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THE INFLUENCE OF DIFFUSION ON STABILITY IN CONTINUOUS/DISCRETE MEDIA

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1. INTRODUCTION

The behavior of coupled dynamic systems is investigated. The model of continuous/discrete medium which contains a network of a finite number of localized (pointwise) systems (elements)connected by means of certain contacts between elements is considered. These elements are distributed quite dense along 1-(or 2-) dimensional continuum or a certain domain in it. Each pointwise system has its own state and is considered as an active element, which influences the surrounding medium, and ice versa. The nearness of these elements has to be enough providing hat local changes of a media caused by activity of one element could influence neighboring elements. Elements could interact y means of "impulses" transmission at short distance or at long-range distance (using "signal channels").

The state of a medium is defined as a distribution off easible parameters (e.g. concentrations). Network describes the exact mechanism of exchange between active elements and is considered as structural parameter (e.g. the topology of an ambient space, the direction of exchange, etc.). The dynamics of local concentrations in medium due to the structural parameters of a system is analyzed. The possibility of directed diffusion process, which leads to the appearance of in homogeneity in the medium has been shown.

In the framework of this model we observed different effects of changing of a concentration in the case of continuous medium. In particular, we found interesting cyclic and like-chaotic regimes, and other nonlinear phenomena. These effects arise in the network due to the translation of the wave of excitation along the certain cycle or due to the interaction among certain cycles.

This model can help to explain some known effects, e.g. potassium' distribution in brain, the accumulation of potassium in the epicenters of epilepsy, etc.

In this article we continue our investigation of the behavior of materially coupled dynamic systems. In our previous works we discussed models of a network of a finite number of localized systems connected through an interaction structure involving migration, diffusion, or other forms of material exchange (see, e.g. [1,2]). On the basis of an analytical criterion for the stabilizing or destabilizing influence of connecting structure, a classification of possible types of connecting structures and of the localized systems themselves was given. Here more special mechanism of coupling is considered: a passing of directed electrical impulses in the network leads to a dislocation of a substance, which conduct these impulses, in the opposite direction. In biological systems this effect could form some in homogeneities in substance distribution.

2. PHENOMENOLOGICAL JUSTIFICATION OF A MODEL

In biological realm we observe recently the enormous surge of information dealing with the intercellular communication in various tissues, including the brain, by means of electrolytes, second messengers and metabolites [3]. The transmission of electrical impulses in brain is accompanied by calcium-potassium pump. So, there is an experimental evidence that electrical activity in brain is usually connected with particular processes, such as intercellular communication by means of some substances. And vice versa: the proper chemical substances can regulate electrical signaling in brain. Unfortunately, space does not allow us to give a complete exposition of variety of experimental data, and we present only a few important examples. We do feel, however, that it is important for nonlinear analysts to know that such experimental results exist and that it allows us to legitimate our model.

One of the hallmarks of the human epileptic brain during periods of time in between seizures is the presence of brief bursts of focal neuronal activity known as interictal spikes. Often such spikes emanate from the same region of brain from which the seizures are generated [4,5]. Several types of in vitro brain slice preparations, usually after exposure to convulsant drugs that reduce neuronal inhibition, exhibit population burst-firing activity that in many ways seems analogous to the interictal spike [6]. One of these preparations is the high potassium concentration ($[\mathcal{K}+]$) model, where slices from the hippocampus of the temporal lobe of the rat brain (a frequent site of epileptogenesis in the human) are exposed to artificial cerebrospinal fluid containing 6.5-10 $m\mathcal{M}$ $[\mathcal{K}+]$ [7]. After exposure to high $[\mathcal{K}+]$, spontaneous bursts of synchronized neuronal activity originate in a region known as the third part of the cornu ammonis or CA3 [8]. A detailed computer model of the high $[\mathcal{K}+]$ burst discharges in CA3 successfully replicates many of the experimental findings [9] (reviewed in ref. [10]). Some evidence of determinism was recently identified [11, 12]. Inositol trisphosphate is a second messenger that controls many cellular processes by generating internal calcium signals. It operates through receptors whose molecular and physiological properties closely resemble the calcium-mobilizing ryanodine receptors of muscle. This family of intracellular calcium channels displays the regenerative process of calcium-induced calcium release responsible for the complex spatiotemporal patterns of calcium waves and oscillations. Such a dynamic signaling pathway controls many cellular processes, including fertilization, cell growth, transformation, secretion, smooth muscle contraction, sensory perception and neuronal signaling. Calcium entry into cells can be regulated by a number of mechanisms, for example through channels operated by voltage, by receptors or by second messengers. With regard to the latter, most attention has focused on the inositol phosphates, InsP3 and InsP4 [13]. In some cells, there are suggestions that these inositol phosphates may directly activate specific channels in the plasma membrane. For example, the InsP3-induced entry of calcium in lymphocytes may be mediated by a new InsP3-receptor (IP3R) which contains sialic acid and is localized in the plasma membrane [14] . Similarly, the plasma membrane of olfactory cells seems to have an InsP3-sensitive calcium channel [15]. In addition to these direct effects, InsP3 may stimulate calcium entry indirectly through a more complex mechanism involving the endoplasmic reticulum (ER). Putney [16] coined the term "capacitative entry" to introduce the idea that the influx of external calcium seemed to be regulated by the calcium content of a portion of the ER lying close to the plasma membrane. In some cells, calcium entry is stimulated when the ER stores are artificially emptied by applying the calcium pump inhibitors thapsigargin [17] or 2,5-di-tert-butylhydroquinone, or the calcium ionophore ionomycin. When the ER is fully charged, entry is prevented, but as soon as InsP3 drains calcium out of these stores, the influx of calcium switches on automatically. Such a mechanism is thought to account for the entry of calcium into lacrimal [18] or mast cells following cell perfusion with InsP3. Others, also using lacrimal cells, failed to see such an InsP3-dependent entry unless they added InsP4 [19]. In cells that are oscillating, the magnitude of this influx component through second messengeroperated channels is often rather small and has little effect on the intracellular level of calcium during the interval between spikes, mainly because it is rapidly sequestered by the internal stores. But by charging up these stores, the influx mechanism transforms the cytoplasm into an "excitable medium" [20] , thus setting the stage for the generation of the repetitive calcium spikes

and waves. In effect, these internal stores integrate this small influx over time before periodically releasing the accumulated signal as a regenerative calcium spike. The calcium waves spreading through glial cells may constitute a long-range signaling network acting in concert with conventional neuronal networks. On a more speculative note, an interaction between glial and neuronal oscillators may contribute to the circadian time-keeping mechanism located within the suprachiasmatic nucleus [21] .

3. THE PRINCIPAL MODEL.

We consider a model of a medium which contains a network of a finite number of localized elements (cells) connected by means of certain contacts between elements. These elements distributed quite dense along 1- (or 2-) dimensional continuum or a certain domain in it. Each cell has its own state and is considered as an active element, which influences the surrounding medium, and vice versa. The nearness of these cells has to be enough providing that local changes of a media caused by activity of one cell could influience neighboring cell. Cells could interact by means of "impulses" transmission at short distance or at long-range distance (using "signal channels"). The state of a medium is defined as a distribution of feasible parameters (e.g. concentrations). Network describes the exact mechanism of exchange between active elements and is considered as structural parameter. As we mentioned in the previous paragraph 1, we suppose that coordinated action of both mechanisms together (electrical impulse and intercellular exchange by some substance) could lead to the phenomena we call "directed diffusion". This phenomena consists in the following: the continuous passage of electrical impulse in particular direction through the network could lead to the dislocation of a substance, involved into this process. Such dislocation could be in the same or in the opposit to the electrical impulse direction. So, owerfalls of concentration of the substance could be created in "macrospace" , e.g. in large space of brain.

4. FORMAL DESCRIPTION OF THE MODEL.

Let us consider the local interaction cell-medium in 1-dimensional case (i.e. in chains of cells), where intercellular exchange takes place by means of some particular substance. As it was mentioned, it could be second messenger, or electrolyte, or metabollite, or ions, etc. For our consideration the essential assumption is that we consider the material exchange caused by impulse.

Let us denote $x(i)$ - the concentration of the substance inside cell number i, $y(i-1), y(i)$ - concentrations of the same substance outside the cell to the left and to the right, respectively

$$.....y(i-1) \to x(i) \to y(i)....$$

At the moment t0 the output of substance from $x(i)$ takes place:

$$\begin{aligned} y(i-1) &:= y(i-1) + 0.5x(i), \\ y(i) &:= y(i) + 0.5x(i), \\ x(i) &:= 0, \end{aligned} \qquad (1)$$

Other cells at this moment suppose to be "silent". At the next moment t1 the influx to the cell x(i) is:

$$\begin{aligned} x(i) &:= f(y(i)) + f(y(i-1)), \\ y(i) &:= y(i) - f(y(i)), \\ y(i-1) &:= y(i-1) - f(y(i-1)). \end{aligned} \qquad (2)$$

Let us consider two cells) $x(i)$ and $x(i+1)$ one after the other:

$$....y(i-1) \to x(i) \to y(i) \to x(i+1)... .$$

We suppose that the passing of the electrical impulse through the chain of cells activates the secretion of a substance from the cell $(i+1)$ due to the formula (1), and at the next moment it activates the influx of a substance by previous cell i by the formula (2). So, from (1) and (2) we have:

$$\begin{aligned} x(i) &:= f(y(i) + 0.5x(i+1)) + f(y(i-1)), \\ y(i) &:= y(i) - f(y(i) + 0.5x(i+1)), \\ y(i-1) &:= y(i-1) - f(y(i-1)). \end{aligned} \qquad (3)$$

where $0.5x(i+1)$ is the contribution to the media $y(i)$ from its "right neigbour" the cell x(i+1). It is clear, that depending from function f, the cell $x(i)$ could get in more substance than it was in it at the previous step, and so on. So, we could obtain the dislocation of a substance through the chain under consideration.

5. LINEAR CASE.

Let us consider the simplest case, when f is linear function:

$$f(y) = ay, \qquad (4)$$

where a - coefficient of influx.

Thus the formula (3) will be a linear transformation at each step, and (1) is linear by definition. Let the number of cells will be (3), and let consider the case with one initial buffer $y0$:

$$y0 \to x1 \to y1 \to x2 \to y2 \to x3 \to y3.$$

So, in this case we have a linear transformation of 7-dimensional vector at each step:

$$(y0, x1, y1, x2, y2, x3, y3) := (y0, x1, y1, x2, y2, x3, y3).$$

From (1)-(4), after complete passing of the impulse through the chain (e.g. cell $x1$ secretion, $x2$ secretion, $x1$ influx, $x3$ secretion, $x2$ influx, $x3$ influx) we can get (7*7)-matrix of linear transformation:

$$\begin{pmatrix} (1-a) & (1-a)/2 & 0 & 0 & 0 & 0 & 0 \\ a & a & a & a/2 & 0 & 0 & 0 \\ 0 & (1-a^2)/2 & (1-a^2 & 0 & 0 & 0 & 0 \\ 0 & (1-a^2)/2 & a(1-a) & a/2 & a & a/2 & 0 \\ 0 & 0 & 0 & (1-a^2)/2 & (1-a^2 & (1-a^2)/2 & 0 \\ 0 & 0 & 0 & a(1-a)/2 & a(1-a) & a(1-a)/2+a/2 & a \\ 0 & 0 & 0 & 0 & 0 & (1-a)/2 & (1-a). \end{pmatrix}$$

It is easy to see, that if $a>1$, than after complete passing of the impulse through the chain under consideration the substance will accumulate as follows: $x1 > x2 > x3$. We assume that the initial amounts

of substance are approximately equal for each cell $\chi(i)$ and each medium $y(i)$. If we normalize these amount, we will get: $\chi 1 = 3.5$, $\chi 2 = 2$, $\chi 3 = 1.5$. So even after the first passing of impulse (from the left to the right) we get a dislocation of a substance along the chain in the opposite direction (from the right to the left).

6. MODELS OF NONLINEAR CHAINS

We investigated some peculiarities of directed diffusion in the simplest model of chain. In particular we considered the chain:

buffer1->cell1->medium1->cell2->...->medium(n-1)->celln->buffer2,

where the wave of excitation transmitted from the first cell to the last cell. Initially it was an equal quantity of substance in each cell and each medium. In buffer1 some definite amount of substance has been hold during the process. In *buffer2* the initial amount of substance is equal *0*. The process of propagating of the wave of excitation was defined, as earlier, according to the following scheme: at the first step the whole amount of the substance of cell s came out to the medium *(s-1)* and *s* equally, i.e. one half of the substance came to the left neighboring medium, other half came to the right medium. In particular, at the corresponding step one half of the substance from the last cell with number *n* came to the *buffer2*; at the second step the cell which has been unloaded at the previous step (number *(s-1)*) swallow up the substance from the left and from the right neighboring media:

$$a(\text{medium}(s\text{-}2))^q + a(\text{medium}(s\text{-}1))^q,$$

where a - coefficient of swallowing, q - degree.

A computer simulation of the process shows a large variety of possibilities of directed diffusion for this model. In particular, in the case $q=2$ and the fixed amount of the substance in *buffer1* the amount of the substance in *buffer2* increases when the number of sections (i.e. cells and media) in the chain increases. The corresponding increase of the substance in *buffer2* is almost linear for short chains ($n<15$), and then the process becomes saturated. Further increasing of the length of a chain (n) leads to an opposite effect. The amount of substance accumulated in *buffer2*, being reached some maximum, is starting to decrease, finally going to certain asymptote . This regularity including the volume of swallowed in *buffer2* substance is independent, in some limits, from the volume of substance in *buffer1*. Variation of the volume in *buffer1* in half does not lead to essential changes in volume of substance in *buffer2*.

Changes of degree of nonlinearity q has more essential influence on volume in *buffer2*. Thus, if q=1.5 then accumulation of substance in *buffer2* does not depend in practice from the length of the chain. In this case the accumulation inside cells is much less expressed than in media. But if q=2 the accumulation inside cells and in media is approximately equal .

Further we consider the case of intersected chains. In particular, let us assume that two chains have a common medium in some place.. Here we can see that shorter chain accumulate more substance being intersected, than without intersection. And shorter chain accumulate more than longer one.

So, directed diffusion in fact could be obtained in the model. Correlations among lengths of chains and their intersections could lead to different in homogeneities in distribution of substance. It is interesting to mention that these results are valid without any assumption about constant output of substance from the accumulator, i.e. from *buffer2* to the right (to the surrounding "tissue"). So we obtained not only "pumping" of substance, but an actual formation of local in homogeneity. This in homogeneity, depending on model parameters, could be temporal and then dissolve. Or it could be long-life living (asymptotically).

It is also interesting that inhomogeneities in distribution os substance along the chain has some peculiarities. In some cases the substance is distributed in a very nonlinear shape . Let $\varphi = 2 + \beta(v2)$, where $v2$ - current volume of substance in *buffer2*. If $\beta<0$, then dynamics of "pumping" almost does not depend from the chain length. If $\beta>0$, then pumping occurs in the direction of the wave of excitation, i.e. both directions coincide. In this case the accumulation inside cells is much more essential than in media.

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