

An Extended Analytic Expression for the Membrane Potential Distribution of Conductance-Based Synaptic Noise

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Synaptically generated subthreshold membrane potential (V_m) fluctuations can be characterized within the framework of stochastic calculus. It is possible to obtain analytic expressions for the steady-state V_m distribution, even in the case of conductance-based synaptic currents. However, as we show here, the analytic expressions obtained may substantially deviate from numerical solutions if the stochastic membrane equations are solved exclusively based on expectation values of differentials of the stochastic variables, hence neglecting the spectral properties of the underlying stochastic processes. We suggest a simple solution that corrects these deviations, leading to extended analytic expressions of the V_m distribution valid for a parameter regime that covers several orders of magnitude around physiologically realistic values. These extended expressions should enable finer characterization of the stochasticity of synaptic currents by analyzing experimentally recorded V_m distributions and may be applicable to other classes of stochastic processes as well.

1 Introduction ---

The sustained and intense synaptic background activity typical of cortical neurons in vivo may have significant consequences on their integrative behavior (reviewed in Destexhe, Rudolph, & Paré, 2003). Various methods were proposed to characterize this synaptic “noise” (e.g., Levitan, Segundo, Moore, & Perkel, 1968; Lánský & Lánská, 1987; van Rossum, 2001; Hillenbrand 2002; Tuckwell, Wan, & Rospars, 2002). Synaptic noise may also be modeled by global conductances described by stochastic processes of the Ornstein-Uhlenbeck (OU) type (Destexhe, Rudolph, Fellous, & Sejnowski, 2001). Recently, this system was investigated within the framework of

stochastic calculus, and analytic expressions were obtained for the steady-state membrane potential (V_m) distribution (Rudolph & Destexhe, 2003), as well as for the moments of the underlying three-dimensional Fokker-Planck equation (Richardson, 2004).

The approach proposed in Rudolph and Destexhe (2003) considered the membrane equation subject to conductance-based synaptic noise, based on the distribution of the stochastic processes as well as the expectation values of their differentials. The analytic expression obtained for the amplitude distribution of the V_m was shown to match well numerical simulations in a physiologically relevant but limited parameter space. However, as we show here, this matching does not apply to other parameter regimes, in particular for very small membrane time constants. How can we explain this mismatch, and if possible, how can it be corrected?

In this note, we investigate this problem by first showing that solving stochastic differential equations solely based on the expectation values of differentials of the underlying stochastic processes does not completely capture the spectral properties of the investigated stochastic system. Although these differences are not dramatic if realistic parameter values are considered, they nevertheless can induce deviations of the predicted amplitude distribution for other parameter regimes. This suggests that both the amplitude distribution and the spectral properties of the underlying stochastic processes are needed to fully describe a stochastic system.

We suggest a simple approach to correct for these spectral deviations. We consider a simpler and dynamically different system for which the analytic solution is known. This system is solved using local expectation values (as in Rudolph and Destexhe, 2003), which allows us to estimate the extension needed to incorporate the spectral signature of the stochastic process. We argue that by applying the same extension to the full conductance-based system, we obtain an extended analytic expression for the probability distribution of the V_m at steady state in which spectral deviations are compensated. Finally, we show that this extended expression matches numerical simulations even for extreme parameter regimes covering several orders of magnitude around physiologically realistic parameter values.

2 The Model and Analytic Solution

What will be referred here as the *full conductance-based system* consists in a fluctuating conductance model (Destexhe et al., 2001), based on the passive

membrane equation,

$$\frac{dV(t)}{dt} = -\frac{1}{\tau_m}(V(t) - E_0) - \frac{1}{C}\tilde{g}_e(t)(V(t) - E_e) - \frac{1}{C}\tilde{g}_i(t)(V(t) - E_i), \tag{2.1}$$

where $V(t)$ denotes the membrane potential, C the membrane capacity, $\tau_m = \frac{C}{G_L + g_{e0} + g_{i0}}$ the effective membrane time constant, G_L the leak conductance, and E_0 the average membrane potential in the presence of synaptic noise given by

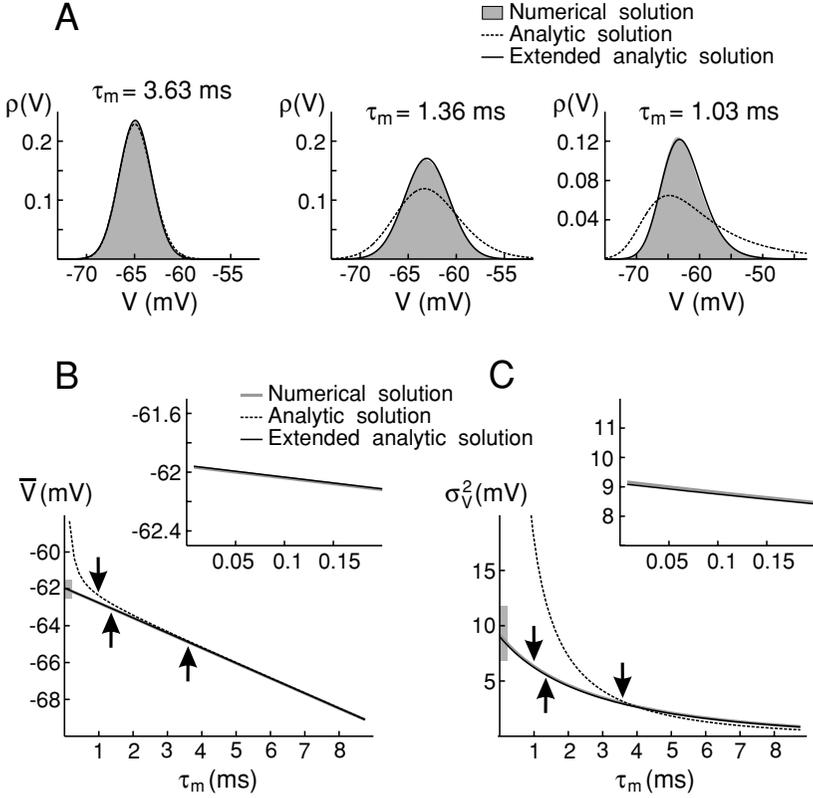
$$E_0 = \frac{G_L E_L + g_{e0} E_e + g_{i0} E_i}{G_L + g_{e0} + g_{i0}}, \tag{2.2}$$

where E_L denotes the leak reversal potential. Note that this notation differs from the one used in Rudolph and Destexhe (2003) by using $C = C_m a$ and $G_L = g_L a$, where a denotes the total membrane area. $\tilde{g}_{\{e,i\}}(t) = g_{\{e,i\}}(t) - g_{\{e,i\}0}$ are excitatory and inhibitory conductances, described by OU stochastic processes,

$$\frac{dg_{\{e,i\}}(t)}{dt} = -\frac{1}{\tau_{\{e,i\}}}(g_{\{e,i\}}(t) - g_{\{e,i\}0}) + \sqrt{\frac{2\sigma_{\{e,i\}}^2}{\tau_{\{e,i\}}}}\xi_{\{e,i\}}(t) \tag{2.3}$$

with mean $g_{\{e,i\}0}$, standard deviation $\sigma_{\{e,i\}}$, and time constant $\tau_{\{e,i\}}$. $\xi_{\{e,i\}}(t)$ denotes gaussian white noise with zero mean and unit standard deviation, and $E_{\{e,i\}}$ are the respective noise reversal potentials for excitatory and inhibitory conductances.

By using the stochastic calculus (see, e.g., Gardiner, 2002), the steady-state subthreshold activity can be characterized in terms of the probability distribution of the membrane potential. To this end, we used a set of differential rules (Itô rules) describing products of differentials, hence infinitesimal displacements, of the corresponding integrated OU stochastic processes for excitatory and inhibitory conductances. With this, the Fokker-Planck equation corresponding to the Langevin equation 2.1 was deduced, which describes the time evolution of the probability $\rho(V, t)$ that the membrane potential takes the value V at time t . In the steady-state limit $t \rightarrow \infty$, this Fokker-Planck equation is explicitly solvable, yielding a membrane



potential distribution given by

$$\rho(V) = N \exp \left[A_1 \ln \left[\frac{\sigma_e^2 \tau_e'}{C^2} (V - E_e)^2 + \frac{\sigma_i^2 \tau_i'}{C^2} (V - E_i)^2 \right] + A_2 \arctan \left[\frac{\sigma_e^2 \tau_e' (V - E_e) + \sigma_i^2 \tau_i' (V - E_i)}{(E_e - E_i) \sqrt{\sigma_e^2 \tau_e' \sigma_i^2 \tau_i'}} \right] \right], \quad (2.4)$$

where

$$A_1 = - \frac{2C(g_{e0} + g_{i0}) + 2CG_L + \sigma_e^2 \tau_e' + \sigma_i^2 \tau_i'}{2(\sigma_e^2 \tau_e' + \sigma_i^2 \tau_i')},$$

$A_2 =$

$$\frac{2C(G_L(\sigma_e^2 \tau_e'(E_L - E_e) + \sigma_i^2 \tau_i'(E_L - E_i)) + (g_{e0} \sigma_i^2 \tau_i' - g_{i0} \sigma_e^2 \tau_e')(E_e - E_i))}{(E_e - E_i) \sqrt{\sigma_e^2 \tau_e' \sigma_i^2 \tau_i' (\sigma_e^2 \tau_e' + \sigma_i^2 \tau_i')}},$$

and $\tau'_{\{e,i\}}$ denote effective noise time constants. This form of $\rho(V)$ differs from the one presented in Rudolph and Destexhe (2003) by the use of “effective” noise time constants, which in general are not equal to $\tau_{\{e,i\}}$. The argumentation leading to this crucial change is the subject of this contribution, along with the deduction of the explicit form of $\tau'_{\{e,i\}}$.

Indeed, by comparing the solution provided in Rudolph and Destexhe (2003) with numerical simulations as well as experimental recordings with artificially recreated synaptic noise in dynamic clamp (Rudolph et al., 2004b), it was shown that this analytic expression characterizes well the subthreshold behavior in a physiologically relevant parameter regime (membrane time constants $\tau_m \geq 3$ ms; see Figures 1A, left, 1B, and 1C, dashed lines). However, marked deviations were found for other parameter regimes, in particular for small membrane areas and small membrane time

Figure 1: Comparison of the V_m distributions obtained numerically and using the extended analytic expression. (A): Examples of membrane potential distributions for different membrane time constants τ_m . In all cases, numerical simulations (gray) are compared with the original analytic solution (Rudolph & Destexhe, 2003, dashed lines) and the extended analytic expression (solid lines) obtained after compensating for the filtering problem (see equations 2.4 and 4.8). (B, C) Mean \bar{V} and variance σ_V^2 of the V_m distribution as a function of membrane time constant. Numerical simulations (gray) are compared with the mean and variance obtained by numerical integration of the original analytic solution (Rudolph & Destexhe, 2003, dashed lines) and the extended analytic expression (see equations 2.4 and 4.8, solid lines). The gray vertical stripes mark the parameter regimes displayed in the insets. Parameter values: $g_L = G_L/a = 0.0452$ mS cm⁻², $C_m = C/a = 1$ μ F cm⁻², $E_L = -80$ mV, $g_{e0} = 12$ nS, $g_{i0} = 57$ nS, $\sigma_e = 3$ nS, $\sigma_i = 6.6$ nS (A, right: $\sigma_e = 3$ nS, $\sigma_i = 15$ nS), $\tau_e = 2.728$ ms, $\tau_i = 10.49$ ms, $E_e = 0$ mV, $E_i = -75$ mV. Membrane area a : $a = 30,000$ μ m² (A, left), $a = 10,000$ μ m² (A, middle), $a = 7,500$ μ m² (A, right), 50 μ m² $\geq a \geq 100,000$ μ m² (B, C). For all simulations, integration time steps of at least one order of magnitude smaller (but at most 0.1 ms) than the smallest time constant (either membrane or noise time constant) in the considered system were used. To ensure that the observed effects were independent on peculiarities of the numerical integration, different values for the integration time step (in all cases, at least one order of magnitude smaller than the smallest time constant in the system) for otherwise fixed noise and membrane parameters were compared. No systematic or significant differences were observed. Moreover, to ensure valid statistics of the membrane potential time course, the simulated activity covered at least 100 s for each parameter set used. Simulations were performed using the NEURON simulation environment (Hines & Carnevale, 1997).

constants $\tau_m \ll 3$ ms (see Figures 1A, middle and right, 1B and 1C, dashed lines).

Two points must be noted related to these deviations. First, in the proposed approach leading to equation 2.1, only moments describing the probability distribution of the OU and integrated OU stochastic process were used. Moreover, in the steady-state limit, only the specific coupling $\sigma_{\{e,i\}}^2 \tau'_{\{e,i\}}$ between the noise variance and time constant enters the solution. Motivated by the fact that the distributions of both white and colored (OU) noise are gaussian, this result suggests that white conductance noise source with an “effective” variance proportional to $\sigma_{\{e,i\}}^2 \tau'_{\{e,i\}}$ will yield equivalent distributions at steady state, and therefore affects the membrane in a statistically equivalent fashion. However, this way, the spectral properties distinguishing white and colored noise will not be respected.

Second, and linked to the first point, no explicit integration of the membrane equation was performed. In this sense, our proposed approach deviates from other approaches (e.g., Manwani & Koch, 1999; Richardson, 2004). Indeed, the restriction to expectation values of differentials allows one to treat the stochastic system, equations 2.1 and 2.3, analytically and to deduce a solution for the corresponding Fokker-Planck equation. On the other hand, as we will show below, this way, the spectral properties of the stochastic variables are not preserved. These properties can be accessed only by integration over the whole time domain.

3 The Filtering Problem

In this section, we demonstrate the core problem by calculating the Fourier transforms of the original Langevin equation, equation 2.1, and that of an infinitesimal displacement of the membrane potential formulated in terms of differentials of the integrated OU stochastic process after application of the stochastic calculus (see equation B.7 in Rudolph & Destexhe, 2003). We then identify the differences between the two power spectra, which can be viewed as resulting from a modification of the spectral properties of the noise processes due to membrane filtering, and argue for a simple way to correct these differences.

Defining $V(\omega)$ and $\tilde{g}_{\{e,i\}}(\omega)$ as the Fourier transforms of $V(t)$ and $\tilde{g}_{\{e,i\}}(t)$, respectively (ω denotes the circular frequency),

$$V(t) = \frac{1}{2\pi} \int_{-\infty}^{\infty} d\omega V(\omega) e^{i\omega t},$$

$$\tilde{g}_{\{e,i\}}(t) = \frac{1}{2\pi} \int_{-\infty}^{\infty} d\omega \tilde{g}_{\{e,i\}}(\omega) e^{i\omega t},$$

the Fourier transform of the membrane equation 2.1 reads

$$\left(i\omega + \frac{1}{\tau_m}\right) \tilde{V}(\omega) = -\frac{1}{2\pi C} \int_{-\infty}^{\infty} d\omega' \{ \tilde{g}_e(\omega') (\tilde{V}(\omega - \omega') - \tilde{E}_e) + \tilde{g}_i(\omega') (\tilde{V}(\omega - \omega') - \tilde{E}_i) \}, \quad (3.1)$$

where $\tilde{V}(\omega) = V(\omega) - E_0$ and $\tilde{E}_{\{e,i\}} = E_{\{e,i\}} - E_0$.

Equation B.7 in Rudolph and Destexhe (2003) provides another expression for an infinitesimal displacement of the membrane potential $V(t)$, deduced within the framework of the calculus of integrated OU stochastic processes $\tilde{w}_{\{e,i\}}(t) = \int_0^t ds \tilde{g}_{\{e,i\}}(s)$. The Fourier transform of this infinitesimal displacement is given by

$$\left(i\omega + \frac{1}{\tau_m}\right) \tilde{V}(\omega) = -\frac{1}{2\pi C} \int_{-\infty}^{\infty} d\omega' \{ \tilde{g}'_e(\omega') (\tilde{V}(\omega - \omega') - \tilde{E}_e) + \tilde{g}'_i(\omega') (\tilde{V}(\omega - \omega') - \tilde{E}_i) \}, \quad (3.2)$$

which can be viewed as the counterpart to equation 3.1. Here, $\tilde{g}'_{\{e,i\}}(\omega)$ denote the Fourier transforms of $g'_{\{e,i\}}(t) = \frac{d}{dt} \tilde{w}_{\{e,i\}}(t) - \frac{1}{C} \alpha_{\{e,i\}}(t)$, where

$$2\alpha_{\{e,i\}}(t) = \sigma_{\{e,i\}}^2 \tau'_{\{e,i\}} \left(1 + e^{-t/\tau'_{\{e,i\}}}\right) + \frac{1}{2\tau'_{\{e,i\}}} \tilde{w}_{\{e,i\}}^2(t) - \sigma_{\{e,i\}}^2 t. \quad (3.3)$$

Note that the Fourier transform of $g'_{\{e,i\}}(t)$ is formally well defined but cannot be calculated explicitly due to the nontrivial form of $\alpha_{\{e,i\}}(t)$.

Indeed, instead of directly evaluating equations 3.1 and 3.2, we follow another path. Comparing both Fourier transforms suggests that the stochastic calculus used in Rudolph & Destexhe (2003) introduces a modification of the spectral structure characterizing the original system. This modification is linked to the term $\alpha_{\{e,i\}}(t)$ (see equation 3.3), whose appearance is a direct consequence of the use of the integrated OU stochastic process and its differentials. As indicated in equation 3.2, this translates into an alteration of the filtering properties described by the stochastic differential equation 2.1. Two points must be mentioned. First, both Fourier transforms, equations 3.1 and 3.2, show the same functional structure, with $\tilde{g}_{\{e,i\}}(\omega)$ in equation 3.1 replaced by the Fourier transform $\tilde{g}'_{\{e,i\}}(\omega)$ of a new stochastic variable $g'_{\{e,i\}}(t)$ in equation 3.2. Second, the functional coupling of $\tilde{g}_{\{e,i\}}(\omega)$ and $\tilde{g}'_{\{e,i\}}(\omega)$ to the Fourier transform of the membrane potential $V(\omega)$ is identical in both cases. This, together with the fact that $V(\omega)$ describe the same state variable,

now provides the basis for deducing an explicit expression for the effective time constants $\tau'_{\{e,i\}}$ and, thus, the extension of equation 2.4.

In order to preserve the spectral signature of $V(t)$, we assume that the functional form of the Fourier transform of the stochastic process $\tilde{g}'_{\{e,i\}}(t)$ is equivalent to that of the OU stochastic process $\tilde{g}_{\{e,i\}}(t)$. The Fourier transform of the latter is given by

$$\tilde{g}_{\{e,i\}}(\omega) = \sqrt{\frac{2\sigma_{\{e,i\}}^2}{\tau_{\{e,i\}}}} \xi_{\{e,i\}}(\omega) \frac{1}{i\omega + \frac{1}{\tau_{\{e,i\}}}}. \quad (3.4)$$

Thus, the above assumption can be restated in more mathematical terms as

$$\tilde{g}'_{\{e,i\}}(\omega) = \sqrt{\frac{2\sigma_{\{e,i\}}^2}{\tau'_{\{e,i\}}}} \xi_{\{e,i\}}(\omega) \frac{1}{i\omega + \frac{1}{\tau'_{\{e,i\}}}}. \quad (3.5)$$

In writing equation 3.5, we further assumed that changes in the spectral properties of $\tilde{g}_{\{e,i\}}(\omega)$ and $\tilde{g}'_{\{e,i\}}(\omega)$ are reflected in changes of the parameters describing the corresponding Fourier transforms. In our case, the latter are the noise time constants $\tau_{\{e,i\}}$. This new “effective” time constants $\tau'_{\{e,i\}}$ will later be used to compensate the change in the spectral filtering properties in the analytic solution, equation 2.4. Note that this restriction to changes in the noise time constants is possible because only the combinations $\sigma_{\{e,i\}}^2 \tau'_{\{e,i\}}$ enter equation 2.4. Thus, each change in $\sigma_{\{e,i\}}$ can be mapped onto a change of $\tau'_{\{e,i\}}$ only. Moreover, due to their definition and equation 3.2, τ'_e and τ'_i undergo mutually independent modifications. In the next section, we explicitly calculate the link between the time constants $\tau'_{\{e,i\}}$ and $\tau_{\{e,i\}}$ and thus provide a solution with which the filtering problem can be resolved. We then justify the validity of the above assumptions and verify the proposed procedure by comparing the obtained results with numerical simulations.

4 One Solution to the Filtering Problem

As motivated above, the changes in the spectral filtering properties of the membrane equation 2.1 are reflected in new effective time constants τ'_e and τ'_i , which enter the steady-state solution 2.4. Moreover, as argued in the last section, this alteration of the spectral signature of the membrane potential $V(t)$ can be accounted for by incorporating the explicit form of these effective time constants $\tau'_{\{e,i\}}$ into equation 2.4. In this section, we propose a way to deduce this explicit form by using a simplified version of the stochastic system.

Due to the complicated functional structure of $\alpha_{\{e,i\}}(t)$, a direct treatment of the Fourier transforms $\tilde{g}'_{\{e,i\}}(\omega)$ is mathematically delicate. Therefore, in order to access $\tau'_{\{e,i\}}$, we followed another approach. We suggested above that an explicit expression of $\tau'_{\{e,i\}}$ as a function of the noise and membrane parameters entering the original system, equations 2.1 and 2.3, alone will allow solving the filtering problem. Such a relation is already provided by the lowest-order moments of the V_m distribution, in particular the variance σ_V^2 of the membrane potential at steady state. Indeed, as we will show below, comparing σ_V^2 obtained by direct integration of the stochastic system (which keeps its spectral structure unaltered), and the σ_V^2 deduced after application of the stochastic calculus proposed in Rudolph and Destexhe (2003), an explicit expression for $\tau'_{\{e,i\}}$ can be deduced.

Unfortunately, for the stochastic system originally described in Rudolph and Destexhe (2003), direct integration does not lead to a closed form. For this reason, we need to choose a simplified stochastic system. Due to the fact that the application of stochastic calculus does not impair the qualitative coupling between the stochastic processes $\tilde{g}_{\{e,i\}}(\omega)$, $\tilde{g}'_{\{e,i\}}(\omega)$ and V_m (compare equations 3.1 and 3.2), a simpler system with the same (conductance) noise processes but different coupling to V_m , such as additive coupling, can be considered. In a recent contribution (Richardson, 2004), such simplified models were investigated, among which an effective time constant approximation described the effect of colored conductance noise by a constant mean conductance and conductance fluctuations that couple to the mean V_m . The latter lead to a term describing current noise. This model is equivalent to equation 2.1, in which $V(t)$ in the noise terms is replaced by its mean E_0 , that is,

$$\frac{dV(t)}{dt} = -\frac{1}{\tau_m}(V(t) - E_0) - \frac{1}{C}\tilde{g}_e(t)(E_0 - E_e) - \frac{1}{C}\tilde{g}_i(t)(E_0 - E_i), \quad (4.1)$$

where $\tilde{g}_{\{e,i\}}(t)$ are given by equation 2.3.

In contrast to equation 2.1, this simplified stochastic system can explicitly be solved by direct integration, which leaves, as required, the spectral characteristics unaltered. The variance of the membrane potential was found to be (Richardson, 2004)

$$\sigma_V^2 = \left(\frac{\sigma_e \tau_m}{C}\right)^2 \frac{\tau_e}{\tau_e + \tau_m} (E_0 - E_e)^2 + \left(\frac{\sigma_i \tau_m}{C}\right)^2 \frac{\tau_i}{\tau_i + \tau_m} (E_0 - E_i)^2. \quad (4.2)$$

An equivalent expression for the membrane potential variance can be deduced by approximating the explicit form of σ_V^2 given in Manwani and Koch

(1999). The latter was directly deduced from the power spectral density of the underlying stochastic processes.

Treating the simplified stochastic system 4.1 within the framework detailed in Rudolph and Destexhe (2003) leads to the following Fokker-Planck equation:

$$\begin{aligned}
 (\partial_t \rho(V, t)) = & -\frac{1}{\tau_m} \rho(V, t) - \frac{V - E_0}{\tau_m} (\partial_V \rho(V, t)) \\
 & - \left(\frac{(E_0 - E_e)^2}{C^2} \alpha_e(t) + \frac{(E_0 - E_i)^2}{C^2} \alpha_i(t) \right) (\partial_V^2 \rho(V, t)). \quad (4.3)
 \end{aligned}$$

For $t \rightarrow \infty$, we obtain the steady-state solution. In this limit, $\partial_t \rho(V, t) \rightarrow 0$, $\rho(V, t) \rightarrow \rho(V)$ and $2\alpha_{\{e,i\}}(t) \rightarrow \sigma_{\{e,i\}}^2 \tau'_{\{e,i\}}$. To obtain the latter, we calculated the expectation value of equation 3.3 and used $\exp[-t/\tau_{\{e,i\}}] \rightarrow 0$ for $t \rightarrow \infty$ as well as the fact that in this limit, the integrated OU stochastic process $\tilde{w}_{\{e,i\}}^2(t)$ yields a Wiener process with two-dimensional cumulant $\langle \tilde{w}_{\{e,i\}}^2(t) \rangle = 2D_{\{e,i\}}t$ where $D_{\{e,i\}} = \sigma_{\{e,i\}}^2 \tau_{\{e,i\}}$ (see equation A.12a in Rudolph and Destexhe, 2003). With this, equation 4.3 takes the form

$$\begin{aligned}
 0 = & -\frac{1}{\tau_m} \rho(V) - \frac{V - E_0}{\tau_m} (\partial_V \rho(V)) \\
 & - \left(\frac{(E_0 - E_e)^2}{2C^2} \sigma_e^2 \tau'_e + \frac{(E_0 - E_i)^2}{2C^2} \sigma_i^2 \tau'_i \right) (\partial_V^2 \rho(V)). \quad (4.4)
 \end{aligned}$$

This equation is obtained from equation 4.3 by performing the limit $t \rightarrow \infty$, in which case the ratio $\frac{t}{\tau_{\{e,i\}}} \gg 1$. Note that this limit is not equivalent to taking the limit $\tau_{\{e,i\}} \rightarrow 0$. As already stated in the original contribution (Rudolph and Destexhe, 2003, see p. 2583, text after equation 3.3), for $t \rightarrow \infty$, the noise time constants $\tau_{\{e,i\}}$ become infinitesimally small compared to the time over which the steady-state probability distribution is obtained. This constitutes the basis for our assumption that the variables $\alpha_{\{e,i\}}(t)$ take a form corresponding to that obtained in the case of a Wiener process.

Equation 4.4 can now explicitly be solved, yielding

$$\rho(V) = e^{-\frac{(V-E_0)^2}{2\sigma_V^2}} \left(C_1 e^{\frac{E_0^2}{2\sigma_V^2}} + C_2 \sqrt{\frac{\pi}{2}} \sigma_V^2 \operatorname{Erfi} \left[\frac{V - E_0}{\sqrt{2\sigma_V^2}} \right] \right), \quad (4.5)$$

where $\text{Erfi}[z]$ denotes the imaginary error function and

$$\sigma_V^2 = \frac{\tau_m \sigma_e^2 \tau_e'}{2 C^2} (E_0 - E_e)^2 + \frac{\tau_m \sigma_i^2 \tau_i'}{2 C^2} (E_0 - E_i)^2 \tag{4.6}$$

the variance of the membrane potential. With the boundary conditions $\rho(V) \rightarrow 0$ for $V \rightarrow \pm\infty$, and normalization $\int_{-\infty}^{\infty} dV \rho(V) = 1$, equation 4.5 simplifies to a gaussian,

$$\rho(V) = \frac{1}{\sqrt{2\pi \sigma_V^2}} e^{-\frac{(V-E_0)^2}{2\sigma_V^2}}. \tag{4.7}$$

This result is the equivalent of equation 2.4, which was deduced from the stochastic system given in equation 2.1, when considering the stochastic system 4.1.

Comparing now the variance of the membrane potential distribution obtained with two qualitatively different methods, equations 4.2 and 4.6, respectively, yield the desired link between the time constants

$$\tau'_{[e,i]} = \frac{2\tau_{[e,i]}\tau_m}{\tau_{[e,i]} + \tau_m}. \tag{4.8}$$

If the argumentation and assumptions made in sections 2 and 3 are valid, then inserting these relations 4.8 in equation 4.7 should allow us to “correct” the change in the spectral signature introduced by reformulating the original stochastic system, equation 4.1, within the framework of stochastic calculus utilizing expectation values of differentials of the governing stochastic variables only.

Moreover, and more crucial, following the above argumentation, equations 4.8 should also provide this “correction” if we apply them to the original stochastic system, equation 2.1. This leads to an extended analytic expression, in which the time constants of the noise are rescaled according to the effective membrane time constant, thus compensating for the filtering effect described in section 3. That this expression leads to significant improvement for fitting numerical simulations, even for extreme parameter values, is tested in the next section.

5 Numerical Simulations ---

To test the validity of the extended analytic expression, we incorporated the effective time constants given in equation 4.8 into the analytic solution of

the full model, equation 2.4, and compared them to numerical simulations of the original equations in extreme parameter regimes that included very small and very large membrane time constants τ_m as well as noise time constants $\tau_{\{e,i\}}$. Using these effective time constants had little effect on parameter regimes for which the agreement was already good (see Figure 1A left; compare dashed and solid lines), but they markedly improved the agreement for other parameter regimes, in particular for very small time constants (see Figure 1A, middle). Indeed, a nearly perfect agreement between mean and variance obtained from numerical simulations and the extended analytic expression was obtained for all parameters so far tested, including membrane time constants down to $\tau_m = 0.005$ ms (see Figures 1B and 1C), which are three orders of magnitude smaller than those observed in real neurons. We also tested noise time constants ranging over seven orders of magnitude ($\tau_{\{e,i\}} = 0.005$ ms to 50,000 ms), whereas physiologically realistic time constants are expected to be of the order of 1 to 100 ms. Moreover, the extended solution can be shown to exactly describe highly asymmetric V_m distributions (see Figure 1A, right) and to correctly provide higher-order moments, like skewness or kurtosis, well within the errors of numerical simulations.

6 Discussion and Conclusion

We have provided an extension of previous work (Rudolph & Destexhe, 2003) in which an analytic solution was obtained for the steady-state V_m distribution of passive membranes subject to conductance-based synaptic noise. We showed here that this previously obtained analytic expression significantly deviates from numerical simulations for certain parameter values, in particular for small membrane time constants. We proposed a way to obtain an extended analytic expression in which this matching problem is solved.

We hypothesized that such deviations are due to a spectral filtering problem inherent to the stochastic calculus used in Rudolph and Destexhe (2003). This hypothesis is supported by the following arguments. First, we explicitly showed that the spectral structure of the stochastic system is altered, presumably consequent to the approach of characterizing stochastic processes and their integrals (in the sense of Riemann-Stieltjes) in terms of their distributions only, that is, the cumulants and moments of their characteristic functions (see Rudolph & Destexhe, 2003). This mathematically well-defined approach to stochastic systems (e.g., Gardiner, 2002) is a description at the level of local expectation values and allowed us to deduce an analytically solvable Fokker-Planck equation directly from equation 2.1, without explicit integration over stochastic variables. However, by strictly

using moments of stochastic processes, alterations of the spectral properties of the stochastic system in question were introduced, as we explicitly showed here by calculating the Fourier transform of the V_m .

Second, the (numerical) observation that the mismatch is larger for small membrane time constants (see Figure 1) can be intuitively justified based on filtering properties. When the membrane time constant is much smaller than the synaptic time constants, the power spectral density of the V_m will be essentially dominated by that of the synaptic processes. If the spectral signature of their effect on the membrane is altered, this will be maximally seen in the power spectral density of the V_m for fast membrane time constants. For slow membrane time constants, the filtering of fast frequencies is more pronounced, and possible alterations in spectral properties will be masked by the RC filtering of the membrane.

Ultimately, the correction needed to recover the correct spectral properties should be directly estimated from the Fourier transform of the V_m . Unfortunately, the complex form of these equations does not permit such a direct estimate, and we had to follow a different way. We used a dynamically different and simplified stochastic system for which direct integration is possible (Richardson, 2004) and applied to it the same stochastic calculus as in Rudolph and Destexhe (2003). Comparing the moments of the V_m distribution allowed us to estimate a correction on the noise time constants to account for filtering effects. Because both systems share the same functional coupling of the V_m and conductances in Fourier space, we argue that the same correction applies to the original full conductance-based system, leading to the extended analytic expression. Indeed, numerical simulations show that the matching for this extended expression with simulations is remarkable—over seven orders of magnitude of the parameters. (NEURON demo programs comparing simulations with the extended analytic expression are available online at <http://cns-iaf.cnrs-gif.fr>.)

We note, however, that the extended analytic expression for the membrane potential distribution of the full conductance-based model presented here does not bypass the two limitations already outlined in the original contribution. First, due to the nature of the distribution of the incorporated conductance noise processes, the presence of unphysical negative conductances cannot be accounted for and will lead to a mismatch between numerical simulations and analytic solution. A possible solution could be to make use of qualitatively different stochastic processes for conductances, for example, described by gamma distributions. Second, eventual changes in the sign of the driving force due to crossing of the conductance reversal potentials will lead to a different dynamic behavior of the numerical model that, due to the exclusive use of expectation values and averages, cannot be

captured in the approach followed here. The expected deviations are most visible at membrane potentials close to the reversal potentials and large values of the involved conductances. Possible solutions here could include the use of different numerical integration methods as well as the use of different boundary conditions (e.g., $\rho(V) \rightarrow 0$ for $V = E_e$ and $V = E_i$). These modifications are currently under investigation.

In sum, this semiheuristic extension of the solution proposed in Rudolph and Destexhe (2003) provides us with an expression that quantitatively fits the steady-state V_m distribution for a considerably larger range of parameter values. Of course, this extended expression is not formally a solution of the original Fokker-Planck equation anymore, and further work is needed to formalize the problem in the appropriate mathematical framework. Another possible extension would be to incorporate other types of synaptic conductances such as the slow types of glutamatergic (NMDA) or GABAergic (GABA_B) currents. Most important, the proposed extension of our previous work should be particularly useful for performing accurate estimates of the mean ($g_{[e,i]0}$) and variance ($\sigma_{[e,i]}^2$) of synaptic conductances by fitting the extended expressions to experimentally recorded V_m distributions (Rudolph, Piwkowska, Badoual, Bal, & Destexhe, 2004b; Rudolph, Pelletier, Paré, & Destexhe, 2004a).

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