Extended Summary

Morphological Noise in a Computational Model of Dendritic Branching.

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Abstract:

We present a computational model of dendritic branching in which several parameters are measured from reconstructed CA1 pyramidal cells, grouped by the corresponding branch diameter, and resampled to create virtual neurons. This model greatly improves over previous studies in which parameters were not grouped by diameter. Further improvement was obtained by separating the distal dendrites in the apical tree. We also investigated the effects of measurement error in the model by systematically adjusting the variability of the parameter distributions. We found the model to be particularly sensible to key parameters (e.g. taper rate) at variability ranges near the experimental values.

The branching pattern of dendrites is vitally important to the behavior of the mammalian nervous system (Schaefer et al., 2003). Computational neuroanatomy attempts to better understand the structure of dendrites through the use of computer algorithms (Ascoli, 1999, 2002; Ascoli et al., 2001; Burke et al, 1992). In one common approach, distributions of morphological parameters measured from real cells are re-sampled to create virtual dendritic trees (Ascoli and Krichmar 2000).

Our general model of dendritic branching has been previously described in detail (Donohue et al., 2002). The flowchart of the specific algorithm used in this study, and the definition of all parameters are provided in Figure 1. Briefly, a set of algorithmic parameters (initial diameter, taper rate, branch pathlength, parent-daughter ratio and daughter ratio) were measured form a publicly available archive of 23 rat hippocampus CA1 pyramidal cells (Pyapali et al., 1998). All model parameters except initial diameter were binned according to the diameter values at which they occurred in the real cells. For each diameter range a bifurcation probability was also computed. During virtual growth, an initial tree diameter is sampled and based on that diameter a taper rate and branch pathlength are sampled. If, depending on the termination probability of the ending diameter, the branch bifurcates, then daughter and parent daughter ratios are sampled to give the daughter diameters. The algorithm then continues treating each daughter branch as a new stem until all branches terminate. The number of bifurcations in the final virtual neuron is taken as an "emergent parameter" that can be compared to the value measured from the real cells to assess the model result.

In previous implementations of this model, the distributions of all parameters (besides termination probability) were extracted from the whole population of dendrites (Donohue et al., 2001, 2002). Binning parameters by diameter vastly improved the model results, presumably by keeping parameter values from being applied to portions of the virtual tree in which they did not occur in the real trees (Donohue et al., 2003).

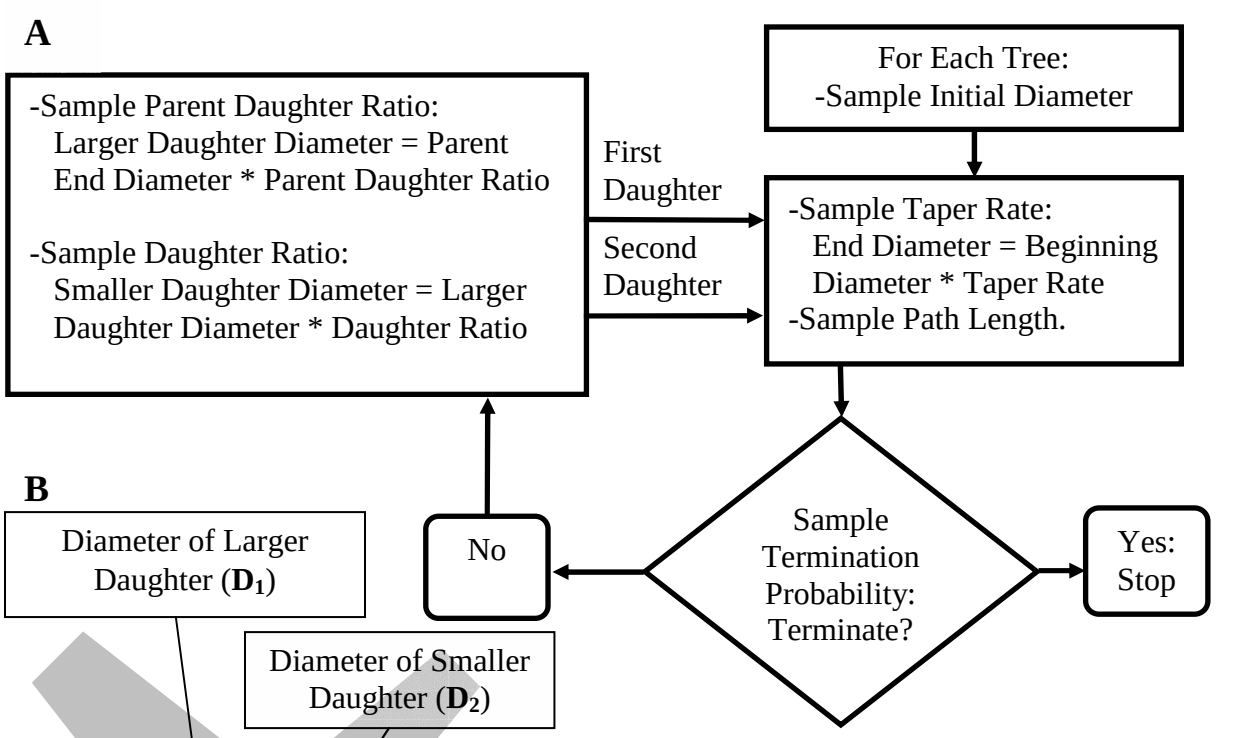

Figure 1a. Algorithm Flowchart. With the exception of initial diameter all of the sampled parameters are binned according to the diameter values at which they occur in real cells. When the virtual cells are being created the parameter values sampled is dependant on the current branch diameter.

Figure 1b. Depiction of the model parameters

For all analysis the apical and basal trees were treated separately. This choice is based on the morphological differences between the two types of trees and the observation that they are located in distinct cellular layers. The possibility that a similar distinction could be applied to different parts of the apical tree was investigated. In particular, the stratum radiatum portion of the apical tree (roughly proximal two thirds) was considered separately from the rest of the tree and the results of the model compared to those from the full tree. This separation further improved the result of the model.

A general difficulty encountered in morphological modeling of dendrites is noise in the data on which these models are based. The effects of measurement errors were investigated by systematically varying the standard deviation values for the parent daughter ratio, daughter ratio, and taper rate parameters individually (Figure 2). The number of bifurcations was relatively stable with regards to daughter ratio. In contrast, both taper rate and parent-daughter ratio were able to cause explosive growth with standard deviation values near those found in real cells. These observations held for both apical and basal trees.

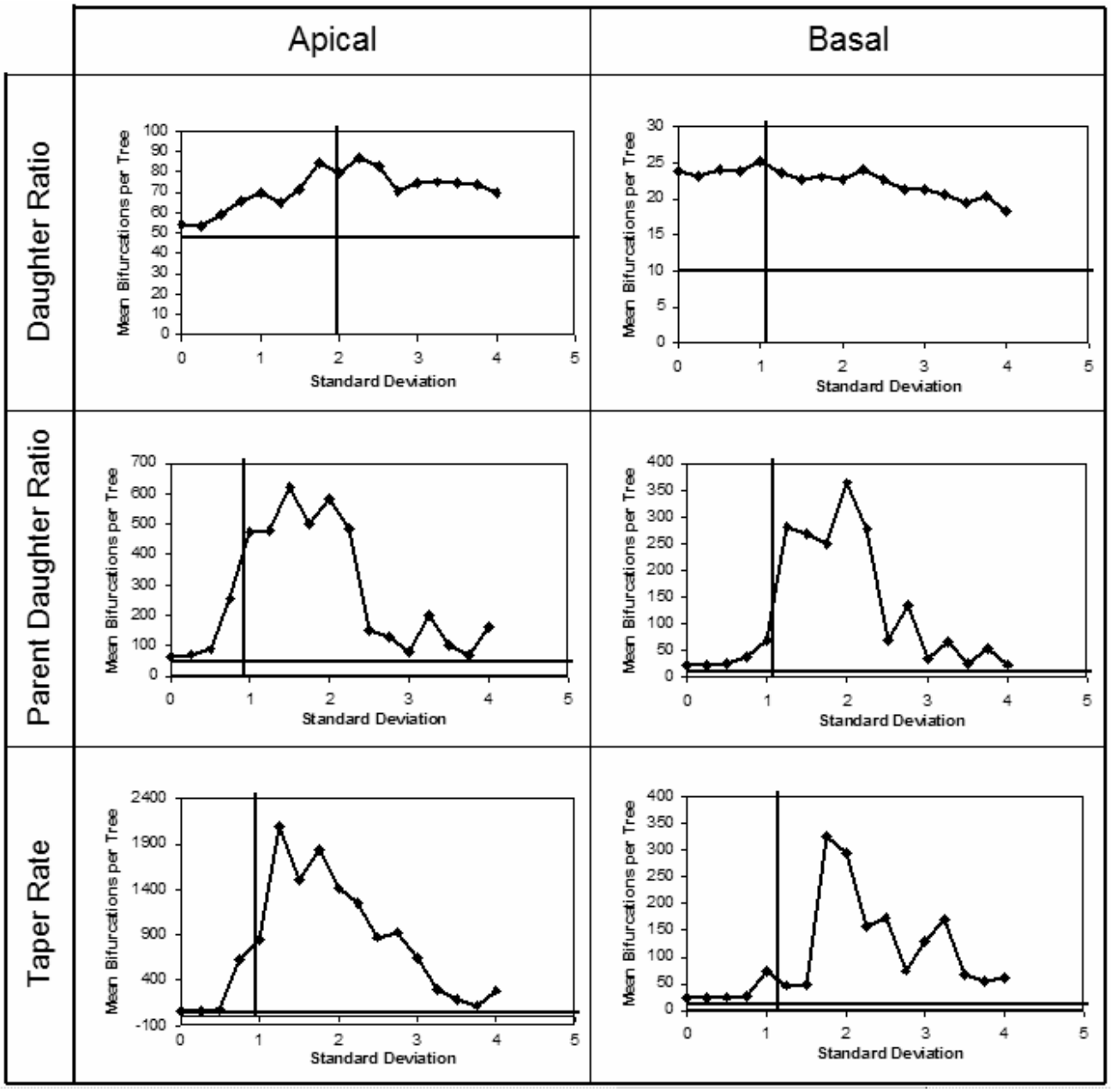

Figure 2. For each graphs, the straight horizontal line shows the average number of bifurcations found in the real cells. The straight vertical line shows the actual standard deviation of parameter values across all diameter bins.

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