*carpus*, and *Gonolobus* were, respectively, 85.7, 85.7, 86.0, and 84.4 g.
11. These were collected in their natural environment in Mayaro, Trinidad, W.I., during December 1967 ($N = 50$, $\bar{X} = 0.115$ g, S.D. $= 0.028$ g).
12. See reviews in: L. P. Brower and J. V. Z. Brower, *Zoologica* **49**, 137 (1964); P. R. Ehrlich and P. H. Raven, *Evolution* **18**, 586 (1965); T. Eisner and J. Meinwald, *Science* **153**, 1341 (1966).
13. J. B. Sale [*East African Wildlife J.* **3**, 127 (1965)] has noted the mammal *Hyrax* feeding upon poisonous plants. H. B. Cott [*Proc. Zool. Soc. London* **123** (1), 123 (1953) and **124** (2), 335 (1954)] has shown that the eggs of certain bird species are unpalatable to mammals.
14. Supported by NSF grant GB4924. We are grateful to Dr. O. M. Buchanan for providing facilities at the William Beebe Tropical Research Station, Professor James Q. Denton for mathematical advice, Dr. Jane V. Z. Brower for critical comments on the manuscript, Dr. David Wetherbee for catching the birds, and Diane Ryerson, Helen Sullivan, and Warren MacAvoy for technical assistance.
* Present address: Department of Biology, Yale University, New Haven, Conn. 06520.
24 June 1968

## Electrotonic Spread of Dendritic Potentials in Feline Pyramidal Cells

Abstract. *In pyramidal cells synaptic activation of the entire apical dendritic tree distal to the branch point of the major shaft can dominate the neuronal firing pattern. Uniform synaptic activation of distant parts of the dendritic tree (~ 750 microns from the soma) would produce potential changes at the soma of 2 to 3 percent of the magnitude of the dendritic potential changes. Even these small somatic potential changes could modulate the frequency of firing of neurons depolarized close to or above firing level by more proximal synaptic inputs.*

Physiologists, anatomists, and information theorists have long pondered the significance of synaptic endings upon distant dendrites of highly branched neurons. Controversy has centered upon the question of whether potentials generated upon distant dentrites would have any significant effect upon the soma and nearby axon hillock region.

We have analyzed the pyramidal cell of the cat motor cortex and estimated the upper and lower limits of attenuation of potential changes between the apical dendritic tree and the soma under "steady-state" conditions, a situation probably frequently approximated in maintained synaptic activity. The fact that the major apical dendritic shaft provides the single intracellular channel for spread of current from apical dendrites to soma simplifies analysis. Furthermore, the steady-state treatment obviates the need to consider membrane capacitances. We can calculate the potential ($V_b$) across the soma and basilar dendrites resulting from a synaptic bombardment of the dendritic tree distal to the major branch point (MBP) which sets up potential decrements ($V_2$ and $V_3$) upon the secondary and tertiary branches, respectively, resulting in a potential ($V_1$) at the MBP (Fig. 1A), where $V_3 \geqq V_2 \geqq V_1$. An equivalent resistive circuit (Fig. 1B) can be constructed from appropriately paired physiologic and new anatomic data. The only physiologic assumptions required are that the resting membrane potential is constant throughout the soma and dendritic trees and that the external resistivity between different leakage resistances and between these resistances and ground is small and can be neglected in these calculations, and the only anatomic assumption required is that any shrinkage during tissue fixation is small and can be neglected in the calculations. It is then required only to find limiting values for the ratio of apical dendritic to basilar dendritic conductance ($\alpha$) which can be done after presentation of the anatomic data. The attenuation ratios ($V_{sb}/V_1$) can then be calculated by application of Kirchoff's laws.

The theoretical advances of Rall (*1*), with applications of cable theory to branching dendritic trees, provided means of determining somatic membrane electrical constants from the type of data obtainable by intracellular microelectrode techniques. These methods were applied to the pyramidal cell of the motor cortex of the cat (*2*). In the best material on identified pyramidal cells the ratio of dendritic conductance to somatic conductance ($\rho$) ranged from 3 to 6.5. By using these respective values of $\rho$, we estimated the somatic membrane specific resistivity as ranging from 1500 to 4000 ohm cm$^2$. Total neuron "input resistances" ($R_I$) have been determined by Takahashi (*3*) and by us (*2*). The average values of $R_I$ for pyramidal cells with rapidly conducting fibers (30 to 60 meter/sec) were $5.9 \pm 2.8$ and $6.7 \pm 1.9$ megohm respectively. For any given value of specific resistivity ($R_m$) and $\rho$, the larger the cell, the smaller is the input resistance. Hence the value of 4.5 megohm, which is representative of the lower values of both groups, can be taken as the input resistance of the largest neocortical pyramidal cells in the cat.

The anatomic problem was to provide measurements on a group of large pyramidal cells comparable to those studied physiologically. Sholl (*4*) in his classic study of dendritic branching had used mostly kittens and had restricted his analysis to apical dendrites branching beyond the MBP. Neither he nor any other anatomist had provided data, crucial for our purposes, on the relations of length and diameter of the major apical dendritic shaft of the mature cat. Therefore, this data is provided by one of us (S.J.).

The brains from two adult cats (2.5 kg) were impregnated by the Golgi-Cox method, dehydrated, embedded in paraffin, and sectioned frontally at 60 $\mu$. All measurements were made $\times$ 1200 with a calibrated eyepiece. The pyramidal neurons were sampled as follows: the count was initiated in the anterior sigmoid gyrus and continued into the posterior sigmoid gyrus. On the examined sections the sample was taken by starting on the lateroventral surface and moving at 1 mm intervals dorsomedially until five cells had been counted. The next section was examined, and the same procedure was followed at 180 $\mu$

Table 1. Calculated values of resistances and electronic attenuations for various values of $\alpha$ and $\rho$.

| Values of | | $R_a$ (megohm) | $R_{sb}$ (megohm) | $R_{L1}$ (megohm) | $R_{L2}$ | $R_{L3}$ | $R_{L4}$ | $R_{L5}$ | $R_{br}$ | $\frac{V_{sb}}{V_1}$ (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| $\alpha$ | $\rho$ | | | | | | | | | |
| | | | | *$R_m = 1500$ ohm cm$^2$* | | | | | | |
| 0.3 | 3 | 25.6 | 5.44 | 134 | 174 | 192 | 236 | 286 | 318 | 27.5 |
| 2 | 3 | 9.0 | 9.0 | 134 | 174 | 192 | 236 | 286 | 318 | 36.2 |
| | | | | *$R_m = 4500$ ohm cm$^2$* | | | | | | |
| 0.1 | 6.5 | 60.4 | 4.88 | 357 | 463 | 513 | 627 | 765 | 849 | 28.6 |
| 1 | 6.5 | 10.5 | 7.94 | 357 | 463 | 513 | 627 | 765 | 849 | 38.1 |

intervals until 50 neurons had been examined. The somata of most examined cells were from layer V close to layer IV, and the major apical dendritic shafts usually branched between layers II and III.

The soma of the pyramidal neuron presents a two-dimensional profile which is triangularly shaped with the base in most instances wider than the apex; the point with greatest curvature was considered the origin of the major apical dendritic shaft (Fig. 1A). Measurements were made across the base of the soma and from base to "height" to estimate somatic size; measurements were also taken at 50 $\mu$ intervals along the apical dendritic shaft (110 cases) to determine its diameter as a function of distance from the soma to the major branch point.

In different cells the major shaft branched at variable distances from the soma (from 100 $\mu$ to 400 $\mu$). It was necessary, in order to evaluate comparably tapering major shafts, to restrict analysis to those cells with shafts branching at a uniform distance from the soma.

A length of 250 $\mu$ was chosen as the longest distance to branch point for which data was available for small (soma surface 600 to 1200 $\mu^2$), medium (1200 to 2250 $\mu^2$), and large (> 2250 $\mu^2$) pyramidal cells. Inasmuch as the $R_I$ value was taken for large pyramidal cells, it was also necessary to take average shaft dimensions from the group of large cells. Subsequent to analysis of these cells, an analysis based on geometric considerations was made to determine whether comparable results would obtain for the small and medium-sized cells.

In the five largest pyramidal cells (soma surface ~ 3000 $\mu^2$), the diameter of the shaft averaged $8.52 \pm 0.48$ and $5.76 \pm 0.65$, $5.44 \pm 0.66$, $4.48 \pm 0.71$, $3.64 \pm 0.64$, and $3.2 \pm 0.55$ $\mu$, respectively, moving out along the shaft in 50 $\mu$ sections until the MBP at 250 $\mu$ was reached. The internal resistivity of mammalian central nervous system cytoplasm may be taken as close to 75 ohm cm (*5*); we then calculated core resistances for each section of the apical shaft, treating it as a truncated cone; the values in megohms were: $R_{c1}$, 0.39; $R_{c2}$, 1.32; $R_{c3}$, 1.66; $R_{c4}$, 2.42; $R_{c5}$, 3.53; $R_{c6}$, 2.19. The relationship of length and diameter for 80 small and medium-sized cells is shown in Fig. 1C.

The total core resistance averaged $11.5 \pm 1.8$ megohm. Between 3 and 12 dendritic side branches measuring 1 to 2 $\mu$ in diameter and about 100 $\mu$ long arose from the major shaft. For our model shaft we will assume six side branches, 1.5 $\mu$ in diameter and 100 $\mu$ long, five of which are evenly spaced between each 50 $\mu$ section and the sixth at the junction with the soma (Fig. 1B). Using the values for specific resistivity, we calculated the "leakage resistances" for each section and side branch (Table 1).

An approximately correct numerical solution for the voltage drop across $R_{sb}$ can now be made for any reliable range of $R_{sb}$ values. To determine $R_{sb}$ we first define a ratio of apical dendritic to basilar dendritic conductance ($\alpha$), where $\alpha = R_b/R_a$ and where $R_a$ and $R_b$ are the apical and basilar dendritic resistances, respectively, as seen from the soma. Using Rall's (*1*) $\rho = (R_a^{-1} + R_b^{-1})/R_s^{-1}$, where $R_s$ is the somatic resistance, and the definition of total input

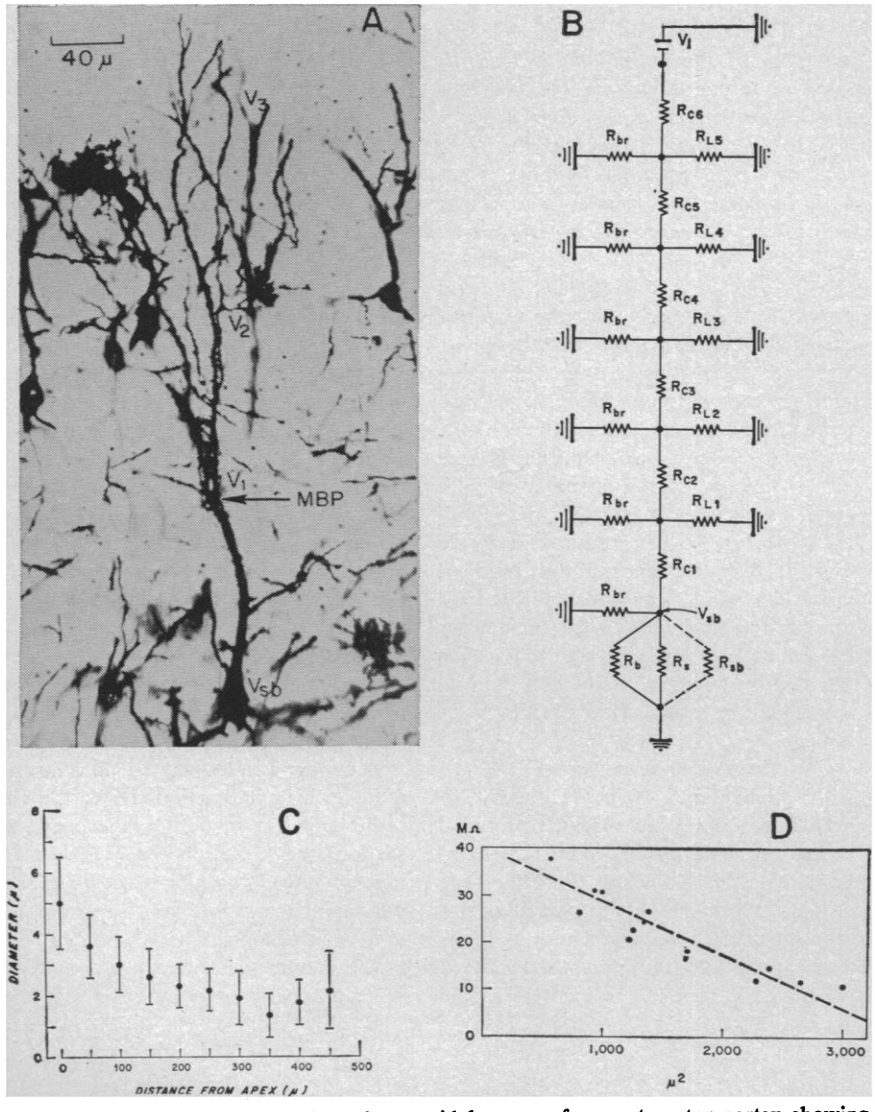


Fig. 1. (A) Golgi-Cox preparation of pyramidal neuron from cat motor cortex showing profuse distal apical dendritic branches separated from the soma by the apical dendritic shaft. A potential change ($V_{sb}$) across the soma and basilar dendrites results from potential changes ($V_2$ and $V_3$) on secondary and tertiary branches, respectively, producing a potential change ($V_1$) at the major branch point (MBP). (B) Steady-state "equivalent" circuit for dendritic shaft showing segmental core resistance ($R_{c1}$ through $R_{c6}$), leakage resistances ($R_{L1}$ through $R_{L5}$) and branch leakage resistances ($R_{br}$). The soma and basilar dendritic resistances ($R_s$) and ($R_b$) are in parallel and may be replaced by an equivalent resistance ($R_{sb}$). (C) Plot of average diameter (with standard deviations) of apical dendritic shaft as a function of distance from apex in 80 small and medium-sized pyramidal cells. (D) Graph shows core resistance of pyramidal cells with apical dendritic shaft branching 250 $\mu$ from the soma as a function of somatic surface area.

resistance ($R_I$), where $R_I^{-1} = R_s^{-1} + R_a^{-1} + R_b^{-1}$ we find that

$$R_{sb} = R_I \frac{(\alpha + 1)(\rho + 1)}{\alpha + \rho + 1}$$

Values are already available for $R_I$ and $\rho$, and the upper and lower limits for $\alpha$ may be easily calculated by assuming either an infinite resistance or a "zero" resistance, respectively, in series with the apical shaft at the MBP and then calculating the total value of $R_a$ as seen from the soma in each case (Table 1). From the previous definitions of $\alpha$, $\rho$, and $R_I$ it then follows that for $\rho = 3$, the maximum possible value for $\alpha$ is 2.0, the minimum is 0.3. For $\rho = 6.5$, the maximum value for $\alpha$ is 1.0, the minimum is 0.1.

In the least favorable case for dendritic electrotonic propagation with low $\alpha$, low $R_m$, and low $\rho$, 27.5 percent of a potential difference produced at the MBP occurred across the soma. In the most favorable case, the higher limit of 38.1 percent was calculated (Table 1).

The anatomic data showed that cells with smaller somatic surfaces gave rise to narrower major shafts. Smaller cells, in general, also gave rise to small axons. The fact that the core resistance of the major shaft relative to the input resistance ($R_{sb}$) is the principal determinant of the potential drop across $R_{sb}$ when the leakage resistances are relatively high encouraged an attempt to see whether the core resistance of the shaft was related to size of the neurons. Core resistances decreased as cell size (surfaces calculated assuming truncated cones) increased (Fig. 1D). This approximately linear relationship suggests that the apical dendritic contribution relative to soma size may be approximately the same for a wide range of pyramidal cell sizes, and that the results on large pyramidal cells may be generally applicable to smaller pyramidal cells.

Sholl (*4*) presented data on the diameter of branching dendrites as a function of distance (extending up to 240 $\mu$) from the MBP. These data, however, were not derived from large cells comparable to those whose major shafts were used in the above calculations. Nor do we have adequate data on the distant branchings of large cells, because it becomes progressively more difficult to obtain full sections of the desired material.

However, for the sake of a rough estimate, a secondary branch 250 $\mu$ long and 2.5 $\mu$ in diameter at the MBP tapering to 2.0 $\mu$ at the end would add a core resistance of 47.8 megohm. When the appropriate leakage resistances are considered, the lower and upper limits for attenuation of a potential change ($V_2$) applied to the end of the secondary branch (500 $\mu$ from the soma) would be 5.5 to 5.8 percent. A tertiary branch 250 $\mu$ long and tapering from 2.0 to 1.5 $\mu$ would add another 75 megohm of core resistance per branch, and similarly considering the range of leakage resistances, the limits for attenuation of potentials ($V_3$) (750 $\mu$ from soma) generated on this tertiary branch would range from 2 to 3 percent.

Somatic potentials of 27.5 to 38.1 percent (estimated lower and upper confidence limits) of a potential difference appearing at the major branch point of the apical dendritic shaft would occur as a result of steady-state synaptic activity in the more distant branches. If it is reasonably assumed that depolarizations of 20 mv can occur over the entire dendritic tree distal to the MBP 250 $\mu$ from the soma, then 5.5- to 7.6-mv depolarizations would occur at the soma. These values are in the same range as the peak depolarizations produced by strong stimulation of the nonspecific thalamic system, a fiber system believed to have the majority of its endings on apical dendrites in the superficial cortical layers (*6*). As depolarizations in this range would bring most neurons to or above firing level, then it can be considered that the apical dendrites, when all are excited, can play a dominant role in determining the neuronal firing pattern. Apical dendrites, 750 $\mu$ distal from the soma, if all depolarized could produce only 2 to 3 percent changes at the soma. If a 20-mv depolarization on these dendrites is assumed, then 0.4 to 0.6 mv of depolarization would occur at the soma. This is a fraction of the depolarization necessary to reach a firing level, usually 5 to 10 mv. However, even a 0.4-mv depolarization can have a marked effect on changing the frequency of firing of a neuron already depolarized close to or slightly above firing level (*7*). In this respect the distant dendrites can play an important modulating role, not so much in setting up sporadic action potentials, but in providing a refinement in the regulation of firing rates of neurons brought close to firing level by afferent systems ending close to the soma (*1*).

Finally, it should be noted that the strength of this assessment of the importance of the apical dendritic tree rests in its quantitative aspect (Table 1), wherein the values depend almost entirely upon anatomic and physiologic measurements and minimally upon factors included as assumptions.

STANLEY JACOBSON
*Department of Anatomy,*
*Tufts Medical School,*
*Boston, Massachusetts*

DANIEL A. POLLEN
*Massachusetts General Hospital,*
*Boston, Massachusetts*

**References and Notes**

1. W. Rall, *Exp. Neurol.* **1**, 491 (1959); *Ann. N.Y. Acad. Sci.* **96**, 1071 (1962); *J. Neurophysiol.* **30**, 1138 (1967).
2. H. D. Lux and D. A. Pollen, *J. Neurophysiol.* **29**, 207 (1966).
3. K. Takahashi, *ibid.* **28**, 908 (1965).
4. D. A. Sholl, *J. Anat.* **87**, 387 (1953).
5. J. S. Coombs, D. R. Curtis, J. C. Eccles, *J. Physiol.* **145**, 505 (1959).
6. A. C. Nacimiento, H. D. Lux, O. D. Creutzfeldt, *Arch. Ges. Physiol.* **281**, 152 (1964); D. A. Pollen, *Electroencephalogr. Clin. Neurophysiol.* **17**, 154 (1964); D. P. Purpura, R. J. Shofer, R. S. Musgrave, *J. Neurophysiol.* **27**, 133 (1964).
7. R. Granit, D. Kernell, G. K. Shortless, *J. Physiol.* **168**, 911 (1963). O. D. Creutzfeldt, H. D. Lux, A. C. Nacimiento, *Arch. Ges. Physiol.* **281**, 129 (1964).
8. We thank Drs. H. D. Lux and C. Feldman for their helpful suggestions.
9. Supported by PHS grants NB 07666-01 and 1-K3-NB-353-01.

9 August 1968

## Antibodies to Deoxyribonucleic Acid Irradiated with Ultraviolet Light: Detection by Precipitins and Immunofluorescence

Abstract. *Two rabbits were immunized with a complex consisting of ultraviolet-irradiated DNA and methylated bovine serum albumin. Serum antibodies reacted only with irradiated DNA, and the serological reaction was shown by immune-precipitation and immunofluorescence.*

Antibodies to DNA have been produced in rabbits immunized with a complex consisting of DNA and methylated bovine serum albumin (*1*). Levine *et al.* (*2*) described antibodies specific for photoproducts of DNA irradiated with ultraviolet light. These antibodies were demonstrated in complement-fixation reactions and were directed against thymine-associated photoproducts. We now