PROPAGATING NERVE IMPULSE IN QUASI-STEADY STATE CONDITIONS*

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The paper presents general facts on the propagation of the neural flow and investigates the propagation of the nerve impulse along the axons in the hypothesis of the quasi-steady state conditions. The steady state conditions suppose constant velocity of propagation, depending nor on the structure of the axon neither on the voltage applied. The resulting equation describing the nerve flow is a wave type equation and some numerical results based on experimental values of the parameters are presented.

Key words: nonlinear dynamics, neural flow, electric circuits.

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1. INTRODUCTION

In this paper we analyse few models of electric circuits which allow to derive some neurophysiologic properties of the neural flow. These circuits are not specific for one single neuron, but they give rather a macroscopic view on the neural flow. It is clear that the propagation of the neural flow is not at all a linear process, that is it is not possible to represent the neural circuits as simple resistive ones. We have to consider elements with nonlinear characteristics $I = f(V)$, whose parallel or serial combination can generate the usual neurological signals. There were many attempts to propose electronic circuits suitable for describing the passage of the neural flow and to find mathematical equations adequate for these signals. The most influential model was proposed in 1952 by Hodgkin and Huxley [1], a model considering "the flow of electric current through the surface membrane of a giant nerve fibre". It is based on a rather complicated differential equation which has been simplified by FitzHugh, Nagumo and other scientists [2]. The aim of this paper is to present a simplified and pedagogical approach to the subject, using very simple electrical circuits. The paper is structured in five different sections. After this introductory part, the next section will introduce the main mechanisms which explain the propagation of the neural flow in terms of electric circuits. The main electric rules which

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apply in these circuits, as for example Ohm law or Kirchhoff laws, will be written down for the considered circuits. Based on these considerations, in the third section we shall effectively explain the so-called subthreshold phenomena in the neural membrane [3]. The main idea of these models is that the membrane behaves as a capacitor with many conducting channels joining its two sides, the extracellular and the cytoplasmic ones. Different types of ions existing around could pass through the channels, either because of the electromagnetic forces (electric current), or because of the diffusion process due to the gradient of ion concentration (diffusive current). Moreover, different physical and chemical interactions existing inside the channel can generate supplementary currents, as a genuine current source. Section four is devoted to the study of a special case of neural flow propagation: the case when the velocity is considered as being constant and the geometric form of the neural impulse can be approximated with a propagating wave. Some concluding remarks will end the paper.

2. CONDUCTION MECHANISMS. GENERAL ASSUMPTIONS

Let us consider the neural flow as an electric current passing through a conductive fibre. As we already mentioned, there are mainly three moving mechanisms for the ions. The first one is given by the existence of the electromagnetic forces generated by the voltage gradient. In this case the current density $\overrightarrow{j_e}$ is proportional with the strength of the electric field $\overrightarrow{E}$, that is with the gradient of the electric potential ϕ:

$$\overrightarrow{j}_e = \sigma \overrightarrow{E} = -\sigma \left(\nabla \phi \right). \tag{1}$$

In the previous relation σ is the conductivity of the medium. It can be proved that in the case of k different types of ions with the mobility $\{u_k, k = 1,2..\}$, valence $\{z_k, k = 1,2,..\}$ and concentrations $\{C_k, k = 1,2...\}$, the conductivity σ in the previous relation can be expressed as:

$$\sigma = \sum_k u_k \frac{z_k}{|z_k|} C_k. \tag{2}$$

The ratio $z_k \,/\, |z_k|$ designates the sign attached to the electromagnetic force and it is considered positive for cations and negative for anions. The relation (1) leads to a linear characteristic of the current intensity, represented as a monotonically increasing function $I_e = f(\phi)$ of the voltage ϕ and it suggests that the neural fibre is equivalent with a linear conductor.

A second mechanism which produces ions displacement through the membrane is related to the existence of a concentration gradient ∇C_k. The density current is given in this case by Fick's first law and it has the form:

$$\overrightarrow{\jmath}_c = -\sum_k D_k z_k F\left(\nabla C_k\right). \tag{3}$$

Here $\{D_k, k = 1, ...\}$ represents the diffusion coefficients of the different types of ions and can be expressed as [4]:

$$D_k = \frac{u_k RT}{|z_k| F}. \tag{4}$$

Unlike (1), the current (3) corresponds to a device whose current-voltage relation is characterized by a monotonically decreasing characteristic. Such a conduction device or structure is called diffuser.

There is a third type of ion flow that can be identified in the neural cells. It corresponds to a current generator and it is due to various chemical phenomena which create supplementary ions. These generators are called *ion pumps* and they can be seen as nonlinear currents $\overrightarrow{\jmath}_{pump}$. Recall that a standard linear dependency of the current intensity I on the potential ϕ can be written as $I = g\phi$, where g denotes the conductivity. Ion pumps are responsible for the electrical activity which appear as neuronal responses to various stimulus and allow a better understanding of spiking neuron networks and the underlying neural code [5]. It is clear that the pumps can not be modulated as linear elements. If it would be so, we could imagine the neural flow as a current passing through a parallel circuit with only linear elements. Following the Kirchhoff laws, we could decompose these currents as:

$$g\phi = (g - d)\phi + d\phi \tag{5}$$

and, for any $d < 0$, we could get a total cancellation of the currents. Thus, to avoid such arbitrary cancellations between conductors and diffusers of equal strength, we shall follow a normalizing rule and we shall always see the neural flow as an overlap between a linear conductor and a nonlinear diffuser with zero maximal diffusion coefficient. This form of decomposition is called canonical. Then, the previous relationship will be used as [6]:

$$I = f(\phi) = g\phi + [f(\phi) - g\phi] := f_e(\phi) + f_d(\phi). \tag{6}$$

Taking into account the three previously mentioned conduction mechanisms, the total density of the current passing through the cell membrane can be written as a sum:

$$\overrightarrow{\jmath}_{total} = \overrightarrow{\jmath}_e + \overrightarrow{\jmath}_c + \overrightarrow{\jmath}_{pump}. \tag{7}$$

After the ions density is established and the chemicals pumps have reached the equilibrium, we can write the equilibrium condition for the ions of type k in the following manner:

$$\vec{j}_{total} = 0 \Rightarrow D_k \nabla C_k = -\frac{C_k z_k F}{RT} \nabla \phi. \tag{8}$$

This leads to the following voltage V_k on the cell membrane at the equilibrium state for the ions of type k:

$$\ln \frac{C_{0,k}}{C_{i,k}} = -\frac{z_k F}{RT}(\phi_{0,k} - \phi_{i,k}) \Rightarrow V_k \equiv \phi_{i,k} - \phi_{0,k} = -\frac{RT}{z_k F} \ln \frac{C_{0,k}}{C_{i,k}}. \tag{9}$$

We denoted by the indexes 0 and i the quantities related with the extracellular, respectively intracellular environments.

3. SUBTHRESHOLD MEMBRANE PHENOMENA IN NEURAL CELLS

Let us consider now the phenomena taking place at the level of the cell membrane. Taking into account the relation (9), one can define the membrane polarization states. The cell membrane is said to depolarize if its voltage moves toward $V \equiv \phi_0 - \phi_i = 0$. If the voltage moves away from this value, the membrane or the channel is said to hyperpolarize. Concerning the energy spread inside the membrane during the electric conduction, it can be expressed as:

$$W_e \equiv q(\phi_0 - \phi_i) = zF(\phi_0 - \phi_i) = zFV_m. \tag{10}$$

The relation (9), known as the Nernst-Plank equation for neuron, describe the flux of k ions through membrane at the equilibrium. Usually, three types of ion should be considered:potassium, sodium and chlorine. A total equilibrium condition for these three categories of ions supposes that the following (Donnan) condition is observed:

$$\frac{C_{0,\mathrm{K}}}{C_{i,\mathrm{K}}} = \frac{C_{0,\mathrm{Na}}}{C_{i,\mathrm{Na}}} = \frac{C_{i,\mathrm{Cl}}}{C_{0,\mathrm{Cl}}}. \tag{11}$$

This condition translated in the language of (9) gives:

$$V_m = -\frac{RT}{F} \ln \frac{P_{\mathrm{K}} C_{i,\mathrm{K}} + P_{\mathrm{Na}} C_{i,\mathrm{Na}} + P_{\mathrm{Cl}} C_{0,\mathrm{Cl}}}{P_{\mathrm{K}} C_{0,\mathrm{K}} + P_{\mathrm{Na}} C_{0,\mathrm{Na}} + P_{\mathrm{Cl}} C_{i,\mathrm{Cl}}}. \tag{12}$$

The coefficients $\{P_k, k = 1,2,3\}$ have expressions coming directly from Nernst-Planck equation. There are values of the potential V_{Na},V_{K} and V_{Cl} for which the conduction of respectively ions is stopped. These values are called rest potentials.

Coming back to the conducting phenomena through neural cell, the most usual model is the model of a capacitor in parallel with some conducting channels. The expression for the total transmembrane current density is the sum of ionic components $\overrightarrow{j}_e$, $\overrightarrow{j}_c$ and $\overrightarrow{j}_{pump}$ and the capacitive current $j_{cap} = c\frac{dV_m}{dt}$, with c representing the

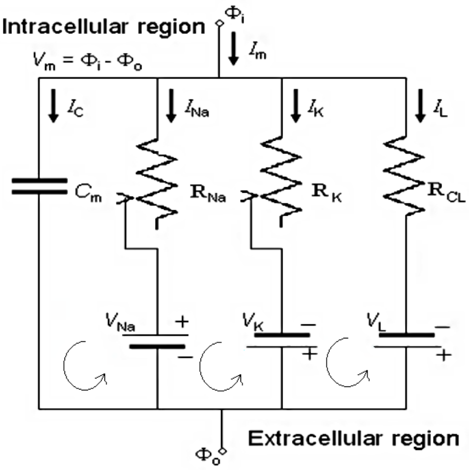

Fig. 1 – Linear and nonlinear elements in the membrane cell

membrane capacitance per unit length. Following Kirchhoff law, we have:

$$\jmath_{total} \equiv c\frac{dV_m}{dt} + g_{\mathrm{Na}}(V_m - V_{\mathrm{Na}}) + g_{\mathrm{K}}(V_m - V_{\mathrm{K}}) + g_{\mathrm{Cl}}(V_m - V_{\mathrm{Cl}}). \qquad (13)$$

This equation take into consideration an homogeneous distribution of the potential along the membrane. Hodgkin-Huxley model [1] introduced a more realistic dependency of the potential, not only on time, but also on the longitudinal coordinate of the axon, $\phi = \phi(t,x)$. According with this model, the total membrane current satisfies an equation which can be written in the form:

$$\jmath_{total} \equiv \sum_k \jmath_k + c\frac{\partial V}{\partial t} = \frac{1}{r_k + r_0}\frac{\partial^2 V}{\partial x^2}. \qquad (14)$$

We used the notations r_k the intercellular axial resistance per unit length of axon for the ions of type k and r_0 the interstitial resistance per unit length. In practice, the resistance of the external medium per unit length r_0 is usually omitted. As far as r_k, it can be expressed considering the axon as a cable of radius a with the axial resistivity ρ_k as:

$$r_k = \frac{\rho_k}{\pi a^2}. \qquad (15)$$

Imposing to the currents $\jmath_k$ in (14) to have the expressions appearing in (13), and taking into account (15), we get a final equation known as the cable equation for axon:

$$\frac{a}{2\rho_k}\frac{\partial^2 V_m}{\partial x^2} = C_m\frac{\partial V_m}{\partial t} + G_{\mathrm{Na}}(V_m - V_{\mathrm{Na}}) + G_{\mathrm{K}}(V_m - V_{\mathrm{K}}) + G_{\mathrm{Cl}}(V_m - V_{\mathrm{Cl}}). \qquad (16)$$

It has the form of a differential equation linear in the membrane potential V_m, where we introduced the unit length quantities $C_m \equiv \frac{c}{2\pi a}, G \equiv \frac{g}{2\pi a}$. A more general form of this equation has been studied in [7] and the invariant quantities have been pointed out.

4. MEMBRANE POTENTIAL UNDER THE STEADY-STATE CONDITIONS

Let us consider the particular case in which we suppose that the neural flow travel along the axon with constant velocity Θ. Under these conditions, the impulse maintains its original form during the propagation, hence the assumption that it obeys the wave equation is quite natural. Such a regime is called steady-state regime and it is described by an equation of the form:

$$\frac{\partial^2 V_m}{\partial x^2} = \frac{1}{\Theta^2}\frac{\partial^2 V_m}{\partial t^2}. \tag{17}$$

From (17) and (16) we obtain an equation for the membrane potential which is still linear in potential, as long as the velocity is considered as being constant.

$$\frac{a}{2\rho_k \Theta^2}\frac{\partial^2 V_m}{\partial t^2} = C_m \frac{\partial V_m}{\partial t} + G_{\mathrm{Na}}(V_m - V_{\mathrm{Na}}) + G_{\mathrm{K}}(V_m - V_{\mathrm{K}}) + G_{\mathrm{Cl}}(V_m - V_{\mathrm{Cl}}). \tag{18}$$

The experiments show that the propagation velocity of the nerve impulse is directly

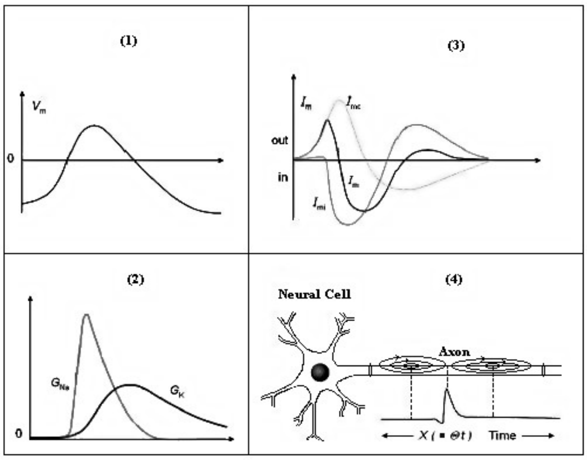

Fig. 2 – Numerical analyses

proportional to the square root of axon radius a in unmyelinated axons: $\Theta^2 \sim a$, so the previous equation takes a simpler form. The aim of this section is to present some results pointed in literature [4] coming from numerical simulations concerning the membrane potential solution of the equation (18). We used the electric model of the membrane represented in Fig. 1 in the above and the values of the constants appearing in equation (18) given by practical measurements are: $C_m = 1$ µ F/cm^2; $G_{\mathrm{Na,max}} = 120$ ms/cm^2; $G_{K,\mathrm{max}} = 36$ ms/cm^2; $G_L = 0.3$ ms/cm^2; $V_{\mathrm{Na}} = -61\log_{10}(15/150) = +61$ mV; $V_{\mathrm{K}} = -61\log_{10}(150/5.5) = -88$ mV. The resting voltage of the cell was measured to be -70 mV, $a = 0.00001$ m, and respectively $\rho_i = 0.02758$ kΩ·cm.

5. CONCLUSIONS

The membrane voltage V_m during activation, the sodium and potassium conductances G_{Na} and G_{K}, the transmembrane current I_m, as well as its capacitive and ionic components I_{mC} and I_{mL}, are illustrated for a propagating nerve impulse in the figure from above. The results show that, under the hypothesis of a propagation of the neural flow with a constant velocity, there are axial points of the axon where both the voltage and the density of the neural flow vanish. These points are spread along the axon and their spatial periodicity is proportional with the square root of the axon transversal radius. A systematic presentation of the numerical results, as well as other important mathematical models for the neural flow will be presented in a forthcoming paper.

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