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COMPUTER MODELING OF AUTO-OSCILLATING PHENOMENA IN NEURON COMPLEXES

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Abstract—*Program model of auto-oscillating phenomena in complexes of natural neurons is represented. Model was elaborated basing on our experimental results of electrical currents studying in natural brain neurons.*

Index Terms—Program model; auto-oscillations; molecular currents; neuron.

I. INTRODUCTION

First research on transmembrane electrical currents was carried out in 1775 by Luigi Galvani. Even though the scientist did not understand the full significance of his own discovery, he gave the birth to the following researches in field of intercellular and transmembrane currents. By the middle of 60`s the world starts investigation in this direction on micro- and nano-level. Today the experiments with the propagation of electrical signals in neuronal and muscular media and how the charge is transferred by cell membrane are reviewed in details in numerical publications [1], [2], [4] – [6]. First investigations were performed at micro-level with the help of voltage clamp method. Further development of science allowed to use more specific and cleaner materials and thus better results were obtained with help of brand new patch-clamp method, developed in 1976. Since then the real science has started. Other sources of experimental data are taken into account for modeling are electrophysiological experiments (patch-clamp, voltage clamp, and others [2], [3], [6], [7]. In our investigations the results of such electrophysiological experiments were combined with optical ones to analyze whether attempts of some biotechnical systems construction and functions are possible [3], [6], [7]. Samples of the brain neurons were inquired into the biotechnical system as rectangular 2D plate with cultured brain neurons constructed as 2D matrix (Figs 1 and 2). In details such construction we have observed in our previous publications [3], [7].

II. TASK STATEMENT

Basing on prototype physic and mathematic models of auto-oscillations in natural excitable media to develop the program model of these phenomena for 2D natural neuronal complexes, including electrical auto-wave propagation from the center of this structure.

III. MATHEMATIC MODELING OF ELECTRICAL CURRENTS IN EXCITABLE CELLS AND THEIR ASSEMBLES

Some results of mathematic modeling of electric currents propagation in neuronal complexes are given below basing on works of [2], [8]. Let's imagine this task as existing complex of active elements at planar 2D neuronal matrix. Signal of excitation here is going from a source as electric current that causes a number of concentric waves. Actually, such system is an artificial neuronal network where electrical currents carry excitation from one active element to another. Neuron by itself may be in 3 states: rested, excited, and refracted (analogously to the system at Fig. 1). At resting state a neuron may stay enough long if its transmembrane potential φ doesn't exceed some threshold φ_*. At moment when the potential become equal to φ_* neuron exceeds and exists in this state during time t_a, and then potential falls to "0". If to define the "age" of neuron τ, as the time from the last excitation, the last condition may be written as

$$\varphi(\tau,t)\,|_{\tau=t_a}=0, \tag{1}$$

where t is a current time. If $\tau > t_a$ neuron potential satisfies the condition

$$C\frac{d\varphi}{dt}=i-g\varphi(\tau,t),\frac{1}{2}, \tag{2}$$

where is $\tau=\tau(t)$; C is capacity, g is membrane conductance; i is summary synaptic current depended on the state of neighbors of studied neuron.

Let's suppose that the neuron threshold depends on its age $\varphi_*=\varphi_*(\tau)$, and $\varphi_*(\tau)$ is a monotonously decaying function τ, defined as $\tau > t_r$, where t_r is a refracted time. In area $\tau < t_r$, the neuron has unlimited threshold, and refracted time of this neuron is defined as the state with unlimited threshold. Variable t_r is an absolute refractivity when a neuron cannot be excited by any outer influence. Relative refractivity is described by the concrete type $\varphi_*(\tau)$. So, the neuron "lives" up to any maximal age τ_m, defined by equation

$$\varphi(\tau_m,t)=\varphi_*(\tau_m). \tag{3}$$

During the excitation a neuron "is" of age $\tau=0$, and the cycle is repeated again. At this stage the different neuron states may be defined as:

1. $0 < \tau < t_a$ – the state of excitation;

2. $0 < \tau < t_r$ – the state of refractivity (absolute);

3. $\tau > t_r$ – the state of the rest or relative refractivity (equal notions).

Let's observe the interaction between the neurons and geometry of the links that define synaptic current. This current transmits the information signal from neuron to neuron in plane of 2D matrix in our constructed system (Fig. 2). If the velocity of nervous impulse spread is constant one, the delay in time will be r/υ, where r is a distance between the neurons; v is velocity of impulses.

Let's suppose that the current at defined synapse is $i_s(\tau_s)$ where τ_s is a time, calculated from the moment of excitable impulse income to a synapse. The distribution of neurons with the same number of parameters is $\eta = \{C, g, t_a, \varphi_*\}$, according to the age may be defined as $a_\eta(r, \tau, t)$, where r is coordinate in space. The number of synapses that reach one neuron from volume element dr' may be defined as $K(r, r')dr'$. For such a case the synaptic current to neuron with coordinate (r) at moment t from neurons with parameters is:

$$di = f(\eta)d\eta \int dr \int d\tau_s a_\eta \left(r', t - \frac{|r - r'|}{v}, \tau_s \right) \times K(r, r') i_s(\tau_s), \tag{4}$$

where $f(\eta)$ is a density of neurons according to parameters. We suppose that φ_* may be defined by one or few parameters. If to find a sum in (4) according to all possible parameters, the synaptic current may be written as:

$$i(r,t) = \int d\eta \int dr' \int d\tau_s f(\eta) K(r,r') a_\eta \times \left(r', t - \frac{|r - r'|}{v}, \tau_s \right) i_s(\tau_s). \tag{5}$$

Expression of (5) is true only under the condition that duration of i_s does not exceed the maximal age. Let's suppose that $i_s(\tau_s) = 0$ if $\tau_s > t_s < t_r$, so, "working time" of the synapse t_s is less than refractive time of any neuron. At the end of mathematic task formulation let's examine the distribution of changes of age. For the first, we can put a condition

$$a_\eta(r, t, \tau) = a_\eta(r, t - \tau, 0), \ \tau < \tau_m, \tag{6}$$

For the second, if the total number of neurons is constant in time

$$\int_0^{\tau_m(\eta, r, t)} a_\eta(r, t, \tau) d\tau = 1. \tag{7}$$

After substitution (6) to (7) we obtain the equation for the density of neurons at initial age $a_\eta(r, t, 0)$:

$$\int_{1-\tau_m(\eta, r, t)}^{t} a_\eta(r, t', 0) dt' = 1. \tag{8}$$

Using (6) let's transform (5) into:

$$i(r,t) = \int d\eta \int dr' \int d\tau' f(\eta) K(r,r') a_\eta \times \left(r', t - \frac{|r - r'|}{v} - \tau', 0 \right) i_s(\tau'). \tag{9}$$

Equations (2), (3), (8), (9) together with additional condition (1) describe the dynamics of neuron network completely, if respective initial conditions are put. Such conditions are defined by function $a_\eta(r, t, 0)$, at enough large interval at the space $\{\eta, r\}$.

Let's suppose that for independent from coordinates r initial conditions for the case $K(r, r') = K_1(|r - r'|)$, where K_1 is a defined function. Our task is the search solutions for the system of equations (2), (3), (8), and (10) as consequence of Eg. (9):

$$i(t) = \int d\eta f(\eta) \int_0^\infty K(\xi) d\xi \int_0^{\tau_m(\eta, t)} d\tau' a_\eta \times \left(t - \frac{\xi}{v} - \tau', 0 \right) i_s(\tau'). \tag{10}$$

where $K(\xi) = 4\pi\xi K_1(\xi)$.

From (10) one can find:

$$i = \int d\eta f(\eta) \int_0^\infty K(\xi) d\xi a_\eta \int_0^{t_s} i_s(\tau') d\tau' = \int_0^\infty K(\xi) d\xi \int_0^{t_s} i_s(\tau) d\tau \int a_\eta f(\eta) d\eta = NQ \int a_\eta f(\eta) d\eta, \tag{11}$$

where $N = \int K(\xi) d\xi$, $Q = \int i_s d\tau'$, a_η is stationary value $a_\eta(t, 0)$.

From (8) may be fond

$$a_\eta = \frac{1}{\tau_m(\eta)}. \tag{12}$$

After examination of $\tau_m(\eta)$ may be shown that the solution for (1) for any $i(t)$ is another (13):

$$\varphi(\tau, t) = \frac{1}{C} \int_{t - \tau_m + t_a}^{t} e^{-\alpha(t - t')i}(t') dt', \tag{13}$$

where $\alpha = g / C$.

Substituting of (13) into (3) one can find equation for $\tau_m(\eta)$:

$$\varphi_*(\tau_m) = \frac{i}{g}\left[1 - e^{-\alpha(\tau_m - t_a)}\right]. \quad (14)$$

It's clear that (14) may be solved only under the condition

$$\lim_{\tau\to\infty} \varphi_*(\tau) < \frac{i}{g}, \quad (15)$$

It is possible to demonstrate that the write part of (11) grows monotonously according to i, up to the limit

$$\int_0^\infty K(\xi)d\xi \int_0^{t_s} i_s(\tau)d\tau \int \frac{f(\eta)}{t_r}d\eta. \quad (16)$$

It is necessary to mention that stationary states of neurons may be characterized as multiple in a case when the neurons are distributed according to different thresholds. Another possibility for multiple stationary states gives a quick transformation of a neuron from the state of relative refractivity to the state of the rest (Fig. 1). Really, let' examine the case when all neurons in a network are absolutely equal, and $f(\eta) = \delta(\eta - \eta_0)$. It means that (11) may be transformed into

$$i = \frac{NQ}{\tau_m}. \quad (17)$$

And together with (14) gives

$$\varphi_*(\tau_m) = \frac{NQ}{g\tau_m}[1 - e^{-\alpha(\tau_m - t_a)}]. \quad (18)$$

Multiple thresholds have only networks that have a neuron with "zero" conductivity g. Such a state is unique one, and does not depend on types of functions $f(\eta)$, and $\varphi_*(\tau)$. Let's examine such a case. If $g = 0$ (14) may be transformed into (19)

$$\varphi_*(\tau_m) = \frac{1}{C}(\tau_m - t_a). \quad (19)$$

It is clear that for any function $\varphi_*(\tau)$ the (19) has a solution. It is possible to demonstrate that

$$\frac{\partial\tau_m}{\partial i} = -\frac{\tau_m - t_a}{i - C\frac{\partial\varphi_*}{d\tau}\Big|_{\tau=\tau_m}} \le 0. \quad (20)$$

Any non-trivial solution of (11) satisfies the condition

$$NQ\int\left(-\frac{\partial\tau_m}{\partial i}\right)\tau_m^{-2} f(\eta)d\eta < 1. \quad (21)$$

From (20) may be found that $\frac{\bar{d}\varphi_*}{d\tau} \le 0$:

$$-\frac{\partial\tau_m}{\partial i} \le \frac{\tau_m - t_a}{i}. \quad (22)$$

Substituting (22) into (21) one can obtain

$$\begin{aligned} -NQ\int\frac{\partial\tau_m}{\partial i}\tau_m^{-2} f(\eta)d\eta \\ \le NQ\int(\tau_m - t_a)\tau_m^{-2} i^{-1} f(\eta)d\eta \\ < NQ\int f(\eta)\tau_m^{-1} i^{-1} d\eta = 1. \end{aligned} \quad (23)$$

Comparing the last terms in (12) one can obtain (21). Let's examine the conditions of solution existence in a case of $g = 0$. Because of (21), non-trivial solutions exist if-and-only-if

$$-NQ\lim_{\tau\to\infty}\int\frac{\partial\tau_m}{\partial i}\tau_m^{-2} f(\eta)d\eta > 1, \quad (24)$$

Taking into account (19) may be obtained the condition

$$NQ\overline{C^{-1}\varphi_*^{-1}(\infty)} > 1, \quad (25)$$

Where the line signifies averaging with the weight $f(\eta)$:

$$\overline{C^{-1}\varphi_*^{-1}(\infty)} = \int_0^\infty dC\int_0^\infty d\varphi_*(\infty)\frac{f(C, \varphi_*(\infty))}{C\varphi_*(\infty)}. \quad (26)$$

Sometimes it is useful to have indirect characteristics of neuronal network with neuron distribution according to their age $a(\tau)$ without dependence on other parameters of neurons. Clear and simple expression for $a(\tau)$ we have for

$$f(\eta) = \delta(g)\,\delta(t_r - t_a) f_1(t_r, \varphi_*^0), \quad (27)$$

where $\varphi_*^0 = \text{const} = \varphi_*(\tau)$ for $r > t_r$. $\tau_m > \tau$, integrating for the neurons for which $\tau_m > \tau$, one can have

$$a(\tau) = \int dt_r \int d\varphi_*^0 \frac{(\varphi_*^0, t_r)}{t_r + \varphi_*^0 / i}. \quad (28)$$

Synaptic current in (28) one can find from equation:

$$i = NQ\int_0^\infty dt_r \int_0^\infty d\varphi_*^0 \frac{f_1(\varphi_*^0, t_r)}{t_r + \varphi_*^0 / i}. \quad (29)$$

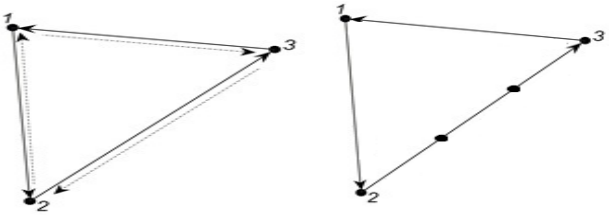
IV. DESCRIPTION OF "QUASI SCREEN" WITH BIONIC ELEMENTS FOR BIOTECHNICAL SYSTEM

This model we have presented previously in [3], [7], and it is a prototype for our novel program model. Our "quasi screen" with bionic elements for biotechnical system may be imagined as 2D neuron matrix on plastic plate with cultural brain neurons in dissociated culture incorporated into electric circle with standard measuring and data stored devices. 2D neuron matrix also may be imagined as a model like chessboard (or "screen") with alternating rows and

columns that separate the cells which contain optically active elements. Designing of such a "screen" in modern biophysical laboratories are absolutely real. This "screen" is specially designed plastic lining with specific "chess-like" geometric profile, armed with electrodes. The structure of such a "screen" we described previously in details [3], [7].

V. Dynamics of neuron characteristics changes in 2D neuron matrices

According to the results of the experimental neuron reaction studying, the receipt of the excitation signal can be represented as three consecutive phases that have their physical, biochemical and physiological sense (Fig. 1). Besides of them we suggest to include to our model other points too, for more adequate reflexion of studied phenomena.



a b

Fig. 1. Three stages of screen pixel functioning: each pixel of the screen works by three-member cycle (a), three-member cycle with 2 intermediary substates (b)

At the "screen" at Fig. 2 the bionic elements are depicted by the circles at defined positions on screen matrix. Fig. 2 demonstrates the model at 101th second from process start. It is possible to see that one element is at the second phase, some other elements are at phase number three (compare with Fig. 1).

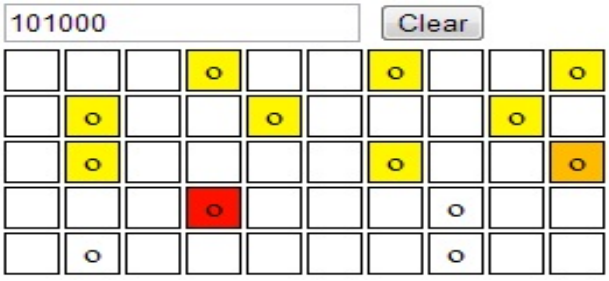


Fig. 2. Working model at 101th second from process start

V. Dynamics of neuron Modeling of auto-oscillating processes, as the result of wave generation in 2D neuron matrix performance

In prototype given above electrical signal is propagated linearly from the left side to the right one (see Fig. 2). Auto-oscillating model described in this subchapter has the following differences (Figs 3, 4, 5, 6).

There is 1 auto-oscillating cell in the centre of 2D model. This cell is called "rhythm-initiator." Actually, this cell (neuron) is the source of electrical excitation in system.

Waves of electrical excitation are propagated spherically from the source to neurons located at the branches. In other words, information from the centre is propagated spherically to the boundaries of 2D matrix.

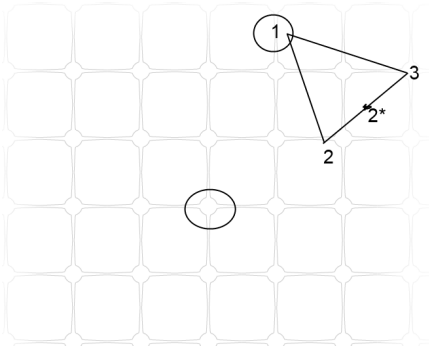


Fig. 3. Rhythm-initiator is in steady condition

Each pixel (neuron, cell) of 2D matrix may be in 4 states (see Fig. 1): *1* is a steady condition; *2* is a state of maximal excitation; at points between *2–3* excitation decreases; *3* is a stage of refractivity. The first state (steady condition state) on triangular is denoted by number 1 and corresponds to described phases 1 and 4 (achromatic). It means that any applied voltage sufficient for system starting can launch the rhythm-initiator and as result, oscillation of the whole matrix.

On modeled auto-oscillating matrix this condition looks as at Fig. 3.

As soon as rhythm-initiator is launched, it gets excited and switches to maximum excitation condition, as shown on Fig. 4. Here $I = I_{max}$

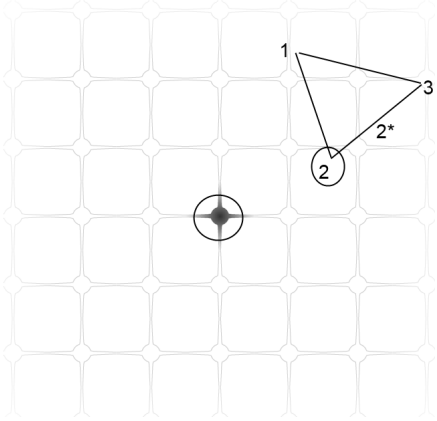


Fig. 4. Rhythm-initiator is in maximum excitation condition

At the maximum excitation condition, the rhythm-initiator transfers the signal to the neighbor neurons and starts decreasing. This process of decreasing can be denoted by 2* on the triangular model

(compare with Fig. 1). It is located between points of maximal excitation (2) and refractivity (3). Now its current I is equal to $I_{max}/2$ [1], [2].

But the surrounding neurons have received the pulse and excited to their maxima, which is clearly seen from Fig. 5.

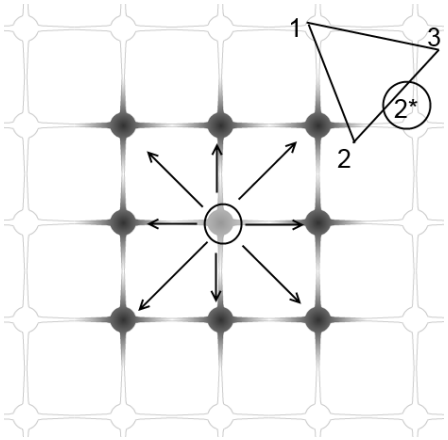


Fig. 5. Excitation decreases

Marked by the circle pale neuron is understood as one that decreases, but surrounding cells just got excited and now equal to $I = I_{max}$, when the rhythm-initiator is equal $I = I_{max}/2$ [2], [8].

The third condition is represented by rhythm-initiator, that is now in refractivity condition $I = 0$ and prepares for new cycle of pulse transmission, the neurons that surround it are in condition when excitation is half decreased, i.e. $I = I_{max}/2$, and the outer circle of neurons is in maximal excitation condition $I = I_{max}$. An example of this condition is represented on Fig. 6.

Given upper figure let us understand that, neuron, that has ability of self-oscillation transmits its puls to the neighbor neurons or cells, that in their turn, being switched by rhythm-initiator, transmit received pulse, signal further to surrounding them neurons. For transition of system from point *3* to point *1*, ΔT is the time of refraction is necessary

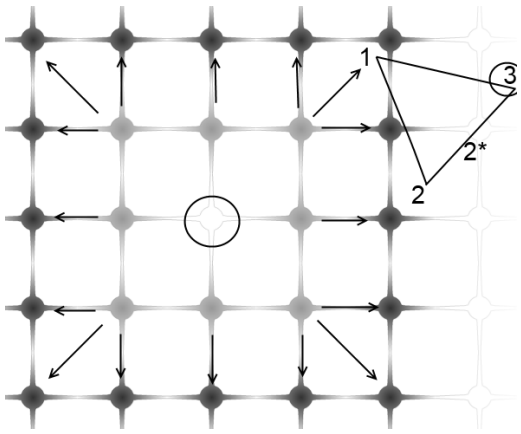


Fig. 6. Refractivity of rhythm-initiator

VI. CONCLUSIONS

In living organisms in nature the sorts of the cells we studied and used for program model may be located in three following places: in brain centre, where such neurons support the vital activity (breathing); in case of pathology some brain cells may start to behave as such auto-oscillating neurons causing the epilepsy; is cardiac cells in the heart. Such cells have characteristics of nerve and muscle cells both, that is why the heart beats during all the time of organism life. In conclusions of our work done we have to list obtained results:

1. Physical and mathematic models for the propagation of generated auto-oscillations for biotechnical system are suggested and examined.

2. Program model for propagation of generated auto-oscillations for biotechnical system was elaborated.

3. Such program models may be useful for laboratory practice as well as for teaching of university courses in biophysics, biocybernetics and related disciplines.

REFERENCES

[1] Kostyuk, P. G.; Kryshtal, O. A. Mechanisms of nervous cell electrical excitability. Moscow. Nauka. 1981. 204 p. (in Russian).

[2] Sigworth, F.; Sackman, B.; Neher, E. Single channel registrations. Moscow. Mir. 1987. 448 p. (in Russian).

[3] Shutko, V. M.; Klyuchko, E. M. "Liquid crystal nanostructures in neurons and the development of screens for television systems on their base." *Vistnyk of Engineer Academy of Sciences*. 2012. no. 3–4. pp. 170–173. (in Ukrainian).

[4] Krishtal, O.; Kiskin, N.; Tsyndrenko, A.; Klyuchko, E. "Pharmacological properties of amino – acid receptors in isolated hippocampal neurons." *Walter de Gruyte.* Berlin (Germany), Receptors and ion channels. 1987. pp. 127–137.

[5] Akaike, N.; Kawai, N.; Kiskin, N. I.; Klyuchko, E. M.; etc. "Spider toxin blocks excitatory amino-acid responses in isolated hippocampal pyramidal neurons." *Neuroscience Letters*. 1987. vol. 79. pp. 127–137.

[6] Klyuchko, E. M.; Hairutdinov R. R. "Modeling of electrical signals transmission along the neuron and its nanostrucrures." *Electronics and control systems*. 2011. no. 2(28). pp. 120–124. (in Ukrainian).

[7] Klyuchko, E. M.; Pashkivsky, A. O.; Sheremet, D. U. "Computer modeling of some nanoelements for radiotechnic and television systems." *Electronics and control systems*. 2012. no. 3 (33). pp. 102–107. (in Ukrainian).

[8] Cherny, V. V., Chismadzhev, Yu. A. Membrana: ion channels. Edited Yu. A. Chismadzhev. Moscow. Mir. 1981. 320 p. (in Russian).

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В. М. Шутко, О. М. Ключко. Програмне моделювання автоосциляторних явищ у комплексах нейронів

Наведено результати програмного моделювання автоосциляторних явищ у комплексах природних нейронів. Модель створено на основі експериментальних результатів з дослідження електричних струмів у природних нейронах мозку.

Ключові слова: програмна модель; автоколивання; молекулярні струми; нейрон.

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В. Н. Шутко, Е. М. Ключко. Программное моделирование автоосциляторных явлений в комплексах нейронов

Приведены результаты программного моделирования автоосциляторных явлений в комплексах природных нейронов. Модель была разработана на основе экспериментальных результатов по исследованию электрических токов в природных нейронах мозга.

Ключевые слова: программная модель; автоколебания; молекулярные токи; нейрон.

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