

Introduction to Physiology. Excitable tissues. Membrane potentials. Muscle Physiology.

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DEFINITIONS

- **Excitability** is defined as the reaction or response of a tissue to the irritation or stimulation. It is a physicochemical changes. The muscle can be excited by both direct stimulation and indirect (through its nerve) stimulation.
- **Lability** is a functional mobility of tissues. It is limit rhythm of impulses which excitable tissue is able to give in course of minute. Nervous tissue possesses maximal lability.
- **Refractoriness** is non-excitability state.



Excitement specific signs are:

- 1) muscular contraction;
- 2) nervous impulse conduction;
- 3) secret releasing.

Non-specific signs of excitement are:

physicochemical and biochemical reactions.

Irritators are divided into groups:

1. By energetic nature:

Physical:

- a) Mechanical stimulus (pinching)
- b) Electrical stimulus (electric shock)
- c) Thermal stimulus (by applying heated glass rod or wire);

Chemical – acids, alkalis and so on;

Physicochemical - oncotic and osmotic pressure.

Biological – hormones, vitamins, mediators.

Social – word.

2. By force – subliminal, threshold (liminal), supraliminal.

3. By biological role – adequate and non-adequate.

4. By distance of action – contact and distant.

QUALITIES OF STIMULUS

To excite a tissue, the stimulus must possess two characters namely:

- intensity or strength;
- duration

Intensity of Stimulus

The intensity of a stimulus is of five types namely:

1. Subminimal stimulus – less than threshold stimulus.
2. Minimal stimulus – the stimulus whose strength (or voltage) is sufficient to excite the tissue is called threshold or liminal or minimal stimulus.
3. Submaximal stimulus.
4. Maximal stimulus – giving maximal answer reaction.
5. Supramaximal stimulus – giving answer reaction inhibiting (force pessimum).

Irritation laws

I. Law of irritation force

The stronger is irritation, the more is answer reaction (but only up to definite limits).

This law is limited on one hand by threshold force and on another hand by force pessimum.

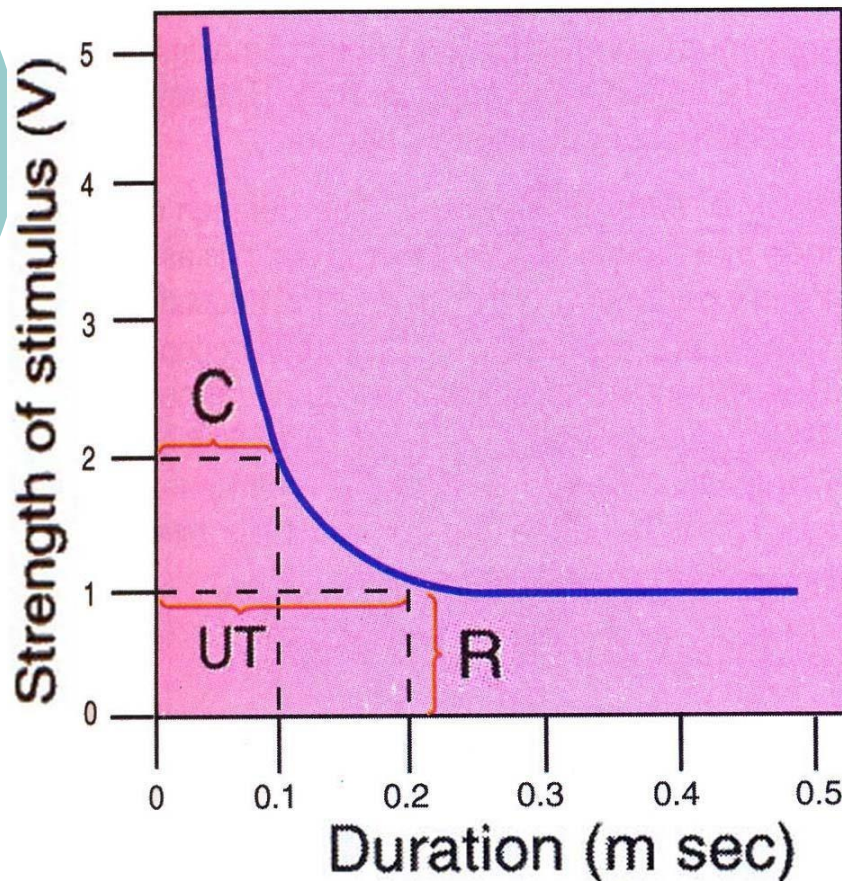
II. Law "everything" or "nothing"

Excitatory tissue does not answer to subliminal stimuli and gives its maximal reaction to the threshold stimuli.

III. Law of force (strength)-duration

The duration of a stimulus to excite a tissue depends on the strength of the stimulus. For a weak stimulus, the duration must be longer and for a stronger stimulus, the duration is short.

EXCITABILITY CURVE OR STRENGTH-DURATION CURVE



Strength duration curve.

R = Rheobase.

UT = Utilization time.

C = Chronaxie.

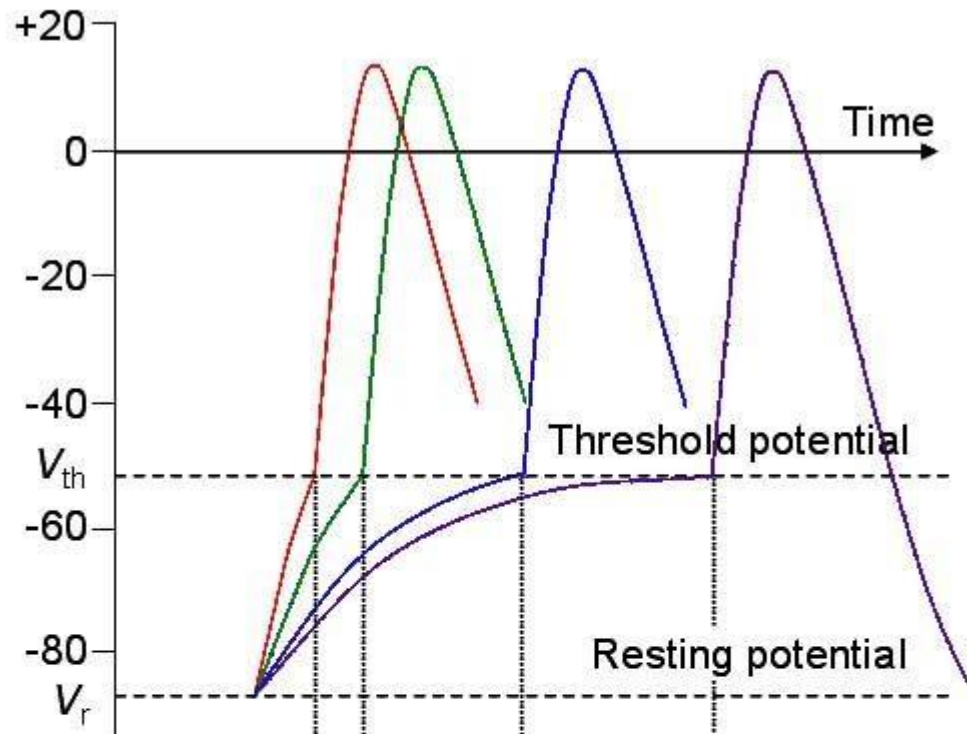
The excitability curve demonstrates the exact relationship between the strength and the duration of a stimulus. So, it is also called the strength—duration curve.



Characteristic Features of the Curve

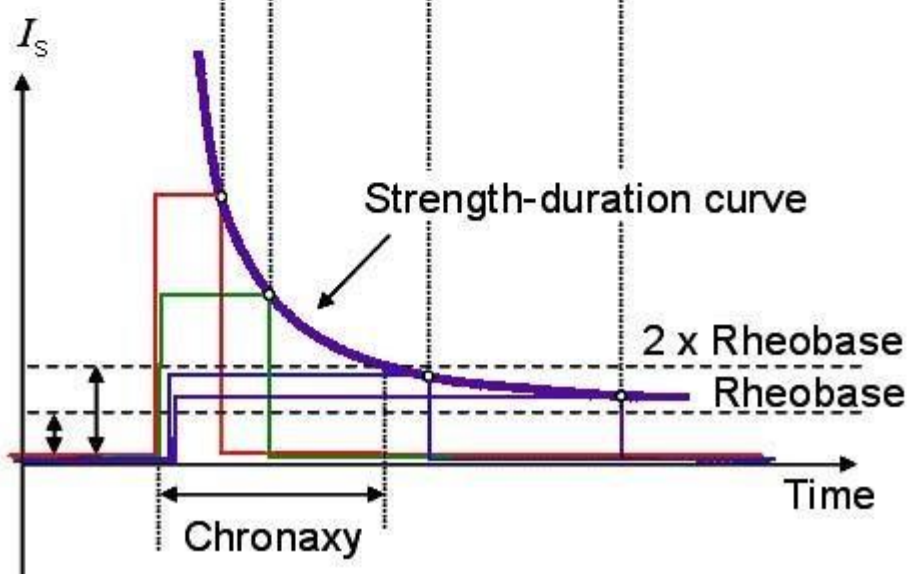
- 1. Rheobase:** This is the least possible, i.e. (minimum) strength (voltage) of stimulus which can excite the tissue.
- 2. Utilization time:** It is the minimum time required for a rheobasic strength (threshold strength) to excite the tissue.
- 3. Chronaxie:** It is the minimum time, at which a stimulus with double the rheobasic strength (voltage) can excite the tissue.

A V_m [mV]



**STRENGTH-DURATION
CURVE:**
*action potential
in excitability cell*

B





Characteristic Features of the Curve

Importance of Chronaxie

The value of chronaxie is used to compare the excitability in different tissues. The measurement of chronaxie determines the excitability of tissue. Longer the chronaxie, lesser is the excitability. Chronaxie in human skeletal muscles varies from 0.08 milliseconds to 0.32 milliseconds. In frog's skeletal muscle, it is about 3 milliseconds.

Chronaxie is 10 times more in skeletal muscles of infants than in the skeletal muscles of adults. It is longer in paralyzed muscles than the normal muscle. And, in progressive neural diseases, chronaxie is prolonged gradually.

Chronaxie is shortened by increased temperature and prolonged in cold temperature. Chronaxie is shorter in red muscles than in white muscle.



ELECTRICAL CHANGES DURING MUSCULAR CONTRACTION

I. RESTING MEMBRANE POTENTIAL

The potential difference between inside and outside of the cell under resting condition is known as resting membrane potential. There is negativity inside the muscle fiber in relation to the outside. This potential difference is constant and is called resting membrane potential.

II. ACTION POTENTIAL

When the muscle is stimulated, a series of changes occur in the membrane potential, which is called action potential.

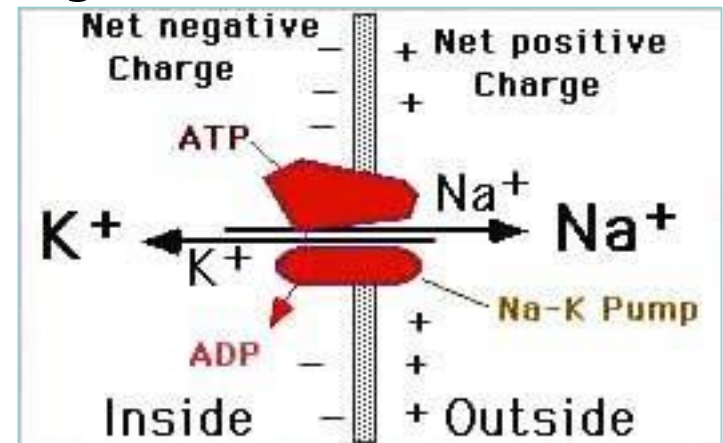
ELECTRICAL CHANGES DURING MUSCULAR CONTRACTION

I. RESTING MEMBRANE POTENTIAL

The potential difference between inside and outside of the cell under resting condition is known as resting membrane potential. There is negativity inside the muscle fiber in relation to the outside. This potential difference is constant and is called resting membrane potential.

In human nervous fibres, the resting membrane potential is -70 mV.

In human skeletal muscle, the resting membrane potential is -90 mV.

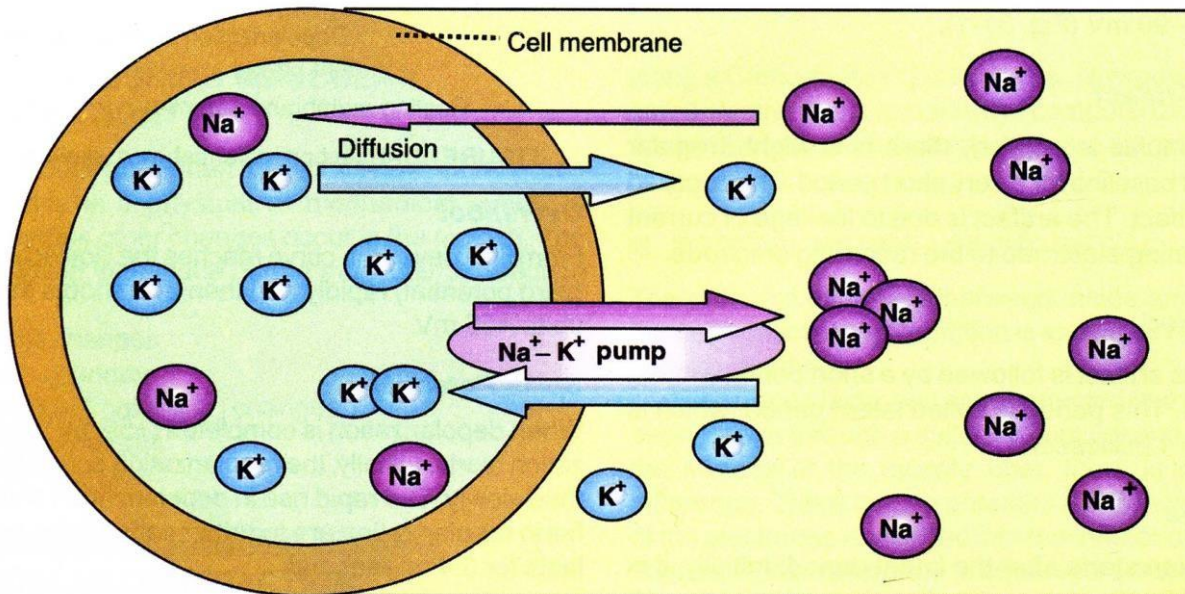


IONIC BASIS OF ELECTRICAL EVENTS

Resting Membrane Potential - positivity outside and more negativity inside the cell.

The ionic imbalance is produced mainly by two transport mechanisms in the cell membrane.

1. Sodium-potassium pump and
2. Selective permeability of cell membrane.

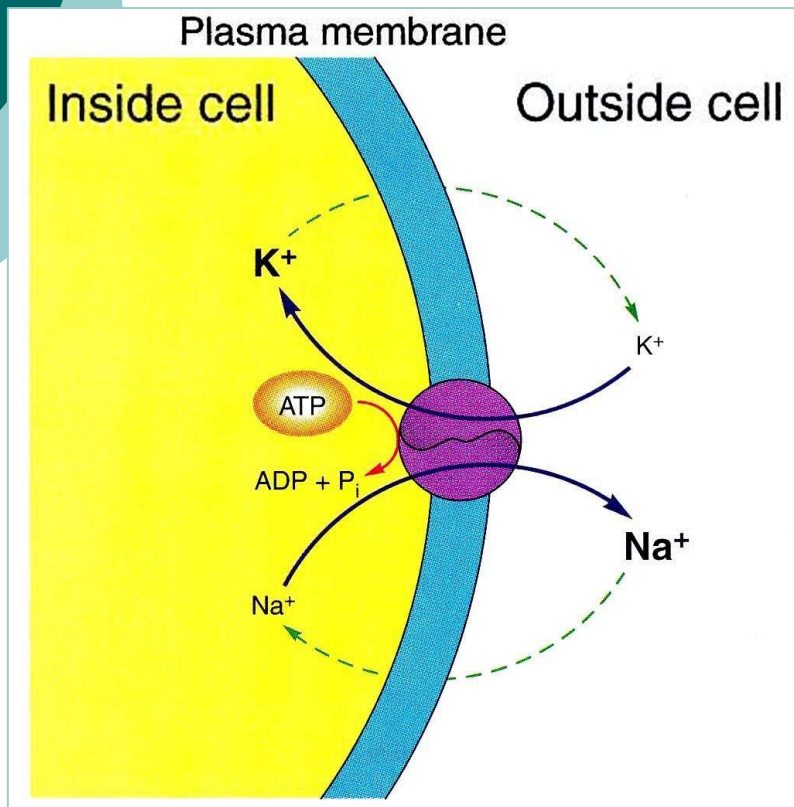


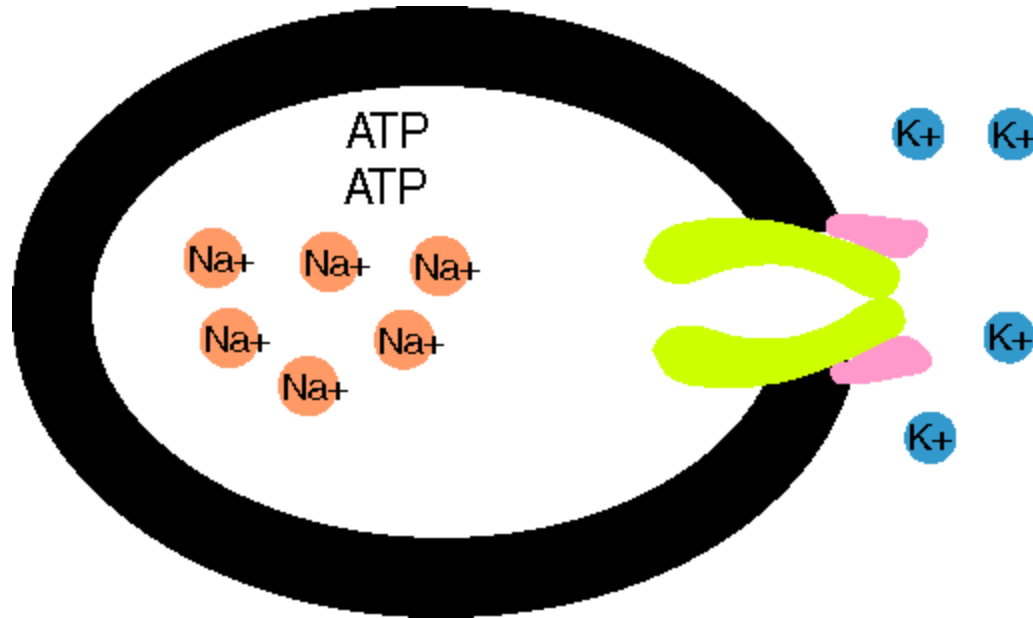
IONIC BASIS OF ELECTRICAL EVENTS

1. Sodium-potassium Pump.

This moves **three sodium ions** out of the cell and **two potassium ions** inside the cell by using energy from ATP. This leads to negativity inside and positivity outside the cell.

Development of resting membrane potential by Sodium-potassium (Na^+/K^+) pump and diffusion of ions. Na^+/K^+ pump actively pumps three Na^+ ions out and two K^+ into the cell. However, the diffusion of K^+ out of the cell is many times greater than the diffusion of Na^+ ions inside the cell because many of the K^+ leak channels are opened and many of the Na^+ leak channels are closed.





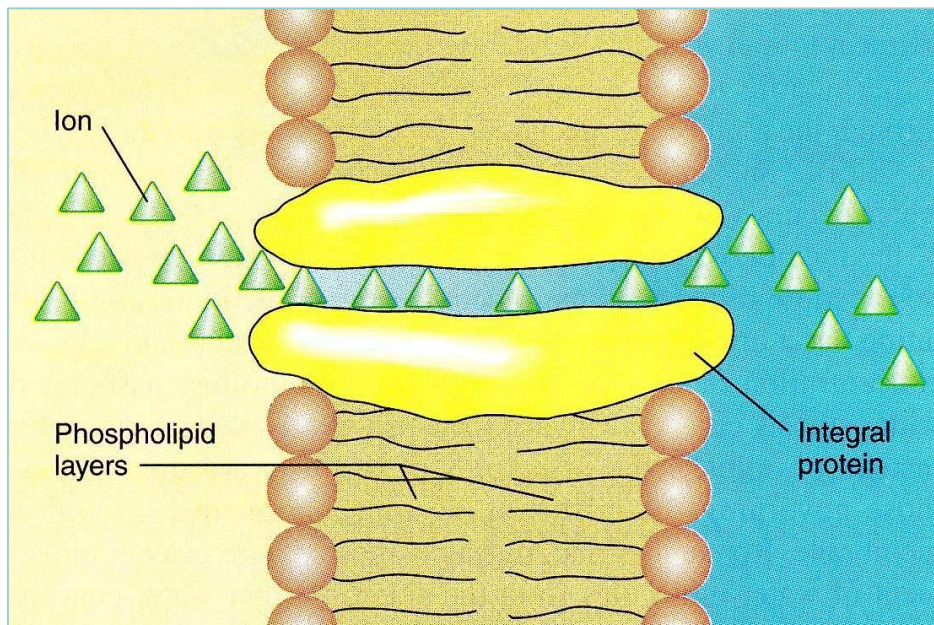
The sodium-potassium pump (Na⁺-K⁺ ATPase) maintains concentration gradients of both sodium (higher outside the cell) and potassium (higher inside the cell).

IONIC BASIS OF ELECTRICAL EVENTS

2. *Selective Permeability of Cell Membrane.*

The sodium (Na^+) and chloride (Cl^-) ions are more outside and potassium (K^+) ions are more inside.

Inorganic ions (such as Na^+ and K^+) are able to penetrate through pores within integral proteins that span the thickness of the double phospholipid layers.

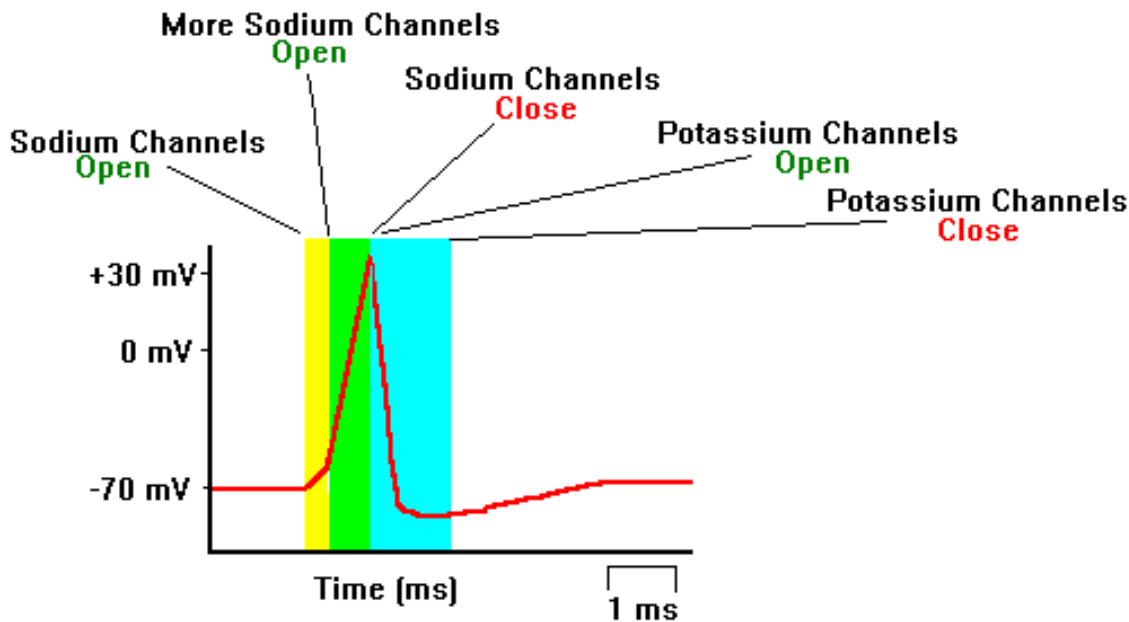


Cell membrane is about twenty times more permeable to potassium (K^+) than to sodium (Na^+); consequently, K^+ diffuses much more rapidly than Na^+ .

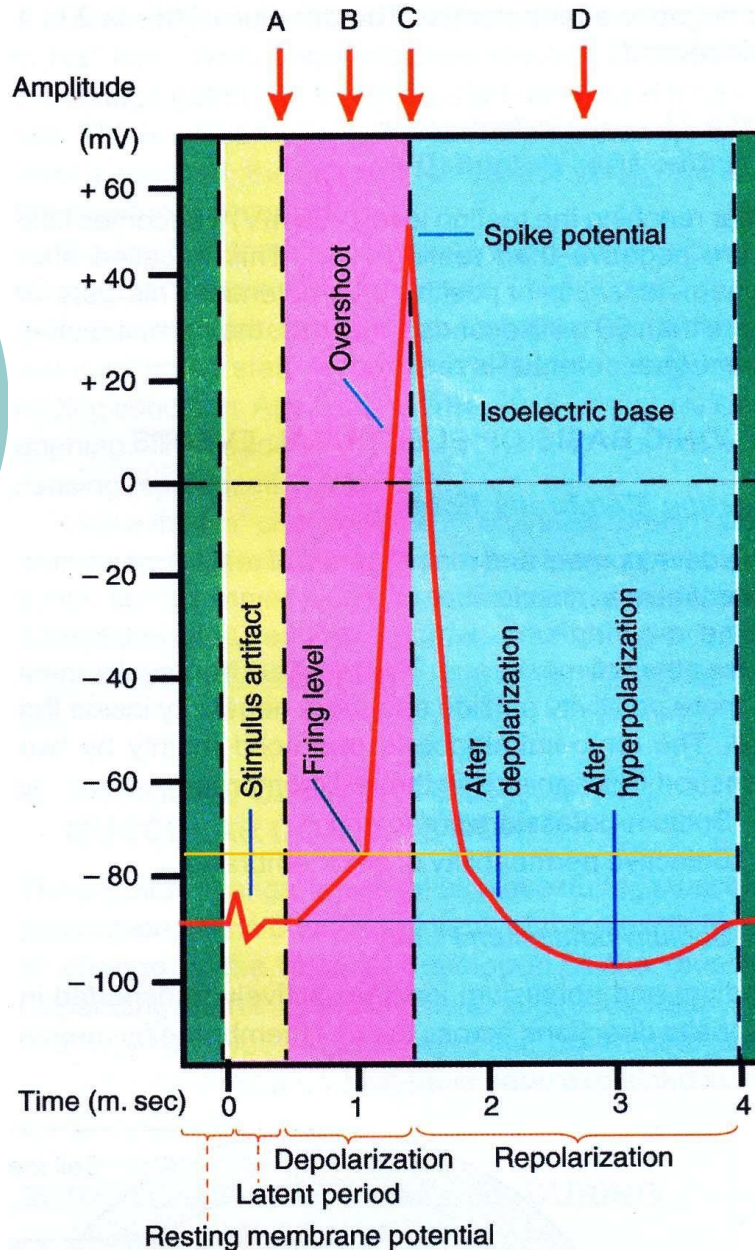
II. ACTION POTENTIAL

When the muscle is stimulated, a series of changes occur in the membrane potential, which is called action potential. The action potential occurs in two phases:

- a) Depolarization and
- b) Repolarization



II. ACTION POTENTIAL



Action potential in a skeletal muscle

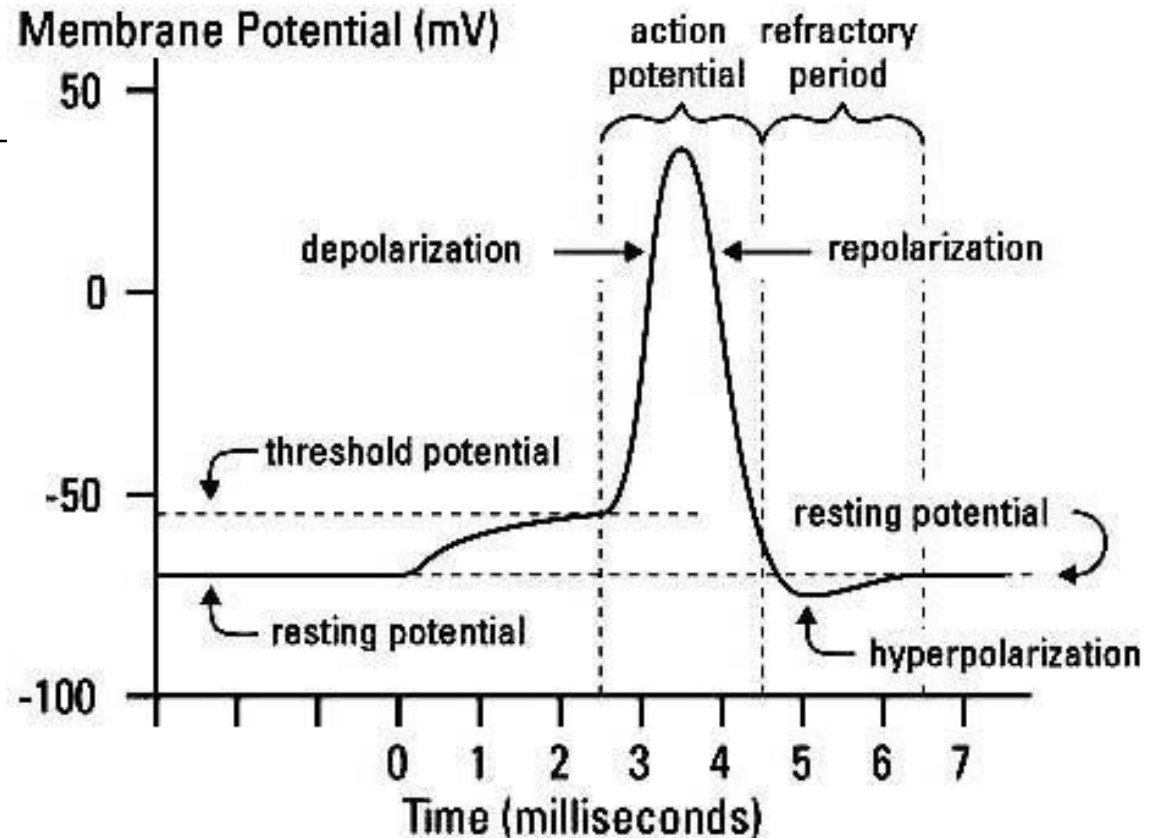
Depolarization

When the impulse reaches the muscle, the polarized condition (-90 mV) is altered. The interior of the muscle becomes positive and outside becomes negative. This condition is called depolarization.

Repolarization

Within a short time, the muscle obtains the resting membrane potential once again. Interior of the muscle becomes negative and outside becomes positive. So, the polarized state of the muscle is re-established. This process is called repolarization.

ACTION POTENTIAL CURVE



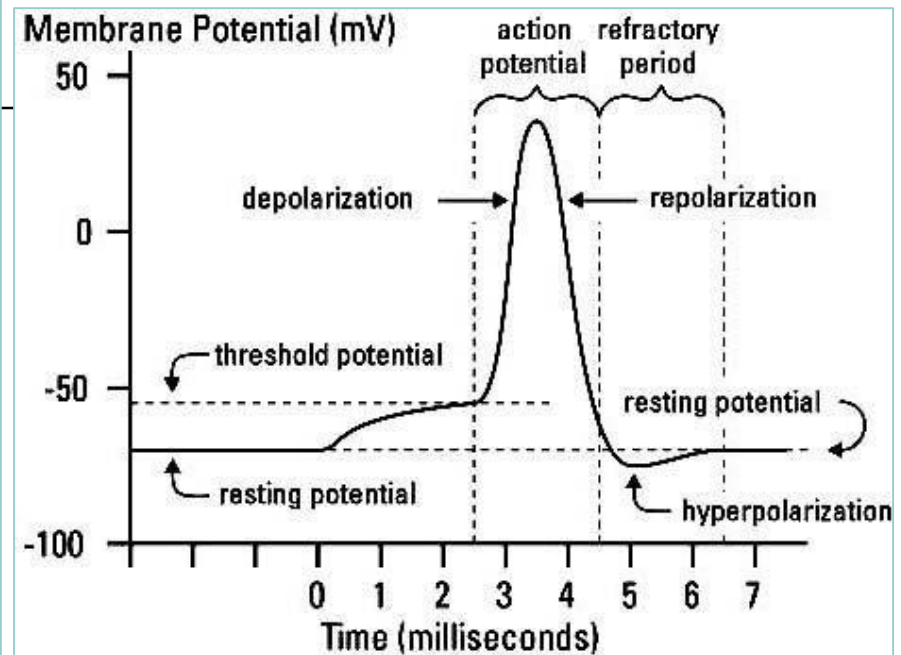
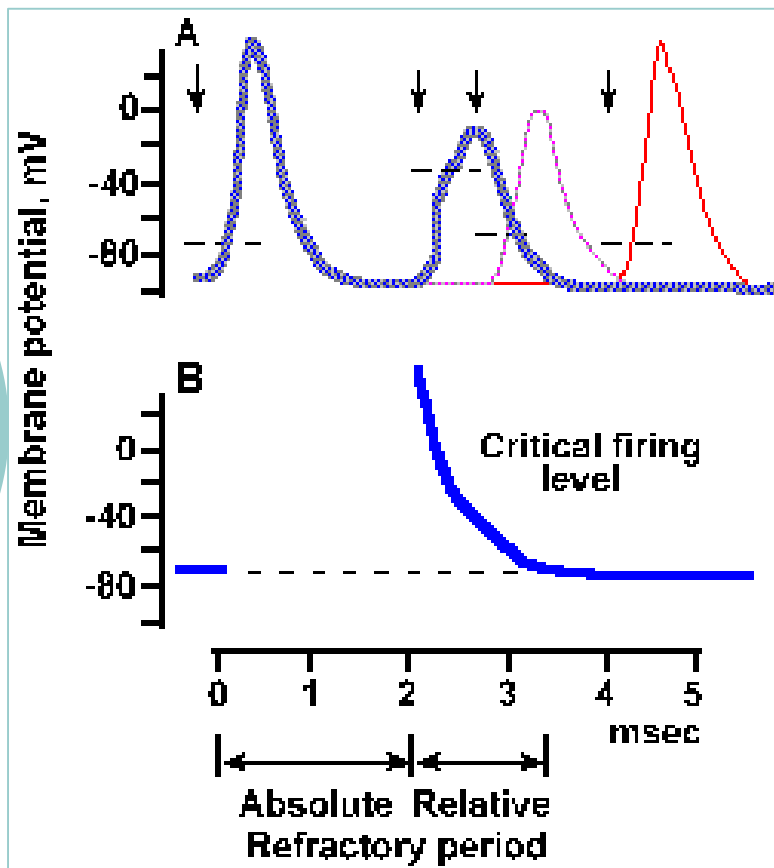
Stimulus Artifact

When a stimulus is applied, there is a slight irregular deflection of baseline for a very short period. This is called stimulus artifact or local potential.

Latent Period

The stimulus artifact is followed by a short period without any change. This period is called latent period, which is about 0.5 to 1 millisecond.

ACTION POTENTIAL CURVE



Firing Level (Threshold Potential, Critical Depolarization Level)

Depolarization starts after the latent period. The point at which, the rate of depolarization increases is called firing level or critical depolarization level.

Overshoot

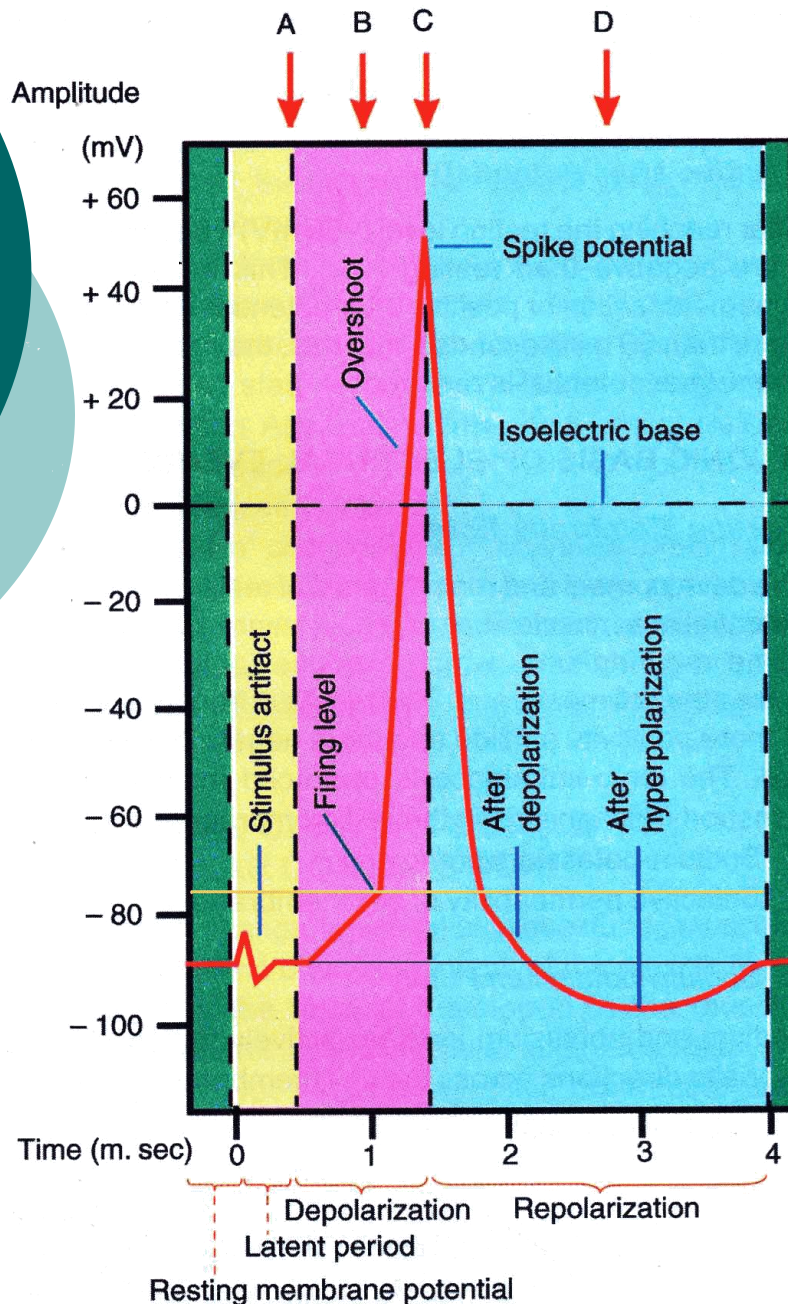
From firing level, the curve reaches the isoelectric potential (zero potential) rapidly and then overshoots the zero line up to +55 mV (**spike potential**).

ACTION POTENTIAL CURVE

Afterpotential.

Then **After Hyperpolarization** (or positive after Potential) and **After Depolarization** (or negative after Potential) occur.

After reaching the resting level (-90 mV) it becomes little more negative than resting level. This is called after hyperpolarization or positive after potential. This lasts for more than 50 milliseconds. After this, the normal resting membrane potential is restored.



During the onset of **depolarization**, there is slow influx of Na^+ ions. When depolarization reaches 7 to 10 mV, the voltage gated Na^+ channels start opening at a faster rate. This is called Na^+ channel activation. When the firing level is reached, the influx of Na^+ ions is very great and the **overshoot** occurs.

But the Na^+ transport is short lived. This is because of rapid inactivation of Na^+ channels. Thus, the Na^+ channels open and close quickly. At the same time, the K^+ channels start opening. This leads to efflux of K^+ ions out of the cell, causing **repolarization** thereby.

Hyperpolarization reason is excessive efflux of K^+ ions through opened K^+ channels out of the cell.

REFRACTORY PERIOD

Refractory period is the period at which the muscle does not show any response to a stimulus.

Types of Refractory Period :

Refractory period is of two types

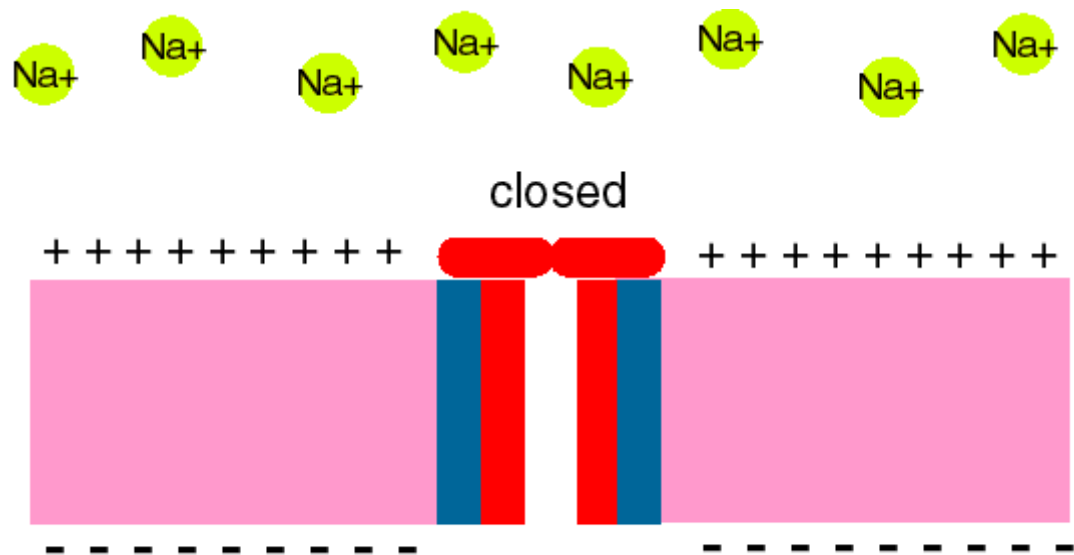
- 1. *Absolute refractory period*:** is the period during which the muscle does not show any response at all, whatever maybe the strength of stimulus.
- 2. *Relative refractory period*.** This is the period, during which the muscle shows some response if the strength of stimulus is increased to maximum.

Refractory Period in Skeletal Muscle

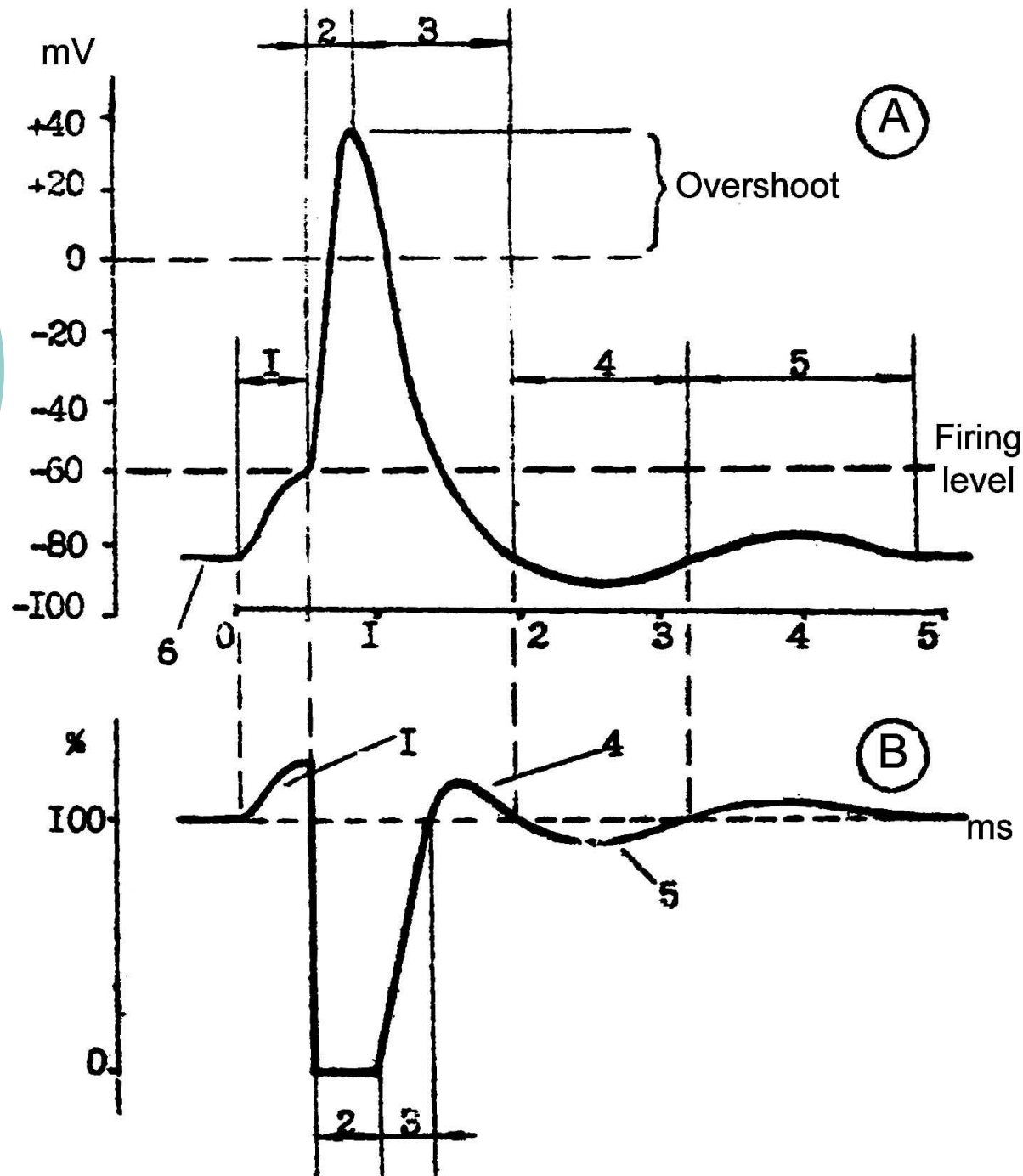
In skeletal muscle, the absolute refractory period falls during first half of latent period (0.005 sec). And, relative refractory period extends during second half of latent period (0.005 sec). Totally, it is 0.01 sec.

Drugs That Affect Neural Control of Skeletal Muscles

| Drug | Origin | Effects |
|------------------------|---|--|
| Botulinum toxin | Produced by <i>Clostridium botulinum</i> (bacteria) | Inhibits release of acetylcholine (Ach) |
| Curare | Resin from a South American tree | Prevents interaction of Ach with the postsynaptic receptor protein |
| α -Bungarotoxin | Venom of <i>Bungarus</i> snakes | Binds to Ach receptor proteins and prevents Ach from binding |
| Saxitoxin | Red tide (<i>Gonyaulax</i>) algae | Blocks voltage-gated Na ⁺ channels |
| Tetrodotoxin | Pufferfish | Blocks voltage-gated Na ⁺ channels |
| Nerve gas | Artificial | Inhibits acetylcholinesterase in postsynaptic membrane |
| Neostigmine | Nigerian bean | Inhibits acetylcholinesterase in postsynaptic membrane |
| Strychnine | Seeds of an Asian tree | Prevents IPSPs in spinal cord that inhibit contraction of antagonistic muscles |



REFRACTORY PERIOD



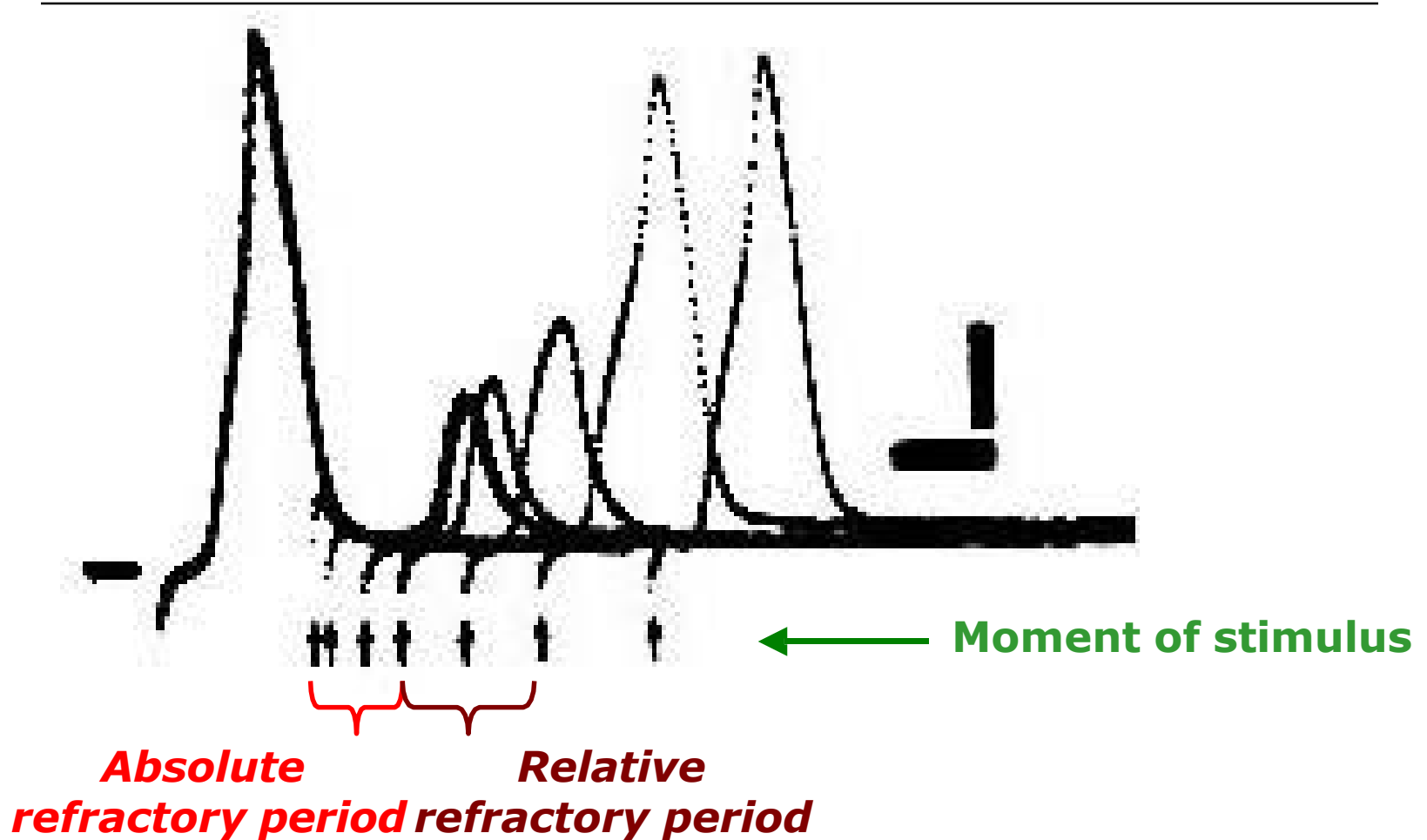
A)

1 – latent period,
2 – depolarization,
3 – repolarization,
4 – after
hyperpolarization,
5 – after
depolarization,
6 – resting level.

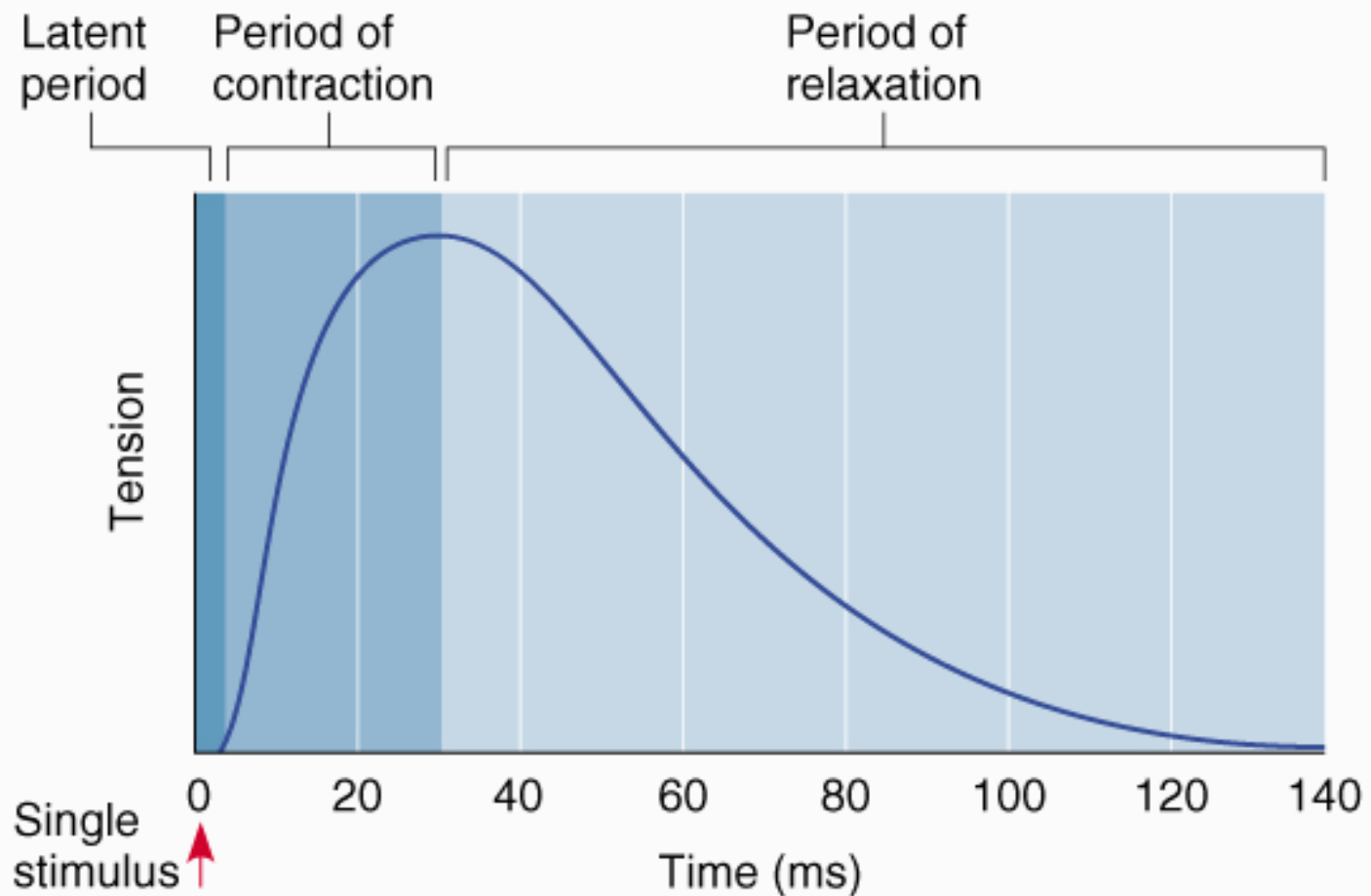
B)

1, 4 – supernormal
period,
2 – absolute
refractory period,
3 – relative
refractory period,
5 – subnormal
period.

REFRACTORY PERIOD (ACTION POTENTIAL)

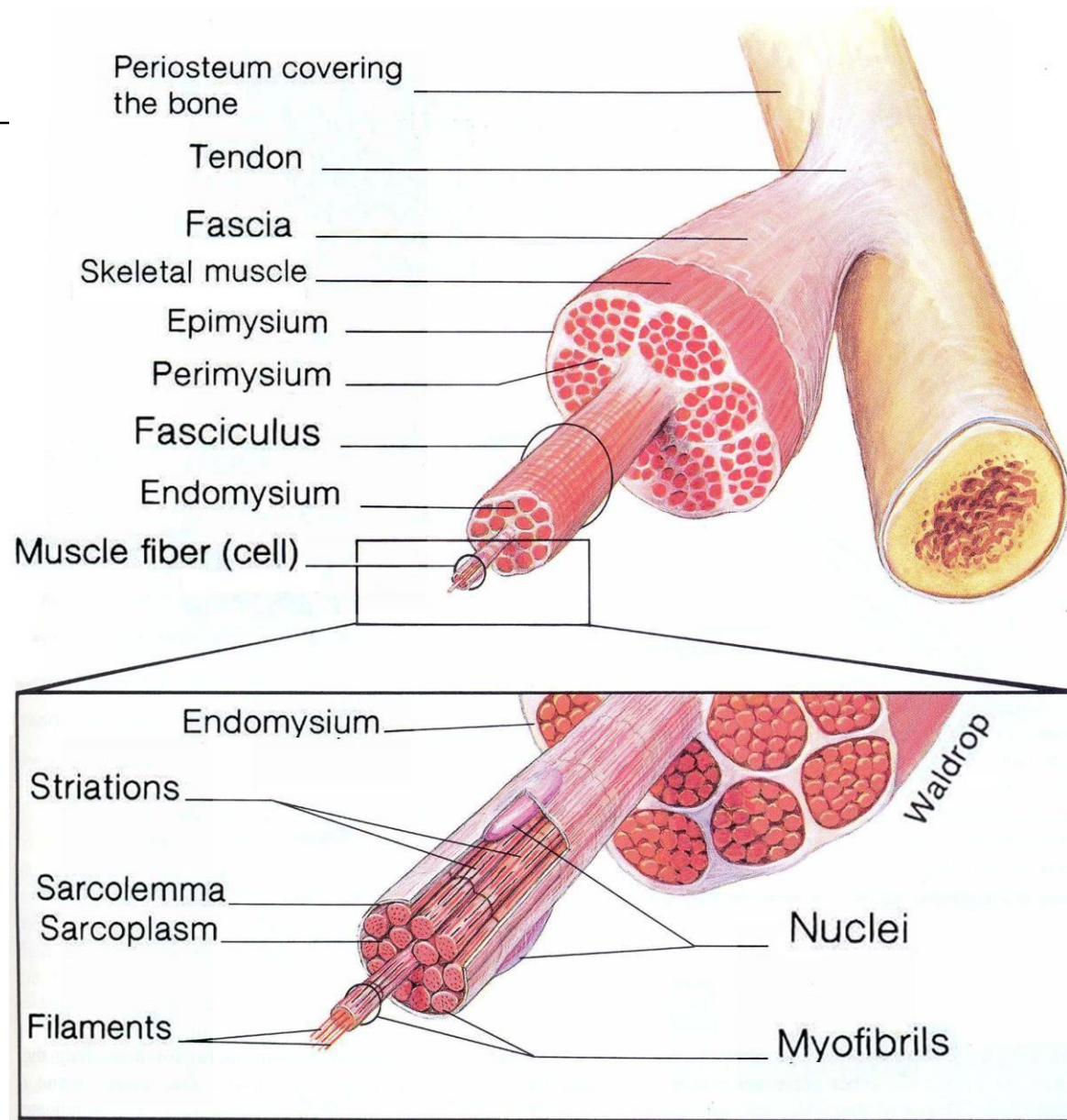


SIMPLE MUSCLE CONTRACTION (TWITCH)



(a)

SKELETAL MUSCLE STRUCTURE



SKELETAL MUSCLE STRUCTURE

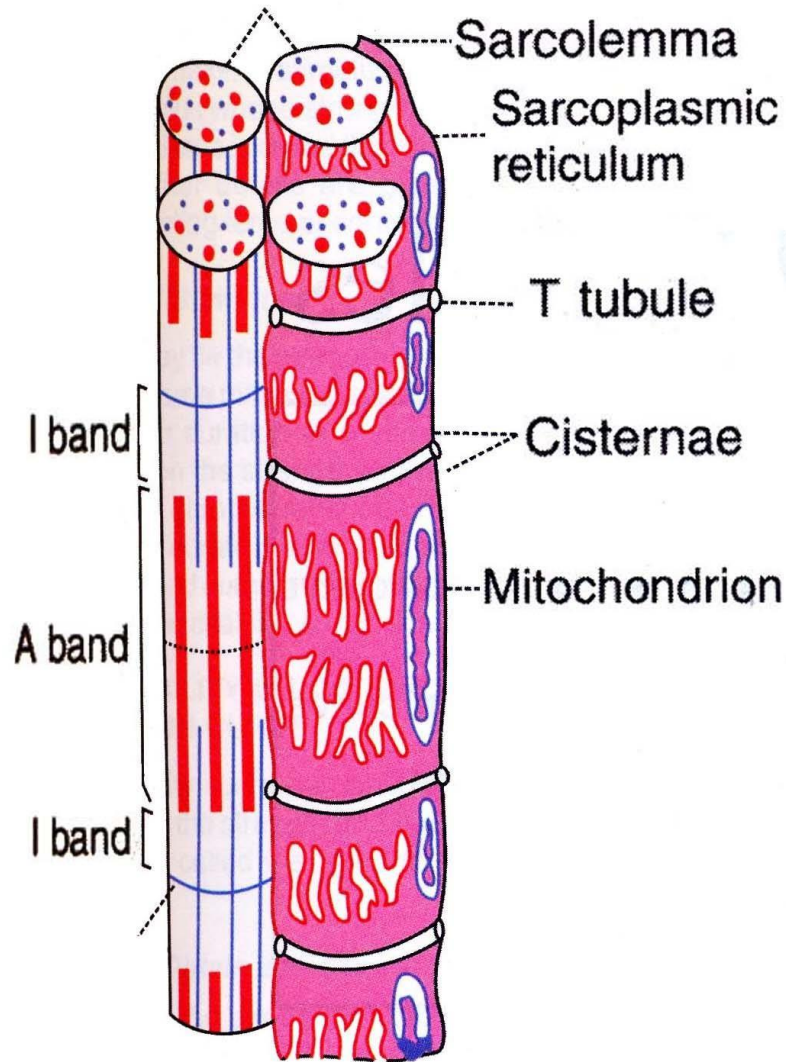
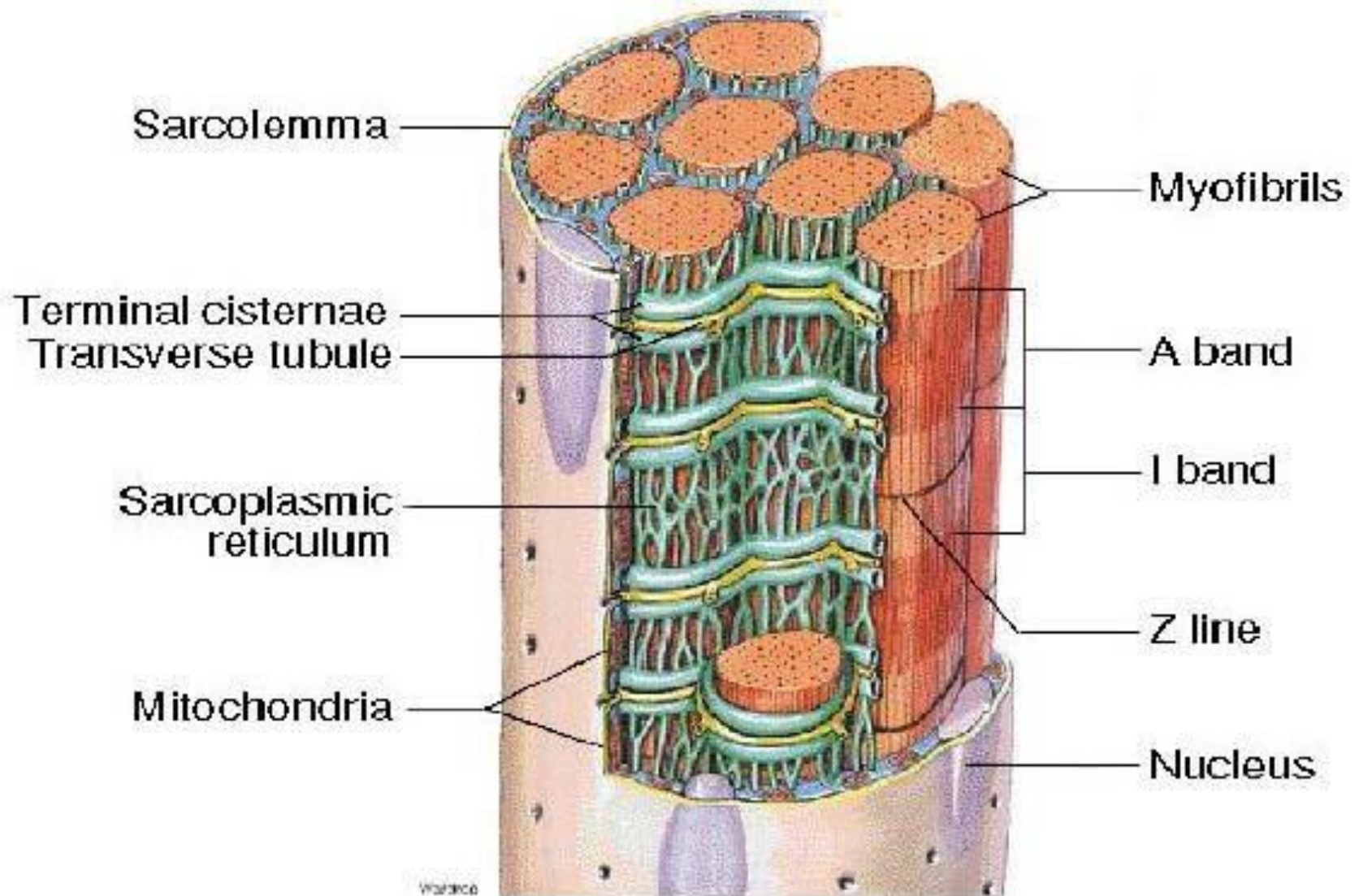
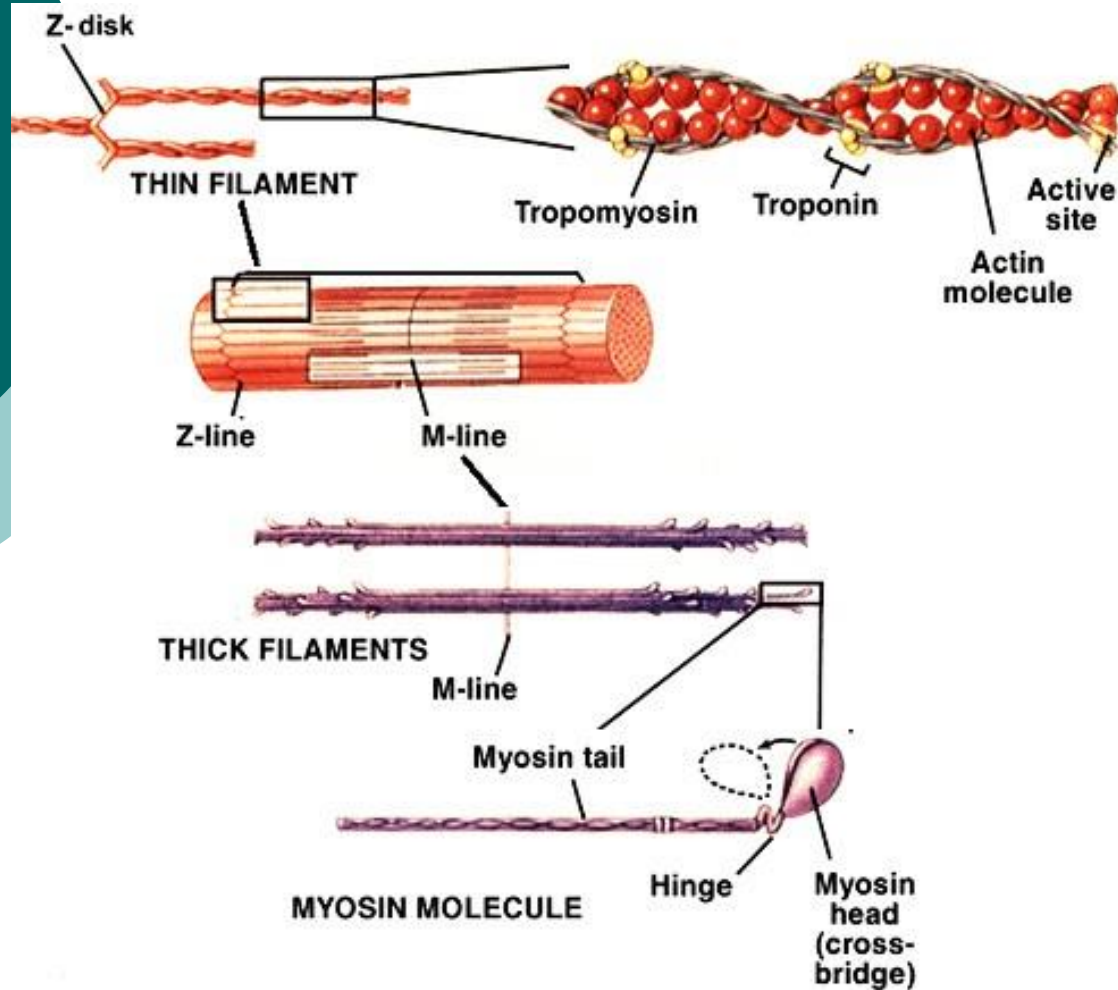


Diagram showing the relation between sarcotubular system and parts of sarcomere.

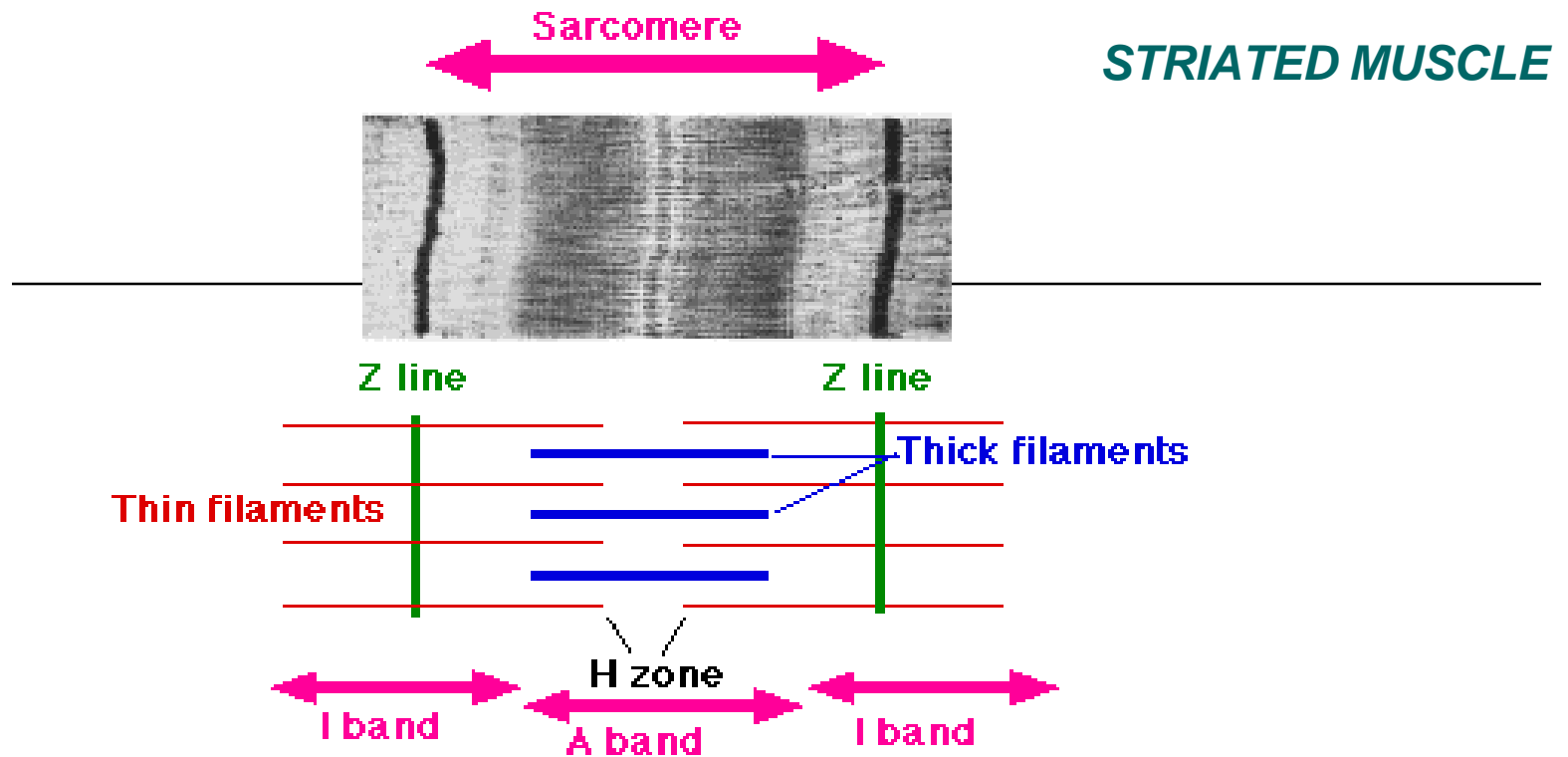
Only few microfilaments are shown in the miofibril drawn on the right side of the diagram.

Sarcoplasmic reticulum





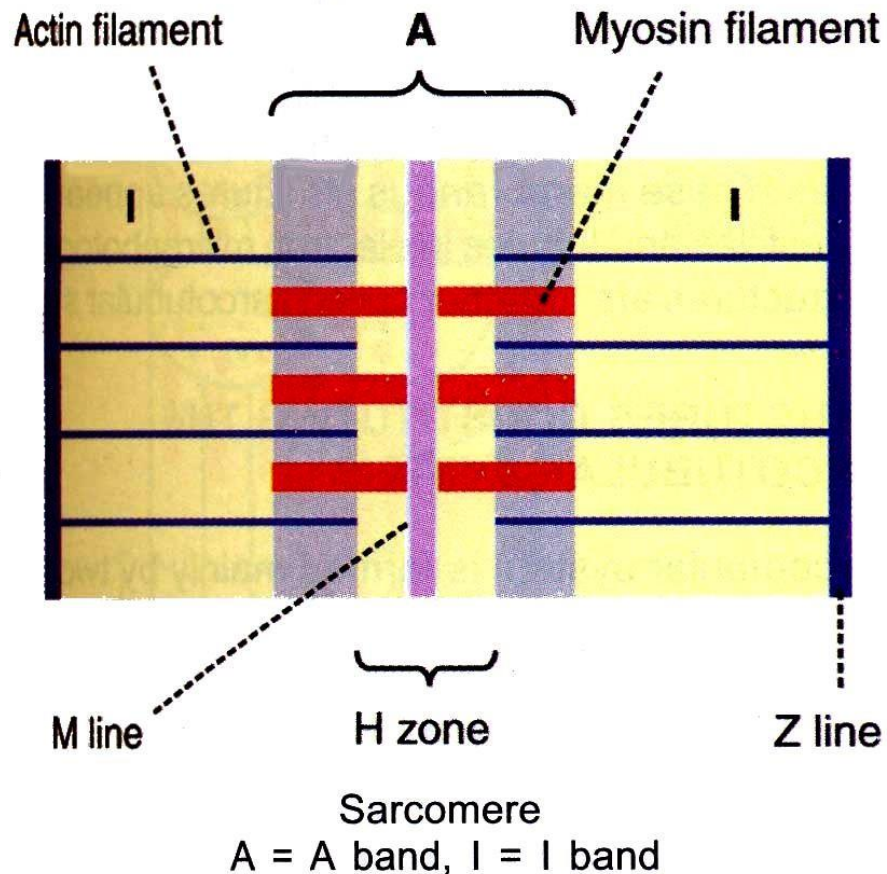
In each sarcomere, thin myofilaments extend in from each end. Thick myofilaments are found in the middle of the sarcomere. Under microscopy, the ends of a sarcomere (where only thin myofilaments are found) appear lighter than the central section (which is dark because of the presence of the thick myofilaments). Thus, a myofibril has alternating light and dark areas because each consists of many sarcomeres lined up end-to-end.



This is why skeletal muscle is called STRIATED MUSCLE (i.e., the alternating light and dark areas look like stripes or striations). The light areas are called the I-BANDS and the darker areas the A-BANDS. Near the center of each I-BAND is a thin dark line called the Z-LINE. The Z-LINE is where adjacent sarcomeres come together.

Thus, a **sarcomere** is the area between Z-lines.

SKELETAL MUSCLE STRUCTURE



Sarcomere is the **structural and functional unit** of the skeletal muscle. In the middle of A-band, there is a light area called H-ZONE. In the middle of H-zone lies the middle part of myosin filament. This is called W-line.

I-BAND is divided into two equal portions means of a narrow line called Z-line.

MUSCLE PROTEINS

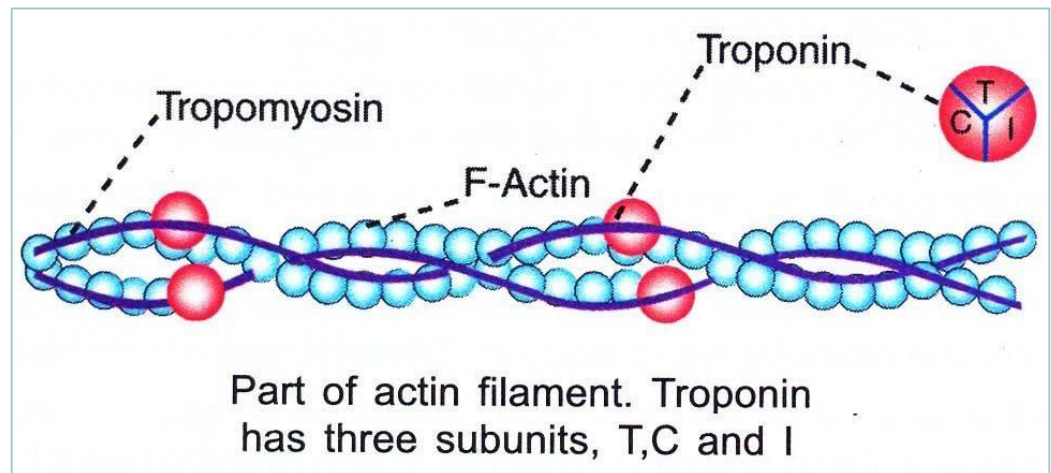
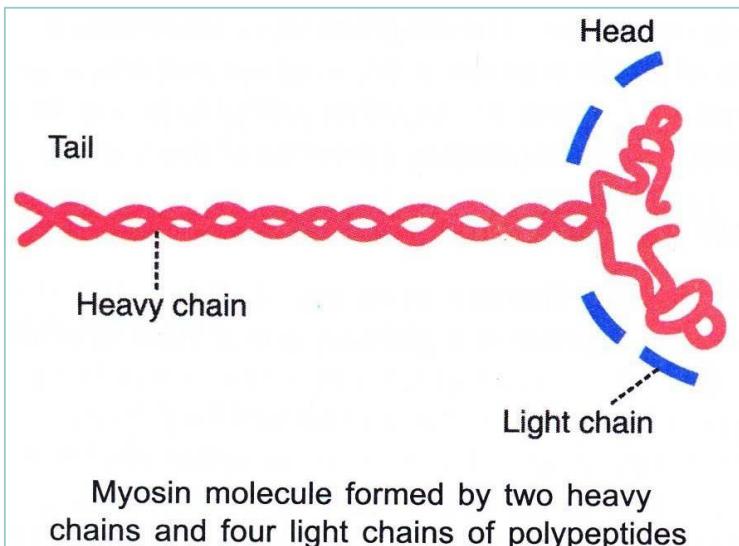
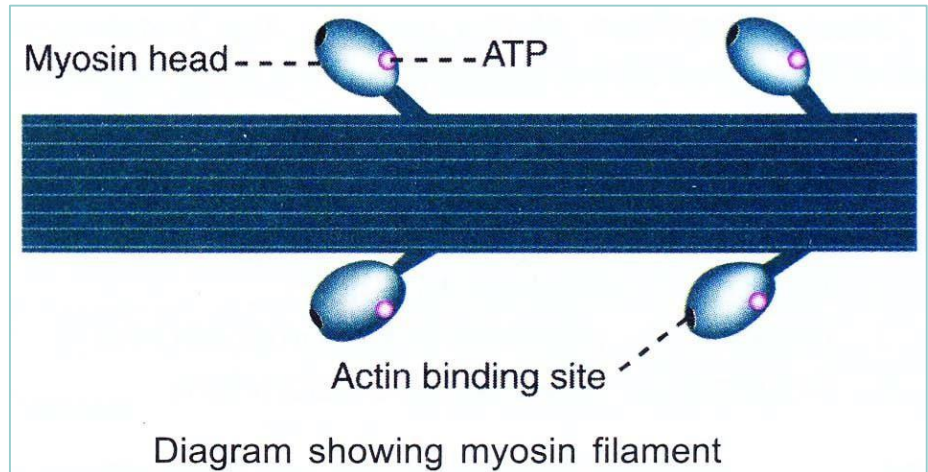
Proteins presents in the muscle:

I. Effectory:

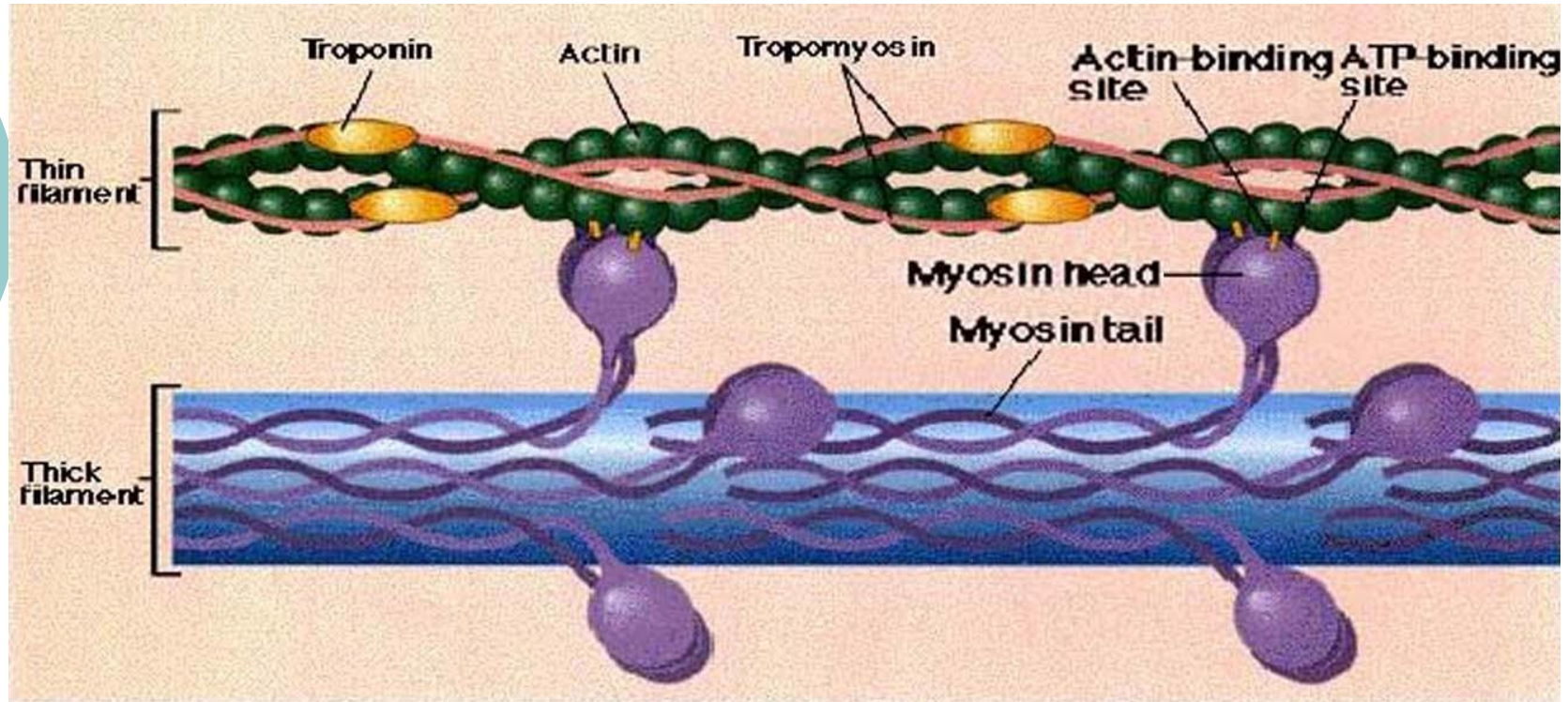
- 1) Myosin
- 2) Actin.

II. Regulatory:

- 1) Tropomyosin
- 2) Troponin



MUSCLE PROTEINS



Thick myofilaments are composed of a protein called MYOSIN. Each myosin molecule has a tail plus a head that projects out from the core of the filament. These myosin heads are also commonly known as CROSS-BRIDGES.

The MYOSIN HEAD has several important characteristics:

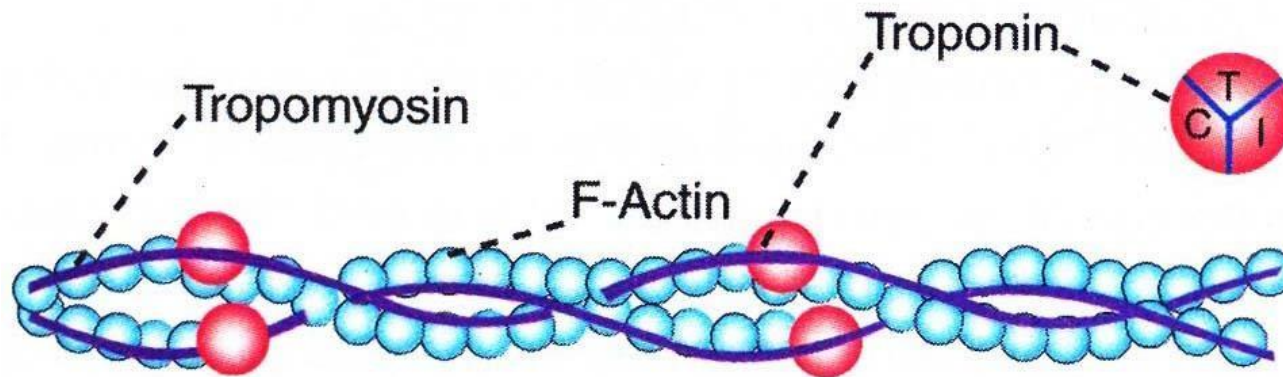
it has ATP-binding sites into which fit molecules of ATP.

it has ACTIN-binding sites into which fit molecules of ACTIN.

it has a "hinge" at the point where it leaves the core of the thick myofilament. This allows the head to swivel back and forth, and the "swivelling" causes muscle contraction.

MUSCLE PROTEINS

Thin myofilaments are composed of 3 types of protein: ACTIN, TROPONIN, and TROPOMYOSIN.



Part of actin filament. Troponin has three subunits, T,C and I

MUSCLE PROTEINS

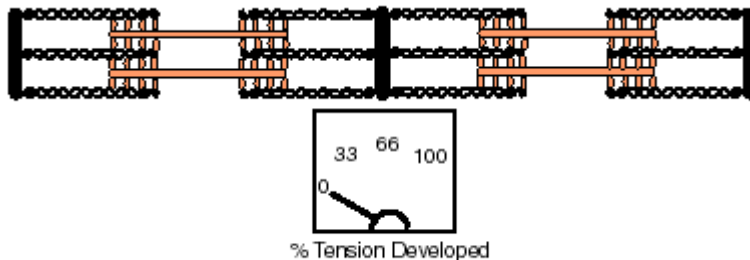
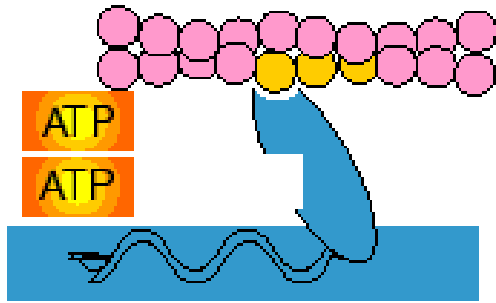
These 3 proteins play a key role in muscle contraction:

- ACTIN - when actin combines with MYOSIN HEAD the ATP associated with the head breaks down into ADP. This reaction released energy that causes the MYOSIN HEAD to SWIVEL.
- TROPOMYOSIN - When MYOSIN HEADS remain in contact with TROPOMYOSIN muscle remains relaxed.
- TROPONIN molecules have binding sites for calcium ions. When a calcium ion fills this site it causes a change in the shape and position of TROPONIN. And, when TROPONIN shifts, it pulls the TROPOMYOSIN to which it is attached. When TROPOMYOSIN is moved, the MYOSIN HEAD that was touching the tropomyosin now comes in contact with an underlying ACTIN molecule.

Muscle contraction

- 1 - Because skeletal muscle is voluntary muscle, contraction requires a nervous impulse. So, step 1 in contraction is when the impulse is transferred from a neuron to the SARCOLEMMA of a muscle cell.
- 2 - The impulse travels along the SARCOLEMMA and down the T-TUBULES and then to the SARCOPLASMIC RETICULUM (SR).
- 3 – impulse open the calcium gates in the membrane of the SR. As a result, CALCIUM diffuses out of the SR and among the myofilaments.
- 4 - Calcium fills the binding sites in the TROPONIN molecules.
- 5 - Movement of TROPOMYOSIN permits the MYOSIN HEAD to contact ACTIN.
- 6 - Contact with ACTIN causes the MYOSIN HEAD to swivel.

Muscle contraction



- 7 - During the swivel, the MYOSIN HEAD is firmly attached to ACTIN. So, when the HEAD swivels it pulls the ACTIN (and, therefore, the entire thin myofilament) forward. (Many MYOSIN HEADS are swivelling simultaneously, and their collective efforts are enough to pull the entire thin myofilament).
- 8 - At the end of the swivel, ATP fits into the binding site on the cross-bridge and this breaks the bond between the cross-bridge (myosin) and actin. The MYOSIN HEAD then swivels back and ATP breaks down to ADP and P then the cross-bridge again binds to an actin molecule.
- 9 - As a result, the HEAD is once again bound firmly to ACTIN. HEAD will bind to a different ACTIN molecule because it swivelled back. Once the HEAD is attached to ACTIN, the cross-bridge again swivels, **so step 7 is repeated.**

Muscle contraction

Skeletal muscle relaxes when the nervous impulse stops. The CALCIUM PUMP in the membrane will now transport the calcium back into the SR.

So, calcium is the "switch" that turns muscle "on and off" (contracting and relaxing).

When a muscle is used for an extended period, ATP supplies can diminish. As ATP concentration decreases, the MYOSIN HEADS remain bound to actin and can no longer swivel. This decreasing in ATP levels in a muscle causes MUSCLE FATIGUE even if calcium level is sufficient.

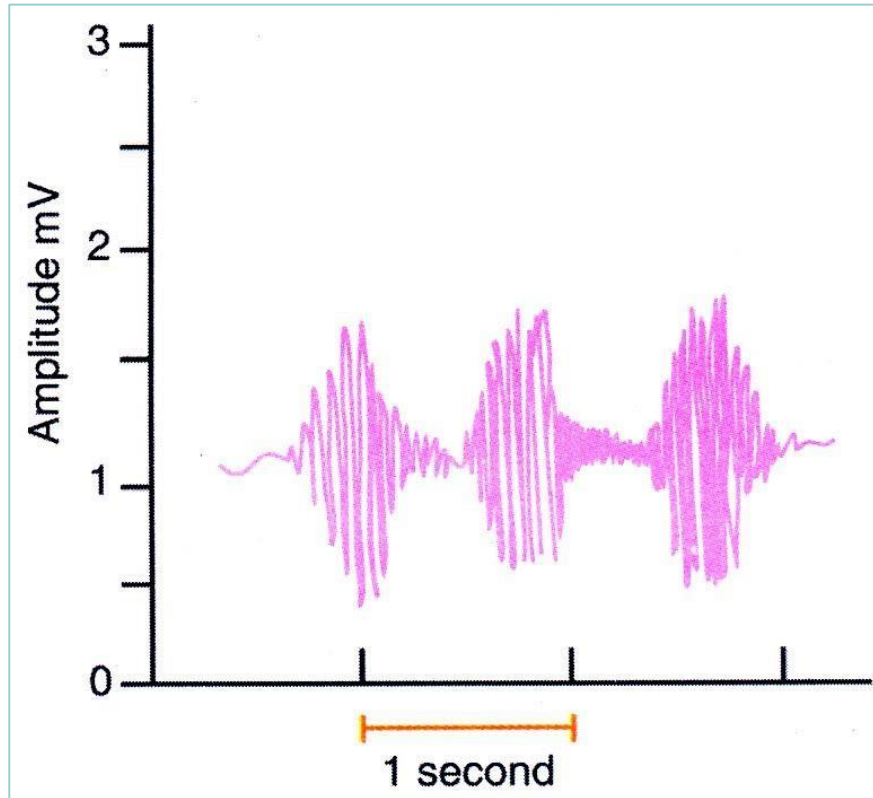
Electromyography

Electromyography is study of electrical activity of the muscle. The record of the electrical activity of the muscle is called Electromyogram (EMG).

Two types of electrodes are used for recording the electrical activities of the muscle:

1. The surface or skin electrodes for studying the activity of a muscle.
2. The needle electrodes for studying the electrical activity of a single motor unit.

Electromyography



3 main types:

- 1) local;
- 2) interferential;
- 3) stimulatory.

Motor unit is the structural basis for electromyogram. The electrical potential developed by the activation of one motor unit is called motor unit potential. This lasts for 5 to 8 milliseconds and has amplitude of 0.5 mV. Mostly it is monophasic (see figure).

Electrical potential recorded from the whole muscle shows smaller potentials if the force of contraction is less. When force is increased, due to the recruitment of more and more number of motor neurons, larger potentials are obtained.

Practical importance:

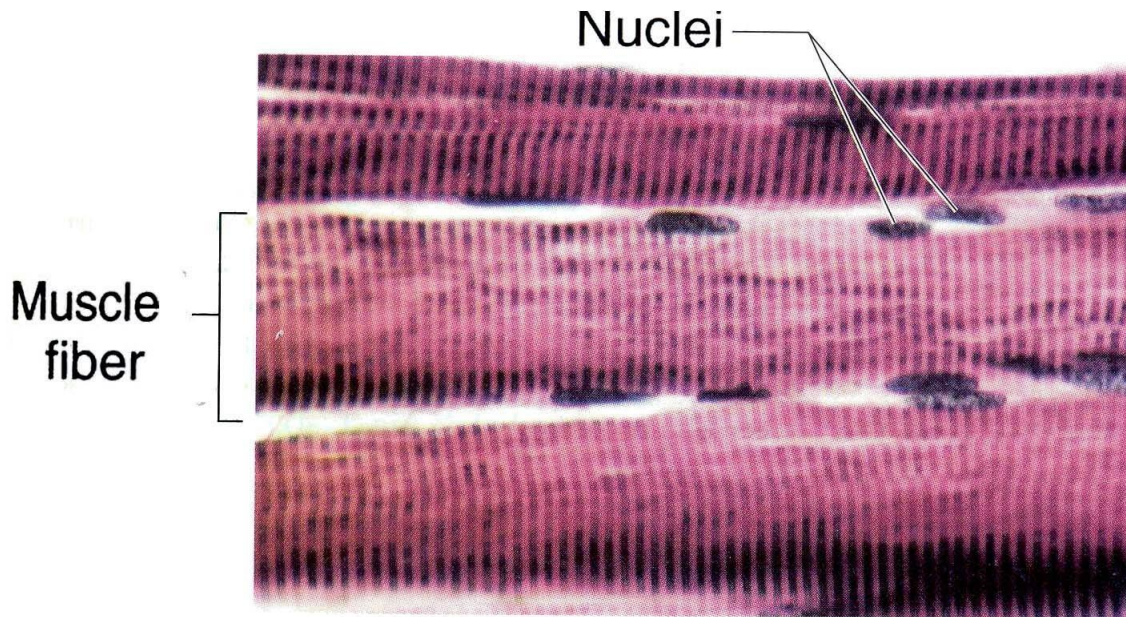
Electromyogram is useful in the diagnosis of neuro-muscular diseases.

1. Motor neuron lesions;
2. Peripheral nerve injury;
3. Myotonia and
4. Myasthenia gravis.

Besides neurology, EMG gives useful information in traumatology, orthopedics, pediatrics, dentistry.

Properties of Skeletal Muscles

1. EXCITABILITY
2. CONTRACTILITY
3. MUSCLE TONE



The appearance of skeletal muscle fibers through a light microscope.



CONTRACTILITY

The skeletal muscle gives response to a stimulus in the form of contraction.

TYPES OF CONTRACTION

- i. Isotonic contraction and
- ii. Isometric contraction

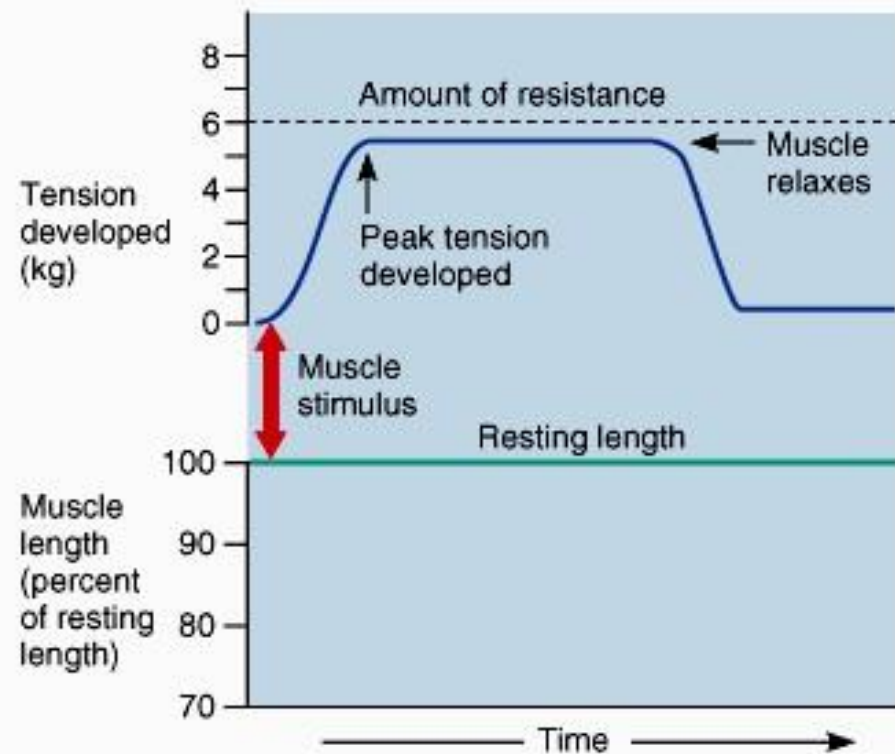
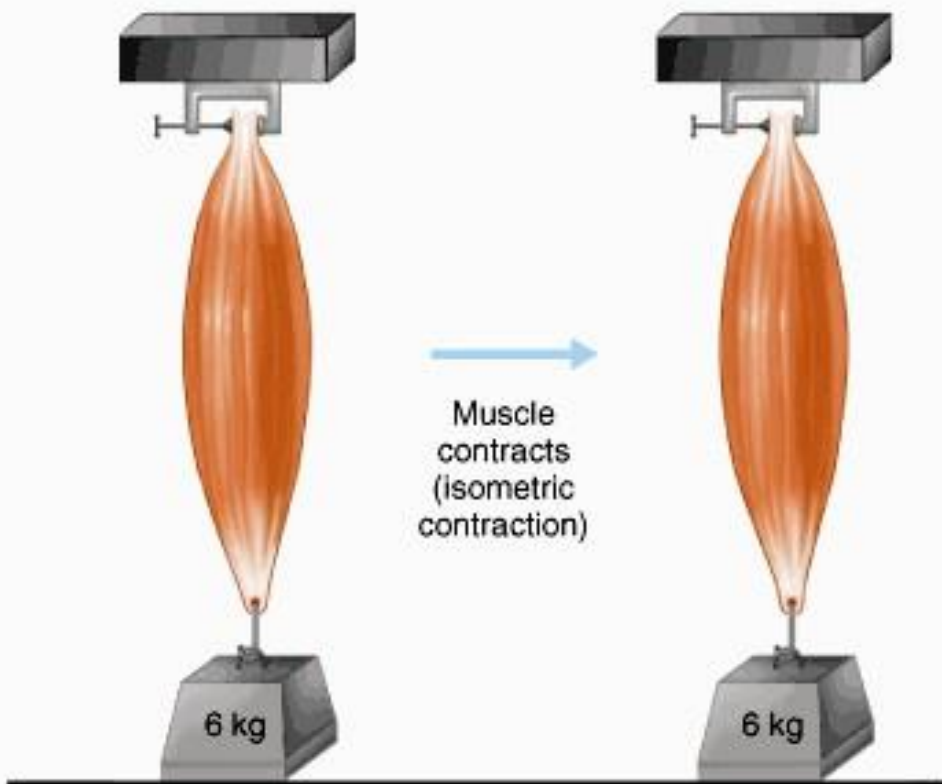
Isotonic Contraction

This is the type of contraction, in which the tension remains the same whereas the change occurs in the length of the muscle fiber. Example is the simple flexion of arm.

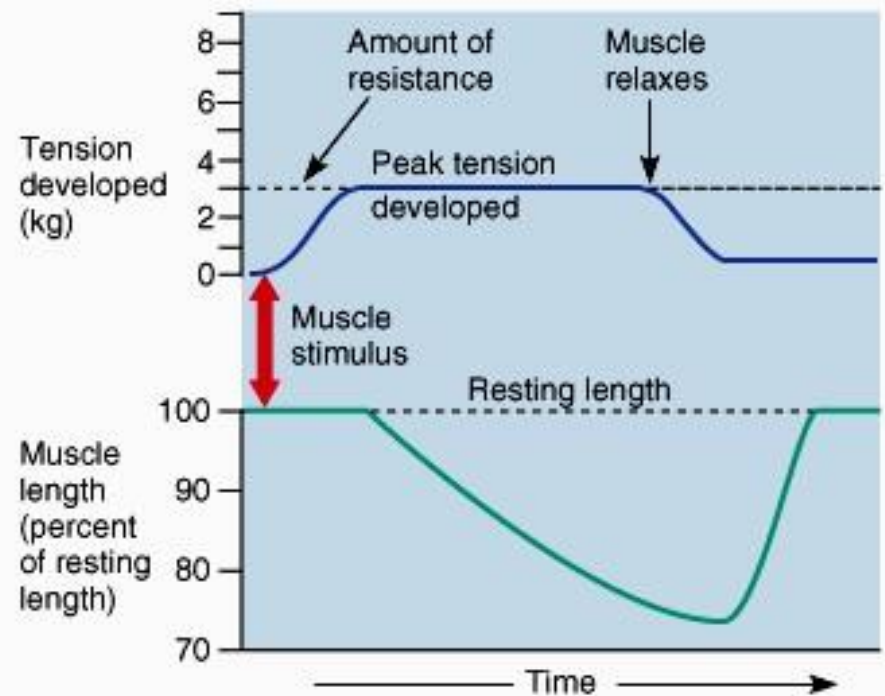
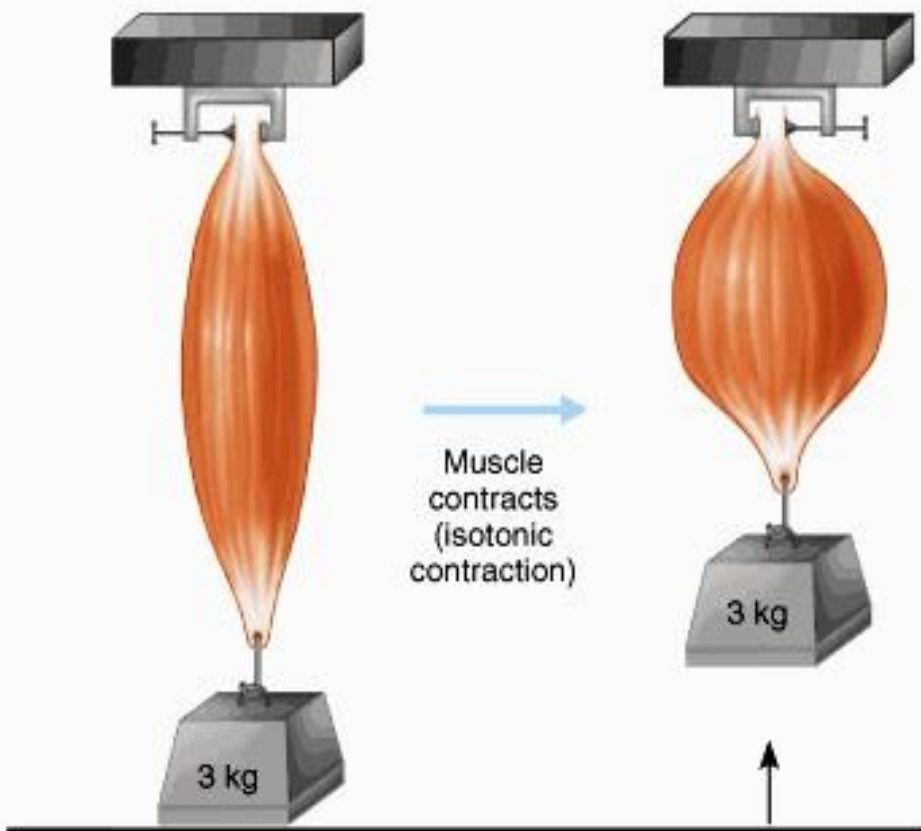
Isometric Contraction

In this type, the length of muscle fibers remains the same and the tension is increased. Example is pulling any heavy object.

Auxotonic Contraction is a combination of isotonic and isometric contraction. The example is tongue contractions.



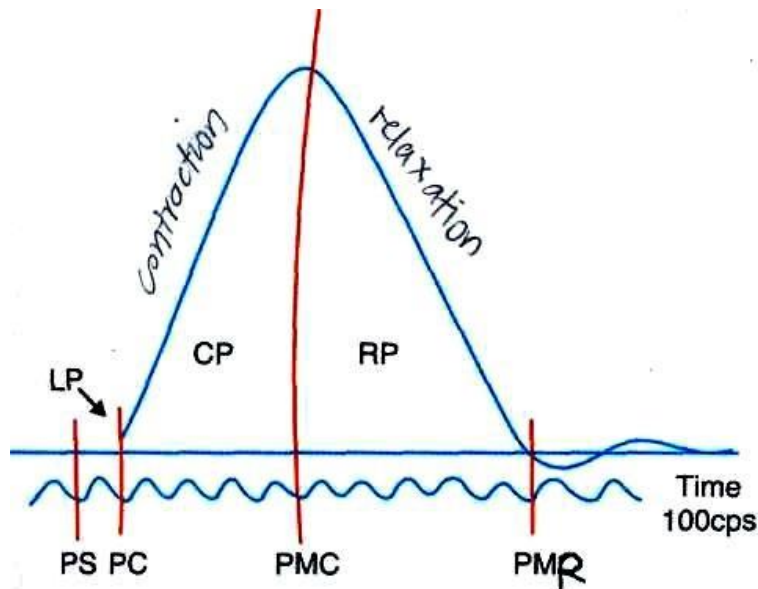
(b) Isometric contraction



(a) Isotonic (concentric) contraction

SIMPLE MUSCLE CONTRACTION

When the stimulus with threshold strength is applied, the muscle contracts and then relaxes. The contraction is recorded as upward deflection from the base line. And, relaxation is recorded as downward deflection back to the base line.



Isotonic simple muscle curve.

PS = Point of stimulus.

PC = Point of contraction.

PMC = Point of maximum contraction.


LP = Latent period (0.01 sec).

CP = Contraction period (0.04 sec).

RP = Relaxation period (0.05 sec)

All these four points divide the entire simple muscle curve into 3 periods.

- 1. Latent period - LP**
- 2. Contraction period -CP**
- 3. Relaxation period - RP**



Based on the contraction time, the skeletal muscles are classified into two types, the red muscles and white muscles. Similarly, depending upon contraction time and myosin ATP-ase activity the muscle fibers are also divided into two types, type I and type II fibers.

Type I fibers (slow fibers) have small diameter.

Type II fibers (fast fibers) have large diameter.



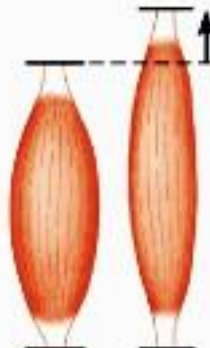
Large number of muscle fibers activated



Large muscle fibers



Tetanic contraction adequately stretches the series-elastic elements



Muscle and sarcomere length slightly over 100% of resting length

(a) Increased contractile force



Predominance of fast glycolytic (fatigable) fibers



Small load



Predominance of slow oxidative (fatigue-resistant) fibers

(b) Increased contractile velocity

(c) Increased contractile duration

Features of red and white muscles

| Red (slow) muscle | Pale (fast) muscle |
|---|--|
| 1. Myoglobin content is more. | Myoglobin content is less |
| 2. Sarcoplasmic reticulum is less extensive | Sarcoplasmic reticulum is more extensive |
| 3. Blood vessels are more extensive | Blood vessels are less extensive |
| 4. Mitochondria are more in number | Mitochondria are less in number |
| 5. Response is slow with long latent period | Response is rapid with short latent period |
| 6. Contraction is less powerful | Contraction is more powerful |
| 7. This muscle is involved in prolonged and continued activity. | This muscle is not involved in prolonged and continued activity. |
| 8. Fatigue occurs slowly | Fatigue occurs quickly |
| 9. Depends on cellular respiration for ATP production | Depends on glycolysis for ATP production |



FACTORS AFFECTING FORCE OF CONTRACTION

The force of contraction of the skeletal muscle is affected by the following factors:

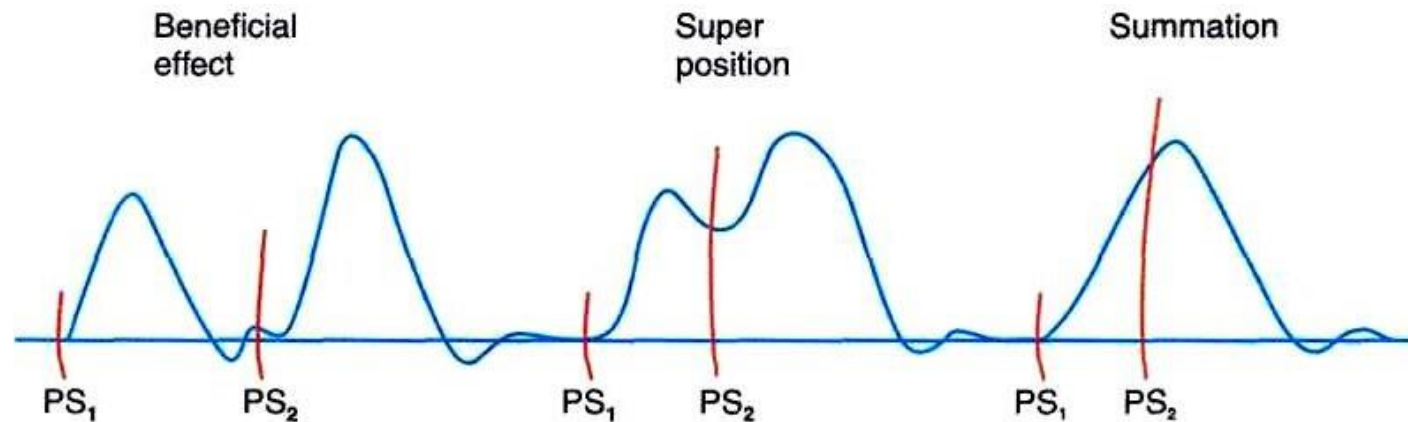
- A. Strength of stimulus
- B. Number of stimulus
- C. Temperature and
- D. Load

Effect of Frequency of Stimulus

The force of contraction of the muscle is affected by changing the frequency of stimuli. One stimulus produces simple muscle twitch. However, two or more than two (multiple) stimuli are produce different effects.

Effects of Two Successive Stimuli

When two stimuli are applied successively to a muscle, three different effects are noticed depending upon the interval between the two stimuli.



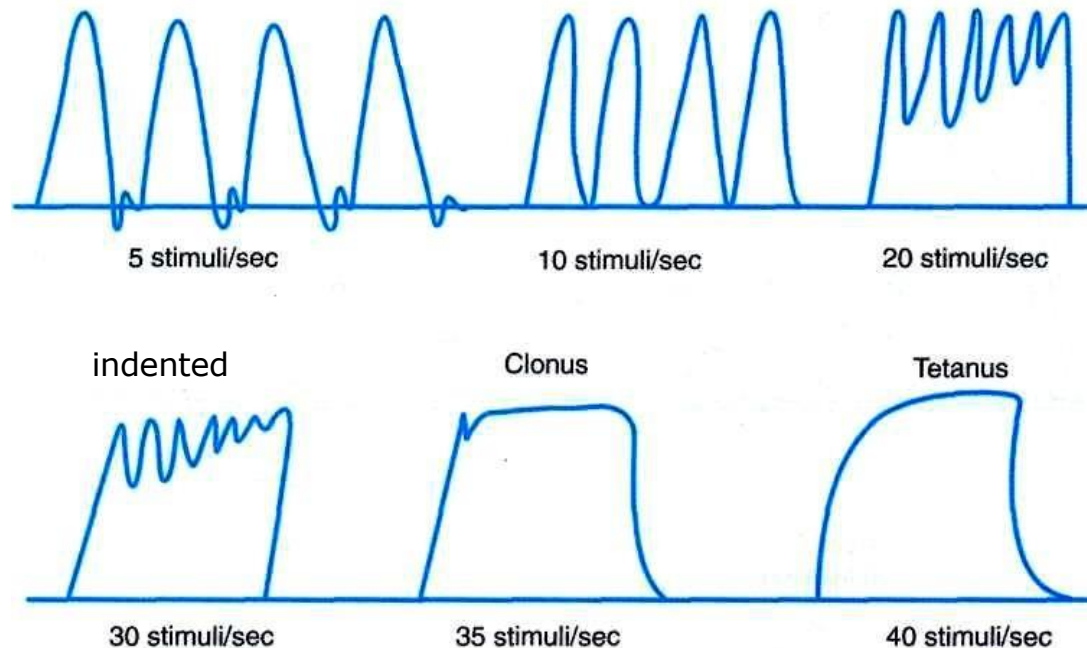
Effects of two successive stimuli.

PS1 = Point of first stimulus. PS2 = Point of second stimulus.

The muscle gives **simple contraction (twitch)** to singular irritation (stimulus).

Incomplete (unfused, indented) tetanus occurs when repeated stimuli are made in relaxation period (with the frequency equal to 15 impulses per 1 min).

Complete (fused, smooth) tetanus takes place when repeated stimuli are performed in contraction period (with the frequency 30 impulses per 1 min).



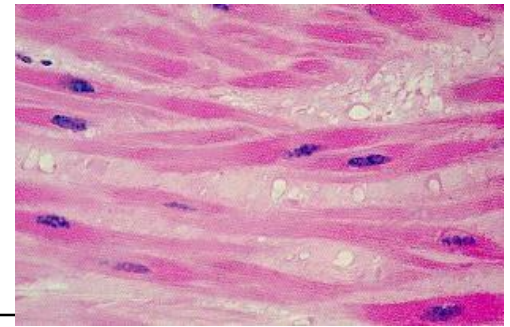
Genesis of tetanus and tetanus curves

Tetanus

Record of frog skeletal muscle, which caused by electrical stimulus with difference frequency.



SMOOTH MUSCLES



Smooth muscles are nonstriated (plain) and non-voluntary muscles. These muscles form the major contractile tissues of various organs. Smooth muscles are distributed on the walls of digestive tract, secretory glands, respiratory tract, urinary bladder, ureters, urethra, arteries, veins, muscles of iris and ciliary body of eyeball.

Each muscle fiber contains myofibrils. The myofibrils are made up of muscle proteins. But, there are no dark and light alternate bands. This is the cause for nonstriated appearance of the smooth muscle.

The smooth muscle fiber contains actin, myosin and tropomyosin components. But troponin or tropomyosin like substance is not present. When smooth muscle fiber is excited, the calcium ions enter the sarcoplasm from extracellular fluid. Calcium ions combine with protein called calmodulin leading to initiation of contraction.

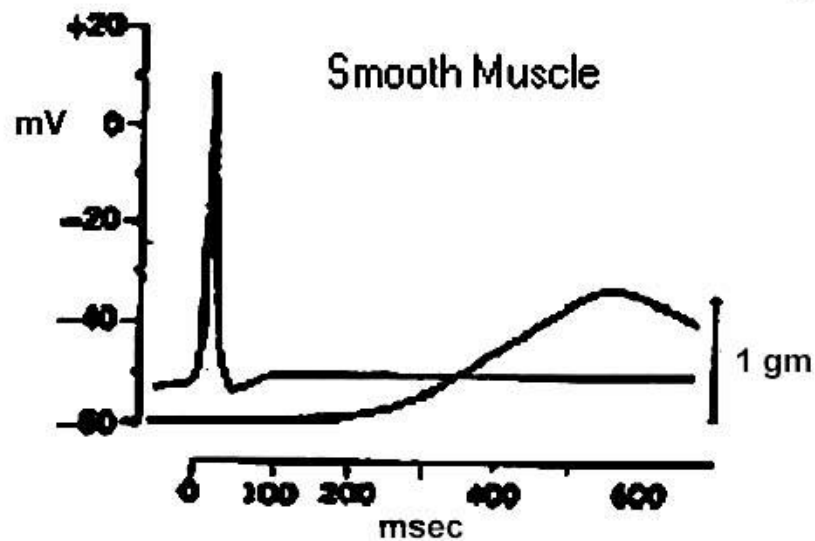
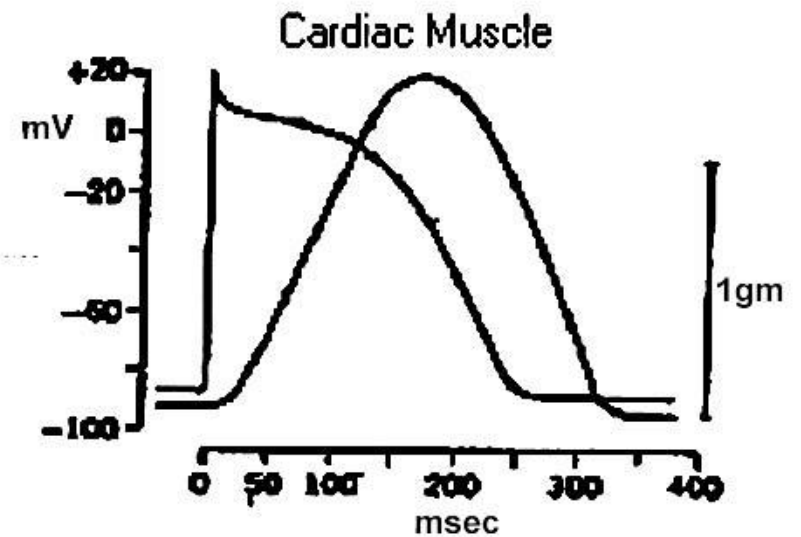
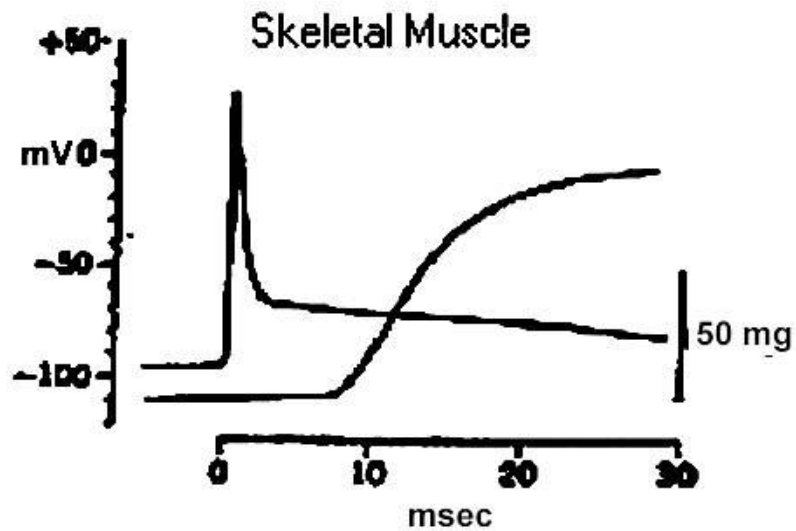
Depolarization is due to entry of calcium ions rather than sodium ions.

Smooth muscles are supplied by both sympathetic and parasympathetic nerves.

There are three general physiological characteristics that apply across all categories of smooth muscle.

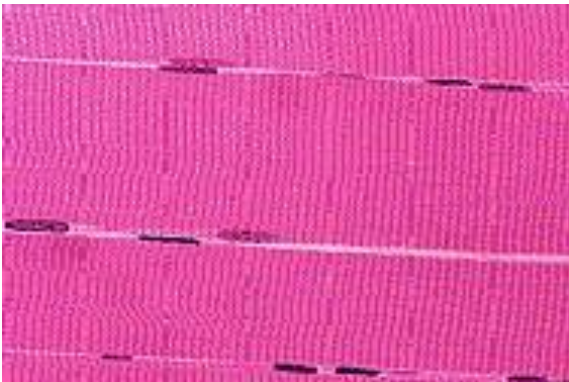
1. They are capable of slow sustained contractions maintained with a minimum energy expenditure.
2. Motor innervation is exclusively via the autonomic nervous system.
3. They exhibit a degree of intrinsic tone (A basal level of active resting tension upon which contractions or relaxations are superimposed).

MUSCLES

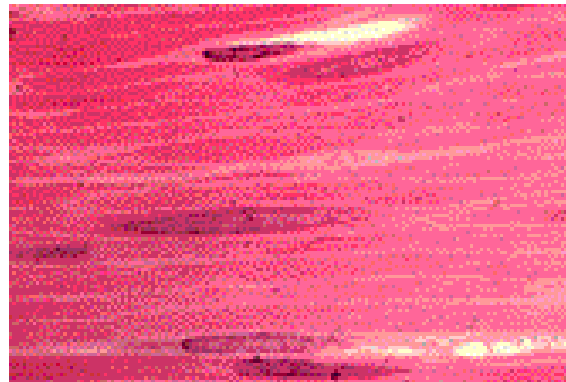


MUSCLES

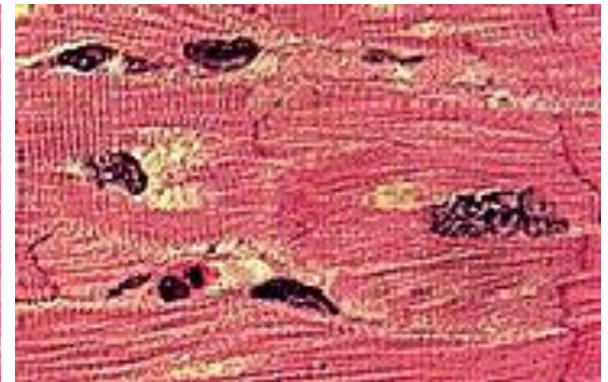
STRIATED MUSCLES



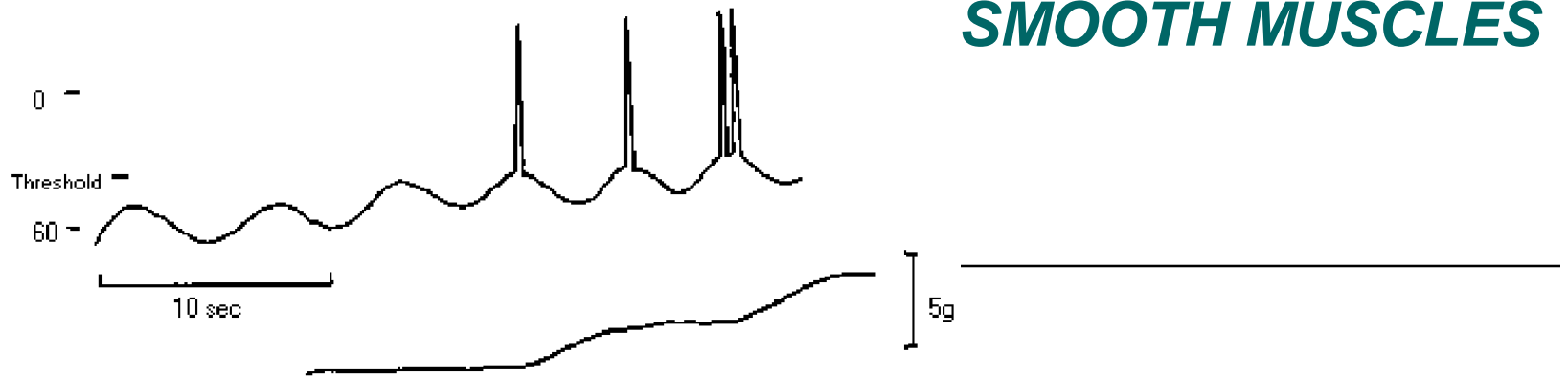
SMOOTH MUSCLES



CARDIAC MUSCLE



SMOOTH MUSCLES



In pacemaker cells and those near it which are electrically coupled by the low-resistance nexuses there is a regular slow oscillation of the resting membrane potential known as slow waves. If the peak of the slow wave exceeds a critical potential level or threshold it results in the generation of one or more action potentials. The action potential is propagated throughout the electrically coupled smooth muscle cells and triggers a tension response as shown in the figure below. The slow wave depolarization cycle appears to be based on cyclic activity of an electrogenic sodium pump. It is highly dependent on metabolic activity and can be blocked by agents which specifically block active pumping of sodium. The action potential which is triggered by the slow wave results from a transient increase in conductance for both sodium and calcium. If sodium is removed from the extracellular fluid electrically stimulated action potentials remain relatively unaltered if calcium concentrations are maintained. Under these conditions the tension response is also intact, pointing out the importance of calcium influx during the action potential for activation of the contractile system. The contractile response increases in relation to the positive amplitude of the slow wave. This is related to longer period during which threshold is exceeded and the generation of multiple action potentials and a proportional increase in tension.

SMOOTH MUSCLES

For intestinal smooth muscle this spontaneous pacemaker activity is modulated by cholinergic and adrenergic neuronal inputs. Acetylcholine results in a depolarization which shifts the slow wave upward to exceed the threshold for a greater period of time during each cycle and increasing the contractile response. Sympathetic activity has a hyperpolarizing influence pulling the peak of the slow wave below threshold and thus reducing electrical activity and tension generation. Neither of the neurotransmitters appears to substantially alter the slow wave itself but rather reset the baseline about which it oscillates. This relation of excitation and inhibition to cholinergic and adrenergic neurotransmission is not universal in smooth muscle. For example some vascular smooth muscle responds to adrenergic stimulation with excitation and to cholinergic stimulation with relaxation. These topics will be considered in greater detail in the physiology and pharmacology of the autonomic nervous system later in your training.

SKELETAL AND SMOOTH MUSCLES COMPARATIVE CHARACTERISTIC

| <i>Characteristic</i> | <i>Skeletal muscles</i> | <i>Smooth muscles</i> |
|---------------------------------|---|--|
| They are the structural part of | fulcral-motor apparatus | inner organs and vessels membranes (tunics) |
| They have | no plastic tonus | plastic tonus |
| They have | fast short-termed depolarization and short absolute refractory period | slow depolarization and long-termed absolute refractory period |
| They have | no the ability for differentiation and division | the feature of differentiation, division and regeneration under injury |

SKELETAL AND SMOOTH MUSCLES COMPARATIVE CHARACTERISTICS

(continuation)

| <i>Characteristic</i> | <i>Skeletal muscles</i> | <i>Smooth muscles</i> |
|------------------------------|---|---|
| They are innerved by | somatic nervous system | vegetative nervous system and have their own innervation apparatus (metasympathic nervous system) |
| They are contracted | under impulses transduction through the motor nerves from spinal motoneurons (automatism absence) | both under impulses that occur in muscles themselves (automatism existance) and impulses transduction through vegetative nerves |
| They have the ability to | fast phasic contractions | long-termed tonic contractions |

SKELETAL AND SMOOTH MUSCLES COMPARATIVE CHARACTERISTICS

(continuation)

| <i>Characteristic</i> | <i>Skeletal muscles</i> | <i>Smooth muscles</i> |
|---|---|---|
| They realize arbitrary muscular movements that are accompanied by | significant energy loss | insignificant energy loss |
| They have | weak sensitivity to chemical substances | high sensitivity to chemical, pharmacological, endogenous |
| They react to medicines | in some extent | in large extent |

SKELETAL AND SMOOTH MUSCLES COMPARATIVE CHARACTERISTICS

| <i>Index</i> | <i>Skeletal muscles</i> | <i>Smooth muscles</i> |
|--------------------------------------|--------------------------------|--|
| Chronaxy, msec | 0,08-0,4 | 2,0-3,0 |
| Refracterity period,sec | 0,005-0,01 | 0,3-0,4 |
| Contraction velocity | Large | Small |
| Fatigue | They are getting tired quickly | They have ability to long-termed contraction (plastic tonus) |
| Exaltation conducting velocity, msec | 6,0-11,0 | 1,0-4,0 |
| Muscles structural parts | Muscular fibres | Non-striated myocytes |
| Striating (strias) | Present | Absent |

SKELETAL AND SMOOTH MUSCLES

COMPARATIVE CHARACTERISTICS

(continuation)

| <i>Index</i> | <i>Skeletal muscles</i> | <i>Smooth muscles</i> |
|-------------------------------------|---|---|
| Contractile proteins localization | Actin and myosin fibres are alternated | Contractile proteins don't have special order |
| Separate contraction longitude, sec | 0,1 0,01 sec – latent period; 0,04 sec – shortage period; 0,05 sec – relaxation period | 1,0 |
| Laws of work | whole muscle – force law; separate fibre – “everything or nothing”; “time-force” law. | None of them |

SKELETAL AND SMOOTH MUSCLES COMPARATIVE CHARACTERISTICS (continuation)

| <i>Index</i> | <i>Skeletal muscles</i> | <i>Smooth muscles</i> |
|---------------------|--|--|
| Main features: | excitability; conductivity; contractility; elasticity (ability to develop tension at stretching); lability | Its elasticity is more expressed in comparison with the skeletal one; plastic tonus – ability to long-termed contraction without further relaxation (f.ex., any vessel can't be dilated or constricted in the maximal extent); answer reaction to stretch (staining) – contraction; automatism (all myocytes) |

SKELETAL AND SMOOTH MUSCLES COMPARATIVE CHARACTERISTICS (continuation)

| <i>Index</i> | <i>Skeletal muscles</i> | <i>Smooth muscles</i> |
|--------------------------------|--|--|
| Tetanus existence | There are 2 main tetanus kinds: complete or smooth; incomplete or infused. | Smooth muscle doesn't give any tetanus |
| Action potential peculiarities | 6 phases | it is located at zero level for a long time; exaltation period is absent |

SKELETAL AND SMOOTH MUSCLES COMPARATIVE CHARACTERISTICS

Ca-dependent contraction part

| <i>In skeletal muscles</i> | <i>In smooth muscles</i> |
|--|---|
| Essence: locuses for myosin binding must become opened on actin; in another situation myosin can be connected with actin. Events algorithm (order): | Essence: myosin light chains should be phosphorylated because myosin head can bind and decompose ATP and interact with actin only under phosphorylation state. Events algorithm (order): |
| 1. Contractive impulse | 1. Contractive stimule (nervous impulse, hormone) |
| 2. Impulse passage through cytomembrane | 2. Calcium channels opening in cytomembrane, smooth endoplasmic reticulum, mitochondria |

SKELETAL AND SMOOTH MUSCLES COMPARATIVE CHARACTERISTICS

Ca-dependent contraction part (*continuation*)

| <i>In skeletal muscles</i> | <i>In smooth muscles</i> |
|---|--|
| 3. Impulse coming through T-tubes membrane | 3. Ca binding with calmodulin (1 molecule of protein calmodulin binds 4 Ca-ions) – it is called to be trigger moment of muscular contraction |
| 4. Inositol-phosphate producing from T-tubes membranes lipids | 4. Complex “calcium+calmodulin” activates myosin light chains kynase |
| 5. Inositol-phosphate diffusion to endoplasimic reticulum | 5. Myosin light chains kynase phosphorylates myosin head light chains and they can bind and decompose ATP as well as be binded with actin under such a state |

SKELETAL AND SMOOTH MUSCLES COMPARATIVE CHARACTERISTICS

Ca-dependent contraction part (*continuation*)

| <i>In skeletal muscles</i> | <i>In smooth muscles</i> |
|--|---------------------------------|
| 6. Inositol-phosphate interaction with own receptors on reticulum membrane | |
| 7. Calcium channels opening in reticulum membranes | |
| 8. Calcium exit from reticulum to cytosol (Ca concentration under resting conditions in cytosol is equal to 10^{-7} - 10^{-8} mmol/l, at contraction – 10^{-5} mmol/l) | |
| 9. Ca diffusion to myofibrils | |

SKELETAL AND SMOOTH MUSCLES COMPARATIVE CHARACTERISTICS

Ca-dependent contraction part (*continuation*)

| <i>In skeletal muscles</i> | <i>In smooth muscles</i> |
|---|---------------------------------|
| 10. Ca binding with troponin C – trigger mechanism of contraction | |
| 11. Sites for myosin binding get opened on actin | |
| 12. Now myosin can bind actin | |

SKELETAL AND SMOOTH MUSCLES COMPARATIVE CHARACTERISTICS

Further events (common for skeletal and smooth muscles) – ATP-dependent contraction part

1. Myosin head binds ATP molecule.
2. Myosin head decomposes ATP till ADP and phosphate, ADP and phosphate are remained binded with myosin head; myosin head containing ADP and phosphate is turned and is binded to actin.
3. ADP and phosphate are disconnected from myosin head binding to actin; at the moment myosin head makes rowing movement and myosin molecule passes alongside actin molecule (with other words, myosin molecule stretches actin out to itself).
4. Myosin head binds new ATP molecule and right after this it is disconnected from actin and acquires its initial location.
5. So, muscle can neither contract nor relax without ATP. Myosin head possesses ATP-ase activity only under contraction condition.



CARDIAC MUSCLE

Cardiac muscle forms the musculature of the heart. These muscles are striated and involuntary. Cardiac muscles are supplied by both sympathetic and parasympathetic divisions of autonomic nervous system.

Contraction period is divided into **phases**:

- 1) systole (of atriums and ventricles) – contraction;
- 2) diastole (of atriums and ventricles) – relaxation.

Myocardium works according to **law “everything or nothing”**.

CARDIAC MUSCLE

2 types of myocardiocytes:

- 1) typical (working, contractive) – possess excitability, contractility and conductivity;
- 2) atypical (automatical) – heart conductive system – possess excitability, conductivity and automatism.

Tetanus is absent.

In typical cardiomyocytes – fast increasing action potential with long absolute refractory period.

In atypical cardiomyocytes (mainly in sino-atrium node) – slow increasing action potential with spontaneous secondary diastolic depolarisation due to which continued non-stopped heart contraction is possible during all human life.