ELSEVIER

# Synaptic background activity affects the dynamics of dendritic integration in model neocortical pyramidal neurons

Michael Rudolph[a,b], Nicolas Hô[b], Alain Destexhe[a,b,*]

[a]Unité de Neurosciences Intégratives et Computationnelles, CNRS, UPR-2191, Avenue de la Terrasse, 91198 Gif-sur-Yvette, France
[b]Départment de Physiologie, Université Laval, Pavillon F. Vandry, Qué., Canada G1K 7P4

## Abstract

Neocortical pyramidal neurons in vivo are subject to an intense synaptic background activity which may significantly impact on dendritic integration, but this aspect is largely unexplored. Here we use computational models of morphologically-reconstructed pyramidal neurons, in which synaptic background activity was simulated according to recent measurements in cat parietal cortex. We show that background activity markedly enhances voltage attenuation, which results in a relative electrotonic "isolation" of different dendritic segments. On the other hand, the active propagation of action potentials in dendrites is minimally affected. The consequence is that inputs are integrated locally and their impact on the soma is independent on their position in the dendritic tree. We conclude that background activity sets up a dynamics of dendritic integration which is radically different compared to quiescent states. © 2001 Elsevier Science B.V. All rights reserved.

*Keywords:* Cerebral cortex; Dendritic integration; Synaptic background activity; Computational models

## 1. Introduction

The membrane potential ($V_m$) of neocortical neurons in vivo is continuously fluctuating due to the presence of synaptic background activity [1,5,13–16], which reflects the ongoing activity in the cortical network. This activity may influence

---

dendritic integration due to tonically-activated synaptic conductances in dendrites. This theme was explored by modeling studies [2,3,7,12,17] which have suggested that these conductances indeed affect dendritic integration and impose strict conditions of convergence or coincidence for synaptic inputs to discharge the cell.

The electrophysiological properties of synaptic background activity were characterized recently in cat parietal cortex by comparing intracellularly recorded pyramidal neurons in vivo before and after application of tetrodotoxin (TTX) [7,16]. It was found that background activity accounts for up to 80% of the input conductance, depending on the type and depth of the anesthesia. An important conductance increase due to background activity was also evidenced in cerebellar Purkinje cells [10].

In this paper, we explore possible consequences of synaptic background activity on dendritic integration, based on models of morphologically-reconstructed pyramidal neurons of cat parietal cortex.

## 2. Methods

Computational models were designed based on four morphologically-reconstructed neocortical pyramidal cells from cats (one from layer II–III, two from layer V and one from layer VI), which were obtained from two previous studies [4,9]. The cell primarily used here is depicted in Fig. 1A. All results were robust to change in the cellular morphology provided all conductance densities were kept equivalent in the different models.

The passive properties were adjusted to intracellular recordings obtained in the absence of synaptic activity [7]. Different combinations of passive parameters were used, such as a supplementary shunt conductance of $10\,nS$ in the soma due to electrode impalement, different values of the axial resistivity ($80–250\,\Omega\,cm$) and different distributions of leak conductances in soma and dendrites (non-uniform distributions taken from Ref. [18]).

Voltage-dependent conductances were inserted in soma, dendrites and axon and were described by Hodgkin–Huxley type models [11] (see details in Ref. [7]). Synaptic currents were simulated by kinetic models of glutamatergic (AMPA, NMDA) and GABAergic ($GABA_A$) receptor types [6]. Quantal conductances were estimated from miniature synaptic events and were $1200\,pS$ for AMPA and $600\,pS$ for $GABA_A$ [7]. Metabotropic receptors were not included.

The densities of synapses in different regions of the cell were estimated from morphological studies in neocortical pyramidal cells (reviewed in Refs. [8,19]). The number of synapses per $100\,\mu m^2$ of membrane were: 10–20 ($GABA_A$, soma), 40-80 ($GABA_A$, axon initial segment), 8–12 ($GABA_A$, dendrites) and 55–65 (AMPA-NMDA, dendrites), leading to a total of 16 563 glutamatergic and 3376 GABAergic synapses for the layer VI cell shown in Fig. 1A.

The release conditions corresponding to synaptic background activity were estimated based on recent data from intracellular recordings in cat parietal cortex before and after application of TTX [7,16]. To match in vivo recordings, high-frequency
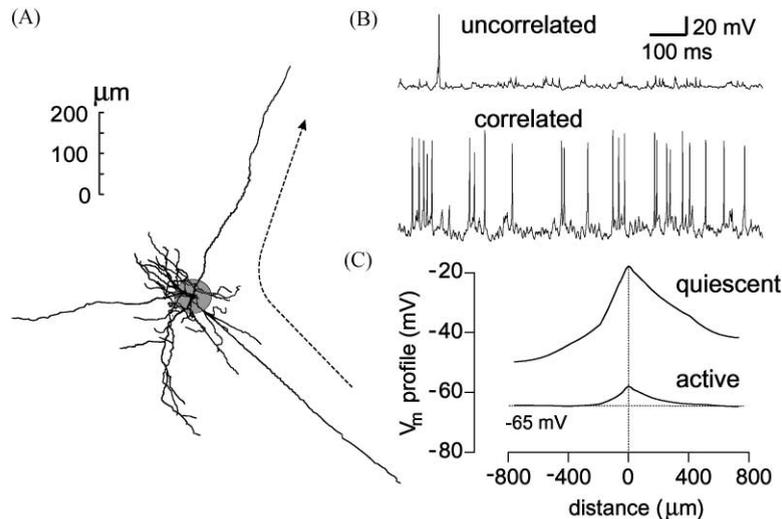
Fig. 1. Synaptic background activity enhances voltage attenuation in cortical pyramidal neurons. (A) Morphologically-reconstructed layer VI pyramidal neuron from cat parietal cortex used for simulations. The shaded area indicates the proximal region including all dendritic branches laying within a radius of 40 µm from the soma. Inside that region there were no excitatory synapses, whereas inhibitory synapses were spread over the whole dendritic tree. (B) Correlated Poisson-like distributed random synaptic background activity based on experimental measurements leads to tonic firing behavior and membrane potential fluctuations. (C) Somatodendritic membrane potential profile at steady-state following injection of current in the soma ( + 0.8 nA). The distance is indicated along the path shown by the dashed line in (A), In the absence of synaptic activity (quiescent) there was moderate attenuation. In the presence of background activity (active) the average dendritic profile (calculated over 1000 trials) revealed a marked attenuation of the steady-state voltage.

release conditions with a significant correlation had to be introduced, such that the model displayed $V_m$ fluctuations (Fig. 1B), low input resistance and depolarized $V_m$ consistent with in vivo measurements [7]. These conditions corresponds to all presynaptic terminals releasing randomly according to Poisson processes (average rates of 1 Hz at glutamatergic and 5.5 Hz at GABAergic synapses).

## 3. Results

The model of synaptic background activity in pyramidal neurons of cat parietal cortex is shown in Fig. 1B. Using this model, we investigated how the presence of background activity affects cellular responses. The first effect of background activity is an enhancement of voltage attenuation due to an important tonic conductance activated by synaptic bombardment. This effect was predicted by previous theoretical studies [2,3,7,12,17]. Intracellular measurements [7,16] confirmed that an important conductance is activated by background activity in vivo. The effect of this conductance on voltage attenuation is illustrated in Fig. 1C. In control conditions (absence of
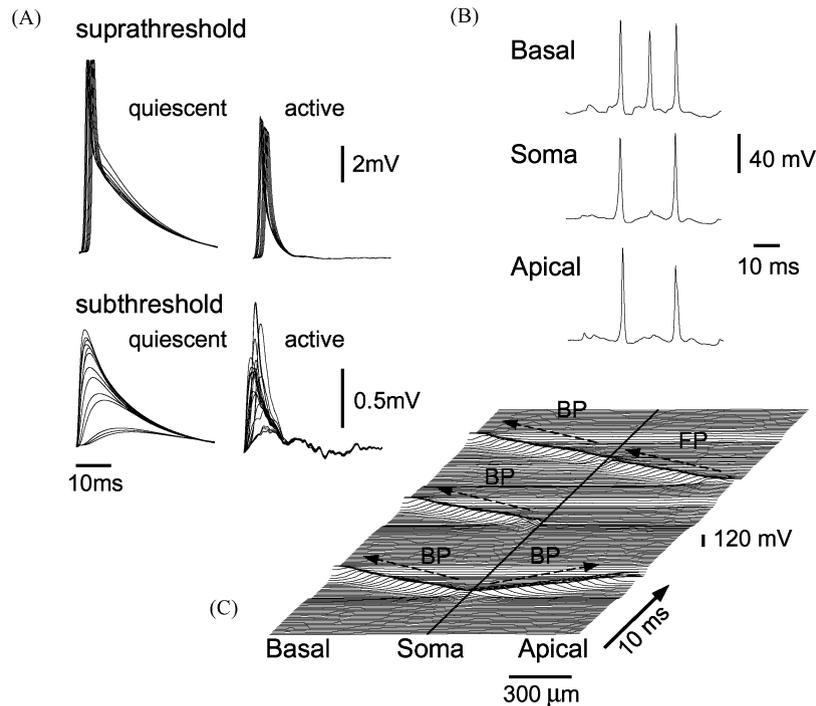
Fig. 2. Initiation and active propagation of dendritic spikes in the presence of synaptic background activity. (A) Somatic EPSPs for synaptic stimulations at various sites of the dendritic tree. For suprathreshold synaptic stimulation (100 synapses), dendritic spikes are initiated under quiescent as well as active conditions, leading to a nearly location independent somatic response (upper panels). In contrast, subthreshold stimulation (3 synapses) leads to a clear location-dependence in the quiescent case, whereas in the active case the latter is diminished due to the active propagation of dendritic spikes. (B) Membrane potential in the soma and the two extremities of apical and basal dendrites. (C) Somatodendritic membrane potential profile (same path as in Fig. 1A) in the presence of synaptic background activity as a function of time. Spike initiation sometimes occurred close to the soma and led to back-propagating action potentials in dendrites (BP). In other instances, spike initiation occurred distally and led to forward-propagating action potentials to the soma (FP).

background activity), current injection in the soma led to about 50% attenuation in distal dendrites (Fig. 1C, quiescent). In the presence of background activity, the same current injection elicited a smaller voltage transient in soma, due to the smaller input resistance, but attenuation of this signal in distal dendrites was increased by about 5-fold (Fig. 1C, active).

In contrast to the marked effect on voltage attenuation, we found that background activity had little effect on the active propagation of action potentials in dendrites. This is illustrated in Fig. 2A. During spontaneous activity, action potentials were generally initiated in axon or in dendrites. In almost 100% of the cases the action potential propagated across the dendritic structure, either backpropagating from proximal to distal sites (BP in Fig. 2C), or propagating from a distal initiation site to the soma (FP in Fig. 2C).
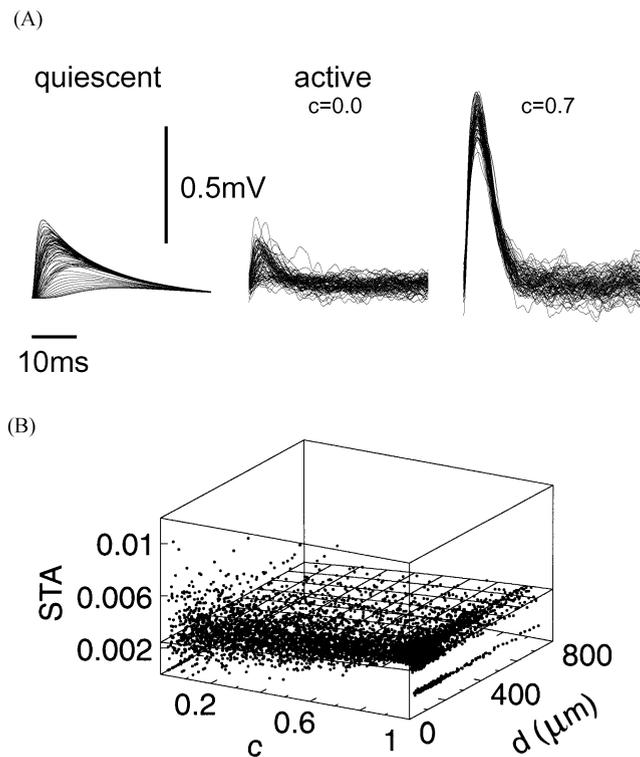
(A)



(B)



Fig. 3. Somatic responses to synaptic inputs in the presence of synaptic background activity. (A) Somatic EPSP traces for subthreshold synaptic stimulation (1 synapse) at different path distances. The impact on the soma shows a clear location dependence in the quiescent case (no background activity) due to the voltage attenuation of the passive signal, which decreases under active conditions. Correlation in the background activity leads to a marked increase in the EPSP amplitude due to the initiation and propagation of dendritic spikes. (B) Spike-triggered average (STA) analysis of the model in the presence of synaptic background. The impact of single synaptic events on spikes elicited at the soma shows a remarkable independence from the site of the synaptic events, indicated by the path distance $d$, for a variety of model parameter settings, such as the background correlation $c$.

These two properties may have important consequences on how the cell processes synaptic inputs. To investigate further the ability of the cell to respond to synaptic inputs in the presence of background activity, we considered next subthreshold stimulation in different compartments of the dendritic tree, which did not elicit dendritic spikes. In the quiescent case we observed the expected exponential decrease of the evoked somatic EPSP peaks with increasing path distance of the stimulation site as a result of passive voltage attenuation (Fig. 3A, left plot). Contrary, in the active case the decrease of the EPSP peaks was much smaller and showed a marked dependence on the level of correlation present in the background activity (Fig. 3A, middle and right plot).

Qualitatively similar results were obtained by analyzing the spike–triggered average of the model in the presence of synaptic background activity (Fig. 3B). The impact of single synaptic events on spikes elicited at the soma showed a remarkable independence from the site of synaptic events for a variety of model parameter settings, such as the background correlation or the release frequency of the excitatory background (data not shown).

## 4. Discussion

We have shown that synaptic background activity is responsible for an augmentation of voltage attenuation, which results in a relative electrotonic "isolation" of different dendritic segments. On the other hand, the active propagation of action potentials in dendrites is minimally affected by background activity. As a result of these two properties, stimulating different regions of the dendritic arbor shows remarkably similar responses at the soma, suggesting that distal dendrites have a roughly equivalent impact as proximal dendrites.

These results show that the dynamics of dendritic integration is radically different in the presence of background activity compared to quiescent states. Individual dendritic segments tend to become electrotonically isolated and integrate inputs independently. As a consequence, the spatial and temporal coincidence requirements markedly depend on whether or not background activity is present. In other words, the level of activity of the network has a profound influence on neuronal responsiveness. This model prediction suggests that the conclusions drawn from experiments in which the network is in a quiescent state (in vitro, deep anesthesia) may not be correct and should be investigated in states where the network activity is comparable to wakefulness.

## Acknowledgements

## References

[1] R. Azouz, C. Gray, Cellular mechanisms contributing to response variability of cortical neurons in vivo, J. Neurosci. 19 (1999) 2209–2223.

[2] J.N. Barrett, Motoneuron dendrites: role in synaptic integration, Fed. Proc. 34 (1975) 1398–1407.

[3] O. Bernander, R.J. Douglas, K.A. Martin, C. Koch, Synaptic background activity influences spatiotemporal integration in single pyramidal cells, Proc. Natl. Acad. Sci. USA 88 (1991) 11569–11573.

[4] D. Contreras, A. Destexhe, M. Steriade, Intracellular and computational characterization of the intracortical inhibitory control of synchronized thalamic inputs in vivo, J. Neurophysiol. 78 (1997) 335–350.

[5] D. Contreras, I. Timofeev, M. Steriade, Mechanisms of long-lasting hyperpolarizations underlying slow sleep oscillations in cat corticothalamic networks, J. Physiol. 494 (1996) 251–264.

[6] A. Destexhe, Z. Mainen, T.J. Sejnowski, Kinetic models of synaptic transmission, in: C. Koch, I. Segev (Eds.), Methods in Neuronal Modeling, MIT Press, Cambridge, MA, 1998,, pp. 1–26.

[7] A. Destexhe, D. Paré, Impact of network activity on the integrative properties of neocortical pyramidal neurons in vivo, J. Neurophysiol. 81 (1999) 1531–1547.

[8] J. DeFelipe, I. Fariñas, The pyramidal neuron of the cerebral cortex: morphological and chemical characteristics of the synaptic inputs, Prog. Neurobiol. 39 (1992) 563–607.

[9] R.J. Douglas, K.A. Martin, D. Whitteridge, An intracellular analysis of the visual responses of neurones in cat visual cortex, J. Physiol. 440 (1991) 659–696.

[10] M. Hausser, B.A. Clark, Tonic synaptic inhibition modulates neuronal output pattern and spatio-temporal synaptic integration, Neuron 19 (1997) 665–678.

[11] A.L. Hodgkin, A.F. Huxley, A quantitative description of membrane current and its application to conduction and excitation in nerve, J. Physiol 117 (1952) 500–544.

[12] W.R. Holmes, C.D. Woody, Effects of uniform and non-uniform synaptic activation-distributions on the cable properties of modeled cortical pyramidal neurons, Brain Res. 505 (1989) 12–22.

[13] I. Lampl, I. Reichova, D. Ferster, Synchronous membrane potential fluctuations in neurons of the cat visual cortex, Neuron 22 (1999) 361–374.

[14] M. Matsumura, T. Cope, E.E. Fetz, Sustained excitatory synaptic input to motor cortex neurons in awake animals revealed by intracellular recording of membrane potentials, Exp. Brain Res. 70 (1988) 463–469.

[15] L.G. Nowak, M.V. Sanchez-Vives, D.A. McCormick, Influence of low and high frequency inputs on spike timing in visual cortical neurons, Cereb. Cortex 7 (1997) 487–501.

[16] D. Paré, E. Shink, H. Gaudreau, A. Destexhe, E.J. Lang, Impact of spontaneous synaptic activity on the resting properties of cat neocortical neurons in vivo, J. Neurophysiol. 79 (1998) 1450–1460.

[17] M. Rapp, Y. Yarom, I. Segev, The impact of parallel fiber background activity on the cable properties of cerebellar Purkinje cells, Neural Computation 4 (1992) 518–533.

[18] G. Stuart, N. Spruston, Determinants of voltage attenuation in neocortical pyramidal neuron dendrites, J. Neurosci. 18 (1998) 3501–3510.

[19] E.L. White, Cortical Circuits, Birkhauser, Boston, 1989.