

The operating mode of cortical neurons: Integrators or coincidence detectors?

Michael Rudolph and Alain Destexhe

*Unité de Neurosciences Intégratives et Computationnelles, CNRS
UPR-2191, Bat. 33, Avenue de la Terrasse 1, 91198 Gif-sur-Yvette, FRANCE
Michael.Rudolph@iaf.cnrs-gif.fr*

Abstract

The question whether cortical neurons operate as integrators or coincidence detectors is subject of a yet unsolved debate, which directly links to the problem of neural coding. We investigated the operating mode of model neocortical pyramidal neurons with active dendrites in states of high background activity comparable to that present *in vivo*. The simulations show that cortical neurons are capable to operate in a continuum between coincidence detection and temporal integration, depending on the background activity. The results suggest that background activity plays a central role in sharpening cortical responses, providing a way to modulate networks between integration and coincidence detection.

Key words: cerebral cortex, synaptic background, computational models

1 Introduction

Much experimental and theoretical work has been dedicated to answer the question of whether individual neurons encode and process information by using precise spike timings, thus working as coincidence detectors, or spike rates, thus working as temporal integrators [15,12,13,8,14,3]. Recent theoretical studies suggest that cortical neurons could operate according to both of these modes, depending on the temporal characteristics of their input [9,7].

Here, we computational investigated this problem using detailed biophysical models of morphologically-reconstructed pyramidal neurons of cat parietal cortex with active dendrites, subject to synaptic background activity which was constrained by recent *in vivo* measurements [5,10]. We show that the integration of multisynaptic input patterns and, thus, the operating mode of cortical neurons can be controlled by the activity of the network.

2 Methods

Computational models were designed based on a morphologically-reconstructed layer VI neocortical pyramidal cell of cat parietal cortex (Fig.1A, [2]). Passive model parameters were estimated by matching the model to passive responses obtained intracellularly after application of TTX and synaptic blockers [5,10]. Three types of active currents (sodium current, delayed-rectifier and voltage-dependent potassium currents simulated by Hodgkin-Huxley type models) were incorporated with densities according to recent measurements [5].

Synaptic currents included AMPA and GABA_A receptors, which were simulated by using two-state kinetic models [4] with quantal conductances estimated from miniature synaptic events [5]. Synaptic densities were estimated from morphological studies in neocortical pyramidal cells, leading to a total of 16563 glutamatergic and 3376 GABAergic synapses.

Synaptic background activity was simulated by a Poisson-like release activity with average rates of 5.5 Hz for GABA_A and 1.0 Hz for AMPA synapses. The statistics of the background activity was modified by introducing a redundancy in the Poisson-distributed random numbers assigned to the presynaptic terminals. A Pearson's correlation coefficient of about 0.1 characterizes the statistics in the investigated correlated case (see [5,6,11] for details).

Synaptic stimulation consisted in activating N Gaussian-distributed excitatory synaptic inputs randomly distributed in the dendrites. Their level of simultaneity was controlled by adjusting the dispersion in time, according to a Gaussian distribution of standard deviation σ_{in} [9,7]. Examples of individual events are shown in Fig.1B (grey).

3 Results

The operating modes of the model neuron were investigated by changing the parameters of the Gaussian input N and σ_{in} , as well as the level of background activity. Three cases were investigated: quiescent (no background activity) and active (*in vivo*-like) conditions with uncorrelated and correlated background activity.

In all investigated cases, the cumulated output spikes depicted as a function of time resemble Gaussian shaped distributions (Fig.1B, black), characterized by the total number of output spike events N_{resp} and the width σ_{out} , with the mean of the output distribution shifted by the mean latency t_{lat} against the center of the Gaussian input signal. Under quiescent conditions, the cell was

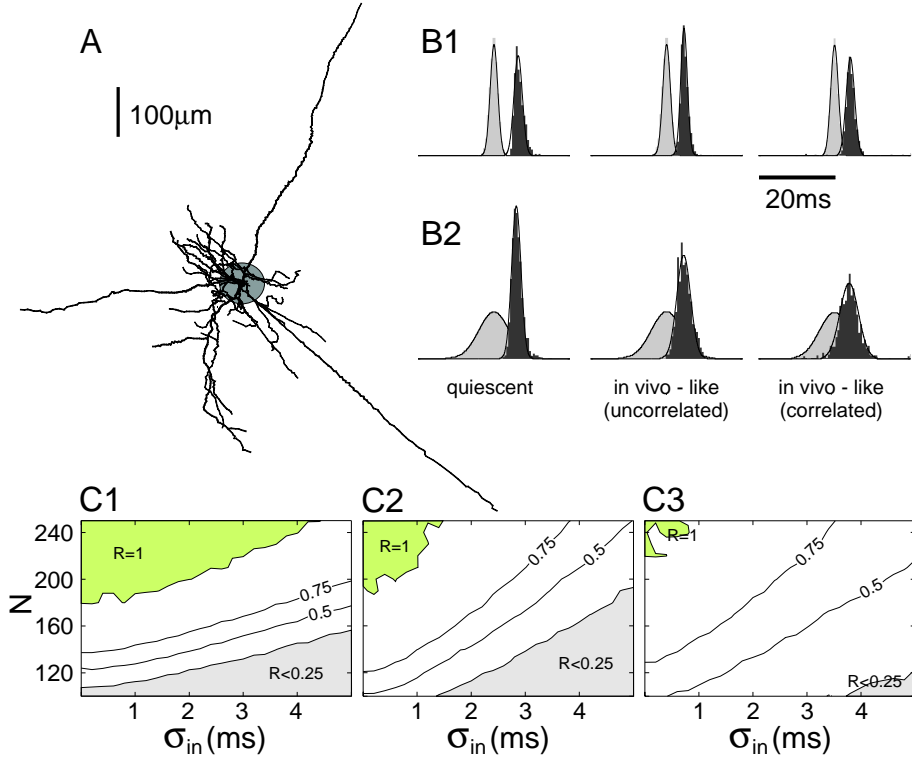


Fig. 1. **A.** Morphologically-reconstructed neocortical pyramidal layer VI neuron of a cat incorporated in the modeling studies. The shaded area (radius $\leq 40 \mu\text{m}$) marks the proximal region with no excitatory synapses. **B.** Representative examples of Gaussian-distributed synaptic stimuli (B1: $N = 130, \sigma_{in} = 1 \text{ ms}$; B2: $N = 220, \sigma_{in} = 4 \text{ ms}$; B3: $N = 220, \sigma_{in} = 4 \text{ ms}$). **C.** Reliability $R = N_{resp}/N_{Gauss}$, where N_{resp} denotes the total number of spikes in response to N_{Gauss} Gaussian events, with which the Gaussian events drive the postsynaptic response (C1: quiescent, C2: uncorrelated, C3: correlated).

capable to respond reliably ($R \sim 1$, Fig.1C1) to events of nearly all widths, with a mean latency t_{lat} increasing with weaker (decreasing N) and more dispersed (increasing σ_{in}) input signals (Fig.2A1).

In contrast, the region with $R \sim 1$ decreased in the presence of uncorrelated and correlated background activity (Fig.1C2 and C3) due to the spontaneous discharge activity caused by the synaptic background, and R displayed an overall weaker dependence on N . The presence of background activity markedly decreased t_{lat} (Fig.2A2 and A3), especially for higher σ_{in} , yielding a t_{lat} which was nearly independent of σ_{in} and N .

It is interesting to note that σ_{out} is proportional to t_{lat} only in quiescent conditions (Fig.2B1) with nearly no dependence on N . Contrary, in the presence of synaptic background activity, in addition to the overall decrease of t_{lat} and increasing range of covered σ_{out} , there was no longer a linear relation between t_{lat} and σ_{out} (Fig.2B2 and B3).

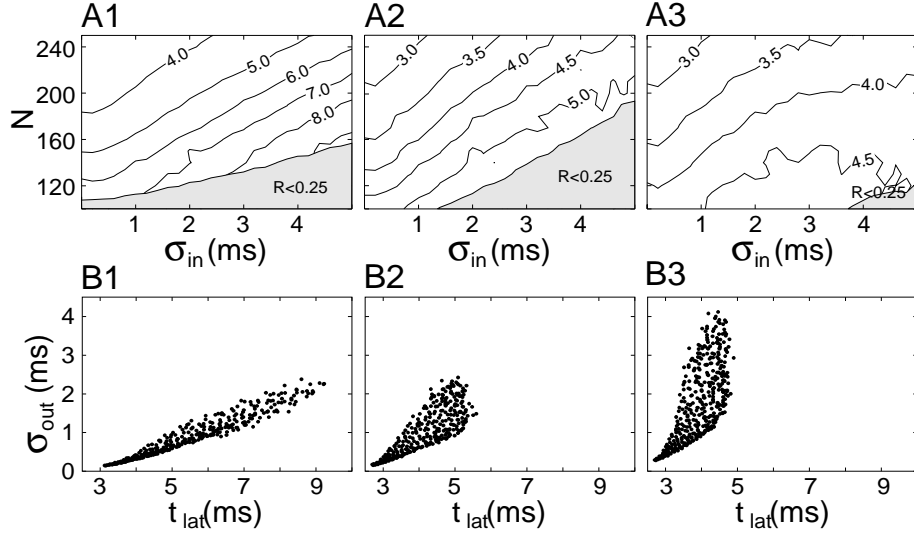


Fig. 2. **A.** The mean latency t_{lat} as a function of the Gaussian stimuli characteristics in the quiescent case (A1) and under uncorrelated (A2) and correlated (A3) *in vivo*-like conditions. **B.** Relation between t_{lat} and the output jitter. Whereas in the quiescent case (B1) there is a linear relation, allowing to determine the time of the input events by measuring the jitter of the output, no corresponding relation can be evidenced under *in vivo*-like conditions (B2 uncorrelated, B3 correlated).

To analyze directly the impact of the input synchronization on the output jitter of the cell, we investigated the behavior of the ratio $\xi = \sigma_{in}/\sigma_{out}$. The input parameter range for which $\xi \geq 1$ was large under quiescent conditions (Fig.3A1) and decreased markedly in the presence of background activity (Fig.3A2 and A3). In all cases σ_{out} was roughly proportional to σ_{in} . In the quiescent state and for uncorrelated background activity, tightly synchronized input distributions (small σ_{in}) caused less jitter in the timing of output spikes (Fig.3B1 and B2, σ_{out} is considerably smaller than σ_{in}), in agreement with previous modelling studies [9,7]. Only in the presence of correlated background activity the slope increased and was close to one for a broad range of input settings (Fig.3B3), suggesting that under these conditions the cell nearly *conserves the synchronization of the input signal*.

4 Conclusions

In this paper we have investigated the operating modes of cortical neurons by using multisynaptic inputs whose dispersion in time was varied. Taken together, the results suggest that cortical neurons are capable of responding to synaptic inputs reliably with various degrees of precision, depending on the synchrony in the multisynaptic input pattern as well as the synaptic background activity [1,7]. Given that for tight input synchronization (small σ_{in}) the cell detects the coincident occurrence of synaptic inputs, whereas for large

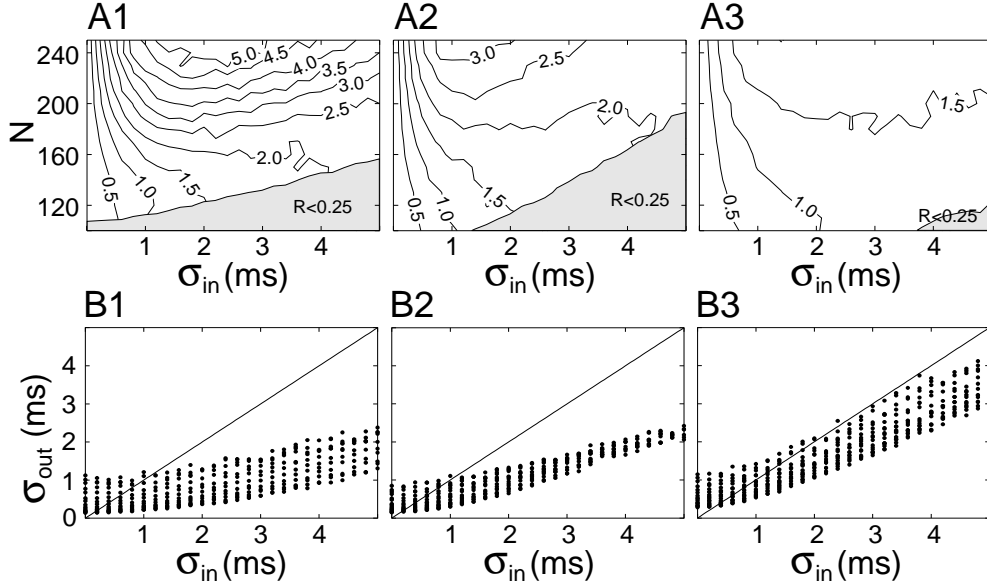


Fig. 3. **A.** $\xi = \sigma_{in}/\sigma_{out}$ as a function of the input settings. In all three cases, the input parameter range covers settings for which $\xi \sim 1$. This range markedly increases for the correlated case (B3). **B1** and **B2** show the results for quiescent and uncorrelated *in vivo*-like conditions, respectively. **B.** Relation between output jitter and the synchrony in the input. In all three cases (C1 quiescent, C2 *in vivo*-like uncorrelated, C3 *in vivo*-like correlated) σ_{out} is roughly proportional to σ_{in} , but with a slope (solid lines) smaller than one. Only in the correlated case the slope is close to unity, suggesting a neuronal response which preserves the synchrony in the input signal.

σ_{in} the cell rather integrates input signals dispersed in time, the simulations show that cortical cells can operate in a continuum between coincidence detection and temporal integration.

Depending on the background activity, the neuron was capable to modulate the degree of conservation of the input synchronization, with a near conservation ($\sigma_{out} = \sigma_{in}$) for background activity at a level comparable to measurements in cat parietal cortex *in vivo* [10,5]. This finding may have important consequences at the network level, because the relation between input and output jitter will determine the synchronization of discharges across successive layers of interconnected neurons, or within successive cycles of an oscillation occurring within a recurrent network. The model predicts that networks can determine the time evolution of the synchrony and, thus, tune their operating mode by modulating the level of spontaneous activity. The further investigation of this type of dynamics as well as its possible role in information processing should be investigated by future network models.

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