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IMPACT OF TOPOLOGICAL VARIABILITY ON DENDRITIC GEOMETRY

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ABSTRACT

The development of neuronal branching patterns mainly proceeds by branching events at terminal segments. The randomness in the occurrences of these events is the major cause of the variability that is observed in the final topological structures of neuronal trees. A general observation in neuronal trees is the existence of a branch power relation between the diameters of the segments at branch points. Because of this correlation, total area and volume will become dependent on branching pattern topology. A quantitative assessment of this finding is given. How topological variation propagates into variation in total area and volume, using topological growth models for producing random tree topologies and a simple metrical parametrization is discussed.

Keywords: Dendrites, morphology, variability, growth.

1. Introduction

The geometry of natural dendritic branching patterns shows large variability, as is demonstrated in many studies of neuronal morphologies (e.g., [1–3], [5–7], [12–15]. This variability is expressed in the number of segments, the length and diameter of segments, and the way the branching pattern is embedded in the three-dimensional space. An additional source of variability is in the topological structure, i.e., the connectivity pattern of the segments. This variation occurs because of the many ways to connect segments in the formation of a tree. The variability in the local elements also propagates into global geometrical measures of the branching pattern, like total area, volume, path lengths and radial distances.

So far, the interest in the literature has not been focussed on variability in itself. Nevertheless, it is expected that variability in structure also results in variability in functional operation. Additionally, variability has its origin and the mechanisms underlying its expression may also be dominant in the emergence of the dendritic morphological features themselves. The recent findings concerning topological variability may serve as an example. It has been shown that dendritic branching patterns have a topological variability that can fully be explained by their growth

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patterns [10]. The primary source of variability is the randomness by which branching events occur at the segments in the tree during outgrowth.

In the separation of metrical and topological aspects, it was initially assumed that these aspects are independent. This assumption may be violated, however, when structural correlations exist within the branching patterns. One such correlation, observed in many dendrites, concerns the branch power relation between the diameters of parent and daughter segments at branch points [4, 5]. An immediate consequence of this rule is that the diameters of the segments become dependent upon the connection pattern of the segments, i.e., their topological structure.

The question, addressed in this paper, is how and to what extent the topological variation will propagate via the branch power rule into a variation in the global metrical properties area and volume.

It will be approached by calculating the area and volume of trees with a fixed and simple metrical parametrization but with full variability in their topological structures.

2. Dendritic Topology

For a given number of segments there are many ways to connect these segments in the formation of a binary branching pattern, as is shown in Fig. 1 for trees of degree 8, i.e., with 8 terminal segments. The tree types are characterized by their tree asymmetry, defined by the mean asymmetry in subtree pairs at all the branch points [10]. The tree asymmetry measure has a value of 0 for strict symmetrical and a value approaching 1 for strict asymmetrical trees.

Natural tree types do not occur with equal probabilities. These probabilities appear to depend strongly on the growth pattern as could be demonstrated by [8], [9] and [10], using a two-parameter (Q-S) growth model. The parameter Q in this model relates the branching probabilities of intermediate and terminal segments, while parameter S determines the order dependency [9]. Characteristic modes of growth are the random terminal growth mode, $(Q, S) = (0, 0)$, allowing only terminal segments to branch, each with the same probability, and the random segmental growth mode, $(Q, S) = (0.5, 0)$, allowing all segments to branch with equal probability.

Figure 1 shows a symmetrical tree (a), an asymmetrical tree (b) and random trees for the random terminal growth mode (c-h) and the random segmental growth mode (i-n). Note, that the trees in (i-n) have on the average greater tree asymmetry values than the trees in (c-h).

The analysis of observed dendritic branching patterns has revealed that their tree-type frequencies correlate with a mode of growth that is close to the random terminal growth mode [10]. For that reason, we will use this growth mode to produce random trees with a realistic topological variability. The way to produce random trees is described in [10].

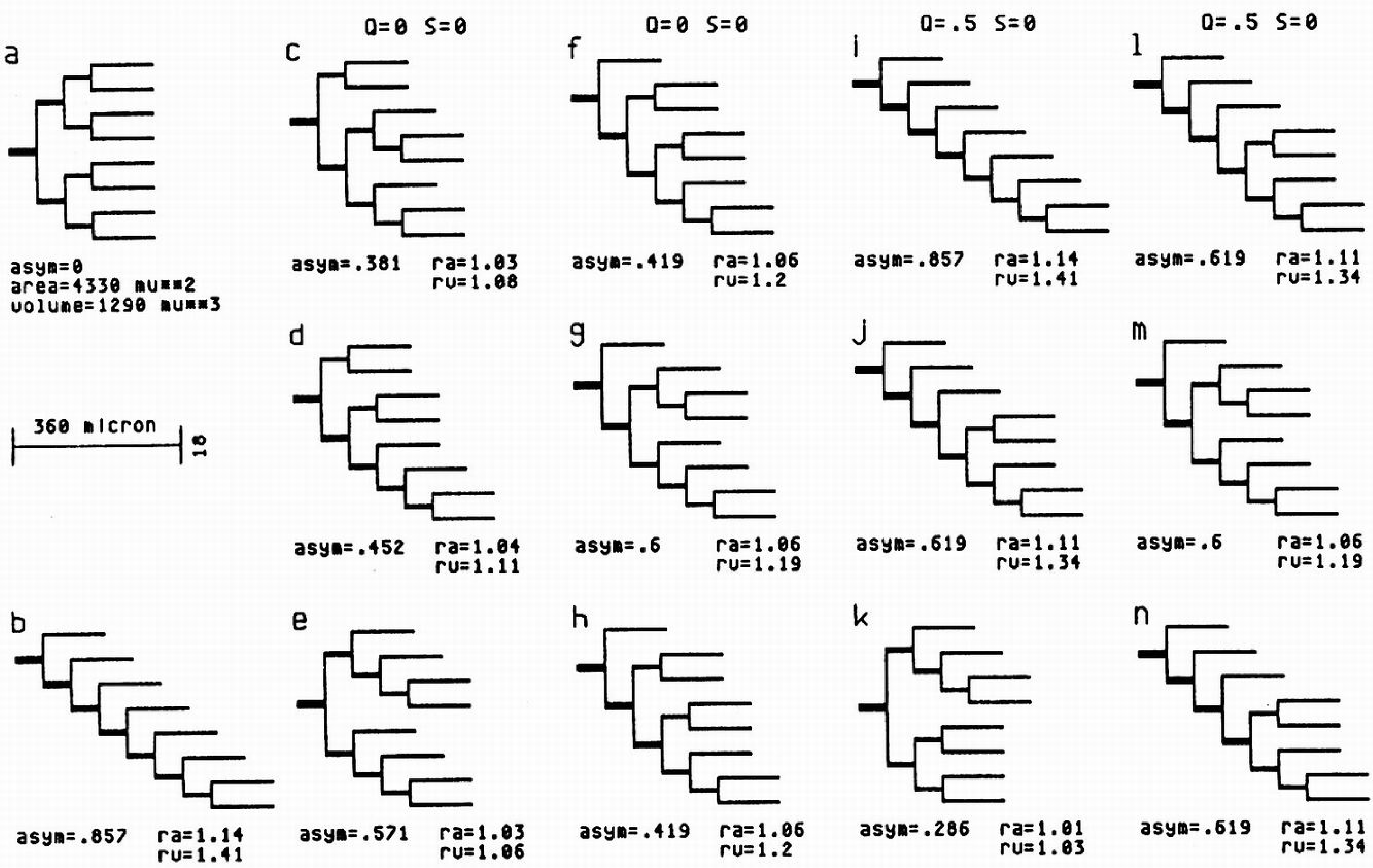

Fig. 1. Illustration of a symmetrical tree (a), an asymmetrical tree (b) and random trees, produced by the random terminal growth mode $(Q, S) = (0, 0)$ (c-h) and the random segmental growth mode $(Q, S) = (0.5, 0)$ (i-n). The trees are of degree 8 and characterized by their tree asymmetry values ("asym"). Terminal segments have a length of $l_t = 132\,\mu$m and diameter $d_t = 0.7\,\mu$m, the length ratio of intermediate and terminal segments equals $r = 0.45$ while the branch power is taken equal to $e = 1.5$. The area ("ra") and volume ("rv") of each tree are calculated relative to the symmetrical tree. Note, that these outcomes are independent of the actual choice of l_t and d_t.

3. Topological Structure, Dendritic Area and Volume

3.1. *Geometrical Parametrization*

A simple parametrization of the dendritic geometry is assumed. All segments have a fixed length, l_t for terminal and l_i for intermediate segments. The diameter of terminal segments will be fixed at d_t. A branch power relation is assumed between the diameters of a parent and its daughter segments at a branchpoint, i.e., $d_p^e = d_1^e + d_2^e$. Then, the diameter of an intermediate segment s is determined by the number of terminal segments n_s in its remote subtree as

$$d_s^e = n_s d_t^e \quad \text{or} \quad d_s = d_t n_s^{1/e} . \tag{1}$$

3.2. *Dendritic Area and Volume*

A dendritic tree of degree n has in total $2n - 1$ segments of which n terminal and $n - 1$ intermediate segments. The membrane area of such a tree is equal to the sum of the area of all its terminal and intermediate segments

$$A = \pi \sum_{s=1}^{2n-1} d_s l_s = \pi \left[n d_t l_t + l_i \sum_{k=1}^{n-1} d_k \right] \tag{2}$$

when d_s and l_s denote the diameter and length of segment s. Assuming a branch power relation (Eq. (1)) we obtain

$$A = \pi d_t l_t \left[n + \frac{l_i}{l_t} \sum_{k=1}^{n-1} n_k^{1/e} \right] = A_t [n + r S_A] \,. \tag{3}$$

Here, A_t denotes the terminal segment area $A_t = \pi d_t l_t$, $r = l_i / l_t$ denotes the length ratio of intermediate and terminal segments and $S_A = \sum_{k=1}^{n-1} n_k^{1/e} = \sum_{k=1}^{n-1} (d_k / d_t)$ denotes the sum of intermediate segment diameters, normalized with respect to the terminal segment diameter d_t.

In a similar way the dendritic volume can be expressed as

$$V = V_t [n + r S_V] \tag{4}$$

with V_t denoting the volume of a terminal segment and $S_V = \sum_{k=1}^{n-1} n_k^{2/e} = \sum_{k=1}^{n-1} (d_k / d_t)^2$ denotes the sum of squared normalized diameters of intermediate segments.

The quantities S_A and S_V are functions of the degree n, the branchpower e and of the topological structure. Separating in Eqs. (3) and (4) the contributions by terminal and intermediate segments we obtain $A^{\mathrm{term}} = n A_t$, $V^{\mathrm{term}} = n V_t$, $A^{\mathrm{int}} = A_t r S_A$ and $V^{\mathrm{int}} = V_t r S_V$. The relative contributions of intermediate segments to total area and volume and to the terminal segment contributions can be expressed as

$$\frac{A^{\mathrm{int}}}{A} = \frac{r S_A}{n + r S_A}, \qquad \frac{V^{\mathrm{int}}}{V} = \frac{r S_V}{n + r S_V},$$

and (5)

$$\frac{A^{\mathrm{int}}}{A^{\mathrm{term}}} = \frac{r S_A}{n}, \qquad \frac{V^{\mathrm{int}}}{V^{\mathrm{term}}} = \frac{r S_V}{n} \,.$$

In conclusion, Eqs. (3)–(5) show that the terms S_A and S_V play a crucial role in both dendritic area and volume as well as in the relative contributions of intermediate and terminal segments to these global geometrical properties.

3.3. *Effect of Topology on S_A and S_V*

The terms S_A and S_V depend on the connection pattern of intermediate segments as an immediate consequence of the branch power relationship. This is clearly demonstrated by their outcomes for trees of different topologies, given in Table 1. Both S_A and S_V become larger when the trees become more asymmetrical. This effect becomes stronger for decreasing branch power. Of course, the terms S_A and S_V increase with increasing degree n, i.e., when the trees become larger.

Table 1. Influence of the topological arrangement of intermediate segments on the sum of normalized diameters $S_A = \sum_{k=1}^{n-1}(d_k/d_t)$ and the sum of squared normalized diameters $S_V = \sum_{k=1}^{n-1}(d_k/d_t)^2$ of intermediate segments. The calculations are done for individual symmetrical and asymmetrical trees and for sets of random trees, produced by the random terminal and random segmental growth mode. For each set, 1000 trees were generated from which mean S_A and S_V values are calculated The results are obtained for two values of the degree n and three values of the branch power e.

$n = 8$	S_A				S_V			
	sym	$Q = 0$	$Q = 0.5$	asym	sym	$Q = 0$	$Q = 0.5$	asym
$e = 1$	24.00	27.30	30.16	35.00	112.00	138.81	163.79	203.00
$e = 1.5$	15.39	16.82	17.96	20.07	38.78	45.78	51.56	62.04
$e = 2$	12.49	13.41	14.06	15.31	24.00	27.57	30.13	35.00
$n = 16$	S_A				S_V			
	sym	$Q = 0$	$Q = 0.5$	asym	sym	$Q = 0$	$Q = 0.5$	asym
$e = 1$	64.00	76.60	94.58	135.00	480.00	651.16	923.22	1495.00
$e = 1.5$	37.13	41.70	48.38	63.00	117.87	147.25	195.25	295.86
$e = 2$	28.97	31.70	35.21	43.47	64.00	76.71	94.51	135.00

Because S_A and S_V are functions of the topological structure, they will show variation when random trees are produced. Therefore, the columns "$Q = 0$" and "$Q = 0.5$" contain mean values, obtained by generating 1000 random trees according to the corresponding growth mode. The coefficients of variation $cv(S_A)$ and $cv(S_V)$ for these sets are given in Table 3. The outcomes demonstrate that the coefficients of variation increase with increasing tree asymmetry, increasing degree and with decreasing branch power.

3.4. *Propagation of Variance in S_A and S_V into Total Area and Volume*

Equations (3) and (4) show how the total dendritic area A and volume V depend on the terms S_A and S_V, while these terms in turn depend sensitively on the topological structure, as is demonstrated in Table 1. This finding is also illustrated in Fig. 1, which shows how area and volume differs between a symmetrical, an asymmetrical and a number of random trees. To calculate quantitatively how $cv(S_A)$ and $cv(S_V)$ propagate into $cv(A)$ and $cv(V)$, respectively, we will assume that the variation in the other terms A_t or V_t, n and r is zero. Then, using Eqs. (3) and (4), the standard deviations in A and in V can be given by

$$\sigma(A) = A_t r \sigma(S_A) \quad \text{and} \quad \sigma(V) = A_t r \sigma(S_V)\,. \tag{6}$$

Realizing that $cv(x) = \sigma(x)/x$ we obtain for the coefficients of variation $cv(A)$ and $cv(V)$

$$cv(A) = \frac{S_A}{S_A + n/r} cv(S_A) \quad \text{and} \quad cv(V) = \frac{S_V}{S_V + n/r} cv(S_V)\,. \tag{7}$$

4. Results

4.1. *Area and Volume Ratios*

The role of topology in dendritic area and volume is clearly expressed by calculating the area or volume of a tree relative to the most symmetric tree. In the ratios $A(\text{tree})/A(\text{sym})$ and $V(\text{tree})/V(\text{sym})$, the terminal segment area A_t and volume V_t will cancel and the ratios remain only as functions of n, r, e and, S_A and S_V. Figure 2 shows that the topological difference between symmetric and asymmetric trees can result in large differences in area and volume (for instance up to a factor 3 in the case of $e = 1$ for the present parameter set). Trees with realistic topologies (e.g., produced by the random terminal growth model) have outcomes much closer to those of the corresponding symmetrical trees.

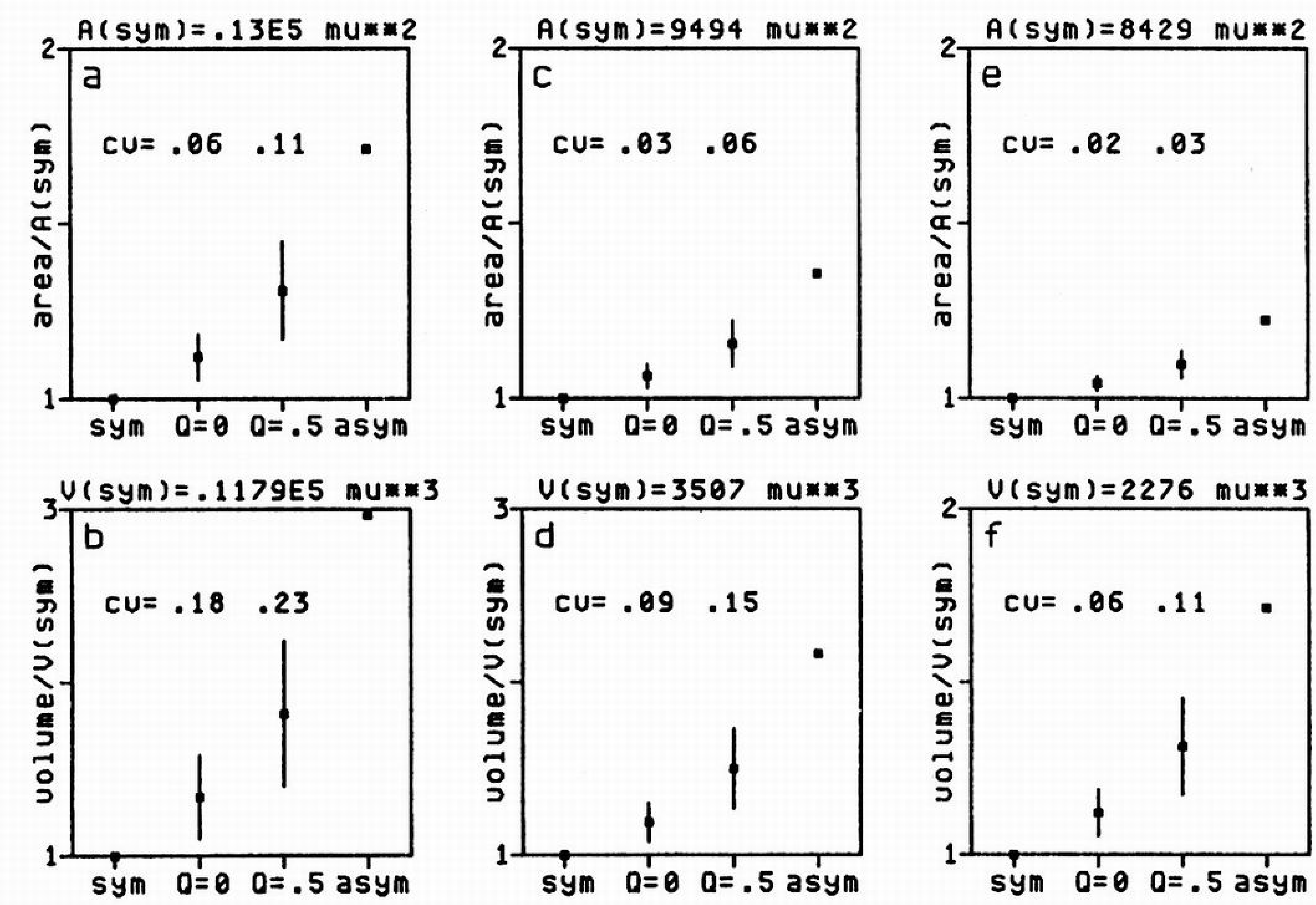

Fig. 2. Illustration of the effect of the topological structure of dendritic trees on area and volume. Each panel gives the result of a symmetrical tree ("sym"), an asymmetrical tree ("asym") as well as of random trees, produced by the random terminal growth mode ("$Q = 0$") and the random segmental growth mode ("$Q = 0.5$"), all of degree 16. Terminal segments have a length $l_t = 132\,\mu$m and diameter $d_t = 0.7\,\mu$m, the length ratio of intermediate and terminal segments equals $r = 0.45$. Area and volume are calculated relative to the symmetrical trees (printed above the panels). The figure illustrates the effect of topology within each panel, as well as the effect of the branch power with values $e = 1$ (panels a and b), $e = 1.5$ (panels c and d) and $e = 2$ (panels e and f). In addition, the figure illustrates the effect of topology and branch power on the coefficients of variation in the area and volume of the random trees. Note, that these outcomes are independent of the actual choice of l_t and d_t.

4.2. *Contribution of Intermediate and Terminal Segments to A and V*

Topology plays a role only via the summed area A^{int} and volume V^{int} of the intermediate segments. Therefore, the relative contribution of intermediate and terminal segments to the total area $A^{\text{int}}/A^{\text{term}} = rS_A/n$ and volume $V^{\text{int}}/V^{\text{term}} = rS_V/n$ [Eq. (5)] determine the extent of this role. For this reason, the ratios S_A/n and S_V/n are calculated for different topologies and for several values of the parameters e and n and presented in Table 2. Actual area and volume ratios are then easily obtained by multiplying these outcomes with the value for $r = l_i/l_t$. From Table 2, it can be concluded that the contribution of intermediate segments to area and volume is consequently larger than of terminal segments, in the case of $r = 1$. This result is based on the fact that intermediate segments have greater diameters than terminal segments as a consequence of the branch power relationship. In the case of unequal lengths of intermediate and terminal segments, say $r < 1$, it is possible that the product terms rS_A/n and rS_V/n become smaller than one, implying that terminal segments then will dominate in their contribution to area and volume. Note, that the coefficients of variation, calculated for S_A and S_V, and given in Table 3, also apply to the ratios S_A/n and S_V/n.

Table 2. Values for the ratios S_A/n and S_V/n, calculated using the outcomes of Table 1. These quantities indicate the ratio of the contributions of intermediate and terminal segments to the total area and volume, respectively, assuming equal segment lengths. In the case of unequal segment lengths, the ratios $A^{\text{int}}/A^{\text{term}} = rS_A/n$ and $V^{\text{int}}/V^{\text{term}} = rS_V/n$ can easily be obtained by multiplying the presented numbers in this table with the value for $r = l_i/l_t$.

$n = 8$	S_A/n				S_V/n			
	sym	$Q = 0$	$Q = 0.5$	asym	sym	$Q = 0$	$Q = 0.5$	asym
$e = 1$	3.00	3.43	3.79	4.38	14.00	17.51	20.61	25.38
$e = 1.5$	1.92	2.11	2.25	2.51	4.85	5.76	6.48	7.75
$e = 2$	1.56	1.67	1.76	1.91	3.00	3.42	3.79	4.38
$n = 16$	S_A/n				S_V/n			
	sym	$Q = 0$	$Q = 0.5$	asym	sym	$Q = 0$	$Q = 0.5$	asym
$e = 1$	4.00	4.75	5.94	8.44	30.00	40.11	58.07	93.43
$e = 1.5$	2.32	2.61	3.01	3.94	7.37	9.22	12.14	18.49
$e = 2$	1.81	1.97	2.20	2.72	4.00	4.74	5.88	8.44

4.3. *Topology-Induced Variation in A and V*

Like the quantities S_A and S_V, $cv(S_A)$ and $cv(S_V)$ also are functions of n, e and topology only, and thus independent of the actual lengths and diameters of the segments. The propagation of $cv(S_A)$ and $cv(S_V)$ (Table 1) into A and V is described by Eq. (7), and thus depends additionally on the parameter r, the length ratio of intermediate and terminal segments. The coefficients $S/[S + n/r]$ in Eq. (7) are smaller than one. Therefore, $cv(S_A)$ and $cv(S_V)$ represent maximal values for the coefficients of variation in A and V.

Like $cv(S_A)$ and $cv(S_V)$, $cv(A)$ and $cv(V)$ also increase with increasing asymmetry and decrease with increasing branch power. For instance, in the given examples in Fig. 2 with $r = 0.45$, values of 10 and 24 percent, respectively, are obtained for trees, produced by the random segmental growth model, with a branch power of $e = 1$. For trees with realistic topological variation (produced by the random terminal growth model) and with a branch power of $e = 1.5$, these values are 3 and 10 percent, respectively.

Table 3. Coefficients of variation in S_A and S_V for the sets of random trees in Table 1, generated by the random terminal growth mode ($Q = 0$) and the random segmental growth mode ($Q = 0.5$). Note, that these *cv*-values also apply to S_A/n and S_V/n in Table 2.

$n = 8$	S_A		S_V	
	$Q = 0$	$Q = 0.5$	$Q = 0$	$Q = 0.5$
$e = 1$	0.08	0.10	0.14	0.17
$e = 1.5$	0.06	0.07	0.11	0.13
$e = 2$	0.04	0.06	0.08	0.10
$n = 16$	S_A		S_V	
	$Q = 0$	$Q = 0.5$	$Q = 0$	$Q = 0.5$
$e = 1$	0.09	0.14	0.18	0.24
$e = 1.5$	0.05	0.10	0.12	0.19
$e = 2$	0.04	0.07	0.09	0.14

5. Discussion

The present study has demonstrated that topological variation propagates into variation of area and volume. It is shown how the topological configuration of the intermediate segments influences, via the branch power relation, the diameter distribution of these segments and consequently the total area and volume. The extent of this variability propagation is estimated using a simple geometrical parametrization of dendritic geometry. Maximal attainable values for the coefficients of variation in area and volume, caused by the topological variability, could be estimated (Table 3). For instance, for trees with realistic topological variability ($Q = 0$), branch power $e = 1.5$ and degree $n = 16$, these values are 5 and 12 percent, respectively.

For the present study, fixed segment lengths are assumed. This is not a realistic assumption. Especially terminal segment lengths vary substantially within a dendrite. This fact, however, will not interfere with the present conclusions because the parameters l_t, A_t and V_t can be interpreted as the mean length, area and volume of terminal segments, respectively. Likewise, l_i can denote the mean length of intermediate segments.

Experimental data of coefficients of variation in dendritic area and volume show in general much larger outcomes than that presented in this paper. For instance, $cv(A)$ in cat motorneurons can range from 0.29 [3] up to 0.74 [2] and $cv(V)$ ranges from 0.49 [12] up to 0.92 [2]. Clearly, the observed variability also originates from variation in other parameters like the degree n, the lengths l_i and l_t and the branch-power e. For a proper comparison these variations should also be included in the analysis, which is the subject of the present research. Dendritic topology plays a role in dendritic function. It has a clear impact on the electrotonic length of the dendrite, on dendritic input conductance and is involved in signal transfer properties as is recently demonstrated in [11]. The present study has shown how area and volume are involved in these structure-function relationships in dendrites.

6. Acknowledgements

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