3.1 Introduction by Donald R. Humphrey

Rall, W. (1962). Electrophysiology of a dendritic neuron model. *Biophys. J.* 2:145–167.

"Electrophysiology of a Dendritic Neuron Model" (Rall 1962) was at the time a remarkable paper, but it is even more so in retrospect. It was presented first at a Symposium on Mathematical Models and Biophysical Mechanisms, held at the International Biophysics Congress in Stockholm in 1961, and published subsequently in the proceedings of the symposium in the *Biophysical Journal.* With simple but elegant illustrations, Rall outlines in this paper a mathematical model of the neuron that, in this and subsequent forms, has allowed neuroscientists to address fundamental questions about the properties of nerve cells that were previously intractable. To appreciate the significance of this and related work by Rall of about the same time (Rall 1959, 1960, 1961), it is helpful to know the scientific milieu in which it emerged. Only 15 years had elapsed since the classic experiments by Hodgkin and Rushton (1946) on electrotonus in crustacean nerve fibers. Only ten years had elapsed since the prize-winning experiments by Hodgkin and Huxley (1952a,b) on the ionic bases of the action potential, and those by Fatt and Katz (1951) on the end-plate potential. In all these classic experiments, the core conductor (cable) model was used as a theoretical tool to estimate membrane parameters or to relate ionic currents and membrane potentials. But there was no hint in any of these papers as to how the model might be extended to studies of the electrophysiology of neurons, where branching dendrites and complex geometries appeared, for all but the simplest of applications, to be well beyond the scope of available theory.

Yet there was clearly a need for an appropriate model of the neuron. Anatomical data had established that dendrites were the major recipients of synaptic input in the central nervous system, where dendritic surface areas are 10 to 100 times those of the soma (Ramón y Cajal 1909; Fox and Barnard 1957; Sholl 1955; Young 1958). And though only a few years had elapsed since the first intracellular recordings from spinal motoneurons (e.g., Brock et al. 1953; Frank and Fuortes 1955; Eccles 1957), a large body of evidence had accumulated about the electrophysiological properties of these cells. Yet there was no clear vision as to how these data might be used to answer many fundamental questions about cellular function. For example, are dendritic membranes passive or excitable (e.g., Fatt 1957; Freygang and Frank 1959; Nelson and Frank 1964)? If dendritic membranes are passive, are the synapses on distal parts effective in modulating neuronal excitability; that is, what is the effective electrotonic length constant of a cell's dendritic tree (Eccles 1964; Rall 1967)? How are excitatory and inhibitory synapses distributed over the soma-dendritic surface of spinal motoneurons, and how do their effects sum at cellular trigger zones (Smith et al. 1967)? Finally, how could one interpret the extracellular potentials that are generated by neurons to approach these and other important questions (Fatt 1957; Rall 1962; Nelson and Frank 1964; Humphrey 1976)?

In this and related papers, Rall set forth the elements of a dendritic neuron model that allowed quantitative approaches to these and many other fundamental questions. Though it was necessary to make simplifying assumptions about dendritic branching in this initial formulation, the major geometrical features of the neuron were captured. Moreover, this model led to the development of more sophisticated, compartmental models, which can be extended to cases of unequal dendritic branching (e.g., Rall 1964). During the next decade, the basic model outlined in this paper was used to address the fundamental questions about spinal motoneurons previously enumerated (Nelson and Frank 1964; Burke 1967; Smith et al. 1967; Rall 1967); to determine the biophysical factors that contribute to a dominance of synaptic over action-potential currents in the generation of electroencephalographic potentials (Humphrey 1968); to relate intracellular and extracellular potentials in stellate-shaped and in cortical pyramidal cells (Nelson and Frank 1964; Humphrey 1968, 1976); to estimate the excitability of the dendrites of cerebellar Purkinje cells (Llinas et al. 1968a,b); and, perhaps most significantly, to provide the first direct evidence for functional dendrodendritic synapses in the mammalian nervous system (Rall and Shepherd 1968).

The work summarized in this and in other papers by Rall over the next decade is thus a landmark in computational neuroscience; indeed, the full potential of his theoretical insights have yet to be reached. It is a distinct privilege, therefore, to introduce this classic paper to the reader, and to be among the many researchers who know Wil Rall as a friend and as a neuroscientist of the highest stature.

References

Brock, L. G., Coombs, J. S., and Eccles, J. C. (1953). The recording of potentials from motoneurons with an intracellular electrode. *J. Physiol.* (Lond.), 122:429–461.

Burke, R. E. (1967). Composite nature of the monosynaptic excitatory postsynaptic potential. *J. Neurophysiol.*, 30:1114–1137.

Eccles, J. C. (1957). *The Physiology of Nerve Cells.* Baltimore: Johns Hopkins Univ. Press.

Eccles, J. C. (1964). *The Physiology of Synapses.* New York: Academic Press.

Fatt, P. (1957). Electric potentials occurring around a neurone during its antidromic activation. *J. Neurophysiol*, 20:27–60.

Fatt, P., and Katz, B. (1951). An analysis of the end-plate potential recorded with an intracellular electrode. *J. Physiol.* (Lond.), 115:320–370.

Fox, C. A., and Barnard, J. W. (1957). A quantitative study of the Purkinje cell dendritic branchlets and their relationship to afferent fibers. *J. Anat. Lond.*, 91:299–313.

Frank, K., and Fuortes, M. G. F. (1955). Potentials recorded from the spinal cord with microelectrodes. *J. Physiol.* (Lond.), 130:625–654.

Freygang, W. H., Jr., and Frank, K. (1959). Extracellular potentials from single spinal motoneurons. *J. Gen. Physiol.*, 42:749–760.

Hodgkin, A. L., and Huxley, A. F. (1952a). Currents carried by sodium and potassium through the membrane of the giant axon of Loligo. *J. Physiol.* (Lond.), 117:449–472.

Hodgkin, A. L., and Huxley, A. F. (1952b). A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol.* (Lond.), 117:500–544.

Hodgkin, A. L., and Rushton, W. A. H. (1946). The electrical constants of a crustacean nerve fiber. *Proc. Roy Soc. B. Lond.*, 133:444–479.

Humphrey, D. R. (1968). Re-analysis of the antidromic cortical response. II. On the contribution of cell discharge and PSPs to the evoked potentials. *Electroenceph. Clin. Neurophysiol.*, 25:421–442.

Humphrey, D. R. (1976). Neural networks and systems modeling. In *Biological Foundations of Biomedical Engineering*, ed. by J. Kline. Boston: Little, Brown and Company.

Llinàs, R., Nicholson, C., Freeman, J., and Hillman, D. E. (1968a). Dendritic spikes and their inhibition in alligator Purkinje cells. *Science*, 160:1132–1135.

Llinàs, R., Nicholson, C., and Precht, W. (1968b). Preferred centripetal conduction of dendritic spikes in alligator Purkinje cells. *Science*, 163:184–187.

Nelson, P. G., and Frank, K. (1964). Extracellular potential fields of single spinal motoneurons. *J. Neurophysiol.*, 27:913–927.

Rall, W. (1959). Branching dendritic trees and motorneuron resistivity. *Exp. Neurol.*, 1:491–527.

Rall, W. (1960). Membrane potential transients and membrane time constant of motoneurons. *Exp. Neurol.*, 2:503–532.

Rall, W. (1961). Theory of physiological properties of dendrites. *Ann. N.Y. Acad. Sci.*, 96: 1071–1092.

Rall, W. (1962). Electrophysiology of a dendritic neuron model. *Biophys. J.*, 2:145–167.

Rall, W. (1964). Theoretical significance of dendritic trees for neuronal input-output relations. In *Neural Theory and Modeling*, ed. R. Reiss. Stanford, CA: Stanford Univ. Press.

Rall, W. (1967). Distinguishing theoretical synaptic potentials computed for different soma-dendritic distributions of synaptic input. *J Neurophysiol.*, 30:1138–1168.

Rall, W., and Shepherd, G. M. (1968). Theoretical reconstruction of field potentials and dendrodendritic synaptic interactions in olfactory bulb. *J. Neurophysiol.*, 31:884–915.

Ramón y Cajal, S. (1909). *Histologie du Système Nerveux de l'Homme et des Vertébrés.* Vol. 1. Paris: Maloine.

Sholl, D. A. (1955). The surface area of cortical neurons. *J. Anat. Lond.*, 89:571–572.

Smith, T. G., Wuerker, R. B., and Frank, K. (1967). Membrane impedance changes during synaptic transmission in cat spinal motoneurons. *J. Neurophysiol.*, 30:1072–1096.

Young, J. Z. (1958). Anatomical considerations. *EEG Clin. Neurophysiol., Suppl.* 10:9–11.