

Stimulus-evoked Synchronization in Neuronal Models

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Abstract

It is known that stimulus-evoked synchronization among neurons occurs in widely separated cortical regions. In this paper we test that how common, *random but not deterministic* inputs can synchronize groups of neurons with their parameters inside physiologically plausible regions. When a common, random input is presented, we find that a group of neurons—of integrate-and-fire or Hodgkin-Huxley models—are capable of rapidly synchronizing their firing. Interestingly the optimal average synchronization time occurs when the efferent spikes have a high coefficient of variation (CV) of interspike intervals (greater than 0.5), or equivalently, when neurons receive balanced inputs.

Introduction How do neurons couple with each other to fire *synchronously* is an important issue both theoretically and experimentally [6, 7, 14, 15, 17, 19]. It has been widely accepted that information is encoded by neurons via a variety of schemes: from the classical view of rate coding to the modern view involving time coding [7]. A typical example of time coding is brain waves, oscillating at about 40 Hz for a group of neurons—the so called gamma

rhythm, which appear to be involved in higher mental activity and therefore are considered to be essential for processing information by the brain [17]. However how neurons 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 synchronization, networks of model neurons have been extensively studied in the literature. We mention but a few studies. In [8] the authors proved the existence of the Lyapunov function for a specific case of interactions. In [23] two identical interacting neurons were investigated and it was found that whether two neurons 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 neuron are frequently stochastic. If a low amplitude random noise is added to the system discussed in [23] then the coherent behaviour simply disappears, as theoretically studied in [12] (see Fig. 5 below). Furthermore and most importantly, experimental results [15] tell us that neurons 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 neurons in widely separated areas (see further discussion below on local interactions and [18]). The purpose of the paper is to reveal when and how efficiently common inputs ensure neurons

to fire synchronously.

We first consider two identical neurons with different initial states but subjected to common, stochastic inputs propagating along excitatory and inhibitory synapses. The two neurons can be viewed as located either in separate areas (with no local interaction), or they receive inputs from many other neurons and therefore the contribution of each to the process of synchronization is much smaller than surrounding inputs, or that local interactions ensure them to receive common inputs. Under *different (independent)* stimuli the synchronization is not observable, but under *same* stimuli the neuronal activities quickly cohere with each other. This suggests that one of the most important factors which synchronizes neuronal activities is their *common* inputs. Let us call the time at which two neurons synchronize the *synchronization time*. Interestingly the shortest synchronization time averaging over different initial states is attained when the CV of efferent spike trains of individual neurons is greater than 0.5, i.e. inside a high CV region. Our results further reveal one of the functional roles of balanced inputs which are automatically maintained with the spike-timing-dependent synaptic plasticity rule[22]. Further numerical examples and theoretical results on the synchronization of a large group of neurons are also included and properties of synchronization time are discussed. Finally we also show that spiking reliability observed in [13] is simply a consequence of stochastic inputs.

The Models We consider a group of leaky integrate-and-fire neurons, 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 neurons with rate $N_E \times$

λ_E and $N_I \times \lambda_I$, where $N_E(N_I)$ is the number of total active excitatory (inhibitory) synapses and λ_E (λ_I) is the firing rate of EPSPs (IPSPs) of each excitatory (inhibitory) synapse. Suppose that $x_i(t)$ is the membrane potential of the i -th neuron at time t then $x_i(t)$ are governed by the following dynamics with initial state x_i

$$dx_i(t) = -\frac{1}{\gamma}(x_i(t) - V_{rest})dt + I_{syn,i}(t) \quad (1)$$

where synaptic inputs $I_{syn,i}(t) = aN_i^E(t) - bN_i^I(t)$, $1/\gamma$ 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. (1) is usually called the integrate-and-fire (IF) model and it has been intensively studied for exploring properties of biological neurons.

The classical Hodgkin-Huxley (HH) model is also taken into account, denoting $V_i(t)$ as the membrane potential of i th cell at time t . We refer the reader to [1] for details of all parameters and notation. Synaptic inputs $I_{syn,i}(t)$ are defined as above.

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

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

is their synchronization time.

For the convenience of discussion we have fixed a few parameters in our numerical simulations $N_E = 100$ (see [20] for a discussion on this choice),

$\lambda_E = \lambda_I = 100Hz$ and $\gamma = 20.2 \pm 14.6msec$ [1, 3, 4]. We have used the same set of parameters elsewhere [1, 2, 3, 4]. Note that the intensity of incoming signals is $10,000Hz = N_E \times \lambda_E$ which is also equivalent to $N_E = 300, \lambda_E \sim 33Hz$. We use step size of 0.01 msec in the simulations of the IF model (Euler scheme), and the Runge-Kutta method with variable step size in the HH model.

Examples 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 eq. (1) is run under the assumption that $N_i^E(t), i = 1, \dots, m$ ($N_i^I(t), i = 1, \dots, m$) are independently and identically distributed (i.i.d.), i.e. inputs with zero correlation.

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

For one hundred IF neurons defined by eq. (1), we use the following parameters in simulations shown in Fig. 1: $N_I = 80$ (see Fig. 3 below), $a = b = 0.5mV, V_{thre} = 20mV, V_{rest} = 0mV, \gamma = 20.2msec$ [3]. In fig. 1 (Left) a common input is turned on at time=500 msec (turned off at time=700msec) and 1500 msec (turned off at 1800msec), namely the synaptic input of the i th neuron now takes the form

$$\begin{aligned} & [\delta(aN_1^E(t) - bN_1^I(t)) + (1 - \delta)(aN_i^E(t) - bN_i^I(t))]I_{\{t \in \mathcal{T}\}} \\ & + [aN_i^E(t) - bN_i^I(t)]I_{\{t \notin \mathcal{T}\}} \end{aligned} \quad (2)$$

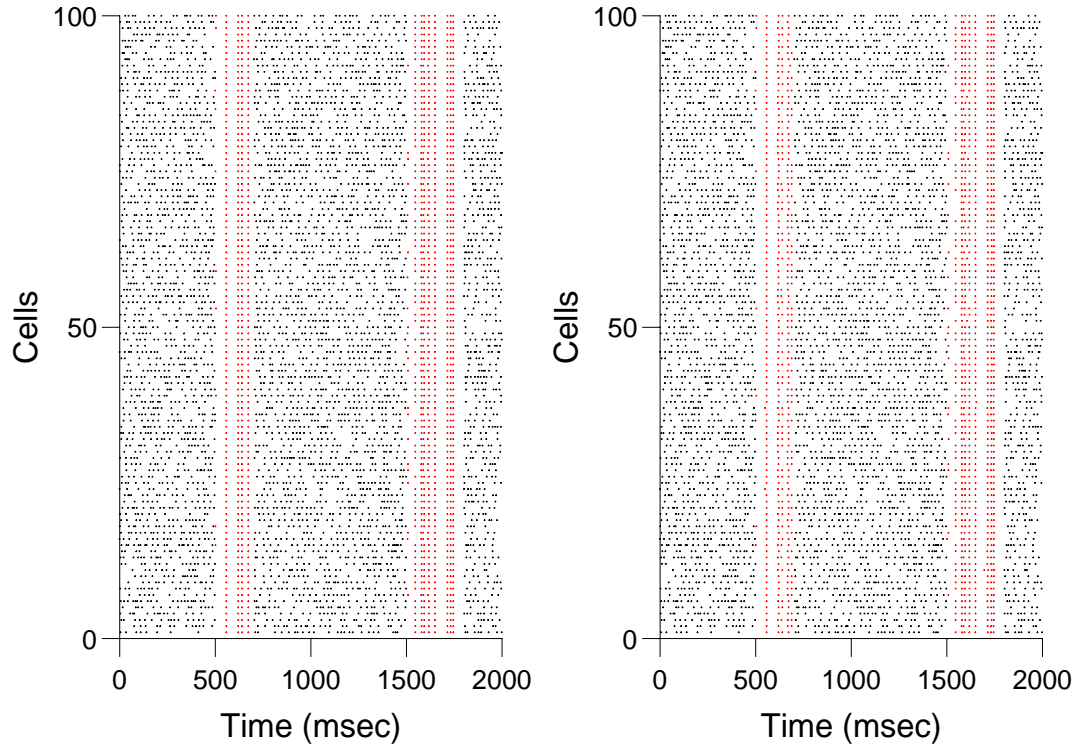


Figure 1: One hundred IF neurons rapidly synchronize when a common stimulus is turned on (see text for further explanation). (Left) All inputs are common. (Right) 90% inputs are common and 10% are i.i.d.

where $\mathcal{T} = [500, 700] \cup [1500, 1800]$, $\delta = 1$ for 100% common inputs, $\delta = .9$ for 90% common inputs, and $I_{\mathcal{T}}$ is the indicator function for the set \mathcal{T} . It is easily seen that the group of neurons synchronize after a few spikes (see Fig. 3), although the number of neurons we consider here is large. In fig. 1 (Right) 90% inputs are common and 10% are i.i.d.. This is of course closer to the input in real biological systems. As one can expect that 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 extensive. Note that mean input (see Eq. (4) below) is $\mu = 0.5 \times 100 \times 0.1 - 0.5 \times 80 \times 0.1 = 1mV$, which is far below the threshold. Nevertheless $\gamma\mu$ is close to the threshold (see table 1). It is recently reported that learning rules in time domain automatically maintain neuron inputs at the level of $\gamma\mu \sim V_{thre}$ [22].

For the HH model we use the same parameters of synaptic inputs as the IF model above, except that $N_I = 40$ (see Fig. 4 below). In Fig. 2 (left) a common input is turned on at time =500 msec (turned off at time=700 msec) and 1500 msec (turn off at 1800 msec). Again it is easily seen that the group of neurons synchronize after a few spikes (one or two). In Fig. 2 (right) 90% inputs are common and 10% are i.i.d., synchronization is still extensive and rapid.

Note that N_I in both simulations for the IF and HH model is chosen based upon estimation in Fig. 3 and Fig. 4, optimal points for synchronization time.

Two IF neurons ($i = 1, 2$, Eq. (1)) It is well known that the following stochastic differential equation is a good approximation to the synaptic in-

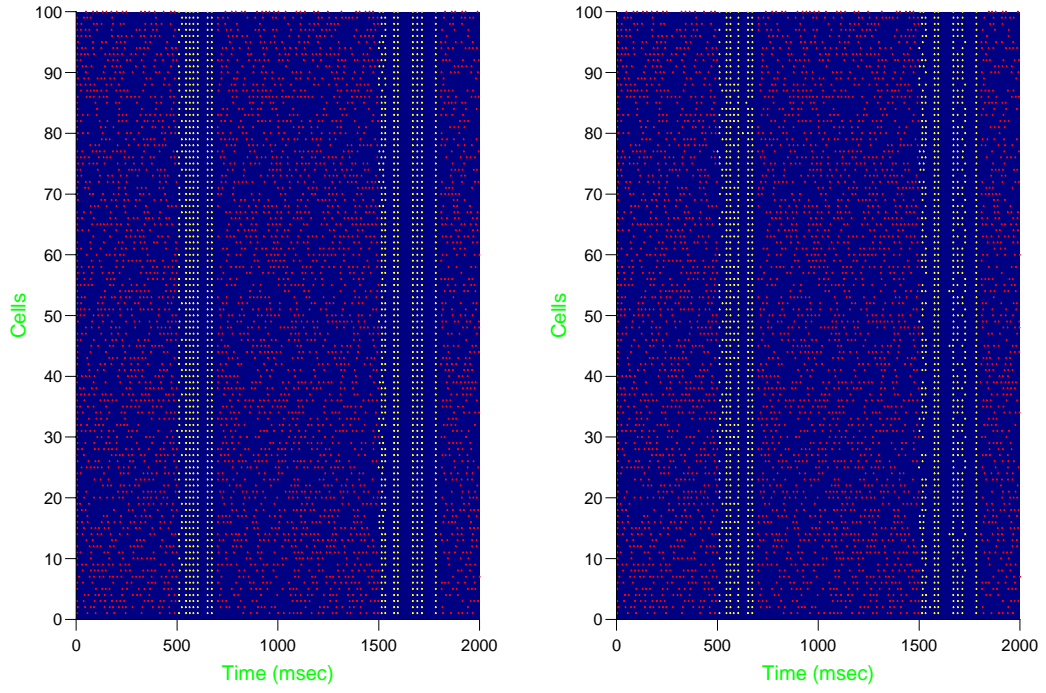


Figure 2: One hundred HH neurons easily synchronize when a common stimulus is turned on (see text for further explanation). (Left) All inputs are common. (Right) 90% inputs are common and 10% are i.i.d.

puts

$$I_{syn,i}(t) \sim \mu t + \sigma B_1(t) \quad (3)$$

where B_1 is the standard Brownian motion and

$$\mu = aN_E\lambda_E - bN_I\lambda_I, \quad \sigma = \sqrt{a^2N_E\lambda_E + b^2N_I\lambda_I} \quad (4)$$

Analytically the stochastic differential equation defined by Eq. (3) is easier to tackle than the jump process defined by Eq. (1). We will restrict ourselves to eq. (3) in the following theoretical discussion, but use solely the jump processes in numerical simulations. Denote $T(m)$ as the time when all m neurons synchronize i.e.

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

We then have the following conclusion.

The probability to synchronize at times $T(2)$ smaller than T , denoted by $P(T)$, approaches to one as T tends to infinity.

Let $y(t) = |x_1(t) - x_2(t)|$. The following consideration illustrates the idea behind the conclusion above [5]. With probability one we have the following events. 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 neuron 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 neuron will be near the threshold as well and an impulse will easily ensure it to hit

the threshold. More specifically without loss of generality we suppose that $x_1 > x_2 = V_{rest}$ and so $T_1^{(1)} \leq T_1^{(2)} \leq T_2^{(1)} \leq T_1^{(2)} \leq \dots$. We have (see [5])

$$\begin{aligned} \lim_{T \rightarrow \infty} P(T) &= P(T(2) < \infty) = \sum_i P(T(2) = T_i^{(2)}, T(2) \neq \\ &\quad T_k^{(2)}, k = 1, \dots, i-1) \\ &= \sum_i P(T(2) = T_1^{(2)}) (1 - P(T(2) = T_1^{(2)}))^{i-1} \\ &= 1 \end{aligned}$$

since $P(T(2) = T_1^{(2)}) > 0$. Therefore decay and random inputs are two vital important factors for the model to show coherent behaviour.

Although the conclusion above tells us that two neurons will synchronize but it does not tell us how quickly they will do so. Unfortunately to find an analytical formula for $T(2)$ 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.

We have reported in early papers [3, 4] that the CV of efferent spikes of the IF 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. 3 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 neurons to synchronize. For example when $r > 0.5$

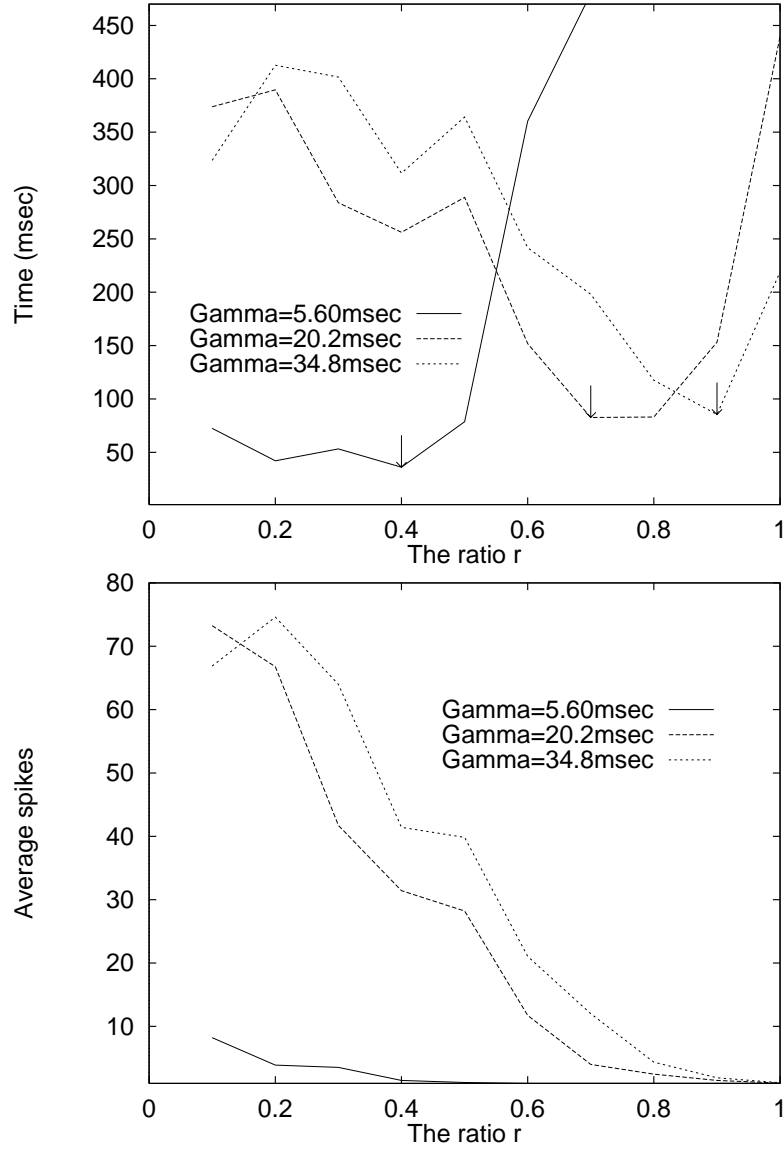


Figure 3: Average synchronization time and spike of two IF neurons with different initial states. The average synchronization time and spike number are obtained for $x_2(0) = 1, 2, \dots, 19$ and $x_1(0) = V_{rest}$. Arrows in figure indicate the optimal average synchronization time. Note that the y-axis of average spikes starts at $y = 1$. When $\gamma = 20.2\text{msec}$ and $r = 0.8$ in average only about 2.47 spikes are needed to synchronize their activities, comparing with Fig. 1.

and $\gamma = 5.6msec$ two neurons fire together from the first spike.

Interestingly (see table 1) the optimal average synchronization time of two neurons is about at $r = r_0$ satisfying $CV(r_0) \geq 0.5$. It has been reported experimentally that the CV of efferent spike trains of neurons in visual cortex is above 0.5[21, 20]. This implies that the optimal average synchronization time is attained when the output of a neuron is inside the region with a high CV (see [1, 4]).

γ	ST	CV
5.60msec	36.0msec	.6
20.2msec	82.6msec	.5
34.8msec	85.4msec	.7

Table 1: Optimal average synchronous time (ST) and CV of efferent spike trains of the IF model.

The conclusions above can be generalized to a group of IF neurons with or without reversal potentials, and we refer the reader to our earlier publications [5] for further details.

From table 1 we see that the shortest synchronization time is attained when $\gamma\mu \sim V_{thre}$. Fig. 3 together with table 1 also reveal one of the functional roles of inputs with the property of $\gamma\mu \sim V_{thre}$ [22], i.e. to optimize the synchronization time. It is recently reported that learning rules in time domain automatically ensure that the relationship $\gamma\mu \sim V_{thre}$, called balanced inputs¹ in [22], is true.

Hodgkin-Huxley neurons We generalize the theory above to the Hodgkin-

¹We consider two cases of input here: when $\mu = 0$ or $r = 1$ it is exactly balanced EPSPs and IPSPs inputs; when $\gamma\mu \sim V_{thre}$ it is balanced inputs

Huxley model, based upon numerical simulations. However the following arguments provide us with rational reasons to explain that why similar phenomena are true for the HH models. Denote V_k, V_{Na}, V_L as the reversal potentials of K, Na channels and leakage, g_L, g_{Na}, g_k as the conductance of K, Na channels and leakage, and V_{re} as the resting potential (see [1] and references therein for the definition of other variables m, n, h). We rewrite the HH model in the following way

$$CdV = -\bar{g}_L(V - V_{re})dt + \bar{g}_{Na}m^3hdt - \bar{g}_kn^4dt + d\bar{I}_{syn}(t) \quad (5)$$

where $\bar{g}_L = g_{Na}m^3h + g_kn^4 + g_L \geq 0$ is the actual leakage of the model (depending on time), $\bar{g}_{Na} = g_{Na}(V_{Na} - V_{re}) > 0$, $\bar{g}_k = g_k(V_{re} - V_k) > 0$, and $\bar{I}_{syn}(t) = I_{syn}(t) + g_L(V_L - V_{re})t$.

Eq. (5) has advantage over the original form of the HH model: firstly each term gives us a clear physical meaning as we mentioned above; secondly it is analogous with the IF model, and so we can generalize results from the IF model to the HH model; thirdly since all ionic channels have their reversal potentials and so Eq. (5) is universal for all biophysical models in the following sense: for a given biophysical model we can rewrite the model in a way similar to Eq. (5). According to our theory on the IF model, we know that the decay term and random inputs ensure the synchronization and thus it is natural to expect that our theory will be true for all biophysical models, although here we confine ourselves to the HH model.

For the synchronization time of the HH model we have similar conclusions as for the IF model, as shown in Fig. 4: the optimal synchronization time occurs neither the neuron receives pure EPSP inputs ($r = 0$) nor balanced

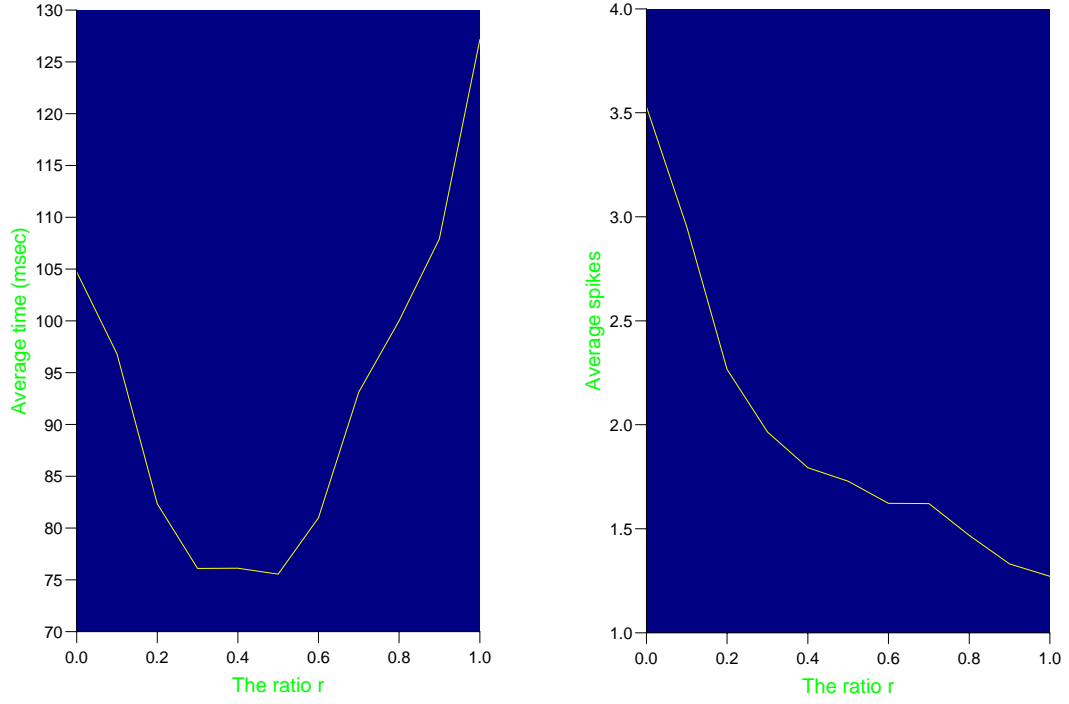


Figure 4: Average Synchronization time and spike of two Hodgkin-Huxley neurons with different initial states. The average synchronization time and spike number are obtained for $V_2(0) = -80, -79.85, \dots, -65mV$ and $V_1(0) = V_{re}$.

EPSP and IPSP inputs ($r = 1$).

Discussion We have shown and proved that the IF model is capable of synchronizing within a finite time and numerically that the time for them to synchronize is almost instantaneous. The conclusions are then generalized to the HH model, based upon numerical simulations. Our results might provide a possible mechanism for the phenomena of stimulus-evoked synchronization in widely separate cortex areas which has been observed in experiments [18]. On the other hand our results also lay a foundation for further investigation, in particular on the role of local interactions. 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 the synchronous neurons to receive common inputs. With balanced inputs, the synchronization time attains its minimum.

To further show the implications of our results in the present paper, we simulate 100 neurons with stochastic and deterministic inputs with small random perturbations, as shown in Fig. 5. It is easily seen that random, rather than deterministic inputs synchronize neuronal activities. We already know from the results above that neurons with stochastic, common inputs are easily to synchronize. Let us now look at the case of deterministic inputs. Suppose that two neuron are driven by a constant input and the first neuron fires before the second neuron with a time difference of t , then this difference will be always present and so it is difficult for them to synchronize, as shown in Fig. 5.

This explains the phenomenon observed in [13] if we think of cells in Fig.

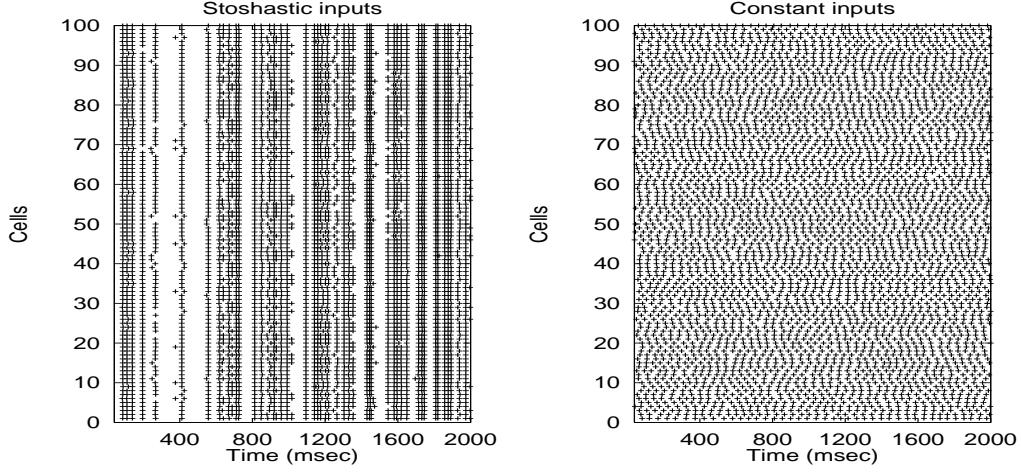


Figure 5: Stochastic inputs (Eq. (2)) and deterministic inputs ($[\delta 10/9 dt + (1 - \delta)(aN_i^E(t) - bN_i^I(t))]I_{\{t \in \mathcal{T}\}}$, see Eq. (2)) with $\delta = 0.9$ and random initial states of the membrane potentials, $\mathcal{T} = [0, 2000]$ msec. At $t = 0$ membranes of cells with deterministic inputs are equal to that with stochastic inputs. For the stochastic input case, the output firing rate is around 23.5 Hz, for the deterministic case, it is around 21.5 Hz. Other parameters are as in Fig. 1. It is easily seen that neurons with stochastic inputs synchronize their activity, but not with deterministic inputs.

4 as trails in Fig. 1 in [13], provided that $(1 - \delta)100\%$ inputs (i.i.d. part, it is 10% in Fig. 5) are feedback from other neurons. To understand the reliability of spiking time, many recent research activity has been devoted to the similar phenomenon and this is also the focus of recent years discussions on whether neuron interspike intervals are reliable or not.

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