SHAPING NEURONAL DENDRITES: INTERPLAY OF TOPOLOGICAL AND METRICAL PARAMETERS

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ABSTRACT

The functional role of a neuron within a network is influenced by the geometry of its dendrites. In the present study we have used a new model of dendritic arborization to analyze how metrical and topological parameters interact to shape a certain dendritic tree. One of the specific questions addressed is how to change topological variability in a systematic way while preserving the metrical features. The second problem concerns the effect of topology on the relationship between dendritic size and the distribution of dendritic surface area with radial distance from soma. The simulation results reproduce features of dendritic architecture found in neocortical pyramidal cells and cat superior colliculus neurons.

Keywords: Neuronal dendrites, parametrization, topological asymmetry.

1. Introduction

In many neurons of the central nervous system, dendrites constitute more than 90 % of the membrane surface area, thus receiving the majority of synaptic inputs. The structure of the dendrites therefore can influence the way in which the neuron processes incoming synaptic potentials (see, e.g. [6, 8, 12]).

Intracellular staining techniques (HRP, Biocytin etc.) as well as the use of Golgi impregnation have enabled quantitative studies of dendritic morphology in various neuron species, comprising motorneurons (e.g. [5]), pyramidal cells of the cortex [4] and superior colliculus neurons [7]. As yet, most quantitative descriptions of neuronal dendrites have considered either metrical features (dimensions and statistical variability of soma size, diameters and lengths of dendritic segments, surface area and volume of the dendritic trees) and correlations between them, or topological characteristics (the types and variability of the connectivity pattern of the dendritic segments). Metrical and topological aspects of dendritic shape, however,

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are obviously intermingled, and their relative contribution must be assessed. In the present study we have analyzed how metrical and topological parameters interact to shape individual dendritic trees. After summarizing measures of metrical tree properties, parameters of topological variability are introduced which have been proved powerful descriptors. Based on experimental findings in the neuron species cited above, a small set of basic variables is specified which completely determines a dendritic tree. The model system devised to simulate dendritic trees possesses a unique feature in that it allows to control topological features independently from the metrical parametrization. Elsewhere this model has been employed to study the impact of topological variability on dendritic information processing [12].

Two specific questions are addressed in this article which may be regarded as part of the aim to derive general rules of dendritic organization. The first is the metrical normalization problem for dendritic trees, i.e. how to change topological variability in a systematic way while preserving the metrical features. The second problem concerns the effect of topology on the relationship between dendritic size and the distribution of dendritic surface area with radial distance from soma (see [3]). To test the model performance, we have used it to produce topology-determined features of dendritic architecture which could be shown to resemble the findings in rat neocortical pyramidal cells [4] and cat superior colliculus neurons [7].

2. Parameters of Dendritic Shape

From the literature a variety of parameters describing specific aspects of dendritic architecture can be extracted, including correlations between these parameters (e.g. [1–5,7]). Parameters of dendritic shape may be differentiated into global (tree) characteristics (e.g. total membrane surface area, total volume, number of dendritic terminals) and local, segmental quantities (diameters and lengths of intermediate and terminal segments, branching diameter ratio, segment taper etc.), see [2]. The local parameters of dendritic shape give rise to the global characteristics branching pattern, total cross-sectional area, volume, dendritic length and surface area. Obviously, the connectivity pattern of the segments in the dendritic tree — termed "tree topology" — decisively influences the way of making the global shape from segmental quantities. In the following, we will focus on topology while metrical complexity and variability of segments is strongly reduced.

2.1. *Metrical Parameters*

2.1.1. *Segmental Parameters*

Basic to the metrical description of dendrites are the dimensions of their segments. Assuming simple cylindric shape, segment dimensions are defined by lengths and diameters. Curvature and taper of segments will be not considered in this study. The 3-dimensional orientation of the segments is assumed to be in radial direction with respect to the soma.

Segment diameter. Although segment diameters exhibit large variation, a common feature in most neurons studied so far is the steep decline of segment diameter with branching order. According to Hillman [1], diameters of terminal segments are constrained by values of less than 1 μm. In many neurons, the diameter relationship at points where segments branch, i.e. between diameters of the parent (d_p) and daughter segments $(d_1$ and $d_2)$ has been described by the branch power, viz. the exponent e fullfilling the equation $d_p^e = d_1^e + d_2^e$.

Segment length. Distributions of segment lengths also show large variation. A general observation in many dendrites, however, is that terminal segments have a greater mean length than intermediate segments (e.g. [4, 7]). Typical values for the distribution means of intermediate and terminal segment lengths are given below. More specific findings such as order dependency of terminal segment lengths will not be included here.

2.1.2. Global Parameters

The combination of segmental parameters forms a set of global parameters which are used to relate the shape of a neuron to its function. The major parameters considered here are total surface area, volume and length of the dendritic segments and their spatial distribution.

2.2. Dendritic Topology

Categorizing dendritic trees according to topological type depends on the patterning of segments, and is independent of metrical and orientation features. For a given number of segments only a finite number of different connectivity patterns (tree types) is possible, although this number rapidly increases with the number of terminal segments (the degree of the tree) [10]. An efficient measure for tree topology is the tree asymmetry [11], defined as the mean value of the asymmetry of its partitions

$$A_t = \frac{1}{n-1} \sum A_p(r_i, s_i). \tag{1}$$

The summation runs over all $n - 1$ branch points of the tree with degree n while the partition (r_i, s_i) denotes the degrees of both subtrees at branch point i, and A_p denotes the partition asymmetry

$$A_p = \frac{|r - s|}{r + s - 2} \qquad \text{if} \quad r + s > 2 \quad \text{and} \quad A_p(1,1) = 0. \tag{2}$$

The values of tree asymmetry range from zero for perfectly symmetrical trees to approaching one for most asymmetrical trees [11]. From experimental observations on neuronal dendritic trees we know that the various tree types do not occur with equal likelihood. Model studies on the growth of tree patterns have shown that among the large number of possible tree types only a limited number of them have

a higher probability of occurrence which depends on the mode of growth of the dendrites. In the QS model [9], the growth of trees is described by a series of branching events during which a new terminal segment is attached to an existing one. The parameter Q defines the ratio for the branching probabilities of intermediate and terminal segments, and the parameter S defines how the branching probabilities depend on the branching order. Two particular growth modes have received much attention, viz. the random terminal growth mode in which only terminal segments branch with the same probability (i.e. $Q = 0$, $S = 0$), and the random segmental growth mode in which all segments with equal probability branch ($Q = 0.5$, $S = 0$). In a recent study it was shown that the expectation of the tree asymmetry depends strongly on the mode of growth and that the expected value is almost independent of tree degree [11]. Observed mean ($\pm$SD) values for the tree asymmetry are, e.g., 0.38 ($\pm$0.22) for basal dendrites of pyramidal cells and 0.43 ($\pm$0.26) for dendrites of multipolar nonpyramidal neurons [11]. By appropriate parameter choices, the QS model could reproduce these observed asymmetry values.

3. Parametrization of Dendritic Trees and Model Construction

In order to analyze the impact of topology on dendritic shape, the complexity and variability of segmental dimensions was excluded. Therefore, we used a fixed parametrization for the metrical properties. First, all terminal segments have equal diameter d_t. Second, a branch power relation was used for calculating the diameters of intermediate segments. The diameter d_s of an intermediate segment s is obtained then by

$$d_s = d_t \, n_s^{1/e}, \tag{3}$$

where n_s denotes the degree of the subtree emanating from segment s. In particular, we yield for the root diameter d_r

$$d_r = d_t \, n^{1/e}, \tag{4}$$

from which follows that the root diameter d_r is independent of the topological tree type. Finally, lengths l_i and l_t of intermediate and terminal segments, respectively, were taken fixed, resulting in a fixed length ratio $r_{it} = \frac{l_i}{l_t}$. Different topological tree types were produced with the QS growth model, using $(Q, S) = (0, 0)$ (random terminal growth mode) and $(Q, S) = (0.5, 0)$ (random segmental growth mode). The most symmetrical and asymmetrical trees were also included to cover the total range of topological variation.

Thus, generation of dendritic trees proceeded in two steps: (1) a topological "skeleton" of a certain asymmetry value A_t was produced via the (Q, S) model to which (2) "flesh" was attached using a specific metrical parametrization.

4. Simulation Results

By choosing specific sets of segmental parameters, two basic types of dendritic trees were modeled. Type 1 dendritic trees were generated to reproduce the main features
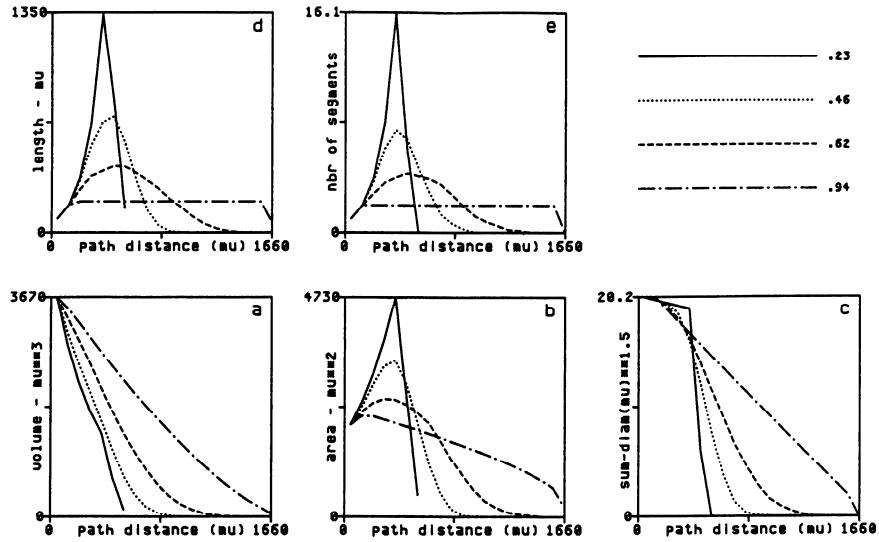
(a)
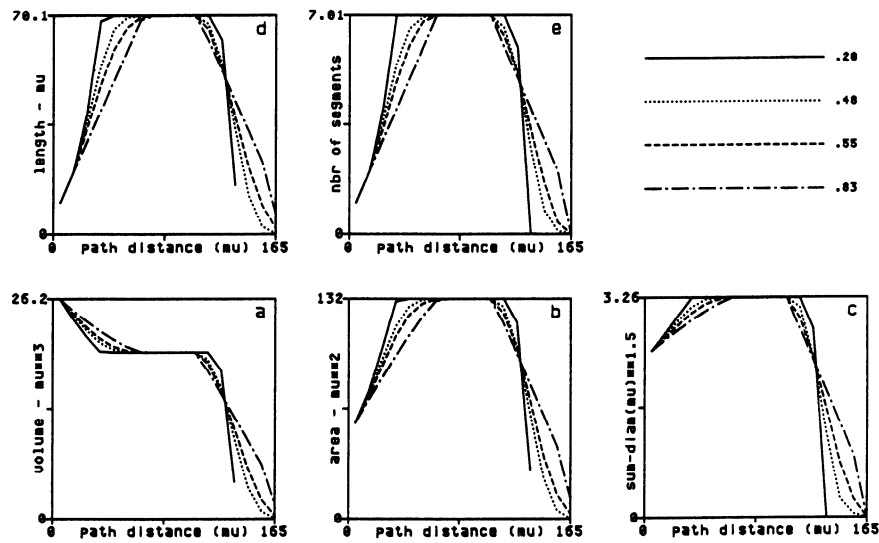
(b)

Fig. 1. Path distance analyses for (a) Type 1 and (b) Type 2 dendritic trees. Displayed are the distribution of aggregate dendritic length, number of segments, volume, surface area and $\sum d^{3/2}$, each per 85 μm (Type 1) and 10 μm (Type 2) bin length, as functions of path distance from the soma. Each plate contains four curves, corresponding to the asymmetry values of the most symmetrical (0.20) and most asymmetrical tree (0.83), and the mean asymmetry values of 100 trees grown in the random segmental (0.55) and terminal growth mode (0.48).
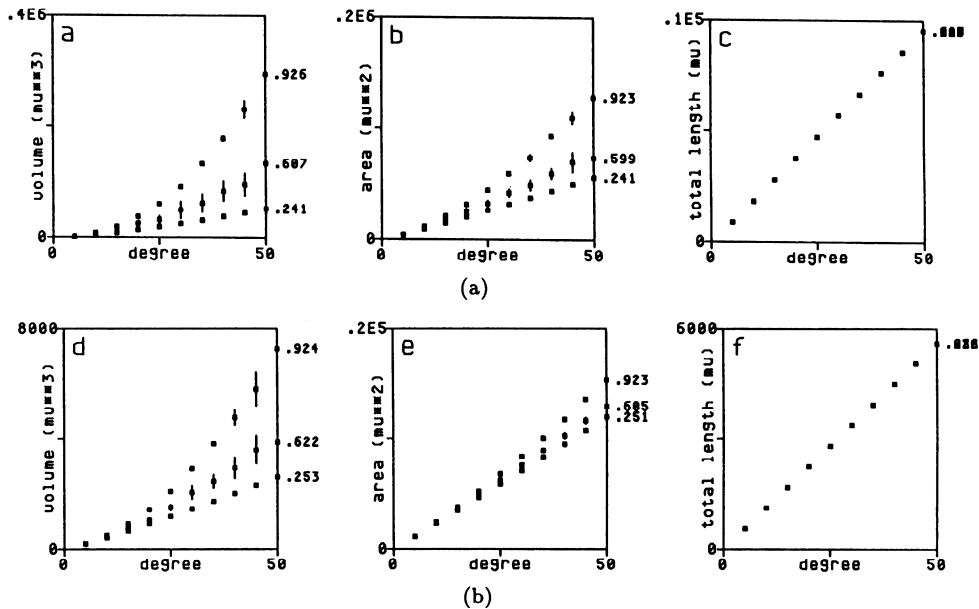
Fig. 2. The global parameters of dendritic shape — total volume, surface area and dendritic length — as functions of degree and topology for (a) Type 1 and (b) Type 2 trees. Each plate displays three curves, labeled with the mean asymmetry values of 50 random trees obtained for symmetrical trees $(Q, S) = (0, 4)$, trees grown in the random segmental mode $(Q, S) = (0.5, 0)$ and asymmetrical trees $(Q, S) = (0.99, 0)$.

of large multipolar neurons, such as spinal motorneurons [5] and superior colliculus neurons [7] of the cat. Parameter values used for the simulations were taken from [7]: degree $n = 19$, length of terminal segments $l_t = 107$ μm, segment length ratio $r_{it} = 0.8$, diameter of terminal tips $d_t = 1$ μm and branch power $e = 1.47$.

With Type 2 dendritic trees, the main features of smaller neurons, such as the basal dendrites of neocortical pyramidal cells of the rat should be reproduced. The parameter values used for generating Type 2 trees were taken from [4]: degree $n = 7$, length of terminal segments $l_t = 102$ μm, segment length ratio $r_{it} = 0.1$, diameter of terminal tips $d_t = 0.6$ μm and branch power $e = 1.75$.

The results of the first set of simulations are presented in Fig. 1. This figure depicts the radial extent and spatial distribution of several characteristic quantities for trees with variable topological asymmetry. Displayed is the distribution of accumulated dendritic length, number of segments, dendritic volume, surface area and dendritic trunk parameter $\sum d^{3/2}$ (the latter parameter is an often used morphological predictor of the passive electrotonic structure of the tree, cf. [8]). With increasing asymmetry value the spatial distribution of the quantities is changed: dendrites extend further, the height of the peak is decreased but its location remains more or less unchanged. This is in good accordance with findings in motorneurons where such differences have been ascribed variations within and between cell classes [1, 9]. In Type 2 dendrites, the spatial distribution curves reproduce the situation found

in the basal dendrites of pyramidal cells [4]. For example, the number of segments in the model shows the same course with distance from the root of the dendrite as in Larkman's experimental data: a rapid increase for the first 40–50 μm, followed by a plateau extending to 100–120 μm and a steep decline down to 160 μm. This general picture is only slightly modified by topological variation (Fig. 1).

In the second set of simulations, the tree size (degree n) was varied while all the other values of the parametrization remained fixed. We found that the relative impact of topological variability strongly depends on tree size. The metrical parametrization used determines the basic level specified by the symmetrical trees (Fig. 2). By comparing Type 1 and Type 2 tree simulations, it turns out that among the metrical parameters branch power seems to have the most remarkable effect on the global tree parameters. Total dendritic length does not depend on tree asymmetry for the metrical parametrization used.

5. Discussion

The impact of topological asymmetry on global features of dendritic shape has been studied, using a new model which allows to control the topological type (and thus the asymmetry) of the tree while preserving the segmental characteristics. From the various relations proved to exist between the parameters of a dendritic tree, we have selected that between stem diameter and degree (via branch power) to attach metrical dimensions to the topological "skeleton" of the tree grown by the QS model. To test the model performance, we have applied it to reproduce features in the original data on superior colliculus neurons, motorneurons and cortical pyramidal cells that have not been explicitly included in the model construction. The simulation results might be summarized as follows. Dendritic trees of Type 1 and Type 2 are distinctly different with respect to the distributional relationships studied. Strictly speaking, topological variability is of significant influence in Type 1 trees whereas it has negligible impact on Type 2 dendrites. Thus, it provides a natural explanation for the observed differences in the degree of "remoteness" of dendritic trees, i.e. the radial extent and spatial distribution of surface area, volume and dendritic length found within and between neuron species. These findings are in accordance with experimental results on many neuron types, stating that large dendritic trees are not scaled-up versions of the smaller trees (e.g., [3]). A prediction of the simulation results is that for larger dendritic trees, the variability in topology should have substantial effect on the strength of the correlation between stem diameter and total surface area or volume: the larger the tree, the weaker the correlation may be. These results are of general importance in analyses of neuronal form-function relationship where the relative contribution of topology is assessed [12].

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