Dynamical behaviour and coupling synchronization of oscillatory activities in a cell system of neural network

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Abstract

The paper mainly described a mathematical model of calcium ion oscillation of non-excitable cells. Based on the model, complex oscillations caused by variations of bifurcation parameters were analysed in detail and effects of variation of parameters to synchronization were discussed when the coupling intensity of two gaps-junction- coupled calcium ion cells was certain. Through numerical simulation, under less stiffness of coupling and among a certain scope of parameters, the phenomenon that the larger the parameters were, the easier the system occurred approximate synchronization were further illustrated.

Keywords: cluster oscillation, bifurcation, fast-slow dynamics, synchronization

1 Introduction

Calcium is the most important second messenger used to activate various cellular processes relaying information within cells to regulate their activity. The calcium signal is a transient increase of the intracellular concentration [1-3], the increase of Ca^{2+} dues to entry through the cell membrane and release from internal storage compartments especially the endoplasmic reticulum (ER) and the sarcoplasmic reticulum, which results in many cells to the formation of spatiotemporal signals in form of waves of high Ca^{2+} concentration travelling across the cell and global oscillations. The information transmitted by these signals arrives as a stimulus at the plasma membrane and is translated into intracellular Ca^{2+} oscillations.

A lot of researches show that many cell functions are closely related to the changes of intracellular calcium concentration [4-6], such as muscle excitation contraction coupling, neurotransmitter release, maintenance of cell membrane excitability, regulation membrane on various ion permeability and hormone secretion. The major intracellular calcium libraries have IP3 Ca^{2+} library, Ryanodine Ca^{2+} library, Ca^{2+} library of interactions between endoplasmic reticulum, mitochondria and so on. Many scholars [7-14] established the model of the calcium oscillation and studied the calcium oscillation and synchronous behaviour in nonlinear dynamics method, revealed the oscillation complex dynamic behaviour of the biological cell system, and found that the oscillation mode, such as cycle, quasi-periodical, chaotic and integer times, the model can well simulate the oscillations of intracellular calcium, so get the very extensive research.

Synchronization of coupled systems is a new research field of nonlinear dynamics, coupling synchronization is a basic phenomenon of nonlinear dynamics. Synchronization of coupled neurons system has been a preliminary study, for example, Zheng Y H [15] have studied synchronization in ring coupled chaotic neurons with time delay, Ge M L [16] have studied synchronization oscillatory on the electrically coupled chay neurons. Studies show that Ca^{2+} transfers from a cell to another cell, intercellular coupling make multicellular calcium oscillations perform synchronization. So the study of synchronous calcium oscillations behaviour in biological cells under the reasonable parameters in changing conditions has important significance. In the paper, dynamical behaviour and coupling synchronization of oscillatory activities in a parameter changing range is analysed and the effect of synchronization of the two gaps-junction-coupled calcium ion cells is discussed on the basis of Borghans model [4].

2 Dynamical model

To study the dynamical behaviour and coupling synchronization of oscillatory activities and the effect of synchronization of the two gaps-junction-coupled calcium ion cells, the model proposed by Borghans et al [4] was used in the paper. The model consists of three basic model compartments, which is the cytosol, the endoplasmic reticulum (ER) and the mitochondria (for details see reference [6]). Consequently, the three main variables are: free Ca^{2+} concentration in the cytosol (Ca_{cyt}), free Ca^{2+} concentration in the ER (Ca_{er}), and concentration of the inositol 1, 4, 5-trisphosphate (IP_3). The evolution of the model system is descried by the following differentials. The Ca_{cyt} changes due to the influx of extracellular Ca^{2+} (J_{in}), the passive efflux of Ca^{2+} changes from the cytosol

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into the extracellular medium (J_{out}), and from the intracellular Ca^2 store into the cytosol (J_{er}). Moreover, Ca^2 is pumped into (J_{pump}) and released from (J_{leak}) the intracellular store. The evolution of the model system is descried by the following differential equations:

$$\frac{dCa_{cyt}}{dt} = J_{in} + J_{leak} - J_{pump} + J_{er} - J_{out}\,, \tag{1}$$

$$\frac{dIP_3}{dt} = J_A - J_D - J_C\,, \tag{2}$$

$$\frac{dCa_{er}}{dt} = J_{pump} - J_{leak} - J_{er}\,, \tag{3}$$

where:

$$J_{in} = k_{in1} r + k_{in2}\,, \tag{4}$$

$$J_{leak} = rk_{leak} \frac{IP_3^{\,4}}{IP_3^{\,4} + k_a^{\,4}} \frac{Ca_{er}^{\,2}}{Ca_{er}^{\,2} + k_y^{\,2}} \frac{Ca_{cyt}^{\,4}}{Ca_{cyt}^{\,4} + k_z^{\,4}}\,, \tag{5}$$

$$J_{pump} = k_{pump} \frac{Ca_{cyt}^{\,2}}{Ca_{cyt}^{\,2} + k_2^{\,2}}\,, \tag{6}$$

$$J_{out} = k_{out} Ca_{cyt}\,, \tag{7}$$

$$J_{er} = k_f Ca_{er}\,, \tag{8}$$

$$J_A = rk_p\,, \tag{9}$$

$$J_C = \varepsilon IP_3\,, \tag{10}$$

$$J_D = k_d \frac{IP_3^{\,2}}{IP_3^{\,2} + K_p^{\,2}} \frac{Ca_{cyt}^{\,4}}{Ca_{cyt}^{\,4} + K_d^{\,4}}\,. \tag{11}$$

In the paper, we take k_{pump} as parameter to consider the influence of the oscillation to the model, other parameters are listed in the Table 1, among of them, the unit of k_{leak}, k_{in1}, k_{in2}, k_p and k_d is $\mu M\text{min}^{-1}$ and the unit of k_f and k_{out} is min^{-1}, the unit of k_2, k_a, k_y, k_z, K_d and K_p is μM.

TABLE 1 Model parameters for all calculated results unless stated

parameter	k_{leak}	k_{in1}	k_{in2}	k_p	k_d	k_f	k_{out}	k_2
value	19.5	1.0	2.0	2.5	80	1.0	10	0.1
parameter	k_a	k_y	k_z	K_d	K_p	r	ε	
value	0.4	0.2	0.3	0.4	1.0	1.12	0.1	

3 Analysis of corresponding dynamical behaviour

3.1 BIFURCATION ANALYSIS OF FAST AND SLOW DYNAMICS

Regarding of the system, we use method of fast and slow dynamics. Take the third equation as tardyon system and other equations as tachyon systems, which mean that Ca_{er} works as slow parameter and studies the model through changing the value of k_{pump}. When k_{pump} = 6.6 the system appears the cluster oscillation pattern shown in the Figure 1a. We use the fast and slow dynamics fork graph in Figure 1b to analyze its dynamics characteristics and type of the cluster oscillation.

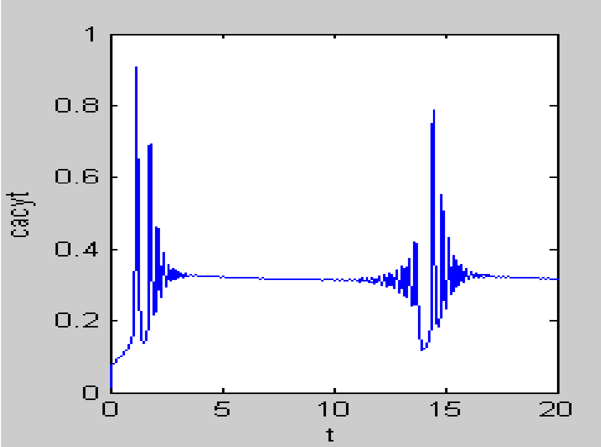

FIGURE 1a the time series of busting oscillations of the whole system

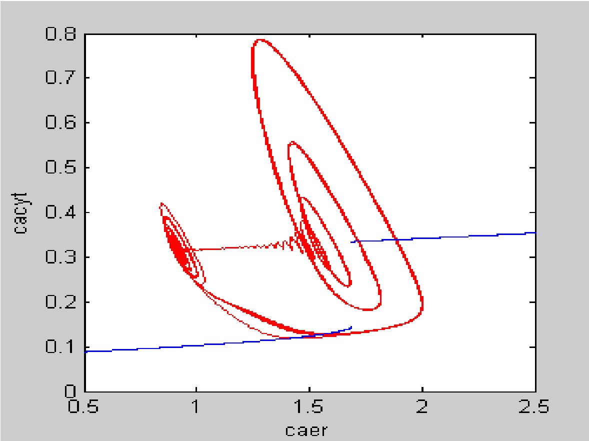

FIGURE 1b the bifurcation diagram of fast subsystem with Ca_{er} as the bifurcation parameter, the red closed trajectories represents for the phase diagram of (Ca_{er}, Ca_{cyt})

The balanced point of fast parameter system along with the change of its slow parameter Ca_{er} forms a resembling S-shape bifurcation line (the part between two full lines is the unstable part) on (Ca_{er}, Ca_{cyt}) plane in Figure 1b, and Figure 1a adds the corresponding Ca_{cyt} time course diagram. S-shape bifurcation line formed in fast parameter system can divide into upper, middle and below parts. In Figure 1a there exists a point-point bursting, whose main characteristic is that whatever bursting is active or resting, it all rely on the stabilize state of fast parameter system. Oscillation of point-point bursting is very commonly seen in the cytoplasm calcium oscillation model and can be well described by fast and slow dynamics.

The upper and below parts of bifurcation line of fast parameter system are made up of stable points, while the middle part consists unstable points. Observed Figure 1b in anticlockwise direction, the beginning and the ending of oscillation accompany with a folding bifurcation, and with the increasing of the time, the below part loses the stable state step by step through a folding bifurcation until reaches the stable upper part where Ca_{cyt} achieves its first maximum value as spiking. Therefore, when $k_{pump} = 6.6$, cluster oscillation pattern of the model presents "fold/fold" point-point cluster oscillation. Point-ring calcium oscillation might occur in the model with the change of k_{pump} when takes Ca_{er} as the slow parameter.

3.2 OVERALL BIFURCATION ANALYSIS ON k_{pump}

When parameter k_{pump} changes in [5, 16] of system (1), we use C language and four order Runge-Kutta method with variable step size to make numerical simulation. The overall bifurcation diagram of the entire system is shown in Figure 2a. Concluded from the figure, calcium oscillation only occurs in a limited range: first it starts from a stable state to an unstable state through a hopf bifurcation and then reaches the final stable state through a hopf bifurcation. When $k_{pump} = 5.862$, system occurs hopf bifurcation to generate limit cycle and enters in the oscillation state. When $k_{pump} = 15.31$, again system enters in the stable state through a hopf bifurcation. We testify the result by observing Figure 2b. To learn the dynamic characteristic of the model perfectly, we analyse phase diagrams by setting the different parameters of k_{pump}.

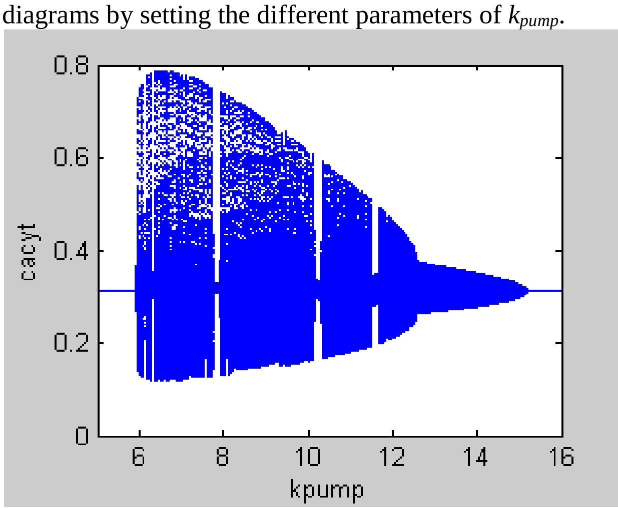

FIGURE 2a the bifurcation diagram of Ca_{cyt} versus the bifurcation parameter k_{pump}

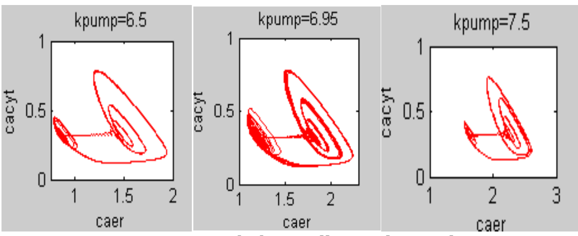

FIGURE 2b the small periodic window

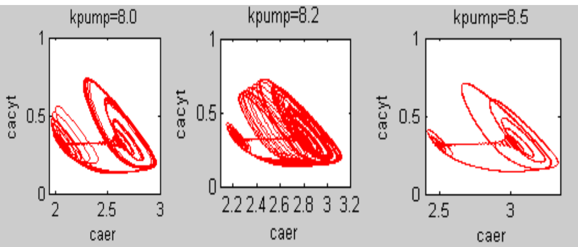

FIGURE 2c the small periodic window

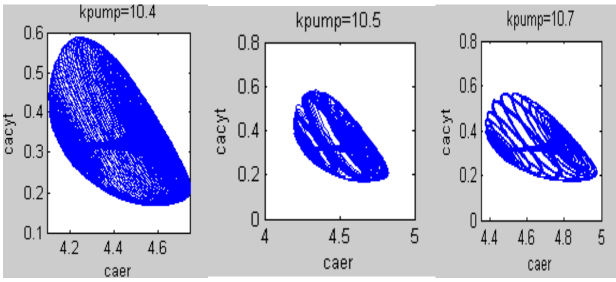

FIGURE 2d the small periodic window

With the increasing of parameter k_{pump}, oscillation system gets into the bursting state that we can observe the periodic bursting, quasi-periodic bursting and chaotic bursting. It is rarely seen in the calcium oscillation mathematics model about quasi-periodic phenomenon [8], which is able to well observe in this model with the changing of parameter k_{pump}, moreover some relatively narrow quasi-periodic windows such as Figure 2b, Figure 2c and Figure 2d can also be found. Quasi-periodic phenomenon is normally judged by calculating its corresponding Lyapunov exponents value, because when the exponent value is larger than 0, the corresponding oscillation is in chaotic state and when the value is smaller than 0, the oscillation is in stable state, however, when Lyapunov exponent equals with 0, the oscillation is in periodic state. Quasi-periodic phenomenon can also be differentiated from phase diagrams, normally a circular ring can be observed in corresponding phase diagrams. In Figure 2b system is in periodic movement when $k_{pump} = 6.5$; in quasi-periodic movement when $k_{pump} = 10.5$ for we can see a circular ring clearly in the second phase diagram of Figure 2d. When $k_{pump} = 10.4$, however, system lies in chaotic movement state. If k_{pump} continues to increase, system repeats periodic-quasi-periodic-chaotic movements.

4 Analysis of gap-junction-coupled synchronization of two calcium oscillation cells

Study of synchronization started from 1673, till now many scholars from variety fields have obtained some significant results [15-21]. Synchronization phenomenon broadly exists in biological cell system and plays important role in some basic activities of organism. Synchronization only occurs under smaller coupling intensity for chaotic system [19]. This paper mainly studies two Borghans models through junction coupling and the effect of synchronization with the changing of bifurcation under small coupling intensity. The coupling system consists with the following equations, among of them, $D(ca_{cyt2} - ca_{cyt1})$ and $D(ca_{cyt1} - ca_{cyt2})$ are coupling terms, D is coupling intensity and its value is in (0,0.1). Values of other parameters are same with the system listed in Table 1.

$$\frac{dca_{cyt1}}{dt} = J_{in} + J_{leak} - J_{pump} + J_{er} - J_{out} + D(ca_{cyt2} - ca_{cyt1}), \tag{12}$$

$$\frac{dIP_{31}}{dt} = J_A - J_D - J_C, \tag{13}$$

$$\frac{dca_{er1}}{dt} = J_{pump} - J_{leak} - J_{er}, \tag{14}$$

$$\frac{dca_{cyt2}}{dt} = J_{in} + J_{leak} - J_{pump} +, J_{er} - J_{out} + D(ca_{cyt1} - ca_{cyt2}), \tag{15}$$

$$\frac{dIP_{32}}{dt} = J_A - J_D - J_C, \tag{16}$$

$$\frac{dca_{er2}}{dt} = J_{pump} - J_{leak} - J_{er}. \tag{17}$$

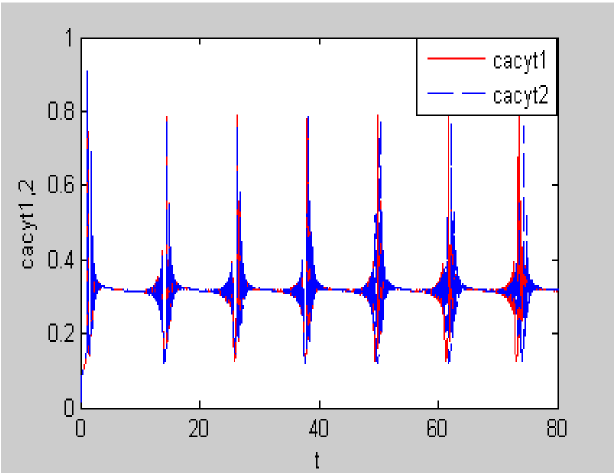

FIGURE 3a the time series of bursting oscillations when k_{pump} = 6.6

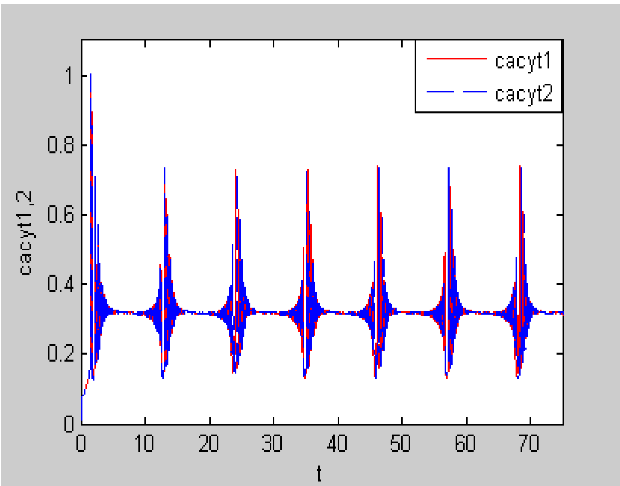

FIGURE 3b the time series of bursting oscillations when k_{pump} = 8

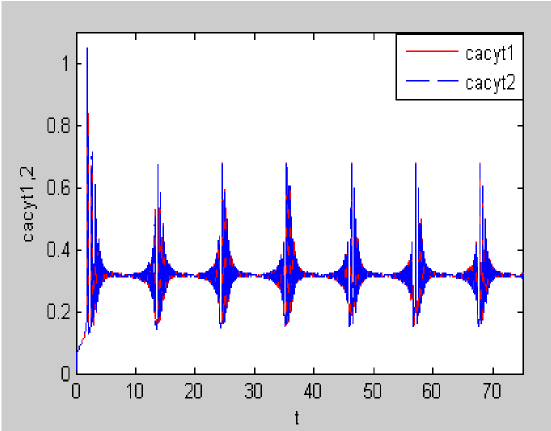

FIGURE 3c the time series of bursting oscillations when k_{pump} = 8

FIGURE 3 the time series of Cacyt in the first (red solid line) and in the second (blue dotted line) coupled cell when D=0.001

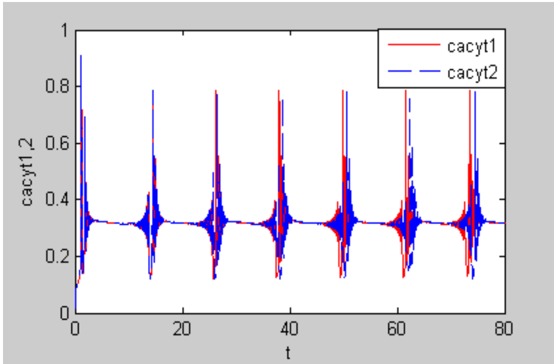

FIGURE 4a the time series of bursting oscillations when k_{pump} = 6.6

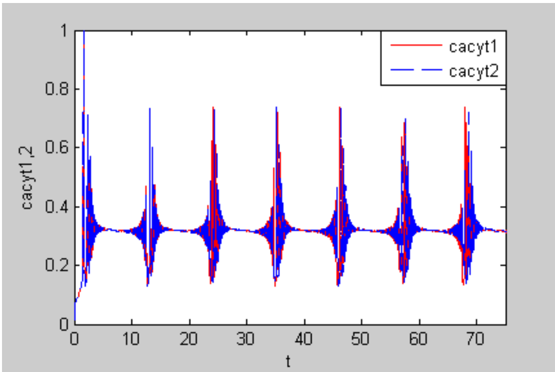

FIGURE 4b the time series of bursting oscillations when k_{pump} = 8

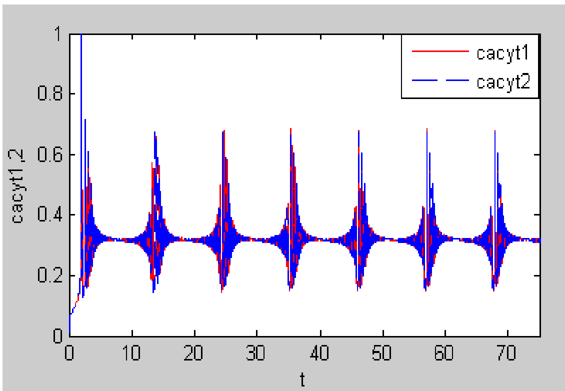

FIGURE 4c the time series of busting oscillations when k_{pump} = 9

FIGURE 4 the time series of Ca_{cyt} in the first (red solid line) and in the second (blue dotted line) coupled cell when D=0.003

Seen from Figure 3, when coupling intensity is fixed (D = 0.001) and other parameters remains unchanged and parameter k_{pump} changes in a certain range, coupling system achieves approximate synchronization but not completely synchronization with the increasing of k_{pump}. Similarly, when D = 0.003, observed from Figure 4, we can conclude that, when k_{pump} = 6.6, two coupling system don't synchronize; when k_{pump} = 8, two coupling system gradually synchronize approximately; when k_{pump} = 9, system reaches approximate synchronization. Thus, we can conclude: when coupling intensity is confirmed, the occurrence of approximate synchronization of two gap-junction-coupled biological cells is related to the values of the parameters. In this system, in a certain range, the larger the parameters are, the easier the system is likely to occur approximate synchronization.

5 Conclusions

For Borghans model of non-excitable calcium ion oscillation, we firstly took the calcium ion concentration in endoplasmic reticulum as the slow-change parameter and mainly researched the dynamical mechanism of the "fold/fold" point-point cluster oscillation generated in the model when k_{pump} = 6.6 using fast and slow dynamic bifurcation method. Of course, if k_{pump} were given other values, the model might have other complex oscillation patterns. Secondly, we analysed the overall bifurcation diagram taking k_{pump} as the bifurcation parameter and got complex calcium oscillation patterns through the diagram and the corresponding phase diagrams. In some small intervals of k_{pump}, quasi-periodic movements can be observed. For instance, the system went through the periodic, quasi-periodic and chaotic oscillation patterns orderly when the value of k_{pump} was 6.5, 8, 8.2. When k_{pump} equalled to 8.4 to 10.0, the above process repeated. Finally, the paper mainly discussed the synchronization problem of two gap-junction-coupled calcium ions. Through the analysis and numerical simulation, we found that complete synchronization could not happen. The value of k_{pump} can affect the synchronization of the coupling model when the coupling intensity is confirmed. To be specific, in the changing range of k_{pump}, the larger the value is, the closer the coupling system approach to the approximate synchronization state. These results are helpful to the understanding of the effect of k_{pump} in complex calcium oscillations.

Cluster oscillation pattern has attracted more and more concentrations of scholars for its varied cluster types, and synchronization of coupling biological cells plays a significant role in biology information transmission and coding, therefore, studying the synchronization problem of coupling cluster oscillation has a positive guiding meaning to solve some practical issues.

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