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# Inverse stochastic resonance induced by synaptic background activity with unreliable synapses

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ABSTRACT

Inverse stochastic resonance (ISR) is a recently pronounced phenomenon that is the minimum occurrence in mean firing rate of a rhythmically firing neuron as noise level varies. Here, by using a realistic modeling approach for the noise, we investigate the ISR with concrete biophysical mechanisms. It is shown that mean firing rate of a single neuron subjected to synaptic bombardment exhibits a minimum as the spike transmission probability varies. We also demonstrate that the occurrence of ISR strongly depends on the synaptic input regime, where it is most prominent in the balanced state of excitatory and inhibitory inputs.

## 1. Introduction

As is well known, neurons communicate with each other through synapses and the process called synaptic transmission. Synaptic transmission is an essentially probabilistic process due to the random neurotransmitter release of the synaptic vesicles. At some synapses the stochastic nature of synaptic communication may give rise to highly *unreliable* transmission which has been confirmed by well-designed biological experiments [1–8]. For example, in the cortex, it is found that the probability of neurotransmitter release in response to a single spike can be as low as 0.1 or lower, indicating that as many as 90% out of all arriving presynaptic inputs fail to evoke a postsynaptic response [4]. Moreover, some recent theoretical studies have also suggested that the transmission unreliability might be a part of the neural computation in the brain and possibly have significant implications in information processing [8–15].

On the other hand, in the past decades, noise in neurons has attracted more and more attention due to its potential facilitating effects on information processing in nervous system. Researchers especially paid close attention to stochastic resonance (SR) mechanism whereby generally feeble input information can be amplified and optimized by the assistance of noise [16–22]. More precisely, when the noise level is small, the neurons are not able to detect the signal due to its small amplitude, but as the noise raises, the temporal output becomes highly correlated with the signal resulting an increase in signal to noise ratio. Finally, for very large noise intensities, the neuronal output is dominated by the noise and the signal cannot be detected. Such an input–output relationship of neurons exhibits a well-known bell-shaped structure as a function of noise intensity. Besides the noise, information transmission delays among neurons are crucial for the SR in neural systems. In [23,24], it has been identified that the synaptic transmission delays lead to emergence of multiple stochastic resonance peaks in networks of neurons, indicating that noise and information transmission delays can play complementary roles in warranting optimal detection of weak signals. In contrast to SR, recent studies have concentrated on an inhibitory effect of noise in rhythmically firing neurons [25–30], that is, there exists a pronounced minimum in the firing rate as the noise level increases. Such an inhibition effect of noise has also been demonstrated experimentally in squid giant axon operating as a pacemaker [31]. Since the dependency of neuronal response on noise is reverse of that in SR mechanism, this new phenomenon is called *inverse stochastic resonance* (ISR). In most previous modeling studies on ISR, noise has been generally considered an external additive noisy current source appearing in the membrane potential equation, and assumed to be originated from the cumulative effect of overall noise sources. However, such an approximation in noise modeling is lack of mimicking the actual biophysical conditions and does not provide us a clear understanding the phenomenon with concrete biological mechanisms.

Due to the large number of synaptic contacts in *in vivo* conditions, neurons are exposed to intense and random incoming excitatory and inhibitory spike inputs. Based on the experimental findings from electrophysiological studies [32–35], this synaptic

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background activity is widely accepted to be the major source of noise in neurons. It is thus necessary to carry out further studies by considering the realistic models of synaptic noise to clarify the underlying biophysical mechanisms which give rise to ISR. In this work, we investigate the ISR by using a detailed modeling approach for the synaptic background activity with unreliable synapses. We mainly examine influence of synaptic unreliability as well as other important some background activity parameters, such as the synaptic input regime, presynaptic firing rate and coupling strength on the occurrence of ISR.

## 2. Mathematical model and setup

The system under study consists of a postsynaptic neuron which receives uncorrelated network activity from a finite number of excitatory and inhibitory neurons. The time evolution of membrane potential of the postsynaptic neuron is modeled based on the second-order Morris–Lecar (ML) equations as follows [36,37]:

$$C\frac{dv}{dt} = -g_{\mathrm{Ca}}m_\infty(v)(v - V_{\mathrm{Ca}}) - g_{\mathrm{K}}w(v - V_{\mathrm{K}}) - g_L(v - V_L) + I_{app} + I_{syn}(t) \tag{1a}$$

$$\frac{dw}{dt} = \phi\frac{w_\infty(V) - w}{\tau_w(V)} \tag{1b}$$

where $v$ and $w$ represent the membrane voltage and the activation of delayed-rectifier $\mathrm{K}^+$ current, respectively. $C$ is the membrane capacity per unit area and $\phi$ is a constant that determines scaling rate for $\mathrm{K}^+$ channel opening. The parameters $g_x$ $(x = \mathrm{Ca}, \mathrm{K}, L)$ are the maximal conductance of calcium, potassium and leakage channels, respectively. $V_{\mathrm{Ca}}$, $V_{\mathrm{K}}$ and $V_L$ denote the corresponding equilibrium potentials. The parameters $m_\infty$ and $w_\infty$ stand for the fraction of open calcium and potassium channels at steady state, respectively; and they are given by the following equations:

$$m_\infty(V) = 0.5\left[1 + \tanh\left(\frac{v - V_1}{V_2}\right)\right] \tag{2a}$$

$$w_\infty(V) = 0.5\left[1 + \tanh\left(\frac{v - V_3}{V_4}\right)\right] \tag{2b}$$

with a time constant for the activation of potassium channels:

$$\tau_w(V) = 0.5\left[\cosh\left(\frac{v - V_3}{2V_4}\right)\right]^{-1} \tag{2c}$$

where $V_1$ and $V_3$ are the activation midpoint potentials at which the corresponding currents are half activated; $V_2$ and $V_4$ denote the slope factors of the activation. Finally, $I_{app}$ is an external current stimulus in $\mu\mathrm{A/cm^2}$. Notably, ML neuronal model can demonstrate two different types of neuronal excitability (i.e. class I and class II excitability) when the model variables are set appropriately. Here, following the previous computational studies on ISR [25–30], we consider the class II excitability and set the ML model parameters as: $C = 20\ \mu\mathrm{F/cm^2}$, $g_L = 2.0\ \mu\mathrm{S/cm^2}$, $g_{\mathrm{Ca}} = 4.4\ \mu\mathrm{S/cm^2}$, $g_{\mathrm{K}} = 8.0\ \mu\mathrm{S/cm^2}$, $V_{\mathrm{K}} = -84$ mV, $V_L = -60$ mV, $V_{\mathrm{Ca}} = 120$ mV, $V_1 = -1.2$ mV, $V_2 = 18$ mV, $V_3 = 2$ mV, $V_4 = 30$ mV and $\phi = 0.04$.

Finally, in Eq. (1a), $I_{syn}$ is the total synaptic current introduced into the neuron due to the network activity. We assume that the model neuron receives a large number of excitatory and inhibitory spike inputs from totally $N$ presynaptic neurons. The ratio of excitatory to inhibitory synaptic contacts is taken as $N_E : N_i = 4 : 1$ to ensure physiological values found in *in-vivo* conditions [38,39]. By considering the presynaptic neurons as a group that generates independent Poisson spike trains with the same input firing rate $f_{in}$, the total synaptic current reaching the soma of the postsynaptic neuron is given by:

$$I_{syn}(t) = w_{exc}\left[\sum_{k=1}^{N_e}\sum_{l} h_k^l\delta\left(t - t_k^l\right) - K\sum_{m=1}^{N_i}\sum_{n} h_m^n\delta\left(t - t_m^n\right)\right] \tag{3}$$

where $w_{exc}$ represents the coupling strength for the excitatory synapses and $K$ is the relative strength between inhibitory and excitatory synapses. $t_k^l$ is the discharge time of the $l$-th spike at the excitatory presynaptic neuron $k$, and $h_k^l$ is the synaptic transmission reliability parameter of this spike which is used to mimic whether the spike transmission is successful or not. Similarly, $t_m^n$ is the discharge time of the $n$-th spike at the inhibitory presynaptic neuron $m$, and $h_m^n$ is the synaptic transmission reliability parameter. The reliability of spike transmission is modeled based on the stochastic Bernoulli on–off process by assuming $h_k^l = 1$ or $h_m^n = 1$ with probability $p_s$, and $h_k^l = 0$ or $h_m^n = 0$ with probability $1 - p_s$, where $p_s$ is defined as the successful transmission probability of spikes [10,18,40–42].

## 3. Results and discussions

We systematically analyze the ISR phenomenon in a single neuron subjected to a synaptic background activity, and discuss the relative contributions of different synaptic subunits on such a phenomenon. In the results presented below, the total number of input synapses is set $N = 5000$. Because it is a slow varying parameter compared with other system parameters, we do not change its value. Following the procedure in [25–28], the temporal output of the neuron is recorded for $T = 20\,000$ ms (after eliminating 1000 ms time interval as transient), and then the mean firing rate is calculated by counting the number of spikes and dividing it by the recording interval $T$. For statistical accuracy, the entire procedure is repeated 1000 times with random initial conditions of $(v_0, w_0)$, and we finally compute the mean firing rate as the measure of ISR.

As a starting point, we first consider the balanced state of excitatory and inhibitory synaptic inputs, and investigate whether the ISR can be induced in this special regime by the synaptic background activity with unreliable synapses. To do so, we set the system parameters as $K = 4$, $w_{exc} = 0.05$, $f_{in} = 32$ Hz, and compute the mean firing rate as a function of successful transmission probability $p_s$ for several typical values of the applied current $I_{app}$. Fig. 1 features the obtained results. As seen in Fig. 1, with decreasing values of $p_s$ (right to left), all the mean firing rate curves drop at first until reaching some minimum and then begin to rise, except $I_{app} = 88$, and finally attain to some saturated values. It is also seen that the minimum in mean firing rates occur at some corresponding optimal $p_s$, indicating that appropriate tuning of synaptic reliability can suppress the spiking activity even in the presence of suprathreshold input current $I_{app}$. This is a clear signature of synaptic transmission reliability induced ISR. Furthermore, it is evident that ISR can significantly be modulated by $I_{app}$: inhibition effect of synaptic transmission reliability on neuronal firing tends to disappear as $I_{app}$ increases.

The underlying effects of $p_s$ and $I_{app}$ on the occurrence of synaptic reliability induced ISR can be understood by considering the dynamical structure of the model neuron. The bifurcation diagram in Fig. 2 shows that the deterministic ML model equations may exhibit different solutions as $I_{app}$ varies. Namely, when $I_{app} < 88.29 = I_1$, there is only a stable equilibrium, generally known as "stable fixed point (SFP)", corresponding to the resting state of the membrane potential. At $I_1$, a saddle node bifurcation gives rise to occurrence of stable and unstable limit cycles. Notably, the stable limit cycle (SLC) corresponds to regular spiking behavior of the neuron. With further increase in $I_{app}$, although the SLC does not change very much, the unstable limit cycle (ULC) collapses onto the SFP at $I_2 = 93.86$ through a subcritical Hopf bifurcation.