Review

Brain States: Top-Down Influences in Sensory Processing

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All cortical and thalamic levels of sensory processing are subject to powerful top-down influences, the shaping of lower-level processes by more complex information. New findings on the diversity of top-down interactions show that cortical areas function as adaptive processors, being subject to attention, expectation, and perceptual task. *Brain states* are determined by the interactions between multiple cortical areas and the modulation of intrinsic circuits by feedback connections. In perceptual learning, both the encoding and recall of learned information involves a selection of the appropriate inputs that convey information about the stimulus being discriminated. Disruption of this interaction may lead to behavioral disorders, including schizophrenia.

General Theoretical Framework

Though neuroscientists are beginning to establish how the activation of cortical regions and the responses of cortical neurons correlate with behaviors, the enduring mystery is what is the nature of a *brain state*, the fundamental algorithm, at the level of cortical circuitry, by which cognition arises. To derive this algorithm, one must analyze brain circuits in a behavioral context. The classical view of information processing in the brain is based on a hierarchical organization. In the visual system, pathways start from the analysis of very simple, local attributes, and representation of visual information becomes progressively more complex as one moves up the hierarchy. However, from a computational point of view, it is unlikely that feedforward mechanisms alone can achieve flexible and invariant pattern recognition in a complex and rapidly changing environment. Recent findings have changed radically the view of the role, range, and functional diversity of top-down interactions in the cortex. We have learned that the function of any area of the cerebral cortex, including that of primary visual cortex, is subject to top-down influences of attention, expectation, and perceptual task. Internal representations of the world, acquired by experience, affect our brain's strategy for analyzing visual scenes. Vision is an active process, and the function of any cortical area is not fixed—each area runs different "programs" according to context and to the current perceptual requirements. Visual processing therefore involves countercurrent streams of information flow, and the operation of primary visual cortex involves an interaction between bottom-up information coming from the retina and feedback connections coming from higher-order cortical areas.

The general idea of top-down influence is that complex information that is represented at higher stages of processing influences simpler processes occurring at antecedent stages. Whereas some of the earlier work on spatial attention—the most studied instance of top-down modulation—suggested that significant influences of attention are found only at high levels in the visual pathway, it is becoming increasingly clear that even at the earliest stages in cortical sensory processing the functional properties of neurons are subject to influences of attention, as well as other forms of top-down modulation. The view of the perceptual role of attention has gone beyond the simplistic metaphor of attention acting as a "spotlight." The notion of attention itself may be inadequate as a descriptor of the full range of top-down influences that are exerted. Top-down influences have been shown to operate over a large variety of categories, including features, surfaces, objects, object categories, temporal context, and virtually any other perceptual group. Furthermore, the *effect* of top-down processing is not best represented as that resulting from a spotlight. Instead, the effects can be of many different kinds, not only augmenting or multiplying responses but also sharpening tuning curves, controlling contextual influences, or acting as a modulator of plasticity. One therefore has to either expand the definition of attention or describe a range of top-down influences that extend beyond the conventional use of the term.

The emerging evidence suggests that any cortical area is an adaptive processor. Rather than performing a fixed and stereotyped operation on input coming from the retina, it makes different calculations according to the immediate sensory and behavioral context. This moment-by-moment functional switching is likely mediated by an interaction between feedback connections from higher- to lower-order cortical areas and intrinsic cortical circuits. The role of top-down influences is then to set the cortex in a specific working mode according to behavioral requirements that are updated dynamically. In effect, these ideas reverse the central dogma of sensory processing, with a flow of information from higher- to lower-order cortical areas playing a role equal in importance to the
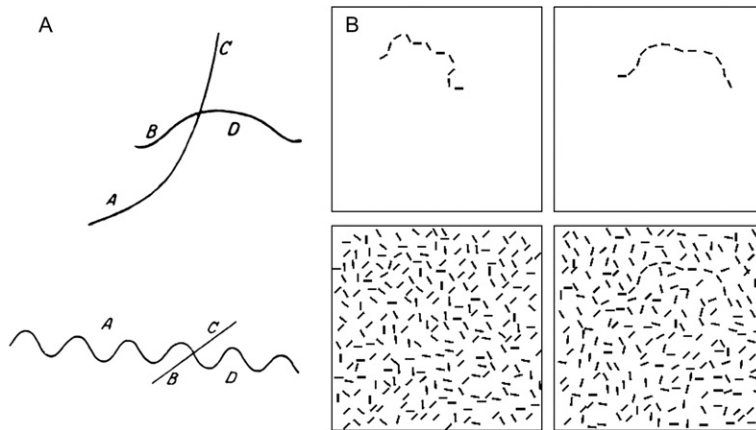
Figure 1. Gestalt Rules of Perceptual Organization

Certain contours are perceptually linked as a result of their geometric relationships.
(A) (Top) In this image, taken from the work of Max Wertheimer (1938b), one naturally associates line segments A and C as belonging to a common contour and dissociates segments A and D into separate contours, since A and C maintain the same orientation and curvature. This is known as the principle of "good continuation." (Bottom) The linkage of line elements can follow the organization of complex forms, such as the components A and D of the sinusoidal figure.
(B) Similar rules apply to contour saliency, where the relationships between line segments (relative orientation, proximity) govern the ability of the contour to pop out from a background of randomly oriented and positioned lines (adapted from Field et al., 1993). The contour on the right, composed of similarly oriented consecutive line elements, pops out when embedded in a background of randomly oriented and positioned lines. The contour on the left, where there is more change in the orientation of adjacent line elements, does not pop out and requires an extended search process to find.

feedforward pathways. The construction of a subjective percept involves making the best sense of sensory inputs based on a set of hypotheses or constraints derived by prior knowledge and contextual influences. Conversely, the top-down expectations and hypotheses are set by feedforward information, the sensory evidence. Under this view, there is no starting point for information flow. Even the prefrontal cortex, arguably the highest-order area in hierarchical views, can be set in different modes depending on task requirements. A strictly linear hierarchy would leave the highest levels without a source of top-down influences, so is it reasonable to speak at all of a starting point of information flow? Rather, in accordance with other theories of brain function (Mackay, 1956; Sporns et al., 1991; Mumford, 1992; Ullman, 1995, 1996; Di Lollo et al., 2000; Roelfsema et al., 2000; Rowe et al., 2002; Dehaene et al., 2003b; Lee and Mumford, 2003; Deco and Rolls, 2004, 2005), we propose that perception results from a reverberation (or resonance) between feedforward and top-down information. The ignition of such reverberation may differ in different contexts from an external stimulus to an internal state. In this view, the brain goes through a succession of *brain states*, with each state serving as the source of top-down influences for the subsequent state. In this dynamic process, task requirements and hypothesis setting are updated by sensory evidence, which in turn causes cortical areas to execute different programs. We propose that this may have an important role in learning and plasticity, postulating that perceptual learning may involve linking the appropriate intrinsic connections to the feedback signal associated with a particular task.

Here we will consider the kinds of information that may be conveyed by top-down interactions. The higher-order information may include learned, internal representations of the shapes of objects and of the abstract syntax of object relationships. It may also include information about behavioral context, which would include attention, expec-

tation, and perceptual task. We will also discuss ideas about how disruption of top-down influences, or disconnection of cortical *interactions*, may play a role in psychiatric disorders such as schizophrenia.

Lessons from Vision: Gestalt Rules, Context, Experience, and Top-Down Control

A classical view of top-down influences was given by the Gestalt psychologists early in the 20th century. They emphasized that the perception of objects was not achieved by an assembly of the parts of objects but rather that perception was based on holistic patterns. This was expressed most succinctly by Max Wertheimer, who observed that "There are entities where the behavior of the whole cannot be derived from its individual elements nor from the way these elements fit together; rather the opposite is true: the properties of any of the parts are determined by the intrinsic structural laws of the whole" (Wertheimer, 1938b). This is illustrated in the principle of "good continuation," where one tends to link line segments that are collinear and have similar orientation and not those making an abrupt change in direction (Figure 1A). This property is seen also in contour saliency, where contours made of line segments that have a gradual change in orientation tend to pop out from complex backgrounds, in contrast to those with random jitter in the orientation in their composite line segments (Figure 1B). The rule of good continuation makes more tractable the problem of how to link the elements of complex scenes into contours belonging to particular objects and segmenting them from the elements of the background.

One sees the rules of perceptual organization reflected in the response properties of neurons in primary visual cortex (V1). This is seen in the dependence of neuronal response upon context and the nature of the receptive field. A single oriented line segment will elicit a brisk response from a neuron when the appropriately oriented line is placed within a small part of visual space, that neuron's

receptive field. When that line is embedded within a complex background of randomly oriented and positioned line elements, the neuron's response is substantially inhibited. If one shifts line elements from the background into alignment with the line within the receptive field, the neuron's response becomes greatly facilitated (Kapadia et al., 1995, 1999; Li et al., 2006). In effect, the response of the neuron is as dependent on the global characteristics of the contour extending well outside the core of the neuron's receptive field as it is on the attributes of the line segment within the receptive field. This kind of effect is termed a "contextual" influence. Contextual influences, exerted on neuronal responses, have been implicated in a number of perceptual functions, including contour integration, surface segmentation, color constancy, and object motion. To what extent are these contextual influences "top-down" versus feedforward, and can one equate these influences with feedback connections from higher- to lower-order cortical areas, or are they derived from connections that are intrinsic to the areas where they are found?

The predominant view of cortical sensory processing is that as one proceeds along the visual pathway from primary visual cortex at the occipital pole to higher-order visual areas in the temporal lobe, neurons become selective to progressively more complex stimuli—"complexification." Early areas are thought to analyze simple attributes, such as orientation, direction of movement, or color, and this analysis is limited to local features within a very restricted window. Higher areas assemble the local stimulus features into more complex shapes, and they integrate information over progressively larger parts of visual space. But both anatomical and physiological evidence shows that even at the earliest stages of cortical processing neurons can integrate information over large areas and that they can be endowed with selectivity for complex shapes.

The belief that a particular property comes from a single source, however, is likely to be an oversimplification. The expression of one input to a neuron may depend on the state of activation of other inputs. The properties expressed by a given neuron or a given cortical area may be a function of an interaction between different cortical areas (McIntosh, 1999, 2000), and more specifically, between local circuits in an area and feedback and feedforward connections from other cortical areas.

Forms of Top-Down Control

Top-down influences are sometimes equated with attention, and attention is often thought of in terms of spatial attention, the location of attentional focus. But spatial attention is just one of many forms of attentional influence, and just about anything can be attended, including objects, features (such as orientation or color), motor actions, and time. Other top-down influences include perceptual task, priming, expectation, and hypothesis testing. Parsing the forms of top-down and attentional influence into different categories is not straightforward, since there is an overlap between them and some of the differences

may be merely semantic. It is difficult, for example, to separate object expectation from object-oriented attention, or perceptual task from feature-oriented attention. The important thing to note is the amount of information carried by top-down influences as a whole. They do not represent only a spatial coordinate, but the rich diversity of one's internal representations of object identity and task sequencing.

Attention is also not an all-or-none phenomenon, but can be graded in intensity. In fact, one of the difficulties in studies on attention is to ensure that an unattended stimulus is in fact unattended, because it is difficult to drive attention to zero unless the task at the attended location is highly demanding of attentional resources (Joseph et al., 1997). Another reason why the attentional spotlight is not the best metaphor is that attention has properties that encompass attended objects. In a way, the focus of attention fills the boundaries of the attended object and is therefore referred to as object-oriented attention. Attention can also be directed toward a feature, such as color or orientation, and as such is distributed across the visual field. There are other potential forms of top-down control, however. These include perceptual task, where the discrimination or detection task that is performed at the attended location affects the ways in which the visual stimulus is processed. Expectation may also play a role, whereby internal representations of objects can influence how scenes are segmented. This may represent a form of hypothesis testing, such that before objects are identified, the visual system compares stored representations of object forms against bottom-up information on stimulus characteristics. A dramatic demonstration of the specificity of top-down influences is seen in priming. One can construct an image containing an embedded figure that is nearly impossible to interpret (Figure 2; Porter, 1954). If one briefly views a more fully rendered version of the image (Figure 3) and then views the initial, ambiguous version of the same image, the figure becomes immediately apparent. Thus expectation of a particular figure contributes to figure/ground segregation. The role of object expectation is also seen in the classic vase/face ambiguous figure, which can be consciously shifted from one object percept to another (Rubin, 1915). Computational models of scene segmentation that utilize top-down representation of object shape work much better than segmentation models that rely on bottom-up mechanisms (Ullman, 1995; Deco and Rolls, 2004, 2005).

Several lines of evidence support the idea that attention can be directed to an entire object (for reviews see Driver and Baylis, 1998; Scholl et al., 2001). Two judgments that concern the same object can be made simultaneously without loss of accuracy, whereas two judgments that concern different objects cannot (Duncan, 1984). Moreover, it is easier to divide attention between elements of the same, rather than different, perceptual groups (Baylis and Driver, 1993; Egly et al., 1994; Watson and Kramer, 1999; Lamy and Egeth, 2002). One demonstration of coherent-motion-defined object-oriented attention is

Figure 2. Priming Perceptions of Embedded Figures
The segmentation of this black & white image into object and background is extremely difficult. It is made much easier when the viewer is primed with a more fully rendered version of the figure—see Figure 3. Therefore, the intermediate-level process of scene segmentation is aided by high-level internal representations of object forms. From Porter (1954).

obtained at the surface segmentation level. Two overlapping patterns of dots rotating in opposite directions yield the percept of two superimposed transparent surfaces. Attending to one set of dots impairs subjects' ability to make judgments about the other set. Since the two sets of dots are overlapping, the cueing effect cannot be explained by spatial attention (Valdes-Sosa et al., 1998, 2000; Rodriguez et al., 2002). This is true even when the color of the two moving surfaces is identical, implying that attention is not directed to space or color, but rather to the whole surface (Mitchell et al., 2003). When the two surfaces are presented in a rapid succession, following a classical attentional blink paradigm, perception of the first surface severely limits the ability to perceive the second (Pinilla et al., 2001). Finally, it has been shown that when the two surfaces are presented in binocular rivalry, directing attention to one of the surfaces enhances its saliency and access to conscious perception (Mitchell et al., 2004), thus indicating that object-based attention acts as a modulator to conscious selection. Object-level attention modulation of performance has been studied in other forms of bistable perception, showing attentional control over ambiguous figure reversal (Liebert and Burk, 1985; Peterson, 1986; Gomez et al., 1995; Toppino, 2003).

Neuropsychological evidence also shows that perceptual groups define units of attentional selection. For example, in neglect (considered a landmark of spatial attention, since it normally impairs patients from seeing a portion of the visual field), the boundary between the attended and neglected visual field locations can be determined by the midline of an attended object, as opposed to the visual field midline (Driver et al., 1994; Tipper and Behrmann, 1996; Behrmann and Plaut, 2001). Also, it has been shown that spatial extinction in a parietally damaged patient was less severe when bilateral stimuli formed a common surface, even if this required visual filling-in to yield illusory Kanizsa figures or completion of partially occluded figures (Mattingley et al., 1997). These two examples, however, have a somewhat ambiguous interpretation. It can be argued that spatial selection is the dominant mechanism

of top-down control and that the object merely defines the region in space to which attention has to be directed.

Additional evidence that spatial attention cannot account for all forms of top-down control comes from experiments in which simultaneous attention to multiple object features (beyond form or spatial extent) are studied. An object can be defined as a cluster of features, grouping elements of different dimensions: color, space, orientation, and so on. In this description, an object evolving in time (moving, deforming, rotating…) can be seen as a trajectory in feature space. An important demonstration of object-directed attention involves experiments in which subjects are asked to track an evolving object, changing in three different feature dimensions: color, space, and spatial frequency. Attending to a feature of an object enhances one's ability to discriminate its other features (Blaser et al., 2000), thus showing that performance enhancement transfers to judgments of multiple dimensions of the same object.

An important effort has been devoted to understanding what subsets of feature space may be grouped as an object and how this relates to perceptual groups that may be attended. The Gestalt psychologists established a series of fundamental principles that govern perceptual grouping (Wertheimer, 1938a). However, *gestaltian* principles do not fully account for the elements in feature space to which attention can be guided (Scholl et al., 2001). Grouping operations depend on the identification of objects and object parts, which may vary on many geometric and semantic factors (i.e., a door may be a whole object made of pieces, or a part of a house made of door, windows, etc…). The versatile and intrinsically dynamic nature of grouping operations is demonstrated by the Marroquin pattern (Marroquin, 1976; Marr, 1982) illustrated in Figure 4. When attending to an invariant static pattern, circular shapes appear and vanish dynamically at various locations. Following Kofka (Kofka, 1935), Palmer and Rock (1994) proposed a scheme for perceptual organization that incorporates the Gestaltian principles of grouping, based on hierarchies of objects and object parts. A first

categorization of object into parts is based on regions of uniformly connected (UC) visual properties, such as luminance, color, or texture. These regions, in turn, can be parsed into branches whose borders are defined by concave discontinuities of edges (Marr and Nishihara, 1978; Hoffman and Singh, 1997; Barenholtz et al., 2003; Feldman, 2003; Feldman and Singh, 2005, 2006). A series of experiments have shown that attention can be driven to single-UC regions (Baylis and Driver, 1995; Watson and Kramer, 1999; Lamy and Egeth, 2002). In an experiment in which object-geometric dimensions (the concavities breaking an object in distinct UC regions) as well as top-down expectation (through priming or explicit instructions) were manipulated, it was shown that attention can be driven to different representational levels in the object hierarchy, including a single UC, a set of UCs, or the whole object (Watson and Kramer, 1999).

Thus, based on explicit instructions or previous knowledge, attention can be directed to parts or the whole of an object. Presenting large letters composed of smaller letters to subjects, Ward demonstrated that switching attention from parts to wholes is a slow process (on the order of seconds) (Navon, 1977; Ward, 1982). In a more recent experiment, attempting to link previous results, it has been proposed that the whole-object-attentional effect is manifested in tasks that require multiple responses with focal attention. It is presumed that the attentional jumps between parts of an object are easier than attentional jumps across objects (Lamy and Egeth, 2002). In a modified version of the MOT paradigm described before, in which subjects track moving objects, it was shown that if target-distractor pairs are merged by connecting links, performance was severely diminished. This indicated that attending to multiple elements becomes more difficult when they belong to distinct objects (Watson and Kramer, 1999; Scholl et al., 2001). While all previous examples have been confined to two-dimensional images, very similar results are obtained in 3D, where the main result is that attention is deployed in a seemingly automatic manner to surfaces (He and Nakayama, 1995), a natural extension of the uniformly connected regions described previously.

Attention can act at a number of levels and can be applied to a large family of cognitive processes (Miller, 2000). Attention can be directed toward actions, resulting in an increased activity in prefrontal, premotor, and parietal cortex, compared with unattended performance of the same movements (Jueptner et al., 1997; Rowe et al., 2002). Attention can be directed to time, and the degree of attention paid to an object or situation modulates its subjective duration (Hicks et al., 1976; Macar et al., 1994). In a judgment task, attentional modulation was tested by changing the content of the task from a color to a temporal judgment while the stimulus remained constant (a series of colored disks presented at different durations). It was found that area V4 was the only region that was more active when attention was deployed to color, while an extended corticostriatal network, most prominently in the preSMA, was more active when attention

was deployed to time. Thus, the network involved in the attentional modulation to time overlaps with the network involved in attention to movement. Attention can also be driven to specific task configurations relating sensory information to motor actions, as reflected in task-switching paradigms, where reaction times and error rates increase when subjects change between different task configurations (Allport et al., 1994; Sigman and Dehaene, 2006).

While this indicates that attentional control can be driven in an endogenous and voluntary fashion to a variety of cognitive processes, it has been known since the early work of Posner (Posner, 1980) that attention can also be engaged by exogenous factors. These two systems of deployment of attention interact in a nontrivial fashion and under many circumstances, a phenomenon of "attentional contagion," i.e., shifting between different forms of attention can be observed. For instance, the abrupt onset of a task-irrelevant distractor induces the spread of attention to an object at the same location (Yantis and Jonides, 1984; Remington et al., 1992; Yantis, 1993). This appears to be a very general observation and has been interpreted evolutionarily as a hard-wired system tuned for the detection of new objects (Yantis and Hillstrom, 1994), although the automatic shift of attention may be inhibited when attention is focused in advance on another location in the scene (Yantis and Jonides, 1990; Theeuwes, 1991). Another transformation of attention is observed in the motor domain. Selective attention shapes motor control, determining which of the various objects in the visual field is to be the target used to plan and guide movement, as for instance in the planning of saccades (Kowler et al., 1995). Similarly, motor action automatically deploys visual attention, indicating a tight coupling between attention (as manifested in selection-for-perception) and selection of a motor plan, including saccades (Deubel and Schneider, 1996) and also manual reaching (Deubel et al., 1998).

Another form of top-down control relating perception and action involves a concept known as "efference copy" or "corollary discharge" (Sperry, 1950). The classic example of efference copy relates to the perceptual stability of the world when one is executing eye movements. We are able to distinguish between the movement of the visual scene across the retina that is induced by eye movements from that caused by actual object movement. In the former, objects still appear to be stationary, in the latter, objects appear to move, even though the sensory input may be the same. This is presumed to be due to a "copy" of the signal that is sent to the oculomotor system to move the eye also being sent to the sensory pathways to cancel the movement signal. The origin of this signal has been suggested to involve a pathway from the superior colliculus to the mediodorsal thalamus to the frontal eye fields (Sommer and Wurtz, 2004). The role for motor and proprioceptive signals in modifying receptive fields includes maintaining a stable representation of object position in extrapersonal space during eye, head, and body movements. In area LIP, neurons transiently shift their receptive fields before a saccadic eye movement, responding to

stimuli that will be brought into their receptive fields as a result of the saccade (Duhamel et al., 1992). The value of this transient shifting of receptive fields is thought to be obtaining a predictive map of the visual world that will exist after the eye movement. This phenomenon of shifting receptive fields has potential utility in another way, by increasing the amount of cortical territory dedicated to attended parts of the visual field, or magnification factor, as has been reported for area MT (Womelsdorf et al., 2006).

To an extent, some forms of top-down influences may be equivalent. A shape-discrimination task may be the same as object-oriented attention, since the attention would have to encompass the form of the attended shapes. But the key issue is how much information is con-

veyed by the top-down signal and how much information is returned by the lower stages as a result. There is considerably more information, for example, in an instruction to discriminate a square from a triangle at an attended location than merely to attend to that location. The change in response properties at the earlier stage resulting from the top-down signal can also be quantified in terms of information—how well the response of the neuron is predictive of the attribute being discriminated. The nature of the effect of top-down influences on response properties has been characterized in various ways. Some experiments show that attention facilitates responses to stimuli lying within the receptive field. These studies describe the attentional influence as being a "gain-control" or a change in response equivalent to that elicited by increasing stimulus contrast (Treue and Martinez Trujillo, 1999; Reynolds et al., 2000; Williford and Maunsell, 2006). A related model of attentional influence is one of competition, where two stimuli within the receptive field compete for determining the cell's response, and this competition is won out by which of these stimuli are attended. But this view may only reveal the tip of the iceberg of attentional effects. Another view is how attention plays a role in mediating contextual influences. In areas where attention to a single, isolated stimulus does not alter neuronal responses, contextual interactions, the influence of stimuli surrounding a central line element, can be dramatically altered by top-down influences. Depending on the nature of the task, attention can either serve to bind stimulus elements inside and outside the receptive field or segregate them (Ito and Gilbert, 1999; Li et al., 2006).

Extending this idea, we propose that there is not a unique answer to the question of what is the unit of attentional selection, but rather this may depend on the type of stimulus representation used in performing a given task and the specific actions involved. It has been shown, for example, that selection may be object based when a task requires shape judgments and space based when position constitutes the relevant dimension of the task
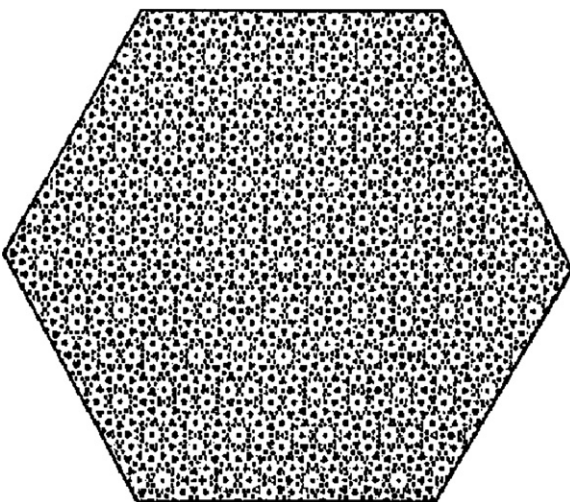

Figure 4. Object-Oriented Attention Seen in the Marroquin Figure (Marroquin, 1976)
As one views this textured pattern, different shapes appear, showing the ability of attention to be object directed. One alternately perceives circles of different size.

(Vecera and Farah, 1994). While there are critics to this particular experiment (see, for example, Kramer et al., 1997), other experiments have shown that the allocation of attention mimics the requirements of the task (Ito et al., 1998; Ito and Gilbert, 1999; Watson and Kramer, 1999; Lamy and Egeth, 2002). Thus, under top-down control, a large variety of perceptual categories (space, features, parts, objects) can be attended (Yantis, 1992). However, there seems to be a specific mechanism of spontaneous direction of attention. To resolve its certainly difficult characterization, spontaneous direction of attention has been often referred to as the form of attention that seem impossible to avoid (as in pop-out, for example) (Schneider and Shiffrin, 1977). Essentially, the default mode of attention seems to be directed to uniformly connected perceptual groups, such as Gestalt bound perceptual groups, or surfaces (He and Nakayama, 1995; Driver and Baylis, 1998; Scholl et al., 2001). The spontaneous attention to basic perceptual groups, determined by geometric or feature continuity, seems to follow the ontogeny of object identification (Kovacs, 2000; Carey and Xu, 2001). The initial structures used for scene categorization during early cognitive development are uniformly connected groups. As adults, we direct attention to the structures we first learned. This suggests that spontaneous allocation of attention is directed to overlearned structures repeatedly present in the ensemble of sensory stimuli throughout our early lives (Gilbert et al., 2001; Sigman and Gilbert, 2000; Sigman et al., 2001).

In summary, attention can be directed to a large variety of perceptual groups. The nature of this selection is determined by two critical factors: bottom-up geometric factors, as determined by Gestalt principles of continuity, and top-down factors, which can be directed by previous experience (priming), explicit semantic instruction, context, or task necessities. Thus, the "units of attention" are intrinsically related to the rules of perceptual grouping and their relation to action or representation as imposed by a particular task or context. As we discuss below, these rules are represented in bottom-up processes, but are engaged by top-down control. In a similar manner to what happens with perceptual learning, the phenomenology of attention does not determine its own idiosyncrasy but rather seems to be malleable to the context of the processes and the task in which it participates. This, as will be discussed later, may be critical to understanding the neurophysiology of attention, which, we propose, is not located within a particular area or groups of areas but rather changes the workings of the specific areas involved in each task.

Role of Top-Down Influences in Different Cortical and Thalamic Areas

In investigating the strength and character of top-down influence in any cortical area, one must take into account the functional role of that area. Stimuli that engage the functional specialization of an area show much stronger attentional influences than stimuli that are irrelevant to that area's function. This also relates to the interaction between contextual influences and top-down influences. The size and prevalence of attentional effects consequently depend on the nature of the visual stimulus and on the behavioral paradigm. Some of the original reports of attentional effects were reported for area V4, where subjects were cued to attend to one of two or more discrete stimuli in the receptive field (Moran and Desimone, 1985; Motter, 1994; Reynolds et al., 1999). Attention to direction of motion has strong effects on direction-selective neurons in area MT (Treue and Maunsell, 1996). In area V1, if one presents an isolated, single bar or grating stimulus within the receptive field, the responses of neurons change very little when the animal attends to that bar versus attending to a different location, relative to that seen in other visual areas (Haenny and Schiller, 1988; Motter, 1993; McAdams and Maunsell, 1999). But when the target is presented within a larger and more complex context, much larger attentional effects are seen (Motter, 1993; Ito and Gilbert, 1999; Crist et al., 2001; Li and Gilbert, 2002; Li et al., 2006). The strongest effects are seen for stimuli that invoke the higher-order, context-dependent integrative properties of the area. Area V1, for example, has been suggested to play a role in contour integration. A stimulus consisting of a contour made of line elements lying both within and outside the receptive field and embedded within a complex background shows very strong attentional effects, particularly when attention is engaged in detecting the contour. The response of a neuron can be doubled when the animal is doing a contour-detection task at the receptive field location relative to when it is doing a different task away from the receptive field (Li et al., 2006). The salient finding of the studies on V1 is that attentional effects are most strongly exerted on contextual influences. This principle is seen in feature-based attention, where attention affects the effect of motion in a surrounding stimulus on the perceived motion of a central target (Tzvetanov et al., 2006). The strength of attentional effects is also dependent on the nature of the perceptual task— different tasks performed at the same attended locations elicit very different degrees of attentional modulation in different cortical areas (Watanabe et al., 1998). Thus, the idea that attentional effects get progressively stronger as one moves up the visual pathway toward higher-order areas—the attentional version of the idea of progressive hierarchical complexification—seems to be biased by specific experimental settings. With the appropriate visual stimulus and behavioral task, one can see as strong attentional effects in V1 as one sees in higher areas using other stimuli and discrimination tasks. We therefore propose that early visual areas are not inherently less susceptible to top-down influences than higher areas. These influences may not even be specific to cortex, but wherever one sees feedback connections, including thalamus (O'Connor et al., 2002; Kastner et al., 2006). This study showed even stronger attentional effects in the LGN than in V1/V2. Top-down influences are not unexpected in the LGN since it receives input from many more V1 neurons,

by orders of magnitude, than it receives from the retina. It has been proposed that the effective size of this modulation, which in this particular experiment are larger than what is found in V1 and V2, might be related to the fact that the LGN receives a larger amount of feedback inputs than areas in early visual cortex, including projections from the thalamoreticular nuclei. However, as we discuss here, while there may be a bias on the amount of top-down influences determined by anatomical factors, the range and magnitude of top-down influences may depend drastically on the computation required by a specific task. Thus, it is difficult to determine an absolute estimation of the magnitude of these interactions from a single experiment.

Neural correlates of top-down influences are seen in a number of perceptual tasks. In a curve-tracing task, cells are more strongly activated when their receptive fields lie along the curve being traced than when they are on unattended curves (Roelfsema et al., 1998, 2003). Another example of task-dependent effects in V1 is seen in perceptual "pop out" of shapes that differ in their shading characteristics. The differential responses to these stimuli are strongest when they are used by the animals in a detection task (Lee et al., 2002). The fact that top-down influences extend well beyond the idea of an attentional spotlight is seen in experiments on attention to feature, where the modulation is dependent on the orientation or color (in area V4) or direction of movement (in area MT) of a stimulus for neurons tuned to the attended feature, regardless of stimulus location (Motter, 1994; McAdams and Maunsell, 1999; Treue and Martinez Trujillo, 1999; see Treue, 2001, for review).

Top-down influences may play a role in visual memory, recruiting the same areas that are involved in processing a visual stimulus in the recall of that stimulus. This has been seen with fMRI, where activation in primary visual cortex is reported in individuals who are imagining a visual stimulus (Kosslyn, 1994; Roland and Gulyas, 1994; Buckner and Wheeler, 2001; Slotnick et al., 2005). A particularly intriguing example of cortical activation by visual memory has recently been reported based on single-unit recordings in area MT of behaving monkeys. This area is ordinarily activated only by moving stimuli, for example a patch of moving dots, not by static shapes. However, when animals were trained to associate a static shape, an arrow, with the moving dots, then the shape stimulus alone could elicit responses in MT (Schlack and Albright, 2007). This activation was interpreted as representing the recall of the associated moving stimulus. Alternatively, one might argue that the activation represents encoding novel information about static stimuli in MT, which exhibits the function required to analyze those stimuli when the animals are performing the task that is relevant to those stimuli. Either explanation argues for a strong top-down influence in the activation of this area.

Other evidence for a top-down interaction between the representation of object shape and lower levels of visual processing is seen in binocular rivalry. When the two eyes are presented with different images, subjects perceive an alternation between one image and the other. The locus of this competition is a matter of considerable controversy, with some arguing that it occurs only in higher-order visual areas and others showing effects in area V1 and even in the LGN (Logothetis et al., 1996; Lumer et al., 1998; Tong et al., 1998; Polonsky et al., 2000; Wunderlich et al., 2005). But the locus of the competition may depend partly on the kinds of stimuli used, such that the use of gratings as the competing stimuli results in a competition at early levels (Polonsky et al., 2000), while houses and faces result in an extrastriate competition (Tong et al., 1998). The nature of the competition suggests that rivalry is not embedded in a single area but involves an interaction between multiple areas. When two images are cut up into a set of patches, with different parts of the two images presented to either eye, the perceived alternation occurs between the complete, assembled objects rather than between the divided images seen by each eye, e.g., the competition is object rather than explicitly eye oriented (Figure 5; Kovacs et al., 1996; Lee and Blake, 2004). For this to occur, it is necessary to combine information about object identity as well as about eye of origin. But while complex shapes are represented in higher-order areas, eye specificity is represented in earlier visual areas. The requirement for this experiment, then, is to select the appropriate information coming from either eye to assemble a unified object percept and to suppress the conflicting information coming from the other locations in either eye. One way this can be achieved is through a top-down interaction between the higher- and lower-order areas.

The other side of the issue of the cortical or thalamic targets of top-down influences is the sites of origin from where these influences arise. The potential candidates include parietal areas, which represent saliency maps and mediate shifts in the locus of attention, frontal areas, which are involved in control of task execution, and temporal areas, which contain internal representations of object shapes and can therefore play a role in priming, expectation, and shape discrimination. These areas are highly interconnected and are often simultaneously engaged when executing perceptual tasks. There are multiple routes, both direct and indirect, by which information in these areas may influence processing in early sensory cortex. For example, area V1 receives direct, though weak, projections from inferotemporal cortex, but it also receives strong projections from area V2 and V4, which in turn receive feedback from higher areas, including temporal lobe. Therefore, feedback can be mediated via a cascade of descending connections crossing many cortical areas.

The Brain Circuitry of Top-Down Influences
Starting from the idea that top-down effects involve an interaction between behavioral states such as attention or expectation and stimulus context, one can ask whether this interaction occurs at higher-level areas, and the product of the interaction fed back to early areas, or whether this interaction occurs in the early areas themselves.

Figure 5. Top-Down Influences in Binocular Rivalry
The image of the monkey and the forest scene are cut and joined to form two complementary images, each containing pieces of the two images. When each composite image is shown to either eye, one sees alternating percepts of either the monkey or forest scene, as shown at top, rather than the jumbled images that are shown to either eye. Therefore, the competition between the eyes is local and is governed by the global properties of the coherent scenes, which act in a top-down matter to gate eye-specific information. This is thought to be top-down, since the eye of origin information is present at lower stages in the visual pathway, whereas the higher-order areas that represent the objects are binocular (Kovacs et al., 1996).

There is an ongoing debate as to whether the contextual interactions seen in early areas such as V1 are themselves mediated by local connections versus feedback. With the caveat that one cannot assume that all contextual interactions come from the same source, there is evidence that interactions involved in contour integration are mediated at least in part by long-range horizontal connections formed by cortical pyramidal cells within V1. These connections enable their target neurons to integrate information over an area of cortex representing an area of visual space that is much larger than the receptive fields of neurons (as defined by simple stimuli, such as a single oriented line segment) (Gilbert and Wiesel, 1979; Stettler et al., 2002). In support of this idea, the spatial extent and orientation dependence of the horizontal connections match the perceptual characteristics of contour saliency (Li and Gilbert, 2002; Stettler et al., 2002; Li et al., 2006). Another suggested route for contextual influences is feedback coming from higher-order cortical areas (Angelucci et al., 2002; Shmuel et al., 2005), though we suggest that the role for feedback is to provide *behavioral context*, as opposed to stimulus context. Even though the long-

range horizontal connections within V1 have properties that are coincident with the perceptual characteristics of contour saliency, the effectiveness of these connections is under top-down control. The observation that responses in V1 neurons show a stronger relationship to contour saliency when animals perform a contour-detection task suggests that the contour-related properties of V1 neurons result from an interaction between feedback and local circuits (Li et al., 2006).

It has traditionally been thought that timing of neuronal responses can be used as a clue to understand the anatomical and physiological basis of cortical interactions. The underlying assumption is that influences coming from higher-order areas would involve longer delays from the onset of a cell's response than influences arising within the same cortical area (Lamme, 1995). However, there are two fundamental problems with this assumption. First, measurements of conduction velocity of cortical feedback showed that it is faster than that of intrinsic connections, leading some to expect that delayed influences were indicative of input from local sources (Hupe et al., 2001; Bair et al., 2003). A similar demonstration of extremely fast feedback influences comes from a TMS study in humans (Pascual-Leone and Walsh, 2001). When a pulse is applied in the V5/MT region in humans, it generates the impression of a moving set of light speckles. The perception of the moving phosphene can be disrupted if a second pulse is applied in area V1 at 5 and 40 ms after the first pulse, but not when the pulse in V1 was applied before the pulse in V5. This suggests that the pulse in V1 prevents proper transmission of information through feedback projections reaching V1 and that this feedback propagation of information can be extremely fast. A second fundamental difficulty with the use of timing to infer functional and anatomical connectivity is that dissociation between timing of neural events and synaptic delays is found in simple decision tasks. Neurons in the parietal cortex integrate information of sensory stimulation, and this accumulation process starts after a latency of about 200 ms (Gold and Shadlen, 2000). This latency cannot be explained simply by synaptic delays, and it has been proposed that the delay, which is relatively fixed for a given task, may be related to the duration of an initial processing stage that is required to engage a large-scale reverberation involving top-down interactions (Sigman and Dehaene, 2005, 2006). Similarly, the rather long latencies, beyond 100 ms, observed in some contextual influences in monkeys (Lamme, 1995) and humans (Martinez et al., 1999, 2001) are well out of the range of what one would expect even from slow conduction velocities. Thus, it is overly simplistic to suppose that a functional property that appears with a delay in a response arises because of slow conduction velocities. Rather, they may reflect the time required for the network to settle into a state, a process that can involve either intrinsic connections, feedback, or both.

While some contextual influences have properties that suggest a role of intrinsic horizontal connections in their

generation, the finding that they can also be influenced by attention suggests an interaction between feedback connections to an area and local circuits within that area. The Gestalt rules of perceptual completion were an early suggested manifestation of top-down influences, though there is disagreement concerning the relative role of feedback and intrinsic connections in generating these rules. Here we emphasize, however, that in addition to *sensory context* one needs to consider the pathways that convey *behavioral context*, which includes attention, expectation, perceptual task, and hypothesis testing.

The anatomical pathways that can carry top-down influences include numerous feedback connections from higher- to lower-order visual areas. V1 receives strong feedback connections from multiple visual areas, including V2, V4, MT, and inferotemporal cortex. It has also been suggested that top-down influences could be mediated by a cortex-to-thalamus-to-cortex pathway (Sherman, 2005). In such a context of fully reciprocal connectivity, it is worth asking whether the terms "higher" and "lower" are appropriate at all. Indeed, as we pointed out earlier, V1 is required for conscious perception even in the absence of bottom-up information (i.e., when the stimulus does not start in the retina). During imagery or magnetic stimulation, a stimulus can only become conscious if V1 function is not disrupted. This has led to the proposal that V1 and V2 may work as "active blackboards" that integrate and sustain the result of computations performed in higher areas (Mumford, 1991; Hupe et al., 2001). But this can only be a part of this story, and assuming that information flow starts in higher-order areas that use V1 and V2 as buffers may be as oversimplistic as a fully feedforward scheme. Instead, in the most general situation, there is a massive signaling between mutually connected cortical regions, leading to reentry and reverberation (Sporns et al., 1991). In this scheme, as has been proposed by Mumford and colleagues, the best description of V1 is not the first stage in a feedforward pipeline (or the last in a fully top-down conception of brain function) but rather the unique high-resolution buffer in the visual system for geometric calculations (Mumford, 1991; Lee and Mumford, 2003). Massive parallel reentry and signaling across all cortical areas may lead potentially to an explosive combination of possible neuronal states. It has been proposed that this process is constrained by a selection system based on a reward mechanism acting on different temporal scales, from the few hundred milliseconds of a single trial to long-term learning (Sporns et al., 1991).

This broadly connected network can be triggered in different manners. Depending on the way in which expectation is triggered relative to stimulus onset, top-down influences may either be exhibited simultaneously with the initial response to the stimulus or with some delay. For example, when an animal is cued before the stimulus is presented to perform either a three-line bisection task or a vernier discrimination task, the difference in the responses associated with the two tasks begins from the first spike. On the other hand, when performing a con-

tour-detection task where the location of the embedded contour is unknown, the response associated with the presence of a contour in the receptive field occurs with a delay of ~100 ms (Figure 6; Li et al., 2004, 2006). This delay in the modulation of the feedforward response is similar to what has been found in other experimental manipulations in which the triggering of attention is determined by stimulus characteristics (Lamme, 1995; Roelfsema et al., 1998). Another example is seen in area LIP, where the component of neurons' responses to a probe indicating saccade plan occurs 115 ms after probe onset (Bisley and Goldberg, 2006). When the stimulus itself is the cue to determine where attention should be directed, the differential response reflecting the attentional effects occurs with a delay after stimulus onset. But the examples presented above are somewhat artificial circumstances, in that we are normally under the influence of continuous expectations, rather than just a transient attentional state following a discrete stimulus appearance. Ordinarily one is exposed to a constant stream of stimuli that are always under the influence of a set of prior expectations, and the responses of neurons in our visual cortices are never purely sensory or bottom up. It has been proposed that in this dynamic setup, two partially segregated networks may play distinct roles. The first system includes the temporoparietal cortex and inferior frontal cortex, which works as a "circuit breaker" for the dorsal system, redirecting attention to salient and unexpected events. The second system, including parts of the intraparietal cortex and superior frontal cortex, is involved in preparing goal-directed actions by exerting a specific pattern of top-down influences (Corbetta and Shulman, 2002).

We have previously stated that top-down interactions can be of many different kinds, not only augmenting or multiplying responses but also sharpening tuning curves, controlling contextual influences, or acting as a modulator of plasticity. This leads to questions concerning a plausible biophysical basis of top-down influences that may involve an interaction between feedback connections and local circuits. We have suggested that the task-dependent changes in the functional properties of neurons involve gating of horizontal inputs by feedback connections. Our theory is that although a neuron may receive thousands of inputs from intrinsic connections, only a small fraction of these connections are expressed, or effective, under any particular behavioral context. This allows neurons to multiplex their function in a state-dependent manner, taking on different functional roles when the animal performs different perceptual tasks. In this manner, rather than performing a stereotyped operation on sensory input, each cortical area is an "adaptive processor," running different algorithms under the instruction of feedback from higher-order areas. In a way, this theory of neuronal function mimics a well known concept in genetics and cell biology. All cells in an organism contain the same genome and thus potentially may perform identical operations. Yet, their broad morphological and biochemical diversity and functional repertoire is set by a specific pattern of gene
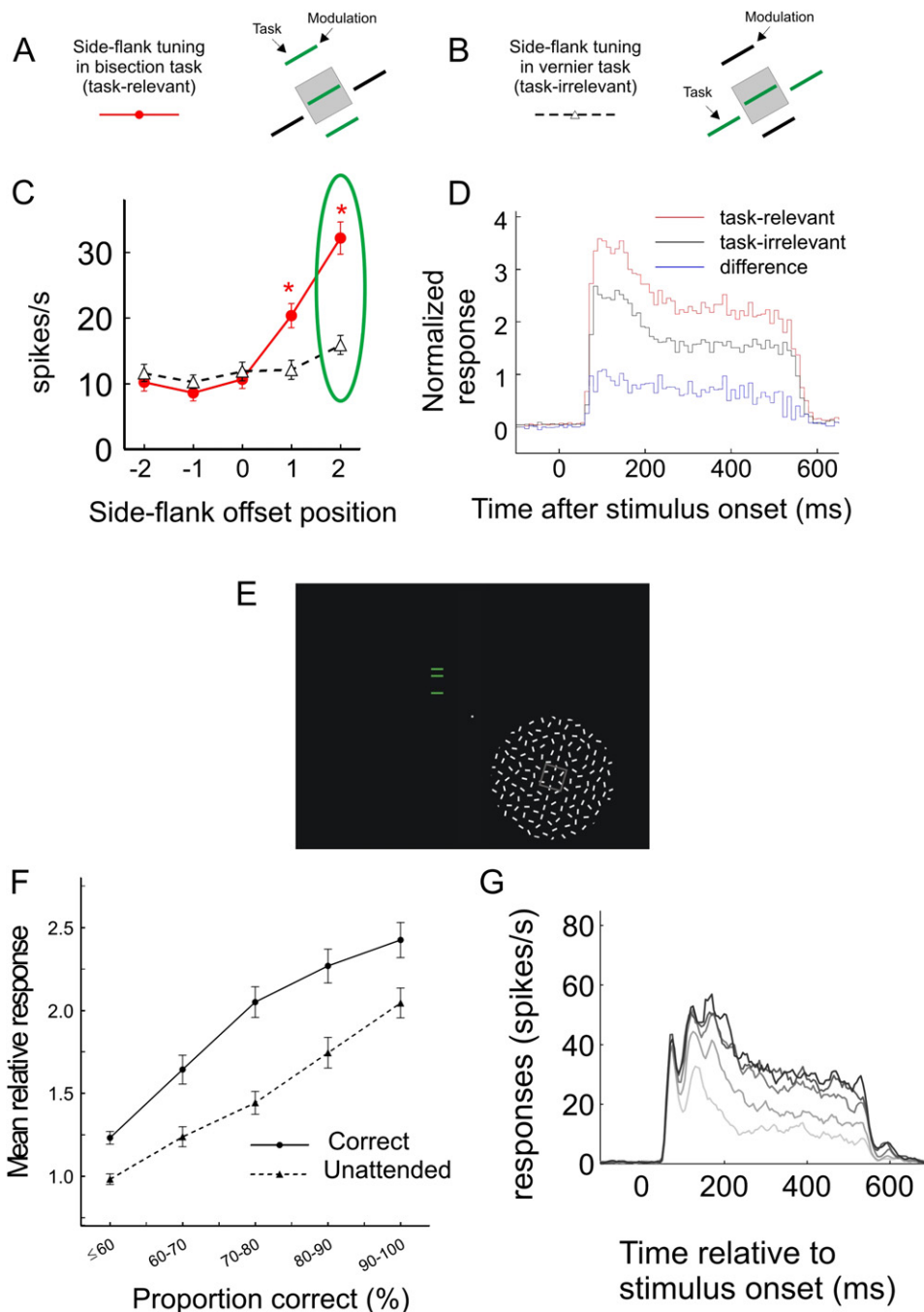
Figure 6. Task-Specific Modulation of Visual Responses in Area V1

(Top) In this experiment, animals were trained to do either a three-line bisection task (A) or a vernier discrimination task (B) with the set of five lines. The set of visual stimuli consisted of 25 conditions: five offsets of the parallel lines used in the three-line bisection task times five offsets of the collinear lines used in the vernier discrimination task. From this set of stimuli, tuning curves were generated based on the neurons' responses to the five offset positions of the parallel or collinear lines. In the example shown (C), the neuron showed more modulation to the offset of the parallel lines when the animal performed the three-line bisection task than when performing the vernier task. In this experiment, the animals were precued to the task before the stimulus appeared. The difference in response when the animal performed the two tasks began from the very beginning of the response (D). (Bottom) Effect of contour saliency on responses when animals perform a contour detection task. (E) Animals were trained to either detect a contour in a complex background or to do a three-line bisection task in the hemifield opposite to the embedded contour. (F) As contours became more salient, the response of neurons in V1 increased. This increase was more marked when the animal performed the contour-detection task than when they did the bisection task. (G) This facilitation occurred with ~100 ms delay after response onset (bottom right). Error bars represent ± SEM. (Adapted from Li et al., 2004; Li et al., 2006.)

expression. Some aspects of this expression pattern are set in a slow temporal scale that determines basic structural aspects of the cell, i.e., its morphology, membrane properties, etc…. Other aspects of the gene expression pattern are regulated by context, determined through specific biochemical pathways, and allow changing, in a dynamic fashion, the operational mode of any given cell. A homeostatic equilibrium is reached when this signaling between cells (the same cells are vulnerable to context, and then, the newly expressed genes set a new context for the cells they signal) reaches a dynamically stable configuration.

While this sets the functional and computational basis of the workings of top-down influences, the biophysical mechanisms by which neuronal circuits are set into different states or programs remains largely unknown. An interesting observation is the growing literature showing that there are default brain "states," with massive amounts of spontaneous activity, perhaps much of it subthreshold, occurring even in the absence of a sensory stimulus. Even when the brain is "at rest," broadly distributed networks of correlated activity are active (Fox et al., 2005, 2006). It has also been reported with optical imaging using voltage-sensitive dyes, where it has been suggested that spontaneous regional fluctuations in activity are as large as the activity evoked by a visual stimulus (Arieli et al., 1996; Petersen et al., 2003). The spontaneous fluctuations in brain activity observed with fMRI and optical imaging have been observed with intracellular recording as UP and DOWN states: spontaneous depolarization and hyperpolarizations in membrane potential that last for seconds (Stern et al., 1997; Lampl et al., 1999; Cossart et al., 2003; Petersen et al., 2003; Haider et al., 2006). Although UP and DOWN states have been shown to be more prominent in sleep than in the awake state (Steriade et al., 2001), these state changes have been seen in whisker barrel cortex of awake mice, where up and down states exist, and the kinetics and magnitude of the membrane-potential shifts change from periods of rest to periods of active whisking (Crochet and Petersen, 2006). These distinct cortical default states can have profound influences on stimulus-evoked activity, and thus, one is tempted to argue that they may account for the presetting of cortical state by expectation or perceptual task. Perhaps related to this, cortical areas show significant "baseline" activity in subjects performing a pattern-detection task, even when the stimulus is absent (Ress et al., 2000). While the link between specific top-down influences and brain states is an intriguing idea, and while fMRI studies have related to a certain extent the workings of one of these prior networks to top-down modulation (Corbetta and Shulman, 2002), some caveats remain. First, it will be valuable to demonstrate a direct link between the different manifestations (fMRI, optical imaging, intracellular recordings) of this state alternation. Second, there is a need for evidence to directly relate the dynamics of these state alternations to a behavioral context, to specific engaging and disengaging of top-down influences. Finally, one must determine

whether the binary nature of neuronal states can account for the broad diversity of top-down influences.

Top-Down Influences and Perceptual Learning
A further insight into the biophysical basis of top-down influences comes from the relationship between top-down influences and perceptual learning. Perceptual learning refers to the unconscious improvement in stimulus discrimination and detection that occurs after exposure to the stimulus for an extended period of time. It has been shown that perceptual learning in shape discrimination or in search tasks involves an alteration in the functional properties of neurons in early visual cortex (Crist et al., 2001; Schoups et al., 2001; Li et al., 2004). The functional change can involve a sharpening of orientation tuning of V1 neurons in animals trained on an orientation-discrimination task (Schoups et al., 2001) and a change in contextual influences in animals trained on a shape-discrimination task (Crist et al., 2001; Li et al., 2004). As shown in Figure 6, the tuning of V1 neurons for the offset of parallel lines changes when animals perform a three-line bisection task, where the parallel lines are relevant to the task, relative to when the animals perform a vernier discrimination task with the identical five-line stimulus (Crist et al., 2001; Li et al., 2004). In the example shown, the cell carries more information about the relative position of the three parallel lines when the animal is doing a task that engages those lines, and this differential tuning is seen for over half of the neurons in V1. The critical point here, and where top-down influences come into play, is that the functional properties associated with learning of this perceptual discrimination are only expressed when the subject is performing the trained task. Notably, the top-down influence here is not the gain control seen in other attentional studies, since the shape change in the tuning curve cannot be accounted by a multiplicative change in responses.

Top-down influences are also evident in fMRI studies of human subjects trained on a search task involving a target embedded in an array of distractors. After practice on this task, subjects become adept at determining whether the target is present, and this is associated with a shift in the representation of the trained target from higher to lower retinotopically mapped visual cortical areas, as evidenced by an increase in the activation in V1/V2 when subjects search for the trained versus untrained targets (Sigman and Gilbert, 2000; Gilbert et al., 2001). Here again top-down interactions come into play: there is no difference in activation when the subjects are searching for the trained target when it is present and seen compared with when it is absent. The change in activation with the trained target, in this case, is primarily associated with the act of searching for the target and not with the presence of the target. The idea here is that the effect of V1 activation by training is the engagement of V1 in the task via top-down influences.

Findings that the response properties of V1 neurons change according to object expectation and perceptual task contribute to the idea that neurons multiplex their

function on a moment-to-moment basis, performing different analyses according to the behavioral context. Also, the changes induced during learning themselves require top-down influences, since one generally needs to attend to the task or stimulus in order for its properties to be encoded. Thus both the encoding and recall of the learned information are subject to top-down influences. The observation that top-down effects are most strongly exerted on contextual influences suggests that learning involves setting up the appropriate interaction between feedback connections and the local circuits that provide contextual information (such as the long-range horizontal connections). This idea is represented schematically in Figure 7. The idea that top-down influences involve a gating of local circuits by feedback suggests a novel mechanism, at the level of circuitry, by which learning occurs. The dominant theory of the synaptic mechanism for learning has been the Hebbian rule, where neurons that have correlated firing will strengthen their mutual interaction, potentiating the strength of synapses they form with each other. The alternative idea that we propose is one that involves changes in the interaction between neuronal inputs. Here, particular ensembles of feedback connections selectively gate subsets of horizontal connections. This requires one set of inputs to selectively *address* another set of inputs allowing a small proportion of intrinsic inputs to be expressed under any given behavioral context. In this view, a given set of horizontal inputs modulate a target cell's responses in a way that enables the subject to perform a particular discrimination task, thereby increasing the amount of information carried in service of that task. The requirement of that system is to identify which subsets of inputs are useful for performing that task and to have those inputs expressed when the subject is doing the task. The process of learning, then, would involve linking the appropriate intrinsic connections to the feedback signal associated with a particular task, which is what we refer to as the addressing process. Then, whenever the feedback signal assumes that state, those sets of intrinsic connections are expressed, and other connections are suppressed. This process would not require modulation of synaptic weights, such as seen with LTP and LTD, but it is possible that both synaptic modification and changes in addressing would work cooperatively to encode learned information.

State Switching of Cortical Function

In one sense, the idea of cortex as adaptive processor, whereby neuronal function is constantly changing, might seem incompatible with the need to maintain a stable representation of the sensory environment. The resolution to this conundrum is that representations appear on an as-needed basis. They never disappear and are present in a latent form in synaptic weights of all the connections within an area, but not all connections are enabled at all times. The classic view of how neurons represent information is one of the "labeled line." A neuron's firing is interpreted by subsequent processing stages as indicative of
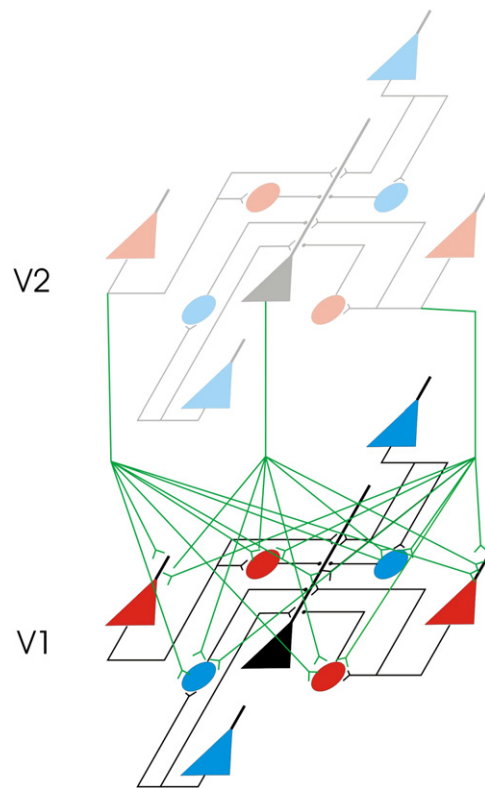

Figure 7. Schematic Representation of Circuits Involved in Top-Down Influences, with an Interaction between Feedback and Local Circuits

An important unanswered question is the specific biophysical nature of top-down connections and how this may relate to their broad range of functional influences. The simplest form of an influence may be implemented by a direct connection from neurons in higher cortical regions to pyramidal neurons in V1. This model may explain the response selection ("spotlight") form of attentional influence, but top-down influences have been shown to target specifically contextual and integrative properties of V1 neurons, suggesting a gating of subsets of neuronal inputs. This requires an interaction between neural networks, with, for example, feedback targeting inhibitory interneurons so as to neutralize the action of intrinsic horizontal connections within V1.

the presence of a stimulus endowed with a particular set of attributes (orientation, color, etc.), and the relative responses of neurons with different line labels determine how the stimulus is perceived. The idea of top-down-mediated functional multiplexing suggests that a neuron's line label actually changes, and its response is appropriately interpreted by the higher areas because these areas sent the instruction of which function to perform, and the areas receiving the top-down signal send a return signal that is the result of that calculation. Second, it should be pointed out that an area performing one function does not wipe the slate entirely clean for performing other functions. Rather, there is an enrichment of the information related to the immediate behavioral context, but there is still some information carried by that area related to the other functions it is capable of performing. The end result, however, is that the range of functions that an area is capable

of performing is much more diverse than what one would see if neuronal properties were fixed. The effect of this is that the representation of information is at the level of synapses rather than cells, and since this involves several orders of magnitude more elements, an individual cortical area can serve many more functions.

An interesting observation related to the multiplexing idea deals with the proportion of neurons in a cortical area whose responses are related to a given task. One can imagine two possible scenarios: either there is a compartmentalization of function, with small numbers of neurons specializing in a given task, or a more distributed function, with essentially all neurons carrying information related to all the tasks the area performs. The growing body of evidence points more toward the latter: whether one looks at how neurons in V1 carry information related to a three-line bisection task or how neurons in the frontal lobe modulate their responses in a way related to executive control in a particular task, the proportion of neurons involved always seem to be on the order of 50% (Miller, 2000; Li et al., 2004). And as the task is shifted, the set of neurons involved are highly overlapping with those engaged in the first task. If the other mode of representation, involving compartmentalization, had been involved, one would have been confronted with a needle-in-the-haystack problem, where it would be nearly impossible to find the small proportion of neurons that encoded information relevant to a particular task. The high proportion of neurons involved in some experiments may reflect the large amount of training the animals received in acquiring the task and the dominance of that task in the animals' experience during an extended period of data collection. However, the point remains that neurons can multiplex their functional roles, calling up different functional states according to the immediate task demands.

The state-switching or multiplexing of a single neuron (or neuronal ensemble) can occur dynamically within a single task. This has been shown in a two-interval frequency somatosensory discrimination task, which requires a sequence of computations: encoding the first frequency, maintaining this value in memory, comparing it with the second frequency, and establishing a binary (categorical) decision (Machens et al., 2005). It has been shown that the same neuron performs subsequently all these computations, suggesting that processing modules can "rapidly reconfigure their dynamical properties, switching between different behaviors as the cognitive flow requires." Moreover, a simple model has shown that this behavior can be accounted for by a simple circuit that is modulated by an external current, and this suggests that even the prefrontal cortex may be driven by external modulation in different processing modes.

The idea that the operation of a cortical area such as V1 is dependent on top-down control is one that can be generalized to all brain areas, and this mechanism has potential implications for understanding the mechanism of behavioral disorders. Clearly, attentional influences have been identified in numerous areas across the visual pathway. Moreover, the observation that even in frontal cortex the same neurons can be engaged in multiple tasks suggests that such top-down modulation operates even at the highest levels. Even in the hippocampus, which is thought to encode information about short-term memories, there is evidence of top-down mechanisms at play (Kentros et al., 2004). Other sensory systems, including the auditory system, show task-dependent modification of functional properties. In ferrets trained to do different auditory tasks—either tone detection or frequency discrimination—neurons in A1 responded differently to the identical auditory stimulus, depending on the behavioral context (Fritz et al., 2005).

We have argued that top-down control enables lower-order cortical areas to encode information about more complex stimulus attributes and that with learning there is a shift in the representation of shape information from higher- to lower-order areas. This raises the following question: is there a privileged route by which this information can access the decision-making apparatus, without recapitulating representation of that information along the entire pathway? If the shift in representation serves to alter the cortical strategy for analyzing a stimulus for more rapid and parallel processing, one would expect that the result of the analysis by early visual areas would get to the areas involved in the response without having to be processed in intermediate areas. Again, the solution here might be related to the process by which higher areas query or send instruction to the lower areas, and to the issue of where the top-down signal is coming from. Learning would be a matter of associating the areas engaged with making the decision with the areas in which the information required for making the decision is represented.

Disruption in the Balance of Top-Down Control in Psychiatric Disorders

The idea of dynamic cortical states and the role of top-down influences in sensory processing have a potential bearing on behavioral disorders. For instance, a failure in a form of efference copy has been posited to underlie certain positive symptoms of schizophrenia, including auditory hallucinations and delusions of alien control (Feinberg, 1978; Frith, 1992). A similar control mechanism exists in the auditory system: auditory responses to uttered speech are attenuated when compared to a playback of the same speech (Ford et al., 2001). This attenuation is mediated by top-down connections between the frontal lobes, where speech is generated to the temporal lobes, where it is heard (Paus et al., 1996; Mrsic-Flogel et al., 2005) and is absent in schizophrenic patients (Ford et al., 2001), providing support for a theory of schizophrenia that involves a disruption of these interactions (Feinberg, 1978; Frith, 1992). According to this theory, the lack of the efference copy in schizophrenic patients precludes them from distinguishing self-generated from externally generated percepts, and this may underlie positive symptoms such as auditory hallucinations, delusions, or alien control (Feinberg, 1978; Frith, 1992). People

suffering from this disorder hear the sounds and words that they themselves are generating as coming from an alien source. Lacking the efference copy, however, they are unable to identify these sounds as coming from themselves. The defective recognition of one's own actions in patients with schizophrenia is also manifested in visuomotor control (Spence et al., 1997; Franck et al., 2001), suggesting a modality-independent difficulty in monitoring and recognizing self actions (Frith et al., 2000).

In addition to stabilizing the image during ocular movements, efferent copy serves, during normal motor function, to simulate and correct motor plans. Thus, in a dysfunction of such a system two behaviors are expected: (1) deficit in rapid error correction, which is based in the possibility of predicting an action before it is made and, and (2) difficulty coping with unexpected sensory feedback that requires a model of the expected feedback from the motor action (Macaluso et al., 2000). Both deficits are observed in patients with schizophrenia: they cannot make rapid error corrections (Frith and Done, 1989) nor cope with distortions of motor output, as evidenced by the fact that they experience delusions when hearing their own voice fed back at a different pitch (Cahill et al., 1996).

The theory that auditory hallucinations may result from misattributed internally generated sounds is also supported by imaging studies performed during hallucinatory episodes (Silbersweig et al., 1995; Shergill et al., 2000, 2004) that have shown the involvement of subcortical activity as well as regions involved in speech generation and auditory perception. Moreover, activation in the left inferior frontal gyrus precedes the activation in the temporal gyri, supporting the hypothesis that activation of sensory areas is driven in a top-down fashion by regions mediating the generation of inner speech (Shergill et al., 2004).

The corollary discharge dysfunction may reflect a more generic deficit in top-down influences, reflecting what has been proposed as a disconnection syndrome (Friston et al., 1995; Friston, 2005). Indeed, a variety of experiments have shown a consistent bias in performance deficits: schizophrenic patients may elicit normal behavior in tasks relying on bottom-up processing but are often impaired in tasks that rely heavily on top-down control. For instance, in the masking paradigm (a stimulus is rendered invisible by a mask), changing the order of the mask and the stimulus yields different levels of top-down involvement. Forward masking (the mask precedes the stimulus) is based on retinal and cortical bottom-up mechanisms (Saccuzzo et al., 1996), and backward masking involves a dynamic competition between bottom-up and re-entrant top-down flows of visual information processing (Di Lollo et al., 2000; Enns, 2004). Schizophrenic patients show a deficit in backward (Green et al., 1999; Dehaene et al., 2003a) but not in forward masking (Saccuzzo et al., 1996). A similar dissociation is observed in memory recall paradigms, were schizophrenic patients show unimpaired recollection of implicit memory, for example in stem-completion tasks (Gras-Vincendon et al., 1994; Huron et al., 1995) but are impaired when explicit (conscious) recollec-

tion is required (Huron et al., 1995; Kazes et al., 1999). Thus, more generally, modulation of sensory or mnemonic information by top-down or executive control seems to be impaired in schizophrenia.

A key aspect of top-down influences in normal function is their interaction with perceptual-learning and contextual influences (Ito et al., 1998; Gilbert et al., 2001; Li et al., 2004; Sigman and Dehaene, 2005), selecting relevant information and acting as a modulator of plasticity. Interestingly, this interaction between learning and top-down influences seems to be particularly affected in schizophrenia (Friston et al., 1995; Friston, 2005). Schizophrenic patients manifest a difficulty in learning and representing behaviorally relevant percepts when the selection of relevant information is determined by prior knowledge. This selection process involves activity of the medial frontal gyrus, a region involved in top-down control (MacDonald et al., 2005). On the other hand, the same patients have no deficit in the same tasks when relevant information is conveyed by a distinctive physical property and thus can be distinguished through bottom-up mechanisms (Silverstein et al., 1996). In a contour-integration task, perceptual learning, top-down effect, and their interaction can be studied by performing the task in different presentation orders: increasing difficulty or random order. In the increasing difficulty order contour-detection thresholds are lower, which is thought to indicate top-down influences (the contour is easier to see once it has been seen) (Kovacs, 2000; Li et al., 2006). Chronic schizophrenic patients show impaired learning and an interaction between learning and presentation order manifesting reduced top-down influences in contour detection (Silverstein et al., 2006). This finding is consistent with other observations indicating that schizophrenic patients' perceptual organization breaks down as the elements to be grouped become more distant or less symmetrical, seeming to imply more generally a breakdown of Gestalt organizational processes in schizophrenic patients (Shallice et al., 1991; Frith, 1992; Silverstein and Uhlhaas, 2004).

Thus, numerous lines of evidence point to a functional deficit of top-down control in schizophrenic patients. Whether this can account for the entire pathophysiology of the disease is of course by no means clear. It is worth exploring, however, whether this reversal of the central dogma of feedforward cortical processing in the developing concept of top-down influences may be important not only in our understanding of the normal processing of sensory information but in developing insights into the mechanisms underlying numerous behavioral disorders.

Conclusion

An increasing body of evidence, coming from many sources, points toward a model of sensory processing whereby each cortical area acts as an adaptive processor, undergoing state changes to execute different algorithms depending on behavioral context. Under normal circumstances, each cortical state creates a set of expectations for the subsequent state, and the top-down signal affects

the way the sensory information is analyzed, so that neural responses at all levels of processing reflect this convergence between expectation and sensory evidence. This considerably enriches the functional diversity of each area and the kinds of information that each area conveys to other areas. As a consequence, any given percept or behavior corresponds to a state of interaction between cortical areas, rather than to the activity of specific cortical modules. We have proposed that this interaction is manifest in the way that feedback connections address subsets of intrinsic cortical connections, and the functional properties of a neuron depend on which subset is gated at any given time. The mechanism of perceptual learning may involve the setting up of this addressing, such that both the encoding and recall of learned information involves the appropriate selection of the inputs that convey information about the stimulus being discriminated. This theory of cortical interaction may prove useful in understanding the mechanisms underlying both normal brain function and behavioral disorders.

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