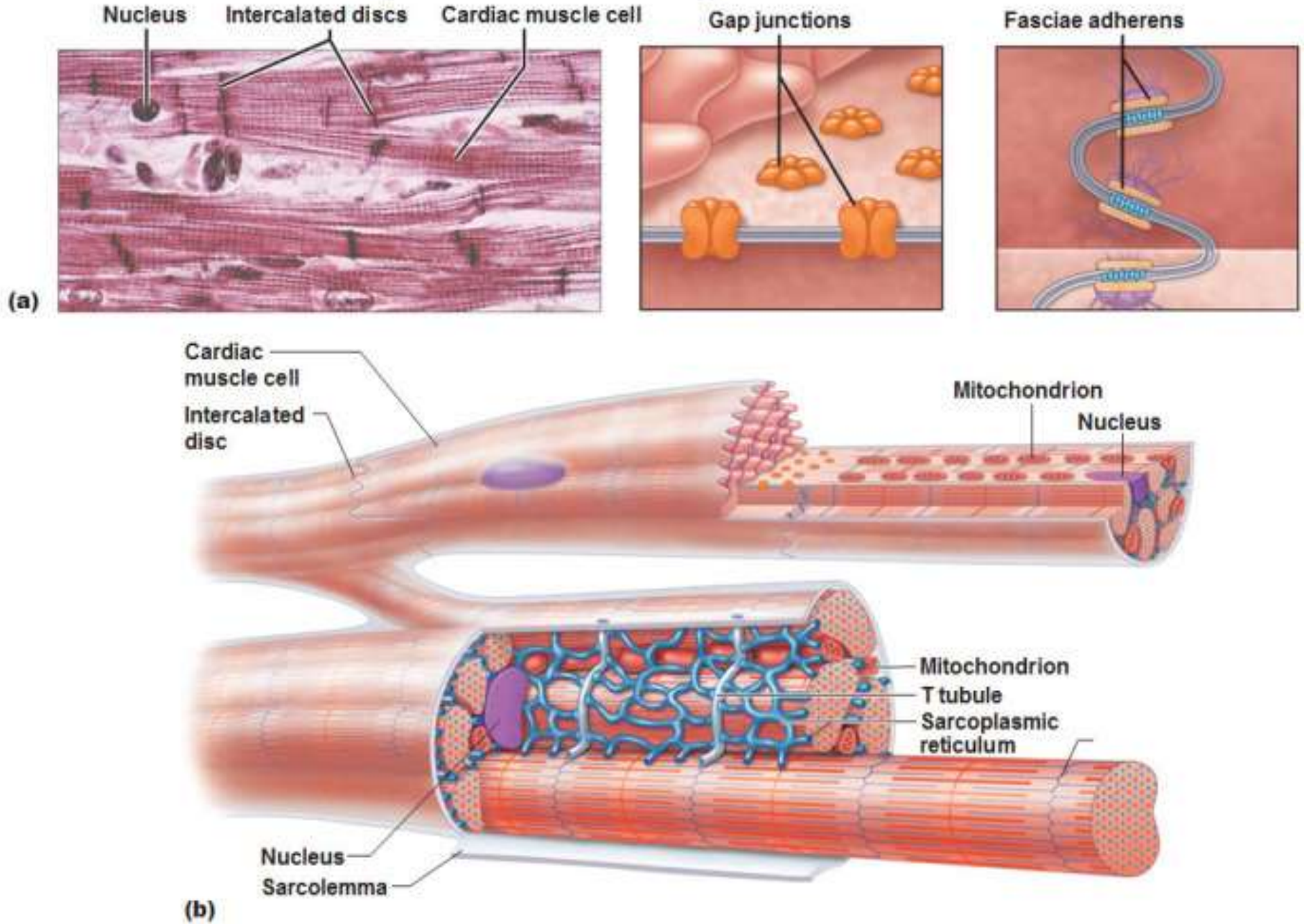
Cardiac muscle-

- CM does not require nerve stimulation. It has its own intrinsic or inherent ability to generate action potentials rhythmically
- This is done by normal pacemaker, the SA node which depolarizes faster than any other part of the heart muscle
- Although it is innervated by the sympathetic & parasympathetic nervous systems
- But its function is limited to altering or regulating the heart rate which is set normally by pacemaker
- The CM action potential is 150 msec in the atria & 300 msec in ventricles
- Contraction time lasts as long is the action potential does
- This extended period provides time for pumping the blood out of the ventricles & filling them again before the next beat
- Hypertrophy (↑in cell size) occurs in CM when the heart has excessive work to do

- Also in man this condition is sometimes called athletes heart
- Brisket disease (high mountain disease of cattle involves enlargement of the heart as well as edema of the brisket & involvement of the lungs)

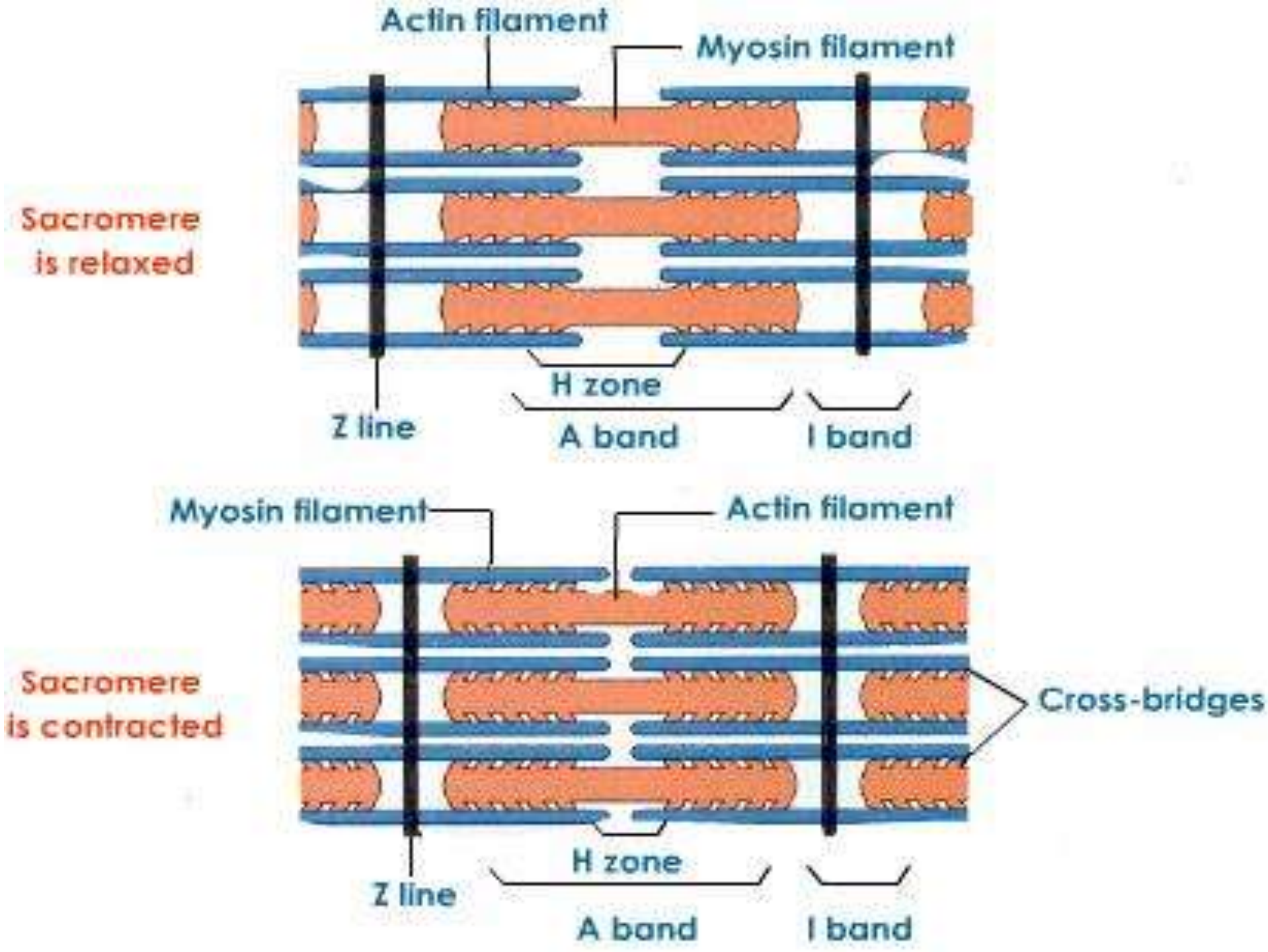


Microscopic Anatomy of Cardiac Muscle



Skeletal muscles-

- When an action potential generates along the muscle fibre (sarcolemma), the fibre begins to contract after an initial latent period of about 3 msec
- The action potential is initiated by the firing of a motor neuron whose axon branch terminates at neuromuscular junction (t tubules) near the mid point of muscle fibre
- T tubules causes current to flow in the longitudinal tubules
- To complete the electrical circuit, the current then transverse the walls of the longitudinal tubules into the sarcoplasm & hence, back outward through cell membrane
- A local circuit of ionic current flow occurs throughout the entire muscle fibre with each action potential
- An electrical potential applied directly to the opening of a t tubule at the surface of a muscle fibre will cause contraction of that half of sarcomere supplied by the tubule


Actin filament
Myosin filament
Sacromere
is relaxed
H zone
Z line
A band
I band
Myosin filament
Actin filament
Sacromere
is contracted
Cross-bridges
H zone
Z line
A band
I band

- Therefore, the spread of electrical current inward through t tubules when an action potential passes has direct electrical effect on the interior of the muscle fibre to cause attraction between the actin & myosin filaments

Myosin & Actin filaments-

- Each thick filament in a sarcomere is a bundle of about 200 myosin molecules having 2 parts
  - Light meromyosin (LMM)- It lies parallel to other LMM molecules making up the length of the thick filament
  - Heavy meromyosin (HMM)- It projects outward like an arm from the end of the LMM filaments
    - Arm projecting- it is flexible like a hinge, where it joins the LMM & also to the head
    - Head attached to the free end of the arm
- These hinged HMM particles called cross-bridges, protrude from all around the thick filaments

- They away from the centre in both directions, so there are no cross-bridges in the centre of the thick filament
- Each thin filament is made up of 3 components; actin, tropomyosin & troponin
- The base unit is the F-actin molecule consists 2 long strands around each other in spiral
- Each strand is made up of hundreds of G-actin molecules
- Lying in the grooves of 2 F-actin spiral chains are tropomyosin molecules attached together to form large strands
- The 3^{rd} protein, troponin is attached to each other tropomyosin molecule & together are called troponin-tropomyosin complex
- The presence of ca^{2+} also causes the myosin molecules to develop an ATPase capability i.e., myosin has the capability of splitting ATP & liberating energy from this molecule

RATCHET theory for muscle contraction-

- In resting state the -ve charges of the ATP bound with the cross bridges of the myosin filaments & the -ve charges of actin filament causes these two to remain in the uncombined state with no attractive forces both them
- On the appearance of Ca^{++} the following amounts occur:
  - The Ca^{++} bind with -ve reactive sites of the ATP on the myosin cross bridges & at the same time with the -ve reactive sites on the actin filaments pulling these filament together
  - It is assured that the cross bridges having strong electronegativity in the resting state because of the presence of ATP normally project straight outward from the mysoin filaments because the shank of the filament is also -vely charged

- When Ca^{++} bind with the ATP on the cross bridges, the negativity of the cross bridge become neutralized. Therefore, the bridges now bend inward toward the axis of the myosin filament. This also pulls the axis of the myosin filament, thus shortening of the muscle
- When the cross bridges fold in against the shank of the myosin filament causes the ATP to split immediately to ADP. This breaks the Ca linked connections between the myosin cross bridges & actin, but in mean time the actin filament has been pulled along the axis of the myosin filament
- Subsequent similar reactions occurs at other cross bridges and the actin filament is pulled another step
- Energy from other sources such as creatinin phosphate causes almost immediate reconstitution of the ADP to ATP. Therefore, the cross bridges that has folded inward now bend outward again & bind with other Ca^{++} to pull the actin filament another step

Relaxation:

- Muscle contraction will continue as long as there is an excess of Ca^{++} ions present in the sarcoplasm, but when the effect of the current spread at the triads ends
- The Ca^{++} is then sequestered back into the longitudinal tubules
- Ion pumps in the membrane of the sarcoplasmic reticulum use the energy of ATP to pump the Ca^{++} from the sarcoplasmic fluid back into the tubules, ready for the next depolarization
- Only a small amount of Ca^{++} is left out in the sarcoplasm of the relaxed muscle not enough to act on the troponin tropomyosin complex
- Therefore, during relaxation the thin & thick filaments are dissociated, allowing the elasticity of the muscle to return into its resting length, which pulls the Z line & thin filaments back to their original positions

Summary of Excitation and contraction:

- Nerve impulse arrives at neuromuscular junction; ACh released from synaptic vesicles & diffuses across synaptic cleft to bind to receptors on muscle cell membrane
- Binding of ACh leads to initiation of membrane action potential which spreads over entire muscle cell surface membrane & via T- tubules into the interior of cell
- Action potential in T- tubules membrane inhibit the Ca^{++} pump of the adjacent terminal cisterns of sarcoplasmic reticulum; Ca^{++} rushes out of the terminal cisterns into the sarcoplasm
- Ca^{++} binds to the troponin component of the troponin tropomyosin complex, moving the complex away from its position blocking the binding sites on the actin chains
- Myosin head (HMM) with attached ATP molecules bind to the new exposed actin chains
- The ATP molecules are hydrolyzed to yield energy which derives the change in the angle of myosin heads & pulls the attached actin chain towards the middle of the sarcomere

- New ATP molecules bind the vacant ATPase sites on the myosin heads; the myosin heads detach from the actin chains & return to their original angle & are attached to new binding sites on the still exposed actin chains. (This process repeats as long as Ca^{++} is bound to the troponin tropomyosin complex
- The Ca^{++} pumps of the sarcoplasmic reticulum recover from the period of inhibition by the muscle cell membrane action potential; Ca^{++} removed from the troponin molecules & pumped back into the sarcoplasmic reticulum
- The troponin tropomyosin complex resumes its blocking positions on the actin chain; further binding of myosin heads to actin chains is presented & the muscle cell relaxes

Effect of Temperature:

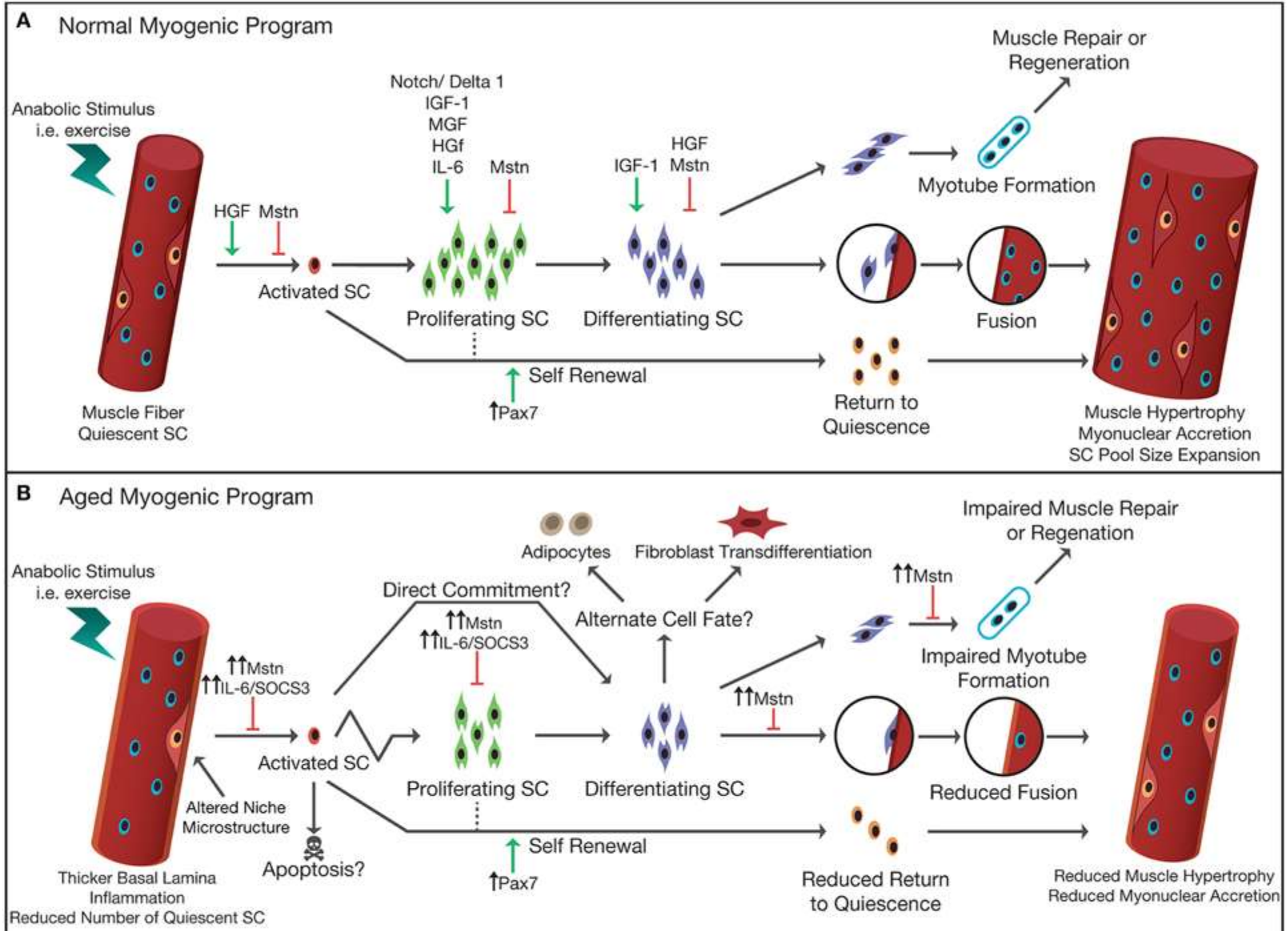
- Whenever environment temperature is much below the normal body temperature, heat production by muscles is a definite advantage
- When air temperature is extremely low, muscles may undergo spasmodic contractions called shivering to produce enough heat to maintain normal body temperature.

Stimulus for muscle contraction:

- Due to an ↑ed permeability of membrane, an electrical action potential is produced by change in the balance of ions on the inside & outside of the nerve fiber
- However, it does not travel beyond the nerve endings
- Instead the depolarization of the nerve ending releases a chemical neurotransmitter ACh from synaptic vesicles at the neuromuscular junction
- The released ACh crosses the cleft between the nerve ending & the muscle fibre membrane to initiate a depolarization wave
- This excitation wave reaches the sarcotubular system & initiates the contraction by subsequent release of Ca^{++}
- The depolarization wave initiated by ACh is due to ↑ed permeability of the muscle fibre membrane to Na^{+} & the wave reaches the individual myofibrils by the way of triads, which are where the longitudinal sarcoplasmic reticulum lies in juxtaposition with the T tubules that pass all the way though a muscle fiber at the junction of the A & I bands

- The T- tubules may pass through the Z line in some species
- The sarcoplasmic reticulum is the longitudinal tubular network within the fiber contains Ca^{++} stores which are released when the membrane depolarization is spread throughout the fiber preceding contraction of the whole muscle fiber
- Ach initiates the impulse for muscle contraction & are inactivated by an enzyme called actelycholinesterase
- Acetylcholinesterase in turn is irreversibly inhibited by certain alkyl-phosphates (insectisides) such as malathion, parathion, diazinon, thymen etc
- When use any of the organic phosphates is improperly tends to extremely dangerous
- Some of the symptoms like constriction of the pupil of the eye, Cramps, vomiting, diarrhea & weakness
- The organophosphates are anti-cholinesterases and they inhibit the action of muscular spasm & asphyxiation
- Neastigmine & physotigmins are commonly used as anti-cholinesterase drugs

- Another group of drugs that affects the neuromuscular junction are the curariform drugs
- These drugs act like curare which is the deadly poison that South Americans Indianas use on their arrowheads
- It binds to the post-junctional membrane so that Ach cannot act on it to produce an end plate potential (EPP)
- Also curare is not destroy by acetylcholinesterase (AchE); muscle contraction cannot be produced because of action potential is not elicited
- Death can result from asphyxiation because the muscles needed for breathing are unable to contract
- Gallamine will do this in varying degree depending on the concentration
- Another group of drugs block the release of ACh from the nerve terminal is botulins toxin causes food poisoning as deadly
- Flaccid paralysis results because Ach is blocked & no action potentials can be produced for muscle contraction. This condition gives rise to the term “limber neck” for poisoning with botulinus toxin


A
Normal Myogenic Program
Anabolic Stimulus
i.e. exercise
Muscle Fiber
Quiescent SC
HGF
Mstn
Activated SC
Notch/ Delta 1
IGF-1
MGF
HGf
IL-6
Mstn
Proliferating SC
IGF-1
HGF
Mstn
Differentiating SC
Muscle Repair or
Regeneration
Myotube Formation
Fusion
Self Renewal
↑Pax7
Return to
Quiescence
Muscle Hypertrophy
Myonuclear Accretion
SC Pool Size Expansion
B
Aged Myogenic Program
Anabolic Stimulus
i.e. exercise
↑↑Mstn
↑↑IL-6/SOCS3
Thicker Basal Lamina
Inflammation
Reduced Number of Quiescent SC
Altered Niche
Microstructure
Activated SC
Apoptosis?
Direct Commitment?
↑↑Mstn
↑↑IL-6/SOCS3
Proliferating SC
Adipocytes
Fibroblast Transdifferentiation
Alternate Cell Fate?
Differentiating SC
↑↑Mstn
Impaired Muscle Repair
or Regenation
↑↑Mstn
Impaired Myotube
Formation
Reduced Fusion
Self Renewal
↑Pax7
Reduced Return
to Quiescence
Reduced Muscle Hypertrophy
Reduced Myonuclear Accretion

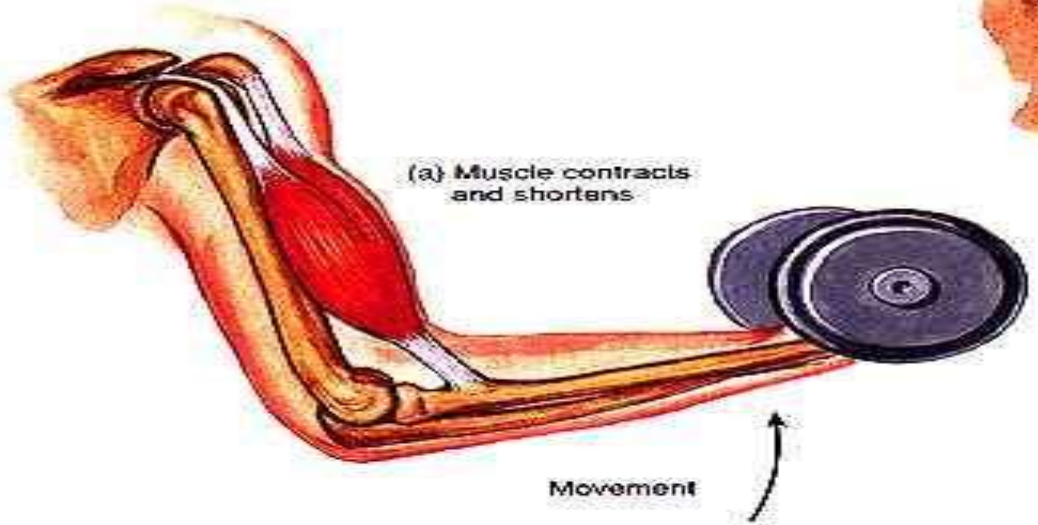
Isometric versus Isotonic Contraction:

Contraction is said to be isometric when muscle does not shortens during contraction & isotonic when it shortens but the tension on the muscle remains constant

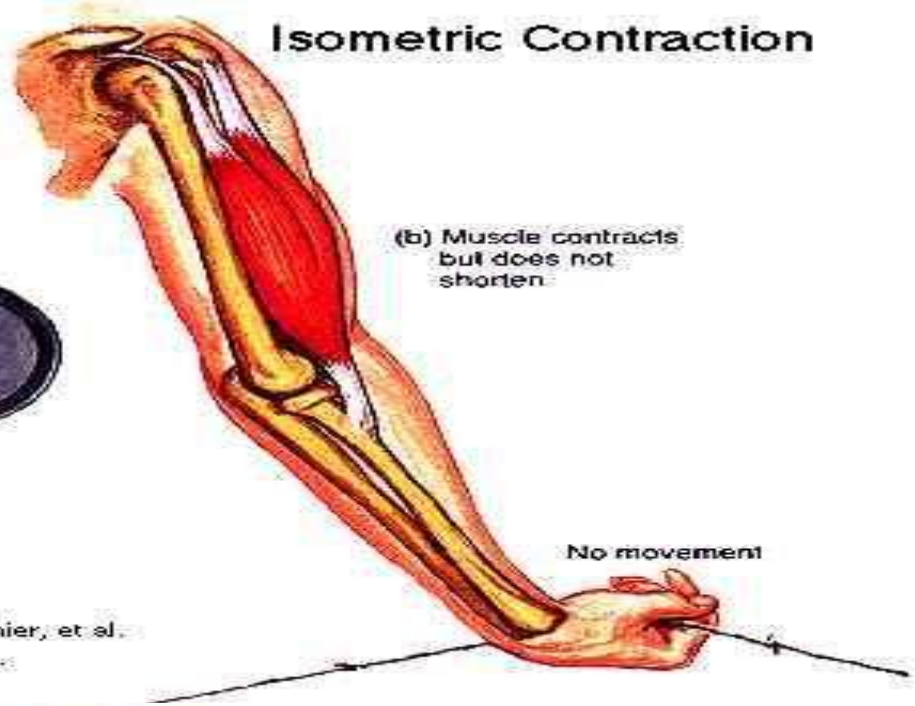
Difference both isometric & isotonic contraction:

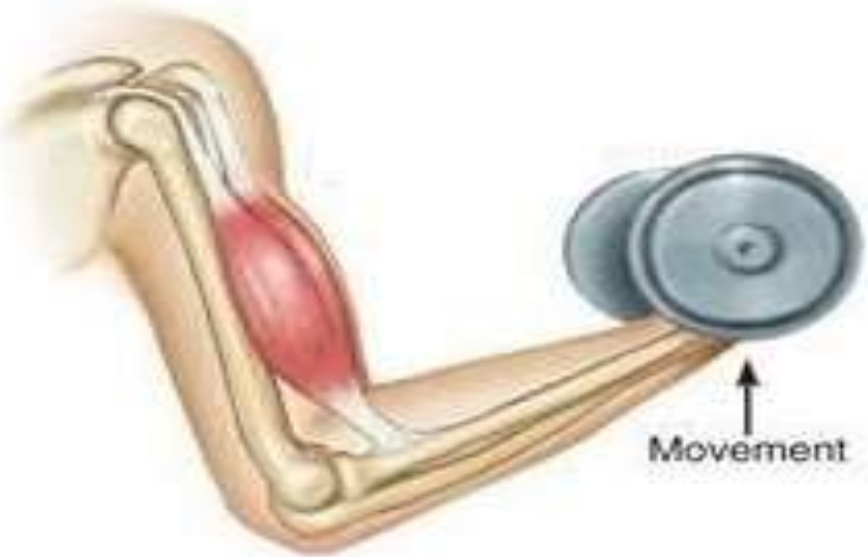
- Isometric contraction does not require slidling of myofibrils among each other
- Isotonic contraction, a load is moved which involves the phenomenon of inertia. Therefore, an isotonic contraction is likely to last considerably longer than an isometric contraction of the same muscle
- Muscles can contract both isometric & isotonic, but most contract are actually a mixed of the two
- When a person stand, he tenses his quadriceps to tighten the knee joints & to keep the legs stiff- **Isometric condition**
- When a person lifts a weight using his biceps- **Isotonic condition**

Isotonic Contraction



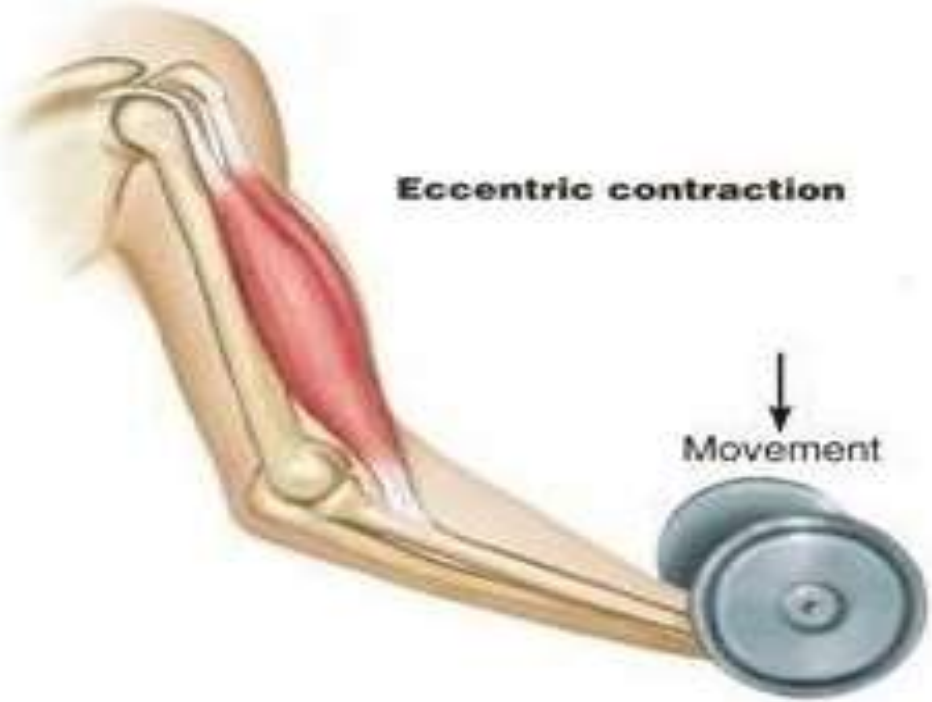
Isometric Contraction





Concentric contraction

Eccentric contraction



- Contractions of leg muscles during running are a mixture of both to keep the limb stiff when the legs hit the ground & isotonic mainly to move the limb

All or None law: It states that when a muscle fibre is contract, the whole fibre contracts & it will contract to the maximum of its ability under the particular condition or it will not contract at all

- A stimulus to a muscle fibre either causes an action potential to travel ones the entire fibre causing contraction or it fails to stimulate the muscle fibre at all
- It applies to a single muscle fibre or motor unit
- It doesn`t state that a muscle fibre will always contract to its maximum
- However has a direct relationship to the strength of the contraction because the larger the stimulus the more motor units are caused to contract

Muscle twitch- It is a single brief response of a single motor unit & so twitch is the smallest quantum of contraction possible. It has 3 phases

- A latent period- between the application of the stimulus & the beginning of the muscle
- A period of contraction- during which the muscles shortens
- A period of relaxation

Physiological properties of muscles: The primary function of muscle is to contract; develop tension & shortens (relaxation)

- **Concentric contraction-** It is the usual form of contraction in which the muscle moves a bone or segment by shortening. Flexion of elbow by contraction of the biceps brachii

- **Isometric contraction-** It occurs naturally whenever a limb or portion of the body is held stationary against equal resistance as gravity. To hold the head up in a fixed position, the dorsal neck muscle must contract isometric
- **Eccentric contraction-** It occurs in the extensor muscles of the neck when an animal lowers its head gradually. Antagonistic muscles may also unsuccessfully opposing the actions of a prime mover
- **Isotonic contraction-** It refers to a contraction in which the length of the muscle changes but the tension remains the same. This occurs primarily when a muscle lifts a given weight

Factors affecting contraction:

- **Summation-**
  - **Multiple motor unit (recruitment):-** It occurs when more motor units are stimulated to contract simultaneously in

the gross muscle. Therefore, more muscle fibres & bundles are contracting & producing greater strength in the whole muscle

- **Wave summation-** It occurs when the frequency of stimulation is ↑^{ed} to a motor unit. i.e., the frequency of stimulation is such that the 1st contraction is not over by the time, the 2nd contraction begins
- **Tetany-** When the frequency of stimulation becomes so rapid that no further ↑ in frequency will ↑ the tension of contraction. Then the greatest force that muscle can develop will have been reached. It is caused by Clostridium tetani which produces spasm of the massester muscles
- **Fatigue-** It is a ↓ in work capacity caused by work itself. The length of the muscle tension/contraction can be maintained depends on the ability to supply energy in the form of ATP & Ca to the contractile protein filaments. As ATP supply ↓^{ed}, the force of contraction ↓es & the muscle gets weaker and the prolonged period is k/a muscle fatigue.

Muscle contraction compresses the blood vessels in the muscle & thereby ↓ blood flow during prolonged contraction. This produces ischemia (lack of blood) which along with fatigue & the build up of lactic acid may cause muscle cramps.

- **Rigor-** If most of the ATP becomes depleted in a muscle, the myosin heads can`t separate from the actin in the thin filament & the Ca can no longer be sequestered back into the sarcoplasmic reticulum by the Ca pump. Therefore, relaxation can`t occur because the actin & myosin filaments become bound in a continuous contracted state. This is the state of extreme fatigue i.e., rigor
- **Rigor mortis-** It is essentially the same except that it occurs a few hours after death
- **Tone**- It refers to the slight tension exhibited by all muscles at rest. Due to continuous transmission of impulses at very low frequency from the spinal cord to the muscles, it keeps

in a state that is receptive to the contraction-strength stimuli & prevents them from hanging flaccid as occurs in paralysis. When an animal becomes anxious, fearful or excited, the muscle tone becomes intensified. During sleep, muscle tone is low to allow for optimal relaxation.

Measurement of contraction- Abnormalities of contraction as well as normal function can be tested by a procedure called electromyography.