3.2 Editorial Comment with an Excerpt from Rall (1992)

Rall, W. (1992). Path to biophysical insights about dendrites and synaptic function. In *The Neurosciences: Paths of Discovery II*, ed. F. Samson and G. Adelman. Boston: Birkhauser.

Because of space limitations we have chosen not to reprint this paper by Rall (1962b). The paper's first half reviewed the modeling perspective gained in several earlier papers (Rall 1957, 1959, 1960, 1962a). The second half presented new results on computed extracellular potential fields and transients. Some of these were published only in that paper, while others were included in Rall 1977, which also is not reprinted in this collection. In order to describe explicitly these computed extracellular potentials here, we include two illustrations from the Rall 1962b, together with some explanatory commentary.

At the time of these extracellular field computations (early 1960s), neurophysiologists were taught that a positive extracellular voltage, recorded relative to a distant (indifferent) electrode, signifies that the recording electrode is located near nerve membrane acting as a current source (i.e., outward membrane current), and that a negative extracellular voltage signifies that it is located near nerve membrane acting as a current sink (i.e., inward membrane current). Although this does hold true for an axon, the fact that this simple rule does not hold for a neuron with several dendrites was clearly demonstrated by these computed results. This was important to the interpretation of recorded extracellular potentials from cat spinal cord, in response to antidromic activation of a single motoneuron (Fatt 1957; Nelson and Frank 1964).

Rall's insights about these spinal cord extracellular potentials are well explained by the following excerpts taken from an essay (Rall 1992).

> My dendritic modeling efforts also followed a parallel path that was concerned with extracellular potentials. In 1960, with the help of Ezra Shahn and Jeanne Altmann, I computed extracellular potential fields of simplified dendritic neurons, for the instant of peak action potential in the soma membrane, assuming one or more long dendritic cylinders with passive membrane properties (details can be found on pages 156–163 of Rall 1962b). This required considerable physical labor, because it involved piece-meal computations using large batches of punched cards with an IBM-650 computer. We hand-plotted equi potential contours for the case of a single passive dendrite and a case of seven passive dendrites [shown here as figure 1]. We found the extracellular potential field to be negative (relative to a distant reference electrode) everywhere near the soma and proximal dendrites, and found only weakly positive sleeves surrounding distal dendritic membrane. The physical intuitive explanation of this is that the soma surface provides the sink for all of the extracellular current, which converges radially into the soma; if the sources were all at infinite distance, the equi-potential contours would be spherical

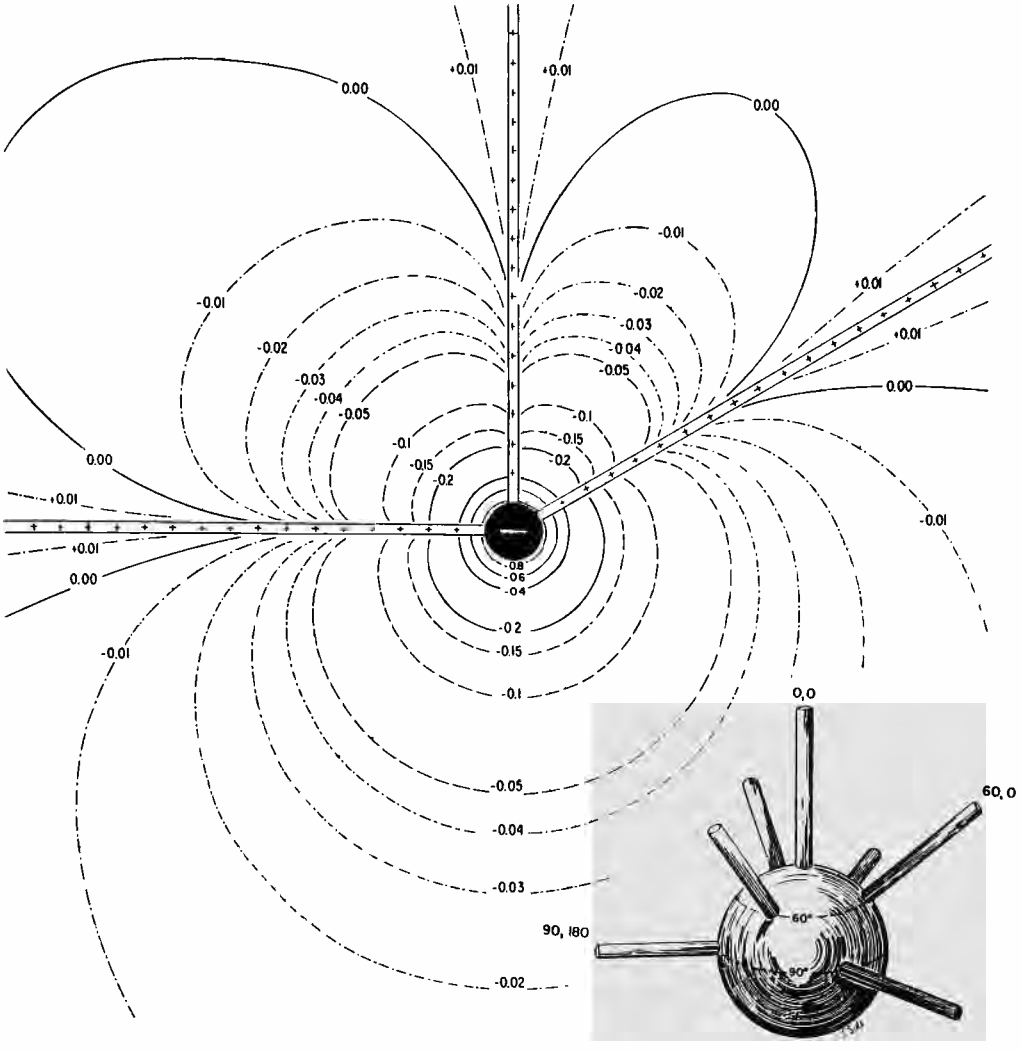

Figure 1
Computed isopotential contours for a spherical soma with seven cylindrical dendrites, of which only three can be seen in the plane shown at upper left. As indicated by the inset at lower right, three dendrites were equally spaced at 60 degrees from the polar axis, and three more dendrites were equally spaced at the equator. The three-dimensional equipotential surfaces are shown cut by a plane that includes the polar axis, one 60-degree dendrite, and one 90-degree dendrite. The soma was the sink for extracellular current current; the dendritic cylinders were distributed sources of extracellular current matching the passive electrotonic spread along the dendrites at the time of the peak of the somatic antidromic action potential. Here, the dendritic length constant was set equal to 40 times the somatic radius. The numbers labeling the contours correspond to the quantity $V_e/(I_N R_e/4\pi b)$, where I_N is the total current flowing from dendrites to soma, R_e represents the extracellular volume resistivity, and b represents the soma radius. For the particular case of the peak somatic action potential in a cat motoneuron, this numerical quantity expresses the value of V approximately in millivolts. This is because of the following order of magnitude considerations: I_N is of the order 10^{-7} A, because the peak intracellular action potential is of the order 10^{-1} V, and the whole neuron instantaneous conductance is of the order 10^{-6} siemens; also, $R_e/4\pi b$ is of the order 10^4 ohms, because the soma radius, b, lies between 25 and 50 μm, and the effective value of R_e probably lies between 250 and 500 ohm cm; see Rall 1962b for more detail. This appeared first as figures 8 and 9 of Rall 1962b; the combined figure appeared as figure 14 of Rall 1977.

surfaces, all of them negative (relative to a distant reference electrode), with the greatest negativity at the soma surface; the negative magnitude would fall off inversely with radial distance (a Coulomb potential). However, the current sources are actually distributed (at a low surface density) over the widely distributed dendritic surface; alone, this low density source current would produce a small positive potential relative to a distant sink. But, because proximal dendritic locations are actually near the soma, the small positive source component is outweighed by the much larger negative potential associated with the radial current into the soma sink. Thus, the extracellular potential is negative at a proximal dendritic source location (an explicit numerical example can be found on pages 158–160 of Rall 1962b). This new physical intuitive insight was important because it had been conventional dogma to say that an extracellular positivity is always associated with a current source (as is indeed true for an axon). The new insight holds for dendritic neurons, and especially for multipolar dendritic neurons. It follows, of course, that when the soma membrane is a source of extracellular current to all of the dendrites, the extracellular potential (relative to a distant reference electrode) is then positive everywhere except for sleeves of weak negativity associated with distal dendrites.

Also around this time, I discussed with Karl Frank and Philip Nelson the problems of interpreting extracellular potential transients generated by antidromic activation of a single motoneuron in cat spinal cord (Nelson, Frank, and Rall 1960; Rall 1962b; Nelson and Frank 1964; see also Fatt 1957). They performed careful experiments in which they recorded the evoked potential transients at many different locations; for locations near the soma, their larger transient (the AB spike) was diphasic, consisting of a brief large negative spike followed by a smaller and slower positive phase, as illustrated by the theoretical curve at lower left in figure 2. Paul Fatt and others had interpreted such diphasic transients as evidence for action potential propagation in the dendrites. However, my computations demonstrated that this transient could be successfully simulated with a model that assumed the dendritic membrane to be entire passive (figure 2) (additional details are provided by pages 160–163 of Rall 1962b). This computation did not prove the dendrites to be passive, but it did help to tip the scales in a careful discussion of the issues (see Nelson and Frank 1964).

This new result was included in presentations at the first International Biophysics Congress, held at Stockholm in 1961. It depends on the fact that an action potential involves two active phases: rapid membrane depolarization by active inward Na^+ ion current, and then rapid membrane repolarization by active outward K^+ ion current. When the dendritic membrane is assumed to be passive, the impulse cannot propagate actively in the dendrites. However, the rapid active membrane repolarization at the soma does produce a reversal in the direction of current flow between the soma and dendrites. In the computed diphasic $(-, +)$ extracellular voltage transient (lower left in figure 2) the large negative peak corresponds to extracellular current flowing radially inward from the passive dendritic membrane to the actively depolarizing soma membrane; then, the subsequent, smaller positive phase corresponds to reversed extracellular current flow, from the rapidly repolarizing soma membrane radially outward to the passively depolarized dendritic membrane. This insight was essential to the interpretation of antidromically evoked extracellular potential transients in cat spinal cord (Nelson and Frank 1964), and also later, in the olfactory bulb of rabbit (Rall and Shepherd 1968).

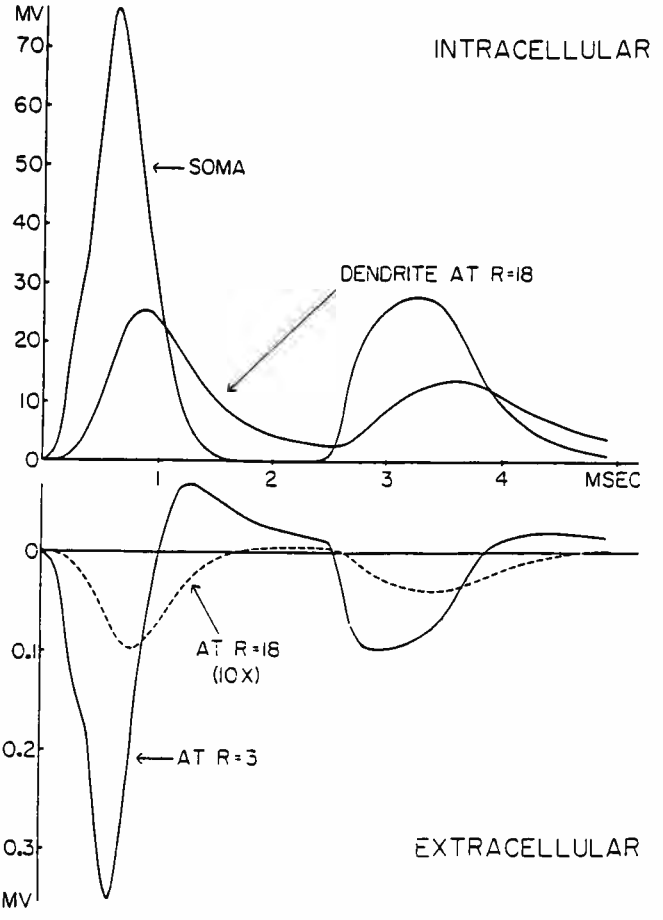

Figure 2
Computed theoretical relation between intracellularly recorded and extracellularly recorded antidromic action potentials, as a function of time.

Uppermost curves: Intracellular potential vs. time. The large-amplitude intracellular curve was given; it corresponds to experimental intracellular recordings made by Nelson and Frank (1964); the full-sized "AB spike" was believed to represent antidromic invasion of both axon hilloc and soma membrane, while the subsequent, smaller "A spike" was believed to represent a spike at the axon hilloc that fails to invade a refractory soma membrane. The lower-amplitude intracellular curve represents the theoretical effect of passive electrotonic spread into a dendritic cylinder of infinite length, computed for a dendritic location at a radial distance $R = 18$, that is, 18 times the soma radius (this corresponds to a dimensionless electrotonic distance of 0.425 from the soma, or about 600 μm in the examples considered).

Lowermost curves: Extracellular potential vs. time. The extracellular curves were computed on the assumption of radial symmetry. The curve for a radial distance $R = 3$ has a shape that is very similar to that at $R = 1$, except the amplitude is about 5 times less. The dashed curve, for a radial distance $R = 18$, has had its amplitude multiplied by 10 to aid the comparison of shape; see Rall 1962b for more detail.

This figure appeared first as figure 11 of Rall 1962b, and also as figure 13 of Rall 1977.

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