35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Reverse Stochastic Resonance in a Hippocampal CA1 Neuron Model

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Abstract: ***Stochastic resonance (SR) is a ubiquitous and counter- intuitive phenomenon whereby the addition of noise to a non-linear system can improve the detection of sub-threshold signals. The "signal" is normally periodic or deterministic whereas the "noise" is normally stochastic. However, in neural systems, signals are often stochastic. Moreover, periodic signals are applied near neurons to control neural excitability (i.e. deep brain stimulation). We therefore tested the hypothesis that a quasi-periodic signal applied to a neural network could enhance the detection of a stochastic neural signal (reverse stochastic resonance). Using computational methods, a CA1 hippocampal neuron was simulated and a Poisson distributed subthreshold synaptic input ("signal") was applied to the synaptic terminals. A periodic or quasi periodic pulse train at various frequencies ("noise") was applied to an extracellular electrode located near the neuron. The mutual information and information transfer rate between the output and input of the neuron were calculated. The results display the signature of stochastic resonance with information transfer reaching a maximum value for increasing power (or frequency) of the "noise". This result shows that periodic signals applied extracellularly can improve the detection of subthreshold stochastic neural signals. The optimum frequency (110Hz) is similar to that used in patients with Parkinson's suggesting that this phenomenon could play a role in the therapeutic effect of high frequency stimulation.***

Index Terms—Terms—Action potential, Stochastic resonance, Synaptic noise, Numerical method, Monte Carlo simulation

INTRODUCTION

The detection of subthreshold signals can be improved by additive noise in nonlinear threshold systems, and is known as stochastic resonance (SR) [1]. SR has been originally observed in many physical systems such as Schmitt triggers [2] and ring lasers [3]. SR has been further observed in biological systems such as peripheral nerves [4,5,12] and the central nervous system [6,7,8]. In particular we recently found that information transmission of stochastic neural signals in single neurons and in neural network can be maximized by the addition of Gaussian noise [9,10].

Here, we test the hypothesis that information transmission of neural stochastic signals can also be maximized by introducing a quasi-periodic sub-threshold biphasic stimulation. Since such periodic signals are routinely applied to neural tissue (i.e. DBS), this study should provide information about the effect of electrical stimulation on information transfer within the brain.

METHODS

Neural Model:

A CA1 hippocampal neuron was modeled with 5 compartments in the basal dendrites, 1 for the soma, and 20 compartments in the apical dendritic branches (Figure 1a). The soma contained 1 sodium, 1calcium, and 5 potassium channels (**K**DR , **K**M , **K**A , **K**CT and **K**AHP). The model parameters were adapted from those in [6,9,10,11].

The subthreshold neural input current, $\mathbf{I_{signal}(t)}$ was injected into the distal portion of the apical dendrite (24th compartment, see Fig. 1). $I_{signal}(t)$ was set to be an impulse response function, $h(t) = a_{signal} \exp(-\alpha t)$, where α= 1000 Hz and a_{signal} = 0.6 nA. The interval between the stimuli, T_s, was generated by using random numbers with the gamma distribution. The intensity or mean signal frequency, λ_s was set at 5Hz whereas the shape parameter, κ, was varied from κ= 1 (exponential distribution, homogeneous Poisson process) to κ= 100 with the scaling parameter set at $\theta = (\kappa/\lambda_s)^{-1}$ (Fig. 2a).

The extracellular periodic electric stimulus ("noise"), $\mathbf{I_{ext}(t)}$, was generated by a point current source located 0.1 mm from the neuron as shown in Fig. 1 and simulated based on a modified McNeal model [13]. The volume conductor was assumed to be purely resistive and isotropic (300 Ω.cm). The electric stimulus, $I_{ext}(t)$ was as a biphasic pulse with an amplitude of 6 μA and the pulsewidth of 80 μs. The interval between pulses was also generated randomly using a gamma

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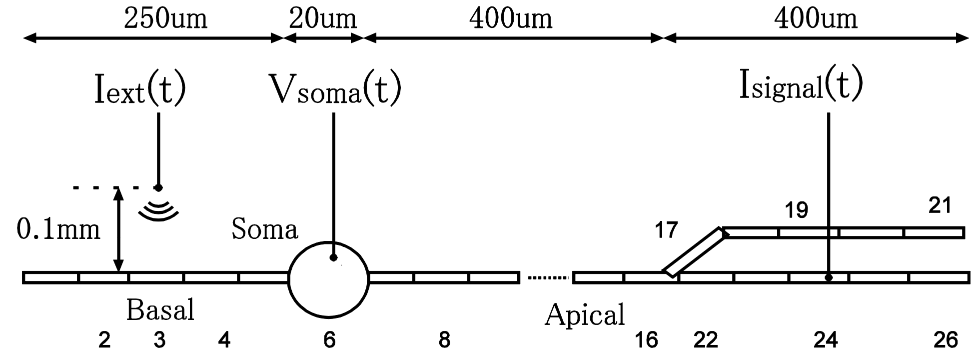

Fig. 1. Pyramidal cell model: The model consists of a basal dendrite, soma, and apical branches. The synaptic signal current was injected into the distal portion of the apical dendrites (24^{th} compartment). The subthreshold extracellular periodic electric stimuli **Iext(t)**, was assumed to be a point current source located 0.1 mm away from the midpoint of the basal dendrite (3^{rd} compartment). The volume conductor was assumed to be a purely resistive isotropic conducting medium (resistivity = 300 Ω.cm).

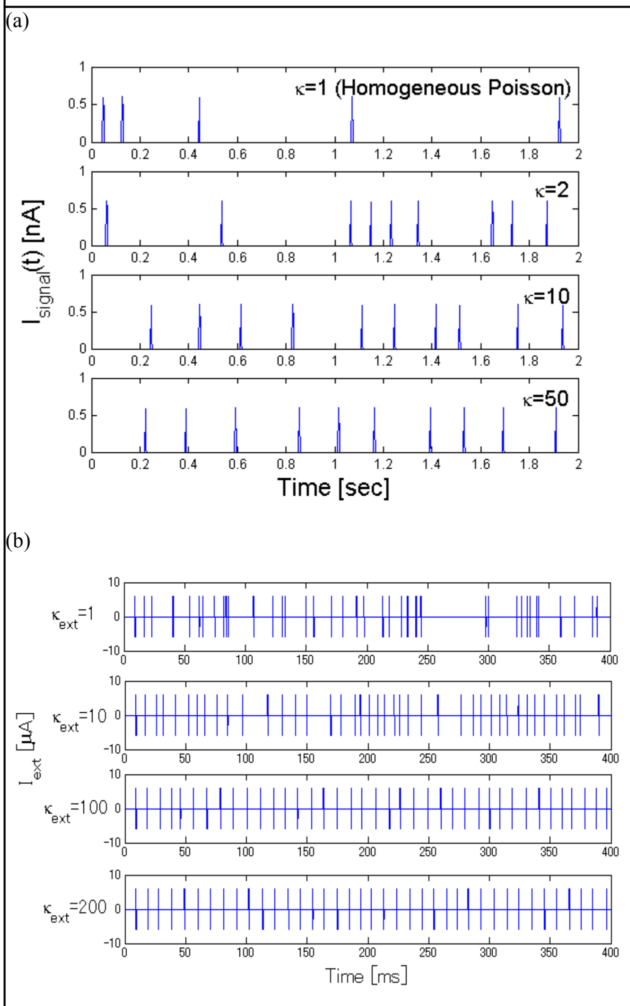

Fig. 2 "Input and noise" waveforms: (a) The subthreshold neuronal signal was a filtered impulse response, h(t) = Aexp(-αt) where α= 1000 Hz and the amplitude A of 0.6 nA with an intensity of 5 Hz. A random number with a gamma distribution was used to set the intervals of stimuli. The shape parameter κ was variable and the scaling parameter set at $\theta = (\kappa/\lambda s)^{-1}$. κ was varied from 1 to 100. (b) The extracellular periodic stimuli were applied with a constant amplitude of Aext =6 μA and pulse width PW= 80μA.

distribution. The mean frequency was varied in order to change the power of the extracellular signal and determine the frequency dependence of the resonance phenomenon. The shape parameter, κ_{ext}, was varied from 1 (exponential distribution, homogeneous Poisson process) to 100 with the scaling parameter set at $\theta_{ext} = (\kappa_{ext}/\lambda_{ext})^{-1}$ to generate the constant mean frequency (Fig. 2b). A periodic stimulus was also generated with constant interval with frequency $\mathbf{f}_{ext}$.

Signal Processing:

The information rate was calculated from the inter-spike intervals by subtracting the 'noise entropy' from the total entropy as follows [13]:

$$I_{rate}\left(I_{signal}(t),T\right)= R\times\left(H_{total}(T)-H_{noise}(T\mid I_{signal}(t))\right)$$

where

$$H_{total}(T)=-\sum_{i=0}^{\infty}p(T_i)\log p(T_i)$$

and:

$$H_{noise}(T)=-\sum_{i=0}^{\infty}p(T_i\mid I_{signal}(t))\log p(T_i\mid I_{signal}(t))$$

$p(T_i)$ and $E[]$ are the normalized probability density function of the inter-spike intervals, and the expectation operation, respectively. R is the mean spike rate (Hz). The noise entropy, H_{noise}, was calculated by applying the expectation operator of each signal sample, whereas the total entropy, H_{total}, was obtained from 100 trials.

RESULTS

The effect of increasing the frequency (or power) of the external stimulation on the mutual information between input and output was first examined. A single trial is shown in Fig. 3. The subthreshold input signal was generated by a homogeneous Poisson process (κ= 1), I_{signal} with the amplitude of 0.6 nA and the mean frequency of λ_s = 5 Hz (top panel in Fig.3abc). The extracellular stimulus was generated using gamma distribution with κ_{ext}=100. I_{ext} had an amplitude of 6 μA (middle panels in Fig.3abc). The transmembrane potentials recorded at the soma (bottom

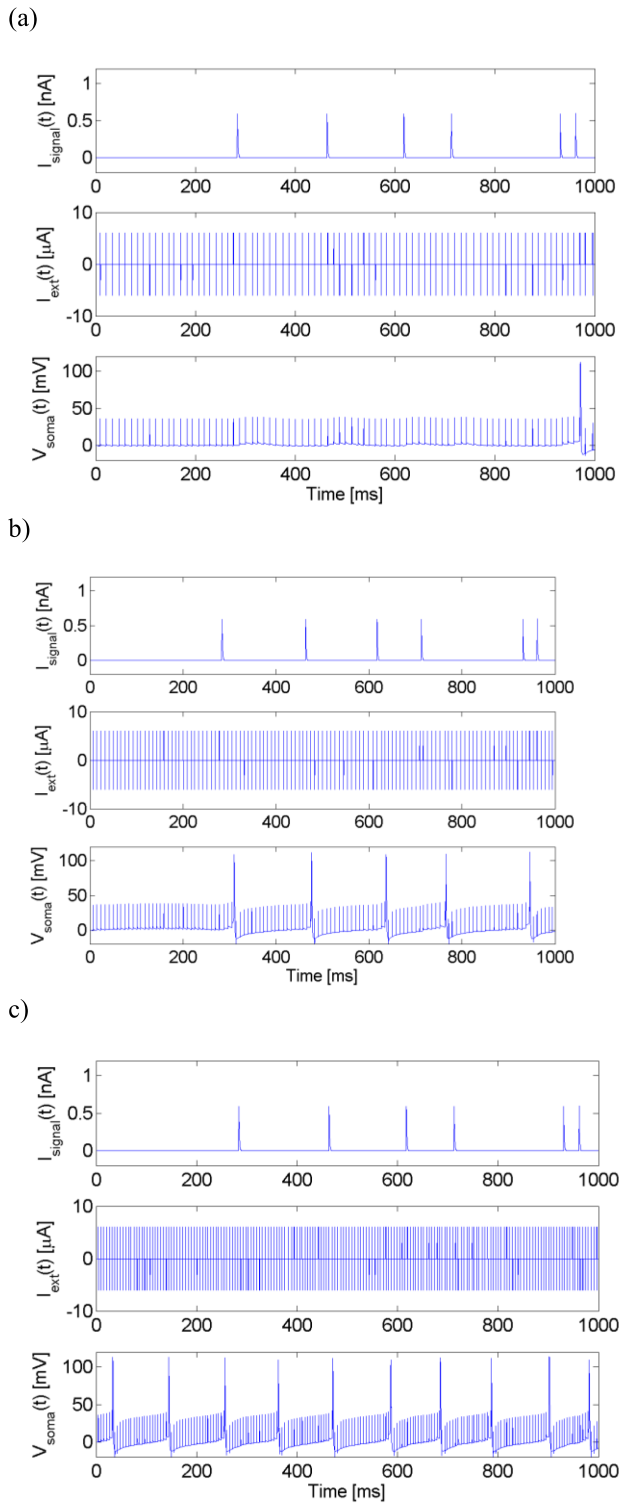

Fig. 3 Effect of increasing the frequency (or power) of the external stimulation on the mutual information between input and output. Top: The subthreshold synaptic signals was generated by a homogeneous Poisson process (κ=1), Middle: Extracellular subthreshold stimulating currents was applied as nearly periodic intervals (κext.= 100) and with constant width of pulse (80 μA). Bottom: Transmembrane potentials recorded at the soma. The mean frequency of extracellular stimuli (f ext.) was varied to reveal a resonance phenomenon: 80 Hz in (a), 120 Hz in (b) and

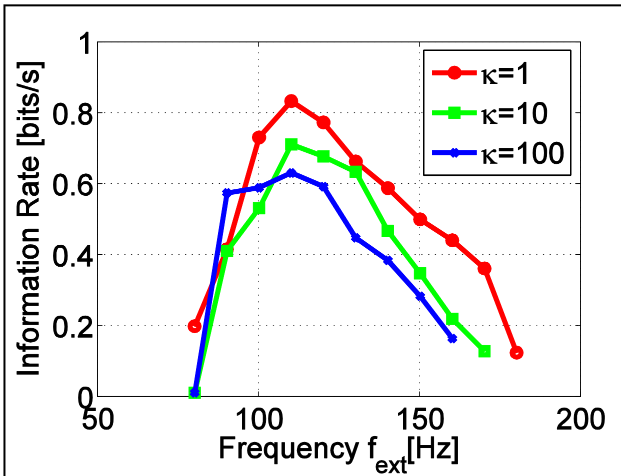

Fig. 4 Information rate as a function of frequency of extracellular stimulation, f_{ext}. The extracellular stimuli were applied with κ_{ext} =100. The information rate calculated from inter-spike interval histograms [9] reached a maximum value at a specific frequency respective condition of shape parameter κ.

panels in Fig.3abc). The mean frequency of extracellular stimuli, λ_{ext} was set at 80 Hz in (a), 120 Hz in (b) and 180 Hz in (c). At frequencies lower than λ_{ext}=80 Hz, (figure 3(a), action potentials were not be observed since both signal and extracellular stimuli were subthreshold. However, as the mean frequency increases above 100 Hz, spike trains could be observed (Fig 3b). As the frequency increased further, the number of spikes decreased indicating a strong resonance effect (Fig 3c).

The information rate (IR) was calculated and is plotted versus frequency in Figure 4 for three values of κ. The information rate reaches a maximum value at a specific frequency (λ_{ext} = 110Hz) indicating a strong resonance effect. Figure 4 also shows that the effect is independent of κ indicating that this reverse stochastic resonance effect can be observed for both quasi-periodic or highly periodic signals.

DISCUSSION

Stochastic resonance data are normally plotted as SNR or IR versus noise power. In fig 4, the data are shown as IR versus frequency. However, the mean power of the extracellular signal is proportional to the mean frequency of the signal since the pulse width is constant. Therefore, figure 4 shows a standard stochastic resonance plot but with stochastic signals as input signals and quasi-periodic signals as “noise”. This is the reverse of normal stochastic resonance whereby the signal is periodic and the noise is stochastic. Hence the phenomenon was called “reverse stochastic resonance”. It should be distinguished from the phenomenon called “inverse stochastic resonance” whereby applied stochastic noise can inhibit neural firing when reaching an optimum value [15]. Since the optimum frequency for the maximum effect of the stimulation is similar to the optimum frequency for stimulation in DBS, these results suggest that subthreshold stimulation at frequencies similar to DBS of neural pathways could enhance information transfer in the nervous system and could be a possible mechanism to explain the effect of DBS.

CONCLUSIONS

- These simulations show that periodic and quasi-periodic signals can also generate a stochastic resonance phenomenon when applied to stochastic signals
- This phenomenon is reverse to normal stochastic resonance with periodic input and stochastic noise
- The frequency that maximizes information rate is similar to the optimum frequency for the control of movement artifacts with DBS (110Hz)

ACKNOWLEDGMENTS

This research was supported by an endowment from the Lindseth family to Case Western Reserve University HM is grateful for financial support from the Institute of Science and Technology at Kanto Gakuin University.

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