1.16 Neural Wiring Optimization

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Glossary

adjacency rule	"If components are connected, then they are adjacent." A wire-saving heuristic for laying out a system; also a simple wire-cost measure for such layouts.
component placement optimization	The positioning of a system of interconnected components to minimize total connection cost.
network optimization theory	The characterization of minimized use of limited connection resources (e.g., wire length) in a system.
NP-hard	A set of problems, each conjectured to require computation time typically on the order of a brute-force search of all possible solutions, and often therefore intractable.
size law	For some optimized systems, the smaller a subset, the poorer its optimization.
Steiner tree	A minimum-cost arbor connecting a set of terminal loci, which may include branch junctions not at terminals.

Long-range connections in the brain are a critically constrained resource, hence there may be strong selective pressure to finely optimize their deployment. The formalism of scarcity of interconnections is network optimization theory, which characterizes the efficient use of limited connection resources. The field matured in the 1970s for microcircuit design, typically to minimize the total length of wire needed to make a given set of connections among components. When this simple 'Save wire' idea is treated as a generative principle for nervous system organization, it turns out to have applicability: to an extent, 'instant brain structure – just add wire minimization'. The most salient caveat is that, in general, network optimization problems are easy to state, but enormously computationally costly to solve exactly; those reviewed here are NP-hard. We focus on the Steiner tree concept and on component placement optimization, with emphasis on the latter.

1.16.1 Neuron Arbor Optimization

The basic concept of an optimal tree is as follows: given a set of loci in 3-space, find the minimum-cost tree that interconnects them, e.g., the set of interconnections of least total volume. If branches are permitted to join at sites other than the given terminal loci (the leaves and root), the minimum tree is of the cheapest type, a Steiner tree. If the synapse sites and origin of a dendrite or axon are treated in this way, the optimization of the dendrite or axon can be evaluated. Approximately planar arbors in 2-space are easier to study. The most important feature of naturally occurring arbors – neuronal, vascular, plant, water drainage networks, etc. – is that, unlike much manufactured circuitry, for each internodal junction, trunk costs (e.g., diameter) are higher than the two branch costs. When such Y junctions are examined in isolation, positioning of the junction sites shows minimization of total volume cost to within approximately 5% of optimal (Cherniak, 1992). Furthermore, the relation of branch diameters to trunk diameter fits a simple fluid-dynamical model for minimization of wall drag of internal laminar flow: neuron arbors act like flowing water.

This Y-tree cost minimization constitutes local optimization. Only one interconnection pattern or topology is involved. Such small-scale optimization does not entail larger-scale optimization, where local trade-offs are often required. When more complex portions of a total arbor are analyzed, the optimization problem becomes a global problem, with an exponentially exploding number of alternative possible interconnection topologies. For example, a nine-terminal tree already has 135 135

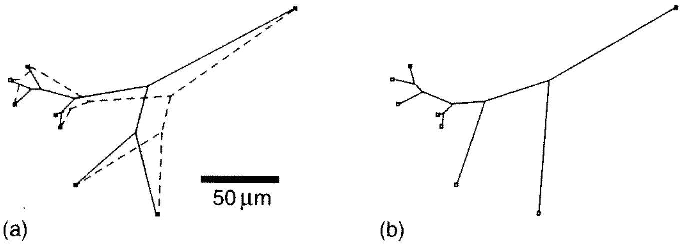

Figure 1 Actual vs. optimal neuron arbors, mouse thalamus extrinsic axon, ascending reticular formation (from data of Scheibel and Scheibel, 1966). The arbor best fits a minimized-volume model. a, Wire-frame representation of an eight-terminal subtree of an observed arbor. Actual tree, with actual topology in its actual embedding, appears as dashed lines. Optimal embedding with respect to volume minimization of the actual topology is superimposed as solid lines. The cost in volume of the actual arbor exceeds that of the optimized embedding of its topology by 2.20%. b, "Best of all possible topologies" connecting the given terminal loci: the optimal topology with respect to volume, optimally embedded. The volume cost of the actual arbor exceeds that of the optimal topology by 2.47%. Only 10 of the 10 395 possible alternative topologies here (approximately 0.14%) have lower total volume costs, when optimally embedded, than the actual topology (Cherniak *et al.*, 1999).

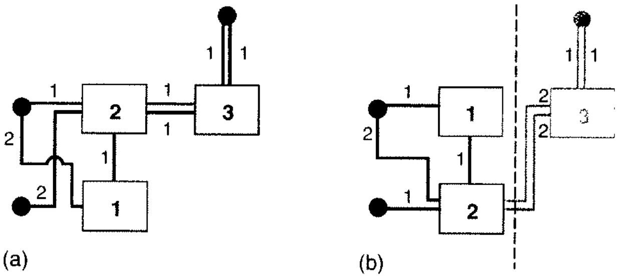

Figure 2 Simple illustration of component placement optimization: minimization of total length of connections. The complete system here consists of a 2-D array of movable components (1, 2, and 3) with given interconnections. All connections are of equal cost per unit length. Component 1 connects to a fixed edge terminal and also to 2; component 2 connects to two fixed edge terminals, and to 1, and also twice to 3; component 3 also connects twice to a fixed edge terminal. a, A globally optimal layout of the three components (cost: 10); cost includes a decussation (connection crossing). b, A complete layout that lacks the decussation, but now is suboptimal (cost: 11). Note also that if the system subset is restricted to only components 1 and 2, including connections to edge terminals, then their layout in (b) is cheaper than their layout in (a), with total connection length reduced from 6 to 5. Hence, these layouts also illustrate global optimization (a) at the trade-off expense of a locally suboptimal cost (b); connection minimization of a total system does not entail connection minimization of its subsets. (A similar pattern holds here for the simpler connection cost measure of adjacency-rule violations explained in text (Cherniak *et al.*, 2004).)

alternative topologies, each of which must be generated and costed to verify the best solution (see Figure 1). Neuron arbor samples, each with three internodal Y junctions, minimize their volume to within approximately 5% of optimal (Cherniak *et al.*, 1999). This optimality performance is consistent for dendrites (rabbit retina ganglion and amacrine cells, and cat retina ganglion cells) and also for some types of axons (intrinsic and extrinsic mouse thalamus).

1.16.2 Component Placement Optimization

Another key problem in microcircuit design is component placement optimization (also characterized as a quadratic assignment problem): given a set of interconnected components, find the placement of the components on a two-dimensional (2-D) surface that minimizes the total cost of connections (e.g., wire length). Again, this concept seems to account for aspects of neuroanatomy at multiple hierarchical levels.

"Why the brain is in the head" is a one-component placement problem. That is, given the positions of receptors and muscles, positioning the brain as far forward in the body axis as possible minimizes total nerve connection costs to and from the brain, because more sensory and motor connections go to the anterior than to the posterior of the body. This seems to hold for the vertebrate series (e.g., humans) and also for invertebrates with sufficient cephalization to possess a main nervous system concentration (e.g., nematodes).

Multiple-component problems again generally require exponentially exploding costs for exact solutions; for an *n*-component system, *n*! alternative layouts must be searched (see Figure 2). One neural wiring optimization result is for placement of the 11 ganglionic components of the nervous system of the roundworm *Caenorhabditis elegans*, with ~1000 interconnections. This nervous system is the first to be completely mapped (Wood, 1988), which enables fair approximation of wire lengths of connections. When all 39 916 800 alternative possible ganglion layouts are generated, the actual layout turns out in fact to be the minimum wire-length layout (Cherniak, 1994a). Some optimization mechanisms provide convergent support for this finding: a simple genetic algorithm, with wire cost as fitness measure, will rapidly and robustly converge on the actual optimal layout (Cherniak *et al.*, 2002). Also, a force-directed placement (mesh of springs) algorithm, with each connection approximated as a microspring acting between ganglion components, attains the actual layout as a minimum-energy state, without much trapping in local minima (Cherniak *et al.*, 2002).

There is statistical evidence that this brain as microchip framework also applies in the worm down to the level of clustering of individual neurons into ganglionic groups and to soma positioning within ganglia to reduce connection costs (Cherniak, 1994a).

Finally, the wiring-minimization approach can be applied to placement of functional areas of the mammalian cerebral cortex. Since wire lengths of intrinsic cortical connections are difficult to derive, one strategy is to explore a simpler measure of connection cost, conformance of a layout to an adjacency rule: if components *a* and *b* are connected, then *a* and *b* are adjacent. An exhaustive search of all possible layouts is still required to identify the cheapest one(s). One promising calibration is that the actual layout of the nematode ganglia is among the top layouts with fewest violations of this adjacency rule. For 17 core visual areas of macaque cortex, the actual layout of this subsystem ranks in the top 10^{-7} layouts best fitting this adjacency costing; for 15 visual areas of cat cortex, the actual layout ranks in the top 10^{-6} of all layouts (Cherniak *et al.*, 2004; see Figure 3) (see The Role of Vision in the Origin and Evolution of Primates, Primate Brain Evolution in Phylogenetic Context, Visual Cortex: Evolution of Maps and Mapping, Captured in the Net of Space and Time: Understanding Cortical Field Evolution, The Evolution of Visual Cortex and Visual Systems).

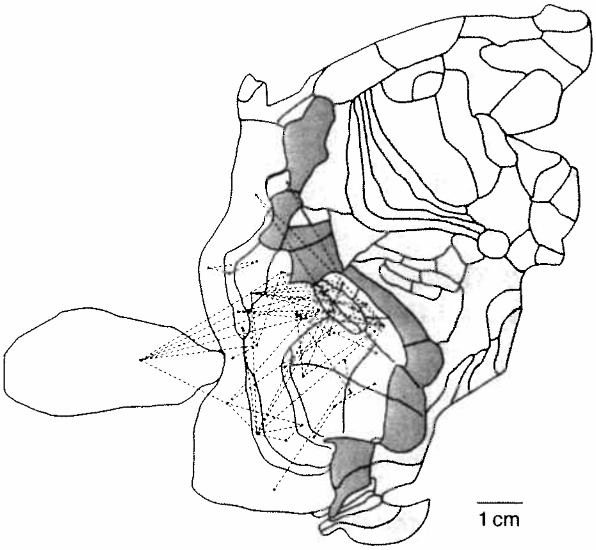

Figure 3 Parcellation of functional areas of macaque cerebral cortex (after Felleman and Van Essen, 1991). Component placement optimization analysis of a layout of 17 core areas (white) of visual cortex, along with immediately contiguous edge areas (dark gray). Reported interconnections among core areas are indicated by dotted lines. Rostral is to the right. In a connection cost analysis, this actual layout of the core visual system ranks in the top one-millionth of all alternative layouts (Cherniak *et al.*, 2004).

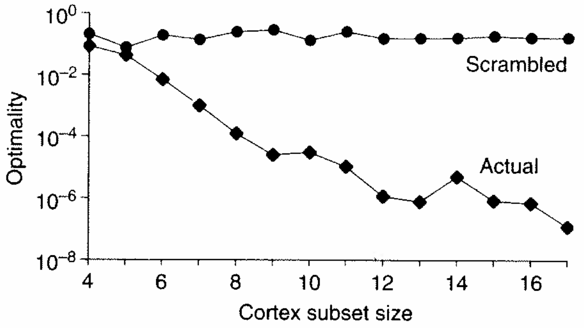

Figure 4 Size Law for macaque visual cortex areas. The system of components here consists of 17 contiguous visual areas of macaque cortex, as in Figure 3. A layout is scored in terms of its violations of the adjacency rule. A series of nested compact subsets of the set of visual areas was generated; each subset was compared with all possible alternative layouts of that subset for adjacency-rule optimality. As subset size increases, optimality ranking of the actual layout consistently improves (with two exceptions, $p < 0.02$). For comparison, the corresponding analysis for a layout of the 17 visual areas with their adjacencies randomly shuffled shows no trend toward improving optimality. Note that this analysis includes only 17 of the total 73 areas of macaque cortex.

In general, a Size Law seems to apply to cases with such local–global trade-offs: the larger proportion of a total system the evaluated subsystem is, the better its optimization (see Figure 4). Similar findings have also been reported for rat olfactory cortex and for rat amygdala (Rodriguez-Esteban and Cherniak, 2005). For the largest systems studied (visual, auditory, and somatosensory areas of cat cortex), there is evidence of optimization approaching limits of current detectability by brute-force sampling techniques. A similar Size Law pattern also appears to hold for Steiner tree optimization of neuron arbor topologies (see Figure 1). The picture then is of limited connections deployed very well, a predictive success story. The significance of ultrafine neural optimization remains an open question. Levels of connection optimization in the nervous system seem unlike levels of optimization elsewhere in organisms.

1.16.3 Optimization: Mechanisms and Functional Roles

Mechanisms of neural optimization are best understood against the background that the key problems of network optimization theory are NP-complete, hence exact solutions in general are computationally intractable. For example, blind trial and error exhaustive search for the minimum-wiring layout of a 50-component system (such as all areas of a mammalian cerebral cortex), even at a physically unrealistic rate of one layout per picosecond, would still require more than the age of the Universe (Cherniak, 1994b). Instead, even evolution must exploit quick and dirty approximation/probabilistic heuristics.

One such possible strategy discernible above is optimization for free, directly from physics. That is, as some structures develop, physical principles cause them automatically to be optimized. We reviewed above some evidence for arbor optimization via fluid dynamics, and for roundworm ganglion layout optimization via mesh of springs force-directed placement simulation. Although neuron arbors appear to optimize on an embryological timescale, component placement optimization appears to proceed much more slowly, on an evolutionary timescale. For component placement optimization, there is the chicken–egg question of whether components begin in particular loci and make connections, or instead start with their interconnections and then adjust their positions, or some mix of both causal directions. It is worth noting that both a force-directed placement algorithm for ganglion layout and genetic algorithms for layout of ganglia and of cortex areas suggest that simple 'connections → placement' optimization processes can suffice.

Wiring optimization is, of course, subject to many basic constraints and so cannot be ubiquitous in the nervous system; the question is where it does in fact occur and how good it is. Trade-offs of local optimality for better cost minimization of a total system (as Figure 2 illustrates) are one way in which global optimization can be obscured.

If the brain had unbounded connection resources, there would be no need or pressure to refine employment of wiring. Thus, to begin with, the very fact of neural resource limitations appears to drive 'Save wire' fine-grained minimization of connections. Another part of the functional role of such optimization may be the picture here of 'physics → optimization → neuroanatomy'. Perhaps such an economical means of self-organizing complex structure generation eases transmissibility through the information bottleneck of the genome. This constitutes a thesis of nongenomic nativism, that some innate complex biological structure is not encoded in DNA, but instead derives from basic physical principles (Cherniak, 2005).

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