

Bottom-up and top-down dynamics in visual cortex

James Schummers, Jitendra Sharma and Mriganka Sur*

*Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology,
Cambridge, MA 02139, USA*

Abstract: A key emergent property of the primary visual cortex (V1) is the orientation selectivity of its neurons. Recent experiments demonstrate remarkable bottom-up and top-down plasticity in orientation networks of the adult cortex. The basis for such dynamics is the mechanism by which orientation tuning is created and maintained, by integration of thalamocortical and intracortical inputs. Intracellular measurements of excitatory and inhibitory synaptic conductances reveal that excitation and inhibition balance each other at all locations in the cortex. This balance is particularly critical at pinwheel centers of the orientation map, where neurons receive intracortical input from a wide diversity of local orientations. The orientation tuning of neurons in adult V1 changes systematically after short-term exposure to one stimulus orientation. Such reversible physiological shifts in tuning parallel the orientation tilt aftereffect observed psychophysically. Neurons at or near pinwheel centers show pronounced changes in orientation preference after adaptation with an oriented stimulus, while neurons in iso-orientation domains show minimal changes. Neurons in V1 of alert, behaving monkeys also exhibit short-term orientation plasticity after very brief adaptation with an oriented stimulus, on the time scale of visual fixation. Adaptation with stimuli that are orthogonal to a neuron's preferred orientation does not alter the preferred orientation but sharpens orientation tuning. Thus, successive fixation on dissimilar image patches, as happens during natural vision, combined with mechanisms of rapid cortical plasticity, actually improves orientation discrimination. Finally, natural vision involves judgements about where to look next, based on an internal model of the visual world. Experiments in behaving monkeys in which information about future stimulus locations can be acquired in one set of trials but not in another demonstrate that V1 neurons signal the acquisition of internal representations. Such Bayesian updating of responses based on statistical learning is fundamental for higher level vision, for deriving inferences about the structure of the visual world, and for the regulation of eye movements.

Introduction

The primary visual cortex (V1) has long been studied as a model of the general principles of cortical functioning. In particular, the emergent property of orientation tuning in V1 provides an interesting test case for the role of different classes of inputs in

shaping the functional response properties of cortical neurons. Much work has attempted to distinguish whether orientation selectivity is derived from "feedforward" inputs from the thalamus, or "recurrent" inputs within the cortical circuit. There is substantial evidence for an important role of both types of inputs in shaping the tuning properties of V1 neurons, with a growing consensus that the dynamics and plasticity of tuning involves both inputs. Beyond the limited scope of orientation tuning, the issue has broad implications for the mode in which cortical

*Corresponding author. Tel.: +1-671-253-8784; Fax: +1-617-253-9829; E-mail: msur@mit.edu

circuits operate. Do cortical neurons inherit their properties from the specific configuration of feedforward inputs, or does the cortical circuitry itself generate new properties based on features of the recurrent circuitry and top-down inputs?

The feedforward model of orientation tuning was the first proposed (see Static linear feedforward models), and many conceptual models of cortical function are based on the principle of strong feedforward determination of response properties. However, there is increasing evidence that the local circuitry can dramatically influence the responses of V1 neurons. As a consequence of the orderly mapping of orientation onto the 2D cortical sheet, the local cortical networks are diverse, and this diversity has implications for both intracortical computations and the stability of response properties. Several lines of evidence suggest that the local cortical circuit may be a meaningful functional unit of cortical computations. Thus, the response properties of individual neurons cannot be fully understood except in the context of these circuits. We have shown that a careful balance of inhibition and excitation can elegantly generate, and maintain, sharp orientation tuning across a diversity of local circuit layouts. This balance may be more or less delicate at different locations in the orientation map, and thus render tuning more or less susceptible to perturbations of excitation or inhibition.

In order for V1, and other “lower” cortical areas, to perform useful computations for vision, action, and behavior, they need to have access to information from “higher” cortical areas that monitor the behavioral and cognitive contingencies of the task at hand. Recent evidence from several studies, including those from our laboratory, has bolstered the view that even in V1, which may not explicitly code for task dependent features, the responses are strongly dependent on a number of influences that reflect behavioral contingencies in alert animals. This suggests that “top-down” inputs from higher cortical areas can modulate the response properties of V1 neurons. In some cases, the changes in V1 responses are fairly complex, beyond simple up or down scaling of response magnitude.

Models of V1 function based on feedforward principles tend to portray V1 neurons as static linear spatio-temporal filters. Such models have difficulty accounting for complex top-down response

modulation. However, a view of V1 with balanced excitation and inhibition in the local circuitry can accommodate changes in tuning properties by top-down inputs. Interestingly, neurons at specific cortical locations, for example near pinwheel centers of the V1 orientation map, should be more modifiable within this framework. Given that top-down influences are variable from cell to cell, we tentatively propose that these differences may relate to position in the orientation map. Confirmation of this hypothesis will require technical advances that enable recording from neurons at specific sites in the orientation map in awake, behaving animals.

The orientation map and local circuits

Orientation tuning is a prominent feature of the receptive fields of neurons in V1. Since the original description of this response property over four decades ago (Hubel and Wiesel, 1962), tremendous effort, both experimental and theoretical, has been devoted to describing the synaptic mechanisms responsible for generating this tuning (Vidyasagar et al., 1996; Sompolinsky and Shapley, 1997; Ferster and Miller, 2000). To a large extent this debate can be simplified to a question of whether orientation tuning is created by the feedforward inputs from the LGN, or recurrent connections within the cortical circuit. In this context, it is important to note that the cortical circuit is not uniform with respect to the layout of orientation; orientation is represented in a map of orientation preference, with a pinwheel configuration. Pinwheel centers are tiled regularly across the cortical surface, and orientation preference is represented radially on the spokes around the pinwheel center. Figure 1A shows an example of such an orientation map, measured by optical imaging of intrinsic signal responses to drifting gratings. The preferred orientation at each point on the cortical surface is represented by the color code indicated at the upper right corner of the map. Pinwheel centers are the points at which all of the orientations converge. Orientation domains are the regions of relatively constant orientation preference interspersed between the pinwheel centers. This structure of the orientation map needs to be taken into account in order to understand the role of intracortical circuits in orientation tuning.

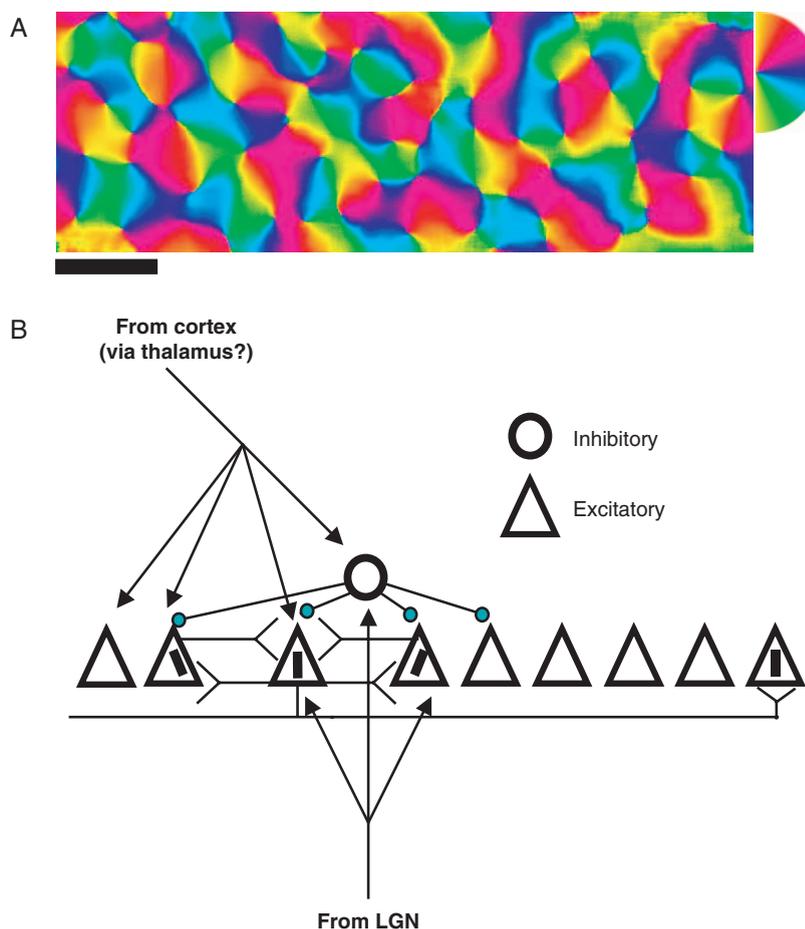


Fig. 1. Schematic depiction of cortical circuitry relevant for orientation tuning and dynamics. A. Orientation preference map obtained with optical imaging of intrinsic signals in cat area V1. Each pixel represents the preferred orientation, computed as the vector average of responses to eight orientations of drifting grating. The orientation value is continuously color coded as indicated in the hemisphere at the upper right corner of the map. The scale bar represents 1 mm of cortical distance. B. Cartoon representation of the components of the cortical circuit involved in creating or modifying orientation tuning. Excitatory neurons are depicted as triangles, and inhibitory neurons as circles. Interareal excitatory connections are depicted by arrow heads; intra-areal excitatory connections by viper-tongues; intra-areal inhibitory connections by gray circles. The feedforward inputs from the LGN synapse on excitatory and inhibitory neurons within one hypercolumn. Intracortical excitatory connections impinge on both local and long range excitatory neurons. Excitatory to inhibitory connections are not shown for the sake of clarity. Inhibitory connections are local within one hypercolumn. Feedback connections from higher visual cortical and eye movement areas contact excitatory and inhibitory neurons.

Another issue that has been heavily debated is the role of inhibition in shaping the orientation tuning of V1 neurons. Most current models of orientation tuning incorporate inhibition to some extent, but its particular role is not fully resolved. Figure 1B shows a schematic representation of the different classes of inputs to, and within, V1 that are likely to play some role in generating or shaping orientation tuning.

The feedforward inputs from the LGN contact both excitatory and inhibitory neurons over a limited cortical extent. They play an important role in the initial generation of tuning, though the degree to which they bias, or determine, tuning remains debated. With a limited extent of less than one hypercolumn, local cortical projections densely interconnect local excitatory (and inhibitory — not shown

for clarity) neurons. Long-range projections between separated iso-orientation columns may play a role in modulating receptive field properties, but will not be discussed in detail here (see [Gilbert, 1992](#); [Somers et al., 2001](#); [Angelucci et al., 2002](#); [Lund et al., 2003](#) for a review of these projections). Top-down projections from higher cortical areas in the visual pathway send numerous projections to both excitatory and inhibitory neurons in V1. They may to some considerable extent, be routed through the thalamus ([Sherman and Guillery, 2002](#)). This cartoon demonstrates the key components of the circuits discussed below.

Static linear feedforward models

The first model to propose a mechanistic explanation for the orientation selectivity of neurons in V1 was proposed by [Hubel and Wiesel \(1962\)](#). Their proposal was intuitive and straightforward; the elongated receptive field of a layer IV simple cell could be created by the convergence of inputs from LGN neurons with receptive fields lying along the axis of elongation of the cortical cell. If the ON and OFF subfields of the input LGN receptive fields lined up, this would create alternating bands of ON and OFF response in simple receptive fields, as found in cat neurons. This arrangement would then lead to greater response to bars flashed or drifted along the extended axis of the receptive field than to bars presented along the narrow axis. This model has come to be called the feedforward model, because it relies solely on the arrangement of the afferent projections to V1, and not on the interactions or circuitry within V1.

This model has received substantial experimental support of several types. The proposal that the elongated ON and OFF subfields in simple receptive fields are inherited from direct projections of LGN neurons is strongly suggested by cross-correlation studies. Reid and Alonso found that pairs of LGN-V1 neurons were much more likely to exhibit cross-correlation histograms indicative of a direct synaptic connection if the subfield sign (ON or OFF), size and position of both matched closely ([Reid and Alonso, 1995](#); [Alonso et al., 2001](#)). Cell pairs with overlapping location, but with mismatched subfield sign were

generally not strongly connected, suggesting a strong specificity of connectivity consistent with the feedforward model.

A second aspect of the model has also received experimental support. [Lampl et al. \(2001\)](#) were able to predict the degree of orientation tuning of responses to drifting grating stimuli with a simple model built from the responses to small flashed spots ([Lampl et al., 2001](#)). This suggests that, as originally proposed, the orientation tuning, measured with bar or grating stimuli can be explained by the spatial profile of the ON and OFF subregions of the field. Another way to view this result is that the responses of simple cells are fairly linear: the response to any arbitrary stimulus can be predicted based on a characterization of the spatial map of the ON and OFF regions.

The idea that simple cell receptive fields are linear has been important in driving the thinking about simple cells and the function of V1 in visual processing. It has long been recognized that spatial integration in V1 simple cells is fairly linear, and generally non-linear in complex cells ([Movshon et al., 1978a](#)). This is a useful distinction, and to a large extent, a reasonable simplification of the behavior of V1 neurons. Simplification can be dangerous, however, and extensions of the linearity of simple cells to a thinking that V1 acts simply as a bank of linear filters can overlook many important behaviors of V1 as a whole. Hierarchical models of V1 tend to oversimplify the behavior of V1 neurons, and may bias us to miss some of the interesting and important aspects of V1 (reviewed in [Riesenhuber and Poggio, 2000](#)). We will highlight several features of orientation tuning in V1 that suggest a more dynamic processing of bottom-up and top-down inputs.

Mechanisms that balance excitation and inhibition

Feedforward models of orientation tuning generally disregard the influence of recurrent cortical circuitry. However, the local cortical inputs to cortical neurons are numerically the majority ([Ahmed et al., 1994](#)), and physiological estimates suggest that they provide roughly 60–70% of the excitatory drive to layer IV neurons ([Reid and Alonso, 1995](#); [Ferster et al., 1996](#); [Chung and Ferster, 1998](#); [Ferster and Miller, 2000](#); [Alonso et al., 2001](#)). Outside of layer IV, the recurrent local projections likely provide almost all of the

excitatory drive. Thus, even if feedforward inputs to layer IV are the major determinant of tuning width, the intracortical inputs can have a strong influence on tuning.

This influence has been demonstrated by a series of experiments that reversibly blocked a subset of the inputs by iontophoresis (Crook and Eysel, 1992; Crook et al., 1997; Crook et al., 1998). When the blocked inputs are orthogonally oriented, the tuning width broadens substantially, but when they are iso-oriented, the effect on tuning is minimal. This finding strongly suggests the existence of strong orthogonal inputs, which are presumably inhibited during normal circuit functioning. A number of other results have also implied a role of inhibition in regulating the sharpness of tuning. Local blockade of inhibition surrounding the recording site can lead to a dramatic decrease in orientation selectivity (Sillito, 1975; Sillito et al., 1980; Sato et al., 1996; Crook et al., 1998; Eysel et al., 1998). Responses of a test grating are suppressed by a second superimposed grating, and the suppression is often maximal with orthogonally orientated mask gratings (Bonds, 1989). These results led to an alternate model of orientation tuning, the cross-inhibition model. In this scheme, non-selective inputs from the LGN are sculpted by orthogonally oriented cortical inhibition to generate sharp tuning. However, two of the main predictions of this model have not been borne out. Blockade of inhibition, intracellularly, in a single neuron, had no demonstrable effect on the sharpness of tuning of that neuron (Nelson et al., 1994). Furthermore, measurements of inhibitory synaptic inputs to V1 neurons have shown that inhibition tends to be strongest at the preferred orientation, rather than at the orthogonal orientation (Ferster, 1986; Anderson et al., 2000; Martinez et al., 2002; Monier et al., 2003). Intriguingly, it is clear that this is not the situation for every cell, suggesting that multiple mechanisms may act to create orientation tuning (Volgushev et al., 1993; Vidyasagar et al., 1996; Martinez et al., 2002; Schummers et al., 2002; Monier et al., 2003). Some of the possible factors responsible for this diversity are discussed below.

None of these results can clearly elucidate a circuit mechanism by which inhibition in the local cortical circuit generates orientation tuning. Taken together, however, they strongly suggest that inhibitory

circuitry plays some role in orientation tuning. In fact, the feedforward model requires strong cortical inhibition to account for the contrast invariance of tuning in V1 (Troyer et al., 1998, 2002). While the specific role of inhibition remains to be clarified, the inhibitory regulation of tuning in two respects is examined. First, the importance of inhibition may be more crucial near pinwheel centers in the orientation map. Second, the balance of inhibition and excitation may be a target for modulation by bottom-up and top-down modulation, and the outcome of this interaction with local circuits may be richer than a simple increase or decrease of gain.

To investigate the influence of local cortical circuits on the computation of orientation tuning, we have combined optical imaging of orientation maps and whole cell recording of synaptic integration in individual neurons in V1. Figure 2 illustrates the main results of the measurements of membrane potential (V_m) as a function of orientation map location. Neurons were recorded at sites near pinwheel centers, or far from pinwheel centers, in orientation domains. For each cell, tuning curves were generated for the subthreshold V_m response amplitude as well as the average suprathreshold firing rate. The V_m amplitude was taken as an estimate of the amount of synaptic input to the cell for that stimulus orientation. Figure 2A shows a schematic representation of the average tuning curves for neurons near pinwheel centers (left column), and in orientation domains (right column). As seen in the bottom panel, the tuning curves for firing rate are nearly identical, as has also been reported with extracellular measurements (Maldonado et al., 1997; Dragoi et al., 2001). However, the tuning curves of subthreshold input are different. Near pinwheel centers, the tuning curve is flatter, with much less difference in response amplitude between preferred and orthogonal orientations. By comparison, the tuning curve of orientation domain neurons is more peaked, suggesting a much larger differential in the synaptic input between preferred and orthogonal. The spike threshold is positioned such that the portion of the V_m tuning curve above threshold (the “tip of the iceberg”) is equally narrow for the two tuning curves. This suggests that, to some extent, the tuning of synaptic inputs reflect the tuning of the local network.

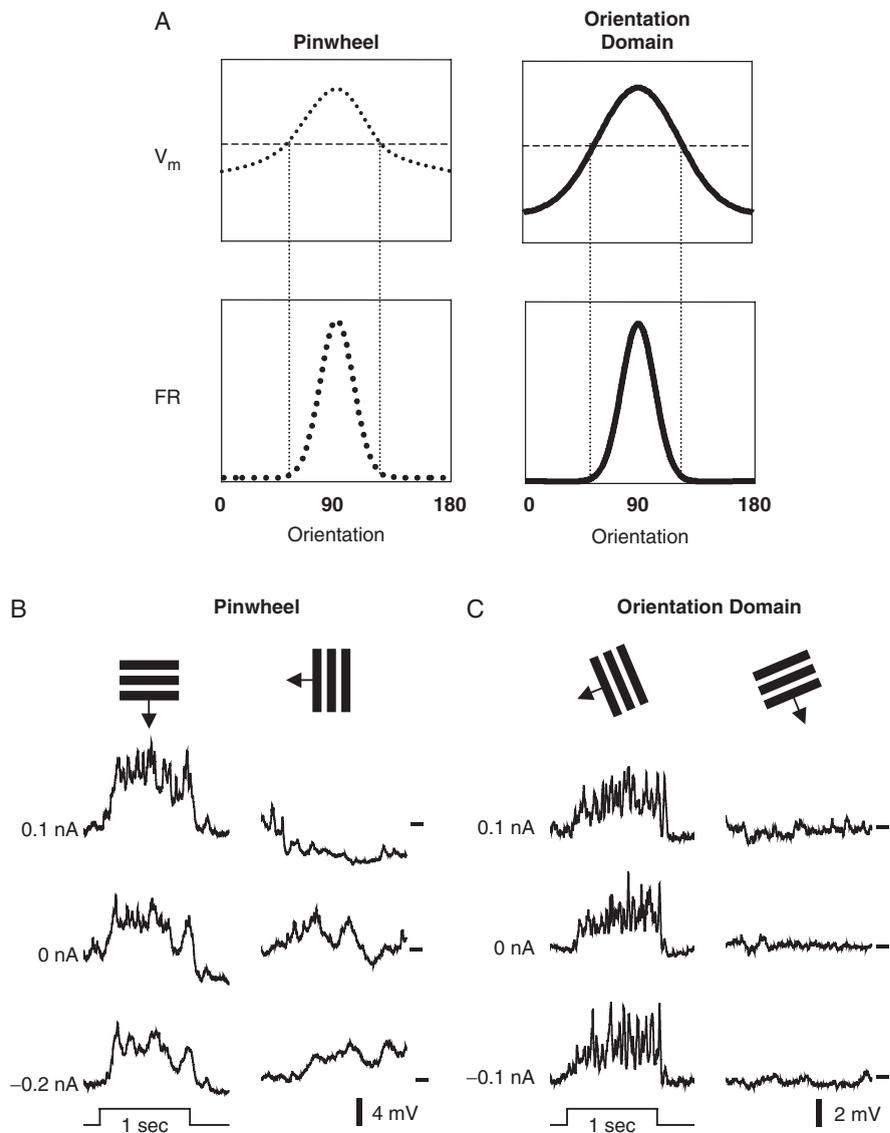


Fig. 2. Subthreshold excitation and inhibition to neurons near pinwheel centers are broader than to orientation domains. A. Schematic depiction of the tuning curves measured near pinwheel centers (left column) and in orientation domains (right column). Mean membrane depolarization (V_m) tuning curves are shown in the top row, and firing rate (FR) tuning curves are shown in the bottom row. Pinwheel neurons have broad subthreshold depolarization, as shown by the V_m curve, with a pedestal (response amplitude at the orthogonal orientation) approximately half the amplitude of the tuning curve peak. The spike threshold is demarcated by the horizontal dashed line. The entire subthreshold portion of the tuning curve is relatively close to the threshold compared with orientation domain neurons. Vertical dashed lines demonstrate the correspondence between the crossing of threshold in the V_m tuning curves, and the firing rate tuning curves. Tuning curves are based on measurements reported in Schummers et al. (2002). B. Demonstration of inhibitory inputs during orthogonal stimulus presentation in a pinwheel center neuron (left column), and the lack thereof in an orientation domain neuron (right column). Each row plots the visually evoked membrane potential for the preferred and orthogonal orientations in the presence of one of three levels of constant current injection. Positive 0.1 nA depolarizes the cells and reveals inhibition as hyperpolarization of V_m . Negative 0.2 nA hyperpolarizes the cells and amplifies the excitatory depolarization of V_m . These examples suggest that the response to orthogonal orientations in pinwheel neurons is composed of both inhibition and excitation, whereas in orientation domain neurons, it is composed of neither. Adapted from Schummers et al. (2002).

As depicted in Fig. 2A, the synaptic inputs on the flanks of the tuning curves of pinwheel center cells push the V_m close to, but not over, the spike threshold. This seems like a precarious balancing act, considering that the spiking response is sharply tuned. How are the synaptic inputs regulated to keep the flank of the tuning curve subthreshold? A likely explanation is that inhibition actively prevents depolarization from leading to spiking. There is qualitative evidence to suggest this is a reasonable explanation. Figure 2B demonstrates an example of V_m responses in a cell near a pinwheel center that suggest inhibition during the orthogonal stimulus (left), and a cell in an orientation domain that does not (right). The responses of the cell were measured under three conditions for each stimulus: resting potential, hyperpolarizing current, and depolarizing current. When the pinwheel cell was hyperpolarized, there was a large stimulus-evoked depolarization that was roughly half the amplitude of the depolarization in response to the preferred orientation. However, when the cell was depolarized, the response to the orthogonal was not hyperpolarizing, suggesting that there was strong inhibitory synaptic input. This was not the case for the orientation domain cell shown on the right. Under all current injection conditions, there was almost no change in V_m in response to the orthogonal grating, suggesting that there was no synaptic input, excitatory, or inhibitory. These examples suggest two conclusions: (1) pinwheel neurons receive strong inputs at all orientations, whereas orientation domain cells only receive inputs near the preferred orientation, commensurate with orientation representation in the orientation map surrounding these sites, and (2) the response at the orthogonal orientation (and at other non-preferred orientations) in pinwheel cells is composed of both excitation and inhibition, which balance each other and help to clamp the V_m below spike threshold and elicit sharp spike tuning (Marino et al., 2003).

These results highlight the important idea that there is a large diversity in the orientation tuning properties in V1. Several recent studies have explicitly examined the diversity in the shapes of tuning curves, and the synaptic mechanisms that might be responsible for these differences (Martinez et al., 2002; Ringach et al., 2002; Schummers et al., 2002; Monier et al., 2003). This diversity is by no means

newly discovered (see, for instance Gilbert, 1977; Volgushev et al., 1993; Vidyasagar et al., 1996), but the importance of it has largely been ignored. In particular, models of orientation tuning have generally assumed a prototypical tuning curve for all V1 neurons (Ben-Yishai et al., 1995; Douglas et al., 1995; Somers et al., 1995; Carandini and Ringach, 1997). Naturally, as early attempts to understand network level interactions capable of generating tuning, these simplifying assumptions were necessary. More recent computational models have begun to incorporate features of the orientation map, including pinwheel center organization, into network models of orientation tuning (McLaughlin et al., 2000; Pugh et al., 2000; Kang et al., 2003). Not surprisingly, adding this extra level of complexity has revealed several new insights into the network organization of orientation tuning, including the possible dependence of tuning features on location in the orientation map (Schwabe et al., 2003). As the field moves towards more complete, and therefore sophisticated models of the V1 network, the diversity of response features in individual neurons may be more closely related to features of the network architecture.

Adaptation-induced orientation shifts

The results of the intracellular experiments described in the previous section demonstrate that the synaptic inputs underlying orientation tuning are not the same at all locations in the orientation preference map. Near pinwheel centers, the visually evoked depolarization at orthogonal orientations is strong, yet does not lead to spiking. These inputs are kept below threshold by strong inhibition, which is necessary to balance the excitation, and keep tuning sharp. It is therefore likely that the tuning of neurons near pinwheels is likely to be a more careful balance of excitation and inhibition. It might follow then, that pinwheel neurons are more sensitive to changes in the intracortical inputs. We speculate that manipulation of the local intracortical circuit would have a larger effect on tuning curves in neurons near pinwheel centers. Experiments described above, in which inputs are blocked in adjacent columns, would presumably have a greater effect on neurons near pinwheel centers (Crook et al., 1997, 1998). Indeed, in the experiments

of Crook and colleagues, tuning curves were most affected when sites 500 μm away with orthogonal tuning were blocked. It is likely, based on the structure of the orientation preference map, that neurons with orthogonal representation 500 μm from one another are located near pinwheel centers. We suggest, therefore that the effects of such manipulation of the balance of intracortical inputs would be strongest in neurons near pinwheel centers.

This issue has been addressed by experiments that subject neurons to visual pattern adaptation. Pattern adaptation is induced by prolonged visual stimulation by a stimulus with constant features, such as orientation, contrast and/or spatial frequency. In sensory pathways, as in many other brain areas, prolonged synaptic activation leads to a decrease in the strength of cortical activation. There is good evidence in both the visual and somatosensory pathways that sensory adaptation has strong effects at an earlier level than primary cortex (Chung et al., 2002; Solomon et al., 2004). There is also evidence for an intrinsic cellular component to adaptation in V1 neurons (Anderson et al., 2000; Carandini, 2000; Sanchez-Vives et al., 2000a, 2000b). It is likely that both mechanisms contribute to some degree to pattern adaptation in V1.

When the receptive fields of V1 neurons are subjected to adaptation with oriented gratings, the tuning curves of many neurons are altered (Dragoi et al., 2000; Dragoi and Sur, 2003). In particular, the response at the adapting orientation is decreased, the tuning curve broadens, and the preferred orientation of the neuron shifts away from the orientation of the adapting stimulus, i.e., the adaptation leads to a repulsive shift in tuning (all three features are required to explain the population shift in activity consistent with the psychophysical tilt after effect: Sur et al., 2002). What can the response changes after adaptation tell us about the role of different circuits in producing orientation tuning in V1 neurons? An important result that helps answer this question is that the effect of adaptation depends on the location of a neuron in the orientation preference map. Figure 3 demonstrates this effect. Figure 3A–C depicts the effect of adaptation on a neuron in an orientation domain. The location of the cell in the orientation map is shown in Fig. 3A. The pool of intracortical inputs likely to be integrated at the

recording site is located within the dashed white circle. The orientation tuning of this pool is depicted by the histogram in Fig. 3B. The tuning of this histogram is fairly sharp, with most of the inputs coming from a narrow range of orientation, close to the preferred orientation of the recorded cell. This suggests that for this neuron, the influence of the cortical circuit is likely to be constrained to orientations similar to its tuning curve peak. Figure 3C shows the effect of adaptation on the tuning curve of this cell. There is no substantial change in tuning following adaptation with an orientation on one flank of the tuning curve (depicted by the vertical dashed arrow). In sharp contrast, the neuron depicted in Fig. 3D–F shows a dramatic effect of adaptation, with a reduction in response at orientations at and near the adapting orientation, a broadening of the tuning curve, and a shift in the preferred orientation away from the adapting orientation, created by an increase in the response to orientations on the flank of the tuning curve away from the adapting orientation (Fig. 3F). This neuron is located at a pinwheel center (Fig. 3D), and the distribution of orientations in the local circuit is therefore broad (Fig. 3E).

The contrasting effects of adaptation on these two cells suggest that the orientation representation in the local network is a critical factor in determining the effect of pattern adaptation. Indeed, there is a relationship between the orientation selectivity of the local representation, and the magnitude of the effects of adaptation. Figure 4 shows that both the magnitude of tuning shift (Fig. 4A), and the magnitude of change in response magnitude on the near flank of the tuning curve (Fig. 4B) are strongly related to the selectivity of the local orientation representation. Interestingly, the selectivity of the subthreshold V_m tuning is also linearly related to the selectivity in the local orientation map (Fig. 4C). This suggests that the broad subthreshold inputs from the local circuit may provide the synaptic substrate for orientation shifts induced by adaptation. Neurons in orientation domains only receive inputs from a narrow range of orientations, and cannot therefore be modified by adapting stimuli outside that range. Neurons near pinwheel centers, on the other hand, receive substantial subthreshold inputs over a broad range of orientations, and the spike tuning can be shifted by alterations of the excitatory and/or

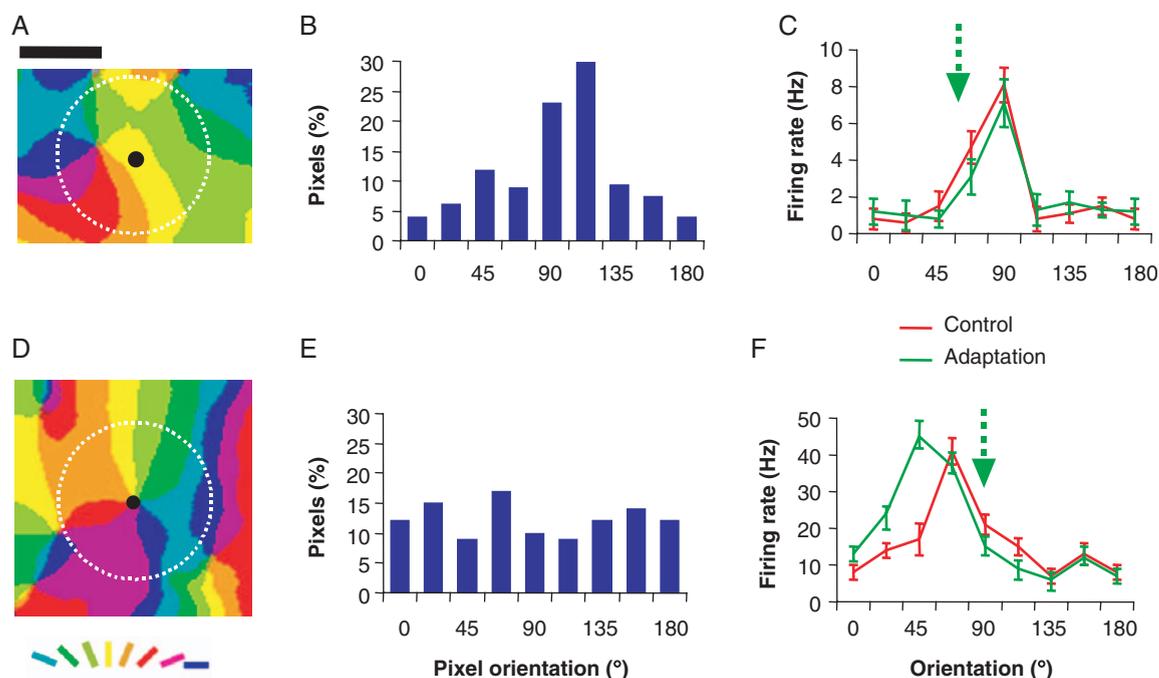


Fig. 3. Adaptation-induced tuning curve changes depend on location in the orientation map. A–C. Adaptation in a neuron located in an orientation domain. A. Orientation map surrounding the location of the recorded cell. Scale bar represent 500 μm . Dashed white line represents a radius of 500 μm centered on the recording site. Orientation color code is as depicted by the color scale in D. B. Histogram of the distribution of preferred orientation values within the white circle in the orientation map in A. Bars are normalized to yield a percentage of total area. C. Firing rate tuning curves obtained pre-adaptation and post-adaptation, color coded as in the legend below the graph. The orientation of the adapting stimulus is indicated by the vertical dashed arrow. D–F. Adaptation in a neuron located in a pinwheel center. All conventions as in A–C. Adapted from [Dragoi et al. \(2001\)](#).

inhibitory synaptic weights across a broad range of orientations. The relationship between the selectivity of the local circuit and the behavior of individual neurons highlights an important point. Pinwheel centers and orientation domains represent the extremes of a continuum of local orientation representation within the map of orientation preference. The inputs to any neuron are in part determined by the representation in the local network. These inputs provide a balance of excitation and inhibition, which regulates the responses and produces invariant output (spike) tuning. The balance can be more critical at some points (pinwheel centers) than others (orientation domains), and thus perturbations of inputs results in larger shifts near pinwheel centers.

In other words, the effects of changes in feedforward inputs can be better understood as influencing

the local network as a whole than by influencing individual neurons in isolation. A similar view has previously been put forward in the context of the influence of stimuli in the receptive field surround on responses to stimuli in the receptive field center ([Somers et al., 1998](#)). In a network model of long-range connections in V1, [Somers et al. \(1998\)](#) showed that the contrast-dependent effects of long-range inputs, while counter-intuitive from the perspective of their effect on a single cell, arise naturally through excitatory/inhibitory balance in the local cortical circuit. The same principle may apply to the orientation-dependent effects of specific adaptation of feedforward inputs. In light of the diversity of local networks inherent from the orientation map structure, we can further propose that the influence of changes in inputs on single neurons (be they feedforward, long-range intracortical, or top-down), will be

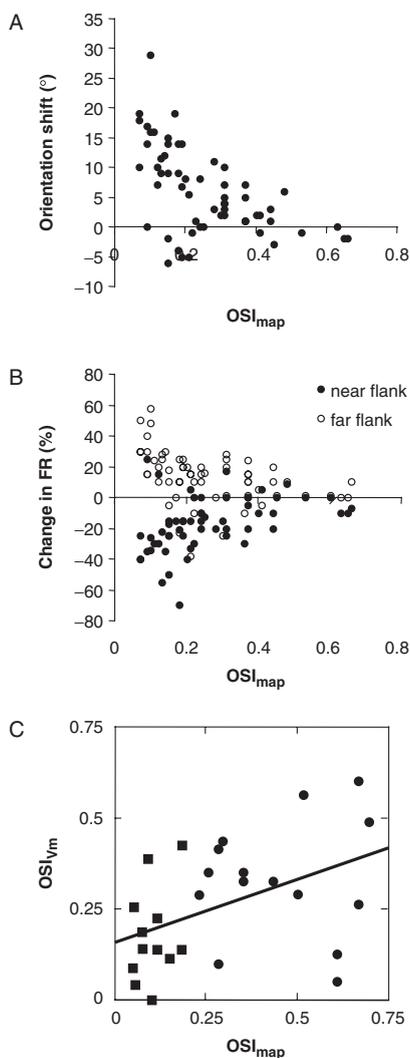


Fig. 4. Adaptation effects vary systematically with position in the orientation map. A. Scatter plot of the magnitude of adaptation-induced orientation shift, as a function of the OSI of the local patch of cortex surrounding the recording site (OSI_{map}). B. Scatter plot of the adaptation-induced changes in response amplitude as a function of OSI_{map} for the same population of cells as in B. Blue points represent changes in firing rate (FR) on the near flank of the tuning curve — orientations intermediate between the preferred orientation and the adapting orientation. Red points indicate changes in firing rate on the far flank — orientations on the opposite side of the preferred orientation, relative to the adapting orientation. C. Scatter plot of the OSI of the membrane depolarization (*V*_m) tuning curves as a function of OSI_{map}. Squares represent neurons classified as pinwheel center neurons, and circles those designated as orientation domain neurons. Adapted from Dragoi et al. (2000) and Schummers et al. (2002).

refracted through the structure of the local orientation representation.

Top-down influences on orientation tuning

New evidence from several laboratories indicates that visual processing even in the early cortical stages is not merely a bottom-up process of sorting and onward transmission of afferent information, but rather is powerfully modified by internal states such as attention, expectation, or past history of the stimulus. There is considerable anatomical support for the idea that higher order cortical processes can influence early sensory areas through an extensive network of intra-areal connections that are highly reciprocal (Felleman and Van Essen, 1991; Salin and Bullier, 1995; Angelucci et al., 2002). A more intriguing proposal is that top-down influences, and cortico-cortical interactions in general, occur via driving cortical projections through specific thalamic nuclei (Sherman and Guillery, 2002). Top-down or state-dependent inputs can have diverse effects; they can influence perception by increasing stimulus selectivity (by enhancing relevant and/or suppressing irrelevant information), or aid in decision making or guide sensory-motor systems according to behavioral contingencies. In sum, the new findings indicate that early visual cortical areas (or even subcortical structures) are part of a distributed rather than simply a hierarchical network for vision, and that bottom-up and top-down processes interact dynamically so as to continuously recalibrate neuronal responses to behaviorally relevant stimuli.

A recent report used an interesting variation of adaptation to study object based attention in human lateral occipital cortex (LOC), considered to be homologous to inferotemporal (IT) cortex in monkeys (Murray and Wojciulik, 2004). It is generally believed that attention increases neuronal responses to the attended location or stimulus, via either a multiplicative or an additive process. An alternative possibility is that attention causes an increase in selectivity of a specific subpopulation of neurons that responds to the attended stimulus. The authors repeatedly presented the same stimulus in pairs of either the same orientation or different orientations. The subjects' task was to either perform color

matching or orientation matching between successive pairs. It was found that the fMRI signal was sharply enhanced when subjects performed orientation matching, and therefore attended to the stimulus orientation. A likely explanation for this finding is that attention increased sensitivity to orientation differences or narrowed the tuning of the sub-population of neurons, thereby increasing the selectivity of these neurons.

One direct consequence of an adaptive process in early visual cortex that enhances sensitivity to changes relates to saccadic behavior during natural vision. Natural viewing involves rapid saccadic eye movements (3–4 saccades per second) interspersed by periods of brief fixation (Yarbus, 1967). During these fixation epochs, neurons encounter image patches that are well correlated in local image features, such as orientation (Dragoi et al., 2002). Brief exposure to such spatially correlated image patches induces short term adaptation that results in reduction in response of neurons at their preferred orientation, thereby possibly reducing the correlation among neuronal responses (Attneave, 1954; Yarbus, 1967; Barlow, 1990). A close examination of saccadic behavior of humans and monkeys during viewing of natural scenes reveals that a substantial percentage of saccades are made to image locations that are uncorrelated in their local attributes. Therefore a brief fixation is typically followed by a saccade to an entirely different part of the scene where the change in local statistics (e.g., orientation) is maximal. In a recent study the role of brief adaptation on orientation discrimination in humans and monkeys was explored (Dragoi et al., 2002). It was found that short-term adaptation by oriented gratings, on the time scale of visual fixation during natural viewing, markedly improves orientation discrimination for orthogonal orientations. We further explored the effect of rapid adaptation on single neuron responses in V1. Specifically, we were interested in the temporal dynamics of orientation tuning under simulated conditions of brief fixational adaptation. By employing a reverse correlation procedure, the dynamics of orientation tuning were captured on a millisecond time scale and allowed us to uncover effects of brief adaptation on the development of orientation tuning. Single neurons exhibited distinct behaviors with and without brief adaptation: adapting orientations near

the preferred orientation of the cells delayed the development of orientation tuned response; conversely response tuning was accelerated after adapting to an orthogonal orientation. Importantly, adaptation near the preferred orientation suppressed responses on the near flank of the tuning curve, broadened the tuning width, and shifting the preferred orientation away from the adapting stimulus. On the other hand, orthogonal adaptation maintained the optimal orientation but sharpened the orientation tuning of the neurons.

These findings are in contrast with the prevalent notion that the role of visual attention is to create a saliency map of the visual scene, which the system arrives at through a “guesswork” based on the relative strength of stimulus features, and which guides decision processes and visuomotor behavior (Treue, 2003). At least one aspect of the visual saccade system seems to be an adaptive process that accentuates differences in image statistics, by a dynamic interaction between top-down and bottom-up influences. Short-term adaptation sharpens neuronal selectivity and continuously updates processing of the visual scene.

Extra-retinal influences on bottom-up processes

Vision, and the response of cortical neurons, is influenced not only by spatial statistics but also by the temporal statistics of visual stimuli. For example, a central aspect of visual processing is the acquisition of an internal representation of stimulus location derived from the temporal order or history of stimulus appearance. Most investigations of the control of visually guided movements have focused on how parietal and frontal cortex, in conjunction with brain stem circuits, are involved in target selection and eye movement control (Platt and Glimcher, 1999; Schall and Thompson, 1999; Corbetta and Shulman, 2002; Glimcher, 2002). However, recent work has claimed a role for early visual cortex in saccade planning and decision making (Schiller and Tehovnik, 2001; Nakamura and Colby, 2002). Recently, the influence of the temporal order of stimuli presented at specific locations on performance in a gaze direction task was examined. The behavioral data point to acquisition of an internal representation

of stimulus location based on prior presentations, and the physiological data show a surprising and substantial involvement of V1. The results are consistent with early visual cortex being a key part of a distributed network of cortical areas that is involved in acquiring the internal representation (Sharma et al., 2003).

A gaze direction task was devised in which subjects could acquire information about future stimulus locations in one task condition but not in another. The task consisted of the appearance of a fixation spot at one of three locations on a computer screen placed in front of a subject. In one condition, the location of the fixation spot varied randomly from trial to trial (termed “randomized” trials), while in the other, the spot appeared repeatedly at the same location for a succession of trials (termed “grouped” trials). Subjects did not receive any prior cue as to which sequence was in effect. Human subjects were asked to indicate where the target would appear next as trials progressed in either the randomized or the grouped sequence. While the probability of successful prediction in the randomized trials was independent of trial number, the prediction probability in the grouped trials tracked the Bayesian target probability as the trials progressed. That is, a significant reduction was noticed in prediction uncertainty when the grouped trials were presented compared to randomized trials. Thus, the manner of stimulus presentation, and the order of stimulus appearance at a given location, provided information about future stimulus locations, which observers could assimilate.

Next, alert monkeys were trained in a similar task. Once the fixation spot appeared in one of the three locations, animals made a saccade and achieved stable fixation. Their latency to achieve fixation in the randomized and grouped task conditions was measured. It has been shown previously that the saccade latency to a visual target is a sensitive indicator of the likelihood of the target’s appearance (Luce, 1986; Kowler, 1990; Carpenter and Williams, 1995). Similar to human performance in the two task conditions, it was reasoned that fixation latency would shorten as monkeys attained knowledge of target location, but not otherwise. As expected, fixation latency was approximately constant from trial to trial in the randomized condition but shortened significantly as trials progressed in the grouped condition.

Importantly, the performance of humans and monkeys was consistent with the Bayesian probability of target appearance. These findings indicate the acquisition of an internal representation of stimulus location with successive trials in the grouped condition of the task, in both humans and monkeys.

While the monkeys performed the fixation task in the two trial conditions, the single neuron responses in V1 to oriented sinusoidal gratings presented in the receptive field of neurons within 3–5 degrees from the fixation spot were also recorded. It is known that integration of retinal and extra-retinal inputs to the brain is essential for localization of stimuli in space, allocation of attention, or dynamic stabilization of receptive fields (Andersen et al., 1985; Downing, 1988; Motter and Poggio, 1990). A number of studies have reported that responses of a subset of V1 neurons are modulated by the direction of gaze (Weyand and Malpeli, 1993; Guo and Li, 1997; Trotter and Celebrini, 1999; Rosenbluth and Allman, 2002). It is however unclear if the modulation in V1 response is purely gaze related or other top-down processes play a role in this response modification. Our findings demonstrate that V1 responses are modulated by gaze direction in a task dependent manner. Figure 5A depicts orientation tuning curves of a V1 neuron in randomized and grouped trials in three gaze directions. The response of the neuron was significantly modulated when stimuli appeared at a particular gaze direction in a particular sequence: stimuli appearing in a grouped sequence at one location caused neurons to respond significantly more (or, in other neurons, less) than when stimuli appeared randomly. In other words, responses to the same visual stimulus (a grating of optimal orientation for a neuron), presented at the same location (and hence subtending the same angle of gaze), are altered when stimuli are presented in one sequence of trials (the grouped sequence) than in another (the random sequence). It is important to note that each recorded neuron had its own preference for modulation in a particular gaze direction and there was no systematic bias in the neuronal population for a particular orientation or gaze direction. On a population basis, more than 40% of the recorded neurons responded in a manner similar to the neuron of Fig. 5A. An internal representation index (IRI) that signifies response difference in the two trial conditions regardless of

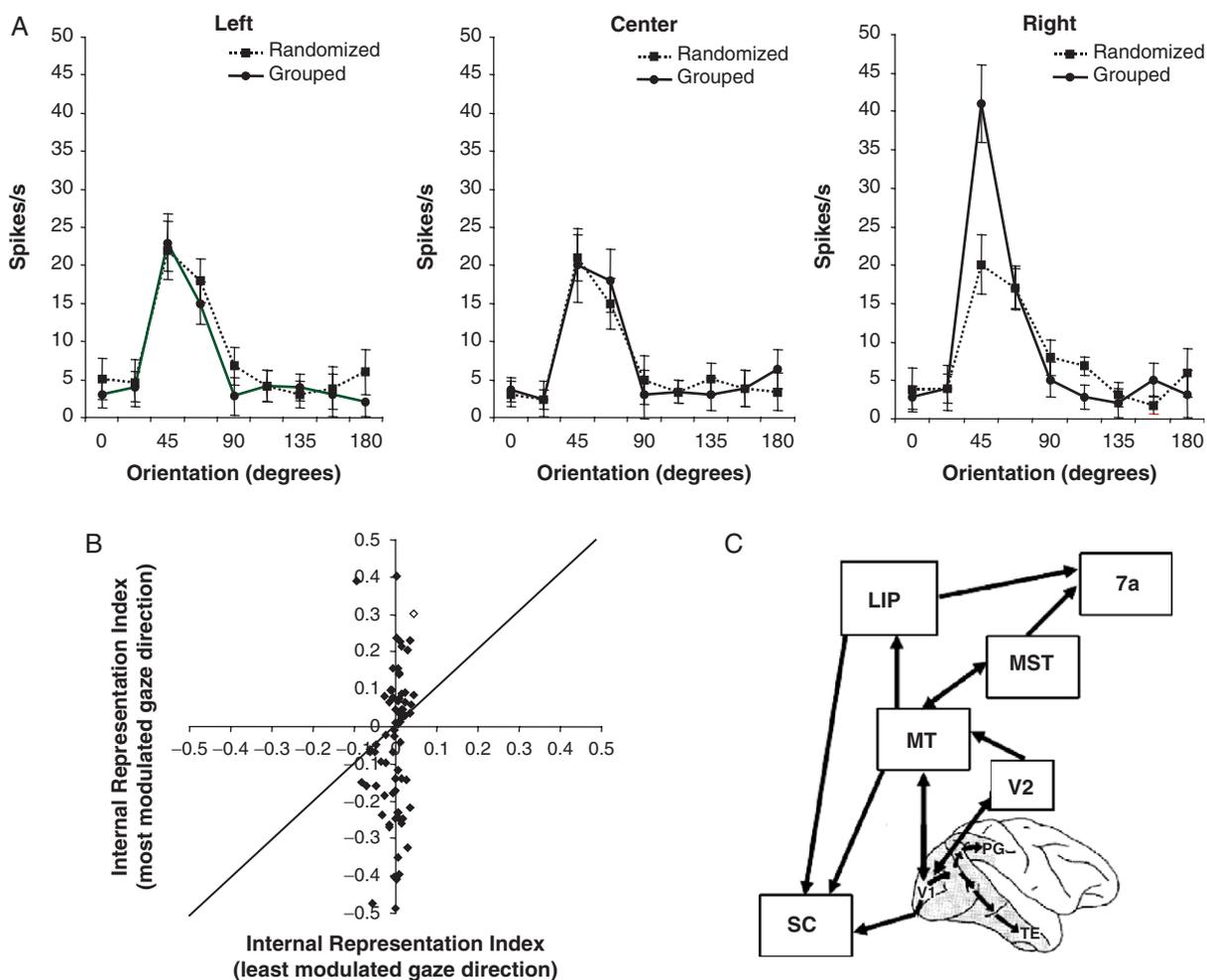


Fig. 5. Modulation of orientation selective responses of V1 neurons in alert monkeys by an internal representation of stimulus location. A. Orientation tuning curves of a V1 neuron when a fixation spot was presented in left, center and right locations on a screen in front of the animal. The darker curves are derived from ‘grouped’ trials while the lighter ones are from ‘randomized’ trials. There was a significant increase in response in the grouped condition when the monkey’s gaze was directed to the right. B. Scatterplot of the response index of the population data ($n=67$ cells) in the least modulated gaze direction compared to most modulated gaze direction. The cell of panel A is shown as a red dot. C. Schematic diagram showing interconnectivity among visual cortical areas (of both dorsal and ventral streams) and motor outputs to the superior colliculus (SC). V1 is an integral part of this distributed network that is involved in processing bottom-up and top-down interactions. Abbreviations, primary visual cortex (V1); secondary visual cortex (V2); middle temporal area (MT); lateral intraparietal cortex (LIP); medial superior temporal area (MST). Adapted from Sharma et al. (2003).

gaze direction was calculated. Figure 5B shows the population IRI data calculated for the best modulated gaze direction of individual neurons versus the least modulated gaze direction. Positive IRI values indicate a response increase in grouped trials. These data demonstrate that a substantial proportion of V1 neurons represent in their responses the probability of

target appearance derived from the temporal sequence of stimuli.

How might V1 neurons dynamically alter their responses to signal such an internal representation? The modulation of V1 responses constitutes an active shaping of the orientation tuning curve, for responses to the preferred orientation are specifically and

selectively modified as the representation is acquired. Orientation selective responses are similarly modified after visual discrimination learning or during short-term visual memory (Gilbert et al., 2001; Schoups et al., 2001; Super et al., 2001). The response change in V1 neurons during the grouped condition involves the integration of top-down inputs carrying task-dependent signals with bottom-up ones carrying visual signals. Top-down signals are likely to arise from the parietal and frontal cortex, which are known to play a key role in saccade decisions and commands (Andersen et al., 1997; Glimcher, 2001; Schall, 2001; Goldberg et al., 2002). As shown in the cartoon in Figure 5C, V1 is part of this network and receives feedback projections from these areas. Such feedback would in turn modulate the strength of recurrent connections between local V1 neurons (Dragoi and Sur, 2000; Somers et al., 2001), that modify the amplification of feedforward inputs to V1 neurons, and constitute a plausible mechanism by which orientation tuning can be altered as trials progress.

Finally, what does a change in orientation tuning as a function of stimulus sequence imply for vision? It is possible, even likely, that the change in response constitutes a motor signal rather than a purely sensory one. V1 projections importantly target not only higher sensory cortical areas, but also subcortical targets such as the superior colliculus which are involved in eye movements. It is suggested that the output of a cortical area is interpreted differently depending on the role of the target: structures concerned with visual processing would read the V1 output as providing information about the image, whereas structures concerned with eye movements would utilize the output for modulating gaze. On this view, no area of the cortex, not even the primary visual cortex, is only a sensory area — rather, every area potentially contributes to movement as well. Indeed, it has been cogently argued that mechanisms of perception necessarily include action, with the thalamus involved critically in receiving copies of the efferent output (Guillery and Sherman, 2002).

Conclusions

This chapter has analyzed evidence that orientation tuning in V1 can be dynamically modified by changes

in bottom-up and top-down inputs. Manipulation of bottom-up inputs by adaptation or pharmacological blockade can lead to changes in tuning properties. Behavioral tasks that require the use of visual information for completion can also lead to changes in orientation tuning. These inputs most likely exert their effects on V1 by interactions at the level of the local cortical circuit, rather than on individual neurons. The local network is characterized by balanced excitation and inhibition, which naturally regulate tuning. Thus, by tapping into network at the level of the local circuitry, bottom-up and top-down inputs can modify tuning in complex and behaviorally useful ways. We have shown that the balance of inhibition and excitation is particularly important near pinwheel centers in the orientation maps. Short-term modification of bottom-up inputs by orientation adaptation has much greater effects at these locations. It is suspected that pinwheel centers may be more susceptible to top-down modification in orientation space as well.

References

- Ahmed, B., Anderson, J.C., Douglas, R.J., Martin, K.A. and Nelson, J.C. (1994) Polyneuronal innervation of spiny stellate neurons in cat visual cortex. *J. Comp. Neurol.*, 341: 39–49.
- Alonso, J.M., Usrey, W.M. and Reid, R.C. (2001) Rules of connectivity between geniculate cells and simple cells in cat primary visual cortex. *J. Neurosci.*, 21: 4002–4015.
- Andersen, R.A., Essick, G.K. and Siegel, R.M. (1985) Encoding of spatial location by posterior parietal neurons. *Science*, 230: 456–458.
- Andersen, R.A., Snyder, L.H., Bradley, D.C. and Xing, J. (1997) Multimodal representation of space in the posterior parietal cortex and its use in planning movements. *Annu. Rev. Neurosci.*, 20: 303–330.
- Anderson, J.S., Carandini, M. and Ferster, D. (2000) Orientation tuning of input conductance, excitation, and inhibition in cat primary visual cortex. *J. Neurophysiol.*, 84: 909–926.
- Angelucci, A., Levitt, J.B., Walton, E.J., Hupe, J.M., Bullier, J. and Lund, J.S. (2002) Circuits for local and global signal integration in primary visual cortex. *J. Neurosci.*, 22: 8633–8646.
- Attneave, F. (1954) Some informational aspects of visual perception. *Psychol. Rev.*, 61: 183–193.
- Barlow, H.B. (1990) A theory about the functional role and synaptic mechanism of after-effects. In: Blakemore, C. (Ed.),

- Vision: Coding and Efficiency, Cambridge University Press, Cambridge, UK, pp. 363–375.
- Ben-Yishai, R., Bar-Or, R.L. and Sompolinsky, H. (1995) Theory of orientation tuning in visual cortex. *Proc. Natl. Acad. Sci. USA*, 92: 3844–3848.
- Bonds, A.B. (1989) Role of inhibition in the specification of orientation selectivity of cells in the cat striate cortex. *Vis. Neurosci.*, 2: 41–55.
- Carandini, M. (2000) Visual cortex: Fatigue and adaptation. *Curr Biol.*, 10: R605–607.
- Carandini, M. and Ringach, D.L. (1997) Predictions of a recurrent model of orientation selectivity. *Vision Res.*, 37: 3061–3071.
- Carpenter, R.H. and Williams, M.L. (1995) Neural computation of log likelihood in control of saccadic eye movements. *Nature*, 377: 59–62.
- Chung, S. and Ferster, D. (1998) Strength and orientation tuning of the thalamic input to simple cells revealed by electrically evoked cortical suppression. *Neuron*, 20: 1177–1189.
- Chung, S., Li, X. and Nelson, S.B. (2002) Short-term depression at thalamocortical synapses contributes to rapid adaptation of cortical sensory responses in vivo. *Neuron*, 34: 437–446.
- Corbetta, M. and Shulman, G.L. (2002) Control of goal-directed and stimulus-driven attention in the brain. *Nat. Rev. Neurosci.*, 3: 201–215.
- Crook, J.M. and Eysel, U.T. (1992) GABA-induced inactivation of functionally characterized sites in cat visual cortex (area 18): effects on orientation tuning. *J. Neurosci.*, 12: 1816–1825.
- Crook, J.M., Kisvarday, Z.F. and Eysel, U.T. (1997) GABA-induced inactivation of functionally characterized sites in cat striate cortex: Effects on orientation tuning and direction selectivity. *Vis. Neurosci.*, 14: 141–158.
- Crook, J.M., Kisvarday, Z.F. and Eysel, U.T. (1998) Evidence for a contribution of lateral inhibition to orientation tuning and direction selectivity in cat visual cortex: Reversible inactivation of functionally characterized sites combined with neuroanatomical tracing techniques. *Eur. J. Neurosci.*, 10: 2056–2075.
- Douglas, R.J., Koch, C., Mahowald, M., Martin, K.A. and Suarez, H.H. (1995) Recurrent excitation in neocortical circuits. *Science*, 269: 981–985.
- Downing, C.J. (1988) Expectancy and visual-spatial attention: effects on perceptual quality. *J. Exp. Psychol. Hum. Percept Perform.*, 14: 188–202.
- Dragoi, V. and Sur, M. (2000) Dynamic properties of recurrent inhibition in primary visual cortex: contrast and orientation dependence of contextual effects. *J. Neurophysiol.*, 83: 1019–1030.
- Dragoi, V. and Sur, M. (2003) Plasticity of orientation processing in adult visual cortex. In: Chalupa, L.M. and Werner, J.S., (Eds.), *The Visual Neurosciences*, MIT Press, Cambridge, pp. 1654–1664.
- Dragoi, V., Sharma, J. and Sur, M. (2000) Adaptation-induced plasticity of orientation tuning in adult visual cortex. *Neuron*, 28: 287–298.
- Dragoi, V., Rivadulla, C. and Sur, M. (2001) Foci of orientation plasticity in visual cortex. *Nature*, 411: 80–86.
- Dragoi, V., Sharma, J., Miller, E.K. and Sur, M. (2002) Dynamics of neuronal sensitivity in visual cortex and local feature discrimination. *Nat. Neurosci.*, 5: 883–891.
- Eysel, U.T., Shevelev, I.A., Lazareva, N.A. and Sharaev, G.A. (1998) Orientation tuning and receptive field structure in cat striate neurons during local blockade of intracortical inhibition. *Neuroscience*, 84: 25–36.
- Felleman, D.J. and Van Essen, D.C. (1991) Distributed hierarchical processing in the primate cerebral cortex. *Cereb Cortex*, 1: 1–47.
- Ferster, D. (1986) Orientation selectivity of synaptic potentials in neurons of cat primary visual cortex. *J. Neurosci.*, 6: 1284–1301.
- Ferster, D. and Miller, K.D. (2000) Neural mechanisms of orientation selectivity in the visual cortex. *Annu. Rev. Neurosci.*, 23: 441–471.
- Ferster, D., Chung, S. and Wheat, H. (1996) Orientation selectivity of thalamic input to simple cells of cat visual cortex. *Nature*, 380: 249–252.
- Gilbert, C.D. (1977) Laminar differences in receptive field properties of cells in cat primary visual cortex. *J. Physiol.*, 268: 391–421.
- Gilbert, C.D. (1992) Horizontal integration and cortical dynamics. *Neuron*, 9: 1–13.
- Gilbert, C.D., Sigman, M. and Crist, R.E. (2001) The neural basis of perceptual learning. *Neuron*, 31: 681–697.
- Glimcher, P. (2002) Decisions, decisions, decisions: choosing a biological science of choice. *Neuron*, 36: 323–332.
- Glimcher, P.W. (2001) Making choices: the neurophysiology of visual-saccadic decision making. *Trends Neurosci.*, 24: 654–659.
- Goldberg, M.E., Bisley, J., Powell, K.D., Gottlieb, J. and Kusunoki, M. (2002) The role of the lateral intraparietal area of the monkey in the generation of saccades and visuospatial attention. *Ann. N Y Acad. Sci.*, 956: 205–215.
- Guillery, R.W. and Sherman, S.M. (2002) The thalamus as a monitor of motor outputs. *Philos. Trans. R Soc. Lond. B Biol. Sci.*, 357: 1809–1821.
- Guo, K. and Li, C.Y. (1997) Eye position-dependent activation of neurones in striate cortex of macaque. *Neuroreport*, 8: 1405–1409.
- Hubel, D.H. and Wiesel, T.H. (1962) Receptive fields, binocular interaction and functional architecture of the cat's visual cortex. *J. Physiol.*, 160: 106–154.
- Kang, K., Shelley, M. and Sompolinsky, H. (2003) Mexican hats and pinwheels in visual cortex. *Proc. Natl. Acad. Sci. USA*, 100: 2848–2853.

- Kowler, E. (1990) The role of visual and cognitive processes in the control of eye movement. *Rev. Oculomot. Res.*, 4: 1–70.
- Lampl, I., Anderson, J.S., Gillespie, D.C. and Ferster, D. (2001) Prediction of orientation selectivity from receptive field architecture in simple cells of cat visual cortex. *Neuron*, 30: 263–274.
- Luce, R.D. (1986) *Response Times: Their Role in Inferring Elementary Mental Organization*, Oxford Press, New York.
- Lund, J.S., Angelucci, A. and Bressloff, P.C. (2003) Anatomical substrates for functional columns in macaque monkey primary visual cortex. *Cereb Cortex*, 13: 15–24.
- Maldonado, P.E., Godecke, I., Gray, C.M. and Bonhoeffer, T. (1997) Orientation selectivity in pinwheel centers in cat striate cortex. *Science*, 276: 1551–1555.
- Marino, J., Schummers, J. and Sur, M. (2003) Input conductance at different locations within V1 orientation map. *Soc. Neurosci. Abstr.*, 29.
- Martinez, L.M., Alonso, J.M., Reid, R.C. and Hirsch, J.A. (2002) Laminar processing of stimulus orientation in cat visual cortex. *J. Physiol.*, 540: 321–333.
- McLaughlin, D., Shapley, R., Shelley, M. and Wielaard, D.J. (2000) A neuronal network model of macaque primary visual cortex (V1): orientation selectivity and dynamics in the input layer 4Calpha. *Proc. Natl. Acad. Sci. USA*, 97: 8087–8092.
- Monier, C., Chavane, F., Baudot, P., Graham, L.J. and Fregnac, Y. (2003) Orientation and direction selectivity of synaptic inputs in visual cortical neurons: a diversity of combinations produces spike tuning. *Neuron*, 37: 663–680.
- Motter, B.C. and Poggio, G.F. (1990) Dynamic stabilization of receptive fields of cortical neurons (VI) during fixation of gaze in the macaque. *Exp. Brain Res.*, 83: 37–43.
- Movshon, J.A., Thompson, I.D. and Tolhurst, D.J. (1978a) Receptive field organization of complex cells in the cat's striate cortex. *J. Physiol.*, 283: 79–99.
- Movshon, J.A., Thompson, I.D. and Tolhurst, D.J. (1978b) Spatial summation in the receptive fields of simple cells in the cat's striate cortex. *J. Physiol.*, 283: 53–77.
- Murray, S.O. and Wojciulik, E. (2004) Attention increases neural selectivity in the human lateral occipital complex. *Nat. Neurosci.*, 7: 70–74.
- Nakamura, K. and Colby, C.L. (2002) Updating of the visual representation in monkey striate and extrastriate cortex during saccades. *Proc. Natl. Acad. Sci. USA*, 99: 4026–4031.
- Nelson, S., Toth, L., Sheth, B. and Sur, M. (1994) Orientation selectivity of cortical neurons during intracellular blockade of inhibition. *Science*, 265: 774–777.
- Platt, M.L. and Glimcher, P.W. (1999) Neural correlates of decision variables in parietal cortex. *Nature*, 400: 233–238.
- Pugh, M.C., Ringach, D.L., Shapley, R. and Shelley, M.J. (2000) Computational modeling of orientation tuning dynamics in monkey primary visual cortex. *J. Comput. Neurosci.*, 8: 143–159.
- Reid, R.C. and Alonso, J.M. (1995) Specificity of monosynaptic connections from thalamus to visual cortex. *Nature*, 378: 281–284.
- Riesenhuber, M. and Poggio, T. (2000) Models of object recognition. *Nat. Neurosci.*, 3 Suppl: 1199–1204.
- Ringach, D.L., Shapley, R.M. and Hawken, M.J. (2002) Orientation selectivity in macaque V1: diversity and laminar dependence. *J. Neurosci.*, 22: 5639–5651.
- Rosenbluth, D. and Allman, J.M. (2002) The effect of gaze angle and fixation distance on the responses of neurons in V1, V2, and V4. *Neuron*, 33: 143–149.
- Salin, P.A. and Bullier, J. (1995) Corticocortical connections in the visual system: structure and function. *Physiol. Rev.*, 75: 107–154.
- Sanchez-Vives, M.V., Nowak, L.G. and McCormick, D.A. (2000a) Membrane mechanisms underlying contrast adaptation in cat area 17 in vivo. *J. Neurosci.*, 20: 4267–4285.
- Sanchez-Vives, M.V., Nowak, L.G. and McCormick, D.A. (2000b) Cellular mechanisms of long-lasting adaptation in visual cortical neurons in vitro. *J. Neurosci.*, 20: 4286–4299.
- Sato, H., Katsuyama, N., Tamura, H., Hata, Y. and Tsumoto, T. (1996) Mechanisms underlying orientation selectivity of neurons in the primary visual cortex of the macaque. *J. Physiol.*, 494(Pt 3): 757–771.
- Schall, J.D. (2001) Neural basis of deciding, choosing and acting. *Nat. Rev. Neurosci.*, 2: 33–42.
- Schall, J.D. and Thompson, K.G. (1999) Neural selection and control of visually guided eye movements. *Annu. Rev. Neurosci.*, 22: 241–259.
- Schiller, P.H. and Tehovnik, E.J. (2001) Look and see: how the brain moves your eyes about. *Prog. Brain Res.*, 134: 127–142.
- Schoups, A., Vogels, R., Qian, N. and Orban, G. (2001) Practising orientation identification improves orientation coding in V1 neurons. *Nature*, 412: 549–553.
- Schummers, J., Marino, J. and Sur, M. (2002) Synaptic integration by V1 neurons depends on location within the orientation map. *Neuron*, 36: 969–978.
- Sharma, J., Dragoi, V., Tenenbaum, J.B., Miller, E.K. and Sur, M. (2003) V1 neurons signal acquisition of an internal representation of stimulus location. *Science*, 300: 1758–1763.
- Sherman, S.M. and Guillery, R.W. (2002) The role of the thalamus in the flow of information to the cortex. *Philos. Trans. R Soc. Lond. B Biol. Sci.*, 357: 1695–1708.
- Sillito, A.M. (1975) The contribution of inhibitory mechanisms to the receptive field properties of neurones in the striate cortex of the cat. *J. Physiol.*, 250: 305–329.
- Sillito, A.M., Kemp, J.A., Milson, J.A. and Berardi, N. (1980) A re-evaluation of the mechanisms underlying simple cell orientation selectivity. *Brain Res.*, 194: 517–520.
- Solomon, S.G., Peirce, J.W., Dhruv, N.T. and Lennie, P. (2004) Profound contrast adaptation early in the visual pathway. *Neuron*, 42: 155–162.

- Somers, D., Dragoi, V. and Sur, M. (2001) Orientation selectivity and its modulation by local and long-range connections in visual cortex. In: Payne, B.R. and Peters, A., (Eds.), *The Cat Primary Visual Cortex*, Academic Press, Boston, pp. 471–520.
- Somers, D.C., Nelson, S.B. and Sur, M. (1995) An emergent model of orientation selectivity in cat visual cortical simple cells. *J. Neurosci.*, 15: 5448–5465.
- Somers, D.C., Todorov, E.V., Siapas, A.G., Toth, L.J., Kim, D.S. and Sur, M. (1998) A local circuit approach to understanding integration of long-range inputs in primary visual cortex. *Cereb Cortex*, 8: 204–217.
- Sompolinsky, H. and Shapley, R. (1997) New perspectives on the mechanisms for orientation selectivity. *Curr. Opin. Neurobiol.*, 7: 514–522.
- Super, H., Spekreijse, H. and Lamme, V.A. (2001) A neural correlate of working memory in the monkey primary visual cortex. *Science*, 293: 120–124.
- Sur, M., Schummers, J. and Dragoi, V. (2002) Cortical plasticity: time for a change. *Curr. Biol.*, 12: R168–70.
- Treue, S. (2003) Visual attention: the where, what, how and why of saliency. *Curr. Opin. Neurobiol.*, 13: 428–432.
- Trotter, Y. and Celebrini, S. (1999) Gaze direction controls response gain in primary visual-cortex neurons. *Nature*, 398: 239–242.
- Troyer, T.W., Krukowski, A.E. and Miller, K.D. (2002) LGN input to simple cells and contrast-invariant orientation tuning: an analysis. *J. Neurophysiol.*, 87: 2741–2752.
- Troyer, T.W., Krukowski, A.E., Priebe, N.J. and Miller, K.D. (1998) Contrast-invariant orientation tuning in cat visual cortex: thalamocortical input tuning and correlation-based intracortical connectivity. *J. Neurosci.*, 18: 5908–5927.
- Vidyasagar, T.R., Pei, X. and Volgushev, M. (1996) Multiple mechanisms underlying the orientation selectivity of visual cortical neurones. *Trends Neurosci.*, 19: 272–277.
- Volgushev, M., Pei, X., Vidyasagar, T.R. and Creutzfeldt, O.D. (1993) Excitation and inhibition in orientation selectivity of cat visual cortex neurons revealed by whole-cell recordings in vivo. *Vis. Neurosci.*, 10: 1151–1155.
- Weyand, T.G. and Malpeli, J.G. (1993) Responses of neurons in primary visual cortex are modulated by eye position. *J. Neurophysiol.*, 69: 2258–2260.
- Yarbus, A.L. (1967) *Eye Movement and Vision.*, Plenum Press, New York.