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A spatial stochastic neuronal model with Ornstein–Uhlenbeck input current

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Abstract. We consider a spatial neuron model in which the membrane potential satisfies a linear cable equation with an input current which is a dynamical random process of the Ornstein–Uhlenbeck (OU) type. This form of current may represent an approximation to that resulting from the random opening and closing of ion channels on a neuron's surface or to randomly occurring synaptic input currents with exponential decay. We compare the results for the case of an OU input with those for a purely white-noise-driven cable model. The statistical properties, including mean, variance and covariance of the voltage response to an OU process input in the absence of a threshold are determined analytically. The mean and the variance are calculated as a function of time for various synaptic input locations and for values of the ratio of the time constant of decay of the input current to the time constant of decay of the membrane voltage in the physiological range for real neurons. The limiting case of a white-noise input current is obtained as the correlation time of the OU process approaches zero. The results obtained with an OU input current can be substantially different from those in the white-noise case. Using simulation of the terms in the series representation for the solution, we estimate the interspike interval distribution for various parameter values, and determine the effects of the introduction of correlation in the synaptic input stochastic process.

1 Introduction

Early experimental studies of the electrophysiological activity of neurons revealed a surprising degree of variability in their firing behaviour, as characterized by the probability distribution function of the interspike interval (ISI); that is, the time between consecutive action potentials. In one such study, Burns and Webb (1976) found that the ISI distribution in cat cerebral cortex neurons in "spontaneous" activity was approximately lognormal whenever the mean firing rate was greater than about 2.5 spikes per second. On the other hand, more-slowly firing cells had ISI densities with long tails, which was as predicted by simple leaky integrate-and-fire (Lapicque) models with considerable amounts of inhibition (Tuckwell 1978). In another extensive early study (Whitsel et al. 1977), the variability in the response of macaque monkey somatosensory cortical neurons to tactile stimuli was found to be heterogeneously distributed across the neuronal population, and depended on mean firing rate. The implication of these and many similar findings is that mammalian CNS neurons rarely if ever fire in regular or predictable temporal patterns. The nature of the information coding by such cells is not obvious and has become a major concern in theoretical neuroscience (see, for example, Konig et al. 1996). Many issues have thus arisen with regard to the role of variability in nervous system function (see, for example, Mainen and Sejnowski 1995; Troyer and Miller 1997; Shadlen and Newsome 1998; Feng and Brown 1999; Salinas and Sejnowski 2000). Noise may be useful in that it enhances firing rates (Tuckwell and Richter 1978) and has been considered even essential for brain functioning by some authors (Arhem and Johansson 1996; Freeman 1996). It is useful to consider therefore the effects of noise at the level of the neuron itself, and in particular to include as much anatomical and physiological detail as possible without making a model excessively complicated. Some authors have considered the spatial extent of the neuron with stochastic compartmental models using software packages (Softky and Koch 1993) such as NEURON. Other authors have proceeded with linear approximations in a similar discrete approach (Lansky and Rodriguez 1999). Nevertheless, in many theoretical investigations the spatial extent of nerve cells has been ignored despite early deterministic studies, of spatially extended neurons, represented by cylindrical cables (summarized in Tuckwell 1988, Chap. 6). Such studies

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may sometimes be simplified by using an equivalent cylinder (Rall 1989) or its generalized version (Walsh and Tuckwell 1985).

In our previous work on the effects of noise on neural activity, we have employed a passive cable model representing a cylindrical nerve segment or whole neuronal dendritic tree with the appropriate mapping (Wan and Tuckwell 1979; Tuckwell et al. 1984). Although the synaptic inputs may give rise to rapid and significant changes in postsynaptic membrane potential, a diffusion approximation was used to smooth out the input by employing a white-noise input current with drift at a given spatial location. We obtained expressions for the first- and second-order moments of the voltage over the neuron's surface, including the two-point covariance, and studied the role of input position in determining the nature of the distribution function of ISIs, both with analytical and simulation techniques. Only a few other theoretical results of an analytical nature have been obtained for such spatially extended neuron models with stochastic input currents (Poznanski and Peiris 1996). Many related experimental results are summarized in Segundo et al. (1994).

In a point leaky integrate-and-fire or Lapicque model neuron, excited synaptically at event times in a homogeneous Poisson process $N = \{N(t), t \geq 0\}$ with rate parameter ν, the neuron's depolarization, $V(t)$, can be obtained from the following pair of stochastic ordinary differential equations:

$$C\frac{\mathrm{d}V}{\mathrm{d}t} = -\frac{V}{R} + I$$

$$\frac{\mathrm{d}I}{\mathrm{d}t} = -\alpha I + \epsilon\frac{\mathrm{d}N}{\mathrm{d}t} \quad .$$

Here C is the membrane capacitance, R is the resistance, $I(t)$ is the synaptic input current at time t and ϵ is the magnitude of the current delivered at each input event, which arises due to the stochastic firing in excitatory presynaptic fibers which connect with the given neuron over its soma dendritic surface, including synapses at dendritic spines. Thus, at the event times in the Poisson process, the postsynaptic current jumps by ϵ and then decays with a time constant $1/\alpha$. This means that the postsynaptic potentials (PSPs) have finite rise times as is observed experimentally. We note, however, that there are two factors responsible for the gradual rather than abrupt change in voltage in response to synaptic activation. One is that the input currents are not, by virtue of synaptic dynamical processes, impulse functions as in Stein's (1965) original model. The other factor which strongly influences the rise time of a PSP, as seen at the soma, is the electrotonic distance of the activated synapse(s) from the soma (see, for example, Tuckwell 1988, Chap. 6). Now the term $\epsilon(\mathrm{d}N/\mathrm{d}t)$ in the equation for the synaptic input current can be approximated by a smoother white-noise version (diffusion approximation), in which case we put

$$\mathrm{d}I = -(\alpha I + \beta)\mathrm{d}t + \gamma\,\mathrm{d}W \quad ,$$

where $\beta = \epsilon\nu$ and $\gamma = \sqrt{\nu\epsilon^2}$, and $W = \{W(t), t \geq 0\}$ is a standard (zero mean, variance t) Wiener process.

We will investigate a spatial neuron model which has the same kind of synaptic input current as in the above point model. The use of a spatial model has the advantage that both of the factors responsible for the graded response at the soma or trigger zone mentioned in the previous paragraph are taken into account in a natural way. By means of this approach, we may also address the quantitative aspects of the effects of the random opening and closing of ion channels on a neuron's surface (Chow and White 1996). These may be due to the arrival of stimulant (e.g. odorant) molecules at receptor molecules (Rospars et al. 1994), as such a process (primitively a birth and death process) is known to be able to be approximated by an Ornstein–Uhlenbeck (OU) process (OUP) (Tuckwell 1987). Such an investigation will be carried out in a later article.

2 The spatial model and its general solution

We consider a spatial neuron which extends from $x = a$ to $x = b$ with depolarization $V(x,t)$ at the space-point x and time-point t. Time is in units of the membrane time constant τ and distance is in units of the space constant λ. In terms of membrane biophysical constants, we have $\tau = r_\mathrm{m}c_\mathrm{m}$ and $\lambda = \sqrt{r_\mathrm{m}/r_\mathrm{i}}$, where r_m is the membrane resistance of unit length times unit length, c_m is the membrane capacitance per unit length and r_i is the internal resistance per unit length. We assume cylindrical symmetry for simplicity.

Stimulating the model neuron are n_E excitatory and n_I inhibitory synaptic inputs at electrotonic distances $x_{\mathrm{E},j}$ and $x_{\mathrm{I},k}$ from the soma, respectively, where $j = 1, \ldots, n_\mathrm{E}$ and $k = 1, \ldots, n_\mathrm{I}$. The arrival times of these inputs are assumed to be at the event times of temporally homogeneous Poisson processes $N_{\mathrm{E},j}$ and $N_{\mathrm{I},k}$ with rate parameters $\nu_{\mathrm{E},j}$ and $\nu_{\mathrm{I},k}$, respectively. We then have

$$\frac{\partial V}{\partial t} = -V + \frac{\partial^2 V}{\partial x^2} + \frac{r_\mathrm{m}}{\lambda}\left[\sum_{j=1}^{n_\mathrm{E}} \delta(x - x_{\mathrm{E},j})I_j^\mathrm{E}(t) + \sum_{k=1}^{n_\mathrm{I}} \delta(x - x_{\mathrm{I},k})I_k^\mathrm{I}(t)\right] \quad , \tag{1}$$

where the jth excitatory current $I_j^\mathrm{E}(t)$ satisfies

$$\frac{\mathrm{d}I_j^\mathrm{E}}{\mathrm{d}t} = -\alpha_{\mathrm{E},j}I_j^\mathrm{E} + A_{\mathrm{E},j}\frac{\mathrm{d}N_{\mathrm{E},j}}{\mathrm{d}t} \quad , \tag{2A}$$

and where $\alpha_{\mathrm{E},j}$ is the reciprocal of its time constant of decay and the units of the $A_{\mathrm{E},j}$ are the same as those of the I_j^E. Similarly for the kth inhibitory current:

$$\frac{\mathrm{d}I_k^\mathrm{I}(t)}{\mathrm{d}t} = -\alpha_{\mathrm{I},k}I_k^\mathrm{I}(t) + A_{\mathrm{I},k}\frac{\mathrm{d}N_{\mathrm{I},k}}{\mathrm{d}t} \quad . \tag{2B}$$

All the $A_{\mathrm{E},j}$ are positive and all the $A_{\mathrm{I},k}$ are negative. In (1), $\delta(.)$ is the Dirac delta function. The currents here are in amperes and x, $\delta(x - x_{\mathrm{E},j})$ and $\delta(x - x_{\mathrm{I},k})$ are dimensionless. The distances $x_{\mathrm{E},j}$ and $x_{\mathrm{E},k}$ are also in units of λ.

A synaptic event makes the corresponding input current rise locally quickly and then decay exponentially. The corresponding local change in V is a postsynaptic potential with a finite rise time and an approximately exponential decay, with amplitude diminishing as distance from the source increases. Postsynaptic currents (and potentials) from a space–time sequence of inputs undergo spatial and temporal summation. To describe completely the space–time evolution of the neuronal potential, initial conditions must be specified for V, as well as for all the (synaptic) input currents and their corresponding driving Poisson processes: see below, where it will be seen that any random or deterministic initial conditions may be easily taken into account.

It is again advantageous to replace the currents with discontinuous changes by smoothed versions. Thus we put

$$\mathrm{d}I_j^{\mathrm{E}} = (-\alpha_{\mathrm{E},j} I_j^{\mathrm{E}} + A_{\mathrm{E},j} v_{\mathrm{E},j})\mathrm{d}t + \sqrt{A_{\mathrm{E},j}^2 v_{\mathrm{E},j}}\,\mathrm{d}W_{\mathrm{E},j} \ , \tag{3A}$$

for $j = 1, 2, \ldots, n_{\mathrm{E}}$,
and

$$\mathrm{d}I_k^{\mathrm{I}} = (-\alpha_{\mathrm{I},k} I_k^{\mathrm{I}} + A_{\mathrm{I},k} v_{\mathrm{I},k})\mathrm{d}t + \sqrt{A_{\mathrm{I},k}^2 v_{\mathrm{I},k}}\,\mathrm{d}W_{\mathrm{I},k} \ , \tag{3B}$$

for $k = 1, 2, \ldots, n_{\mathrm{I}}$, where the $\{W_{\mathrm{E},j}\}$ and $\{W_{\mathrm{I},k}\}$ are all independent standard Wiener processes, on the assumption that there is no correlation between individual synaptic inputs. Of course, in many cases of interest, such as for cortical pyramidal cells, the latter assumption will be violated for individual synapses, but the approach can be justified by lumping together similar close-by synapses with a common driving source; or, alternatively, correlation can be introduced between the various inputs. Thus each input current is being approximated by an OUP (Uhlenbeck and Ornstein 1930). The effects of replacing Poisson processes by diffusion approximations have been elaborated on in articles referred to in Tuckwell (1989).

Since the system under consideration is linear, it is notationally convenient in the first instance to consider just a single input site at $x = x_0$, so

$$\frac{\partial V}{\partial t} = -V + \frac{\partial^2 V}{\partial x^2} + \frac{r_{\mathrm{m}}}{\lambda}\delta(x - x_0)I(t) \tag{4A}$$

$$\frac{\mathrm{d}I}{\mathrm{d}t} = -\alpha I + A\frac{\mathrm{d}N}{\mathrm{d}t} \ , \tag{4B}$$

where A is positive (excitatory) or negative (inhibitory). In the white-noise version the latter equation is replaced by

$$\mathrm{d}I = (-\alpha I + \mu)\mathrm{d}t + \sigma\,\mathrm{d}W \ , \tag{4C}$$

where $\mu = Av$ and $\sigma = \sqrt{A^2 v}$.

We now suppose that the initial voltage distribution is $V_0(x), a \le x \le b$, and the initial value of the input current is I_0, where both of these quantities are possibly stochastic. For the Wiener process, the initial value is $W(0) = 0$ with probability equal to one. We note that the input current I is independent of V, so one may integrate (4B) independently of (4A). This gives

$$I(t) = I_0\,\mathrm{e}^{-\alpha t} + \mu\mathrm{e}^{-\alpha t}\int_0^t \mathrm{e}^{\alpha t'}\mathrm{d}t' + \sigma\,\mathrm{e}^{-\alpha t}\int_0^t \mathrm{e}^{\alpha t'}\mathrm{d}W(t') \ . \tag{5}$$

Now, as is usually the case, we may impose boundary conditions at $x = a$ and $x = b$ which are of such a nature that a Green's function can be obtained for the partial differential equation (4A) without the source terms. These boundary conditions include sealed-end conditions and lumped-soma termination conditions (see, for example, Tuckwell 1988). Letting the Green's function solution be G, the depolarization is given by

$$V(x,t) = \int_a^b V_0(y)G(x,y;t)\mathrm{d}y + \frac{r_{\mathrm{m}}}{\lambda}\int_0^t G(x,x_0;t-s)I(s)\mathrm{d}s \ . \tag{6}$$

One may then substitute (5) for I here to obtain an explicit expression for $V(x,t)$. From such a solution one may obtain information concerning subthreshold responses, such as moments and spectral densities, and also address the problem of determining the properties of the time taken to generate an action potential – the ISI random variable. We will also be able to examine the limiting case of $\alpha \to \infty$, whereupon the input current itself is a white-noise as in Wan and Tuckwell (1979).

3 Subthreshold response

3.1 Mean

We may readily obtain the moments by straightforwardly taking expectations in appropriate combinations of integrals such as (6). We use overbars to denote expected values of the given random variables, $v(y)$, the initial (random) distribution of potential and I_0, the initial (random) value of the applied current. This gives, for the mean depolarization,

$$\mathrm{E}[V(x,t)] = \int_a^b \bar{v}(y)G(x,y;t)\mathrm{d}y + \frac{r_{\mathrm{m}}}{\lambda}\int_0^t G(x,x_0;t-s)\Big(\frac{\mu}{\alpha} + \mathrm{e}^{-\alpha s}\Big[\bar{I}_0 - \frac{\mu}{\alpha}\Big]\Big)\mathrm{d}s \ . \tag{7}$$

When, as is often assumed, the neuron is initially at resting voltage along its entire length, and the initial current is also zero, we have the simplified result

$$\mathrm{E}[V(x,t)] = \frac{r_{\mathrm{m}}}{\lambda}\frac{\mu}{\alpha}\int_0^t G(x,x_0;t-s)\big(1 - \mathrm{e}^{-\alpha s}\big)\mathrm{d}s \ . \tag{7A}$$

This can be compared with the corresponding result for the white noise current $I = \mu + \sigma(\mathrm{d}W/\mathrm{d}t)$,

$$\mathrm{E}[V_{\mathrm{W}}(x,t)] = \frac{r_{\mathrm{m}}}{\lambda}\mu \int_0^t G(x,x_0;t-s)\mathrm{d}s \ . \tag{7B}$$

3.2 Covariance and variance

To obtain the second-order moments, we make the simplifying assumption that the initial conditions are deterministic so that $v(y) = \bar{v}(y)$ and $I_0 = \bar{I}_0$, whereupon we find that

$$\begin{aligned} &K(x_1,t_1;x_2,t_2) \\ &\quad = \mathrm{cov}[V(x_1,t_1),V(x_2,t_2)] \\ &\quad = \left(\frac{r_{\mathrm{m}}\sigma}{\lambda}\right)^2 \mathrm{E}\left[\left(\int_0^{t_1} G(x_1,x_0;t_1-s_1)\mathrm{e}^{-\alpha s_1}\int_0^{s_1} \mathrm{e}^{\alpha t_1'}\mathrm{d}W(t_1')\mathrm{d}s_1\right)\right. \\ &\qquad \times \left.\left(\int_0^{t_2} G(x_2,x_0;t_2-s_2)\mathrm{e}^{-as_2}\int_0^{s_2} \mathrm{e}^{\alpha t_2'}\mathrm{d}W(t_2')\mathrm{d}s_2\right)\right] , \end{aligned}$$

which can be simplified to

$$\begin{aligned} K(x_1,t_1;x_2,t_2) = \left(\frac{r_{\mathrm{m}}\sigma}{\lambda}\right)^2 \frac{1}{2\alpha}\int_{s_1=0}^{t_1}\int_{s_2=0}^{t_2} & G(x_1,x_0;t_1-s_1) \\ & \times G(x_2,x_0;t_2-s_2)\mathrm{e}^{-\alpha(s_1+s_2)} \\ & \times \left[\mathrm{e}^{2\alpha\min(s_1,s_2)} - 1\right]\mathrm{d}s_1\,\mathrm{d}s_2 \ , \end{aligned} \tag{8}$$

where $\min(s_1,s_2)$ denotes the smaller of the two variables s_1 and s_2. In particular, the variance of the depolarization at the space–time point (x,t) is

$$\begin{aligned} \mathrm{var}[V(x,t)] = \left(\frac{r_{\mathrm{m}}\sigma}{\lambda}\right)^2 \frac{2}{\alpha}\int_{s_1=0}^{t}\int_{s_2=0}^{s_1} & G(x,x_0;t-s_1) \\ & \times G(x,x_0;t-s_2)\mathrm{e}^{-\alpha s_1}\sinh(\alpha s_2)\mathrm{d}s_1\,\mathrm{d}s_2 \ . \end{aligned} \tag{9}$$

This may be compared with the variance in the case of a white-noise input current

$$\mathrm{var}[V_{\mathrm{W}}(x,t)] = \left(\frac{r_{\mathrm{m}}}{\lambda}\right)^2 \sigma^2 \int_0^t G^2(x,x_0;t-s)\mathrm{d}s \ . \tag{9A}$$

We note that: (i) $V(x,t)$ is a Gaussian random variable (in the absence of thresholds), so its probability distribution is completely determined by (7A) and (9); and (ii) $\{V(x,t), t \geq 0\}$ is, for fixed x, a Gaussian random process, so this process is completely describable (again in the absence of a threshold) through its mean value function (7A) and the covariance kernel (8) with $x_1 = x_2 = x$.

3.3 Computations for sealed ends

The calculation of moments for specific boundary conditions for which a Green's function G can be found is straightforward. The parameter space is large, however, so we will focus attention on the effects of changes in the parameter α, which is the reciprocal of the time constant of decay of the synaptic current at its site of origin. To illustrate such effects we choose, as a first approximation for a physiological neuron, conditions for a cylinder of length L such that there is no current escaping at the end points $x = 0$ and $x = L$. This gives the conditions on the spatial derivatives $V_x(0,t) = 0$ and $V_x(L,t) = 0$, with the subscripts here denoting partial differentiation. Using the eigenfunction expansion for G gives the results

$$\mathrm{E}[V(x,t)] = \frac{r_{\mathrm{m}}}{\lambda}\frac{\mu}{\alpha}\sum_{n=0}^{\infty} v_n(t)\phi_n(x)\phi_n(x_0) \ , \tag{10}$$

where

$$v_n(t) = \begin{cases} \frac{1}{\mu_n^2} - \frac{\mathrm{e}^{-\alpha t}}{\mu_n^2-\alpha} + \frac{\alpha\,\mathrm{e}^{-\mu_n^2 t}}{\mu_n^2(\mu_n^2-\alpha)}, & \mu_n^2 \neq \alpha; \\ \frac{1}{\alpha}(1-\mathrm{e}^{-\alpha t}) - t\mathrm{e}^{-\alpha t}, & \mu_n^2 = \alpha \ . \end{cases}$$

and

$$\phi_n(x) = \begin{cases} \frac{1}{\sqrt{L}}, & n = 0; \\ \sqrt{\frac{2}{L}}\cos\left(\frac{n\pi x}{L}\right), & n = 1,2,\ldots \end{cases}$$

with $\mu_n^2 = 1 + \frac{n^2\pi^2}{L^2}$ for all n.

The variance of $V(x,t)$ is given explicitly as the following double-infinite series with a similar expression for the covariance of the voltage at various combination of space–time points:

$$\begin{aligned} &\mathrm{var}[V(x,t)] \\ &\quad = \left(\frac{r_{\mathrm{m}}}{\lambda}\right)^2 \frac{\sigma^2}{2\alpha}\sum_{m=0}^{\infty}\sum_{n=0}^{\infty} v_{mn}(t)\phi_m(x)\phi_m(x_0)\phi_n(x)\phi_n(x_0) \end{aligned} \tag{11}$$

where the time-dependent coefficients are, in general, given by

$$\begin{aligned} v_{mn}(t) = \frac{\rho_{mn}}{\mu_{mn}} &- \frac{\mathrm{e}^{-2\alpha t}}{(\mu_m^2-\alpha)(\mu_n^2-\alpha)} + \frac{2\alpha}{\mu_m^4-\alpha^2}\frac{1}{\mu_n^2-\alpha}\mathrm{e}^{-(\mu_m^2+\alpha)t} \\ &+ \frac{2\alpha}{\mu_n^4-\alpha^2}\frac{1}{\mu_m^2-\alpha}\mathrm{e}^{-(\mu_n^2+\alpha)t} - \frac{2\alpha\,\mathrm{e}^{-\mu_{mn}t}}{\mu_{mn}(\mu_m^2-\alpha)(\mu_n^2-\alpha)} \end{aligned}$$

with

$$\mu_{mn} = \mu_m^2 + \mu_n^2$$

and

$$\rho_{mn} = \frac{1}{\mu_m^2+\alpha} + \frac{1}{\mu_n^2+\alpha} \ .$$

However, in the special case $\alpha = 1$, we have

$$v_{00}(t) = \tfrac{1}{2}\left[1-\mathrm{e}^{-2t}\right] - \left[t+t^2\right]\mathrm{e}^{-2t}$$

$$v_{m0}(t) = v_{0m}(t) = \frac{1}{\mu_m^2+1}\left[\frac{1}{2}+\frac{1}{\mu_m^2+1}\right] - \frac{\mathrm{e}^{-2t}}{\mu_m^2-1}\left[t+\frac{1}{2}\right] + \frac{2\mathrm{e}^{-(\mu_m^2+1)t}}{\mu_m^4-1}\left[t+\frac{1}{2}\right] .$$

The mean and variance of $V(x,t)$ for these boundary conditions for the case where $I(t)$ is purely Gaussian white noise were given in Wan and Tuckwell (1979), and hence we may ascertain the effects of temporal correlation in the noise on these moments for various locations of the synaptic input. The spatial factors in the moments and distribution of the voltage are the same for an OUP current input as for a white-noise input, as only the temporal components of the eigenfunction expansions differ. It is noted that when $\alpha < \infty$, the variance of $V(x,t)$ is finite for all x and all t, in contrast to the white-noise case where $\mathrm{var}[V(x,t)]$ becomes unbounded at the stimulus location x_0 and $t > 0$.

3.4 Values of α

In order to choose values of α which are appropriate for real neurons, we consider illustrative examples from the hippocampus and cerebral cortex. First, we appeal to the results of Destexhe et al. (1994) which were obtained by the probabilistic modelling of ion channel kinetics at various types of central synapses. For example, for the glutamate AMPA/kainate synapse on hippocampal pyramidal cells, the time constant of decay of postsynaptic currents was about 2.7 ms, although this figure was apparently obtained on the assumption of an isopotential neuron. Using the R_m, R_i and C_m values from Carnevale et al. (1995), we find that the membrane time constants for CA1 pyramidal cells, CA2 pyramidal cells and granule cells are 30, 70 and 40 ms, respectively. Since time in (4A) and (4B) is in units of the membrane time constant, we find that the corresponding values of α may be estimated as 11.1, 25.6 and 14.8, respectively. For neocortical pyramidal cells (rat), we may use the data of Rapp et al. (1996). The membrane time constant of 50 ms and an estimated time constant of decay (based on the "alpha-function" conductance change of Rapp et al. 1996) of the postsynaptic current of 3 ms, gives $\alpha = 16.7$. Furthermore, using standard (cat) motoneuron data (summarized in Tuckwell 1988) we find that a value of α of about 3.3 would be appropriate for excitatory synapses on this cell. It is therefore of interest to consider values of α in the range from about 1 to 30.

3.5 The white-noise limit

In the case of a train of purely Poisson-input currents, to which Gaussian white-noise is an approximation, the postsynaptic currents are essentially delta functions. In the present case, the covariance of the process satisfying the stochastic equation (4B) is

$$\mathrm{cov}[I(s), I(t)] = \frac{\sigma^2}{2\alpha}\left[\mathrm{e}^{-\alpha(t-s)} - \mathrm{e}^{-\alpha(t+s)}\right] , \qquad (12)$$

where $s \le t$. Since white-noise is delta-correlated, the limiting case $\alpha \to \infty$ is of interest. However, just letting $\alpha \to \infty$ is not useful, because it makes I more and more deterministic as it approaches the solution of $\mathrm{d}I/\mathrm{d}t = -\alpha I$. In the limit we want

$$I \to \mu + \sigma\frac{\mathrm{d}W}{\mathrm{d}t} .$$

Since

$$\frac{1}{\alpha}\frac{\mathrm{d}I}{\mathrm{d}t} = -I + \frac{1}{\alpha}\left[\mu + \sigma\frac{\mathrm{d}W}{\mathrm{d}t}\right] ,$$

it is necessary to increase μ and σ by the same factor by which α is increased as the limit is taken. This is achieved by setting $\mu = k_1\alpha$ and $\sigma = k_2\alpha$, where k_1 and k_2 are constants. It can be verified that in the limit $\alpha \to \infty$ the covariance function (12) does become a delta function. It can be readily seen from the expansions (10) and (11) that as $\alpha \to \infty$,

$$\begin{aligned}\mathrm{E}[V(x,t)] &\to \frac{r_\mathrm{m}}{\lambda}k_1\sum_{n=0}^{\infty}\frac{1-\mathrm{e}^{-\mu_n^2 t}}{\mu_n^2}\phi_n(x)\phi_n(x_0)\\ &= \mathrm{E}[V_\mathrm{W}(x,t)] ,\end{aligned}$$

and that

$$\begin{aligned}&\mathrm{var}[V(x,t)]\\ &\to \left(\frac{r_\mathrm{m}}{\lambda}\right)^2 k_2^2\sum_{m=0}^{\infty}\sum_{n=0}^{\infty}\frac{1-\mathrm{e}^{\mu_{mn}t}}{\mu_{mn}}\phi_m(x)\phi_m(x_0)\phi_n(x)\phi_n(x_0)\\ &= \mathrm{var}[V_\mathrm{W}(x,t)] .\end{aligned}$$

3.6 Numerical results

The mean depolarization in the absence of a threshold was determined for a cable with sealed-end conditions for a typical neuronal electrotonic length of $L = 1.5$. The driving input OUP current was placed at a site either near the origin (trigger zone), with $x_0 = 0.25$, or at a more distal site, with $x_0 = 0.75$. Results were computed from the above series expressions and also verified by simulations whose main purpose was in the estimation of ISI (see Sect. 4). The remaining parameters were chosen to make the time course of the voltage correspond to physiologically realistic values. Since r_m/λ simply, multiplies I, this factor was set at unity, whilst α, μ and σ were varied – in accordance with the above discussion on the limiting case of white noise – in such a way that $\mu/\alpha = \mathrm{constant} = 15$ and $\sigma/\alpha = \mathrm{constant} = 10$. For the mean, terms to $m = 6$ were employed in the sums, although calculations were also performed for larger values of m, giving essentially the same numerical results.

The mean depolarization versus time for various α is shown in Fig. 1a. For $x_0 = 0.75$ (top part), the asymptotic or steady-state mean of about 9 mV is attained by

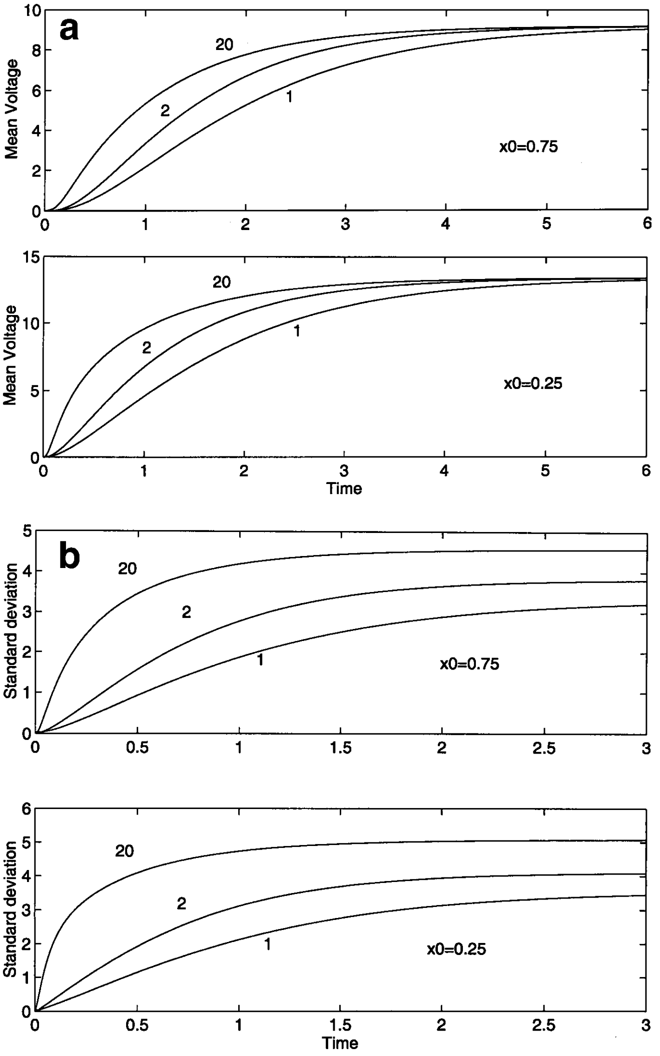

Fig. 1. **a** The computed mean depolarization, $V(0, t)$, at the trigger zone, is shown as a function of time for various α (values indicated near each curve), in the absence of any threshold for firing of the nerve cell. The neuronal electrotonic length is $L = 1.5$, and we show the results for a synaptic input remote from the origin at $x_0 = 0.75$ in the *upper part* and nearer to the origin at $x_0 = 0.25$ in the *lower part*. Note that the larger the value of α, the closer the input process is to a purely white noise. **b** The standard deviation of $V(0, t)$ versus t for various α corresponding to the results shown in **a** for the mean

about $t = 6$, where time is in units of time constants. In the bottom part of Fig. 1a are shown the results for $x_0 = 0.25$, and these are similar in structure but that now the steady-state mean is considerably greater at about 14 mV. The effects of varying α within the physiological range are greatest for α of order 1, and are then most appreciable at small times. For example, changing α from 1 to 2 makes a substantial difference in the time at which a given subthreshold voltage is attained. It is clear that the larger the value of α, the sooner a given voltage is reached, with the fastest growth in the purely white-noise case.

Figure 1b shows the standard deviation of the depolarization $V(0, t)$, obtained by summing the expansion (11), versus time corresponding to the results for the mean of Fig. 1a. The differences here as α changes at the lower end of the range of physiological values are somewhat more pronounced than those of the mean. When $x_0 = 0.75$ (top part of figure) and $\alpha = 1$ and $\alpha = 2$, the steady-state values are attained by about $t = 2$ and $t = 1.75$, respectively whereas for $\alpha = 20$ the steady state is achieved by about $t = 1$. For the case of an input closer to the origin (soma, trigger zone) the steady-state standard deviations are larger and are attained somewhat more rapidly. In fact, with $\alpha = 20$ the steady state is attained by about $t = 0.75$. In all cases the results in the purely white-noise case, corresponding to $\alpha = \infty$, differ considerably from those for small values of α which may occur for some synaptic inputs in physiological neurons.

4 Interspike intervals

In non-linear partial differential equation models for nerve membrane potential, such as the Hodgkin–Huxley model or the emulating Fitzhugh–Nagumo model, there is no need to impose a threshold condition because it is an intrinsic property of the dynamical system. However, in linear cable models there is no natural threshold, and the ISI can be determined in several ways, as was described previously for the purely white-noise case (Tuckwell et al. 1984; Tuckwell 1989). Here we will assume a simple threshold condition, namely that an action potential is generated if the depolarization at some fixed space point, akin to a trigger zone, reaches a constant value θ. Then, assuming this spike-generating zone is located at $x = 0$, we may put for the ISI

$$T = T_\theta + T_R \ ,$$

where T_R is a refractory period and

$$T_\theta = \inf\{t | V(0, t) \geq \theta\} \ ,$$

where the latter quantity the time of first passage of the potential at the trigger zone to the threshold level.

Now, even for one-dimensional models such as the OU diffusion approximation (Gluss 1967; Johannesma 1968; Roy and Smith 1969), the determination of the moments of the firing time has been possible by analytical and numerical techniques (Ricciardi and Sacerdote 1979; Wan and Tuckwell 1982) but the firing-time distribution is most easily studied by simulation methods (Giraudo and Sacerdote 1998). For the present model, it is feasible to make a numerical determination of the moments and distribution of the firing time by solving the (linear) partial differential equations for these quantities which arise from a Kolmogorov equation approach as was attempted in the white-noise case (Tuckwell et al. 1984). However, this method leads to an unwieldy numerical computation and will be deferred to a later work. We have thus proceeded directly with a numerical solution of the stochastic partial differential equations using standard methods that have been described previously (Tuckwell et al. 1984). Thus, a time-dependent component $u(t)$, say, of the Fourier

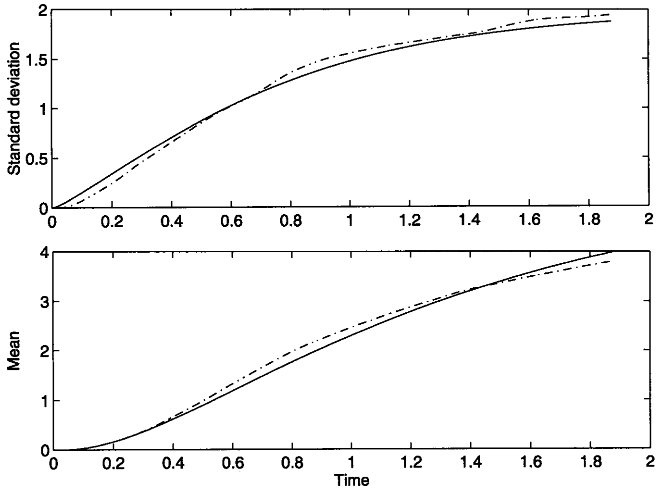

Fig. 2. A comparison of analytical (*solid lines*) and simulation (*dash-dot lines*) results for the mean and standard deviation of the voltage at $x = 0$ as functions of time for $\alpha = 2$, $\mu = 15$, $\sigma = 10$ and $x_0 = 0.5$. For details see text

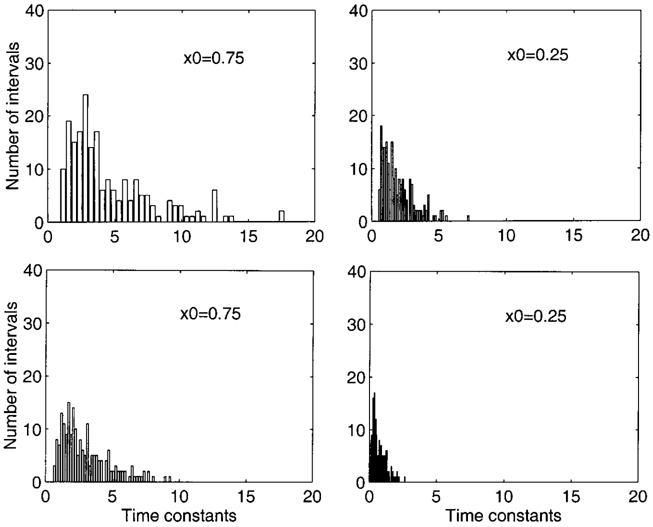

Fig. 3. Interspike interval (ISI) histograms obtained by simulation of the voltage at the origin with a fixed threshold for firing. The *upper two histograms* are for $\alpha = 2$, whereas for the *lower ones* are for $\alpha = 20$

decomposition of $V(x;t)$ satisfying the ordinary stochastic differential equation

$$\mathrm{d}u = f(u)\mathrm{d}t + g(u)\mathrm{d}W \ ,$$

is approximated through the scheme

$$u_{j+1} = u_j + f(u_j)\Delta t + g(u_j)N_j\sqrt{\Delta t} \ ,$$

where u_j, $j = 0, 1, 2, \ldots$, is an approximation to $u(j\Delta t)$, and N_j, $j = 0, 1, 2, \ldots$, is a sequence of independent standard normal random variables. In order to assess the accuracy of the numerical solutions of the stochastic partial differential equation (4A) with I satisfying (4C), a comparison was made of the mean and variance calculated analytically from the series expressions (10) and (11), respectively, with those obtained using the numerical solution.

A typical comparison is made in Fig. 2, where we show an example of the mean and standard deviation of $V(0, t)$ as functions of time, as calculated using the two methods. The results shown are obtained with $\alpha = 2$, $\mu = 15$, $\sigma = 10$ and $x_0 = 0.5$. In the simulations the time step is 0.0025, there are 200 trials and terms to $m, n = 10$ in the Fourier series are employed. In this and other cases examined, the results obtained by simulation of the solutions of the stochastic partial differential equation are in good agreement with those obtained analytically.

Since there are a large number of parameters and a large number of different types of neurons, a systematic study is not feasible here. Hence we have again elected to ascertain the effects of introducing and varying the decay time constant of the input current for a limited set of parameter values.

Figure 3 shows ISI histograms for the linear cable model with an OU input current based on 200 trials, but without the inclusion of any refractory period. For the two histograms shown in the upper part of this figure, the value of α is 2, whereas for those in the lower part $\alpha = 20$, representing the case closer to purely white noise. Except in the case $x_0 = 0.25, \alpha = 20$, where the cell is firing the most rapidly, the interval distributions resemble gamma densities which are a common form of experimentally (and theoretically) determined distribution. When $x_0 = 0.25, \alpha = 20$, the distribution is almost exponential. The effects of changing α from 2 to 20 are very pronounced.

This is further highlighted in the results for the mean and standard deviation of the ISI which are shown in Fig. 4a and b. In obtaining these results, ten different values of α were used from 1 to 30, and three values of the input position, $x_0 = 0.25, 0.5$ and 0.75, for a neuron with a total electrotonic length of $L = 1.5$. Broadly speaking, as α goes from 1 to 30, the mean interval and the standard deviation of the interval drop by about 50%. The decline in the mean and variance are due to the increasing variance of the input noise, which speeds up the attainment of threshold. Actually, there are only small decreases in these quantities when α is increased beyond 10. However, for the extreme cases when α is very small, corresponding to very slowly decaying input currents, the mean and standard deviation of the ISI are much greater than in the purely white-noise case. In Fig. 4c we show, as a function of α, the coefficient of variation of the ISI. Here values of α between 1 and 30 were employed for the same input positions as in Fig. 4a and b. Only for the case $x_0 = 0.25$, closest to the soma, does any significant change occur in the coefficient of variation as the parameter α changes, although there seems to be a slight increasing trend in this quantity as α increases.

5 Conclusions

Since the pioneering work of Rall, the cable model neuron has been used to understand integrative phenomena in neurons, with the possibilities of studying the interaction between various inputs and the roles of dendritic geometry. Since the activity of neurons is

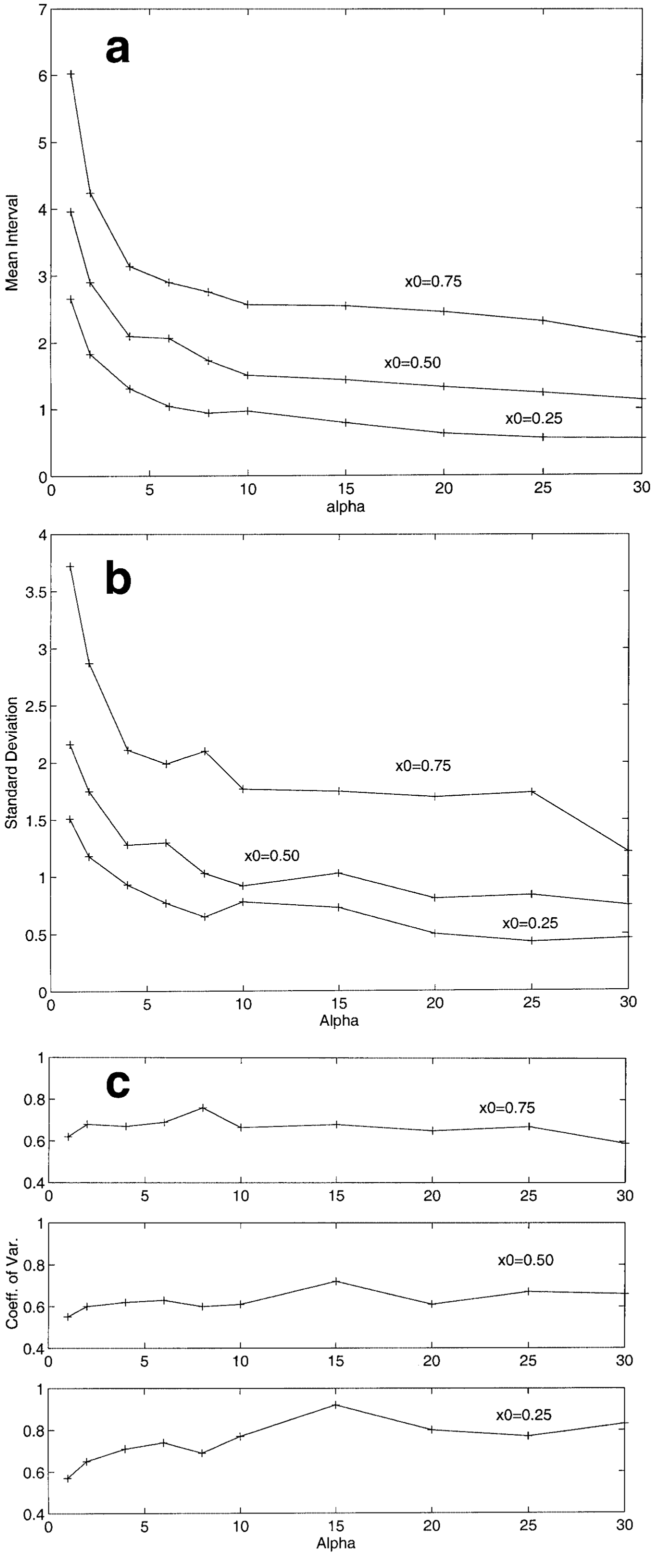

Fig. 4. **a** The mean ISI, obtained by simulation, vs. α for an input at three different distances from the soma of the neuron with $x_0 = 0.75$, $x_0 = 0.5$ and $x_0 = 0.25$. **b** The standard deviation of the ISI corresponding to the results for the mean shown in Fig. 3a. **c** The coefficient of variation of the ISI corresponding to the results in **a** and **b**

usually stochastic in nature, it is natural to extend a study of such cable models to the stochastic case. In previous work with stochastic partial differential equation models of neurons, synaptic inputs have been assumed – ndash;as they also usually are in one-dimensional models – to be Gaussian white noise as an approximation to Poisson inputs. Here we have let the time constant of decay of the synaptic input current be positive and in the range of physiological values. This has led to the use of an OUP to represent the input current. The results presented here for the cable model show that omitting the correlation in the input current may lead to rather large differences in the subthreshold voltages for realistic choices of the parameters of both the neuron and the input current. The differences between the statistical properties of the membrane potential and the firing time of the neuron for the purely white-noise case, and those for the more realistic model with an OUP as the input current, are considerable enough to make the purely white-noise approach sometimes questionable if accurate estimates are required. Allowing for the exponential decay of the synaptic input current seems, based on the examples considered in the present article, to be important if α is less than about 10.

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