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The Response of a Spatially Distributed Neuron to White Noise Current Injection*

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Abstract. The depolarization of a passive nerve cylinder or dendritic tree in the equivalent cylinder representation is assumed to satisfy the cable equation. We consider in detail the effects of white noise current injection at a given location for the case of sealed end boundary conditions and for an initial resting state. The depolarization at a point is a Gaussian random process but is not Markovian. Expressions (infinite series) are obtained for the expectation, variance, spatial and temporal covariances of the depolarization. We examine the steady state expectation and variance and investigate how these are approached in time over the whole neuronal surface. We consider the relative contributions of various terms in the series for the expectation and variance of the depolarization at x 0 (soma, trigger zone, recording electrode) for various positions of the input process. It is found that different numbers of terms must be taken to obtain a reasonable approximation depending on whether the stimulus is at proximal, central or distal parts of the dendritic tree. We consider briefly the interspike time problem and see in an approximate way how spatial effects are important in determining the mean time between impulses.

1. Introduction

Many models for the response of nerve membrane potential to random synaptic input have been proposed and analyzed in the last decade. A description of such models and an account of the progress made with them are contained in the monograph by Holden (1976).

In most of these stochastic models the state of the neuron is represented by a single variable, such as the depolarization at a point. Letting this quantity be $V(t)$ at time t, and employing a simple R-C circuit for a patch of membrane, we can write the stochastic equation

$$dV = -sVdt + \sum_{i=1}^{n} a_i dP(f_i;t), \qquad V(0)=0, \tag{1}$$

where $s=(RC)^{-1}$ is the reciprocal of the membrane time constant, and $P(f_i;t)$ is a Poisson process of rate parameter f_i. An event in the process $P(f_i;t)$ makes V undergo a jump of magnitude a_i, which may be positive or negative depending on whether the input process is excitatory or inhibitory. Equation (1) is essentially the model proposed by Stein (1965) for which many results have been obtained for the moments of the time between action potentials (see for example, Tuckwell and Richter, 1978; Cope and Tuckwell, 1979, and references therein). A modification of Stein's model which incorporates a more complete description of the processes of synaptic transmission has been derived and analyzed (Tuckwell, 1979). This modified Stein model is governed by the stochastic differential equation

$$dV = -sVdt + (V_E - V)a_E dP(f_E;t) + (V_I - V)a_I dP(f_I;t), \tag{2}$$

where V_E and V_I are the excitatory and inhibitory reversal potentials, a_E and a_I are positive constants and f_E, f_I are the rate parameters of the excitatory and inhibitory input processes.

The random processes described in these models have sample paths with discontinuites. They have also been studied through their diffusion approximations, which we denote by $\hat{V}(t)$. For (1), we have

$$d\hat{V} = (-s\hat{V} + a)dt + bdW(t), \tag{3}$$

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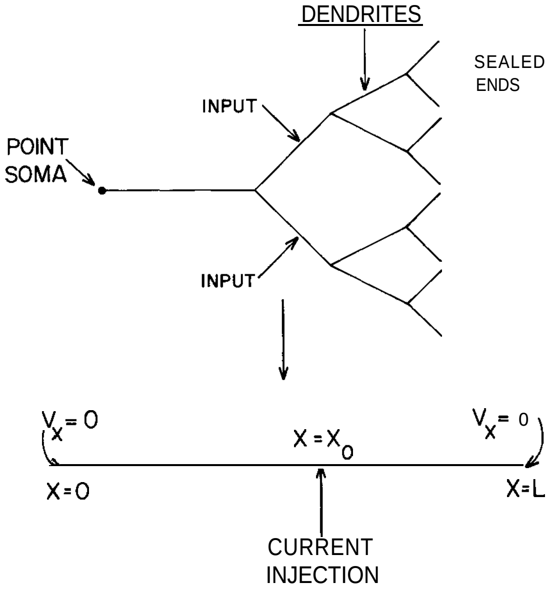


Fig. 1. A nerve cylinder of length L and with sealed ends is stimulated with white noise current at $x=x_0$. The dendritic tree, with inputs as shown, may be mapped, under certain conditions, onto this cylinder. The numerical results in subsequent figures are for (6) with $a=b=L=1$

where a and b are constants and $W(t)$ is a standard Wiener process of mean zero and variance t This model has been extensively studied (Gluss, 1967; Roy and Smith, 1969 ; Capocelli and Ricciardi, 1971). A diffusion analog of (2)

$$d\hat{V}=[(-s+a_1)\hat{V}+b_1]dt+c\hat{V}dW(t), \tag{4}$$

where a_1, b_1, and c are constants, was proposed by Johannesma (1968) but results for this model have not been obtained.

Equations (1)-(4) summarize the point models whose generalization to include spatial effects we will begin to study here. Neurons are spatially distributed and often have branching dendritic trees. Synaptic inputs may occur both on the somatic region and the dendrites. The response at a localized patch of membrane to inputs which occur at spatially remote points has been much studied in deterministic neural modelling (Rall, 1959, 1964, 1967, 1969; Rall and Rinzel, 1973; Rinzel, 1975). Our aim here is to consider this kind of problem when inputs occur randomly in time at a given location on the neuron's surface.

Our starting point is the cable equation satisfied by the depolarization of the nerve cell membrane. Such an equation has been found to adequately describe the subthreshold behaviour of axon cylinders and can also govern the distribution of the potential in a dendritic tree if this can be represented by an "equivalent cylinder". In the case of no inputs, $V(x, t)$, the depolarization at the space point x at time t, will satisfy

$$\frac{\partial V}{\partial t}=-V+\frac{\partial^2 V}{\partial x^2}, \tag{5}$$

where the physical parameters such as membrane resistance have been scaled out so that t is measured in units of the "passive membrane time constant", x is measured in units of the "characteristic length" and the electrotonic length is L. Suppose now that a "white noise" current with drift is injected at the point $x=x_0$ (Fig. 1). We may then write

$$\frac{\partial V}{\partial t}= -V+ \frac{\partial^2 V}{\partial x^2}+\delta(x-x_0)\left[a+b\frac{dW}{dt}\right], \tag{6}$$

where a is the drift parameter and b is the variance parameter of the noise. This equation forms the basis of most of the work to be presented here.

A few comments are in order to relate (6) to the electro-physiological problem of interest. The appearance of the delta function, $\delta(x-x_0)$, implies that the sources are active only on a very small patch of a nerve cylinder membrane. Such an experimental arrangement was achieved for a space clamped squid axon by Guttman et al. (1974). For a dendritic tree, the use of the delta function implies that we are considering random input at a few synapses which are about the same electrotonic distance from the soma. If some of these synapses are excitatory and others inhibitory, then (6) can be considered to be a smoother version of

$$\frac{\partial V}{\partial t}=-V+\frac{\partial^2 V}{\partial x^2}$$
$$+\delta(x-x_0)\left[a_E\frac{dP}{dt}(f_E;t)-a_I\frac{dP}{dt}(f_I;t)\right], \tag{7}$$

where $P(f_E;t)$ and $P(f_I;t)$ are independent Poisson processes of rate parameters f_E and f_I and where a_E and a_I are positive constants. Equation (7) can in turn be considered to be a (spatially) smoothed version of

$$\frac{\partial V}{\partial t}=-V+\frac{\partial^2 V}{\partial x^2}+\delta(x-x_E)a_E\frac{dP}{dt}(f_E;t)$$
$$+\delta(x-x_I)a_I\frac{dP}{dt}(f_I;t), \tag{8}$$

where x_E and x_I, the location of the excitatory and inhibitory synapses, respectively, do not differ by very much. Equation (6) can be generalized to handle an arbitrary number of input processes at the points x_i, $i=1,\ldots,n$

$$\frac{\partial V}{\partial t}=-V+\frac{\partial^2 V}{\partial x^2}+\sum_{i=1}^{n}\delta(x-x_i)\left[a_i+b_i\frac{dW_i}{dt}\right], \tag{9}$$

where the a_i, b_i are constants and the W_i are (possibly independent) Wiener processes. This equation in turn can be considered a smoothed version of

$$\frac{\mathbf{av}}{\partial t} = -V + \frac{\partial^2 V}{\partial x^2} + \sum_{i=1}^{n} \delta(x-x_i)\left[a_i \frac{dP(f_i;t)}{dt}\right], \tag{10}$$

where the a_i may be positive (excitatory) or negative (inhibitory). Furthermore, we may generalize (2) to include spatial effects by writing

$$\frac{\partial V}{\partial t} = -V + \frac{\partial^2 V}{\partial x^2} + \sum_{i=1}^{n} \delta(x-x_i)[V_i - V]a_i \frac{dP}{dt}(f_i;t), \tag{11}$$

where x_i is the location of the i-th synaptic input whose reversal potential is V_i with Poisson rate f_i, and where the a_i are positive constants.

We note that the Wiener processes $W(t)$ and the Poisson processes $P(f;\ t)$ can be replaced by more general random processes but these standard processes are expected to be reasonable approximations under many circumstances. Equations (7) through (11) provide the basis of further work in this series. For the present we will focus on the problem of a cable with white noise current injection at a single space point as described by (6). We will find expressions for the mean and variance of the depolarization as well as its spatio-temporal covariance. We will investigate how various eigenfunctions contribute to the moments of the depolarization and hence be able to conclude when a single component approximation [such as described by (1)-(4)] to the spatial model can be expected to perform reasonably well. We will also consider the problem of determining the time between impulses of a neuron under the assumption of a threshold depolarization at the trigger zone.

2. **The Cable Equation with White Noise Current Injection at a Point**

Various boundary conditions may be imposed on the stochastic partial differential (6) corresponding to cases of "sealed end", "killed end" or lumped soma at one end in the case where the equivalent cylinder representation of the dendritic tree is being employed (Rall, 1969). For clarity, we limit ourselves in this study to the sealed end conditions

$$\left.\frac{\partial V}{\partial x}\right|_{x=0} = \left.\frac{\partial V}{\partial x}\right|_{x=L} = 0\,, \tag{12}$$

and assume that the nerve membrane is initially in its resting state so that

$$V(x,0) = 0\,.$$

It should be evident from the subsequent development that other boundary conditions and/or an inhomogeneous initial condition can also be handled by the same method of solution.

Upon writing

$$F(x,t) \equiv \delta(x-x_0)f(t) \equiv \delta(x-x_0)\left[a + b\frac{dW}{dt}\right], \tag{14}$$

we observe that the solution of the initial-boundary value problem defined by (6), (12), and (13) can be expressed in terms of the associated Green's function (see Stakgold, 1968 for example)

$$V(x,t) = \int_0^t \int_0^L G(x,\xi,t-\tau)F(\xi,\tau)d\xi d\tau\,. \tag{15}$$

The Green's function, $G(x,\xi,t-\tau)$, is the cable response to a point source of unit strength applied at the point ξ and the instant τ, i.e.

$$G_t = G_{xx} - G + \delta(x-\xi)\delta(t-\tau)\,. \tag{16}$$

For a sealed end cable, we have for $t > \tau$

$$G(x,\xi,t-\tau) = \sum_{n=0}^{\infty} e^{-\mu_n^2(t-\tau)}\phi_n(x)\phi_n(\xi) \qquad (t>\tau) \tag{17}$$

with

$$\phi_0(x) = \frac{1}{\sqrt{L}},\ \phi_n(x) = \sqrt{\frac{2}{L}}\cos\left(\frac{n\pi x}{L}\right) \qquad (n=1,2,3,\ldots)\,, \tag{18}$$

$$\mu_n^2 = 1 + \frac{n^2\pi^2}{L^2} \qquad (n=0,1,2,3\,,\ldots), \tag{19}$$

and G $\equiv$ 0 for $t < \tau$. The expansion (17) is a Fourier series representation of $G(x,\xi,t-\tau)$ in terms of the eigenfunctions of the (ordinary) differential operator $d^2(\ )/dx^2 - (\ )$ associated with the cable equation and a reflecting boundary condition at each end of the interval $[0,L]$.

With F(x, t) given by (14) we may carry out one integration in (15) to get

$$\begin{aligned} V(x,t) &= \int_0 G(x,x_0,t-\tau)f(\tau)d\tau \\ &= av(x,t;x_0) + bu(x,t;x_0)\,, \end{aligned} \tag{20}$$

where

$$v(x,t;x_0) \equiv \sum_{n=0}^{\infty} \frac{1-e^{-\mu_n^2 t}}{\mu_n^2}\phi_n(x)\phi_n(x_0)\,, \tag{21}$$

$$u(x,t;x_0) \equiv \int_0 G(x,x_0,t-\tau)w(\tau)d\tau \tag{22}$$

with $w(\tau)d\tau \equiv dW(\tau)$.

It is instructive to note that (20) may be written as

$$V(x,t)=\sum_{n=0}^{\infty}V_n(t)\phi_n(x)\,, \tag{23}$$

where

$$\begin{aligned}V_n(t)&=\phi_n(x_0)\int_0^t e^{-\mu_n^2(t-\tau)}f(\tau)d\tau\\ &=\phi_n(x_0)\int_0^t e^{-\mu_n^2(t-\tau)}[a+bw(\tau)]\,d\tau\end{aligned} \tag{24}$$

or

$$dV_n=[-\mu_n^2V_n+a\phi_n(x_0)]dt+b\phi_n(x_0)dW \quad (t>0) \tag{25}$$

$$V_n(0)=0 \tag{26}$$

for n= 0, 1,2 ,... . Therefore, each process $V_n(t)$ is an Ornstein-Uhlenbeck process (O.U.P.) (see for example Jaswinski, 1970) which has as its foundation the classical model for the velocity of a Brownian motion particle (Uhlenbeck and Ornstein, 1930). Thus each component process $V_n(t)\phi_n(x)$ in the normal mode decomposition (23) (Van Lear and Uhlenbeck, 1931) is also an O.U.P. It is well known that an O.U.P. is Gaussian and Markov; the mean and variance of the component O.U.P.'s in (23) are

$$E[V_n(t)]\equiv\langle V_n(t)\rangle=\frac{a\phi_n(x_0)}{\mu_n^2}[1-e^{-\mu_n^2t}] \tag{27}$$

and

$$\begin{aligned}\mathrm{Var}\,[V_n(t)]&\equiv\langle V_n^2(t)\rangle-\langle V_n(t)\rangle^2\\ &=\frac{b^2\phi_n^2(x_0)}{2\mu_n^2}[1-e^{-2\mu_n^2t}]\end{aligned} \tag{28}$$

respectively, with $\langle\alpha\rangle$ denoting the average of α. Furthermore, we can obtain from (24) and the fact that $\langle w(\tau_1)w(\tau_2)\rangle=\delta(\tau_1-\tau_2)$ the covariance of two different component O.U.P.'s which will be useful in finding an expression for the variance of $V(x;t)$:

$$\begin{aligned}\mathrm{Cov}[\,V_m(t)\,V_n(t)]&\equiv\langle V_m(t)\,V_n(t)\rangle-\langle V_n(t)\rangle\langle V_m(t)\rangle\\ &=b^2\phi_n(x_0)\phi_m(x_0)\\ &\quad\cdot\int_0^t\int_0^t e^{-[\mu_n^2(t-\tau_1)+\mu_m^2(t-\tau_2)]}\\ &\quad\cdot\langle w(\tau_1)w(\tau_2)\rangle d\tau_2d\tau_1\\ &=b^2\phi_n(x_0)\phi_m(x_0)\int_0^t e^{-(\mu_n^2+\mu_m^2)(t-\tau_1)}d\tau_1\\ &=\frac{b^2\phi_n(x_0)\phi_m(x_0)}{\mu_m^2+\mu_n^2}[1-e^{-(\mu_m^2+\mu_n^2)t}]\,.\end{aligned} \tag{29}$$

Note that even though the individual O.U.P.'s which constitute $V(x,t)$ are Markovian, it is clear that the depolarization at a point is not a Markov process. Physically, this is understandable because specifying the potential at a single point at a given instant of time does not determine the potential at that point at any future time; $V(x,t)$ for a given x depends on the potentials at all other points of the cable at the same earlier time. Mathematically, this dependence is a consequence of the Green's function representation for the initial value problem [with $F(x,t)$ 0 and] with reflecting boundaries (Stakgold, 1968). Hence, it is not meaningful to talk about the transition probability density for $V(x,t)$ at a fixed x. The same Green's function representation does show that specifying V for the entire cable at any instant of time determines the depolarization for all points in the cable thereafter. As such, the depolarization $V(x,t)$ is a Markov random field.

3. **Mean, Variance and Covariance of the Depolarization**

a) Expected Value

With the expression (27) for (K(t)), we get formally from (23)

$$\begin{aligned}E[V(x,t)]\equiv\langle V(x,t)\rangle&=\sum_{n=0}^{\infty}\langle V_n(t)\rangle\phi_n(x)\\ &=a\sum_{n=0}^{\infty}\frac{1-e^{-\mu_n^2t}}{\mu_{nn}^2}\phi_n(x_0)\phi_n(x)\\ &=av(x,\,t\,;x_0)\,.\end{aligned} \tag{30}$$

The same result can also be obtained by ensemble averaging both sides of the Green's function representation (20) and using the fact that W is of zero mean. The series (30) converges uniformly and absolutely since $\mu_n^2=1+O(n^2)$; therefore, the expected value of $V(x,\,t)$ is bounded for all x in $[0,L]$ and all $t>0$ and we have the following result:

The expected depolarization at the point x at time t for the nerve cylinder with sealed ends at x 0 and $x=L$, driven by a white noise current of strength a at the point x_0, is given by the infinite series (30) *with a steady state value*

$$av(x,\infty;x_0)=a\sum_{n=0}^{\infty}\frac{\phi_n(x_0)\phi_n(x)}{\mu_n^2}\,. \tag{31}$$

The two series (30) and (31) converge rather slowly at and near the point of application of the external stimulus (see Sect. 4). It is therefore extremely useful from a computational viewpoint to have an alternative expression for expected steady state depolarization the which does not involve an infinite series. To find such an expression, we take expectations in (6), (12), and (13) to get the following initial-boundary value problem for the expected value $\langle V(x,t)\rangle$

$$\langle V\rangle_t = \langle V\rangle_{xx} - \langle V\rangle + a\delta(x-x_0)\,, \tag{32}$$

$$\langle V(x,0)\rangle = \langle V(0,t)\rangle_x = \langle V(L,t)\rangle_x = 0\,. \tag{33}$$

The exact solution of this problem is of course given by (30). But the steady state value $\langle V(x,\infty)\rangle \equiv \bar{v}(x\,;x_0)$ is now seen to be the solution of the boundary value problem

$$\bar{v}'' - \bar{v} = -a\delta(x-x_0)\,, \qquad \bar{v}'(0) = \bar{v}'(L) = 0\,, \tag{34}$$

where a prime indicates differentiation with respect to x. In other words, $\bar{v}(x\,;x_0)$ is the Green's function for the operator $(\;)'' - (\;)$ with reflecting end conditions and is easily found by known methods (Stakgold, 1968) to be

$$\bar{v}(x\,;x_0) = \begin{cases} \dfrac{a\cosh(L-x_0)\cosh(x)}{\sinh(L)} & (x<x_0) \\[2ex] \dfrac{a\cosh(x_0)\cosh(L-x)}{\sinh(L)} & (x>x_0) \end{cases} \tag{35}$$

Thus, we have the following supplementary result:

The mean steady state depolarization for the nerve cylinder with sealed ends is given by the expression (35) or by the infinite sum (31).

It is not difficult to see that the expression (31) is in fact the eigenfunction expansion of (35) and is not as well suited for evaluating $\bar{v}(x\,;x_0)$ at the point x_0.

b) Variance

To find an expression for the variance of $V(x,t)$, *we* use the normal mode decomposition (23) and the expression (29) for the covariance, Cov [K(t), $V_m(t)$], in

$$\mathrm{Var}[V(x,t)] \equiv \langle V^2(x,t)\rangle - \langle V(x,t)\rangle^2 \tag{36}$$

to get formally

$$\begin{aligned} \mathrm{Var}[V(x,t)] = {} & \sum_{m=0}^{\infty}\sum_{n=0}^{\infty} [\langle V_n(t)V_m(t)\rangle \\ & - \langle V_n(t)\rangle\langle V_m(t)\rangle]\phi_m(x)\phi_n(x) \\ = {} & \sum_{m=0}^{\infty}\sum_{n=0}^{\infty} \mathrm{Cov}[V_m(t), V_n(t)]\phi_m(x)\phi_n(x) \\ = {} & b^2 \sum_{m=0}^{\infty}\sum_{n=0}^{\infty} \frac{[1-e^{-(\mu_m^2+\mu_n^2)t}]}{\mu_m^2+\mu_n^2} \\ & \cdot \phi_m(x_0)\phi_m(x)\phi_n(x_0)\phi_n(x)\,. \end{aligned} \tag{37}$$

The same result can also be obtained by using the Green's function representation (20) for $V(x,t)$ in (36) and the fact that W is a standard Wiener process. It is not difficult to show by an integral test that the double infinite series (37) diverges at $x=x_0$. With the help of the Dirichlet series and Abel's summation, we can also establish the convergence of the series for $x \neq x_0$. We omit the details of these analyses here, since a different representation of the variance of $V(x,t)$ will be obtained below by way of the spatial covariance of V which more readily displays these properties, and merely state the following result:

The variance of the depolarization at a point $x \neq x_0$ at time t for the nerve cylinder with sealed ends at x 0 and $x=L$, driven by a white noise current with variance parameter b at x_0, is given by the infinite series (37) with a steady state value

$$\mathrm{Var}[V(x,\infty)] = b^2 \sum_{m=0}^{\infty}\sum_{n=0}^{\infty} \frac{\phi_m(x_0)\phi_n(x_0)\phi_m(x)\phi_n(x)}{\mu_m^2+\mu_n^2} \quad (x \neq x_0)\,. \tag{38}$$

With regard to the divergence of (37) and (38) at $x=x_0$, we note that the energy in an element of the cable of length dx at the point x at time t is $\frac{1}{2}cV^2(x,t)dx$ where c is the capacitance per unit cable length. Hence, the mean square value and the variance of $V(x,t)$ are measures of the average energy per unit cable length in the cable at x and t. An ideal white noise has a flat spectrum and therewith unbounded average energy. With an ideal white noise input concentrated at the point x_0, we should expect the average energy per unit cable length, and thereby the variance of V, to be unbounded there also. A similar singular behavior in the variance of the response of other physical systems driven by an ideal white noise at a point has been found in (Wan, 1972, 1973) and references therein. In the appendix an alternative expression will be derived for the variance which shows that it has a *logarithmic* singularity at $x=x_0$ [see (A 13)].

c) Covariance

We may obtain the covariance of $V(x,t)$ and $V(y,\tau)$, defined as,

$$r(x,t\,;y,\tau) = \langle v(x,t)v(y,\tau)\rangle - \langle v(x,t)\rangle\langle v(y,\tau)\rangle\,, \tag{39}$$

readily from the integral representation (2). We have, for $t>\tau$,

$$\begin{aligned} r(x,t\,;y,\tau) = {} & b^2 \left\langle \int_0^t G(x,x_0\,;t-t_1)w(t_1)dt_1 \cdot \int_0^\tau G(y,x_0\,;\tau-\tau_1)w(\tau_1)d\tau_1 \right\rangle \\ = {} & b^2 \sum_{n=0}^{\infty}\sum_{m=0}^{\infty} \frac{e^{-\mu_m^2 t}[e^{\mu_m^2\tau} - e^{-\mu_n^2\tau}]}{\mu_m^2+\mu_n^2} \\ & \cdot \phi_m(x_0)\phi_n(x_0)\phi_m(x)\phi_n(y)\,, \end{aligned} \tag{40}$$

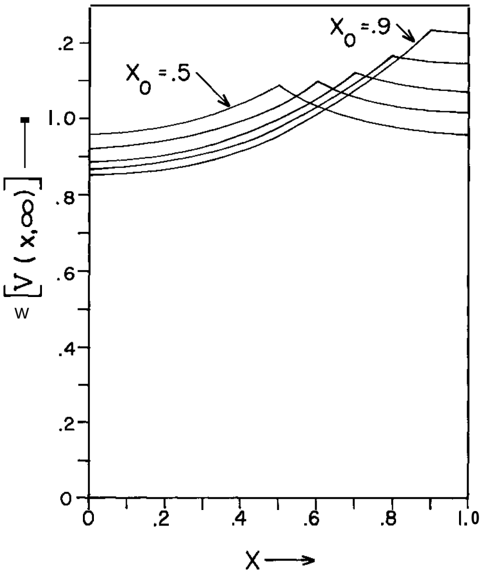


Fig. 2. The spatial distribution of the steady state mean depolarization for white noise current injection at $x_0 = 0.5, 0.6, 0.7, 0.8$, and 0.9

where we have used the expansion (17) and the covariance kernel of white noise. Though we will not numerically consider the covariance in the sequel, we point out that at $x = y, r(x, t; x, \tau)$ is not amenable to the usual spectral analysis with $a = 1$.

4. **Numerical Results and Discussion**

a) Expected Value

The model Eq. (6) we have analyzed can be regarded as representing a single passive nerve cylinder with sealed ends or a branching dendritic tree in the equivalent cylinder representation with a point soma at one end. In either case, a white noise current with a constant mean strength a is injected at the point x_0. The corresponding expected value of the depolarization is determined by the initial-boundary value problem (32) and (33). Evidently, it is the same as the depolarization $V^*(x, t)$ of a nerve cylinder subject to a deterministic input current of strength a at the point x_0, i.e.,

$$V_t^* = V_{xx}^* - V^* + a\delta(x - x_0), \tag{41}$$

$$V^*(x, 0) = V_x^*(0, t) = V_x^*(L, t). \tag{42}$$

This kind of deterministic problem has been considered briefly in papers by Rall and Rinzel (I973) and Rinzel and Rall (1974) which are mainly concerned with the related problem of a neuron with deterministic current injection at a branch terminal. Our complete solution for the stochastic problem contains the complete solution of the deterministic problem (41) and (42), namely Eqs. (30), (31), and (35). We have obtained from this complete solution numerical results for the expected value of the depolarization for white noise current injection at x_0 for various values of x_0. We shall assume that the point soma is located at x 0 so that $x = L$ represents the distal end of the dendritic tree. It has been pointed out that when we use the equivalent cylinder representation for the dendrites, an input located at an electrotonic distance x_0 from the soma means an input occurs on all branches of the tree at points which are that same electrotonic distance from the soma. If we consider input on a single branch a more complicated boundary value problem arises (see for example, Rall and Rinzel, 1973). Our results also have direct application to a passive nerve cylinder (e.g. unmyelinated axon). For the results to have physiological significance for the case of random synaptic input on the dendrites, the synapses at all points an electrotonic distance x_0 from the soma must be active. This may not be an unreasonable assumption when one considers how a given set of afferent fibers may distribute over the entire dendritic tree of a particular neuron [e.g. in the case of Ia endings on cat spinal motoneurons - see Conradi (1969) and Koziol and Tuckwell (1978)].

The mean electrotonic lengths of cat spinal motoneuron dendrites were found to be between 1.1 and 1.5 space constants by Barrett and Crill (1974). In the numerical results to be reported we have set $L = 1$ as a physiologically representative value. Since we are only interested here in qualitative effects we set $a = b = 1$ in (6); all distances will be in units of the characteristic length and all times will be in units of the time constant.

In Fig. 2 we show the computed expectation of the steady state $(t = \infty)$ depolarization as a function of distance from the soma for stimuli at $x_0 = 0.5$, 0.6, 0.7, 0.8, and 0.9. The distribution of depolarization is of course symmetrical about $x = 0.5$ when the stimulus is at $x_0 = 0.5$. These results are obtained from the expression (35) which shows that the expected steady state depolarization is proportional to the input current strength a. The results for $x_0 = 0.1, 0.2, 0.3$, and 0.4 are the reflections about $x = 0.5$ of the results for $x_0 = 0.9$, 0.8, 0.7, and 0.6 respectively. In each case shown in Fig. 2 the peak value of the expected depolarization occurs at the stimulus point and the slope has a discontinuity at that point. If we employ the equivalent cylinder picture for the dendritic tree and now regard the stimulus as representing synaptic input at x_0 it is interesting to examine the effect of varying x_0 on the response at the soma $(x = 0)$, which will often be the approximate location of the trigger zone of the neuron. We see from (35) that $\bar{v}(0; x_0) = a \cosh(L - x_0)/\sinh(L)$, and, since for a given neuron

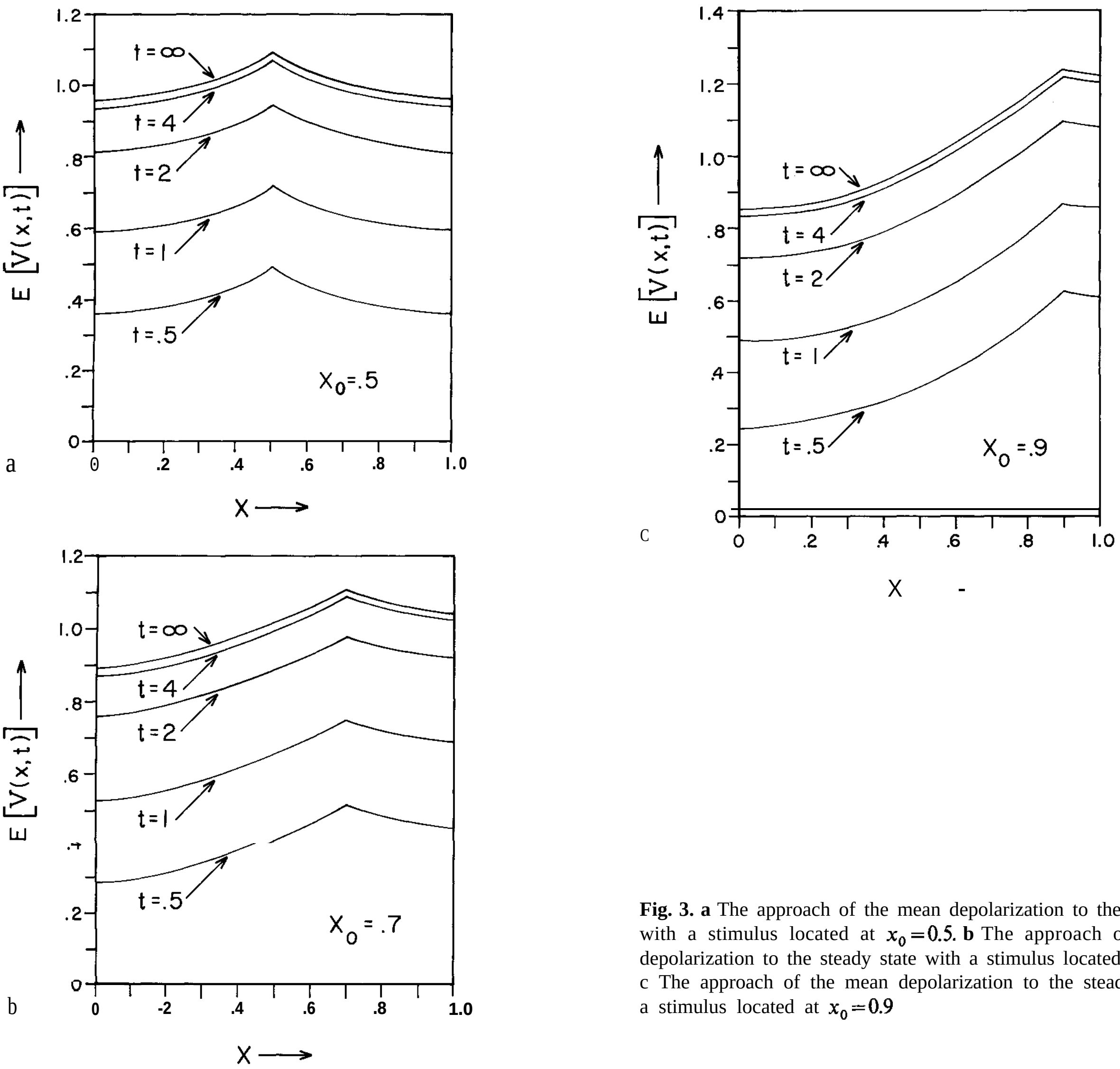


Fig. 3. a The approach of the mean depolarization to the steady state with a stimulus located at $x_0 = 0.5$. **b** The approach of the mean depolarization to the steady state with a stimulus located at $x_0 = 0.7$. c The approach of the mean depolarization to the steady state with a stimulus located at $x_0 = 0.9$

the denominator of this expression is constant, we have the following result :

The mean steady state depolarization at the soma is proportional to the hyperbolic cosine of the electrotonic distance between the source point and the distal end of the dendritic tree.

The maximum value of this mean steady state depolarization for fixed L and fixed a occurs when x_0 0 + (the soma) in which case

$$\max[\bar{v}(0;x_0)] = \bar{v}(0;0+) = a \coth L \tag{43}$$

and its minimum value occurs when $x_0 = L-$,

$$\min[\bar{v}(0;x_0)] = \bar{v}(0;L-) = a \operatorname{cosech} L. \tag{44}$$

(If the mean current strength, a, is negative, then the average steady state depolarization will also be negative which means of course an overall hyperpolarized state.)

It is noteworthy from Fig. 2 that in the steady state the mean depolarization does not vary appreciably over the entire neuronal structure. Furthermore, the value of this mean depolarization, in particular at the soma $(x = 0)$, is fairly insensitive to the location of the point of current injection.

Figure 3a–c show how the steady state is approached in time for values of $x_0 = 0.5$, 0.7, and 0.9 respectively. In all cases we have again taken $a = L = 1$. The most striking feature of these results is the way in which the mean depolarization given by (30) approaches the steady state value almost uniformly over the whole neuronal structure. To see why this is so, note that the series (30) may be written as

$$E[V(x,t)] = av(x,\infty;x_0) - a\sum_{n=0}^{\infty} \frac{e^{-\mu_n^2 t}}{\mu_n^2}\phi_n(x_0)\phi_n(x), \tag{45}$$

where $av(x,\infty;x_0)$ is the eigenfunction expansion (3 1) of the steady state expected value. Since $\mu_n^2 = 1 + n^2\pi^2/L^2$, the time dependent part of $E[V(x,t)]$ in (45) at one or more units of passive membrane time constant after the start of the current injection is dominated by the first term of the series so that

$$E[V(x,t)] \simeq av(x,\infty;x_0) - \frac{a}{L}e^{-t}. \tag{46}$$

Hence the nearly uniform approach of $E[V(x,t)]$ to its steady state value.

It is evident from the partial differential equation (32) satisfied by the expected value of $V(x,t)$ that it has a discontinuous first spatial derivative at x_0 for all $t>0$, similar to the discountinuity in the first derivative of its steady state value as given by (35). Therefore, the convergence of the series (31) and (30) is understandably slow near $x=x_0$; often fifty or more terms of the series are required for four significant figure accuracy.

It has been found that postsynaptic potential transients in cat spinal motoneurons can be accurately described by just the first few terms of their eigenfunction representation (see Rall, 1969 and references therein for relevant experimental results and analyses). For our nerve cylinder with a continuous current injection at a point, it is of interest to carry out the corresponding investigation of the relative contribution of the individual terms in the various eigenfunction expansions. To see the number of terms in the series for $\langle V(x,t)\rangle$ required for the partial sum to be experimentally indistinguishable from the actual value of $\langle V(x,t)\rangle$, we define the partial sums

$$U_m(x,t;x_0) \equiv a\sum_{n=0}^{m} \frac{1-e^{-\mu_n^2 t}}{\mu_n^2}\phi_n(x_0)\phi_n(x) \tag{47}$$

so that $\langle V(x,t)\rangle = U_\infty(x,t;x_0)$. Figure 4a shows the values of the partial sums U_0, U_2, U_4, and U_{10} evaluated at x 0 (soma) for a stimulus at $x_0 = 0.5$ when $a=L=1$.

Note that in this case, because

$$U_m(0,t;\tfrac{1}{2}) = 1 - e^{-t} + 2\sum_{n=1}^{m} \frac{\{1-e^{-(1+n^2\pi^2)t}\}}{1+n^2\pi^2}\cos\left(\frac{n\pi}{2}\right), \tag{48}$$

$U_0 = U_1$, $U_2 = U_3$, etc., because cos $(n\pi/2)$ is zero when n is odd. It was found by computing U_m $(0, t; \frac{1}{2})$ for large m that U_{10} is to four significant figures the same as the expected depolarization in this case. From Fig. 4a, we see that the first term of the series (30) overestimates $\langle V(0, t))$ by about 7% when $t = 1$ and by about 5 % for large t (> 5). If we approximate $\langle V(0, t))$ by the first two nontrivial terms (i.e., by U_2) the error is reduced to 1% or less for all t.

Figure 4b and c show how the various terms in the series contribute to the expected depolarization at x 0 (soma) and $x=L$ (distal end of dendrites) when the stimulus is located at $x_0 = 0.9$. These results will be the same as those at $x=L$ and $x = 0$ respectively when the stimulus is at $x_0 = 0.1$. We will refer to the results in Fig. 4b and c as the response at $x = 0$ with stimuli at 0.1 and 0.9, respectively. Again we found numerically that the convergence of the series (30) is essentially complete when eleven terms (i.e. U_{10}) are included. When the stimulus is at $x_0 = 0.1$, quite electrotonically close to the soma (Fig. 4b), the first term in the series (30), i.e. U_0 $(0, t; 0.1)$, underestimates the actual response by about 30% when $t = 1$ and eventually $(t = 10)$ *under*-estimates it by about 20%. Including the next term reduces these errors to about one fifth, and the effect of extra terms is quite negligible. When the stimulus is remote from the soma $(x_0 = 0.9)$ the first term in the series for $\langle V(0;t)\rangle$ overestimates the response by about 30% at $t = 1$ and eventually (by $t = 10$ say) overestimates it by about 16 %. Including the next term (i.e. U_1) underestimates the somatic response by a few percent and including three terms (i.e. U_2) gives an extremely accurate estimate of $\langle V(0,t)\rangle$. These observations will be useful later in making approximations to the spatial model neuron described by (6), particularly for preliminary estimates of the mean first passage time.

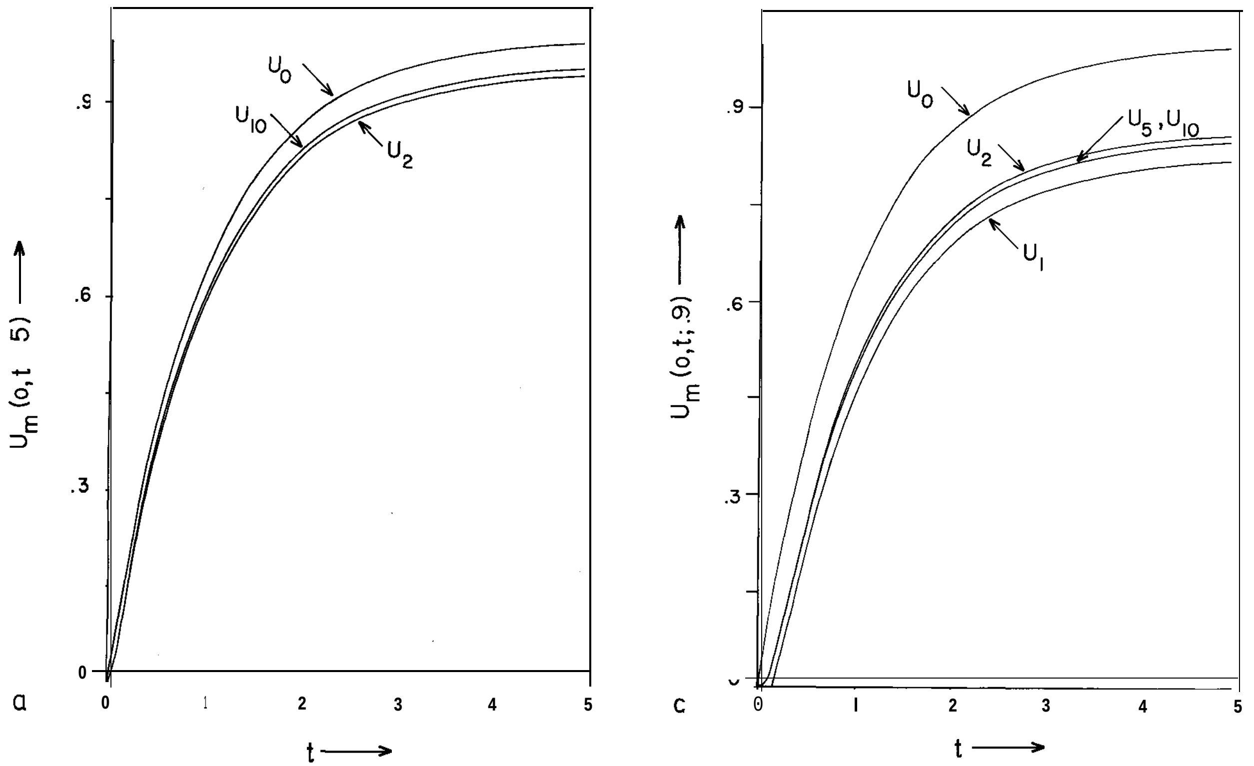
At this point, it is worth mentioning that all the results we have obtained so far in this report apply equally well to the cable equation model for a neuron driven by Poisson inputs at x_0 according to (7) where now the quantity a is replaced by $f_E a_E - f_I a_I$ because if we take expectations in (7), we obtain

$$\langle V\rangle_t = -\langle V\rangle + \langle V\rangle_{xx} + \delta(x-x_0)[f_E a_E - f_I a_I] \tag{49}$$

which is the same as (32) with a replaced by $[f_E a_E - f_I a_I]$.

b) Variance

We also computed, from the appropriate series, the variance of the depolarization of the nerve cylinder when driven by a white noise current at the point x_0 with $a = b = L = 1$. Figure 5 shows the steady state standard deviation, $\sigma[V(x,\infty)] = \sqrt{\mathrm{Var}\,[V(x,\infty)]}$, plotted against electrotonic distance for values of $x_0 = 0.5$, 0.7, and 0.9. As pointed out above, the variance of the depolarization is not defined at the stimulus point and the standard deviation in each case becomes infinite at x_0. When $x_0 = 0.5$ the standard deviation is symmetric about x_0 and does not begin to depart much from its values at the ends of the cylinder until within about 0.1 characteristic lengths of the



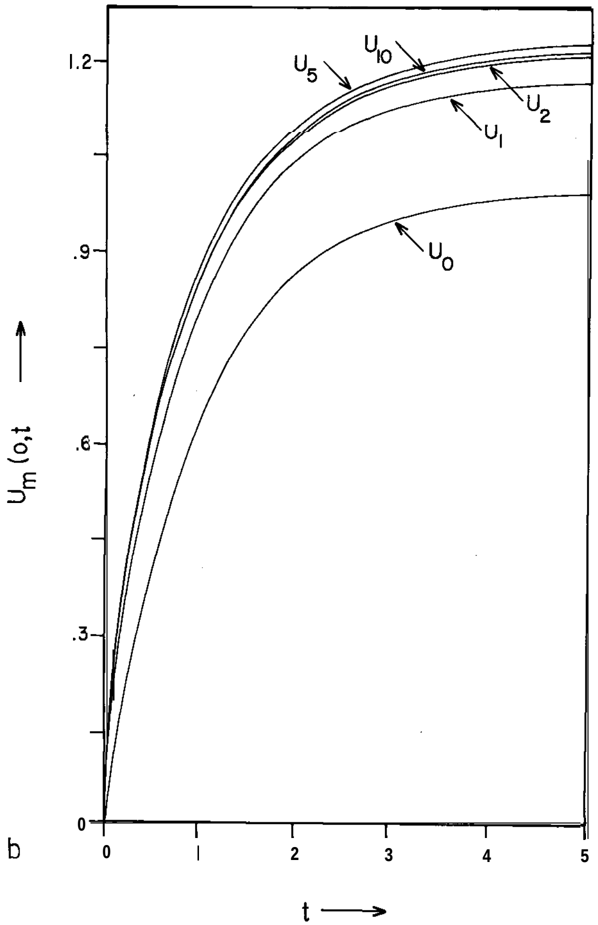


Fig. 4. a Convergence of the partial sum, U_m, to the mean depolarization at $x = 0$ with the stimulus at $x_0 = 0.5$. **b** Convergence of the partial sum, U_m, to the mean depolarization at x 0 with the stimulus at $x_0 = 0.1$. c Convergence of the partial sum, U_m, to the mean depolarization at $x = 0$ with the stimulus at $x_0 = 0.9$

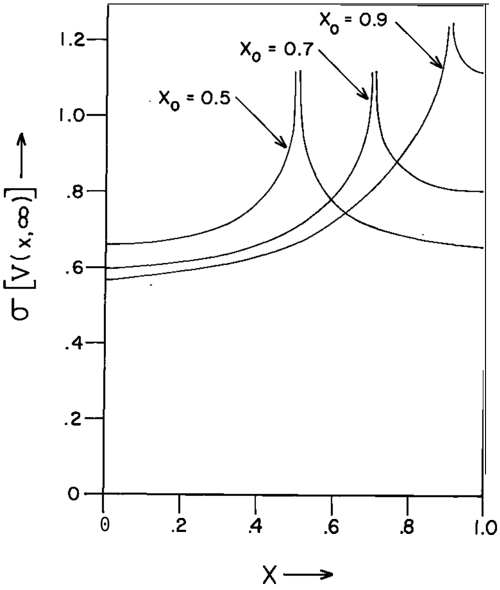


Fig. 5. The spatial distribution of the steady state standard deviation of the depolarization for white noise current injection at $x_0 = 0.5, 0.7$, and 0.9

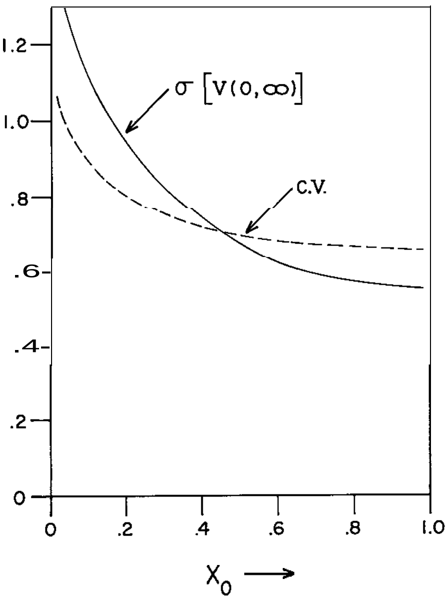


Fig. 6. The steady state standard deviation and coefficient of variation of the somatic depolarization as a function of the position of the stimulus

stimulus. When the stimulus is at $x_0=0.7$ (0.3) and $x_0=$ 0.9 (0.1) the standard deviation of the steady state depolarization becomes a much more rapidly changing function of position so that spatial effects are much more important. We point out that when we used the double sum (38) to numerically determine the steady state variance accurate to four significant figures, we had to employ about $[20]^2$ terms (i.e. both m and n from 0 to 20) when $|x-x_0|$ was about 0.1; up to $[100]^2$ terms when $|x-x_0|$ was about 0.03 ; and up to $[150]^2$ terms when $|x-x_0|$ was about 0.02. By comparison, when the alternative series (A13) was employed, the same accuracy was attained for $|x-x_0|\geqq 0.02$ when the summations were truncated at $m=n=\pm$ 5, i.e. about $[11]^2$ terms.

Since in the equivalent cylinder representation, we regarded x 0 as the position of a point soma with synaptic input at x_0, it is of interest to see how the variance of the somatic response depends on input location for a fixed stimulus strength : This is shown in Fig. 6 where we have plotted the standard deviation of the steady state somatic depolarization versus stimulus position. When the input is at the distal end of the dendritic tree (cylinder) the standard deviation is about 0.55. Moving the stimulus to the half-way point $x_0=0.5$ only increases the standard deviation to about 0.66, whereas a dramatic increase occurs when the stimulus moves closer to the soma. When $x_0=$ 0.1, the standard deviation has become twice its value when the stimulus was at the distal end of the dendritic tree. Eventually, of course, the standard deviation becomes infinite in the limit as $x_0\to 0^+$.

To consider the standard deviation of V(0, co) without considering the mean would be misleading in a discussion of how noisy the somatic response is to a noisy input at x_0. We have also shown in Fig. 6 how the *coefficient* of *variation* of $V(0,\infty)$ (i.e. its standard deviation divided by its mean) depends on the stimulus position for the given input process. It can be seen that when $x_0=$ 1.0, the coefficient of variation is about 0.65. When the stimulus is at the electrotonic center of the nerve cell, the coefficient of variation is 0.69 which is a change of only 0.6 %. When the stimulus is even closer to the soma $(x_0=0.2)$, the coefficient of variation of the steady state depolarization has still only increased to about 0.8. Thus over the whole range of stimulus locations from quite proximal to the extreme distal end of the dendritic tree, only relatively small changes in the noisiness of the steady state somatic response occur for a random input channel. The variability of the steady state somatic response is practically independet of stimulus location provided the latter is in the distal half of the dendritic tree. Thus, no input in this part of the neuronal structure is "seen" more clearly by the integrating part (trigger zone) of the neuron than any other input. It will be of interest in future work to see if this invariance extends to the whole neuronal structure when a more elaborate somatic circuit (than a point model) and a non-delta correlated input current are incorporated in the model of the neuron.

We now turn our attention to the manner in which the variance of $V(x,t)$ approaches its steady state value over the neuronal structure as time increases. For input currents at $x_0=0.5$, 0.7, and 0.9 we show in Fig. 7a–c, the variance of the depolarization as functions of electrotonic distance at $t=$ 0.5, 1,0, and 2.0. Again for these curves we have set $a=b=L=$ 1. In all cases the variance in the steady state is virtually indistinguishable from the results for $t=$ 2. Furthermore, just as the expectation of $V(x,t)$ approaches $E[V(x,\infty)]$ practically uniformly in x, so too does its variance. The explanation for this uniform behaviour is similar to that adduced for the expectation.

Finally we consider the relative contributions of the various terms in the double sum (37) to the variance of $V(x,t)$. To do this, we define the partial sums

$$W_k(x,t;x_0)=b^2\sum_{m=0}^{k}\sum_{n=0}^{k}\frac{[1-e^{(\mu_m^2+\mu_n^2)t}]}{\mu_m^2+\mu_n^2}\cdot\phi_m(x_0)\phi_m(x)\phi_n(x_0)\phi_n(x)\,. \quad (50)$$

We restrict our attention to the soma and compare the values of W_k there, for various k, when stimuli are located at $x_0=0.5, x_0=0.1$, and $x_0=0.9$. For a stimulus at the midpoint of the cylinder (Fig. 8a) we see that $W_0(0,t;$ 0.5) overestimates the variance of the

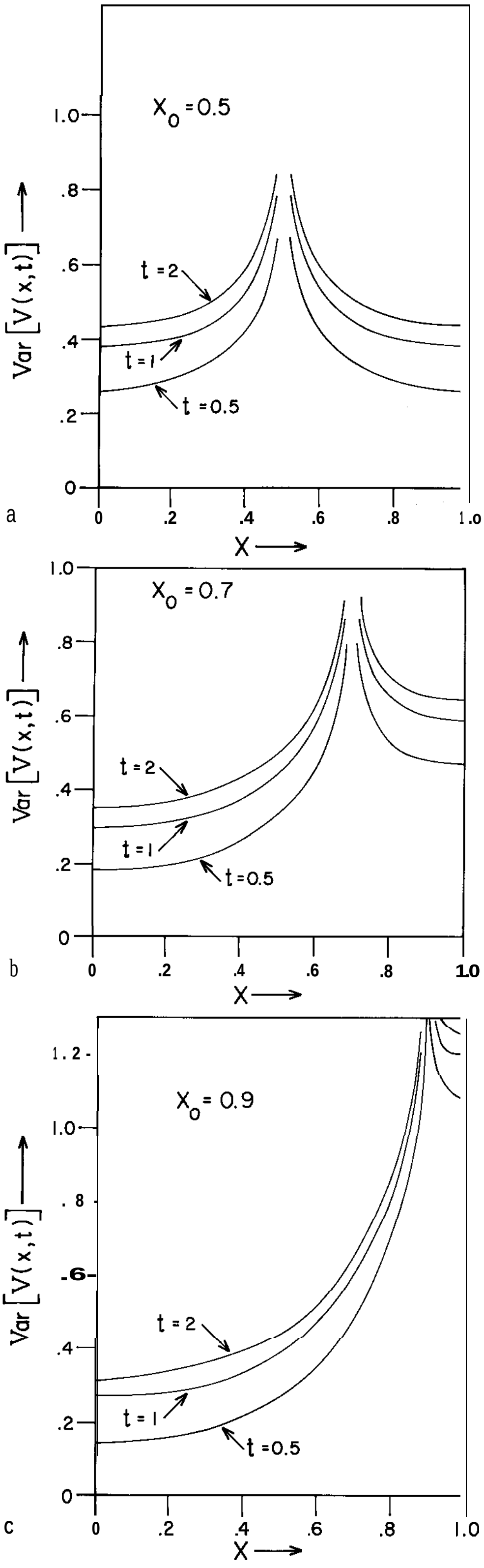


Fig. 7. a The approach of the variance of the depolarization to the steady state with a stimulus located at $x_0 = 0.5$. At $t = 2$ the steady state is virtually achieved. b The approach of the variance of the depolarization to the steady state with a stimulus located at $x_0 = 0.7$. At t=2 the steady state is virtually achieved. c The approach of the variance of the depolarization to the steady state with a stimulus located at $x_0 = 0.9$. At $t = 2$ the steady state is virtually achieved

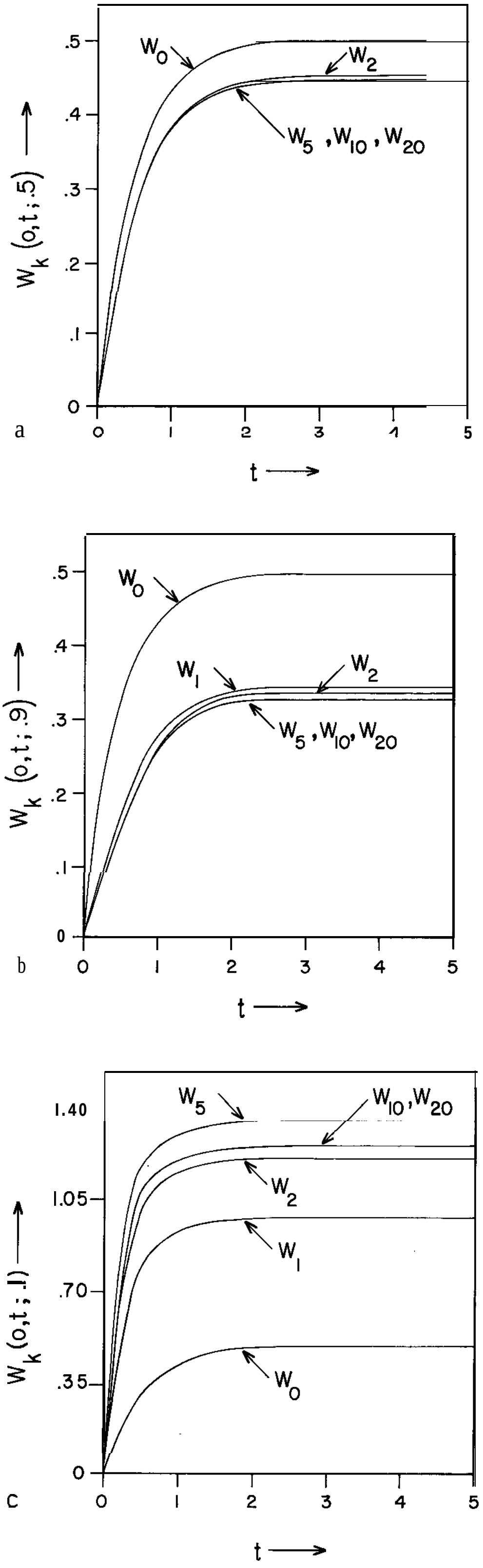


Fig. **8.** a Convergence of the partial sums, W_k, to the variance of the depolarization at x 0 for a stimulus located at $x_0 = 0.5$. b Convergence of the partial sums, W_k, to the variance of the depolarization at $x = 0$ for a stimulus located at $x_0 = 0.9$. c Convergence of the partial sums, W_k, to the variance of the depolarization at $x = 0$ for a stimulus located at $x_0 = 0.1$

depolarization by about 11% at $t=1$ and the error remains unchanged for large $t\,(t>5)$. This is equivalent to an error of only about 6 % in the standard deviation of $V(0,t)$. For this case $W_1=W_0$ and W_2 is only about 1% larger than the actual variance for large values of t. We may conclude that the first term in the expansion (23) at $x=0$ provides a reasonably accurate approximation to the random depolarization there when white noise stimulus is close to the electrotonic center of the nerve cylinder (dendritic tree), at least for the values of the parameters we have considered.

The results shown in Fig. 8b are for W_k with $k=0$, 1, 2, 5, 10, 20, evaluated at $x=0$ when the stimulus is at $x_0=0.9$ and $b=L=1$. (The results for $k=5, 10$, and 20 are indistinguishable in the figure.) Here we find that $W_0(0,t;\ 0.9)$ overestimates the variance of the somatic depolarization by about 60 % at $t=1$, the error being reduced slightly to about 50% at $t>5$. The next approximation, $W_1(0,t;\ 0.9)$ provides a dramatic decrease in the error. The value of W_1 at $t=1$ differs only by about 3.5 % from the actual variance and by about the same percentage at $t>5$. It is apparent that W_2 differs by only about 1% from W_∞ in this case. We conclude that when the stimulus is remote from the recording electrode ($x=0$, soma) the first two terms in the expansion (23) may provide a reasonably accurate description of the random depolarization there.

The third case we consider is that where the white noise stimulus is electrotonically close to the recording electrode (soma, trigger zone). In Fig. 8c, we show $W_k(0,t;\ 0.1)$ for $k=0, 1, 2, 5, 10$, and 20. Here the variance of $V(0,t)$ is severely underestimated by that of the first term in the expansion (23), the relative error being about 64 % at $t=1$ and about 61% at $t=10$. The value of W_1 is also considerably different from the actual variance, the error now being about 22%. Including 3 terms in the expansion (23) (i.e. W_2) underestimates the variance by only about 4%. Somewhat paradoxically, including six terms in the expression for $V(0,t)$ leads to an *overestimate* of Var $[V(0,t)]$ by nearly 8%. Thus if one wishes to approximate $V(0,t)$ by the sum of the Ornstein-Uhlenbeck processes $V_n(t)\phi_n(0)$ one must take at least three of these processes when the white noise stimulus is near the point at which the response is being evaluated.

c) *The Interspike Time Problem*

In the introduction of this paper, we pointed out that point models had been used to investigate the firing time distribution of neurons with random input. In these models, the firing time is the time of first passage of a Markov process through some threshold. Suppose we are only interested in the response at the soma ($x=0$) and use the decomposition (23) to write $V(0,t)$ as an infinite sum of Ornstein-Uhlenbeck processes

$$V(0,t)=\sum_{n=0}^{\infty} V_n(t)\phi_n(0)\,. \tag{51}$$

The numerical results for $x_0=0.5$ shown in Figs. 4a and 8a tell us that when the white noise stimulus is close to the halfway point between the soma and the distal end of the dendritic tree, then a reasonably good approximation for the random process $V(0,t)$ will be

$$V(0,t)\simeq V_0(t)/\sqrt{L}\,, \tag{52}$$

where, from (18), (19), and (25), the random process $V_0(t)$ is an Ornstein-Uhlenbeck process satisfying the stochastic initial value problem

$$dV_0=\left(-V_0+\frac{a}{\sqrt{L}}\right)dt+\frac{b}{\sqrt{L}}\,dW,\qquad V_0(0)=0 \tag{53}$$

W being a standard Wiener process. Hence, with correct interpretation of the parameters, a single component model is quite adequate under these circumstances; correspondingly, the point model results for firing time are expected to provide reasonable approximations for the spatial model. On the other hand, when the input arrives either close to or remote from the soma, it is seen from the numerical results in Fig. 4b and c and 8b and c that a single component model generally does not provide an adequate representation for the depolarization of the neuron. These numerical results also suggest that for white noise stimuli near the distal end of the dendritic tree, a reasonable approximation for the process $V(0,t)$ is

$$V(0,t)\simeq\frac{1}{\sqrt{L}}\left[V_0+2V_1(t)\right]\,, \tag{54}$$

where $V_0(t)$ is as described before and $V_1(t)$ is another Ornstein-Uhlenbeck process satisfying the stochastic intial value problem

$$dV_1=\left[-\left(1+\frac{\pi^2}{L^2}\right)V_1+a\sqrt{\frac{2}{L}}\cos\left(\frac{\pi x_0}{L}\right)\right]dt$$
$$+b\sqrt{\frac{2}{L}}\cos\left(\frac{\pi x_0}{L}\right)dW,\qquad V_1(0)=0\,. \tag{55}$$

Note that we have $V_1(t)\equiv 0$ for $x_0=L/2$. While the two component approximate representation (54) is known to be Gaussian (see Sect. 2) and the determination of its mean and covariance poses no difficulty, the associated firing time problem is much more difficult compared to the single component case as the sum of V_0 and V_1 is not a Markov process. The same remark applies to any multi-component approximation of $V(0,t)$ and to the exact infinite series representation (51) itself.

We hope to address ourselves to the important firing time problem in future articles. Like other previous investigations, we will be concerned mainly with the determination of the random variable $T_\theta(x)$ which is the time of first passage of the depolarization at the point x to the level 8 given some initial distribution of depolarization, a resting state in our case. That is,

$$T_\theta(x)=\inf\{t|V(x,t)\geqq\theta|V(x,0)=0\}\ . \tag{56}$$

In particular, if we locate the trigger zone of the neuron at the soma (x =0) then the interspike time would be approximately given by $T_\theta(0)$. This is only approximately true for the following reason. If the depolarization reaches 8 at the point then this may lead to the generation of a nerve impulse. However, other conditions could also lead to generation of an impulse. For example, it may be sufficient that V(x, t) exceeds some value $\theta'(<\theta)$ over an extended patch of neuronal membrane. If we assume this patch is localized between x_1 and x_2 then one might consider the random variable

$$\begin{aligned}T_{\theta'}(x_1,x_2)=\inf_t\{t|V(x,t)\\ \geqq\theta',\forall x\in(x_1,x_2)|V(x,0)=0\}\ .\end{aligned} \tag{57}$$

It can be seen that the calculation of the random variable $T_{\theta'}(x_1,x_2)$, which allows for spatial as well as temporal summation in the generation of the action potential, is an extremely difficult task. The determination of $T_\theta(0)$ should be somewhat more tractable because it is the time of first passage of a Gaussian process to the level θ. However, there is no general first passage time theory for Gaussian processes, though some results have been obtained for the Ornstein-Uhlembeck process and other particular Gaussian processes (Wang and Uhlenbeck, 1943 ; Slepian, 1961; Kielson and Ross, 1976).

For point models such as described by (1)-(4), one may estimate the expectation of the time for V to first reach $\theta, \hat{T}_\theta$, by solving the equation

$$E[V(\hat{T}_\theta)]=\theta\ . \tag{58}$$

This requires that E[V(t)] does in fact cross 8 at some finite time and is expected to be reliable when the variability (i.e. variance of V relative to the mean) is small because most of sample paths in that case follow E[V(t)] rather closely. We adopt here a corresponding procedure for estimating the mean of $T_\theta(0)$ as $\hat{T}_\theta(0)\equiv t'$ *by solving* [cf. eq. (30)]

$$\frac{a}{L}\left[(1-e^{-t'})+2\sum_{n=1}^{\infty}\frac{1-e^{-\mu_n^2t'}}{\mu_n^2}\cos\left(\frac{n\pi x_0}{L}\right)\right]=\theta\ . \tag{59}$$

In this approximation, the expected time between two nerve impulses (in units of the membrane time constant) depends on two dimensionless parameters: (I) the ratio of the distance between the source point and the trigger zone to the neuron length, x_0/L, and (II) the ratio of threshold depolarization to mean input "current strength" per unit electrotonic length, $\theta/(a/L)$. Though the dependence of the mean interspike time on these quantities is not always reliably indicated by (59), new insight may be gained into the firing patterns of neurons by the above procedure in comparison with the heretofore obtained results using models which ignored the spatial extent of the neuron.

For example, if we take just the first term in (59), we find

$$t'\cong\ln\left[\frac{1}{1-\theta L/a}\right] \tag{60}$$

which tends to zero with $\theta L/a$ and to infinity as $\theta L/a$ tends to one. Thus, a single component approximation (which is essentially equivalent to a point model) does not exhibit any dependence of t' on the position of the stimulus and limits the *maximum depolarization* realizable (the maximum mean depolarization) to *a/L,* the input current strength per unit electrotonic length. For a threshold depolarization value 8 small compared to *a/L, t'* depends essentially linearly on $\theta/(a/L)$; in fact we have $t'\simeq\theta L/a$.

For a two component approximation (59) becomes

$$\begin{aligned}&\left[1+\frac{2\cos(\pi x_0/L)}{1+\pi^2/L^2}e^{-\pi^2t'/L^2}\right]e^{-t'}\\ &\quad\cong\left[1+\frac{2\cos(\pi x_0/L)}{1+\pi^2/L^2}\right]\frac{\theta L}{a}\end{aligned} \tag{61}$$

In contrast to (60), the relation (61) shows an effect of the position of the stimulus on t'. To a first approximation, this effect amounts to a change of the maximum depolarization realizable to

$$(a/L)[1+2\cos(\pi x_0/L)/(1+\pi^2/L^2)]$$

Consistent with out earlier discussion on the two component model, the use of relation (61) should be contemplated only when the stimulus is remote from the soma. For $x_0/L>\frac{1}{2}$, *we* have cos $(\pi x_0/L)<0$; the effect of spatial extent of the neuron in this case is a reduction of the maximum allowable depolarization.

We may use the approximation (61) to obtain preliminary insight into the importance of the spatial relation of the input and the trigger zone in determining the average interspike interval. It is clear that for a typical motoneuron, with $L\simeq1$, that

$$\frac{2\cos(\pi x_0/L)}{1+\pi^2/L^2}e^{-t'(1+\pi^2/L^2)}\ll e^{-t'}\ , \tag{62}$$

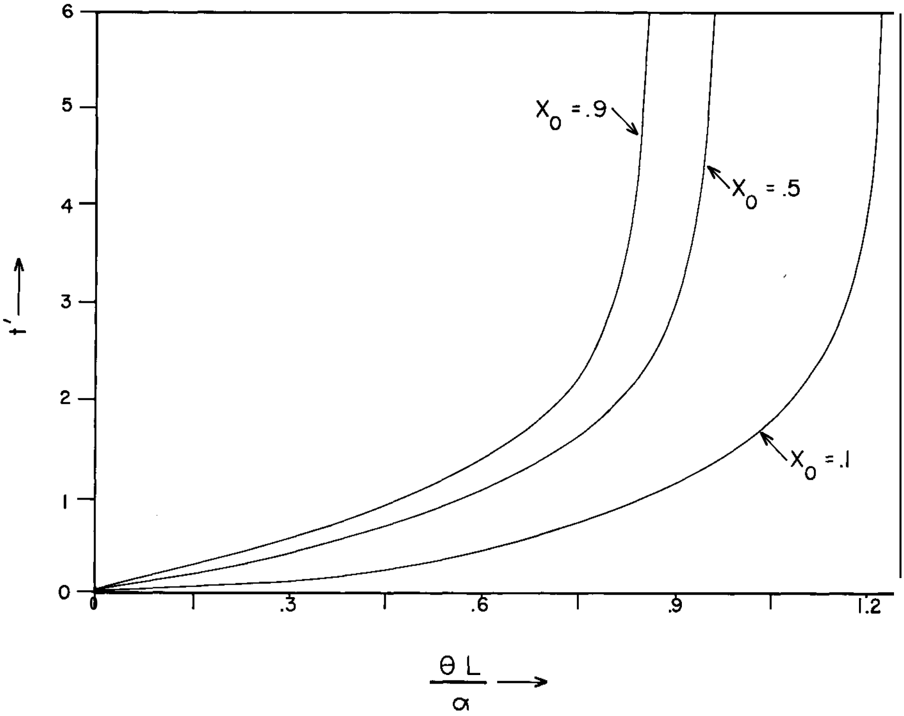


Fig. 9. Approximate mean interspike times for white noise current injection at $x_0 = 0.1$, 0.5, and 0.9 as a function of the normalized threshold variable $\theta L/a$ for $L = 1.0$

whereupon (61) yields

$$t' \simeq -\ln\left[1 - \frac{\theta L}{a} - \frac{2\cos(\pi x_0/L)}{1+\pi^2/L^2}\right]. \tag{63}$$

With $\theta/a = 0.2$, $L = 1$, this formula gives t'= 0.223,0.297, 0.368,0.429,0.470, and 0.485 with x0/L = 0.5, 0.6,0.7, 0.8, 0.9, and 1.0 respectively, whereas the single component approximation, (60), gives $t' = 0.223$ independent of the location of the stimulus. It can be seen in this approximate treatment that the interspike time may more than double for a given input and threshold as the location of the point of stimulation moves from the center to the distal end of the dendritic tree.

It should be emphasized, however, that our interest in the one and two term approximation of (59) lies in the qualitative features of t', particularly its qualitative dependence on $\theta L/a$ and x_0/L. The actual dependence of t' on these same two quantities is already contained in our solution for $E[V(0,t)]$, *e.g.* Fig. 4a-c. For completeness, we show in Fig. 9 some typical (exact) dependence of t' on $\theta/(a/L)$ and (x_0/L) for $L = 1.0$.

5. Conclusions

We have considered the cable equation for a potential V(x, t) driven by white noise current injection at a point with sealed end boundary conditions. If the equivalent cylinder representation is valid, this can be employed as a model for a neuron with a branching dendritic tree, receiving inputs randomly at all points which are the same number of characteristic lengths from the end $x = 0$. With the condition $\partial V/\partial x$ 0 at $x = 0$ we can consider this to be the location of a “point soma”.

Deterministic treatments of problems similar to that considered here have employed eigenfunction expansions for the depolarization V(x, t). It is found here that a similar approach can be adopted in the random input case except that the terms in the expansion are now random processes. In the case of white noise current injection at a point, these individual terms are Ornstein-Uhlenbeck processes and V(x, t) is Gaussian but not Markov. For this same stimulus, we found expressions for the mean and variance of the depolarization as well as the temporal-spatial covariance of the depolarization.

As time goes by, the mean depolarization approaches a steady state for which we found an explicit expression. At the soma, this steady state mean depolarization has a simple dependence on the hyperbolic cosine of the electrotonic distance between the source and the distal end of the neuronal structure. The effects of different stimulus locations was investigated. It was found that the steady state mean depolarization is usually not particularly sensitive to the input location except when it is near the end points. We found that the approach in time to the steady state is nearly uniform over the neuronal surface which was explained by the dominance of the first two terms in the expansion for E[V(x, t)].

The series for the variance of V(x, t) converges everywhere except at the location of the stimulus where there is a logarithmic singularity (see the Appendix). We calculated the steady state standard deviation for various input locations and have shown the results graphically. The coefficient of variation of the steady state depolarization at the soma was found to be quite insensitive to input locations provided the stimulus is not proximal to the soma. The approach of the variance to its steady state value was also found to be fairly uniform over the neuronal surface. As we pointed out in Sect. 3, the logarithmic singularity of the variance of V(x, t) is due to the concentration of the ideal white noise current injection at a point of the cable. In reality, the input is distributed over a finite interval of the cable, however small. The variance of the depolarization for that case has been found to be finite at all locations including the interval of the stimulus and its eigenfunction expansion converges uniformly and absolutely. These and other results for a distributed stimulus will be reported in a future publication.

As mentioned in the introduction, previous models for neuronal response to random input have not included a space variable. This is tantamount to taking a single component of the expansion for V to represent V(x, t). Here, we investigated in detail how good on approximation to the response at x = 0 one obtains by truncating the series for the mean and variance after a certain number of terms. We found that the number of terms needed to obtain a reasonable approximation depends on the location of the stimulus. When the input is near the electrotonic center of the neuronal structure a single component approximation is reasonably accurate. However, in this single component model the overall electrotonic length parameter L, which does not appear in the conventional single component models, was found to play a significant role. When the stimulus is far from the center, one may obtain a reasonable approximation for the statistics of V(0, t) by taking the sum of first two components in the expansion.

We have taken a preliminary look at the interspike time problem. When a space variable is included there are many conditions [configurations for V(x,t)] which could lead to spike generation. We investigated only one, namely that the mean depolarization at the soma reach a threshold level. We were then able to find approximate expressions for the mean interspike time and see the important effect of the location of the input on its value when the stimulus is remote from the soma.

We have considered a particular problem which seemed a natural starting point to more realistic considerations of neuronal activity with random input. It is apparent that the techniques we have employed are applicable to absorbing ("killed") end boundary conditions, more elaborate models of the somatic region (such as those mentioned in the Introduction) and multiple inputs. We intend to consider such problems in later papers.

Appendix

Let

$$\begin{aligned} s(x,y,t) &\equiv \langle V(x,t)V(y,t)\rangle - \langle V(x,t)\rangle \langle V(y,t)\rangle \\ &\equiv S(x,y,t) - a^2 v(x,t;x_0) v(y,t;x_0) \end{aligned} \qquad \text{(A1)}$$

be the *spatial covariance* of V at the two points x and y along the cable at time t. Evidently, both s and S are defined for $0 \leqq x, y \leqq L$ and $t \geqq 0$. From the definition of S and the partial differential equation (6), we get

$$\begin{aligned} S_t &= \langle V_t(x,t)V(y,t)\rangle + \langle V(x,t)V_t(y,t)\rangle \\ &= S_{xx} + S_{yy} - 2S \\ &\quad + [\langle F(x,t)V(y,t)\rangle + \langle V(x,t)F(y,t)\rangle], \end{aligned} \qquad \text{(A2)}$$

where a subscript t, x or y denotes partial differentiation with respect to that variable and where the load-response cross correlation function $\langle F(\xi,t)V(\eta,t)\rangle$ can be expressed in terms of the Green's function as

$$\langle V(\xi,t)F(\eta,t)\rangle = \int_0^t \int_0^L G(\xi,z;t-\tau)\langle F(z,\tau)F(\eta,t)\rangle dz d\tau . \qquad \text{(A3)}$$

But we have from (14)

$$\begin{aligned} \langle F(z,\tau)F(\eta,t)\rangle &= \delta(\eta - x_0)\delta(z - x_0)[a^2 + b^2\langle w(t)w(\tau)\rangle] \\ &= \delta(\eta - x_0)\delta(z - x_0)[a^2 + b^2\delta(t-\tau)] \end{aligned} \qquad \text{(A4)}$$

so that

$$\begin{aligned} &\langle V(\xi,t)F(\eta,t)\rangle \\ &= \delta(\eta - x_0)\int_0 G(\xi,\ x_0,\ t-\tau)[a^2 + b^2\delta(t-\tau)]d\tau \\ &= \delta(\eta - x_0)\left[a^2\int_0^t G(\xi,x_0,t-\tau)d\tau + \frac{b^2}{2}G(\xi,x_0,0+)\right] \\ &= \delta(\eta - x_0)\left[a^2 v(\xi,t;x_0) + \frac{b^2}{2}\delta(\xi - x_0)\right]. \end{aligned} \qquad \text{(A5)}$$

Therewith, (A2) can be written as

$$\begin{aligned} S_t &= S_{xx} + S_{yy} - 2S \\ &\quad + a^2[\delta(x-x_0)v(y,t;x_0) + \delta(y-x_0)v(x,t;x_0)] \\ &\quad + b^2\delta(x-x_0)\delta(y-x_0). \end{aligned} \qquad \text{(A6)}$$

We use the definition of spatial covariance (Al) to transform (A6) into the following partial differential equation for $s(x,y,t)$

$$s_t = s_{xx} + s_{yy} - 2s + b^2\delta(x-x_0)\delta(y-x_0), \quad (0 \leqq x, y \leqq L, t > 0). \qquad \text{(A7)}$$

We also obtain from (12), (13), (33), and (A6) the following auxiliary conditions for $s(x,y,t)$:

$$\begin{aligned} s(x,y,0) &= s_x(0,y,t)=s_x(L,y,t) \\ &= s_y(x,0,t)=s_y(x,L,t)=0\,. \end{aligned} \tag{A8}$$

[For example, we have $s_x(L,y,t)=S_x(L,y,t) - a^2 v_x(L,t;x_0)v(y,t;x_0)=\langle V_x(L,t)V(y,t)\rangle=0.$] The initial-boundary value problem (A7) and (A8) completely determines the spatial covariance $s(x,y,t)$. Upon setting $y=x$ in the solution of this problem, we will get Var $[V(x,t)]$ since

$$\begin{aligned} s(x,x,t) &= \langle V^2(x,t)\rangle - a^2 v^2(x,t;x_0) \\ &= \langle V^2(x,t)\rangle - \langle V(x,t)\rangle^2 = \mathrm{Var}[V(x,t)]\,. \end{aligned} \tag{A9}$$

From (A7), we see that the steady state value of $s(x,y,t)$, denoted by $\bar{s}(x,y;x_0)$, is the solution of the boundary value problem

$$\bar{s}_{xx} - \bar{s}_{yy} - 2\bar{s} = -\delta(x-x_0)\delta(y-x_0)\,, \tag{A10}$$

$$\bar{s}_x(0,y;x_0)=\bar{s}_x(L,y;x_0)=\bar{s}_y(x,0;x_0)=\bar{s}_y(x,L;x_0)=0\,. \tag{A11}$$

In other words, $\bar{s}(x,y;x_0)$ is the Green's function of the boundary value problem. Unlike the one dimensional boundary value problem (34), we do not have an elementary solution for the two dimensional problem (A10) and (A11). However, it is known (Stakgold, 1968) that a solution (in fact, the fundamental solution) of (48) is

$$K_0(\sqrt{2}|\underline{x}-\underline{x}_{00}^{(1)}|) \equiv K_0(\{2[(x-x_0)^2+(y-x_0)^2]\}^{1/2})$$

where $\underline{x}=(x,y)$ and $\underline{x}_{00}^{(1)}=(x_0,x_0)$ and where $K_0(u)$ is the zeroth order modified Bessel function of the second kind, analytic for all $u>0$ and with the following asymptotic properties (Abramowitz and Stegun, 1965)

$$\begin{aligned} &K_0(u) \sim -\ \ln(u) \quad (u\to 0)\,, \\ &K_0(u) \sim \sqrt{\frac{\pi}{2u}}\,e^{-u} \quad (u\to\infty)\,. \end{aligned} \tag{A12}$$

We use this solution to generate the following solution of the boundary value problem (A10) and (A11) by the method of images (Stakgold, 1968)

$$\begin{aligned} \bar{s}(x,y;x_0) = \frac{1}{2\pi} \sum_{m=-\infty}^{\infty} \sum_{n=-\infty}^{\infty} &\cdot [K_0(\sqrt{2}|\underline{x}-\underline{x}_{mn}^{(1)}|) + K_0(\sqrt{2}|\underline{x}-\underline{x}_{mn}^{(2)}|) \\ &+ K_0(\sqrt{2}|\underline{x}-\underline{x}_{mn}^{(3)}|) + K_0(\sqrt{2}|\underline{x}-\underline{x}_{mn}^{(4)}|)]\,, \end{aligned} \tag{A13}$$

where

$$\begin{aligned} \underline{x}_{mn}^{(1)} &= (2mL+x_0,\,2nL+x_0)\,, \\ \underline{x}_{mn}^{(2)} &= (2mL-x_0,\,2nL+x_0)\,, \\ \underline{x}_{mn}^{(3)} &= (2mL+x_0,\,2nL-x_0)\,, \\ \underline{x}_{mn}^{(4)} &= (2mL-x_0,\,2nL-x_0)\,. \end{aligned} \tag{A14}$$

Note that $\underline{x}_{mn}^{(k)} \neq (x_0,x_0)$ except when $m = n$ 0 and $k=1$. Therefore, away from the point (x_0,x_0), the series (A13) converges rapidly because of the exponential decay of K_0 for large arguments. As $|\underline{x}-\underline{x}_{00}^{(1)}|\to 0$, the series tends to $-\ln(\sqrt{2}|\underline{x}-\underline{x}_{00}^{(1)}|) = -\ln(\{2[(x-x_0)^2 + (y-x_0)^2]\}^{1/2})$ because of the logarithmic behavior of K_0 for small arguments.

Since the solution of the boundary value problem (48) and (49) is unique and since $s(x,x,t)=\mathrm{Var}[V(x,t)]$, *we* can state the following result:

The variance of the steady state depolarization at the point $x \neq x_0$ of the nerve cylinder with sealed ends is given by either the series (38) or equivalently by the series (A13) with y set equal to x.

The series (38) may be obtained from the eigenfunction expansion of $\bar{s}(x,y;x_0)$ with y set equal to x. In view of the exponential decay property of K_0 for large arguments, the representation (A13) (with $y=x$) is more suitable for an efficient evaluation of the steady state variance for $x \neq x_0$. More importantly, we now see that the divergence of the series (38) at $x=x_0$ is due to the logarithmic singularity in the steady state variance at that location.

The method of images can also be used to obtain the solution of the initial-boundary value problem (A7) and (A8) for $s(x,y,t)$. Such a solution enables us to explicitly exhibit the nature of the singularity of the variance of $V(x,t)$ at $x=x_0$.

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