

EXCITABLE TISSUES

- * Chapter overview
 1. Physiology of the nerve.
 - Electrical changes.
 - Excitability changes.
 - Chemical changes.
 - Thermal changes.
 2. Physiology of skeletal muscle.
 - Electrical changes.
 - Excitability changes.
 - Mechanical changes.
 - Chemical changes.
 - Thermal changes.
 3. Physiology of smooth muscle.
- * Self assessment questions.



I: Physiology of the nerve:

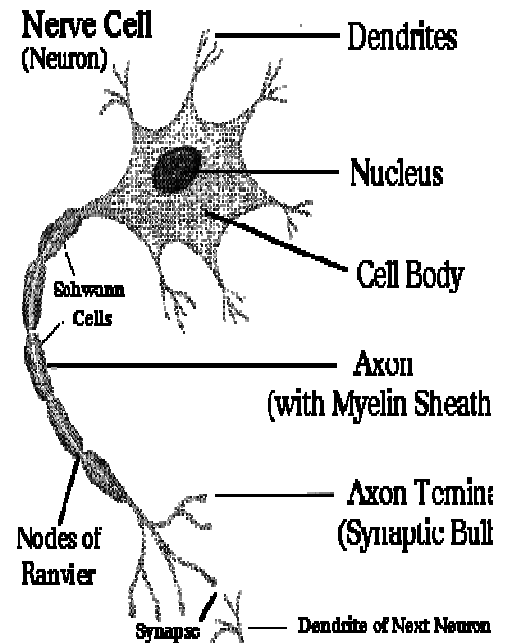
* Types of nerve fibers:

(1) Myelinated nerve fibers:

- Axon is surrounded by myelin sheath & outer neurilemmal sheath.
- The myelin sheath is absent at the end of the axon & at gaps 1 mm "Nodes of Ranvier"

(2) Unmyelinated nerve fibers:

- Axon is only covered by neurilemmal sheath which has an important role in nerve regeneration.
- Under the neurilemma, there are many nuclei which are called schwann cells.



* Changes occurring in a nerve during activity:

- | | |
|-------------------------|--------------------------|
| (1) Electrical changes. | (2) Excitability changes |
| (3) Metabolic changes . | (4) Thermal changes |

(I) Electrical changes "action potential":

(1) Resting membrane potential "RMP".

1- Definition:

- It's the potential difference created across the cell membrane by the metabolic processes of the fiber during rest.

2- Normal value:

- Nerve fiber : - 70 mv → It's negative as the inside of membrane is negatively charged relative to the outside
- Skeletal muscle : - 90 mv
- Cardiac muscle : - 85 mv
- Smooth muscle : -60 mv

3: Causes:

- It's caused by unequal distribution of cations & anions on both sides of the membrane due to:

(I) Selective permeability across cell membrane:

(1) The chief ions of outer surface of the membrane are Na^+ , Cl^- , HCO_3^- & small amount of K^+ & The chief ions of inner surface are K^+ & protein with little amount of Na^+ , Cl^- , HCO_3^- .

(2) Concentration of Na^+ on the outer surface of membrane is 15 times greater than on the inner surface.

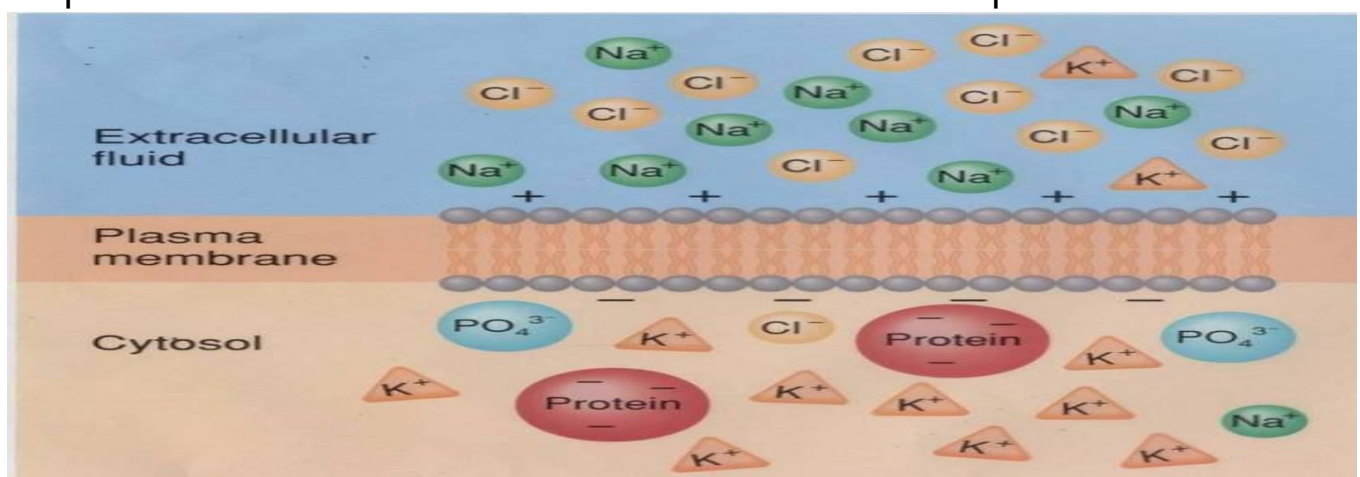
While concentration of K^+ on the inner surface of membrane is 30 times greater than on the outer surface.

(3) Under resting condition, the permeability of the membrane to various ions is a matter of selection, the membrane is:

- Impermeable to proteins which create negative charge on the inner surface of the membrane.
- Freely permeable to Cl^- , HCO_3^- which diffuse to intracellular surface
- Permeability of K^+ is high "50 - 100 times than Na^+ " & to extracellular surface.

(4) The permeability of the channels is controlled by opening or closing of leak channels **"gating of protein channels"**

(5) Migration of ions cannot continue because once the state of equilibrium is reached → the membrane becomes polarized.



(II) Na⁺-K⁺ pump "electrogenic pump"

(1) The Na⁺-K⁺ pump is an active transport mechanism since it occurs against both concentration & electrochemical gradient. i.e: uphill → Transport Na⁺ to the exterior of the cell & K⁺ to the interior of the cell.

(2) There is a carrier protein formed of 2 separate globular proteins which have 3 receptor sites for Na⁺ towards the interior of the cell & 2 receptor sites of K⁺ towards the outer surface.

(3) The inner part of this carrier protein has ATPase activity.

→ Activation of ATPase function occurs once the binding sites of the carrier proteins (2 for K⁺, 3 for Na⁺) are bounded with them.



→ The energy causes conformational change in the protein carrier, extruding the 3 Na⁺ ions to outside & 2K⁺ ions to inside.

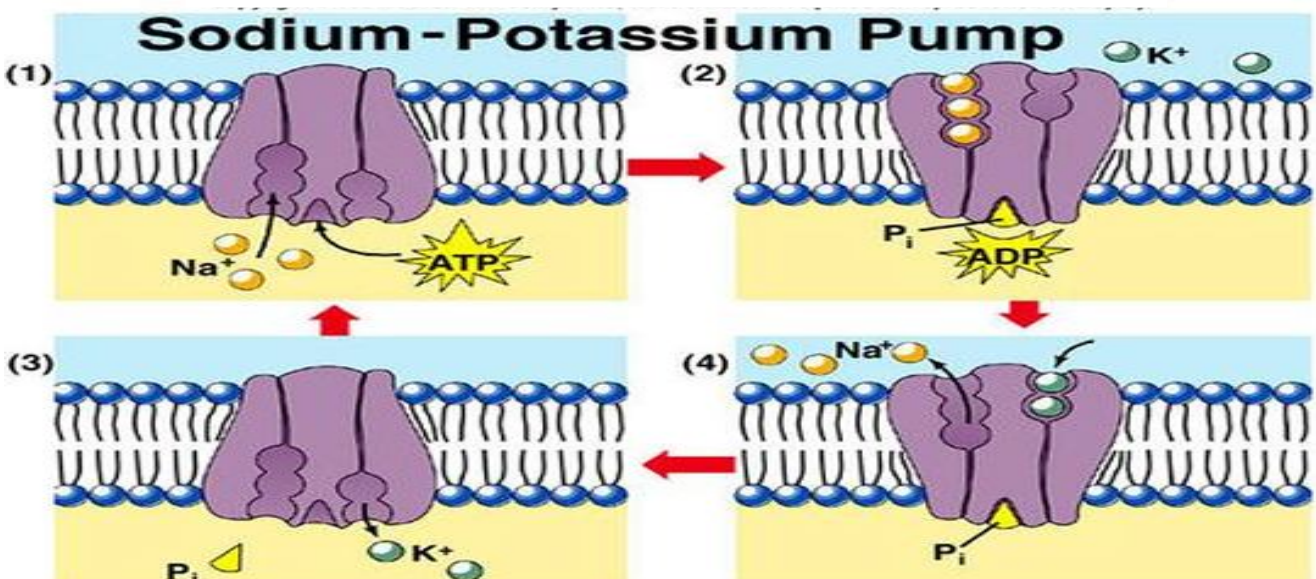
(4) Importance of Na⁺-K⁺ pump:

1-Maintains the Na⁺ & K⁺ concentration gradients across the cell membrane.

2-Establishes a negative electrical potential inside the cells, which helps to transmit signals throughout the nervous system.

3-Maintains intracellular k⁺ level necessary for protein metabolism

4-Maintain osmotic equilibrium.



(2) Action potential

1- Definition:

-It's the electrical changes accompanying the propagation of excitation wave along the nerve fiber.

2-Recording:

-By using 2 electrodes, one on the outer surface of the membrane & the other on its inner surface, both connected to Cathode ray oscilloscope (CRO).

3- Electrical changes:

(1) Stimulus artifact: indicates the time of application of the stimulus to the nerve fiber, followed by a latent period.

(2) Latent period: represents time taken by the excitation wave to travel from the site of stimulation to the recording electrodes.

(3) Initial slow depolarization: membrane potential decrease below 70 mv till it reach 50 mv. The point which called **"Firing level"**.

(4) Rapid complete depolarization: The potential difference decrease till zero **"Isopotential"**.

(5) Reversal of polarization: "overshoot" the outer side of the membrane becomes -ve & the inner side become +ve charged → the potential difference become +35 mv.

So the magnitude of the action potential = 70 mv + 35 mv = 105 mv.

(6) Rapid repolarization: membrane potential falls rapidly.

(7) Slow repolarization: When the repolarization reach 70% & it reaching the firing level slowly **"after depolarization"**

(8) After hyperpolarization: after reaching the firing level, outer side of the membrane becomes positive than resting condition.

(9) The membrane potential reach its **resting membrane potential**.

3. Causes:

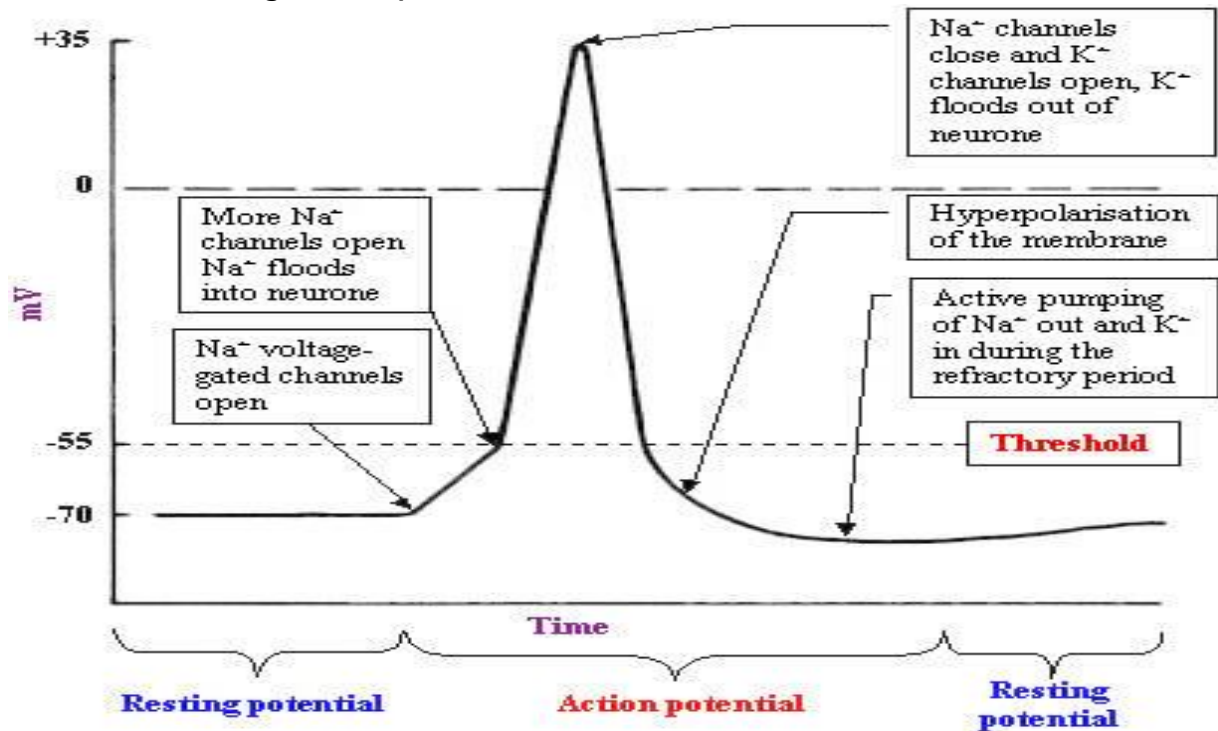
-The rapid rise & rapid fall are the spike potential of the nerve.

(1) The ascending limb of the spike potential is due to:

Na^+ influx through opening of voltage gated Na^+ channels leading to depolarization of the membrane followed by reversal of polarity.

(2) The descending limb of the spike potential is due to:

K^+ outflux leading to repolarization of the membrane.



(3) All or non rule "All or nothing principle"

*** Definition:**

-stimulation of single nerve fiber by a stimulus of threshold "minimal" intensity or over → give maximal response, but its stimulation by subthreshold "subminimal" give no response at all.

*** It's applied in**

- | | |
|-------------------------|----------------------------------|
| 1- Single nerve fiber | 2- Single skeletal muscle fiber. |
| 3- Whole cardiac muscle | 4- Most of the smooth muscles |

*** Not applied in**

- | | |
|----------------------|---------------------------|
| 1- Mixed nerve trunk | 2- Whole skeletal muscle. |
|----------------------|---------------------------|
- because increasing the intensity of the stimulus from threshold to maximal, increase the magnitude of response but single fiber inside nerve trunk or whole skeletal muscle obeys all or non rule.

(4) Local excitatory state (L.E.S)

-Subthreshold stimuli are not to produce an action potential, but they don't pass with effect, they lead to:

A)↓ Resting membrane potential below the firing level.

B)Slight ↑ in excitability below the level which produce a response.

C)Application of multiple subthreshold stimuli can be summated to give a response "reaching to the firing level"(Temporal summation)

(5) Properties of the nerve:

I: Excitability:

1.Definition:

-It's the power to response to a stimulus.

2- Types of stimuli:

1- Electrical

2- Chemical

3- Mechanical

4- Thermal

3- Electrical stimuli:

- Electrical stimulation is preferred because:

1. It's similar to natural stimuli in our body.
2. The intensity & duration can be easily measured.
3. Have no permanent damage effect.

-Types of electrical stimuli:

1. Galvannic current: low voltage – long duration
2. faradic "induced" current: high voltage + short duration.
3. square – wave pulses: very high voltage + very short duration.

4. Factors affecting effectiveness of a stimulus:

(I) Rate of application of the stimulus:

-Sudden application of a current of a certain intensity is more effective than if it's gradually applied,as gradual application leads to adaptation or accommodation.

(II) Strength & duration of the stimulus "strength duration curve"

*Definition:

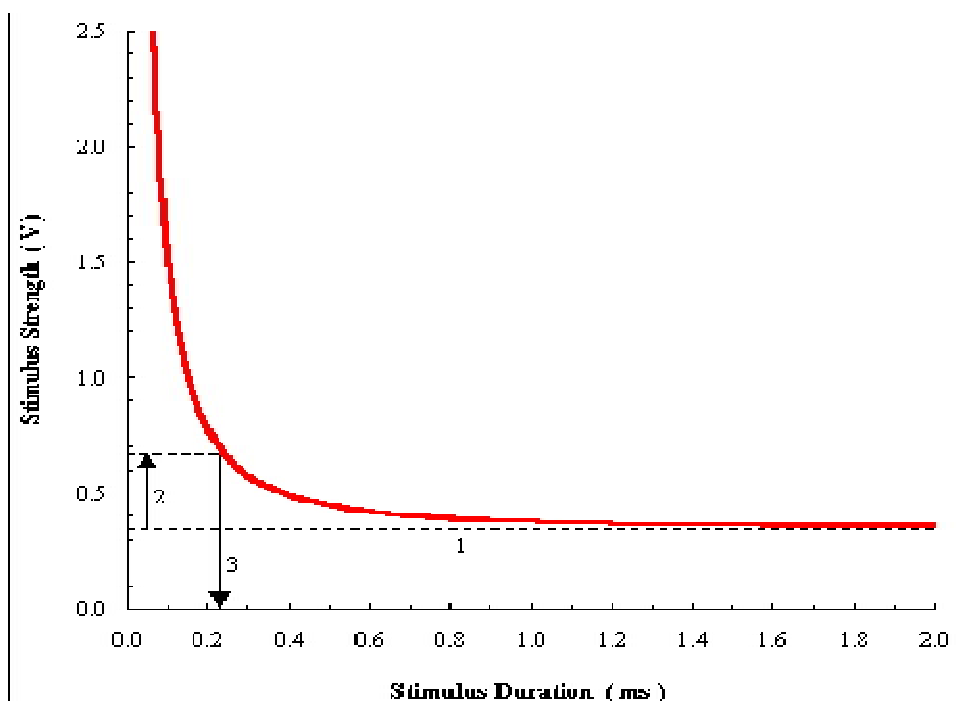
-It's the curve in which the strength of the current is plotted against the time needed by it to excite the tissue.

*Analysis:

- (1) Within limits, the stronger the current. The shorter is the time needed to excite the tissue.
- (2) There's a minimal or threshold current intensity (R) below which no excitation occurs, whatever the duration **"Rheobase"**
- (3) Time needed by the rheobase "threshold current of unlimited duration" to give a response is called **"Utilization time (UT)"**
- (4) There is minimal time (**T**) which is required for excitation below which no current however strong, can excite the tissue.

*Uses:

- Used for comparison between excitability of different tissues & the same tissue under different conditions.
- To compare the excitability by using one point on the curve, **chronaxie (c)** is the minimal time needed by double the rheobasic strength to excite the tissue.



5. Factors which affect the excitability of the nerve fiber :

(I) Concentration of ions in Extracellular fluid (ECF):

- Ca^{++} concentration

- Low Ca^{++} in ECF, \uparrow excitability of the nerve by \uparrow the permeability of the membrane to Na^+
- $\uparrow \text{Ca}^{++}$ in ECF \rightarrow \downarrow excitability by stabilization of the membrane.

- K^+ concentration

- $\uparrow \text{K}^+$: concentration in ECF \rightarrow \uparrow excitability of nerve due to it \downarrow RMP.
- $\downarrow \text{K}^+$: concentration in ECF \rightarrow \downarrow excitability if nerve due to it \uparrow RMP.

- Na^+ concentration:

- $\uparrow \text{Na}^+$ concentration in ECF \rightarrow facilitate depolarization & \uparrow Excitability of the nerve.
- $\downarrow \text{Na}^+$: concentration in ECF \rightarrow \downarrow excitability of nerve.

II chemical factors:

- local anaesthetics as procaine \downarrow permeability of the nerve fiber to Na^+ ions by acting on Na^+ channels making them difficult to open "Membrane stabilizers"

III Electrical changes:

- Electronic potentials are localized potential occurred by stimulation of the nerve fiber by subthreshold stimuli "local response"
- If the stimulation electrode is cathode, it called "catelectrode"
- If the stimulation electrode is anode, it called "Anelectrode"
- On making the current:
 - *The cathode adds more $-$ ve charge at the outer surface of the membrane \rightarrow partial depolarization \rightarrow \uparrow excitability of the nerve.
 - *The anode adds more $+$ ve charge at the outer surface of membrane \rightarrow Hyperpolarization \rightarrow decrease excitability of the nerve.

II: Adaptation:

- On stimulation of a nerve with a constant current \rightarrow no response occurs during passage of this current due to adaptation of the nerve fiber to the current very rapidly.

III: Infatigability:

-The nerve fibers are not readily fatigued by repeated stimulation.

IV: conductivity:

*Definition:

- propagation of the action potential on an excitable membrane.

*Types:

I: conduction in unmyelinated nerve fibers:

- (1) Stimulus \rightarrow \uparrow permeability of Na^+ ions at the excited point \rightarrow depolarization of this area of the membrane.
- (2) local circuit of the current flows between the depolarized area of the membrane & the adjacent resting membrane area & repeated this process.
- (3) Spread of action potential in the form of local circuit in both directions away from stimulus until all membrane become depolarized.
- (4) Repolarization occurs at the point of the stimulus & spreads in the direction of depolarization.

*Velocity of conduction $0.5 - 3 \text{ m/s/sec}$.

(II) Conduction in myelinated nerve fibers:

- (1) Myelin sheath is insulator to the passage of electric current.
- (2) Nodes of Ranvier are the most excitable regions of the nerve fiber due to absence of the myelin sheath.
 \rightarrow They are the site which the impulse starts & the site which the migration of ions necessary for conduction of impulse takes place.
- (3) The internodes are areas of resistance or block to the passage of the impulse which jumps the internodes from one node to the next one "Saltatory conduction"

(4) Value of saltatory conduction:

1. \uparrow velocity of conduction along the fiber $\rightarrow 3 - 120 \text{ m/s/sec}$
- B- Depolarization is limited to the node $\rightarrow \text{Na}^+$ leakage is minimum
 \rightarrow save energy required by Na^+ pump to extrude Na^+ to outside.

II:Excitability changes (Refractory periods):

-The conduction of nerve impulse alters the excitability of the fiber in the following order:

(1) The absolute refractory period (ARP):

- It's the period during which the excitability is zero & no other stimuli whatever its strength may be, can excite the fiber.
- This is due to the depolarized state of the membrane as it must be repolarized before it can response to a second stimuli.
- It coincides with the ascending limb of the spike & the upper third of the descending limb.

(2) The relative refractory period (R.R.P)

- It's the period during which the excitability is recovered but still below normal level, stronger stimulus is needed to excite the fiber.
- It coincides with middle third of the descending limb of the spike.

(3) Super normal phase:

- It's the period during which the threshold to stimulation is decreased & excitability is increased.
- It coincides with after depolarization phase of action potential.

(4) Subnormal phase:

- It's the period during e the threshold to stimulation is increased the nerve excitability is decreased .
- It coincide with the after hyperpolarization phase of action potential

III:Chemical or metabolic changes:

(1) During rest: -The energy is spent to:

1. maintain the polarized state of the membrane.
2. maintain ionic composition across the cell membrane constant→
The $\text{Na}^+ - \text{K}^+$ pump derives energy from the breakdown of ATP.

(2) During activity:

- The energy expenditure is doubled to restore the polarized state of the membrane.
- The following chemical reactions occurs:

(I) Break down of ATP:

-ATP → ADP + Pi + E

(II) Breakdown of creatine phosphate:

-CP → creatine + Pi + E .

(III) Breakdown of glycogen "glycolysis":

-Glycogen $\xrightarrow[\text{in presense of } O_2]{\text{Glycolysis}}$ Pyruvic acid $\xrightarrow[+O_2]{\text{Oxidation}}$ $\text{Co}_2 + \text{H}_2\text{O} + \text{E}$
in absence of $O_2 \rightarrow$ lactic acid.

IV: Thermal changes:

-During activity, heat production is doubled that produced during rest.

(1) Initial heat:

-due to migration of ions during the spike "action potential"

(2) Delayed heat:

-it concides with the recovery "Recovery heat", it's divided into:

(I) Early rapid phase: which is equal to the initial.

(II) Slow phase: continues 10-30 minutes depending on type of fiber.

-It's 9 times the magnitude of the initial

-But if no O_2 initial= delayed.

II: Physiology of skeletal muscle:

1- Types of muscles:

	Skeletal muscle	plain muscle	cardiac muscle
Histology	striated muscle	unstraited muscle	striated muscle
Contraction	- voluntary. - neurogenic	- involuntary - myogenic	- involuntary - myogenic
Role of nerves system on contraction.	Nerve operated "Contract only in response to nervous stimuli"	Nerve regulated "contraction regulated by A.N.S	Nerve regulated contraction regulated by A.N.S

2- Structure of skeletal muscle:

(1) **The skeletal muscle** is formed of muscle fibers.

(2) **Muscle fiber** is surrounded by a membrane called "Sarcolemma" that prevent the cytoplasmic continuity of adjacent muscle fiber several nuclei are present underneath the sarcolemma.

(3) Each skeletal muscle fiber is composed of parallel longitudinal **fibrils** which are embedded in sarcoplasm giving the fiber its longitudinal striations.

(4) Each fibril is composed of **several proteins**:

* myosin & actin → muscle proteins needed for contraction.

*troponin & tropomyosin are muscle proteins needed for relaxation.

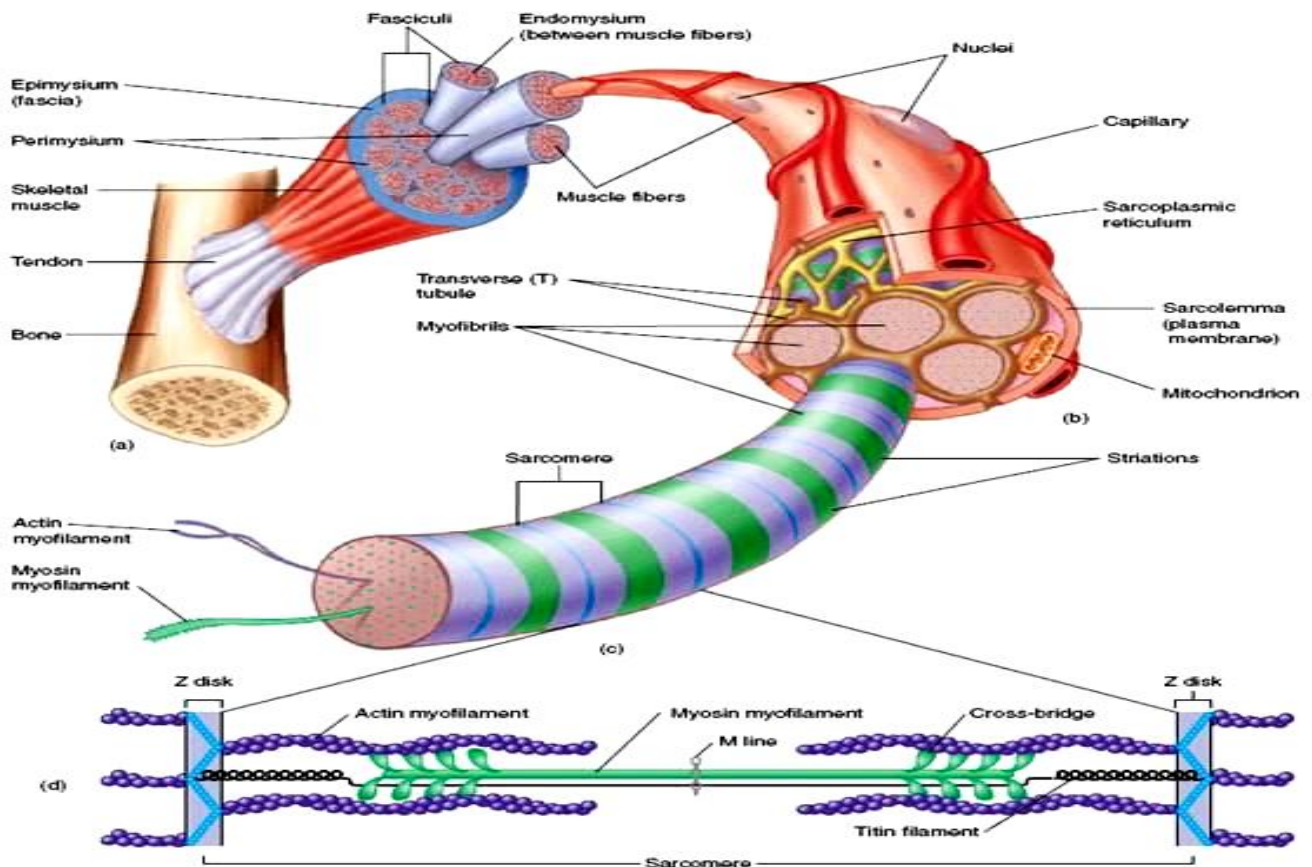
(5) **The cross - striations** characteristic of skeletal muscle give rise to dark & light bands alternating together:

*Dark band "A band": has a light zone in their middle (H membrane).

*Light band "I band": has dark line in its center called "Z line"

*The structure between 2 successive z line is called "Sacromere" which is the contractile unit of the muscle.

(6) Actin filaments occupy I band & held together at their middle by the z membrane. but the myosin filaments occupy A band.



3- Types of skeletal muscle:

	<u>Red muscle</u> (Type I)	<u>Pale muscle</u> (Type II)
Fibrils	-Thick fibrils embedded in a bundant sacroplasm.	-Thin fibrils embedded in little sacroplasm
Myoglobin	-Sacroplasm contains myoglobin " red pigment" which combined with O ₂ .	-Sacroplasm contains little or no myoglobin.
Contraction	contract slowly	contract quickly
Fatigue	Less rapidly to occur.	get fatigued early.
Blood capillary	Numerus to supply extra amount of O ₂ "red fiber"	Few blood capillaries "pale fibers"
Mitochondria	Greatly increased to support aerobic oxidation	Few "anerobic oxidation"
Function	Long slow contraction which maintain body position	Fine skilled movements as hand muscle

-In human being, muscle are mixed from the 2 types but there are muscles made completely of one type.

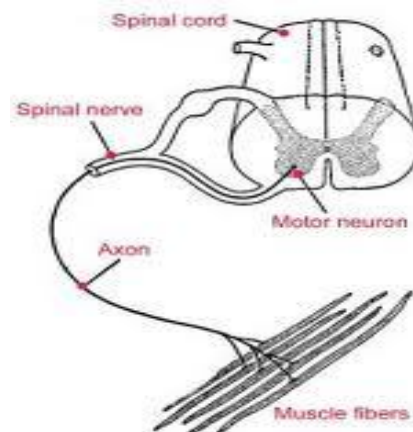
-A third type of muscle :**intermediate "fast oxidative"**

They have the charactersitics of the 2 types, increase ATPase activity as fast areobic fibers & increased oxidative capacity as slow anaerobic fibers.

4-Nerve supply of skel etal muscle:"Motor Unit"

-Which consist of:

- (1) Anterior horn cell (AHC)
- (2) It's axon
- (3)Membrane of muscle fibers supplied by it.



5- Changes occurring in the muscle in activity:

- (1) Electrical changes.
- (2) Excitability changes.
- (3) Mechanical changes.
- (4)Chemical "Metabolic" changes.
- (5)Thermal changes.

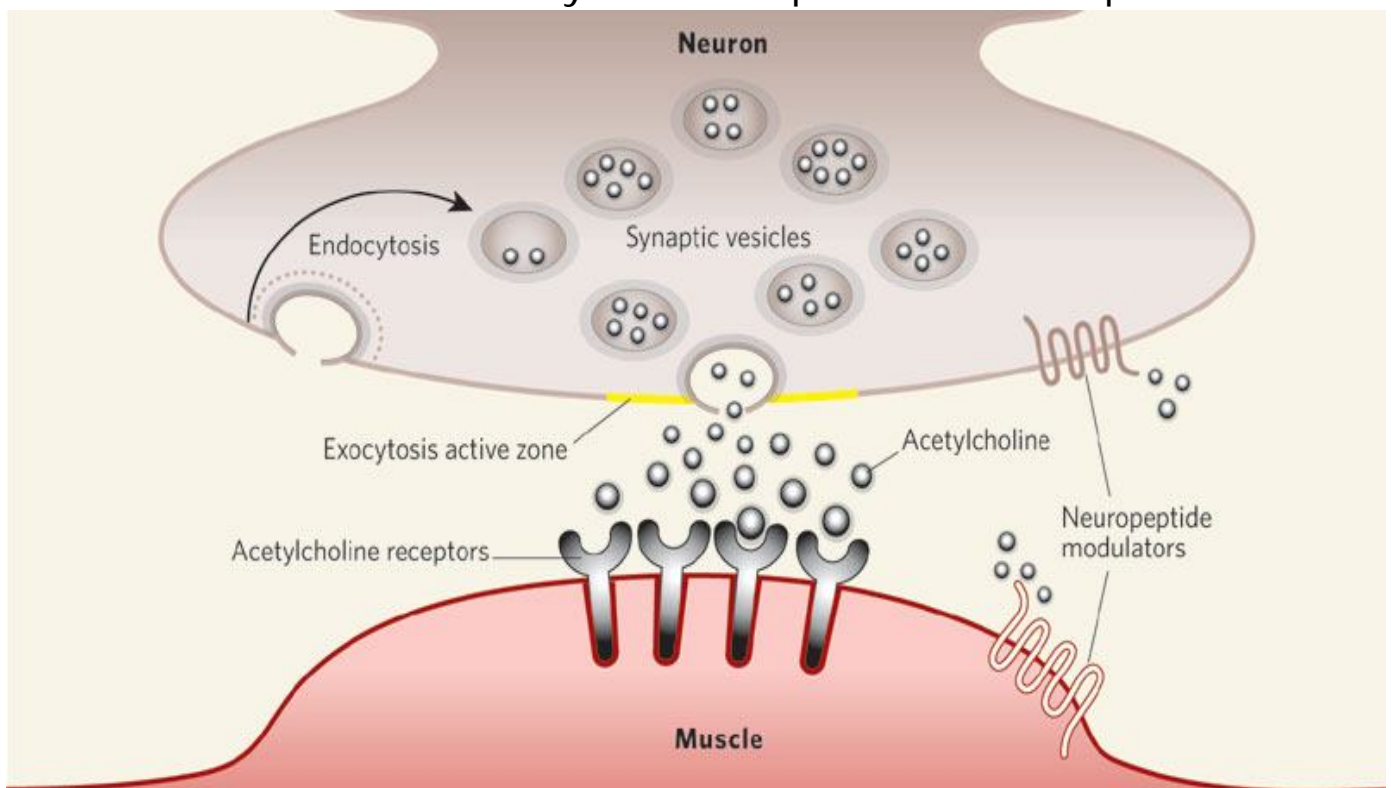
(I) Electrical changes:

-They are the same as in the nerve with some difference:

	Nerve fiber	Skeletal muscle
(1) RMP	- 70 mv	- 90 mv
(2)Magnitude	105 mv (70 + 35)	130 mv (90 + 40)
(3)Duration of action potential	2 - 4 msec	1 - 5 msec
(4)Velocity of conduction	5 m/sec	3 - 5 m/sec
(5) Response	Followed by conduction of nerve impulse	Followed by contraction "after 2 msec"

-Mechanism of neuromuscular transmission at motor end plate:

- (1) Excitation of neuromuscular junction by a nerve impulse → Ca^{++} influx from extracellular fluid into the nerve terminal membrane.
- (2) Ca^{+2} ions attached to Ach vesicles to the membrane & rupture → release of Ach into synaptic cleft.
- (3) The channels on muscle outer surface acts as a receptor for Ach which cause conformational changes in the channel to open the gate for about one millisecond → rapid influx of sodium ions to the interior of the muscle fiber → generation of an action potential.
- (4) This localized action potential generated is called "The endplate potential" (EPP) → a localized unpopulated potential when it reaches a certain value "Threshold potential", it fires the development of action potential on both sides of the motor end plate along the sarcolemmal membrane → muscular contraction.
- (5) Fate of Ach: rapidly destroyed after 1 msec by cholinesterase enzyme in the cleft itself → to prevent re-excitation of the muscle fiber after recovery from the previous action potential.



*** Properties of neuromuscular transmission:**

1- Unidirectional

-Occurs in one direction from the nerve to the muscle & not in the opposite direction.

2- Delay

-There is some delay about 0.5msec in neuromuscular transmission.
-This time is used for release of Ach + its binding to the receptors at the outer surface of the membrane + occurring of EPP till reaching the firing level to generate action potential.

3. fatigue:

-The neuromuscular junction is the site in the neuromuscular system which suffer from fatigue.

(II) Excitability change:

*** It's same that occurring in the nerve fiber except:**

1-The total refractory period is too short "2 msec".

2-It end at the beginning of the mechanical response "muscle contraction" so The electrical changes always proceeding the mechanical response → There's summation for contraction in response to multiple successive stimuli.

(III) Mechanical changes

***Definition:**

-The ability of the muscle to convert the electrical energy into mechanical energy.

***Types of muscular contraction:**

	Isotonic Contraction	I sometric contraction
-length of fibers	shortening	Constant
- Tension	constant	I ncreased
- work done	25% of energy is converted to work 75% to heat.	No work is done so all energy produced is converted to heat.

*Molecular basis of muscular contraction:

[1] Contraction of muscle occur by sliding of the thin filament of the myofibrils over the thick filaments.

[2] The thick filament is formed of protein called myosin → which is rod shaped with many cross bridges or heads protruded from its surface except central part.

[3] The thin filaments is formed of 3 proteins: Actin, Troponin & tropomyosin

* **Actin:** The main protein present in the thin filament, globular in shape

- There's many bindings sites along it for the myosin heads.

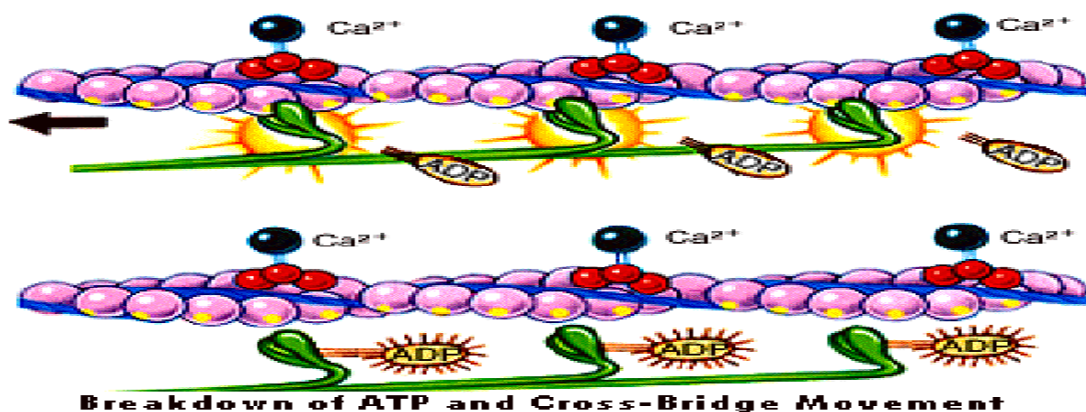
* **Tropoin:** It's the protein for muscle relaxation, globular in shape.

- There are 3 troponin I, T, C. (I) attached to actin, (T) attached to tropomyosin & (c) attached to Ca^{++} ions.

* **Tropomysosin:** it's a protein for muscle relaxation.

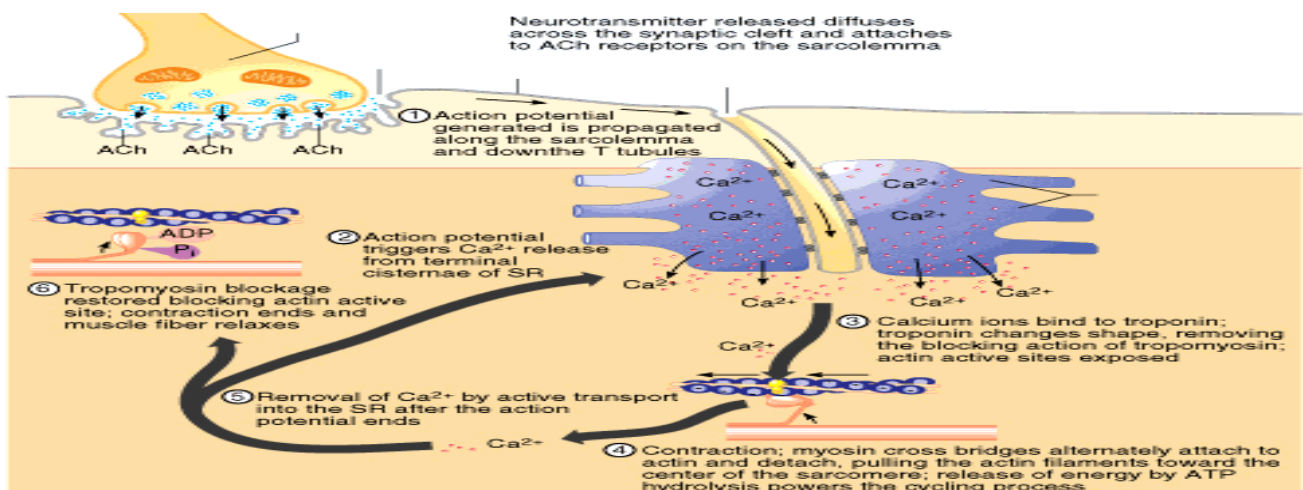
[4] During rest "relaxation": Troponin T is tightly bound to tropomyosin forming troponin – tropomyosin complex → which covers the binding sites for myosin heads on the actin filament → Inhibition of contraction.

[5] During contraction: once troponin C is combined with Ca^{++} ions → disappear of troponin – tropomyosin action by moving of tropomyosin laterally → uncovering of binding site of myosin heads in the actin filaments → contraction occurs.



(5)Excitation–contraction coupling:"Mechanism of muscle contraction":

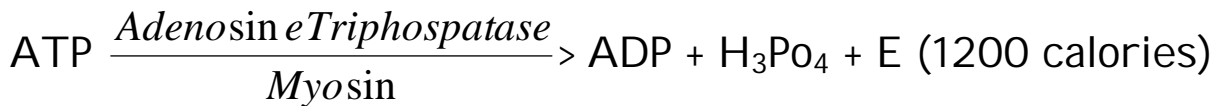
- [1]Stimulation of myelinated motor nerve supplying a skeletal muscle
→ generation of action potential → spreads along both sides of the sarcolemmal membrane.
 - [2] The action potential spreads to the depth of the myofibrils via T-Tubules system "Extending from the sarcolemmal membrane"
 - [3] Release of Ca^{++} ions from the lateral sacs of the sarcoplasmic reticulum & its diffusion to the thick & thin filaments.
 - [4] Binding of Ca^{++} to troponin C → uncover of the binding sites of myosin on the actin filaments due to inhibition of troponin - tropomyosin complex.
- ATP is splitted to supply energy needed for muscular contraction.
- [5]Formation of cross linkages between myosin and actin → sliding of the thin filaments over thick filaments → muscular contraction.
 - [6]More & more shortening is obtained by disconnection, swiveling & reconnection of myosin heads to binding sites on actin filaments.
 - [7]Active reuptake of Ca^{++} by the sarcoplasmic reticulum to be stored for the next action potential. The energy needed is obtained from breakdown of ATP.
 - [8]Once Ca^{++} is reuptaked by sarcoplasmic reticulum,the interaction between myosin & actin stops & muscular relaxation occurs.



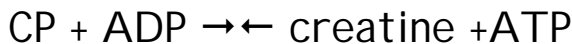
(IV) Chemical changes:

-The energy needed for contraction is supplied from the ATP & creatine phosphate & glycogen.

[1] Breakdown of ATP:



[2] Resynthesis of ATP anaerobically from CP:



[3] Energy needed for resynthesis of ATP & CP: comes from:

* Glycogen \rightarrow pyruvic acid \rightarrow (O₂) \rightarrow H₂O + CO₂ + E
no O₂ \rightarrow lactic acid + E

[4] oxidation of blood fatty acid:

-mainly used in the muscle at rest & after contraction "during recovery"

V: Thermal changes "heat production"

[1] Initial heat"

-It starts before the shortening of the muscle, it's subdivided into:

- (A) Activating heat \rightarrow Due to conduction of the spike & changes produced by it start shortening.
- (B) Shortening heat \rightarrow due to changes in the structure of the muscle in shortening.
- (C) Relaxation heat \rightarrow due to breakdown of ATP for active reuptake of Ca⁺⁺
- (d) Maintenance heat \rightarrow If the muscle contract tetanically, extra heat is produced to maintain the contracted state.

[2] Recovery "delayed heat":

-It's waste heat from resynthesis of glycogen & any CP not resynthesized anaerobically.

- If no O₂: It's diminished but not completely abolished.

[6] Some important skeletal muscle conditions:

(A) Muscle hypertrophy:

*Definition:

- It's the increase in the size of the muscle fibers.
- It's differ in hyperplasia (increase in cell number).

*Cause:

- Very forceful muscle activity exerted even for a short time daily (especially isometric contraction).

*Result:

- Increase the power of contraction of muscle, the nutrient & energy stores.

(B) Muscle atrophy:

*Definition:

- Decrease in the muscle size which occurs when the muscle is not contracted.

*Causes:

- 1.Placing the limbs in casts hinder its contraction.
- 2.Muscle denervation

*Treatment:

- Electrical stimulation which prevent atrophy even if the muscle is denervated.

(C) Muscle fatigue:

*Deninition:

- It's atemporary decreas in the work capacity of skeletal muscles following prololoned or forceful contraction by 1-2 minutes

*Causes:

- 1.Depletion of energy producing substances(ATP-CrP-Glycogen).
- 2.Accumilation of lactic acid.
- 3.Reduction in the nerve transimission at neuromuscular junction.

(D) Muscle contracture "cramps"

*Definition:

- Sustained muscular contraction when the muscle is fatigued.

*Cause:

- Depletion of ATP which is required for active reuptake of Ca^{++} after contraction is decreased, consequently muscle relaxation fails.

(c) Muscle denervation

*Causes:

- Skeletal muscle is nerve dependent, so destruction of a motor nerve supplying a skeletal muscle as in case of:
 - 1- Myasthenia gravis.
 - 2- Cutting of motor nerve by cut wound.
 - 3- AHC lesion as in "poliomyelitis".

*Manifestation:

- 1- Atrophy of the muscle → converted to fibrous tissue.

- 2- Muscle fasciculation:

- They are jerky contraction due to pathological discharge from AHC.
- They particularly occurs in poliomyelitis & are visible by eye & felt by patient.

- 3- Muscle Fibrillation:

- They are irregular contractions which not visible by the eye but can be recorded by electromyogram.
- They caused by hypersensitivity of denervated muscle by small amount of Ach present in the blood stream.

- 4- Reaction of degeneration:

- It means the changes in electrical response of degenerated muscle.
- These changes are:

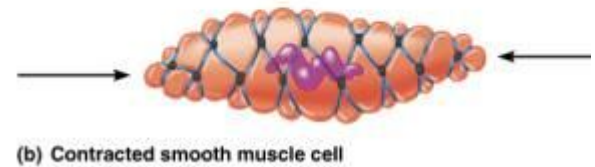
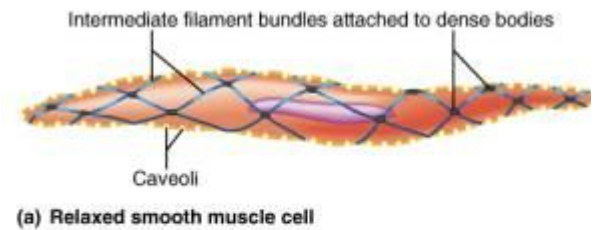
- a) ↓ Excitability (↑chronaxia)
- b) Normal healthy muscle responds to both galvanic & faradic current but, degenerated muscle responds to galvanic current only.
- c) In healthy muscle the cathode closing contraction (CCC) is higher than the anode closing contraction (ACC) but there, $CCC < ACC$.

III: Physiology of smooth muscle:

1. Smooth muscle structure:

1-Actin & myosin filaments are present, but the ratio between myosin to actin are 1:13 (compared to 1:2 in skeletal muscle).

2-Actin is attached to dense bodies which either attached to the cell membrane or to each other by protein. (they are analog of Z-line)



3.Thin filaments are actin & tropomyosin (no troponin).

4.No sarcomeres & no T-tubules.

5.Sarcoplasmic reticulum is less developed.

2.Types of smooth muscle:

	Visceral unitary muscle	Multi-units muscle
site	Wall of GI T, urinary tract & many blood vessels.	-Wall of blood vessels, ciliary muscle, iris of eye & piloerector muscle.
Arrangement	-arranged in bundles -gap junctions between the fibers. -cell membrane of different fibers come in contact with each others.	-separate muscle fibers
Contraction	Action potential spread to all fibers so contract in syncytial fashion.	Each fiber responds independent from the other
Control	Mainly by non nervous stimuli	By autonomic nervous system.

3.Contractile process in the smooth muscle:

*It's like that occurs in the skeletal muscle except:

1.The contractile unit is formed from many radiating actin filaments from 2 dense bodies.

2.Some of the dense bodies of adjacent cells are attached together by intercellular protein bridge, which transmits the force of contraction from one cell to other.

3.Instead of troponin, smooth muscle contraction needs another protein called calmodulin which combines with Ca^{++} .

4.The process of attachment & detachment of actin & myosin is much slower than skeletal muscle due to reduced ATPase activity of myosin heads.

5.The energy needed for sustained contraction is very small, only one ATP is needed for contraction whatever its duration.

6.For relaxation to occur, Ca^{++} is removed by Ca^{++} pump to SR, the pump is slower than skeletal muscle so contraction takes more time.

7. Smooth muscle in arterioles & other organs maintains a moderate degree of contraction without fatigue, called **smooth muscle tone**

8.Sources of Ca^{++} in smooth muscle:

-The sarcoplasmic reticulum is rudimentary, so Ca^{++} influx in smooth muscle from ECF on arrival of action potential.

-Some smooth muscle contains a moderately developed sarcoplasmic reticulum near the cell membrane which has invagination called caveoli (like T-tubules).



4. Properties of the smooth muscle:

I: Electrical properties:

-RMP: -50 mv.

-Action potential :2 types depend on the types of fibers

1. Spike potential: occurs in most of visceral type.

2. Action potential with plateau: occurs in the vascular smooth muscle, ureter & uterus.

II: Excitability & conductivity:

-They are less excitable than skeletal muscle with long chronaxia.

-Factors increase excitability:

1. O₂ lack, Excess CO₂, decrease H⁺ & increase K⁺

2. Acetylcholine, oxytocin, vasopressin & estrogen.

-Factors decrease excitability:

-Increase Ca⁺⁺ & increase H⁺

-Epinephrine & progesterone.

III: Contractility & rhythmicity:

-Some smooth muscle are self excitatory "spontaneously stimulated"
Slow wave potential, when it reaches the threshold (-35mv), fires action potential leading to muscle contraction.

1. Rhythmic contraction:

-Occurs in self excitable fibers which act as pacemaker.

-It's due to leaking of Na⁺ ions from the membrane leading to gradual decrease in potential to the firing level.

2. Tonic contraction:

-It's due to repetitive action potential, so contractions are summated giving tetanic contractions.

-They maintain steady pressure on the intestinal contents & maintain ABP in the wall of blood vessels.