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Noise induced calcium oscillations in a cell exposed to electromagnetic fields[1]

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Abstract. The effects of noise on the calcium oscillations in a cell exposed to electromagnetic fields are described by a dynamic model. Noise is a very important factor to be considered in the dynamic research on the calcium oscillations in a cell exposed to electromagnetic fields. Some meaningful results have been obtained here based on the discussion. The results show that the pattern of intracellular calcium oscillations exposure to electromagnetic fields can be influenced by noise. Furthermore, the intracellular calcium oscillations exposure to electromagnetic fields can also be induced by noise. And the work has also studied the relationships between the voltage sensitive calcium channel's open probability and electromagnetic field. The result can provide new insights into constructive roles and potential applications of selecting appropriate electromagnetic field frequency during the research of biological effect of electromagnetic field.

Keywords: Calcium oscillations, noise, electromagnetic fields, open probability

1. Introduction

It is well known that intracellular calcium oscillations play a significant role in the process of cell regulation, e. g., calcium oscillations can increase the efficiency and specificity of gene expression, and regulate cellular process from egg fertilization to cell death, etc. [1, 2]. Intracellular calcium concentration ($[Ca^{2+}]_i$) exposure to electromagnetic fields was measured by many researchers [3-6], and the biological effects of electromagnetic fields should be noted. A number of theoretical models have been proposed to explain the oscillatory behavior of calcium ions in a cell exposed to electromagnetic fields [7-11]. For example, Huang et al. [8] reported the influence of electromagnetic fields on intracellular calcium concentration through the experiment research of osteoblasts [8]. Zhang et al. found that the frequency factor and the energy factor results at the window effects [9]. Another work has shown that cytosol calcium oscillation could be induced by some types of electromagnetic fields [10].

Noise plays a constructive role in many nonlinear systems and its effect has been widely studied in the past two decades. As a result of the number of membrane receptors, ion channels, and calcium ions

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in some organelles is very low [12], noise effects cannot be neglected. Now that noise is an important factor to be considered, its effects on the process of dynamic research should be taken into consideration further. Are there effects of noise on the calcium oscillations in a cell exposed to electromagnetic fields? This is a starting point from which the work would analyze in the following discussion.

In this paper, the Goldbeter model [13] is applied to get insight into the effects of noise on the behavior of calcium oscillations in a cell exposed to electromagnetic fields. The results show that the pattern of cytosol calcium oscillations exposure to electromagnetic fields can be influenced as well as induced by noise.

2. The model

Following the previous work [10], the effects of noise on the intracellular calcium oscillations exposure to electromagnetic fields will be discussed. For the dynamic model, X is cytosolic calcium concentration and Y is calcium concentration in the $InsP_3$-insensitive pool. And the dynamic model is described by the following set of equations:

$$\frac{dX}{dt} = \upsilon_0 \times \frac{P_0}{P_0'} - \upsilon_1 + \upsilon_2 + k_f Y - kX + \sqrt{2D}\xi(\mathrm{t}) \tag{1}$$

$$\frac{dY}{dt} = \upsilon_1 - \upsilon_2 - k_f Y \tag{2}$$

Eqs. (1) and (2) were originally proposed by Goldbeter [13] to explain calcium oscillations in a cell. Detailed description of other parameters in this model can be found in reference [13], and the parameter values in Eqs. (1) and (2) are chosen according to reference [13]. The number of reaction molecules is often low in a cell [14]. Then noise resulted from random fluctuations should be considered in this model. D denotes the intensity of Gaussian white noise $\xi(t)$ with zero mean value $<\xi(t)>=0$ and unit variance $\langle \xi(t)\xi(t') \rangle = \delta(t-t')$.

The experiment of Grassi, et al. [15] showed that the Ca^{2+} current through a calcium channel is almost unaffected by electromagnetic fields. And the enhancement of Ca^{2+} current density was due to the increased number of voltage-gated Ca^{2+} channels. Ebrahimian [16] had also drawn a conclusion that low frequency electromagnetic fields with 50 Hz frequency will directly lead to change in bioelectric activities neurons through a change in amount and rate of open and close ion channels. In conclusion, the exposure of cells to electromagnetic field results in changes in membrane potential. And the open probability of voltage sensitive calcium channel will be changed also. Thus the rate of Ca^{2+} and the pattern of calcium oscillations will be modulated. υ_0 represents the influx rate of Ca^{2+} into the cell. The exposure of cell to electromagnetic field will modify υ_0 as $\upsilon_0 \times P_0 / P_0'$ in Eq. (1). P_0' is open probability of voltage sensitive calcium channel without electromagnetic field exposure, and P_0 is open probability during electromagnetic field exposure.

Because of the similarity for sodium and calcium ion channel topology, this work suppose that the voltage sensitive calcium channel's open probability is similar to the open probability of N_a^+ channel [17].

Thus, we assume P_0' to be

$$P_0' = \frac{1}{1+e^{-\frac{zF(V_0-V_H)}{RT}}} \tag{3}$$

in which z is the values for the equivalent number of gating particles, V_H is the voltage at which the channel is open 50% of the time, V_0 is the initial equilibrium membrane potential, T is the absolute temperature, R is the universal gas constant, and F is the Faraday constant.

According to Neves, et al. [18], 60 Hz electric field with low amplitudes can change the membrane potential in pancreatic $\beta-$ cells. Then the work considers that the membrane potential is changed into $V_0 + V_m cos\omega t$ when the cell is exposed to extremely low frequency (ELF) electromagnetic fields. V_m is the peak value of the AC voltage across the membrane, and ω is the angular frequency of the electromagnetic fields. The value of V_m is given by the result of [19].

$$V_m = \frac{\omega B_0 cd}{2} \cdot \frac{\sigma_i}{\sigma_m}, \quad \omega = 2\pi f \tag{4}$$

Where B_0 represents magnetic density, c represents the distance between cell and the center of electromagnetic field, d represents the thickness of the plasma membrane. σ_i and σ_m represent conductivity of the intracellular fluid and membrane. In the following discussion, P_0 is written as

$$P_0 = \frac{1}{1+e^{-\frac{zF(V_0+V_m\cos\omega t-V_H)}{RT}}} \tag{5}$$

V_0 is chosen as -80mV, d is 20 nm, $\sigma_i/\sigma_m = 5\times10^8$, $z = 3.7$, $c = 5cm$ and $V_H = -67.5mV$, see [17] and [19] for more details.

3. Results and discussion

Based on Eq. (5), some meaningful results have been obtained. Figure 1 shows the relationship between the voltage sensitive calcium channel's open probability and electromagnetic field intensity when the electromagnetic frequency is 50 Hz. The results show that the open probability of voltage sensitive calcium channel increases with the enhancements of electromagnetic field intensity at first. Then P_0 keeps in about 50% when electromagnetic field intensity (B_0) is greater than 4 mT.

In Figure 2, we present P_o as a function of electromagnetic frequency f. One can see from Figure 2 that, P_o keeps in peak when the electromagnetic frequency f is 15 Hz and 60 Hz. And it is in trough when the electromagnetic frequency f is 35 Hz and 85 Hz. This means that we would observe obvious biological effect when we select appropriate electromagnetic field frequency during the

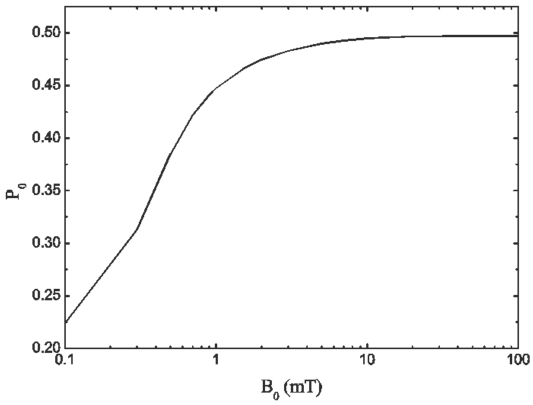

Fig. 1. The relationship between voltage sensitive calcium channel's open probability and electromagnetic field intensity.

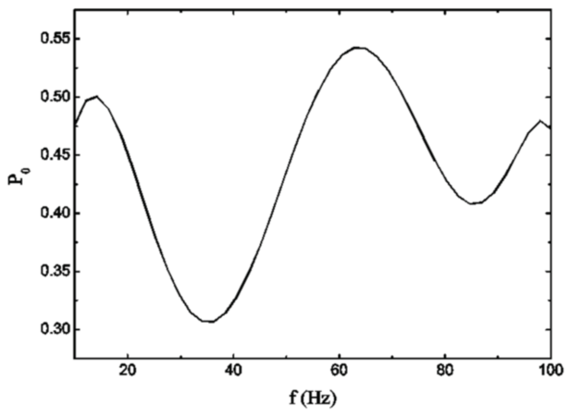

Fig. 2. The relationship between the voltage sensitive calcium channel's open probability and electromagnetic frequency.

research of biological effect of electromagnetic field.

The effects of noise on the calcium oscillations in a cell exposed to electromagnetic fields are discussed here. The curves of intracellular calcium concentration are presented in Figures 3(A) and 3(B) when the amplitude of electromagnetic fields B_0 is 10 mT. In Figures 3(A) and 3(B), the curves of calcium oscillations are given when electromagnetic field frequencies are 50 and 100 Hz, respectively. It can be well observed that the pattern of calcium oscillations changes with the increasing noise intensity.

Figure 4 shows that calcium oscillations cannot appear when there are no effects of noise on the cell (i.e. $D=0$) under conditions that $B_0 = 0.01mT$ and $f = 50Hz$. And calcium oscillations can be induced clearly with the increasing noise intensity. This can be explained by the fact that the calcium oscillations could be induced by noise when the cell is exposed to some types of electromagnetic fields.

4. Conclusion

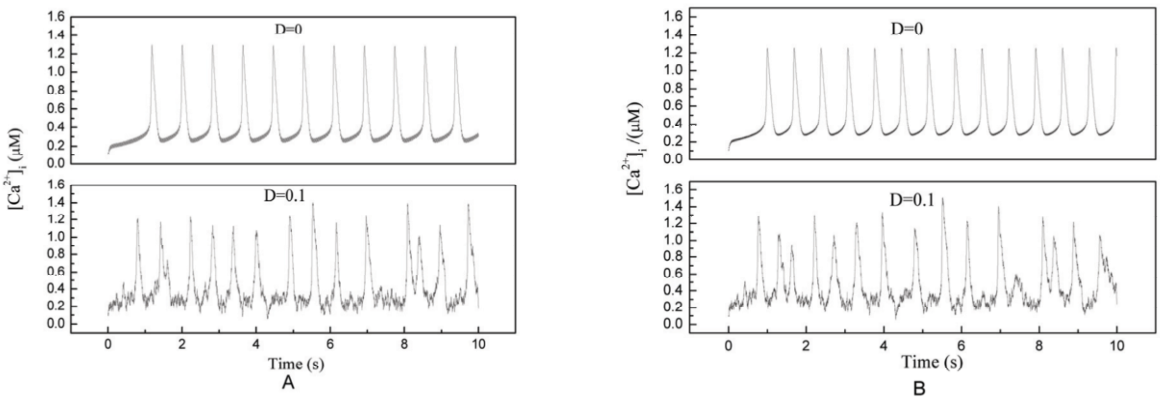

Fig. 3. Time evolution of the intracellular calcium concentration with different noise intensity. (A) $f = 50Hz$; (B) $f = 100Hz$

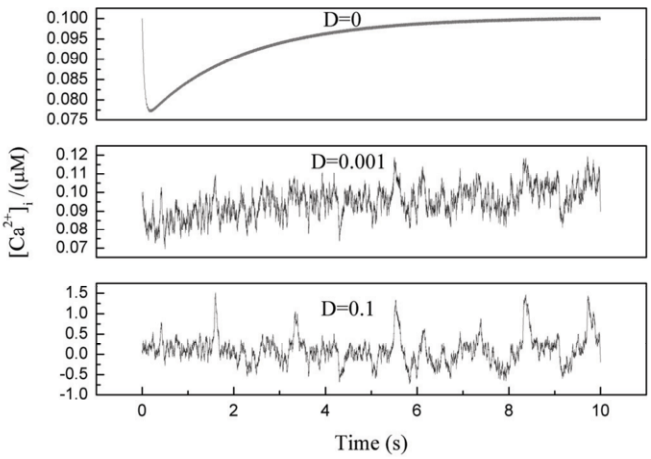

Fig. 4. Time evolution of the intracellular calcium concentration with different noise intensity. ($B_0 = 0.01mT$, $f = 50Hz$).

In this paper, the effects of noise on the calcium oscillations in a cell exposed to electromagnetic fields were discussed. Noise is a very important factor to be considered in the dynamic research of the calcium oscillations in a cell exposed to electromagnetic fields. The work has shown that the pattern of intracellular calcium oscillations exposed to electromagnetic fields can be influenced as well as induced by noise. And the work has also studied the relationships between the open probability of voltage sensitive calcium channel and electromagnetic field. The result provides new insights into constructive roles and potential applications of selecting appropriate electromagnetic frequency during the research of biological effect of electromagnetic field.

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