Optimal Sizes of Dendritic and Axonal Arbors in a Topographic Projection

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Chklovskii, Dmitri B. Optimal sizes of dendritic and axonal arbors in a topographic projection. *J. Neurophysiol.* 83: 2113–2119, 2000. 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) and the number of input neurons synapsing on each output neuron (convergence), I determine the widths of axonal and dendritic arbors which minimize the total volume of axons and dendrites. Analytical results for one-dimensional and two-dimensional projections 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 anatomic data for retinal, cerebellar, olfactory bulb, and neocortical neurons the morphology and connectivity of which are known. The rule may be used to infer connectivity of neurons from their morphology.

INTRODUCTION

Understanding brain function requires knowing connections between neurons. However, experimental studies of interneuronal connectivity are difficult and the connectivity data are scarce. At the same time, neuroanatomists possess much data on cellular morphology and have powerful techniques to image neuronal shapes. In this situation I propose the use of morphological data to infer interneuronal connections. Any such inference must rely on rules which relate shapes of neurons to their connectivity.

The purpose of this paper is to derive such a 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 (Fig. 1). As a result, the output neurons form an orderly map of the input layer.

I characterize interneuronal connectivity for a topographic projection by divergence and convergence factors defined as follows (Fig. 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 Fig. 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 toward cell bodies (Cajal 1995a). 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 the synapses. For example, consider a wiring diagram with $D = 1$ and $C = 6$ (Fig. 2*A*). Narrow axonal arbors may synapse onto wide dendritic arbors (Fig. 2*B*) or wide axonal arbors may synapse onto narrow dendritic arbors (Fig. 2*C*). I call these arrangements type I and type II, correspondingly. The question is: which type is 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 whereas 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 (Fig. 2*B*) 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 (Cajal 1995b; Cherniak 1992; Chklovskii and Stevens 1999; Mitchison 1991; Young 1992): 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 wiring *length* minimization. My results are trivially extended to the case of unequal fiber diameters as shown below.

Purves and co-workers (Purves and Hume 1981; Purves and Lichtman 1985; Purves et al. 1986) have previously reported empiric observations which may be relevant to the present

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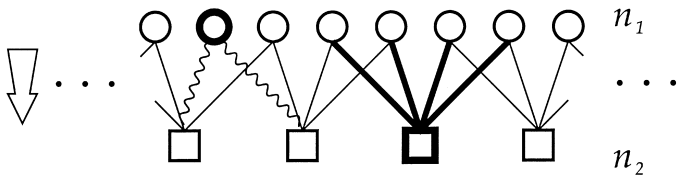

FIG. 1. Wiring diagram of a topographic projection between input (○) and output (□) layers of neurons. Divergence, D, is the number of outgoing connections (here, $D = 2$) from an input neuron (wavy lines). Convergence, C, is the number of connections incoming (here, $C = 4$) to an output neuron (bold lines). Arrow, direction of signal propagation.

theory. They found a correlation between convergence and complexity of dendritic arbors in sympathetic ganglia. Conclusive comparison of this data with the theory requires establishing topographic (or some other) wiring diagram and measuring axonal arbor sizes in this system.

In the next section I consider a one-dimensional version of the problem. In this version, wire length is minimized by wide dendritic and no axonal arbors (type I) in case of divergence less than convergence and by no dendritic and wide axonal arbors (type II) in the opposite case. Next, I consider a two-dimensional version of the problem. If both convergence and divergence are much greater than one, the optimal ratio of dendritic and axonal arbors equals the square root of convergence/divergence ratio.

I test the rule on the available anatomic data. For several projections between retinal, cerebellar, olfactory bulb, and neocortical neurons, arbor sizes agree with the rule. Finally, I discuss other factors which may affect arbor sizes.

TOPOGRAPHIC PROJECTION IN ONE DIMENSION

Consider two parallel rows of evenly spaced neurons (Fig. 1) with a topographic wiring diagram characterized by divergence, D, and convergence, C. The goal is to find axonal and dendritic arbor sizes which minimize the combined length of axons and dendrites. I compare different arbor arrangements by calculating wire length per unit length of the rows, L. I assume that input/output rows are close to each other and include in the calculation only those parts of the wiring which are parallel to the neuronal rows.

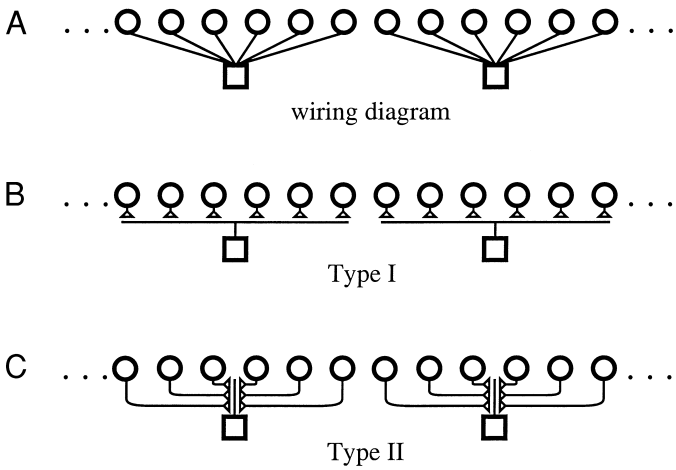

FIG. 2. Two different arrangements implement the same wiring diagram. *A*: topographic wiring diagram with $C = 6$ and $D = 1$. *B*: arrangement with wide dendritic arbors and no axonal arbors (type I). *C*: arrangement with wide axonal arbors and no dendritic arbors (type II). Because convergence exceeds divergence, type I has shorter wiring than type II.

I start by considering a special case where each input neuron connects with only one output neuron ($D = 1$) (Fig. 2*A*). There are two limiting arrangements satisfying the wiring diagram: type I has wide dendritic arbors and no axonal arbors (Fig. 2*B*); type II has wide axonal arbors and no dendritic arbors (Fig. 2*C*). Intuitively, the former arrangement has smaller wire length: short axons synapsing onto a common buslike dendrite is better than long axons from each input neuron synapsing onto a short dendrite. To confirm this I calculate wire length in the two extreme arrangements for $D = 1$ (see METHODS)

$$L_{\mathrm{I}} = (1 - 1/C) \tag{1}$$

$$L_{\mathrm{II}} = \begin{cases} C/4, & C - \text{even} \\ (C - 1/C)/4, & C - \text{odd} \end{cases} \tag{2}$$

These results show that for $D = 1$ and $C \leq 3$ the two arrangements have the same wire length. For $D = 1$ and $C > 3$ the arrangement with wide dendritic arbors and no axonal arbors (type I) has smaller wire length than the arrangement with wide axonal arbors and no dendritic arbors (type II).

I can readily apply this result to another special case, $C = 1$, by invoking the symmetry of the problem in respect to the direction of the signal propagation. I can interchange the words "axons" and "dendrites" and variables D and C in the derivation and use the above argument. For $C = 1$ and $D \leq 3$ the two extreme arrangements have the same wire length, whereas for $D > 3$ the arrangement with wide axonal arbors (type II) has shorter wiring than the arrangement with wide dendritic arbors (type I).

Next, I consider the case when both convergence and divergence are greater than one ($D, C > 1$). For the two extreme arrangements I get (see METHODS)

$$L_{\mathrm{I}} = D(1 - 1/C) \tag{3}$$

$$L_{\mathrm{II}} = C(1 - 1/D) \tag{4}$$

Comparison of the two expressions reveals the following: if divergence is less than convergence, then the optimal arrangement has wide dendritic and no axonal arbors (type I). If divergence is greater than convergence, then the optimal arrangement has wide axonal and no dendritic arbors (type II). If convergence and divergence are equal, both arrangements have the same wire length.

I can restate this result by using the identity between the divergence/convergence ratio and the neuronal density ratio (see METHODS): In the optimal arrangement the sparser layer has wide arbors, whereas the denser layer has none.

So far I compared extreme arrangements with wide arbors in one row and none in the other. What about intermediate arrangements, with both axonal and dendritic arbors of nonzero width? To address this question I consider the limit of large divergence and convergence factors ($C, D \gg 1$). I find wire length as a function of the axonal arbor size s_a (see METHODS)

$$L(s_a) = n_1 s_a \left(1 - \frac{D}{C}\right) + D \tag{5}$$

Because $0 < s_a < C/n_1$, I find the following: If $D/C < 1$, then the minimal wire length is achieved when $s_a = 0$, arrangement with wide dendritic and no axonal arbors (type I). If $D/C > 1$,

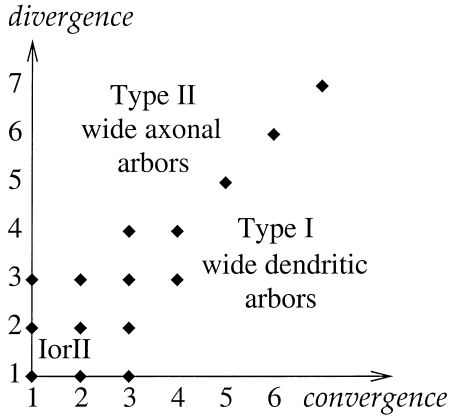

FIG. 3. Phase diagram for the one-dimensional projection. Optimal arrangements for possible pairs of convergence and divergence are shown. ◇, projections where wire length is minimized by both wide axonal and wide dendritic arbor arrangements.

then the minimal wire length is achieved when $s_a = C/n_1$ arrangement with wide axonal and no dendritic arbors (type II). If $D/C = 1$, then all possible axonal arbor widths give the same wire length.

This proves that for C, $D \gg 1$ extreme arrangements minimize wire length. In cases of small C and D I checked intermediate solutions one by one. In many cases intermediate arrangements have the same wire length as the extreme solution. However, only for a few "degenerate" D, C pairs there are equally good intermediate arrangements with the reverse ratio of average axonal and dendritic arbor sizes relative to the extreme solution.

My results are conveniently summarized on the phase diagram in Fig. 3, which shows optimal arrangements for various pairs of divergence and convergence factors. I mark the degenerate D, C pairs by diamonds on the phase diagram (Fig. 3).

What if axons and dendrites have different cross-sectional areas? The principle of wiring economy requires that wire volume rather than wire length should be minimized. I can modify the arguments of this section by including the cross-sectional areas of the processes. I find for D, $C \gg 1$ that if divergence/convergence ratio is less than the ratio of axonal and dendritic cross-sections, then the optimal arrangement has wide dendritic and no axonal arbors (type I). In the opposite case I find wide axonal and no dendritic arbors (type II).

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 wire length 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 (Fig. 4*A*). Two extreme arrangements satisfy the wiring

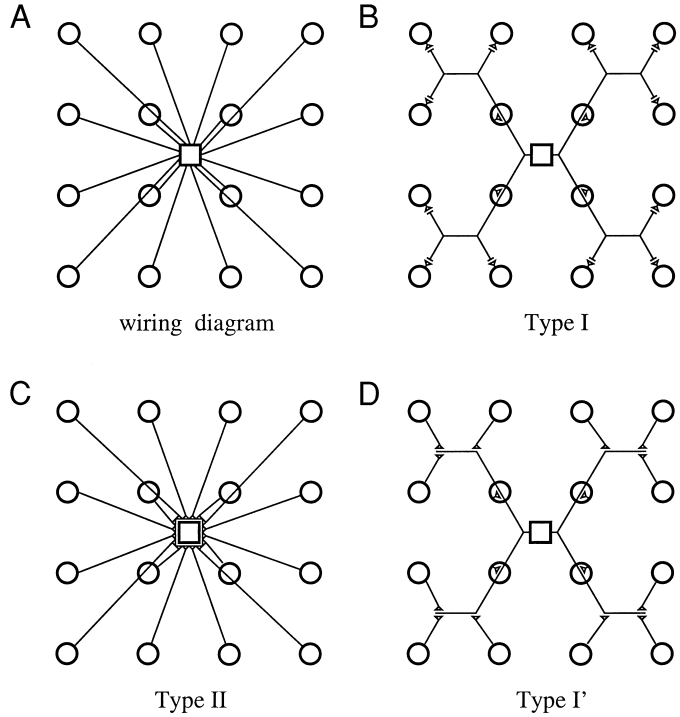

FIG. 4. Different arrangements implement the same wiring diagram in 2 dimensions. *A*: topographic wiring diagram with $D = 1$ and $C = 16$. *B*: arrangement with wide dendritic arbors and no axonal arbors (type I). *C*: arrangement with wide axonal arbors and no dendritic arbors (type II). Because convergence exceeds divergence, type I has shorter wiring than type II. *D*: intermediate arrangement which has the same wiring length as type I.

diagram: type I has wide dendritic arbors and no axonal arbors (Fig. 4*B*); type II has wide axonal arbors and no dendritic arbors (Fig. 4*C*). I take the branching angles equal to 120°, an optimal value for constant cross-sectional area (Cherniak 1992). Assuming "point" neurons, the ratio of wire length for type I and II arrangements

$$\frac{L_{\mathrm{I}}}{L_{\mathrm{II}}} \approx 0.57 \tag{6}$$

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 nonzero axonal arbors that give the same wire length. One of them is shown in Fig. 4*D*. Degenerate arrangements have axonal arbor width $0 < s_a < 1/\sqrt{n_1}$, where the upper bound is given by the approximate interneuronal distance. This means that the optimal arbor size ratio for $D = 1$

$$\frac{s_d}{s_a} > \sqrt{\frac{n_1}{n_2}} \tag{7}$$

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 wire length. These arrangements have arbor size ratio

$$\frac{s_d}{s_a} < \sqrt{\frac{n_1}{n_2}} \tag{8}$$

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. Unlike the one-dimensional projection, optimal sizes of both axons and dendrites turn out to be nonzero.

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 (Fig. 5). 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 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 (Fig. 5). 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 wire length. Details of the calculation are given in METHODS.

Here, I give an intuitive argument for why in the optimal layout both axonal and dendritic size are nonzero. 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 of which the 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 neuron (large divergence, $D \gg 1$), many dendrites run in parallel inefficiently carrying the same signal. A nonzero axonal arbor rectifies this inefficiency by carrying signals to several dendrites along one wire.

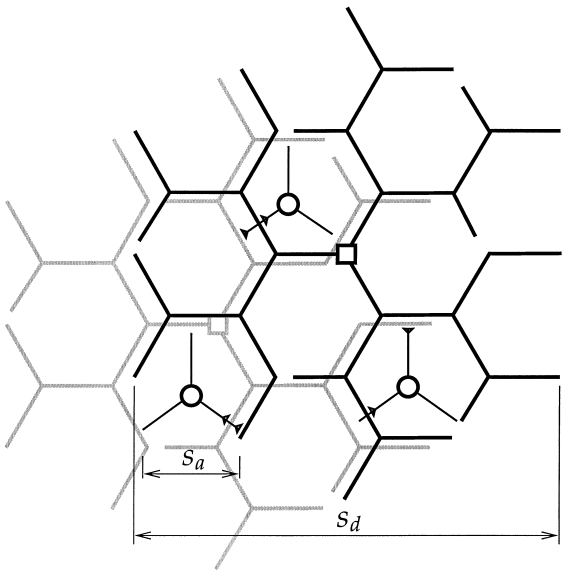

FIG. 5. Topographic projection between the layers of input (○) and output (□) neurons. For clarity, out of the many input and output neurons with overlapping arbors only a few are shown. Number of input neurons is greater than number of output neurons ($C/D > 1$). Input neurons have narrow axonal arbors of width s_a connected to the wide but sparse dendritic arbors of width s_d. Sparseness of dendritic arbor is given by s_a because all input neurons spanned by the dendritic arbor have to be connected.

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

$$\frac{s_d}{s_a} = \sqrt{\frac{C}{D}} = \sqrt{\frac{n_1}{n_2}} \tag{9}$$

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

So far I treated axons and dendrites on equal footing. In real brains, however, axons are usually thinner than dendrites reflecting electrophysiological differences between them. Because the wiring economy principle requires minimizing the total volume occupied by axons and dendrites, expressions of this section must be modified. This is easily done by taking fixed average axonal and dendritic cross-sectional areas, h_a and h_d, and minimizing the total volume. For example, by repeating the calculations shown in METHODS, I get a modified expression for the optimal arbor size ratio

$$\frac{s_d}{s_a} = \sqrt{\frac{Ch_a}{Dh_d}} = \sqrt{\frac{n_1 h_a}{n_2 h_d}} \tag{10}$$

There is an interesting consequence of the total volume minimization. A straightforward calculation shows that in the optimal arrangement the total axonal volume of input neurons is equal to the total dendritic volume of the output neurons.

COMPARISON OF THE THEORY WITH ANATOMIC DATA

This theory makes predictions relating convergence/divergence ratio of a neuronal projection to the relative sizes of axonal and dendritic arbors. To test these predictions I analyze real neuronal projections for which both neuronal morphology and connectivity are known. These projections take place between various classes of retinal, cerebellar, olfactory bulb, and neocortical neurons.

Retinal neurons

Retinal neurons are well suited for testing the theory because their connectivity and morphology are well known. Moreover, because retinal neurons use mostly graded potentials, their axons and dendrites can be treated on the same footing. In particular, I assume that their cross-sectional areas are the same.

I consider several projections between pairs of neuronal classes. In all cases divergence is either equal or close to one. Thus 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. 7*).

I present the data on the plot of the relative arbor diameter, s_d/s_a, versus the square root of the relative densities, $(n_1/n_2)^{1/2}$ (Fig. 6). Because neurons located in the same layer may belong

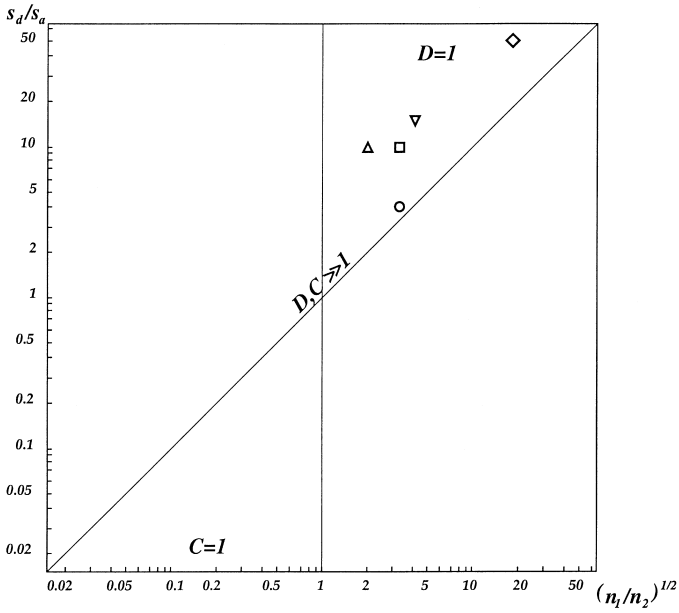

FIG. 6. Anatomic data for several pairs of retinal cell classes which form topographic projections with $D = 1$. All data points fall in the triangle above the $s_d/s_a = (n_1/n_2)^{1/2}$ line in agreement with the theoretical prediction (*Eq. 7*). The following data has been used: ○, midget bipolar → midget ganglion (Dacey 1993; Milam et al. 1993; Watanabe and Rodieck 1989); □, diffuse bipolar → parasol ganglion (Grunert et al. 1994; Watanabe and Rodieck 1989); ▽, rods → rod bipolar (Grunert and Martin 1991); △, cones → HI horizontals (Wassle et al. 1989); ◇, rods → telodendritic arbors of HI horizontals (Rodieck 1989).

to different classes each having different arbor size and connectivity, I plot data 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.

This shows that even though the actual retinal circuit is more complicated than a single projection between two neuronal classes, the theory gives a reasonable first-order approximation.

Cerebellar neurons

High level of regularity and high convergence and divergence factors in cerebellum make it a natural choice to test the predictions. I apply the theory to the projection from granule cell axons (parallel fibers) onto Purkinje cells. Because these cells form the majority of connections in the molecular layer, I can neglect other cell types and assume a single projection. Although divergence factor can be a few hundred, the ratio of granule cells to Purkinje cells is 3,300 (Andersen et al. 1992), indicating a high convergence/divergence ratio. In this case the theory 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 400 μm, *Eq. 9* predicts axonal arbor of about 7 μm. This is close to the distance between two adjacent Purkinje cell arbors of about 9 μm. Because the length of parallel fibers is >7 μm, absence of axonal arbors comes as no surprise.

Olfactory bulb neurons

Another part of the brain containing projections with high convergence and divergence factors is the olfactory bulb. The basic circuit of this part is reminiscent of the retinal circuit (Shepherd and Koch 1998). I focus on the projection between mitral and granule cells in the external plexiform layer. Again, I can neglect other projections because the majority of the synapses in the layer are between mitral and granule cells. This projection is peculiar in that synapses are dendro-dendritic. However, the theoretical predictions should not be affected by this fact. The ratio of granule to mitral cells is about 100:1 (Shepherd and Koch 1998). In this case the theory predicts the ratio of dendritic arbor diameters to be 10. This is in agreement with observed arbors sizes 1,200 μm (mitral secondary dendrites) (Shepherd and Greer 1998) and 50–200 μm (granule dendrites) (Shepherd and Greer 1998).

Neocortical neurons

In cerebral cortex, axons and dendrites take up approximately equal fractions of the total volume, ≈0.3 each (Braitenberg and Schuz 1998). This is unlikely to be an accidental coincidence because the linear dimensions of axons and dendrites are different. Axons of a given neuron are typically three times thinner than dendrites while being on average ten times longer (Braitenberg and Schuz 1998). Because the volume scales with the length times diameter squared, it comes out roughly the same for both types of processes.

This fact can be explained by the present theory as a result of volume minimization for a circuit with high divergence and convergence values. In cerebral cortex the majority of connections are intracortical (Ahmed et al. 1994; LeVay and Gilbert 1976; Peters et al. 1994). If I assume that each cortical neuron receives inputs from N other cortical neurons in its vicinity and sends outputs to N, other cortical neurons then cortical connections can be viewed as a topographic projection from the cortical neurons onto themselves. Diameters of axonal and dendritic fibers are determined by requirements on their electrophysiological properties. Then the minimal total volume of axons and dendrites is achieved by choosing arbor sizes in accordance with *Eq. 10*. This results in axons and dendrites occupying the same volume.

In general, application of the rule requires some care because it was derived for a simplified model. I considered a topographic projection only between a single pair of layers. However, neurons often make connections to different layers. In particular, dendritic arbors of the output layer may be determined by connections other than to the input layer. For example, consider the topographic projection from thalamus to the primary visual cortex. One may think that because the density of magnocellular thalamic afferents is smaller than neurons in layer 4Cα (80 mm^{-2} compared with 1.8×10^4 mm^{-2}) (Peters et al. 1994), then the axonal arbors should be wider than the dendritic ones. Although this is true [600 μm (Blasdel and Lund 1983) compared with 200 μm (Wiser and Callaway 1996)], the majority of inputs to layer 4Cα are intracortical (Peters et al. 1994) Therefore the dendritic arbor size may be determined by these other projections.

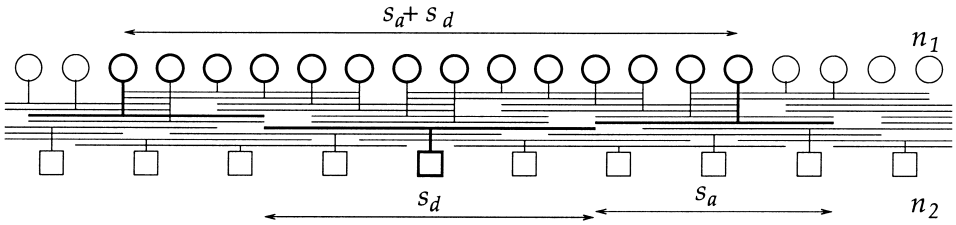

FIG. 7. Topographic projection between the rows of input (○) and output (□) neurons. Density of input neurons is greater than the output, $C/D > 1$. Sizes of the axonal arbors are s_a and of dendritic arbors are s_d. We show in bold the cell bodies of the C input neurons projecting to one output neuron (bold).

OTHER FACTORS AFFECTING ARBOR SIZES

I have argued that the relative size of axonal and dendritic arbors is related to the convergence/divergence ratio due to simple geometric constraints. One may object to this theory on the grounds that axons and, especially, dendrites perform functions other than linking cell bodies to synapses and, therefore the size of the arbors may be dictated by these other considerations. Although I cannot rule out these effects, I believe that the *primary* function of axons and dendrites is to connect cell bodies to synapses to conduct nerve pulses between them. Indeed, if neurons were not connected, more sophisticated effects such as nonlinear interactions between different dendritic inputs could not take place. Therefore in the first-order approximation the most basic parameters of axonal and dendritic arbors such as their size should follow from considerations of connectivity. When the details of nonlinear interactions in dendrites become well understood, their impact on the arbor size can be incorporated in the theory.

One may argue that there is another geometric constraint on the dendritic arbor size: dendritic surface area may be needed to accommodate all the synapses. However, this argument does not specify arbor sizes; a compact dendrite of elaborate shape can have the same surface area as a wide dendritic arbor. Moreover, the density of synapses on dendrites seems to be highly variable indicating that the limit of synapses per unit area is not reached in real brains. Therefore this argument seems unlikely to determine arbor sizes.

Finally, agreement of the predictions with the existing anatomic 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.

In conclusion, I propose a rule relating connectivity of neurons to their morphology based on the wiring economy principle. This rule may be used to infer connections between neurons from the sizes of their axonal and dendritic arbors.

METHODS

I frequently use the following identity (Purves et al. 1986) relating convergence/divergence ratio and neuronal densities ratio

$$\frac{C}{D} = \frac{n_1}{n_2} \tag{11}$$

To prove it, I calculate the number of connections (or synapses, if connections are monosynaptic) per unit length in two ways. The number of connections (or synapses) is the number of input neurons, n_1, times divergence, D. At the same time, the number of connections (or synapses) is the number of output neurons, n_2, times convergence, C. Because the answer should not depend on the argument, $n_1 D = n_2 C$ and *Eq. 11* follows trivially.

Projection in one dimension

First, consider the case of $D = 1$. In type 1 arrangement (Fig. 2*B*), the size of a dendritic arbor, s_d, is the interneuronal spacing $1/n_1$ times the number of interneuronal intervals covered by the arbor, $C - 1$

$$s_d = (C - 1)/n_1 \tag{12}$$

The number of dendritic arbors per unit length is equal to the density of output neurons n_2. The combined dendritic arbor length per unit length is $n_2 s_d$. Because the axonal arbors do not contribute, the total wire length per unit length

$$L_1 = n_2 s_d = n_2(C - 1)/n_1 \tag{13}$$

By using *Eq. 11* and recalling that $D = 1$, I get *Eq. 1*.

In type II arrangement (Fig. 2*C*), the wire length is equal to the sum of the lengths of axons converging on each output neuron multiplied by the neuronal density in the output layer n_2

$$L_{II} = \begin{cases} n_2[(C-1) + (C-3) + \cdots + 1]/n_1 = n_2 C^2/4n_1, & C - \text{even} \\ n_2[(C-1) + (C-3) + \cdots + 0]/n_1 = n_2(C^2-1)/4n_1, & C - \text{odd} \end{cases} \tag{14}$$

Using *Eq. 11* I express the result in terms of convergence alone ($D = 1$) and get *Eq. 2*.

Now consider the case of D, $C > 1$. By using *Eq. 11*, I find from *Eq. 13* that

$$L_1 = D(1 - 1/C) \tag{15}$$

This is *Eq. 3* of the main text. By using the symmetry in respect to the direction of signal propagation I find *Eq. 4* of the main text.

Next, I consider an arrangement with arbitrary sizes of axonal, s_a, and dendritic, s_d, arbors (Fig. 7) in the limit of D, $C \gg 1$. To satisfy the wiring diagram each input neuron must connect with D output neurons and each output neuron must connect with C input neurons. This places a constraint on the sum of axonal and dendritic arbor widths

$$s_a + s_d = D/n_2 = C/n_1 \tag{16}$$

Therefore axonal arbor width can take values $0 < s_a < C/n_1$. The total wire length per unit length is

$$L = s_a n_1 + s_d n_2 \tag{17}$$

Using *Eqs. 11* and *16*, I get *Eq. 5* of the main text.

Projection in two dimensions

I consider the case of C, $D \gg 1$ (Fig. 5). The following calculation is valid to the leading order in D and C: I omit numerical factors of order one which depend on the precise geometry of axonal and dendritic arbors. The total length of a dendritic arbor, l_d, is equal to the number of periods in the mesh s_d^2/s_a^2 times the mesh size, s_a

$$l_d = \frac{s_d^2}{s_a} \tag{18}$$

The size of the dendritic arbor, s_d, follows from expressing convergence as the product of the area covered by the dendritic arbor times the density of input neurons $C = s_d^2 n_1$

$$s_d^2 = \frac{C}{n_1} \tag{19}$$

Substituting this into *Eq. 18* I find

$$l_d = \frac{C}{n_1 s_a} \tag{20}$$

The length of an axonal arbor is approximately given by its size

$$l_a = s_a \tag{21}$$

Then the total wire length per unit area is

$$L = l_d n_2 + l_a n_1 = \frac{C n_2}{n_1 s_a} + s_a n_1 \tag{22}$$

To find the optimal axonal arbor size s_a, I differentiate wire length in respect to s_a and set the derivative to zero

$$\frac{\partial L}{\partial s_a} = -\frac{C n_2}{n_1 s_a^2} + n_1 = 0 \tag{23}$$

Solution of this equation gives the optimal size of an axonal arbor, s_a

$$s_a = \sqrt{\frac{C n_2}{n_1^2}} = \sqrt{\frac{D}{n_1}} \tag{24}$$

By using *Eq. 19* I get the size of the dendritic arbor

$$s_d = \sqrt{\frac{C}{n_1}} \tag{25}$$

The last two equations combined give *Eq. 9* of the main text.

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