

The Response of a Nerve Cylinder to Spatially Distributed White Noise Inputs

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The response of a passive nerve cylinder (or dendritic tree in the equivalent cylinder representation) to random white noise input currents is determined. Results for the mean, variance and covariance of the depolarization are obtained for an arbitrary number of independent spatially distributed inputs. The case of a cylinder with sealed ends is considered in detail. The differences that arise when the input currents are distributed over a small but finite region of space instead of concentrated at a point are investigated. In the case of distributed inputs, the expectation is smoother near the stimulus and the variance becomes finite over the entire cable length including the region of the applied stimulus. Away from the stimulus, there are no appreciable differences between the responses for the two cases. The interaction between an excitatory input and an inhibitory input at various locations is examined and one case of more than two inputs is also analysed to study effects which could not have been discerned from point models for a neuron with random inputs.

1. Introduction

We will investigate in this paper the response of the cable model of a passive nerve membrane when white noise input currents are distributed spatially over different segments of the cable. This extends the work of our previous paper (Wan & Tuckwell, 1979) where the input current was concentrated at a point.

Motivation for studying this problem comes from three sources. The first is the experimental use of white noise currents to directly stimulate a nerve cell. This was done for the squid axon under space clamp by Guttman *et al.*

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(1974) and for *aplysia* neurons by Bryant & Segundo (1976). Secondly, many central nervous system neurons have their somadendritic surfaces densely packed with synapses (see for example, Conradi, 1969), at which input currents occur when presynaptic fibers are active. The trains of activity in the pre-synaptic fibers can be thought of as random point processes and many inputs will occur at about the same electrotonic distance from the soma which are excitatory and inhibitory. The input current thus performs at a given location a random walk of which a smoothed version is a white noise. Thirdly, the neuronal response to random inputs has often been studied by means of models which assume a lumped circuit for the whole cell so that variations in voltage over the neuronal surface are neglected [see Holden (1976) for a review]. The spatial distribution of the response voltage for different input currents should be investigated to assess the adequacy of these point models.

As a first step toward a better understanding of spatial variations in neuronal response with random inputs, we have analyzed in our previous paper the depolarization of a passive nerve cylinder with white noise input current at a point (Wan & Tuckwell, 1979). Let $V(x, t)$ be the depolarization at position x and time t with x measured in units of the "characteristic length" and time measured in units of the membrane time constant. In the cable model with a point source, V satisfies the partial differential equation:

$$V_t = -V + V_{xx} + \delta(x - x_0) \left(a + b \frac{dW}{dt} \right), \quad (0 < x < L, t > 0), \quad (1)$$

where W is a standard Wiener process, a represents the strength of the input current and b its variance parameter, the current being applied at the point x_0 . In equation (1), a subscript x or t indicates partial differentiation with respect to the subscript variable. We considered this equation in detail in conjunction with the initial condition

$$V(x, 0) = 0, \quad (2)$$

and the boundary conditions

$$V_x(0, t) = V_x(L, t) = 0 \quad (3)$$

representing sealed ends at $x = 0$ and $x = L$. The numerical results obtained there were particularly useful for delineating the adequacy of point models away from the source point. At the source point, the idealized white noise point source input gives rise to an unbounded variance of the depolarization corresponding to the unbounded energy of the source.

In real physiological or experimental situations the stimuli (whether it be a stimulating electrode or a natural synaptic input) will have a finite spatial

extent. We will show that the variance of $V(x, t)$ for such stimuli is finite everywhere, including the location of the stimulus. It will be found that if the spatial extent of the input is small, then the variance of the response away from the source and the mean depolarization throughout the cable differ negligibly from the case of a point source for the same total current. We will delimit the region of applicability of the point source solution for real physiological or experimental situations where the spatial extent of the stimuli is indeed small in this context. Attention will be focused on cables with sealed ends but expressions for the mean, variance and covariance of the depolarization can also be found for various boundary conditions including "killed end" and "lumped soma at one end" using the appropriate eigenvalues and eigenfunctions listed in the Appendix.

The same method of solution will be used to obtain the response of the cable to multiple localized distributed white noise input currents. A closed form expression will be given for the steady state expectation. Since the initial boundary value problem is linear, the solution for the multiple input problem is simply a superposition of the solutions of the relevant single source problems as long as the inputs are (statistically) independent. We study the interaction between stimuli at different locations on the neuronal surface. When an excitatory input is close to the soma, the introduction of an inhibitory input generally increases the interspike time. Our results indicate that the probability of a threshold crossing is not likely to be very sensitive to the position of that inhibitory input along the cable. Such effects could not have been discerned from point models for a neuron with random inputs.

2. Theory of a Passive Nerve Cylinder with Spatially Distributed White Noise Inputs

For a white noise stimulus extending uniformly from $x_0 - \varepsilon/2$ to $x_0 + \varepsilon/2$, the cable response is the solution of

$$\frac{\partial V}{\partial t} = -V + \frac{\partial^2 V}{\partial x^2} + h(x; x_0, \varepsilon) \left(\alpha + \beta \frac{dW}{dt} \right), \quad (4)$$

with appropriate initial and boundary conditions, where

$$h(x; x_0, \varepsilon) = \begin{cases} 1, & x_0 - \varepsilon/2 < x < x_0 + \varepsilon/2, \\ 0, & \text{otherwise.} \end{cases} \quad (5)$$

This function rises from value 0 at $x_0 - \varepsilon/2$ to the value 1 at which it stays until x equals $x_0 + \varepsilon/2$ whereupon it drops to zero again, as depicted in Fig. 1. In equation (4), $W(t)$ is again a standard Wiener process. Thus the white

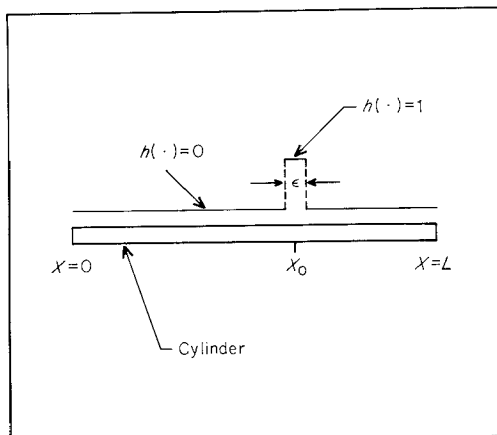


FIG. 1. Depicting the cable of length L with sealed ends at $x=0$ and $x=L$. The input occurs over a finite region centered on x_0 and of total width ϵ .

noise input current has a total value

$$\begin{aligned}
 I(t) &= \int_{x_0 - \epsilon/2}^{x_0 + \epsilon/2} \left(\alpha + \beta \frac{dW}{dt} \right) dx \\
 &= \alpha \epsilon + \beta \epsilon \frac{dW}{dt},
 \end{aligned}
 \tag{6}$$

with mean $\alpha \epsilon$ and s.d. $\beta \epsilon$.

When there are N white noise inputs centered on x_i ($i=1, 2, \dots, N$) with spatial extents ϵ_i and with current density parameters α_i and β_i , the depolarization satisfies the equation

$$\frac{\partial V}{\partial t} = -V + \frac{\partial^2 V}{\partial x^2} + \sum_{i=1}^N h(x; x_i, \epsilon_i) \left(\alpha_i + \beta_i \frac{dW_i}{dt} \right),
 \tag{7}$$

where $h(x; x_i, \epsilon_i)$ is defined as in (5). It is assumed that $W_1(t)$, $W_2(t), \dots, W_N(t)$, are independent standard Wiener processes. We will only be interested in cases where the localized inputs centered at various x_i do not overlap in space though our method of solution applies to overlapping stimuli cases as well providing that the cable does in fact represent a single nerve cylinder. However, in the equivalent cylinder representation of a dendritic tree (see Rall, 1964, 1969; Rinzel, 1975), different parts of the dendritic tree may map to (nearly) the same value of x in the equivalent cable so that there may be significant overlapping of inputs in this represen-

tation. We do not consider this type of situation but point out that the input currents clearly do not always just add in this case.

With appropriate boundary conditions for (7) we employ the initial data $V(x, 0) = 0$, and suppose that $\{\mu_n^2\}$ is the sequence of eigenvalues and $\{\phi_n\}$ the normalized spatial eigenfunctions of the problem. Then the expected value of $V(x, t)$ is

$$E[V(x, t)] = \sum_{i=1}^N \alpha_i \sum_n \frac{\phi_n(x) \psi_n(x_i, \varepsilon_i)}{\mu_n^2} (1 - e^{-\mu_n^2 t}), \quad (8)$$

with a steady-state value of

$$E[V(x, \infty)] = \sum_{i=1}^N \alpha_i \sum_n \frac{\phi_n(x) \psi_n(x_i, \varepsilon_i)}{\mu_n^2} \equiv \sum_{i=1}^N V_i^*(x), \quad (9)$$

and the variance of the depolarization is

$$\text{Var}[V(x, t)] = \sum_{i=1}^N \beta_i^2 \sum_n \sum_m \frac{\phi_n(x) \phi_m(x) \psi_n(x_i, \varepsilon_i) \psi_m(x_i, \varepsilon_i)}{(\mu_n^2 + \mu_m^2)} [1 - e^{-(\mu_n^2 + \mu_m^2)t}], \quad (10)$$

with steady-state value

$$\text{Var}[V(x, \infty)] = \sum_{i=1}^N \beta_i^2 \sum_n \sum_m \frac{\phi_n(x) \phi_m(x) \psi_n(x_i, \varepsilon_i) \psi_m(x_i, \varepsilon_i)}{(\mu_n^2 + \mu_m^2)}, \quad (11)$$

where

$$\psi_n(x_i, \varepsilon_i) = \int_{x_i - \varepsilon_i}^{x_i + \varepsilon_i} \phi_n(y) dy. \quad (12)$$

The derivation of these results and an expression for the covariance can be found in the Appendix.

(A) SEALED END BOUNDARY CONDITIONS

With reflecting boundary conditions as in equation (3), we have

$$\phi_n(x) = \begin{cases} \frac{1}{\sqrt{L}}, & n = 0 \\ \sqrt{\frac{2}{L}} \cos\left(\frac{n\pi x}{L}\right), & n = 1, 2, \dots, \end{cases} \quad (13)$$

and

$$\mu_n^2 = 1 + \frac{n^2 \pi^2}{L^2}, \quad n = 0, 1, 2, \dots \quad (14)$$

From the definition in equation (12) we have

$$\psi_n(x_i, \varepsilon_i) = \begin{cases} \varepsilon_i/\sqrt{L}, & n = 0 \\ \frac{2\sqrt{2L}}{n} \cos\left(\frac{n\pi x_i}{L}\right) \sin\left(\frac{n\pi\varepsilon_i}{2L}\right), & n = 1, 2, \dots \end{cases} \quad (15)$$

The expectation of $V(x, t)$ is then given by equation (9) with the summation over n from 0 to ∞ and with the ϕ_n , μ_n^2 and ψ_n given by (13), (14) and (15) respectively. The variance is given by equation (10) with the summations over n and m from 0 to ∞ .

We note that the previous point stimulus results are obtained in the limit as $\varepsilon_i \rightarrow 0$, keeping $\alpha_i\varepsilon_i = a_i$ and $\beta_i\varepsilon_i = b_i$ finite. We have in fact

$$\lim_{\varepsilon_i \rightarrow 0} \alpha_i \psi_0(x_i, \varepsilon_i) = \frac{\alpha_i \varepsilon_i}{\sqrt{L}} = a_i \phi_0(x_i), \quad (16)$$

and, for $n > 0$,

$$\begin{aligned} \lim_{\varepsilon_i \rightarrow 0} \alpha_i \psi_n(x_i, \varepsilon_i) &= \lim_{\varepsilon_i \rightarrow 0} \alpha_i \varepsilon_i \cos\left(\frac{n\pi x_i}{L}\right) \sqrt{\frac{2}{L}} \frac{\sin(n\pi\varepsilon_i/2L)}{(n\pi\varepsilon_i/2L)} \\ &= a_i \phi_n(x_i). \end{aligned} \quad (17)$$

There is one major difference in the results for the variance for the point stimulus and the stimulus that is distributed in space. The series

$$\text{Var}[V(x, t)] =$$

$$\sum_{i=1}^N \beta_i^2 \sum_{n=0}^{\infty} \sum_{m=0}^{\infty} \frac{\phi_n(x) \phi_m(x) \psi_n(x_i, \varepsilon_i) \psi_m(x_i, \varepsilon_i) [1 - e^{-(\mu_n^2 + \mu_m^2)t}]}{(\mu_n^2 + \mu_m^2)} \quad (18)$$

converges for all x including $x = x_i$, the centers of the applied stimuli, whereas the corresponding series for point sources diverged logarithmically at these points (Wan & Tuckwell, 1979). The different behavior is due to the fact that in addition to the $n^2 + m^2$ behavior of the denominator from $\mu_n^2 + \mu_m^2$ we have the additional factor nm there coming from $\psi_n \psi_m$.

We also note that a closed form expression may be obtained for the steady-state mean depolarization (9) for the spatially distributed input in (7).

For sealed end boundary conditions, we have from the Appendix

$$V_i^*(x) = \begin{cases} \frac{2\alpha_i \cosh(x-L) \cosh x_i \sinh(\varepsilon_i/2)}{\sinh L}, & (x > x_i + \varepsilon_i/2), \\ \frac{\alpha_i}{\sinh L} \left\{ \sinh L - \left[\cosh(x-L) \sinh\left(x_i - \frac{\varepsilon_i}{2}\right) \right. \right. \\ \left. \left. + \cosh x \sinh\left(L - x_i - \frac{\varepsilon_i}{2}\right) \right] \right\}, & (x_i - \varepsilon_i/2 < x < x_i + \varepsilon_i/2), \\ \frac{2\alpha_i \cosh x \cosh(L-x_i) \sinh(\varepsilon_i/2)}{\sinh L}, & (x < x_i - \varepsilon_i/2). \end{cases} \quad (19)$$

Thus, the steady-state expectation can be found from (9) and (19) for an arbitrary number of non-overlapping stimuli without the need to obtain the sum of an infinite series. Also, it can be easily shown that in the limit as $\varepsilon_i \rightarrow 0$, the mean depolarization approaches its values for the case of point stimuli.

(B) OTHER END CONDITIONS

We will confine ourselves in this article to the response of a cable with sealed ends to different localized distributed white noise inputs. Expressions for the mean and variance of the depolarization of a cable with other end conditions (e.g. "killed end" and "lumped soma at one end") can be obtained from equations (8)–(12) using the appropriate eigenvalues $\{\mu_n^2\}$ and eigenfunctions $\{\phi_n(x)\}$ listed in the Appendix.

3. Results for One Input

For a single input, the parameters of the model are: (i) the total electrotonic length of the cable, L ; (ii) the location of the center of the stimulus, x_0 ; (iii) the spatial extent of the stimulus, ε ; (iv) the mean input current density on the interval $(x_0 - \varepsilon/2, x_0 + \varepsilon/2)$, α ; and (v) the standard deviation (s.d.) of the input current density on $(x_0 - \varepsilon/2, x_0 + \varepsilon/2)$, β . In the equivalent cylinder representation, the point $x = 0$ may be taken to be the location of a point soma (or trigger zone) and the point $x = L$ corresponds to the extreme ends of the dendritic tree. An input at x_0 will, in this picture, mean active inputs at all parts of the dendritic tree at this distance from the soma. In the numerical results to be presented, we will always have $L = 1$ which is in the range for cat spinal motoneurons (Barrett & Crill, 1974).

(A) EXPECTATION OF THE DEPOLARIZATION

The steady-state expectation of the depolarization was calculated using equation (19) at various positions along the cable for stimuli centered at $x_0 = 0.5, 0.7, 0.9$ and for stimuli of extent $\epsilon = 0.002, 0.004, 0.006, 0.008$ and 0.010 . The "normalization" condition $\alpha\epsilon = 1$ and $\beta\epsilon = 1$ [equation (6)] facilitates a comparison with the point source case. The results for each of the above values of ϵ differ very little from the corresponding point source results [see Wan & Tuckwell (1979, fig. 2)] except that now $E[V(x, \infty)]$ has a continuous spatial derivative for all x in $(0, L)$ whereas in the case of a point source this derivative is not continuous at x_0 . This is illustrated in Fig. 2 where we show the steady state depolarization in the vicinity of a point source at $x_0 = 0.1$ and a distributed source of width $\epsilon = 0.01$ centered on $x_0 = 0.1$. In each case the total mean current is the same. The values of

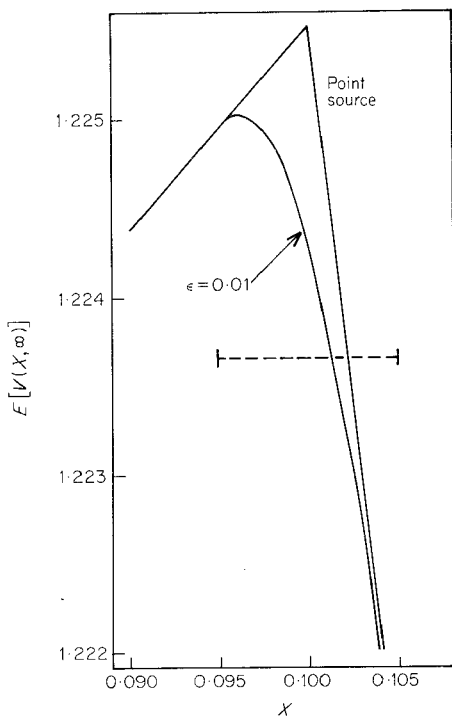


FIG. 2. Details of the steady-state expectation of the depolarization near the stimulus for the case of a point source at $x_0 = 0.1$ and a distributed source of extent $\epsilon = 0.01$ centered on $x_0 = 0.1$.

$E[V(x, \infty)]$ for the two cases differ only in a region of very small spatial extent around the center of the stimulus. Graphically, this difference amounts to a kink in $E[V(x, \infty)]$ at the source point for the point source case while no such kink exists for a spatially distributed source. Hence for these small values of ε the only effect on the expectation of the steady-state depolarization of distributing the input current over a finite region is to smooth out the expectation around x_0 .

We found that the expected response as ε varies (within the range indicated above) for fixed $\alpha\varepsilon$ was surprisingly insensitive to the value of ε . To translate this into more meaningful language, let us suppose that the input current corresponds to a synaptic input centered on x_0 and extending over an effective distance of ε characteristic lengths. This means that ε represents the "length of apposition", in characteristic lengths, of the synapse with the post-synaptic cell. It may therefore be stated that the effectiveness of a synapse at a given location is, for a given mean current strength per unit length α , directly proportional to the "length of apposition" of the synapse with the postsynaptic cell. Furthermore, the steady-state expectation is, for a given length of apposition, proportional to the current density per unit length α . These remarks apply for a fixed stimulus center, x_0 .

It is more pertinent to consider a constant current density per unit area at a synapse on a dendritic tree. Since ε corresponds to the diameter of a synapse (the length of apposition), then for a given current density per unit area the effectiveness of a synapse is proportional to the square of its diameter (in characteristic lengths). A synapse with $\varepsilon = 0.001$ would thus be 100 times as effective as a synapse with $\varepsilon = 0.0001$, or, 100 synapses with $\varepsilon = 0.0001$ would be required to have the same effect at the soma as 1 synapse with $\varepsilon = 0.001$ if located at about the same position.

The question arises as to whether in a real physiological situation the values of ε employed are representative. For a cat spinal motoneuron of total electrotonic length 1.5 there are on average about 23 000 synapses (Koziol & Tuckwell, 1978). Since there are about 15 primary dendrites, the order of magnitude of ε in characteristic lengths is very roughly estimated at 0.001, though the figure for some synapses will be larger and for others smaller. Thus the above remarks on the effectiveness of synapses are applicable in some real physiological situations because they are based on values of ε at and above the appropriate range.

The time dependence of the expectation of $V(x, t)$ was found by computing its value from the series (8) and the expressions (13) and (15) for ϕ_n and ψ_n respectively for various values of x and t . The results are again similar to the point source case. For example, the approach to the steady state is

practically uniform in space as mentioned in our previous report (Wan & Tuckwell, 1979).

(B) VARIANCE OF THE DEPOLARIZATION

In the steady state, the variance of the depolarization in the case of a single input centered at x_0 of spatial extent ε is given by

$$\text{Var} [V(x, \infty)] = \beta^2 \sum_{n=0}^{\infty} \sum_{m=0}^{\infty} \frac{\phi_n(x)\phi_m(x)\psi_n(x_0, \varepsilon)\psi_m(x_0, \varepsilon)}{\mu_n^2 + \mu_m^2}. \quad (20)$$

We here consider the case of sealed end boundary conditions in which case the functions ϕ_n and ψ_n are given by equations (13) and (15) respectively. Again we computed the sum to a finite number of terms and studied the convergence of the sum as the number of terms became larger.

The convergence of the series (20) is reasonably rapid providing x is not very close to the center, x_0 , of the stimulus. For example, with $x_0 = 0.1$, $\varepsilon = 0.01$ and $\beta\varepsilon = 1$, the value of the variance away from the x_0 is accurate to within 1% with n and m taken up to 9. With this number of terms the s.d. $\sigma[V(0, \infty)]$ is computed to be 1.131; when n and m are taken up to 99, the value obtained is 1.124.

As pointed out previously, the variance of the depolarization for a point source at x_0 has a logarithmic singularity at x_0 . For a distributed stimulus centered at x_0 with a spread ε which is small compared to the cable length L , the values of $\text{Var} [V(x, \infty)]$ at and near x_0 still reflect this singular behavior. Thus in contrast to the behavior at $x = 0$ the convergence of the series (20) at $x = x_0 = 0.1$ is slow. In one case with $\varepsilon = 0.002$, the computed value of the standard deviation at the source point with $(450)^2$ terms is still about 5% from the estimated correct value. The amount of computing needed to obtain a reasonably accurate estimate of the variance at and near the stimulus was reduced by using suitable extrapolation techniques (Bender & Orszag, 1978, ch. 8).

The steady-state s.d. was computed for various stimulus positions and different values of ε . This quantity is shown in Fig. 3 as a function of distance, x , for $x_0 = 0.5, 0.7, 0.9$, with $\varepsilon = 0.005$, $\beta\varepsilon = 1$ and $L = 1$. Values near x_0 were computed by four iterations of the Shanks transformation (Bender & Orszag, 1978). In all cases, the s.d. rises to a sharp maximum around the spatial extent of the source. These results should be compared with those in fig. 5 of Wan & Tuckwell (1979) where the corresponding results are shown for a point source. The values obtained in the two cases are similar except near x_0 . When the source is distributed over a small but finite region of the cell the s.d. $\sigma[V(x, t)]$ is finite for all x .

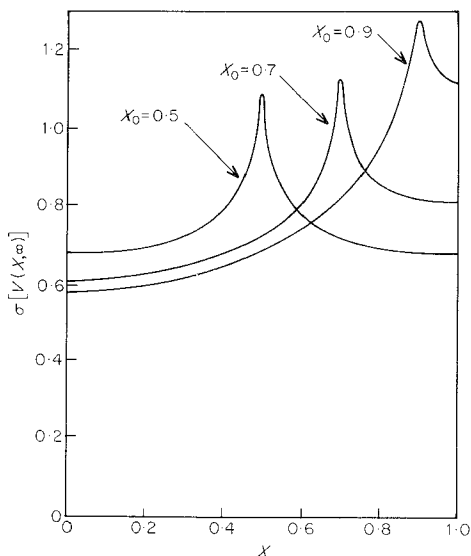


FIG. 3. The steady-state s.d. of the depolarization distributed stimuli of extent $\epsilon = 0.01$ centered at various locations along the cable.

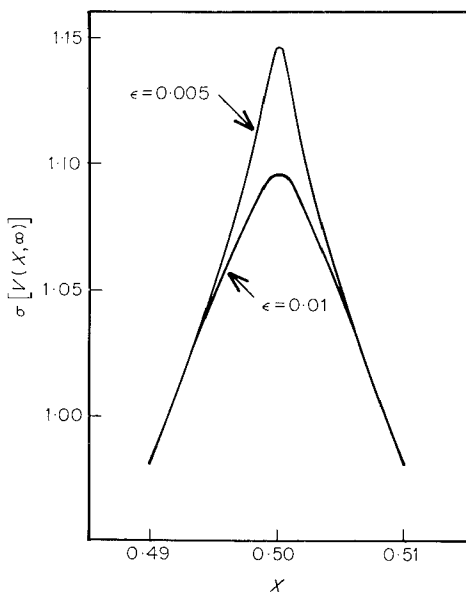


FIG. 4. Details of the s.d. of the steady-state depolarization near the region of application of the stimulus for sources of extents $\epsilon = 0.01$ and $\epsilon = 0.005$.

The s.d. for $\varepsilon = 0.005$ and $\beta\varepsilon = 1$ with the source point at $x_0 = 0.5$ was also computed to see how sensitive the response was to the width of the source. As expected its value practically coincides with that for $\varepsilon = 0.01$ except in a small neighborhood of x_0 . To illustrate the quantitative differences we show the values of $\sigma[V(x, \infty)]$ at values of x between 0.49 and 0.51 for these two values of ε in Fig. 4. The difference in the values of $\sigma[V(x, \infty)]$ becomes negligible at a distance of about 0.005 from x_0 . The peak of the s.d. for $\varepsilon = 0.005$ is sharper than that for $\varepsilon = 0.01$.

We also computed the variance of $V(x, t)$ for various values of t . The results showed the same kind of qualitative behavior as for a point source in that the approach to the steady state is fairly uniform over the entire cable length. The reader can see figs 7(a), (b) and (c) of Wan & Tuckwell (1979) to obtain the basic behavior of the variance as time increases.

4. Interaction Between Stimuli

In the last section, we discussed results for the case of a cable equation driven by a single spatially distributed white noise input current. For an arbitrary number of random inputs, the expectation of $V(x, t)$ is just the sum of the expectations obtained when each input is taken separately since the system under study is still governed by equation (7) which is linear. Furthermore, if the various inputs are independent random processes, then the variance of $V(x, t)$ is the sum of the variances when each input is taken separately. If the expectation of $V(x, t)$ is $E[V]$ for a stimulus with $\alpha = 1$ with extent ε centered on x_0 , then the expectation of $V(x, t)$ with the same stimulus except now of strength $\alpha = \bar{\alpha}$ is just $\bar{\alpha}E[V]$, as can be seen from equation (8). Similarly if the variance of $V(x, t)$ is $\text{Var}[V]$ with $\beta = 1$, then the variance for $\beta = \bar{\beta}$ is $\bar{\beta}^2 \text{Var}[V]$ as can be seen from equation (10). This observation makes it possible to compute the mean and variance of $V(x, t)$ when independent inputs of various strengths and variance parameters are simultaneously active at x_1, \dots, x_N from the results for a single stimulus of strength $\alpha = 1$ and $\beta = 1$ at each point x_i , $i = 1, \dots, N$ (with the same extents). Also, if the results are known for a stimulus centered on x_0 , then by symmetry they are automatically known for a stimulus at $L - x_0$.

We have obtained results for two inputs, one of which is excitatory and the other inhibitory to illustrate the kinds of effects that may occur. Figures 5(a), (b) and (c) illustrate the interaction between two stimuli when the distance between them changes. In each case, the inhibitory and excitatory stimuli have extent $\varepsilon = 0.01$, their strengths being equal and opposite such that $|\alpha|\varepsilon = 1$ and both have variance parameters satisfying $\beta\varepsilon = 1$. The effect of the inhibitory input is, naturally, to greatly depress the mean level of

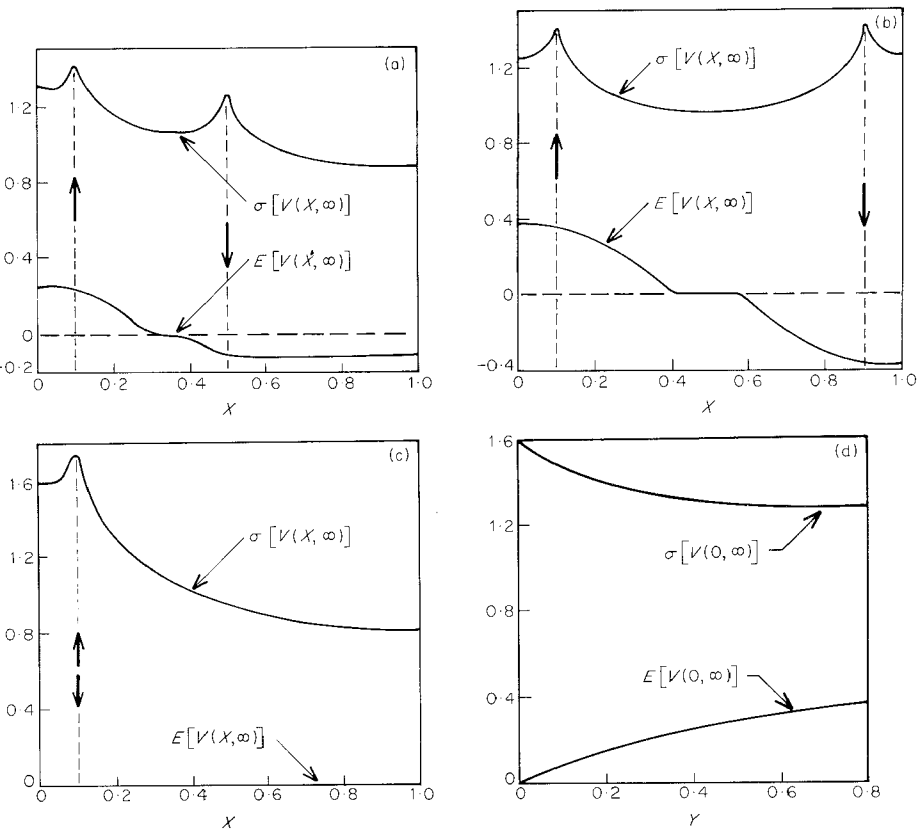


FIG. 5. (a) Variation of the steady-state expectation and the s.d. along the cable with excitation and inhibition of equal magnitudes at $x=0.1$ and $x=0.9$ respectively. (b) As in (a) but with the inhibition at $x=0.5$. (c) As in (a) but with the inhibition at $x=0.1$. (d) Response (steady-state mean and s.d. of V) at the soma as the distance between the inhibitory and excitatory input varies, the latter input being fixed at $x=0.1$.

excitation throughout the cell. Thus, even though the s.d. of the depolarization at the soma is increased moderately, the inhibitory input is expected to greatly increase the interspike time if the cell has a trigger zone near the soma. This had been pointed out in studies of point models for a neuron receiving random excitation and inhibition (Tuckwell, 1975; Cope & Tuckwell, 1979).

Figure 5(a) shows the steady-state results for the expectation and s.d. of $V(x, t)$ for a cylinder with $L=1$ when an excitatory input is close to the soma at $x_1=0.1$ and the inhibitory input is distal to the soma at $x_2=0.9$. The s.d. is

symmetric about $x = 0.5$ and the expectation is antisymmetric about the same point. The mean level of excitation is quite high near the soma ($x = 0$), drops to zero in the "center" of the cell and becomes negative at the end remote from $x = 0$. Note however that while the level of mean excitation is close to zero in the "central" parts of the cell, the s.d. of the response there is about 70% of its maximum value which occurs at $x = 0.1$ and $x = 0.9$. Thus with noisy input, the central and distal parts of the cell are on average depressed; but there is a certain probability that this is not actually the case and a considerable contribution towards a threshold crossing to produce an action potential may come from the apparently depressed part of the cell. This becomes even more noticeable when, as shown in Fig. 5(b), the excitatory input is located in the same position ($x_1 = 0.1$) but the inhibitory input is moved closer to $x_2 = 0.5$. The mean level of excitation is of course less than in Fig. 5(a) but from $x = 0.3$ to $x = 1$ where the mean depolarization is either close to zero or negative, the s.d. of $V(X, \infty)$ is almost as large as it is near $x = 0$ so that again there is a chance of a contribution to a threshold crossing from the depressed parts of the cell. The extreme case is shown in Fig. 5(c) where the excitatory and inhibitory inputs are practically at the same location. (These were placed at $x = 0.095$ and 0.105 to ensure that the sources did not overlap in space.) Now the mean level of excitation is zero throughout the whole cell but the standard deviation is large and threshold crossings, if they occur, must originate purely from the noisiness of the input processes.

It is also of interest to consider in detail how the response at the soma ($x = 0$) changes with an inhibitory input at various distances from the excitatory input for a fixed excitatory input close to the soma. We computed for a nerve cylinder with $L = 1$, the mean and s.d. of V at $x = 0$ in the steady state with an excitatory input at $x = 0.1$ and an inhibitory input at positions between $x = 0.1$ and $x = 0.9$. The two results are shown in Fig. 5(d). As the distance between the inputs increases from zero to 0.8 characteristic lengths, the expectation of $V(0, \infty)$ increases from 0 to 0.35 whilst its s.d. decreases from 1.6 – 1.25 . Thus, though the expectation increases radically, the standard deviation decreases only by 20% as the distance between the excitatory and inhibitory inputs increases from 0 to $\frac{4}{5}$ of the cable length.

We note the following with regard to the firing of the nerve cell. There are two factors which promote the threshold crossing of V . One is the passage of $E[V]$ close to threshold, the other comes from the large fluctuations of V about its mean value, even when $E(V)$ is not close to threshold. As the distance between the inhibitory and excitatory inputs increases (with the latter at 0.1), the possibility of a threshold crossing due to the approach of $E[V]$ to threshold increases while the contributions from the fluctuations

about the mean decrease. These kinds of effects could not have been observed with a single component model. We will investigate these aspects further by means of computer simulations and other methods of attack on the first passage problem in a future article.

One could investigate the effect of numerous different combinations of excitatory and inhibitory inputs at various locations. We present here only results for one case of more than two inputs. Figure 6 shows in dashed lines

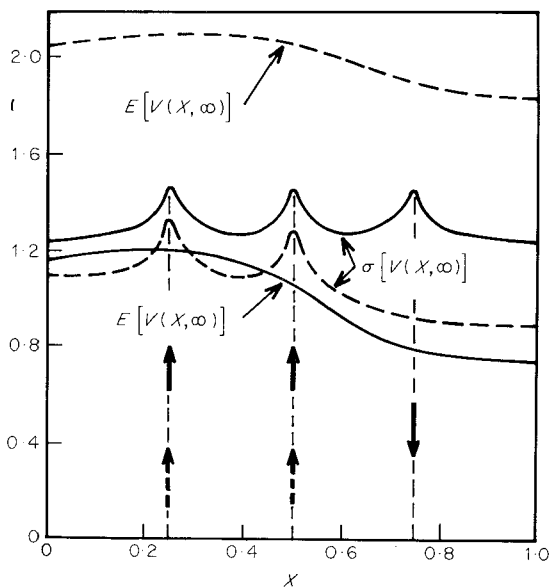


FIG. 6. Showing the steady state mean and s.d. along the cylinder with three inputs of equal magnitudes; the two excitatory inputs being at $x = 0.25$ and $x = 0.50$, the inhibition being at $x = 0.75$. For comparison, the results are shown without the introduction of the inhibitory input.

the effects of two excitatory inputs at $x = 0.5$ and $x = 0.25$ of equal strength. The mean level of excitation is high throughout the whole cell and the s.d. of $V(x, \infty)$ is also fairly uniform. The effects of introducing an inhibitory input of the same strength at $x = 0.75$ are shown by solid curves in the same figure for comparison. The overall level of mean excitation drops substantially and fairly uniformly throughout the cell, whilst the s.d. increases only slightly. The probability of a threshold crossing is thus greatly reduced by the introduction of the inhibitory input even though its location is remote from the soma.

5. Summary and Conclusions

Many nerve cells receive thousands of synaptic inputs and the manner in which inputs arrive over the soma-dendritic surface is often essentially random. Previous models of stochastic neural activity have ignored the spatial extent of the cell. It has been realized in deterministic neural modeling that the location of an input has an important influence on the effects of that input at the soma. We have begun to study these spatial effects in the case of a nerve cell receiving random input. Our previous paper (Wan & Tuckwell, 1979) addressed the case of an input concentrated at a single space point and the results have been extended here to incorporate the more realistic case where the inputs are distributed over finite lengths of the nerve structure.

We have decided to consider first the problem of a nerve cylinder driven with spatially distributed white noise input currents. Under some conditions this nerve cylinder can represent a symmetric dendritic tree. The effects of random inputs on a single branch of a dendritic tree has not yet been addressed.

We have derived explicit expressions for the mean and variance of the depolarization of a nerve cylinder in the case of sealed end boundary conditions and an arbitrary number of independent spatially extended white noise inputs. The general expressions may be used, with the appropriate set of $\{\mu_n^2\}$ and $\{\phi_n\}$ (see Appendix), for other boundary conditions.

With a cable of total electronic length $L = 1$ we considered inputs whose extent, in characteristic lengths, was of order $\varepsilon = 0.01$ and less, as this was expected to cover the range of values for synaptic inputs for real neurons, e.g. spinal motoneurons. The greatest effect of having a finite extent of the stimulus is to make the variance of the depolarization finite everywhere, whereas with point inputs the variance is infinite at the stimulus positions. The expectation is also made smooth around the stimulus positions when the inputs have finite extent.

We have also considered the interaction of independent spatially distributed white noise input currents at various locations on the neuronal surface. Though there are numerous combinations of excitatory and inhibitory input locations that could be considered, we restricted our attention mainly to the case of one excitatory and one inhibitory input and briefly considered the introduction of a third input. One interesting result that came from having excitation close to the soma and inhibition at various distances was that the probability of a threshold crossing may not be very sensitive to the position of the inhibitory input. Such effects, which will be considered in more detail in subsequent papers, could not have been discerned from point models for a neuron with random input.

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APPENDIX

Suppose $\{\mu_n^2\}$ and $\{\phi_n\}$ are the sequences of eigenvalues and normalized spatial eigenfunctions of (7) and the relevant boundary conditions. For a general initial condition $V(x, 0) = g(x)$, the solution of the initial-boundary value problem for $V(x, t)$ is

$$V(x, t) = \int_0^L g(y)G(x, y, t) dy + \sum_{i=1}^N \int_0^t \int_0^L G(x, y, t-s)h(y; x_i, \epsilon_i)[\alpha_i + \beta_i w_i(s)] dy ds, \quad (A1)$$

where the Green's function (see Stakgold, 1968, for example) is

$$G(x, y, t-s) = \sum_n \phi_n(x)\phi_n(y) e^{-\mu_n^2(t-s)}, \quad (A2)$$

and where (the white noise) w_i is the formal derivative of W_i .

The expectation of $V(x, t)$ is just

$$E[V(x, t)] = \int_0^L g(y)G(x, y, t) dy + \sum_{i=1}^N \alpha_i \int_0^t \int_0^L G(x, y, t-s)h(y; x_i, \epsilon_i) dy ds. \quad (A3)$$

From now on we will assume the entire membrane is initially at a resting level so that $g(y) = 0$; we then have

$$E[V(x, t)] = \sum_{i=1}^N \alpha_i \sum_n \phi_n(x) e^{-\mu_n^2 t} \int_0^t \int_0^L \phi_n(y) h(y; x_i, \varepsilon_i) e^{\mu_n^2 s} ds dy. \quad (\text{A4})$$

After performing the s -integration and noting that

$$\int_0^L \phi_n(y) h(y; x_i, \varepsilon_i) dy = \int_{x_i - \varepsilon_i}^{x_i + \varepsilon_i} \phi_n(y) dy \equiv \psi_n(x_i, \varepsilon_i), \quad (\text{A5})$$

we get the expression (8) for the mean depolarization.

We can evaluate the covariance of $V(x_1, t_1)$ and $V(x_2, t_2)$ by utilizing the same Green's function representation of V and the relation

$$E[w_i(t_1)w_j(t_2)] = \delta_{ij}\delta(t_1 - t_2), \quad (\text{A6})$$

where δ_{ij} is the Kronecker delta with $\delta_{ii} = 1$ and $\delta_{ij} = 0$ ($i \neq j$), which follows from the fact that the w_i are independent for different i and delta-correlated in time. We will omit the quadruple integrals and note that the result for $t_2 \geq t_1$ is

$$\begin{aligned} \text{Cov}[V(x_1, t_1), V(x_2, t_2)] &= \sum_{i=1}^N \beta_i^2 \sum_n \sum_m \frac{\phi_n(x_1)\phi_m(x_2)\psi_n(x_i, \varepsilon_i)\psi_m(x_i, \varepsilon_i)}{(\mu_n^2 + \mu_m^2)} \\ &\times e^{-\mu_n^2(t_2 - t_1)} [1 - e^{-(\mu_n^2 + \mu_m^2)t_1}]. \end{aligned} \quad (\text{A7})$$

Setting $t_1 = t_2 = t$ and $x_1 = x_2 = x$ gives the variance of the depolarization in equation (10).

The infinite series solutions for the expected value and second moment of the depolarization $V(x, t)$ are to be used in conjunction with the appropriate eigenvalues $\{\mu_n^2\}$ and eigenfunctions $\{\phi_n(x)\}$ for the prescribed end conditions. The case of two sealed ends is discussed in the main body of this paper. The following is a list of eigenvalues and eigenfunctions for the cable equation (7) for different combinations of end conditions. We give these here for ease of reference as most of them can be found in the papers dealing with the deterministic cable equation (e.g. Rall, 1969; Rinzel, 1975).

Killed Ends

$$V(0, t) = V(L, t) = 0, \quad (\text{A8})$$

$$\mu_n^2 = 1 + \left(\frac{n\pi}{L}\right)^2 \quad (n = 1, 2, \dots), \quad (\text{A9})$$

$$\phi_n(x) = \sqrt{\frac{2}{L}} \sin\left(\frac{n\pi x}{L}\right). \quad (\text{A10})$$

Killed Ends at $x = 0$ and Sealed End at $x = L$

$$V(0, t) = V_x(L, t) = 0, \quad (\text{A11})$$

$$\mu_n^2 = 1 + \left[\frac{(2n+1)\pi}{2L}\right]^2 \quad (n = 0, 1, 2, \dots), \quad (\text{A12})$$

$$\phi_n(x) = \sqrt{\frac{2}{L}} \sin\left(\frac{(2n+1)\pi x}{L}\right). \quad (\text{A13})$$

Sealed End at $x = 0$ and Killed End at $x = L$

$$V_x(0, t) = V(L, t) = 0, \quad (\text{A14})$$

$$\mu_n^2 = 1 + \left[\frac{(2n+1)\pi}{2L}\right]^2 \quad (n = 0, 1, 2, \dots), \quad (\text{A15})$$

$$\phi_n(x) = \sqrt{\frac{2}{L}} \cos\left(\frac{(2n+1)\pi x}{2L}\right). \quad (\text{A16})$$

Lumped Soma at $x = 0$ and Sealed End at $x = L$

$$V_x(0, t) - k[V(0, t) + V_t(0, t)] = V_x(L, t) = 0, \quad (\text{A17})$$

$$\mu_0^2 = 1, \quad \mu_n^2 = 1 + \left(\frac{\sigma_n}{L}\right)^2 \quad (n = 1, 2, 3, \dots), \quad (\text{A18})$$

$$\phi_0(x) = \frac{1}{\sqrt{L}}, \quad \phi_n(x) = \sqrt{\frac{2/L}{1 + \sin(2\sigma_n)/(2\sigma_n)}} \cos\left[\frac{\sigma_n}{L}(L-x)\right], \quad (\text{A19})$$

where $\sigma_1, \sigma_2, \dots$ are the zeros of

$$\tan \sigma + \left(\frac{k}{L}\right)\sigma = 0. \quad (\text{A20})$$

Lumped-Soma at $x = 0$ and Killed End at $x = L$

$$V_x(0, t) - k[V(0, t) + V_t(0, t)] = V(L, t) = 0, \quad (\text{A21})$$

$$\mu_n^2 = 1 + \left(\frac{\gamma_n}{L}\right)^2 \quad (n = 1, 2, 3, \dots), \quad (\text{A22})$$

$$\phi_n(x) = \sqrt{\frac{2/L}{1 - \sin(2\gamma_n)/(2\gamma_n)}} \sin \left[\frac{\gamma_n}{L} (L-x) \right], \quad (\text{A23})$$

where $\gamma_1, \gamma_2, \dots$ are the zeros of

$$\cot \gamma + \left(\frac{k}{L} \right) \gamma = 0. \quad (\text{A24})$$

We note that a closed form expression can be obtained for the steady-state expected value of the depolarization for the spatially distributed input in (7). If $V^*(x) = E[V(x, \infty)]$, then the steady-state mean depolarization $V^*(x)$ must satisfy

$$-\frac{d^2 V^*}{dx^2} + V^* = \sum_{i=1}^N \alpha_i h(x; x_i, \varepsilon_i). \quad (\text{A25})$$

Let $G^*(x, x_0)$ be the associated Green's function which satisfies

$$-\frac{d^2 G^*}{dx^2} + G^* = \delta(x - x_0), \quad (\text{A26})$$

with the relevant boundary conditions. For sealed end boundary conditions, we have from Wan & Tuckwell (1979)

$$G(x, x_0) = \begin{cases} \cosh(L - x_0) \cosh x / \sinh L, & (0 < x < x_0), \\ \cosh x_0 \cosh(L - x) / \sinh L, & (x_0 < x < L) \end{cases} \quad (\text{A27})$$

The solution for $V^*(x)$ is then

$$V^*(x) = \sum_{i=1}^N \alpha_i \int_0^L G(x, x_0) h(x_0; x_i, \varepsilon_i) dx_0 = \sum_{i=1}^N V_i^*(x), \quad (\text{A28})$$

which defines $V_i^*(x)$.

For each i there are three cases to consider, to the left of the stimulus, at the stimulus and to the right of the stimulus. (We assume that the stimulus at x_N , the greatest of the x_i , is such that $x_N + \varepsilon_N/2 < L$ and that of x_1 , the least of the x_i , is such that $x_1 - \varepsilon_1/2 > 0$.) Then for $x < x_i - \varepsilon_i/2$,

$$V_i^*(x) = \frac{\alpha_i \cosh x}{\sinh L} \int_{x_i - \varepsilon_i/2}^{x_i + \varepsilon_i/2} \cosh(L - x_0) dx_0 \quad (\text{A29})$$

which upon evaluation and simplification becomes

$$V_i^*(x) = \frac{2\alpha_i \cosh x \cosh(L - x_i) \sinh(\varepsilon_i/2)}{\sinh L}, \quad (x < x_i - \varepsilon_i/2). \quad (\text{A30})$$

In the interval of the stimulus at x_i we have

$$V_i^*(x) = \frac{\alpha_i}{\sinh L} \times \left[\cosh(x-L) \int_{x_i - \varepsilon_i/2}^x \cosh x_0 dx_0 + \cosh x \int_x^{x_i + \varepsilon_i/2} \cosh(L-x_0) dx_0 \right] \quad (\text{A31})$$

which upon evaluation and simplification gives

$$V_i^*(x) = \frac{\alpha_i}{\sinh L} \left\{ \sinh L - \left[\cosh(x-L) \sinh\left(x_i - \frac{\varepsilon_i}{2}\right) + \cosh x \sinh\left(L - x_i - \frac{\varepsilon_i}{2}\right) \right] \right\} \\ (x_i - \varepsilon_i/2 < x < x_i + \varepsilon_i/2). \quad (\text{A32})$$

To the right of the stimulus,

$$V_i^*(x) = \frac{\alpha_i \cosh(x-L)}{\sinh L} \int_{x_i - \varepsilon_i/2}^{x_i + \varepsilon_i/2} \cosh x_0 dx_0 \quad (\text{A33})$$

which can be written as

$$V_i^*(x) = \frac{2\alpha_i \cosh(x-L) \cosh x_i \sinh(\varepsilon_i/2)}{\sinh L}, \quad (x > x_i + \varepsilon_i/2). \quad (\text{A34})$$

The three different expressions for $V_i^*(x)$ for $x < x_i - \varepsilon_i/2$, $|x - x_i| < \varepsilon_i/2$ and $x > x_i + \varepsilon_i/2$, respectively, are to be used in the expression $V^*(x) = \sum_{i=1}^N V_i^*(x)$ to get the steady-state mean depolarization for an arbitrary number of non-overlapping stimuli without summing the infinite series (9). The resulting $V^*(x)$ approaches the corresponding result for point stimuli as $\varepsilon_i \rightarrow 0$.