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ANTONIO BORSELLINO COLLEGE ON NEUROPHYSICS

(15 May - 9 June 1995)

"Emergence of Radial and Modular Units in Neocortex"

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These are preliminary lecture notes, intended only for distribution to participants.

EMERGENCE OF RADIAL AND MODULAR UNITS IN NEOCORTEX

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INTRODUCTION

Our strategy here is to compare the cortical organization of phylogenetically distant species. We can view the shared features as themes conserved during the course of evolution and the features of cortical organization that differ among species as variations on a common theme. We will compare the most primitive dorsal cortex found among living vertebrates, the visual cortex of turtles, with the somatic sensory field of mammalian neocortex. The comparison is based on classical cell morphology combined with modern intracellular and extracellular electrophysiology, tract tracing, and receptive field mapping.

The most fundamental difference between the reptilian and mammalian cortex is the organization of thalamocortical projections. In the turtle, individual thalamic fibers form synapses across the entire horizontal extent of the dorsal cortex. In contrast, thalamocortical axons in mammals originate in distinct cell clusters and terminate within strips of discrete columnar modules. Each cortical module, roughly one half millimeter in diameter, is in turn assembled from a set of narrow radial units. Receptive field studies of the somatic sensory cortex of the cat provide insights into the functional significance of radial and modular units.

The evolution of the cluster-to-module projection is accompanied by a new cell type in mammalian neocortex. Description of the cellular morphology of reptilian and mammalian cortex has a distinguished history; our approach here is to forgo traditional classifications in favor of a scheme consisting of three broad classes of neuron. Turtle dorsal cortex is made up of just two of these classes, the excitatory output cell and the inhibitory local cell. Mammalian neocortex includes both of the above and a third class as well, the excitatory local cell. The excitatory local cell of neocortex replaces the tangential thalamic fibers of turtle dorsal cortex as the chief substrate for the horizontal propagation of activity; while this cell is specialized for spreading activity vertically among the cells in the various layers of a radial unit, its unique integrative function is to interconnect cells located in separate radial units and modules.

We suggest that mammalian somatic sensory cortex is a mosaic of modular and radial units, both types of unit demonstrable by anatomical and receptive field methods. When viewed in this way, the rodent cortical whisker representation — rather than a unique pattern of organization — is best considered a modest specialization of the general mammalian plan of neocortex.

CELL TYPES COMMON TO PRIMITIVE CORTEX AND NEOCORTEX

Excitatory output cell

Turtle dorsal cortex is a three-layered cortex; a single layer of tightly packed cell bodies with a dendritic zone above and below (Johnston, 1915). The vast majority of the cells in the main cell layer are *excitatory output cells*: pyramidal cells whose axons enter the white matter and form asymmetric synapses with distant (more than a millimeter away) targets. The apical den-

The Neocortex, Edited by B. L. Finlay *et al.*
Plenum Press, New York, 1990

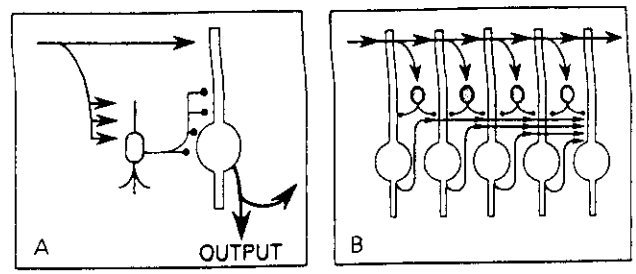

Figure 1. Synaptic and topographic organization of turtle dorsal cortex. (A) Thalamic afferents (originating in top left corner of frame) terminate densely upon the inhibitory local cell (shaded) and less densly upon the apical dendrite of the excitatory output cell. The inhibitory cell forms synapses on the dendrites and soma of the output cell. (B) Each thalamic afferent courses through the molecular layer in the anterolateral to posteromedial direction and forms synaptic contacts across a wide extent of dorsal cortex. The excitatory output cells give rise to intracortical collaterals.

drites of the excitatory output cells form a molecular layer as they extend toward the pial surface, and their basal dendrites form a subcellular neuropil between the lamina of cell bodies and the ependymal cells lining the ventricle.

The dominant input to the excitatory output cells is the thalamic projection. Thalamic fibers enter the molecular layer just beneath the pial surface in the anterolateral region of cortex and form synaptic contacts on successively more posterior and medial apical dendrites as they travel tangentially (Figure 1). Thus, one key function of the thalamocortical projection in turtles is the *horizontal* dissemination of sensory information; circumscribed clusters of cortical cells never constitute the target of lateral geniculate nucleus fibers in the turtle.

The output cell axons course in the medial direction, giving rise to collateral branches to other cortical excitatory output cells. The axons depart the cortex through the subcellular zone. They descend from cortex through the medial wall cortex, and course through the hypothalamus as far posteriorly as the midbrain tegmentum (Hall et al., 1977).

In mammals, as in turtles, there exists a cell with at least part of its axon projecting through the white matter, and whose axon terminals contain clear round vesicles and form asymmetrical (presumably excitatory) synaptic contacts (Winfield et al., 1981). This *excitatory output cell* is well suited to transfer information to distant sites; that is, to cortical targets more than a millimeter away or to subcortical structures. Previous studies using a variety of techniques have consistently shown that an excitatory output cell is nearly always a pyramidal neuron. Pyramidal cells are the most numerous elements in mammalian cortex (Winfield et al., 1980) and are found in all cellular layers.

Before the excitatory output cell axon reaches the white matter it gives rise to numerous collateral branches that distribute within the grey matter. The extent of spread varies widely from neuron to neuron (Gilbert and Wiesel, 1981; Lorente de No, 1949). After the axon enters the white matter it projects to an ipsilateral cortical, a contralateral cortical, or a subcortical target.

Inhibitory local cell

Scattered throughout the three layers of turtle cortex is a population of aspiny stellate cells which contains glutamic acid decarboxylase (GAD; the synthetic enzyme for GABA) and forms symmetrical (presumably inhibitory) synaptic contacts (unpublished observations). These neurons receive a high density of thalamic fiber terminals and, in turn, project to nearby cells in the cortex. The GABAergic neurons in turtle cortex are *inhibitory local cells* in as much as their axons have never been found to project out of cortex.

The neocortex of mammals also contains a population of GAD-positive cells which forms symmetric synapses and whose axons do not travel in the white matter (Ribak, 1978). The *inhibitory local cells* make up about 20-25% of all neurons in neocortex (Hendry et al., 1987) and exist as several subclasses, each with a distinct morphology. For the present purpose it suffices to say that most inhibitory local cells have the morphology of a nonpyramidal neuron with aspiny or sparsely spiny dendrites (Somogyi et al., 1981).

SYNAPTIC ORGANIZATION OF THALAMIC INPUTS

Certain fundamental features of the connectivity between thalamic inputs and cortical excitatory and inhibitory neurons have been faithfully conserved during the evolution of neocortex. In both turtle dorsal cortex (Ebner and Colonnier, 1978) and mammalian neocortex (Colonnier, 1968) thalamic fibers terminate as round vesicle containing profiles that form asymmetrical contacts and are presumed excitatory synapses. In the turtle, thalamic fibers synapse upon both inhibitory and excitatory neurons; terminations are particularly dense upon the dendrites of aspiny stellate cells (Figure 1A). The total number of thalamic synapses upon excitatory output cells is six times the number of thalamic synapses upon inhibitory local cells. However, because excitatory output cells greatly outnumber inhibitory local cells, there is, on average, a six fold greater number of thalamic synapses per inhibitory local cell (Smith et al., 1980). Inhibitory local cells in turn synapse densely upon nearby excitatory output cells.

In neocortex, as in turtle dorsal cortex, fibers from thalamic primary sensory relay nuclei terminate densely upon inhibitory local cells (White, 1979). For example, following destruction of the ventrobasal (VB) thalamic nucleus in mouse, degenerating thalamic axon terminals made the most synapses per unit length of dendrite with aspiny stellate cells, followed in decreasing order by layer IV spiny stellate cells, layer III pyramidal cells, and layer V pyramidal cells (White, 1978). On the soma of one aspiny bipolar cell, 67% of the synapses were made with thalamic fibers (Keller and White, 1987). Inhibitory local cells synapse upon excitatory output neurons, and typically the position of these synapses (e.g., the axon hillock or the initial segment) allows the inhibitory cell to exert a particularly strong influence on the excitatory output cell (Jones and Powell, 1969).

EXCITATORY LOCAL CELLS OF NEOCORTEX

Our argument began with the principle that in turtle cortex all excitatory cells are output neurons (the only local cells in turtle cortex are inhibitory) while in mammalian cortex an additional excitatory cell type is present whose axon remains within the grey matter. The axon of the *excitatory local cell* terminates in its entirety within a few hundred μm (horizontally and vertically) of the cell body. Nearly every excitatory local cell is a spiny stellate cell (Lund, 1984). Typically, the axon descends toward the white matter for a short distance before turning upward and arborizing. The functional significance of a cell type specialized for excitatory communication with nearby neurons will become evident as we discuss the modular and radial units of neocortex.

MODULAR UNITS OF NEOCORTEX

Thalamocortical projection as the anatomical basis of the modular unit

It is worth reiterating the contrast between the topographic organization of the mammalian thalamocortical projections and that of the turtle. In the turtle, fibers from the lateral geniculate nucleus course horizontally across several millimeters of cortex. Individual axons from the geniculate contact the dendrites of a series of cortical neurons, each axon influencing a wide domain of cortex (Figure 1B). As a consequence, receptive fields of turtle dorsal cortex neurons typically include nearly the entire representation of the retina (Mazurskaya, 1972; Orrego and Lisenby, 1962). A thalamocortical axon which terminates in the molecular layer is conserved in mammalian neocortex; it arises mainly in "nonprimary" thalamic relay nuclei, such as the posterior nucleus or the pulvinar. However, the projection from primary thalamic relay nuclei takes a form not found in reptiles. A case in point is the somatic sensory system. Individual fibers from VB of cat (Landry and Deschenes, 1981) and monkey (Garraghty et al., 1989) ascend orthogonal to the cortical surface and terminate mainly in layers IIIB and IV, often with collateral branches to other layers. In the horizontal dimension, *the terminal field of each fiber is restricted to one or a few circumscribed terminal arbors* ranging from 200 to 800 μm in diameter (Figure 2A, B).

What is the relationship between the terminal fields of neighboring thalamic cells? Is there evidence that multiple thalamocortical arbors are grouped together into a larger unit? The findings of Jones and colleagues (Friedman and Jones, 1980; Jones et al., 1982) in monkeys, based on anterograde and retrograde transport methods, do indeed provide support for an organizing principle larger than the single thalamocortical cell. Narrow cortical domains, or *modules*, are the the targets of rodlike clusters of thalamic cells. The same conclusion was reached based

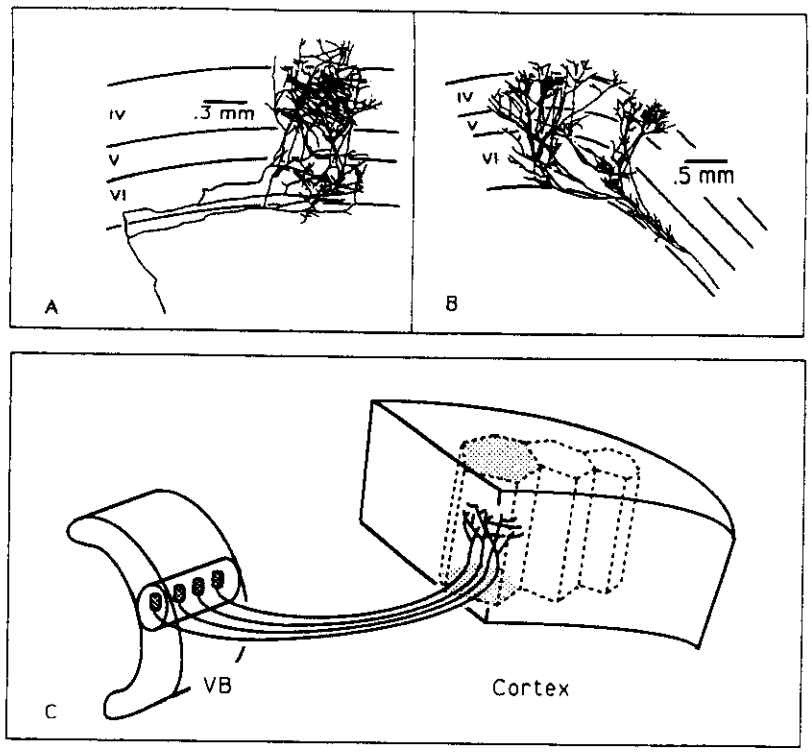

Figure 2. Mammalian plan of the projection from VB thalamus to somatic sensory cortex. In (A) the fiber arborizes in a single discrete module. In (B) the fiber arborizes in two separate modules. The thalamocortical topography is illustrated in (C). A rodlike cluster of cells in VB projects to a cortical module (collaterals to other modules not illustrated). The cell cluster in VB is one of several which form a lamellae and project, as a group, to a strip of modules. Parts (A) and (B) adapted from Figures 5 and 7 of Landry and Deschenes (1981).

on cortical projections from cat VB (see Figure 1 of Kosar and Hand, 1981). This is not to say that the projection of each cell cluster in the thalamus is restricted to a single cortical module; rather, the set of clusters contained within a lamella of VB projects to a strip of modules, each cluster projecting most densely to one module in particular (Figure 2C). The diameter of a module, as defined by bulk labeling of thalamic fibers, is between 200 and 800 μm — the same size range as the individual VB terminal arbors. It should be emphasized that the patterns of retrograde thalamic label and anterograde cortical label do not support the idea that the cortical terminal fields of neighboring thalamic cells are partially shifted and overlapping relative to one another. If that were the case, as the size of the cortical horseradish peroxidase (HRP) injection increased, the label would be transported to an enlarged but continuous thalamic region. Instead, multiple separate, distinct thalamic cell clusters are labeled. Similarly, as the size of the thalamic injection is increased, the resulting transport to cortex labels multiple separate patches (modules) rather than a single field of ever larger diameter.

Physiological detection of the modular unit

The question we take up here is whether the module identified by anatomical methods also can be defined by physiological methods. We continue to concentrate on the somatic sensory field of neocortex, and we review in some depth recent results from studies on the topography of the cortical body representation (Diamond, 1989; Favorov and Diamond, 1990; Favorov et al., 1987). The starting point in our search for a module is the assumption that neurons located within the same module will have relatively similar receptive fields, and neurons located on opposite sides of a module boundary will have less similar receptive fields. Using two different receptive field methods we demonstrate that the above assumption is valid, and that the module is therefore a physiological as well as an anatomical unit.

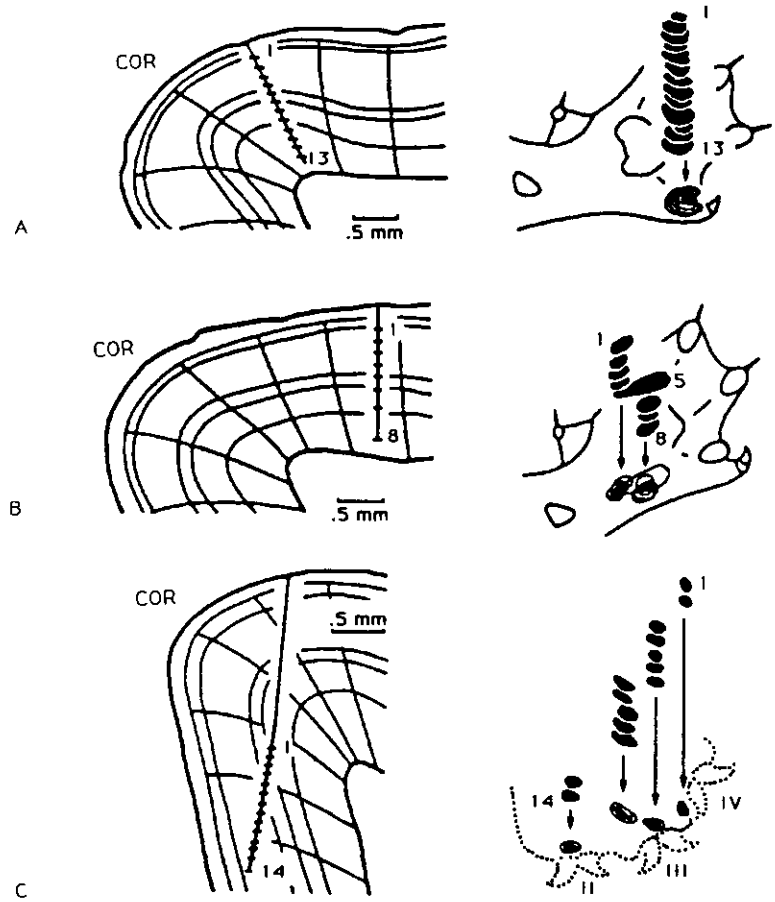

Figure 3. Sequences of minRFs reveal boundaries of modular units. MinRFs were mapped every 100-200 μm along the microelectrode track. Left column: drawing of cortical sections at low magnification to show the location of recording sites along each penetration (dashed lines). Thin lines parallel to the cortical surface indicate cortical layers and lines orthogonal to the surface indicate orientation of vertical cell cords. Right column: minRF sequences; the numbers from top to bottom identify the location of the recording site in cortex. The minRFs are also shown projected onto the skin of the distal forelimb. (A) Penetration remains within a single module. (B) Penetration crosses a modular boundary. At the depth of the fifth recording site, the electrode tip lies on the boundary between two modules. (C) A nearly tangential penetration crosses three boundaries. The minRFs shift from digit IV to III to II. COR- coronal sulcus. Adapted from Favorov and Diamond (1990).

The first method, the minimal receptive field (*minRF*) method, uses ketamine general anesthesia coupled with gentle (barely suprathreshold) tactile stimulation to render the receptive field of cortical cells as small as possible. The method is designed to identify the main input to the small cluster of cortical neurons within roughly 50 μm of the recording site. In penetrations of the primary somatic sensory cortical field (cytoarchitectonic areas 3b and 1) minRFs were mapped at intervals of about 150 μm along the electrode track. When the penetrations were very close to radial, all minRFs occupied nearly the same position on the skin (Figure 3A). In penetrations with an oblique trajectory, successive minRFs fell into groups that resemble separate stacks of pancakes: within a stack minRFs are nearly completely overlapping while adjacent stacks are separated by an abrupt change in the location of the minRF to a different skin site (Figure 3B). Penetrations tangential to the cortical surface resulted in multiple distinct stacks of minRFs (Figure 3C).

In no penetration (out of 21), either radial off-radial or tangential, were minRFs distributed across the skin in a continuous, gradually shifting manner. Instead, each time a shift of the minRF occurred— from one stack of pancakes to the next — the move happened abruptly, as the electrode tip travelled only about 40-50 μm in the plane of the cortical surface. Our interpreta-

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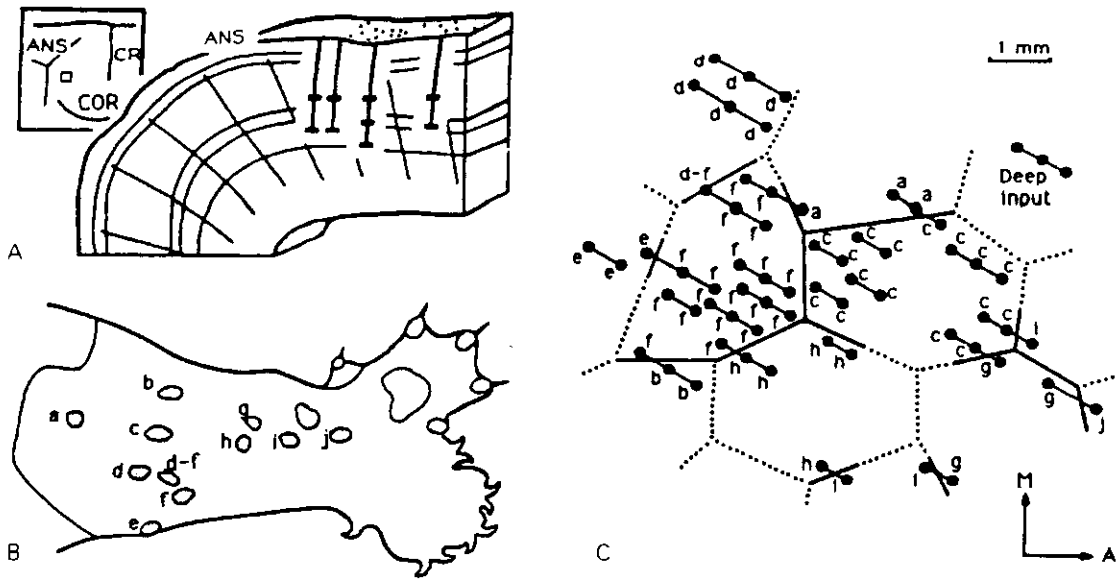

Figure 4. Closely spaced grid of penetrations reveals the size and shape of modules. (A) Diagram to show the location of penetrations between the ansate (ANS), cruciate (CR) and coronal (COR) sulci (small square in inset). (B) Each of 61 minRFs was located within one of 10 discrete spots, labeled a-j (one minRF was located midway between d and f). (C) Surface view of cortex to show recording sites (filled circles). Connected recordings sites are from the same penetration. Each recording site is labeled according to the location of its minRF, a-j. Boundaries crossed by a penetration are shown as solid lines and estimated boundaries are shown as dotted lines. Adapted from Favorov and Diamond (1990).

tion is that the point in cortex where the minRF shifts from one location to another marks a topographic boundary — presumably the edge of a modular unit. When the electrode tip lies exactly on the boundary between two modules (as in the fifth recording site of Figure 3B) neural activity originating in both modules is detected by the recording electrode. This results in a "transitional" minRF encompassing the minRFs of two modules.

Size and shape of the module

To determine the geometry of the modular unit in cat somatic sensory cortex, minRFs were mapped in a grid of closely spaced penetrations. The main result is that all the minRFs were grouped within 10 discrete spots on the skin, labeled **a-j** (Figure 4B). When each cortical recording site is labeled according to its minRF, it becomes clear that the recording sites yielding the same minRF are grouped near one another. Based on those penetrations which crossed topographic boundaries, it is possible to draw the outlines around two distinct cortical regions, labelled **c** and **f**. The geometry of regions **c** and **f** gives us the size and shape of the module: a discrete column with a roughly hexagonal outline. Within a single module, the minRF is the same throughout — this shared minRF is the *receptive field center* of the module. Shifts in the minRF occur only at the borders of a module. Additional experiments indicated that the size of a module depends on the location of its receptive field center: when the receptive field center is on the distal forelimb the module's diameter is about 450 μm, and when the receptive field center is on the forearm (e.g. near the elbow) the module's diameter is about 250 μm.

To this point we have reviewed both anatomical and physiological evidence for modular units in somatic sensory cortex. The units are similar in size whether defined by i) the topography of the skin representation (Diamond et al., 1987; Favorov and Diamond, 1990; Favorov et al., 1987; Favorov and Whitsel, 1988), ii) the projection of clusters of VB cells (Friedman and Jones, 1980; Jones et al., 1982; Kosar and Hand, 1981), or iii) the terminal fields of individual VB fibers (Landry and Deschenes, 1981; Garraghty et al., 1989).

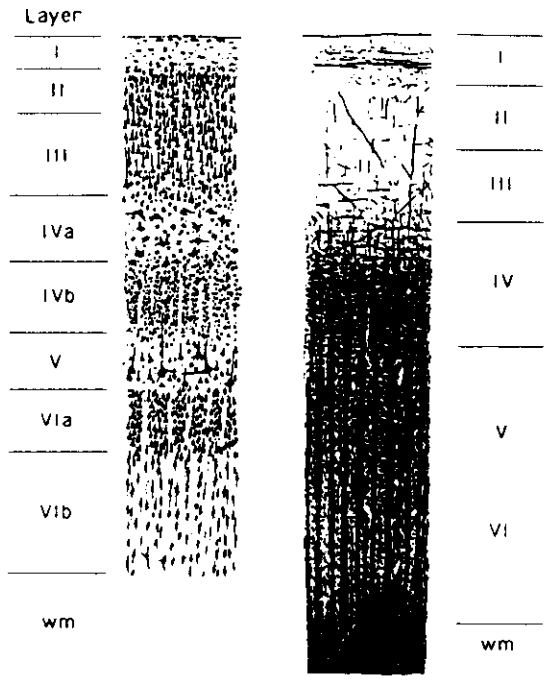

Figure 5. Anatomical correlates of the radial unit. Left: Cell bodies aligned in radial units in the visual cortex of man. Nissl stain. Adapted from Figure 1 of Cajal (1899). Right: Myelinated fibers aligned in vertical arrays in the sphenoidal gyrus of man showing the same radial orientation. Weigert-Pal method. Adapted from Figure 2 of Cajal (1900).

RADIAL UNITS OF NEOCORTEX

Anatomical basis of the radial unit

Apart from three obvious horizontal layers, the distribution of neurons in turtle dorsal cortex seems unpatterned; there is no reason to suspect any grouping of cells into multicellular units smaller than a cortical field or subdivision. In the mammalian neocortex, the opposite is true. An unmistakable grouping of cell bodies into vertical cords one to four cells wide, extending from layer II to VI, is frequently evident, as illustrated in the drawings of the human cerebral cortex by Cajal (Figure 5, Left). It was also apparent to Cajal that axons and dendrites in cortex are grouped into distinct vertical cords (Figure 5, Right). Typically, the centers of adjacent cellular cords are separated by about 30-50 μm. Bundles of apical dendrites of pyramidal cells are one component of the vertical arrays in cortex (Peters and Walsh, 1972). The apical dendrites of layer V cells form the core, and as they ascend toward the cortical surface they are joined by the apical dendrites of more superficial cells. Other nonpyramidal cell types, for example double bouquet or bipolar cells, also have narrow dendritic trees oriented toward the cortical surface and probably contribute to the organization of such vertical cords (Jones, 1975).

Functional correlate of the radial unit

It is reasonable to anticipate that the anatomically defined narrow vertical cord of cell bodies and processes — *the radial unit* — has a physiological counterpart. In this section we raise the question, How is the radial unit manifest in neuronal response properties? We will provide evidence that the neurons within a radial unit in somatic sensory cortex discharge in a cooperative manner during tactile stimulation.

Because the minRF is based on the responses of a cluster of neurons located within an approximately 50 μm diameter of the electrode tip (Favorov and Diamond, 1990), the method does not have adequate spatial resolution to identify an entity as narrow as the radial unit. Detecting a

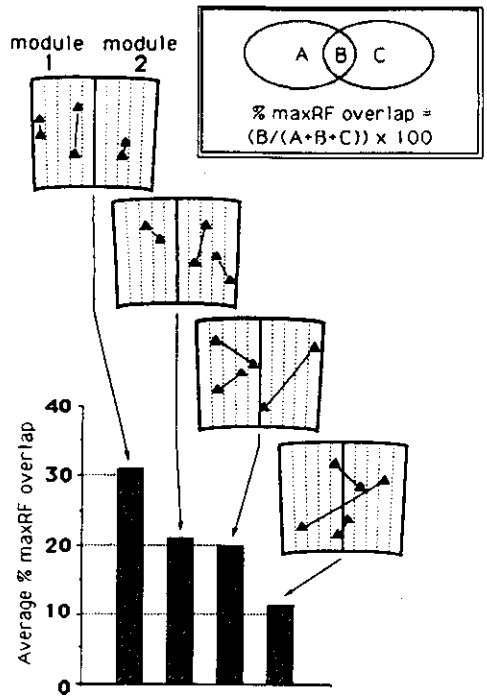

Figure 6. Radial and modular units are reflected in receptive field measurements. The inset in the upper right gives the formula for computing precent maxRF overlap. The columns represent two separate cortical modules, labeled module 1 and module 2; dashed lines delineate radial units. Four possible relative locations of pairs of neurons are illustrated from top left to bottom right: two cells in the same module and same radial unit; two cells in the same module and adjacent radial units; two cells in the same module and nonadjacent radial units; two cells in different modules (the two radial units may be adjacent or remote).

The histogram shows the average maxRF overlap for pairs of neurons with the indicated relative locations. Note that neuron pairs from the same radial unit have a realtively high degree to maxRF similarity (31% overlap). Also note that for neuron pairs from the same module but different radial units, the degree of maxRF similarity is independent of the distance between the two neurons.

functional correlate of the radial unit requires a receptive field method that selects and analyzes neural activity with higher precision. The maximal receptive field method (*maxRF*) is one such technique: unlike the minRF method, the maxRF method maps the entire skin field projecting, even if weakly, to a single cortical neuron; in practice it is necessary to record single cell responses in the absence of anesthesia to reveal the weak inputs. If the set of neurons making up a radial unit constitutes a functional entity — such that they tend to fire synchronously during tactile experience — then their coactivity will be reflected by a large shared area of peripheral receptor input. We can predict therefore that, on average, two neurons located in the same radial unit will have more similar maxRFs than two neurons located in different radial units. MaxRFs are usually much larger and more variable than minRFs (Favorov and Diamond, 1990). The amount of input common to pairs of neurons is measured here by the *percent of maxRF overlap*, as illustrated in Figure 6, inset.

Analysis of the maxRFs of 1111 pairs of neurons (where both members of the pair were located within the same module) indeed identifies a functional correlate of the radial unit. Pairs of neurons separated by less than about 10 μm in the horizontal dimension exhibit an average of 31% maxRF overlap, whereas pairs of neurons separated by 40-100 μm in the horizontal dimension exhibit an average of only about 21% maxRF overlap. Our interpretation is shown in Figure 6: two neurons located in the same radial unit share, on average, a greater area of maxRF overlap than two neurons located in separate radial units, *even when the two radial units are contiguous.* This finding implies that neurons located in the sameradial unit are more likely to be coactive

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during tactile experience than neurons in different radial units. The estimate of maxRF overlap for members of the same radial unit is likely an underestimate, since some pairs separate by just 10 μm may reside in separate radial units.

Based on Figures 3 and 4 (which showed that the same minRF is mapped throughout a module) we should anticipate some kinship between the maxRFs of two neurons located within the same module, even if the two neurons are located on opposite sides of the module. The specific question is, What is the nature of the movement across the skin of successive maxRFs as the recording electrode advances at an oblique angle across a modular unit? The answer is that, for any two neurons located within the same module, the average maxRF overlap is about 20%, *independent of the horizontal distance separating the two neurons*: the pair of neurons may be located in two neighboring radial units (i.e., separated by just 40-100 μm in the plane of the cortical surface), or in two radial units at opposite edges of the module (i.e., separated by any distance between 100 and 500 μm). This relationship among the radial units of a module means that a recording microelectrode traveling horizontally across a sampling single neurons from successive radial units, will fail to detect any systematic and continuous shift in maxRF position. The jitter in maxRF position can be pictured as a "random walk".

At the boundary of the module the electrode tip passes from a radial unit belonging to one module to a radial unit belonging to a second module. With this last, seemingly equivalent, advance of the electrode the maxRF position shifts markedly: pairs of neurons located on opposite sides of a module boundary exhibit an average of only 12% maxRF overlap, even if the two neurons are located in adjacent radial units (Figure 6). Comparable results have been obtained in the somatic sensory cortex of monkeys (Favorov and Whitsel, 1988).

DISTRIBUTION OF ACTIVITY WITHIN AND AMONG RADIAL UNITS: THE EXCITATORY LOCAL CELL REVISITED

What is the role of the excitatory local cell, the cell type posited as novel to mammalian neocortex? On the basis of their morphology and connections, it is reasonable to suspect that many types of excitatory local cells are specialized for the vertical distribution of information within a radial unit. For example, spiny stellate cells in layer IV receive a dense thalamic input and some of these cells possess narrow cartridge-like axonal arbors which terminate in asymmetric synapses on the dendritic spines of pyramidal and perhaps stellate neurons above and below layer IV (Jones, 1975). Thus, it is easy to imagine that a thalamic volley arriving in layer IV of a radial unit would rapidly and powerfully influence the neurons located above and below layer IV. This idea is supported by comparing in reptiles (Kriegstein and Connors, 1986) and mammals (Connors et al., 1982) the sequence of membrane potentials recorded from cortical neurons after stimulation of thalamic afferents. Output cells in an in vitro slice of turtle cortex respond to low intensity orthodromic stimulation with a pure inhibitory postsynaptic potential (IPSP). As the intensity of the stimulus is increased toward threshold, an excitatory postsynaptic potential (EPSP) is evoked, but it is still preceded by an IPSP (Figure 7A). In an *in vitro* slice of mammalian neocortex *the earliest response to a weak afferent volley is an EPSP rather than an IPSP* (Figure 7B). Since the amplitude of the EPSP is increased in the presence of bicuculline (Chagnac-Amitai and Connors, 1989), our interpretation is that in neocortex the same short latency inhibitory influences seen in turtle cortex are at work, but they are overridden by a concomitant burst of excitatory input, arising in part from the excitatory local cells. The role of the excitatory local cell in the vertical propagation of activity can also be seen in the analysis of maxRF overlap; recall the comparatively high measure of maxRF overlap (31%) observed within a narrow radial unit (Figure 6).

The morphology of the excitatory local cell also is appropriate for spreading activity across horizontal distances of roughly less than a millimeter. Strong interconnection of the excitatory local cells residing within the same module could be a contributing factor in the receptive field similarity observed within a module (20% average maxRF overlap). In other words, one function of excitatory local cells could be to link the cells within a module so that they become activated by the same tactile event. On the other hand, sets of neurons located on opposite sides of a module border (12% average maxRF overlap) would be less likely to be activated by the same stimulus: these neurons receive significantly different thalamic inputs and their excitatory local cells may be weakly interconnected. The effectiveness of the synapses between neurons of the same or different modules may be regulated through postulated rules of synaptic modification (Bear et al., 1987).

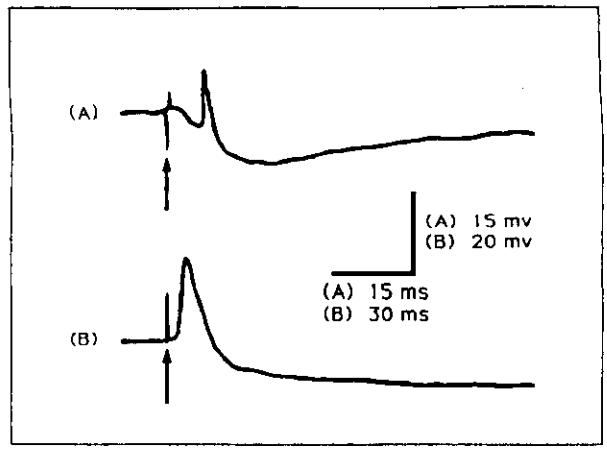

Figure 7. Influence of the excitatory local cell on excitatory output cell responses is seen in the PSP sequence evoked by an afferent volley. Intracellular recordings of the membrane potential of excitatory output cells in response to electrical stimulation of input fibers in vitro. Arrows indicate stimulus artifact. (A) In the turtle, even near the spike threshold, the initial response is an IPSP, which is followed by an EPSP. Adapted from Figure 2 of Kriegstein and Connors (1986). (B) In guinea pig, the initial event is an EPSP generated, we would argue, by the influence of excitatory local cells. Adapted from Figure 12 of Connors et al. (1982).

SPECIALIZATION OF THE MAMMALIAN PLAN OF CORTEX

The modular and radial organization of cat somatic sensory cortex is the general mammalian plan which allows us to look for variations on the theme. In some rodents the extraction of information from the environment is dominated by the whisker sensory system (Vincent, 1912). The somatic cortical field of many rodent species exhibits anatomical and physiological specializations which provide marvelous examples of the adaptation of the nervous system to their environmental niche. While these specializations are commonly viewed as setting the somatic cortex of rodents apart from that of other mammals, we interpret them as modifications of the same plan of organization that characterizes the cortical body representation in other mammals, such as cat and monkey.

The mystacial vibrissae of mice and rats are distributed across five rows on the muzzle, designated row A to row E. Each densely innervated whisker follicle — e.g. C2 — is associated with a corresponding cluster of neurons along the central somatosensory pathway. For example, in the C2 cluster of the principal trigeminal nucleus all neurons are best activated by movement of whisker C2. In turn, each cell cluster of the principal trigeminal nucleus projects to a distinct cluster of cells (called a "barreloid") in VB. A discrete bundle of fibers arises from each barreloid and arborizes within a circumscribed cortical locus of about 300-400 μm diameter (Jensen and Killackey, 1987; Killackey, 1973). The terminal field of barreloid cells is correlated with dense clusters of stellate cells in layer IV; the "barrels" of barrel field cortex (Woolsey and Van der Loos, 1970).

From this outline, the barrel, together with the column of cells above and below it, can be seen as analagous to the modular unit of the cat. As in the cat, the modular unit of rodent cortex has been identified by two receptive field methods — the minRF method (Welker, 1971) and the maxRF method (Simons, 1978). The receptive field center of a modular unit in rodent barrel field cortex is a single whisker, the "principal" whisker. The major difference between the cat and the rodent, according to our interpretation, is that in the rodent fiber bundles from VB are strictly segregated one from another. Indeed, the segregation is so absolute that the axon terminals from the medial division of the posterior nucleus (PO), a second thalamic nucleus carrying information from whiskers to cortex, are specifically excluded from the VB termination zone; instead, PO fibers project to the "septa" surrounding each barrel (Lin et al., 1987). Van der Loos has suggested that in the embryo the density of sensory receptors in the developing whisker follicle induces these discrete, segregated cellular groupings at subsequent stations along the sensory pathway (see Van der Loos in this volume).

Armstrong-James and colleagues (Armstrong-James and Callahan, 1990; Armstrong-James et al., 1990a; Armstrong-James et al., 1990b; Armstrong-James and Fox, 1987) have formulated a model of the vertical and horizontal integrative function of the modules in rodent cortex. Their conclusion is that input from the receptive field center - the principal whisker - arrives in a module as a direct thalamic volley. Input from the surrounding receptive field - the non-principal whiskers - arrives in a cortical module only at longer latencies after relays in surrounding modules. While this scheme is fundamentally the same as that proposed for cat and monkey cortex (Diamond, 1989), it stands in sharp contrast to the scheme of integrative function of turtle dorsal cortex shown in Figure 1.

Figure 1 returns us full circle to the purpose of this chapter, the comparison of neocortex with primitive cortex. In mammals the type of afferent pathway found in turtles — a superficial trajectory coursing parallel to the cortical surface — remains only in the olfactory and hippocampal regions. In neocortex the multiple waves of cell migration lead to a vastly increased number of cells in comparison to turtles. Yet these additional cells are not merely a multiplication of the same cell types found in reptiles. Rather, an entirely new cell type, a short axon cell with excitatory local connections, emerges. We have argued here that the function of the excitatory local cell is intricately related with the cluster-to-module thalamocortical projection. Thus, the main idea of this chapter is that a novel type of thalamocortical projection has evolved hand in hand with a novel type of intrinsic cortical organization. One implication of this idea is that the evolution of a specialized form of thalamic projection (one related to a species' unique behavior) can stimulate the evolution of a new cortical area. Examples of specialized forms of thalamocortical projection include those pathways segregated by function (e.g. the X, Y, and W pathways through the cat lateral geniculate nucleus and the tone-specific pathways through the bat medial geniculate nucleus) or topography (e.g. the barreloids-to-barrels pathways of rodent). The specialized thalamic projection induces a new cortical area: new modules with specialized form and function.

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