72

EFFECTS OF INPUT SYNCHRONY ON THE RESPONSE OF A MODEL NEURON

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ABSTRACT

For a model neuron with 3 conductances, we studied the dependence of the average spike rate on the degree of synchrony in its synaptic inputs. The effect of synchrony was determined as a function of three parameters: number of inputs, average input frequency and the size of unitary EPSPs.

1 INTRODUCTION

It is generally believed that the firing rates of neurons carry information, but additional information could also be coded in the relative timing of spikes among groups of neurons. In the latter mechanism, synchronous activity, i.e., the near-simultaneous occurrence of spikes in multiple neurons, is of particular relevance. Indeed, cross-correlation histograms between spike trains from mammalian neocortical neurons often exhibit a central peak [4]. Recently, widespread synchronous cortical activity has been observed in the visual cortex of cats [3, 5] and in sensorimotor cortex of awake monkeys [8]. Afferent inputs to a neuron clearly cause more effective depolarization if they arrive synchronously. Postsynaptic potentials have finite time constants and their amplitudes are often a small fraction of the threshold depolarization necessary to evoke a spike. Therefore, near-simultaneous occurrence of excitatory postsynaptic potentials (EPSPs) would be more effective in depolarizing cells to threshold than asynchronous arrival. Relatively few studies have investigated this mechanism parametrically, using simulations [1, 2, 6, 9].

A primary aim of our simulations was to determine quantitatively how the output of a biophysically realistic model neuron depends on the degree of synchrony in its inputs. We systematically explored the effect of four basic parameters on the average output frequency ($\mathbf{f_o}$): (1) **N**, the number of active inputs converging on the model neuron, (2) $\mathbf{f_i}$, the average frequency of the inputs, (3) **w**, the synaptic strength, or equivalently, the size of the unitary EPSP, (4) **s**, the degree of synchrony among the afferents (varied from 0 to 100%).

2 METHODS

The simulated neuron modeled a cortical pyramidal neuron with five compartments, a soma and four apical dendritic compartments. The membrane time constant was 15 msec. Three Hodgkin-Huxley type membrane currents were included in the soma: fast sodium, delayed rectifier potassium and an A-like potassium current to allow low-frequency firing in response to injected current. The dendritic compartments had no active currents. The parameters for the kinetics of the currents were similar to those of the three-channel model of Lytton and Sejnowski [7]. The maximal conductances of the three types of channels were adjusted to reproduce action potential waveforms and frequency-current relation seen in cortical pyramidal neurons. The intrinsic parameters of the model were then fixed at these values for all further simulations. Excitatory synaptic inputs occurred on the second dendritic compartment and produced a conductance change with a timecourse similar to the fast glutamate synapses in the cortex. The strength of the input connections was varied by changing the maximal synaptic conductance. Inhibitory inputs were not included in these simulations. Each input was modeled as a Poisson spike train; all inputs had the same mean rate in a given simulation. Synchronization was simulated by lumping the synchronized inputs into one source, whose strength was increased proportionately. The synchrony among the inputs was measured by a synchrony factor **s**, which was varied from 0 to 1 in steps of 0.1. For example, at "0.7 synchrony", 70% of the afferents had identical spike trains. The average number of spikes per second ($\mathbf{f_o}$) computed over 5 s of simulation was used as the index of the output. All simulations were performed using the GENESIS program on a Sun 4 workstation [10].

3 RESULTS

For each combination of the four parameters, **N**, $\mathbf{f_i}$, **w** and **s**, we determined the average frequency of the output over 5 seconds of simulation. The results are discussed in two sections, each describing the effect of increasing synchrony on $\mathbf{f_o}$ when one variable was systematically varied, with the other two fixed. In general **N** and $\mathbf{f_i}$ need not be independently varied since each input is a Poisson process and so is the sum of Poisson processes. Therefore, only the variation in $\mathbf{f_i}$ is discussed, although simulations were also performed for variation in **N**.

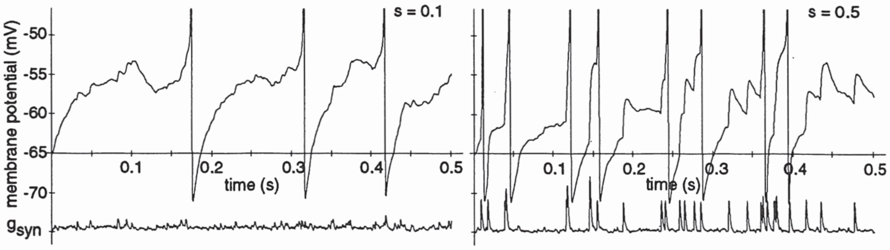

Figure 1 Membrane potential of the soma compartment and the total synaptic conductance ($\mathbf{g_{syn}}$ in arbitrary units). For both panels **N** = 100, $\mathbf{f_i}$ = 50 Hz and w = 100μV. The degree of synchrony in the inputs were 10% (left) and 50% (right). Action potentials are clipped.

(1) *s and w varied, N and f_i held constant:* Fig. 1 shows the membrane potential trajectories and the synaptic conductance changes for two levels of input synchrony with the other parameters fixed (**N** = 100, **w** = 100 μV and $\mathbf{f_i}$ = 50 Hz). At low level of synchrony (s = 0.1), the membrane trajectories were was relatively smooth and the firing was regular. At a synchrony level of 0.5, the membrane potential was strongly affected by the synchronized input, which produced large EPSPs. The average firing rate was higher than in the low-synchrony condition. Fig. 2 shows a typical family of curves depicting the dependence of $\mathbf{f_o}$ on **w** and **s**, for **N** = 100 and $\mathbf{f_i}$ = 50 Hz. For low values of **w** (< 125 μV), the output increased monotonically with increasing synchrony. For instance, with 100 inputs firing at 50 Hz, each input producing an EPSP of 100 μV, no spike was evoked in the model neuron with **s** = 0, and at 100%

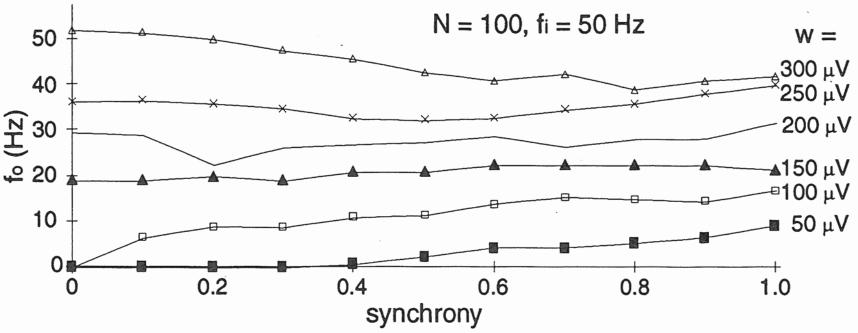

Figure 2 Variation of output frequency ($\mathbf{f_o}$) with synchrony and size of EPSP.

synchrony ($\mathbf{s} = 1$), the average output was 17 Hz. For larger EPSPs (> 300 μV) the output frequency actually decreased with increasing synchrony. This occurred when the EPSP size was such that, at low synchrony $\mathbf{f_o}$ was greater than $\mathbf{f_i}$. At very high synchrony the inputs are effectively lumped into one source, and since each EPSP can lead to no more than one spike, $\mathbf{f_o}$ cannot be greater than $\mathbf{f_i}$. In fact, $\mathbf{f_o}$ is less than $\mathbf{f_i}$ since the synchronized input sometimes occurs during the afterhyperpolarization following a previous spike and fails to evoke another spike. At low levels of synchrony the individual synaptic currents add up more smoothly and lead to a relatively regular firing rate, which can be greater than $\mathbf{f_i}$. For the same reason the variance of $\mathbf{f_o}$ increased with increasing synchrony. When the inputs were highly synchronized, the output spikes were more tightly linked with the inputs and therefore tended to have the same Poisson statistics as the inputs. Simulations for other values of $\mathbf{N}$ and $\mathbf{f_i}$ produced results qualitatively similar to those in fig. 2.

(2) *s and f_i varied, N and w held constant:* At low values of $\mathbf{f_i}$, increasing synchrony led to an increase in $\mathbf{f_o}$. For sufficiently large values of $\mathbf{f_i}$, $\mathbf{f_o}$ was greater than $\mathbf{f_i}$ at $\mathbf{s} = 0$. In this regime, increasing $\mathbf{s}$ resulted in a decrease in $\mathbf{f_o}$ for the same reason discussed above (i.e., at high synchrony $\mathbf{f_o}$ cannot exceed $\mathbf{f_i}$).

It is of interest to determine the values of $\mathbf{N}$, $\mathbf{f_i}$ and $\mathbf{w}$ for which synchrony in the inputs can enhance the firing rate of the cell. Synchrony was considered to have a significant effect on $\mathbf{f_o}$ if $\mathbf{f_o}$ increased by at least 10% when synchrony was changed from 0 to 1. With this criterion, synchrony had a significant effect on $\mathbf{f_o}$ if the product ($\mathbf{P}$) of the three factors $\mathbf{N}$, $\mathbf{f_i}$ and $\mathbf{w}$, was less than 0.5 Vsec^{-1}. That is: $\mathbf{P} = \mathbf{Nwf_i} \leq 0.5$ Vsec^{-1}. This particular cut-off for P depends on the parameters of the model cell. For instance, if the time constant of the membrane is reduced, synchrony is effective for a greater range of $\mathbf{P}$.

4 DISCUSSION

Our primary objective was to determine parametrically the conditions under which synchrony in synaptic inputs can lead to an increase in the average output firing rate of a biologically realistic model of a cortical neuron. Interestingly, the simulations revealed that greater synchrony does not always increase the average firing rate. When input firing rates, number of inputs and unitary EPSPs are small, synchrony can significantly increase the output firing rate; for these parameters anynchronous inputs generate relatively smooth membrane potential trajectories, whereas synchronized inputs can cause large deviations in the membrane potential that trigger spikes (Fig. 1). However, when $\mathbf{N}$,

$\mathbf{f_i}$ and $\mathbf{w}$ are large, asynchronous inputs generate a relatively smooth steady depolarization that can produce output rates higher than the firing rates of the individual inputs. In contrast, highly synchronized inputs generate large compound EPSPs that cause one spike at most, so $\mathbf{f_o}$ cannot be greater than $\mathbf{f_i}$. Consequently, in this parameter regime, greater synchrony can actually decrease $\mathbf{f_o}$. This situation will change if some intrinsic membrane properties (such as calcium currents) can generate multiple spikes per EPSP.

Our simulations have relevance to biological neurons *in vivo*. Unitary EPSPs in cortical pyramidal neurons are in the range of a few hundred μV [4]. However, *in vivo* intracellular recordings in awake monkeys show large membrane potentials fluctuations up to 10 mV, suggesting synchronous occurrence of PSPs (Matsumura, Chen and Fetz, unpublished observations). Pyramidal cells typically fire one spike and repolarize much like our model neuron. Assuming an average input firing rate of 25 Hz and unitary EPSPs of 100 μV, synchrony would increase the frequency of target neurons, if the number of active inputs is less than 200, as seems likely. Although the results presented were obtained under steady state conditions, preliminary simulations suggest similar results for time-varying inputs: transient changes in $\mathbf{f_i}$ cause bigger changes in $\mathbf{f_o}$ if synchrony is increased in parallel, at least when $\mathbf{P} < 0.5 \text{ Vsec}^{-1}$.

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