

## SOME ASPECTS OF CABLE THEORY WITH SYNAPTIC REVERSAL POTENTIALS\*

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### Abstract

A partial differential equation for the electrical potential across nerve membrane is considered. On the assumption of a space clamp, expressions are obtained for the synaptic reversal potentials in terms of the Nernst potentials of the various ion species present. The cable equation with reversal potentials is then derived. Its solutions are obtained exactly in terms of Green's functions for the usual cable equation for the cases of (i) a repetitive train of excitatory impulsive conductance changes; and (ii) a synaptic input whilst a steady current is applied at the soma. The importance of including the reversal potentials when studying a model neuron's response to multiple synaptic inputs is emphasized.

### 1. Introduction

The cable equation which has most often been employed to describe the sub-threshold electrical potential in axons and dendrites can be written

$$(1.1) \quad r_m c_m V_t = \frac{r_m}{r_i} V_{xx} - V + r_m I_A,$$

where  $c_m$  is the membrane capacitance per unit length ( $F \text{ cm}^{-1}$ ),  $r_i$  is the internal or axial resistance per unit length ( $\Omega \text{ cm}^{-1}$ ),  $r_m$  is the membrane resistance of unit length times unit length ( $\Omega \text{ cm}$ ),  $I_A$  is the applied current density ( $A \text{ cm}^{-1}$ ),  $V = V(x, t)$  is the depolarization in volts,  $x$  is the distance in cm and  $t$  is time in sec. (Note that subscripts  $t$  and  $x$  indicate partial derivatives with respect to these variables.)

Equation (1.1) was found to apply to crab axons by comparing measured and predicted voltage distributions in response to currents of various strengths (Hodgkin and Rushton, 1946). Rall (1959, 1960) employed (1.1) for calculating the steady state and transient potentials in model neurons with dendritic trees and initiated a long

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\*Dedicated to Hiroko Suzuki.

sequence of such investigations (see Rall, 1977, for a summary) which is still on-going (Ashida, 1985; Durand, 1984; Walsh and Tuckwell, 1985).

When the only current applied to a nerve cell is one experimentally injected or when a synaptic input occurs when the cell is uniformly at rest, (1.1) may often provide an adequate representation (see Equ. (4.5) below). However, when a cell is not at resting level and a synaptic input occurs, (1.1) needs modifying to allow for the phenomenon of synaptic reversal potentials.

It is well established (see for example Eccles, 1964; Krnjevic, 1974) that when a synapse, whose activation is mediated by the release of transmitter from the presynaptic terminal, is active, the permeabilities of the postsynaptic membrane to various ions undergo local changes. However, the mathematical treatment of ionic fluxes through the various specialized ion channels under the combined effects of electrical and diffusive forces is too difficult.

To simplify matters, it is assumed that the membrane offers a certain resistance to the current flow for each ion type, thus preserving the concept that each ion type has its own specialized channels. It is further assumed that the magnitude of the current due to an ionic species is proportional to the difference between the existing membrane potential and the Nernst potential for that species.

Consider a small, uniformly polarized patch of membrane, and suppose that the current through it due to ion species  $i$  is  $I_i$ . Let the Nernst potential be  $V_i$  for that type of ion. Then it is assumed that the following equation holds:

$$(1.2) \quad I_i = g_i(V_i - V),$$

where  $V$  is the membrane potential. Equation (1.2) is taken as the *definition of*  $g_i$ , which is called the (chord) conductance of that patch of membrane to ion species  $i$ .

The inclusion of these ionic currents in cable theory is as follows. Let there be  $n$  ion species to which the membrane is permeable. Suppose that  $V_i$ , assumed constant, is now the Nernst potential for the  $i$ -th species minus the resting membrane potential. If  $V$  is the depolarization, or membrane potential minus the resting potential, then equation (1.2) still applies.

Suppose further that the conductance per unit length at  $(x, t)$  for ion species  $i$  is  $g_i(x, t)$ , with units  $\Omega^{-1} \text{cm}^{-1}$ . We introduce, for reasons which will shortly become clear, a *pump current*  $P$  (with units  $A \text{cm}^{-1}$ ) which contains ion fluxes due to active transport. Then, by considering the membrane current in  $[x, x + \Delta x]$ , we obtain the following equation satisfied by the depolarization:

$$(1.3) \quad c_m V_t = \frac{1}{r_i} V_{xx} + \sum_{i=1}^n g_i(V_i - V) - P + I_A.$$

The usual contributions to the ionic current come from sodium ions, potassium ions, chloride ions, with calcium, magnesium and other cations sometimes being included in special circumstances.

*An alternative form of equation (1.3) and its connection with the usual cable equation*

Equation (1.3) is rarely encountered as such although it should be used in most cases for investigating the effects of synaptic inputs. Without the pump term  $P$ , it is the basic equation of the Hodgkin-Huxley (1952) theory. We will now obtain a version of (1.3) which makes clear its connection with the usual cable equation (1.1).

To this end, we separate each ionic conductance  $g_i$  into a component  $\tilde{g}_i$ , constant in space and time, which we associate with the resting membrane, and another component  $\Delta g_i$ , which depends on  $x$  and  $t$ :

$$(1.4) \quad g_i(x, t) = \tilde{g}_i + \Delta g_i(x, t).$$

Thus  $\Delta g_i$  is the increase in conductance relative to resting level, per unit length, for ion species  $i$ . Substituting in (1.3) we obtain

$$(1.5) \quad c_m V_t = \frac{1}{r_i} V_{xx} + \sum_{i=1}^n \tilde{g}_i V_i - V \sum_{i=1}^n \tilde{g}_i + \sum_{i=1}^n \Delta g_i(V_i - V) - P + I_A.$$

Define

$$(1.6) \quad g_m = \frac{1}{r_m} = \sum_{i=1}^n \tilde{g}_i,$$

which is the resting membrane conductance per unit length,  $r_m$  being the resting membrane resistance of unit length times unit length. When there is no applied current, so  $I_A = 0$ , and when  $\Delta g_i = 0$ , so that the ionic conductances have their resting values, there must be zero ionic current. This requires the condition

$$(1.7) \quad P = \sum_{i=1}^n \tilde{g}_i V_i,$$

so that the resting pump rate counters the resting ionic fluxes in order to maintain equilibrium. Then (1.5) can be written

$$(1.8) \quad c_m V_t = \frac{1}{r_i} V_{xx} - \frac{V}{r_m} + \sum_{i=1}^n \Delta g_i(V_i - V) + I_A.$$

Converting to dimensionless space and time variables, in which the units of space and time are the resting membrane's space and time constants, we now have

$$(1.9) \quad V_t = V_{xx} - V + r_m \sum_{i=1}^n \Delta g_i(V_i - V) + r_m I_A.$$

It is now possible to determine the relation between the usual cable equation (1.1) and the modified equation (1.3). Either one lumps synaptic and other ionic currents into the term  $I_A$  and neglects the other forcing term: or one assumes that  $V_i$  is so large

and changes in  $V$  are so relatively small that  $\Delta g_i(V_i - V)$  can be regarded as independent of  $V$ . The latter may be a valid approximation when considering the sodium ion current, but not usually the potassium and chloride currents.

Equation (1.9) may be further rewritten

$$(1.10) \quad V_t = V_{xx} - V + \sum_{i=1}^n \Delta g_i^* (V_i - V) + r_m I_A$$

where

$$(1.11) \quad \Delta g_i^* = \frac{\Delta g_i}{\sum_{i=1}^n \tilde{g}_i},$$

is a dimensionless quantity, being the ratio of the increase in the membrane conductance for species  $i$  to the total resting membrane conductance.

## 2. Equations for the Potential with Space Clamp and Synaptic Input-Reversal Potentials

*Solution of the space-clamped version of Eq. (1.10) with  $I_A = 0$*

First consider the space-clamped version of (1.10). That is, set the space derivative (and hence  $V_{xx}$ ) equal to zero and deal with a small patch of membrane across which the potential is uniform in space. Then, in the absence of applied currents,  $V = V(t)$  satisfies the ordinary differential equation

$$(2.1) \quad \frac{dV}{dt} = -V + \sum_{i=1}^n \Delta g_i^*(t) [V_i - V].$$

During a synaptic event, the ionic conductances will undergo brief increases. These may have different durations for each ion species but we will assume that simultaneous step changes in the conductances occur for each ion type. We let the step changes start at  $t=0$  and end at  $t=t_1$ :

$$(2.2) \quad \Delta g_i^*(t) = a_i [H(t) - H(t - t_1)], \quad t_1 > 0,$$

where  $H(\cdot)$  is the unit step function and the  $a_i \geq 0$  are constants. Prior to the conductance increase we assume

$$(2.3) \quad V(0^-) = V_0.$$

We find, on defining

$$(2.4) \quad A = 1 + \sum_{i=1}^n a_i,$$

$$(2.5) \quad B = \sum_{i=1}^n a_i V_i,$$

that whilst the conductances are switched on,

$$(2.6) \quad V(t) = \frac{B}{A} + \left( V_0 - \frac{B}{A} \right) e^{-At}, \quad 0 \leq t < t_1.$$

If the conductances were switched on indefinitely,  $V$  would approach the steady state value

$$(2.7) \quad V(\infty) = \frac{B}{A}.$$

The change in  $V(t)$  from the beginning to the end of the conductance increases is

$$(2.8) \quad V(t_1) - V_0 = \left( \frac{B}{A} - V_0 \right) (1 - e^{-At_1}).$$

Thus whether the change is positive or negative depends on both the initial value  $V_0$  and the quantities  $A$  and  $B$ . Since  $A$  is necessarily positive, we see that synaptic potentials elicited from rest ( $V_0 = 0$ ) will be excitatory if  $B > 0$  and inhibitory if  $B < 0$ . For an excitatory synapse the change in depolarization will be positive if  $V_0 < B/A$  and negative if  $V_0 > B/A$ . Thus the quantity  $B/A$  is a "reversal potential" and we have:

$$(2.9) \quad V_{\text{rev.}} = \frac{\sum_{i=1}^n a_i V_i}{1 + \sum_{i=1}^n a_i}.$$

This expression is linear in the Nernst potentials for the various ions. In general, however,  $V_{\text{rev.}}$  is not linear in the individual Nernst potentials, except when only one ion species is involved. This deficiency can be traced to the inconsistency of (1.2) with constant field theory.

For  $t \geq t_1$ , when the conductance increases are switched off, the depolarization will be

$$(2.10) \quad V(t) = \left( \frac{B}{A} - V_0 \right) (1 - e^{-At_1}) e^{-(t-t_1)}.$$

Thus whilst the synapse is active, the time constant is  $1/A$  of its value during the passive decay stage.

*Response to synaptic input in the presence of injected current*

In certain experiments (see for example Coombs, Eccles and Fatt, 1955a, 1955b), a constant current  $I_0$ , which may be depolarizing or hyperpolarizing, is injected into a nerve cell. Then, usually after a steady state has been attained, synaptic inputs are activated. For this situation in the space-clamped case we have, with synaptic input conductance changes lasting from  $t=0$  to  $t=t_1$ ,

$$(2.11) \quad \frac{dV}{dt} + V = \sum_{i=1}^n a_i [H(t) - H(t-t_1)] [V_i - V] + V_0, \quad t > 0,$$

where, now,

$$(2.12) \quad V_0 = r_m I_0,$$

is the steady state voltage under the application of the current  $I_0$ .

If the steady state has been achieved by the time the synaptic input occurs, then we must solve (2.11) with the initial condition

$$(2.13) \quad V(0) = V_0.$$

The potential whilst the synapses are active is given by

$$(2.14) \quad V(t) = V_0 + \frac{\tilde{B}}{A} (1 - e^{-At}), \quad 0 \leq t \leq t_1,$$

where

$$(2.15) \quad \tilde{B} = \sum_{i=1}^n a_i (V_i - V_0).$$

The resulting change in potential is thus positive if  $\tilde{B} > 0$  and negative if  $\tilde{B} < 0$ . Equivalently, the response is depolarizing (excitatory) if  $V_0 < \sum a_i V_i / \sum a_i$  and hyperpolarizing (inhibitory) if  $V_0 > \sum a_i V_i / \sum a_i$ . Hence the reversal potential is

$$(2.16) \quad V_{\text{rev.}} = \left( \sum_{i=1}^n a_i V_i \right) / \left( \sum_{i=1}^n a_i \right).$$

If only sodium and potassium ions are involved, this formula becomes, using an obvious notation:

$$(2.17) \quad V_{\text{rev.}} = \frac{(a_{Na}/a_K) V_{Na} + V_K}{(a_{Na}/a_K) + 1}$$

Formula (2.17) is given in Kuffler and Nicholls (1976, p. 167).

### 3. Derivation of the Cable Equation with Synaptic Reversal Potentials

We will derive a version of (1.9), valid under certain assumptions, which is particularly useful in delineating excitatory and inhibitory inputs. First we distinguish those ionic conductance changes induced by excitatory synaptic input from those due to inhibitory input. If  $n_E$  ion species are involved in excitation and  $n_I$  in inhibition, then

$$(3.1) \quad V_t = -V + V_{xx} + r_m \left[ \sum_{i=1}^{n_E} \Delta g_{i,E} (V_{i,E} - V) + \sum_{i=1}^{n_I} \Delta g_{i,I} (V_{i,I} - V) \right] + r_m I_A$$

$$= -V + V_{xx} + r_m \left[ \sum_{i=1}^{n_E} \Delta g_{i,E} \left\{ \frac{\sum \Delta g_{i,E} V_{i,E}}{\sum \Delta g_{i,E}} - V \right\} + \sum_{i=1}^{n_I} \Delta g_{i,I} \left\{ \frac{\sum \Delta g_{i,I} V_{i,I}}{\sum \Delta g_{i,I}} - V \right\} \right] + r_m I_A.$$

If there is only one ion species involved in excitation and only one involved in inhibition, then the Nernst potentials  $V_{1,E}$  and  $V_{1,I}$  will be the synaptic reversal potentials which we denote by  $V_E$  and  $V_I$ . Then (3.1) becomes

$$(3.2) \quad V_t = -V + V_{xx} + r_m [\Delta g_E (V_E - V) + \Delta g_I (V_I - V)] + r_m I_A,$$

where  $\Delta g_E(x, t) = \Delta g_{1,E}(x, t)$  and  $\Delta g_I(x, t) = \Delta g_{1,I}(x, t)$ .

We will show that (3.2) is sometimes applicable in situations where there are several ion species involved in the synaptic transmission. Consider a single excitatory synapse extending from  $x_E$  to  $x'_E$  which is activated from  $t_E$  to  $t'_E$ , the (assumed) constant magnitudes of the conductance increases for the  $i, E$  ion species being  $a_{i,E}$ . Then

$$(3.3) \quad \Delta g_{i,E}(x, t) = a_{i,E} [H(x_E) - H(x'_E)] [H(t_E) - H(t'_E)], \quad i = 1, \dots, n_E.$$

Assume a similar set of conductance changes for an inhibitory synapse. Then, substituting in (3.1) gives

$$(3.4) \quad V_t = -V + V_{xx} + r_m \left[ \{H(x_E) - H(x'_E)\} \{H(t_E) - H(t'_E)\} \left( \sum_{i=1}^{n_E} a_{i,E} \right) \times \left\{ \frac{\sum a_{i,E} V_{i,E}}{\sum a_{i,E}} - V \right\} + \{H(x_I) - H(x'_I)\} \{H(t_I) - H(t'_I)\} \left( \sum_{i=1}^{n_I} a_{i,I} \right) \times \left\{ \frac{\sum a_{i,I} V_{i,I}}{\sum a_{i,I}} - V \right\} \right] + r_m I_A$$

where  $H(x_E)$  has been used to abbreviate  $H(x - x_E)$  etc.

But

$$(3.5) \quad \frac{\sum_i a_{i,E} V_{i,E}}{\sum_i a_{i,E}} = V_E,$$

and

$$(3.6) \quad \frac{\sum_i a_{i,I} V_{i,I}}{\sum_i a_{i,I}} = V_I,$$

are, according to (2.16), the excitatory and inhibitory reversal potentials. If we set

$$(3.7) \quad \Delta g_E = \sum_{i=1}^{n_E} a_{i,E}$$

$$(3.8) \quad \Delta g_I = \sum_{i=1}^{n_I} a_{i,I},$$

then (3.4) becomes identical to (3.2). Furthermore, if there are several synapses of either excitatory or inhibitory character, and these are active on several different time intervals, then, providing the corresponding conductance changes are of the kind in Eq. (3.3), equation (3.2) will still apply. It can be seen that this represents a simplification even though (3.2) is no easier to solve than the more general equation (3.1). Although something is lost in going from (3.1) to (3.2), the latter is more widely used because it makes more transparent the contributions from excitation and inhibition. Any solutions obtained for Eq. (3.2) can of course be employed for (3.1) with a change of symbols.

#### 4. Response to Impulsive Conductance Changes

Although synaptic conductance changes are sustained in time, if they are short-lasting it is often expeditious to consider them as instantaneous (MacGregor, 1968). In this section we will consider the response of a nerve cell to (1) a periodic train of excitation and (2) a synaptic input whilst a steady current is injected at the origin (soma).

##### 4.1 A periodic train of excitation

Suppose a sequence of excitatory conductance impulses arrives at the space point  $x = x_E$ , being separated in time by  $T$  time units. The partial differential equation for  $V$  is then

$$(4.1) \quad V_t = V_{xx} - V + a_E \delta(x - x_E) (V_E - V) \sum_{n=0}^{\infty} \delta(t - nT),$$

where  $a_E$  is a constant and  $V_E$  is the excitatory reversal potential for the given synapse. We will not specify the domain in space but assume that a Green's function can be found for the usual cable equation  $V_t = V_{xx} - V$  on this domain. Let  $G(x, y; t)$  be this Green's function. Then applying the usual Green's function method of solution, the solution of

$$(4.2) \quad V_t = V_{xx} - V + g(x, t) (V_E - V),$$

with initial condition

$$(4.3) \quad V(x, 0) = v(x),$$

is

$$(4.4) \quad V(x, t) = \int G(x, y; t) v(y) dy + \int \int [V_E - V(y, s)] g(y, s) G(x, y; t - s) ds dy.$$

Thus the "source term" is  $(V_E - V)g$ , differing from the usual cases in that it involves  $V$ , the function which is sought.

If an impulsive conductance change occurs at  $t=0$  and the potential is initially zero, then

$$(4.5) \quad V(x, t) = a_E V_E G(x, x_E; t), \quad 0 < t \leq T.$$

This is the response to a single impulse and does not differ in form from that of the neuron without synaptic reversal potentials.

Now we regard

$$(4.6) \quad V(x, T) = a_E V_E G(x, x_E; T),$$

as the initial condition when the next impulsive conductance change occurs. Let  $t' = t - T$  so  $t'$  measures the time elapsed since the second synaptic input. Applying formula (4.4) again,

$$(4.7) \quad V(x, t') = \int a_E V_E G(y, x_E; T) G(x, y; t') dy + \int \int a_E [V_E - V(y, s)] \delta(y - x_E) \delta(s) G(x, y; t' - s) ds dy.$$

The first integral may be evaluated by using the (semigroup) property of the Green's function

$$(4.8) \quad \int G(x, y; s) G(z, x; t) dx = G(z, y; s + t).$$

Evaluating the double integral gives

$$a_E [V_E - V(x_E, t' = 0)] G(x, x_E; t') = a_E [V_E - V(x_E, T)] G(x, x_E; t').$$

Using (4.6) we get,

$$(4.9) \quad V(x, t) = a_E V_E G(x, x_E; t) + a_E V_E G(x, x_E; t - T) [1 - a_E G(x_E, x_E; T)], \quad T < t \leq 2T$$

In particular,

$$(4.10) \quad V(x, 2T) = a_E V_E [1 - a_E G(x_E, x_E; T)] G(x, x_E; T) + a_E V_E G(x, x_E; 2T)$$

Proceeding to the next time interval,  $2T < t \leq 3T$ , we find in the same way that  $V(x, 3T)$  consists of a linear combination of  $G(x, x_E; T)$ ,  $G(x, x_E; 2T)$  and  $G(x, x_E; 3T)$ . We infer that in general  $V(x, nT)$  can be expressed as a linear combination of  $G(x, x_E; T)$ ,  $\dots$ ,  $G(x, x_E; nT)$ .

A recursive formula for  $V(x, nT)$

Let us therefore put

$$(4.11) \quad V(x, nT) \doteq \sum_{k=1}^n a_{nk} G(x, x_E; kT),$$

where the constant coefficients  $a_{nk}$  are found as follows. For  $nT < t \leq (n+1)T$ , put  $t' = t - nT$ . Then in this time interval,

$$(4.12) \quad \begin{aligned} V(x, t') &= \int \sum_{k=1}^n a_{nk} G(y, x_E; kT) G(x, y; t') dy \\ &+ \int \int G(x, y; t' - s) a_E [V_E - V(y, s)] \delta(y - x_E) \delta(s) ds dy \\ &= \sum_{k=1}^n a_{nk} G(x, x_E; t' + kT) + a_E G(x, x_E; t') [V_E - V(x_E, t' = 0)] \end{aligned}$$

or

$$(4.13) \quad \begin{aligned} V(x, t) &= \sum_{k=1}^n a_{nk} G(x, x_E; t - nT + kT) \\ &+ a_E G(x, x_E; t - nT) \left[ V_E - \sum_{k=1}^n a_{nk} G(x_E, x_E; kT) \right], \\ &nT < t \leq (n+1)T. \end{aligned}$$

Substituting  $t = (n+1)T$  in this formula,

$$(4.14) \quad \begin{aligned} V(x, (n+1)T) &= \sum_{k=1}^n a_{nk} G(x, x_E; (k+1)T) \\ &+ a_E G(x, x_E; T) \left[ V_E - \sum_{k=1}^n a_{nk} G(x_E, x_E; kT) \right] \\ &= a_E \left[ V_E - \sum_{k=1}^n a_{nk} G(x_E, x_E; kT) \right] G(x, x_E; T) + \end{aligned}$$

$$\begin{aligned} &+ \sum_{k=1}^n a_{nk} G(x, x_E; (k+1)T) \\ &\doteq \sum_{j=1}^{n+1} a_{n+1,j} G(x, x_E; jT). \end{aligned}$$

( $\doteq$  means we are defining new symbols.)

We can now read off the recursive relation which gives, in summary,

$$(4.15) \quad V(x, nT) = \sum_{k=1}^n a_{nk} G(x, x_E; kT)$$

$$(4.16) \quad a_{11} = a_E V_E,$$

$$(4.17) \quad a_{n+1,1} = a_E \left[ V_E - \sum_{k=1}^n a_{nk} G(x_E, x_E; kT) \right],$$

$$(4.18) \quad a_{n+1,k} = a_{n,k-1}, \quad k = 2, 3, \dots, n+1.$$

The full time dependent solution is given by (4.13) when the coefficients  $a_{nk}$  are found from (4.16)–(4.18).

Assuming that the cell is capable of producing spikes, and given a suitable threshold condition and boundary conditions, the time interval between output spikes can be computed from the above formulas. Such calculations cannot be done analytically and are quite lengthy, especially for finite cables. MacGregor (1968) has performed such calculations for excitatory inputs at various locations for an infinite cable with an assumed exponentially decaying threshold at the soma ( $x=0$ ). An interesting claim was that the frequency transfer curves saturate at high input frequencies due to the diminution of the amplitude of the postsynaptic potentials.

*The steady state*

Experimental evidence (see for example Curtis and Eccles, 1960) points to the existence of a steady state distribution of potential when subthreshold synaptic inputs are stimulated indefinitely. Examination of the recursion relations (4.17) and (4.18) shows that  $a_{\infty k} = a$ ,  $k = 1, 2, \dots$ . Hence, from (4.17),

$$(4.19) \quad a = \frac{a_E V_E}{1 + a_E \sum_{k=1}^{\infty} G(x_E, x_E; kT)}$$

and the steady state distribution of potential at the time of arrival of the input is

$$(4.20) \quad V^*(x) = a \sum_{k=1}^{\infty} G(x, x_E; kT).$$

Whereas formulas (4.19) and (4.20) enable the steady state voltage to be found at the times of arrival of the synaptic input, in order to find the steady state distribution of potential *between* inputs,  $V^*(x)$  must be used as the initial condition in conjunction with an impulsive conductance change at " $t=0$ " (quotes indicate that reference is to infinite times). From formula (4.4), the steady state *epsp* is given by

$$(4.21) \quad \tilde{V}(x,t) = \int V^*(y)G(x,y;t)dy + a_E \int_0^t \int_0^t [V_E - \tilde{V}(y,s)] \delta(s) \delta(y-x_E) G(x,y;t-s) ds dy$$

for " $0 < t \leq T$ " in the steady state. On substituting for  $V^*$  from (4.20) and using (4.7), there results

$$(4.22) \quad \tilde{V}(x,t) = a \sum_{k=1}^{\infty} G(x, x_E; t+kT) + a_E [V_E - V^*(x_E)] G(x, x_E; t)$$

If this is truly the steady state potential it must return at " $t=T$ " to its value at " $t=0$ ". It will be verified, with the aid of (4.19), that this is indeed the case; namely, that

$$(4.23) \quad \tilde{V}(x, T) = V^*(x).$$

The results obtained for the steady state *epsp* under repetitive impulsive conductance changes should correspond, in a first approximation, to the experimental results on repetitive monosynaptic excitation of various nerve cells reported by Eccles (1964, p. 84 *et seq.*). Terminal responses were measured for various frequencies of stimulation, corresponding to different and approximately known values of  $T$ . It is possible that on evaluation of the formulas for  $V^*(0)$  and  $V(0,t)$ , " $0 < t \leq T$ ", which give the voltage at the origin (soma), the parameters  $a_E$ ,  $V_E$  and  $x_E$  could be estimated from the experimental data, thus providing information on the nature and location of the synaptic transmission.

#### 4.2 Synaptic Input with Steady Current at the Origin

Let an excitatory impulsive conductance change, representing synaptic input, occur at the point  $x_0$  at time  $t=0$ . Then the voltage satisfies

$$(4.24) \quad V_t = V_{xx} - V + a_E [V_E - V(x,t)] \delta(x-x_0) \delta(t), \quad 0 < x < L.$$

Suppose that prior to the arrival of the synaptic input, a constant current  $I_0$  was injected at the origin (soma) and a steady state distribution of potential,  $U(x)$ ,  $0 \leq x \leq L$ , had been attained throughout the cell. To be specific, suppose a lumped soma boundary condition is appropriate at  $x=0$  and a sealed end condition applies at  $x=L$ . Thus,

$$(4.25) \quad V_x(L,t) = 0,$$

$$(4.26) \quad V(0,t) + V_t(0,t) - \gamma V_x(0,t) = I_0 R_s,$$

where  $R_s$  is the soma resistance and  $\gamma$  is the ratio of the conductance of a characteristic length of the trunk to the conductance of the soma. The initial condition is

$$(4.27) \quad V(x,0) = U(x).$$

The response is the same as if  $V(x,t)$  satisfied the equation

$$(4.28) \quad V_t = V_{xx} - V + a_E [V_E - U(x_0)] \delta(x-x_0) \delta(t),$$

with the same boundary data. Then the potential is given by

$$(4.29) \quad V(x,t) = U(x) + W(x,t),$$

where  $W$  satisfies

$$(4.30) \quad W_t = W_{xx} - W + a_E [V_E - U(x_0)] \delta(x-x_0) \delta(t),$$

$$(4.31) \quad W(0,t) + W_t(0,t) - \gamma W_x(0,t) = 0,$$

$$(4.32) \quad W_x(L,t) = 0.$$

That is,  $W$  is a constant multiple of the Green's function,  $G(x, x_0; t)$ , for the usual cable equation. Hence

$$(4.33) \quad V(x,t) = U(x) + a_E [V_E - U(x_0)] G(x, x_0; t).$$

If other boundary conditions are applied at  $x=0$  and  $x=L$ , then the Green's function to be used in this formula is the one appropriate to those boundary conditions.

Equation (4.33) gives for the potential at  $x=0$  (soma, assumed site of recording electrode),

$$(4.34) \quad V_s(t) = U(0) + a_E [V_E - U(x_0)] G(0, x_0; t).$$

If  $U(x_0) = V_E$  there will be no observable response at the soma to the synaptic input. Let the value of the potential at the origin, at which the response to an excitatory input becomes hyperpolarizing, be  $U_R$ . To find the true reversal potential, the formula for the steady state potential under the application of the constant current  $I_0$  at the origin must be employed. This gives, in the case of a sealed end at  $x=L$ ,

$$(4.35) \quad V_E = \frac{U_R \cosh(L-x_0)}{\cosh L},$$

for the actual reversal potential. Thus a knowledge of both the location of the input and the electrotonic length of the nerve cylinder is needed to accurately obtain the reversal potential if the latter is judged from observations of the somatic response.

## 5. Concluding Remarks

Synaptic reversal potentials were introduced into differential equations for nerve membrane potential after it was realized that the action of neurotransmitters was to change the postsynaptic membrane's permeability or conductance to various ionic species. In their theory of the action potential in squid axon, which does not involve synaptic transmission, Hodgkin and Huxley (1952) employed separate Nernst potentials and separate conductances for  $Na^+$ ,  $K^+$  and "leakage" ions. Fatt and Katz (1953) introduced a variable membrane conductance to represent inhibitory neuromuscular synapses in crab. Eccles (1957) employed circuits with variable conductances in series with batteries to represent both excitatory and inhibitory synapses in spinal motoneurons.

In Rall's first papers (1959, 1960) on cable theory for dendritic trees, the usual cable equation was employed, but these were not concerned with synaptic input. In two subsequent papers (Rall 1962a, 1962b) the excitatory and inhibitory reversal potentials were used and incorporated into a differential equation but the applications considered were somewhat artificial. In most subsequent papers by Rall and other authors (e.g., Jack and Redman, 1971; Ianssek and Redman, 1973), the reversal potentials were ignored. Although this provides a less complete description, the omission of reversal potentials was not especially significant because these authors were concerned with *epsp*'s elicited from resting level.

MacGregor (1968) employed an excitatory synaptic reversal potential in a calculation of the response of an infinite cable to an impulsive conductance change and of the response to a sequence of such inputs. He emphasized how nonlinear interactions between synaptic inputs would be significant for synapses close in space when they were activated at points close in time. Barrett and Crill (1974) also employed the cable equation with reversal potentials in their computation of motoneuron responses to synaptic input. More recently, Koch, Poggio and Torre (1983) and Koch and Poggio (1985) have incorporated synaptic reversal potentials in finding the response of model nerve cells with dendritic trees to various patterns of synaptic inputs.

It is clearly important, based on the results obtained thus far, that synaptic reversal potentials should be included in calculating nerve cell subthreshold responses to multiple synaptic inputs. This is true despite the fact that using (1.9) or (3.2) instead of (1.1) often means a more difficult computational problem.

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