

## Supplemental Methods

### Mathematical model of the “bursting” spontaneous activity

We employed a minimal “rate model” (Dayan & Abbott, 2001; Amit & Tsodyks, 1991; Wilson & Cowan, 1972) to describe the mean firing rate of a homogenous neuronal population, recurrently connected by short-term depressing synapses and including neuronal spike-frequency adaptation. Recurrent excitation (i.e. a positive feedback) determines the tendency of the network to ignite epochs of sustained firing, while intrinsic or synaptic refractoriness (i.e. a delayed negative feedback) terminate these epochs and determine the irregular “bursting” behavior (see Giugliano *et al.*, 2004 for a discussion).

The collective firing rate  $R$  of an ensemble of cultured neurons can be inferred from the knowledge of the single-cell stationary frequency-current response function  $R = \Phi(m_x, s_x^2)$ , extended to account for the response to input fluctuations and identified experimentally in Giugliano *et al.* (2004). As reviewed in La Camera *et al.* (2008),  $m_x$  and  $s_x^2$  approximately represent the time-varying mean and variance of the overall input synaptic current  $I_x$  to a generic unit of the network (Amit & Brunel, 1997). Although it neglects a precise biophysical account of neuronal excitability, such a description was shown to hold even in dynamical regimes (Köndgen *et al.*, 2008; La Camera *et al.*, 2004; see Giugliano *et al.* 2008 for a review).  $I_x$  results from presynaptic spiking activity, constituted of individual postsynaptic currents with an instantaneous rise time and exponential decay, mathematically described as  $g_x \exp(-t / \tau_x)$  for  $t > 0$ , where  $g_x$  is the peak postsynaptic current.

In the diffusion approximation (Lánský & Sato, 1999),  $I_x$  is equivalent to a continuous random walk with gaussian amplitude and correlation-length  $\tau_x$ . Then, mean  $m_x$  and variance  $s_x^2$  of such a stochastic process evolve according to a first-order dynamics,  $\tau_x dm_x / dt = -m_x + m_0$ , analogously for  $s_x^2$  replacing  $\tau_x$  by  $\tau_x / 2$  (Gardiner, 1985).

The steady-state values  $m_0$  and  $s_0$  arise from the statistics of the presynaptic activity and account for both external  $m_{ext}$ ,  $s_{ext}$  (background) inputs and recurrent synaptic contributions (Amit & Brunel, 1997; Rauch *et al.*, 2003):  $m_0 = g_x N C R \tau_x + m_{ext}$  and  $s_0^2 = g_x^2 N C R \tau_x / 2 + s_{ext}^2$ . In this context,  $m_{ext}$  and  $s_{ext}$  refers to spontaneous synaptic release and other sources of cellular randomness (see Giugliano *et al.*, 2004

and references therein).  $N$  and  $C$  indicate the number of neurons constituting the network and their probability of pair-wise (random) connectivity, respectively. The impact of single-cell spike-frequency adaptation was introduced as in La Camera *et al.* (2004),  $R = \Phi(m_x - I_{ahp}, s_x^2)$ , with  $I_{ahp}$  being an activity-dependent after-hyperpolarizing current that evolves in time as  $\tau_{ahp} dI_{ahp} / dt = I_{ahp} + \alpha R$ . A similar model was studied in Giugliano *et al.*, (2004), similarly assuming  $I_{ahp}$  to fluctuate slowly compared to  $I_x$  and therefore mainly contributing to  $m_x$  and not to  $s_x^2$  (La Camera *et al.*, 2004). Short-term synaptic depression and facilitation (Markram *et al.*, 1999) were also introduced in the model. Similarly to  $I_{ahp}$ , short-term plasticities were dominated by slow fluctuations and approximated by their mean-field description (Tsodyks *et al.*, 1998).  $g_x$  was therefore a function of both time and presynaptic activity  $R$ , as  $g_x = g_0 u x / U$ , with  $dx/dt = (1 - x) / D - u x R$  and  $du/dt = (U - u) / F + U(1 - u) R$ .

Finally, finite-size effects have been introduced by replacing  $R$  with  $R + \eta (R / N)^{0.5}$ , where  $N$  is the size of the network and  $\eta$  a sequence of normally-distributed pseudo-random numbers with unitary variance. This introduces coherent random fluctuations in the network model, accounting for the divergence from the theoretical (mean-field) approximation that strictly holds in the limit of a infinitely large networks (Mattia & Del Giudice, 2002; see also Holcman & Tsodyks, 2006).

Summarizing, the model is constituted of five ordinary differential equations (S.2, S.3, S.5, S.8 and S.9), and fully described as:

$$R = \Phi(m_x - I_{ahp}, s_x^2); \quad R \rightarrow R + \eta (R / N)^{0.5} \quad (\text{S.1})$$

$$\tau_{ahp} dI_{ahp} / dt = I_{ahp} + \alpha R \quad (\text{S.2})$$

$$\tau_x dm_x / dt = -m_x + m_0 \quad (\text{S.3})$$

$$m_0 = g_x N C R \tau_x + m_{ext} \quad (\text{S.4})$$

$$0.5 \tau_x ds_x^2 / dt = -s_x^2 + s_0^2 \quad (\text{S.5})$$

$$s_0^2 = g_x^2 N C R \tau_x / 2 + s_{ext}^2 \quad (\text{S.6})$$

$$g_x = g_0 u x / U \quad (\text{S.7})$$

$$dx/dt = (1 - x) / D - u x R \quad (\text{S.8})$$

$$du/dt = (U - u) / F + U (1 - u) R \quad (\text{S.9})$$

The profile of  $\Phi(\cdot)$  was chosen as in Giugliano *et al.* (2004) – parameters of Table 1. We considered the rate-model (eqs. S.1-S.9) to account for the electrical activity in a small network, composed of 100 neurons (i.e.  $N = 100$ ) randomly connected with a probability of 25% – 56% (i.e.  $C = 0.25 - 0.56$ ). Synapses were short-term depressing (i.e. recovery from depression  $D = 255$  ms, instantaneous recover from facilitation  $F = 1$  ms) with an effective probability of release in the range 10% – 100% (i.e.  $U = 0.1 - 1$ ). The remaining parameters were chosen as  $\alpha = 6.23$  pA s,  $\tau_{ahp} = 700$  ms,  $\tau_x = 10$  ms, and  $g_0$  in the range 5 – 20 pA.

## Supplemental References

Amit DJ, Brunel N (1997) Model of global spontaneous activity and local structured activity during delay periods in the cerebral cortex. *Cereb Cortex* **7**(3):237-52.

Amit DJ, Tsodyks MV (1991) Quantitative study of attractor neural networks retrieving at low spike rates, *Network* **2**:259–94.

Gardiner CW (1985) Handbook of stochastic methods. Springer.

Holcman D, Tsodyks MV (2006) The Emergence of Up and Down States in Cortical Networks, *PLOS Comp Biol* **2**:e23.

Köndgen H, Geisler C, Fusi S, Wang X-J, Lüscher H-R, Giugliano M (2008). The dynamical response properties of neocortical neurons to temporally modulated noisy inputs *in vitro*. *Cereb Cortex* **18**(9):2086-97.

La Camera G, Giugliano M, Senn W, Fusi S (2008) The response of cortical neurons to *in vivo*-like input current: I. Noisy inputs with stationary statistics. *Biol Cybern*, special issue (in press).

La Camera G, Rauch A, Lüscher H-R, Senn W, Fusi S (2004) Minimal models of adapted neuronal response to *in vivo*-like input currents. *Neural Comp* **16**(10):2101-24.

Lánský P, Sato S (1999) The stochastic diffusion models of nerve membrane depolarization and interspike interval generation. *J Peripher Nerv Syst* **4**(1):27-42.

Markram H, Wang Y, Tsodyks MV (1999) Differential signaling via the same axon from neocortical layer 5 pyramidal neurons, *Proc Natl Acad Sci USA* **95**:5323–8.

Mattia M, Del Giudice P (2002) Population dynamics of interacting spiking neurons. *Phys Rev E* **66**(5):051917.

Rauch A, La Camera G, Lüscher H-R, Senn W, Fusi S (2003) Neocortical pyramidal cells respond as integrate-and-fire neurons to *in vivo*-like input currents, *J Neurophysiol* **90**:1598–612.

Tsodyks MV, Pawelzik K, Markram H (1998). Neural networks with dynamic synapses, *Neural Comp* **10**:821–35.

Wilson HR, Cowan JD (1972) Excitatory and inhibitory interactions in localized populations of model neurons, *Biophys J* **12**:1–24.