Microcircuits in visual cortex

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The microcircuity of the neocortex is bewildering in its anatomical detail, but seen through the filters of physiology, some simple circuits have been suggested. Intensive investigations of the cortical representation of orientation, however, show how difficult it is to achieve any consensus on what the circuits are, how they develop, and how they work. New developments in modeling allied with powerful experimental tools are changing this. Experimental work combining optical imaging with anatomy and physiology has revealed a rich local cortical circuitry. Whereas older models of cortical circuits have concentrated on simple 'feedforward' circuits, newer theoretical work has explored more the role of the recurrent cortical circuits, which are more realistic representations of the actual circuits and are computationally richer.

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Current Opinion in Neurobiology 2002, 12:418–425

0959-4388/02/$ – see front matter

Abbreviations

2D	two-dimensional
3D	three-dimensional
LGN	lateral geniculate nucleus

Introduction

Francis Crick once advised: 'if you do not make headway studying a complex system, study its structure and knowledge of its function will follow automatically' (cited in [1]). Explorers of neocortical microcircuits have traditionally chosen the reverse strategy: they study function and use it to infer structure. How successful have they been? Very — if textbooks and computational models of cortical microcircuits are any indication. Despite the recent flowering of anatomical studies associated with physiological recordings in slices of cortex maintained *in vitro*, these new studies have had remarkably little influence on modern ideas of microcircuits in visual cortex. This is quite unlike the central significance that anatomy has had for concepts of hierarchical processing and for notions of feedforward and feedback processing between cortical areas.

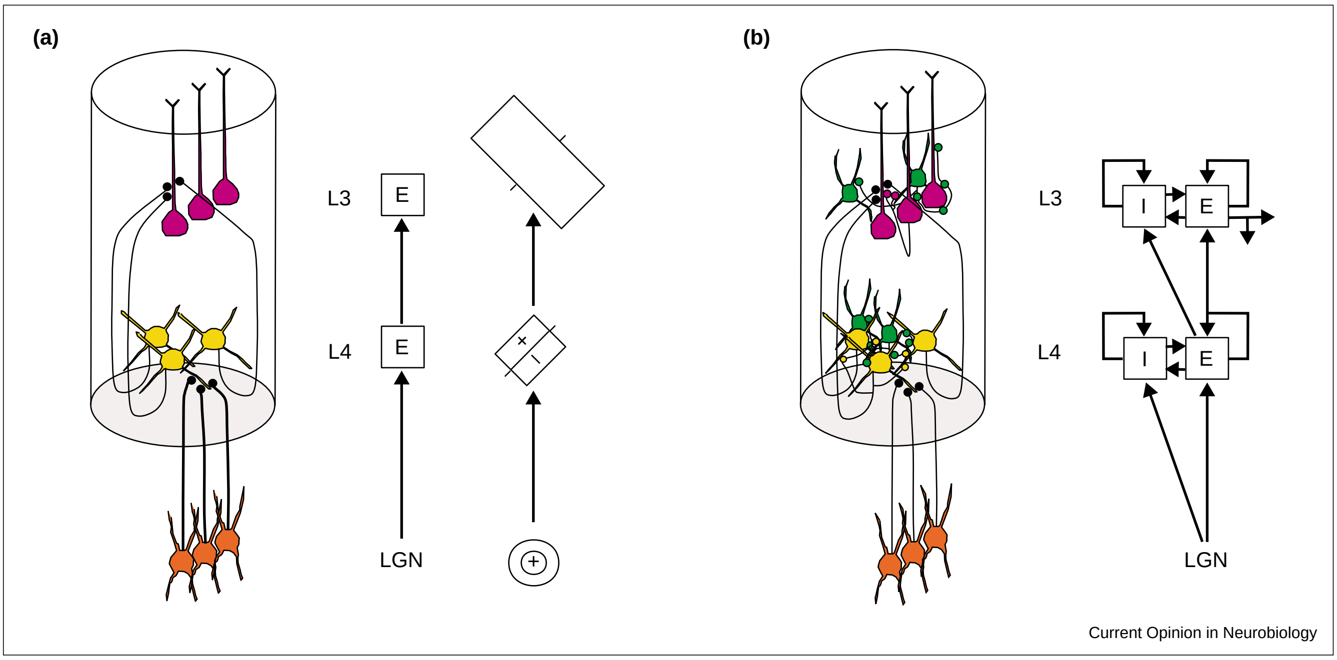
It could be argued that the relative lack of impact of anatomical discoveries in cortical slices is because the work in slices has been directed to questions of neuronal biophysics and synaptic physiology and not to the structural basis of the functional microcircuits. Also, most cortical slice studies use rodent somatomotor cortex and not the visual cortex of the cat or monkey, which have been the major models for investigations of cortical circuits. A more fundamental reason may be that most of the progress in our understanding of cortical microcircuits has come about through the approach deployed with effortless brilliance by Hubel and Wiesel [2]. They first constructed a hierarchical model (Figure 1a) of the microcircuit in visual cortex on the basis of the receptive fields and of the lamina in which neurons were recorded [2]. The power of their approach was that it mattered not whether one or one hundred cell types were involved, whether the synapses depressed or potentiated, or what glutamate receptor subtypes and ion channels were present: the baffling complexity of microanatomy and microphysiology was simply irrelevant. Thus, despite its ripe age, their model continues to be remarkably agile and it remains the textbooks' favorite. It has had the good fortune to be insoluble by past and current techniques and thus it continues to tantalize successive generations of experimentalists. Most modelers of cortical microcircuits have followed suit and taken the first stage of the hierarchy — the generation of orientation-selective 'simple cells' from a row of relay cells in the lateral geniculate nucleus (LGN) of the thalamus — as their test case.

With this history as ambience, it is no surprise to discover that recent publications on cortical microcircuits maintain this bias of approach and interest. According to the dictum, 'anatomy tells you what could be, physiology tells you what is' (JA Movshon, personal communication), *in vivo* physiology and modeling continue to be the main tools used to solve the structure of cortical microcircuits. Where real structural studies are made *in vivo*, it is usually at the level of populations of labeled neurons observed through the light microscope. Thus, although the anatomical basis of the visual field map (retinotopy) and the segregated inputs of left and right eyes (ocular dominance) appear to be fully explained by the distribution of the eye-specific thalamic inputs to layer 4 [3], to date, no anatomical circuits have been demonstrated for the cortical properties of orientation tuning, binocular disparity, direction selectivity and contrast adaptation, amongst others. Yet, this apparent lack of progress is deceptive, for many of the elements required for a new synthesis are already here. The new experimental and theoretical evidence reviewed here indicates that feedforward inputs to cortical layers from the thalamus are not the sole determinant of the specificity of neurons, even in the orientation domain. Rather, local recurrent cortical circuits (Figure 1b) play an important role in the organization of such specificity at the level of single neurons and at the level of cortical maps (Figure 2).

Wiring the cortex

On the basis of the retinotopic map derived from the mapping of thalamic afferents, the primary visual cortex elaborates an impressive range of spatial and temporal

Figure 1

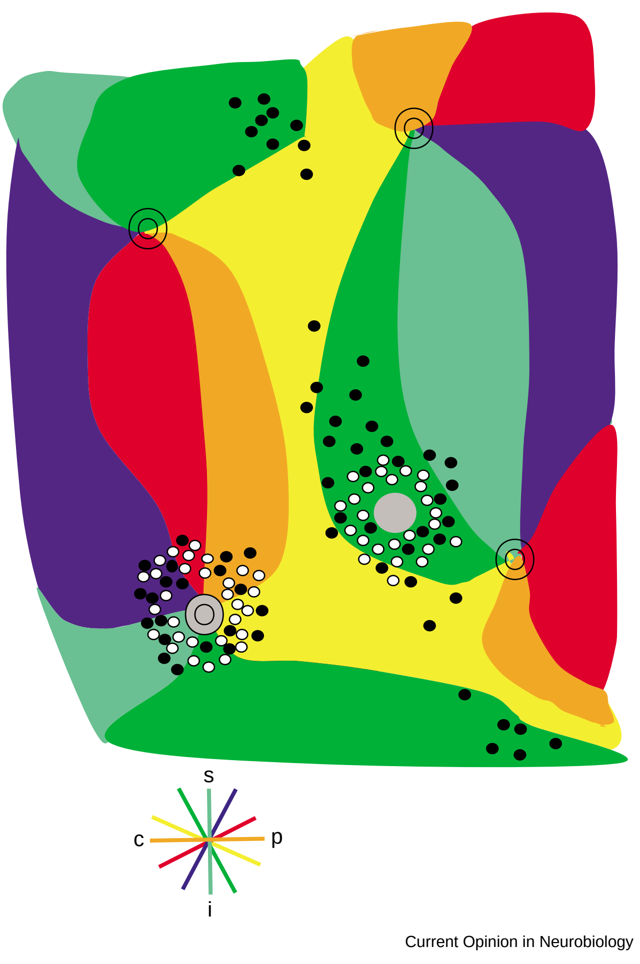


Schematics of the vertical columns of visual cortex. **(a)** The hierarchical model of Hubel and Wiesel. It has two stages: neurons of the LGN with their concentric centre-surround receptive fields converge on layer 4 (L4) neurons to form 'simple' receptive fields. The layer 4 neurons then converge on layer 3 (L3) neurons to form 'complex' receptive fields. Both simple and complex cells lie within the same orientation column, indicated by cylinder. The cardinal characteristic of the complex cells is their position invariance – an optimal oriented stimulus placed anywhere in the receptive field gives the same response. Responses of simple cells are highly position-dependent and sign-dependent. Only feedforward excitatory connections are considered in their model. Lefthand column indicates schematic of circuitry, righthand columns the receptive field structure of neurons at the three stages of the hierarchy. **(b)** An alternative hierarchy. Layers 3 and 4 contain excitatory (E) and inhibitory (I) neurons that are recurrently connected in every possible combination. Most recurrent connections to any neuron are from neighbors. It is out of this collective computation that the functional maps are formed.

properties. Because these properties are generated by cortical microcircuits, it is important to discover the rules and constraints governing the layout of the wiring in the microcircuits. However, such investigations are relatively rare. Stevens [4•] proposed that amongst visual cortical properties, it is only the need to represent orientation with the same fidelity as the retinotopic map that drives the significant increase in the total number of cortical neurons relative to lateral geniculate relay neurons. In general, any additional parameter that needs to be represented in visual cortex means additional constraints on the way in which the neurons wire themselves together; thus, it is crucial to understand the nature of the cortical representations of dimensions such as space, motion, and orientation. It is a fortuitous coincidence that, thanks to optical recordings of the intrinsic signals in the visual cortex, we know more about the representation of the orientation of stimuli than we do about any visual property other than retinotopy. This attention to the two-dimensional (2D) organization of the orientation domain, as it is expressed in superficial cortical layers, has resulted in many delightful papers. The beautiful false-color images used to illustrate the orientation maps have seduced many editors searching for an eye-catching cover picture for their journals (Figure 2). However, the 2D maps themselves are intriguing because they contain large regions where orientation preferences of neurons change slowly, interspersed with point singularities, called 'pinwheels' or 'orientation centers', where orientation preferences change rapidly. Such images have been the inspiration for models of cortical wiring, where the goal is to discover whether the maps are in some way optimal solutions to the constraint of reducing wiring length [5,6•]. The significance of exploring this domain is that it places important constraints on the 2D intracortical connections and offers experimentally testable predictions.

Algorithms for self-organizing maps have been successful in describing the basic features of cortical maps [7–9]. One issue they have addressed is the relationship between the orientation map and the retinotopic and eye dominance maps [10]. The basic assumption of these models is that computations in cortex are local; thus, optimally, all the neurons that represent the different parameters in a given part of the visual field should be neighbors and have the shortest interconnections. In visual cortex, the two dimensions of retinotopic space, and one each of orientation and ocular dominance, have to be represented on a 2D cortical surface. In reducing the dimensions, distortions are introduced to the map. In the case of near optimal solutions (i.e. those requiring the minimum 'wire') the most rapid

Figure 2



Schematic of connectivity within the orientation map of visual cortex. Optical recordings of intrinsic signals rendered in false color provide striking images of the tangential organization of the cortical orientation map. The maps are generated by presenting stimuli at different orientations and recording the ‘intrinsic’ optical signals associated with metabolic or electrical activity in the superficial layers of the cortex. The intrinsic signals associated with the different orientation are then color-coded and presented in a composite orientation map. The maps have orientation centers, or pinwheels, indicated by the four donuts, separated by relatively linear iso-orientation zones where slow changes in orientation preference occur across the iso-orientation bands. Injections of anterograde and retrograde tracers (dark circle on the bottom left donut) into the orientation centers produce symmetric labeling of inhibitory (indicated by white dots) and excitatory (black dots) axons and/or cells. Tracer injections into the linear zones (dark circle towards the center/right) produce labeling distributed along the visual field axis corresponding to the cells’ preferred orientation. The star indicates orientation preferences of the optical map. Visual space is also mapped in 2D on the cortical surface. Visual fields: s, superior; i, inferior; c, central; p, peripheral. Not shown to scale.

changes in orientation occur in places where the retinal position changes most slowly. Inconveniently, the opposite was found in one experimental study in the cat: the most rapid changes in orientation were associated with the most rapid changes in retinal position [11]. Mitchison and Swindale [12] attempted to accommodate these new results by adding a variant of Hebbian synaptic learning to the Kohonen self-organizing algorithm [7]. In Kohonen’s algorithm, synapses in a patch of the map are strengthened regardless of whether the neurons they contact are also active. This is sometimes called ‘volume learning’ and the Hebbian variant requires the additional constraint that synapses are only strengthened when the postsynaptic neurons are also sufficiently active. Mitchison and Swindale’s [12] modifications were only partially successful, because the correlation between changes in orientation and changes in retinal position were weak, albeit positive. Worse still, they found that rapid changes in orientation were also correlated with abrupt changes in ocular dominance in their model. This does not occur experimentally [10], which argues against purely Hebbian learning mechanisms being involved in map formation. For good measure, Mitchison and Swindale cautioned against a thorough overhaul of models before species other than the cat were examined. Sure enough, the ferret [13••] and the tree shrew [14] do not have distorted maps; thus, on the basis of the present data, the cat’s visual cortex seems to be anomalous. However, new models have concentrated on explaining the cat data [15,16•]. Surprisingly, a consensus has emerged that the orientation map reflects the architecture and activity patterns of lateral connections within the cortical circuits, and not simply the feedforward pattern of thalamic connections [11,12,13••].

Thinking laterally

In the feedfoward model of orientation selectivity, a row of LGN neurons converges on a single cortical neuron to create a cortical receptive field that is longer than it is wide (Figure 1a). This anisotropy in the LGN connections to layer 4 neurons is the means by which orientation selectivity is generated by the feedforward connections. One alternate view to feedforward patterning is that lateral connections of cortical neurons generate the spatial anisotropy inherent in orientation preferences [17•,18,19]. In the monkey, the axons of the non-orientation-selective layer 4cβ cells have few lateral connections, whereas the orientation-sensitive layer 4cα cells have strong lateral projections [19]. In cat layer 4, spiny stellate cells are orientation selective and have extensive lateral connections [20]. Layer 3 neurons in the cat also extend their axons along the retinotopic axis of the cortical map that corresponds to their orientation preference [18]. Previous attempts in macaque monkeys to discover an orientation-related anisotropy of intracortical connections outside layer 4 foundered, because of the high degree of anisotropy generated when the visual fields of the left and right eyes are mapped into separate ‘ocular dominance’ stripes. By contrast, the tree shrew, which separates the left and right eye input to cortex into sublayers rather than bands [21,22], provides a particularly florid expression of the anatomical pattern seen in the cat [23] (Figure 2).

The confounding ocular dominance system is more weakly expressed in New World monkeys than in the Old World macaque, which means that, locally, the retinotopic map is almost isotropic. A similar elongation of axon collaterals is found in the New World primate as exists in the cat and the tree shrew [17•]. However, the anisotropy is small, ~1.7 times long as it is wide. The long axis is ~3 mm, which means that any neuron could connect monosynaptically to another neuron with adjacent but non-overlapping receptive fields. However, it must be noted that this extent of collaterals may be an overestimate, because the tracer used in this study might also label the local axon collaterals of distant neurons whose axons transport the label retrogradely. A related study in the cat [24••], using similar methods, explored the topography of lateral connections in layer 3, to and from the pinwheel or orientation centers — the points in the orientation map upon which all orientations converge [10]. Unlike the connections made in iso-orientation domains [25], the pattern of labeling to and from the centers was circularly symmetric (~1.6 mm in diameter). This resembles the pattern seen in layer 4 of the cat, where the lateral extent of labeling was ~1–2 mm, with little clustering or asymmetry [26]. The interpretations of these anatomical studies are somewhat hampered by the fact that the putative inhibitory and excitatory connections are not always differentiated.

Bold attempts were made previously to identify the lateral connections of inhibitory and excitatory neurons within the orientation map in adult ferret visual cortex [27]; the latest such attempts are as technically demanding [28••]. Roerig and Chen [28••] made optical recordings of the orientation maps in ferret cortex *in vivo*: they then sliced the cortex horizontally and used photo-released glutamate to stimulate presumed monosynaptic inhibitory and excitatory inputs onto single pyramidal cells in known orientation domains in superficial and deep layers (orientation tuning is poor or absent in layer 4 neurons in ferret [29]). About 90% of the recorded inputs originated from neurons lying within 500 μm of the recorded pyramidal cell. Inhibitory potentials were more common close to the recorded cell, whereas excitatory connections were more common at longer distances and had a stronger preference for the iso-orientation domains than the inhibitory connections. This is similar to the pattern seen in the cat, although anatomical connections in the ferret extend twice as far as in the cat [24••,26,30•]. The excitatory currents originating from iso-orientation domains were also larger in amplitude on average than those originating from neurons in other orientation domains. These currents arise from clusters of neurons, so this amplitude may indicate that relatively more neurons connect from iso-orientation domains. However, overall, the individual neurons received <50% of their input from neurons whose orientation preference was close (within 30°) to theirs. Simply on the basis of random connectivity, it would be expected that inhibitory neurons, which make dense local axonal arbors, would connect on average more to their neighboring cells, which have similar orientation preferences [30•] (Figure 1b).

Taken together, these studies appear to rule out explanations of orientation that rely on high specificity of connections between cortical neurons. Of course, even if local connections were highly specific for orientation, we would be none the wiser as to the mechanisms underlying the generation of orientation specificity. Nevertheless, these studies have brought a new degree of technical sophistication to experimental studies of cortical microcircuitry.

Wetware

The task of elucidating the circuits for basic functions such as orientation and direction selectivity might seem simpler in the cat than in the ferret, tree shrew, or monkey — all species where the orientation and direction selectivity of neurons in layer 4, the major thalamorecipient layer, is weak or absent [22,29,31]. The simplification offered by the model of Hubel and Wiesel [2] is that the pattern of convergence of thalamic connections on layer 4 neurons generates the receptive field properties of the first stage of the hierarchy. Thus, local connections between cortical neurons are ignored in favor of a feedfoward circuit (Figure 1a). Cross-correlating the activity of the presynaptic and postsynaptic neurons allows an exploration of the rules governing the thalamic connections to orientation-sensitive neurons in layer 4 of the cat. This electro-anatomical method assumes that a monosynaptic connection exists between two neurons when a spike in one cell is followed, after a delay of a few milliseconds, by a spike in a second cell. However, even in optimal conditions, where the monosynaptic connection is strong, cross-correlation shows only the physiological expression of a part of the underlying circuit under the given stimulus conditions, not the whole circuit itself. Nonetheless, cross-correlation studies have made strong claims in support of the Hubel and Wiesel model and have recently extended their simple cell model by claiming that the feedforward input is not only spatially specific, but also specific in terms of timing, strength of connection, and size of thalamic input [32•]. Cross-correlation techniques further show that monosynaptic connections exist between layer 4 simple cells and layer 3 complex cells within the same orientation column [33•]. These latter results ‘provide strong support for one of the main tenants (sic) of the hierarchical model’ [33•]. Such cross-correlation studies do not explain the operation of a cortical circuit of the observed three-dimensional (3D) organization and richness of behavior of the visual cortex, but what they do support is a strong claim that connections between cortical neurons are highly specific. If true, how does such connectional specificity develop?

Map-making

Although orientation specificity is present at birth in many species, one view is that it arises not through epigenesis, but through activity-dependent learning. Here, theorists continue to have a field day [16•,34•,35•] but experimentalists who share their devotion to nurture as an organizing principle have found it hard to obtain unequivocal evidence that neural activity is the primary factor driving the development of orientation selectivity. The main paradigm for activity-dependent learning involves rearing animals in restricted environments (e.g. in the dark, or with both eyes closed, in stroboscopic lighting, or 'stripe-rearing') where the animals live in a pop-art world of high contrast vertical or horizontal stripes. The conventional assumption is that the changes such deprivation induces are due to some form of Hebbian learning. In the most recent account in ferrets, the particular form of the deprivation had a marked influence on visual maps [36••]. The maps in animals with both eyes closed during development were far more rudimentary than in eye-open animals reared in the dark. The interpretation offered is that light scattering through the closed eyelids disrupts the normal orientation-based correlations in activity that lead to a sharpening of the orientation circuits by a Hebbian process [36••]. Both forms of deprivation produced marked reductions in the extent and in the degree of clustering of lateral connections of layer 3.

Immaculate timing is crucial for Hebbian synaptic modification, whether it be to potentiate or depress a synapse. Recent *in vivo* studies use protocols that provide far better temporal control of presynaptic and postsynaptic activity than restricted rearing experiments [37••,38,39]. These studies produce conditioned shifts in the orientation of neurons. One important discovery in the context of the present discussion is that the orientation preferences of layer 4 neurons are not modifiable [37••]. This is reminiscent of the finding that layer 4 neurons do not respond rapidly to monocular deprivation, whereas neurons in other layers do [40,41••]. The synapses in the major thalamorecipient layer, it seems, are not so 'plastic'. Nevertheless, recent models [35•] are still strongly centered on specificity 'learned' at geniculocortical synapses in layer 4. Work on hierarchical networks that use temporal learning rules and natural stimuli to learn complex receptive fields may indicate another route of understanding the development of specificity [42•]. Indeed, over the years, the thought has occured to a number of prominent investigators that the key features that we regard as 'cortical' may truly be an invention of the recurrent circuits of cortex itself and not solely due to an ingenious construction of feedforward thalamic connections [11,17•,23].

Food for thought

To be fair, feedforward models have evolved. So much so that they are reminiscent of the fabled 'stone soup', in which the more supplementary ingredients added to the basic recipe of boiled stone, the better the taste. As more of the known cortical microcircuits have been included in computational models, they have come to exhibit a richer range of cortical-like behaviors. Indeed, in matter, if not yet in the minds of their inventors, the current crop of feedforward circuits is indistinguishable from earlier versions of recurrent circuits founded on observed cortical anatomy [43–45]. This convergence offers the enticing prospect of consensus on what the structure of the basic microcircuit is, even if there are still strong differences of opinion concerning its function. For example, one persistent misconception about feedback or recurrent circuits is that they are inherently much slower than feedforward circuits and that the selectivity they generate must sharpen over time [46]. In fact, models of recurrent circuits indicate that sharp tuning is present from the first spike, despite a broadly tuned feedforward input [44,47••]. Thus, local recurrent processing doesn't necessarily slow interareal transmission [48•]. Recordings with a voltage-sensitive dye in the recurrent circuits of the cat's visual cortex have now tracked the time course of orientation-tuned responses [49••]. As with intracellular experiments [46], these recordings reveal that orientation tuning does not sharpen with time, but that the response to the non-preferred (orthogonal) orientation is suppressed relative to the preferred. Thus, instead of 'sharpening' the orientation-tuning curve, the suppression (inhibition) appeared to increase the difference between the preferred and non-preferred responses.

Although recurrent models nominally include more of the actual cortical circuitry than feedforward models, they have remained minimalist with regard to cell types, 3D organization and dynamics. As to the architecture, most assume that the lateral connections of the cortex are isotropic and that inhibitory connections form the surround and excitatory connections dominate the center [15,16•,34•,44,50]. This Mexican Hat pattern is the inverse of the actual structure (Figure 2). For reasons of stability, inhibition dominates model recurrent networks, although this seems at odds with the cortical microcircuits in which only 25% of neurons are inhibitory and ~80% of the synapses made by excitatory cells are with other excitatory cells. Even modelers trying to use a more realistic connectivity make the inhibitory synapses so much stronger than the excitatory ones that they effectively generate a Mexican Hat [51,52•]. With a Mexican Hat connectivity, neurons located in the orientation centers have an advantage, theoretically at least, because all orientations provide them with inhibition and this generates a more sharply tuned output from a broadly tuned input than does iso-orientation or cross-orientation inhibition. This access to all orientations may help explain the marked short-term orientation plasticity seen in neurons near orientation centers [53•].

Conclusions

Work on cortical microcircuits is being done in the conceptual framework that is 40 years old and based on investigations in cat area 17 [2]. This framework offers a simple feedforward hierarchy to explain the formation of specific receptive fields (Figure 1a). Thus, papers on cat microcircuits still begin with sentences such as: 'Although separated by a single synapse, thalamic cells and cortical simple cells have very different response properties' [32•]. This focus on the thalamocortical synapse obscures the truth that, even in layer 4 of the cat, 95% of the synapses on a simple cell come from other cortical neurons, which are themselves connected in a multisynaptic network [54]. It is this collective computation that needs to be understood, not just the pattern of feedfoward thalamic connections that contribute a few percent of cortical synapses and a small fraction of the total synaptic drive [43,44,54]. Similarly, layer 3, the second tier in the hierarchical model (Figure 1a,b), receives only ~20% of its excitatory connections from layer 4. Approximately 75% of its connections arise from its neighbors in layer 3 (T Binzegger, R Douglas, KAC Martin, unpublished data). Nevertheless, conceptually and experimentally, it has proved difficult to go beyond the thalamocortical synapse and to get to grips with the essential multilayered recurrence of the local cortical circuit. Many modelers still select details of the cortical wiring in the hope that they will eventually describe physiological phenomena, rather than attempting to discover the principles by which cortical microcircuits are built and operate. The devil, it seems, is still in the details.

It is clear that we simply do not understand much of the detailed structure of cortical microcircuits or their relation to function. Our present models are highly abstracted versions of the known fragments of the microcircuits. Perhaps because we are overawed by the structure of cortical microcircuits, we have not yet learned to think about them in their own terms — as highly successful adaptations that solve the difficult problems of vision in the natural world. Nevertheless, experimentalists and theoreticians increasingly share the same brain and this offers new hope for rapid progress on the hard problems of cortical microcircuitry. Many of the clues we need are already available. In particular, we certainly cannot continue to neglect the details of microstructure and physiology that have been gathered in recent years from *in vitro* experiments. But, whatever the model, the simple truth still remains: 'what chiefly distinguishes cerebral cortex from other parts of the nervous system is the great diversity of its cell types and interconnections. It would be astonishing if such a structure did not profoundly modify the response patterns of the fibres coming into it' [2].

Acknowledgements

I thank the Human Frontier Science Program and the European Union for support, members of Information Networking Institute for critical readings, and John Anderson for artwork.

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The authors if this paper present the most advanced account of thalamo-cortical cross-correlation studies. They document both temporal and spatial relations between the LGN and layer 4 simple cells while adroitly skirting the vexed issue of how the two major types of LGN neurons, the X and Y cells, project to the simple cells in area 17.

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A cross-correlation study of connections between layer 4 and layer 3 in the cat visual cortex. The authors show that γ-amino butyric acid (GABA)-inactivation of the A-layer in the lateral geniculate nucleus silences connected neurons both in the thalamus and in the cortex. Their results directly contradict earlier findings of Malpeli *et al*. [55], who found that layer 3 neurons remained active after LGN A-layers were inactivated. Although they claim that the findings strongly support the hierarchical model, the method is inherently unable to demonstrate that complex cell responses are due solely to simple cell input, as the hierarchical model requires. Accompanying panygeric [56].

34. • Burger T, Lang EW: Self-organization of local circuits and cortical orientation maps: a nonlinear Hebbian model of the visual cortex with adaptive lateral couplings. *Z Naturforsch* 2001, 56:464-478.

Burger and Lang discover that when left (nearly) to their own devices, local neocortical circuits create Difference of Gaussian (DOG) patterns of connectivity. This model does not explain the mechanisms that lead to the alternate architecture seen in the brain.

35. • Kayser AS, Miller KD: Opponent inhibition: a developmental model of layer 4 in the neocortical circuit. *Neuron* 2002, 33:131-142.

Here, the authors further explore the ability of Hebb's eponymous synapses to generate opponent inhibition in which inhibition is evoked by stimuli that are anticorrelated with those that excite the cell. The claim is that opponent inhibition is the mechanism whereby cortical neurons respond specifically, regardless of the contrast of the stimulus.

36. •• White LE, Coppola DM, Fitzpatrick D: The contribution of sensory experience to the maturation of orientation selectivity in ferret visual cortex. *Nature* 2001, 411:1049-1052.

In this study, the authors indicate the involvement of Hebbian learning mechanisms in the development of the orientation map in the visual cortex. Simple eyelid closure has a far more catastrophic effect on the map than dark-rearing – a result with curiously Beckettian resonance [57].

37. •• Schuett S, Bonhoeffer T, Hübener M: Pairing-induced changes of orientation maps in cat visual cortex. *Neuron* 2001, 32:325-337.

Schuett *et al*. apply a Hebbian paradigm to induce acute changes in the orientation maps of anaesthetized kittens.

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41. •• Trachtenberg JT, Stryker MP: Rapid anatomical plasticity of horizontal connection in the developing visual cortex. *J Neurosci* 2001, 21:3476-3482.

This fascinating study shows rapid changes in horizontal connections in superficial layers of visual cortex following monocular eye closure in kittens. A complement to [39].

42. • Einhäuser W, Kayser C, König P, Körding KP: Learning the invariance properties of complex cells from their responses to natural stimuli. *Eur J Neurosci* 2002, 15:1-14.

A new attempt to explain how, in a feedforward circuit, complex cells could acquire their property of spatial invariance from simple cells by exploiting the temporal structure of natural images.

43. Douglas RJ, Martin KAC, Whitteridge D: A canonical microcircuit for neocortex. *Neural Comput* 1989, 1:480-488.

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46. Gillespie DC, Lampl I, Anderson JS, Ferster D: Dynamics of the orientation-tuned membrane potential response in cat primary visual cortex. *Nat Neurosci* 2001, 4:1014-1019.

47. •• Lui SC, Kramer J, Indiveri G, Delbrück T, Burg T, Douglas R: Orientation-selective aVLSI spiking neurons. *Neural Netw* 2001, 14:629-643.

The authors present an analogue Very Large Scale Integrated (VLSI) that emulates a visual system of retina and cortex, using integrate-and-fire neurons and a soft winner-take-all cortical microcircuit. Here, a VLSI system is used to compare spatial and temporal dynamics of feedforward and feedback models in real-time computations. Sharp orientation selectivity is present from the first spike in recurrent circuits, despite a broadly oriented input.

48. • Panzeri S, Rolls ET, Battaglia F, Lavis R: Speed of feedforward and recurrent processing in multilayer networks of integrate-and-fire neurons. *Network* 2001, 12:423-440.

Panzeri *et al*. simulate interareal transmission with the surprising result that recurrent networks add little to the processing time needed by purely feedforward networks.

49. •• Sharon D, Grinvald A: Dynamics and constancy in cortical spatiotemporal patterns of orientation processing. *Science* 2002, 295:512-515.

The authors use voltage-sensitive dyes with high temporal resolution to study the evolution of the orientation response in superficial layers of cat cortex. The study contains a timely plea from the savant of Rehovot to combine feedforward and recurrent models of orientation selectivity.

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• cortex. *Nature* 2001, 411:80-86.
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57. Beckett S: Watt. John Calder: London; 1976:231.