Local optimization of neuron arbors

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Abstract. How parsimoniously is brain wiring laid out, that is, how well does a neuron minimize costs of connections among its synapses? Neural optimization of dentritic and axonic arbors can be evaluated using a generalization of the Steiner tree concept from combinatorial network optimization theory. Local branch-junction geometry of neuronal connecting structures fits a volume minimization model well. In addition, volume of the arborizations at this neighborhood level is significantly more strongly minimized than their length, signal propagation speed, or surface area. The mechanism of this local volume optimization resembles those involved in formation of nonliving tree structures such as river junctions and electric-discharge patterns, and appears to govern initial nerve growth-cone behavior through vector-mechanical energy minimization.

Introduction

For recent models of massively interconnected and parallel computation in the brain, a natural question concerns how well available neural connectivity is actually deployed. Real-world neuron fibers are not infinitesimally thin wires, but rather a limited resource for the intensive connectivity demands of massively parallel circuitry. Applying concepts from combinatorial network optimization theory to neuroanatomy, looking at "trees in the brain," reveals that the branch-junction geometry of the dendritic and axonic structures that interconnect a neuron's synapses conforms well to a local optimization model. What is most strongly minimized at the individual junction level is total volume of the arborizations, rather than connection length, signal propagation speed, or surface area. Supporting data comes from a wide range of species, developmental stages, and brain regions.

Neurons solve a generalization of a small-scale "Steiner tree" optimization problem about as well as a variety of other tree-like structures throughout nature, some of them non-living. This suggests the possibility that the mechanism of local network optimization in

the brain may involve basic physical processes only: the genome seems to get the anatomy of local neural junction optimization automatically and directly from energy-minimization phenomena involving classical mechanics, as they apply to initial growth-cone budding behavior in the branch junction vicinity. A basic insight of computational complexity theory is that good local optimization does not necessarily yield good global or large-scale optimization, since achieving the latter tends to be extremely computationally costly. Actual neural network volume minimization appears to bear out this distinction, in that longer-range neuron arbor optimization seems not to be as good as local optimization of the junctions composing the arbors.

1 Network optimization

One of the main problems of network optimization theory is: Given a set of nodes located in 3-space, find the set of arcs (of constant cost per unit of length) that links all nodes and has shortest total length. If the interconnecting network, which takes the form of a tree, may have branch junctions only at the nodes themselves, it is a *minimal spanning tree*. If the network is permitted also to have isolated junctions not at the node loci, it is a *Steiner tree* (see Fig. 1). For a given set of nodes, total length of its Steiner tree will be equal to or less than total length of its minimal spanning tree. In addition, isolated junctions of Steiner trees will always consist of three intersecting arcs or branches; bifurcations, not trifurcations or greater branchings, yield the shortest network (Georgakopoulos and Padimitriou 1987). Also, the three arcs of each junction will be coplanar. At these isolated Steiner junctions, it can be proved that the angles formed by each adjacent pair of arcs must be 120° (Courant and Robbins 1969, p. 354). It also follows that the optimizing angle will turn out to remain unchanged for any node location lying collinear with an arc.

A number of highly efficient exact algorithms are known for generating minimal spanning trees; they work well in practice today on quarter-million node
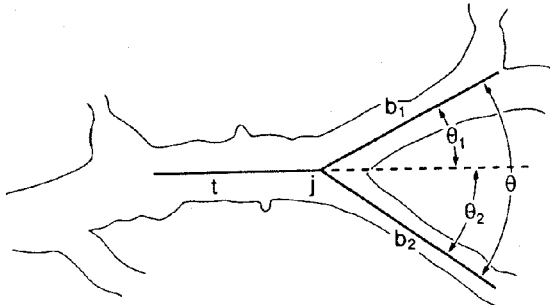
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Fig. 1. Bifurcating junction in a neuron arbor: t, trunk; b_1, b_2, branches; j, internodal junction. Internal angle $\theta = \theta_1 + \theta_2$. The "Y-tree" diagram is superimposed upon a simplified outline of a junction in the data set from the dendritic arbor of a cat cortical stellate neuron. (Scale: length of line segment $b_1 = 10\mu m$)

sets. However, the problem of finding a Steiner tree for a given set of nodes is a member of the class of NP-hard problems studied in computational complexity theory (Garey and Johnson 1979). NP-hard problems are at least as computationally costly as NP-complete ("Nondeterministic Polynomial time-complete") problems, of which the best known is the Travelling Salesman problem; even the latter are strongly conjectured to be intrinsically computationally complex. As a practical matter, each typically is intractable, that is, exact solutions are extremely computationally difficult because of the combinatorial explosion of possibilities that appear to have to be exhaustively searched. For example, the largest unconstrained Travelling Salesman problem that had been exactly solved as of the mid-1980's had only 318 nodes (Lawler et al. 1985, p. 14). Steiner problems of 100 nodes are beyond current computing capabilities (Bern and Graham 1989, p. 88).

In this context, the task of optimal wiring layout of a mammalian brain with billions of neurons may seem of a difficulty not easy even to comprehend. Consider a simplification of a part of the network optimization problem for a single human cortical neuron: Given a set of synaptic target loci fixed in 3-space (rather than, more realistically, a set of embryologically moving targets), the cell is to generate the axonic arborization that connects to all these synaptic sites, and is of minimum total length. The task as thus conceived is a pure connectivity-minimization problem, ignoring other functional roles and constraints of cell architecture, such as electrophysiological signal processing. When synapses and cell body are viewed as the only nodes in the optimization problem, one immediately sees that neurons do not form minimal spanning trees, since branch junctions generally do not occur at synapses. Instead, neurons seem to be forming arborizations that are candidates for the more economical Steiner trees, with isolated internodal junctions.

A typical primate cortical pyramidal neuron has around 1,000–5,000 synapses (Cherniak 1990), so even if human neurons were forming perfect Steiner trees,

there is at least presently no way in which we could directly prove this. Demonstration of this optimality – as opposed to various types of weaker probabilistic approximation – would be computationally inaccessible, and so unknowable, to us. However, verifying sufficiently small-scale local optimization of neuronal arbors is quite computationally feasible. We therefore first turn to the more manageable project of evaluating maximally local minimization, namely, at individual internodal junctions of a neuron's arbors. One can immediately observe that, throughout the cerebral cortex, and indeed most of the central nervous system, bifurcating and planar junctions do heavily predominate, in accordance with the optimization theorems mentioned above.

2 Variable-cost models

The next question concerning local optimization is, do these internodal junctions form 120° branch angles, as specified by the theorem described above? Quite consistently, they do not. Indeed, with the main exception of some hexagonal tessellation phenomena, nature generally – animal, vegetable, mineral – seems to abhor 120° junctions in branching structures: For individual neurons (dendrites and axons), nerve tracts, glia, blood vessels (arterial and venous), lung bronchi, plant arbors and their roots, corals, antlers, tissue wrinkles; rivers (both fan-in and fan-out), geological cracks, and electric discharge patterns. Instead, there is a rough but robust tendency toward bifurcations with an internal angle of about half of this (see Tables 1 and 2). The simplest explanation to begin with is that in nature, generally not all connecting arcs are equal; in some relevant sense, "trunks" (nearer to some origin) cost more per unit length than their branches. The earlier 120° junction theorem holds only on the assumption that all 3 arcs at internodal junctions are of equal cost per unit length. If a trunk-arc costs more than the mean cost of its two branch-arcs, then the cost-minimizing solution will involve taking the 120° solution and trading off costlier trunk t in exchange for more of the cheaper branches b_1, b_2 (see Fig. 1). As a result, the internal angle θ ($= \theta_1 + \theta_2$) between the branches will be narrowed below 120°.

This qualitative idea can be refined into a simple function from cost per unit length of branches and trunk to the internal angles θ_1, θ_2 that would minimize overall cost of the junction, conceived of by itself as a simple "Y"-shaped tree. A formalism of this type was in fact derived by Murray (1926, 1927), although of course not within the more recent network optimization framework of the present discussion (see also Uylings 1977). The model was proposed for plant arbors and arteries, but little quantitative data supporting empirical applicability of the model was published there or subsequently (see Zamir 1976; Woldenberg and Horsfield 1983; Roy 1983).

To summarize briefly the derivation of the local optimization model: First, the total cost of such a

Y-tree is expressed as a trigonometric function of angles θ_1 and θ_2 and arc-costs. Let w_0 be the cost per unit length of trunk t, and w_1, w_2 be the corresponding costs of branches b_1, b_2 respectively. Since we are interested not in the absolute value, but relative cost comparisons, the total cost function can be simplified by dropping terms that remain constant with changes in θ_1 and θ_2. Total cost w of the Y-junction is then:

$$w = \frac{w_1}{\sin \theta_1} + \frac{w_2}{\sin \theta_2} - \frac{w_0 \cos \theta_1}{\sin \theta_1} . \tag{1}$$

A plot of this total Y-tree cost index as a function of the total internal branch angle θ for, e.g., a symmetrically branched tree with trunk/mean branch cost ratio of 1.75, indicates that there does exist a minimum total cost, for $\theta = 58°$. In short, for a general solution, the derivative of total cost w with respect to θ_1 and θ_2 is taken. (See Zamir 1976 for a recent presentation of this type of analysis.) When $\partial w / \partial \theta_1, \theta_2$ is then set equal to 0 and solved for θ_1 and θ_2 to find its minimum, the cost-minimizing angles θ_1 and θ_2 are given by:

$$\cos \theta_1 = \frac{w_0^2 + w_1^2 - w_2^2}{2 w_0 w_1} , \tag{2}$$

$$\cos \theta_2 = \frac{w_0^2 + w_2^2 - w_1^2}{2 w_0 w_2} . \tag{3}$$

One point brought out by this derivation is that the actual given distances between nodes connected by a junction, or even the proportions involved, still do not enter into determination of the optimizing junction angles. Some useful lemmas follow from these formulas. The total internal angle θ between branches b_1 and b_2, which is $\theta_1 + \theta_2$, will minimize the cost of the Y-junction when

$$\cos \theta = \frac{w_0^2 - w_1^2 - w_2^2}{2 w_1 w_2} . \tag{4}$$

For the special case of constant-cost arcs that we began with above, where $w_0 = w_1 = w_2$, this formula indeed does yield a cost-minimizing θ of 120°. Another important special case is the symmetrical-branch junction, where $w_1 = w_2$. The above formula can then be simplified, with w_1 and w_2 normalized at 1 so that w_0 expresses trunk to mean branch cost ratio, to

$$\cos \theta = \frac{w_0^2 - 2}{2} . \tag{5}$$

In addition, the above general formula (4) implies that, for maximally assymmetric junctions, where arc-weights tend toward $w_0 = w_1$ with $w_2 = 0$ (i.e., b_2 is relatively thin), the optimizing solution is to set $\theta = 90°$. Finally, it is interesting that if $w_0 \geqslant (w_1 + w_2)$ (so that no "economy of scale" is gained in trunk cost over combined branch costs), the optimizing internal angle will be $\theta = 0°$; in effect, the cost-minimizing solution would thereby be no trunk at all.

Are observations of actual neuroanatomy consistent with a hypothesis that neurons in fact locally optimize their arborizations in accordance with the above model? Before this can be checked, an additional assumption is needed, regarding what is the "cost" the neurons are supposed to be locally minimizing. Perhaps the simplest working hypothesis to begin with is that the cost minimized is just total volume of the Y-junctions (cf. Cajal's qualitative "laws of protoplasmic economy" (1972, vol I, chap 5)). Given that neuron fibers are not infinitely fine, like geometrical line segments, the overall volume constraints of a finite nervous system are fundamental. Also, a widespread feature of tree-like structures in nature, including neurons, is that some connecting arcs – trunks – have greater volume per unit length than others; a variable-cost arc model therefore seems a promising starting point.

One can immediately note some familiar, informal qualitative neuroanatomical observations that fit such a local optimization model. The intersection of branches with the apical dendrite of pyramidal cells progresses from right angles for junctions at the wide base of the apical dendrite to more acute angles with decreasing diameter of the tapering shaft; a similar pattern is common for plant trunks. This phenomenon conforms to the case above where optimal branch angle is 90° if a branch has a relatively small diameter compared to the trunk and the other branch of the junction. Similarly, many types of dendritic spines show strong diameter assymmetry with respect to the branches from which they sprout, and consequently tend toward 90° junction angles. At symmetrical axon bifurcations, the decrease in diameter from trunk to branches typically is less than for symmetrical dendrite branchings; consequently, such axon junction angles stay wider, and closer to the constant-cost optimum of 120°, than the dendrite junctions do.

3 Materials and methods

For this exploratory study, in order to maximize sensitivity of goodness of fit tests of the model as discussed below, the widest range of types of junctions was sought for sampling. Data was chosen in terms of best-quality available sources – for example, high-contrast micrographs of representative structures without anatomical irregularities or evidence of distortion from tissue fixation shrinkage. Pictures, principally published camera lucida drawings of Golgi preparations, were selected for a broad variety of neuron types, of animals, and of developmental stages. Neuron pictures included dendritic arbors of cortical pyramidal and stellate, retinal ganglion, Purkinje, in vitro cultured hippocampal, and insect cells; and cortical axonic arbors (see Table 1). Non-neuronal junctions included both living cases, with measurements from a camera lucida drawing of an astrocyte, from a 2 m tall eucalyptus sapling, elm tree roots, and human retinal capillary networks (arterial and venous); and non-living structures, with measurements from a photograph of a Lichtenberg electric discharge pattern, a river delta, and a set of erosion gulleys (see Table 2). Branch widths were measured from the pictures by microscope with ocular and scalar micrometers, and, because of swelling typically found at

Table 1. Local branch optimization law: neuronal junction observations. All arbors are dendritic, unless indicated otherwise. Values in parentheses are number of junctions measured

Neuron junctions	Mean trunk/branch area ratio	Mean observed angle	Mean pred-obs angle diff
Pyramidal			
cerebral cortex,			
rabbit (8) (Cajal 1972: I, p 60)	1.64	77.8	−10.4
visual cortex,			
human infant (8) (Cajal 1972: II, p 534)	1.87	58.4	−14.6
frontal cortex,			
human infant (8) (Cajal 1972: II, p 544)	1.75	68.0	13.8
primary visual cortex,			
rabbit (8) (Shkol'nik-Yarros 1971, p 143)	1.51	76.0	6.0
motor cortex,			
human (7) (Shkol'nik-Yarros 1971, p 250)	1.49	71.0	14.6
primary auditory cortex,			
cat (8) (Winer 1984a, p 485)	1.83	61.4	−16.4
primary visual cortex,			
macaque (8) (Valverde 1985, p 454)	1.54	65.8	15.7
hippocampus, mouse, in vitro			
(8) (Banker and Waxman 1988, p 76)	1.82	61.9	−16.9
Stellate			
somatosensory cortex,			
mouse (4) (White 1981, p 159)	1.73	54.5	−2.3
primary auditory cortex,			
cat (8) (Winer 1984b, p 520)	1.74	70.9	−7.8
suprageniculate nucleus,			
cat (8) (Winer and Morest 1983, p 26)	1.77	51.3	−0.3
Axonic arbor			
afferent, human cortex			
(11) (Lorente de No 1949, p 296)	1.37	75.1	18.0
afferent, primary visual cortex,			
monkey (8) (Shkol'nik-Yarros 1971, p 63)	1.34	87.4	11.4
intrinsic, medial geniculate, cat			
(9) (Winer and Morest 1984, p 358)	1.63	76.2	−5.4
bitufted neuron, primary auditory cortex,			
cat (8) (Fairen et al. 1984, p 210)	1.55	94.9	−14.2
recurrent, striate cortex,			
macaque (7) (Valverde 1985, p 454)	1.68	80.7	−6.7
Ganglion cell, retina,			
dog (8) (Marenghi in Rodieck 1973, p 481)	1.71	48.4	13.9
cat (8) (Dann et al. 1988, p 1492)	1.92	56.9	−17.5
trout (8) (Collin 1989, p 155)	1.38	80.6	12.3
Purkinje,			
mouse (12) (Cajal 1972: II, p 11)	1.59	81.3	−7.6
30 day rat (12) (Bradley and Berry 1976, p 136)	1.58	79.3	0.9
50 day rat (12) (Berry and Bradley 1976, p 9)	1.60	66.9	10.0
Dragonfly larva,			
motor (9) (Zawarzin in Cohen 1970, p 800)	1.97	53.7	−7.2
sensory (7) (Zawarzin in Kuhlenbeck 1967, p 161)	1.60	50.7	19.1
Cricket interneuron (15) (Nevin 1989)	1.51	81.6	1.3
Neuron means (217)	1.64	70.3°	+0.6°

the immediate junction point, taken at about one to two trunk-diameters from the junction point. "Local" for neurons thereby fell in the 1–10 μm range. The goal was to measure about eight "clean" junctions, typically of a single neuron, from each neuron picture. Junctions excluded were within half a cell body diameter of the cell body, at synaptic spines, at final branchings where resolution was failing as indicated by gaps in fibers, or where irregularities such as synaptic swellings were present. Number of junctions measured per picture ranged from 4 to 12. For area calculation, cross-sections were assumed (except for water channels) to be approximately circular.

4 Results

An initial empirical question is whether, on the above model, there is any possible volume optimization problem in the first place: Is the trunk-to-branch cost ratio – here, the ratio of cross-sectional areas – below the "break-even" value of 2.00 explained above? Although individual junctions sometimes reach 2.00, Tables 1 and 2 indicate that, quite widely in nature, pooled sets of samples of neural as well as non-neural structures satisfy this condition, with a mean ratio of 1.68. Earlier studies by Rall (1959) of neuron fiber diameters at junctions also confirm a trunk/branch ratio below 2.00.

Table 2. Local branch optimization law: non-neuronal junction observations. Values in parentheses are number of junctions measured. Data given without citation was originally collected by author[a]

Non-neuron junctions	Mean trunk/branch area ratio	Mean observed angle	Mean pred-obs angle diff
Living			
Neuroglia, fibrous astrocyte (8)			
(Rio Hortega in Hosokawa and Mannen 1963, p 14)	1.69	70.2	−7.2
Capillaries, human retina (Siegelman and Ozanics 1982, p 497)			
arterial (5)	1.61	78.4	−3.2
venous (8)	1.82	66.1	−8.0
Eucalyptus sapling			
branches (22)	1.83	64.2	−3.9
Elm tree			
roots (8)	1.85	46.5	−2.3
Non-living			
Lichtenberg electric discharge (8)			
(Sander 1987, p 100)	1.95	48.1	−15.3
Delta, Colorado River (8)			
(aerial photograph, Gulf of California)	1.97	51.8	0.1
Converging erosion gulleys (6)			
(La Jolla, California)	1.47	68.8	15.0
Non-neuron means (73)	1.80	61.4°	−3.8°

[a] For river delta and erosion gulley data, predictions are derived from channel widths; predictions are unaffected by specific channel width/depth ratios, so long as they remain constant for trunk and branches at each junction

The main question then is, how well do neuron arbors fit the network optimization model? For satisfactory direct angle measurement, the key requirement on the above picture set was that all elements of each junction studied lie at least approximately in the picture-plane. This appeared achievable, since Uylings and Smit (1975) had reported that rabbit striate cortex pyramidal cell dendrite branchings deviated little from planarity. It had been accomplished in some cases through sectioning the cell so that only structures in a relatively thin slice remained (White 1981), or through the intrinsically rather planar global arbor anatomy of the cell type (e.g., retinal ganglion cells and Purkinje cells), or through representational conventions for drawings (e.g., Cajal and Lorente de No), or through in vitro culture of the cells on flat glass plates (e.g., Banker and Waxman 1988).

As shown in Table 1, mean neuronal junction angle was 70.3°, falling far below 120°. Overall mean difference between predicted junction angle and observed angle (the latter subtracted from the former) is small, +0.6° for 217 neuronal junctions; for comparison, mean predicted-observed angle difference for 73 non-neural junctions is −3.8°. In addition, the density of these errors for junction-groups approximates a normal probability distribution around zero. Also, the correlation was determined between mean predicted and observed angles for the set of arbor samples (see Table 3): As a variance-suppression strategy, pooled groups of junctions sampled together – with a mean of about 8 junctions per group – were taken as the unit of analysis (since grand means in Table 3 are means of these group means, they diverge slightly from those in Table 1 and 2). With r = 0.710, the mean predicted angles rather strongly correlate with the mean observed angles for the neuron arbor samples; at r = 0.857, the correlation is somewhat higher for the non-neuron samples. If the model fit the data perfectly – i.e., predicted = observed values – the linear regression line here would have a slope of 1, with y intercept at 0. In fact, the best-fit line for the neuron samples has a shallower slope of 0.516; the non-neuron data has a slightly steeper slope of 0.611. A calibration study by direct computer-assisted 3-D microscopy of whole-mounted cricket dendrites (Nevin 1989) agrees with the above "by-hand" data (see Table 1), as also does preliminary data using these computer techniques for rat hippocampus granule cell dendritic arbors.

Table 3. Analysis of arbor data by sample groups. Mean sample size: 8.8 junctions. See Table 1 for listing of neuron samples, Table 2 for non-neuron samples

Neuron arbor samples (25)		
	Predicted (x)	Observed (y)
Mean	69.6°	62.2°
SD	17.4°	12.6°
Linear regression	slope 0.516	y intercept 33.3°
Correlation	r = 0.710	p < 0.001

Non-neuron arbor samples (8)		
	Predicted (x)	Observed (y)
Mean	58.7°	61.8°
SD	16.3°	11.6°
Linear regression	slope 0.611	y intercept 25.9°
Correlation	r = 0.857	p < 0.01

5 Arbor optimization

How good in fact is a mean 0.6° departure of neuron junctions from the volume-minimizing angles? The mean optimizing performance of neural and non-neural samples described above seems at least comparable. In addition, the above hypothesis that the minimized cost is local junction volume can be compared for goodness of fit to actual neuron data with some important alternative candidates. First, suppose that the cost minimized instead is local junction surface area. For circular branch cross-section of radius r, volume per unit length of branch is πr^2, while surface area is $\pi 2r$. Thus, for example, a symmetrical tree trunk/branch ratio cost of 1.75 where cost = volume would decrease for cost = surface area to a cost of only $\sqrt{1.75}$, that is to 1.32. The optimal angle θ would thereby increase by 67%, from 58° to 97°. The general picture is that optimal branch angles for surface area minimization are much larger than for volume minimization. Correspondingly, a salient difference between performance of the volume and area minimization models for neurons can be seen in their mean predicted-observed error, which is +31.6° for the area minimization model, over an order of magnitude greater than for the volume model. Furthermore, the volume minimization model consistently outperforms the area minimization model: the mean value of the angle errors for each arbor sample is smaller for the volume model in all but one of 25 cases ($p < 0.001$, by a sign test); similarly for all non-neuron samples ($p < 0.01$). Both neural and non-neural samples therefore fit a volume-minimization hypothesis significantly more closely than an area-minimization hypothesis.

Local volume-minimization also appears to dominate over the important desideratum of signal propagation-time minimization. For, suppose delay is directly proportional to path length. We saw earlier that a conventional constant arc-cost Steiner tree, with 120° junctions, minimizes simple Euclidean length of the total arbor; 120° junctions versus 60° ones save 30% of the length w of a normalized Y-tree. All neuronal observation sets of Table 1 clearly favor junction volume minimization over length minimization. In addition, larger fiber diameters, other things being equal, yield higher axon conduction and dendritic graded potential propagation velocities; consequently, larger-diameter trunk ought even to be *preferred* over thinner branches for propagation-time minimization. Therefore, junctions actually wider than the constant arc-cost 120° should be observed for symmetrical-branch junctions. But in fact they are rare: only one occurs among the 290 junctions summarized in Tables 1 and 2.

Finally, the considerable variance in individual junction angle predictions should be noted – as can be seen in higher standard deviations for predicted (42.4°) versus observed (22.3°) neuron angles, and the consequent flattening of slope of the linear regression line. While subtle "chaotic" and/or stochastic phenomena might be involved, the simplest source of this variance would just be in random errors of measurement of branch diameters that are propagated through the optimization model to the predicted θ. For, the formula makes θ sometimes highly sensitive to branch diameter variation: for example, where trunk and branches have respective diameters of 18.5, 18, and 6, a less than 3% decrease in trunk diameter yields a 50% increase in θ. Since diameter observations would be susceptible to at least $\pm 3\%$ error under the best conditions, the unavoidable error-induced variability in predicted angles will be appreciable. (A smaller measurement bias is also present in angle observations whenever a Y-junction can rotate about its trunk on an axis parallel to the picture plane; such junction rotation here would always decrease the apparent angle.)

Goodness of fit studies for local optimization models of types similar to the one proposed here have been reported for arteries (Zamir 1976; Woldenberg and Horsfield 1983) and river junction geomorphology (Roy 1983); they evaluate performance of the alternative cost assumptions of volume, surface area, required "pumping" power, and hydrodynamic drag. However, these studies have not yielded results that supported one of these cost-minimization hypotheses significantly more strongly than the others. Since each of the studies appears to have taken individual junctions rather than aggregated data from related junction groups as the unit of analysis, one possible explanation for their inconclusiveness might be that the unavoidably high variance described above is swamping any actual effects. An additional strategic point is that, for a given number of observations and level of variance, the wider the range over which the observations are collected (here, range of trunk and branch weights), the greater will tend to be the power of the experiment; the broad variety of junction types sampled here would therefore also tend to improve sensitivity of the goodness of fit tests.

6 Optimization mechanisms

How in fact would neuron arbor junctions arrive at angles that, for their branch diameters, minimize local volume out to around a dozen μm from the junction point? One clue is that, as we have seen, ensembles of neuronal and non-neuronal junctions appear to approximate volume-minimizing behavior comparably well; similarly for neuronal versus non-living ones. Since river junctions and electric discharge patterns must be generated by basic physical processes not mediated by DNA code, the possibility arises that neuron junction anatomy might stem from a similar elementary process, where the genome in effect can exploit this simple physical mechanism to achieve local optimization. This suggestion is reinforced by the fact that the volume minimization law relating branch costs and angles is exactly equivalent to the "triangle of forces" law ("Lamy's theorem," in Thompson (1961 p. 91)) derivable in vector mechanics: Let three cords correspond to the three arcs of the network optimization problem, with the cords fastened together at the junction point.

Each cord is pulled away from the junction by a weight that corresponds to the cost per unit length of each of the three network arcs. Then the angles formed between the cords are given by the above cost-minimization laws.

Thus, an idea worth exploring is that a wide range of local volume-minimizing tree-forming phenomena, from the micron to the kilometer scale, may all arise by similar simple "tug of war" energy-minimization mechanisms. In the case of neurons, perhaps the simplest model would be drawn from fluid statics. Suppose that, at a Y-junction, some intracellular extruding pressure exerted forces that affect branch orientation only upon the cross-sectional disk of the trunk and each branch as it leaves the junction joint zone; then, for any positive intracellular pressure, forces on each element would be proportional to its cross-sectional area, and so by the triangle of forces law, the three arcs would go into vector equilibrium at the volume-minimizing angle. Such a process would yield quick convergence on the equilibrium state; developmental and phylogenetic data are consistent with such rapid dynamics, in that neurons that are embryologically and evolutionarily more primitive appear to conform to the optimization law about as well as more advanced ones. An alternative model involving instead mechanical tension exerted on the two branches during development by the growth cone at each tip, as the cone's filopodia pull it across the substratum (cf. Bray 1987), seems less plausible for this initial branch-budding stage, because the trunk lacks a growth cone to exert the required third traction force. (It should be mentioned that fluid-dynamic accounts of observed neuronal trunk/branch cross-sectional area ratios in turn can also be derived.)

7 Global optimization

A simple local network volume minimization model turns out to fit rather well to neuroanatomical junction observations – without introduction of, e.g., the ideas of optimization of subtle electrophysiological signal-processing roles for the junctions, or of the abstract flow of information through them. One rationale for so simple an anatomy-generating process can be seen in a dilemma Nature confronts: Human brain wiring is among the most complex structures known in the universe, yet its layout information must pass through the "genomic bottleneck" of very limited DNA information-representation capacity (Cherniak 1988). The harmony of local neuroanatomy and vector mechanics suggested by the above account would lower this hereditary information load by giving the genomic DNA local network optimization automatically and comparatively cheaply. Indeed, similar genomically compact structure-optimizing strategies for self-organization may be widespread among organisms.

It is worth noting that even if a wide range of junctions, neural and non-neural, approximate a pure local volume-minimization model fairly well, extrapolation of the model to large-scale global optimization of neuron arbors remains at least an open question. In the first place, local network optimization is not a sufficient condition for global optimization; the distinctive character of the intractability of NP-complete/hard combinatorial problems like Steiner tree is that exact solution of small "local" cases can remain quite feasible, while moderately larger "global" cases are often surprisingly unmanageable – even with resources of cosmic scale (Cherniak 1986). The energy-minimization mechanism for local optimization sketched here can only operate where internodal junctions have *already* formed; some entirely different type of process is required to solve the distinctively *combinatorial* optimization problem of where to sprout these Steiner junctions in the first place.

And in fact, a variety of direct observations at least prima facie suggest long-range overall neuron arbor departure from simple volume-minimizing Steiner tree optimality. One major type of symptom is branch wiggle: For instance, cat intrinsic cortical axons in Winer and Morest (1983, pp. 9, 20, 25) show double hairpin turns. A "best of all possible brains" explanation for such repeated zigzags and switchbacks might be that the long-range optimization problem is really more constrained – e.g., these meanders indicate that a branch tip must in fact navigate a dense obstacle course around other brain structures toward its target. Even without such a maze-running puzzle confronting each branch, one would expect its initial local angle setting to have to undergo later mid-course corrections – unless, implausibly, the neuron of origin had complete information in advance about the locus of the ultimate destination of the branch. Thus, local junction optimization will not suffice for more global wiring problems. As mentioned earlier, second-guessing Nature to verify global connectivity optimization is a task of dramatically high computational cost for human investigators; we must adopt weaker probabilistic and/or approximation methods. Perhaps the global problem is simply intrinsically intractable for Nature as well as ourselves, and so even Nature must employ "quick but dirty" heuristics (Cherniak 1991). Hence, whether the observed apparent large-scale non-optimality is because Nature's agenda here involves perfected compromises in a complex, multi-dimensional problem-space, or because Nature itself in fact must employ probabilistic/approximation procedures, is a large topic that will require further study.

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