EPJ B
Condensed Matter and Complex Systems
www.epj.org

Eur. Phys. J. B **61**, 499–503 (2008) DOI: 10.1140/epjb/e2008-00095-y

Impact of network activity on noise delayed spiking for a Hodgkin-Huxley model

M. Ozer and L.J. Graham

EDP SCIENCES
Società Italiana di Fisica
Springer

Eur. Phys. J. B **61**, 499–503 (2008)
DOI: 10.1140/epjb/e2008-00095-y

THE EUROPEAN PHYSICAL JOURNAL B

Impact of network activity on noise delayed spiking for a Hodgkin-Huxley model

M. Ozer[1,2,a] and L.J. Graham[2]

[1] Zonguldak Karaelmas University, Engineering Faculty, Department of Electrical and Electronics Engineering, 67100 Zonguldak, Turkey
[2] Laboratory of Neurophysics and Physiology, UMR 8119 CNRS, Université Paris Descartes, 45 rue des Saint-Peres, 75006 Paris, France

Received 19 september 2007 / Received in final form 28 January 2008
Published online 7 March 2008 –

Abstract. In a Hodgkin-Huxley neuron model driven just above threshold, external noise can increase both jitter and latency of the first spike, an effect called "noise delayed decay" (NDD). This phenomenon is important when considering how neuronal information is represented, thus by the precise timing of spikes or by their rate. We examine how NDD can be affected by network activity by varying the model's membrane time constant, τ_m. We show that NDD is significant for small τ_m or high network activity, and decreases for large τ_m, or low network activity. Our results suggest that for inputs just above threshold, the activity of the network constrains the neuronal coding strategy due to, at least in part, the NDD effect.

PACS. 05.40.-a Fluctuation phenomena, random processes, noise, and Brownian motion – 87.10.+e General theory and mathematical aspects – 87.16.-b Subcellular structure and processes

1 Introduction

Neurons transmit information about their inputs by transforming them into the spike trains, and the question of which coding scheme is represented by these trains is much debated. In principle, information in spike trains may be in the average rate of firing [1,2] or in the timing of spikes [3,4]. However, a temporal coding scheme can make more efficient use of the capacity of neuronal connection than those that rely simply on the firing rate [5]. Experimental studies have indicated a significant role for the precise timing of the spikes in neuronal coding [6,7]. Reinagel and Reid [8] also indicated that the precise spike times contain more information about the input than firing rate alone based on the information-theoretical analyses of the neuronal spike trains in the lateral geniculate nucleus.

In the context of temporal coding, Pankratova et al. [9] recently analyzed the influence of external noise on the timing of the first spike with a Hodgkin-Huxley (H-H) neuronal model driven by a noisy suprathreshold periodic forcing, and showed that although the noise increases the first spike latency and thus delays signal detection, a proper choice of the frequency for the suprathreshold periodic forcing could minimize this effect. They also plotted the dependence of the mean latency on the noise for different values of the driving frequencies, obtaining a non-monotonic behavior at the frequency boundaries of the suprathreshold spiking regime. At these boundaries, and at small noise amplitudes, the mean latency is mainly insensitive to the noise. As the noise increases past a critical value, however, a further increase strongly increases the mean latency, thus imparting a significant delay in the stimulus detection by the neuron. After the latency reached a maximum value, a further increase in the noise caused a decrease of the latency. The authors attributed the noise-dependent increase of the latency to a phenomenon called noise delayed decay (NDD), which is described in potential systems [10], and suggested that their results demonstrated the first example of NDD in excitable systems.

Given the significant impact of NDD on first-spike timing, and thus its importance for neuronal coding, our aim here is to extend this analysis to the in vivo setting of an active network. Neurons in vivo are embedded in a network of active cells, where each neuron receives thousands of synaptic inputs [11]. This massive input can significantly modify the integrative capabilities of the neuron, most fundamentally by a decrease in the membrane time constant (τ_m) due to an increase in the average membrane conductance. In this context, Bernander et al. [12] studied the overall effect of the synaptic input on the temporal integrative properties of individual cortical pyramidal cells,

[a] e-mail: mahmutozer2002@yahoo.com

and found that realistic values of synaptic input can decrease the effective time constant by a factor of ten. Rapp et al. [13] studied the same problem by considering parallel fiber background activity on the cable properties of cerebellar Purkinje cell and arrived at similar conclusions. In the present paper, we studied how the NDD effect changes with the network activity, by changing the time constant of the neuron model.

2 Model and methods

We use the same model and the parameters by Pankratova et al. [9], where the time evolution of the membrane potential for the Hodgkin-Huxley model [14] is given as follows:

$$C_m\frac{d\nu}{dt}+G_{\rm Na}(\nu-\nu_{\rm Na})+G_{\rm K}(\nu-\nu_{\rm K}) + G_L(\nu-\nu_L)=A\sin(2\pi ft)+\xi(t) \quad (1)$$

where ν denotes the deviation of the membrane potential from its equilibrium value in units of mV, and $C_m = 1\ \mu$F cm^{-2} is the membrane capacity. $G_{\rm Na}$, $G_{\rm K}$ and G_L represent sodium, potassium and leakage conductances, respectively. $\nu_{\rm Na} = 115$ mV, $\nu_{\rm K} = -12$ mV and $\nu_L = 10.6$ mV are the reversal potentials for the sodium, potassium and leakage channels, respectively. A denotes the amplitude of the sinusoidal forcing current, which is set to 4 μA/cm^2 as by Pankratova et al. [9]. $\xi(t)$ represents a white Gaussian noise with zero mean and an autocorrelation function $\langle\xi(t)\xi(t+\tau)\rangle = D\delta(t)$. In the model, the leakage conductance is assumed to be constant, G_L, and determines the average or resting membrane time constant by the relation $\tau_m = C_m/G_L$, whereas the sodium and potassium conductances dynamically change according to the following equation:

$$G_{\rm Na}=g_{\rm Na}^{\max}m^3h, \quad G_{\rm K}=g_{\rm K}^{\max}n^4 \quad (2)$$

where $g_{\rm Na}^{\max} = 120$ mS cm^{-2} and $g_{\rm K}^{\max} = 36$ mS cm^{-2} are the maximal sodium and potassium conductances, respectively. m and h denotes the activation and inactivation gating variables for the sodium channel, respectively, and the potassium channel includes an activation gating variable, n. In the H-H model, activation and inactivation gating variables change over time in response to the membrane potential with first-order differential equations as follows [14]:

$$\frac{dm}{dt}=\alpha_m(1-m)-\beta_m m, \quad (3a)$$

$$\frac{dh}{dt}=\alpha_h(1-h)-\beta_h h, \quad (3b)$$

$$\frac{dn}{dt}=\alpha_n(1-n)-\beta_n n, \quad (3c)$$

where α and β are the voltage-dependent rate functions defined in units of (ms) as follows [14]:

$$\alpha_m=0.1\frac{25-\nu}{\exp[(25-\nu)/10]-1}, \beta_m=4\exp(-\nu/18), \quad (4a)$$

$$\alpha_h=0.07\exp(-\nu/20), \beta_h=\frac{1}{1+\exp[(30-\nu)/10]}, \quad (4b)$$

$$\alpha_n=0.01\frac{10-\nu}{\exp[(10-\nu)/10]-1}, \beta_n=0.125\exp(-\nu/18). \quad (4c)$$

We define the latency to the first spike as the time, relative to stimulus start time, of the first upward crossing of the membrane potential past a fixed detection threshold value, taken here as 20 mV, as by Pankratova et al. [9]. We obtain the mean latency of an ensemble of first spikes by averaging their latencies overrealizations as follows:

$$\langle t\rangle=\frac{1}{N}\sum_{i=1}^{N}t_i \quad (5)$$

where t_i is the response time for ith realization. We also consider the standard deviation of the latencies, or temporal jitter, as follows:

$$\sigma_L=\sqrt{\langle t^2\rangle-\langle t\rangle^2} \quad (6)$$

where$\langle t^2\rangle$represents the mean squared latency.

In order to calculate both the mean latency and jitter, we averaged the first spike latencies over $N = 3\ 000$ realizations. In the simulations, we assumed that the initial conditions for each realization are the same as in [9], namely that the neuron is in its stable resting state (external current set to 0).

3 Results

The firing current threshold of a Hodgkin-Huxley neuron subject to periodic forcing changes in a frequency-dependent manner for a fixed stimulus strength [9]. For a sinusoidal stimulus with an amplitude of 4 μA/cm^2, the model studied here displays a suprathreshold regime for a frequency range of 16–144 Hz [9]. Since the NDD effect is maximal at the frequency boundaries of the suprathreshold regime, we first reexamined the behaviour of the model at a stimulus frequency of 18 Hz, that is just above threshold, over a large range of the external noise, following Pankratova et al. [9] (Fig. 1). In the absence of noise, the model neuron fires the first-spike at 11 ms. We then computed the mean latency and jitter for different values of the external noise. As Pankratova et al. [9] showed, both the mean latency and jitter exhibit a non-monotonic behavior: increasing with the noise, reaching some maximum and then decreasing. When the noise strength is small, the mean latency values are close to the deterministic value, and the jitter is below 1 ms, indicating high temporal precision. As the noise strength increases, the

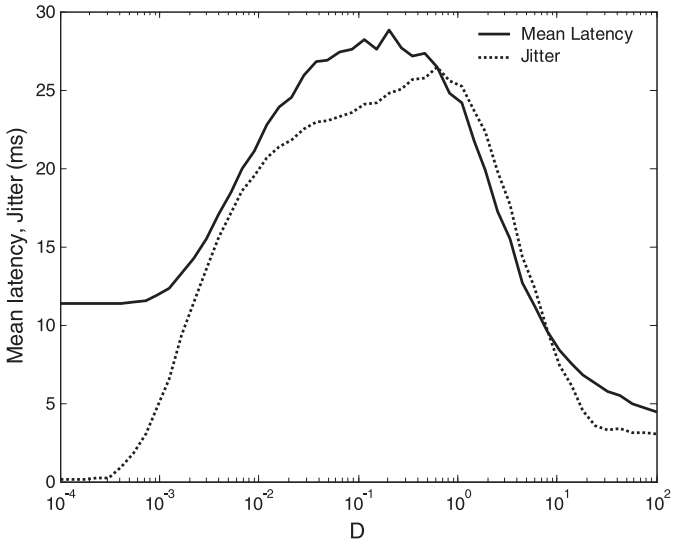

Fig. 1. The mean latency and jitter versus the noise intensity in response to the suprathreshold periodic stimulus with a frequency of 18 Hz and a magnitude of 4 μA/cm^2.

NDD effect strongly appears: Both the mean latency and jitter increase substantially, displaying a pronounced peak as a function of noise strength. Given that the ratio of the peak latency over the deterministic value is about 2.5, with a jitter of about 26 ms, the NDD effect can cause the neuron to fire with a very low temporal precision. After reaching some maximum for the mean latency and jitter, a further increase in the noise intensity decreases both. Although the mean latency eventually decreases to a value (around 4.5 ms) which is below the deterministic value (11 ms), the jitter saturates at a non-zero value (around 3 ms), indicating a significant distribution of the latency values even when the noise accelerates the overall response of the neuron.

We then investigated how the NDD effect might be influenced by network activity, by changing the time constant of the neuron model and measuring spike latencies to the same 18 Hz periodic forcing. The leakage conductance of the model, G_L, was set to values between 0.01–0.3 mS cm^{-2}, corresponding to a range of membrane time constants from 100 ms to 3.3 ms, consistent with experimentally measured values in neocortical pyramidal neurons [15–17]. We computed the normalized mean latency and jitter for five different values of the membrane time constant (Fig. 2; for comparison, the membrane time constant τ_m in [9] is 3.3 ms). We find that as the noise increases from small values, the mean latency remains constant, near the deterministic one, over a larger range of the noise intensity for larger values of τ_m (Fig. 2a). The jitter displays a similar behavior, being less dependent on the noise, and small, for larger membrane time constants, indicating that the model neuron fires the first-spike with higher precision in the absence of the synaptic input. Although for the larger values of τ_m (10–100 ms) high noise intensities increase mean spike latency, this occurs over a narrow range of the higher noise strength with a lower

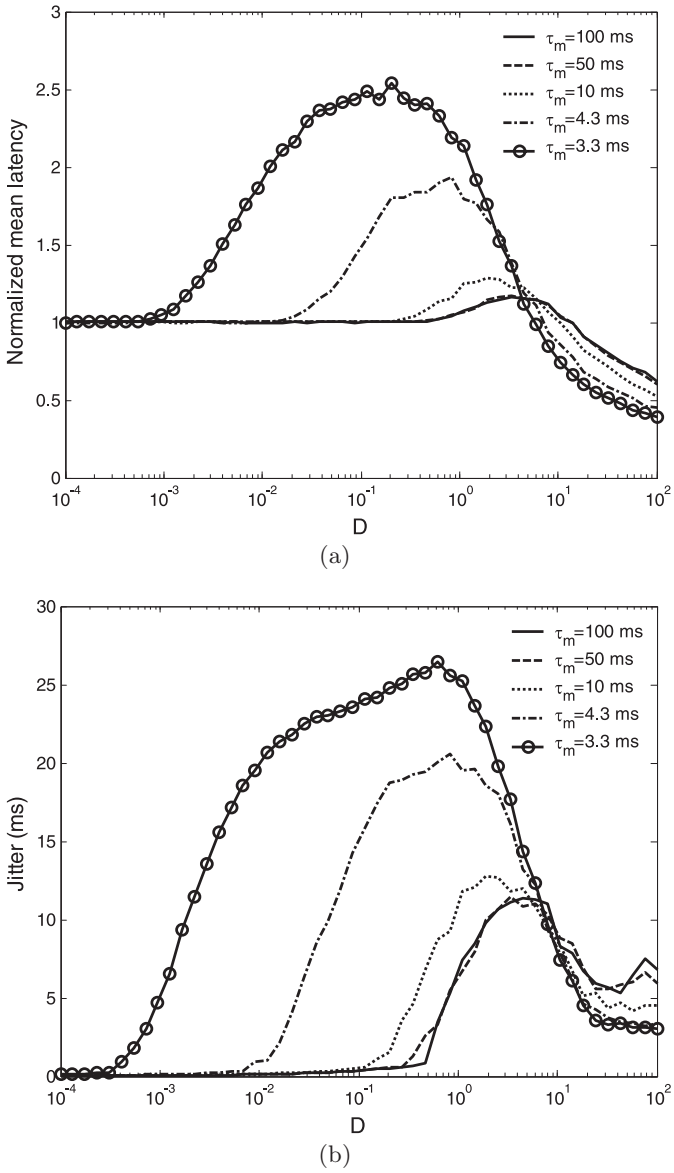

Fig. 2. The statistics of the latency for five different values of the time constant (f = 18 Hz): (a) the normalized mean latency versus the noise strength, (b) the jitter versus the noise strength.

peak (a smaller NDD effect), beyond which a further increase in the noise results in a decrease of the mean latency below the deterministic value. In addition, there is no qualitative difference in the latency versus noise for these larger time constants. We also observed that there is no almost a quantitative difference in the latency and its jitter versus noise for both time constants of 50 and 100 ms.

In contrast, when τ_m is smaller due to the overall synaptic activity, a significant NDD effect on the first-spike timing emerges. For small values of τ_m, a one millisecond decrease in τ_m strongly amplifies the NDD effect; increasing the maxima of the mean latency and jitter, and

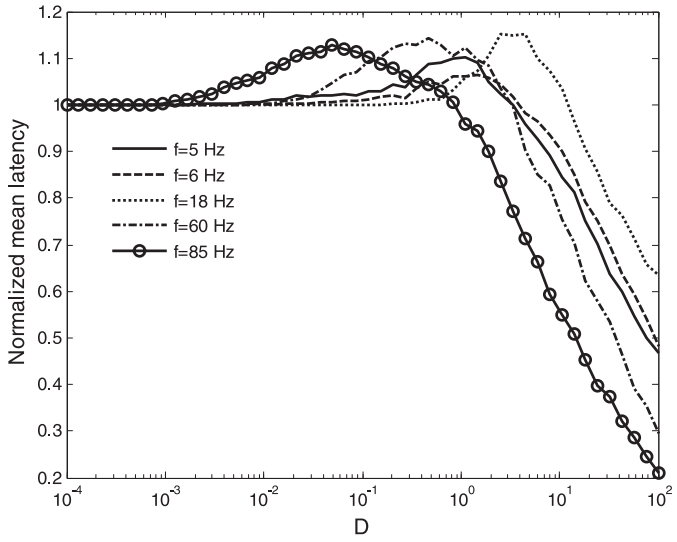

Fig. 3. The normalized mean latency versus the noise intensity in response of the neuron model with a time constant of 100 ms to the suprathreshold periodic stimulus of five different frequencies (5, 6, 18, 60 and 85 Hz). The frequencies of 5 and 6 Hz are just above the lower frequency threshold of 4 Hz, 18 Hz is well within the suprathreshold regime, and 60 and 85 Hz are close to the upper frequency threshold of 86 Hz.

decreasing the minimum noise intensity for which NDD is evident.

For the H-H model, an increase in the membrane time constant changes the frequency range of the suprathreshold periodic current threshold, shifting the lower boundary for firing toward a lower frequency. Thus, for a fixed input of some frequency and amplitude that is above threshold for a fast τ_m, a slower time constant results in that input being increasingly suprathreshold, which in turn is sufficient to decrease the NDD effect. To explore this relationship further, we then investigated how the membrane time constant per se affected NDD independently of a change in the current threshold, by adjusting the input frequency to bring it again to the just suprathreshold range for a slow membrane time constant of 100 ms. For this value of τ_m and the same input strength as before, the suprathreshold regime covers a frequency range of 4–86 Hz, as compared to 16–144 Hz when τ_m is 3.3 ms. We examined the NDD effect for suprathreshold frequencies near both the lower and upper boundaries (5, 6, 60 and 85 Hz), as well as for the now strongly suprathreshold frequency of 18 Hz, and we computed the normalized mean latency as a function of external noise as before (Fig. 3). With no noise, the neuron fires the first-spike at 22, 19, 12, 26 and 43 ms, corresponding to input frequencies of 5, 6, 18, 60 and 85 Hz, respectively. The mean latency remained near the deterministic value until over a narrow range of strong noise we observed a smaller increase in mean latency (a smaller NDD effect) and then a decrease in latency for even larger noise, similar to that found earlier for the larger values of τ_m with the 18 Hz input (Fig. 2a). Increasing the frequency toward the upper boundary (60 and 85 Hz) decreases the minimum noise strength for which the NDD effect is evident. However, we find that the peak value of the latency almost gets similar values for all frequencies regardless of their closeness to the current threshold. These results indicate that the NDD effect is not only dependent on the closeness of the input to threshold, but also on the membrane time constant, which serves as a scaling factor, such that the NDD effect is large when τ_m is small, and vice versa.

4 Discussion

We examine how the NDD effect of a H-H neuron subject to periodic forcing can be affected by network activity. The firing current threshold of a H-H neuron subject to a periodic forcing changes in a frequency-dependent manner [9], such that a stimulus with some fixed amplitude is suprathreshold within a limited frequency range. Stimuli just inside the lower and upper boundaries of that range are just above threshold, which is a requirement for the significant NDD effect. For an input near the lower boundary of the suprathreshold range, we considered the impact of different levels of network activity by varying τ_m. We also examined the system behavior for different input frequencies, near threshold and well suprathreshold, during low network activity, thus with a large value of τ_m. Our results illustrate how the overall activity of a neuronal network can alter the temporal integrative properties of the individual neurons in terms of the NDD effect of the first-spike timing. An increase in the time constant changes the frequency range of the suprathreshold current threshold, shifting it towards lower frequencies. Therefore, for a given input just above the lower suprathreshold boundary, an increase in the time constant causes disappearance of the NDD effect in part because the stimulus becomes increasingly suprathreshold (Fig. 2). We also showed, however, that a large membrane time constant decreases the NDD effect even when the input is kept near the thresholds (Fig. 3) defined by the lower and upper frequency boundaries of the suprathreshold regime. Therefore, in addition to the fact that the NDD effect only emerges near threshold, we suggest that the membrane time constant serves as a scaling factor by increasing or decreasing the NDD effect when it exists. When the membrane time constant is small, the neuron responds quickly to input fluctuations instead of temporally integrating them, whereas a longer time constant enables the cell to more strongly integrate the input. In this context, the NDD effect on first-spike timing depends on the higher sensitivity of the cell to noise when the time constant is low. As the time constant increases, the sensitivity of the cell decreases, and therefore the NDD effect decreases, even for just suprathreshold inputs. We conclude that the NDD effect on first-spike timing near the frequency boundaries of the suprathreshold spiking regime is a function of both the noise as well as the overall activity of the network, acting through the membrane time constant.

For an input whose frequency is just below the upper suprathreshold boundary, increasing the membrane time constant from a small value will also eliminate the NDD

effect as for inputs near the lower boundary, but for a different reason. Since an increase in the time constant shifts the entire suprathreshold regime toward lower frequencies, an input near the upper boundary for a fast membrane time constant will fall into the subthreshold regime for a slow time constant. Thus, in this case the NDD effect disappears simply because the input (with no noise) is no longer able to trigger spikes.

Robustness of spike timing to physiological noise is suggested as a prerequisite for a spike-timing as opposed to a spike-rate code [18]. Our results suggest that for a periodic forcing that is just above threshold, the NDD effect may limit the neuron to spike-rate coding when the membrane time constant is small. The NDD effect decreases either when the membrane time constant is large or if the input becomes strongly suprathreshold, suggesting operating regimes in which the neuron may also exploit a spike time code. Since the overall level of the synaptic input is the major determinant of the time constant [12], these results suggest in particular that the functional code used by neurons for inputs that are just suprathreshold may rely qualitatively on the network activity.

5 Conclusion

In a Hodgkin-Huxley neuron driven just above threshold, external noise can increase not only the jitter but also the latency of the first spike, an effect called "noise delayed decay" (NDD). We show that the NDD effect on the first-spike timing near the frequency boundaries of the suprathreshold spiking regime is not only a function of the noise, but also a function of the overall activity of the network as it modulates the membrane time constant of the cell.

The authors would like to thank to anonymous reviewers for their valuable comments. This work was supported by a grant from The Scientific and Technological Research Council of Turkey (TUBITAK), 219.01-880-5768 to Dr. Mahmut Ozer, and a HFSP grant (RGP0049/2002) and an Agence Nationale Recherche grant (FUNVISYNIN) to Dr. Lyle J. Graham.

References

1. E.D. Adrian, J. Physiol. (Lond.) **61**, 49 (1926)
2. A.P. Georgopoulos, A.B. Schwartz, R.E Keftner, Science **233**, 1416 (1986)
3. M. Abeles, *Corticonics: Neural Circuitry of the Cerebral Cortex* (Cambridge, Cambridge University Press, 1991)
4. M. Abeles, H. Bergman, E. Magalit, A. Vaadia, J. Neurophysiol. **70**, 1629 (1993)
5. F. Rieke, D. Warland, R. de Ruyter van Steveninck, W. Bialek, *Spikes - Exploring the Neural Code* (Cambridge, MIT Press, 1996)
6. W. Bair, C. Koch, Neural Comput. **8**, 1185 (1996)
7. S. Panzeri, R.S. Petersen, S.R. Schultz, M. Lebedev, M.E. Diamond, Neuron **29**, 769 (2001)
8. P. Reinagel, R.C. Reid, J. Neurocsi. **20**, 5392 (2000)
9. E.V. Pankratova, A.V. Polovinkin, E. Mosekilde, Eur. Phys. J. B **45**, 391 (2005)
10. N.V. Agudov, A.N. Malakhov, Int. J. Bifurcati. Chaos **5**, 531 (1995); A.N. Malakhov, A.L. Pankratov, Physica C **269**, 46 (1996); R.N. Mantegna, B. Spagnolo, Phys. Rev. Lett. **76**, 563 (1996); N.V. Agudov, Phys. Rev. E **57**, 2618 (1998), N.V. Agudov, A.N. Malakhov, Phys. Rev. E **60**, 6333 (1999)
11. A.U. Larkman, J. Comp. Neurol. **306**, 332 (1991)
12. Ö. Bernander, R.J. Douglas, K.A.C. Martin, C. Koch, Proc. Natl. Acad. Sci. USA **88**, 11569 (1991)
13. M. Rapp, Y. Yarom, I. Segev, Neural Comput. **4**, 518 (1992)
14. A.L. Hodgkin, A.F. Huxley, J. Physiol. (Lond.) **117**, 500 (1952)
15. B.W. Connors, M.J. Gutnick, J. Prince, J. Neurophysiol. **48**, 1302 (1982)
16. B. Delord, A.J. Klaassen, Y. Burnod, R. Costalat, E. Guigon, NeuroReport **8**, 1019 (1997)
17. L.J. Borg-Graham, C. Monier, Y.F. Fregnac, Nature **389**, 369 (1998)
18. S. Schreiber, J.M. Fellous, P. Tiesinga, T.J. Sejnowski, J. Neurophysiol. **91**, 194 (2004)