Resting membrane potential and Action potential

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PROGRAMME OUTCOMES

- PO1- Demonstrate comprehensive knowledge and application of the Trisutra concept to explore root causes, identify clinical manifestations of disease to treat ailments and maintain healthy status.
- PO2- Demonstrate knowledge and skills in Ayurveda, acquired through integration of multidisciplinary perspectives and keen observation of clinical and practical experiences.

COURSE OUTCOMES

- CO1- Explain all basic principles & concepts of Kriya Sharir along with essentials of contemporary human physiology and biochemistry related to all organ systems.

- **Teaching learning methods-** lecture with power point presentation
  Domain- Cognitive/comprehension
  Must to know / desirable to know / Nice to know- Must to know
  Millers pyramid- Knows how(applied knowledge)

- **RESTING MEMBRANE POTENTIAL**
- Resting membrane potential is defined as the electrical potential difference (voltage) across the cell membrane (between inside and outside of the cell) under resting condition.
- It is also called membrane potential, transmembrane potential, steady potential, transmembrane potential difference or trans membrane potential gradient.
- When two electrodes are placed on the surface of a cell and are connected through a suitable amplifier to a cathode ray oscilloscope (CRO i.e. voltage amplifier recorder system), no potential difference is observed. However, if one electrode is inserted into the interior of the cell, a constant (or steady) potential difference is observed between the inside and the outside of the cell at rest, called as the Resting Membrane Potential.

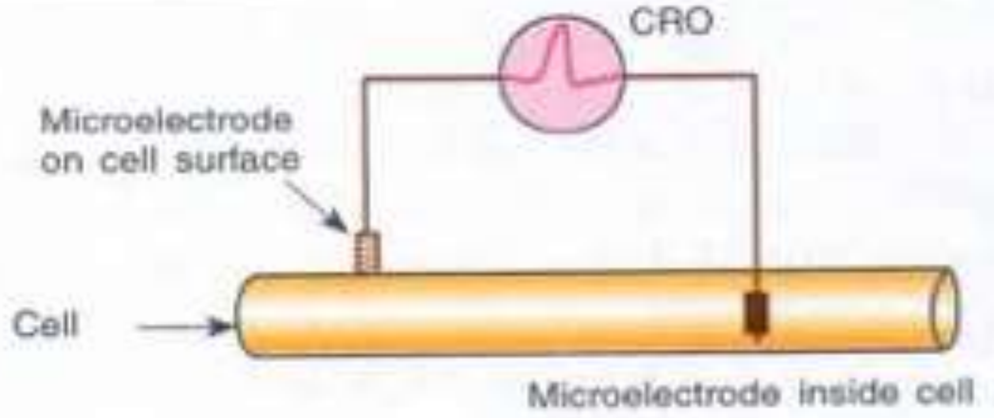


Fig. 4.1 Arrangement to record resting membrane potential (R.M.P.)

- This is also termed as steady potential or transmembrane potential and indicates the resting state i.e. **state of polarisation** of the cell membrane.
- It is written with a minus sign, signifying that inside is negative relative to the exterior. Its magnitude varies considerably from tissue to tissue ranging from -1OmV to -1OOmV.

Ionic Basis of Resting Membrane Potential

- Development and maintenance of resting membrane potential in a muscle fiber or a neuron are carried out by movement of ions, which produce ionic imbalance across the cell membrane. This results in the development of more positivity outside and more negativity inside the cell. Ionic imbalance is produced by two factors:

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

1. Sodium-potassium pump

- Sodium and potassium ions are actively transported in opposite directions across the cell membrane by means of an electrogenic pump called sodium-potassium pump. It moves three sodium ions out of the cell and two potassium ions inside the cell by using energy from ATP. Since more positive ions (cations) are pumped outside than inside, a net deficit of positive ions occurs inside the cell. It leads to negativity inside and positivity outside the cell.

2. Selective permeability of cell membrane

- Permeability of cell membrane depends largely on the transport channels. The transport channels are selective for the movement of some specific ions. Their permeability to these ions also varies. Most of the channels are gated channels and the specific ions can move across the membrane only when these gated channels are opened. Two types of channels are involved:
- **i. Channels for major anions like proteins**
- **ii. Leak channels.**

i. Channels for major anions (negatively charged substances) like proteins

- Channels for some of the negatively charged large substances such as proteins, organic phosphate and sulfate compounds are absent or closed. So, such substances remain inside the cell and play a major role in the development and maintenance of negativity inside the cell (resting membrane potential).

ii. Leak channels

- Leak channels are the passive channels, which maintain the resting membrane potential by allowing movement of positive ions (Na^+ and K^+) across the cell membrane.
- Three important ions, sodium, chloride and potassium are unequally distributed across the cell membrane. Na^+ and Cl^- are more outside and K^+ is more inside.
- Since, Cl^- channels are mostly closed in resting conditions Cl^- are retained outside the cell. Thus, only the positive ions, Na^+ and K^+ can move across the cell membrane.

- Na+ is actively transported (against the concentration gradient) out of cell and K+ is actively transported (against the concentration gradient) into the cell. However, because of concentration gradient, Na+ diffuses back into the cell through Na+ leak channels and K+ diffuses out of the cell through K+ leak channels.
- In resting conditions, almost all the K+ leak channels are opened but most of the Na+ leak channels are closed. Because of this, K+, which are transported actively into the cell, can diffuse back out of the cell in an attempt to maintain the concentration equilibrium. But among the Na+, which are transported actively out of the cell, only a small amount can diffuse back into the cell. That means, in resting conditions, the passive K+ efflux is much greater than the passive Na+ influx. It helps in establishing and maintaining the resting membrane potential.

- After establishment of the resting membrane potential (i.e. inside negativity and outside positivity), the efflux of K+ stops in spite of concentration gradient. It is because of two reasons: i. Positivity outside the cell repels positive K+ and prevents further efflux of these ions ii. Negativity inside the cell attracts positive K+ and prevents further leakage of these ions outside.
- After establishment of the resting membrane potential (i.e. inside negativity and outside positivity), the efflux of K+ stops in spite of concentration gradient.
- **Importance of intracellular potassium ions**
- Concentration of K+ inside the cell is about 140 mEq/L. It is almost equal to that of Na+ outside. The high concentration of K+ inside the cell is essential to check the negativity.
- Normally, the negativity (resting membrane potential) inside the muscle fiber is –90 mV and in a nerve fiber, it is –70 mV. It is because of the presence of negatively charged proteins, organic phosphates and sulfates, which cannot move out normally.
- Suppose if the K+ is not present or decreased, the negativity increases beyond –120 mV, which is called hyperpolarization. At this stage, the development of action potential is either delayed or does not occur.

- **ACTION POTENTIAL**
- Action potential is defined as a series of electrical changes that occur in the membrane potential when the muscle or nerve is stimulated.
- **ORIGIN**
- Excitable cells e.g. nerve and muscle cells, generate action potentials when they are stimulated by a change in membrane potential. It is due to the disturbance in the ionic equilibrium across the receptive zone of the cell membrane i.e. changes in the conduction of ions across the cell membrane that are produced by alterations in the ion channels.

- **PHASES**
- The phases of action potential produced by various cell types differ slightly but their origin is the same. The phases of the nerve cell action potential are described here as follows:

l. During resting (polarised) state, the inside of nerve is negative and the outside of nerve is positive and the resting membrane potential in most of neurons is -70 mV.

2. When a stimulus is applied there is a brief irregular deflection of the base line, the **stimulus artifact**. It marks the point of stimulus. The stimulus artifact is followed by an isopotential interval or latent period which ends with the next potential change.

3. The first manifestation of the approaching impulse is a beginning of **Depolarization** or Reverse Polarization of membrane. Depolarization means reduction in the membrane potential from its negative value towards zero.

4. After an initial 15 mV(-55mV) of depolarization the rate of depolarization increases; the point at which this change in rate occurs is called the **firing level** (or threshold excitation).

- **5.** The tracing rises rapidly, then reaches and overshoots the zero potential line to approx. +35 mV.
- **6.** It then reverses and falls rapidly towards the resting level, called **Repolarization.**
- **7.** When repolarization is about 70% completed, the rate of repolarization decreases and tracing approaches the resting level more slowly.
- The sharp rise and the rapid fall are the **Spike Potential** of the axon, and the slower fall at the end of the process is the **After Depolarization**.
- 8. After reaching the previous resting level, the tracing becomes slightly more negative than its resting value for quite some time. This small but prolonged increase in membrane potential is called **After hyperpolarization**.

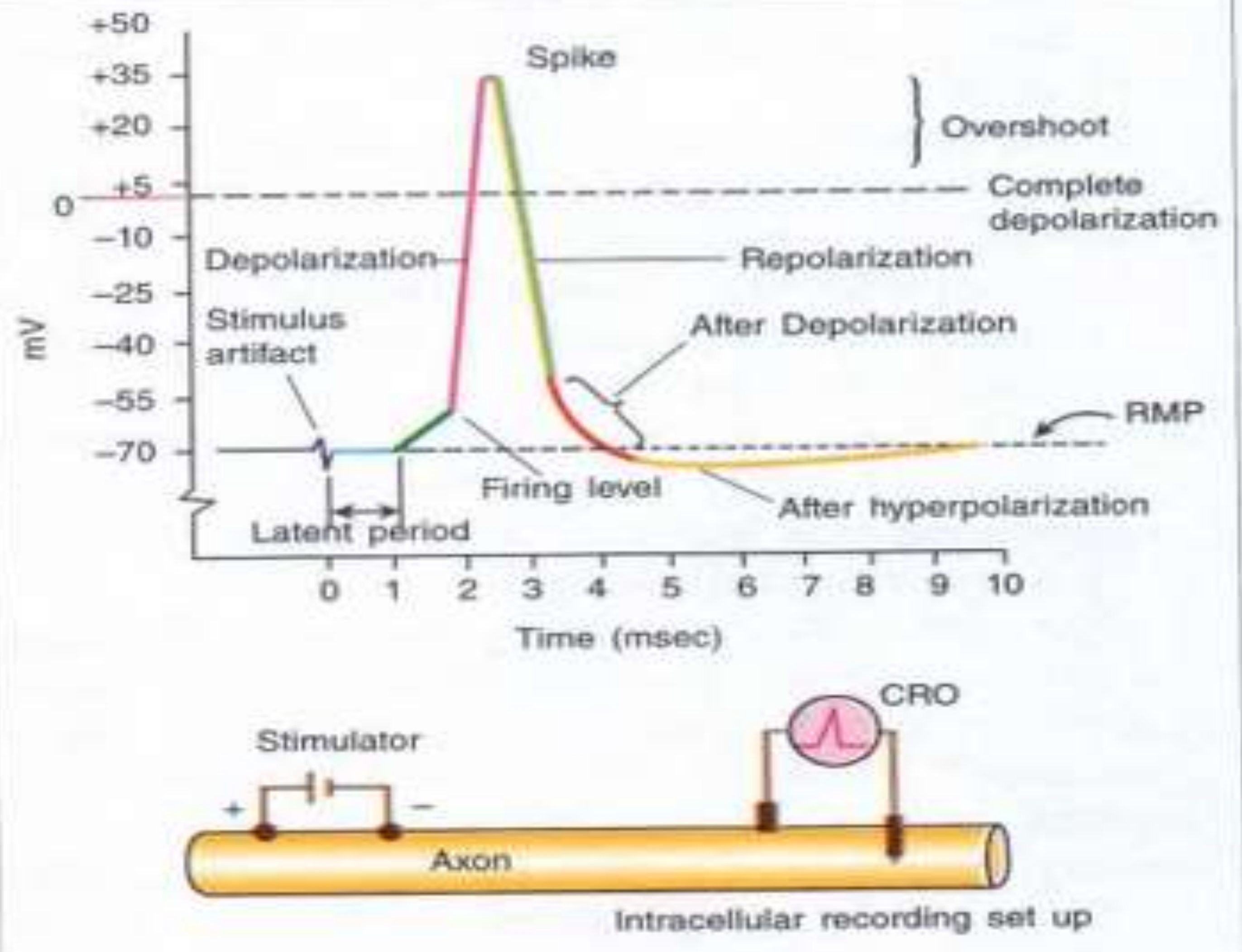
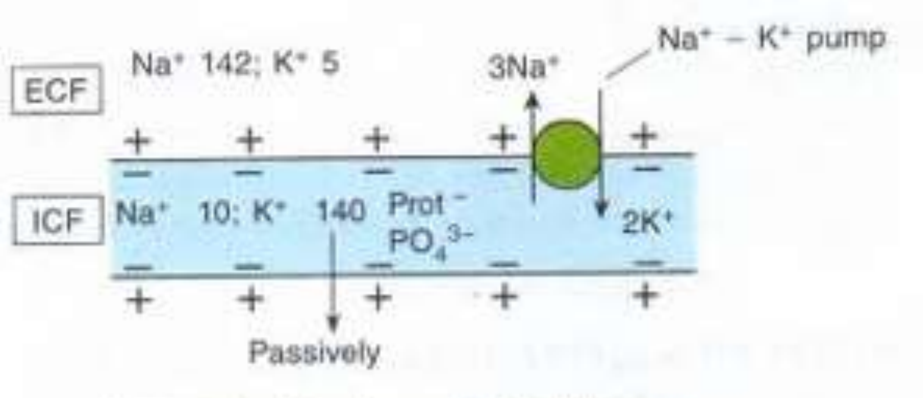


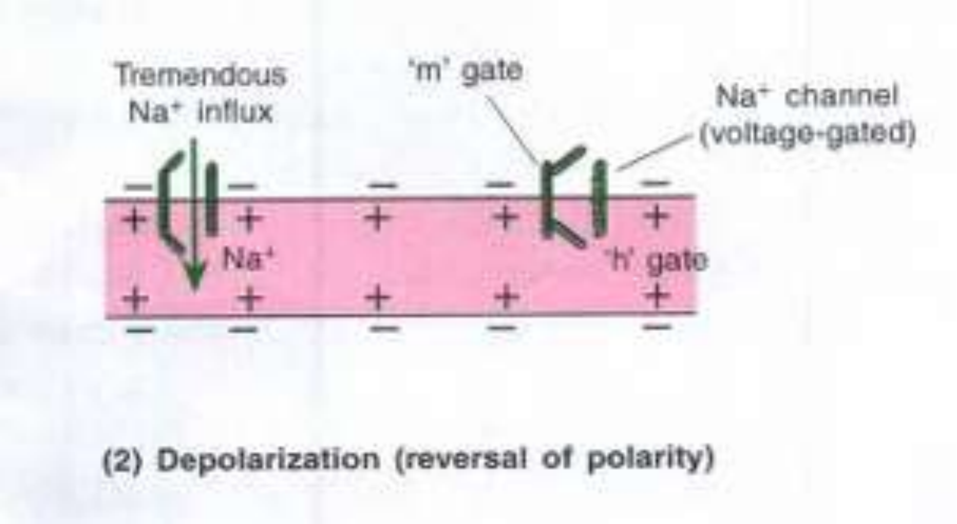
Fig. 4.2 Action potential in a neuron (intracellular recording)

- After depolarization lasts for approx. 4 msec. while after hyperpolarization is 1-2 mV in amplitude and lasts for approx. 35-40 msec. These potentials represent recovery processes in the neurons.
- If the nerve has been conducting repetitively for a long time, the after hyperpolarization is usually quite large. 'Depolarization' decreases the stability of the membrane, while 'hyperpolarization' increases the stability.
- **IONIC BASIS (MECHANISM OF DEVELOPMENT) OF ACTION POTENTIAL**
- **1. Resting (polarised) state:** R.M.P. At rest, inside of the membrane is negative and outside is positive. Since K+ permeability is greater than Na+ permeability, therefore, K+ channels maintain the RMP.



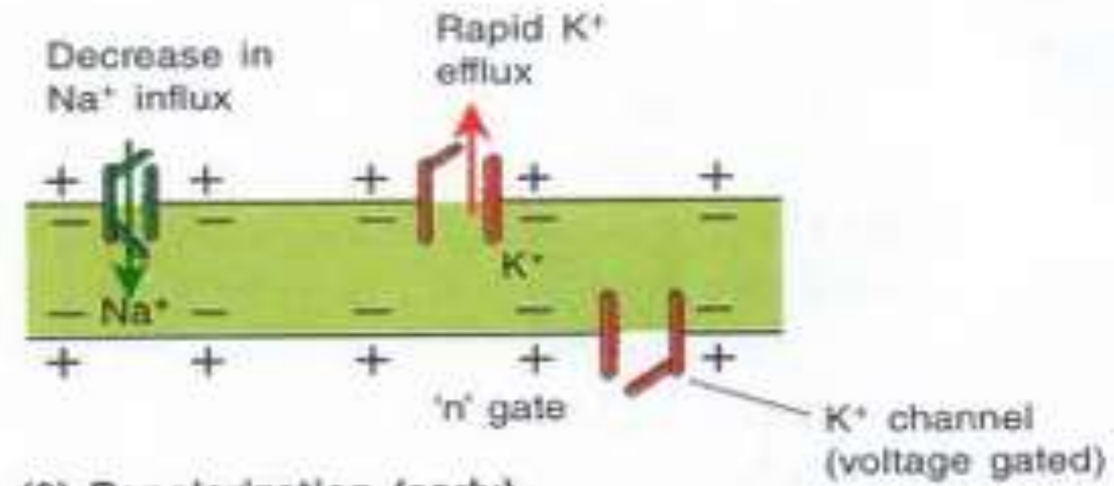
(1) Resting Membrane Potential

- **2. Depolarization:** During the onset of depolarization, voltage gated sodium channels open and there is slow influx of Na+. When depolarization reaches 7 to 10 mV, the voltage gated Na+ channels start opening at a faster rate. It is called Na+ channel activation. When the firing level is reached, the influx of Na+ is very great and it leads to overshoot.
- But the Na+ transport is short lived. It is because of rapid inactivation of Na+ channels. Thus, the Na+ channels open and close quickly.



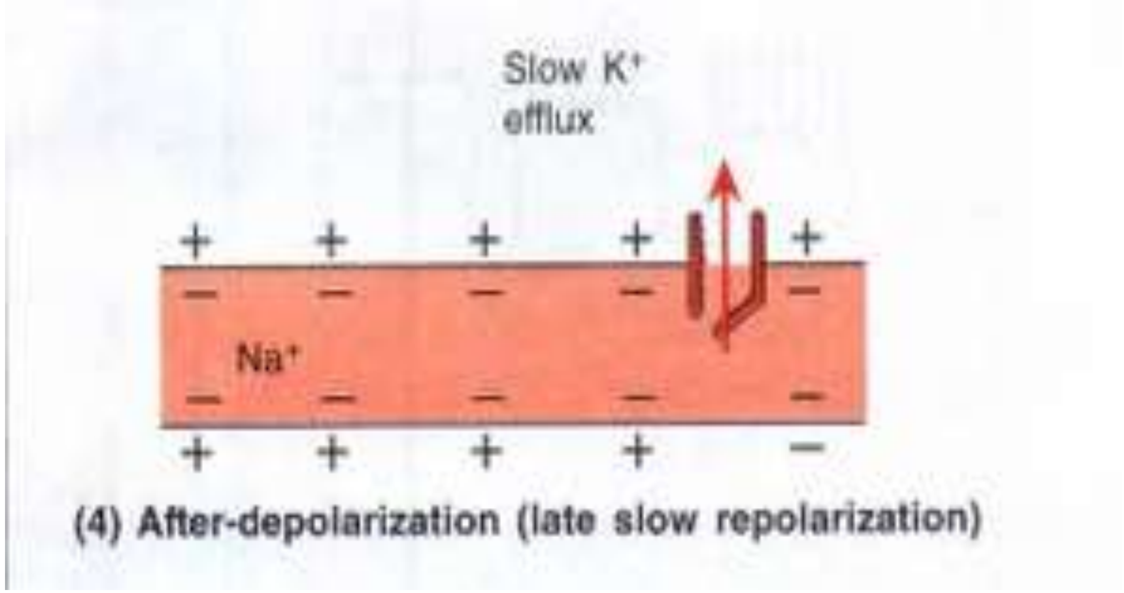
3. Repolarization

Repolarization starts with K+ efflux due to opening of voltage gated K+ channels and decreases in further Na+ influx. The opening of voltage gated K+ channels is slower and more prolonged than the opening of Na+ channels. K+ efflux cause net transfer of positive charge out of the cell that serve to complete repolarization.



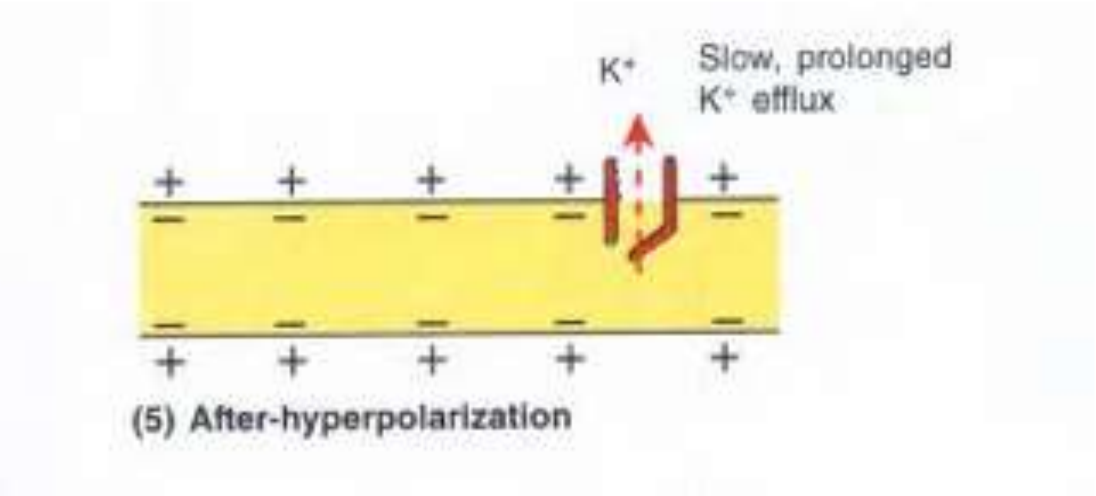
(3) Repolarization (early)

4. After depolarization: At the termination of spike potential K+ conduction is slowed down and thus a few milliseconds are delayed in restoring the membrane potential. This last phase of slow K+ efflux is called after depolarization.



- **5. After hyperpolarization**

With the disappearance of the after depolarization, though the resting membrane potential is achieved yet the resting ionic status (composition) is not established. It is achieved by slow return of the K+ channels to the closed state (although the membrane permeability to Na+ has returned to baseline levels)



- **Applied Aspect**
- **1.** Generation of action potential is prevented by local anaesthetics such as xylocaine as it blocks opening of the sodium channels thereby reducing membrane excitability.
- **2**. Decreasing extracellular Na^+ concentration decreases the size of the action potential but has little effect on the RMP.
- **3.** Decrease in extracellular $[Ca^{2+}]$ causes activation (opening) of Na^+ channels. This increases the excitability of nerve by decreasing the amount of depolarization necessary to initiate the action potential. Conversely, an increase in extracellular $[Ca^{2+}]$ decreases membrane permeability to Na^+ and stabilizes the membrane by decreasing excitability.

Revision exercise

- Describe briefly the properties of action potential.
- Draw well labelled diagram of mechanism of conduction of action potential in a neuron.

MCQs

1. Resting nerve membrane is more permeable to K+ than to Na+ by:

(a) 1-5 times (b) 20-50 times(c) 50-100 times (d) 200-500 times

2. Presence of Ca2+ on nerve membrane may play a significant role in:

(a) Operation of sodium-potassium pump (b) Regulation of K+ outflow

(c) Keeping Na+ gates closed (d) Preventing protein anion from going out

3. All or none law refers to:

(a) Resting potential (b) Excitatory postsynaptic potentials

(c) Spike potential (d) Strength of contraction

4. True about the extracellular recording of action potential:

(a) One electrode is placed on the surface and other is inserted into the interior of the cell

(b) It cannot record changes in membrane potential

(c) It cannot record resting membrane potential

(d) It can provide a record for accurate analysis of the action potential

5.Resting membrane potential is also referred as:

(a) Equilibrium potential (b) Generator potential

(c) Spike potential (d) Steady potential

6. What provides most of the energy that is used to maintain a normal resting membrane potential of about 70 millivolts inside the nerve?

(a) The chloride pump (b) The calcium pump

(c) The sodium potassium pump (d) Diffusion of chloride ions

7.The repolarization of an action potential is associated with all of the following except:

(a) Loss of positive charges from inside the cell

(b) Return of the membrane potential towards its resting value

(c) Closure of sodium channels in the cell membrane

(d) Decreased potassium permeability of the cell membrane

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THANKS