

How Cortical Interconnectedness Varies with Network Size

Charles F. Stevens*

*Section of Molecular Neurobiology, Yale University School of Medicine,
New Haven, CT 06510 USA*

When model neural networks are used to gain insight into how the brain might carry out its computations, comparisons between features of the network and those of the brain form an important basis for drawing conclusions about the network's relevance to brain function. The most significant features to be compared, of course, relate to behavior of the units. Another network property that would be useful to consider, however, is the extent to which units are interconnected and the law by which unit-unit connections scale as the network is made larger. The goal of this paper is to consider these questions for neocortex. The conclusion will be that neocortical neurons are rather sparsely interconnected — each neuron receives direct synaptic input from fewer than 3% of its neighbors underlying the surrounding square millimeter of cortex — and the extent of connectedness hardly changes for brains that range in size over about four orders of magnitude. These conclusions support the currently popular notion that the brain's circuits are highly modular and suggest that increased cortex size is mainly achieved by adding more modules.

1 Introduction

Different mammalian species have brains of very different sizes — man's brain is more than a thousand times larger than that of a mouse — but homologous areas are thought to have the same circuits and to operate in the same way. Thus, evolution has scaled what we believe to be the same basic network up many fold and this presents the opportunity to examine how connectedness varies with the size of the network.

Since neuronal intercommunications occur at synaptic contacts, estimates of connectedness can be made by simply counting the number of synapses on a neuron. Direct counting is impracticable, however, because a cubic millimeter of cortex contains on the order of a billion synapses. This paper presents a simple theory that provides a way of characterizing connectedness from measurements on cortical thickness and surface area.

* Address correspondence to The Salk Institute, P.O. Box 85800, San Diego, CA 92138-9216.

Such data are available for many species so that the way connectedness is scaled can be assessed over a very wide range, about four orders of magnitude, of cortex sizes.

2 A Scaling Law

Brain size will be specified by N , the total number of neurons in neocortex, or in some defined subsystem in neocortex. The goal, then, is to find an expression for the average number of synapses a cortical neuron receives (and gives) as a function of brain size.

I begin with a consideration of how the average number of synapses per cortical neuron, $q(N)$, scales with brain size N . Consider some reference brain, a mouse or cat brain, for example, with size n and $q(n)$ synapses per neuron. If evolution scales this brain by a factor $s = N/n$ to a new brain of size N , q should change as

$$q(sn) = f(s)q(n),$$

where $f(s)$ is some function that gives the increase in q for the larger brain over the reference one. Because we believe all mammalian brains, no matter how large or small, conform to the same general design and operate in the same general way, $f(s)$ should vary continuously with s and the particular brain we select as a reference should not alter the scaling function $f(s)$. A standard result for homogenous functions (Aczel 1969) implies, then, that $f(s)$ is a power function

$$f(s) \sim s^b$$

for some constant b . Rearrangement of the preceding equations gives the scaling law

$$q(N) = q(n)(N/n)^b$$

If every neuron were connected to a constant fraction of the neurons in every sized cortex then b would be 1, whereas if each neuron were connected to the same number of others independent of brain size then b would equal zero; if the degree of interconnectedness decreases as brains became larger (perhaps larger, more powerful brains operate more efficiently by sharing information over a smaller number of units), b would be negative.

3 Relating Measurable Quantities

The next goal in our development is to recast the preceding equation into a form that relates quantities for which data are available so that the accuracy of the scaling law can be evaluated, and so that $q(n)$ and b can be determined.

Two experimental observations provide the key for relating the quantities in the scaling law to measured features of cortical structure. The first is that the density of synapses in cortex, r , is constant (within measurement error) across cortical layers, regions, and species (Aghajanian and Bloom 1967; Armstrong-James and Johnson 1970; Cragg 1967, 1975a,b; Schüz and Palm 1989; Jones and Cullen 1979; O'Kusky and Colonnier 1982; Rakic *et al.* 1986; Vrensen *et al.* 1977) and has an average value:

$$r = 0.6 \times 10^9 \text{ synapses/mm}^3$$

The second experimental observation is that the number of neurons that underlies a square millimeter of cortical surface, p , is also about constant (Powell 1981; Rockel *et al.* 1980) across cortical regions and species (with the exception of primate area 17 where it is also constant across species, but differs in magnitude from other cortical areas):

$$p = 1.48 \times 10^5 \text{ neurons/mm}^2$$

(for primate area 17

$$p = 3.57 \times 10^5 \text{ neurons/mm}^2)$$

This quantity p is constant in spite of variations in cortical thickness.

The average number of synapses per cortical neuron is, by definition, the total number of cortical synapses Q divided by the number of neurons N . From the experimental observations presented above

$$Q = rV$$

where V is the total cortical volume and is given by the product of the average cortical thickness T and the cortical surface area A :

$$V = AT$$

N is, according to the preceding, given by

$$N = pA$$

This means that the average number of synapses per cortical neuron $q(N)$ is

$$q(N) = Q/N = rAT/pA = rT/p$$

From the scaling law, however,

$$q(N) = q(n)(N/n)^b = (rt/p)(A/a)^b$$

where a is the surface area and t the cortical thickness of the reference brain. If $q(N)$ is eliminated between these last two equations, a relationship between cortical surface area and thickness results:

$$T/t = (A/a)^b$$

Cortical thickness and surface area data available in the literature thus provide a way of testing the scaling law and of evaluating the constant b .

Because the scaling law is a power relation, the most convenient form for comparisons with experimental data is obtained by taking logarithms of the preceding equation:

$$\log(T) = b \log(A) + [(\log(t) - b \log(a))]$$

A double logarithmic plot of cortical thickness T versus surface area A should be linear, then, with a slope that gives b , the parameter that characterizes neuronal interconnectedness as a function of brain size.

4 Conclusions

Data are available in the literature for evaluating b in two contexts, a particular cortical subsystem, primate (and one tree shrew) area 17, and the entire cortex from a variety of mammalian species. The advantage of using data from primate primary visual cortex is that this cortical region is comparable from one species to another, but the disadvantage is that a relatively narrow range of cortical sizes is available. Using data for the entire mammalian cortex means that different functional regions might be compared from species to species, but a four order of magnitude range of brain sizes is available. In so far as cortex is uniform, as many believe (Creutzfeldt 1977; Eccles 1984; Lorente de No 1949; Powell 1981), the comparison of mammalian cortex across species is appropriate. If the cross species comparison is invalid, then my conclusions are limited to the primate visual area.

Figure 1 presents $\log(T)/\log(A)$ for primate area 17. The data for cortical sizes in this figure vary over a 50-fold range and conform to the expectations of the scaling law with $b = 0.07$ (least-squares fit). Prothero and Sundsten (1984) have gathered data for thickness and surface area of total mammalian neocortex from 15 species (7 animal orders) and find the regression line for a double logarithmic plot like that in Figure 1 has a slope of 0.09. Their data (in their Figures 1 and 3) range in cortical size over about four orders of magnitude.

The scaling law for interconnectedness does indeed seem to provide an adequate fit for the experimental data, and the value of b is small, but not zero. This implies that each neuron is connected to an almost-constant number of other neurons irrespective of brain size. The quantity $q(n)$ for a 1-mm-thick reference cortex is 4.12×10^3 synapses per neuron (1.71×10^3 for primate area 17). This means that a particular neuron could receive synaptic connections from less than 3% of the neurons underlying the surrounding square millimeter of cortex, so that brain cells are rather sparsely interconnected. Other, but less complete, data for hippocampus (Stevens, unpublished) suggest that interconnectedness grows slowly (less than linearly) with hippocampal size. The sparseness in interconnections places limits on models for neuronal circuits, and suggests,

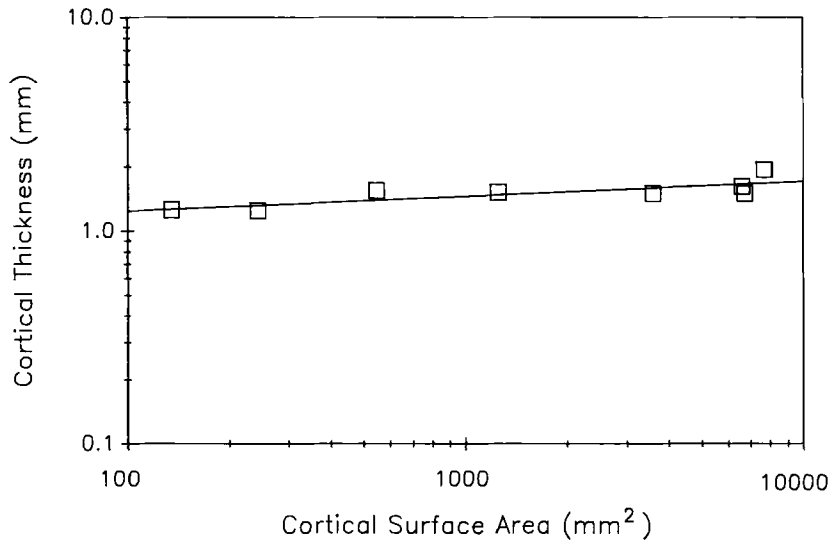


Figure 1: A double logarithmic plot of cortical thickness (in mm) as a function of cortical surface area (in mm²) for area 17. Data derived from cortical volumes given by Frahm *et al.* (1984) and cortical thickness given by Rockel *et al.* (1980). Animals represented, in order of increasing cortical size, are tree shrew (Scandentia), galago (Prosimian), marmoset, squirrel monkey, macaque, baboon, chimpanzee, and man (Simians). The regression line is

$$\log(T) = 0.07 \log(A) - 0.047$$

where T is cortical thickness (mm) and A the surface area (mm²).

for example, that any large content-addressable memories present in cortex seem not to be based on rich connectedness of large populations of neurons. Further, network models that provide realistic representations of cortical circuits should also embody a scaling law like that used by the brain.

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References

- Aczél, J. 1969. *Applications and Theory of Functional Equations*. Academic Press, New York.
- Aghajanian, G. K., and Bloom, F. E. 1967. The formation of synaptic junctions in developing rat brain: A quantitative electron microscopic study. *Brain Res.* **6**, 716–727.
- Armstrong-James, M., and Johnson, R. 1970. Quantitative studies of postnatal changes in synapses in rat superficial motor cerebral cortex. *Z. Zellforsch* **110**, 559–568.
- Cragg, B. G. 1967. The density of synapses and neurones in the motor and visual areas of the cerebral cortex. *J. Anat.* **101**, 639–654.
- Cragg, B. G. 1975a. The density of synapses and neurons in normal mentally defective and ageing human brains. *Brain* **98**, 81–90.
- Cragg, B. G. 1975b. The development of synapses in the visual system of the cat. *J. Comp. Neurol.* **160**, 147–168.
- Creutzfeldt, O. D. 1977. Generality of the functional structure of the neocortex. *Naturwissenschaften* **64**, 507–517.
- Eccles, J. C. 1984. The cerebral neocortex. A theory of its operation. In *Cerebral Cortex*, Vol. 2, *Functional Properties of Cortical Cells*, E. G. Jones and A. Peters, eds., pp. 1–36. Plenum Press, New York.
- Frahm, H. D., Heinz, S., and Baron, G. 1984. Comparison of brain structure volumes in insectivora and primates. V. Area striata (AS). *J. Hirnforsch* **25**, 537–557.
- Jones, D. G., and Cullen, A. M. 1979. A quantitative investigation of some presynaptic terminal parameters during synaptogenesis. *Exp. Neurobiol.* **64**, 245–259.
- Lorente de No 1949. Cerebral cortex: Architecture, intracortical connections, motor projections. In *Physiology of the Nervous System*, J. Farguhar Fulton, ed., pp. 288–315. Oxford University Press, London.
- O’Kusky, J., and Colonnier, M. 1982. A laminar analysis of the number of neurons, glia, and synapses in the visual cortex (area 17) of adult macaque monkeys. *J. Comp. Neurol.* **210**, 278–290.
- Powell, T. P. S. 1981. Certain aspects of the intrinsic organisation of the cerebral cortex. In *Brain Mechanisms and Perceptual Awareness*, O. Pompeiano and C. Ajmone Marsan, eds., pp. 1–9. Raven, New York.
- Prothero, J. W., and Sundsten, J. W. 1984. Folding of the cerebral cortex in mammals. A scaling model. *Brain Behav. Evol.* **24**, 152–167.
- Rakic, P., Bourgeois, J.-P., Eckenhoff, M. F., Zecevic, N., and Goldman-Rakic, P. S. 1986. Concurrent overproduction of synapses in diverse regions of the primate cerebral cortex. *Science* **232**, 232–235.
- Rockel, A. J., Hiron, R. W., and Powell, T. P. S. 1980. The basic uniformity in structure of the neocortex. *Brain* **103**, 221–244.
- Schüz, A., and Palm, G. 1989. Density of neurons and synapses in the cerebral cortex of the mouse. *J. Comp. Neurol.* **286**, 442–455.

Vrensen, G., De Groot, D., and Nunes-Cardozo, J. 1977. Postnatal development of neurons and synapses in the visual and motor cortex of rabbits: A quantitative light and electron microscopic study. *Brain Res. Bull.* 2, 405–416.

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