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Pellionisz A, Llinás R.

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PURKINJE CELLS

A. PELLIONISZ and R. LLINÁS

Department of Physiology and Biophysics, New York University School of Medicine,
New York 10016, U.S.A.

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A COMPUTER MODEL OF CEREBELLAR PURKINJE CELLS

A. PELLIONISZ and R. LLINÁS

Department of Physiology and Biophysics, New York University School of Medicine, New York, NY 10016

Abstract—A mathematical computer model of frog Purkinje cells is generated on the basis of present-day morphological and physiological data. The model utilizes passive cable equations and the Hodgkin & Huxley equations describing ionic conductances in excitable membranes. It comprises 62 compartments, the active and passive properties being specified independently for each compartment. The morphological properties of the model were obtained from computer reconstruction and direct observation of Golgi-stained Purkinje cells. Three forms of activation were utilized to test the adequacy of the model: (1) antidromic invasion, (2) orthodromic invasion via the parallel fiber–Purkinje cell synapse, and (3) climbing fiber activation. It was shown that the electrophysiological parameters available in the literature make it possible to construct a model capable of demonstrating most of the electrical properties of Purkinje cells, such as antidromic invasion and the ability to generate simple spikes and spike bursts. Questions such as the mechanism of generation of climbing fiber bursts were analyzed. The model may be used as a heuristic tool to help in the analysis and interpretation of electrophysiology and as a prototype element in the construction of more complex computer simulations of neuronal circuits.

RIGOROUS mathematical models of the electrical activity of central neurons, besides being a powerful tool to test and interpret experimental data, can also be an essential component in the development of computer simulation of neuronal networks. Our interest in the Purkinje cell stems from its well understood morphology and function. In fact, this cell is unique in that its input, the climbing and the mossy–parallel fiber systems, have been totally described anatomically and functionally. Further, these inputs are extremely different from each other and represent the limits of afferent innervation. On the one hand, the climbing fiber input establishes a one-to-one pattern of innervation with the Purkinje cell and is probably the most specific afferent in the central nervous system. In contrast, at the other extreme of the continuum, the mossy fiber–parallel fiber complex represents the largest and most dispersed input to any central cell (Ramón y Cajal, 1911; cf. Palay & Chan-Palay, 1974). From an electrophysiological point of view, the Purkinje cell is probably one of the most exhaustively studied neurons (cf. Eccles, Ito & Szentágothai, 1967; LLINÁS, 1969).

On a more general level the integrative properties of the Purkinje cell have gained further interest since the demonstration of dendritic electroresponsiveness (cf. LLINÁS & NICHOLSON, 1969, 1971; LLINÁS & HESS, 1976). This latter variable emphasizes the need for a modeling technique capable of handling a partially or totally active dendritic tree. The developing of such a model for the Purkinje cell offers the particular advantage that it must reproduce the responses to three distinctly different forms of activation, (1) the antidromic invasion, (2) orthodromic parallel fiber meditated single spikes, and (3) the climbing fiber-activated spike burst. Meeting these stringent requirements provides an assurance of adequacy and a clarification of the mechanisms generating the complex bursting discharges which thus far have been purely speculative (Eccles, LLINÁS & Sasaki, 1966; Martínez, Crill & Kennedy, 1971).

Given the morphological richness of the Purkinje cell dendritic arborization, the very useful equivalent cylinder assumption developed for the spinal motoneuron (Rall, 1962a,b) will not be used here. While this decision introduces significant computational difficulties, it does, however, extend the model to trees not following the 3/2 constraint implicit in this concept. In fact, a preliminary quantitative analysis on frog Purkinje cells shows that the actual branching power averages 1.75 (J. McLaren, personal communication).

In an important new development in neuronal modeling for the spinal motoneuron, Dodge & Cooley (1973) combined the idealized equivalent cylinder cable model of Rall with the mathematical formulation of Hodgkin & Huxley (1952) for membrane ionic permeabilities. The model is composed of non-uniform cable segments representing the cellular morphology. In the present paper Dodge & Cooley's model is further developed and applied to Purkinje cells. The neuron is divided into a multitude of spatial components lumped together by the cable equations; the electrical phenomena in each compartment are governed by either the Hodgkin–Huxley equations (in the compartments representing excitable sections of the neuron membrane) or by passive R.C. properties. In this paper only passive dendritic arborizations will be considered; a future publication will consider

Abbreviation: EPSP, excitatory postsynaptic potential.

.ABBR.
active dendritic properties. A preliminary note (Pellionisz & Llinás, 1975) has been published on the present study.

**METHODS**

The Purkinje cells of the model are represented by different types of dichotomous tree dendritic structures. The morphogenesis of these trees provides a variant of the skeleton of branch-arborization in respect of lengths and angular deviations of branches on the 29 × 29 two-dimensional lattice of (10 μm spacing). As is shown in Fig. 1 A, which demonstrates the basic neuronal elements of the circuitry model (cf. Pellionisz, Llinás & Perkel, 1977), the Purkinje cell bodies are distributed on a staggered arrangement. The Purkinje cell dendritic trees are gradually thinned towards the distal end to provide a clarity of the positioning of trees and an impression about the density of the dendritic structure (Fig. 1 B). For illustrative reasons, three representative dendritic arbors are depicted in Fig. 1 C–E. Close to one-half of the 29 × 29 matrix points are marked by dots. Each dot represents one complete spiny branchlet on the tree. Variation of the branch distribution in these dendritic trees is indicated in Fig. 1. In C minimum dendritic overlapping is observed, and in D a large degree of overlapping is shown. In E dendritic trees with clear dendritic asymmetry is illustrated. These skeleton trees represent the distribution of the Purkinje cell’s smooth dendrites and are considered an adequate model for the development of a connectivity circuit in which a rigid characterization of the neuronal connectivity is largely avoided.

**Morphological structure of the Purkinje cells**

All Purkinje cell dendritic arborizations are represented as a set of cable segments. Each segment has a uniform diameter but the different segments have different diameters (Fig. 1 F). The basic dimensions were obtained from Golgi-stained preparations (Hillman, 1969b) and electron micrographs (Sotelo, 1969). In establishing the diameters of the dendritic segments a crucial parameter is the exponent p in the equation for parent and daughter branches (Rall, 1962a).

\[ a_1^p + a_2^p = a_k^p \]

which for the equivalent cylinder model is 3/2. However, since preliminary measurements (J. McLaren, personal communication) indicate that this figure for first bifurcation of the Purkinje cell dendritic tree averages 1.75, this latter figure is used in the models presented in this paper.

**Axon.** The axon is constructed as consisting of three different structural parts, each being a uniform cylinder: (i) Initial segment of axon (normally with length of 25 and diameter of 2 μm). (ii) Myelinated segments (of 200 μm length and 3 μm diameter). (iii) Axonal node of Ranvier (cylinder of 3 μm length and 2 μm diameter).

The morphological structure of such a Purkinje cell is shown in Fig. 1 F. Note that different scales apply for dendritic diameter and branch length and for the length and diameter of axonal segments.

**Compartmentalization of the Purkinje cell model**

Compartmentalization of the Purkinje cell model is shown in Fig. 2. As seen in A, each of the seven myelinated segments, the seven Ranvier nodes, and the axonal initial segments is considered as a separate spatial compartment. The electrical parameters utilized were 100 Ω/cm, for the intracellular medium, 6000 Ω/cm² and 1 μF/cm² (Dodge & Cooley, 1973) for the specific resistivity and capacitance of the soma, dendrites and nodes and infinite resistance, and 0.05 μF/cm² for resistance and capacitance of the internode respectively. The spherical soma is equated to a cylinder of identical volume and is represented as a separate compartment. The dendritic branches are broken into thirds where the midsection represents a simple cylindrical compartment, while the adjoining three sections, at each branch, represent a combined spatial compartment. Thus, while the Purkinje cell model had a variety of dendritic branching patterns, it consisted, in every case, of 62 spatial compartments.

Each cylindrical compartment (e.g. axonal compartments, dendritic midsections, or the two adjoining thirds at the upper end of the top branches) is equated to an equivalent cylinder of two halves while the branching compartments have a three cylindrical equivalent (Fig. 2 B). If in the i neighbor compartments the diameters of cylindrical segments are \( a_i \), the lengths are \( L_i \), and the compartment receives \( k \) activated spines, then the \( V \) membrane potential in the equivalent circuit (C in Fig. 2) is determined by the following equations:

\[ R_i = \frac{4L_i}{a_i^2} \]

\[ R_m = R_{\text{min}} / k \]

\[ C = c \cdot \sum_{i=1}^{n} d_i^2 \cdot \pi \cdot L_i \]

where \( r_i \) is the specific resistance of the internal medium, \( c \) is the specific cross-membrane capacitance of the membrane and \( R_{\text{min}} \) is the resistance represented by one spine.

**Time function of membrane potential and Hodgkin & Huxley equations**

The following equations apply for the membrane potential \( V \) as determined by the \( I_m \) transmembrane current, \( I_L \) longitudinal current (inside the cylindrical segment) and the \( I_S \) synaptic current.

\[ 0 = C \frac{\delta V}{\delta t} + I_m + I_L + I_S \text{ where} \]

\[ I_m = \frac{1}{R_{\text{Na}}} (V - V_{\text{Na}}) + \frac{1}{R_k} (V - V_{k}) + \frac{1}{R_L} (V - V_l) \]

\[ I_L = \sum_{i=1}^{n} \frac{1}{R_s} (V - V_s) \text{ and } I_S = \frac{1}{R_p} (V - V_{\text{syn}}). \]

Where \( V_{\text{Na}}, V_k \) and \( V_{\text{syn}} \) are the equilibrium potential values for the \( Na^{+} \) and \( K^{+} \) ions and for the synaptic depolarization (with the assumed values of 115 mV, −5 mV and
Fig. 1. Simplified models of Purkinje cells as utilized in the computer simulation of frog cerebellum (Pellionisz et al., 1977). A: the overall organization of the model; Purkinje cells lie between granular layer (on left) and molecular layer (at right). The bodies of the Purkinje cells are represented by dots; only a few dendritic trees are illustrated. In B, somatic locations of Purkinje cells (dots) and their dendritic trees (gradually thinned out in number towards the closer end for easier visualization) viewed from above. In C, D and E: representative Purkinje cell dendritic 'skeletons'. Dots represent location for spiny branchlets where the crossing parallel fiber establishes contact with the Purkinje cell spines. In F, a more detailed account of the model. Note different dimensional scales for the dendritic and axonal length and their width.
FIG. 2. Multicompartamental model of the Purkinje cell. The model consists of 31 dendritic branches, 15 bifurcation points, a soma, an initial segment and 7 nodes and myelinated segments. Each of these 62 compartments are represented by a cylindrical spatial segment of uniform diameter; or, for the branching compartments, a combination of three cylinders as shown in B. The equivalent electrical circuit is shown in C, where \( R_l \) represents the longitudinal resistance of the cylindrical compartment and the rest represents the electrical equivalent of the membrane as described by Hodgkin & Huxley (1952), all of the parameters being set individually for each compartment. D–E–F show the assumed electrical properties of three representative compartments: a low excitability branching point (upper row in D–E–F), the soma (second row) and nodes of Ranvier (lowest row) being of increasing excitability. Numerical solutions expressing the waveform of membrane potential change (D), the membrane currents (E), and the \( m, n, h \) variables in Hodgkin-Huxley equations (F) are shown as a function of time following the brief current pulse injection illustrated in F.

90 mV respectively), \( V_L \) is the e.m.f. (0 mV) for 'leakage' current. The neighboring compartmental potential values are denoted by \( V \).

The \( R_{Na}, R_K \) and \( R_L \) cross-membrane resistance values for Na\(^+\), K\(^+\) and leakage currents are determined as follows:

\[
\frac{1}{R_{Na}} = g_{Na} \cdot S \\
\frac{1}{R_K} = g_{K} \cdot S \\
R_L = R_{m}/S
\]

where \( S \) is the combined surface area of the \( i \) cylinders involved in one compartment:

\[
s = \sum_{i=1}^{i} \pi d_i L_i.
\]

While the specific cross-membrane resistance (\( R_m \)) is assumed to be constant (normally taken as 6000 \( \Omega/cm^2 \)), the Na and K conductances follow those of Hodgkin & Huxley (1952), in which the actual \( g_{Na} \) and \( g_{K} \) values are at all times determined by the average \( \bar{g}_{Na} \) and \( \bar{g}_{K} \) but are changing with the \( V \) membrane potential and time as determined by the equations:

\[
g_{Na} = m^4 h \bar{g}_{Na} \\
g_{K} = n^4 \bar{g}_{K}.
\]

Here the dimensionless variables of \( k = m, n \) and \( h \) follow the equation

\[
dk/dt = z_k (1 - k) - \beta_k \cdot k.
\]

The \( \alpha \) and \( \beta \) constants are deduced from those in Frankenhauser & Huxley (1964) with only minor modifications:

\[
z_m = 0.36 \frac{V - 22.0}{1 - \exp(22.0 - V)/3} \\
\beta_m = 0.40 \frac{13.0 - V}{1 - \exp(13)/30} \\
z_n = 0.02 \frac{V - 35.0}{1 - \exp(45.0 - V)/10} \\
\beta_n = 0.25 \frac{10.0 - V}{1 - \exp(V - 10.0)/10} \\
z_h = 0.35 \frac{- 10.0 - V}{1 - \exp(V + 10.0)/7} \\
\beta_h = 0.05 \frac{V - 45.0}{1 - \exp(45.0 - V)/10}.
\]

These sets of parameters were established through the procedure of requiring an adequate rising time and propagation of the action potential (see Hardy, 1973) and also a capability of firing with a frequency exceeding 500 Hz, as it can be recorded experimentally (Llinas, Bloedel & Hillman, 1969). Since the morphological and electrical properties of any of the 62 compartments could be adjusted independently, this provided the possibility of studying the significance of the different parameters in overall integrative properties. Especially important were
those relating to $g_{Na}$ and $g_{K}$. An example of this versatility is illustrated in Fig. 2 D-F where the excitability is increased from close to zero at the upper portion of the dendritic tree (top row) to a moderate level at the somatic compartment (middle row). The axonal nodes exhibit their usual high excitability (lower row). This individual treatment of spatial compartments was considered essential in order to study potential inhomogeneities of the excitability on the dendritic tree (so-called 'hot spots') associated with dendritic spikes (LLINÁS & NICHLSON, 1971). The present paper aims at modeling the frog Purkinje cell in which dendritic spikes are not prominent, the dendritic compartments (unless otherwise specified) being considered non-excitatory, passive cables.

Computational methods

The set of equations was solved numerically using a PDP-15 computer (Digital Equipment Corp.) with floating point processor and 32K 18-bit core memory, and the data monitored on a Tektronix 611 storage oscilloscope and stored via DEC-pack cartridge disc. The data later could be displayed using either the passive storage oscilloscope or the dynamic graphic-15 display, therefore enabling both the selecting and composing of static pictures or production of spatio-temporal display by computerized cinematographic methods.

The numerical integration was chosen as the classical Euler (explicit) integration form which requires suitably limited $dx$ and $dt$ to avoid instabilities of the computation. While the program automatically monitored the $dv$ increment in every compartment and accordingly relaxed or restricted the time increment of the integration (within the extremes of 200 ns and 25 $\mu$s) separately, in an asynchronous manner for every compartment, still the computation involved in the solution of Hodgkin-Huxley and cable equations makes this 67 compartment model work about $5 \times 10^5$ times slower than the real time activity of Purkinje cells.

The traditional questions of boundary problems in a spatially limited model were handled in two different ways: the axonal end of the distal compartment could either have the option of 'open end' (connected to the isopotential extracellular fluid by short circuit) or 'sealed end', in which the next to last compartment echoed the potential of the last compartment with an identical value. While the uppermost dendritic branches were always considered sealed, the axonal ending could be set either way. The short circuited 'cut' ending of axon introduces a clearly visible distortion of action potential on the last nodes which is the reason for using a relatively long axon consisting of seven myelinated segments.

RESULTS

The simulation of electrical activity of Purkinje cells is particularly advantageous since this cell produces three markedly different types of activation all of which have been studied in great detail. Thus, any Purkinje cell model which claims to be adequate, at least at first approximation, must satisfy the rather stringent requirement of producing appropriate potential waveforms for all of these three forms of activation. Namely, the propagation of the action potential evoked by antidromic electrical stimulation must result in a firing of the initial segment of the axon and then the soma itself. The depolarization, however, should rapidly decrease upward on the dendritic structure (cf. LLINÁS et al., 1969; FREEMAN & NICHLSON, 1975). The orthodromic activation via parallel fiber synaptic input must be graded and must generate unitary simple action potentials. The model should also be able to generate the complex spike bursts which follow the climbing fiber activation (ECCLES et al., 1966; LLINÁS et al., 1969) without any parameter modification.

Antidromic activation

The spatio-temporal display of the membrane potential waveforms throughout the 62 compartment model in the case of antidromic activation is shown in Fig. 3. In this particular example the main trunk and all dendritic branches are passive RC cables. The specific Na and K conductance figures were chosen in order to arrive at an appropriate spike propagation speed through the axon and a proper waveform for the action potential. Thus $g_{Na} = 600 \Omega^{-1}/cm^2$ and $g_{K} = 100 \times 10^{-9} \Omega^{-1}/cm^2$ were assumed for the excitable Ranvier nodes and soma. A $50\%$ increase of these values was assumed for the initial segment. With these values a $10\, nA$ stimulus applied to the sixth Ranvier node generated the antidromic invasion seen in Fig. 3. Display of the intracellular voltage across the different segments indicates a rapid reduction of $V_r$ with distance from the soma, as expected from the analysis of field potentials (LLINÁS et al., 1969; FREEMAN & NICHLSON, 1975).

Orthodromic activation by parallel fibers

The orthodromic activation of Purkinje cells following parallel fiber stimulation via surface electrodes has been carefully investigated in many different preparations (ECCLES et al., 1966; LLINÁS et al., 1969) and some theoretical consideration has been given to the possible impact of differences in integration of input carried by different spatial patterns of parallel fiber input (LLINÁS, 1971). Simulation of this type of Purkinje cell activity was obtained by current injections distributed over the dendritic tree via the dendritic spines. Thus, as seen in Fig. 2 B, the cylindrical spatial compartments may have different numbers of activated spines. The activated spine is represented by a $100 \Omega^{-1}$ conductance increase allowing a synaptic current to be injected as shown in the equivalent circuit of Fig. 2 C.

Thus for orthodromic activation evoked by, let us say, a horizontal strip of activated parallel fibers, we assumed that each of the 16 uppermost branches received five continuously 'open' synapses during a $0.5 \, ms$ time interval. This case is shown in Figs. 3 B and 4. The off-line display of data provided a good opportunity to compare the results in the conventional electrophysiological manner (as two-dimensional graphs of time-function of membrane potential at one spatial location) with the simultaneous visualization of the depolarization wave throughout the den-
Fig. 3. A: Numerical solution for membrane potential against time throughout the 62 compartmental model in the case of simulated antidromic invasion of the Purkinje cell. All compartments of the dendritic tree are passive. Since the lowermost node in the axon has a boundary condition of an 'open end' (short circuited to the equipotential extracellular field), the action potential of the distal three nodes is distorted. The invasion of the soma and lower dendritic branches is clearly illustrated. As expected, the invasion is blocked at the base of the dendritic arbor and produces a slight depolarization on the most peripheral branches. This remote electrotonic invasion produces an after-depolarization at somatic level. B: Orthodromic activation of the model by parallel fiber synaptic input on the uppermost dendritic branches of the tree (horizontal distribution). At the right, numerical solution for membrane potential against time indicates a large depolarization at the peripheral dendritic branches which produces a prolonged EPSP at somatic level. A second slightly longer input (0.05 ms) produced an orthodromic action potential with 2 ms latency which propagated along the axon.

Fig. 4. Numerical solution for a just threshold orthodromic activation of Purkinje cell model. At the left schematic representation of the Purkinje cell, the density of 'hatching' is a function of the spatial distribution of potential at 1 ms after the onset of computation. On the right is continuous display of computed potential against time at the different neuronal compartments. Time and voltage calibration as indicated.
FIG. 5. Numerical solution illustrating vertical integration of an orthodromic input applied to one side of the dendritic tree. The amplitude and duration of the input are identical to that in Fig. 4, the only difference being the spatial distribution of the input. The schematic diagram to the left was taken at 2.5 ms from the onset of computation (arrow).

EPSP evoked at somatic level differed markedly both in amplitude and rising phase with different localization of parallel fiber input in varying distance from the soma. Accordingly the EPSP evoked at somatic level produced a practically immediate action potential of soma and initial segment, and the spike propagated along the axon. Moreover, the initial spike of short latency was followed, slightly more than 2 ms later, by a second propagating spike. Only after this short 'burst' was a general decay of the depolarization visible throughout the model. Interestingly, the second spike was initiated almost simultaneously at the initial segment and soma, followed by outward propagation towards the dendrites and axon.

Activation of Purkinje cell by climbing fiber

The distribution of membrane potential in the case of a climbing fiber activation of the same model Purkinje cell is shown in Fig. 6 B and compared with the actual record from a frog Purkinje cell (Fig. 6 A). This highly stereotyped all-or-none spike, which is followed by several (normally 3–5 but in some cases up to 12) oscillatory wavelets, has been observed frequently in the cerebellum of the frog (LLINÁS et al., 1969; FREEMAN, 1969; FABER & KORN, 1970; RUSHMER & WOODWARD, 1971; LLINÁS, PRECHT & CLARKE, 1971; HACKETT, 1972, 1976). While the climbing fiber–Purkinje cell synapse is well understood morphologically (LARRAMENDI & VICTOR, 1967; HILLMAN, 1969b) and electrophysiologically (ECCLES et al., 1966; LLINÁS & NICHOLSON, 1976), the exact mechanism which generates this characteristic spike burst has remained unclear hitherto and only speculative statements are available (ECCLES et al., 1966; MARTINEZ et al., 1971).

Climbing fiber activation of the Purkinje cell model was simulated by activating five synapses on each

Fig. 6. Climbing fiber activation of Purkinje cell. In A, sample of actual intracellular recording of the climbing fiber evoked spike burst in a frog Purkinje cell. The first spike is followed by a highly stereotyped pattern of wavelets. B: Numerical solution illustrating action potential waveform at Purkinje cell somatic level by a synaptic input equivalent to the distribution of climbing fiber synapses. The similarities with the experimental results are evident. In C similar activation as in B illustrating membrane potential throughout the 62 compartments. For further explanation, see text.
Purkinje cell model

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dendritic branch for a duration of 0.5 ms with a linear shift in the onset with respect to distance. The somatic onset of depolarization was defined as zero time and 0.5 ms at the uppermost branches. The overall membrane potential waveform at somatic level is shown in Fig. 6 B and was considered an adequate analog of the experimental data. Thus, the large initial spike is followed by a second depolarization of about 50-60% amplitude and a set of such wavelets which wax and wane.

Display of membrane potential change along the cell puts in evidence a possible mechanism for the generation of the waveform. Apparently the peaks of the burst are generated by the repetitive firing of the initial segment (followed shortly by the somatic firing) rather than in the dendrites as originally proposed (Eccles et al., 1966; Martinez et al., 1971). It is clear that in this model the firing pattern is evoked by the delayed repolarization of the dendritic tree which drives the somatic and initial segment compartments into a short burst of repetitive firing. The model also suggests a possible explanation for the fragile nature of some of the spike peaks, as opposed to the stable components of this burst. Furthermore, the results are consistent with similar findings in the cat Purkinje cells. For instance, the last of the three spike wavelets in the climbing fiber bursts shows the most variability (also in extracellular records) (cf. Llinás & Volkind, 1973). As indicated by the model, this phenomenon may be produced by the antidromic invasion of the propagating axonal action potential into the soma. This feature appears to result from the impedance mismatch and loose coupling of the somatic and the initial segment and axon regions, due to morphological and excitability differences.

Similar phenomenology may also be found using a different dendritic branch configuration with parameters otherwise identical to those of the model used in Fig. 6. One such example is illustrated in Fig. 7 A and B, where the basic pattern of complex spike is similar to the previous case. This is in accordance with the fact that the complex spike waveform is a highly stereotyped response, quite similar from cell to cell, although these cells exhibit more than trivial morphological differences.

Reversal of the climbing fiber evoked EPSP

The reversal properties of EPSP evoked by a climbing fiber-like activation is illustrated in Fig. 8 B. Figure 8 A shows actual intracellular recordings from a cat Purkinje cell, the EPSP showing a characteristic biphasic reversal as a depolarizing current of increasing amplitude is applied across the somatic membrane (Llinás & Nicholson, 1976). As seen in Fig. 8 B in a purely passive model with an $E_{EPSP}$ of $-10$ mV, the results from the model show striking similarities with the experimental results, even in quantitative terms. The biphasic reversal of climbing fiber-evoked EPSP at 11.7 nA outward current injection is shown in detail in Fig. 8 C. As expected from theoretical treatment of distributed synaptic inputs (Rall, 1967; Calvin, 1969), the EPSP in the upper branches is not reversed, producing the late depolarizing portion of the biphasic EPSP reversal.

Modification of branching and internal resistance parameters

The functional importance of different parameters in this model can also be studied with great ease. Given the large number of possible permutations of these parameters, only one representative example will be illustrated. The antidromic invasion of a Purkinje cell is shown after the introduction of two small changes in the model (Fig. 9 A), and the results may be compared to those shown in Fig. 3. In the present case the branching power is set to 1.25 and the inter-
FIG. 8. Reversal of climbing fiber evoked EPSP. A: Experimental results obtained in a mammalian Purkinje cell. The climbing fiber EPSP is reversed by membrane depolarization (from LLINÁS & NICHOLSON, 1976). In B, calculated climbing fiber EPSP at the Purkinje cell soma during trans-somatic current injections of increasing amplitudes. These results may be compared with those in A. In C, calculated distribution of potential at different portions of the Purkinje cell model for an intrasomatic current injection of 11.7 nA (time and voltage calibration as indicated). The parallel recording demonstrates that while the EPSP would be totally reversed at somatic level (due to depolarization surpassing the EPSP equilibrium potential) the upper branches are less depolarized by the applied current and therefore the CF-evoked EPSP does not reverse there. This produces the biphasic character of EPSP at somatic level.

FIG. 9. Functional implications of varying morphological and physiological parameters: Numerical solutions for antidromic (A) or climbing fiber (B) activations. In A the internal resistance of the branches is increased by assuming a faster taper of dendritic diameter with distance. As a result, the antidromic invasion is delayed and the dendritic invasion minimal. In B the excitability of initial segment is reduced by 30% and a climbing fiber activation is simulated, as in Fig. 3. Note that while the general pattern of complex spike at somatic level is retained, these spikes do not propagate along the axon.
analysis of morphofunctional states but also the possible implication of certain pathological conditions. This means that rather than idealizing the rich variety of neurons into a single model, the functional features of neurons with special geometry of dendritic trees may be approached.

Obviously some of the most important problems to be tackled relate to the significance of possible spatial inhomogeneities in excitability. The number of instances where more than one site of spike initiation appears to be present in central neurons is quite appreciable (Eccles, Libet & Young, 1958; Lorente de Nó & Condouiris, 1959; Spencer & Kandel, 1961; Purpura, 1967; Llinás & Nicholson, 1969, 1971; Kidokoro, 1969; Kuno & Llinás, 1970; Korn & Bennett, 1971; Baker & Precht, 1972; Czéh, 1972; Precht, 1975; Llinás & Hess, 1976; Zipsber & Bennett, 1976). The problems relating to such parameters and their probable functional nuances as circuit modifiers may become of significance in the study of such important functions as learning, which may in fact be subserved by subtle modifications of neuronal excitability or geometry.

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A. PELLIONISZ and R. LLINÁS


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