Neurophysiology

Physiology excitable tissues

(Nerve Fibers)

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Excitable tissues

excitable

Non-excitable

neuron

muscle

Red cell

GIT

- Nerve
- Muscle
  - Skeletal
  - Cardiac
  - Smooth

- RBC
- Intestinal cells
- Fibroblasts
- Adipocytes

EXCITABLE TISSUE :

- When an ***external stimulation*** (electrical , chemical ,mechanical ,physical) is applied , an ***electrical activity*** is ***generated*** and ***conducted*** along their fibers

Neurons and Neuroglia

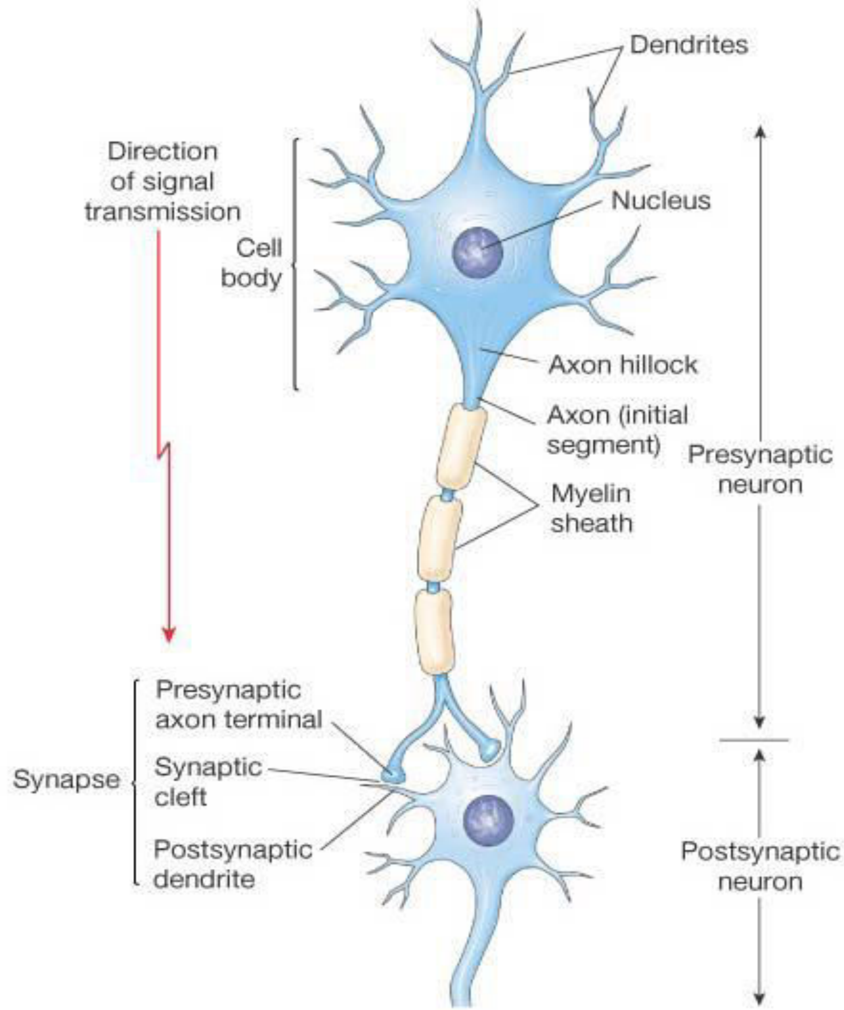
The human central nervous system (CNS) contains about **100 billion** neurons (electrical impulse conducting cells). It also contains **10-50 times** this number of glial cells (supporting cells).

The neurons are the basic building blocks of the nervous system, their specialized function is to integration and transmission of nerve impulses.

Morphology of the nerve cell

Neurons in the CNS have different shapes and size; however most of them have the same parts:

A. Dendrites
B. Cell Body (soma)
C. Axon
D. Nerve ending
E. Myelin



- Cell body: contains nucleus, cytoplasm and cell organelle.
- Dendrites: are multiple small projections from the cell body, their function is acting as receptors of nerve impulses from another nerve cell and transmit the impulses toward the cell body.

- Axon: originate from thickened area of the cell body called **axon hillock**. the first part of the axon is called **initial segment**, the axon ends by dividing into terminal branches each ending by a number of **synaptic knobs** .The function of the axon is transmission of nerve impulses to the nerve ending.

- Nerve ending: terminal parts of the axon, they divide into a number of **synaptic knobs** is called (**terminal buttons**) contain granules or vesicles in which the **synaptic transmitters** secreted by the nerve are stored.

- Myelin: is a sheath of **protein-lipid complex** that wrapped around the axon of many nerve fiber (myelinated).***<u>In the CNS it is formed by the oligodendrocyte and in the PNS is formed by shwan cells</u>***.

*the myelin sheath envelops the axon except at their ending and at Ranvier nodes which are a periodic constrictions. The myelin sheath is considers as electrical insulator.

*some nerves are unmyelinated thus simply surrounded by shwan cells without the wrapping that forms myelin.

*in the multiple sclerosis crippling autoimmune disease patchy destruction of myelin occur in CNS.

*the **loss of myelin is associated with delayed or blocked conduction** in the demyelinated axon.

Functional organization of neurons

There are 4 functional zones in neurons :

- **1) Receptor Zone** : it is represented by **soma** and **dendrites** , where nervous **impulses are received** ,**integrated** and multiple graded electro genesis occurs
- **2) Initial Segment Zone** : represented by the **initial segment** of the axon where **origination of conducted impulses** occurs

- **3) Axonal Zone** : **transmission & conduction** of impulses , represented by axon and its branches
- **4) Nerve Ending Zone**: where impulses causes **secretion of synaptic neurotransmitters** to affect other tissues (gland ,skeletal muscles) ,represented by synaptic vesicles

Protein Synthesis and Axoplasmic Transporort

- Neurons are secretory cells that synthesize proteins in cell body by endoplasmic reticulum and Golgi apparatus, then, the proteins are secreted from axonal endings (synaptic vesicles) , therefore ,there should be a method of transportation between cell body and terminals called " **AXOPLAXMIC TRANSPORT** " ,it occurs along the microtubules , the axoplamic transport divided in to two types :

- 1) **Anterograded Transport** : transporting substances from soma to axonal endings , occurs at 2 speeds :

- A) *Fast* : occurs at rate (*400 mm\day*) , transports cell organelles (synaptic vesicles) mediated by Kinesin (microtubular protein)
- B) *Slow* : occurs at rate *(0.5- 10 mm\day*), it involes the polymerization and depolymerization of cytoskeleton
- 2) **Retrograde Transport** : the transport from axon terminal to soma , at rate of (*200 mm\day*) , involoves the transport of used vesicles, viruses , Nerve Growth Factors (NGF) , mediated by cytoplasmic Dyenin (microtubular protein)

Excitation and neuronal conduction

Nerve cells have a low threshold for excitation. The stimulus may be electrical, chemical, or mechanical. Two types of physicochemical disturbances are produced:-

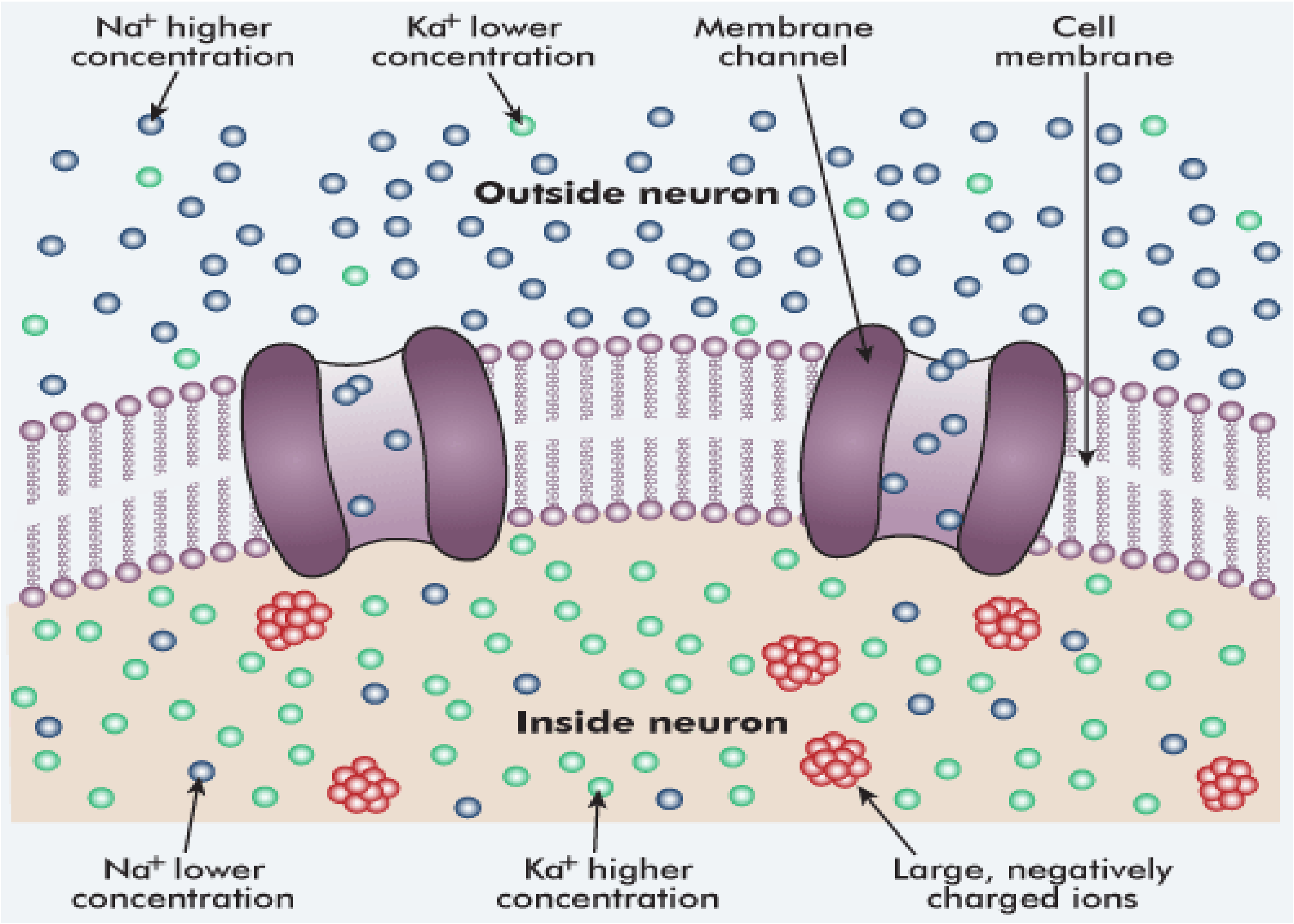
1. ***Local, non propagated*** potentials called generator, or electrotonic potentials. (CNS)
2. ***Propagated disturbances***, the action potentials (or nerve impulses- PNS).

Resting Membrane Potential

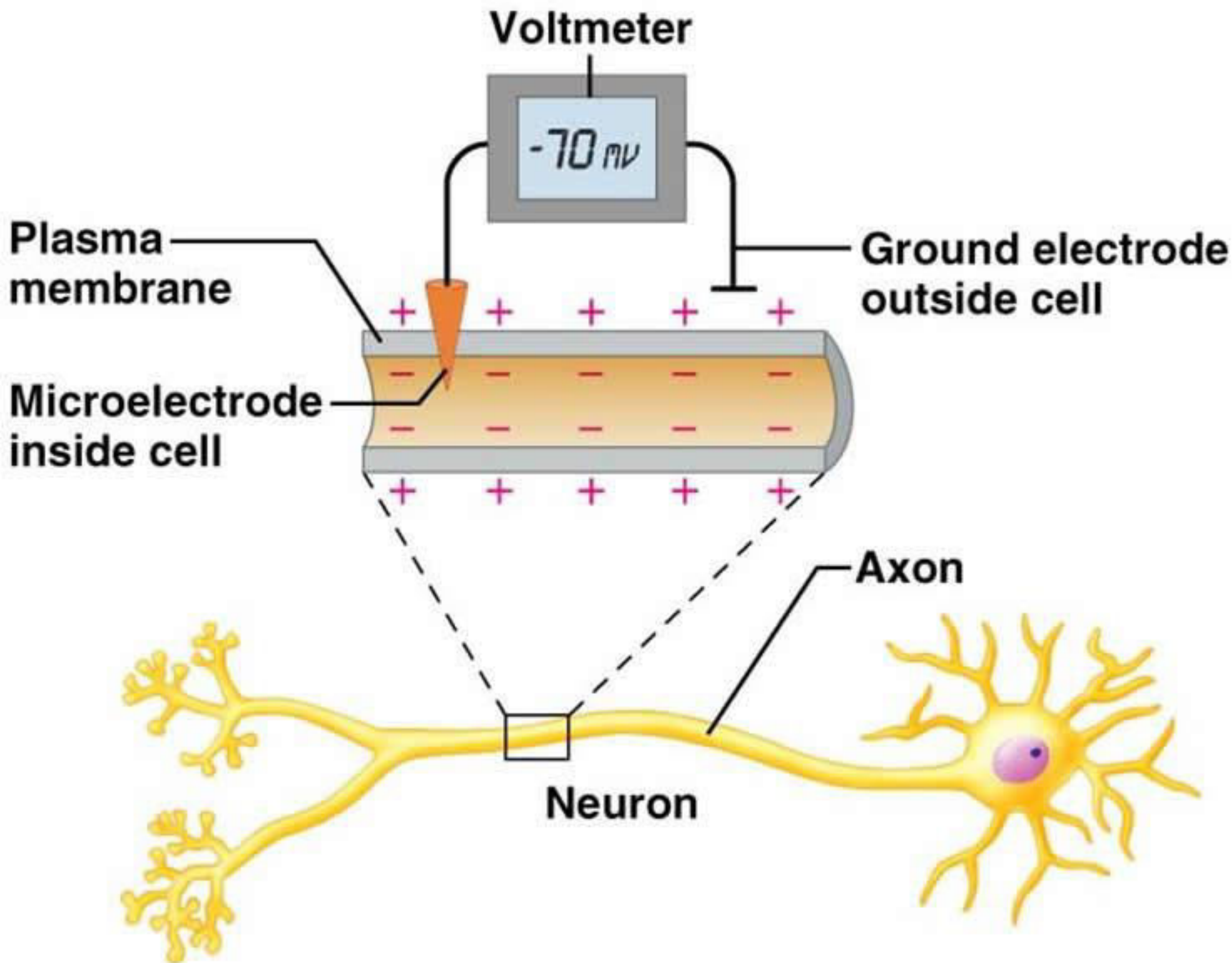
Distribution of ions

(intracellular and extracellular) :

- **Na^+ (outside): 142 mEq/L**
- **Na^+ (inside): 14 mEq/L**
- **K^+ (outside): 4 mEq/L**
- **K^+ (inside): 140 mEq/L**



Na+ higher concentration
Ka+ lower concentration
Membrane channel
Cell membrane
Outside neuron
Inside neuron
Na+ lower concentration
Ka+ higher concentration
Large, negatively charged ions


Voltmeter
-70 mV
Plasma membrane
Ground electrode outside cell
Microelectrode inside cell
Axon
Neuron

THE IONIC BASIS OF RMP

- How The RMP is maitaned nearly -70 mv ??
- There are three primary factors :
- 1) Active **(Na+ – K+) pump**
- 2) Membrane permeability (difference between Na , K)
- 3) Presence of **anions** inside the cell

- In neurons, like other cells , there is **an active (Na^+ - K^+) pump** system that pushes Na^+ actively to the outside of the cell and draws K^+ actively to the inside of the cell.

- As a result, Na^+ will accumulates outside the cell while K^+ inside the cell, Na^+ ions tries to enter inside the cell passively down its concentration gradient , but since the cell membrane is much more permeable (50-100) times to K+ than Na+, so passive K+ efflux (from inside to outside) is more than the passive Na+ influx (from outside to insid) leading to accumulation of more positive charges outside the cell than the inside.

- Moreover, there are proteins (negatively charged) inside the cell that cannot get out increasing the negativity inside , all the three factors cause the cell (neuron) to be polarized in the resting state, it's RMP.

Resting Membrane Potential of Nerves

The resting membrane potential of large nerve fibers when not transmitting nerve signals is about –70 millivolts. That is, the potential *inside the fiber is 70* millivolts more negative than the potential in the extracellular fluid on the outside of the fiber.

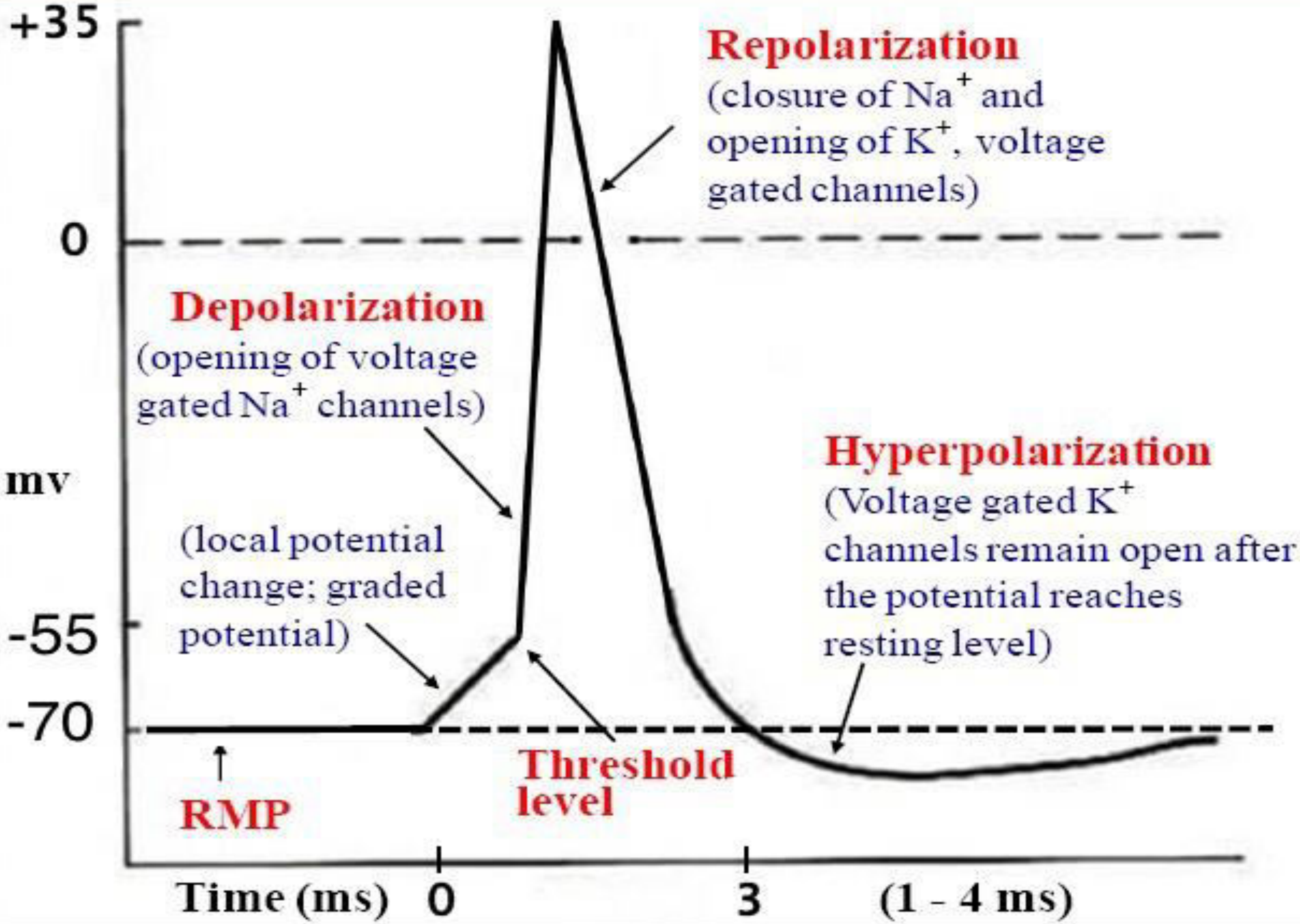
- ***<u>Resting Stage.</u>***

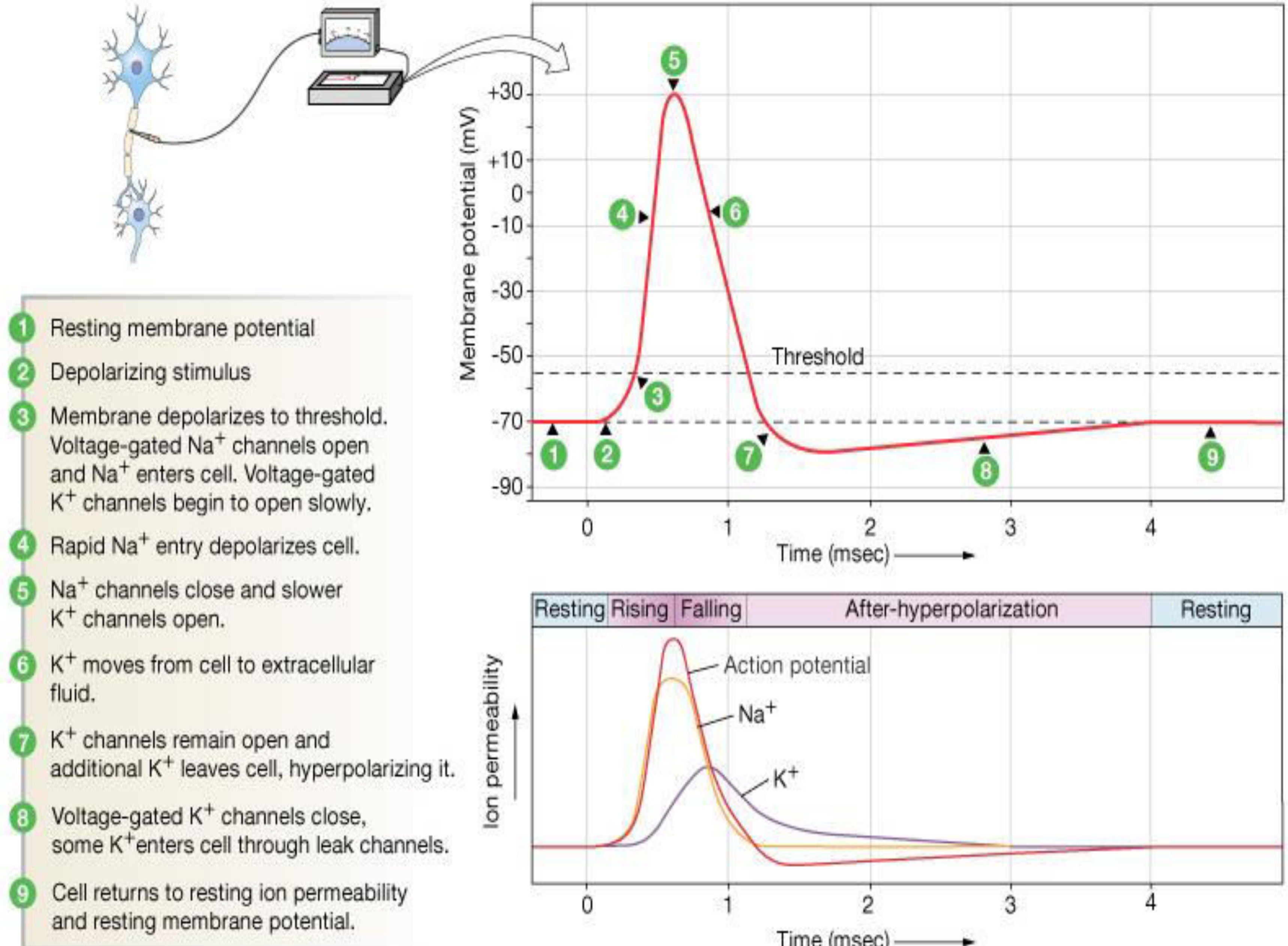
This is the resting membrane potential before the action potential begins. The membrane is said to be “polarized” during this stage because of the –70 millivolts negative membrane potential that is present.

- ***<u>Nerve Action Potential</u>***

Nerve signals are transmitted by *action potentials*, which are *rapid changes in the membrane potential that spread rapidly along the nerve fiber membrane.*

Action potential





1 Resting membrane potential
2 Depolarizing stimulus
3 Membrane depolarizes to threshold. Voltage-gated Na+ channels open and Na+ enters cell. Voltage-gated K+ channels begin to open slowly.
4 Rapid Na+ entry depolarizes cell.
5 Na+ channels close and slower K+ channels open.
6 K+ moves from cell to extracellular fluid.
7 K+ channels remain open and additional K+ leaves cell, hyperpolarizing it.
8 Voltage-gated K+ channels close, some K+ enters cell through leak channels.
9 Cell returns to resting ion permeability and resting membrane potential.
Membrane potential (mV)
+30
+10
0
-10
-30
-50
-70
-90
Threshold
0
1
2
3
4
Time (msec)
Resting
Rising
Falling
After-hyperpolarization
Resting
Ion permeability
Action potential
Na+
K+
0
1
2
3
4
Time (msec)

- These are the only electrical responses of neurons and other excitable tissues, and they are the main language of the nervous system. They are due to changes in the conduction of ions across the cell membrane that are produced by alterations in ion channels.
- The impulse is normally transmitted (conducted) a long the axon to its termination.

- Each action potential begins with a sudden change from the normal resting negative membrane potential to a positive potential and then ends with an almost equally rapid change back to the negative potential.
- To conduct a nerve signal, the action potential moves along the nerve fiber until it comes to the fiber’s end. The successive stages of the action potential are as follows

- ***Depolarization Stage.***

At this time, the membrane suddenly becomes **very permeable to sodium ions,** allowing tremendous numbers of positively charged sodium ions to diffuse to the interior of the axon. The normal “polarized” state of –70 millivolts is immediately neutralized by the inflowing positively charged sodium ions, with the potential rising rapidly in the positive direction. This is called d*epolarization*

- In large nerve fibers, the great excess of positive sodium ions moving to the inside causes the membrane potential to actually “overshoot” beyond the zero level and to become somewhat positive. In some smaller fibers, as well as in many central nervous system neurons, the potential merely approaches the zero level and does not overshoot to the positive state.

- ***Repolarization Stage.***

Within a few 10,000ths of a second after the membrane becomes highly permeable to sodium ions, the sodium channels begin to close and the potassium channels open more than normal. Then, rapid diffusion of potassium ions to the exterior

- re-establishes the normal negative resting membrane potential. This is called *repolarization* of the membrane. To explain more fully the factors that cause both depolarization and repolarization, we need to describe the special characteristics of two other types of transport channels through the nerve membrane: the voltage-gated sodium and potassium channels.

The Events That Cause the Action Potential

During the resting state, before the action potential begins, the conductance for potassium ions is 50 to 100 times as great as the conductance for sodium ions. This is caused by much greater leakage of potassium ions than sodium ions through the leak channels.

- However, at the onset of the action potential, the sodium channels instantaneously become activated and allow up to a 5000-fold increase in sodium conductance. Then the inactivation process closes the sodium channels within another fraction of a millisecond.

- The onset of the action potential also causes voltage gating of the potassium channels, causing them to begin opening more slowly a fraction of a millisecond after the sodium channels open. At the end of the action potential, the return of the membrane potential to the negative state causes the potassium channels to close back to their original status, but again, only after an additional millisecond or more delay.

Initiation of the action potential

A Positive-Feedback Vicious Cycle Opens the Sodium Channels.

As long as the membrane of the nerve fiber remains undisturbed, no action potential occurs in the normal nerve. However, if any event causes enough initial rise in the membrane potential from –90 millivolts toward the zero level, the rising voltage itself causes many voltage-gated sodium channels to begin opening.

This allows rapid inflow of sodium ions,which causes a further rise in the membrane potential, Thus, opening still more voltage-gated sodium channels and allowing more streaming of sodium ions to the interior of the fiber. This process is a positive-feedback vicious cycle that, once the feedback is strong enough, continues until all the voltage-gated sodium channels have become activated (opened).

Threshold for Initiation of the Action Potential

An action potential will not occur until the initial rise in membrane potential is great enough to create the vicious cycle described in the preceding paragraph.. A sudden rise in membrane potential of 15 to 30 millivolts usually is required.

Therefore, a sudden increase in the membrane potential in a large nerve fiber from –90 millivolts up to about –65 millivolts usually causes the explosive development of an action potential. This level of –65 millivolts is said to be the *threshold* for stimulation.