Biophysical Journal Volume 65 July 1993 15-16

Transients in Neuron with Arbitrary Dendritic Branching and Shunted Soma

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In this issue, three papers (1–3) present an important advance in our mathematical solutions for voltage transients in a neuron represented as a branched structure with passive cable properties. In a remarkable research collaboration Guy Major, Jonathan Evans, and Julian Jack provide us with their meticulous solution of the mathematical complications that result from including arbitrary branch lengths and diameters, together with a shunted soma membrane. These papers provide a careful presentation of the analytical solutions, and an insightful discussion of applications of these theoretical results to voltage clamp and current clamp experiments.

Among many interesting results are parameter dependencies revealed by the mathematics; some are obvious, but others are not. The amplitude terms of impulse responses are independent of R_m, and are inversely proportional to C_m; also, (in the absence of a shunt) the amplitudes are independent of R_i. Fast components of waveforms are independent of R_m and of the shunt conductance; their time constants are proportional to R_iC_m. The largest time constants increase with R_m, and are decreased by the presence of a soma shunt, while the smaller time constants are almost independent of the soma shunt. When fitting model transients to experimental transients, the fast amplitudes constrain C_m, the fast time constants constrain R_i, slow amplitudes constrain the soma shunt estimate, and the slower time constants finally constrain R_m. Insufficient data (at early and/or late times in a transient) can leave estimates underconstrained; this can result in significant nonuniqueness of fit (1).

Explicit examples include a hippocampal CA1 pyramidal cell (with its full morphology); also, several reduced models are evaluated, using tables and computed transients (1). Problems that arise when estimating time constants from experimental transients are illustrated and discussed (1–3); other examples and related discussion are provided by Holmes, Segev, and Rall (1992), and in a review by Rall, Burke, Holmes, Jack, Redman, and Segev (1992) (see references in Ref. 1).[1]

Because voltage clamp methods are used to elucidate membrane channel properties, it is important that the limitations of this technique for branched neurons be explored both analytically and numerically. For a voltage clamp to the soma of a dendritic neuron, explicit examples demonstrate the inadequacy of voltage clamp for many purposes (3), and this is judged likely to be a robust result (3). These results confirm and significantly extend those of Rall and Segev (1985) and of Jackson (1992) (see references in Ref. 2).

It has been known for 30 years that transients in dendritic neurons can be represented as sums of exponential decays, where the values of the coefficients depend on the point of observation and on the initial condition (or location of inputs), while the time constants depend only on eigenvalues of the system (4, 5). Simplifying assumptions were used to reduce a dendritic neuron to a uniformly passive membrane cylinder with sealed-ends; the classical method of separation of variables yielded the simple eigenvalues, $\alpha_n = n\pi/L$, and the simple eigenfunctions, $V_n(x,t) = \cos(\alpha_n x/\lambda)\ \exp(t/\tau_n)$, where the time constants, τ_n, are defined as $R_mC_m/(1 + \alpha_n^2)$ (see Refs. 4 and 5).

How does the more general case differ from this idealized case? The eigenvalues, eigenfunctions, and expressions for the coefficients become much more complicated! Useful insights were gained from several intermediate cases. The effects of membrane nonuniformity were treated early (4), for two regions having different amounts of uniformly distributed synaptic excitatory conductance and/or synaptic inhibitory conductance; the appropriate eigenvalues and eigenfunctions were found and used to calculate illustrative examples, including nonuniform synaptic potentials (4). Coupling two or more cylinders with different electrotonic lengths also complicates the transcendental equation (5); examples that explain how the difference in L changes the eigenvalues, eigenfunctions, and coefficients were recently provided in the appendix of (Holmes, Segev, and Rall (1992); see Ref. 1).

Effects of branching were elucidated first for a case of symmetric branching which also satisfied equivalent cylinder constraints; superposition and symmetry were used to find eigenfunctions which correspond to charge equalization between each branch and its sister branch (Rinzel and Rall (1974); see Ref. 1). Because these eigenfunctions have zero value at their mid-point (where the sister branches take origin from their parent branch), they contribute nothing to proximal voltage transients (e.g., in the parent branch); thus, they contribute only to voltage transients in these branches, in response to inputs in these branches. Such insights provide a basis for qualitative understanding of eigenfunctions and eigenvalues to be expected with less symmetric branching. Explicit lumping of the soma membrane complicates the eigenvalues (5) and also compromises simple orthogonality of the eigenfunctions (Rall (1977); see Ref. 1). Shunting or reduced resistance of the lumped soma membrane introduces further complications which were addressed by Iansek and Redman (1973), Durand (1984), Kawato (1984), as well as others cited in Refs. 1 and 2.

The present papers (1–3) show how to compute eigenvalues (for arbitrary branching) by means of a recursive method that proceeds stepwise from terminal branches to the soma (or to another point of interest); this process resembles the recursive calculation of input conductance in arbitrarily branched dendritic trees (Rall (1959); see Ref. 1). A different method of obtaining essentially equivalent eigenvalues uses matrix inversion with a compartmental (6) representation of the system; this method has been illustrated by Holmes, Segev, and Rall (1992) (see Ref. 1). Very

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[1] References cited by author and year can be found within the article cited by number.

different methods are those of Butz and Cowan (1974), and Holmes (1986), both cited in Ref. 1; note also a recent path integral approach (7). All of these methods assume a linear system. Of course, nonlinear membrane properties can be put into a compartmental model (6); if completely specified for every compartment, the nonlinear consequences can be explored by numerical simulations. Here (1–3), linearity is used to provide a rigorous analytical focus on the complicating effects of different branching morphologies, together with a shunted soma.

REFERENCES

1. Major, G., J. D. Evans, and J. Jack. 1993. Solutions for transients in arbitrarily branching cables: I. Voltage recording with a somatic shunt. *Biophys. J.* 65:423–449.
2. Major, G., J. D. Evans, and J. Jack. 1993. Solutions for transients in arbitrarily branching cables: II. Voltage clamp theory. *Biophys. J.* 65:450–468.
3. Major, G. 1993. Solutions for transients in arbitrarily branching cables: III. Voltage clamp problems. *Biophys. J.* 65:469–491.
4. Rall, W. 1962. Theory of physiological properties of dendrites. *Ann. N. Y. Acad. Sci.* 96: 1071–1092.
5. Rall, W. 1969. Time constants and electrotonic length of membrane cylinders and neurons. *Biophys. J.* 9:1483–1508.
6. Rall, W. 1964. Theoretical significance of dendritic trees for neuronal input-output relations. *In* Neural Theory and Modeling. R. F. Reiss, editor. Stanford Univ. Press, Palo Alto, CA. 73–97.
7. Cao, B. J., and L. F. Abbott. 1993. A new computational method for cable theory problems. *Biophys. J.* 64:303–313.