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Signal power amplification of intracellular calcium dynamics with non-Gaussian noises and time delay☆

Wei-Long Duan[a], Chunhua Zeng[b,*]

[a] City college, Kunming University of Science and Technology, Kunming 650051, PR China
[b] State Key Laboratory of Complex Nonferrous Metal Resources Clean Utilization/Faculty of Science, Kunming University of Science and Technology, Kunming 650093 PR China

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ABSTRACT

The effect of non-Gaussian noises on stochastic resonance of intracellular Ca^{2+} concentration in intracellular calcium oscillation(ICO) system with time delay is investigated by means of second-order stochastic Runge–Kutta type algorithm. By simulating the signal power amplification(SPA), the results indicate: there are respectively continuous values and a value of the parameter p(which is used to control the degree of the departure from the non-Gaussian noise and Gaussian noise.) to enhance reverse resonance in the behavior of SPA vs. p in cytosol and calcium store, namely continuous reverse resonance occurs in cytosol and reverse resonance occurs in calcium store. Moreover, SPA monotonically decreases as non-Gaussian noises strengthen, and SPA fast decays to constant as correlation time of non-Gaussian noises increases.

1. Introduction

In many studies on ICO, there are a variety of channels showing calcium-induced calcium release and a variety of models to describe ICO [1–4]. Many interesting phenomena have been found such as stochastic resonance [5,6], reverse resonance [6–8], coherence resonance [7], oscillatory coherence [9], resonant activation [10], bistability solutions with hysteresis [11], calcium puffs [12], various spontaneous Ca^{2+} patterns [13], colored noise-optimized calcium wave [14], stochastic backfiring [15], stability transition [16], and dispersion gap and localized spiral waves [17]. More importantly, Matjaž Perc et al. [18–21] has found that noise and other stochastic effects indeed play a central role [18,19] in system. Recently, calcium wave instability [22,23] has also been studied.

Martin Falcke et al. [15,17,24–29] has intensively studied ICO. For instance, a discrete stochastic model for calcium dynamics in living cells [24], spatial and temporal structures in intracellular Ca^{2+} dynamics caused by fluctuations [25], and key characteristics of Ca^{2+} puffs in deterministic and stochastic frameworks [28]. Additionally, they clearly showed that real ICO is non-Gaussian [29]. As stated in above, stochastic resonance and reverse resonance have been discovered in ICO. Thus, in this paper, we study the effect of non-Gaussian noise on stochastic resonance of ICO. For the role of noise on some stochastic systems, there are also some research [30–35].

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* Corresponding author.
E-mail addresses: yndwl@sina.com.cn (W.-L. Duan), zchh2009@126.com (C. Zeng).

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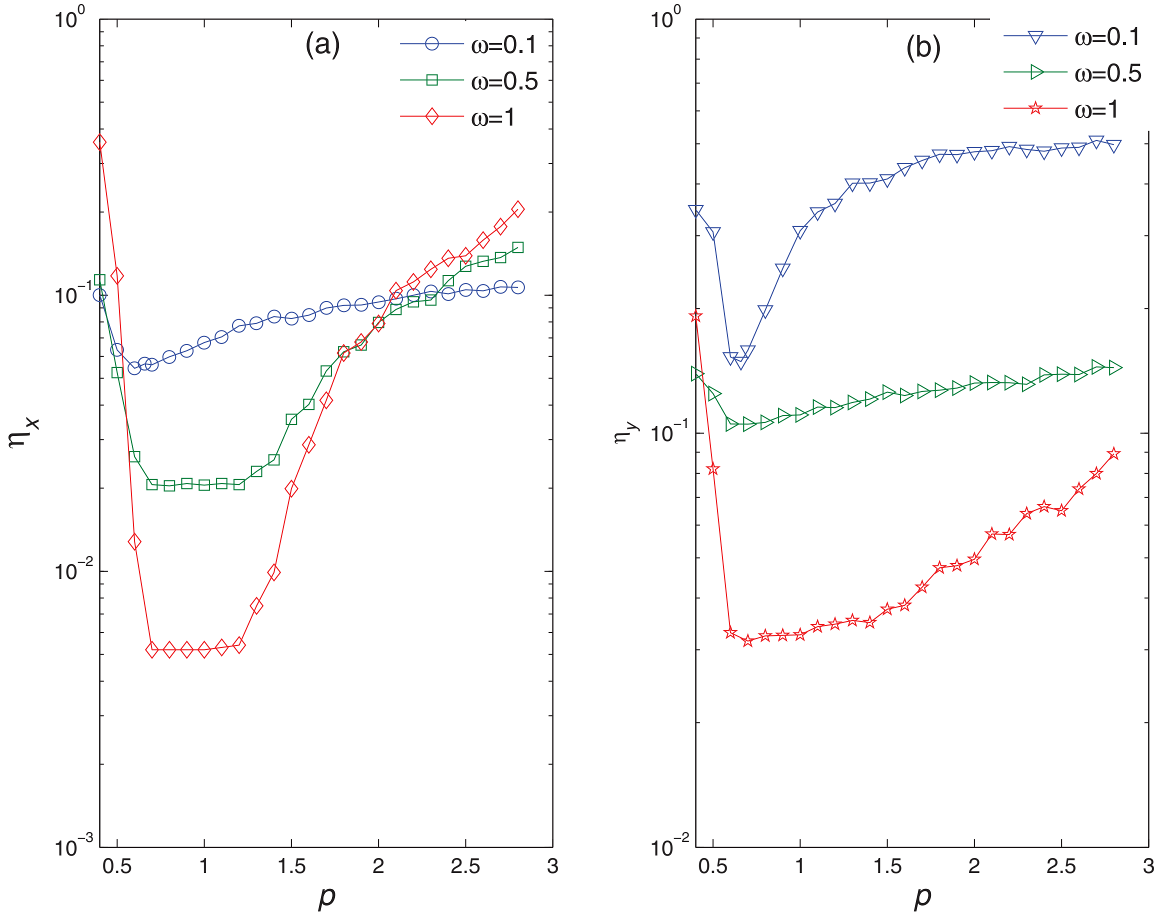

Fig. 1. The SPA η_x(see Fig. 1(a)) and η_y(see Fig. 1(b)) vs. parameter p of non-Gaussian noises.

2. The model for ICO with non-Gaussian noises and time delay

In order to study easily, taking into account same time delay τ in processes of active and passive transport of Ca^{2+} in a real cell. In this paper, x and y denote the concentration of free Ca^{2+} of cytosol and calcium store in a cell, respectively. Based on calcium-induced calcium release, the Langevin equations of ICO system can be read as follows according to our previous results [7,8]:

$$d_t x = A_1(x; x_\tau, y_\tau) + B_1(x; x_\tau, y_\tau)\eta_1(t), \tag{1}$$

$$d_t y = A_2(x, y; x_\tau) + B_2(x, y; x_\tau)\eta_2(t), \tag{2}$$

with

$$A_1(x; x_\tau, y_\tau) = v_0 + v_1\beta_0 - v_2 + v_{3\tau} + k_f y_\tau - kx, \tag{3}$$

$$A_2(x, y; x_\tau) = v_{2\tau} - v_3 - k_f y, \tag{4}$$

$$B_1(x; x_\tau, y_\tau) = \sqrt{v_1^2\beta_0^2 + 2v_1\beta_0\lambda W + W^2}, \tag{5}$$

$$B_2(x, y; x_\tau) = \sqrt{\frac{v_{2\tau} + v_3 + k_f y}{V}}, \tag{6}$$

$$W(x; x_\tau, y_\tau) = \sqrt{\frac{v_0 + v_1\beta_0 + v_2 + v_{3\tau} + k_f y_\tau + kx}{V}}, \tag{7}$$

and

$$v_2 = \frac{V_2 x^2}{x^2 + k_1^2}, v_3 = \frac{V_3 x^4 y^2}{(x^4 + k_2^4)(y^2 + k_3^2)}, \tag{8}$$

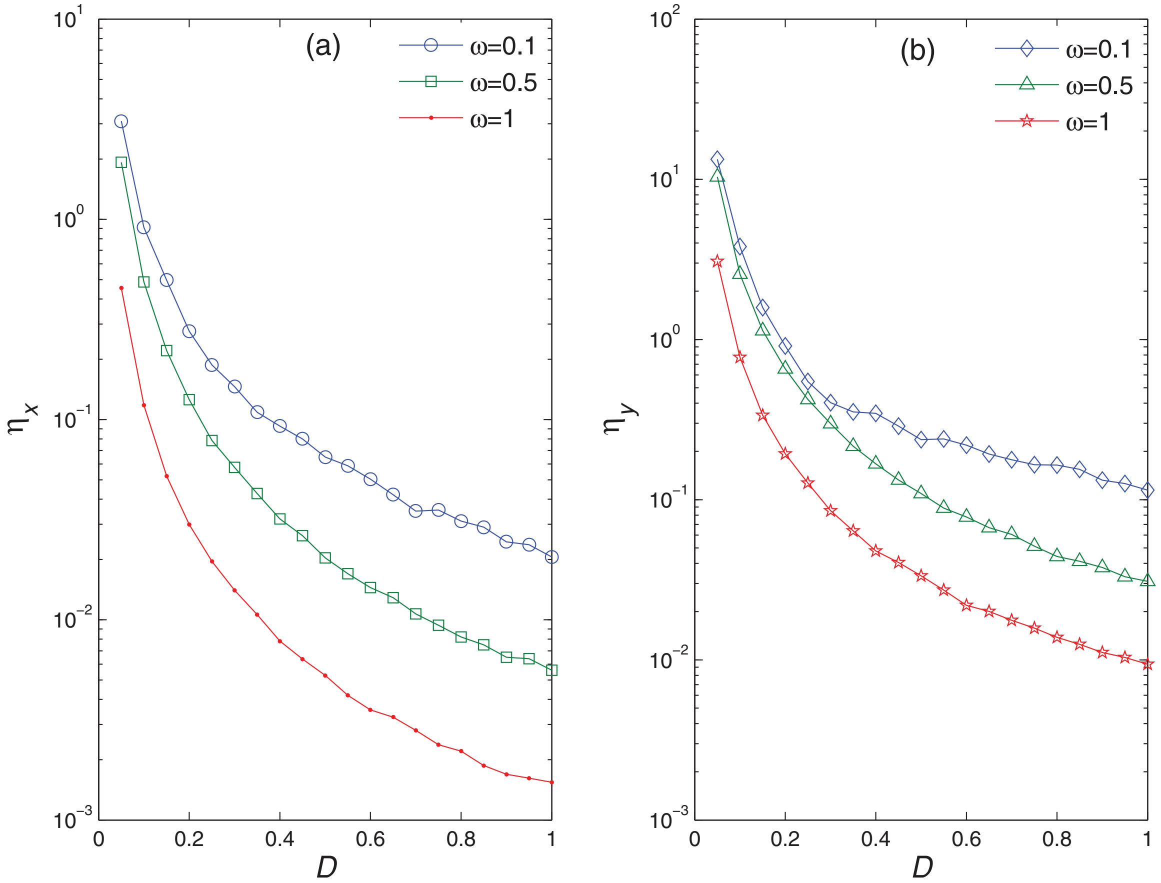

Fig. 2. The SPA η_x(see Fig. 2(a)) and η_y(see Fig. 2(b)) vs. intensity D of non-Gaussian noises.

$$v_{2\tau}=\frac{V_2x_\tau^2}{x_\tau^2+k_1^2}, v_{3\tau}=\frac{V_3x_\tau^4y_\tau^2}{(x_\tau^4+k_2^4)(y_\tau^2+k_3^2)}. \tag{9}$$

Here v_0 is the steady flow of Ca^{2+} to the cytosol, v_1 is the maximum rate of the stimulus induced influx of Ca^{2+} from the extracellular medium, β_0 is the external control parameter that denotes the degree of extracellular simulation. The rates v_2 and v_3 refer, respectively, to pumping of Ca^{2+} into calcium store and to release of Ca^{2+} from store into cytosol in a process activated by cytosolic Ca^{2+}. $v_{2\tau}$ is v_2 with time delay, and $v_{3\tau}$ is v_3 with time delay. k_fy is a diffusional flow of Ca^{2+} from store to cytosol, kx denotes the uptake from the cytosol, V is the system size. V_2 and V_3 denote the maximum values of the rates v_2 and v_3, respectively. The parameters k_1, k_2, and k_3 are threshold constants for pumping, release, and activation of release by Ca^{2+} and by inositol 1,4,5-trisphosphate. $W=W(x;x_\tau,y_\tau)$, $x_\tau=x(t-\tau)$, $y_\tau=y(t-\tau)$. λ denotes cross-correlation degree of internal and external noise before merger [11].

The noises $\eta_1(t)$ and $\eta_2(t)$ are considered as non-Gaussian noises which are characterized by the following Langevin equation [36]:

$$\frac{d\eta_i(t)}{dt}=-\frac{1}{\tau_1}\frac{d}{d\eta_i}V_{ip}(\eta_i)+\frac{\sqrt{2D}}{\tau_1}\xi_i(t), i=1,2. \tag{10}$$

Where $\xi_i(t)$ is a standard Gaussian white noise of zero mean and correlation $\xi_i(t)\xi_i(t')=\delta(t-t').V_{ip}(\eta_i)$ is given by

$$V_{ip}(\eta_i)=\frac{D}{\tau_1(p-1)}\ln\left[1+\frac{\tau_1}{D}(p-1)\frac{\eta_i^2}{2}\right], \tag{11}$$

and the statistical properties of non-Gaussian noise $\eta_i(t)$ is defined as

$$\langle\eta_i(t)\rangle=0, \tag{12}$$

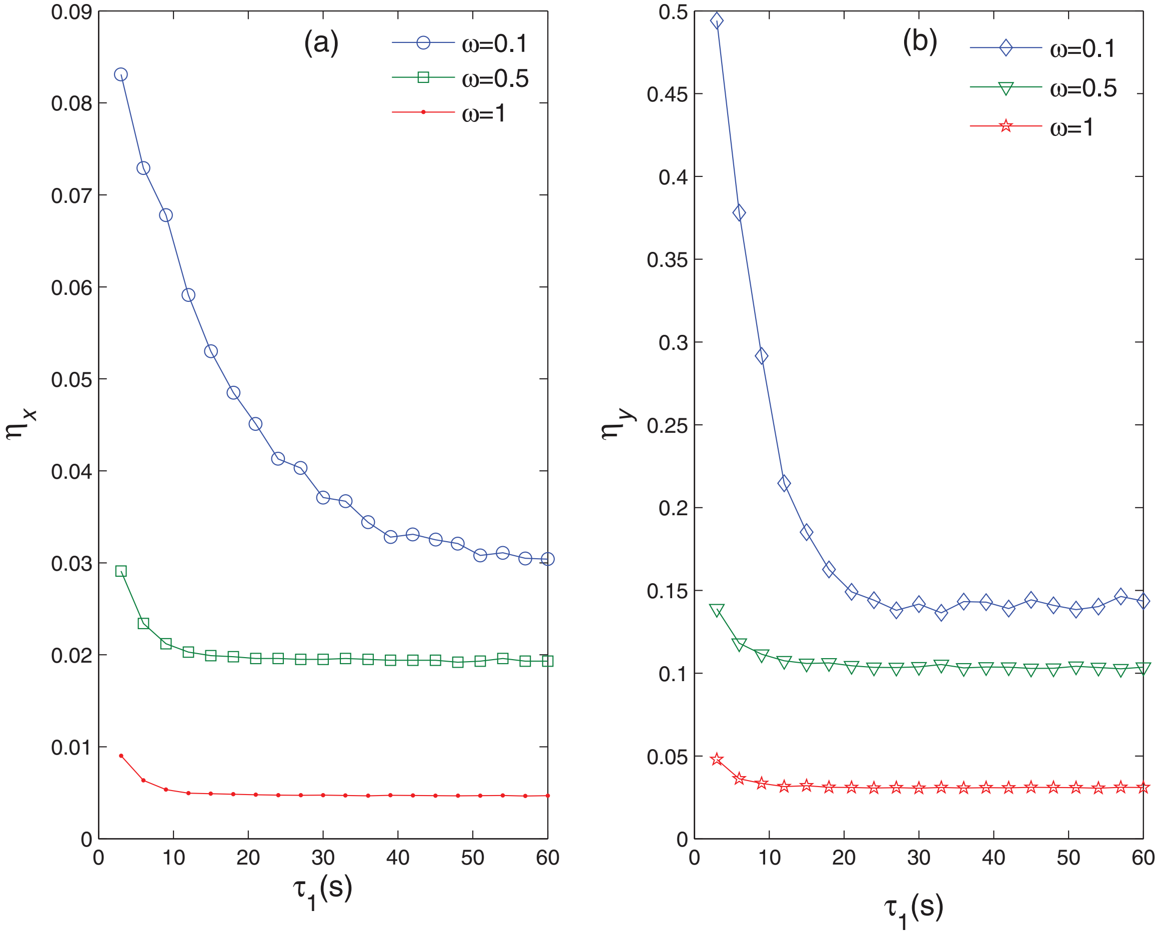

Fig. 3. The SPA η_x(see Fig. 3(a)) and η_y(see Fig. 3(b)) vs. correlation time τ_1 of non-Gaussian noises.

$$\langle\eta_i^2(t)\rangle = \begin{cases} \frac{2D}{\tau_1(5-3p)}, p\left(\in -\infty, \frac{5}{3}\right), \\ \infty, p \in \left[\frac{5}{3}, 3\right). \end{cases} \tag{13}$$

Where τ_1 denotes the correlation time of the non-Gaussian noises $\eta_i(t)$, and D denotes the noise intensity of Gaussian white noise $\xi_i(t)$. The parameter p is used to control the degree of the departure from the non-Gaussian noise and Gaussian noise. The distribution of the noise is Gaussian for $p = 1$, non-Gaussian with long tail for $p > 1$, and characterized by a "more than Gaussian" cutoff for $p < 1$. Here, in order to study easily, supposing noises $\xi_1(t)$ and $\xi_2(t)$ have same strength D, and non-Gaussian noises $\eta_1(t)$ and $\eta_2(t)$ have same p and correlation time τ_1.

3. The signal power amplification

In order to investigate the roles of non-Gaussian noises on stochastic resonance in ICO system, we respectively employ SPA η_x and η_y of cytosolic and calcium store's Ca^{2+} concentration to characterize the stochastic resonance of system [37–39]:

$$\eta_x = 4D^{-2}|\langle e^{i\omega t}X(t)\rangle|, \eta_y = 4D^{-2}|\langle e^{i\omega t}Y(t)\rangle|, \tag{14}$$

where $X(t)$ and $Y(t)$ are obtained respectively from the ensembles average over the stochastic path $x(t)$ and $y(t)$ realizations, and ω is frequency of Fourier transformation. Through integrating Eqs. (1) and (2) with second-order stochastic Runge–Kutta type algorithm [40], the time series $x(t)$ and $y(t)$ can be obtained(for specific simulation algorithm of ICO system, see Ref. [7], discretize time in steps of size $\Delta = 0.001$s.). After fast Fourier transformation of $X(t)$ and $Y(t)$, one can obtain the amplitude of the first harmonic of the output information η_x and η_y from Eq. (14). By simulating time series, one could obtain many properties of stochastic dynamics system, e.g., in neuronal network system [41–51].

Experimentally, x is in the order of 100–200 nM in basal state [52] and $y = 5$ μM [53], so that the initial values $x(0)$ and $y(0)$ independently take uniformly random from 0.1 ∼ 0.2 μM and 4 ∼ 5 μM. In the condition of time delay, it is rational to let $x(t-\tau) = x(0)$ and $y(t-\tau) = y(0)$ as $t < \tau$. In this paper, the value of parameters are set as: $v_0 = 1$ μM/s, $v_1 = 7.3$ μM/s, $\beta_0 = 0.287$, $k_f = 1$/s, $k = 10$/s, $V_2 = 65$ μM/s, $V_3 = 500$ μM/s, $k_1 = 1$ μM, $k_2 = 0.9$ μM, $k_3 = 2$ μM, $V = 1000\mu m^3$, $\lambda = 0.1$, and $\tau = 0.5$ s.

In the following, by simulating SPA η_x and η_y, we respectively discuss the effect of parameter p, intensity D, and correlation time τ_1 of non-Gaussian noises on stochastic resonance in ICO system.

In Fig. 1, the role of parameter p on stochastic resonance is plotted, here $D = 0.5$ and $\tau_1 = 10$ s. As shown in figure, the SPA η_x(see Fig. 1(a)) exhibits the deeper valley as ω increases, i.e., the larger the ω, the deeper the valley is. Namely, reverse resonance occurs in cytosol, it enhances as ω increases. It's clear, there is only a value of p to indicate reverse resonance when ω is small (e.g., $\omega = 0.1$). Additionally, as ω increases, the bottom of valley becomes flat (e.g., $\omega = 0.5$ and 1), which demonstrates, the presence of some continuous values of p induce reverse resonance, i.e., reverse resonance always happens as long as p takes the value of in this portion. Briefly, in these continuous values of p, continuous reverse resonance happens in cytosol. However, SPA η_y(see Fig. 1(b)) shows a structure of deep valley with small ω (e.g., $\omega = 0.1$), as ω increases, this structure disappears slowly (e.g, $\omega = 0.5$ and 1), i.e., SPA only presents a minimum with small ω. It shows that reverse resonance only occurs in calcium store when ω is small, as ω increases, reverse resonance decreases.

Then, the role of intensity D of non-Gaussian noises on stochastic resonance is studied in Fig. 2, here $p = 0.9$ and $\tau_1 =$ 10s. It is clearly seen that SPA η_x(see Fig. 2(a)) and η_y(see Fig. 2(b)) linearly decrease as non-Gaussian noises strengthen. Moreover, the higher the ω, the smaller the SPA is.

Finally, the role of correlation time τ_1 of non-Gaussian noises on stochastic resonance is studied in Fig. 3, here $p = 0.9$ and $D = 0.5$. Whether SPA η_x(see Fig. 3(a)) or η_y(see Fig. 3(b)) roughly shows same variation as τ_1 prolongs, i.e., both η_x and η_y fast decay to a constant. Moreover, the larger the ω, the faster the decay is and the smaller the SPA is.

4. Conclusions

In view of non-Gaussian noises in transmission processes of intracellular Ca^{2+}, by means of second-order stochastic Runge–Kutta type algorithm, the effect of non-Gaussian noises on stochastic resonance of intracellular Ca^{2+} concentration in ICO system with time delay is investigated.

By simulating SPA η_x and η_y of cytosolic and calcium store's Ca^{2+} concentration, the results indicate that: (1) in cytosol, there is a value of p to induce reverse resonance with small ω, as ω enlarges continuous reverse resonance occurs at portion continuous values of p, and reverse resonance increases as ω increases; in calcium store, though reverse resonance also occurs, it decreases as ω increases. (2) As non-Gaussian noises strengthen, SPA η_x and η_y show decay all the time, the larger the ω, the smaller the SPA is. (3) As correlation time varies, SPA η_x and η_y fast decay to constant, the larger the ω, the faster the decay is and the smaller the SPA is. Therefore, in ICO system, the value of p is main factor to induce reverse resonance, it may has significance to study ICO and cell biology.

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