Chapter 11
Noisy Dendrites: Models of Dendritic Integration In Vivo

Alain Destexhe and Michelle Rudolph-Lilith

Abstract While dendritic processing has been well characterized in vitro, there is little experimental data and models available about the integrative properties of dendrites in vivo. Here, we review existing computational models to infer the dendritic processing of neocortical pyramidal neurons in vivo. We start by summarizing experimental measurements of the “high-conductance states” of cortical neurons in vivo. Next, we show models predicting that, in such states, the responsiveness of cortical neurons should be greatly enhanced, in particular due to the presence of high-amplitude fluctuations (“synaptic noise”). We infer that in dendrites this effect should be particularly strong, leading to the spontaneous activation of dendritic spikes. The presence of noise in dendrites also enhances spike propagation. We show that opposite distance dependencies of spike initiation and propagation result in roughly location-independent synaptic efficacies. In addition, in high-conductance states, dendrites display sharper temporal processing capabilities. Thus, we conclude that noisy active dendrites behave more “democratically,” and that dendrites should have enhanced processing capabilities in vivo.

11.1 Introduction

Activated states of the brain are characterized by intense, irregular, and desynchronized neuronal activity. In awake animals, neurons in different cortical structures display high spontaneous firing rates, from 5 to 20 Hz in cats (Evarts, 1964; Steriade and McCarley, 1990). Moreover, the cerebral cortex shows a very dense connectivity, with each pyramidal neuron receiving between 5,000 and 60,000
synaptic contacts, most of which originate from the cortex itself (DeFelipe and Fariñas, 1992; Braitenberg and Schüz, 1998). As a consequence, many synaptic inputs are simultaneously activated onto cortical neurons in vivo. Indeed, intracellular recordings in awake animals reveal that cortical neurons are subjected to an intense synaptic bombardment and, as a result, are depolarized and have a low input resistance (Matsumura et al., 1988; Baranyi et al., 1993; Steriade et al., 2001) compared to brain slices kept in vitro. This activity is also responsible for a considerable amount of subthreshold fluctuations, called “synaptic noise.” Together these properties characterize what is called the “high-conductance state” of cortical neurons. How such high-conductance and high-noise conditions affect the integrative properties of neurons remains an intense subject of research (reviewed in Destexhe et al., 2003; Destexhe and Contreras, 2006; Destexhe, 2007; Destexhe and Rudolph-Lilith, 2012). Besides few exceptions (Helmchen et al., 1999; Branco et al., 2010; Branco and Häusser, 2011; Lavzin et al., 2012), little is known about the integrative properties of dendrites in vivo.

In this chapter, we start by overviewing experimental measurements of high-conductance states in cortical neurons in vivo. We next review computational models to explore the impact of such states on integrative properties, and what sort of computational advantages may be conferred by synaptic noise in dendrites.

11.2 Characterization of High-Conductance States In Vivo

11.2.1 The Synaptic Noise in Neocortical Neurons In Vivo

In awake animals, the cerebral cortex (and more generally the entire brain) displays an “activated” state, with distinct characteristics compared to other states like slow-wave sleep or anesthesia. These characteristics include a low-amplitude “desynchronized” electroencephalogram (EEG), a depolarized \( V_m \), and irregular firing activity (Fig. 11.1a, Awake). During slow-wave sleep, the EEG and \( V_m \) activity follow low-frequency rhythms (Fig. 11.1a, Slow-Wave Sleep). The most prominent rhythm consists of slow-wave complexes in the EEG, which are paralleled with up/down-state dynamics in the \( V_m \). During the up-state (Fig. 11.1a, gray bars), the \( V_m \) is depolarized and the activity is similar to wakefulness; during the down-state, all cortical neurons are hyperpolarized and do not fire. Several anesthetics, such as urethane or ketamine–xylazine, induce EEG and \( V_m \) dynamics very similar to slow-wave sleep. For instance, ketamine–xylazine anesthesia generates an up/down-state pattern very similar to sleep (Destexhe et al., 2003). For recent reviews on EEG and \( V_m \) dynamics during activated and sleep states, see Steriade (2001, 2003), Steriade and McCarley (1990), and McCormick and Bal (1997).

One of the main interests in dealing with up/down-state patterns is that there is good evidence that the up-states follow dynamics very similar to that of activated states of the brain (for a recent review, see Destexhe et al., 2007). Indeed, at the level of EEG and intracellular activities, the dynamics seen during up-states are
almost undistinguishable from that during wakefulness. An illustrative example of
this similarity is that electrical stimulation of the brain stem (pedonculopontine
tegmentum, or PPT) can transform the up/down-state dynamics into the typical
desynchronized EEG of activated states, which appears as a “prolonged” up-state
(see Steriade et al., 1993; Rudolph et al., 2005). Thus, it seems that the up-states
constitute a relatively good approximation of the network state during activated states. It is important to stress that these states are close, but not identical, as shown for example by conductance measurements (reviewed in Destexhe et al., 2007; Destexhe and Rudolph-Lilith, 2012).

11.2.2 Conductance Measurements

The total excitatory and inhibitory conductance can be estimated from $V_m$ measurements in different ways. Injection of constant current during up/down-states induces a marked change of the $V_m$ during down-states, while the up-state seems much less sensitive to the injected current (Paré et al., 1998; Destexhe et al., 2003). In other words, the up-state has a much larger conductance compared to the down-state. These measurements constitute a first indication that the up-states correspond to a high-conductance state. The same results were obtained with purely subthreshold activity, suggesting that they are not due to the conductances of action potentials.

A second, more direct measurement was obtained by using the “VmD method” (Rudolph et al., 2004; Piwkowska et al., 2008), which estimates the total conductances and their variances by fitting experimental $V_m$ distributions to the Gaussian approximation of an analytical expression for the membrane potential distribution of an effective stochastic membrane model (Rudolph and Destexhe, 2003c, 2005). This approach leads to estimates of the mean excitatory and inhibitory conductances ($g_{e0}, g_{i0}$) and their standard deviations ($\sigma_e, \sigma_i$), respectively, and was successfully applied to intracellular recordings from awake and naturally sleeping cats (Fig. 11.1b; Rudolph et al., 2007). These measurements evidenced that the membrane in these states is indeed in a high-conductance state, with inhibitory conductances in general several-fold larger than excitatory conductances.

This result was consistent with another type of direct measurement, in which intracellular recordings were compared during up-states and after suppression of network activity using TTX (Fig. 11.1c; Paré et al., 1998). Because TTX blocks all sodium channels, it effectively suppresses all action potential-dependent activity and reveals the resting $V_m$ of the neuron. Input resistance ($R_{in}$) measurements showed that, taking the up-states of ketamine–xylazine anesthesia as reference, these active states have about five times more synaptic conductance compared to the resting $V_m$ of the cell (Fig. 11.1c; Paré et al., 1998; Destexhe and Paré, 1999). These results are not affected by the $V_m$ level or by spiking activity as identical results are obtained at hyperpolarized and subthreshold levels. Furthermore, $R_{in}$ measurements correspond to the linear portion of the $I$–$V$ curve, suggesting little or no contamination by intrinsic voltage-dependent currents (Destexhe and Paré, 1999; see also discussion in Monier et al., 2008).

Similar measurements have also been obtained during active states in vivo in other studies, by comparing up- and down-states under various anesthetics such as ketamine–xylazine or urethane, in different species. These estimates are very variable, ranging from up to several-fold smaller $R_{in}$ in up-states (Contreras et al., 1996;
Paré et al., 1998; Petersen et al., 2003; Leger et al., 2005), to nearly identical $R_{in}$ between up- and down-states or even larger $R_{in}$ in up-states (Metherate and Ashe, 1993; Zou et al., 2005; Waters and Helmchen, 2006). It was argued that the latter, rather paradoxical observation, only found in rats so far, is the result of the presence of potassium currents in down-states (Zou et al., 2005), or voltage-dependent rectification (Waters and Helmchen, 2006). Consistent with the latter, blocking $K^+$ currents using cesium-filled electrodes has negligible effects on the up-state, but abolishes the hyperpolarization during the down-states (Timofeev et al., 2001). Moreover, in cats, the $R_{in}$ of the down-state differs from that of the resting $V_m$ (after TTX) by about twofold (Paré et al., 1998). It is, thus, clear that at least the down-state is very different from the true resting $V_m$ of the neuron. Finally, conductance measurements in awake and naturally sleeping animals have revealed a wide diversity between cells in cat cortex (Rudolph et al., 2007), ranging from large synaptic conductances, much larger than the resting conductance, to synaptic conductances smaller or equal to the resting conductance. However, on average, the synaptic conductance was estimated as about three times the resting conductance, where the inhibitory conductance is about twice the excitatory conductance (Rudolph et al., 2007). Strong inhibitory conductances were also found in artificially evoked active states using PPT stimulation (Rudolph et al., 2005), as shown in Fig. 11.1b.

In conclusion, the data reviewed here indicate that in brain activity states with desynchronized EEG, neocortical neurons display a high-conductance state characterized by the following features: (1) a large membrane conductance, which corresponds to a threefold to fivefold decrease in input resistance; (2) an average membrane potential (around $-65$ to $-60$ mV), which is significantly depolarized compared to the natural resting $V_m$ ($-70$ to $-80$ mV); and (3) large amplitude membrane potential fluctuations ($\sigma_V$ of 2–6 mV), which are at least tenfold larger than those seen in the absence of network activity. In addition, the data indicate that these characteristics are attributable mostly to network activity, and that inhibitory conductances account for most of the large membrane conductance. The consequences of this strong synaptic bombardment are considered in the next section.

### 11.3 Computational Consequences of High-Conductance States

#### 11.3.1 Models of High-Conductance States

Since several decades, theoretical studies have been designed to understand the impact of noise on the integrative properties of neurons. The notion of high-conductance state itself, as well as the fact that neurons could integrate differently in such states, was first proposed by modeling studies. By integrating the sustained synaptic conductance arising from network activity into models, Barrett (1975) for motoneurons, and later Holmes and Woody (1989) for pyramidal cells, predicted
that synaptic activity could have a profound impact on dendritic integration. This theme was then investigated using biophysically and morphologically more precise models in cortex (Bernander et al., 1991; Destexhe and Paré, 1999) and cerebellum (Rapp et al., 1992; De Schutter and Bower, 1994). Such models have predicted a number of computational consequences of background activity and high-conductance states characterizing the in vivo state in neurons which will be briefly summarized in the next section.

In addition to morphologically precise computational models, a large number of theoretical studies have also designed simplified and mathematically treatable models to study the effect of noise on neurons. Synaptic activity is commonly modeled by a source of current noise in the neuron (Levitan et al., 1968; Tuckwell, 1988), which leads to a description of the membrane potential in terms of a stochastic process. However, this type of model is too simple to account for the effect of conductances, in particular high-conductance states. For that reason, more recently, another approach was followed which modeled background activity by fluctuating conductances instead of fluctuating currents (Destexhe et al., 2001). In this case, the synaptic conductances are stochastic processes, which, in turn, give rise to a stochastic $V_m$ dynamics. The advantage of this representation is that the high-conductance state of the membrane can be directly reproduced and modulated, for instance, through the independent control of the conductance mean and the variance. The realism and computational simplicity of these models also enable injection into real neurons in order to recreate high-conductance states artificially using the dynamic-clamp technique (reviewed in Destexhe and Bal, 2009).

Another advantage is that such models are simple enough to allow analytical treatment. Various mathematical studies of the firing dynamics of neurons with conductance-based inputs were performed (see for example Burkitt et al., 2003; Moreno-Bote and Parga, 2005; Muller et al., 2007) and have consequences on network dynamics with conductance-based inputs (Meffin et al., 2004; see also Shelley et al., 2002). The $V_m$D method mentioned above is also a direct consequence of this mathematical tractability (Rudolph et al., 2004).

### 11.3.2 Impact of High-Conductance States on Integrative Properties

Computational models have predicted several interesting computational consequences of high-conductance states and synaptic noise (Rudolph and Destexhe, 2003a; reviewed in Destexhe et al., 2003; Destexhe and Rudolph-Lilith, 2012).

#### 11.3.2.1 Probabilistic Responses

A first consequence of the presence of synaptic noise is that the $V_m$ behaves stochastically and, therefore, neuronal responses in high-conductance states are highly
variable (Fig. 11.2a). In such states, it is necessary to use repeated trials for any given stimulus, and the appropriate measure of the response is to compute the probability of emitting spikes. The use of such probabilistic measures are well known in in vivo electrophysiology, where routinely “post-stimulus time histograms” (PSTH) from data are calculated. Here, integrating the response (total “output” of the neuron) after a stimulus yields the total probability that a spike is emitted in response to the given stimulus (Fig. 11.2b).

11.3.2.2 Noise-Induced Enhanced Responsiveness

An important consequence of high-conductance states is not only the transformation of neurons into probabilistic devices, but also the profound impact on their response properties. The response curve (or transfer function), which is obtained by representing the total response probability (integrated over time after stimulus) against stimulus amplitude, is all-or-none for a neuron not subjected to stochastic synaptic activity. This behavior reflects the presence of a fixed spiking threshold (Fig. 11.2b, gray), in which case the emitted spike can only tell whether the stimulus is larger than the threshold. In the presence of synaptic noise, however, the response curve is qualitatively different. It is no longer step-like, but spans a whole range of input amplitudes (Fig. 11.2b, black). In this case, the probability of spiking is indicative of the whole range of input amplitude. Specifically, for small-amplitude inputs (those in the physiological range), which are normally subthreshold, the neuron’s response probability is enhanced (Fig. 11.2b, star). This enhanced responsiveness is a very robust feature of neurons in the presence of synaptic background activity.
(Hô and Destexhe, 2000; Shu et al., 2003). Moreover, the shape of the response function can be altered by changes in the statistics of the background activity. For that reason, this phenomenon has been coined “gain modulation” (Chance et al., 2002), reflecting the fact that the slope of the response curve is modulated by synaptic noise.

Using computational models to independently control the total amount of conductance, and the amount of fluctuations, it was possible to determine their respective role. The conductance alone shifts the response curve (Fig. 11.2b, rightward arrow), while the noise component alone modulates the slope (gain) of the response curve (Hô and Destexhe, 2000; Chance et al., 2002; Shu et al., 2003; Mitchell and Silver, 2003; Prescott and De Koninck, 2003). It is important to note that the type of modulation by noise will depend strongly on the intrinsic properties of the neurons. For that reason, also an inverse gain modulation can be observed (Fellous et al., 2003) and may be explained by potassium conductances (Higgs et al., 2006). Similarly, the dual response (burst vs. single-spike) of thalamic relay neurons is also strongly affected by the presence of synaptic noise, and the two modes may no longer be distinguishable (Wolfart et al., 2005).

It is important to note that the phenomenon of enhanced responsiveness is similar to stochastic resonance phenomena, which have been thoroughly studied by physicists (reviewed in Gammaitoni et al., 1998; Wiesenfeld and Moss, 1995). Stochastic resonance is a noise-induced enhancement of the signal-to-noise ratio in nonlinear systems. It typically presents itself as a peak in the signal-to-noise ratio when the latter is considered as a function of the noise amplitude. Thus, the system appears to “resonate” or to respond optimally for an intermediate but non-vanishing amount of noise. While neurons can also show such behavior when subjected to noise (Levin and Miller, 1996; Stacey and Durand, 2000), the situation is more complex than for classical stochastic resonance phenomena, because in neurons the noise sources are synaptic conductances, and these conductances lead to an additional shunting effect of the cellular membrane (see details in Rudolph and Destexhe, 2001b). As will be shown below, such a modulation of neuronal responsiveness by conductance noise is the basis for the explanation of other neuronal response properties.

### 11.3.2.3 Noisy Dendrites: Equalization of Synaptic Efficacies

Focusing on the dendrites of neocortical neurons, the presence of massive synaptic bombardment may fundamentally change dendritic integration properties, as illustrated in Fig. 11.3. An inherent property of neuronal dendrites and other electrical cable structures is the attenuation of voltage. This is true in particular for pyramidal neurons: synaptic inputs can experience strong attenuation in the neuron at rest (Fig. 11.3a, left). If the high-conductance state of the membrane is integrated as a static conductance component through an increase in the leak conductance of the membrane, the attenuation is much more severe (Fig. 11.3a, middle): already
a  Quiescent  Static conductance  High-conductance

b

c

1.2 nS

4.8 nS

12 nS

AP initiation

Somatic response

AP propagation

Path distance (μm)
probability shows a surprisingly low dependence on the location of inputs in dendrites (Fig. 11.3a, right).

For the explanation of this equalization of synaptic efficacy, the dendritic excitability, combined with noise, plays a critical role. In quiescent conditions, synaptic inputs arising in distal dendrites can elicit a local dendritic spike, but such a
Fig. 11.4 Location independence for different dendritic morphologies. The probability of somatic response to AMPA stimulation (12 nS amplitude) is indicated for different dendritic sites (corresponding branches are indicated by dashed arrows; equivalent electrophysiological parameters and procedures as in Fig. 11.3c) for four different cells (one layer II–III, two layer V, and one layer VI), based on cellular reconstructions from cat cortex (Douglas et al. 1991; Contreras et al. 1997; modified from Rudolph and Destexhe, 2003a; see this paper for details about the model)

Fig. 11.5 Increased temporal resolution with synaptic noise. (a) Location-dependence of the timing of EPSPs. A similar stimulation paradigm as in Fig. 11.3a was used, except that the time-to-peak of averaged synaptic responses is represented against distance to soma. In quiescent conditions (gray), the time-to-peak of EPSPs increased approximately linearly with distance from soma. This location dependence was markedly reduced in the high-conductance state (black). (b) Enhanced temporal resolution of synaptic inputs during high-conductance state. Excitatory synaptic inputs were delivered at different frequencies. The temporal resolution was quantified by computing the ratio between the stimulus interval and the mode of the corresponding interspike interval histogram. In quiescent conditions (gray), the model could respond reliably up to a stimulus frequency of about 50 Hz. In high-conductance states (black), the frequency following was reliable up to much higher frequencies (beyond 100 Hz). (a) modified from Rudolph and Destexhe, 2003a; (b) modified from Destexhe et al., 2003; see these papers for details about the model
also promote fast-propagating action potentials, resulting in a reduced location-dependence of EPSP timing (Fig. 11.5a; Rudolph and Destexhe, 2003a). Here, synaptic noise seems to set the dendrite into a fast-conducting mode, in which the timing of inputs shows reduced dependence on their distance from the soma. This remarkable property is likely to facilitate the association of synaptic inputs arising at distant locations from each other.

The mechanisms underlying this fast-conducting mode depend on several factors. First, the reduction of the membrane time constant due to the high conductance, which can be modeled with an equivalent static conductance, shows a partial increase in the conduction speed of dendritic spikes. Second, varying the presence of sodium conductances also led to intermediate effects on the timing due to the presence of dendritic spikes. Combining both of these effects suggests that this fast conducting mode is due to fast propagation of dendritic spikes in a membrane of fast time constant (see details in Rudolph and Destexhe, 2003a).

Neurons in high-conductance states also display a superior ability to distinguish and process high-frequency inputs, when compared to low-conductance states. This is illustrated in Fig. 11.5b, which shows the temporal resolution of a neuron represented against the input frequency. In quiescent or low-conductance states, neurons can follow inputs (i.e., produce a spike) up to a maximal frequency which is typically around 40–50 Hz (Fig. 11.5b, gray). With synaptic noise, the neuron can lock its response to larger frequencies (up to more than 100 Hz in the example of Fig. 11.5b, black). This property is attributable to the smaller time constant associated with high membrane conductances.

Modeling studies have explored other computational advantages of synaptic noise on temporal processing. If both excitatory and inhibitory conductances are large during high-conductance states, slight variations of either excitation or inhibition can be very effective in modifying spiking probability. As a consequence, neurons can reliably detect faint changes in temporal correlation of their synaptic inputs (Halliday, 1999; Salinas and Sejnowski, 2000; Rudolph and Destexhe, 2001a). This type of response is interesting, because changes in correlation do not change the average conductance nor the average \( V_m \), but they uniquely appear as changes of the level of fluctuations (variances) of the conductances and of the \( V_m \). In this case, neurons respond to a signal which is not carried by the mean activity of conductances, which, thus, constitutes an example of a paradigm which cannot be modeled by rate-based models.

Finally, high-conductance states also impact on the operating mode of cortical neurons. Neurons can operate either as coincidence detectors or as temporal integrators, which determine whether the cortex encodes information by the precise timing of spikes, or by average firing rates. Modeling studies monitored the spike output of neurons submitted to a full spectrum of multisynaptic input patterns, from highly coincident to temporally dispersed (Maršílek et al., 1997; Kisley and Gerstein, 1999). It was found that, in general, the spike output jitter tends to be lower than the input jitter, indicating that neurons tend to synchronize the responses and reduce their temporal dispersion. However, we found that this conclusion is different when simulating high-conductance states. In this case, the temporal
dispersion is nearly identical between input and output (Rudolph and Destexhe, 2003b). This suggests that in high-conductance states, both operating modes can be used robustly and in parallel.

11.4 Conclusions

In this chapter, we have reviewed models of the high-conductance states in cortical neurons, and their predicted consequences on dendritic integration. We have first overviewed experimental results (Sect. 11.2), showing that cortical neurons in vivo are subject to a considerable amount of synaptic noise, and experience what is called a high-conductance state. In Sect. 11.3, we have reviewed models of synaptic noise which have predicted a number of computational consequences of synaptic noise and high-conductance states on neuronal processing.

It is important to note that models are not limited to the sole task of predicting consequences on integrative properties. Simple models, such as the point-conductance model of synaptic noise (Destexhe et al., 2001), can be used to add artificial synaptic noise in neurons in vitro using the dynamic-clamp technique. This mixed modeling-experimental technique is of primary importance, because it allows one to directly test the predictions of the models in real neurons. It can also be used to realize experiments that would not be possible in vivo, such as controlling the amount of synaptic noise, or controlling independently the amount of mean conductances and their fluctuations. Another important application of the point-conductance model is that it can form the basis for methods to analyze experimental data. Such methods include the estimation of synaptic conductances (the VmD method; Rudolph et al., 2004), the estimation of spike-triggered average conductances (Pospischil et al., 2007), or the estimation of synaptic parameters from the power spectrum of the Vm (Destexhe and Rudolph, 2004). These quantities are evaluated from the sole knowledge of the Vm activity, which makes it applicable to standard intracellular recording conditions. In the past years, each of these methods was tested using computational models, as well as in real neurons using the dynamic-clamp technique (reviewed in Piwkowska et al., 2008).

One main consequence of high-conductance states is that the presence of synaptic noise drastically affects the responsiveness of the neurons by changing their response curve or transfer function. The finding that the gain and responsiveness of neurons are enhanced by synaptic noise was first reported from modeling studies (Hô and Destexhe, 2000), and then investigated experimentally using dynamic-clamp injection of in vivo-like synaptic noise (Destexhe et al., 2001; Chance et al., 2002; Fellous et al., 2003; Prescott and De Koninck, 2003; Shu et al., 2003; Wolfart et al., 2005; Higgs et al., 2006; Piwkowska et al., 2008), thus confirming some of the predictions formulated by models. A fascinating possible consequence is that the enhanced responsiveness due to synaptic noise could be used as an attentional mechanism (Hô and Destexhe, 2000; Shu et al., 2003). By modulating the
amount of synaptic noise, it should be possible to switch entire networks from unresponsive to responsive states, an intriguing possibility which should be investigated by designing appropriate experiments and models.

Given these drastic effects of noise on neurons, the fact that synaptic noise has also profound impact on dendritic processing comes to no surprise. Here, the presence of noise affects not only the initiation and propagation of dendritic spikes, but its consequences are very different in different parts of the dendritic tree. Remarkably, it was found that there is a compensation between two opposite distance dependence, leading to a roughly location-independent effect of synaptic inputs on somatic spiking (Fig. 11.3c). Thus, the probabilistic dendrites seem to behave more “democratically,” giving to each synaptic input a roughly equal vote on somatic spiking.

This remarkable property still awaits to be tested experimentally, but such a test is not easy. It would require to modulate the conductance state of the whole extent of the dendrites, and control synaptic inputs of similar weights at different positions. These two conditions constitute clear experimental challenges. However, recently it was shown that it is possible to maintain irregular states of activity (up-down states) in cortical slices (Sanchez-Vives and McCormick, 2000; Silberberg et al., 2004), which would be a possible way towards performing such experiments. From a mathematical point of view, the almost perfect compensation observed for very different distance-dependent profiles (Fig. 11.3c) suggests a simple theoretical explanation for the observed effects. Specifically, it should be possible to reproduce the present observations using simplified models, endowed, for example, with multicompartment tapering dendrites and integrate-and-fire mechanism with noise. This, as well, constitutes a possible direction for future theoretical studies.

Note that the location independence was only studied for isolated excitatory synaptic inputs, and should still be investigated for more complex input combinations, such as multiple excitations and combined excitatory and inhibitory inputs. In such cases, we expect that the proximity of the different inputs on the dendrite will play an important role and may reveal local aspects of dendritic computations, as analyzed previously (Mel, 1994).

Models also showed that synaptic noise enhances the temporal resolution of dendrites, both by setting a fast propagating mode and by enhancing the ability of the neuron to follow high-frequency inputs (Fig. 11.5). Interestingly, the latter type of temporal processing was the first consequence put forward by modeling studies (Barrett, 1975; Holmes and Woody, 1989; Bernander et al., 1991; Rudolph and Destexhe, 2003a,b). Neurons in high-conductance states necessarily have a faster membrane which allows sharper temporal processing. Remarkably, the fast-propagating mode would make the neuron more suitable to act as a coincidence detector. Surprisingly, few experimental studies have investigated these temporal aspects, which constitute other interesting directions for future investigations.

Finally, we did not review here dendrites with calcium currents, although this constitutes an interesting subject to investigate in the presence of synaptic noise as well. It was shown previously that synaptic noise has strong effect on bursting mediated by T-type calcium currents in thalamic relay neurons (Wolfart et al., 2005).
This study revealed that the classic duality of “tonic” and “burst” modes of firing in thalamic relay cells no longer holds in high-conductance states, because, with synaptic noise, bursts and single-spikes participate to all responses. Interestingly, it was observed that intrinsically bursting neurons are much less frequent in vivo compared to in vitro recordings (reviewed in Steriade et al., 1993). Noise modulation of the calcium current in dendrites, as in thalamic neurons, as well as the high synaptic conductances, which are likely to compete with dendritic calcium conductances, may explain why cortical cells are more reticent to burst under in vivo conditions.

In conclusion, modeling studies predict that noisy membranes integrate according to different rules. This concept also applies to dendrites and may be responsible for properties such as equalization of synaptic efficacies and finer temporal processing. Thus, like single neurons, the presence of synaptic noise may also be beneficial to dendrites.

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**References**


De Schutter E, Bower JM (1994) Simulated responses of cerebellar Purkinje cells are independent of the dendritic location of granule cell synaptic inputs. Proc Natl Acad Sci USA 91:4736–4740
Halliday DM (1999) Weak, stochastic temporal correlation of large-scale synaptic inputs is a major determinant of neuronal bandwidth. Neural Comput 12:693–707


Steriade M, Amzica F, Nuñez A (1993) Cholinergic and noradrenergic modulation of the slow (~0.3 Hz) oscillation in neocortical cells. J Neurophysiol 70:1384–1400