

Spatial neuron model with two-parameter Ornstein–Uhlenbeck input current

Henry C. Tuckwell

Max Planck Institute for Mathematics in the Sciences, Inselstr. 22, Leipzig, D-04103 Germany

Received 11 October 2005; received in revised form 8 December 2005

Available online 18 January 2006

Abstract

We consider a new and extended spatial neuron model in which the neuronal electrical depolarization from resting level satisfies a cable partial differential equation. The synaptic input current is also a function of space and time and satisfies a first order linear partial differential equation driven by a two-parameter random process. A natural choice for these random input processes is to make them two-parameter Poisson processes for both excitation and inhibition. For such inputs the mean subthreshold voltage is found in the case of an infinite cable and of finite cables. Assuming uniform amplitudes and rates exact expressions are obtained in the case of particular boundary conditions. We then consider a diffusion approximation and show that the membrane current is a two-parameter Ornstein–Uhlenbeck process, whose statistical properties are derived. Using representations for the voltage in terms of stochastic integrals in the plane we find, in the case of finite space intervals the mean, variance and covariance of the subthreshold voltage. For large times the voltage process is shown to be covariance stationary in time and the corresponding spectral density is found and compared with the result for a purely (two-parameter) white noise driven cable. The limiting white noise case is obtained from the extended model as the decay parameter becomes infinite. Finally, we develop useful simulation methods for the solution of the extended spatial model using properties of stochastic integrals involving eigenfunctions to obtain one-dimensional representations which are easily implemented.

© 2006 Elsevier B.V. All rights reserved.

Keywords: Neuronal model; Stochastic model; Stochastic partial differential equation

1. Introduction

The importance of stochastic effects in the performance of the nervous system has been emphasized in many recent publications. In [1] the stochastic spontaneous background activity within the visual cortex has been shown to shape neuronal responses in the natural perceptual processes. That the activity of cortical and other neurons is highly variable has been known since the pioneering days of microelectrode recordings [2–4]. The subject of the stochasticity of neuronal activity has been energetically studied, especially in recent years after the appearance of several articles which indicated that it was an important effect that needed explanation and elucidation [5,6]. If the brain is to be reliable, how can the activity of its component neurons be so random and unpredictable?

E-mail address: tuckwell@mis.mpg.de.

Modeling the stochastic activity of neurons began even before microelectrode recording had revealed the nature of the excitation and inhibition. In the early part of the second half of the twentieth century the nature of electrophysiological synaptic processes was elucidated [7,8] whereupon in the 1960s diffusion process models began to appear [9,10] (see Ref. [11] for a summary). Analysis continues to the present day with such simple models especially in the framework of the modeling of biological neural networks [12,13].

With the advent of efficient and readily available computing power, nonlinear models, similar in nature to and including the Hodgkin–Huxley model, were employed with random terms [14–20]. Some progress was possible with simulation techniques but analytical work with such models was difficult. Hence it is still important to analyze linear stochastic models, especially spatial ones as in the present paper.

The first analytical studies of a stochastic spatial neuronal model were of a cable with one-parameter Gaussian white noise at discrete points or smeared out over small regions, representing random synaptic input [21–23]. Such cable models are not inapplicable to real neurons with branching structure because of the mapping theorem from dendritic tree to cylinder [24,25]. At about the same time there appeared a model with two-parameter white noise representing a continuous approximation to synaptic input over a dendritic tree [26]. Now in the original Poisson synaptic input model [27] a synaptic event made the membrane potential jump discontinuously to a new value, whereas in real neurons the voltage would change less abruptly. This could be corrected if the current and not the voltage was discontinuous [28] which led to a more natural diffusion approximation. The original white noise cable model could be similarly made more realistic with a discontinuous current rather than voltage in response to synaptic input [29]. In this paper we extend the two-parameter Poisson or white noise driven cable model to include the effects of currents along the whole cable. This gives a new, more applicable and more advanced model than those heretofore employed. All the results obtained are new. We derive several statistical properties of the model and obtain an efficient method of simulation which will be applied in later articles.

2. The model with impulsive input currents

Before considering the diffusion approximation which is inevitably easier to handle, we consider a model in which inputs to the neuron arrive as impulsive currents. A one-dimensional cable model is assumed to represent the neuron which is a valid approach under certain assumptions on neuronal geometry after a mapping from dendritic tree to cylinder is made [8, Chapter 5; 25]. The extent of the cable is assumed to be the interval $[a, b]$, where $-\infty \leq a < b \leq \infty$.

Thus the electrical potential $V(x, t)$ satisfies the following partial differential equation:

$$\frac{\partial V}{\partial t} = -V + \frac{\partial^2 V}{\partial x^2} + I, \quad a < x < b, \quad t > 0, \quad (2.1)$$

where $I = I(x, t)$ is the input current density. The initial condition is given as $V(x, 0)$ which may be random or deterministic, often zero. The boundary conditions are either Dirichlet, Neuman or mixed. There is a special boundary condition which may be applied at the origin called a lumped soma condition [8, Chapter 6].

We will distinguish between excitatory and inhibitory input streams by letting $N_E(x, t)$ and $N_I(x, t)$ be stochastic counting processes for the numbers of excitatory and inhibitory synaptic inputs. That is, for example, $N_E(x, t)$ is a random variable representing the number of points in the rectangle $(a, x] \times (0, t]$ at which excitatory inputs arrive. In general the current density satisfies the partial differential equation

$$\frac{\partial I}{\partial t} = -\alpha I + a_E(x, t) \frac{\partial^2 N_E}{\partial x \partial t} - a_I(x, t) \frac{\partial^2 N_I}{\partial x \partial t}, \quad (2.2)$$

where $a_E, a_I \geq 0$ describe the excitatory and inhibitory synaptic potential amplitudes as functions of space and time. The corresponding rate functions are defined as $\lambda_E(x, t)$ and $\lambda_I(x, t)$ with

$$E(N_E(x, t)) = \lambda_E(x, t)$$

and

$$E(N_I(x, t)) = \lambda_I(x, t),$$

where E denotes expectation. An initial condition can be stated for the current density as $I(x, 0)$, which may be random or deterministic. No boundary conditions are needed for I as it is determined by μ , σ and the two-parameter Poisson processes.

Standard theory for linear partial differential equations states that the solution of (1) is given for each t and x as the random variable

$$V(x, t) = \int_a^b G(x, y; t) V(y, 0) dy + \int_a^b \int_0^t G(x, y; t - s) I(y, s) ds dy, \tag{2.3}$$

where G is the Green’s function for the given boundary conditions.

The mean voltage: The expected value of $V(x, t)$ is thus in general

$$E[V(x, t)] = \int_a^b G(x, y; t) E[V(y, 0)] dy + \int_a^b \int_0^t G(x, y; t - s) E[I(y, s)] ds dy, \tag{2.4}$$

and expressions for higher moments may be similarly obtained. We will for simplicity assume that the initial depolarization is zero for all x corresponding to an initially resting nerve cell.

We will also focus in this section on the following case. The amplitude of the postsynaptic potential may depend on position but not time so that $a_E(x, t) = a_E(x)$, $a_I(x, t) = a_I(x)$. This assumption is in accordance with the known properties of neuronal synapses which are not undergoing changes due to physiological activity as in certain learning paradigms. For the moment, however, we allow the rate of arrival of synaptic potentials to be both time and position dependent.

The current density is in general given by

$$I(x, t) = I(x, 0)e^{-\alpha t} + e^{-\alpha t} \left[\int_0^t e^{\alpha s} \left\{ a_E(x, s) \frac{\partial^2 N_E(x, s)}{\partial x \partial s} - a_I(x, s) \frac{\partial^2 N_I(x, s)}{\partial x \partial s} \right\} ds \right]. \tag{2.5}$$

Taking expectations here and assuming that the postsynaptic amplitudes depend on position only but that the rates may depend on position and time gives

$$E[I(x, t)] = e^{-\alpha t} \int_0^t e^{\alpha s} (a_E(x)\lambda_E(x, s) - a_I(x)\lambda_I(x, s)) ds, \tag{2.6}$$

whereupon

$$E[V(x, t)] = \int_a^b \int_0^t G(x, y; t - s) e^{-\alpha s} \left[\int_0^s e^{\alpha u} \{ a_E(y)\lambda_E(y, u) - a_I(y)\lambda_I(y, u) \} du \right] ds dy. \tag{2.7}$$

We now consider the case where the rates of arrival of the postsynaptic potentials are also constant in time but may depend on position. In particular, we assume there are baseline rates $\bar{\lambda}_E$ and $\bar{\lambda}_I$ for excitation and inhibition, respectively, so that the mean current density is now from (2.6)

$$\begin{aligned} E[I(x, t)] &= e^{-\alpha t} \left[\int_0^t e^{\alpha s} (a_E(x)\bar{\lambda}_E\lambda_E(x) - a_I(x)\bar{\lambda}_I\lambda_I(x)) ds \right] \\ &= \frac{1}{\alpha} (a_E(x)\bar{\lambda}_E\lambda_E(x) - a_I(x)\bar{\lambda}_I\lambda_I(x))(1 - e^{-\alpha t}). \end{aligned} \tag{2.8}$$

Then the mean voltage is given by

$$E[V(x, t)] = \frac{1}{\alpha} \int_a^b \int_0^t G(x, y; t - s) [a_E(y)\bar{\lambda}_E\lambda_E(y) - a_I(y)\bar{\lambda}_I\lambda_I(y)] (1 - e^{-\alpha s}) ds dy. \tag{2.9}$$

Even this case is more general and improves upon the spatio-temporal distribution of synapses discussed in Ref. [26]. In some cases analytical results may be obtained, as we now demonstrate.

2.1. An infinite cable

The Green’s function for the cable equation when $x \in (-\infty, \infty)$ is

$$G(x, y; t) = \frac{e^{-t} e^{-(x-y)^2/4t}}{\sqrt{4\pi t}}, \quad t > 0. \tag{2.1.1}$$

Substituting in (2.9) gives

$$E[V(x, t)] = \frac{1}{\alpha} \int_{-\infty}^{\infty} \int_0^t \frac{e^{-z}}{\sqrt{4\pi z}} e^{-(x-y)^2/4(t-s)} [a_E(y) \bar{\lambda}_E \lambda_E(y) - a_I(y) \bar{\lambda}_I \lambda_I(y)] dy dz.$$

Putting

$$Y(y) = a_E(y) \bar{\lambda}_E \lambda_E(y) - a_I(y) \bar{\lambda}_I \lambda_I(y),$$

and changing variable to $z = t - s$,

$$E[V(x, t)] = \frac{1}{\alpha} \int_{-\infty}^{\infty} dy \int_0^t \frac{e^{-z}}{\sqrt{4\pi z}} e^{-(x-y)^2/4z} (1 - e^{-\alpha(t-z)}) Y(y) dy. \tag{2.1.2}$$

We need to evaluate the two temporal integrals

$$A(x, y, t) = \int_0^t \frac{e^{-z}}{\sqrt{4\pi z}} e^{-(x-y)^2/4z} dz, \tag{2.1.3}$$

$$B(x, y, t) = \int_0^t \frac{e^{-z(1-\alpha)}}{\sqrt{4\pi z}} e^{-(x-y)^2/4z} dz. \tag{2.1.4}$$

To evaluate $A(x, y, t)$ we utilize the following standard integral [8, p. 193]:

$$\int_0^t \frac{e^{-x^2/4T} e^{-T}}{\sqrt{T}} dT = \frac{\sqrt{\pi}}{2} \left\{ \exp(-|x|) \operatorname{erfc} \left[\frac{(|x| - 2t)}{2\sqrt{t}} \right] - \exp(|x|) \operatorname{erfc} \left[\frac{(|x| + 2t)}{2\sqrt{t}} \right] \right\}, \tag{2.1.5}$$

where erfc is the complementary error function defined by

$$\operatorname{erfc}(x) = \frac{2}{\sqrt{\pi}} \int_x^{\infty} e^{-z^2} dz.$$

Thus we obtain

$$A(x, y, t) = \frac{1}{4} \left\{ \exp(-|x - y|) \operatorname{erfc} \left[\frac{(|x - y| - 2t)}{2\sqrt{t}} \right] - \exp(|x - y|) \operatorname{erfc} \left[\frac{(|x - y| + 2t)}{2\sqrt{t}} \right] \right\}.$$

To determine $B(x, y, t)$ we change variable to $z' = z(1 - \alpha)$ to obtain

$$B(x, y, t) = \frac{1}{\sqrt{4\pi(1-\alpha)}} \int_0^{t(1-\alpha)} \frac{e^{-z'}}{\sqrt{z'}} e^{-(\sqrt{1-\alpha}(x-y))^2/4z'} dz'.$$

Using again the standard integral (2.1.5) we obtain

$$B(x, y, t) = \frac{1}{4\sqrt{1-\alpha}} \left\{ \exp(-\sqrt{1-\alpha}|x - y|) \operatorname{erfc} \left[\frac{\sqrt{1-\alpha}|x - y| - 2t(1-\alpha)}{2\sqrt{t(1-\alpha)}} \right] - \exp(\sqrt{1-\alpha}|x - y|) \operatorname{erfc} \left[\frac{\sqrt{1-\alpha}|x - y| + 2t(1-\alpha)}{2\sqrt{t(1-\alpha)}} \right] \right\}.$$

Now the mean voltage along the cable is given by the expression

$$E[V(x, t)] = \int_{-\infty}^{\infty} [A(x, y, t) - B(x, y, t)] Y(y) dy, \tag{2.1.6}$$

which can be computed for any given combination of rate and amplitude functions, $a_E, a_I, \lambda_E, \lambda_I$.

2.1.1. *Uniform synaptic amplitudes and rates*

We assume that the excitatory and inhibitory postsynaptic potential amplitudes are independent of position as are their rates of arrival. In this case we put $a_E(x) = a_E, \lambda_E(x) = \lambda_E, a_I(x) = a_I, \lambda_I(x) = \lambda_I$ and define the net synaptic drive as

$$Y(y) = K = a_E \overline{\lambda_E} \lambda_E - a_I \overline{\lambda_I} \lambda_I.$$

Then from (2.9)

$$E[V(x, t)] = \frac{K}{\alpha} \int_{-\infty}^{\infty} \int_0^t \frac{e^{-(t-s)}}{\sqrt{4\pi(t-s)}} e^{-(x-y)^2/4(t-s)} (1 - e^{-\alpha s}) ds dy.$$

Consider the y integration and put

$$I = \int_{-\infty}^{\infty} e^{-(x-y)^2/4(t-s)} dy,$$

which on putting

$$z = \frac{x-y}{\sqrt{2(t-s)}}$$

yields

$$I = \sqrt{2(t-s)} \int_{-\infty}^{\infty} e^{-z^2/2} dz = 2\sqrt{\pi(t-s)}.$$

Then the expected voltage simplifies to the elementary integral

$$E[V(x, t)] = \frac{K}{\alpha} \int_0^t e^{-(t-s)} (1 - e^{-\alpha s}) ds.$$

This gives the following result:

$$E[V(x, t)] = \frac{K}{\alpha} \left[1 - e^{-t} + \frac{1}{1-\alpha} (e^{-t} - e^{-\alpha t}) \right], \quad \alpha \neq 1,$$

which shows that the mean voltage is independent of position as it is in the purely white case [26]. In the special case $\alpha = 1$ we get

$$E[V(x, t)] = K[1 - e^{-t}(t + 1)].$$

It is immediate that the steady state value of the mean voltage is for all $\alpha > 0$

$$E[V(x, \infty)] = \frac{K}{\alpha}.$$

In Fig. 1 are shown plots of the mean voltage versus time for various values of α . Note that as $\alpha \rightarrow \infty$ the current density and hence the voltage tends to zero. This is in contrast to the limit as $\alpha \rightarrow \infty$ being taken in such a way that a the current density approaches a two-parameter white noise (with drift) as is discussed in Section 3.

2.2. *Finite cables*

For cables of finite length, the Green’s function can be written as Fourier series

$$G(x, y; t) = \sum_n \phi_n(x)\phi_n(y)e^{-\lambda_n t}, \quad t > 0, \tag{2.2.1}$$

where $\{\phi_n\}$ is the set of normalized spatial eigenfunctions and $\{\lambda_n\}$ is the set of corresponding eigenvalues.

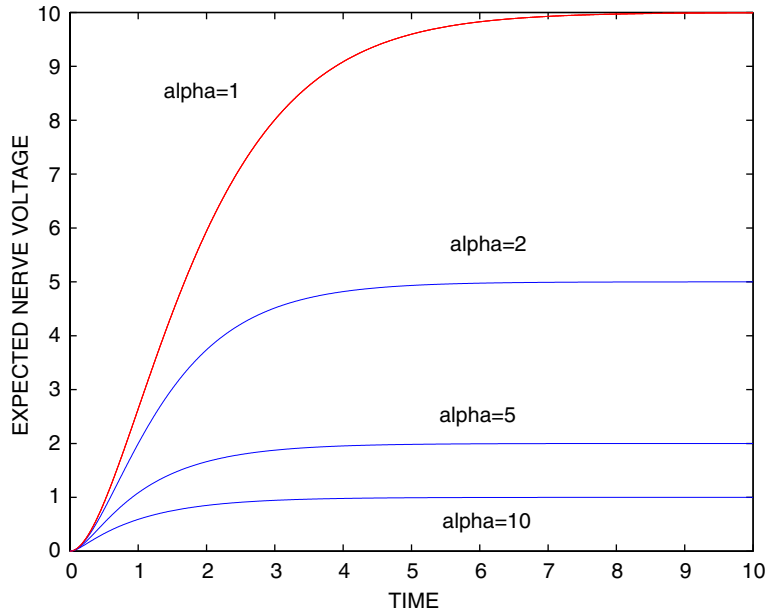


Fig. 1. Showing the mean voltage as a function of time at points on the infinite cable model neuron when driven by a current of uniform intensity. The current density is given by (2.5) of the text. The various values of α , which is the reciprocal of the time constant of decay of the current, are indicated in the figure.

In general we have therefore

$$E[V(x, t)] = \frac{1}{\alpha} \sum_n \int_0^L \int_0^t \phi_n(x)\phi_n(y)e^{-\lambda_n(t-s)} Y(y)(1 - e^{-\alpha s}) ds dy.$$

Upon evaluating the temporal integrals and defining

$$\Phi_n(L) = \int_0^L \phi_n(y) Y(y) dy,$$

we obtain

$$E[V(x, t)] = \frac{1}{\alpha} \sum_n \phi_n(x)\Phi_n(L) \left\{ \frac{1 - e^{-\lambda_n t}}{\lambda_n} - \frac{(e^{-\alpha t} - e^{-\lambda_n t})}{\lambda_n - \alpha} \right\}.$$

For cables on $[0, L]$ there are two sets of boundary conditions we wish to consider. Firstly, when the cable has *sealed ends*

$$V_x(0, t) = V_x(L, t) = 0,$$

where subscripts denote partial differentiation. The remaining case of interest is that of *killed ends*

$$V(0, t) = V(L, t) = 0.$$

For both cases the Green’s function can be expressed as in (2.2.1). For sealed ends the eigenvalues are

$$\lambda_n = 1 + n^2\pi^2/L^2, \quad n = 0, 1, \dots$$

and the normalized (to unity) eigenfunctions are

$$\phi_n(x) = \begin{cases} \frac{1}{\sqrt{L}}, & n = 0, \\ \sqrt{2/L} \cos(n\pi x/L), & n = 1, 2, \dots \end{cases}$$

In the killed ends case, the eigenvalues are

$$\lambda_n = 1 + n^2\pi^2/L^2, \quad n = 1, 2, \dots$$

and the normalized eigenfunctions are

$$\phi_n(x) = \sqrt{2/L} \sin(n\pi x/L), \quad n = 1, 2, \dots$$

2.2.1. Uniform synaptic amplitudes and rates

Making the same assumptions as in Section 2.1.1, we find that for the case of a nerve cylinder of length L with sealed ends the quantities $\Phi_n(L)$ are zero except for $n = 0$ in which case

$$\Phi_0(L) = K\sqrt{L},$$

so that the mean depolarization is

$$E[V(x, t)] = \frac{K}{\alpha} \left[1 - e^{-t} + \frac{1}{1 - \alpha} (e^{-t} - e^{-\alpha t}) \right], \quad \alpha \neq 1.$$

This is the same as the result for the infinite cable, again giving a mean which is independent of position.

In the case of killed ends one obtains

$$\Phi_n(L) = \begin{cases} \frac{2K\sqrt{2L}}{n\pi}, & n \text{ odd,} \\ 0, & n \text{ even.} \end{cases}$$

The mean voltage along the cable is given by

$$E[V(x, t)] = \frac{4K}{\alpha\pi} \sum_{n=1}^{\infty} \frac{\sin(n\pi x/L)}{n} \left\{ \frac{1 - e^{-\lambda_n t}}{\lambda_n} - \frac{(e^{-\alpha t} - e^{-\lambda_n t})}{\lambda_n - \alpha} \right\},$$

where summation is over odd values of n only.

In Fig. 2 are shown the computed expected voltages as functions of time at the centers of cables of lengths 1, 2 and 5 for a value of $\alpha = 2$.

Expressions may be found for such quantities as the variance of $V(x, t)$, the covariance of $V(x, s)$ and $V(y, t)$ and the asymptotic spectral density, but are the same as those obtained below for the diffusion approximation.

3. The diffusion approximation with two-parameter OUP current

As has been done for ordinary differential equation models of neurons [9,10], discontinuities induced by Poisson processes may be smoothed by means of a diffusion approximation. Here a similar procedure sees the partial differential equation (2.2) for the current density replaced by one involving a two-parameter Gaussian white noise with the same drift and variance so that

$$\begin{aligned} \frac{\partial I}{\partial t} = & -\alpha I + a_E(x, t)\lambda_E(x, t) - a_I(x, t)\lambda_I(x, t) \\ & + \sqrt{a_E^2(x, t)\lambda_E(x, t) + a_I^2(x, t)\lambda_I(x, t)} \frac{\partial^2 W}{\partial x \partial t}, \quad a < x < b, \quad t > 0. \end{aligned} \tag{3.1}$$

Here $W(x, t)$ is a two-parameter Wiener process (Brownian motion) with the following elementary properties:

- (i) $W(x, t)$ is a Gaussian random variable with mean 0 and variance xt ;
- (ii) $\text{Cov}[W(x, s), W(y, t)] = \min(x, y) \min(s, t)$.

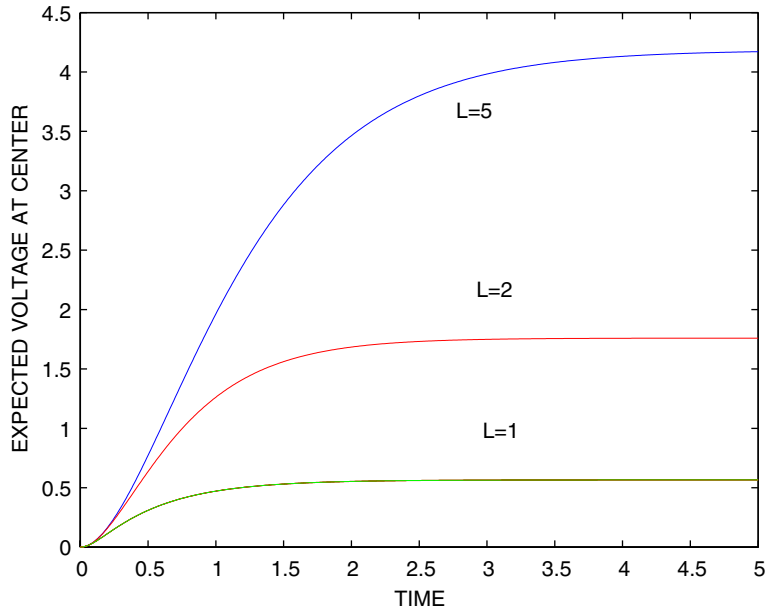


Fig. 2. Showing the mean voltage as a function of time at the centers of cable model neurons with killed end boundary conditions when driven by a current of uniform intensity. The value of α is 2 and $K = 10$. The various values of L are indicated in the figure.

The mixed second order partial derivative of $W(x, s)$, denoted by W_{xs} , is called two-parameter white noise and the following property is useful:

$$\text{Cov}[W_{xs}(x, s), W_{yt}(y, t)] = \delta(x - y)\delta(s - t).$$

This is also useful in the form

$$E[dW(x, s)dW(y, t)] = \delta(x - y)\delta(s - t) dx ds dy dt.$$

Stochastic integrals of Ito type with respect to W are well defined and

$$\int_a^b \int_0^t f(y, s) dW(y, s),$$

where f is deterministic, is a Gaussian random variable of mean zero and

$$\text{Var} \left[\int_a^b \int_0^t f(y, s) dW(y, s) \right] = \int_a^b \int_0^t f^2(y, s) dy ds. \tag{3.2}$$

Let us now define

$$\mu(x, t) = a_E(x, t)\lambda_E(x, t) - a_I(x, t)\lambda_I(x, t)$$

and

$$\sigma(x, t) = \sqrt{a_E^2(x, t)\lambda_E(x, t) + a_I^2(x, t)\lambda_I(x, t)}.$$

The solution of (3.1) must be

$$I(x, t) = I(x, 0)e^{-\alpha t} + e^{-\alpha t} \left[\int_0^t e^{\alpha s} \left(\mu(x, s) + \sigma(x, s) \frac{\partial^2 W}{\partial x \partial s} \right) ds \right]. \tag{3.3}$$

3.1. The membrane current is a two-parameter OUP

The integral

$$J(x, t) = \int_a^x I(y, t) dy$$

over space gives the current flowing into the neuron from the left end point a to $x \leq b$. J is given by

$$J(x, t) = \int_a^x I(y, 0)e^{-\alpha t} dy + e^{-\alpha t} \int_a^x \int_0^t (\mu + \sigma W_{ys}) dy ds.$$

Let us assume that μ and σ are constant. Then ignoring the contribution of the initial value and putting $a = 0$ the mean current is easily found as

$$E[J(x, t)] = e^{-\alpha t} \int_0^x \int_0^t \mu e^{\alpha s} ds dy$$

so

$$E[J(x, t)] = \frac{\mu x}{\alpha} (1 - e^{-\alpha t}).$$

Using (3.2) the variance of J is

$$\text{Var}[J(x, t)] = \sigma^2 e^{-2\alpha t} \int_0^x \int_0^t e^{2\alpha s} dy ds$$

which gives

$$\text{Var}[J(x, t)] = \frac{\sigma^2 x}{2\alpha} (1 - e^{-2\alpha t}).$$

To find the covariance of J at different space and time points we need evaluate

$$\text{Cov}[J(x, s), J(y, t)] = \sigma^2 e^{\alpha(s+t)} \int_0^x \int_0^s \int_0^y \int_0^t e^{\alpha(s'+t')} \delta(x' - y') \delta(s' - t') dx' dy' ds' dt'.$$

Evaluating this integral we obtain

$$\text{Cov}[J(x, s), J(y, t)] = \frac{\sigma^2}{2\alpha} e^{-\alpha(s+t)} \min(x, y) (e^{2\alpha \min(s,t)} - 1).$$

This is the covariance kernel of what we call a two-parameter Ornstein–Uhlenbeck process (see also Ref. [30]).

3.2. Moments of the voltage

It is also clear from (2.3) that V is given by

$$\begin{aligned} V(x, t) &= \int_a^b G(x, y, t) V(y, 0) dy \\ &+ \int_a^b \int_0^t G(x, y, t - s) \left[e^{-\alpha s} \int_0^s e^{\alpha u} \left(\mu(y, u) + \sigma(y, u) \frac{\partial^2 W}{\partial y \partial u} \right) du \right] ds dy. \end{aligned} \tag{3.2.1}$$

Assuming an initial value of V which is zero, this expression splits into a deterministic component which is the mean of V , being the same as (2.7) or (2.9), and a random component involving the stochastic integral with respect to $W(y, u)$

$$V_R(x, t) = \int_0^t \left[\int_a^b \int_0^s e^{\alpha u} G(x, y; t - s) \sigma(y, u) dW(y, u) \right] e^{-\alpha s} ds. \tag{3.2.2}$$

3.2.1. Covariance and variance

It is desired to find the variance of $V(x, t)$ in the general case. To this end we first find the covariance of $V(x, t)$ and $V(\bar{x}, \bar{t})$. We set

$$K(x, t; \bar{x}, \bar{t}) = \text{Cov}[V(x, t), V(\bar{x}, \bar{t})]$$

and find

$$\begin{aligned} K(x, t; \bar{x}, \bar{t}) &= E[V_R(x, t)V_R(\bar{x}, \bar{t})] \\ &= E\left[\int_0^t \left[\int_a^b \int_0^s G(x, y; t-s)e^{2\alpha u} \sigma(y, u) dW(y, u)\right] e^{-\alpha s} ds \right. \\ &\quad \left. \times \int_0^{\bar{t}} \left[\int_a^b \int_0^{\bar{s}} G(\bar{x}, \bar{y}; \bar{t}-\bar{s})e^{2\alpha \bar{u}} \sigma(\bar{y}, \bar{u}) dW(\bar{y}, \bar{u})\right] e^{-\alpha \bar{s}} d\bar{s}\right], \end{aligned} \tag{3.2.3}$$

which on using the covariance property of the two-parameter white noise becomes

$$\begin{aligned} K(x, t; \bar{x}, \bar{t}) &= \int_0^t \int_a^b \int_0^s \int_0^{\bar{t}} \int_a^b \int_0^{\bar{s}} G(x, y; t-s)G(\bar{x}, \bar{y}; \bar{t}-\bar{s})e^{-\alpha(s+\bar{s})} \\ &\quad \times \sigma(y, u)\sigma(\bar{y}, \bar{u})e^{2\alpha(u+\bar{u})}\delta(y-\bar{y})\delta(u-\bar{u}) ds dy du d\bar{s} d\bar{y} d\bar{u}. \end{aligned} \tag{3.2.4}$$

If the integration is performed over u then the remaining part involving \bar{u} is

$$\int_0^{\min(s, \bar{s})} e^{2\alpha \bar{u}} \sigma(y, \bar{u})\sigma(\bar{y}, \bar{u}) d\bar{u}.$$

The case of constant σ : Little progress can be made analytically except when the variance of the input current is not dependent on either distance along the neuron or time. For the rest of the section we assume therefore that $\sigma(x, t) = \sigma$, a constant. The covariance is then

$$\begin{aligned} K(x, t; \bar{x}, \bar{t}) &= \frac{\sigma^2}{2\alpha} \int_0^t ds e^{-\alpha s} \int_0^{\bar{t}} e^{-\alpha \bar{s}} (e^{2\alpha \min(s, \bar{s})} - 1) d\bar{s} \\ &\quad \times \int_a^b \int_a^b G(x, y; t-s)G(\bar{x}, \bar{y}; \bar{t}-\bar{s})\delta(y-\bar{y}) dy d\bar{y}. \end{aligned} \tag{3.2.5}$$

Performing the y integration but relabeling we get the following triple integral:

$$K(x, t; \bar{x}, \bar{t}) = \frac{\sigma^2}{2\alpha} \int_0^t e^{-\alpha s} ds \int_0^{\bar{t}} e^{-\alpha \bar{s}} d\bar{s} \int_a^b (e^{2\alpha \min(s, \bar{s})} - 1)G(x, y; t-s)G(\bar{x}, y; \bar{t}-\bar{s}) dy. \tag{3.2.6}$$

Let us assume that $t_2 \geq t_1$. Then the region of (s, \bar{s}) -integration splits into three natural parts A, B and C, which are indicated in the accompanying sketch (Fig. 3).

Performing the integrations in the three regions gives

$$K(x, t; \bar{x}, \bar{t}) = \frac{\sigma^2}{\alpha} (A_1 + A_2 + A_3), \tag{3.2.7}$$

where

$$A_1 = \int_a^b \left(\int_0^t e^{-\alpha s} G(x, y; t-s) \left\{ \int_0^s \sinh(\alpha \bar{s}) G(\bar{x}, y; \bar{t}-\bar{s}) d\bar{s} \right\} ds \right) dy,$$

$$A_2 = \int_a^b \left(\int_0^t e^{-\alpha s} G(\bar{x}, y; \bar{t}-\bar{s}) \left\{ \int_0^{\bar{s}} \sinh(\alpha s) G(x, y; t-s) ds \right\} d\bar{s} \right) dy,$$

$$A_3 = \int_a^b \left(\int_t^{\bar{t}} e^{-\alpha \bar{s}} G(\bar{x}, y; \bar{t}-\bar{s}) \left\{ \int_0^t \sinh(\alpha s) G(x, y; t-s) ds \right\} d\bar{s} \right) dy.$$

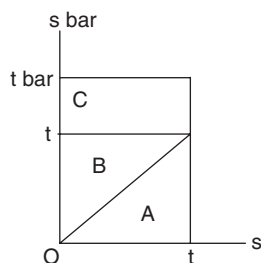


Fig. 3. The three regions of integration in the (s, \bar{s}) plane involved in computing the covariance.

The variance: The variance of $V(x, t)$ which is just $K(x, t; x, t)$ is, in the case of constant σ , from (3.8)

$$\text{Var}[V(x, t)] = \frac{\sigma^2}{2\alpha} \int_0^t ds e^{-\alpha s} \int_0^t e^{-\alpha \bar{s}} d\bar{s} \int_a^b (e^{2\alpha \min(s, \bar{s})} - 1) G(x, y; t - s) G(x, y; t - \bar{s}) dy.$$

This expression yields the following readily computable formula:

$$\text{Var}[V(x, t)] = \frac{2\sigma^2}{\alpha} \int_a^b \left[\int_0^t e^{-\alpha s} G(x, y; t - s) \left(\int_0^s \sinh(\alpha \bar{s}) G(x, y; t - \bar{s}) d\bar{s} \right) ds \right] dy. \tag{3.2.8}$$

Bounded space intervals

Covariance: As seen above, when $-\infty < b < a < \infty$ the Green’s function for the cable equation can be written as an infinite series (2.2.1). Evaluating the integrals A_1, A_2, A_3 defined above, the covariance of $V(x, t)$ and $V(\bar{x}, \bar{t})$ can finally be written as

$$K(x, t; \bar{x}, \bar{t}) = \frac{\sigma^2}{\alpha} \sum_n \phi_n(x) \phi(\bar{x}) \left[T_n(t, \bar{t}) + \frac{1}{2} U_n(t, \bar{t}) \right].$$

Here we have defined

$$T_n(t, \bar{t}) = \frac{e^{\lambda_n(t-\bar{t})} - e^{\lambda_n(t+\bar{t})}}{2\lambda_n(\lambda_n + \alpha)} - \frac{(e^{-\alpha t - \lambda_n \bar{t}} - e^{-\lambda_n(t+\bar{t})})}{\lambda_n^2 - \alpha^2} - \frac{(e^{\lambda_n(t-\bar{t}) - 2\alpha t} - e^{-\lambda_n(t+\bar{t})})}{2(\lambda_n - \alpha)^2} + \frac{(e^{-\alpha t - \lambda_n \bar{t}} - e^{\lambda_n(t+\bar{t})})}{(\lambda_n - \alpha)^2}$$

and

$$U_n(t, \bar{t}) = \frac{1}{\lambda_n^2 - \alpha^2} [e^{\alpha(t-\bar{t})} - e^{-(\alpha \bar{t} + \lambda_n t)} - e^{\lambda_n(t-\bar{t})} - e^{\alpha t + \lambda_n \bar{t}}] + \frac{1}{(\lambda_n - \alpha)^2} [e^{-(\alpha \bar{t} + \lambda_n t)} - e^{\alpha(t+\bar{t})} - e^{-2\alpha t + \lambda_n(t-\bar{t})} - e^{-(\alpha t + \lambda_n \bar{t})}].$$

Variance: From (3.11) or from $K(x, t; x, t)$ we find in the case of a bounded space interval

$$\text{Var}[V(x, t)] = \frac{\sigma^2}{\alpha} \sum_n \phi_n^2(x) V_n(t),$$

where

$$V_n(t) = \frac{1 - e^{-2\lambda_n t}}{2\lambda_n(\lambda_n + \alpha)} - \frac{(e^{-(\lambda_n + \alpha)t} - e^{-2\lambda_n t})}{\lambda_n^2 - \alpha^2} - \frac{(e^{-2\alpha t} - e^{-2\lambda_n t})}{2(\lambda_n - \alpha)^2} + \frac{(e^{-(\lambda_n + \alpha)t} - e^{-2\lambda_n t})}{(\lambda_n - \alpha)^2}.$$

The steady state variance is evidently

$$\text{Var}[V(x, \infty)] = \frac{\sigma^2}{2\alpha} \sum_n \frac{\phi_n^2(x)}{\lambda_n(\lambda_n + \alpha)}.$$

It is of interest to compare this with the steady state variance of the voltage in a cable driven by a Gaussian white noise current density:

$$\text{Var}[V_{WN}(x, \infty)] = \sigma^2 \sum \frac{\phi_n^2(x)}{2\lambda_n}$$

a result which was given in Ref. [26]. The standard deviation is shown as a function of time in Fig. 4.

Asymptotic stationarity and spectral density of the voltage: A process is called weakly stationary (or covariance stationary) if its covariance kernel is a function only of time differences. We can see that the voltage at a space point x becomes weakly stationary as follows. We put $\bar{t} = t + \tau$ and find

$$T_n(t, t + \tau) = \frac{(e^{-\lambda_n \tau} - e^{-\lambda_n(2t+\tau)})}{2\lambda_n(\lambda_n + \alpha)} - \frac{(e^{-\alpha t - \lambda_n(t+\tau)} - e^{-\lambda_n(2t+\tau)})}{\lambda_n^2 - \alpha^2} - \frac{(e^{-2\alpha t - \lambda_n \tau} - e^{-\lambda_n(2t+\tau)})}{2(\lambda_n - \alpha)^2} + \frac{(e^{\alpha t - \lambda_n(t+\tau)} - e^{-\lambda_n(2t+\tau)})}{(\lambda_n - \alpha)^2}$$

and that

$$U_n(t, t + \tau) = \frac{[e^{-\tau} - e^{-\alpha(t+\tau) - \lambda_n t} - e^{-\lambda_n \tau} + e^{-t(\alpha + \lambda_n) - \lambda_n \tau}]}{\lambda_n^2 - \alpha^2} - \frac{[e^{-t(\alpha + \lambda_n) - \alpha \tau} - e^{-\alpha(2t+\tau)} - e^{-2\alpha t - \lambda_n \tau} - e^{-t(\alpha + \lambda_n) - \lambda_n \tau}]}{(\lambda_n - \alpha)^2}$$

Then

$$K(x, t; x, t + \tau) = \frac{\sigma^2}{\alpha} \sum_n \phi_n^2(x) \left[T_n(t, t + \tau) + \frac{1}{2} U_n(t, t + \tau) \right]$$

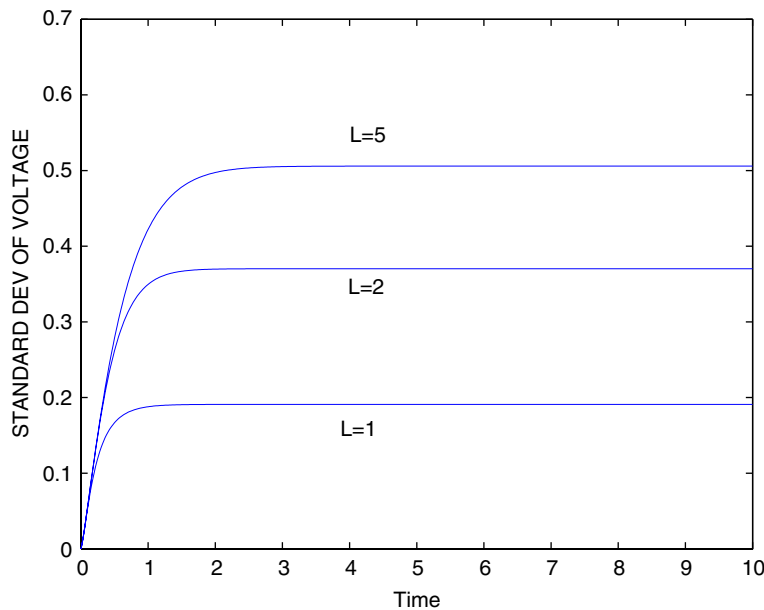


Fig. 4. Showing the standard deviation of the voltage as a function of time at the centers of cable model neurons with killed end boundary conditions when driven by a current of uniform intensity. The value of α is 2 and $\sigma = \sqrt{10}$. The various values of L are indicated in the figure.

Now we can see the asymptotic stationarity by letting as $t \rightarrow \infty$

$$T_n(t, t + \tau) \rightarrow \bar{T}_n(\tau),$$

$$U_n(t, r + \tau) \rightarrow \bar{U}_n(\tau),$$

whereupon

$$K(x, t; t + \tau) \rightarrow \bar{K}(x, \tau)$$

so that the limiting weakly stationary covariance is

$$\bar{K}(x, \tau) = \frac{\sigma^2}{\alpha} \left[\sum_n \phi_n^2(x) \left(\frac{e^{-\lambda_n \tau}}{2\lambda_n(\lambda_n + \alpha)} + \frac{e^{-\tau} - e^{-\lambda_n \tau}}{2(\lambda_n^2 - \alpha^2)} \right) \right]$$

or after a simplification

$$\bar{K}(x, \tau) = \frac{\sigma^2}{2\alpha} \sum_n \frac{\phi_n^2(x)}{\lambda_n^2 - \alpha^2} \left(e^{-\tau} - \frac{\alpha e^{-\lambda_n \tau}}{\lambda_n} \right).$$

This can be compared with the result for the white noise driven cable

$$\bar{K}_{WN}(x, \tau) = \sigma^2 \sum_n \frac{\phi_n^2(x)}{2\lambda_n} e^{-\lambda_n \tau}.$$

The spectral density of the weakly stationary process at space-point x is the Fourier transform

$$f(\omega; x) = \frac{1}{2\pi} \int_{-\infty}^{\infty} e^{-i\omega\tau} \bar{K}(x, \tau) d\tau.$$

The kernel is extended to negative τ as

$$\bar{K}(x, -\tau) = \bar{K}(x, \tau),$$

so that the Fourier transform reduces to

$$f(\omega; x) = \frac{1}{\pi} \int_0^{\infty} \cos(\omega\tau) \bar{K}(x, \tau) d\tau,$$

which on substitution gives

$$f(\omega; x) = \frac{\sigma^2}{2\alpha\pi} \sum_n \frac{\phi_n^2(x)}{\lambda_n^2 - \alpha^2} \left[\frac{1}{1 + \omega^2} - \frac{\alpha}{\lambda_n(\lambda_n^2 + \omega^2)} \right].$$

This can be compared with the corresponding simpler result for the purely two-parameter white noise driven cable [26]:

$$f_{WN}(\omega; x) = \frac{\sigma^2}{2\pi} \sum_n \frac{\phi_n^2(x)}{\lambda_n^2 + \omega^2}.$$

Numerical evaluation and a comparison of these spectral functions will be done in a later article.

3.3. The white noise limit

Here we adhere to the notation of using subscripted variables to represent partial differentiation. It is of interest to see if the purely white noise driven cable

$$V_t = -V + V_{xx} + k_1 + k_2 W_{xt} \tag{3.3.1}$$

can be obtained by limiting operations from the model described in Section 3,

$$V_t = -V + V_{xx} + I, \tag{3.3.2}$$

$$I_t = -\alpha I + \mu + \sigma W_{xt}. \quad (3.3.3)$$

If we let $\alpha \rightarrow \infty$ in (3.3.3), the result is that I becomes more and more deterministic and like the solution of the differential equation $I_t = -\alpha I$. To overcome this problem we put

$$\mu = k_1 \alpha,$$

$$\sigma = k_2 \alpha,$$

where k_1 and k_2 are constants. Now since

$$\frac{I_t}{\alpha} = \frac{\mu}{\alpha} + \frac{\sigma W_{xt}}{\alpha} - I,$$

when we let $\alpha \rightarrow \infty$ we recover

$$I = k_1 + k_2 W_{xt},$$

so that (3.3.1) is recovered in the limit.

3.4. A representation for V useful for simulation

For a model neuron, one quantity to ascertain which is of relevance to the physiological activity of a cell is the amount of time taken before an action potential is emitted, especially when the inputs are stochastic in character as they usually are for actual nerve cells. Simulation of solutions of (3.1) directly seems difficult but fortunately we are able to develop exact expressions for the voltage $V(x, t)$ at any space point in terms of one-dimensional processes which are readily simulated by known methods.

We recall that $V(x, t)$ can be written as

$$V(x, t) = E[V(x, t)] + V_R(x, t),$$

where V_R is a purely random component while $E[V(x, t)]$ is purely deterministic. Since we can find the mean readily analytically, we wish to develop a representation which will enable us to easily simulate V_R . In the case of constant σ and a bounded space interval (3.5) becomes

$$V_R(x, t) = \sigma \int_0^t \left[\int_a^b \int_0^s e^{\alpha u} \sum_n \phi_n(x) \phi_n(y) e^{-\lambda_n(t-s)} dW(y, u) \right] e^{-\alpha s} ds.$$

Now define the process

$$W_n(t) = \int_a^b \int_0^t \phi_n(y) dW(y, s), \quad t \geq 0.$$

It can be shown that firstly $\{W_n(t), t \geq 0\}$ is a standard (one-parameter) Wiener process or Brownian motion. Secondly, the W_n for different n are independent. From the previous equation it follows that

$$dW_n(t) = \int_a^b \phi_n(y) dW(y, t).$$

We may isolate $dW_n(u)$ in the above expression for V_R and obtain

$$V_R(x, t) = \sigma \sum_n \phi_n(x) \int_0^t \int_0^s e^{\alpha u} dW_n(u) e^{-\lambda_n(t-s)} e^{-\alpha s} ds.$$

Now we define another one-parameter process

$$U_n(s) = e^{-\alpha s} \int_0^s e^{\alpha u} dW_n(u), \quad s \geq 0.$$

This gives

$$V_R(x, t) = \sigma \sum_n \phi_n(x) \int_0^t e^{-\lambda_n(t-s)} U_n(s) ds, \quad t \geq 0.$$

Finally, we define

$$V_n(t) = \int_0^t e^{-\lambda_n(t-s)} U_n(s) ds,$$

so that we obtain the following explicit series representation for V_R :

$$V_R(x, t) = \sigma \sum_n \phi_n(x) V_n(t)$$

in which individual terms are independent.

Stochastic differential equations for U_n and V_n : Differentiating throughout the equation defining U_n we find that

$$\frac{dU_n}{ds} = -\alpha U_n + \frac{dW_n}{ds},$$

which can be written in more standard notation as an Ito equation

$$dU_n = -\alpha U_n ds + dW_n,$$

which shows that U_n is a one-parameter Ornstein–Uhlenbeck process. Similarly, differentiating throughout the equation defining V_n we get

$$dV_n = -\lambda_n V_n dt + U_n dt.$$

The pair (U_n, V_n) constitutes a vector-valued Markov process defined by the following system of stochastic differential equations:

$$d \begin{bmatrix} U_n \\ V_n \end{bmatrix} = \begin{bmatrix} -\alpha & 0 \\ 1 & -\lambda_n \end{bmatrix} \begin{bmatrix} U_n \\ V_n \end{bmatrix} dt + \begin{bmatrix} dW_n \\ 0 \end{bmatrix}.$$

Note that U_n is a Gaussian process so V_n is Gaussian and hence too are V_R and V .

To simulate a path for $V(x, t)$ at fixed x we may use the following Euler-type iterative formulas in conjunction with the expected value of $V(x, t)$:

$$U_n(t + \Delta t) = U_n(t) - \alpha U_n(t) \Delta t + N(0, 1) \sqrt{\Delta t},$$

$$V_n(t + \Delta t) = V_n(t) - \lambda_n V_n(t) \Delta t + U_n(t) \Delta t,$$

$$V_R(x, t + \Delta t) = V_R(x, t) + \sigma \Delta t \sum_n \phi_n(x) [U_n(t) - \lambda_n V_n(t)].$$

Here $N(0, 1)$ is a member of a sequence of independent standard normal random variables. These methods will be employed in a forthcoming article.

4. Discussion

Based on experimental observations, the trains of spikes emitted by neurons almost anywhere in the mammalian central nervous system are usually essentially stochastic. There are numerous levels at which the prediction of the properties of such stochastic neuronal spike trains can be made. Simulation studies may use software packages which can be applied to multi-compartmental models where each compartment is represented by a set of nonlinear equations. On the other hand, analytical approaches to point models range from the classical one-dimensional one-parameter Ornstein–Uhlenbeck process to Hodgkin–Huxley or similar equations with various types of Markovian noises.

In the present study the standard models have been extended in a realistic fashion in two ways. Firstly by the inclusion of a continuous space variable which means that the neuronal electrophysiology requires stochastic partial differential equations rather than stochastic ordinary differential equations for its

description. Secondly, the differential equation for the synaptic current rather than that of the voltage is stimulated by an independent-increment process, which means that the neuron is represented by a system of two stochastic partial differential equations rather than one. In Section 2 the independent increment process was Poisson in nature and the mean of the voltage was found analytically. Then we turned to a diffusion approximation in which the Poisson noise was replaced by Gaussian two-parameter white noise. This gave a current which is a two-parameter Ornstein–Uhlenbeck process whose use is also new. With this input, the statistical properties of the voltage were able to be found easily in analytical forms for bounded space intervals. The spectral density of the asymptotically weakly stationary voltage process was found and this may be useful for comparison with experimental recordings from nerve in subthreshold states.

In order to obtain the statistical properties of the firing time, namely the time required for the neuron to reach threshold for action potentials from some initial value, it is required to simulate the voltage process in Monte Carlo trials. Since the voltage in the present model satisfies a stochastic partial differential equation, direct simulation would be very difficult. To this end we have developed in Section 3.4 an algorithm involving stochastic ordinary differential equations that enables voltage at any space point to be easily simulated. However, lack of space has meant that simulation results for the firing time, and other results for the statistical properties of the subthreshold voltage will be presented elsewhere.

Acknowledgements

The author thanks the Max Planck Institute for financial support and Prof. Dr. Juergen Jost for his kind hospitality.

References

- [1] J. Fiser, C. Chiu, M. Weliky, *Nature* 431 (2004) 573.
- [2] G.L. Gerstein, N.Y.-S. Kiang, *Biophys. J.* 1 (1960) 15.
- [3] E.V. Evarts, *J. Neurophysiol.* 27 (1964) 152.
- [4] B.D. Burns, A.C. Webb, *Proc. R. Soc. London Ser. B* 194 (1976) 211.
- [5] M.N. Shadlen, W.T. Newsome, *J. Neurosci.* 18 (1998) 3870.
- [6] W.R. Softky, C. Koch, *J. Neurosci.* 13 (1993) 334–350.
- [7] J.C. Eccles, *The Physiology of Synapses*, Springer, Berlin, 1964.
- [8] H.C. Tuckwell, *Introduction to Theoretical Neurobiology, Linear Cable Theory and Dendritic Structure*, vol. 1, Cambridge University Press, Cambridge, 1988.
- [9] G.L. Gerstein, B. Mandelbrot, *Biophys. J.* 4 (1964) 41.
- [10] B. Gluss, *Bull. Math. Biophys.* 29 (1967) 233.
- [11] H.C. Tuckwell, *Stochastic Processes in the Neurosciences*, SIAM, Philadelphia, 1989.
- [12] M.C.W. van Rossum, G.G. Turrigiano, S.B. Nelson, *J. Neurosci.* 22 (2002) 1956.
- [13] M. Shiino, M. Yamana, *Phys. Rev. E* 69 (2004) 011904.
- [14] M. Badoual, M. Rudolph, Z. Piwkowska, A. Destexhe, T. Bal, *Neurocomputing* 65–66 (2005) 493.
- [15] G. Schmid, I. Goychuk, P. Hanggi, *Phys. Biol.* 1 (2004) 61.
- [16] R.K. Adair, *Proc. Nat. Acad. Sci.* 100 (2003) 12099.
- [17] R. Toral, C. Masollera, C.R. Mirasso, M. Ciszaka, O. Calvo, *Physica A* 325 (2003) 192.
- [18] A. Destexhe, M. Rudolph, J.-M. Fellous, T.J. Sejnowski, *Neuroscience* 107 (2001) 13.
- [19] H.C. Tuckwell, F.Y.M. Wan, *Physica A* 351 (2005) 427.
- [20] B. Doiron, A. Longtin, N. Berman, L. Maler, *Neural Comput.* 13 (2000) 227.
- [21] F.Y.M. Wan, H.C. Tuckwell, *Biol. Cybernet.* 33 (1979) 39.
- [22] H.C. Tuckwell, F.Y.M. Wan, *J. Theor. Biol.* 87 (1980) 275.
- [23] H.C. Tuckwell, F.Y.M. Wan, Y.-S. Wong, *Biol. Cybernet.* 49 (1984) 155.
- [24] H.C. Tuckwell, *Introduction to Theoretical Neurobiology, Nonlinear and Stochastic Theories*, vol. 2, Cambridge University Press, Cambridge, 1988.
- [25] J.B. Walsh, H.C. Tuckwell, *J. Theor. Neurobiol.* 4 (1985) 27.
- [26] H.C. Tuckwell, J.B. Walsh, *Biol. Cybernet.* 49 (1983) 99.
- [27] R.B. Stein, *Biophys. J.* 5 (1965) 173.
- [28] N. Brunel, S. Sergi, *J. Theor. Biol.* 195 (1998) 67.
- [29] H.C. Tuckwell, F.Y.M. Wan, J.-P. Rospars, *Biol. Cybernet.* 86 (2002) 137.
- [30] J.-W. Wen, *J. Zhejiang Univ. (Science)* 2 (2001) 253.