

## Synchronization due to common pulsed input in Stein's model

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It is known that stimulus-evoked oscillatory synchronization among neurones occurs in widely separated cortical regions. In this paper we provide a possible mechanism to explain the phenomenon. When a common, random input is presented, we find that a group of neurones—of Stein's (integrate-and-fire) model type with or without reversal potentials—are capable of quickly synchronizing their firing. Interestingly the optimal average synchronization time occurs when the common input has a high coefficient of variation of interspike intervals (greater than 0.5) for this model with or without reversal potentials. The model with reversal potentials more quickly synchronizes than that without reversal potentials.

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### I. INTRODUCTION

How neurones couple with each other to fire *synchronously* is an important issue both theoretically and experimentally [1–5]. It has been widely accepted that information is encoded by neurones via a variety of schemes: from the classic view of rate coding to the modern view involving time coding [2]. A typical example of time coding is brain waves, oscillating at about 40 Hz for a group of neurones—the so-called gamma rhythms, which appear to be involved in higher mental activity and therefore are considered to be essential for processing information by the brain [4]. However, how neurones respond to external stimuli to organize locally or over a wider range to fire together remains elusive, with a few mechanisms, such as recurrent inhibition, mutual excitation, intrinsic oscillators, and mutual inhibition having been put forward.

For the purpose of elucidating mechanisms of oscillatory synchronisation, networks of integrate-and-fire units have been extensively studied in the literature [6–9]. We mention but a few studies. In Ref. [10] the authors proved the existence of the Lyapunov function for a specific case of interactions. In Ref. [11] two identical interacting neurones were investigated and it was found that whether two neurones fire synchronously or not depends on the rise time of the synapse *per se*; in particular, inhibitory rather than excitatory interactions facilitate the synchronization of neuronal activities.

These studies above are confined to the case of deterministic inputs, but there is a consensus that the inputs and outputs of single neurones are frequently stochastic. If low amplitude random noise is added to the system discussed in Ref. [11] then the coherent behavior simply disappears, as theoretically studied in Ref. [12]. Furthermore, and most importantly, experimental results [3] tell us that neurones in widely separated areas—which implies there is no local interaction among them—are capable of synchronizing with zero time lag. This possibly indicates that inputs play a vital role in the synchronization, at least for neurones in widely separated areas (see further discussion in Secs. VI and VII on local interactions and Ref. [13]). The purpose of the paper, as a first step towards carrying out a systematic study on possible mechanisms of synchronization with stochastic inputs, is to

reveal when and how efficiently common inputs ensure that neurones fire synchronously.

We first consider two identical neurones with different initial states and suppose that they are subjected to common, but stochastic, inputs propagating along excitatory and inhibitory synapses. The two neurones can be viewed as located either in separate areas (with no local interaction), or they receive inputs from many other neurones and therefore the contribution of each to the process of synchronization is much smaller than surrounding inputs, or that local interactions ensure common inputs. Under *different (independent)* stimuli the synchronization is not observable, but under the *same* stimuli the neuronal activities quickly cohere with each other. This suggests that probably one of the most important factors which synchronizes neuronal activities is their *common* inputs. Let us denote the time at which two neurones synchronize as the *synchronization time*. Interestingly, the shortest average synchronization time is attained when the coefficient of variation of interspike intervals [CV (ISI)] of individual neurones is greater than 0.5, i.e., inside a high CV (ISI) region. Although the different roles of noise accompanying the signals in the brain have been explored (see, for example, Ref. [14]), why the brain employs such a noisy signal for processing information remains unclear. Our theory here reveals one possible role of noise: to synchronize neuronal activities quickly. Although here we exclusively consider the case of inputs with zero rise time ( $\delta$ -pulse current input), we expect our conclusions can be generalized to a more realistic case with a nonzero rise time course (see Sec. VI). Further numerical examples and theoretical results on the synchronization of a large group of neurones are included and properties of synchronization time are discussed.

We want to compare our approach and results with those in the literature. Synchronization is obviously one of the most important phenomena observed in nature, but the model mimicking the phenomenon is usually hard to tackle theoretically. One of the most widely used techniques is to transform the variables of the model to phase variables, which provides a uniform and powerful way to deal with the problem [9,12,11]. This naturally requires that all units have a common period of oscillation, independent of each specific firing time as well. Here we consider a stochastic model (not as a small perturbation of a deterministic system), which simply implies that the method mentioned above is not ap-

plicable since we do not have a common period of oscillation [15]. Another powerful technique is to utilize the so-called firing mapping which connects the firing times of successive spikes [16,17]. Unfortunately, the first passage time of Stein's model is so complex that up to today no analytical formula is available in spite of many years research efforts [18]. Hence we are not able to apply these techniques to our problem. Our analytical analysis relies on the following features of the model. With probability one there is a sufficiently long interval over which neither neurone fires so that their membrane potentials have a chance to converge to each other within some  $\epsilon$  distance and the external input then pushes both neurones over the threshold.

On the other hand, here we consider Stein's model, which is derived from the study of neuronal behavior and stochastic inputs (see further discussion in Sec. VII on this issue). Its noise term is proportional to its deterministic inputs. To the best of our knowledge, all results in the literature on synchronization with the presence of noises are based on the assumption of weak noise, i.e., a perturbation of deterministic system [14].

## II. MODELS

We consider a group of leaky integrate-and-fire neurones, with or without reversal potentials, subjected to inputs which are conventionally assumed to be Poisson processes. For  $i = 1, 2, \dots, m$  let  $N_i^E(t)$  and  $N_i^I(t)$  be total excitatory and inhibitory inputs of the  $i$ th neurones with rate  $N_E\lambda_E$  and  $N_I\lambda_I$ , where  $N_E(N_I)$  is the number of total active excitatory (inhibitory) synapses and  $\lambda_E(\lambda_I)$  is the firing rate of excitatory postsynaptic potentials (EPSP's) [inhibitory postsynaptic potentials (IPSP's)] of each excitatory (inhibitory) synapses. Suppose that  $x_i(t)$  is the membrane potential of the  $i$ th neurone at time  $t$ , then  $x_i(t)$  is governed by the following dynamics with initial state  $x_i$ ,

$$\begin{aligned} dx_i(t) &= -\frac{1}{\gamma}x_i(t)dt + a dN_i^E(t) - b dN_i^I(t), \\ x_i(0) &= x_i, \end{aligned} \quad (2.1)$$

where  $1/\gamma$  is the decay rate,  $a > 0$  and  $b > 0$  are the magnitude of each excitatory and inhibitory input. As soon as  $x_i(t)$  reaches a prefixed value  $V_{thre}$ , the threshold,  $x_i(t)$  is reset to  $V_{rest}$ , the resting potential. The model defined by Eq. (2.1) is usually called Stein's model and it has been intensively studied for exploring properties of real neurones.

There is, however, a *severe* flaw for the model defined by Eq. (2.1). We know that the voltage of single neurone is bounded from below, about 10 mV below the resting potential, but  $x_i(t)$  visits any negative value with a positive probability. There are several ways to prevent this from happening. One way is to impose a lower boundary condition for  $x_i(t)$  and thus obtain a different process as considered in Ref. [19]. Obviously this process and  $x_i(t)$  are different; nevertheless, from numerical results the behavior of these two models are very close (not shown). The other more biologically realistic modification is to include reversal potentials in Stein's model [15]:

$$\begin{aligned} dz_i(t) &= -\frac{(z_i(t) - V_{re})}{\gamma} dt + \bar{a}(V_E - z_i(t)) dN_i^E(t) \\ &\quad + \bar{b}(V_I - z_i(t)) dN_i^I(t), \\ z_i(0) &= z_i, \end{aligned} \quad (2.2)$$

$z_i(t), i = 1, 2, \dots, m$  are now birth-and-death processes with boundaries  $V_E$  and  $V_I$  [20]. Once  $z_i(t)$  is below  $V_{re}$ , the resting potential, the decay term  $z_i(t) - V_{re}$  will push the membrane potential  $z_i(t)$  up; whereas when  $z_i(t)$  is above  $V_{re}$  the decay term will hyperpolarize it. When  $z_i(t)$  hits the threshold its value is reset to  $V_{re}$ .

We first consider Stein's model and then move to the model with reversal potentials. For the convenience of discussion we have fixed a few parameters in our numerical simulations  $N_E = 100$  (see Ref. [19] for a discussion on this choice),  $\lambda_E = \lambda_I = 100$  Hz and  $\gamma = 20.2 \pm 14.6$  msec [21]. We have used the same set of parameters elsewhere [22–24,18,25]. Note that the intensity of incoming signals is  $10\,000$  Hz =  $N_E\lambda_E$  which is also equivalent to  $N_E = 300$ ,  $\lambda_E \sim 33$  Hz.

For a given neurone  $i$  let us denote  $T_n^{(i)}$  as the occurrence time of the  $n$ th spike. For two neurones  $i, j$  the time

$$\begin{aligned} T(i, j) &= \inf\{T_n^{(i)} : T_{n+p}^{(i)} = T_{k+p}^{(j)}, n, k = 1, 2, \dots, p \\ &= 0, 1, 2, \dots, \} \end{aligned}$$

is their synchronization time.

## III. EXAMPLE

We begin by giving an exact definition of a common input. A *common input* implies that all  $N_i^E(t) = N_1^E(t)$ ,  $N_i^I(t) = N_1^I(t), i = 1, \dots, m$ , i.e., the correlation between the input signals is one. Without the presentation of a common input the system defined by either Eq. (2.1) or Eq. (2.2) is run under the assumption that  $N_i^E(t), i = 1, \dots, m$ ,  $N_i^I(t), i = 1, \dots, m$  are i.i.d. inputs, i.e., inputs with zero correlation.

Before we analyze the detailed behavior of synchronization of neurones here we first present a numerical example in Fig. 1 to show that, when a common input is presented, how quickly neurones group themselves to fire together.

For 100 Stein neurones defined by Eq. (2.1), we use the following parameters in simulations shown in Fig. 1:  $N_E = 100$ ,  $N_I = 80$ ,  $a = b = 0.5$  mV,  $V_{thre} = 20$  mV,  $V_{rest} = 0$  mV,  $\lambda_E = \lambda_I = 100$  Hz,  $\gamma = 20.2$  msec [18]. In Fig. 1(a) a common input is turned on at time = 1000 msec (turned off at time = 1500 msec) and 2000 msec (turned off at 2300 msec). It is easily seen that the group of neurones synchronize after a few (one to two) spikes, although the number of neurones we consider here is large. In Fig. 1(b) 90% of both excitatory and inhibitory inputs are common and 10% are i.i.d. This is, of course, a more natural scenario in biological systems. As one can expect, the system will not fully synchronize as in the case of 100% common inputs. But it can be easily seen that synchronization is still quite good and quick.

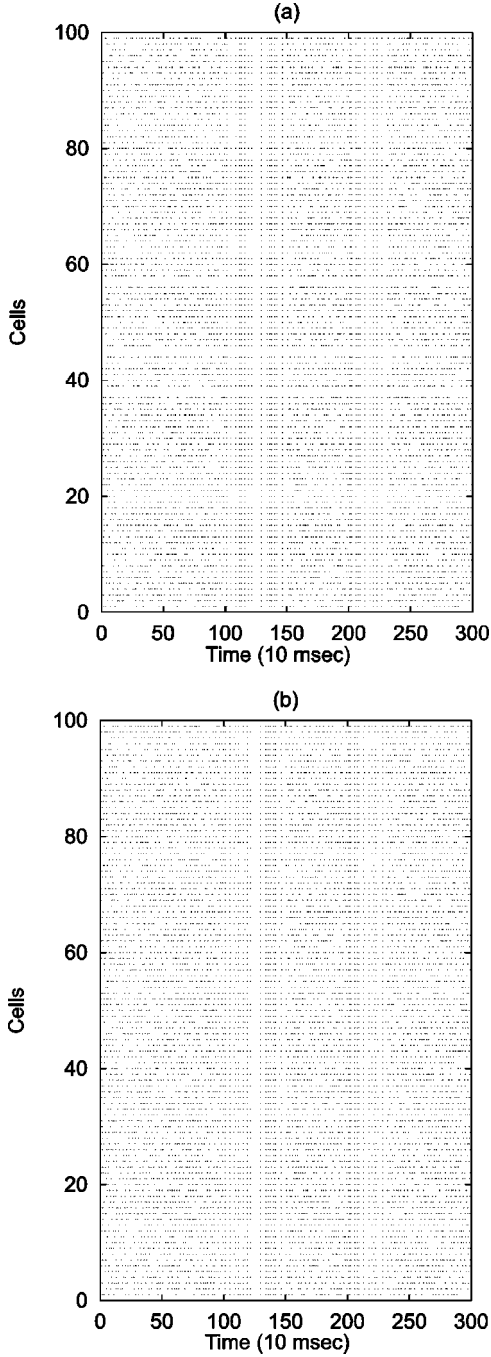


FIG. 1. One hundred Stein neurones easily synchronize when a common stimulus is turned on (see text for further explanation and parameters used in simulations). (a) All inputs are common. (b) 90% inputs are common and 10% are i.i.d.

#### IV. TWO NEURONES

##### A. Stein's model

It is well known that the following stochastic differential equation is a good approximation (the so-called usual approximation) of the dynamics defined by Eq. (2.1):

$$dx_i(t) = -\frac{1}{\gamma}x_i(t)dt + \mu dt + \sigma dB_i(t),$$

$$x_i(0) = x_i, \quad (4.1)$$

where  $B_i$  is the standard Brownian motion and

$$\begin{cases} \mu = aN_E\lambda_E - bN_I\lambda_I \\ \sigma = \sqrt{a^2N_E\lambda_E + b^2N_I\lambda_I} \end{cases} \quad (4.2)$$

Analytically, the stochastic differential equation defined by Eq. (4.1) is easier to tackle than the jump process defined by Eq. (2.1). We will restrict ourselves to Eq. (4.1) in the following theoretical discussion, but use solely Eq. (2.1) in numerical simulations.

Before going on to analyze properties of the system defined by Eq. (4.2), let us say a few words on the example of the previous section. With the parameters given in the previous section, a fully coherent excitatory input causes a voltage increase of  $100 \times 0.5 = 50$  mV. Hence one might conclude that the phenomena observed in Sec. III are rather trivial since a coherent excitatory input will push all cells to fire synchronously. However, Eq. (4.2) tells us that this is definitely not the case. Within a time step  $h > 0$ , the deterministic input to a cell is given by  $\mu = a(N_E\lambda_E - N_I\lambda_I) = 0.5(100 \times 100/1000 - 80 \times 100/1000) = 1$  mV, which is far below any reasonable membrane threshold. Then a natural question is that why all cells so quickly synchronize their firing. Our following theoretical developments partly answer the question.

Let  $T_1^{(1)}, T_2^{(1)}, \dots$  be the firing times of the first neurone and  $T_1^{(2)}, T_2^{(2)}, \dots$  of the second neurone. Without loss of generality we suppose that  $x_1 > x_2 = V_{rest}$  and so

$$T_1^{(1)} < T_1^{(2)} < T_2^{(1)} < T_2^{(2)} < \dots$$

Note that in the definition above, the stopping time  $T_1^{(1)}$  depends on the initial value  $x_1$ . Define

$$y(t) = |x_2(t) - x_1(t)|,$$

we have the following sequence of identities:

$$y(T_1^{(1)}) = y(0) \exp\left(-\frac{T_1^{(1)}}{\gamma}\right), \quad (4.3)$$

$$y(T_1^{(2)}) = \left[V_{thre} - y(0) \exp\left(-\frac{T_1^{(1)}}{\gamma}\right)\right] \exp\left(-\frac{T_1^{(2)} - T_1^{(1)}}{\gamma}\right) \quad (4.4)$$

$$= [V_{thre} - y(T_1^{(1)})] \exp\left(-\frac{T_1^{(2)} - T_1^{(1)}}{\gamma}\right) \quad (4.5)$$

$$\dots, \quad (4.6)$$

$$y(T_n^{(1)}) = [V_{thre} - y(T_{n-1}^{(2)})] \exp\left(-\frac{T_n^{(1)} - T_{n-1}^{(2)}}{\gamma}\right), \quad (4.7)$$

$$y(T_n^{(2)}) = [V_{thre} - y(T_n^{(1)})] \exp\left(-\frac{T_n^{(2)} - T_n^{(1)}}{\gamma}\right) \quad (4.8)$$

since

$$x_i(t) = \exp\left(-\frac{t-T_i^{(m)}}{\gamma}\right)x(T_i^{(m)}) + \mu \int_{T_i^{(m)}}^t \exp\left(-\frac{t-s}{\gamma}\right) ds + \sigma \int_{T_i^{(m)}}^t \exp\left(-\frac{t-s}{\gamma}\right) dB_i(s) \tag{4.9}$$

for  $T_i^{(m)} \leq t \leq T_i^{(m+1)}$ . Therefore the synchronization time  $T(1,2)$  is given by

$$T(1,2) = \inf\{T_n^{(1)}, x_1(T_n^{(1)}) > y(T_n^{(1)}) + V_{thre}\} \wedge \inf\{T_n^{(2)}, x_2(T_n^{(2)}) > y(T_n^{(2)}) + V_{thre}\}. \tag{4.10}$$

The sequence  $y(T_n^{(1)}), y(T_n^{(2)})$  gives us information about the position of one neurone when the other neurone hits the threshold. For example when  $t = T_1^{(1)}$  we see that due to the leakage the difference of the membrane potential between two cells reduces from  $x_1$  to  $x_1 \exp(-T_1^{(1)}/\gamma)$ . Nevertheless at  $t = T_1^{(1)} +$  the difference between these two cells are enlarged provided that  $x_2(T_1^{(1)}) > V_{thre}/2$ . Then starting from  $y(T_1^{(1)} +)$  the difference between them is reduced again. When the sequence of firing times is deterministic the sequence  $y$  defined above gives arise to a mapping on a circle (after normalization) and is well studied in the literature [16]. A variety of different behaviors including chaotic behaviors have been reported. However, in our case we can prove the following theorem.

Suppose that the probability space we consider is  $(\Omega, \mathcal{F}, P)$ . For  $t \in \mathbb{R}^1$  it is reasonable to assume that  $P_x(T_1^{(1)} \geq t) > 0$ , the probability of the event  $\{T_1^{(1)} \geq t\}$  with  $x_1(0) = x$ , is a continuous function of  $x \in (V_{rest}, V_{thre})$  although an analytical formula is not available.

*Theorem 1. Within a finite time two Stein neurones synchronize their firing with probability 1.*

*Proof:* For any subset  $[a, b] \subset [V_{rest}, V_{thre}]$  with  $a > V_{rest}, b < V_{thre}$ , positive number  $\epsilon > 0$ , denote  $\bar{p} = \inf_{x \in [a, b]} P_x(T_1^{(1)} > A) > 0$  where

$$A = -\gamma \ln \frac{\epsilon}{V_{thre}}.$$

This implies that when  $x_1(t)$  hits the threshold at time  $T_1^{(1)} > A, x_2(t)$  is close to the threshold as well, within a distance  $\epsilon$ . Define a set

$$G_n = \{T_n^{(1)} - T_{n-1}^{(2)} > A\}.$$

Discretizing Eq. (4.1) with a time step  $h > 0$ , let

$$\bar{B}_n = B_1(T_n^{(1)} - T_{n-1}^{(2)}) - B_1(T_n^{(1)} - T_{n-1}^{(2)} - h)$$

and

$$F_n = \{\bar{B}_n > (-\mu h + \epsilon)/\sigma\}, \quad \underline{p} = P(F_n) > 0.$$

Note that  $\underline{p}$  is independent of  $n$ . Then we have

$F_n \cap G_n \subset \{x_1(t) \text{ and } x_2(t) \text{ synchronize at time } T_n^{(1)} \text{ no matter where } x_1(T_{n-1}^{(2)}) \text{ is}\}.$

Denote

$$E_n = \{\omega \in \Omega, \omega \in F_n \cap G_n \text{ but } \omega \notin \cup_{i=1}^{n-1} E_i\},$$

we see that

$$\cup_{n=1}^{\infty} E_n \subset \{x_1(t) \text{ and } x_2(t) \text{ synchronize at finite time}\}.$$

Since  $T_i^{(1)}, T_i^{(2)}$  are two renewal processes we thus conclude that

$$P(\cup_{n=1}^{\infty} E_n) = \sum_{n=1}^{\infty} \underline{p} \bar{p}^{n-1} = 1. \tag{4.11}$$

Equation (4.11) together with the arbitrary choice of  $[a, b], h, \epsilon$  imply our desired conclusion.

The following consideration illustrates the idea behind the above proof. Starting from an arbitrary state  $y(0)$  we see that two cells will gradually forget their initial difference, i.e., the term  $y(T_n^{(1)})$  will vanish when  $T_n^{(1)}$  is large. The larger the decay rate  $1/\gamma$  the quicker the system forgets its initial difference. Once the potential of one neurone is near the threshold and an incoming EPSP pushes the membrane potential across it, if  $T_n^{(1)} - T_{n-1}^{(2)}$  is large enough the membrane potential of another neurone will be near the threshold as well and an impulse will easily ensure it to hit the threshold. Therefore decay and pulse inputs are two vital important factors for the model to show coherent behavior.

The theorem above tells us that two neurones will synchronize but it does not tell us how quickly they will do so. Unfortunately, to find an analytical formula for  $T(1,2)$  is a formidable task and we do not even have an exact expression for  $T_n^{(1)}$  except for one special case. For the *perfect* integrate-and-fire model ( $\gamma = \infty$ ) an analytical expression for  $T_n^{(1)}$  is available; however, for reasons discussed above we expect that it is much more difficult for perfect integrate-and-fire units to synchronize.

Define a sequence of random sets  $A_n, D_n$  as

$$A_1 = \{\omega: x_1(T_1^{(1)}) > y(T_1^{(1)}) + V_{thre}\},$$

$$D_1 = \{\omega: x_1(T_1^{(2)}) > y(T_1^{(2)}) + V_{thre}, \omega \notin A_1\}, \tag{4.12}$$

$$A_n = \{\omega: x_1(T_1^{(n)}) > y(T_1^{(n)}) + V_{thre}, \omega \notin (\cup_{i=1}^{n-1} A_i) \cup (\cup_{i=1}^{n-1} D_i)\},$$

$$D_n = \{\omega: x_1(T_1^{(n)}) > y(T_1^{(n)}) + V_{thre}, \omega \notin (\cup_{i=1}^{n-1} A_i) \cup (\cup_{i=1}^{n-1} D_i)\}$$

then we have the following decomposition:

$$T(1,2) = \sum_{i=1}^{\infty} [T_i^{(1)} I_{A_i} + T_i^{(2)} I_{D_i}], \tag{4.13}$$

where  $I$  is the indicator function of a set. Define another quantity

$$S = \sum_{i=1}^{\infty} iI_{A_i}; \quad (4.14)$$

the expectation of  $S$  gives the average number of spikes of the first neurone needed for the two neurones to synchronize, called the average synchronization spike number. Since the output of Stein's model is a renewal process we know the property of  $T_i^{(1)}$  if the corresponding property of  $T_1^{(1)}$  is available.

Note that  $x_1(T_n^{(1)}) = V_{thre}$  when  $x_i$  is defined by a stochastic differential equation which implies in theory that  $A_i, i \geq 1$  given by Eq. (4.12) are all empty. Of course if  $x_i$  is a jump process as we discussed before this case will not happen, both in theory and in numerical simulations. In actual numerical simulation of the usual approximation of Stein's model, this is certainly not the case [26]. For any given  $\epsilon > 0$ , a small positive number which can be neglected in numerical simulations, we have

$$A_1 = \{\omega, y(T_1^{(1)}) < \epsilon\} \quad (4.15)$$

or equivalently

$$A_1 = \left\{ \omega, T_1^{(1)} > -\gamma \ln \frac{\epsilon}{y(0)} \right\}. \quad (4.16)$$

Similarly, we obtain

$$A_n = \left\{ \omega, T_n^{(1)} > -\gamma \ln \frac{\epsilon}{V_{thre} - y(T_{n-1}^{(2)})} + T_{n-1}^{(2)}, \right. \\ \left. T_i^{(1)} < -\gamma \ln \frac{\epsilon}{V_{thre} - y(T_i^{(2)})} + T_i^{(2)}, \quad (4.17) \right.$$

$$\left. T_i^{(2)} < -\gamma \ln \frac{\epsilon}{V_{thre} - y(T_i^{(1)})} + T_i^{(1)}, i = 1, \dots, n-1 \right\}.$$

Hence, in principle, if we know the probability distribution of  $T_1^{(1)}$  we can calculate the synchronization time  $T(1,2)$ .

We have reported in early papers [18,25] that the CV of efferent spikes of the model is an increasing function of the ratio  $r = N_I/N_E$ . With a given  $N_E$  the larger the ratio, the more the randomness of the output spikes and the less deterministic inputs which is given by  $\mu = aN_E\lambda_E - aN_I\lambda_I$ . We see from Fig. 2 that the average synchronization time is not a monotone function of the ratio, while the average synchronization spike number is. The better the balance between the inhibitory and excitatory inputs, the fewer the spikes needed by the neurones to synchronize. For example when  $r > 0.5$  and  $\gamma = 5.6$  msec two neurones fire together from the first spike.

Interestingly, the optimal average synchronization time of two neurones is about at (see Table I)  $r = r_0$  satisfying  $CV(r_0) \geq 0.5$ . It has been reported experimentally that the CV of neurones in visual cortex is above 0.5. This implies

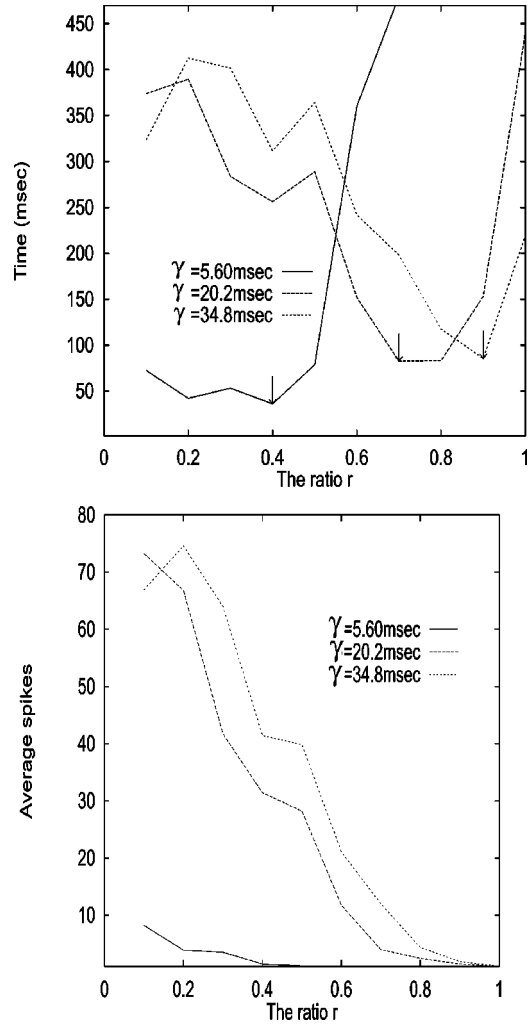


FIG. 2. Average synchronization time and spike of two Stein's neurones with different initial states. The average synchronization time and spike number are obtained for  $x_2(0) = 1, 2, \dots, 19$  and  $x_1(0) = V_{rest}$ . Arrows in figure indicate the optimal average synchronization time. Note that the y axis starts at 1 in the figures.

that the optimal average synchronization time is attained when the output of a neurone is inside the region with high CV.

### B. Stein's model with reversal potentials

As we have reported in our early paper, one essential difference between the model with or without reversal potentials is that the former one has a high CV even when  $r$  is small. Again in numerical simulations we employ the set of parameters in the literature [27] with  $V_E = 50$  mV,  $V_I = -60$  mV,  $V_{th} = -30$  mV,  $V_{re} = -50$  mV.

TABLE I. Optimal average synchronization time and CV of Stein's model.

$\gamma$ (msec)	ST (msec)	CV
5.60	36.0	0.58
20.2	82.6	0.46
34.8	85.4	0.74

Consider two neurones with identical inputs of Stein's model with reversal potentials:

$$\begin{aligned} dz_1(t) &= -[z_1(t) - V_{re}]/\gamma dt + \bar{a}[V_E - z_1(t)]dN_1^E(t) \\ &\quad + \bar{b}[V_I - z_1(t)]dN_1^I(t), \\ z_1(0) &= z_1, \end{aligned} \quad (4.18)$$

and

$$\begin{aligned} dz_2(t) &= -[z_2(t) - V_{re}]/\gamma dt + \bar{a}[V_E - z_2(t)]dN_2^E(t) \\ &\quad + \bar{b}[V_I - z_2(t)]dN_2^I(t), \\ z_2(0) &= z_2. \end{aligned} \quad (4.19)$$

In the following consideration we require  $\bar{a}$  and  $\bar{b}$  satisfying a local balance condition [27]:

$$\bar{a}(V_E - V_{re}) = \bar{b}(V_I - V_{re}).$$

As in the previous subsection let us define  $T_1^{(1)}, T_2^{(1)}, \dots$  as the firing time of the first neurone and  $T_1^{(2)}, T_2^{(2)}, \dots$  of the second neurone. Without loss of generality we suppose that  $x_1 > x_2 = V_{re}$  and so

$$T_1^{(1)} < T_1^{(2)} < T_2^{(1)} < T_2^{(2)} < \dots$$

Denote  $y(t) = |z_1(t) - z_2(t)|$  satisfying (under the condition that a common input is presented)

$$dy(t) = -y(t)/\gamma dt - \bar{a}y(t)dN_1^E(t) - \bar{b}y(t)dN_1^I(t)$$

or equivalently

$$y(t) = y(0)\exp[-t/\gamma - \bar{a}N_1^E(t) - \bar{b}N_1^I(t)] \quad (4.20)$$

with  $\bar{a} > 0$ ,  $\bar{b} > 0$  and  $t < T_1^{(1)}$ . We note the difference of the term  $y(t)$  given by Eqs. (4.3) and Eq. (4.20). With given initial states  $y(0), y(t)$  defined by Eq. (4.3) is smaller than that of Eq. (4.20) since the term  $\bar{a}N_1^E(t) + \bar{b}N_1^I(t) > 0$ . In other words, Stein's model *with reversal potentials* tends to forget the initial state more quickly than Stein's model *without reversal potentials*, which, as we already elucidated in the previous subsection, certainly reduces the synchronization time. On the other hand, when  $z_1(t)$  is near  $V_{th}$  the variation of Stein's model with reversal potentials is

$$\bar{a}^2(V_E - V_{th})^2 N_E \lambda_E + \bar{b}^2(V_I - V_{th})^2 N_I \lambda_I$$

which is greater than the variation of Stein's model without reversal potentials given by (independent of the threshold)

$$a^2 N_E \lambda_E + b^2 N_I \lambda_I.$$

Due to the above reasons we conclude that Stein's model with reversal potentials will more easily synchronize than Stein's model, as confirmed in the following numerical simulations.

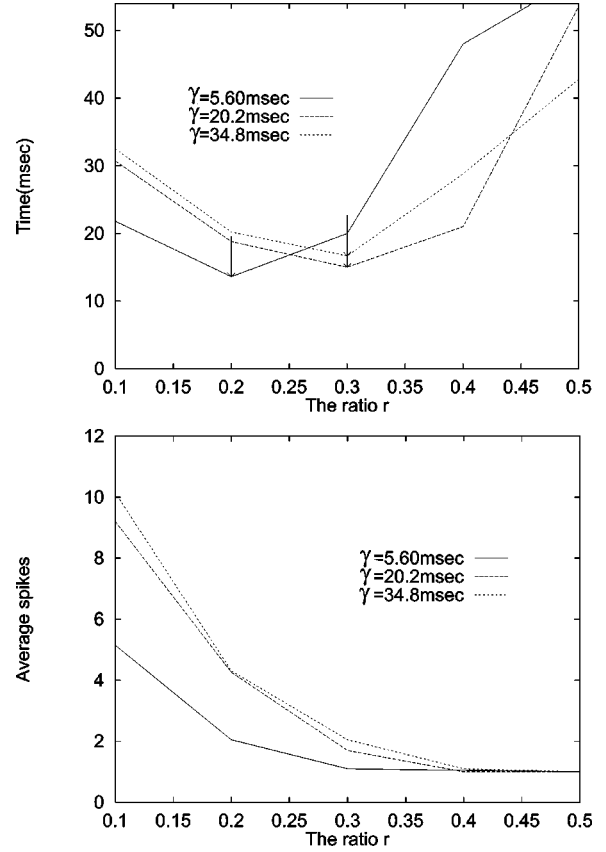


FIG. 3. Average synchronization time and spikes of two Stein's model with reversal potentials (comparing Fig. 2). The average synchronization time and spike are obtained for  $x_2(0) = 1, 2, \dots, 19$  and  $x_1(0) = V_{re}$ . Arrows in the figure indicate the optimal synchronization time.

By applying similar arguments as in the previous subsection we can prove

*Theorem 2. With probability 1 two Stein's cells with reversal potentials synchronize their firing within a finite time.*

From numerical results we observe similar behavior as for Stein's model (see Fig. 3). The average (synchronization) spike is a decreasing function of the ratio. When  $r \geq 0.4$  the average spike is one. Again we want to emphasize that the optimal synchronization time occurs at a point at which its CV is greater than 0.5, as summarized in Table II.

## V. A GROUP OF NEURONES

We numerically simulate a group of neurones with randomly generated initial states inside  $[V_{rest}, V_{thre}]$  for Stein's

TABLE II. Optimal average synchronization time and CV of Stein's model with reversal potentials.

$\gamma$ (msec)	ST (msec)	CV
5.60	13.6	0.61
20.2	15.0	0.63
34.8	16.7	0.62

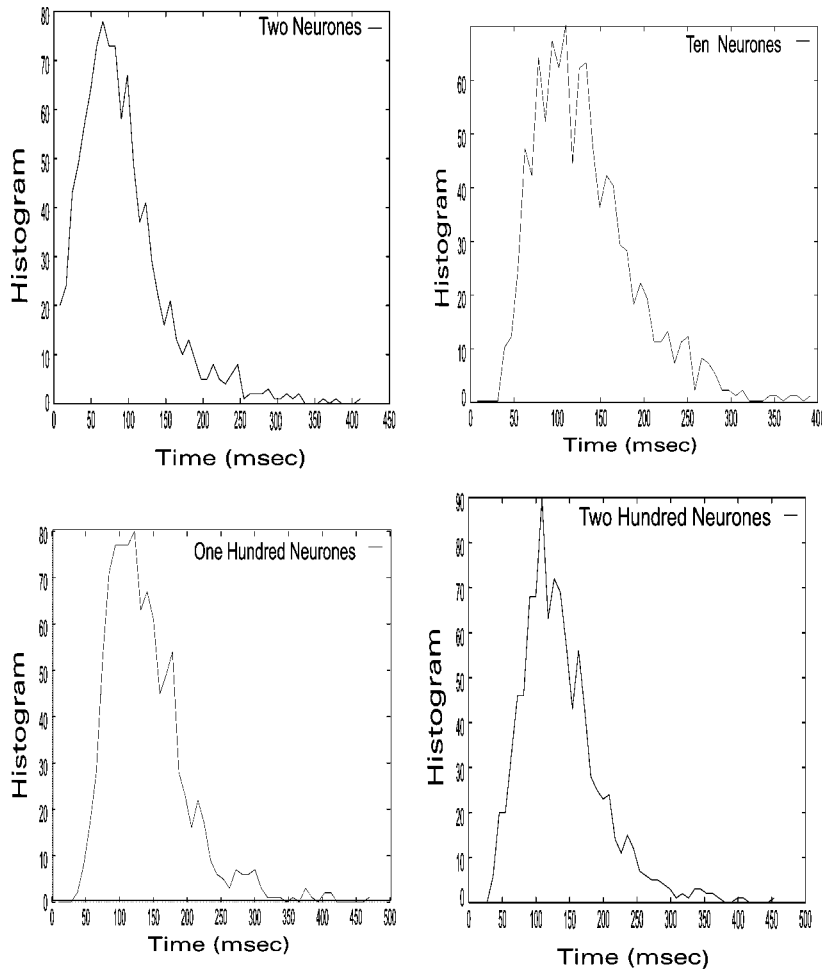


FIG. 4. Histograms of  $T(2), T(10), T(100), T(200)$  vs time in the unit of msec.

model. Denote  $T(m)$  as the time when all  $m$  neurones synchronize i.e.,

$$T(m) = \max\{T(1,i), i = 1, \dots, m\}.$$

In fact, we have

*Theorem 3.* For a group of Stein’s models with or without reversal potentials,

$$P[T(m) < \infty] = 1.$$

The proof of the theorem is similar to that for two cells and so we omit it.

A numerical study of  $T(m)$  will give us informative results on how neurones fire synchronously. Let us consider the dependence of the distribution of  $T(m)$  on  $m$ . We carry out a systematic numerical simulations (see Fig. 4) for the case of  $m = 2, 10, 100, 200$  under the condition that  $\gamma = 20.2$  msec,  $r = 0.8$  which roughly corresponds to the optimal synchronization time in Fig. 2.

When  $m = 2$  we see the possibility of instantaneous syn-

chronization of the two neurones. The left side of the histogram is close to zero. When  $m \geq 10$  the distribution of  $T(m)$  is stabilized. There is a time lag for neurones to synchronize and the peak of the distribution is around 100 msec, i.e., the most likely case is that they ( $m \geq 10$ ) synchronize after about 100 msec (see Fig. 4). Note that here we require all neurones to *exactly* synchronize. In Fig. 1 we have numerically shown that as soon as a common input is presented, all neurones tend to fire together instantaneously.

### VI. WITH LOCAL INTERACTIONS

Our results in the previous sections tell us that a common input can group neurones to fire together in a short time and provide us a mechanism to explain oscillatory synchronization in separated areas in the cortex. It is obvious that neurones are intensively connected via excitatory and inhibitory interactions. What is the implication of our results for locally interacting neurones?

For  $i = 1, \dots, m$ , consider the following models:

$$\begin{aligned} dx_i(t) &= -\frac{1}{\gamma}x_i(t)dt + adN_i^E(t) - bdN_i^I(t) + f_i(x_1, x_2, \dots, x_m; t), \\ x_i(0) &= x_i, \end{aligned} \tag{6.21}$$

where  $f_i$  is a function of  $x_1, x_2, \dots, x_m, t$ . For example, we can take  $f_i(x_1, x_2, \dots, x_m, t) = \sum_j \sum_n w_{ij} \alpha(t, T_n^{(j)}, \Delta_{ij})$  where  $\alpha$  is the  $\alpha$  function and  $\Delta_{ij}$  is the delay of the spike transmission between the  $i$ th and  $j$ th cell. Assume further that  $f_i$  is independent of  $i$ . This is approximately true, for example if we assume that  $T_n^{(j)}, \Delta_{ij}$  are i.i.d. random sequences and  $w_{ij} = w_{|i-j|}$  (the central limit theorem). Then our theorem in the previous section is still true, i.e., neurones will synchronize within a finite time with probability one. Here the synchronization time depends on the choice of  $f$ . It is obviously interesting to find under which conditions on  $f$  synchronization is sped up or slowed down. We explore this in a further paper.

## VII. DISCUSSION

We proved theoretically that Stein's model with or without reversal potentials is capable of synchronizing within a finite time and numerically that the time for them to synchronize is almost instantaneous. Our results might provide a possible mechanism for the phenomena of stimulus-evoked oscillatory synchronization in widely separate cortex areas which has been observed in experiments [13]. On the other hand, our results also lay a foundation for further investigation, in particular on the role of local interactions as we have discussed in the previous section.

According to our results presented here we also want to point out another possible role played by *local connections*, except for its role of speeding up or slowing down the synchronization time: the brain is wired in such a way as to adjust the input of synchronized neurones so that they receive common inputs. Furthermore, it will be interesting to see how the mechanism found here works for more biophysically realistic models like FitzHugh-Nagumo and Hodgkin-Huxley models.

Let us have a comparison between the phenomena of stochastic resonance and the one we observed here, i.e., the optimal synchronization time is obtained at a value at which

the output CV is between 0.5 and 1. For a given stochastic dynamic system with a parameter which is a measurement of the noise in the system, the output signal is optimized at a value of the parameter. This phenomena is called the stochastic resonance. Hence the observed phenomena in this paper can be viewed as a kind of stochastic resonance if the mean synchronization time is thought of as an output and the ratio  $r$  as a measurement of the noise in the system. Although the stochastic resonance has been widely studied in the literature, a convinced biological system which employs it has not yet been found. Our results provide such an example of system which naturally exhibits the stochastic resonance.

Finally, we discuss the implication of random inputs, i.e., Poisson process inputs, in our model. This is a puzzling issue and a solid answer can be provided only in terms of experiments. In Ref. [28] the authors pointed out that "reliability of spike timing depended on stimulus transients. Flat stimuli led to imprecise spike trains, whereas stimuli with transients resembling synaptic activity produced spike trains with timing reproducible to less than one millisecond." However, we must emphasize here that their experiments are carried out in neocortical *slices*. It is interesting to see that the variability of spike trains depend on the nature of inputs, but *in vivo* recording tells us that CV of efferent spikes trains might be very different. For example, it is reported that CV is between 0.5 and 1 for visual cortex (V1) and extrastriate cortex (MT) [29]; even in the human motor cells their CV is between 0.1 and 0.25 (Ref. [30], p. 597). We have concrete examples to show that a group of cells *in vivo* behave totally different from in slices. Oxytocin cells burst synchronously *in vivo*, but this property is totally lost in slice (see Ref. [31] and references therein). Most recently it is reported that random rather than deterministic inputs play an important role in motor planning [32].

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