



Influence of dendritic topology on firing patterns in model neurons

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Abstract

Neuronal electrophysiology is influenced by both channel distribution and morphology. Distinguishing two sources of morphological variability—metrics and topology—we show that model neurons sharing the same channel densities and anatomical size can derive functional differentiation from their dendritic topology. Firing frequencies in these metrically reduced neurons show a strong correlation with both mean path length and total electrotonic transformed size of the dendritic tree. This dependency of spiking behaviour is robust to different modes of stimulation, different tapering powers, and the absence of active dendritic channels. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

Many features of firing patterns arise from distinctive membrane properties, such as the distribution of ion channels. Several studies, however, have emphasised the role of dendritic morphology. For example, Mainen and Sejnowski [4] showed that multi-compartmental models of neocortical neurons that have the same channel densities and kinetics but differ in their dendritic shape and size can generate firing patterns ranging from regular spiking to bursting when stimulated at the soma with a fixed current injection.

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Reduced models consisting of only a dendritic and an axo–somatic compartment can give rise to the same spectrum of firing patterns by varying the ratio of surface area and the electrical coupling between the two compartments [4,7].

These models show that morphology has a influence on cell response, but they do not give insight into the possible separate roles of the two sources of morphological variability: metrics (such as segment lengths and diameters) and topology [5]. By assuming segments to be simple cylinders with fixed lengths and diameters, we reduce the metrical complexity of dendrites. The topological variability, however, is maintained. We show that topology alone can influence the firing patterns of metrically reduced neurons that share not only the same membrane properties but also the same anatomical size.

Furthermore, we study whether the results obtained in compartmental studies like Mainen and Sejnowski's [4] and ourselves still hold under biologically more realistic stimulation regimes than somatic current injection. We show that basically the same results are obtained when randomly firing synapses distributed along the entire surface of the dendrites are used.

2. Somatic vs. dendritic stimulation

Stimulation of a neuron with a fixed current injection at the soma has been used in many theoretical studies that claim the existence of a relationship between neuronal morphology and electrophysiological functioning [4,7]. Although this mode of stimulation is also used in many *in vitro* and *in vivo* studies, the question arises whether the results found can be reproduced under a more biologically realistic stimulation regime, such as synaptic stimulation of the entire dendritic tree.

To test this, we used morphologies and channel distributions as in [4] and simulated them in NEURON [3] using identical physiological parameters for each cell. AMPA-type excitatory synapses [1] were placed uniformly over the dendrites with a density of 1 per $20\mu\text{m}^2$. Each synapse fired according to a Poisson distributed temporal pattern with a mean frequency of 1 Hz.

Fig. 1 shows the four morphologies used and the firing patterns that were recorded at their somas during standard somatic and during synaptical dendritic stimulation. Although the latter results in a noisier firing pattern, both modes of stimulation give a similar dependency of spiking behaviour on dendritic morphology. This can intuitively be explained as follows. Once a spike is initiated, current leaks into the dendrites. Due to active channels this can trigger a dendritic spike, causing an after-depolarization in the soma which can give rise to the observed bursting. Whether the initial spike was due to a somatic current injection or to dendritic stimulation is thus irrelevant to this mechanism.

3. Effect of dendritic topology on firing patterns

To be able to independently control both dendritic shape and size, we constructed sets of metrically reduced model neurons. These can be classified according to their

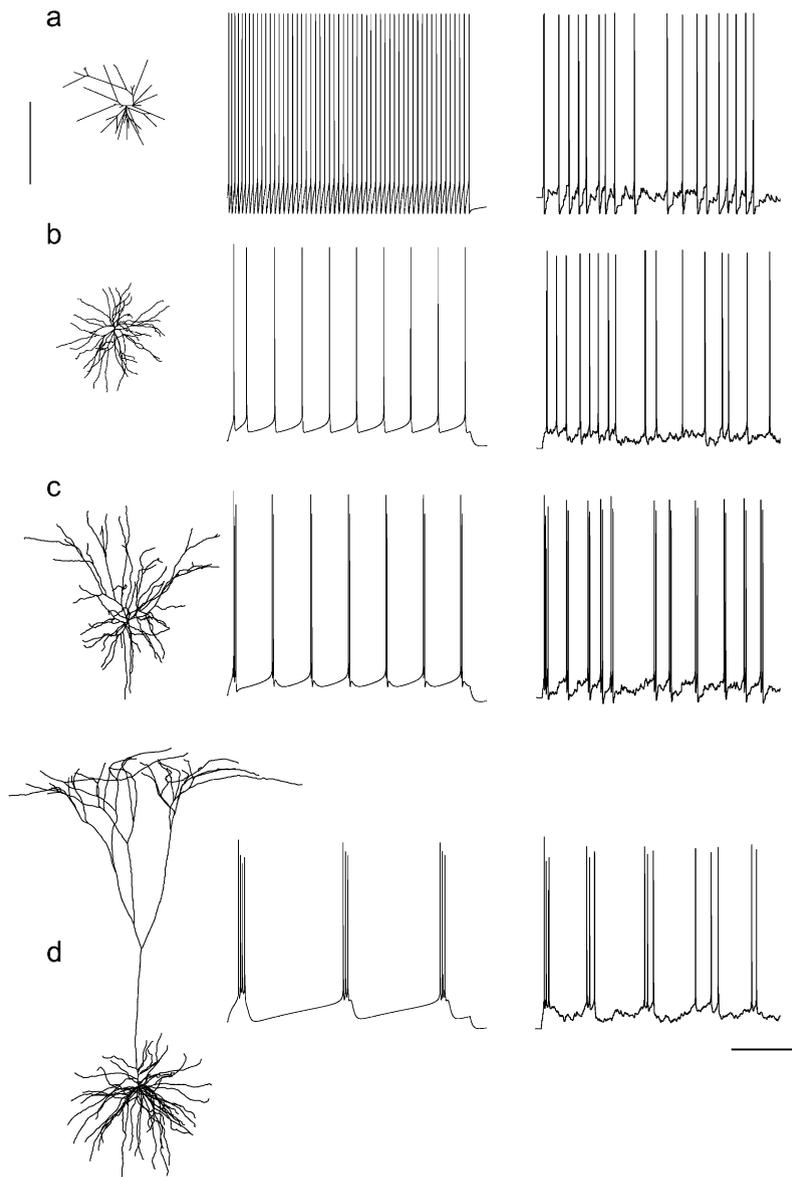


Fig. 1. Firing patterns in model neurons sharing a common distribution of ion channels but with different dendritic morphologies. Left traces show firing patterns during somatic current injection [4]. Right traces are recorded during random synaptic stimulation. Both modes of stimulation give a similar dependency of spiking behaviour on dendritic morphology. (Scale bars: 250 μ m, 250 ms, 25 mV.)

number of end segments, or degree. Each cell of a particular degree consists of the same number of equally sized segments. Thus, the neurons are only topologically different. Fig. 2 shows all degree 8 topologies. The metrically reduced neurons were simulated

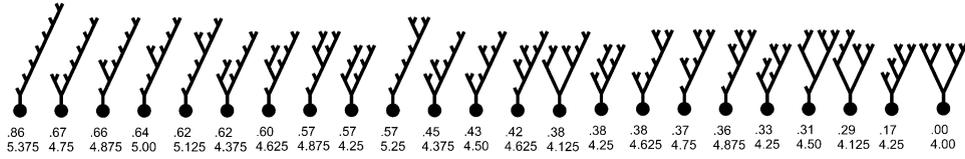


Fig. 2. Degree 8 topologies. Upper index: tree asymmetry. Lower index: normalised mean path length. For display purposes some segments have been lengthened.

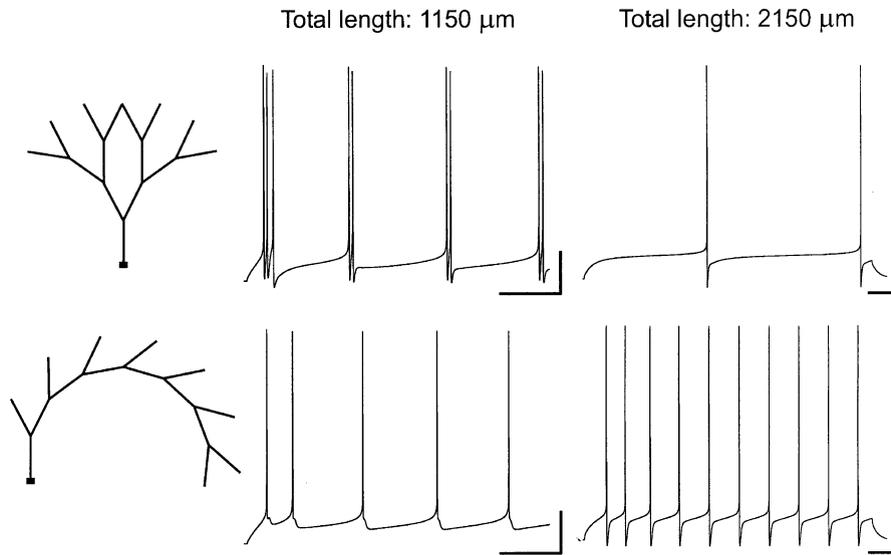


Fig. 3. Different firing patterns in metrically reduced model neurons sharing similar size and channel distribution. Recorded at the axo-somatic compartment during stimulation with a 100 pA current injection. Both spike shape and firing frequency can be influenced by dendritic topology. This is illustrated here in fully symmetric and asymmetric degree 8 neurons with dendritic lengths of 1150 μm and of 2150 μm . (Scale bars: 100 ms, 25 mV.)

using the same channel distribution as used in the previous section. Firing patterns were recorded at the axo-somatic compartment, which was also used for stimulation with a current injection. Fig. 3 shows the firing patterns of a fully symmetric and an asymmetric cell. For these simulations a segment diameter of 5 μm was used. The axo-somatic compartment had a diameter and length of 20 μm . Different topological types produce strikingly different firing patterns. Note that both the firing rate and the type of firing (i.e., regular vs. bursting) can be influenced by dendritic topology. The intuitive explanation for this is that the symmetric tree acts as a more efficient current sink because its dendritic segments are, on average, located closer to the soma.

3.1. Correlations between morphometric parameters and firing frequency

Firing patterns were recorded from every degree 8 topology with total dendritic length of 2150 μm . At this length each cell shows the same type of spiking (i.e., regular, non-adapting), so that the differences in electrophysiological response reduce to differences in firing rate, which were correlated with a variety of morphometric parameters (Fig. 4). We find a weak positive correlation of firing frequency with the tree asymmetry index [6]. Mean path lengths (the sum of all dendritic path lengths measured from tip to soma divided by the number of end segments—varying from approximately 570–770 μm) prove to correlate very strongly with firing frequency (Fig. 4b).

Furthermore, this correlation is maintained when dendritic branching patterns obey Rall's $\frac{3}{2}$ power law (Fig. 4d, e). This law was implemented in two ways. First, we assumed identical end segment diameters for all topologies, which implies, however, that asymmetric topologies get a higher total dendritic surface area. As is known from the two-compartmental models, this results in a lower firing frequency [4,7]. Although the range of the recorded frequencies under this condition was indeed smaller, a strong positive correlation can still be found (Fig. 4d). Such a correlation is also found in the second implementation of the power rule, in which the total surface area is kept constant. This implies we had to assign different end segment diameters to every topological type. As a side effect of this, root-segments become very thick, which explains the low firing rates in Fig. 4e. Finally, without active dendritic channels the correlation between firing rate and topology can still be found (Fig. 4f).

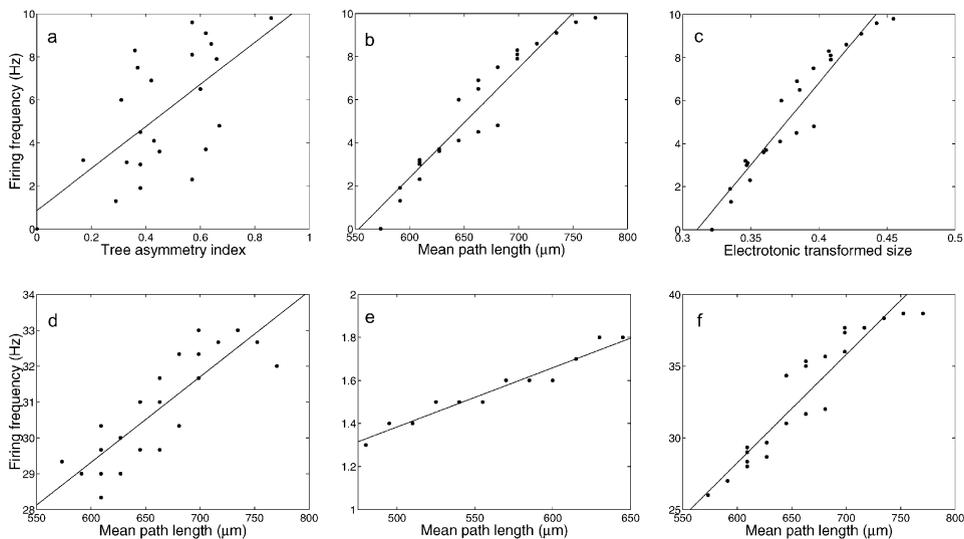


Fig. 4. Correlation between firing rate of degree 8 neurons and various morphometric parameters: (a) tree asymmetry index, (b) mean path length, (c) electrotonic transformed size. Mean pathlength and firing rate still correlate in neurons with tapered dendrites with (d) fixed end segment diameter, and (e) the same surface area as in (a–c). (f) As (b), but without active dendritic channels present.

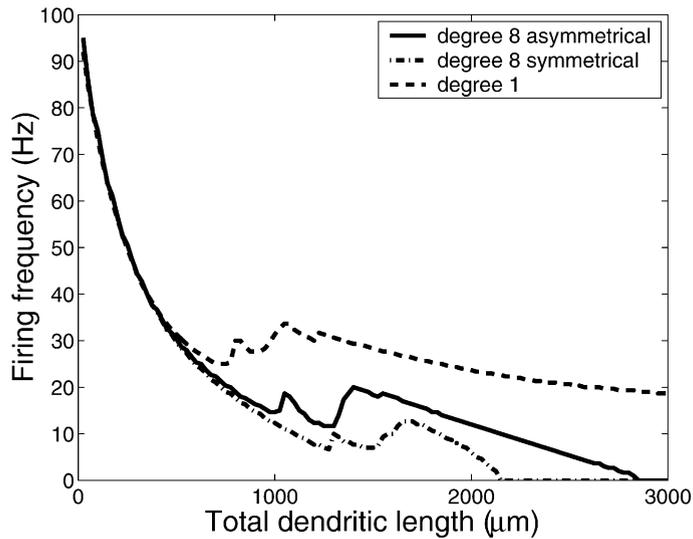


Fig. 5. The influence of size on the firing rate of degree 1 and fully symmetric and asymmetric degree 8 cells. (Segment diameter: $5\ \mu\text{m}$. Max. compartment length: $20\ \mu\text{m}$.)

A third measure we correlated with firing rate is based on the electrotonic transformation [2] which defines electrotonic distance as the natural log of the voltage attenuation between two points on a neuron. The steady state voltage attenuation over every segment in our degree 8 sample was computed using NEURON's impedance class. An advantage of the new definition is that electrotonic lengths can be summed, resulting in a total electrotonic transformed dendritic size. This dimensionless measure also shows a strong correlation with firing rate (Fig. 4c).

3.2. The effect of size on the firing rate of topologically different cells

For a neuron of a given topology we study the relationship between the total dendritic size and firing pattern by increasing the length of the dendritic segments. As is to be expected from Ohm's law and [4,7], the firing frequency drops with increasing dendritic size (Fig. 5). At the same time the differences between topologically different cells become more pronounced. At intermediate sizes a phase transition in firing behaviour occurs: cells start bursting, which explains the humps in the graph. When size is further increased the cells revert to a regular firing pattern. From then on, the firing frequency slowly diminishes. Note that the degree 1 neuron has the highest overall firing rate, which corresponds to its high mean path length value.

4. Conclusions

Metrical reduction of dendritic trees in model neurons enables us to study separately the effects of dendritic shape and size on neuronal firing patterns. Using these models,

we show that neurons which differ only in the topology of their dendritic tree produce different firing patterns during stimulation, even though they share the same channel densities and are of the same anatomical size.

Firing frequencies show a very strong correlation with both mean path length and total electrotonic transformed size of the dendritic tree. This dependency of spiking behaviour is robust to different modes of stimulation, different tapering powers, and the absence of active dendritic channels.

Although further research is needed to determine the usefulness of these correlates as predictors of firing behaviour in non-metrically reduced cells, we conclude that cells sharing the same physical size and channel distribution can still derive functional differentiation from their dendritic topology.

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