



# Multi-channel shot noise and characterization of cortical network activity

Michael Rudolph\*, Alain Destexhe

*Unité de Neurosciences Intégratives et Computationnelles, CNRS, UPR-2191, Bat. 33, Avenue de la Terrasse 1, 91198 Gif-sur-Yvette, France*

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## Abstract

Neurons in cerebral cortex are characterized by a stochastic subthreshold membrane potential ( $V_m$ ) activity, which originates from the ongoing and irregular activity of neurons in the cortical network. Here, we propose a way of characterizing this network activity by using the notion of shot noise applied to pulse-based kinetic models of synaptic conductances. We link the statistical characterization of synaptic conductances in terms of their mean and variance to the activity in the network, in particular the average firing rate of presynaptic neurons and their temporal correlation, thus providing a possible method for characterizing cortical network activity from intracellularly recorded  $V_m$  activity.

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## 1. Introduction

Neurons are subject to many different sources of noise, which may significantly alter their integrative properties [4]. Because of a remarkably dense connectivity [1] and high sustained firing rates [11], synaptic noise is particularly prominent in cerebral cortex. Recently, a model of synaptic noise was proposed based on random-walk processes [3,9]. Although such an effective stochastic representation allows to characterize

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\*Corresponding author. Tel.: +33 169 824177; fax: +33 169 823427.

*E-mail address:* [Michael.Rudolph@iaf.cnrs-gif.fr](mailto:Michael.Rudolph@iaf.cnrs-gif.fr) (M. Rudolph).

synaptic noise in terms of the mean and variance of the total synaptic conductance [10], information about the firing statistics of the presynaptic neurons and, hence, information about the cortical network activity cannot be directly deduced. Here, the notion of shot noise stochastic processes [7] provides a possible solution.

Shot noise processes describe the output of a dynamical system characterized by a quantal response function activated by a sequence of singular impulses occurring at random times [6]. By extending the notion of shot noise to multiple input channels, we will relate the statistical characterization of the total membrane conductance caused by the barrage of synaptic inputs with the statistical properties of the presynaptic activity. The application of this paradigm could provide a method to characterize cortical network activity, in particular correlations in populations of neurons, from intracellular recordings.

## 2. Methods

We considered a single-compartment model described by a passive membrane equation, in which the resulting total synaptic current stemming from  $N$  synaptic terminals was described by  $I_{\text{syn}}(t) = \sum_{n=1}^N g_0 r_n(t)(V(t) - E_e)$ , where  $g_0$  denotes the quantal conductance for each channel.  $r_n(t)$  represent the fraction of postsynaptic receptors in the open state at time  $t$  for each individual synapse. It was described by a pulse-based 2-state kinetic equation [2], for which the time course of the conductance can be solved analytically, yielding a quantal response function  $h(t)$  with exponential rise and decay. Synaptic models for excitatory and inhibitory synapses, modelled by  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic (AMPA) and  $\gamma$ -aminobutyric acid (GABA) postsynaptic receptors [2], were investigated. To simulate synaptic background activity, all synapses were activated randomly according to Poisson processes with mean rate  $\lambda$ . A (temporal) correlation  $c$  among the multiple synaptic input channels was introduced using a “distributed generator algorithm” [8]. Here, at each integration time step,  $N_0 = N + \sqrt{c}(1 - N)$  Poisson-distributed events were generated and randomly distributed among the  $N$  synaptic channels, leading to a redundancy for  $N_0 < N$  ( $0 \leq c < 1$ ).

The application of the presented methods was tested by using a passive multi-compartment model based on a morphologically reconstructed neocortical pyramidal neuron from layer 6 of cat parietal cortex whose response properties matched those obtained in intracellular recordings (for a review see [4]). In order to assess the total synaptic conductances (their mean and standard deviation), an “ideal” voltage clamp was simulated using a somatic electrode [3]. Numerical simulations were performed with NEURON [5].

## 3. Results

Campbell’s theorem [7] gives explicit expressions for the mean and variance of single-channel Poisson-driven shot noise process with integrable quantal response

functions  $h(t)$ . A prerequisite for the applicability of Campbell's theorem is the additive nature of the quantal process in question. This is not true for the 2-state kinetic process considered here, where the change in the fraction of channels in the open state  $r(t)$  at a new release depends on the actual value of  $r(t)$  and, thus, on the release history. However, an additive behaviour is approached for multiple synaptic channels with low release rates  $\lambda$  and small effective time constants  $\ll 1/\lambda$  at each channel. As our simulations show, these conditions are, in general, met by biophysically realistic models of AMPA and GABAergic synapses.

Numerical simulations of multi-channel shot noise processes show that changes in  $\lambda$  lead to proportional changes in the mean and variance of the system's output (Figs. 1A and B). On the other hand, changes in  $c$  without change in the channel rate do not impact on the mean but alter the variance of the resulting output in a nonlinear fashion (Figs. 1B and C). This behaviour can be seen in the corresponding amplitude distributions  $\rho(g)$  (Fig. 1D). Furthermore, a dependence on both  $c$  and  $\lambda$  was also

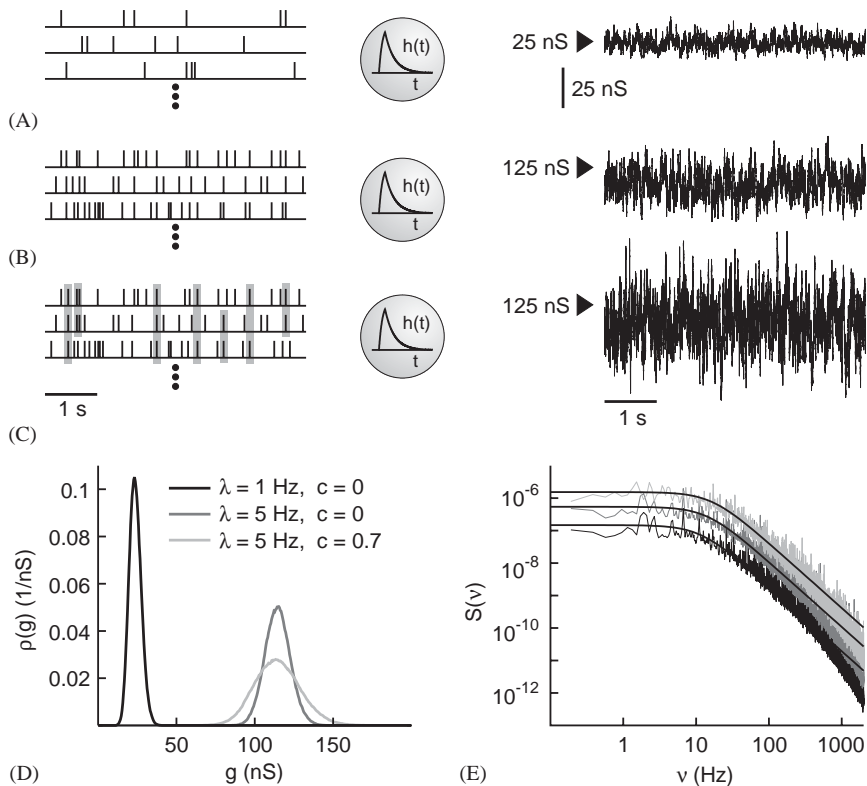


Fig. 1. Changes in the channel frequency lead to proportional changes in the mean and variance of the system's output (compare A and B; A:  $\lambda = 1$  Hz; B:  $\lambda = 5$  Hz;  $c = 0.0$ ), whereas changes in the temporal correlation between individual channels impact only on the variance (compare B and C; B:  $c = 0.0$ ; C:  $c = 0.7$ ;  $\lambda = 5$  Hz). The amplitude distribution  $\rho(g)$  of synaptic conductances (D) and power spectral density (E, grey; black: Lorentzian fit) showed also a dependence on both  $c$  and  $\lambda$ .

found for the power-spectral density  $S(v)$  of the resulting synaptic conductance, whereas the Lorentzian behaviour of the spectral density remained unaltered at lower frequencies (Fig. 1E).

By extending Campbell's theorem to the case of multiple temporally correlated synaptic input channels, we obtained analytic expressions for the mean and variance of the total synaptic conductance:

$$\bar{g} = C_1 \lambda N, \quad \sigma_g^2 = C_2 \lambda N \left( 1 + \frac{N-1}{N + \sqrt{c}(1-N)} \right). \quad (1)$$

Here,  $C_1$  and  $C_2$  are parameters which depend on the synaptic kinetics only. In agreement with numerical simulations, the mean conductance was found to be linearly dependent on  $\lambda$ , but independent on the correlation  $c$  (Figs. 2A and B). The standard deviation  $\sigma_g$ , while being linearly dependent on  $\sqrt{\lambda}$  (Fig. 2C), showed a more complex dependence on  $c$  and the number of input channels  $N$ , with  $\sigma_g^2 \sim N + (N(N-1))/(N + \sqrt{c}(1-N))$  (Fig. 2D). In all cases, the error between numerical and analytic results was small in a wide parameter range, suggesting that the shot noise approach yields a valid approximation for characterizing the effect of multiple synaptic inputs following 2-state kinetic schemes. Note that for  $c = 0$  and large  $N$  the system is not equivalent to a shot noise process of rate  $\lambda N$ , as predicted by Campbell's theorem, but of rate  $2\lambda N$  due to the used shuffling algorithm.

The monotonic dependence of the mean and variance of the total conductance on the channel firing rate and temporal correlation among multiple channels allows to

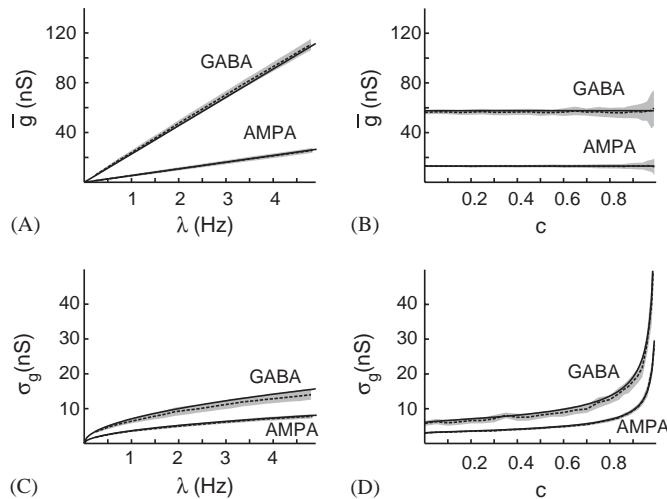


Fig. 2. Dependence of the mean  $\bar{g}$  and standard deviation  $\sigma_g$  of the total synaptic conductances on the frequency  $\lambda$  and correlation  $c$  for AMPA and GABAergic synapses (for kinetic model see Methods). Theoretical values (Eqs. (1); black solid) are compared with numerical results (black dashed: mean value; grey: standard deviation around mean). Parameters values:  $N = 4472$  (AMPA),  $N = 3801$  (GABA); A, C:  $c = 0.7$ ; B, D:  $\lambda = 2.16$  Hz (AMPA),  $\lambda = 2.4$  Hz (GABA).

estimate  $\lambda$  and  $c$  from the sole knowledge of  $\bar{g}$  and  $\sigma_g^2$ :

$$\lambda = \frac{\bar{g}}{C_1 N}, \quad c = \frac{(C_2 \bar{g}(2N - 1) - C_1 N \sigma_g^2)^2}{(N - 1)^2 (C_2 \bar{g} - C_1 \sigma_g^2)^2}. \quad (2)$$

We tested this paradigm in numerical simulations of compartmental models, in which the mean and variance of synaptic conductances were obtained using voltage-clamp [3] or current-clamp [10] protocols. For single-compartment model, the estimations matched perfectly the input values (Figs. 3A and B). In multi-compartment models, however, the method yielded an underestimation of  $\lambda$  and  $c$ , especially for small  $c$  (Figs. 3C and D). Our results show that this effect is related to the filtering effect of the spatially extended dendrites.

#### 4. Conclusions

We investigated the relation between the discharge activity at synaptic terminals, described by pulse-based 2-state kinetic models, and the resulting total conductance

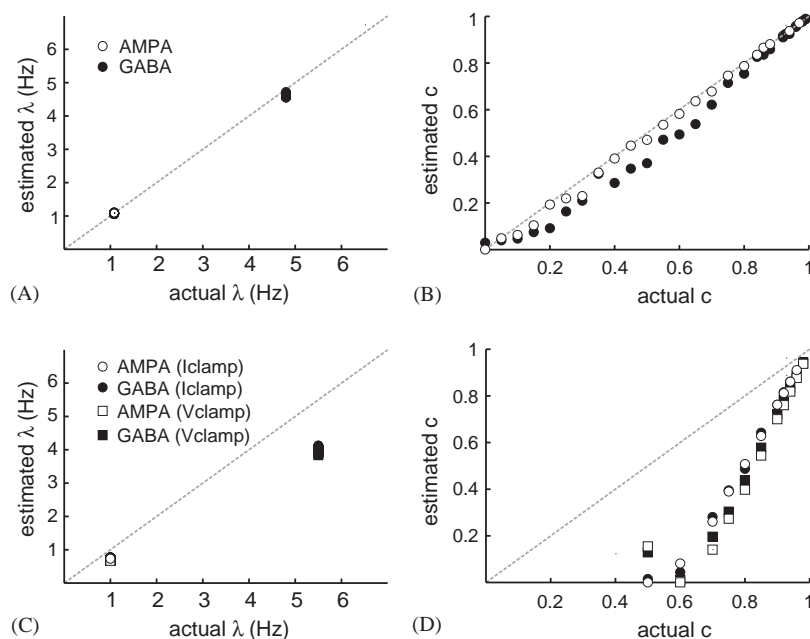


Fig. 3. Estimation of the rate  $\lambda$  and correlation  $c$  from the characterization of the total conductance distribution for different levels of background activity (obtained by change in  $c$  for fixed  $\lambda$ ). Estimated values are shown as functions of the actual values used for the simulations. For the single-compartment model (A, B), excellent estimates were obtained, whereas dendritic filtering in multi-compartment models, for which conductance distributions were obtained by voltage-clamp and current-clamp protocols, gave an underestimation of  $\lambda$  and  $c$  (C, D).

in the framework of shot noise. Although at single terminals the conductance contribution are state-dependent and, thus, not additive, this approach yielded analytic expressions for the mean and variance of the total conductance which were in excellent agreement with numerical simulations for the realistic case of multiple synaptic channels and low channel release rates.

The monotonic dependencies obtained allow us to estimate the firing rate and temporal correlation of multiple synaptic inputs from experimentally obtained distributions. This approach, therefore, could yield a method to characterize statistical properties of network activity from single-neuron activity. Of particular interest here are temporal correlations in the discharge of a large number of neurons, which, although of prime physiological importance, still remains an uncharacterized parameter. The applicability of this paradigm will be the subject of future investigations (research supported by CNRS and HFSP).

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