

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 refractoryness (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 τ_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 τ_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 η 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

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