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"Two Views of the Cerebral Cortex"

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Two Views of the Cerebral Cortex

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1 Introduction

The cerebral cortex, one half of the cerebral grey substance in mice and men, is what any detailed theory of the workings of the nervous system ought to explain, or at least, ought to make use of. In fact, theoretical papers ranging from 1943 to 1985 and from rather realistic views to frankly speculative constructs have made explicit reference to the cortex and perhaps even have influenced the ideas of some experimenters. Cortical anatomists and physiologists, in turn, learned to shape their findings so as to make them acceptable to the theoreticians. The resulting situation of reciprocal positive feedback had some stable solutions:

1. The random network with or without learning. Lashley's philosophy is of this category, as is Hebb's theory of cell assemblies. Rosenblatt's perceptron is also a descendant.
2. The circuit diagram in the spirit of radio engineering. The amplifier entered neurophysiology from communication engineering and with it came various ideas, the most enticing being that of functional secrets embodied in loops of wires connecting tubes, condensers and the like. The neuroanatomists responded quickly with loops of fibres connecting various sorts of neurons in the cortex (Lorente de No and others).
3. The digital computer and a logical theory of nerve nets. This was soon recognized as a misleading analogy, but the digital computer has at any rate among all models of cortical function the unique distinction of being a very useful machine. And the theory formulated by McCulloch and Pitts (1956), made more palatable by Kleene (1956), lent the brain a flair of almightiness which was gratefully recognized by many.

I could mention some more, but I won't. Rather, it is important to realize that the greater part of brain research today ignores the mental schemata 1 to 3 and operates on the basis of more archaic pictures:

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4. The idea of projection, derived from optics. Indeed, this is an enterprise that has not yet been exhausted: Wherever one looks, one finds maps of the body surface or of some sensory space repeated many times in the cortex or in subcortical structures. The brain is reluctant to give up spatial order when it corresponds to something meaningful in the outside world, even after many stages of elaboration. Whether this just reflects convenience of engineering, or some profound reason, we do not know. Projectionist research is still flourishing (see volumes by Woolsey 1981–1982).
5. The idea of localization of function, derived from dualist philosophy. If you are utterly convinced that the connection between mind and brain escapes us as matter of principle, all you can do is find out what part of the brain is related to which faculty of the mind, without asking any further questions about the nature of the connection. This leads to a very useful partition of the brain and to a perhaps less useful dissection of the psyche on anatomical grounds.

I will report in this paper on two different approaches to the cerebral cortex which we have been following in the past years, one in our own histological work on the mouse cortex (Braitenberg 1978a,b), the other one in an analysis of the papers by Hubel and Wiesel and their followers (Braitenberg and Braitenberg 1979, Braitenberg 1983, 1984). Our own work results in a view of type 1 above, while the Harvard papers reflect an extreme type 5 position, possibly with the implied hope of finding a type 2 explanation. Some of the most stunning findings in Hubel and Wiesel's papers carry the principle of localization of function much further than anybody would have believed: "orientation specificity" varying systematically on the surface of the cortex in a succession of strips 30 μm wide, colour specificity being confined to patches not much wider than that (Hubel and Wiesel 1977, Hubel and Livingstone 1982).

In view of these findings it would seem difficult to sustain the essentially random-network philosophy which had grown dear to our hearts on the basis of many anatomical facts. However, I will show that it is possible to make the two points of view quite compatible with each other.

2 The Neuropil in the Mouse Cortex

All the essential features of the cerebral cortex which impress us in human neuroanatomy can be found in the mouse too, except of course for a difference in size by a factor 1000. It is a task requiring some experience to tell a histological section of the mouse cortex from a human one, if the Golgi staining technique is used, and no clues about magnification are provided. With electronmicrographs the task would actually be almost impossible. The task is easiest with a low power photograph of a Nissl preparation (cell body stain). In fact, at the most

microscopical level, the components of the nerve tissue are quite similar in different animals and even in different regions of the brain. On the other hand, a more macroscopical view may readily reveal differences between one piece of brain and the other, the difference being essentially related to the statistics of the distribution of the various components in the tissue. The essential similarity of the neurons as they appear in Golgi preparations of the cortex of mouse and man, the similar shape of their dendritic and axonal ramifications, shows that a common principle is at work in the cerebral cortex of the two species. This principle is quite different from that governing the wiring in other parts of the brain: some of the neuronal shapes in the cerebral cortex are quite characteristic for that level of the nervous system and occur only there. We should like to know why and are looking for an interpretation which provides a good reason for the structural peculiarities of the cerebral cortex.

Before we approach the problem of the shape of the neurons in the cortex, we take a more global view and collect some quantitative data about the densities of the various components in the cerebral cortex of the mouse. The numbers, many of them only approximate, are assembled in Tables 1 and 2. Table 1 contains the raw data. The macroscopical measurements (a, b, c) were taken on frozen sections of formalin fixed material. The areas (a, b) were measured by relatively rough graphic methods. The density of synapses (d) is a quantity affected by a variety of experimental difficulties, and varies somewhat in different areas and layers. Our figure is slightly in excess of other published

Table 1. Measured quantities

a:	Surface area: $2 \cdot 120\,\text{mm}^2$ (including hippoc.)
b:	Surface area: $2 \cdot 65\,\text{mm}^2$ (eulaminate isocortex)
c:	Thickness: 0,8 mm
d:	Density of synapses (isocortex): $10^9\,\text{mm}^{-3}$
e:	Percent type I-synapses: 85% (Wolff 1976)
f:	Density of axons (electronmicroscopy, layer I): $4\,\text{km/mm}^3$
g:	Density of neurons: $2 \cdot 10^5\,\text{mm}^{-3}$
h:	Distribution of cell-types (very rough estimate): 70% Pyramidal, 10% Martinotti, 20% others
	Dendritic length per neuron:
i:	Pyramidal: 3–5 mm
j:	Martinotti: 2–3 mm
k:	Stellate: 4–6 mm
	Axonal length per neuron (not including fiber in white matter):
l:	Pyramidal: 3–6 mm
m:	Martinotti: 3–4 mm
n:	Stellate (large): 10–17 mm
o:	Afferent: 5 mm
	Relative axonal field density:
p:	Pyramidal: 10^{-5}
q:	Martinotti: 10^{-4}
r:	Stellate: 10^{-3}
t:	"Cross section" of basal dendritic tree, Py-neuron (see Braitenberg 1978b)
u:	Number of spines per dendritic length (Py-neuron): $1.5\,\mu\text{m}^{-1}$
v:	Synapses per spine: 1

Table 2. Deduced relations

α (b,c):	Volume isocortex: $2 \cdot 52\,\mathrm{mm}^3$
β (α,d):	Number of synapses: 10^{11}
γ (α,g):	Number of neurons (isoc.): $2 \cdot 10^7$
δ (β,γ):	Synapses/neuron: 5000
c (d,f,ς):	Synapses per length of axon: 1 every 1 to 4 μm
ς (h,l,m,n):	Density of axons: $1 - 4\,\mathrm{km\,mm}^{-3}$
η (i,u):	Number of spines/Py-neuron 5000
θ (g,h,η):	Density of spines $7 \cdot 10^8\,\mathrm{mm}^{-3}$
λ (p,s,t,u,ε):	Probability of 0,1,2...contacts from Py to Py (w_0, w_1, w_2...) at distance 100 μm: $w_0 = 0,9$ $w_1 = 0,09$ $w_2 = 0,004$ same at distance 10 μm: $w_0 = 0,1$ $w_1 = 0,27$ $w_2 = 0,27$ $w_3 = 0,18$

measurements (Cragg 1967) but corresponds to an approximation quoted by many. The distinction of Type I and Type II synapses becomes rapidly very convincing to anybody who had the opportunity to familarize himself with cortical electronmicrographs, but is quite difficult to render objective. In any case, the percentage quoted (Wolff 1975) is very close to our own appraisals in various samples of the mouse cortex. If, by the method of forced choice one classifies synapses according to the well-known criteria, one always ends up with a 4/5 majority, or even slightly higher, of the kind of synapses (Type I) which we like to assume, but never were able to prove to be excitatory. This is a remarkable fact which will detain us later.

The density of neurons (g) in the mouse is almost ten times that in the human cortex. This reflects a difference in the size of the neurons, not so much of their cell bodies but rather of their dendrites and axons which are longer and more ramified and hence occupy proportionally more space when the total number of neurons and their average distances are larger.

A quantity which reflects the complexity of the interactions in the tissue is axonal density (f); the total length of axonal segments in a unit volume. This can be obtained by stereological reasoning on the cross-sections of axons recognizable on electronmicrographs, or from Golgi preparations in which the axonal tree of various neuron types can be measured (l, m, n, o). The total

axonal density can be obtained from these values if the neuronal density (g) and the differential distribution of different neuron types (h) are known (see Table 2, ς). Both methods yield approximately the same result.

Similar measurements can be made on dendrites. It can be seen from the table that the length of all the dendrites of one neuron (i, j, k) is of the same order as that of the axonal tree (l, m, n) and the dendritic density in the tissue is therefore only slightly less than the axonal density.

The remaining measurements are particularly useful if one wants to estimate the influence which the various neurons have upon each other. The relative axonal density (p, q, r) is the proportion of the axonal population contributed by one particular neuron within the territory of its axonal spread. It is interesting to note that even the densest axonal trees of the stellate cells (r) and of the specific thalamo-cortical afferents (not given in the table) represent only one in a thousand axons present within the confines of their termination. Equally interesting, the loosest axonal trees, those of the pyramidal cells (p) seem to be specially made for a wide distribution of signals from each cell.

The "cross-section" of a dendritic tree (t) is defined as the probability of hitting one of the dendrites for a straight fibre entering the region of the dendritic tree in a random direction. For pyramidal cells, which have most of their afferent synapses on dendritic spines, this cross-section was measured on tracings of the dendritic tree including the spines. A closed envelope of the projection connecting all the spine tips was drawn. The area of this envelope, divided by the area of the entire dendritic expansion (i.e. the macroscopical envelope connecting the tips of the dendrites, or alternatively, the circumscribed circle) provides a measure for the probability termed "cross-section".

Finally, the last two quantities were important for assessing the importance of dendritic spines: the density of spines per unit length of (pyramidal neuron) dendrite (u) and the number of synapses on each spine (v), namely 1. .

This crude list of facts, combined in various ways, provides some further quantities more directly relevant for theories of cortical function (Table 2). Besides the more trivial figures volume of the isocortex (α), total number of synapses (β) and of neurons (γ), we get the more interesting ratios. Since cortical synapses as a rule have only one presynaptic and one postsynaptic element we can easily compute the average number of synapses on the dendritic tree of cortical neurons (ς). The number of cortical synapses for which a cortical neuron is presynaptic is only slightly less, because the synapses provided by extracortical afferents are only a small fraction of all synapses, the vast majority being synapses between cortical neurons.

A very useful quantity is (ε), the density of synapses along an axon, which follows simply from the average number of synapses belonging to one neuron and from the average length of the axons of one neuron. There must be a synapse every 1 to 4 μm of axonal length, most of them "en passant", suggesting connections very different from the old picture of terminal boutons situated at the very tip of axonal branches.

The number of spines on all the dendrites of a pyramidal cell (η) is also a derived quantity, since spine counts are always performed on isolated segments of a dendritic tree. From this the density of the spines in the tissue can be derived (θ) which is only slightly less than the density of all synapses in the tissue.

In principle these figures provide the basis for a connectivity matrix of the cortical neurons, but of course the form factors reflecting the shape of dendritic and axonal ramifications are also involved. The probability of a connection between any two neurons in a block of tissue depends crucially on their distance. There are two ways of calculating this for two neighbouring pyramidal cells. One is based on the assumption that the connection is via straight axon collaterals (Fig. 1) and that the form factor on the receiving side is described by the

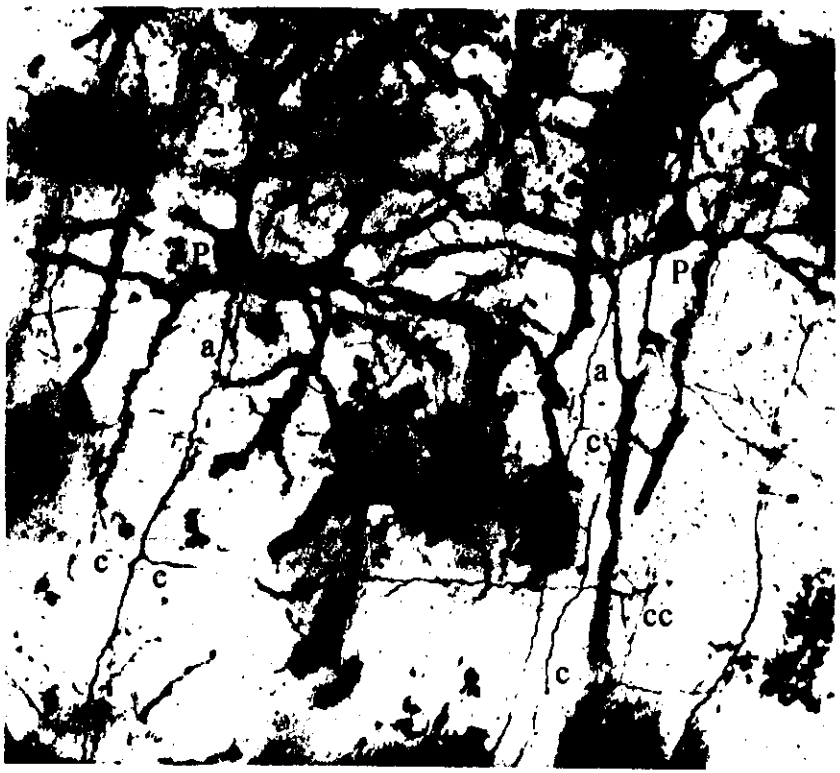

Fig. 1. Two pyramidal cells (*P*) from a Golgi preparation of the mouse cortex. The apical dendrites are cut off. The axons (*a*) leave the cell bodies in a downward direction, giving off straight collaterals of the first (*c*) and second (*cc*) order. Such collaterals are responsible for most of the synapses in the cortex. The target neurons are again other pyramidal cells. Due to their straight course, it is unlikely that such a collateral makes more than one contact with any particular neuron

"cross section" of the dendritic tree (t, Table 1). The other one takes as the axonal and dendritic form factor a certain density of pre- and postsynaptic sites homogeneously distributed within the territory of the axonal expansion of one neuron and the dendritic expansion of the other. If the overlap is known, and if we assume that the presynaptic elements pick their postsynaptic partners at random, we can compute the probability of a connection simply by means of the binomial distribution. The values obtained, for two different distances, are listed in Table 2, λ.

What are the propositions which can be extracted from these anatomical facts for the purpose of a physiological discussion? Four of them are presented in Table 3, and I will discuss their implications.

A and B: It seems that the vast majority of all synaptic contacts within the cerebral cortex are between one class of neurons, the pyramidal cells, and that these are of the excitatory kind, or at least histologically of Type 1, for such are all the synapses residing on the tips of the dendritic spines. This implies a sort of computation which takes us far away from the radio engineering analogy, discussed earlier as the philosophy of Type 2. It is not the combination of a number of components of different kinds, which is at the basis of cortical function, but rather an enormous collection of fundamentally similar neurons connected to each other by a huge number of contacts. The fact that these contacts are all excitatory (the inhibitory ones belong to the stellate cells which have a very different connectivity) is also worth considering. Clearly, for any non-trivial calculation one would be considerably restricted if no inhibitory interactions were available to implement the logical function of negation or negative quantities in arithmetic. But in an associative memory (Palm 1982) a multitude of excitatory contacts is what one would expect. This is our main reason for assigning this role to the cerebral cortex (Braitenberg 1978b).

Proposition C (Table 3) is also interpretable in the same vein. It states that the divergence of signals from one pyramidal cell is as large as it can be: the number of synaptic partners is almost as great as the number of synapses, each of the partners receiving just one or occasionally two synaptic contacts. Again, this is desirable in a network which ought to be prepared to discover, and store as "associations", the largest possible variety of correlations between the activities of the individual elements.

Table 3. Main propositions inferred from Table 1 and 2

A (d, h, θ):
Most synapses are on spines
B (h, A):
Most contacts are Py–Py
C (λ):
The number of neurons afferent to a given Py-Cell is almost as great ($\approx$ 5000) as the number of its afferent synapses. Similarly for efferent synapses
D (B,C):
The cortex is a mixing machine. The activity is relayed in ever new combinations from one set of neurons to the next

The upshot is proposition D: the cortex as a system of fairly uniform units, the pyramidal cells (with a smaller number of neurons of a different kind interspersed) connected to each other by wide-spread but very weak links, so weak, in fact, that the activity of one single cell can hardly exert an appreciable influence on the others. We must assume that the elementary event is constituted by fairly large sets of active pyramidal cells so that fresh sets will be activated in sucession through the synapses preformed in the cortical tissue and moulded by a learning process.

The picture I have in mind is influenced by Hebb's theory of Cell assemblies, by Abeles' "synfire chains", and by various developments of this work by Palm (1982).

There are two observations on cortical structure which are needed to complete the picture.

First, the shape of pyramidal cells. Their dendritic tree has an apical and a basal part, and also their axons are bipartite: long axons reaching distant pyramidal cells and axon collaterals making local connections. The local connections generally attach themselves to basal dendrites of other pyramidal cells, while the distant connections terminate on apical dendrites. We do not know whether the *A*-connections (apical dendrites, long axons) and the *B*-connections (basal-dendrites, axons collaterals) are two separate systems with different tasks, or just (apparently) different for reasons of convenience in the construction of the network during ontogeny. It is difficult to provide a very rich system of connections for millions or billions of neurons arranged in a cup-shaped volume, and one might well come up with the idea of keeping the shorter ones in the volume while letting the longer ones take shortcuts through the surrounding space. There may however be a more interesting distinction between the *A* and *B* systems according to Palm (Palm and Braitenberg 1979). While the probabilities of connections in the *B*-system clearly depend on distances in a smooth fashion, (the "metric system"), no such rule is apparent for the *A* system ("ametric system"). Thus one system may embody, or learn, facts of the world which refer to some metric spaces, (e.g. visual space) and the other facts referring to more abstract realms.

The second observation is about non-pyramidal cells. These are the (smooth) stellate cells, basket cells, chandelier cells in anatomical terminology. The general consensus is that they are inhibitory. The high density of their axons (Table 1, *r*) and especially their specialized endings (baskets, chandelier endings) imply that they have a much stronger grip on their target neurons than the excitatory pyramidal cells. Their role may be merely that of safety devices, strewn among the pyramidal cells to smother the local explosions which are to be expected in a system of overwhelming excitatory connections. But we may also assign them a more interesting role. What an associative memory learns is association of events, in other words positive correlations between the occurrence of events. There have been a number of suggestions of how this may be achieved by a "plastic" mechanism affecting the synapses. If the mechanism is supposed to discover, and translate into synaptic strength, negative as well as positive correlations, say, if the signal "*A* and *B* but not *C*" has to be learned as distinct from "*A* and *B*", then we are either driven to assume a much more complicated elementary learning mechanism than the additive one which is generally postulated, or we must use inhibitory interneurons for the negation. I suggest that at least some of the non-pyramidal cells, in particular those residing in the input layer IV have this function. The next part of this paper, where a special example will be discussed, makes use of this idea.

3 The "Wiring" of Area 17, the Primary Visual Area of the Monkey

Hubel and Wiesel (1977) discovered some facts by microelectrode recording which could be interpreted as indicating very specific connections within the cortical neuropil. The following is a selection of some of their most striking findings:

1. Most neurons in *A* 17 respond best to patterns of light and dark in the visual field ("receptive fields") which are much larger, by a factor 10 or 20, than the distance between points "seen" by neighbouring retinal receptors.
2. The patterns which are most effective are those containing straight borders between light and dark regions presented at a certain fixed orientation characteristic of each neuron.
3. Proceeding through the cortex in any direction parallel to the cortical plane, one encounters neurons whose characteristic orientations vary continuously, with clockwise rotation of the orientations in the visual field sometimes changing smoothly into counterclockwise orientation and vice versa. There are also occasional abrupt changes of the preferred orientation for small displacements of the recoding electrode.

These three facts taken together constitute a puzzle when one tries to reconstruct the intracortical connections which would produce these strange exceptions to the apparent homogeneity of the cortical neuropil.

Figure 2 represents such an attempt. Two neurons, N_1 and N_2, situated in Area 17 at a distance of about 50 μm from each other, have receptive fields F_1 and F_2 in the visual field (a). The fields are about 15 times as large as the distance between two neighbouring points of the elementary grid (dots) corresponding to the resolution of the visual field. Since the plane of the cortex represents the visual field, the two neurons N_1 and N_2 correspond to slightly different positions in the visual field, say to positions shifted by the angle of resolution, i.e. by the distance between neighbours in the elementary grid. Thus we draw F_1 and F_2 slightly apart (in reality there is considerable scatter in the representation of the visual field on most of the neurons in the cortex: the two

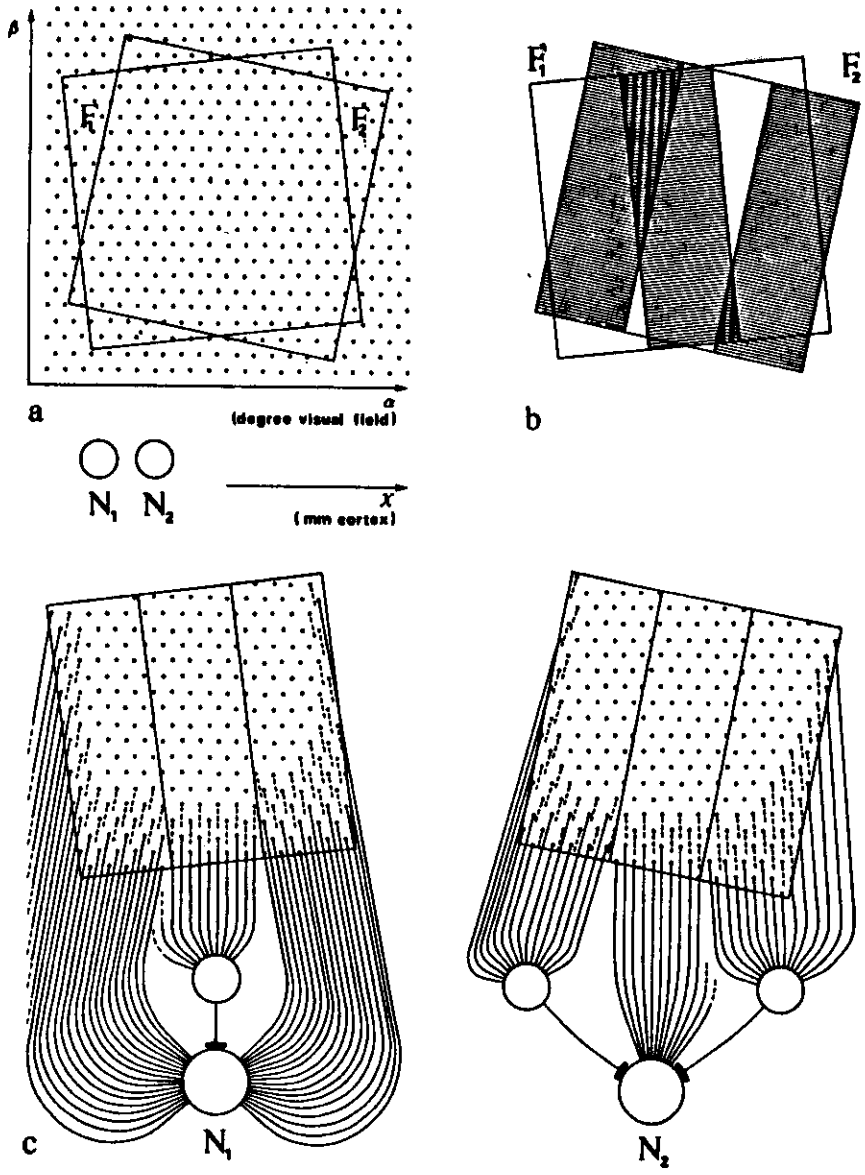

Fig. 2a–c. Illustration of a naive neuronal model explaining some of the effects described by Hubel and Wiesel. **a** The array of *dots* represents the sampling points in a portion of the visual field corresponding to individual cones of the retina. Their separation is about 1 min or arc. E_1 and E_2 are the two receptive fields of a pair of neurons N_1 and N_2 situated in the cortex at a distance of 50 μm from each other. The two fields are rotated 18° one with respect to the other (they belong to different "orientation columns"), and shifted by one minute of arc, the angle corresponding (in the fovea) to 50 μm of cortex. **b** The two fields F_1 and F_2 happen to be of the "simple cell" variety, with well-defined excitatory (*white*) and inhibitory (*cross-hatched*) subfields. E_1 has a central inhibitory region and two excitatory flanks, E_2 vice versa. **c** The wiring responsible for the receptive field characteristics of N_1 and N_2 is shown. Fibres from the receptors (*dots*) reach the cortical neurons directly in the excitatory subfields, via an interposed inhibitory neuron (*smaller circles*) in the inhibitory subfields. The two diagrams of Fig. 2c should be mentally superimposed, to explain the effects described in **a** and **b**

fields F_1 and F_2 could be much farther apart, or entirely superimposed). On the other hand, since distance in the cortex also represents orientation in the visual field, we draw the receptive fields F_1 and F_2 rotated 18° one with respect to the other, for that is roughly the rotation corresponding to 50 μm cortex in many of the published records.

In Fig. 2b the two fields F_1 and F_2 are redrawn with their excitatory (white) and inhibitory (hatched) subfields. This is a feature which is found in many of the receptive fields: in different parts of the field a spot of light may produce an increase or a decrease of the activity of the corresponding neuron. F_1 has a central inhibitory region flanked by two excitatory regions, F_2 the other way round. Figure 2c shows the cortical "wiring" which one would naively assume to be an explanation of the response characteristic of the neurons N_1 and N_2. The two sets of fibres are drawn separately for the two neurons, since their superposition would make the diagram completely incomprehensible. We have to assume at least one inhibitory interneuron for N_1, two for N_2.

There are many more (by a factor of at least 10) neurons in Area 17 than there are incoming fibres from the geniculate body. It is clear that the complete blueprint for all cortical neurons in any small region of cortex according to the principle of Fig. 2c is not only an impossible task for the artist, but a highly improbable feat for the mechanisms of embryogenesis. If such improbable wiring were indeed preformed in the cortex (and that it is not acquired through learning we know from certain experiments: Hubel and Wiesel 1977), we would have to assume an amount of genetic information in the neuropil much richer than one would expect, having accepted the description of the mouse cortex in the first part of this paper.

But there is an alternative explanation of the Hubel and Wiesel effects requiring much less specificity of growth in the cortex (Braitenberg and Braitenberg 1979, Braitenberg 1984, 1985). The main idea was derived from a geometric analysis of the published records showing the variation of orientation specificity of cortical neurons encountered along a straight electrode track. It seemed that the records were more compatible with an inhomogeneity of the cortical neuropil circularly symmetric around centres spaced about half a millimetre apart, rather than with a local anisotropy, the orientation of which changes in one direction only ("orientation strips"), as Hubel and Wiesel had supposed. When this idea was first formulated (Braitenberg and Braitenberg 1979), nothing was known in the histology of Area 17 to justify the assumption of centres with a regular geometric arrangement, but soon afterwards the dis-

covery of the "cytochrome oxidase blobs" (Horton and Hubel 1981, Humphrey and Hendrickson 1980) regularly arranged with the spacing predicted by us came as a pleasant surprise.

However, the coincidence remains simply phenomenological until we are able to show in what way something concentrated in patches in the visual cortex can produce the effects described by Hubel and Wiesel. I offer the following hypothesis (Braitenberg 1983, 1984), best explained on the drawings of Figs. 3 and 4. I assume that the cytochromeoxidase blobs are the site of special inhibitory neurons which exert a strong inhibitory influence on all the (principally pyramidal) neurons in the surrounding region. I also assume that these inhibitors are connected, like the other neurons, to the input fibres in a strictly topographical fashion. The dendritic fields of the inhibitors which receive the input are circular with a diameter slightly less than their separation. The inhibition is so strong that a uniform excitation of a large area is completely smothered by the inhibitors, Fig. 4a. Clearly then only elongated stimuli can be effective which fit into the interstices between the inhibitors so as not to activate them. Moreover, such elongated stimuli have to be oriented tangentially with respect to a neighbouring inhibitor, in order not to affect its dendritic field (Fig. 3). How long straight patterns of excitation affect an array of "hypercolumns", each dominated by a central inhibitor, depends on the orientation of the stimulus with respect to the axes of the geometrical array (Fig. 4). The orientation of the effective stimulus tangential to circles surrounding the hypercolumn centres produces the well-known electrophysiological effects of smooth sequences of orientation along a microelectrode track, including the switching

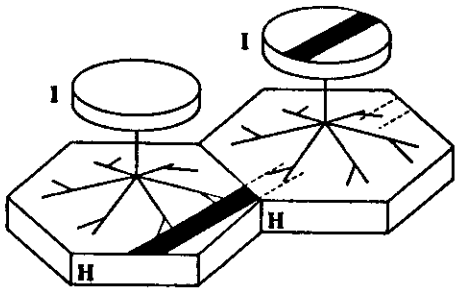

Fig. 3. An alternative model of orientation specificity. The cortex is composed of (schematically) hexagonal "hypercolumns" *H*. In the centre of each hypercolumn there is an inhibitory region, here represented above the hypercolumn as a round box *I*, perhaps to be identified with the dendritic field of an inhibitory neuron. When the central inhibitory region is hit by the stimulus, here represented as a black bar, the corresponding hypercolumn is inhibited and does not respond to the stimulus (*right* hypercolumn). The stimulus is effective only if it passes by the inhibitory region (*left* hypercolumn). Clearly, the hypercolumns respond more readily to elongated stimuli orientated tangentially with respect to the hypercolumn centre, for the same stimuli with a radial orientation tend to hit the inhibitory hypercolumn centre. In this fashion different regions of the periphery of each hypercolumn become sensitive to different orientations tangentially arranged with circular symmetry around the centre

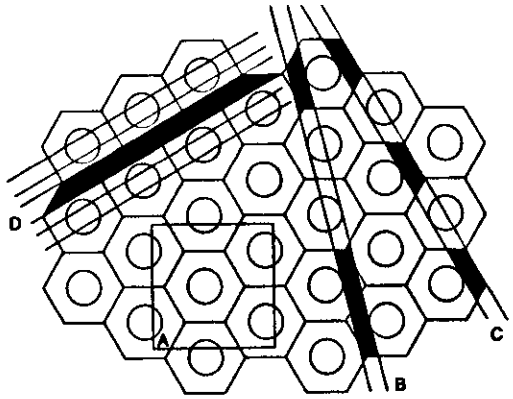

Fig. 4. An array of hypercolumns as in Fig. 3 seen from the top. Regions where pyramidal cells respond to the stimuli *A* to *D* are shown in *black*. The square stimulus *A* does not elicit any response since it falls on all the central inhibitors (*circles*) of the hypercolumns which it touches. *B* and *C* are bars of different orientation. They produce excitation in some hypercolumns where they bypass the inhibitory centres. The position of the active cells within the individual hypercolumns is different for *B* and *C* and is characteristic of the orientation (different regions of each hypercolumn have different orientation specificity). In *D* the stimulus is composed of three parallel stripes. The central one passes between two rows of hypercolumn centres and therefore elicits a continuous response in all the hypercolumns it touches. The two flanking stripes fall on rows of inhibitory regions. This arrangement is possible when the orientation of the stimulus is parallel to one of the axes of the array of hypercolumns. Neurons which respond to such stimulus configurations are called "simple cells" in the Hubel and Wiesel terminology. In our model they should have predetermined orientation in each part of the visual field. Other neurons responding to elongated stimuli with orientations such as in *B* and *C* would be "complex cells"

of the direction of orientation change from clockwise to counterclockwise, and the occasional abrupt change of orientation (Braitenberg 1985).

The model of Figs. 3 and 4 is simplified in many ways but correct in principle. One simplification regards the geometrical pattern of the blobs, which is not so regular in reality. Also, the model fails to distinguish between two kinds of input fibres, "on"-centre and "off"-centre, each already with its structured receptive field, one the negative of the other, one activated by light in the centre and depressed in the periphery, the other one vice versa. In spite of this and other shortcomings, the drawings make the main point, namely that the anisotropy determined by the hypercolumn centres, if they are the site of special neurons, is sufficient to explain the known effects without having to resort to a great deal of highly specified wiring. In fact we did not assume anything but circularly symmetric, perhaps largely random dendritic and axonal distributions of the inhibitory neurons.

We have not yet mentioned the wiring of the other cells, which we assume to be pyramidal cells. They are strongly connected to each other by excitatory connections subject to "plastic" changes in the way of associative learning. Clearly, neurons of the same or of neighbouring hypercolumns which are tuned

to the same orientation will often be activated by the same stimuli in the visual field either at the same time or in close temporal succession. Such neurons, following the laws of associative learning, will strengthen their reciprocal synapses and will form what was called a "cell-assembly" by Hebb. I assume that a receptive field as described by Hubel and Wiesel and their followers is in reality the compound field of many neurons tied together into a cell assembly.

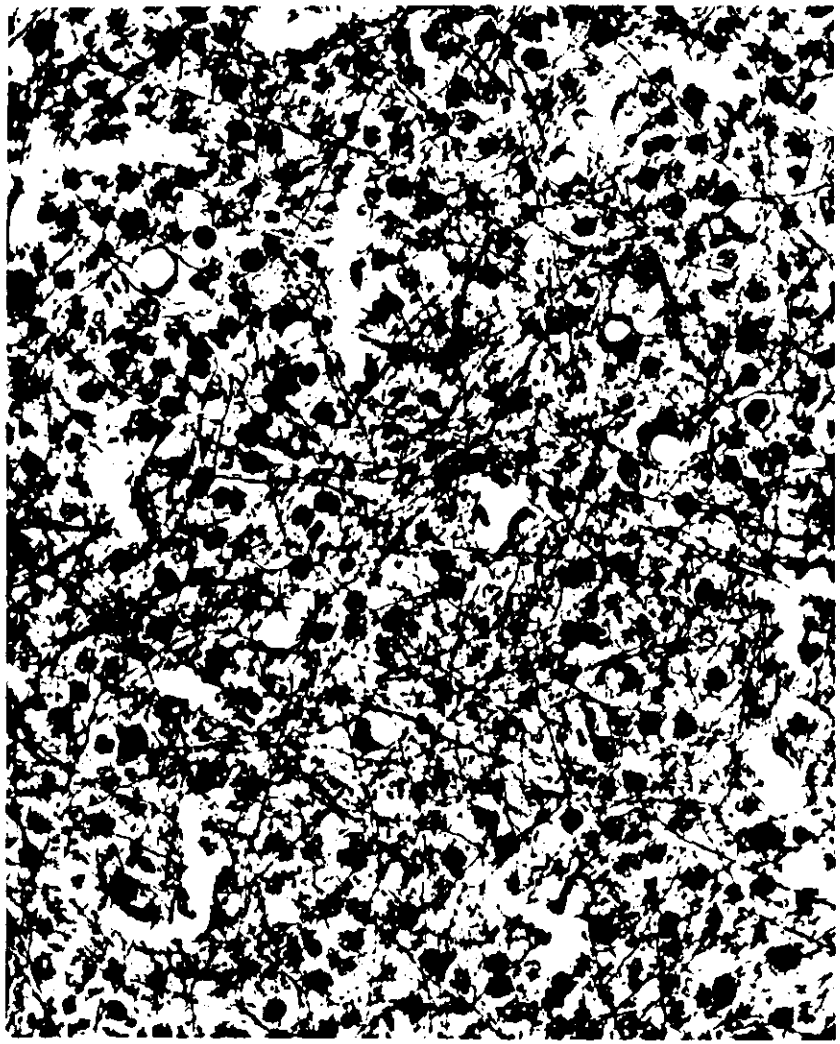

Fig. 5. Horisontal section through layer IVb of Area 17 of the monkey. The orientation of fibres in the anatomical picture appears random, contrary to naive expectation

This is a necessary assumption in our model, which would assign to individual neurons only small fields no larger than a hypercolumn (translating the cortical coordinates into those of the visual field). In reality, the typical field is two or three times hypercolumn size.

The model makes a strong prediction. In Fig. 4 it is obvious that what is called a simple cell in Hubel and Wiesel terminology, namely one with definite parallel excitatory and inhibitory subfields should be oriented along one of the axes of the array of hypercolumns. Cells with receptive fields not so oriented would be "complex". If in a small area of cortex simple and complex cells are sampled, the orientation of the respective receptive fields should be complementary.

Again, the wiring of the pyramidal cells subserving the associative learning and hence the formation of the receptive fields in this model of monkey area 17 is no different from what we had derived from our statistical analysis of the neuropil in the mouse cortex. Thus I have fulfilled my promise of tying together two descriptions of the cortex that initially seemed almost incompatible. A tangential section through layer IVb of the monkey striate cortex (Fig. 5) showing fibres running in all directions is apt to underscore this point.

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