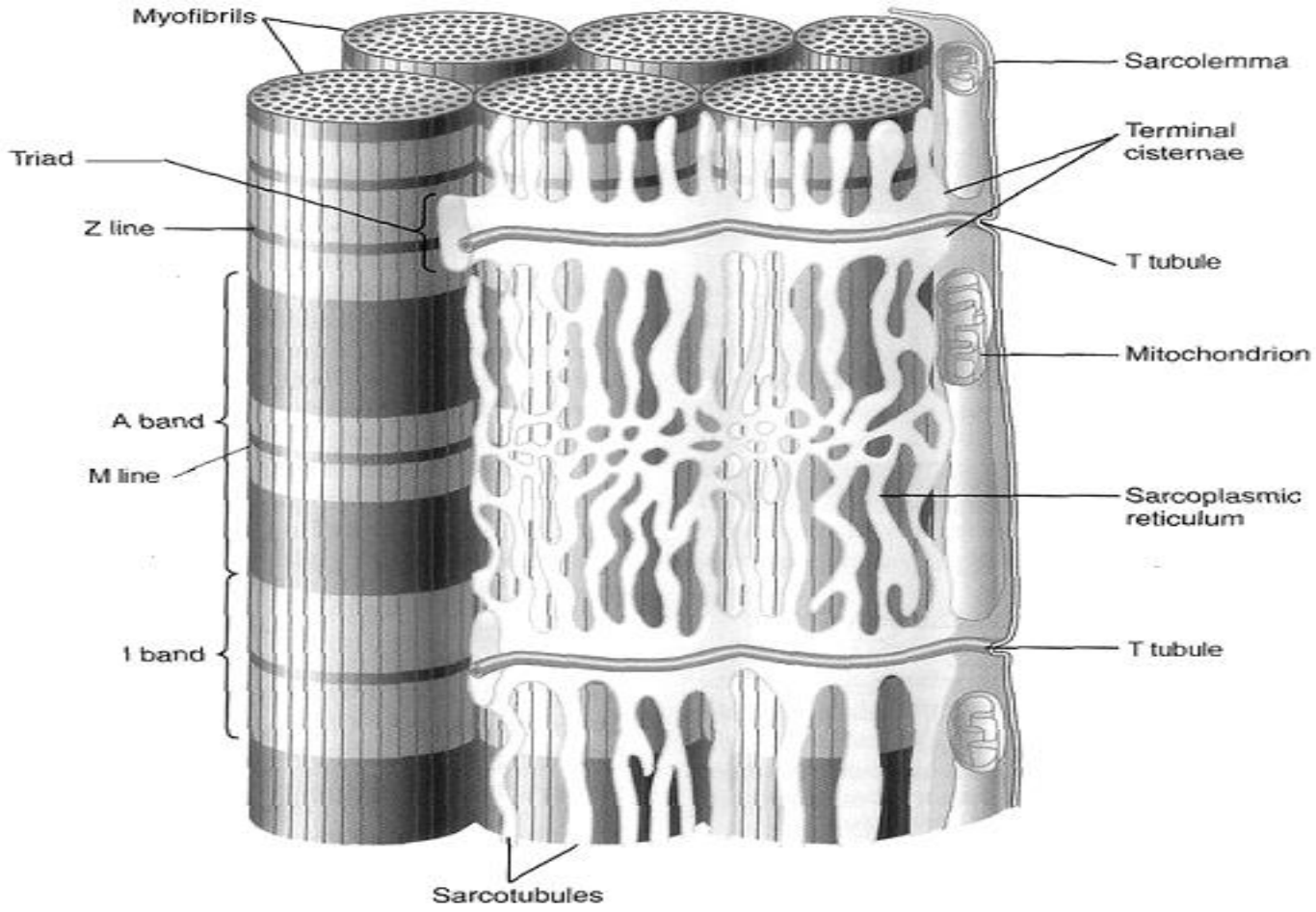
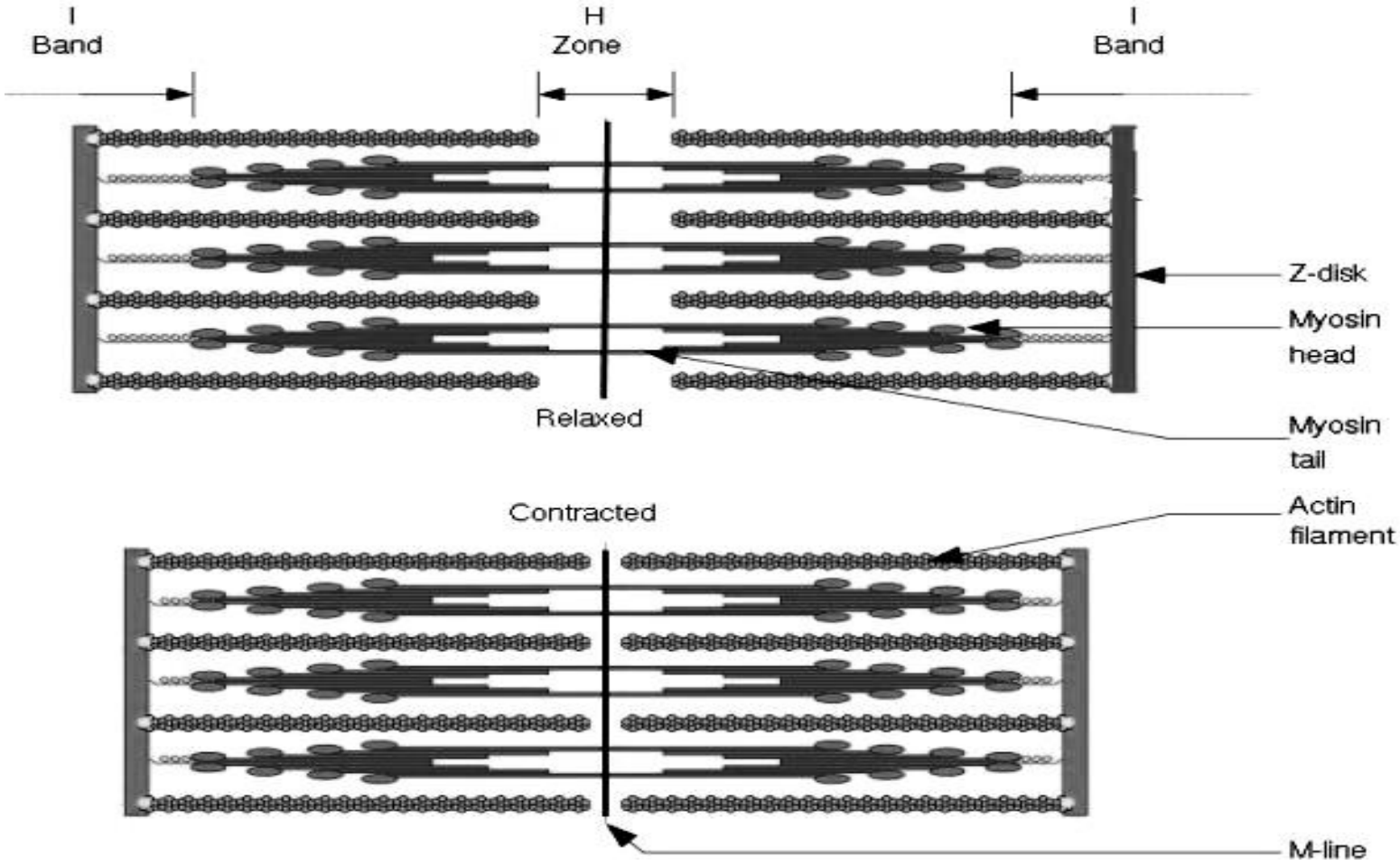
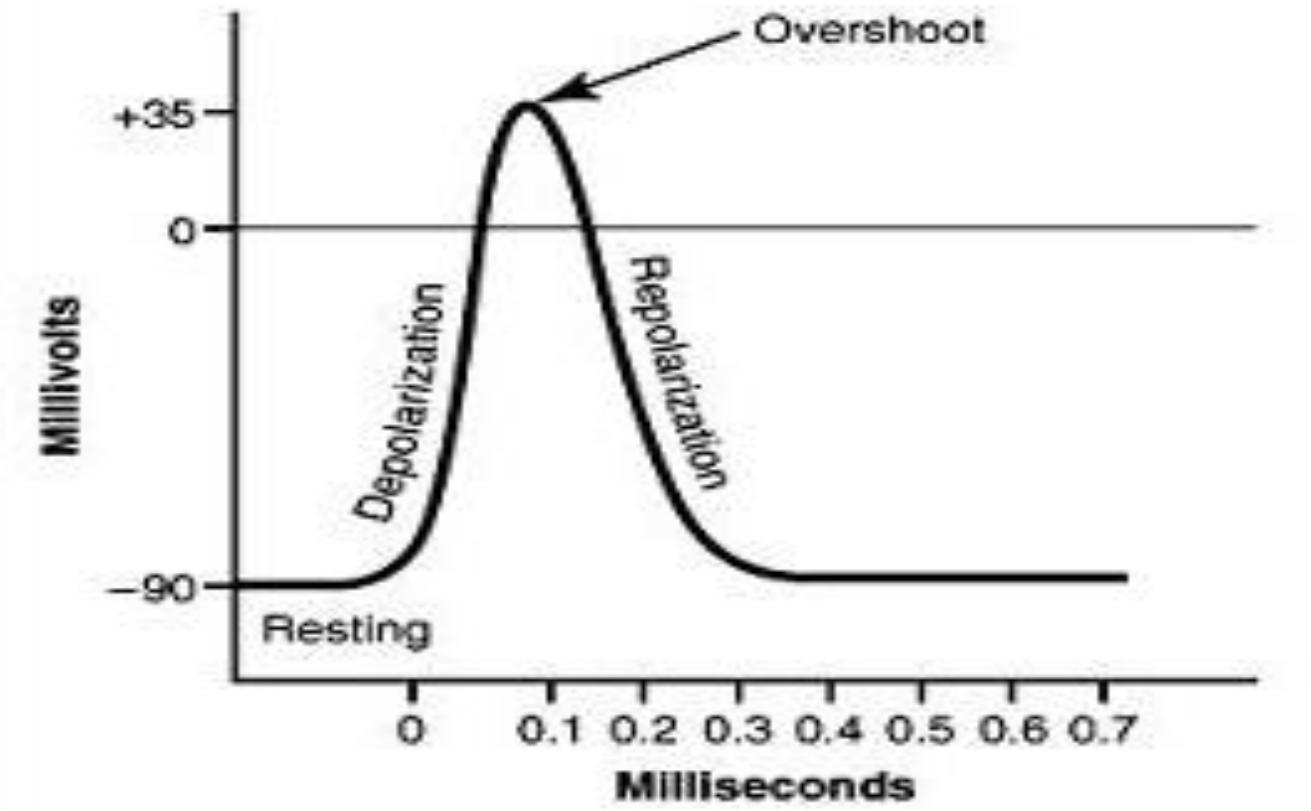
Muscular System


Myofibrils
Sarcolemma
Terminal cisternae
Triad
Z line
T tubule
Mitochondrion
A band
M line
Sarcoplasmic reticulum
I band
T tubule
Sarcotubules


I
Band
H
Zone
I
Band
Z-disk
Myosin
head
Myosin
tail
Relaxed
Contracted
Actin
filament
M-line

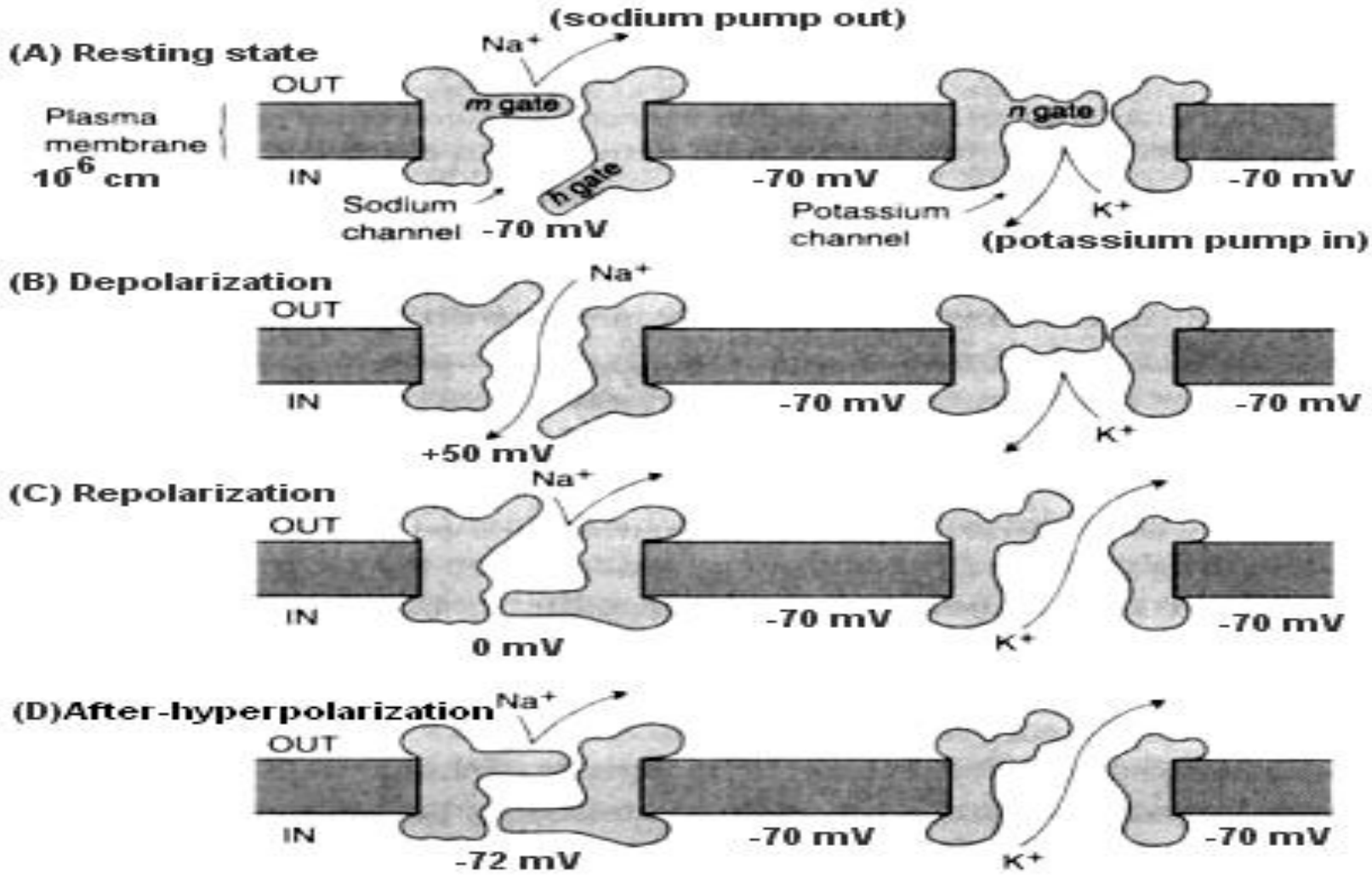
Characteristics	Skeletal muscle	Cardiac muscle	Smooth muscle
Location	Attached to bones (skeleton)	Found only in heart	**Found in the walls of blood vessels and in the organs of digestive, respiratory, urinary and reproductive tracts**
Function	Movement of the body - prevention of movement of body	Pumping of blood	**Control of blood vessel diameter; transport of food through GI tract; emptying of bladder; alteration of pupil diameter; accommodation in eye; hair movement etc**
Anatomical description	Very large, cylindrical, multinucleated cells arranged in parallel bundles	Short cells with blunt, branched ends. Cells joined to others by intercalated discs and gap junctions	**Small, spindle shaped cells joined to each other by gap junctions**
Initiation of contraction	**Only by a nerve cell**	**Spontaneous (pacemaker cells), modified by nerves**	**Some contractions always maintained. Modified by nerves**

Characteristics	Skeletal muscle	Cardiac muscle	Smooth muscle
Voluntary	Yes	No	**No**
Gap junctions	No	Yes	**Yes**
Speed and sustainability of contraction	Fast-50 msec (0.05 sec); not sustainable	Moderate-150 msec (0.15 sec); Not sustainable	**Slow-1-3 sec. Sustainable indefinitely**
Fatigue	Varies widely depending on type of skeletal muscle and work load	Low; relaxation between contractions reduces the likelihood	**Generally does not fatigue**
Striated	Yes	Yes	**No**
Ca^{2+} binding protein	**Troponin**	**Troponiin**	**Calmodulin**


Overshoot
+35
0
−90
Millivolts
Depolarization
Repolarization
Resting
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
Milliseconds

- The *first event* of action potential is characterised by rapid increase in the permeability of membrane to Na^+ ions (5000 folds) to interior of the cell, thus generating more positive electrical potential inside of the cell; this is called the *depolarization* stage.
- This causes more of Na^+ ions flowing into the cell than K^+ ions outflow. The potential inside the cell becomes “zero” or in some cases becomes positive (overshoot).
- This is followed by inactivation of Na^+ channels (closure) that occur within another few milliseconds and the membrane becomes impermeable to Na^+ ions.
- Because the inside of the cell has become positive, Na^+ influx is limited.

- The *voltage gated K^+ channels* open but this is slower and more prolonged. This allows K^+ ions outflow to the exterior of the cell membrane.
- The potential inside cell is re-established to its normal resting level (-90mV). This stage is called as the *repolarisation stage*

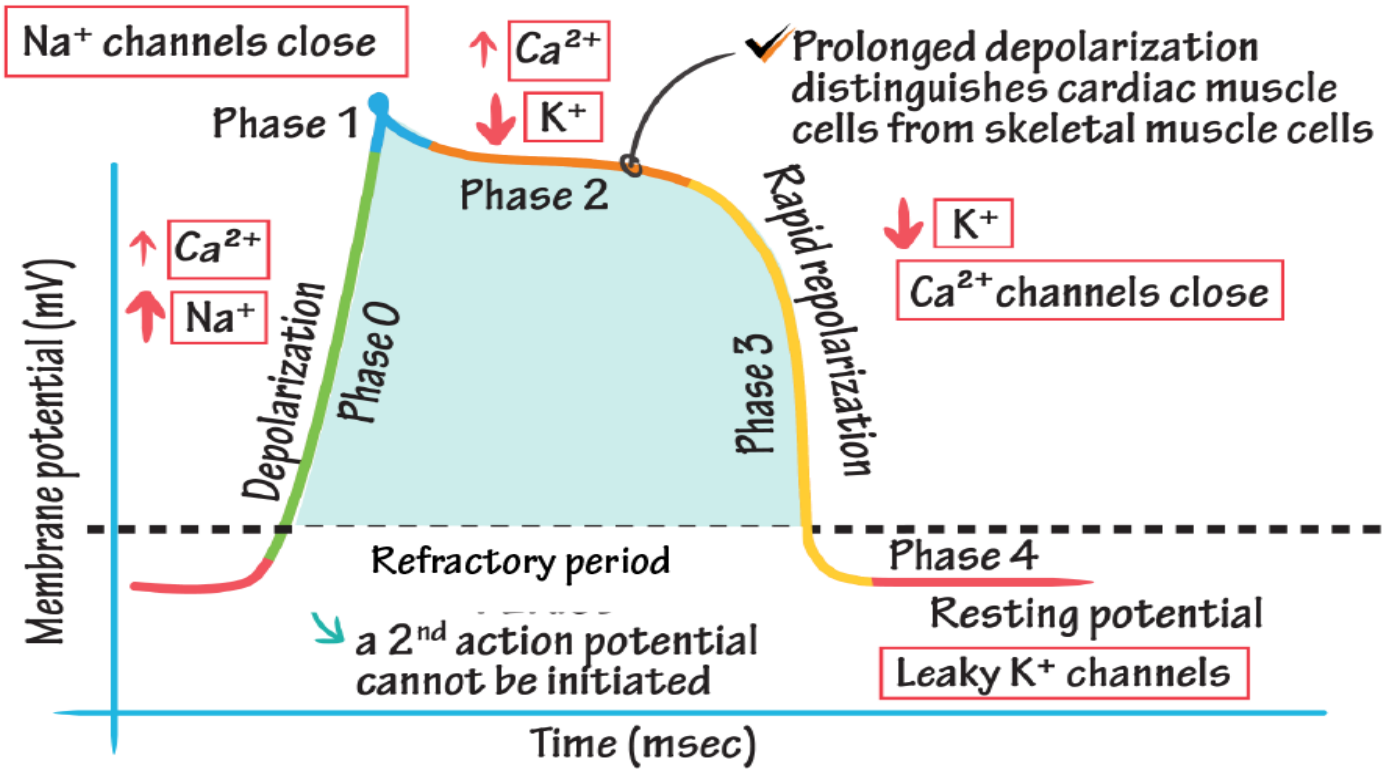

(A) Resting state
(sodium pump out)
Na+
OUT
Plasma membrane
10-6 cm
m gate
n gate
IN
h gate
-70 mV
-70 mV
Sodium channel
-70 mV
Potassium channel
K+
(potassium pump in)
(B) Depolarization
Na+
OUT
IN
-70 mV
-70 mV
+50 mV
K+
(C) Repolarization
Na+
OUT
IN
-70 mV
-70 mV
0 mV
K+
(D)After-hyperpolarization
Na+
OUT
IN
-70 mV
-70 mV
-72 mV
K+

- **Resting membrane potential in cardiac muscle**:
- Cardiac muscle = -85 to -95 mV
- Conduction system = -90 to -100 mV
- Ventricle muscle = -100 to -105 mV
- S.A. node = -50 to -55 mV

ACTION POTENTIAL IN CARDIAC MUSCLE

- Cardiac muscle has an inherent or intrinsic property of generating its own action potentials rhythmically, independent of nerve stimulation. This occurs in the pacemaker cells of the S.A. node, AV node and Purkinje fibres; SA depolarises faster than any other parts of the heart and is the normal pacemaker in heart.
- The cardiac muscle has slower but prolonged action potential than skeletal muscle that lasts for **150msec in atria and 300 msec in ventricle.**
- In cardiac muscle cells, repolarisation does not occur immediately after depolarisation but the positivity remains as a plateau near the peak of the spike potential. This plateau lasts for a few-hundred msec. and prolongs the contraction of the cardiac muscle.

Cardiac Conduction



- *The causes for the prolonged action potential* in cardiac muscle cells are:
- Cardiac muscle has two separate channel systems.
- Voltage activated Na^+ channel (*fast channel*).
- Voltage activated Ca^{2+} channel (*slow channel*).
- The slow channels are slow to open and remain in the open state for a few tenths of a second. The slow channels are activated at a membrane potential of -30 to -40 mV

- Activation of the fast Na^+ channels causes the spike potential of the action potential, whereas the slow channel prolongs the passage of Ca^{2+} ions into the interior of the cell, thus establishes the plateau in the action potential.
- The inflow of Ca^{2+} ions into the cardiac muscle cells decreases K^+ efflux through voltage gated K^+ channels. This delays the K^+ ion permeability to outside which in turn delays the repolarisation process of the action potential in cardiac muscle.
- The prolonged action potential makes the cardiac muscle cells to have longer contraction period than skeletal muscles. Hence the heart muscle unlike skeletal muscle cannot be stimulated into tetany.

ACTION POTENTIAL IN SMOOTH MUSCLES

- The smooth muscles have lower resting membrane potential than skeletal and cardiac muscles.
- The resting potential of the smooth muscle cells range **from –50mV to -60mV.** The action potential is regulated by voltage-gated Ca^{2+} channel.
- Action potential in visceral smooth muscle occurs in two forms:
  - spike potential
  - action potential with plateau
- ***Spike Potential***: Typical spike potential as in skeletal muscle occurs in unitary smooth muscles. These action potentials can be elicited by electrical stimulation, hormones, transmitter substances from nerves, by stretch or spontaneously. It has relatively short duration (5-10m sec)

- *Action potential with plateau* occurs in visceral smooth muscle cells similar to cardiac cells; They prolong the period of contraction and seen in smooth muscles like ureters, uterus and vascular smooth muscles.
- Spontaneous action potentials are generated in smooth muscles.
- Voltage-gated Ca^{2+} channels are more in number in smooth muscle cells than the Na^{+} channels and the Ca^{2+} is the major player in generating the action potential. Since the Ca^{2+} channels are slow to open and slow in closing, smooth muscle contractions are slower but prolonged.
- Muscles contract **200 msec after spike and lasts for 150 msec** after the spike is over.
- Slow wave depolarisation changes the membrane potential by few mV magnitude and spike potentials occur over the membrane potential. The spikes when occur is produced during the end of slow wave potential.

Rhythmicity (*automaticity or spontaneous action potentials)*

- Repetitive discharge of impulses or *rhythmicity* normally occurs in heart muscle (pace maker cells of SA node), smooth muscle and many neurons of CNS.
- **To establish rhythmicity, the resting membrane potential in these tissues is only -55 to -60 mV (less than the normal value of -90mV in skeletal muscle) which is not enough to close the Na^{+} and Ca^{2+} channels. The cause for the less negativity in these cells is that these cell membranes are naturally leaky to Na^{2+} ions.**

Abnormal ion concentrations in extracellular fluid

- Reduction in K^+ concentration in the ECF is ***hypokalemia*** and it makes the membrane potential more negative, and greater intensity of stimulus strength is required to stimulate muscles and the patient will suffer from muscle weakness.
- Eg. **hyperaldosteronsim and in certain kidney diseases**
- Reduced Ca^{2+} concentration in the ECF, *hypocalcaemia* makes the cells to undergo action potential easily which can lead to muscle spasms and cramps; hypocalcaemia occur in vitamin D deficiency, hypoparathyroidism, milk fever in cows
- Hypocalcemia in cows blocks acetylcholine release from synapse between muscle and nerve and causes paresis whereas in dogs and humans, this leads to spontaneous depolarization of nerve cells that produces muscular spasm

MECHANISM OF MUSCLE CONTRACTION

- Skeletal muscles contract in response to stimulation by CNS. The efferent impulses for muscle contraction are carried over motor nerves to muscle
- An action potential travels along a motor nerve to its endings in the muscle fibre
- The endings of the nerve secrete a neurotransmitter – ***acetylcholine*** (Ach).
- The acetylcholine acts on the muscle membrane to open Ach-gated ion channels (*ligand-gated* channels) on the muscle fibre membrane
- Ach channels allow Na^+ ions to flow to the interior of the muscle fibre membrane at the point of the nerve terminal. This initiates an action potential in the muscle fibre
- The action potential travels along the muscle fibre membrane

- The action potential depolarises the muscle cell membrane and also travels deeply into the muscle cell through the T tubule to the terminal cisterna; this releases Ca^{2+} ions into the myofibrils
- The Ca^{2+} ions initiate attraction between actin and myosin filaments, causing them to slide together which is the contraction process
- After a fraction of a second, the Ca^{2+} ions are reuptaken into the sarcoplasmic reticulum, stored until they are released for next contraction.

- This process of an action potential travelling along a nerve fibre that leads to generation of action potential in muscle fibre which releases Ca^{2+} into the sarcoplasm and the Ca^{2+} initiates muscle contraction is referred to as "***excitation-contraction coupling***".

"Walk-Along Theory" of Contraction (Sliding Mechanism of Contraction)

- In the relaxed state, actin filaments from two successive z-discs barely overlap one another and at the same time, lie adjacent to the myosin filaments.
- During contraction, actin filaments slide over the myosin filaments with shortening of sarcomere. The actin filaments are actually pulled inward toward the M line in a ratchet-like manner by myosin.
- The actin and myosin filaments overlap one another to a major extent. The z-discs are also pulled up to the ends of the myosin filaments. **Thus, muscle contraction occurs by *sliding filament mechanism*.**
- The troponin-tropomyosin complex inhibits the active sites on the actin filaments of relaxed muscle. Hence, the myosin heads cannot attach with the active sites of actin to cause contraction.

- In the presence of large amounts of Ca^{2+} ions, the inhibitory effect of T-T complex on the actin filament is removed.
- When Ca^{2+} ions bind with troponin-C, the troponin complex undergoes a conformational change; this moves the tropomyosin molecules deeper into the groove between two stands of actin strands. This effect “uncovers” the active sites of actin, hence the myosin head attaches with the active sites to cause contraction.