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How Does the Slow Injection of a Medicine under the Influence of a Magnetic Field Affects the Spreading of Medical Substances

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Abstract

The problem of excitation and the propagation of a nerve impulse by an axon (nerve fiber) for the case of a noninstantaneous function is studied. The application of no instantaneous step function of the Heaviside type takes into account the time of delay. This generalizes the problem of the propagation of axon excitation to the case of an input impulse function's noninstantaneous action with some increasing excitation. An exact analytical solution to the problem is constructed based on the Laplace integral transform and Ephros theorem. The propagation of the transmembrane potential was studied, in response to the switching on and off, for impulse of a constant current pulse delivered intracellularly at different points in time. The time analysis of excitation propagation along axon at different distances from the excitation point was performed.

Keywords

Noninstantaneous, Excitation, Heaviside Function, Transmembrane Potential, Ephros Theorem, Laplace Transform

1. Introduction

The transient reaction of active nerve fiber is considered under off-cell excitation when excitation impulse is originated from a step function. In this paper, the effect of this deviation on the change of transmembrane potential in time and space was estimated.

In [1], the model of excitation in the nerve was constructed. This model is of a hyperbolic type. They registered potassium and sodium currents of membrane and constructed phenomenological system of equations which describes quite well the process of propagation of nerve impulse. Their model was considerably based on the research of Hodgkin & Rushton (1946) [2], where the instantaneous excitation was introduced earlier.

In [3], singularities of construction of the excitation model on the example of Timoshenko model are considered. In [4], the propagation of medical substance in human tissue was investigated. In [5], complex problem of wave diffraction in elastic medium was analyzed and an exact mathematical solution was presented.

In [6], we use numerical and analytical methods for wave propagation and diffraction analysis. In [7] [8] [9] for mathematical modeling and physiological aspects, we consider nerve metamerism and use wave hyperbolical models [10] of excitation propagation as a generalization of parabolic models.

The theorem from operational calculus was adapted for the construction of solutions and in applying methods of complex analysis.

2. The Effect of Magnetic Field

It is shown that constant magnetic field does not influence the propagation of nerve excitations.

It was experimentally shown in 1980 by V. I. Danilov from JINR, Dubna, that constant in time magnetic fields do not disturb a cell, and the cell still is well functioning, generating electrical impulses with constant frequencies.

3. Traditional Models of Instantaneous Reaction

The Hodgkin-Huxley model was reduced to the Fitzhugh-Nagumo form, the most popular model of excitation medium, which was proposed in 1960 by the American biophysicist Fitzhugh. Later this model has been investigated by Japanese physicist Nagumo, and now it is known as Fitzhugh- Nagumo model.

For distributed medium, it can be presented in the form

$$\begin{aligned} &\varepsilon \frac{\partial V_m}{\partial t} = V_m - V_m^3 - g + D\frac{\partial^2 V_m}{\partial x^2}, \\ &\frac{\partial g}{\partial t} = V_m - a. \end{aligned} \tag{1}$$

where V_m—is the transmembrane potential, ε—a small positive parameter, D—diffusion coefficient and the value a satisfy the inequality $0 < a < 1$.

4. The Effect of Noninstantaneous Excitation

We solve the IBV problem, based on [1], [10] for the differential equation

$$\lambda^2 \frac{\partial^2 V_m(x,t)}{\partial x^2} - \tau \frac{\partial V_m(x,t)}{\partial t} - V_m(x,t) = 0, \quad -\infty < x < \infty, \ t \in (0, t_0], \tag{2}$$

Where $V_m(x,t)$ is an action potential, which satisfies the boundary condition:

$$\left. \frac{\partial V_m(x,t)}{\partial x} \right|_{x=0} = -\frac{I_0 r_i}{2} u(t), \tag{3}$$

with regularity condition on infinity

$$\lim_{|x|\to\infty} V_m(x,t) = 0, \tag{4}$$

And the initial condition

$$V_m(x,t)\big|_{t=0} = 0. \tag{5}$$

Here x is the longitudinal coordinate along with the fiber $(-\infty < x < \infty)$; I_0 —stimulated current, applied to the intercellular space; λ —typical length, $\lambda = \sqrt{r_m/(r_i + r_e)}$; τ —typical time; $\tau = r_m c_m$; r_m is the leakage resistance of membrane on a unit of length; r_i is the internal cell resistance on a unit of length (unitary resistance); r_e is the outer cell resistance on a unit of length (unitary resistance); c_m is capacity.

The problem is solved by the Laplace transform:

$$V_m^L(x,s) = \int_0^\infty V_m(x,t)\mathrm{e}^{-st}\mathrm{d}t. \tag{6}$$

After the Laplace transform (6), the Equation (2) and condition (3) with (5), obtains the following form:

$$\lambda^2 V_m^{L''} - (\tau s + 1)V_m^L = 0, \tag{7}$$

$$\left.\frac{\mathrm{d}V_m^L}{\mathrm{d}x}\right|_{x=0} = -\frac{I_0 r_i}{2}u^L(s). \tag{8}$$

The solution of Equation (7) with taking into account condition (8) and regularity condition (4) is of the form

$$V_m^L(x,s) = \frac{I_0 r_i \lambda}{2}\frac{\mathrm{e}^{-\frac{x}{\lambda}\sqrt{\tau s+1}}}{\sqrt{\tau s+1}}u^L(s), \quad \mathrm{Re}(\tau s + 1) > 0. \tag{9}$$

Figure 1 shows the form of excitation function, constructed as a composition with Heaviside function,

$$u(t) = \begin{cases} 0 & 0 < t < a, \\ 1 - \mathrm{e}^{-b(t-a)} & a < t. \end{cases} \tag{10}$$

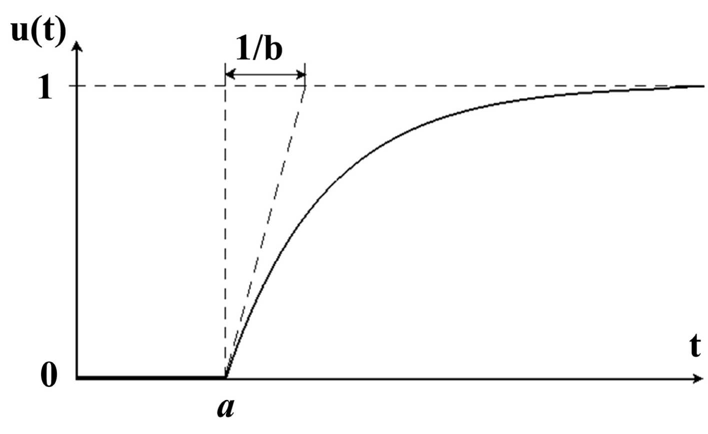

Figure 1. The form of excitation function.

where the value a stands for the delay; b is the increasing function velocity—the rate of function growth (as a result of the step function).

In (10) we use the Heaviside function for $a \to 0$ and $b \to \infty$ or $a \ll 1$.

Then the Laplace transform function (10) has the form

$$u^L(s) = \frac{b\mathrm{e}^{-as}}{s(s+b)}, \tag{11}$$

and the solution V_m^L (9) in (11), has the following form:

$$V_m^L(x,s) = \frac{I_0 r_i \lambda}{2} \frac{\mathrm{e}^{-\frac{x}{\lambda}\sqrt{\tau s+1}}}{\sqrt{\tau s+1}} \frac{b\mathrm{e}^{-as}}{s(s+b)}. \tag{12}$$

Note that $V^L(x,s) = \frac{\mathrm{e}^{-\frac{x}{\lambda}\sqrt{\tau s+1}}}{\sqrt{\tau s+1}} \frac{1}{s(s+b)}$ and using the delay theorem, we get

$$\mathrm{e}^{-as} V^L(x,s) \longrightarrow \begin{cases} V(x,t-a), & 0 \le a < t, \\ 0, & t < a. \end{cases} \tag{13}$$

For the inverse Laplace transform of $V^L(x,s)$, we use the Ephros theorem (generalized theorem of multiplication): given a transform $F(s) \longrightarrow f(t)$ and two analytical functions $G(s)$ and $q(s)$ such that

$$G(s)\mathrm{e}^{-\xi q(s)} \longrightarrow g(t;\xi),$$

then

$$F[q(s)]G(s) \longrightarrow \int_0^\infty f(\xi) g(t;\xi) \mathrm{d}\xi. \tag{14}$$

According to the theorem, let $G(s) = \frac{1}{\sqrt{\tau s+1}}$, $q(s) = \sqrt{\tau s+1}$. The function $g(t;\xi)$ has the form

$$g(t;\xi) = \frac{1}{2\pi i} \int_{c-i\infty}^{c+i\infty} \mathrm{e}^{-\xi\sqrt{s}+st} \frac{\mathrm{d}s}{\sqrt{s}}. \tag{15}$$

then

$$\frac{\mathrm{e}^{-\xi\sqrt{\tau s+1}}}{\sqrt{\tau s+1}} \longrightarrow \frac{\mathrm{e}^{\left(-\frac{t}{\tau}-\frac{\xi^2\tau}{4t}\right)}}{\sqrt{\pi\tau t}}.$$

So for $F(s)$ we get:

$$F(s) = \frac{\tau^2 \mathrm{e}^{-\frac{x}{\lambda}s}}{(s^2-1)(s^2-1+b\tau)}. \tag{16}$$

As a result, $f(x)$

$$f(t) = \frac{\tau}{b} H\left(t-\frac{x}{\lambda}\right)\left[\sinh\left(t-\frac{x}{\lambda}\right) - \frac{1}{\sqrt{1-b\tau}} \sinh\left(\sqrt{1-b\tau}\left(t-\frac{x}{\lambda}\right)\right)\right]. \tag{17}$$

Then for the transform $V^L(x,s)$ we obtain

$$
\begin{aligned}
V^L(x,s) \stackrel{\cdot}{\longrightarrow} & \frac{\tau}{b\sqrt{\pi\tau t}}\int_0^\infty \mathrm{e}^{\left(-\frac{t}{\tau}-\frac{\xi^2\tau}{4t}\right)} H\left(\xi-\frac{x}{\lambda}\right)\left[\sinh\left(\xi-\frac{x}{\lambda}\right)\right. \\
& \left.-\frac{1}{\sqrt{1-b\tau}}\sinh\left(\sqrt{1-b\tau}\left(\xi-\frac{x}{\lambda}\right)\right)\right]\mathrm{d}\xi \\
& =\frac{\tau}{b\sqrt{\pi\tau t}}\int_{\frac{x}{\lambda}}^\infty \mathrm{e}^{\left(-\frac{t}{\tau}-\frac{\xi^2\tau}{4t}\right)}\sinh\left(\xi-\frac{x}{\lambda}\right)\mathrm{d}\xi \\
& -\frac{\tau}{b\sqrt{\pi\tau t}\sqrt{1-b\tau}}\int_{\frac{x}{\lambda}}^\infty \mathrm{e}^{\left(-\frac{t}{\tau}-\frac{\xi^2\tau}{4t}\right)}\sinh\left(\sqrt{1-b\tau}\left(t-\frac{x}{\lambda}\right)\right)\mathrm{d}\xi.
\end{aligned}
\tag{18}
$$

After the few simple transformations, we get

$$
\begin{aligned}
V(x,t)= & \frac{1}{2b}\left[\mathrm{e}^{-\frac{x}{\lambda}}\operatorname{Erf}\left(\frac{x}{\lambda}\frac{\sqrt{\tau}}{2\sqrt{t}}-\frac{\sqrt{t}}{\sqrt{\tau}}\right)-\mathrm{e}^{\frac{x}{\lambda}}\operatorname{Erf}\left(\frac{x}{\lambda}\frac{\sqrt{\tau}}{2\sqrt{t}}+\frac{\sqrt{t}}{\sqrt{\tau}}\right)\right] \\
& -\frac{\mathrm{e}^{-tb}}{2b\sqrt{1-b\tau}}\left[\mathrm{e}^{-\sqrt{1-b\tau}\frac{x}{\lambda}}\operatorname{Erf}\left(\frac{x}{\lambda}\frac{\sqrt{\tau}}{2\sqrt{t}}-\frac{\sqrt{t}}{\sqrt{\tau}}\sqrt{1-b\tau}\right)\right. \\
& \left.-\mathrm{e}^{\sqrt{1-b\tau}\frac{x}{\lambda}}\operatorname{Erf}\left(\frac{x}{\lambda}\frac{\sqrt{\tau}}{2\sqrt{t}}+\frac{\sqrt{t}}{\sqrt{\tau}}\sqrt{1-b\tau}\right)\right].
\end{aligned}
\tag{19}
$$

The final solution of Equation (11) has the form

$$
\begin{aligned}
& V_m(x,t)=0, \quad t<a, \\
V_m(x,t)= & \frac{I_0 r_i\lambda}{4}\left[\mathrm{e}^{-\frac{x}{\lambda}}\operatorname{Erf}\left(\frac{x}{\lambda}\frac{\sqrt{\tau}}{2\sqrt{t-a}}-\frac{\sqrt{t-a}}{\sqrt{\tau}}\right)\right. \\
& -\mathrm{e}^{\frac{x}{\lambda}}\operatorname{Erf}\left(\frac{x}{\lambda}\frac{\sqrt{\tau}}{2\sqrt{t-a}}+\frac{\sqrt{t-a}}{\sqrt{\tau}}\right) \\
& -\frac{\mathrm{e}^{-(t-a)b}}{\sqrt{1-b\tau}}\left[\mathrm{e}^{-\frac{x}{\lambda}\sqrt{1-b\tau}}\operatorname{Erf}\left(\frac{x}{\lambda}\frac{\sqrt{\tau}}{2\sqrt{t-a}}-\frac{\sqrt{t-a}}{\sqrt{\tau}}\sqrt{1-b\tau}\right)\right. \\
& \left.\left.-\mathrm{e}^{\frac{x}{\lambda}\sqrt{1-b\tau}}\operatorname{Erf}\left(\frac{x}{\lambda}\frac{\sqrt{\tau}}{2\sqrt{t-a}}+\frac{\sqrt{t-a}}{\sqrt{\tau}}\sqrt{1-b\tau}\right)\right]\right], \quad 0\le a<t.
\end{aligned}
\tag{20}
$$

The solution (20) corresponds to the current pulse (current supply) I_0 into the intercellular space at the point $x=0$ and gives the membrane behavior at $x>0$. The behavior at $x<0$ can be found from symmetry. Passing to absolute values *x*, $V_m(x,t)$ has the form

$$
\begin{aligned}
V_m(x,t)= & \frac{I_0 r_i\lambda}{4}\left[\mathrm{e}^{-\frac{|x|}{\lambda}}\operatorname{Erf}\left(\frac{|x|}{\lambda}\frac{\sqrt{\tau}}{2\sqrt{t-a}}-\frac{\sqrt{t-a}}{\sqrt{\tau}}\right)\right. \\
& -\mathrm{e}^{\frac{|x|}{\lambda}}\operatorname{Erf}\left(\frac{|x|}{\lambda}\frac{\sqrt{\tau}}{2\sqrt{t-a}}+\frac{\sqrt{t-a}}{\sqrt{\tau}}\right) \\
& -\frac{\mathrm{e}^{-(t-a)b}}{\sqrt{1-b\tau}}\left[\mathrm{e}^{-\frac{|x|}{\lambda}\sqrt{1-b\tau}}\operatorname{Erf}\left(\frac{|x|}{\lambda}\frac{\sqrt{\tau}}{2\sqrt{t-a}}-\frac{\sqrt{t-a}}{\sqrt{\tau}}\sqrt{1-b\tau}\right)\right.
\end{aligned}
$$

$$-\mathrm{e}^{\frac{|x|}{\lambda}\sqrt{1-b\tau}}\operatorname{Erf}\left(\frac{|x|}{\lambda}\frac{\sqrt{\tau}}{2\sqrt{t-a}}+\frac{\sqrt{t-a}}{\sqrt{\tau}}\sqrt{1-b\tau}\right)\Bigg]\Bigg], \quad 0\le a<t. \tag{21}$$

Correctness of the obtained solution (21) was verified by substitution of this solution to (2)-(5).

5. Numerical Calculations

From the solution form (21) such conditions follow:

$$b\tau<1, \quad 0\le\frac{a}{\tau}<\frac{t}{\tau}. \tag{22}$$

According to (22) the condition $\tau<1/b$ holds, where the value $1/b$ characterizes the potential delay.

Calculations are conducted at $\tau=0.01$, and $a/\tau=0.01$.

Distribution of potential is obtained along the space coordinate X in different times $T=0.16, 0.36, 0.7, 1.0$ and potential values in time in different points along $X=0.5, 1.0, 2.0, 3.0$.

From the conducted calculations of transmembrane potential V_m at instantaneous and no instantaneous application, the effect of input delay was evaluated.

Particularly it is shown, that a delay at application increases the time till a stationary state.

Calculations of V_m, as a time function, along the axon were conducted at different distances from the point excitation $X=0.5, 1.0, 2.0, 3.0$. These calculations show that the value of transmembrane potential V_m is reduced, as a function of instantaneity and no instantaneity, both at switching on and off.

6. Conclusion

We present in the paper a full analytical solution for the propagation of the transmembrane potential under the application of a magnetic field. The solution refers to the case when excitation functions are different from the traditional Heaviside step function. The step function is used to manage the delay. Some extensions of the model have been presented. The solution is analyzed in detail for different cases. Our approach is new and it can significantly improve the transfer and absorption of medications especially in problematic cases. Our approach is new and it can significantly improve the transfer and absorption of medications especially in problematic cases

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Hodgkin, A.L. and Huxley, A.F. (1952) A Qualitative Description of Membrane Current and Its Application to Conduction and Excitation in Nerve. *The Journal of*

Physiology, **117**, 500-544. https://doi.org/10.1113/jphysiol.1952.sp004764

[2] Hodgkin, A.L. and Rushton, W.A.H. (1946) The Electrical Constants of a Crustacean Nerve Fiber. *Proceedings of the Royal Society*, **133**, 444-479. https://doi.org/10.1098/rspb.1946.0024

[3] Selezov, I.T. (2020) Timoshenko Equation of Hyperbolic Type and Basic Singularities. Collection of Kiev Polytechnical Institute, Kiev, 81-87.

[4] Gulko, N.G., Selezov, I.T. and Volynsky, R.I. (2020) Mathematical Study of Medicine Propagation in Biological Tissue and Some of Its Applications. *Journal of Applied Mathematics and Physics*, **9**, 127-132. https://doi.org/10.4236/jamp.2021.91009

[5] Khimich, A.N., Selezov, I.T. and Sydoruk, V.A. (2020) Simulation of Elastic Wave Diffraction by a Sphere in Semi Bounded Region. Reports of NAS of Ukraine, Kyiv, No. 10, 22-27. https://doi.org/10.15407/dopovidi2020.10.022

[6] Selezov, I.T., Kryvonos, Y.G. and Gandzha, I.S. (2018) Wave Propagation and Diffraction. Mathematical Methods and Applications. Springer, 237 p. https://doi.org/10.1007/978-981-10-4923-1

[7] Selezov, I.T. and Bersenev, V.A. (2009) Neurometamerism. Mathematical Modeling and Physiological Aspects. AVERS, Kiev, 136 p. (In Russian)

[8] Selezov, I.T. and Kryvonos, Y.G. (2015) Wave Hyperbolic Models of Disturbance Propagation. Naukova Dumka, Kiev, 172 p. (In Russian)

[9] Fitzhugh, R. (1961) Impulses and Physiological States in Theoretical Models of Nerve Membrane. B*iophysical Journal*, **1**, 445-466. https://doi.org/10.1016/S0006-3495(61)86902-6

[10] Joshi, R.P., Mishra, A., Song, J., Pakhomov, A.G. and Schoenbach, K.H. (2008) Simulation Studies of Ultrashort, High-Intensity Electric Pulse Induced Action Potential Block in Whole-Animal Nerves. *IEEE Transactions on Biomedical Engineering*, **55**, 1391-1398. https://doi.org/10.1109/TBME.2007.912424