Optimal sizes of dendritic and axonal arbors

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Abstract

I consider a topographic projection between two neuronal layers with different densities of neurons. Given the number of output neurons connected to each input neuron (divergence or fan-out) and the number of input neurons synapsing on each output neuron (convergence or fan-in) I determine the widths of axonal and dendritic arbors which minimize the total volume of axons and dendrites. My analytical results can be summarized qualitatively in the following rule: neurons of the sparser layer should have arbors wider than those of the denser layer. This agrees with the anatomical data from retinal and cerebellar neurons whose morphology and connectivity are known. The rule may be used to infer connectivity of neurons from their morphology.

1 Introduction

Understanding brain function requires knowing connections between neurons. However, experimental studies of inter-neuronal connectivity are difficult and the connectivity data is scarce. At the same time neuroanatomists possess much data on cellular morphology and have powerful techniques to image neuronal shapes. This suggests using morphological data to infer inter-neuronal connections. Such inference must rely on rules which relate shapes of neurons to their connectivity.

The purpose of this paper is to derive such rule for a frequently encountered feature in the brain organization: a topographic projection. Two layers of neurons are said to form a topographic projection if adjacent neurons of the input layer connect to adjacent neurons of the output layer, Figure 1. As a result, output neurons form an orderly map of the input layer.

I characterize inter-neuronal connectivity for a topographic projection by divergence and convergence factors defined as follows, Figure 1. *Divergence*, D, of the projection is the number of output neurons which receive connections from an input neuron. *Convergence*, C, of the projection is the number of input neurons which connect with an output neuron. I assume that these numbers are the same for each neuron in a given layer. Furthermore, each neuron makes the required connections with the nearest neurons of the other layer. In most cases, this completely specifies the wiring diagram.

A typical topographic wiring diagram shown in Figure 1 misses an important biological detail. In real brains, connections between cell bodies are implemented by neuronal processes: axons which carry nerve pulses away from the cell bodies and dendrites which carry signals
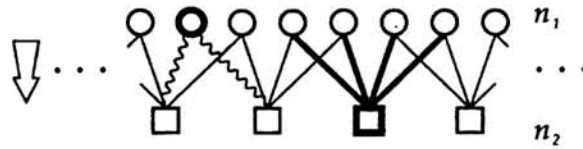
Figure 1: Wiring diagram of a topographic projection between input (circles) and output (squares) layers of neurons. Divergence, D, is the number of outgoing connections (here, $D = 2$) from an input neuron (wavey lines). Convergence, C, is the number of connections incoming (here, $C = 4$) to an output neuron (bold lines). Arrow shows the direction of signal propagation.
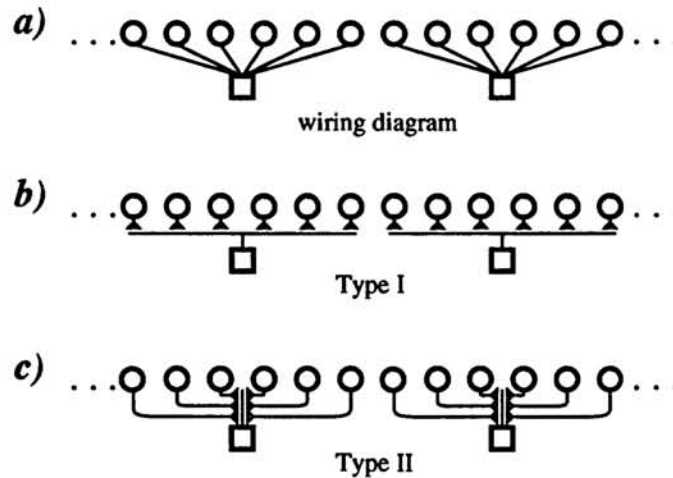

Figure 2: Two different arrangements implement the same wiring diagram. (a) Topographic wiring diagram with $C = 6$ and $D = 1$. (b) Arrangement with wide dendritic arbors and no axonal arbors (Type I) (c) Arrangement with wide axonal arbors and no dendritic arbors (Type II). Because convergence exceeds divergence type I has shorter wiring than type II.

towards cell bodies.[1] Therefore each connection is interrupted by a synapse which separates an axon of one neuron from a dendrite of another. Both axons and dendrites branch away from cell bodies forming arbors.

In general, a topographic projection with given divergence and convergence may be implemented by axonal and dendritic arbors of different sizes, which depend on the locations of synapses. For example, consider a wiring diagram with $D = 1$ and $C = 6$, Figure 2a. Narrow axonal arbors may synapse onto wide dendritic arbors, Figure 2b or wide axonal arbors may synapse onto narrow dendritic arbors, Figure 2c. I call these arrangements type I and type II, correspondingly. The question is: which arbor sizes are preferred?

I propose a rule which specifies the sizes of axonal arbors of input neurons and dendritic arbors of output neurons in a topographic projection: *High divergence/convergence ratio favors wide axonal and narrow dendritic arbors while low divergence/convergence ratio favors narrow axonal arbors and wide dendritic arbors.* Alternatively, this rule may be formulated in terms of neuronal densities in the two layers: *Sparser layer has wider arbors.* In the above example, divergence/convergence (and neuronal density) ratio is 1/6 and, according to the rule, type I arrangement, Figure 2b, is preferred.

In this paper I derive a quantitative version of this rule from the principle of wiring economy which can be summarized as follows. [2, 3, 4, 5, 6] Space constraints require keeping the brain volume to a minimum. Because wiring (axons and dendrites) takes up a significant fraction of the volume, evolution has probably designed axonal and dendritic arbors in a way that minimizes their total volume. Therefore we may understand the existing arbor sizes as a result of wiring optimization.

To obtain the rule I formulate and solve a wiring optimization problem. The goal is to find the sizes of axons and dendrites which minimize the total volume of wiring in a topographic wiring diagram for fixed locations of neurons. I specify the wiring diagram with divergence and convergence factors. Throughout most of the paper I assume that the cross-sectional area of dendrites and axons are constant and equal. Therefore, the problem reduces to the wire *length* minimization. Extension to unequal fiber diameters is given below.

2   Topographic projection in two dimensions

Consider two parallel layers of neurons with densities n_1 and n_2. The topographic wiring diagram has divergence and convergence factors, D and C, requiring each input neuron to connect with D nearest output neurons and each output neuron with C nearest input neurons. Again, the problem is to find the arrangement of arbors which minimizes the total length of axons and dendrites. For different arrangements I compare the wirelength per unit area, L. I assume that the two layers are close to each other and include only those parts of the wiring which are parallel to the layers.

I start with a special case where each input neuron connects with only one output neuron ($D = 1$). Consider an example with $C = 16$ and neurons arranged on a square grid in each layer, Figure 3a. Two extreme arrangements satisfy the wiring diagram: type I has wide dendritic arbors and no axonal arbors, Figure 3b; type II has wide axonal arbors and no dendritic arbors, Figure 3c. I take the branching angles equal to 120^0, an optimal value for constant crossectional area.[4] Assuming "point" neurons the ratio of wirelength for type I and type II arrangements:

$$\frac{L_I}{L_{II}} \approx 0.57. \tag{1}$$

Thus, the type I arrangement with wide dendritic arbors has shorter wire length. This conclusion holds for other convergence values much greater than one, provided $D = 1$. However, there are other arrangements with non-zero axonal arbors that give the same wire length. One of them is shown in Figure 3d. Degenerate arrangements have axonal arbor width $0 < s_a < 1/\sqrt{n_1}$ where the upper bound is given by the approximate inter-neuronal distance. This means that the optimal arbor size ratio for $D = 1$

$$\frac{s_d}{s_a} > \sqrt{\frac{n_1}{n_2}} \tag{2}$$

By using the symmetry in respect to the direction of signal propagation I adapt this result for the $C = 1$ case. For $D > 1$, arrangements with wide axonal arbors and narrow dendritic arbors ($0 < s_d < 1/\sqrt{n_2}$) have minimal wirelength. The arbor size ratio is

$$\frac{s_d}{s_a} < \sqrt{\frac{n_1}{n_2}}. \tag{3}$$

Next, I consider the case when both divergence and convergence are greater than one. Due to complexity of the problem I study the limit of large divergence and convergence ($D, C \gg 1$). I find analytically the optimal layout which minimizes the total length of axons and dendrites.

Notice that two neurons may form a synapse only if the axonal arbor of the input neuron overlaps with the dendritic arbor of the output neuron in a two-dimensional projection, Figure 4. Thus the goal is to design optimal dendritic and axonal arbors so that each dendritic arbor intersects C axonal arbors and each axonal arbor intersects D dendritic arbors.

To be specific, I consider a wiring diagram with convergence exceeding divergence, $C > D$ (the argument can be readily adapted for the opposite case). I make an assumption, to be
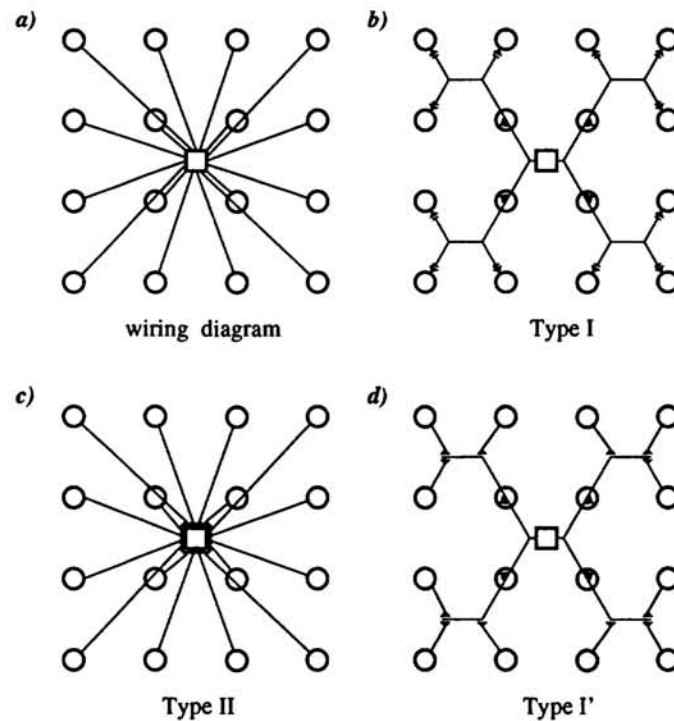
Figure 3: Different arrangements implement the same wiring diagram in two dimensions. (a) Topographic wiring diagram with $D = 1$ and $C = 16$. (b) Arrangement with wide dendritic arbors and no axonal arbors, Type I. (c) Arrangement with wide axonal arbors and no dendritic arbors, Type II. Because convergence exceeds divergence type I has shorter wiring than type II. (d) Intermediate arrangement which has the same wire length as type I.
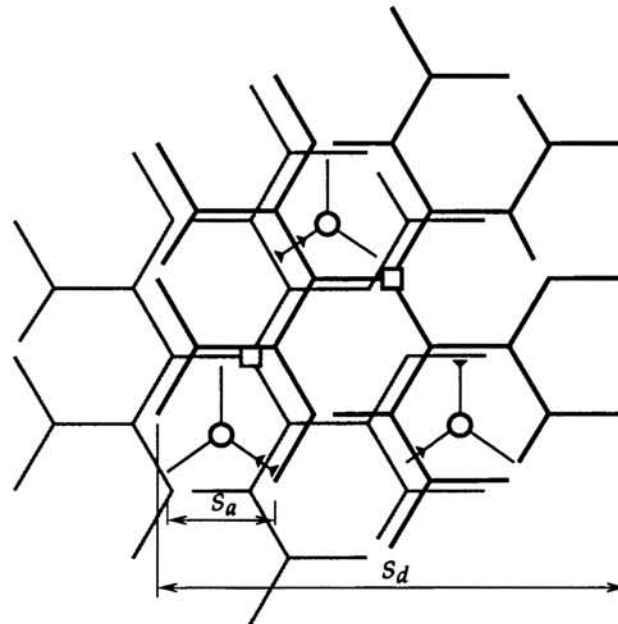

Figure 4: Topographic projection between the layers of input (circles) and output (squares) neurons. For clarity, out of the many input and output neurons with overlapping arbors only few are shown. The number of input neurons is greater than the number of output neurons ($C/D > 1$). Input neurons have narrow axonal arbors of width s_a connected to the wide but sparse dendritic arbors of width s_d. Sparseness of the dendritic arbor is given by s_a because all the input neurons spanned by the dendritic arbor have to be connected.

verified later, that dendritic arbor diameter s_d is greater than axonal one, s_a. In this regime each output neuron's dendritic arbor forms a sparse mesh covering the area from which signals are collected, Figure 4. Each axonal arbor in that area must intersect the dendritic arbor mesh to satisfy the wiring diagram. This requires setting mesh size equal to the axonal arbor diameter.

By using this requirement I express the total length of axonal and dendritic arbors as a function of only the axonal arbor size, s_a. Then I find the axonal arbor size which minimizes the total wirelength. Details of the calculation will be published elsewhere. Here, I give an intuitive argument for why in the optimal layout both axonal and dendritic size are non-zero. Consider two extreme layouts. In the first one, dendritic arbors have zero width, type II. In this arrangement axons have to reach out to every output neuron. For large convergence, $C \gg 1$, this is a redundant arrangement because of the many parallel axonal wires whose signals are eventually merged. In the second layout, axonal arbors are absent and dendrites have to reach out to every input neuron. Again, because each input neuron connects to many output neurons (large divergence, $D \gg 1$) many dendrites run in parallel inefficiently carrying the same signal. A non-zero axonal arbor rectifies this inefficiency by carrying signals to several dendrites along one wire.

I find that the optimal ratio of dendritic and axonal arbor diameters equals to the square root of the convergence/divergence ratio, or, alternatively, to the square root of the neuronal density ratio:

$$\frac{s_d}{s_a} = \sqrt{\frac{C}{D}} = \sqrt{\frac{n_1}{n_2}} \tag{4}$$

Since I considered the case with $C > D$ this result also justifies the assumption about axonal arbors being smaller than dendritic ones.

For arbitrary axonal and dendritic cross-sectional areas, h_a and h_d, expressions of this Section are modified. The wiring economy principle requires minimizing the total volume occupied by axons and dendrites resulting in the following relation for the optimal arrangement:

$$\frac{s_d}{s_a} = \sqrt{\frac{C h_a}{D h_d}} = \sqrt{\frac{n_1 h_a}{n_2 h_d}} \tag{5}$$

Notice that in the optimal arrangement the total axonal volume of input neurons is equal to the total dendritic volume of the output neurons.

3 Discussion

3.1 Comparison of the theory with anatomical data

This theory predicts a relationship between the con-/divergence ratio and the sizes of axonal and dendritic arbors. I test these predictions on several cases of topographic projection in two dimensions. The predictions depend on whether divergence and convergence are both greater than one or not. Therefore, I consider the two regimes separately.

First, I focus on topographic projections of retinal neurons whose divergence factor is equal or close to one. Because retinal neurons use mostly graded potentials the difference between axons and dendrites is small and I assume that their cross-sectional areas are equal. The theory predicts that the ratio of dendritic and axonal arbor sizes must be greater than the square root of the input/output neuronal density ratio, $s_d/s_a > (n_1/n_2)^{1/2}$ (Eq.2).

I represent the data on the plot of the relative arbor diameter, s_d/s_a, vs. the square root of the relative densities, $(n_1/n_2)^{1/2}$, (Figure 5). Because neurons located in the same layer may belong to different classes, each having different arbor size and connectivity, I plot data
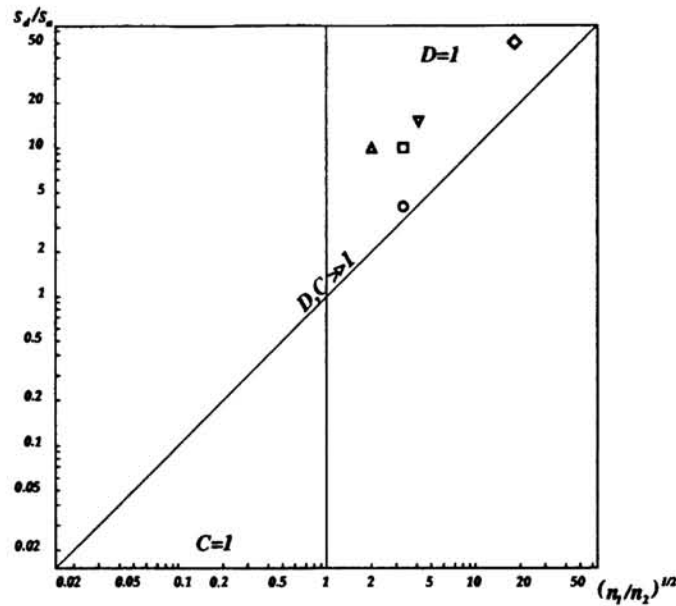
Figure 5: Anatomical data for several pairs of retinal cell classes which form topographic projections with $D = 1$. All the data points fall in the triangle above the $s_d/s_a = (n_1/n_2)^{1/2}$ line in agreement with the theoretical prediction, Eq.2. The following data has been used: $\circ$ - midget bipolar $\rightarrow$ midget ganglion,[7, 8, 11]; $\sqcup$ - diffuse bipolar $\rightarrow$ parasol ganglion,[7, 9]; $\triangledown$ - rods $\rightarrow$ rod bipolar,[10]; $\triangle$ - cones $\rightarrow$ HI horizontals,[12]; $\diamond$ - rods $\rightarrow$ telodendritic arbors of HI horizontals,[13].

from different classes separately. All the data points lie above the $s_d/s_a = (n_1/n_2)^{1/2}$ line in agreement with the prediction.

Second, I apply the theory to cerebellar neurons whose divergence and convergence are both greater than one. I consider a projection from granule cell axons (parallel fibers) onto Purkinje cells. Ratio of granule cells to Purkinje cells is 3300,[14], indicating a high convergence/divergence ratio. This predicts a ratio of dendritic and axonal arbor sizes of 58. This is qualitatively in agreement with wide dendritic arbors of Purkinje cells and no axonal arbors on parallel fibers.

Quantitative comparison is complicated because the projection is not strictly two-dimensional: Purkinje dendrites stacked next to each other add up to a significant third dimension. Naively, given that the dendritic arbor size is about 400μm Eq.4 predicts axonal arbor of about 7μm. This is close to the distance between two adjacent Purkinje cell arbors of about 9μm. Because the length of parallel fibers is greater than 7μm absence of axonal arbors comes as no surprise.

3.2 Other factors affecting arbor sizes

One may argue that dendrites and axons have functions other than linking cell bodies to synapses and, therefore, the size of the arbors may be dictated by other considerations. Although I can not rule out this possibility, the *primary* function of axons and dendrites is to connect cell bodies to synapses in order to conduct nerve pulses between them. Indeed, if neurons were not connected more sophisticated effects such as non-linear interactions between different dendritic inputs could not take place. Hence the most basic parameters of axonal and dendritic arbors such as their size should follow from considerations of connectivity.

Another possibility is that the size of dendritic arbors is dictated by the surface area needed

to arrange all the synapses. This argument does not specify the arbor size, however: a compact dendrite of elaborate shape can have the same surface area as a wide dendritic arbor.

Finally, agreement of the predictions with the existing anatomical data suggests that the rule is based on correct principles. Further extensive testing of the rule is desirable. Violation of the rule in some system would suggest the presence of other overriding considerations in the design of that system, which is also interesting.

Acknowledgements

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