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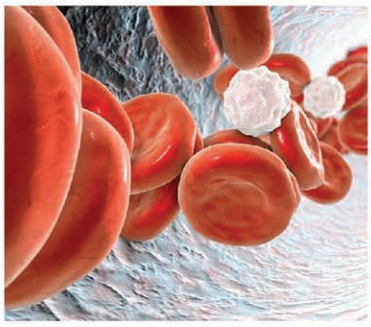

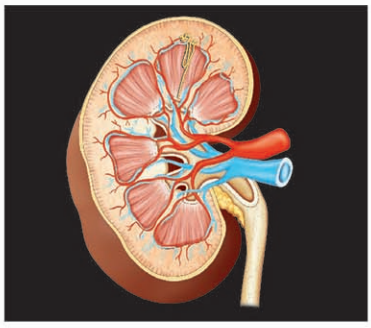



Exam Preparatory Manual for Undergraduates

PHYSIOLOGY

As per the Competency Based Medical Education Curriculum (NMC)

HIGHLIGHTS

- All essential theory and viva questions covered
- Comprehensive yet concise information for exam preparation
- Compact illustrations, line diagrams for better understanding
- Flowcharts and tables for quick revision
- Questions on applied physiology added
- Important notes and Key points have been highlighted

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4
CHAPTER

Membrane Potential

PY1.8 Describe and discuss the molecular basis of resting membrane potential and action potential in excitable tissue.

CHAPTER OUTLINE

- ❖ Membrane potential and its types
  - – Resting membrane potential (RMP)
  - – Action potential
  - – Graded potential
- ❖ Genesis of RMP
  - – Gibbs-Donnan equilibrium
  - – Role of Na^+–K^+ ATPase pump
- ❖ Action potential
  - – Ionic basis
  - – Properties

Q.1. What is membrane potential?

Ans. The cell membranes of all living cells are polarized due to movement of ions into or out of a cell, which creates a charge imbalance between the intracellular fluid (ICF) and extracellular fluid (ECF). This charge imbalance between inside and outside of the cell creates a voltage difference across the cell membrane known as membrane potential. *The membrane voltage, or potential, is determined at any time by the relative ratio of ions, extracellular to intracellular, and the permeability of each ion.*

Q.2. How is the potential difference across the cell membrane measured?

Ans.
- ❒ The potential difference across a nerve cell membrane can be measured with a **microelectrode** whose tip is so small (about a micron) that it can penetrate the cell without producing any damage.
- ❒ The membrane potential is measured using a reference electrode placed in the extracellular solution and a recording electrode placed inside the cell soma. The membrane potential is the difference in voltage between these two regions.

Q.3. Enumerate the different types of membrane potential.

Ans. There are three types of membrane potentials:
1. Resting membrane potential.
2. Action potential.
3. Graded potential: Nonpropagating potential, which decays over a distance, e.g., electrotonic potentials, receptor potentials.

Q.4. What is resting membrane potential (RMP)? Write the factors responsible for genesis of RMP.

Ans. When the cell is quiescent, the potential difference existing across the cell membrane is called the **resting membrane potential (RMP)**. The RMP is a constant voltage difference across the cell membrane during resting state, i.e., when there is no stimulation of the cell. It is expressed as minus voltage indicating that inside is more negative as compared to outside **(Table 1)**.

Factors responsible for genesis of RMP:
- ❒ **Diffusion of ions across the membrane:** Diffusion of ions across the membrane occurs due to *unequal distribution of ions,* i.e., Na^+ and K^+ across the cell membrane. There is more of K^+ inside the cell, i.e., in the ICF and more of Na^+ in the ECF. *This unequal distribution of Na^+ and K^+ is brought about by the following two factors* **(Table 2)**:
  - Gibbs-Donnan equilibrium (passive action).
  - Na^+ -K^+ ATPase (it generates and maintains the unequal distribution of Na^+ and K^+ actively).
- ❒ **Unequal permeability of cell membrane to Na^+ and K^+ ions.**

Table 1: Resting potentials in different cells.

Cell type	*Resting membrane potential (mV)*
Neuron	–70
Skeletal muscle fiber	–90
Smooth muscle cell	–50 to –60
Cardiac muscle fiber	–80

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Table 2: Different concentration of ions across the cell membrane at rest.

Ions	*ICF (mmol/L of HO)*	*ECF (mmol/L of HO)*	*Cross the cell membrane*
Potassium	150	5.5	Yes
Sodium	15	150	No
Chloride	9	125	Yes
Calcium	0.0001	1.2	No
Anion (protein)	65	<5	No

During the resting stage the cell membrane is 20–30 times more permeable to K^+ ions as compared to Na^+ and therefore K^+ diffuses down the concentration gradient or force from high concentration in ICF to lower concentration in ECF. This movement continues till an equal and opposite electrical force (potential) is developed due to the movement of K^+ ion. At this potential/voltage there is no net movement of K^+ ion. The equation relating the electrical potential and concentration gradient of an ion across a permeable membrane at equilibrium is called the **Nernst Equation**.

- **Role of Na^+ K^+ pump:** It is an electrogenic pump. Sodium ions are actively transported across the membrane to maintain the resting membrane potential.

This pump exchanges three sodium ions (which move outside) for two potassium ions (which move inside). Since, more positive ions move outside, it creates a negativity of –4 mV inside the cell (*refer* Chapter 2).

Q.5. Give the physiological significance of Gibbs-Donnan equilibrium.

Ans. The Gibbs-Donnan effect describes the unequal distribution of permeant charged ions on either side of a semipermeable membrane, which occurs in the presence of impermeant charged ions.

At Gibbs-Donnan equilibrium:

- On each side of the membrane, each solution will be electrically neutral.
- The product of diffusible ions on one side of the membrane will be equal to the product of diffusible ions on the other side of the membrane.
- The presence of impermeant ions on one side of the membrane creates an osmotic diffusion gradient attracting water into that compartment, which may cause cell swelling. The cell swelling is prevented by the operation of a sodium potassium pump.

Note: The diffusible cations and total ion concentration is greater in the protein containing compartment.

- The Donnan equilibrium is a completely passive process, i.e., no active transporters are involved in maintaining this equilibrium.

Q.6. What would be the effect of change in ionic composition of ECF on RMP and why?

Ans.

- **Hyperkalemia:** Increase in ECF, K^+ concentration will depolarize the cell and hence the magnitude of RMP will decrease.

The magnitude of RMP depends upon the concentration gradient of that ion to which the membrane is highly permeable. During resting state, the membrane is highly permeable to K^+ because of the presence of K^+ leak channels, and therefore there is diffusion of K^+ from inside of the cell to outside. By increasing ECF K^+ concentration, there is a decrease in K^+ efflux and hence the magnitude of RMP decreases.

- **Hypokalemia:** Decrease in ECF K^+ concentration will hyperpolarize the cell and hence increase the magnitude of RMP.
- **Alteration in ECF Na^+ and Ca^{2+}** will not have much effect on the magnitude of RMP as the membrane is not significantly permeable to these two ions in the resting state.

Q.7. Define an action potential (AP). Add a note on properties of action potential.

Ans. Definition: An action potential is a brief and rapid sequence of changes in the voltage across a membrane of an excitable tissue when a stimulus of threshold strength is applied to it.

Properties of action potential:

- An action potential shows **all-or-none response,** i.e., a stimulus either produces a full-sized (maximal) action potential or fails to do so. It indicates that a threshold stimulus will produce a full-fledged action potential and a further increase in the strength of stimulus (supra-threshold) is not going to increase its size further. Similarly, a subthreshold stimulus will not produce an action potential at all.
- The action potential is capable of **propagating without any decrement,** i.e., there is no change in shape and size of the action potential during propagation.
- An action potential has a **refractory period,** which limits the frequency of the action potentials and ensures their one-way propagation.
- Action potentials **cannot be summated**.
- During action potential there is **reversal of cell membrane polarity,** i.e., the cell interior becomes positive with respect to the exterior.

Q.8. Describe the sequence of events during the development of an action potential in a nerve fiber.

Ans. The **action potential** consists of several components.

- The **threshold** is the value of the membrane potential which, if reached, leads to the all-or-nothing initiation of an action potential.
- The initial or rising phase of the action potential is called the **depolarizing phase** or the **upstroke**.
- The part of the action potential between the 0 mV level and the peak amplitude is the **overshoot**.
- The return of the membrane potential to the resting potential is called the **repolarization phase**.
- There is also a phase of the action potential during which time the membrane potential can be more negative than the resting potential. This phase of

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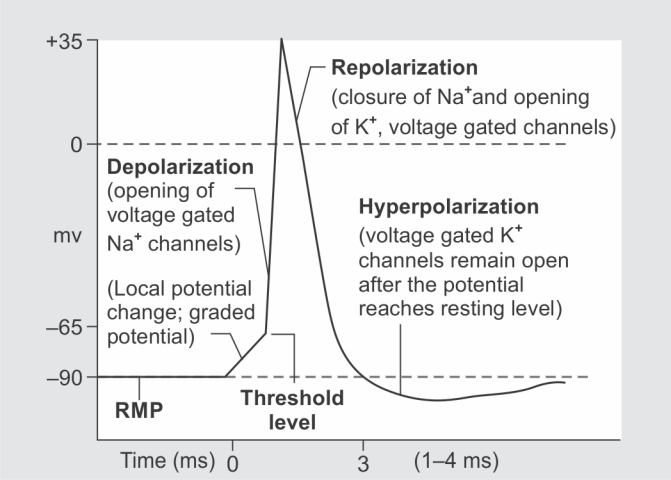

Fig. 1: Ionic basis of action potential in nerve fiber.

the action potential is called the **undershoot** or the **hyperpolarizing after potential**.

Ionic basis of action potential (Fig. 1):

- **Depolarization phase:** When the nerve is stimulated, the polarized state is altered, i.e., the RMP is abolished and the interior of the nerve becomes positive as compared to the exterior. This is called depolarization phase. An action potential begins when a depolarization increases the membrane voltage, so that it crosses a threshold value (around –55 mv).
- **If a threshold is reached**, then an action potential is produced. Action potentials are described as "all or none".
- At threshold, the influx of sodium ions through voltage-gated Na^+ channels makes the membrane potential increase very rapidly, going all the way up to +40 mV.
- **Repolarization:** The sodium channels then self-inactivate (close and become unresponsive to voltage), stopping the influx of sodium. A set of voltage-gated potassium channels open, allowing potassium to rush out of the cell down its electrochemical gradient. These events rapidly decrease the membrane potential, bringing it back toward its normal resting state.
- **Hyperpolarization:** The voltage-gated potassium channels stay open a little longer than needed to bring the membrane back to its resting potential. This results in a phenomenon called "undershoot", in which the membrane potential briefly dips lower (more negative) than its resting potential.
- Eventually, the voltage-gated potassium channels close and the membrane potential stabilizes at resting potential. The sodium channels return to their normal state (remaining closed, but once more becoming responsive to voltage). The action potential cycle may then begin again.

Q.9. Define refractory period and explain its physiological significance.

Ans.
- A refractory period is a short phase during the course of an action potential where another action potential cannot be generated.
- During action potential the cell is completely refractory to further stimulation, i.e., it has a **refractory period**.
- This period can be further divided into the **absolute refractory period** and the **relative refractory period.**
- **Absolute refractory period:** This period occurs because once the sodium channels close after an AP, they enter an inactive state during which they cannot be reopened regardless of the membrane potential. This is known as the absolute refractory period.
- **Relative refractory period:** Slowly the sodium channels come out of inactivation. During this period, the neuron can be excited with stimuli stronger than one normally needed to initiate an AP, as some Na^+ channels are still voltage inactivated. This is known as the relative refractory period.
- Because of the presence of a refractory period, the conduction of impulse in a nerve fiber is possible only in one direction.

Q.10. Discuss the conduction of nerve impulse in myelinated and unmyelinated axons. Write a note on saltatory conduction. How does the diameter of nerve fiber affect the conduction velocity in a nerve fiber?

Ans.
- **Myelinated axons:**
  - In order to allow rapid conduction of electrical signals through a neuron and make them more energy efficient certain neuronal axons are covered by a **myelin** sheath. The myelin sheath surrounds the axon to form an insulating layer.
  - There are periodic gaps along a myelinated axon where there is no myelin and the axonal membrane is exposed. These gaps are called **nodes of Ranvier.** Myelinated sections of the axon lack voltage gated ion channels whereas there is a high density of ion channels in the nodes of Ranvier. For this reason, action potential can only occur at the nodes.
  - The myelin sheath acts as a good insulator so the action potential is able to propagate along the neuron at a higher rate than would be possible in unmyelinated neurons.

The electrical signals are rapidly conducted from one node to the next node. This is known as **saltatory conduction**.

Thus, myelination increases the speed of conduction of action potentials as the action potential "jumps" from node to node.

- **Unmyelinated axons:**
  - Action potentials are propagated along the axons of neurons via local currents. Local current flow following depolarization results in depolarization of the adjacent axonal membrane and where this reaches threshold, further action potentials are

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generated. The areas of membrane that have recently depolarized will not depolarize again due to the refractory period—meaning that the action potential will only travel in one direction.

- These local currents would eventually decrease in charge until the threshold is no longer reached.

The fiber diameter also affects the velocity of action potential propagation as the resistance to local current decreases with increase in the fiber diameter thereby increasing the velocity of conduction.

Note: The most important determinants of conduction velocity in a nerve fiber:
- Myelination
- Fiber diameter

Q.11. How does an action potential differ from an electrotonic/graded potential?

Ans. See **Table 3**.

Table 3: Differences between action potential and electronic potential.

Action potential	*Graded potential*
It is propagated without any decrement	It cannot be propagated. It is a local potential, which dies down over a short distance
It obeys all or none law	Does not obey all or none law
They cannot be summated	Can be summated
Refractory period is present during the course of an action potential	Does not have a refractory period

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Salient Features

This book is written as per the competency-based medical education (CBME) guidelines for the Indian medical graduates. It covers essay type and short-answer questions. Important notes and recent advances have been added. This book fills the niche to provide basic information to an undergraduate in a nutshell. The text provides all the basic information student needs to know. Key words are shown in a bold font so that the student can rapidly go through the book just before the examination. The authors have incorporated many illustrations, tables, text boxes and flowcharts. These can serve as a source of rapid revision of physiology for both undergraduate and postgraduate medical students. It would also be useful for postgraduate entrance examination. The authors emphasize that this is not intended as a textbook of physiology but a supplement for quick revision of the subject before examination.

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They have also published "Practical Physiology—A Student's Workbook" in 2019, which is being used as a practical manual for medical undergraduates all over India.

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