ЖУРНАЛ ФІЗИЧНИХ ДОСЛІДЖЕНЬ
т. 11, № 3 (2007) с. 322–324

JOURNAL OF PHYSICAL STUDIES
v. 11, No. 3 (2007) p. 322–324

STRANGE ATTRACTOR IN KINETIC MODEL OF SYNAPTIC TRANSMISSION

A. V. Chalyi[1], E. V. Zaitseva[2]
[1] *O. O. Bogomolets National Medical University, Department of Medical and Biological Physics, 13 Shevchenko Blvd, Kyiv, UA–01160, Ukraine,*
[2] *Taras Shevchenko National University of Kyiv, Faculty of Physics, Department of Theoretical Physics, 6 Glushkova Pr., Kyiv, UA–03022, Ukraine*
(Received February 15, 2007)

This study is aimed at the creation of a physical model of transmission through a synaptic cleft at the cell-to-cell communication with taking into account such real processes: time-dependent release of mediator (acetylcholine) molecules (ACh) to a synaptic cleft, diffusion of ACh molecules from synaptic cleft, receptor binding of ACh — formation of mediator-receptor complexes (AChR), decay of ACh and AChR by action of a specific ferment — acetylcholinesterase (AChE). The system of three nonlinear differential equations was proposed to characterize the change of concentrations of acetylcholine molecules, mediator-receptor complexes and acetylcholinesterase. The stationary states and types of singular points are studied for the given model of synaptic transmission.

Key words: kinetic model of synaptic transmission, strange attractor, cholinergic synapse.

PACS number(s): 82.40.Ck, 87.10.Ed

The problem of cell-to-cell communication is of the same fundamental importance in animate nature as intermolecular interaction is in abiocoen. Particularly, as is well known [1, 2], the cell-to-cell communication happening as a result of synaptic transmission of information underlies processes of thinking.

Shortly saying one can picture basic processes respondent for synaptic transmission using the following scheme:

$$ACh + R \rightarrow AChR \rightarrow R.$$

It means:

1. Acetylcholine (ACh) is synthesized by cholineacetyltransferase and is stored up in spherical vesicles in presynaptic area; membrane is depolarized while nerve excitation acetylcholine is injected into a synaptic cleft. One should mention here that during this process about 10^4 acetylcholine molecules are released and reach postsynaptic membrane where cholinergic receptors (R) are located.

2. Acetylcholine reacts with a cholinergic receptor forming a complex compound (AChR) which is in dynamic equilibrium with free acetylcholine and receptor. As a result of ACh and R reaction, membrane permeabilities for Na^+ and K^+ ions increase causing membrane depolarization. If ACh concentration is large enough the process of depolarization becomes supraliminal evoking the spreading of synaptic stimulation along the muscle fiber.

3. Acetylcholinesterase hydrolyzes ACh. The process of removing acetylcholine from the receptor location area is very important for the renewal of the initial state of postsynaptic membrane. A large amount of ferment acetylcholinesterase (AChE) is located in postsynaptic membrane area. If AChE is inactivated, the transmission of synaptic stimulation is blocked as a result of ACh accumulation in receptor membrane area.

Models of synaptic transmission were created allowing for concentrations of acetylcholine and non-active receptors [3, 4]. The aim of the present study is to create a more realistic model of synaptic transmission. Here we will consider synaptic transmission in the cleft where muscarinic cholinoreceptors prevail. It is well known that cholinoreceptors of this type are G-protein coupled. This means that for activation they need G-protein to be present. In the present study we will assume that concentration of G-protein is constant and enough for activation, thus, we will not take it into account. Also we will assume that one molecule of acetylcholine activates the receptor and acetylcholinesterase takes part in the decomposition of mediator-receptor complexes. And we will approximate the function of acetylcholine release by the Dirac δ-function.

Thus, we obtain the following system of nonlinear differential equations, where x matches up concentration of ACh, y and z denote concentrations of AChR and AChE, respectively:

$$\frac{dx}{dt} = K\delta(t) - k_1 x(a-y) - k_2 xz - k_3 x + D_1 \Delta x, \quad (1)$$

$$\frac{dy}{dt} = k_1 x(a-y) - k_4 xyz, \quad (2)$$

$$\frac{dz}{dt} = k_5 z - k_2 xz - k_4 xyz - D_3 \Delta z, \quad (3)$$

The first equation describes such processes: velocity of ACh release to synaptic cleft (1st term), the 2nd term gives the velocity of receptor binding of ACh (a is total amount of receptors on the post-synaptic membrane), the 3rd term gives the velocity of ACh decay under the action of AChE, the 4th and the 5th terms describe the process of ACh removing from the synaptic cleft due to back trap and diffusion, respectively. In the second equation the 1st term corresponds to the formation of mediator-receptor complexes (AChR), the 2nd term — velocity of the AChR decay due to AChE. The third equation corresponds to such processes: velocity of AChE release after free ACh and AChR splitting (1st term), 2nd, 3rd and 4th terms have the same meanings as in eqs. (1) and (2). We put sign "+" before $D_1\Delta x$ because we consider the mediator to flow from the synaptic cleft, and sign "−" before $D_3\Delta z$ because we consider cholinesterase to move to the place with a higher ACh concentration. Then we will take a natural assumption that $D\Delta c \approx D\frac{c}{L^2}$ where L is the characteristic geometric size, thus we obtain such a system of equations:

$$\frac{dx}{dt} = K\delta(t) - k_1x(a-y) - k_2xz - k_3x + D_1\frac{x}{H^2}, \quad (4)$$

$$\frac{dy}{dt} = k_1x(a-y) - k_4xyz, \quad (5)$$

$$\frac{dz}{dt} = k_5z - k_2xz - k_4xyz - D_3\frac{z}{L^2}, \quad (6)$$

Here H is the width of synaptic cleft; L is characteristic geometric size of the postsynaptic zone.

In our system of equations we consider the 1st term in (1) to be perturbation in this system. Thus the stationary solutions of system (4)–(6) are as follows:

(a) $x_0 = 0$, $y_0 = g$, $z_0 = 0$,

where g is a certain concentration of activated receptors, obviously $g \le a$; for $k_5 > 0$ (physiological condition), this point is classified as a strange attractor: $\lambda_1 = k_1g + \frac{D_1}{H^2} - k_1a - k_3 < 0$ ($\frac{D_1}{H^2} \approx 10^5, k_1a \approx 2\cdot 10^{12}$, [5]), $\lambda_2 = 0$, $\lambda_3 = k_5 - \frac{D_3}{L^2} > 0$, λ_i are solutions of the corresponding characteristic equation;

(b) $x_0 = m$, $y_0 = a$, $z_0 = 0$,

where m is a certain concentration of free acetylcholine; this solution satisfies system (4)–(6) on condition that $k_3 = 0$; indeed, when time is big enough all free acetylcholine will be trapped back into presynaptic membrane or diffuse from the synaptic cleft, so its velocity of back trap will be zeroth; for this point $\lambda_1 = \frac{D_1}{H^2} - k_3, \lambda_2 = -k_1m < 0$, $\lambda_3 = k_5 + \frac{D_3}{L^2} - k_2m - k_4ma$: this point may be either stable or unstable due to signs of λ_1 and λ_3;

(c) $x_0 = 0$, $y_0 = g$, $z_0 = h$,

where h is a certain concentration of acetylcholinesterase; this solution satisfies system (4)–(6) on conditions that $k_5 = 0$; really, when t is big enough AChE will have split all ACh and AChR and its velocity of release will be zeroth, for this point $\lambda_1 = k_1g + \frac{D_1}{H^2} - k_1a - k_2h - k_3 < 0$, $\lambda_2 = 0$, $\lambda_3 = k_5 - \frac{D_3}{L^2} > 0$, ($k_5 \approx 10^4$, $\frac{D_3}{L^2} \approx 10^{-2}$, [5]), so it is classified as strange attractor. Under normal condition when for sufficiently big time all the ACh are removed from the synaptic cleft due to diffusion and hydrolysis over AChE ($x_0 = 0$), all the mediator-receptor complexes will be split ($y_0 = 0$) and AChE will be free and ready for the new action ($z_0 = h$). It is clearly seen that this condition is the closest to the point (c) if we put $g = 0$.

For $k_5 < 0$ (action of AChE inhibitors):

Point (a):
$x_0 = 0$, $y_0 = g$, $z_0 = 0$,
$\lambda_1 = k_1g + \frac{D_1}{H^2} - k_1a - k_3 < 0$,
$\lambda_2 = 0$,
$\lambda_3 = k_5 - \frac{D_3}{L^2} < 0$.
When the organism is poisoned by AChE inhibitors (phosphororganic substances, for example) all the receptors will be activated ($y_0 = a$) and all molecules of AChE will be bent ($z_0 = 0$). Then point (a) is classified as a limiting cycle.

The same can be applied to point (b):
$x_0 = m$, $y_0 = a$, $z_0 = 0$,
$\lambda_1 = -\frac{D_1}{H^2} - k_3 < 0$,
$\lambda_2 = -k_1m < 0$,
$\lambda_3 = k_5 - k_2m - k_4ma + \frac{D_3}{L^2} < 0$
so point (b) is classified as sink.

Point (c):
$x_0 = 0$, $y_0 = g$, $z_0 = h$,
$\lambda_1 = k_1g + \frac{D_1}{H^2} - k_1a - k_2h - k_3 < 0$,
$\lambda_2 = 0$,
$\lambda_3 = k_5 - \frac{D_3}{L^2} < 0$, so point (c) is a limiting cycle.
Constants m, g, h are certain concentrations of acetylcholine, activated receptors and acetylcholinesterase, their values can be different, they can equal zero, the only limitation is for the concentration of activated receptors: $0 \le g \le a$.

A partial solution of the corresponding linearized system is as follows:

$$\delta x_{ps} = K, \quad (7)$$

Thus, a general solution of system (1)–(3) is following one:

$$x = x_0 + K + F_1\exp(\lambda_1 t) + F_2\exp(\lambda_2 t) + F_3, \quad (8)$$

$$y = y_0 + G_1\exp(\lambda_1 t) + G_2\exp(\lambda_2 t) + G_3, \quad (9)$$

$$z = z_0 + H_1\exp(\lambda_1 t) + H_2\exp(\lambda_2 t) + H_3, \quad (10)$$

where F_i, G_i, H_i can be found from the initial conditions.

It can be easily seen that diffusion of mediator has a stronger influence than lateral diffusion of cholinesterase on the process of synaptic transmission. Diffusion summand gives shifts to values of characteristic equations' solutions but does not change types of singular points, i. e. its contribution to the process of synaptic transmission is not so strong.

The main result of our study is as follows: kinetic model of synaptic transmission with three order parameters demonstrates a strange attractor behaviour under special above-mentioned conditions.

[1] P. G. Kostyuk, V. L. Zima, I. S. Magura, M. S. Miroshnichenko, M. F. Shuba, *Biofizika* (Biophysics) (Oberegy, Kyiv, 2001).
[2] M. V. Volkenshtein, *Biofizika* (Biophysics) (Nauka, Moskow, 1982).
[3] A. V. Chalyi, L. M. Chernenko, in *Dynamic phenomena at interfaces, surfaces and membranes*, edited by D. Beysens, N. Boccara, G. Forgacs (Nova Science Publ., New York, 1993), p. 599.
[4] A. V. Chalyi, K. A. Chalyi, L. M. Chernenko, A. N. Vasil'ev, *Nonlinear dielectric phenomena in complex liquids* **157**, 2004, edited by S. J. Rzoska, V. P. Zhelezny, NATO Sciense Series, Mathematics, Physics and Chemistry (Kluwer Academic Publishers, Dordrecht), p. 143.
[5] N. R. Nigmatullin *et al.*, Neyrofiziologiya **20**, 3, (1988).

ДИВНИЙ АТРАКТОР У КІНЕТИЧНІЙ МОДЕЛІ СИНАПТИЧНОЇ ПЕРЕДАЧІ

О. В. Чалий[1], О. В. Зайцева[2]
[1] *Національний медичний університет, кафедра медичної та біологічної фізики, бульв. Шевченка, 13, Київ, 01160*
[2] *Київський університет імені Тараса Шевченка, фізичний факультет, кафедра теоретичної фізики, просп. Глушкова, 6, Київ, 03022*

Метою цієї роботи є створення фізичної моделі передачі інформації через синаптичну щілину при міжклітинній взаємодії, які враховує такі реальні процеси:

1) вивільнення в синаптичну щілину молекул медіятора (ацетилхоліну), яке залежить від часу;

2) дифузію ацетилхоліну (ACh) із синаптичної щілини;

3) зв'язування ацетилхоліну з рецепторами;

4) дію специфічного ферменту — ацетилхолінестерази (AChE), яка відповідає за руйнування медіятор-рецепторних комплексів. Запропоновано систему трьох нелінійних диференціяльних рівнянь, які характеризують зміну концентрації молекул ацетилхоліну, активованих рецепторів (медіятор-рецепторних комплексів) та ацетилхолінестерази; досліджено стаціонарні стани та тип особливих точок.