DISTINGUISHING THEORETICAL SYNAPTIC POTENTIALS COMPUTED FOR DIFFERENT SOMA-DENDRITIC DISTRIBUTIONS OF SYNAPTIC INPUT

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By means of computational experiments with a mathematical neuron model, it is possible to make many detailed predictions, some of which can be tested by comparison with suitably controlled experimental observations. In particular, a theoretical model which permits a choice of both the time course and the soma-dendritic location of synaptic input, makes it possible to explore the way in which the shape of a synaptic potential can be expected to depend upon these two aspects of synaptic input. It is also possible to explore such related problems as the following: the effect of superimposing various combinations of synaptic input, both excitatory and inhibitory, and at various locations; the effect of applied hyperpolarizing current upon the shape of a synaptic potential; and the detectability at the neuron soma of a synaptic conductance transient located in the dendrites.

Many such computational experiments have been carried out, with two somewhat different objectives in mind. One objective has been to explore and gain insight into the general properties of the theoretical model, while the other objective has been to test the applicability of this theoretical model to the particular case of motoneurons in the cat spinal cord. The experimental observations presented in several companion papers (1, 8, 15) have provided an unusual opportunity for such a comparison of theory and experiment. This comparison has been carried out as a collaborative effort; the implications of this for our understanding of synaptic potentials in cat motoneurons are presented in a separate paper (14). The present paper is not about motoneurons, but about the properties and implications of the more general theoretical model.

There are several positive advantages to separating the consideration of a general model from its application to a particular neuron type. The general model can be tested for applicability to different neuron types; some applications may differ only in the value of the membrane time constant needed to relate a general result to a particular neuron type; other applications may differ in the values of theoretical parameters corresponding to electrotonic length or to the time course of synaptic current; still other applications may require explicit consideration of several sets of dendrites, such as the basal and apical dendrites of pyramidal cells.
Theoretical predictions that cannot be tested experimentally are usually regarded as scientifically meaningless; however, it is important to distinguish between predictions that could never be tested, and others that are testable, in principle, but which require greater experimental control or finesse than is currently available. The present research provides several illustrations of the latter. For example, when synaptic input is located in the dendrites, a comprehensive computation can provide not only the synaptic potential time course predicted to occur at the soma, but also the time course of the synaptic current and the transient membrane depolarization at the dendritic location, as well as the details of the electrotonic spread of current and of membrane depolarization from the dendrites to the soma. Such details are not easily tested in neurons; yet these details can have great value in enriching our physical intuitive understanding of such related events. We can build our physical intuition upon the quantitative answers to precise questions obtained for the theoretical model, and this physical intuition can then be helpful in the interpretation of approximately similar experimental observations.

Several examples of the differences between the brief synaptic potential computed when synaptic input is restricted to the neuron soma or proximal dendrites, and the slower rising and longer lasting synaptic potential computed when synaptic input is restricted to distal portions of the dendrites have appeared as illustrations in previous theoretical papers (12, 13). The earliest theoretical results relating the time course of a synaptic potential to the time course of nonuniformly distributed synaptic current appeared in 1959 (9). The fact that passive decay (as seen at the soma) should be fastest when membrane depolarization is greatest at the soma, and slowest when membrane depolarization is greatest in the dendritic periphery was demonstrated theoretically and illustrated graphically in 1960 (11, p. 515–516, 521, 528–529). The theoretical basis for transforming an extensively branched neuron into an equivalent cylinder, and for representing nonuniform distributions of synaptic excitatory and/or synaptic inhibitory membrane conductance, was presented in 1961, and this theory was used to compute an early illustrative comparison of synaptic potential shapes obtained for synaptic input restricted to half of the soma-dendritic surface (12, Fig. 7). The use of a compartmental model of soma-dendritic surface was introduced in 1962 as means of computing the consequences of many spatio-temporal patterns of synaptic input (13). Because of the new quantitative experimental detail now available (1, 8, 14, 15) the present computations have avoided the artificiality of step changes in synaptic conductance value by introducing a smooth transient synaptic conductance time course as the synaptic input.

METHOD

Compartmental model. For most of these computations, the soma-dendritic surface of a neuron has been represented as mathematically equivalent to a chain of 5 or 10 equal compartments. This concept is illustrated schematically in Fig. 1, where the dashed lines divide
the dendritic branching system into 5 regions of equal membrane surface area. When each such region is approximated as a compartment, in which the membrane capacity and the several parallel membrane conductances (see inset in upper right of Fig. 1) are treated as lumped electric parameters, the essential simplifying assumption is that spatial nonuniformity within each region is completely neglected. Spatial nonuniformity of the whole neuron is represented only by the differences between regions.

Soma and dendritic compartments. With the most commonly used chain of 10 compartments, shown at bottom of Fig. 1, the neuron soma has been identified with compartment 1, while compartment 10 represents a lumping of the most peripheral portions of all dendritic trees belonging to this neuron model. The intermediate compartments represent increments of electrotonic distance, as measured from the dendritic trunks to the dendritic periphery.

Electrotonic distance, $Z$. In a dendritic tree, the electrotonic distance, $Z_i$, from the soma to any dendritic point $x_i$, can be defined by the integral

$$Z_i = \int_0^{x_i} \frac{dx}{\lambda}$$
where \( x \) measures actual distance along the lengths of successive branches from the soma to the point in question, and \( \lambda \) represents the characteristic length (or length constant) which changes with branch diameter at each point of branching. For a branching system that is transformable to an equivalent cylinder (12), or to a chain of equal compartments (13), each dendritic compartment represents not only an equal amount of membrane surface area, but also an equal increment in electrotonic distance (12, 13). Thus, for the 10-compartment chain at the bottom of Fig. 1, the increment per compartment usually had the value, \( \Delta Z = 0.2 \); then the values, \( Z = 1.0 \) in compartment 6, and \( Z = 1.8 \) in compartment 10, express the corresponding electrotonic distances away from the soma compartment. Occasionally, computations were done with \( \Delta Z = 0.1 \), or with \( \Delta Z = 0.4 \) as the electrotonic increment per compartment.

**Mathematical model.** The actual mathematical model is a system of ordinary differential equations which are linear and of first order; some coefficients are constants, but others (those related to synaptic conductance) are functions of time. This system of equations was presented and derived in a previous publication (13).

**Dimensionless variables of the model.** The state of the system at any time is defined by three variables in each compartment. Two of these are independent variables representing synaptic excitatory and inhibitory conductance, while the dependent variable represents membrane potential. When there is externally applied current, this must be considered as an additional independent input variable. Each of these variables has a very specific definition in the mathematical model. Also, each variable is defined as a dimensionless ratio that has a useful physical intuitive meaning.

**Synaptic intensity variables.** The synaptic excitatory intensity, \( \alpha \), and the independent synaptic inhibitory intensity, \( \beta \), must be specified for each compartment. They are defined as the membrane conductance ratios,

\[
\alpha = \frac{G_e}{G_r}, \quad \beta = \frac{G_i}{G_r}
\]

where \( G_e \), \( G_r \), and \( G_i \) are parallel membrane conductances in the electrical equivalent circuit shown as an inset in Fig. 1; \( G_r \) represents resting membrane conductance in series with the resting battery, \( E_r \); \( G_e \) represents synaptic excitatory conductance in series with the synaptic excitatory battery, \( E_e \); \( G_i \) represents synaptic inhibitory conductance in series with the synaptic inhibitory battery, \( E_i \). The values of \( E_e \), \( E_r \), and \( E_i \) are assumed to remain constant. This formal model (12, 13) is only a slight generalization of more familiar membrane models (2, 3, 6). The two variables, \( \alpha \) and \( \beta \), will sometimes be referred to as synaptic input; the time course in each compartment is prescribed and, for all of the present computations, is assumed to be independent of membrane potential and of applied current.

**Membrane potential disturbance, \( v \).** This variable provides a dimensionless measure of the deviation of membrane potential from its resting value. It is defined

\[
v = \frac{(V_m - E_r)}{(E_e - E_i)}
\]

where \( V_m \) represents the potential difference across the membrane (inside potential minus outside potential).

The variable, \( v \), is normalized in the sense that

\[v = 1, \quad \text{when} \quad V_m = E_r\]

Thus, excitatory deviations from the resting potential are represented as positive values on a scale extending from 0 to 1. These positive values of \( v \) correspond to membrane depolarization; this is consistent with the experimentally observed positivity of intracellularly recorded excitatory synaptic potentials. The value, \( v = 1 \), corresponds to the limiting amount of depolarization, for \( \alpha \) very large, and \( \beta \) small, and in the absence of applied current.

Peak amplitudes of \( v = 0.01 \) and \( v = 0.1 \) were obtained in several series of computed synaptic potentials. This means depolarization one-hundredth or one-tenth of the way toward the limiting value. For example, if \( (E_e - E_i) = 70 \text{ mv} \), then \( v = 0.01 \) corresponds to 0.7 mv, and \( v = 0.1 \) corresponds to 7 mv. Negative values of \( v \) represent membrane hyperpolarization. For example, if \( (E_i - E_r)/(E_e - E_i) = -0.1 \), then this value represents the limiting negative value of \( v \) (for \( \beta \) much larger than \( \alpha \), and in the absence of applied current).

**Dimensionless time variable, \( T \).** This variable is defined

\[T = t/\tau\]
where \( t \) represents time and \( \tau \) represents the passive membrane time constant. Results expressed in terms of \( \tau \) can be equally valid for neurons which may have different membrane time constants.

**Dimensionless slope divided by peak.** Although the theoretical slope, \( \frac{dv}{dT} \), is already a dimensionless quantity, the comparison of experimental and theoretical rising slopes of synaptic potentials is facilitated by considering the value of the slope divided by the peak amplitude of the synaptic potential. This dimensionless quantity can be expressed

\[
\frac{(dv/dT)_p}{V_p} = \frac{\tau (dv/dt)_p}{V_p}
\]

where \( V = V_m - E_r \) is in millivolts, \( dV/dt \) is in millivolts per millisecond (i.e., volts per second), and subscript, \( p \), designates the peak value of \( v \) or \( V \). Usually, the slope has been measured at the point where the rising synaptic potential reaches half of its peak amplitude, i.e., the point halfway up; sometimes the slope was also measured at the point halfway down. To compare with experiment, consider, for example, a rising slope of 12 \( \text{v/sec} \) for a synaptic potential having a peak amplitude of 4 \( \text{mv} \), then \( (dv/dt)_p / V_p = 3 \text{msec}^{-1} \), and, for a membrane time constant, \( \tau = 5 \text{ msec} \), we obtain a dimensionless value of 15 for the slope over peak defined above.

**Depolarizing current density.** The dimensionless slope, \( \frac{dv}{dT} \), is also a dimensionless measure of net depolarizing current density. This net current refers to the difference between the actual synaptic current at the region in question, and the loss current composed of electrotonic current spread to neighboring regions and of current that leaks across the local passive membrane resistance. The actual net depolarizing current density can be expressed

\[
C_m \frac{dV_m}{dt} = \left[ C_m (E_r - E_i) / \tau \right] \frac{dv}{dT}
\]

where \( C_m \) represents the membrane capacitance. For example, if \( C_m = 1 \ \mu F/cm^2 \), \( (E_r - E_i) = 70 \text{mv} \), and \( \tau = 5 \text{msec} \), the factor enclosed by the square brackets has a value of 14 \( \mu \text{amp} / \text{cm}^2 \).

**Computation method.** The computations were carried out with the computer program SAAM 22, on the IBM 7094 at the National Bureau of Standards. The computer program is the current version of a program developed over a period of years by Berman, Weiss, and Shahn; it is especially suited for computations with compartmental models, and contains many features that contribute to its versatility. One feature is that the computations can be required to adjust the values of one or more parameters to obtain a least squares fit between the theoretical points and several data points, this feature was used to find, for any given compartmental and temporal distribution of synaptic input, \( \delta \), the magnitude of \( \delta \) that produces a synaptic potential having a prescribed peak value (usually \( v = 0.01 \), or \( v = 0.10 \)). Another feature is that one or more parameters can be required to vary with time in proportion with any prescribed transient function; this feature was used to prescribe smooth time variation of synaptic input, \( \delta \) and/or \( \beta \), in one or more compartments.

**Synaptic transient function.** Most of the computations used a transient of the form defined by

\[
F(T) = \left( T/T_p \right) \exp \left( 1 - T/T_p \right)
\]

where \( T \) represents dimensionless time as a variable starting from zero, and \( T_p \) is a constant to be selected. This transient has the following features, \( F(T) = 0 \) for \( T = 0 \), \( F(T) = 1.0 \), the peak value, at \( T = T_p \), and \( F'(T) \) returns to zero for large values of \( T \). Also \( F(T) = 0 \) at nearly \( T = 0.23 \ T_p \) on the way up, and again at nearly \( T = 2.68 \ T_p \) on the way down; thus the half-width (width at half of peak amplitude) is very nearly \( 2.45 \ T_p \). The area under the entire curve equals \( cT_p \), where \( c \) is the base of the natural logarithms. Graphic examples of this transient are provided by the dotted curves in Figs. 2 and 4. The three particular choices of \( T_p \) used most, 0.02, 0.04, and 0.092, provide the transients referred to in the text as “fast,” “medium,” and “slow” input transients.

**Fast input transient.** This transient reaches its peak at \( T = 0.02 \), and has a half-width (duration at half of peak amplitude) of about 0.049 in units of \( T \). For a membrane time constant of \( \tau = 5 \text{ msec} \), this would imply a peak time of 0.1 msec, and a half-width of about 0.245 msec.

**Medium input transient.** This transient reaches its peak at \( T = 0.04 \), and has a half-
width of about 0.098 in units of $T$. For a membrane time constant of $\tau = 5$ msec, this would imply a peak time of 0.2 msec, and a half-width of about 0.49 msec.

Slow input transient. This transient reaches its peak at $T = 0.092$, and has a half-width of about 0.225 in units of $T$. Also, the area under this curve is 0.25 in units of $T$; this area equals that of a rectangular pulse of unit height and of duration 0.25 in units of $T$, such as the synaptic input used in numerous earlier computations (cf. 13, Fig. 6).

**RESULTS**

I. **Different shapes of computed synaptic potentials**

**Effect of synaptic input location.** Four examples of computed excitatory postsynaptic potentials (EPSP) are illustrated by the solid curves in Fig. 2.

![Graph](http://jnp.physiology.org/)

**FIG. 2.** Comparison of four EPSP shapes computed for a chain of 10 compartments. Dotted curve shows the assumed excitatory conductance transient; it is the medium input time course defined in METHODS. Curve A shows the EPSP for equal input in all compartments. Curves B, C, and D all show an EPSP for equal input in compartment 1 for different cases of synaptic input restricted to 1 of the 10 compartments. For curve B, synaptic input was in compartment 1 alone; for curve C, input was in compartment 4 alone; for curve D, input was in compartment 8 alone. Ordinate scale represents amplitudes relative to each peak amplitude. The same EPSP shapes were obtained for peak amplitudes, $u = 0.01$ and $u = 0.10$; the synaptic intensity required for each case can be found (below) in Table 3.

The obvious differences in shape are due to differences in the location of synaptic input assumed for each computation. Exactly the same time course of synaptic excitatory conductance was assumed in each case; this time course, shown as a dotted curve, is the medium input transient defined above (in METHODS). Curve A shows the EPSP computed for the case of synaptic input distributed equally to all compartments. This EPSP reaches peak value at $T = 0.20$ and has a half-width of 0.88 in units of $T$. Curve A represents not only the EPSP that occurs in the soma compartment, but also the time course of membrane depolarization in every dendritic compartment; there is no electrotonic spread between compartments for this case of equal
synaptic input to all compartments. After the synaptic input transient is completed (after $T = 0.3$ for this medium input transient), the decay of such a spatially uniform EPSP is a simple passive exponential decay.

Curves B, C, and D illustrate 3 examples of EPSP shapes computed in the soma compartment of a chain of 10 compartments when the synaptic input was localized to a single compartment. Thus curve B was obtained when synaptic input was restricted to the soma compartment, curve C was obtained with input restricted to compartment 4, while curve D was obtained with input restricted to compartment 8. Although synaptic excitatory conductance had the same (dotted) time course as for case A, larger synaptic intensities were required in cases B, C, and D, in order to obtain an EPSP of the same peak amplitude as curve A.

Curve B rises about 1.65 times as fast as curve A, reaches its peak in about half the time required by curve A, and has a half-width that is only one-third that of curve A. Also, when both curves have decayed to half of peak amplitude, curve B falls three times as fast as curve A; this faster decay can be understood intuitively as the consequence of electrotonic spread from the soma compartment toward the dendritic compartments (cf. 11, p. 515–516, 528–529).

Curve C is somewhat similar to reference curve A; however, there are significant differences. Curve C rises more slowly and falls more rapidly than curve A; the slower rise can be understood intuitively as the consequence of electrotonic spread from the input compartment (no. 4) toward the soma, while the faster fall is the consequence of electrotonic spread away from compartments 1, 2, 3, and 4, toward the peripheral dendritic compartments.

Curve D is more delayed, rises more slowly, has a more rounded peak, and begins to decline more slowly than the other curves. The half-width value of 1.42, in units of $T$, is nearly five times that of curve B, and is 60% larger than that of curve A. This sluggish rise to a very rounded peak can be understood intuitively as the consequence of electrotonic spread from the distal dendritic input compartment (no. 8) to the soma.

**EPSP shape and amplitude.** The 4 EPSP shapes in Fig. 2 illustrate equally well the results obtained for several different EPSP amplitudes. In particular, 1 complete set of results having the small EPSP peak, $u_p = 0.01$, was compared with another set having a 10-fold larger peak amplitude. When these results were scaled relative to their peak amplitudes (as in Fig. 2), the 2 sets of EPSP curves differed negligibly (i.e., rarely by more than the thickness of the curve). To understand why shape distortions occur for still larger EPSP amplitudes, and why the agreement is not exact even at small amplitudes, it is necessary to remember that the synaptic input has been treated as an excitatory conductance transient. For small amounts of membrane depolarization, the time course of synaptic current is essentially the same as that of the synaptic conductance. For a large transient membrane depolarization at the synaptic input location, the effective driving
potential (for synaptic current) changes enough to cause a significant distortion of synaptic current time course; this can result in a significant change of EPSP shape. In practice, one is usually concerned with small EPSP amplitudes (i.e., less than $v_p = 0.2$). For this range of practical interest, the EPSP shape computed for a given synaptic input location and time course can be regarded as approximately independent of EPSP amplitude.

Quantitative shape indices. The comparison of computed EPSP shapes with experimentally observed EPSP shapes can be facilitated by focusing attention upon a few quantitative measures. Definitions of several shape indices are stated below. These shape indices are used in Table 1 to summarize the computed results obtained for the same medium input transient as in Fig. 2, and for the same chain of 10 compartments having an over-all electrotonic length equal to twice the characteristic length.

Table 1. Quantitative EPSP shape characteristics
(chain of ten compartments: medium & transient)

<table>
<thead>
<tr>
<th>Location of Synaptic Input</th>
<th>All Cpts</th>
<th>Cpt 1</th>
<th>Cpt 2</th>
<th>Cpt 3</th>
<th>Cpt 4</th>
<th>Cpt 5</th>
<th>Cpt 6</th>
<th>Cpt 7</th>
<th>Cpt 8</th>
<th>Cpt 9</th>
<th>Cpt 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of peak (from $T=0$)</td>
<td>0.20</td>
<td>0.11</td>
<td>0.16</td>
<td>0.22</td>
<td>0.29</td>
<td>0.47</td>
<td>0.73</td>
<td>0.86</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to peak (from EPSP foot*)</td>
<td>0.19</td>
<td>0.10</td>
<td>0.14</td>
<td>0.19</td>
<td>0.24</td>
<td>0.38</td>
<td>0.59</td>
<td>0.67</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Same, for $\tau = 5$ msec</td>
<td>0.05 msec</td>
<td>0.5 msec</td>
<td>0.7 msec</td>
<td>0.95 msec</td>
<td>1.2 msec</td>
<td>1.9 msec</td>
<td>2.9 msec</td>
<td>3.3 msec</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Half-width time</td>
<td>0.88</td>
<td>0.29</td>
<td>0.42</td>
<td>0.57</td>
<td>0.73</td>
<td>1.14</td>
<td>1.42</td>
<td>1.46</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Same, for $\tau = 5$ msec</td>
<td>4.14 msec</td>
<td>1.45 msec</td>
<td>2.1 msec</td>
<td>2.8 msec</td>
<td>3.6 msec</td>
<td>5.7 msec</td>
<td>7.1 msec</td>
<td>7.3 msec</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slope/peak: halfway up</td>
<td>9.4</td>
<td>15.5</td>
<td>11.0</td>
<td>8.4</td>
<td>6.8</td>
<td>4.5</td>
<td>2.6</td>
<td>2.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$(dV/dT)/v_p$ for $\tau = 5$ msec</td>
<td>1.0 msec$^{-1}$</td>
<td>3.1 msec$^{-1}$</td>
<td>2.2 msec$^{-1}$</td>
<td>1.7 msec$^{-1}$</td>
<td>1.4 msec$^{-1}$</td>
<td>0.9 msec$^{-1}$</td>
<td>0.6 msec$^{-1}$</td>
<td>0.5 msec$^{-1}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slope/peak: halfway down</td>
<td>$-0.5$</td>
<td>$-1.32$</td>
<td>$-1.05$</td>
<td>$-0.81$</td>
<td>$-0.65$</td>
<td>$-0.48$</td>
<td>$-0.47$</td>
<td>$-0.47$</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Time of foot defined as point of intersection with the base line of a line drawn from the point halfway up, through the point one-tenth way up. Except where noted otherwise, time is dimensionless, $T=t/r$.

Time and peak. It is useful to distinguish between time of peak, measured from the time of synaptic input initiation ($T=0$ in Fig. 2) and time to peak measured from the “foot” of the EPSP. The time, $T=0$, is easy to obtain for a computed EPSP, but is usually not known for an experimental EPSP. The foot of the EPSP is sometimes characterized as the point where EPSP rise can first be detected; an alternative, used here is to define the time of the foot operationally as the point of intersection with the base line, of a line drawn through the two points where the rising EPSP attains 10% and 50% of its peak amplitude. When this operational definition is applied to Fig. 2, the time of foot values, $T=0.05$ and $T=0.14$, are obtained for curves C and D. In Table 1 the values of time to peak (from EPSP foot) range from $T=0.10$ to $T=0.87$ (or from 0.5 msec to 3.3 msec for $\tau = 5$ msec).

Half-width. This quantity provides a useful measure of the sharpness of an EPSP; it is defined as the width of the EPSP at half of peak amplitude. For the series in Table 1, the half-width is about three times the time to
peak, for single compartment locations from 1 to 6; this factor becomes progressively smaller for input locations 8 and 10, but it is more than 4.6 for the case of uniform input to all compartments.

**Rising slope divided by peak.** The slope, $\frac{du}{dT}$, is determined at the point where the rising EPSP attains half of its peak amplitude; this slope is often the maximal rising slope. An amplitude independent quantity is obtained by dividing this slope by the EPSP peak amplitude. The resulting dimensionless shape index values cover a sixfold range, from 2.5 to 15.5 in Table 1. Thus, for a membrane time constant, $\tau = 5$ msec, the quantity, $\frac{(du/dt)/u_p}{\tau}$, ranges from 0.5 msec$^{-1}$ for input to compartment 10 alone, to 3.1 msec$^{-1}$ for input to compartment 1 alone. There is an approximate inverse proportionality between these rising slope/peak values and the time-to-peak values, in other words, the time to peak is approximately 1.6 times the reciprocal of the rising slope/peak value. A similar proportionality was found to apply to many experimental EPSP shapes, and also to theoretical EPSP shapes computed with either the fast or the slow synaptic conductance time course.

**Falling slope divided by peak.** Here the slope, $\frac{dv}{dT}$, is determined at the point where the falling EPSP attains half of the EPSP peak amplitude and this slope value is divided by the peak amplitude. A value of $-0.5$ corresponds to uniform passive decay. The cases where synaptic input was confined to compartments 1, 2, 3, or 4 all fall more rapidly than this because of electrotonic spread out into the peripheral half of the chain, while the cases where synaptic input was confined to compartments 6, 8, or 10 fall slightly more slowly because of electrotonic spread toward the soma from the peripheral half of the chain.

**Plot of half-width versus time to peak.** In comparing these theoretical EPSP shapes with EPSP shapes observed in motoneurons, it was found useful to represent each shape as a point in a two-dimensional plot: the ordinate of each point is the half-width value, while the abscissa is the corresponding time to peak. Several examples of such shape index plots are illustrated in a companion paper (14). Such plots provide a means of grasping and comparing the variety of EPSP shapes found for different values of the theoretical parameters.

**Effects of fast, medium, and slow synaptic input transient.** Table 2 provides a summary comparison of EPSP shapes obtained in three different computational series, using the three cases, fast, medium, and slow, of synaptic conductance time course defined in METHODS. The numerical details of Table 2 are presented with the hope that they may be found useful in the examination of experimental results from various neuron types having different membrane time-constant values, and a similar time course of synaptic current or synaptic conductance; one example of this (for cat motoneurons) is provided in a companion paper (14). Here, comments are made about only a few general aspects of these numerical results. Perhaps most striking is the fact that changing the input time course at single compartmental locations has a proportionately much larger effect for proximal input loca-
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Tions than for distal input locations. For example, both the time-to-peak values and the slope/peak values change by a factor of about 3.5 (fast to slow) for input in compartment 1, compared with a factor of 1.3 (fast to slow) for input in compartment 10; the corresponding factors for half-width are somewhat smaller. The increment of change in time-to-peak values remains more nearly constant; this increment has a value of 0.15 (fast to slow) for input in compartment 1 or 10. This can be understood approximately as follows: this common time increment represents primarily the shift of peak depolarization in the input compartment caused by the change in the synaptic input time course. The half-width does not behave in the same way; the increments themselves decrease as input is shifted to more distal locations, so much so that for inputs in compartment 8 or 10, the EPSP

Table 2. EPSP shape index values comparing effects of fast, medium, and slow synaptic input transients

<table>
<thead>
<tr>
<th>Location of Synaptic Input</th>
<th>All Cpts</th>
<th>Opt 1</th>
<th>Opt 2</th>
<th>Opt 3</th>
<th>Opt 4</th>
<th>Opt 6</th>
<th>Opt 8</th>
<th>Opt 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to peak (from foot)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fast</td>
<td>0.11</td>
<td>.06</td>
<td>.09</td>
<td>.14</td>
<td>.19</td>
<td>.33</td>
<td>.54</td>
<td>.61</td>
</tr>
<tr>
<td>Medium</td>
<td>0.19</td>
<td>.10</td>
<td>.14</td>
<td>.19</td>
<td>.24</td>
<td>.38</td>
<td>.59</td>
<td>.67</td>
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<tr>
<td>Slow</td>
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<td>.21</td>
<td>.25</td>
<td>.31</td>
<td>.37</td>
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<tr>
<td>Fast</td>
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<td>.18</td>
<td>.33</td>
<td>.50</td>
<td>.69</td>
<td>1.12</td>
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<td>.73</td>
<td>1.14</td>
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<td>.53</td>
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<td>.75</td>
<td>.89</td>
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<td>(dV/dT)/Vp, halfway up</td>
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<td>5.1</td>
<td>4.3</td>
<td>3.2</td>
<td>2.4</td>
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</table>

half-width value changes by less than 5% over this range of synaptic input time course. Apparently the EPSP half-width is determined primarily by the slowing and rounding effects of electrotonic spread from these distal input locations. This conclusion receives additional support from the fact that the same half-width values were also obtained with a square synaptic conductance pulse (duration ΔT = .25) at these same distal input locations.

Effect of different electrotonic length. Computations were carried out to discover how the EPSP shape index values change when the chain of 10 compartments is assumed to have a different effective electrotonic length. This is important because of uncertainties about the correct value of the characteristic length constant, λ, even in experimental situations where the actual dimension of the dendritic branches are fairly well known. As defined in METHODS, an electrotonic length increment, ΔZ = 0.2 per dendritic compartment, implies a value, Z = 1.8, for the electrotonic length of the 9 dendritic compartments. This length was used in computing the EPSP shapes of Tables 1 and 2. Other computations were carried out with ΔZ = 0.1, implying
Z = 0.9 for the 9 dendritic compartments, and with ΔZ = 0.4, implying Z = 3.6 for the dendritic chain.

Two useful approximate generalizations can be stated: doubling ΔZ approximately doubles the time-to-peak value obtained for a given input compartment; a smaller factor, between 1.4 and 1.5, of increase was found for the half-width values. More detailed results are summarized in Fig. 3, which uses a common Z scale to plot the dendritic input locations in the 3

![Diagram](http://jn.physiology.org/)

Fig. 3. Effect of dendritic electrotonic length upon EPSP shape index values. Three cases, ΔZ = 0.1, 0.2, and 0.4 per dendritic compartment, are shown. The three sets of compartment numbers, shown at left, are spaced to fit a common ordinate scale, expressed as electrotonic distance, Z, shown at right. For each input location (as ordinate), both the time-to-peak and the half-width values were plotted (as abscissa). The solid lines connect points plotted for case (ΔZ = 0.4) where compartment 10 is Z = 3.6 distant from the soma, implying a value, Z = 3.6, for the dendritic electrotonic length. The dashed lines represent the case (ΔZ = 0.2) implying a value, Z = 1.8, for dendritic electrotonic length. The dotted curves represent the case (ΔZ = 0.1) implying a value, Z = 0.9, for the dendritic electrotonic length. The fast synaptic input transient (see METHODS) was used for all of these cases.

sets of computations; time-to-peak values and half-width values were both plotted (as abscissa), for each of the several input locations (as ordinate). It is instructive to compare two examples of input at the electrotonic distance, Z = 1.2, away from the soma. Both compartment 4 with ΔZ = 0.4, and compartment 7 with ΔZ = 0.2 are at this distance from the soma. In both cases, the time-to-peak value was 0.45 in the EPSP computed at the soma; however, the input in compartment 7 resulted in a longer half-width value (1.31) than that (1.15) for the input in compartment 4. Both this particular difference, and the deviations of the shorter curves from the longer curves in Fig. 3, are consistent with earlier generalizations stating that electrotonic spread toward the soma from the distal half of the chain causes the
early decay to be slower than a spatially uniform decay, while electrotonic spread from the proximal half to the distal half of the chain causes faster early decay. Figure 3 has the merit of displaying both shape index values plotted versus one Z scale that is common to the three cases. For other purposes it is useful to plot each of these half-width values against its corresponding time-to-peak value; such a plot can be found in a companion paper (14, Fig. 6).

Comment on nonuniqueness. From the preceding figures and tables, it is apparent that one cannot infer the location and time course of synaptic input from EPSP shape alone. Most of these computed EPSP shapes can be at least approximately duplicated by several alternative combinations of synaptic input location and time course; by permitting multiple input locations, the number of possible combinations becomes greatly increased (14). When an EPSP is very brief, this restricts consideration to more proximal locations and to faster input transients, but some reciprocity of choice remains within this range. When an EPSP is very slow, either or both slow input time course and electrotonic distance of input location may be responsible. With slow experimental EPSP shapes one must beware of the possible effects of temporal dispersion of synaptic activity. In any given application to experimental EPSP shapes, it is important to assess the extent to which one can safely assume reasonable ranges of values for these three unknowns: synaptic conductance time course, restricted location of synaptic input, and dendritic electrotonic length.

Comment on 5 or 10 compartments. Because quite a few computations were done with a chain of 5 compartments, the effect of this upon EPSP shape merits a brief statement. In particular, comparisons were made between a 5-compartment chain having $\Delta Z = 0.4$ per compartment, and the 10-compartment chain having $\Delta Z = 0.2$ per compartment. The essential difference is a factor of 2 in the coarseness of lumping. As might be expected intuitively, it was found that the EPSP shape computed for synaptic input restricted to 1 coarse lump (e.g., compartment 2 of the chain of 5) was approximately the mean of the 2 EPSP shapes computed for the same synaptic input time course restricted to one or the other of the 2 corresponding finer lumps (e.g., compartment 3 or 4 of the chain of 10).

Combinations of synaptic input locations. It should be noted that the variety of computed EPSP shapes is greatly increased when the synaptic input is not restricted to a single location. Several examples of this are pro-

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1 The mathematical treatment of such equalizing electrotonic spread (12) implies the existence of several equalizing time constants which are smaller than the passive membrane time constant. The relative values of these time constants depend upon the electrotonic length of the equivalent cylinder or chain of compartments. Experimental determination of the first equalizing time constant, relative to the passive membrane time constant provides a means of estimating the underlying electrotonic length of the system. For the particular case of cat motoneuron EPSP's, this experimental determination is complicated by the unknown process that causes EPSP decay to end in an after-hyperpolarization; the response to an applied current pulse appears better suited for this experimental determination, as has recently been verified by P. G. Nelson (personal communication).
vided in a companion paper (14, Fig. 5). Two examples are provided in a later section of the present paper (Fig. 5) in the course of illustrating a more general argument. A brief generalization can summarize the results of many such computations: for any given synaptic excitatory conductance time course, a somatic or proximal dendritic input location contributes especially to the early rising portion of the EPSP, while a distal input location contributes toward a longer half-width and toward a slower rise and fall; the particular time-to-peak value and half-width value depend upon the relative weights of the proximal and distal contributions of the two component EPSP's (see Fig. 5 below for an illustration). It is helpful to note that for EPSP shapes of small amplitude and different input locations, the two component EPSP shapes sum almost linearly. Conditions for nonlinear summation are discussed in a later section of this paper, and (13, 14).

II. Computational dissection of synaptic and other electric current relating transient excitatory conductance to the resulting EPSP

Only when synaptic input is uniform over the entire soma-dendritic surface is it correct to deduce the time course of synaptic current from the EPSP by a simple application of the differential equation

\[ I = C \frac{dV}{dt} - \frac{V}{R} \]

for a single lumped resistance in parallel with a single lumped capacitance. In cases where synaptic input is distributed nonuniformly, unmodified application of the above procedure would be expected to result in erroneous inferences; such errors would be further compounded if incorrect values of the membrane time constant were used (see 11 for a discussion of such errors).

In an actual physiological case of localized dendritic synaptic input, it would be extremely difficult to measure the true time course of synaptic current at the dendritic location, and to compare this with the time course of the electrotonic spread current which actually depolarizes the soma. Here, advantage is taken of the complete information that can be obtained from computational simulation of such situations.

The example illustrated in the right-hand side of Fig. 4 represents a case of synaptic input that was restricted to compartment 6 of a chain of 10 compartments. The dotted curve at upper right represents the time course of the excitatory conductance transient in compartment 6, while the solid curve at lower right represents the resulting EPSP in compartment 1. All of the dashed curves represent electric currents, each of which plays a role in the complex of events relating the EPSP to the conductance transient. The uppermost dashed curve represents the synaptic current that is generated in compartment 6 by the excitatory conductance transient. Its time course
FIG. 4. Computational dissection comparing transients of conductance, current, and voltage in perturbed compartment and in compartment 1, for 2 cases. Top left shows the $E$ transient in compartment 2 of a chain of 10 compartments; this was responsible for all of the current and voltage transients shown on the left side of the figure. Top right shows the $E$ transient in compartment 6 of a chain of 10 compartments; this was responsible for all of the current and voltage transients shown on the right side of the figure. Both $E$ transients are plotted to a common ordinate scale, expressed as dimensionless $E$ values. All of the current transients, shown as dashed lines at left and right, have been plotted to a common ordinate scale; the ordinate scale values express the dimensionless slope, $du/dT$. All of the voltage transients, shown as solid curves at left and right, have been plotted to a common ordinate scale; however, the dimensionless $v$ values are exactly one-tenth of the numerical scale shown; the EPSP peak amplitude in compartment 1 is $v = 0.10$ in both cases.

is very similar (but not identical)$^2$ to that of the conductance transient. This synaptic current is not completely available for depolarizing the membrane capacity in compartment 6; it must also supply the "loss current" consisting of current spread from compartment 6 to compartments 5 and 7, as well as a small leak, or self decay, through the resting membrane resistance of compartment 6.

A graph of this loss current is shown superimposed upon that of the synaptic current, and these two currents can be seen to be of quite comparable

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$^2$ This synaptic current reaches its peak value at $T = 0.075$, which is earlier than the time, $T = 0.092$, of peak conductance. This can be understood in terms of the effective driving potential, $(1-v)$, which falls as the membrane becomes more depolarized. The synaptic current is proportional to the product, $(1-v)E$, in compartment 6. At $T = 0.075$, rounded values are $v = 0.19$ and $E = 9.7$; thus, the synaptic current is proportional to $(0.81)(9.7) = 7.9$, at this time. At $T = 0.092$, rounded values are $v = 0.22$ and $E = 9.9$; thus, the synaptic current is smaller, being proportional to $(0.78)(9.9) = 7.7$, at this later time.
magnitude. The loss current has a smaller and later peak, but for times greater than \( T = 0.19 \), the loss current exceeds the synaptic current. It is the difference between these two currents that must be regarded as the net depolarizing current in compartment 6. This net current is also shown in the figure, together with the voltage transient in compartment 6. This net current peaks earlier and has a peak amplitude that is less than half that of the actual synaptic current; also, this net current is negative for times greater than \( T = 0.19 \), because this is when the loss current exceeds the synaptic current. For the same reason, the peak depolarization in compartment 6 also occurs at \( T = 0.19 \), and the decay from peak depolarization is faster than for a purely passive decay of a uniformly distributed depolarization.

But this is not the end of the story. So far, attention has been focused upon the dendritic location designated as compartment 6. What happens at the soma, here represented as compartment 1? One could present, in turn, the current spread from compartment 6 to 5, then 5 to 4, 3 to 2, and finally 2 to 1; only the net current from compartment 2 to compartment 1 is illustrated in Fig. 4. This current has a much smaller and later peak than the synaptic current or any of the other currents illustrated. However, from the perspective of compartment 1, it is this current that generates the EPSP by flowing into the parallel resistance and capacity of compartment 1.

This EPSP reaches its peak amplitude \((v = 0.1)\) at \( T = 0.62 \), and the early part of its decay is slower than for a case of passive decay of a uniformly distributed depolarization. This slower decay can be attributed to the tail of current spreading to the soma from the dendrites; however, one should hasten to add that this entire EPSP must be attributed to current spread from the dendrites.

Further understanding of these results can be obtained by comparing the right and left sides of this figure. The left side represents a similar computation for the case of synaptic input confined to compartment 2, which may be thought of as corresponding to the proximal portions of the dendritic trunks. The left and right sides have been plotted to the same scale, to facilitate visual comparisons of amplitude and time course. Thus, in compartment 2, with the same excitatory conductance time course, the required amplitude is only one-fourth that required in compartment 6. The synaptic current at left is slightly more than one-fourth that at right. The relation of loss current and synaptic current is qualitatively similar at left and right. The net depolarizing current in the perturbed compartment is smaller and slower at left; the peak is one-fourth as great and the reversal to negative values occurs at \( T = 0.24 \) as compared with 0.19 at right. As before, this necessarily defines the time of peak depolarization in the perturbed compartment, and the decay is more rapid than for passive decay of a uniformly distributed depolarization. The time course of current flowing from compartment 2 to compartment 1 is shown at lower left; this time course is proportional to the difference between the voltage transients in these two compartments, both of which are shown as solid curves at left. This current has
negative values for times greater than $T = 0.36$; this means that the spread of current into the dendrites is sufficient to make the depolarization in compartment 2 decay more rapidly than in compartment 1; after $T - 0.36$, there is a flow of current all the way from compartment 1, through compartment 2, into the dendritic periphery.

Perhaps favorable experimental preparations will permit a test of some of these predictions in the near future. At present, it seems fair to say that such computations help to illustrate the importance of synaptic input location to a consideration of the relation between synaptic current, the loss current due to electrotonic spread, and the net depolarizing current in any given compartment.

III. Synaptic intensity required at different soma-dendritic locations: amount of nonlinearity for different amplitudes and locations

If the same EPSP amplitude is to be obtained, at the soma compartment, it is intuitively obvious that a greater intensity of synaptic excitatory conductance is needed when synaptic input is confined to a single compartment, as compared with equal input to all compartments. Also, for a chain of equal compartments, it would be expected intuitively that the required synaptic intensity would increase with increasingly distal compartmental location, because of the electrotonic attenuation expected during passive spread from the distal compartment to the soma. To go beyond such qualitative expectation, it is best to refer to the computational results.

Rows A and C of Table 3 list the peak values of synaptic excitatory intensity (peak $G$) found necessary to produce the two EPSP series (small and large) whose shapes were illustrated in Fig. 2 and summarized in Table 1; the small EPSP series had peak $v = 0.01$ in the soma compartment, while the large EPSP series had peak $v = 0.10$ in the soma compartment. In rows A and C, it can be seen for both series that the synaptic intensity (peak $G$) required in compartment 1 alone was about 2.4 times that required for equal input to all compartments, and that required in compartment 2 alone was...
about 3.7 or 3.8 times the value for all compartments. For these three synaptic input distributions, the peak ε values of row C are between 10 and 11 times those of row A, indicating approximate linearity over this 10-fold range of EPSP amplitude. Such approximate linearity does not hold, however, for the more distal input locations. In particular, for synaptic input restricted to compartment 10, row A shows a peak ε value that was about 28 times its reference value for all compartments, while row C shows a peak ε value that was about 204 times its reference value. Put another way, the peak ε value of 234 in row C is 76 times that in row A, although it produces an EPSP which is only 10 times larger; this represents a very significant nonlinearity. For input to compartment 8, the row C value is about 19 times the row A value, and for compartment 6, the corresponding factor is about 14; both indicate significant nonlinearity. To understand the essential difference between those cases showing very significant nonlinearity and other cases showing approximate linearity, it is important to examine the amount of depolarization that takes place in the compartment which receives the synaptic input, and to bear in mind that synaptic current is proportional to the product (1-ν)ε, as it varies with time in the input compartment.

**Peak depolarization at input compartment.** The time course of membrane depolarization in the input compartment (as illustrated in Fig. 3) was computed routinely in most of the synaptic potential computations. For each case in Table 3, the peak depolarization at the input compartment is tabulated as a number enclosed by parentheses. It can be seen that the values in row D are all about 10 times those in row B. However, it is instructive that in the extreme case of input to compartment 10, it was not possible for the peak v value in row D to equal 10 times that of row B, because the limiting value of v, for ε very large, is v = 1.0 (see Methods). This means that the 10-fold increase of the EPSP (at the soma) was achieved in spite of the amplitude limitation at the input compartment. The very large synaptic intensity (peak ε = 234) produced an atypical depolarizing transient in compartment 10: its peak occurred earlier (T = 0.06 as compared with T = 0.11), it had a saturated, flat-topped shape, and its area was presumably close to 10 times that of the undistorted depolarizing transient of the small EPSP series. It is not suggested that such extreme cases need occur in nature; equally potent distal synaptic input can be achieved with smaller synaptic intensity over 2 or 3 distal compartments. The essential point is that the 10-fold increase of the EPSP at the soma corresponds, in every case, to a 10-fold increase of the depolarizing transient at the input compartment. The nonlinearities demonstrated by the upper half of Table 3 can thus be ascribed to the more than 10-fold increase of synaptic intensity required to produce the 10-fold increase of depolarization in the input compartment. This nonlinearity is greatest for dendritic input locations where the peak depolarization is greatest. In other words, peak ε must increase more than 10-fold to compensate for the decrease in driving potential (1-ν). This source of non-
linearity was tested quantitatively by means of an additional set of computational experiments.

Nonlinearity of EPSP amplitude increase for a 10% increase of synaptic intensity. For each of the synaptic intensity values in row A of Table 3, another EPSP was computed with a synaptic intensity that was 10% larger in amplitude, but had the same time course as before. The results (not shown in Table 3) demonstrate how the percentage of increase in EPSP amplitude depends upon the amount of depolarization that occurred in the input compartment. When the original peak $v$ in the input compartment was around 0.01, the 10% increase of peak $v$ produced an EPSP amplitude increase of about 9.9%. Original peak $v$ values of 0.041 and 0.063 resulted in EPSP amplitude increases of 9.64% and 9.47%. For the larger EPSP series, original peak $v$ values of 0.405, 0.602, and 0.94, respectively, resulted in EPSP amplitude increases of 6.5, 4.6, and 1.5%, respectively. In most of these cases the percentage increase of EPSP amplitude was fairly well approximated by the expression

$$P \approx 10(1 - 0.9y)$$

where $y$ represents the original peak $v$ value in the input compartment, and $P$ represents the percentage increase of EPSP amplitude for 10% increase of synaptic intensity. As the original peak $v$ value ranges from 0 to 1.0, the quantity inside the parentheses ranges from 1.0 to 0.1; the departure of this quantity from unity is obviously a measure of the nonlinearity for small increments of perfectly synchronous synaptic input at the same location.

This nonlinearity is similar to that derived earlier for muscle end plate potentials (7), and that derived for initial slopes and steady-state depolarizations in response to a step conductance change (12, 13). However, the end-plate potential treatment explicitly neglected reactances, and neither treatment provided for a smooth conductance transient, or for the computed peak of a transient depolarization; also neither calculation of nonlinearity provided for distant input locations. All of these difficulties are provided for in the present computations. Thus, it is useful to have determined that all of these nonlinearities are rather similar, when attention is focused on the membrane depolarization at the site of the conductance transient.

Large nonlinearities implicate dendritic conductance transients. The computed results summarized above provide the theoretical basis for a recognition of the significance of occasional large nonlinearities observed in the summation of EPSP amplitudes (1, 14). First, a significant nonlinearity is, by itself, suggestive evidence for a membrane conductance transient at the input location. Second, when the observed nonlinearity significantly exceeds that which could be accounted for in terms of the peak depolarizations at the soma, this suggests that the synaptic input occurred at dendritic locations, sufficiently distant and sufficiently circumscribed to account for the needed peak depolarization at the input location. It is not necessary that the addi-
tional synaptic input should occur at the same location as the control input; it would be sufficient for the control input to generate a depolarization which, as it spreads to the location of the additional synaptic input, is of sufficient magnitude (at the time of this additional conductance transient) to account for the nonlinearity.

**Synaptic intensity with slow conductance time course.** It should not be surprising that the peak synaptic intensity (peak $\varepsilon$) required to produce a given EPSP amplitude is reduced when the time course of the synaptic conductance is changed from the medium transient to the slow transient. This can be verified in Table 3 for the large EPSP amplitude ($v = -0.10$) at the several input locations tabulated (row $E$ compared with row $C$). Since, for unit peak amplitude, the area under the slow transient is 2.3 times that under the medium transient, it is not surprising that the required peak $\varepsilon$ for uniform input to all compartments was about half as much for the slow conductance transient as for the fast conductance transient (0.58 compared with 1.15); one can understand why the full factor of 2.3 was not obtained by noting that the slow transient has a significant tail at times after the EPSP peak is attained. For input locations near the soma, this factor is even smaller, because the EPSP peak occurs earlier. For input locations beyond compartment 5, the factor relating peak $\varepsilon$ values exceeds 2.3, because the EPSP peaks occur later, and because the fast dendritic transients encroach farther into the nonlinear domain.

One functional implication of this result is that a small amount of temporal dispersion can enhance summation of input to a common peripheral dendritic location, while the same amount of temporal dispersion can reduce the peak summation for brief input delivered to the soma or a proximal dendritic location.

**Synaptic inhibitory conductance intensity at different locations.** The lower part of Table 3 shows the results of a series of computed inhibitory postsynaptic potentials (IPSP). These were computed with the slow conductance time course. It was assumed that the limiting value, $(E_i - E_r)/(E_e - E_r) = -0.1$, and the prescribed IPSP amplitude was half of this ($v = -0.05$), corresponding to $-3.5\text{ mV}$ if $E_e - E_i = 70\text{ mV}$. Because this prescribed IPSP amplitude represents half the limiting amplitude, it should not be surprising that the required peak $g$ values display very significant nonlinearity. If linearity had held perfectly, these peak $g$ values would have been exactly 5 times the peak $\varepsilon$ values for EPSP amplitudes of $v = 0.10$; however Table 3 shows ratios closer to 10, for several input locations. At compartment 6, the nonlinear saturation effect is so great that even a 100 times greater conductance peak is not sufficient. The large $g$ values are needed to compensate for the small driving potential. An interesting functional implication of this result is that distal dendritic synaptic inhibition is not effective in producing an IPSP at the soma, although this same input could be very effective against synaptic excitation delivered to the same dendritic locations (4, 5, 12, 13).

**Combinations of synaptic excitation and inhibition at different locations.** It
proved instructive to compute the results of combining some of the excitatory and inhibitory synaptic inputs that have already been presented separately in rows $E$ and $G$ of Table 3. Thus, for example, when peak $\varepsilon =1.75$ and peak $\gamma =13.9$ were placed simultaneously in compartment 1, the resulting synaptic potential had a peak amplitude, $u = 0.0124$, that was significantly smaller than would have been obtained by a simple summation of the synaptic potential amplitudes, $u = +0.10$ and $u = -0.05$, obtained separately. Quite another result was obtained when peak $\varepsilon =5.01$ and peak $\gamma =72.2$ were placed simultaneously in compartment 4; the resulting synaptic potential had the opposite sign; its peak amplitude, $u = -0.0146$ in compartment 1 resulted from a peak hyperpolarization, $u = -0.0224$, in compartment 4. This rather surprising result can be understood by noting that the peak $\gamma$ value in compartment 4 was more than 10 times the peak $\varepsilon$ value in compartment 4, and this factor more than compensates for the 10-fold smaller inhibitory driving potential. In other words, the synaptic inhibition was more powerful than the synaptic excitation, even though the separate synaptic potential amplitudes, $u = +0.10$ and $u = -0.05$, were the same as above. This extreme example provides a further illustration of the fact that synaptic potentials observed at the soma do not provide a reliable measure of the relative potency of synaptic excitation and inhibition combined at a common dendritic location. It is more than sufficient to account for the observations (14, Fig. 7B) which we have attributed to interaction at a dendritic location.

Other computations, in which synaptic excitation and inhibition were placed in different dendritic trees of the same neuron, demonstrated that such electrotonic separation of input locations can account for the linear summation of EPSP and IPSP that is sometimes observed experimentally (14, Fig. 7A).

IV. Effects of steady hyperpolarizing current upon EPSP shape

There have been numerous experiments and interpretations concerned with the effects of a steady hyperpolarizing current. This current is applied inward across the soma membrane between an intracellular microelectrode and a distant extracellular electrode; after the nerve membrane has reached a steady state of hyperpolarization, an EPSP is evoked by synaptic input; the shape of this EPSP is compared with that obtained without membrane hyperpolarization. The question is: what change in EPSP shape should one expect to find for various soma-dendritic locations of synaptic input? It was pointed out in 1960 (11, p. 522–523 and 528–529) that “... steady state hyperpolarization of the membrane must be greatest at the soma and must decrease electrotonically with distance along the dendrites. Under such conditions (with uniformly distributed synaptic input), both the density of synaptic current and the amount of depolarization caused by the brief excitatory conductance increase must be greatest at the soma. This nonuniformity will cause a more rapid EPSP decay.” At that time, however, a detailed consideration of the effects upon EPSP rising slope as compared with EPSP...
amplitude was not attempted. Also, at that time, the phenomenon of anomalous rectification (8) had not received much attention. Here, attention will be focused upon EPSP properties that can be predicted without complication by anomalous rectification. The focus is upon the consequences of different synaptic input locations when synaptic input is represented as a transient increase of excitatory membrane conductance.

**Expected increase of EPSP slope and amplitude.** For EPSP computations with such steady-state hyperpolarization, should one expect both the rising slope and the peak amplitude of the EPSP to increase by the same factor? The answer is no, in general, but yes for all cases when synaptic input is restricted to a single compartmental location. This answer has been verified by numerous examples of such EPSP computations; it is explained below in physical intuitive terms; a mathematical demonstration will be given elsewhere.

**Electrotonic decrement of steady-state hyperpolarization.** In an equivalent cylinder of electrotonic length, $Z_m$, the relative values of steady-state hyperpolarization, as a function of electrotonic distance, $z$, can be expressed as $\frac{\cosh(Z_m - z)}{\cosh Z_m}$, on the assumption that hyperpolarizing current is applied at one end, $Z = 0$, of the cylinder, and that the other end, $Z = Z_m$, is a sealed end (see ref. 9 or 10, Fig. 3). For a chain of five compartments, with $\Delta Z = 0.4$ per compartment, and with $Z = 0$ in compartment 1, we have $Z_m = 1.6$ at the dendritic terminal in compartment 5. With this value of $Z_m$, consider, for example, a steady-state hyperpolarization that amounts, in compartment 1, to a 20% increase of the synaptic excitatory driving potential. For this case, the decreasing amounts of steady-state hyperpolarization in the four dendritic compartments are 14% in no. 2, 10% in no. 3, and roughly 8% in both nos. 4 and 5.

**Factor of EPSP increase for single input location.** When the synaptic excitatory conductance transient is restricted to a single compartment, the effect of steady-state hyperpolarization is to increase the computed EPSP amplitude by the same factor over its entire time course; thus both the rising slope and the peak amplitude are increased by precisely the same factor. This factor exactly equals the factor of increase in synaptic current, which exactly equals the factor of increase in the excitatory driving potential at the particular compartment in which the synaptic conductance transient is assumed to occur. Only when the synaptic input occurs at the soma will this factor of increase be the same as that of the excitatory driving potential at the soma; then a 20% hyperpolarization at the soma would produce a 20% increase in EPSP slope and amplitude. Such a case is illustrated by curves $A_1$ and $A_2$ in Fig. 5. In contrast, curves $B_1$ and $B_2$ result from synaptic input restricted to compartment 4 of a five-compartment chain. Here the slope and amplitude of curve $B_2$ are only 8% greater than those of curve $B_1$, and this corresponds to the 8% steady-state hyperpolarization in compartment 4 when 20% hyperpolarization is maintained at the soma compartment. In other words, the electrotonic decrement of steady-state hyperpolarization is responsible for a
different increase of excitatory driving potential at each compartmental location, and it is the factor of increase in driving potential at the one-compartment receiving synaptic input that determines the factor of increase in EPSP slope and amplitude. In these cases, EPSP shape is unchanged.

**EPSP shape change with compound synaptic input locations.** When synaptic input is distributed to two or more compartments, the effect of steady-

![Diagram](http://jn.physiology.org/)

**Fig. 5.** Effect of steady-state membrane hyperpolarization (applied at soma), upon computed EPSP shape for (A) proximal input, (B) distal input, and (C) combined proximal and distal input. Subscript 1 designates each control EPSP computed without hyperpolarization. Subscript 2, designates the increased membrane potential transient at the soma compartment obtained with a steady-state hyperpolarization equal to 20% at the soma compartment. Computations were with a five-compartment chain, with \( \Delta Z = 0.4 \); the medium time course of synaptic membrane conductance was used for all cases. Case (A) corresponds to peak \( \varepsilon = 0.10 \) in compartment 1; case (B) corresponds to peak \( \varepsilon = 0.55 \) in compartment 4; case (C) corresponds to a combination of these two inputs; one unit of the ordinate scale corresponds to \( \Delta w = 0.001 \), for these particular peak \( \varepsilon \) values.

state hyperpolarization upon the EPSP is more complicated. The peak amplitude is increased by a factor that is smaller than the factor of increase in the early rising slope; also, the peak occurs earlier in time, and the fall to half of peak amplitude also occurs earlier. These changes, it should be emphasized, are predicted without introducing any complications due to anomalous rectification. These changes can be understood in terms of the different amounts of increase in the synaptic excitatory driving potential at the several compartments receiving synaptic input. The input compartment nearest to the soma has the largest factor of increase in driving potential; this factor largely determines the factor of increase in the early rate of rise of the EPSP. Thus, in Fig. 5, where curves \( C_1 \) and \( C_2 \) were generated by a compound synaptic input (in compartments 1 and 4), the early slope (halfway up) is 20%
greater in $C_2$ than in $C_1$, as it is also in $A_2$ compared with $A_1$. However, the peak amplitude of $C_2$ is only 14% greater than that of $C_1$, and the time of peak is shifted from $T = .43$ to $T = .17$, providing a fairly extreme example of such a shift. Also, one can deduce that $C_2$ falls to one-half of its peak amplitude at an earlier time than does $C_1$, because the peak of $C_2$ is 14% greater, while the tail amplitude of $C_2$ is only 8% greater than that of $C_1$.

This one example shows why it should not be expected, in general, to have EPSP shape remain the same with and without steady-state hyperpolarization. Nevertheless, it should be added that the experimental observations (8) include cases where the rising slope is increased by as much as 20% without any significant increase of peak amplitude; in such cases, the phenomenon of anomalous rectification (8) presumably contributes as much or more to the EPSP shape change as does the compound input location effect illustrated in Fig. 3.

**Different observations with hyperpolarizing current.** It is possible to account for several different experimental observations that might, at first glance, appear to conflict with the theoretical predictions. For example, hyperpolarizing current can produce a large increase of EPSP amplitude with an EPSP shape of very slow time course. These slow EPSP shapes do not imply distal dendritic synaptic input; in all cases that have come to my attention, these shapes can be explained by temporal dispersion of a polysynaptic input that could be somatic or proximal dendritic.

Sometimes a 30-mv hyperpolarization produces as much as a threefold increase of EPSP amplitude. To account for this, one must bear in mind that, when both synaptic excitatory and inhibitory activity are present, the synaptic “equilibrium potential” becomes a weighted mean of the separate excitatory and inhibitory values

$$E_{eq} = E_r + \frac{(E_x - E_r)E + (E_i - E_r)g}{\epsilon + g}$$

see and compare $V^*$ of (12) and $v_s$ of (13). For example, if the effective driving potential, $E_{eq} - V_m$, should happen to be 15 mv, then a 30-mv hyperpolarization would increase the effective driving potential to 45 mv, and this would account for a threefold increase in synaptic potential amplitude. Whenever one cannot exclude the possibility of temporal dispersion or the possibility of mixed excitatory and inhibitory effects, one must beware of requiring the theory to account for the observations without benefit of these additional degrees of freedom.

At the other extreme, there are experiments which produce no significant increase of EPSP amplitude with steady-state hyperpolarizing current. For such cases it is relevant to ask the magnitude of the smallest increase that could have been detected, and then to ask how dendritically remote the synaptic input would have to be to account for this theoretically, without the help of anomalous rectification. Suppose, for example, that the experimental
procedure would fail to detect a 4% increase, and that the hyperpolarization at the soma was 20%; this would require that the electrotonic decrement of the hyperpolarization from the soma to the synaptic input location be a factor of 5 or more. From a table of hyperbolic cosine values, one can see that $Z_m = 2.3$ would be a sufficient dendritic electrotonic length to account for this with terminal dendritic synaptic input. Alternatively, for longer dendritic electrotonic length ($Z_m \geq 4$), the synaptic input location would need only be $Z = 1.6$, to account for this much exponential decrement. In other words, an undetected increase of EPSP amplitude in such experiments need not conflict with theoretical predictions.

V. Detectability at the soma, of transient synaptic conductance at different soma-dendritic locations

The basic question to be answered here is this: given a dendritic synaptic conductance transient which generates an EPSP of respectable size at the soma, should one expect to obtain, with microelectrodes at the soma, experimental evidence that detects the synaptic conductance transient, as distinguished from a synaptic current transient? If experimental methods were perfect, the answer would certainly be yes; however, since there is significant experimental noise to contend with, the question becomes a quantitative one of estimating whether the theoretically predictable effect is large enough to detect by present experimental techniques. In fact, the theoretical results presented below suggest that the predicted effect for proximal dendritic input locations may be above the present threshold for experimental detection, while that for distal dendritic input locations may be below the present threshold for experimental detection. Future experiments may, of course, succeed in shifting the detection threshold.

Computational experiment. Although the experimental approach (15) has been to analyze transients obtained with an a-c impedance bridge technique, my own preference has been to consider a constant current applied at the soma, and to analyze the distortion of the EPSP transient that is theoretically predicted under such conditions. The results of computations for one case of transient dendritic synaptic conductance are illustrated in Fig. 6. In this case, the conductance transient was restricted to compartment 3 of a chain of five compartments (with $\Delta Z = 0.4$ per compartment). A constant current was applied to compartment 1 (the soma) at zero time; the two solid curves at left illustrate the passive response in compartment 1 to depolarizing and hyperpolarizing current. The two solid curves at right illustrate the slower and smaller passive response computed in compartment 3 for the same constant current applied at the soma. These solid curves thus represent control transients of membrane potential obtained in the absence of any synaptic conductance transient. Perfect symmetry between upper and lower curves reflects the fact that all membrane parameters are assumed to remain constant (i.e., independent of membrane potential).

Next, a synaptic conductance transient was introduced in compartment
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3 (at $T = 1.0$) after the initiation of a constant current at $T = 0$. This synaptic conductance had the medium time course (defined in METHODS, and shown at lower right of Fig. 6), and the synaptic intensity was made equal to that which would produce an EPSP amplitude of $v = 0.10$ in compartment 1 in the absence of applied current. The dashed curves in Fig. 6 show the distorted membrane potential transients that were computed for compartments

![Figure 6](image_url)

**Fig. 6.** Transients related to the detectability of a dendritic conductance change. The left side shows transients computed for compartment 1 in a chain of five compartments ($\Delta Z = 0.4$), while the right side shows transients computed for compartment 3. The solid curves at left and right show the voltage transients which result when a constant-current step is applied to compartment 1 at zero time; the upper solid curves result from depolarizing current; the lower solid curves result from hyperpolarizing current. The dashed curves show the change in these voltage transients computed when a brief synaptic excitatory input was put in compartment 3. The synaptic input began at $T = 1.0$, had a peak $E$ value of 9.52, and had the medium time course shown at lower right. The dotted curves show the deviation from the solid curves obtained in computations with the same conductance transient, but with $E_r - E_s$. The same dotted transients were also obtained by computing one-half of the difference between the upper dashed curve and the lower dashed curve. Amplitude scale expresses dimensionless units of $v$.

1 and 3 for both depolarizing and hyperpolarizing applied current. When the peak amplitudes of these dashed curves are measured as departure from the solid curve control transients, a simple generalization becomes apparent. In both compartments, the upper peak (obtained with depolarizing current) has an amplitude that is 10% smaller than it would be in the absence of the applied current, while the lower peak (obtained with hyperpolarizing current) has an amplitude that is 10% larger than it would be in the absence of the applied current. This 10% change in amplitude is easily explained by the effective driving potential in compartment 3 at the time of the synaptic con-
ductance transient; at this time, the two solid curves show depolarization or hyperpolarization corresponding to $v = \pm 0.1$, implying effective synaptic excitatory driving potentials $(1-v)$, that are 10% smaller or larger than the resting value. It should be added that this 10% distortion could be doubled to 20% simply by doubling the intensity of the applied current.

**Computational dissection of distortion due to conductance transient.** The deviation of the dotted curves from the solid curves is a measure of the above distortion alone. This can be obtained in two different ways. The easiest way, computationally, is simply to set the excitatory emf, $E_x$, equal to the resting emf, $E_r$, in all compartments. Then, in the absence of applied polarizing current, the conductance transient would produce no voltage transient whatever, but, in the presence of applied current, the dotted curves are predicted. The effective driving potential for the deviation of the dotted curves from the solid curves is simply the $v = \pm 0.1$ polarization in time of the conductance transient.

The significance of these dotted curves is that they represent the distortion imposed upon the solid control transients by the conductance transient, but without the excitatory emf. It is this distortion that is attributable to the conductance transient alone. It is the detectability of this distortion in compartment 1 that needs to be assessed.

The alternative method of obtaining these dotted curves consists essentially of canceling the effect of $E_x$ by taking a difference between two (dashed curve) transients. At both left and right in Fig. 6, the upper dotted curve can be obtained by taking, for every $T$, one-half the ordinate of the upper dashed curve minus one-half the ordinate of the lower dashed curve. Although the figure may show this imperfectly, this result was computationally precise; it is an exact mathematical consequence of assuming a linear system in which all coefficients, whether constant or time dependent, are independent of the membrane potential, and hence unchanged by both depolarizing and hyperpolarizing applied currents.

**Computed distortion related to a-c bridge imbalance.** The previous paragraph has been explicit about canceling the effect of $E_x$ by taking appropriate differences between transients of opposite polarity, because this concept is rather similar to that of averaging a-c bridge imbalance over all positive and negative phases of the sinusoidal period, as in the experimental method devised by Smith et al. (15). The end result of such averaging may be regarded as roughly comparable to the dotted distortion in compartment 1 of Fig. 6. The a-c method has a number of complications which have been discussed in the Appendix of (15).

**Computed distortion as percent distortion.** As noted earlier, the magnitude of the dotted distortion in Fig. 6 could be increased by increasing the intensity of the applied current. But this would also increase the amplitude of the solid curve control transients and, presumably, also the amplitude of the experimental noise which limits the precision of experimental measurements. Thus, it seems appropriate to express the amplitude of the computed distor-
tion as a percentage of the solid curve control amplitude. In compartment 3, this percentage is 33, but in compartment 1, where experimental observation would have to be made, the percentage distortion is only 3.5, as labeled in Fig. 6. The approximate factor of 10 relating these 2 percentages can be understood as due to a factor of nearly 3 in the electrotonic decrement of membrane polarization from compartment no. 1 to no. 3 at \( T = 1.0 \), and a factor of about 3.3 in the decrement of the transient peak amplitude from compartment no. 3 to no. 1. The resulting 3.5% distortion at the soma compartment probably lies close to the threshold for detection by the experimental techniques of Smith et al. (15).

**Effect of different input locations.** This computational experiment was repeated with different locations of the conductance transient. Each column of

<table>
<thead>
<tr>
<th>A. Perturbed compartment</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>All Five</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. Synaptic intensity (peak ( G )) in perturbed cpt</td>
<td>1.75</td>
<td>4.25</td>
<td>9.52</td>
<td>19.6</td>
<td>44.6</td>
<td>1.15</td>
</tr>
<tr>
<td>C. Time of peak distortion of ( v ) in cpt 1</td>
<td>1.13</td>
<td>1.26</td>
<td>1.42</td>
<td>1.65</td>
<td>1.82</td>
<td>1.15</td>
</tr>
<tr>
<td>D. Distortion of ( n ) in cpt 1 when ( E_r = E_c )</td>
<td>.027</td>
<td>.017</td>
<td>.010</td>
<td>.007</td>
<td>.005</td>
<td>.022</td>
</tr>
<tr>
<td>E. Distortion (( D )) expressed as percent of control response to current step alone</td>
<td>9.8</td>
<td>3.9</td>
<td>3.5</td>
<td>2.3</td>
<td>1.7</td>
<td>8.5</td>
</tr>
<tr>
<td>F. Distribution of ( v ) over five cpts, at ( T = 1.0 )</td>
<td>.266</td>
<td>.163</td>
<td>.098</td>
<td>.061</td>
<td>.044</td>
<td></td>
</tr>
<tr>
<td>G. Relative values of ( F )</td>
<td>1.0</td>
<td>.61</td>
<td>.37</td>
<td>.23</td>
<td>.17</td>
<td></td>
</tr>
</tbody>
</table>

Table 4 summarizes the results of one of these experiments; column 3 is the same as that already illustrated in Fig. 6. In each case, the conductance transient had the same medium time course, and its intensity (row B of table) was made equal to that previously found necessary to produce an EPSP of amplitude, \( v = 0.10 \), under normal conditions. When \( E_r = E_c \), the distortion in compartment 1, for each case, is expressed in dimensionless units of \( v \), in row D of the table. To assess the detectability of each distortion, it is expressed (in row E) as a percentage of the control transient (solid curves at left in Fig. 6) at the time of peak distortion (time shown in row C). This shows that a 9.8% distortion is predicted when the conductance transient occurs in compartment 1, while only a 1.7% distortion is predicted when the conductance transient occurs in compartment 5. Also, for the case of a conductance transient distributed equally to all five compartments, the last column shows a prediction of an 8.5% distortion.

**Detectability.** Thus, an experimental procedure which can detect only those distortions that exceed 3.5% would be expected to detect the distortion caused by the two cases of proximal input (columns 1 and 2), and by the equal input to all five compartments; it would fail to detect the two cases of
distal dendritic input (columns 4 and 5), and might barely detect the case of input to compartment 3 of the chain of five compartments. All of these cases, it should be noted, involve substantial conductance transients, each of which, under normal conditions, would produce an EPSP amplitude of $v \approx 0.10$ at the soma.

Electrotonic spread of membrane polarization provides key. Useful physical intuitive understanding of these results can be gained by comparing rows $D$ and $F$ of Table 4. Row $F$ shows the compartmental distribution of membrane depolarization, $v$ (at $T = 1.0$) due to the depolarizing current step applied to compartment 1 at $T = 0$; this was the same in each experiment. When $E_r = E_0$, these values correspond to what can be regarded as the effective driving potential in each compartment, for a conductance transient applied, at $T = 1.0$, to that compartment. Inspection shows that in each of the experiments, the distortion in compartment 1 (row $D$) is very nearly one-tenth of this effective driving potential (row $F$) of the perturbed compartment; the factor of 10 reflects the fact that the EPSP amplitude had been prescribed as one-tenth the normal driving potential. Also, the relative values (row $G$) of the membrane depolarization at $T = 1.0$ are related to the percent distortion values (row $E$) by nearly a factor of 10. In other words, relative detectability at the soma depends upon the relative amount of electrotonic spread from the testing electrodes to the site of the conductance transient.

Additional generalizations. This simple generalization provides a basis for understanding several other related generalizations. 1) If the transient conductance were initiated earlier than $T = 1.0$ for a constant current applied at $T = 0$, the electrotonic spread into the dendrites would be less, and the detectability of dendritic conductance change would be even worse than in Table 4. 2) From these idealized considerations alone, the detectability of dendritic conductance change would be greatest when the electrotonic spread from the applied current reaches a steady state. This fact can perhaps be exploited with some neuron types; however, in the case of cat motoneurons, anomalous rectification (8) complicates such steady states. 3) High-frequency sinusoidal applied current is useless for testing dendritic conductance change, because most of this current flows across the soma membrane capacitance (see ref. 11, p. 517 and 530). 4) At low frequencies, such as about 100 cycles/sec, a sinusoidal steady state reaches out into the dendrites with a spatial decrement similar to that shown in rows $F$ and $G$. For example, when a sinusoidal frequency of one-half cycle per $\tau$ (100 cycles/sec, if $\tau = 5$ msec) is applied to compartment 1 of a chain of five compartments, the relative steady-state sinusoidal amplitudes were found to be 1.0, 0.55, 0.30, 0.18, and 0.14, respectively (these may be compared with row $G$ of Table 4); also, the steady-state phase lags in compartments 1 through 5 were found to be approximately 45°, 72°, 100°, 125°, and 145°, respectively. 5) The fact that the distortion, row $E$, column 1, in Table 4 is very nearly 10% is no coincidence; it is a consequence of the fact that the magnitude of transient conductance in compartment 1 had already been selected to yield an EPSP amplitude equal
to 10% of the normal driving potential. Thus one can guess, and it was found, that when the magnitude of the transient conductance in compartment 1 is increased (more than doubled) to that required to produce a doubled EPSP amplitude, \( v = 0.20 \), then the percentage distortion corresponding to row \( E \) in the first column of Table 4 becomes increased to very nearly 90%; in fact, the complete series of computational experiments for this larger prescribed EPSP amplitude results in a new set of percentage distortion values which are essentially double those in row \( E \) of Table 4. Similarly for IPSP computations, when the IPSP amplitude was prescribed as halfway from resting potential to the inhibitory equilibrium potential, the percentage distortion values were found to be essentially five times those in row \( E \) of Table 4.

**Time course of transient distortion.** When the conductance transient is confined to a single compartment, the time course of the distortion in compartment 1 is essentially the same as that of the corresponding EPSP. This, it should be emphasized, is significantly slower than the time course of the synaptic conductance transient, as can be seen in Fig. 6 and also in Fig. 4. The situation is more complicated when synaptic conductance transients occur in more than one compartment; it is obviously even more complicated when synaptic inhibition is present as well as synaptic excitation; in these more complicated cases, the distortion should not be expected to have the same time course as the EPSP or the EPSP-IPSP combination. For the particular case of equal conductance transients in all compartments (column 6 of Table 4) the transient distortion peaked earlier and decayed faster than the corresponding EPSP; this distortion can be understood as a weighted sum of five component distortions, with the largest weight attached to the perturbation in compartment 1, and progressively smaller weights attached to the contributions of the other compartments. These theoretical results should serve to illustrate the fact that this transient distortion, which does provide evidence for the presence of a synaptic conductance transient, does not permit a simple inference of the synaptic conductance time course.

**Summary**

Extensive computations have been carried out with a mathematical neuron model which permits a choice of both the time course and the somadendritic location of synaptic input. The results provide quantitative predictions of the way in which the shape of a synaptic potential, as well as other properties of synaptic potentials, depend upon these spatial and temporal aspects of synaptic input. Quantitative details have been summarized in several tables and figures. Also, several qualitative generalizations have been developed as aids to intuitive understanding of these theoretical results. Specific applications of these theoretical results to the interpretation of experimental results from cat motoneurons are presented in a collaborative companion paper (14). The theoretical results have been presented in five parts.
Part I provides details of how the shapes of computed synaptic potentials can be characterized by means of the quantitative shape indices: time to peak, half-width, and rising slope/peak. The dependence of these shape indices upon synaptic input location, time course, and upon dendritic electrotonic length is demonstrated quantitatively and discussed in terms of electrotonic spread over the soma-dendritic membrane surface.

Part II provides a computational dissection of the several electric current transients and membrane potential transients that relate a dendritically located synaptic conductance transient to the resulting synaptic potential at the soma. These quantitative results, although not yet tested experimentally, provide insight into the distinctions that can and should be made between synaptic current, loss current due to electrotonic spread away from the input location, and the resultant, net depolarizing current. Both this net depolarizing current and the resulting membrane potential transient are distinguished at the dendritic input location and at the soma.

Part III provides details of the synaptic conductance intensities required at different locations in order to produce synaptic potentials of certain prescribed amplitudes. The nonlinearities, which tend to be greatest for distal dendritic input locations, are explained in terms of the amount of membrane depolarization occurring at the input location; significant membrane depolarization produces significant reduction in the effective driving potential. Reduced driving potential can be compensated for by increased intensity of synaptic conductance. Many examples of nonlinearity, both for various intensities of synaptic excitation and for combinations of synaptic excitation and inhibition, are illustrated and discussed.

Part IV explains the effects of steady-state hyperpolarizing current upon synaptic potentials in terms of the increase in effective driving potential at each site where a synaptic input conductance transient occurs. For single input locations, the slope and amplitude of the synaptic potential increase by the same factor, leaving the synaptic potential shape unchanged. For compound input locations, it is shown that the contribution of the proximal input location is augmented more than that of the distal dendritic input location (because of electrotonic decrement of the steady-state hyperpolarization), and a change in the shape of the synaptic potential is predicted. Comments are also made regarding anomalous rectification and other unusual observations with polarizing currents.

Part V presents quantitative results that are relevant to the detectability at the soma, of transient synaptic conductance at different dendritic locations. It is shown that relative detectability (for a given size of the control synaptic potential) depends upon the relative amount of electrotonic spread from the testing electrodes to the input location. For a suitable detection threshold, this could explain failure to detect conductance transients at distal dendritic locations under conditions which permit detection of conductance transients at proximal dendritic locations.

A theme common to all of these computations and interpretations is that
results, which may appear paradoxical when examined only at the soma, can be understood quite simply when attention is directed to the synaptic input location with special attention to the effective driving potential there.

REFERENCES