

TEACHING BIOPHYSICS IV: BIOPHYSICAL APPROACH OF MEMBRANE
ACTION POTENTIAL PROPAGATION

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Abstract. This paper describes the propagation of the action potentials (APs) along a neuron as well as the chain of interconnected neurons by means of chemical and electrical synapses. At the level of dendrites, soma, axon, and axonal ramifications, the AP propagation is of electric type, being mediated by ionic currents. The soma membrane depolarizations due to affluent signals sent by dendrites are summed up in space and time. If the depolarization at the level of axonal hillock, is over a threshold, a train of APs is generated and propagated along the axon reaching the presynaptic membranes and producing the fusion of neurotransmitter vesicles, with the presynaptic membrane. The liberated neurotransmitters are passively diffusing in the synaptic cleft reaching the specific receptors embedded in the postsynaptic membrane. Here, they interact specifically with receptors and opens or closes different ionic channels depolarizing the postsynaptic membrane (for excitatory synapses) or hyperpolarizing them (for inhibitory synapses). Also, in this case, if membrane depolarization is beyond a threshold, a train of APs is downstream delivered to the next neuron and so on. The chain of neurons assuring AP propagation could be affected by different anomalies engendering many neural disorders as it is described in the last part of the paper.

Key words: Neuron, axon, synapse, ionic channels, neurotransmitters, action potential propagation

1. INTRODUCTION

This work is the fourth one in a series of teaching biophysics papers aiming to disseminate Biophysics in an accessible manner. The first three papers are dedicated to: specific interactions in living matter [1], transport through cell membranes [2], and biophysical approach of biomolecular motors [3].

Pluricellular animal organisms are endowed with nervous systems more or less complex which, together the endocrine systems, permit their integration and perpetuation in the sometimes hostile life environment.

The most complex nervous system is encountered in human beings coordinating all their actions (e.g., muscle contraction) and processing the significant information carried by the external and internal signals detected by their analyzers (e.g., visual and hearing ones). These processes are possible due to very intricate nervous networks, able to transmit afferent electrical signals to the central nervous system (CNS) and efferent signals towards the effectors.

In order to easily understand the circulation of the myriad electrical signals, called action potentials (AP), through the complex neural networks, both towards

CNS and effectors, it is necessary to firstly know: the morphology of neurons, the synaptic contacts, the types of membrane ionic channels and pumps, the disparity of ions distribution on either side of the neuronal membrane, and the kinds of generation and propagation of AP.

2. ASYMMETRIC IONIC DISTRIBUTION ON EITHER SIDE OF MEMBRANES

All living cells, in their „resting state”, maintains actively a concentration difference of ions on either side of their membrane (Fig. 1) due to the permanent antientropic activity of ionic pumps which populate the membranes as integral proteins. These pumps are driven by the energy liberated by ATP hydrolysis (*vide infra*).

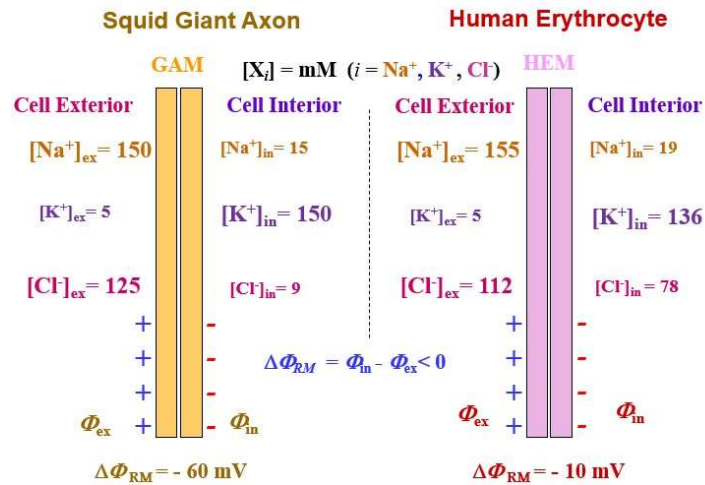


Fig. 1 - The Na⁺, K⁺, and Cl⁻ distribution on either side of giant axon membrane (GAM) of squid and of human erythrocyte membrane (HEM). Φ_{ex} = external potential. Φ_{in} = internal potential. ΔΦ_{RM} = potential difference. [X_i] (i = Na⁺, K⁺, Cl⁻). Vertical yellow and pink rectangles represent the membrane lipid bilayers (4)

3. RESTING MEMBRANE POTENTIALS

The ionic concentration differences on either side of membrane as well as the different ionic permeability coefficients, are causing the electrical polarization of membrane, so that its interior surface is negatively charged, while the external one is positive (Fig. 1).

Therefore, in the “resting state”, the cell membrane is polarized by a potential difference, ΔΦ_{RM}, which, by convention, is negative:

$$\Delta\Phi_{RM} = \Phi_{in} - \Phi_{ex} < 0 \quad (1)$$

where Φ_{in} is the internal potential ($\Phi_{in} < 0$) and Φ_{ex} is the external potential ($\Phi_{ex} > 0$).

This membrane potential difference, commonly incorrectly named membrane potential, is a consequence of the disparity concentration of ions (Na^+ , K^+ , Cl^-), on either side of membrane and also of their different permeability coefficients, P_i ($i = \text{Na}^+$, K^+ , Cl^-) of ions through the membrane.

The *resting potential*, $\Delta\Phi_{RM}$, has a special meaning, in order to be distinguished from other two types of membrane potentials, the *local* and *action potentials*. $\Delta\Phi_{RM}$ can be measured with the aid of a pair of electrodes: a microelectrode (μE) inserted into the cell through the membrane, and a macroelectrode (ME), placed in the exterior cellular medium (5; 6) (Fig. 2).

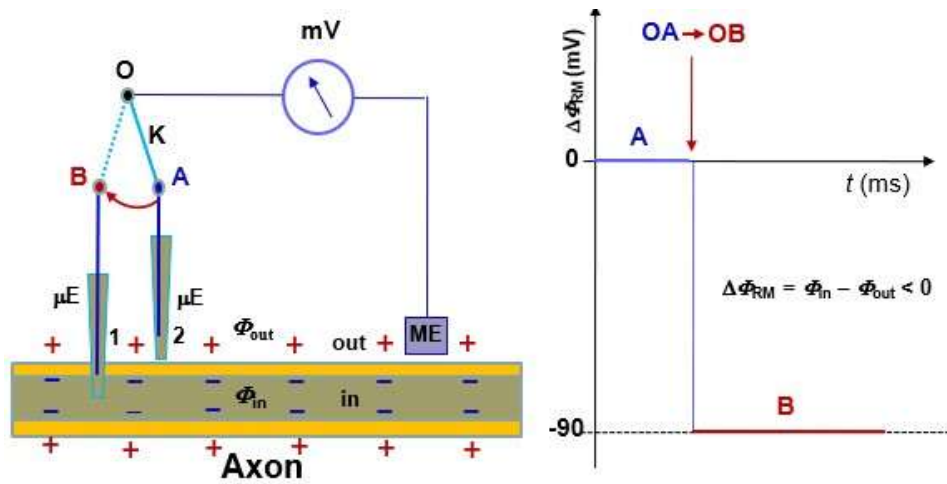


Fig. 2 - The scheme of axon's resting potential measurement. Φ_{in} , Φ_{out} = internal respectively, external electric potential. ME = exterior macroelectrode. μE = glass microelectrodes. The microelectrode 1 (μE) is inserted into the axon. The microelectrode 2 (μE) is placed outside the axon. K = two position key. mV = millivoltmeter (7)

The potential difference, $\Delta\Phi_{RM}$, across a membrane of a resting cell, namely the *resting membrane potential*, can be calculated by the *Goldman-Hodgkin-Katz (GHK) formula* (8; 9):

$$\Delta\Phi_{RM} = -\frac{RT}{F} \ln \frac{P_{Na}[\text{Na}^+]_i + P_K[\text{K}^+]_i + P_{Cl}[\text{Cl}^-]_e}{P_{Na}[\text{Na}^+]_e + P_K[\text{K}^+]_e + P_{Cl}[\text{Cl}^-]_i} \quad (2)$$

where R = universal gas constant; T = absolute temperature; F = Faraday number ($\approx 96,500$ C/mol); $[X]_{i,e}$ = molar concentrations of species X, at the interior and exterior

of the cell; P_i = permeability coefficients of three representative ionic species ($i = Na, K, Cl$).

At $T = 293,15$ K ($t = 20$ °C) the GHK formula becomes a simplified and practical one:

$$\Delta\Phi_{RM} = -58 \lg \frac{P_{Na}[Na^+]_i + P_K[K^+]_i + P_{Cl}[Cl^-]_e}{P_{Na}[Na^+]_e + P_K[K^+]_e + P_{Cl}[Cl^-]_i} \quad (3)$$

The values of $\Delta\Phi_{RM}$ calculated with the aid of practical GHK formula (3) are in a very good agreement with the measured values by the microelectrodes (Fig. 2).

Generally, in the case of excitable cells (neuronal, muscular, and glandular cells), the resting membrane potentials, $\Delta\Phi_{RM}$, are greater, in absolute value, than 50 mV and situated in the range (90 - 100) mV:

$$-100 \text{ mV} < \Delta\Phi_{RM} < -50 \text{ mV} \quad (4)$$

For instance, in the case of squid giant axon, $\Delta\Phi_{GAM} = -61$ mV and, in the case of frog muscle fibre, $\Delta\Phi_{FMF} = -99$ mV (10). By the contrary, in the case of non excitable cells, $|\Delta\Phi_{RM}| < 50$ mV. For instance, for red blood cells, $|\Delta\Phi_{RBC}| = 10$ mV (Fig. 2).

4. IONIC PUMPS

All types of cellular membranes are endowed with a multitude of integral proteins, among which are ionic pumps, able to transport ions against their electrochemical potentials thus counterbalancing the passive diffusion of ions through specific ionic channels (e.g., Na^+ and K^+ channels). By their continuous activity the ionic pumps succeed to maintain the antientropic asymmetry of ions concentration on either side of cell membrane. These pumps are driven by the energy liberated during enzymatic splitting of adenosine triphosphate (ATP) in adenosine diphosphate (ADP) and inorganic phosphate, P (Fig. 3). In the case of neuronal cells, the Na^+K^+ -ATP-ases are consuming an impressive amount (about 70 %) of energy liberated during the cellular catabolism (11).

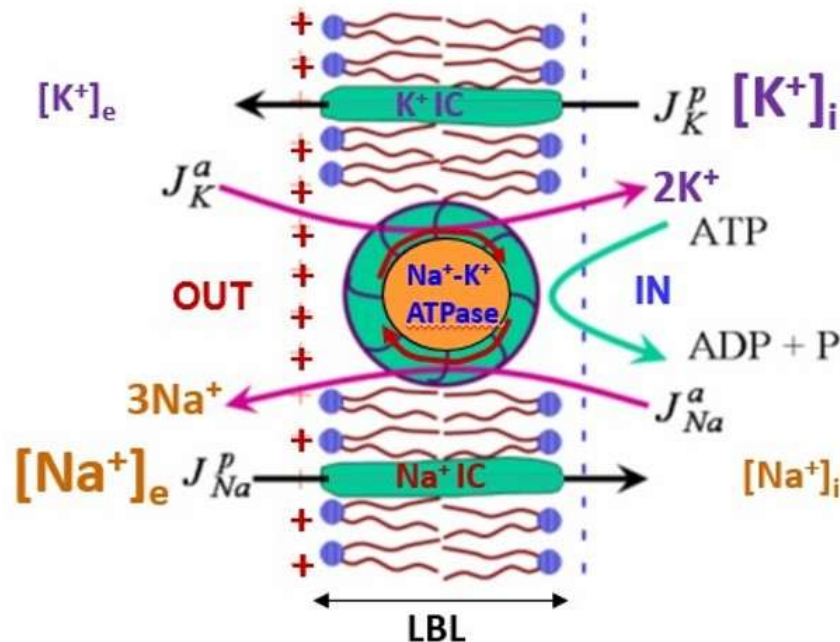


Fig. 3 - A schematic description of ionic pump, ($\text{Na}^+\text{-K}^+\text{ATPase}$), together with the ionic active and passive fluxes. LBL = lipid bilayers. Na^+IC = sodium channel. K^+IC = potassium channel. J^a = fluxes of active transport. J^p = fluxes of passive transport. ATP = adenosine triphosphate. ADP = adenosine diphosphate. P = radical phosphate. $[X_i]$ ($i = \text{Na}^+, \text{K}^+$) = ionic concentration inside (i) and outside (e) the cell (Adapted from 12).

In the case of neuronal cells, the relatively high resting potentials ($50 \text{ mV} < |\Delta\Phi_{\text{RM}}| < 100 \text{ mV}$) are a guarantee for these cells to be excited and generate trains of action potentials which are propagating downwards excitable cells (*vide infra*).

5. NEURONAL MORPHOLOGY

Central nervous system (CNS), composed of the encephal and spinal chord, together the peripheral nervous system (PNS) are composed of a huge number of neurons estimated to be about 86 billion, that is, 86×10^9 neurons (13; 14).

The neurons of CNS and PNS are quite different having in mind their morphology of the soma and axons, their magnitude, and their functions (sensitive, intermediary, and motor). In spite of the large neuron diversity, one can distinguish to all of them some common features and parts: dendrites, soma, axons, and axonal ramifications (Fig. 4).

The role of the dendrites is to collect signals from the other neurons, acting like a reception antenna. After the number of dendrites, one can distinguish the following types of neurons: *i) unipolar* without dendrites; *ii) (pseudo)unipolar*,

without dendrites (found, for example, in the sensory ganglia of cranial nerves V, VII, IX, and X); *iii*) *bipolar* neurons, with a single dendrite (e.g., bipolar cells from retina); *iv*) *multipolar* neurons, (e.g., ganglion cells of retina), with more or less dendrites (e.g., the Purkinje neuron from cerebellum possesses a very large number of dendrites).

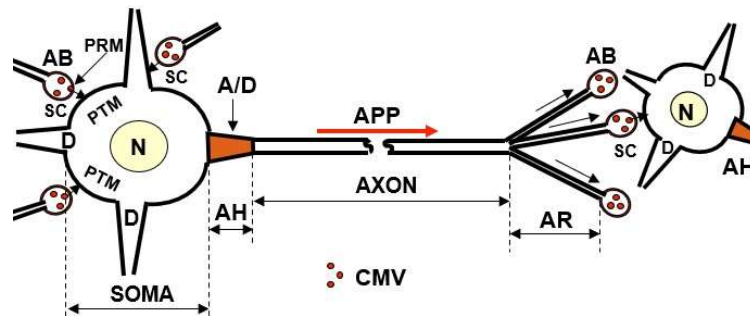


Fig. 4 - The schematic morphology of an interneuron together its synaptic connections. N = nucleus. PRM = presynaptic membranes. PTM = postsynaptic membranes. CMV = chemical messenger vesicles. SC = synaptic contacts. D = dendrites. AH = axonal hillocks. A/D = analog/digital converter. APP = sense of action potential propagation. AB = axonal buttons. AR = axonal ramifications (4).

After the form of soma, there are *pyramidal* neurons (with pyramid-shaped soma) and *stellate* neurons (with star-shaped soma).

Taking into account the axon morphology, there are two types of axons: the *myelinated* and *unmyelinated*. As for the axon length, the axons are short, medium and very long.

By synaptic neurotransmitter criteria, the neurons are of many types: *i*) *cholinergic* liberating acetylcholine; *ii*) (*nor*)*adrenergic* liberating (nor)adrenaline and dopamine; *iii*) *GABAergic* which generate gamma aminobutyric acid (an inhibitory neurotransmitter in CNS); *iv*) *glycinergic* producing glycine (a major inhibitory neurotransmitter in CNS); *v*) *glutamatergic* which liberate glutamate (a very common excitatory neurotransmitter in CNS); and *vi*) *serotonergic* which synthesize the serotonin (5-HT).

The above description of neurons and their component parts provides the very great diversity of neurons composing CNS which gives CNS a large variety of its multiple and complex functions.

6. INTERNEURONAL SYNAPSES

The neurons pertaining to networks of CNS and PNS are not isolated but, on the contrary, they are highly connected morphologically and functionally by a huge number of synapses. It is estimated that the number of synapses exceeds by far the

number of all neurons. Therefore, the huge number of neurons form a complex spatial scaffold of interconnected neurons that permanently modify their states by receiving, processing, and exchanging information through a myriad of synapses, ranging from 10^{14} to 5×10^{14} (15).

There are two distinct classes of synapses: *chemical* unidirectional synapses which can be both excitatory and inhibitory, and *electrical* bidirectional synapses. A brief description will follow.

6.1 Chemical synapses

A chemical synapse consists in the following components: *i) presynaptic space*, *ii) presynaptic membrane (PRSM)*, *iii) synaptic cleft*, a narrow space of about (20-50) nm, and *iv) postsynaptic membrane (PTSM)* (Fig. 5).

In the presynaptic space, there are many small synaptic vesicles (SV) filled with about (6,000-7,000) molecules of neurotransmitters (16; 17).

Towards the axonal button space, PRSM presents the active protein zones which are the sites of neurotransmitter release. The synaptic cleft (SC) is filled with fibrous proteins extending between PRSM and PTSM in order to form a stable structure of the synapse.

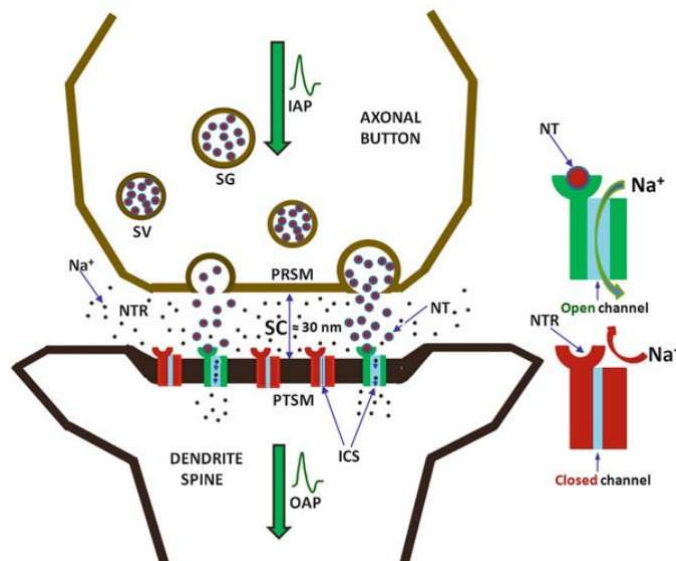


Fig. 5 - Schematic morphology of an axo-dendritic chemical synapse. PRSM = presynaptic membrane. PTSM = postsynaptic membrane. SC = synaptic cleft. SV = synaptic vesicle. SG = secretory granules. NT = neurotransmitter. NTR = neurotransmitter receptor. ICS = ionic channels of the postsynaptic membrane. IAP = incoming action potential. OAP = outgoing action potential (7).

The PSTM is formed of proteins containing neurotransmitter receptors (NTRs) which, by binding the coming neurotransmitters, are modifying the polarization state of the postsynaptic cell membrane, either depolarizing or hyperpolarizing it.

If the Na^+ channels are opened by the coupling to NTRs the excitatory neurotransmitters (e.g., serotonin, acetylcholine) the PTSM depolarization takes place and the synapse is generating an excitatory postsynaptic potential, facilitating the further transmission of the AP.

If, on the contrary, the Cl^- channels are opened by the inhibitory neurotransmitters (e.g., Gly and GABA) the PTSM hyperpolarization takes place and the synapse is generating an inhibitory postsynaptic potential blocking the further transmission of the AP.

6.2 Electrical synapses

Electrical synapses are much simpler than the chemical ones, allowing direct flow of ionic current from a neuron to an adjacent one. These synapses are composed of connexons (interneuron hydrophilic channels) that assemble together forming gap junctions. Unlike chemical synapses, their synaptic cleft is narrower, being of about 3 nm. Each connexon consists of six proteins forming a hydrophilic pore with a diameter of about 2 nm, thus allowing the free diffusion of ions. The channel-connexons are bridging the SC connecting the cytosols of the two adjacent neurons (Fig. 6).

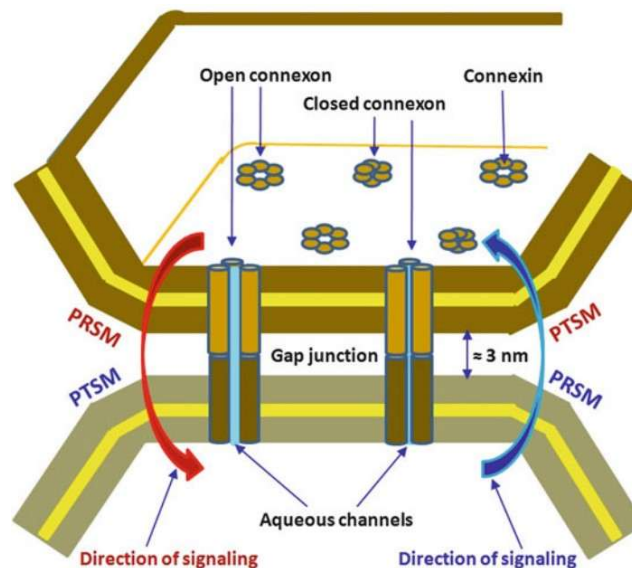


Fig. 6 - Schema of an electrical synapse. PRSM = presynaptic membrane. PTSM = postsynaptic membrane. The directions of signal propagation are indicated, too. This type of synapse is conducting the action potentials bidirectionally (7).

The AP synaptic transmission between the neurons is much faster than in the case of chemical synapses because the diffusion of neurotransmitters, taking place in chemical synapses, is a slow physical process. In the case of electrical synapses, the incoming presynaptic AP induces, almost instantaneously, an outgoing AP in the postsynaptic neuron. In the case of CNS of mammals, the electrical synapses are encountered in brain zones where the activity of neighbour neurons requires a high synchronization (18). In PNS, the electrical synapses occur, for instance, between retina cells. With a few exceptions (17) electrical synapses are conducting the AP in both directions.

7. SELECTIVE NEURONAL IONIC CHANNELS

The membranes of all cells are endowed with *selective ionic channels*. Generally, there are many types of ionic channels activated by voltage, ligand binding, mechanical stress, and even light (e.g., in the case of purple membrane of some halophilic bacteria) (Fig. 7).

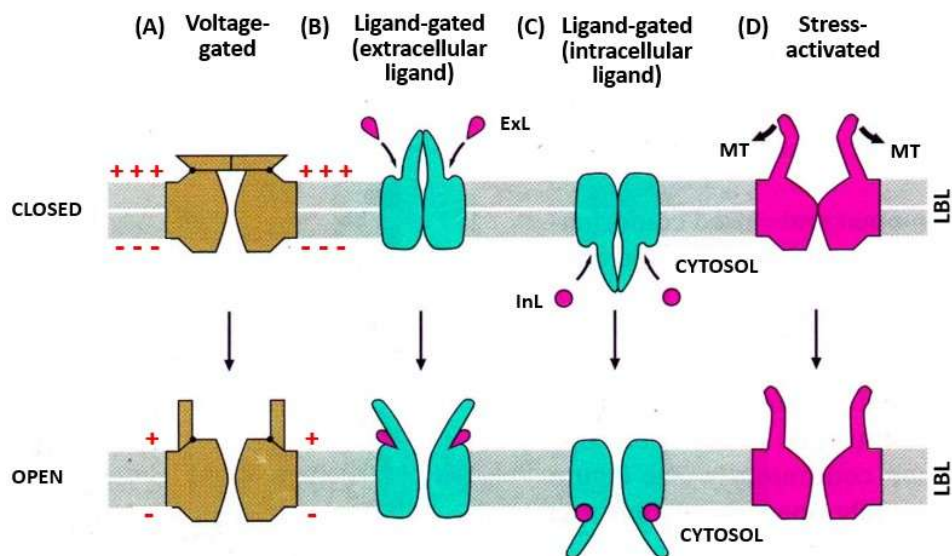


Fig. 7 - Schematic representation of the four types of selective ionic channels in their resting states and activated by voltage, ligands, and mechanical tension. LBL = membrane lipid bilayers. ExL = extracellular ligands. InL = intracellular ligands. MT = mechanical stress (Adapted after the figure designed by James F. Thompson, 2014, without Licence (19))

In the case of action potential (AP) propagation, along a chain of interconnected neurons, the important role is played by the *voltage-gated channels*. The main voltage gated channels of neuronal membrane are the selective Na^+ and K^+ channels which, in different phases of AP, are asynchronously activated becoming selectively permeable either to Na^+ or K^+ .

Having in mind the asymmetry of ion concentration on either side of neuronal membrane (Fig. 1), the voltage activated channels of Na^+ will allow the *inward passive diffusion* of these ions while, on the contrary, the voltage activated channels of K^+ will allow the *outward passive diffusion* of K^+ (*vide infra*).

The density of Na^+ and K^+ channels is significantly greater in the more sensitive parts of the neurons, for instance, the axonal hillock.

8. LOCAL AND ACTION MEMBRANE POTENTIALS

Different types of excitable cells can be activated only under the influence of their adequate stimuli (e.g., electrical, chemical, mechanical), but all the cells are excited by the *electrical stimuli* considered, for this reason, as *universal nonspecific stimuli*.

The behavior of an excitable cell to electrical stimuli, injected into the cell, can be studied using an experimental setup generating rectangular currents of stepwise intensities, J (Fig. 8, up) and recording the time evolution of membrane potential (i.e., $\Delta\Phi_{\text{RM}}$) (Fig. 8, down).

Under the small rectangular electrical stimuli (steps, 1-2, Fig. 8) the membrane potential increases exponentially, and by abruptly stop of stimuli it decays also exponentially (actually, an increase/decrease of membrane potential is a decrease/increase of its absolute value). This type of membrane potential response is called *electrotonic* and is not a specific neuronal response being not abolished by anesthetics.

If the amplitude of the electrical stimulus is further increased (Fig. 8, step 3) but remaining under a certain value (step 4) provoking a small membrane depolarization (smaller than the threshold potential, $\Delta\Phi_{\text{TH}}$), a *transient potential hump*, $\Delta\Phi_L$, is recorded. This response is called *local potential* whose amplitude, in a given axonal point, *decreases exponentially in space* (i.e., the local potential is localized). The local potential is decreasing also in time, eliciting a graded behavior (i.e., its amplitude is proportional with stimulus amplitude). This type of response is neuronal specific being abolished by anesthetics.

If the stimulus intensity, J , is sufficiently strong (e.g., greater than in step 3), so that the membrane depolarization (around cathode) is over the critical value, $\Delta\Phi_{\text{TH}}$, then the temporal evolution of membrane potential is sudden and accelerated, the membrane potential passing rapidly through a series of successive states (A-B-

C-D-E-F-G-H-I), and, finally, reaching the resting potential. This time course of the membrane potential is typical for neurons and is known as *action potential* (AP) which is further propagating along the axonal membrane.

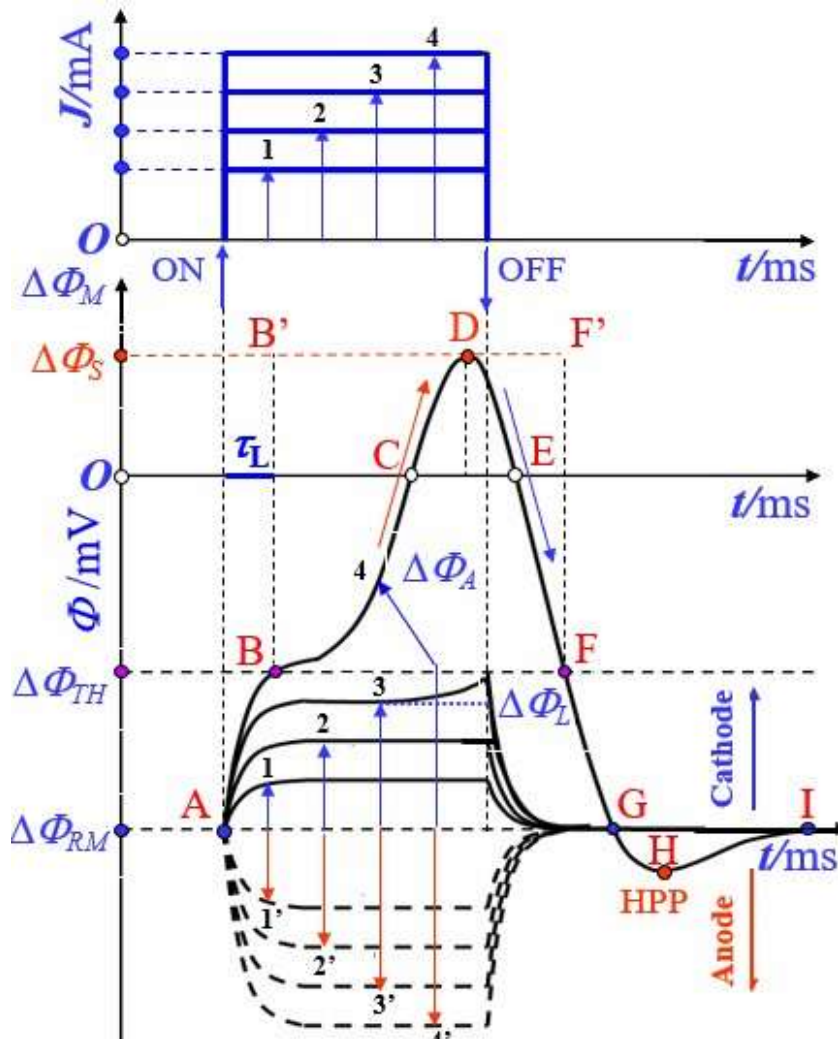


Fig. 8 - The time variation of membrane potential, $\Delta\Phi_M$ (down) under the influence of increasing rectangular currents (up). $\Delta\Phi_{RM}$ = resting potential; $\Delta\Phi_{TH}$ = threshold potential; C-D-E = potential spike; $\Delta\Phi_S$ = spike potential collected around the cathode; $\Delta\Phi_L$ = local potential collected around the cathode; $\Delta\Phi_A$ = action potential; τ_L = latency time; 1, 2 = electrotonic passive potentials. 3 = local potential. 1', 2', 3', 4' = electrotonic passive potentials collected around the anode. HPP = membrane hyperpolarization (Adapted from 12; 20)

9. ACTION POTENTIAL PROPAGATION

As opposed to local potential, the action potential is delocalised and is propagating along the axons and axonal ramifications without decrement respecting the law *all or none*, that is, its amplitude remains the same, irrespective of the excitation intensity above the threshold.

The propagation velocity of AP depends on the type of axons (unmyelinated or myelinated) and on the axon diameter.

9.1 Propagation along unmyelinated axons

The velocity of AP propagation along an unmyelinated axons is greater in larger axons.

In the case of unmyelinated axons (e.g., squid giant axons) AP potential velocity, v , has a small value, because the depolarization of axolemma, near the axonal hillock, is propagating unidirectionally (i.e., orthodromically) by *local Hermann currents*, towards the axonal ramifications, as it is illustrated in Fig. 9A. For instance, the conduction velocity of a typical 0.5 mm diameter of squid giant axon is lesser than 25 m/s.

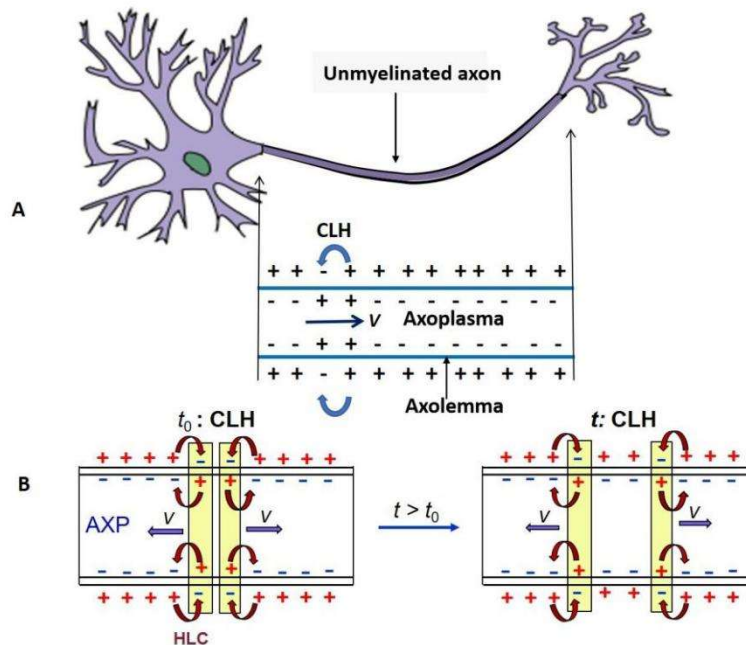


Fig. 9 - Schematic representation of action potential propagation along the unmyelinated axon. LHC = local Hermann currents. AXP = axoplasm. Yellow rectangles = axonal depolarization zones. v = velocity of AP propagation (4; 21).

In the case of an isolated unmyelinated axons, if the electric stimulus is producing a depolarization in the middle of the axons, the depolarization (i.e., AP) is propagating in the both directions (Fig. 9B).

9.2 Propagation along myelinated axons

During living matter evolution, the superior organisms were endowed with a very performant neurons possessing myelinated axons. The axons of myelinated neurons are covered by myelin sheaths, generated by the Schwann cells, separated by naked axolemma portions called Ranvier nodes (Fig. 10 A).

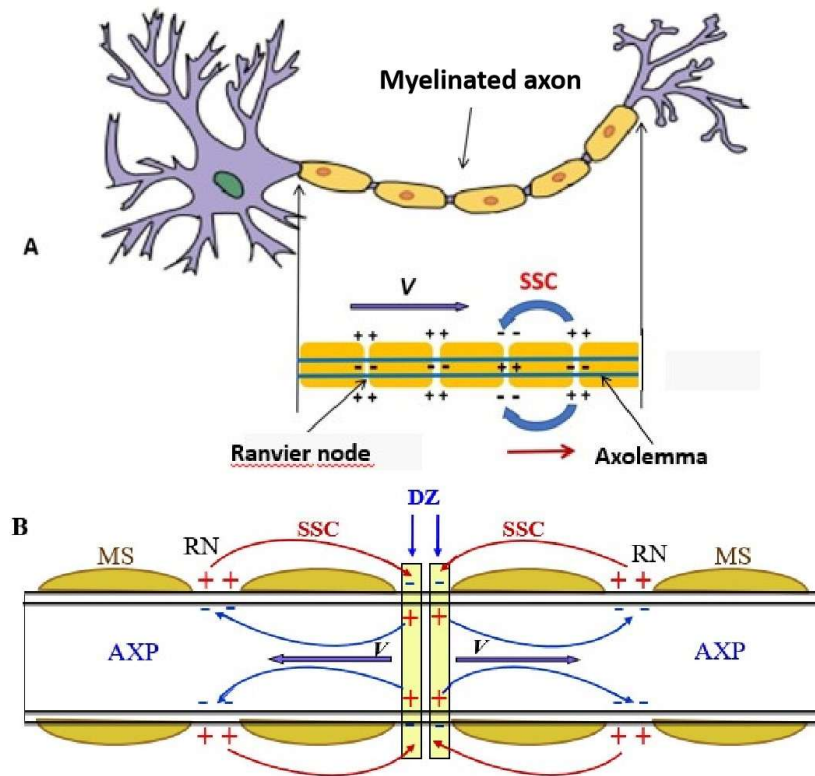


Fig. 10 - Schematic representation of action potential propagation along the myelinated axon. DZ = depolarized zone of axolemma. Yellow rectangles = axonal depolarization zones. SSC = saltatory Stämpfli currents. AXP = axoplasm. MS = myelin sheaths. V = velocity of AP propagation. RN = Ranvier nodes (4; 21).

The myelin sheaths insulate chemically and electrically the axolemma from the external medium. On the contrary, the Ranvier nodes allow the axolemma to communicate with the external medium exchanging ions with it. These „windows” permits also the electrical stimuli to modify the polarization state of axolemma.

Due to this particular morphology, the depolarization of axolemma, near the axonal hillock (Fig. 10A), is propagating, unidirectionally and very rapidly, as an AP wave by *saltatory Stämpfly currents* from a Ranvier node to the next one (Fig. 10A). For this reason the velocity of AP conduction is very high, in some cases attaining the value of 125 m/s. This natural „invention” (i.e., myelinisation) assure a rapid communications among the neurons decreasing substantially the organism reaction time to external stimuli.

In the case of an isolated myelinated axons, if the electric stimulus is inducing a depolarization in the middle of the axon, the depolarization is propagating in the both directions (Fig. 10B).

9.3 Somatic action potential propagation

At the level of neuronal soma, all the APs converging to it, along the upstream dendrites, will provoke partial spatial and temporal depolarizations of its membrane potential. Their effects are summed in space and time producing a continuous increase of membrane depolarization. This depolarization is propagating towards the axonal hillock. If the total depolarization is exceeding a certain threshold value, discrete APs will be emitted by the axon hillock which is behaving alike an analog/digital transducer.

The hillock generated trains of AP are propagating along the axons and to all axonal ramifications, without decrement, reaching the presynaptic membranes or the downstream synapses.

9.4 Synaptic propagation of action potentials

Chemical synapses, involved in the electrical AP transmission or in the blockade of neuronal signals, have a basic role in information processing both in CNS and PNS.

In the case of chemical synapses, the incoming APs towards the presynaptic membranes will provoke the fusion of the synaptic vesicles (located in the axonal buttons) with the presynaptic membrane (PRSM). These vesicles charged with neurotransmitters (e.g. acetylcholine) are trafficked by the kinesin motors, from the axonal ramifications toward the synaptic space. Here, by fusion with PRSM, the neurotransmitters are liberating into synaptic cleft. Then, the neurotransmitters will passively diffuse (due to thermal motion) towards the postsynaptic membrane

(PTSM). This membrane could pertain to a dendrite, a soma or even to an axon of the downstream neuron (Fig. 5).

The postsynaptic membranes are endowed with neurotransmitter receptors attached to ionic channels (e.g., Na^+ channels) which are embedded into them. In the resting states, when the receptors are not occupied by neurotransmitter molecules, the channels are closed. But, by interactions of neurotransmitter molecules with the specific receptors of the PTSM, the channels will open allowing the passive diffusion of Na^+ into the postsynaptic space, provoking the PTSM depolarization.

The more the neurotransmitter vesicles are fusing with PRSM, the more neurotransmitters are liberated into synaptic cleft, and the more neurotransmitter molecules will interact with the PTSM receptors.

If the number of PTSM receptors which interact with the neurotransmitters is sufficiently high, the PTSM will suffer a significant depolarization in the case of excitatory synapses (i.e., beyond a threshold) or a hyperpolarization, in the case of inhibitory synapses. If the chemical synapse is of excitatory type, trains of APs will be generated towards the downstream partners. In the case of inhibitory synapses, the propagation of the signal (i.e., AP) is blocked. In this way, the upstream neuron can influence the state of the downstream neuron.

Therefore, the electrical propagation of APs in upstream neurons is replaced by chemo-physical propagations, at the level of synapses, and thus it is continued by the downstream electrical AP propagations and so on.

Observation. The synaptic AP conduction, taking place at the level of synapses during the AP transmission from a presynaptic to a postsynaptic neuron is lasting about (0.5 - 1.0) ms, being considered as a synaptic delay of AP.

9.4 Neuronal reflex arc

In order to summarize the AP propagation along a chain of contiguous neurons, the successive steps of AP propagation *via* dendrites, soma, axons and synapses, are illustrated in the case of a representative reflex arc, namely, the neuromuscular junction reflex arc (Fig. 11). One can observe that the electrical rapid AP conduction is successively interrupted by the slower physico-chemical conduction at the levels of the synapses.

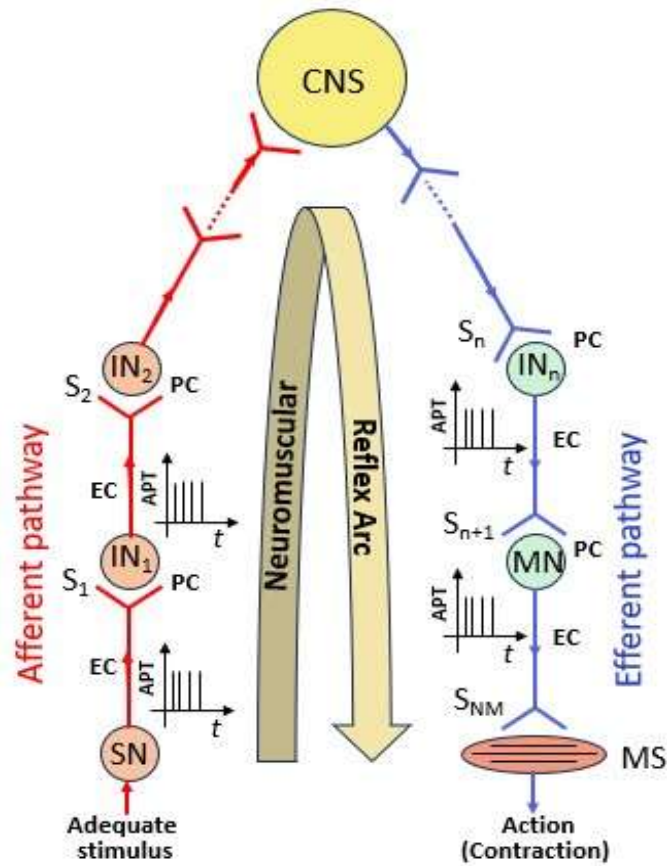


Fig. 11 - Schematic representation of a particular reflex arc, namely the AP afferent alternative propagation (electrical and physico-chemical) from a sensory neuron (SN) towards the CNS (encephal and/or spinal chord) and efferently from here towards a motor neuron (MN) which makes a synapta neuronal junction (S_{NM}) with a muscle (MS). The electrical conduction (EC) along dendrites, soma and axon is converted in physico-chemical conduction (PC) at the level of synapses $S_1, S_2, \dots, S_n, S_{n+1}$. The sensory neuron (SN) is activated by an adequate stimulus (e.g., thermal, mechanical etc.). IN_k ($k = 1, 2, \dots, n$) = intermediary neurons. APT = action potential trains as a function of time, t . As a result of this reflex arc, the muscle responds by a contraction (e.g., a twitch).

10. BLOCKING OF ACTION POTENTIAL PROPAGATION

Knowledge concerning both the morphology and physiology of AP propagation along the multitude of neuronal chains and networks is of great importance for medicine.

In many circumstances, the AP propagation can be blocked this engendering different types of anomalies and even serious diseases.

The AP propagation can be abolished at different levels: ionic channels, axons, synapses, soma, etc.

A great number of diseases, referred to as the *channelopathies*, are the result of defective function of voltage-gated Na^+ , K^+ and Ca^{2+} channels (22; 23; 24; 25). These diseases (e.g., epilepsy, schizophrenia), are due to mutations in the genes that encode ionic channel proteins.

Observation. A salutary effect of normal ionic channel blocking is desired and obtained by different anaesthetics drugs.

As concerns the axons, one of the most grave medical conditions is *multiple sclerosis* due to axon demyelination, impeding the proper AP conduction along the axon.

The decrease of synapse number, the modifications of their morphology and biochemistry provoke the perturbation of neuronal circuits, causing the *synaptopathies* like some psychiatric and neurologic disorders: Alzheimer's disease, schizophrenia, addiction, etc. Also, the chemical synapses are the target for many psychoactive drugs (e.g., morphine, strychnine). For this reason, the synapses constitute important targets for treatments to stop progression and preserve the cognitive and functional abilities in the case of brain diseases (26).

CONCLUSION

The action potential is the main vehicle carrying vital information, regarding both external and internal stimuli, towards the central nervous system (brain and spinal chord) which is able to analyze and optimally process them to send adequate orders to the effectors (muscle, glands) through trains of action potentials.

Because the neuronal chains are composed from contiguous neurons (i.e., connected by synapses) the nervous system uses two alternatives of action potential propagation: one electro-chemical *via* myelinated and unmyelinated axons, and the other chemo-physical by traversing the synaptic cleft.

The first type of conduction is more rapid, especially in the case of myelinated axons, while the synaptic conduction is slower due to neurotransmitter diffusion, which is a rate-limiting step. In spite of this, the global reaction time of a reflex arc, for instance, is relatively short permitting the organism to take the optimal decisions in order to integrate it in the environment and to survive.

Dysfunction of ionic channels, axons, and synapses causes a number of neuronal diseases (for example, *channelopathies*, *synaptopathies*) which engender many psychological and neuronal conditions can be ameliorated or cured by the in deep understanding of the anatomy and physiology of the AP genesis and propagation into neural circuits and networks.

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