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ORIGINAL PAPER

Information processing limits on generating neuroanatomy: global optimization of rat olfactory cortex and amygdala

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Abstract A pattern of widespread connection optimization in the nervous system has become evident: deployment of some neural interconnections attains optimality, sometimes without detectable limits. New results for optimization of layout of connected areas of rat olfactory cortex and of rat amygdala are reported here. One larger question concerns mechanisms—how such minimization is attained. A next question is why a nervous system would optimize rather than just moderately satisfice. A morphogenic proposal that relates these questions is that the means of organizing neural wiring happens also to yield optimization. Some neuroanatomy is generated via "saving wire," and this optimizing is via simple physical processes rather than DNA-mediated mechanisms. Such "non-genomic nativism" is thereby a path around fundamental limitations on generating brains, some of the most complex structures in the known universe.

Keywords Component placement optimization · Network optimization · Non-genomic nativism · Size law · Olfactory cortex · Amygdala

1 Introduction

Neuroconnectivity architecture sometimes shows a virtually perfect network optimization, rather than just network satisficing. Such connection minimization for layout of neural components has been reported for the nematode nervous system [1], cat sensory cortex areas, and macaque visual cortex areas [2]; corresponding arbor optimization also applies for some types of dendrites and axons [3]. This contrasts with the usual picture for biological design, of only moderately good engineering: e.g., the first chapter of Darwin's *Descent of Man* enumerated many examples of rudimentary structures that are no longer functional.

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Instead, it is almost as if neural connections had an unbounded cost. These connection cost-minimization problems are a major hurdle of microcircuit design and are known to be NP-complete, i.e., de facto intractable [4]. Computational costs of solving problems of comparatively small size typically grow exponentially to cosmic scale: solving some could consume more space and/or time than exist in the known universe.

How does biology effectively solve such cosmically costly problems? Some evidence has suggested that the optimal biological structure here arises "for free, directly from the physics." That is, simple physical processes, such as vector-mechanical ("tug of war") energy-minimization, yield the connection minimization [5]. In this way, physics links to neurobiology—in particular, neuroanatomy—via optimizing. Fine-grained economizing of connection deployment is then a means to self-organization of neurobiological structure:

$$\text{Physics} \rightarrow \text{Optimization} \rightarrow \text{Neuroanatomy}.$$

Another case of biological optimization provides some perspective on neural optimization: an amoeboid organism, the plasmodium of the slime mould *Physarum polycephalum*, is capable of solving a maze—that is, not just finding some path across a labyrinth, but a shortest path through it to food sources [6]. Generating this minimum-length solution is an impressive network optimization feat for any simple creature. However, it should be noted that this "shortest-path" problem is not of high computational intractability; in particular, it is not NP-complete [4]. "Greedy algorithms" can solve it and also can be implemented as simple vector-mechanical "tug of war" processes. Nonetheless, that a slime mould can optimize its path through a network converges with observations of network optimization in nervous system anatomy. The latter results entail solution of computationally complex (i.e., NP-complete) problems, namely component placement [1] and the Steiner tree problem [3]. Such consilience lends support to the neuroanatomical findings.

2 Rat olfactory cortex and amygdala

One issue is whether essentially three-dimensional neural organizations can be analyzed in the same fashion as the *Caenorhabditis elegans* ganglia system or the mammalian cortex, which can be roughly modeled as, respectively, virtually one- and two-dimensional in their layout composition. To start addressing these questions, we analyze here two anatomically and physiologically well-understood neural formations of another mammal: rat olfactory cortex and amygdala.

Rat olfactory cortex The rat olfactory cortex extends over the ventral part of the telencephalon, folding like a section of a conical surface with the tip of the cone in the olfactory tubercle. The areas near the tip, such as the ventral tenia tecta and the anterior olfactory nucleus, wrap around the full circumference. The rat olfactory system includes both the primary olfactory cortex and other not strictly cortical parts [7]. Connectivity data was compiled from [7–9] and topological mapping from [7], including the subdivision suggested by [10]. See Fig. 1.

Rat amygdala Several nuclei and other cell masses in the medial part of the temporal lobe form the rat amygdaloid complex. Its almond-shaped structure has a three-dimensional organization, with nuclei adjacent across different spatial dimensions rather than only via

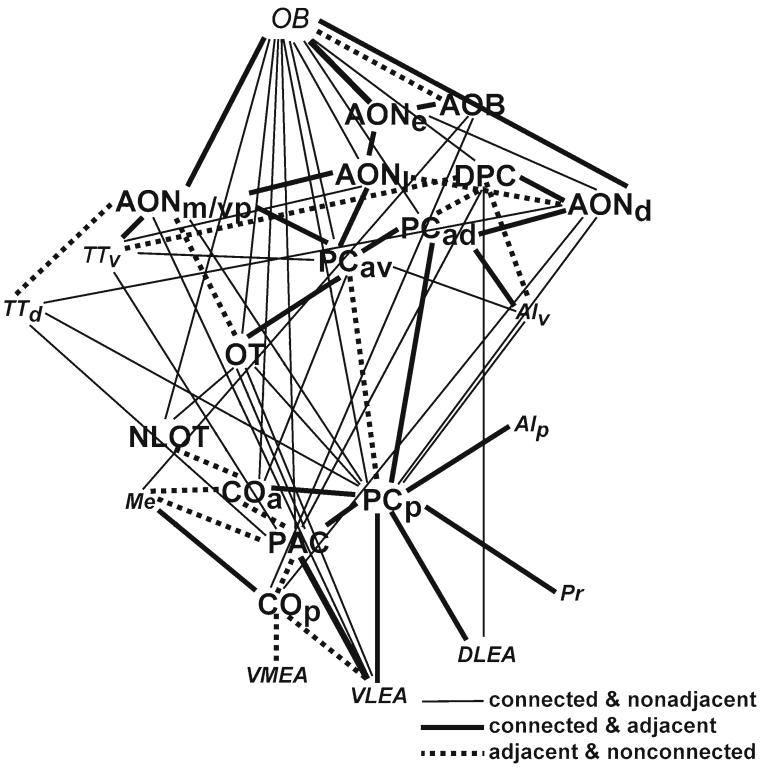

Fig. 1 Rat olfactory cortex represented as a network: interconnections and topological interrelations among areas. Fourteen core areas for optimization analysis of their layout are shown with *boldface labels*; immediately surrounding edge areas are in *italic*. Their connections and adjacencies are designated by *links* as explained in key. For successive subset sizes 1–14, see Table 1. Relative positions of area labels are approximate (based on data from [9])

edge contiguity. Connectivity data were collected from [11] and anatomical mapping of divisions and subdivisions from [11–13]. See Fig. 2.

For evaluation of layout optimality, the procedure [2] outlined was followed, compiling anatomical topology and connectivity data for functional areas of rat olfactory cortex and of rat amygdala. Strength of connection was not included: each connected area pair was assigned a value of 1 in the connectivity matrix regardless of connection magnitude, while unconnected pairs were assigned a value of 0. Area pairs situated immediately alongside each other were assigned an adjacency matrix value of 1, while area pairs that were not next to each other were assigned an adjacency matrix value of 0.

For a given layout of interconnected areas, the wire length cost measure of dis-optimality used was an "all or nothing" surrogate in place of a less manageable distance metric. This consists of cost-counting all area pairs that are connected but not adjacent. Each system is thereby evaluated for its conformity to an adjacency rule: if components are connected, then they are adjacent to each other. E.g., as can be seen in Tables 1 and 2, respectively, the actual layout of olfactory cortex has cost = 9, and the actual amygdala layout has cost = 48 (adjacencies do not include tangential contiguity, where only corners of two areas touch).

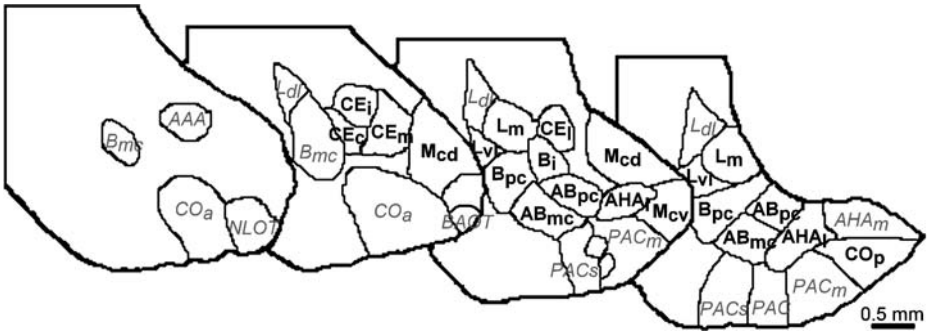

Fig. 2 Rat amygdala represented as a stack of slices: topological interrelations among areas. Fourteen core areas for optimization analysis of their layout are shown with *boldface labels*; immediately surrounding edge areas are in *italic*. For interconnections, and successive subset sizes 1–14, see Table 2 (schematic based on [13])

To generate alternative layouts from the actual one, area positions were randomly rearranged, exhausting all combinatorial possibilities (for a system of 14 areas, $n = 14! = 8.7 \times 10^{10}$ placements). For each layout possibility, the above connection cost measure was

Table 1 Combined connection and adjacency matrix for rat olfactory cortex

	PC_{av}	$AON_{m/vp}$	AON_l	AON_e	AOB	DPC	AON_d	PC_{ad}	PC_p	PAC	Co_p	Co_a	NLOT	OT
PC_{av}														
$AON_{m/vp}$	**1**													
AON_l	**2**	**1**												
AON_e	0	0	**1**											
AOB	0	0	0	**1**										
DPC	0	0	0	0	0									
AON_d	0	0	**0**	1	0	**1**								
PC_{ad}	**1**	0	0	0	0	**0**	**2**							
PC_p	**0**	1	0	0	0	0	1	**2**						
PAC	0	0	0	0	0	1	0	0	**2**					
Co_p	0	0	0	0	1	0	0	0	0	**0**				
Co_a	1	0	0	0	0	0	0	0	**2**	**0**	0			
NLOT	0	0	0	0	0	0	0	0	0	0	0	**0**		
OT	**1**	**0**	0	0	0	0	0	0	1	1	0	0	1	
TT_V	1	**1**	1	0	0	**0**	0	0	0	1	0	0	0	0
OB	2	**2**	2	**2**	**0**	2	**2**	2	2	2	0	1	2	1
TT_d	0	**0**	0	0	0	0	1	0	1	1	0	0	0	0
Me	0	0	0	0	1	0	0	0	0	**0**	**2**	**0**	0	0
VMEA	0	0	0	0	0	0	0	0	0	0	**0**	0	0	0
VLEA	0	1	0	0	0	0	0	0	**1**	**2**	**0**	0	0	1
DLEA	0	0	0	0	0	2	0	0	**2**	0	0	0	0	0
Al_v	1	0	0	0	0	**0**	0	**1**	1	0	0	0	0	0
AL_p	0	0	0	0	0	0	0	0	**1**	0	0	0	0	0
Pr	0	0	0	0	0	0	0	0	**1**	0	0	0	0	0

The series of 14 core areas (PC_{av} − OT) are listed in the order that they are successively added to the analyzed subset. Below are listed the ten edge-ring areas (TT_v − Pr) for a full size 14 core. See Fig. 1. Connections of an area to itself are excluded. Bold values designate topological contiguity of an area pair.
0 no known connection between a pair of areas, *1* connection in one direction, *2* two-way connection

Table 2 Combined connection and adjacency matrix for rat amygdala

	AB_{pc}	B_i	L_m	L_{vl}	B_{pc}	AB_{mc}	AHA_l	CE_l	CE_c	CE_m	CE_i	M_{cd}	M_{cv}	CO_p
AB_{pc}														
B_i	**2**													
L_m	2	2												
L_{vl}	2	**2**	**0**											
B_{pc}	**2**	**2**	**2**	**2**										
AB_{mc}	**2**	**2**	2	2	**2**									
AHA_l	**2**	2	2	1	2	**2**								
CE_l	1	**1**	0	1	**2**	1	1							
CE_c	1	1	1	1	2	1	1	**2**						
CE_m	1	**1**	0	1	2	1	1	**2**	**2**					
CE_i	0	0	0	0	0	0	0	**2**	2	**1**				
M_{cd}	2	1	2	2	2	2	**2**	0	1	**1**	0			
M_{cv}	2	1	2	2	1	**2**	**2**	0	1	1	0	**2**		
CO_p	1	1	1	1	1	2	**2**	0	0	0	0	2	2	
AHA_m	2	1	1	1	2	1	**1**	0	1	1	0	2	1	**1**
L_{dl}	2	2	**1**	**1**	2	2	2	1	1	1	0	1	1	1
B_{mc}	1	**2**	1	**2**	2	2	1	1	**1**	**1**	0	1	0	1
NLOT	1	1	0	1	1	1	1	0	0	0	0	0	0	1
BAOT	1	0	0	0	0	1	1	0	0	0	0	1	1	1
CO_a	2	2	1	2	2	2	2	2	2	**2**	0	**2**	**2**	2
M_r	1	0	0	0	1	1	1	0	0	0	0	**1**	1	1
M_c	2	0	0	0	0	2	**2**	0	1	**1**	0	**2**	**2**	2
PAC	1	1	2	2	1	**1**	**1**	0	0	0	0	1	1	2
PAC_m	**1**	0	0	1	1	**1**	**1**	0	0	0	0	0	**0**	**1**
PAC_s	1	1	1	1	1	**1**	1	0	0	0	0	1	1	**1**

As in Table 1, the series of 14 core areas ($AB_{pc} - CO_p$) are listed in the order they are successively added to the analyzed subset. Below are listed the 11 edge-envelope areas ($AHA_m - PAC_s$) for a full size 14 core. See Fig. 2

determined and compared with the wire cost of the actual layout. The optimality rank score of the actual layout was computed by comparing the wire cost of that layout with the cost of every other alternative layout of that size.

In addition, to assess optimality rank changes in relation to subsystem size, the optimality rank for increasingly larger nested subset sizes was obtained, beginning from a compact central group of four contiguous areas. For each subset size, the optimality analysis included

Table 3 Connections and contiguities between neural components

		Rat olfactory cortex contiguous pairs			Rat amygdala contiguous pairs		
		Yes	No	Total	Yes	No	Total
Connected pairs	Yes	23	30	53	48	129	177
	No	15	163	178	2	66	68
	Total	38	193	231	50	195	245
Significance of effect		$p < 0.0001$			$p < 0.0001$		
Magnitude of effect		$r_\Phi = 0.40$			$r_\Phi = 0.27$		

Each system tends to conform to the adjacency rule: a significantly greater proportion of connected than nonconnected component pairs are contiguous. Connection and adjacency data for rat olfactory cortex system are from Table 1 above, for rat amygdala system from Table 2. Each consists of 14 core components. Connections and adjacencies to immediately surrounding edge components are also included

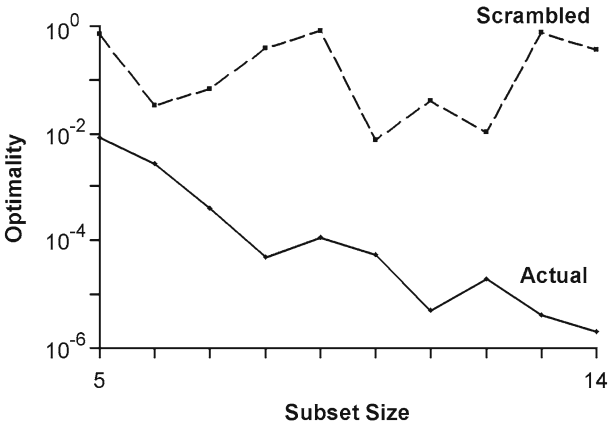

Fig. 3 Rat olfactory cortex layout optimization analysis: plot of optimality rankings for a series of nested subset sizes of the 14 area core shown by *solid line*. For comparison, a randomly generated layout with the areas' relative positions scrambled and their interconnections preserved is similarly analyzed for a succession of progressively larger subsets (*dashed line*). A size law—increasing optimality with increased subsystem size—is apparent for the actual layout but not for its scrambled version. Optimality rank for the complete olfactory system is in the top 2×10^{-6} of all possible alternative layouts of the 14 areas

the "edge-ring" areas immediately surrounding the "core" subset for wire cost computation, but only the areas belonging to the core subset were permuted. See Tables 1 and 2 for the sequence of areas added to the core in rat olfactory cortex and rat amygdala, respectively, and for the ring areas with full size 14.

2.1 Results

As a preliminary analysis: do the rat systems even conform to the adjacency rule (connected → adjacent) to a statistically significant extent? Table 3 shows they each in fact do.

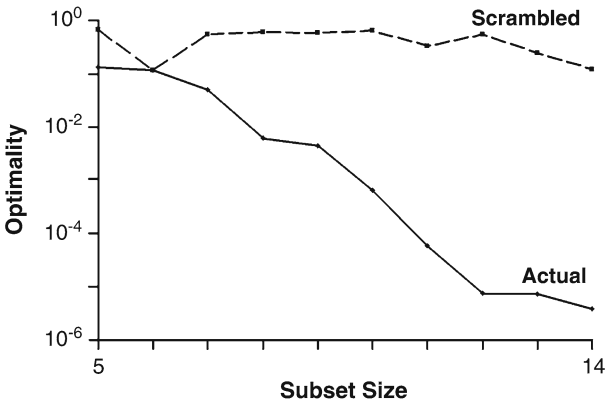

Fig. 4 Rat amygdala layout optimization: optimality-rank plot for nested subset series as in Fig. 3 above. Optimality rank for the complete amygdala system analyzed is in top 3.9×10^{-6} of all possible layouts of the full 14 areas

However, while this simple test is consistent with connection cost minimization, verifying layout optimization still in addition requires exhaustive search of alternative layouts.

Such brute-force search methods shows that rank optimality for the rat olfactory cortex is in the top 2×10^{-6} of all layouts (Fig. 3) and that the amygdala is in the top 3.9×10^{-6} (Fig. 4). That is, the actual layout of each complete system analyzed falls in the cheapest one millionth of all possible alternative layouts. These high optimality ranks are comparable to cat and macaque visual cortex [2] and to *C. elegans* ganglia [1].

Furthermore, a size law appears as subset size increases, indicating a significant trend of increasing optimization across each complete neural system. Each component area added to the system analysis improves optimality exponentially. For olfactory cortex, the best-fit line for optimality of the series of subsets of actual layout gives $r^2 = 0.90$, ($p < 0.0001$). For amygdala, the best-fit line for optimality of the subset series of actual layout: $r^2 = 0.96$, ($p < 0.0001$). A scrambled layout of each system's components shows no such size law trend.

3 Discussion

The above results converge with earlier "connective tissue" minimization findings for other animals (nematode, cat, macaque) and for other neural structures (entire nervous system, cerebral cortex) and for other types of optimization (neuron arbors, as well as component placement). The rat observations suggest optimization of neural layouts to a level that yields costs in the best one millionth of all layouts. For comparison, we reported dendrite and axon optimization of similar-sized arbor topology (in contrast to topology embedding) that did not even reach the top one thousandth [3], perhaps because this tree optimization occurs over only an embryological, not evolutionary, timescale.

The size law also raises the possibility of extrapolation, that larger neural systems that take into account more connected components may attain even better cost minimization. And, in fact, another study [2] describes results for the 39 component cat sensory cortex system (visual, auditory, and somatosensory) where optimization falls in the top one billionth of all layout possibilities.

Such a best-in-a-billion optimization model seems a predictive success story. Yet, against the familiar background of biological satisficing, this neural minimizing may appear gratuitous. There are many other competing design desiderata besides "saving wire." Extreme connection minimization itself in turn stands in need of explanation. One type of account might simply be that brain function demands every micron of connectivity available. However, the existence of neural plasticity—the capacity of nervous systems to regain functionality after even extensive damage—seems to weaken such an approach; connection–optimization after recovery seems improbable. Another possible rationale is in terms of limitations on generation of neuroanatomy. Some brains are the most complex physical structures known in the universe. Yet, plans for their construction must fit through the "genomic bottleneck," the limited information–transmission capacity of the genome [14].

The ganglia of *C. elegans* are positioned in the layout that has the minimum wire cost out of all 40 million alternatives [1]. This optimal layout can be attained by a simple "mesh of springs" force-directed placement procedure, where each of the one thousand connections is treated as a micro-spring acting upon its ganglia [5]. The worm layout is among the most complex biological structures known to be derivable in this way "for free," directly

from simple physical processes without intervention by DNA mechanisms. In this way, perhaps, physics generates other neuroanatomy, thereby lowering the information load on the genome and also, in the process, yielding optimality.

Such an account is an innateness hypothesis: there is inborn structure—not only at the abstract cognitive level (e.g., of linguistic competence) but also at the brain hardware level. The harmony of physics and neuroanatomy yielding optimization is an instance of self-organizing biological structure. Such an account is a kind of non-genomic nativism, where the "blank slate" of the nervous system is in fact instead preformatted—however, not via the genome but by the underlying physical and mathematical order of the universe [15, 16].

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