

Simple model neurons with AMPA and NMDA filters. The role of the synaptic time scales

Rubén Moreno-Bote and Néstor Parga

*Departamento de Física Teórica, Universidad Autónoma de Madrid, 28049
Cantoblanco, Madrid, Spain.*

Abstract

Cortical neurons receive inputs that are filtered by a variety of synaptic types with very different time constants. We study the response properties of a leaky integrate-and-fire (LIF) model neuron in the presence of both fast AMPA and slow NMDA filters and find an analytical formula valid when the membrane time constant τ_m of the neuron is short. When the NMDA/AMPA abundances are similar to those found in cortex, the neuron mainly responds to particular large fluctuations in its inputs. These results suggest that NMDA filters play a crucial role in shaping the neuron response in cortex.

Key words: Integrate-and-fire neuron; AMPA and NMDA filters; neuron response; slow filters.

1 Introduction

Spikes arriving at cortical neurons can generate at the same time fast and slow unitary currents at their membranes. Fast AMPA receptors filter presynaptic inputs with a time constant $\tau_{AMPA} \sim 1 - 10ms$, while NMDA receptors filter them with a longer time scale $\tau_{NMDA} \sim 100ms$ (2). Because both receptor types normally coexist in cortical neurons, the information contained in the inputs is present in the membrane potential at these two time scales. Using a simple model neuron with AMPA and NMDA filters we show that, for values of NMDA/AMPA ratio abundances found in cortex (5; 6), these neurons acquire specific detection capabilities which are not present in neurons with only AMPA synapses. This work generalizes the results found in (1), where a neuron with a single type of filter was shown to behave as a coincidence detector of events with a temporal scale similar to the filter's time constant. All the

results can be seen from simulations as well as from an analytical expression for the output mean firing rate of the model neuron (eq. (8)), which we derive by means of simple arguments.

2 Model neuron and mean firing rate

The membrane potential V of the model neuron obeys

$$\tau_m \dot{V} = -V + \tau_m I(t) \quad (1)$$

$$I(t) = I_{AMPA}(t) + I_{NMDA}(t) , \quad (2)$$

where $I_{AMPA}(t)$ and $I_{NMDA}(t)$ are the pre-synaptic currents filtered by AMPA and NMDA synapses. A spike is produced whenever V reaches a threshold value Θ , after which it is reset to H .

Cortical neurons receive a large number of presynaptic spikes through their AMPA and NMDA receptors. Their contribution to the total input current can be described by two white noise processes with means μ_{AMPA} and μ_{NMDA} , and variances σ_{AMPA}^2 and σ_{NMDA}^2 (8; 3). In this model, the presynaptic signal generates the following AMPA and NMDA currents

$$\begin{aligned} \tau_{AMPA} \dot{I}_{AMPA}(t) &= -I_{AMPA}(t) + \mu_{AMPA} + \sigma_{AMPA} \eta(t) , \\ \tau_{NMDA} \dot{I}_{NMDA}(t) &= -I_{NMDA}(t) + \mu_{NMDA} + \sigma_{NMDA} \eta(t) , \end{aligned} \quad (3)$$

where $\eta(t)$ is a Gaussian white noise with zero mean and unit variance. Notice that since both filters receive the same spikes, they integrate the same white noise, what introduces a high degree of correlation between both currents (as will be checked later; see top panels in Fig. (1)). Writing the current without driving forces is justified because V is very far from the reversal potential of excitatory synapses for typical (under threshold) values.

We start by providing a qualitative derivation of an expression for the firing rate of this model neuron valid for $\tau_{NMDA} \gg \tau_m$ and τ_{AMPA} comparable to τ_m (or longer), which is the realistic case. Since the synaptic time constants are either longer (τ_{NMDA}) or at most comparable (τ_{AMPA}) to τ_m , we assume that the current is approximately constant during a time period τ_m , that is $I(t) = I$. A LIF neuron receiving such a constant current fires at the instantaneous constant rate (8)

$$\nu^{-1}(I) = \tau_m \ln \left(\frac{\tau_m I - H}{\tau_m I - \Theta} \right) . \quad (4)$$

The current defined in eqs. (2,3) is a random variable which we describe with a density distribution $\rho(I)$. Then, the mean firing rate can be computed by averaging the rate at constant current, eq. (4), with the density $\rho(I)$:

$$\nu_{out} = \int_{I_{min}}^{\infty} dI \rho(I) \nu(I) , \quad (5)$$

where the integral extends from $I_{min} = \Theta/\tau_m$. This *threshold current* is the minimal current required for the neuron to fire (see eq. (1)). To evaluate the firing rate we still need the distribution $\rho(I)$ for the stochastic process defined in eqs. (2,3). Since it is Gaussian (9), it is fully determined by its mean μ and variance σ_I^2 . The mean is simply the sum of the AMPA and NMDA mean currents, $\mu = \mu_{AMPA} + \mu_{NMDA}$. To obtain the variance we first solve eqs. (3) with the initial condition $I_k(0) = 0$ ($k = AMPA, NMDA$) to obtain

$$I_k(t) = \mu_k(1 - e^{-t/\tau_k}) + \frac{\sigma_k}{\tau_k} e^{-t/\tau_k} \int_0^t ds e^{s/\tau_k} \eta(s) . \quad (6)$$

The variance σ_I^2 is computed as

$$\begin{aligned} \sigma_I^2 &= \lim_{t \rightarrow \infty} \langle (I_{AMPA}(t) + I_{NMDA}(t) - \mu)(I_{AMPA}(t) + I_{NMDA}(t) - \mu) \rangle \\ &= \frac{1}{2} \left(\frac{\sigma_{AMPA}^2}{\tau_{AMPA}} + \frac{\sigma_{NMDA}^2}{\tau_{NMDA}} + 4 \frac{\sigma_{AMPA} \sigma_{NMDA}}{\tau_{AMPA} + \tau_{NMDA}} \right) . \end{aligned} \quad (7)$$

The first two terms are the current variances generated by the AMPA and NMDA input fluctuations, while the third positive term arises from the correlations between AMPA and NMDA input fluctuations. Notice that if AMPA and NMDA filters were driven by two independent white noises, the third term would not be present. Notice also that the effect of combined AMPA and NMDA events is to increase the synaptic noise relative to that provided by independently driven synapses, with the same variances. Computing μ and σ_I^2 in the way just described, the firing rate eq. (5) can be finally written as

$$\nu_{out} = \int_{I_{min}}^{\infty} \frac{dI}{\sqrt{2\pi}\sigma_I} e^{-(I-\mu)^2/2\sigma_I^2} \nu(I) . \quad (8)$$

This expression generalizes the result recently found in (1) for a current filtered through a single slow synaptic filter. The firing rate for this particular case is readily obtained from eq. (8) by setting to zero the mean and variance of one of the two receptors.

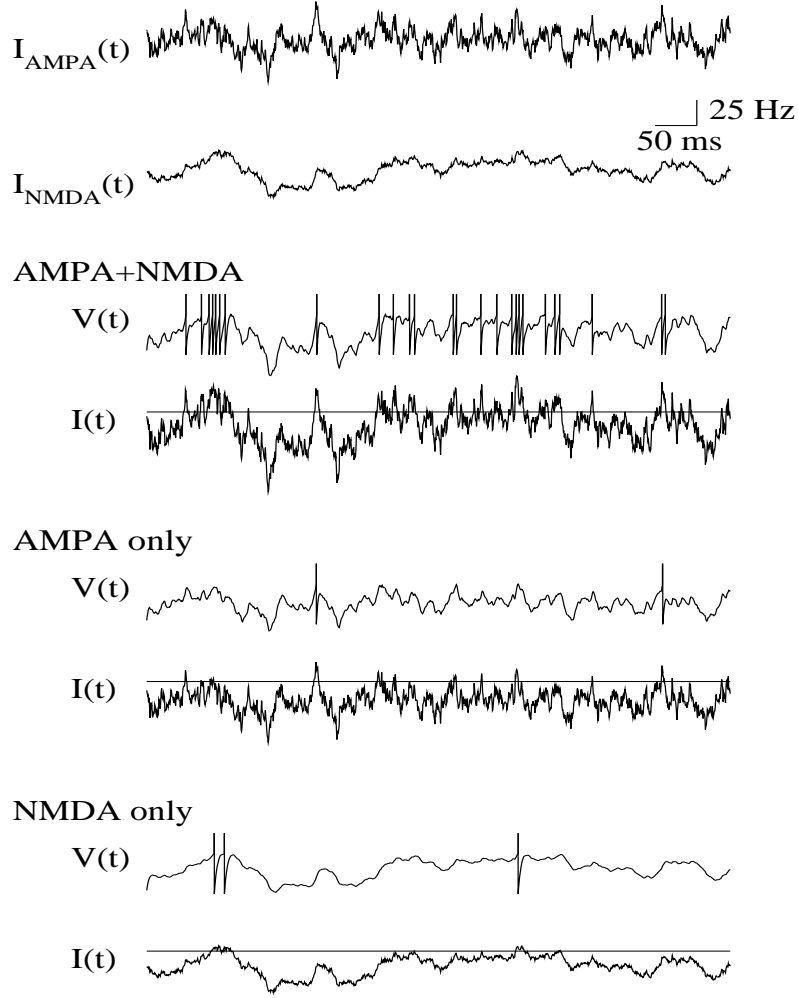


Fig. 1. Simulated membrane potential and *AMPA* and *NMDA* synaptic currents traces (eqs. (1-3)). All traces last for one second. The top two traces are the *AMPA* and *NMDA* synaptic currents obtained by filtering the same signal (Gaussian white noise) with the corresponding synaptic time constants: $\tau_{AMPA} = 5ms$ and $\tau_{NMDA} = 100ms$. Pairs of membrane potentials and synaptic currents are then showed for three different cases: 1) *AMPA + NMDA*: both *AMPA* and *NMDA* currents are present; 2) *AMPA*: only the *AMPA* current is present; and 3) *NMDA*: only the *NMDA* current passes through the synapse. The straight lines in the current traces are the threshold current I_{min} . For the three cases, the mean current is $\mu = 160Hz$. In case 1) $\sigma_{AMPA}^2 = 1Hz$ and $\sigma_{NMDA}^2 = 20Hz$, while in 2) the second variance is zero and in 3) the first one is zero. Neuronal parameters are $\tau_m = 5ms$, $H = 0.8$ and $\Theta = 1$ (without units). With this choice the neuron is in the subthreshold regime ($\mu\tau_m < \Theta$).

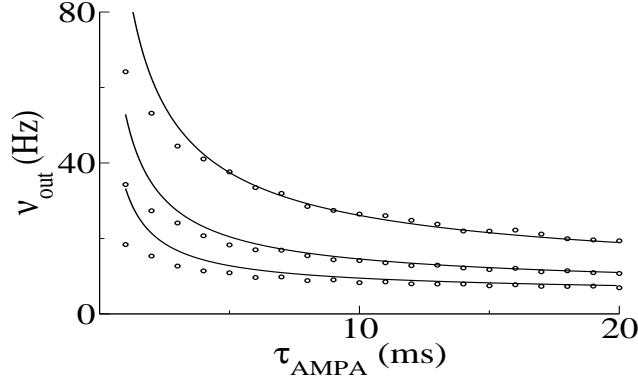


Fig. 2. Simulated (circles) and predicted (full curves) mean firing rates as a function of τ_{AMPA} for $\sigma_{AMPA}^2 = 2, 1$ and $0.5 Hz$ (from top to bottom). The parameters of the NMDA channel are kept fixed at $\tau_{NMDA} = 100ms$ and $\sigma_{NMDA}^2 = 20Hz$. The other parameters are as in Fig. (1).

3 Results

To illustrate how the behavior of the neuron depends on the nature of their synapses, we have plotted in Fig. (1) the voltage traces when the neuron receives 1) a sum of AMPA and NMDA synaptic currents, 2) only AMPA current, and 3) only NMDA input. The comparison is done at a fixed mean current. The AMPA and NMDA currents have been generated using eqs. (1-3) (top two traces). When the neuron integrates both AMPA and NMDA currents, there is a big chance of evoking action potentials when the total current $I(t)$ is above the threshold level $I_{min} = \Theta/\tau_m$. Remind that if, otherwise, $I(t) < I_{min}$, spikes cannot be evoked. We want to determine whether this “threshold effect” is due to either the AMPA or the NMDA filters, or whether it arises as a cooperative effect derived from the coexistence of both filters. To this end we have plotted the voltage responses when an AMPA current is injected with no additional NMDA current, and when an NMDA current is injected in the absence of AMPA current. With only AMPA, the threshold effect is not present: although $I(t)$ exceeds I_{min} several times, action potentials are sparse. However, with only NMDA current, the neuron fires if and only if $I(t) = I_{NMDA}(t)$ is above I_{min} . These results show that the detection behavior is only present when strong enough NMDA synapses drive the neuron. The reason for this behavior is that NMDA synapses are slow filters, and whenever a large fluctuation exists, it survives for a time long enough to produce action potentials (1). It has been shown that the NMDA/AMPA ratio of post-synaptic current amplitudes in cortex is ~ 0.3 (4; 5), which corresponds to a ratio of $\sigma_{NMDA}^2/\sigma_{AMPA}^2 \sim 36$ for Poisson spike trains. The threshold effect is present for this and close values of the ratio. Much smaller ratios give however behaviors similar to those obtained with only AMPA filters. The behavior we have observed seems to be agree in part by Fig. (3 C) of reference (6). There it is shown that, for a cortical neuron recorded *in vitro* with AMPA and NMDA

injected currents, action potentials are evoked mainly when the fluctuations in the NMDA current are large and positive, similarly to what we have obtained.

The mean firing rate given by this formula is compared with simulation results in Fig. (2). Notice that the prediction is excellent for $\tau_{AMPA} > \tau_m = 5ms$, but it is also in good qualitative agreement with the simulated data for $\tau_{AMPA} < \tau_m$.

4 Conclusions

We have shown that simple model neurons with the NMDA/AMPA abundances found in thalamocortical (4) and cortical synapses (5) only fire when particular fluctuations in their input current occur. As our results show, this behavior is absent when the neuron have only AMPA synapses or when the abundance of NMDA is low. We suggest that NMDA filters are crucial in shaping the response of cortical neurons and provide them with particular signal detection capabilities.

References

- [1] R. Moreno-Bote and N. Parga. The role of synaptic filtering on the firing response of simple model neurons. *Physical Review Letters*, 92(2) 028102, 2004
- [2] MF Bear, BW Connors and MA Paradiso. *Neuroscience: Exploring the Brain*. Wiliams & Wilkins, Baltimore, 1996.
- [3] A. Destexhe, M. Rudolph, J. M. Fellous and T. J. Sejnowski. Fluctuating synaptic conductances recreate in vivo-like activity in neocortical neurons. *Neuroscience*, 107:13–24, 2001.
- [4] M.C. Crair and R.C. Malenka. A critical period for long-term potentiation at thalamocortical synapses. *Nature*, 375:325–328, 1995.
- [5] C.I.O Myne, K. Sugino, G.G. Turrigiano and B. Nelson. The NMDA-to-AMPA ratio at synapses onto layer 2/3 pyramidal neurons conserved across prefrontal and visual cortices. *J. Neurophysiol.*, 90:771–79, 2003.
- [6] A. Harsch and H. P. C. Robinson. Postsynaptic variability of firing in rat cortical neurons: the roles of input synchronization and synaptic NMDA receptor conductance. *J. of Neurosc.*, 20(16):6181–92, 2000.
- [7] Ö. Bernander, R. J. Douglas, K. A. Martin, and C. Koch. Synaptic background activity influences spatiotemporal integration in single pyramidal cells. *Proc. Natl. Acad. Sci. USA*, 88:11569–11573, 1991.
- [8] H. C. Tuckwell. *Introduction to theoretical neuroscience. Vol. 1 and 2*. Cambridge UP, Cambridge UK, 1988.

- [9] H. Risken. *The Fokker-Planck equation*. 2nd Ed. Springer-Verlag, Berlin, 1989.