

On Shunting Inhibition*

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Abstract. The interaction between excitation and inhibition is analyzed for nerve cylinders when reversal potentials for synaptic action are included. Both impulsive and sustained conductance changes are employed to model synaptic action.

Exact results, in terms of Green's functions are obtained for the solutions of the cable equation with reversal potentials when there are impulsive conductance changes. The amplification factor for an inhibitory input due to a prior excitatory input is found exactly. In the case of an infinite cylinder, the dependence of this factor on the spatial separation of the excitatory and inhibitory synapses is one plus a Gaussian density function. Similar results apply when excitation follows inhibition. There is shunting inhibition even for impulsive conductance changes in the cable, but it is very different from that for sustained conductance changes. The interaction of excitation and inhibition is also studied in the full cable equation with reversal potentials and sustained conductance changes. An exact result is obtained for the potential in response to simultaneous excitation and inhibition at the same space point in an infinite cable. The effects of timing and spatial separation of inputs is analyzed in a finite nerve cylinder by numerically integrating the cable equation by the Crank-Nicolson method. Shunting inhibition is found to be most effective, for the chosen parameter values, when inhibition quickly follows excitation. The EPSP amplitude at the soma is found to be roughly proportional to the distance from the soma to the site of inhibition when the excitation is at the center of the nerve cylinder.

of a nerve cylinder was derived, taking into account synaptic reversal potentials. That equation may be written

$$V_t = V_{xx} - V + r_m [g_E(V_E - V) + g_I(V_I - V)] + r_m I_A, \quad (1.1)$$

where $V = V(x, t)$ is the depolarization from resting potential, r_m is the resting membrane resistance of unit length times unit length, V_E and V_I are the reversal potentials for excitatory and inhibitory synaptic action, $g_E = g_E(x, t)$ and $g_I = g_I(x, t)$ are the synaptically induced changes in conductance per unit length, and I_A is the applied current density (per unit length). Note that in (1.1) the subscripts x and t denote partial derivatives with respect to those variables.

Equation (1.1) has solutions with richer behaviours than those of the usual cable equation,

$$V_t = V_{xx} - V + r_m I_A, \quad (1.2)$$

which had often been employed in early studies of theoretical motoneuron response to synaptic input (see Rall 1977, and references therein). Recently the importance has been realized of including synaptic reversal potentials in modeling neuronal response to multiple synaptic inputs, especially when those inputs are juxta-posed in space-time (Koch et al. 1983; Turner 1984). One example of the richer behaviour of solutions of (1.1) is afforded by the phenomenon of *shunting inhibition* which has been invoked by Koch et al. to explain the firing behaviours of cat retinal ganglion cells in response to stimuli moving in certain directions.

In this paper the interaction between synaptic inputs is investigated with particular reference to the relative timing of excitatory and inhibitory inputs. It will be seen that the impulsive conductance changes lead to quite different, even qualitatively different, results from the sustained conductance changes. For an earlier review containing a discussion of nonlinear interactions in dendritic trees, see Redman (1976).

1 Introduction

In a previous paper (Tuckwell 1985), the cable equation for the electrical potential across the membrane

* Dedicated to Jane Pauley

2 Cable Equation with Impulsive Conductance Changes

We are here concerned with the interaction of excitation and inhibition when these are represented by impulsive conductance changes in the cable equation with reversal potentials.

Excitation Before Inhibition

If an excitatory input occurs at $t=t_E$ at $x=x_E$ and an inhibitory one occurs at $t=t_I$ at $x=x_I$, then the appropriate equation for V is

$$V_t = V_{xx} - V + a_E[V_E - V]\delta(x - x_E)\delta(t - t_E) + a_I[V_I - V]\delta(x - x_I)\delta(t - t_I). \quad (2.1)$$

We do not specify the spatial domain but assume that an appropriate Green's function $G(x, y, t)$ for that domain and the given boundary conditions can be found.

The first case we consider is $t_E < t_I$ so that the excitation arrives first. Before the inhibition arrives,

$$V(x, t) = a_E V_E G(x, x_E; t - t_E), \quad t_E < t < t_I. \quad (2.2)$$

We may then employ the function

$$V(x, t_I) = a_E V_E G(x, x_E; t_I - t_E) \quad (2.3)$$

as the initial condition for an inhibitory pulse at $t=t_I$. Thus, with $t' = t - t_I$ we have from the standard Green's function formula for the solution,

$$V(x, t) = \int G(x, y; t') v(y) dy + a_I \int_0^{t'} [V_I - V(y, s)] \delta(y - x_I) \delta(s) G(x, y; t' - s) ds dy, \quad (2.4)$$

with

$$v(x) = V(x, t_I - t_E), \quad (2.5)$$

the result

$$V(x, t) = a_E V_E \int G(y, x_E; t_I) G(x, y; t') dy + a_I [V_I - V(x_I, t_I - t_E)] G(x, x_I; t'). \quad (2.6)$$

Using the general formula

$$\int G(x, y; s) G(z, x; t) dx = G(z, y; s + t), \quad (2.7)$$

we reduce (2.6) to

$$V(x, t) = a_E V_E G(x, x_E; t - t_E) + a_I V_I G(x, x_I; t - t_I) - a_E a_I V_E G(x_I, x_E; t_I - t_E) G(x, x_I; t - t_I), \quad t > t_I. \quad (2.8)$$

It is apparent that the response is the sum of the responses to the individual excitatory and inhibitory inputs, less an interference term which is proportional to $a_E a_I V_E$ and which goes to zero as the time interval between inputs gets larger. Thus the total response is not the sum of the individual responses, a phenomenon

often referred to as *nonlinear summation*. We may put therefore

$$\text{RESPONSE} = \text{EPSP} + \text{IPSP} - \text{INTERFERENCE TERM}. \quad (2.9)$$

This contrasts, of course, with the superposition principle which applies to solutions of the usual cable equation. Note that in this case the magnitude of the interference term does not depend on V_I , the inhibitory reversal potential.

It is useful to rewrite (2.8) as

$$V(x, t) = a_E V_E G(x, x_E; t - t_E) + a_I V_I G(x, x_I; t - t_I) \cdot \left[1 - \frac{a_E V_E}{V_I} G(x_I, x_E; t_I - t_E) \right], \quad V_I \neq 0. \quad (2.10)$$

If we assume that the inhibitory reversal potential satisfies

$$V_I < 0 \quad (2.11)$$

then

$$1 - \frac{a_E V_E}{V_I} G(x_I, x_E; t_I - t_E) > 1. \quad (2.12)$$

Thus if an inhibitory input by itself results in an IPSP, then the inhibitory input is enhanced by a previous excitatory input.

To quantify the magnification of the second response due to the prior input we define an *amplification factor* which is the ratio of the response to the second input in the presence of the previous one to the response to the second input by itself. In the present case (excitation followed by inhibition) the amplification factor is

$$A_{E,I} = 1 + \left| \frac{a_E V_E}{V_I} \right| G(x_I, x_E; t_I - t_E), \quad V_I \neq 0. \quad (2.13)$$

Of course this formula is valid for many kinds of boundary condition.

Properties of $A_{E,I}$

(i) $A_{E,I}$ is an increasing function of both a_E and V_E . Thus the larger the isolated EPSP the larger the amplification of the subsequent inhibitory response. In fact since the isolated EPSP amplitude at any space point is $a_E V_E$ multiplied by the maximum value of the Green's function at that space point, the *amplification factor increases linearly with EPSP amplitude*. The *increase (not $A_{E,I}$) in the magnitude of the response to the inhibitory input is also inversely proportional to absolute value of the inhibitory reversal potential*.

(ii) $A_{E,I}$ must achieve a maximum when $x_E = x_I$, for fixed values of the remaining parameters. When the

spatial domain of the solution is infinite we must have

$$A_{E,I} \xrightarrow{|x_E - x_I| \rightarrow \infty} 1, \quad (2.14)$$

since, of course, at infinite separation there will be no interaction between the two inputs.

(iii) There is a value of the time interval, $t_I - t_E$, between the inputs at which the amplification factor $A_{E,I}$ attains a maximum, for fixed values of the remaining input parameters. This is due to the fact that the Green's function $G(x_E, x_I; t_I - t_E)$ rises to a maximum as $t_I - t_E$ increases from zero and then decays monotonically to zero. Hence, as $t_E - t_I \rightarrow \infty$ the factor $A_{E,I}$ tends to unity:

$$A_{E,I} \xrightarrow{t_E - t_I \rightarrow \infty} 1. \quad (2.15)$$

Statements (2.14) and (2.15) can be summarized simply by saying that as the distance in space-time

$$d = \sqrt{(x_E - x_I)^2 + (t_E - t_I)^2} \quad (2.16)$$

between the two kinds of input event increases, the interaction between the responses tends to zero.

A relatively easy quantitative grasp of the behaviour of $A_{E,I}$ can be obtained by considering the case of an infinite spatial domain. In this case the Green's function is

$$G(x, y; t) = \frac{e^{-t}}{\sqrt{4\pi t}} e^{-(x-y)^2/4t}, \quad t > 0, \quad (2.17)$$

so that the amplification factor is

$$A_{E,I} = 1 + \left| \frac{a_E V_E}{V_I} \right| \frac{e^{-(t_I - t_E)} e^{-(x_I - x_E)^2/4(t_I - t_E)}}{\sqrt{4\pi(t_I - t_E)}}. \quad (2.18)$$

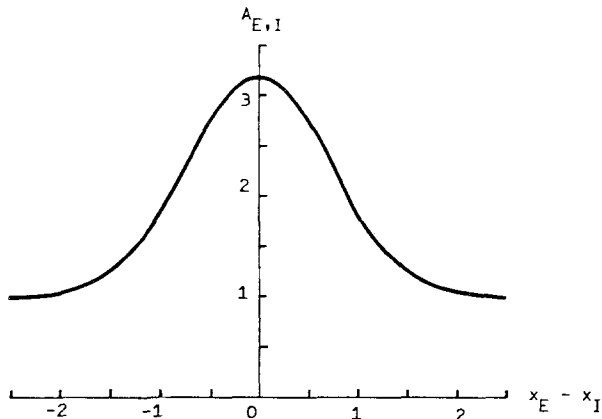


Fig. 1. The amplification factor $A_{E,I}$ for an inhibitory response when there is preceding excitation as given in (2.18) for the infinite cable. The abscissa is $x_E - x_I$, the distance between the excitatory and inhibitory inputs. Parameter values: $a_E = 1$, $V_E = 50$, $V_I = -10$, $t_I - t_E = 0.25$

Thus, as a function of the distance between the synapses, the amplification factor has the form of unity plus a normal density function. At certain fixed values of the remaining parameters, $A_{E,I}$ will appear as in Fig. 1.

Excitation Simultaneous with Inhibition

When $t_E = t_I$ so that excitatory and inhibitory conductance changes arrive at precisely the same time the response is just

$$V(x, t) = a_E V_E G(x, x_E; t - t_E) + a_I V_I G(x, x_I; t - t_E), \quad t > t_E. \quad (2.19)$$

Thus the superposition principle does apply in this exceptional case and the amplification factor is unity.

Excitation Following Inhibition

If $t_E > t_I$, the response after the arrival of the excitatory input is, by analogy with (2.8),

$$V(x, t) = a_I V_I G(x, x_I; t - t_I) + a_E V_E G(x, x_E; t - t_E) - a_E a_I V_I G(x_E, x_I; t_E - t_I) G(x, x_E; t - t_E), \quad t > t_E. \quad (2.20)$$

The resulting depolarization is the sum of the individual responses plus an interference term which is proportional to $a_E a_I V_I$. Thus we have

$$\text{RESPONSE} = \text{IPSP} + \text{EPSP} + \text{INTERFERENCE TERM}. \quad (2.21)$$

It is now useful to note that (2.20) can be written

$$V(x, t) = a_I V_I G(x, x_I; t - t_I) + a_E V_E G(x, x_E; t - t_E) \cdot \left[1 - \frac{a_I V_I}{V_E} G(x_E, x_I; t_E - t_I) \right], \quad V_E \neq 0. \quad (2.22)$$

Since we must have

$$V_E > 0 \quad \text{and} \quad V_I < 0 \quad (2.23)$$

we find that the amplification factor is

$$A_{I,E} = 1 + \left| \frac{a_I V_I}{V_E} \right| G(x_E, x_I; t_E - t_I), \quad V_E \neq 0. \quad (2.24)$$

In general, however, we expect

$$A_{I,E} \ll A_{E,I} \quad (2.25)$$

because $V_E \gg |V_I|$. That is, the amplification of an excitatory input due to a prior inhibitory stimulation is usually negligible compared with the effect of a conditioning inhibitory input on an excitatory one.

2.1 Numerical Results

To see more graphically the effects of timing of the excitation and inhibition we evaluated the ratio q of the

EPSP amplitude to the amplitude of an isolated EPSP. The latter is, at space point x ,

$$\text{EPSP}^* = \max_{t>0} a_E V_E G(x, x_E; t). \quad (2.1.1)$$

For *excitation preceding inhibition* define

$$V_{EI}(t) = \begin{cases} a_E V_E G(x, x_E; t - t_E), & t_E < t < t_I, \\ a_E V_E G(x, x_E; t - t_E) + a_I V_I G(x, x_I; t - t_I) \\ - a_E a_I V_E G(x_E, x_E; t_I - t_E) G(x, x_I; t - t_I), \\ & t > t_I. \end{cases} \quad (2.1.2)$$

The amplitude of the EPSP is then

$$\text{EPSP} = \max_{t>t_E} V_{EI}(t)$$

and, with all parameters fixed except t_E, t_I ,

$$q(t_E - t_I) = \frac{\text{EPSP}}{\text{EPSP}^*}. \quad (2.1.3)$$

When *excitation and inhibition are simultaneous*

$$\text{EPSP} = \max_{t>0} a_E V_E G(x, x_E; t) + a_I V_I G(x, x_I; t) \quad (2.1.4)$$

and $q(0)$ is just the ratio of this quantity to EPSP^* .

Finally, for *excitation following inhibition*, we define

$$V_{IE}(t) = \begin{cases} a_I V_I G(x, x_I; t - t_I), & t_I < t < t_E, \\ a_I V_I G(x, x_I; t - t_I) + a_E V_E G(x, x_E; t - t_E) \\ - a_E a_I V_I G(x_E, x_I; t_E - t_I) G(x, x_E; t - t_E), \\ & t > t_E. \end{cases} \quad (2.1.5)$$

The EPSP amplitude is

$$\text{EPSP} = \max_{t>t_I} V_{IE}(t) \quad (2.1.6)$$

and q is defined as above.

The quantity q was evaluated for various values of $t_E - t_I$ for the following values of the parameters:

$x=0$, representing a soma; $a_E=0.1$, $a_I=0.2$, $V_E=50$, $V_I=-10$. In one set of calculations $x_E=0.5$ and $x_I=0.55$ so that the inhibition is distal to the excitation; in the other set of calculations $x_I=0.50$ and $x_E=0.55$ giving inhibition proximal to the excitation.

Figure 2a and b shows a graph of q versus $t_E - t_I$ when the inhibition is distal to the excitation. In Fig. 2a, the excitation arrives first and the abscissa is $t_I - t_E$, which is positive. The ratio q of EPSP amplitude to the isolated EPSP amplitude is very small for small time intervals between the two inputs indicating that a severe depression of the amplitude of the response to excitation will occur if the inhibitory pulse *quickly follows* the excitation. From Fig. 2b q is shown for the inhibition arriving ahead of the excitation. Although the depression of the EPSP amplitude is not as great,

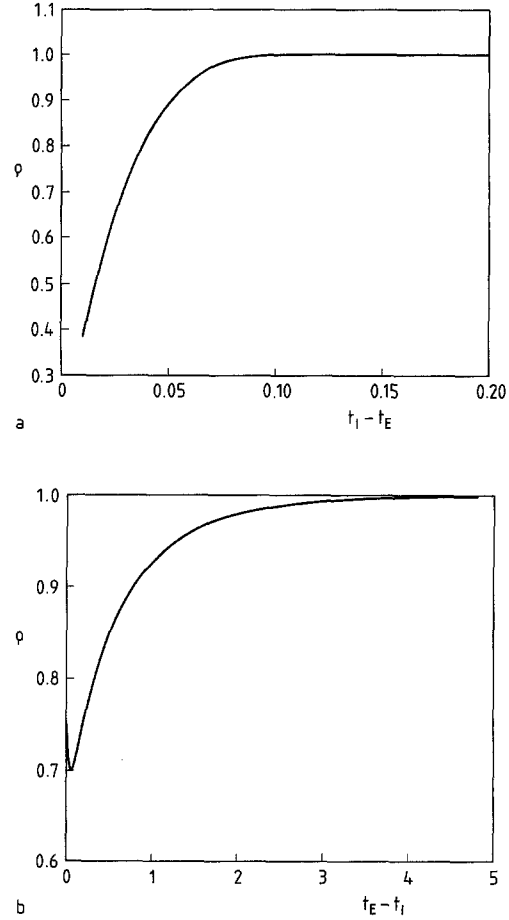


Fig. 2. a Ratio of somatic EPSP amplitude to that of an isolated EPSP when inhibition is distal to excitation. Here the excitation arrives first and the abscissa is $t_I - t_E$. The inputs are at $x_E=0.5$, $x_I=0.55$; for remaining parameter values see text. The value of the ratio at $t_I - t_E=0$ is 0.650. b As in a except the inhibition arrives first and the abscissa is $t_E - t_I$

there are sizeable reductions for large time delays between the 2 inputs. Thus inhibition arriving later has a more drastic effect if it comes quickly enough and inhibition arriving sooner has a less drastic effect but the effect persists for much longer (of order 10 times as long). The function $q(t_E - t_I)$ is apparently not continuous at $t_E - t_I=0$ because $q(0)$ in the present case is 0.650.

Figure 3a and b shows the results for inhibition proximal to the excitation and correspond to 3a and b. The depression of the response at $x=0$ is greater as expected. The values of $q(0)$ in this case was 0.557.

2.2 The Case $V_I=0$

The case $V_I=0$ is of special interest because of its relevance to shunting inhibition. If we put $V_I=0$ in (2.8), (2.19), and (2.20) we obtain for *inhibition after the*

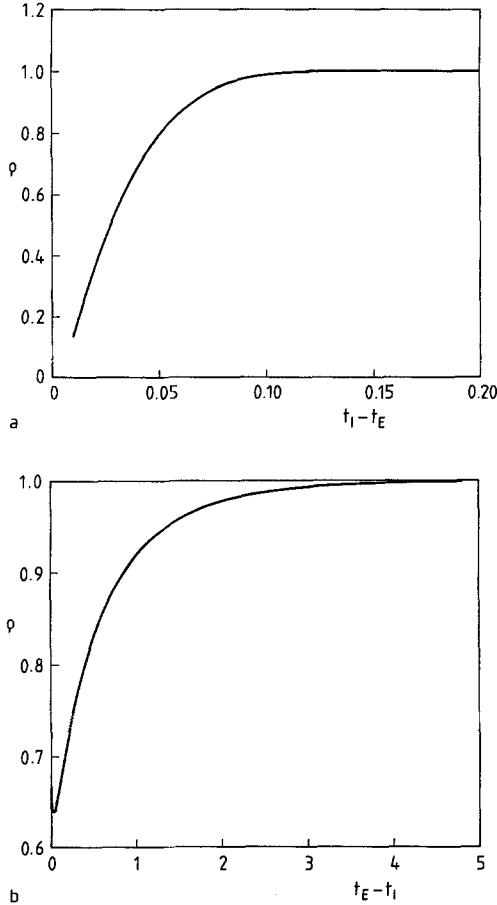


Fig. 3. a As in Fig. 2a except that the inhibition is now proximal to the excitation: $x_I = 0.5$, $x_E = 0.55$. The abscissa is $t_I - t_E$ as the excitation arrives first. The value of the ratio at $t_I - t_E = 0$ is 0.557. **b** As in **a** except now the inhibition arrives first so the abscissa is $t_E - t_I$

excitation,

$$V_{EI}(x, t) = a_E V_E G(x, x_E; t - t_E) - a_E a_I V_E G(x_I, x_E; t_I - t_E) G(x, x_I; t - t_I) \quad (2.2.1)$$

whereas for inhibition and excitation simultaneous,

$$V(x, t) = a_E V_E G(x, x_E; t - t_E), \quad (2.2.2)$$

and for inhibition preceding the excitation,

$$V_{IE}(x, t) = a_E V_E G(x, x_E; t - t_E). \quad (2.2.3)$$

It can be seen that when $V_I = 0$ the inhibitory input has no effect whatsoever on the membrane potential of the cell if it arrives before or at the same time as the excitation. However, when the inhibition follows the excitation it may effect a large depression of the response despite the fact that by itself it elicits no response at all. This is the form of *shunting inhibition* for the cable model with impulsive conductance changes.

3 Cable Equation with Sustained Conductance Changes

We are here concerned with the cable equation with reversal potentials when there are synaptically induced conductance changes which persist in time.

In the case of an excitatory conductance change by itself, leading to the generation of an EPSP, we write

$$V_t = V_{xx} - V + a_E \delta(x - x_E) [H(t - t_E) - H(t - t'_E)] \cdot [V_E - V], \quad (3.1)$$

where a_E , $V_E \geq 0$, x_E is the location of the excitatory input and the induced conductance change lasts from t_E to t'_E . This kind of conductance change was employed by Barrett and Crill (1974) who calculated the rising phases of corresponding EPSP's. Calculations of complete EPSP's are given in Tuckwell (1986, Chap. 7).

Interaction of Excitatory and Inhibitory Inputs

We approach a study of the interaction of excitation and inhibition by employing the equation,

$$V_t = V_{xx} - V + a_E \delta(x - x_E) [H(t - t_E) - H(t - t'_E)] \cdot [V_E - V] + a_I \delta(x - x_I) [H(t - t_I) - H(t - t'_I)] \cdot [V_I - V]. \quad (3.2)$$

Thus, in addition to the excitatory input there may be an inhibitory one persisting in time from t_I to t'_I at the space point x_I . We will first obtain an exact result for an infinite cable in a special case and then numerically integrate (3.2) to study the interactions between inputs generally.

3.1 An Exact Calculation - Excitation and Inhibition Simultaneous and at the Same Value of x in an Infinite Cable

In general the calculations of solutions of (3.2) are cumbersome. However, when $t_E = t_I$ and $x_E = x_I$ in the case of an infinite cable, an exact solution may be found whilst the conductance increases are occurring. Notice that $x_E = x_I$ does not exclude anatomical reality since excitatory and inhibitory synapses may occur on opposite (or other nonintersecting) surfaces on a nerve cylinder.

The method of finding $V(x, t)$ is by Laplace transforms, a similar calculation being given in Jack et al. (1975) and Tuckwell (1986) in the case of excitation only. If we define the Laplace transform of $V(x, t)$ as

$$V_L(x; s) = \int_0^{\infty} e^{-st} V(x, t) dt, \quad (3.3)$$

then we find

$$V_L(x; s-1) = \frac{e^{-|x-x_E|} (a_E V_E + a_I V_I)}{2(s-1) \left(\sqrt{s + \frac{a_E + a_I}{2}} \right)}. \quad (3.4)$$

The inverse transform is found to be [see Abramowitz and Stegun (1965) for a table of relevant transforms]

$$\begin{aligned}
 V(x, t) = & \frac{a_E V_E + a_I V_I}{2} \left[\frac{e^{-|x-x_E|}}{a_E + a_I + 2} \operatorname{erfc} \left(\frac{|x-x_E|}{2\sqrt{t}} - \sqrt{t} \right) \right. \\
 & + \frac{e^{|x-x_E|}}{a_E + a_I - 2} \operatorname{erfc} \left(\frac{|x-x_E|}{2\sqrt{t}} + \sqrt{t} \right) \\
 & + \frac{2(a_E + a_I)}{4 - (a_E + a_I)^2} \exp \left\{ \frac{(a_E + a_I)|x-x_E|}{2} \right. \\
 & \left. + \left(\frac{(a_E + a_I)^2}{4} - 1 \right) t \right\} \\
 & \left. \times \operatorname{erfc} \left(\frac{|x-x_E|}{2\sqrt{t}} + \frac{(a_E + a_I)\sqrt{t}}{2} \right) \right]. \quad (3.5)
 \end{aligned}$$

In the special case $a_E + a_I = 2$ we have

$$\begin{aligned}
 V(x, t) = & \frac{a_E V_E + a_I V_I}{8} \left[e^{-|x-x_E|} \operatorname{erfc} \left(\frac{|x-x_E|}{2\sqrt{t}} - \sqrt{t} \right) \right. \\
 & + 4e^{|x-x_E|} \left\{ \sqrt{\frac{t}{\pi}} \exp \left(- \left(\frac{|x-x_E|}{2\sqrt{t}} + \sqrt{t} \right)^2 \right) \right. \\
 & \left. \left. - \left(\frac{1}{4} + \frac{|x-x_E|}{2} + t \right) \operatorname{erfc} \left(\frac{|x-x_E|}{2\sqrt{t}} + \sqrt{t} \right) \right\} \right]. \quad (3.6)
 \end{aligned}$$

Although the infinite cable provides only an approximate basis for real nerve cells, the formulas in (3.5) and (3.6) are nevertheless useful because they are exact and hence readily available for computation. Formula (3.5) enables one to see immediately how the excitatory and inhibitory contributions interact: - this expression is linear in $a_E V_E + a_I V_I$ but is nonlinear in $a_E + a_I$.

The response at $x=0$ (soma) was calculated from (3.5) for various parameter values as follows and for $0 < t \leq 3$, assuming an initially resting cell:

(i) *Excitation only (E)*. $a_E = 0.2$, $V_E = 50$, $a_I = 0$, $V_I = 0$.

(ii) *Inhibition only (I)*. $a_I = 1$, $V_I = -5$, $a_E = 0$, $V_E = 0$.

(iii) *Excitation and inhibition together (E, I)*. $a_E = 0.2$, $V_E = 50$, $a_I = 1$, $V_I = -5$.

(iv) *Excitation and inhibition together when $V_I = 0$* . $a_E = 0.2$, $V_E = 50$, $a_I = 1$.

The results of these calculations are shown plotted in Fig. 4. Here $V(0, t)$, the somatic potential is graphed against time for cases (i)–(iv) above. In addition, the algebraic sum of the potentials for cases E and I is shown. The nonlinear summation of excitatory and inhibitory responses is indicated by the values of $V(0, t)$ at $t=3$. We find

$$V(0, t=3)_E + V(0, t=3)_I = 1.70,$$

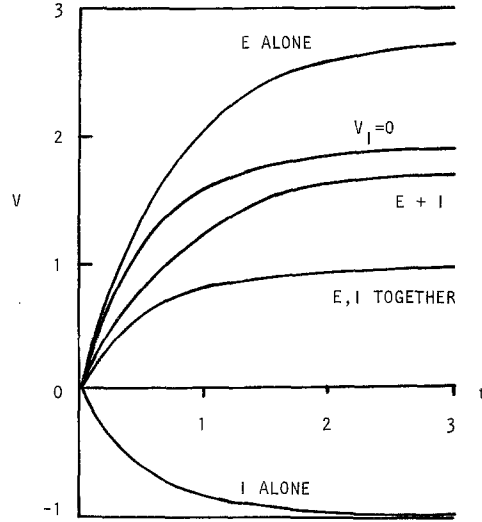


Fig. 4. Exact results for the infinite cable with reversal potentials and sustained conductance changes. The somatic potential is shown as a function of time in the four cases: excitation only (*E*); inhibition only (*I*); excitation and inhibition simultaneous (*E* with *I*); shunting inhibition ($V_I = 0$). Also shown is the algebraic sum (*E* + *I*) of the excitatory and inhibitory responses. For parameter values see text

whereas

$$V(0, t=3)_{E,I} = 0.939,$$

so the reduction is to about 55% of the algebraic sum. In the shunting inhibition case ($V_I = 0$) the potential at $t=3$ is 1.88, representing a reduction to 69.6% of the potential in the case of excitation only.

To conclude this subsection we give, for completeness, the Laplace transform of the potential for the infinite cable when $x_E \neq x_I$ whilst the excitatory and inhibitory conductance changes are (simultaneously) occurring:

$$\begin{aligned}
 V_L(x; s-1) = & \left[a_E e^{-|x-x_E|\sqrt{s}} \left(V_E \sqrt{s} + \frac{a_I V_E}{2} \right. \right. \\
 & \left. \left. - \frac{a_I V_I}{2} e^{-|x_E-x_I|\sqrt{s}} \right) \right. \\
 & \left. + a_I e^{-|x-x_I|\sqrt{s}} \left(V_I \sqrt{s} + \frac{a_E V_I}{2} - \frac{a_E V_E}{2} e^{-|x_E-x_I|\sqrt{s}} \right) \right] / \\
 & \left[2(s-1) \left\{ s + \frac{(a_E + a_I)\sqrt{s}}{2} + a_E a_I (1 - e^{-2|x_E-x_I|\sqrt{s}}) \right\} \right]. \quad (3.7)
 \end{aligned}$$

Although this expression is amenable to inversion by way of infinite series expansions, this aspect will not be pursued here.

3.2 Numerical Solutions – Shunting Inhibition

The Laplace transform method of solution is useful, especially for the infinite cable, for finding the response during the time interval in which the first conductance increase occurs. The decay phase following the first conductance increase may be found by numerical solution of an integral equation (see Tuckwell 1986, Chap. 7). However, if there is a *subsequent* conductance increase, as for example if inhibition follows excitation with a time interval between them, the Laplace transform – integral equation approach becomes overburdensomely complicated. It is then advantageous to turn to numerical methods of solution of the partial differential equation (3.2).

To this end the Crank-Nicolson method of solution was employed, in which the finite-difference approximation

$$V(i\Delta x, j\Delta t) \cong U_{ij}, \quad i=0, 1, \dots, m; \quad j=0, 1, \dots, n, \quad (3.8)$$

is made. In these calculations a finite space interval of length L was used, so we always have $m\Delta x=L$. The required derivatives are approximated by

$$V_i(x, t) \cong \frac{U_{i,j+1} - U_{ij}}{\Delta t} \quad (3.9)$$

$$V_{xx} \cong \frac{1}{2\Delta x^2} [U_{i+1,j+1} - 2U_{i,j+1} + U_{i-1,j+1} + U_{i+1,j} - 2U_{i,j} + U_{i-1,j}]. \quad (3.10)$$

The boundary conditions at $x=0$ and $x=L$ were chosen to be sealed end conditions, which yields

$$\begin{cases} U_{-1,j} = U_{1,j} \\ U_{m-1,j} = U_{m+1,j} \end{cases} \quad (3.11)$$

One assumes for any j that the U_{ij} 's are known and then proceeds to find the $U_{i,j+1}$'s in order to advance the domain of the known solution by Δt . This involves the solution of a tridiagonal system of equations which may be solved without matrix inversion (see, for example, Ames 1977). The delta functions in space at x_E and x_I were incorporated by making the nonhomogeneous (input) terms in the finite-difference approximation zero except at one space point (one value of i) for excitation and one space point for inhibition. Throughout the calculations the following quantities were held fixed.

Parameters Which Were Not Varied. In both sets of calculations we have

$$\begin{cases} \Delta t = 0.01, \Delta x = 0.01, L = 1, \\ a_E = 20, V_E = 50, a_I = 200, V_I = 0, \\ x_E = 0.5, t'_E - t_E = t'_I - t_I = 0.5. \end{cases} \quad (3.12)$$

The values of the somatic potential were obtained as a function of time. The EPSP amplitude was taken as the maximum value of the depolarization, there sometimes being two peak values. The amplitude of the EPSP in the absence of any inhibitory inputs was 3.62 mV.

Variation in Time Interval Between Excitation and Inhibition. With the above parameters fixed, the reduction of EPSP amplitude induced by an inhibitory input at $x_I=0.2$ was determined. The time interval between the onset of the inhibition and the onset of the excitation was varied through positive and negative values.

The % reduction of the EPSP amplitude is shown as a function of $t_E - t_I$ in Fig. 5. It can be seen that shunting inhibition is, according to the calculated results shown, most effective when it commences just after the excitation is switched on. This is in contradistinction to the findings of Fatt and Katz (1953), but the origin of the inhibition in their experiment has been shown to be presynaptic.

Effect of Changing the Position of the Inhibitory Input. With the parameters given in (3.12) again held fixed, the location of the inhibitory input, x_I , was varied. The time interval between excitation and inhibition was fixed with the excitation commencing 0.15 time units before the inhibition. This was the timing (see Fig. 5)

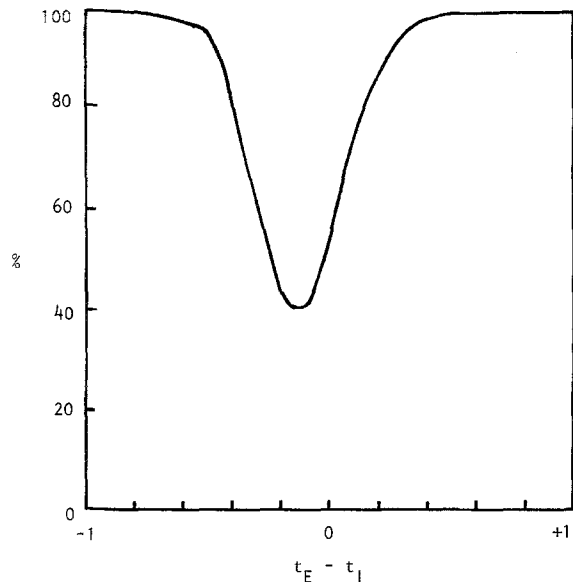


Fig. 5. Somatic EPSP amplitude as a percentage of the amplitude of an isolated EPSP for the shunting inhibition case ($V_I=0$) in a finite cable with reversal potentials, sustained conductance changes and sealed ends. The abscissa is $t_E - t_I$, where t_E, t_I are the start times for the excitatory and inhibitory conductance increases. The results were obtained by numerical integration of the cable equation. For parameter values see text

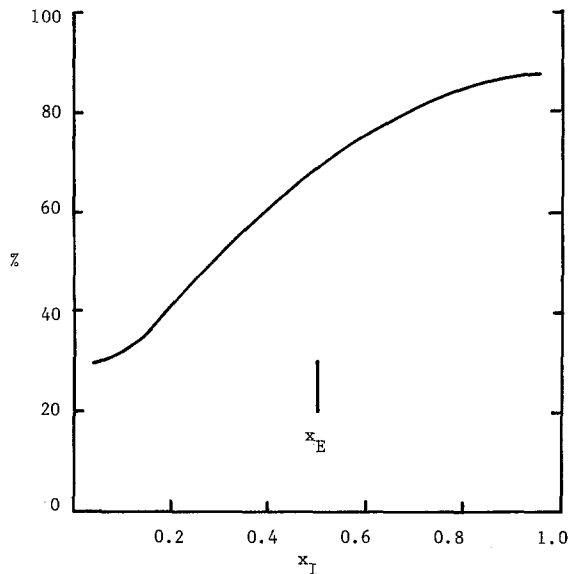


Fig. 6. Somatic EPSP amplitude as a percentage of that of an isolated EPSP when $V_I=0$ in the finite cable as a function of the distance from soma to the inhibitory input. The position of the excitatory input is fixed at $x_E=0.5$, the center of the cylinder. For parameter values, see text

which had led to maximal depression of the EPSP when $x_I=0.2$.

The % depression (i.e., EPSP amplitude as a % of the amplitude of an isolated EPSP) of the response is plotted as a function of x_I in Fig. 6. For this set of results it is seen that the EPSP amplitude is approximately proportional to the distance from the soma to the site of inhibitory action. This result is obtained, however, in a special case so that a general conclusion of this nature is not possible.

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