Development and Plasticity of Cortical Processing Architectures

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One of the basic functions of the cerebral cortex is the analysis and representation of relations among the components of sensory and motor patterns. It is proposed that the cortex applies two complementary strategies to cope with the combinatorial problem posed by the astronomical number of possible relations: (i) the analysis and representation of frequently occurring, behaviorally relevant relations by groups of cells with fixed but broadly tuned response properties; and (ii) the dynamic association of these cells into functionally coherent assemblies. Feedforward connections and reciprocal associative connections, respectively, are thought to underlie these two operations. The architectures of both types of connections are susceptible to experience-dependent modifications during development, but they become fixed in the adult. As development proceeds, feedforward connections also appear to lose much of their functional plasticity, whereas the synapses of the associative connections retain a high susceptibility to use-dependent modifications. The reduced plasticity of feedforward connections is probably responsible for the invariance of cognitive categories acquired early in development. The persistent adaptivity of reciprocal connections is a likely substrate for the ability to generate representations for new perceptual objects and motor patterns throughout life.

A fundamental characteristic of the cerebral cortex is the similarity of its organization across different areas (*1*). This suggests that the cortex performs computational operations of a general nature that support functions as diverse as perception, motor programming, remembering, planning, language processing, and reasoning. The exact nature of these omnipotent processing algorithms remains elusive, but the wealth of data gathered over the past few decades permits some educated guesses. Analyses of sensory systems suggest that one basic function of cortical modules is to detect consistent relations among incoming signals—often referred to as features—and to represent such relations by responses of neurons. The iteration of this process is thought to lead eventually to descriptions of the consistent constellations of elementary features that characterize individual perceptual objects. Cortical representations of motor programs are assumed to have a similar format in which descriptions refer to the spatiotemporal relations among activated muscles.

Because the number of possible feature constellations that are examined and eventually represented is astronomical, it is essential that cortical processing algorithms be capable of coping with combinatorial problems. I propose that the cortex uses two main coping strategies. First, hard-wired neurons detect and represent relations that are particularly frequent and important. Second, dynamic grouping mechanisms, which allow for a flexible recombination of responses from hard-wired neurons, enable higher order relations to be analyzed and represented successively within the same hardware. Because most of the relevant published data are from the mammalian visual system, the two strategies and their associated adaptive mechanisms will be discussed in this context.

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Two Strategies, Two Classes of Connections

Neurons in the primary visual cortex of mammals (V1) evaluate particular spatial and temporal relations among the responses of retinal ganglion cells and represent these relations by their feature-specific responses. Among the extracted features are the location, orientation, and polarity of luminance gradients; their direction of motion; their spectral composition; and their interocular disparity, which indicates viewing distance. For the extraction of these features, the signals of retinal ganglion cells must be correlated with one another; this appears to be achieved by the selective recombination of inputs, as first proposed by Hubel and Wiesel (*2*) and supported by several recent studies (*3*). Thus, to detect and to represent the joint firing of ganglion cells responding to the vertical outlines of an object, inputs from vertically oriented rows of ganglion cells are made to converge selectively on individual cortical cells (Fig. 1). It is likely that this strategy of input recombination is also used to evaluate other relations that are analyzed at the level of V1 and that the same basic operations are iterated in prestriate cortical areas. As suggested by the substantial divergence of projections beyond V1 and by the functional specialization of neurons in prestriate areas, many of these operations appear to be performed in parallel, with each area evaluating a particular subset of higher order relations in feature space (*4*).

Interestingly, however, this strategy of recombining inputs and generating cells with selective response properties is not pursued to exhaustive descriptions, either of the elementary features represented in V1 or of the immensely more complex constellations of features of natural objects. At all processing stages, neurons remain broadly tuned to variations of stimulus parameters along different feature dimensions. The responses of individual cells are ambiguous, and a full description of a particular feature or constellation of features can be obtained only by evaluating jointly the graded responses of a population of neurons. Such coarse coding may appear uneconomical, because it seems to require even more neurons to describe a particular feature or constellation of features than would a strategy that uses the responses of individual, sharply tuned cells as descriptors. However, broadly tuned individual cells respond to many different features, and as a consequence, populations coding for different features overlap. Thus, a single cell can participate at different times in the analysis and representation of different features, and this ability can be exploited to reduce substantially the number of required representational units (*5*).

The problem with overlapping population codes is, however, that natural visual scenes usually contain many image components that are adjacent or overlapping in both Cartesian and feature space and thus evoke simultaneous responses in overlapping populations of broadly tuned cells. The advantage of population coding cannot be exploited unless the responses related to a particular feature are identified and labeled in a way that assures their joint evaluation at subsequent processing stages and prevents false conjunctions with responses evoked by unrelated features. Such a strategy requires a dynamic selection process that enables the grouping of distributed neuronal responses in ever-changing constellations. As a result of dynamic grouping, signals are selected at one level and are reassociated in a flexible and context-dependent way at the next level through the

feedforward connections. This process allows for the dynamic rerouting of signals within a fixed hardware configuration, and it circumvents the combinatorial explosion of representational units that would result if every possible feature or constellation of features had to be analyzed by selective recombination of feedforward connections and represented by sharply tuned neurons. The process can therefore be iterated over successive processing stages to analyze and represent, in a versatile way, relations of ever-increasing complexity up to the level where the represented relations describe whole perceptual objects.

I propose that a system exploiting this strategy needs two classes of connections: (i) feedforward connections that are responsible for the generation of neurons with feature-selective receptive fields (RFs), and (ii) reciprocal connections among these neurons that serve to dynamically associate them into assemblies. To economize neurons, the feedforward connections should generate cells with a preference for frequently occurring features that are suitable for the definition of perceptual objects. The reciprocal connections, in contrast, should not contribute to the feature-specific RF structure but should allow for a maximum of combinatorial freedom in associating feature-coding cells. Thus, the constraints for the architecture, development, and use-dependent malleability of the two classes of connections are different. Before reviewing the evidence on the development and adaptivity of feedforward (feature-extracting) and reciprocal (assembly-forming) connections, the organization and putative mode of action of the latter require brief discussion. The two classes of connections are described in Fig. 1.

Strategies for Response Selection

The dynamic selection and association of responses for further joint processing is best accomplished by enhancing their saliency. In principle, there are two strategies to raise the saliency of distributed responses: The selected neurons can be made to discharge more vigorously, or they can be made to discharge in precise temporal synchrony. Both mechanisms enhance the impact of the selected responses, the first profiting from temporal and the second from spatial summation of synaptic potentials in the target cells. Grouping through synchronization has the additional advantage that it can operate at a fast time scale because no temporal integration is required and selection can occur at the level of individual action potentials. This mechanism allows

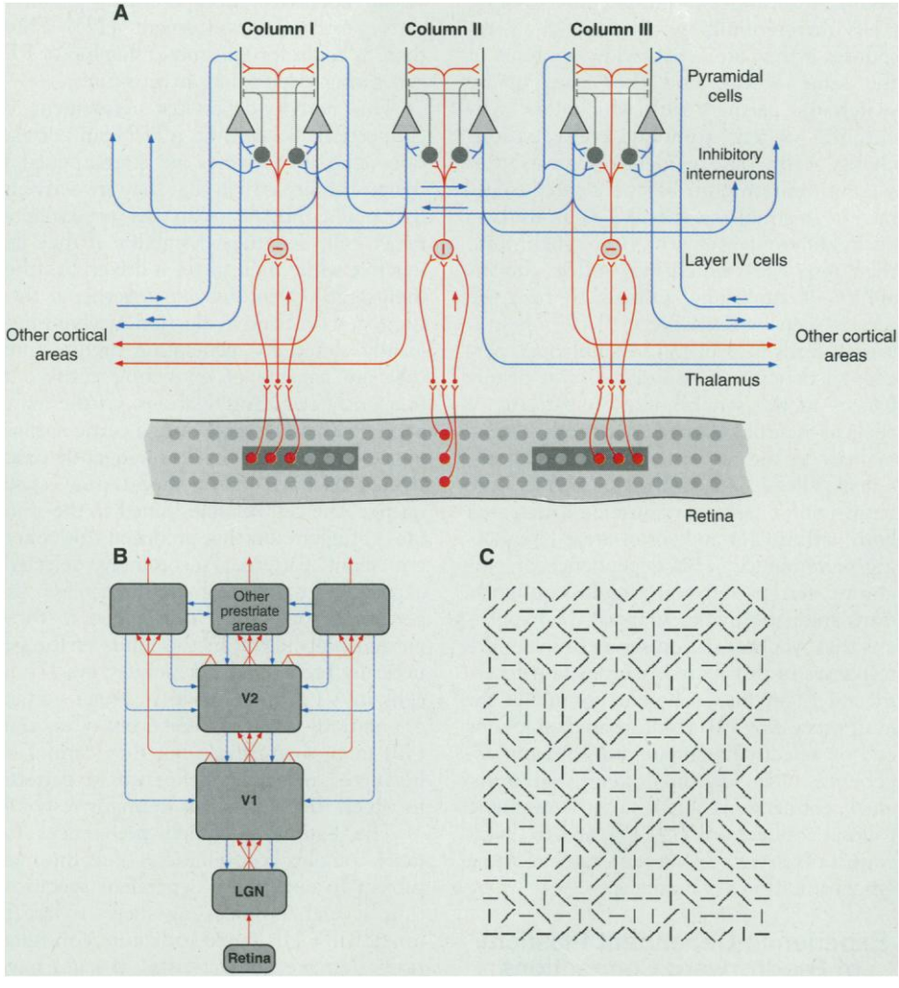

Fig. 1. Schematic representation of feedforward RF-generating connections (red) and reciprocal assembly-forming connections (blue). (**A**) Connections within the primary visual cortex; (**B**) connections between different areas of the visual cortex (LGN, lateral geniculate nucleus). The assumption is that the preference of cortical neurons for particular features results from the specific combination of converging feedforward connections, as exemplified here for cells tuned to horizontally oriented (columns I and III) and vertically oriented (column II) contours. The output of retinal ganglion cells (red dots in retina) that are aligned in horizontal rows (columns I and III) or vertical rows (column II), respectively, converges after relay in the thalamus onto cortical cells in layer IV. Because of this specific combination of inputs, layer IV cells acquire orientation-selective RFs tuned to vertical and horizontal orientations. The output of the orientation-selective layer IV cells is then further relayed onto pyramidal cells in other cortical layers, and these in turn project with feedforward connections to prestriate visual areas (B). This wiring diagram is highly simplified and omits most of the sophistication of intracortical circuitry. As shown in (B), it is assumed that this strategy of evaluating and representing particular relations among input signals by selective recombination of feedforward connections is iterated over the subsequent processing stages in prestriate visual areas. The assembly-forming connections are assumed to originate from and to terminate on pyramidal cells, thus assuring reciprocal excitatory interactions. In addition, they terminate on inhibitory interneurons that in turn synapse on pyramidal cells. As shown in (B), grouping functions are also attributed to the reciprocal connections among cortical areas occupying the same level in the processing hierarchy and to the back-projections from higher to lower processing stages. The latter are thought to bias grouping as a function of computational results obtained at the respective higher level. The general organization of these ensemble-forming interareal connections resembles that of the intra-areal grouping connections: They originate from pyramidal cells, are excitatory, and terminate both on pyramidal cells and on interneurons in the target areas. In the present example, the tangential intra-areal grouping connections (A) are proposed to preferentially link columns responsive to collinear contours; there is some experimental support for this architecture (62) (see arrangement of shaded RFs in the retina). The effect of the resulting grouping is that signals evoked by collinear contour borders are selected and bound preferentially for joint evaluation at subsequent processing stages. (**C**) An example of perceptual grouping on the basis of vicinity and collinearity. The collinearly arranged line segments defining the outlines of a diamond are grouped together and pop out from the randomly distributed line segments of the background. The figure can be segregated from the ground because of the enhanced saliency of figure-defining contour elements.

for multiplexing of grouping operations and may be beneficial when several groups need to be established simultaneously within the same cortical area.

The available evidence suggests that both strategies are used. The discharge rate of cells in V1 can be modified in a context-dependent way by concurrent stimuli that are remote from the classical RF (6), and cells in V1 that respond to the component features of a perceptual figure respond more vigorously than cells that respond to similar features that are not part of a figure (7). These findings support the hypothesis of response selection by modulation of the discharge rate. Experiments on response selection by attentional mechanisms also show an enhancement of selected responses (8).

The recently developed technique of recording discharges from more than one cell simultaneously has shown that cortical cells can synchronize their discharges with a precision in the range of milliseconds (9–17). Cells preferentially synchronize their responses if they are activated by contours of the same object, and they can rapidly switch the partners with which they synchronize when stimulus configurations change (18). The evidence suggests that synchronization probability is related to behavior. In strabismic cats, V1 neurons driven by different eyes no longer synchronize their responses, which may reflect the inability of strabismic animals to fuse the images seen by each eye (19). When strabismus leads in addition to amblyopia, perceptual deficits are associated with disturbances in the synchronization patterns of cortical neurons rather than with abnormalities in the response properties of individual cells (20). In animals trained to solve sensorimotor tasks, synchronicity increased both within (21) and across areas (16) during performance. This dependence of synchronization patterns on stimulus configurations and performance supports the hypothesis that synchronization serves to select the responses of distributed neurons and to associate them into coherent assemblies for joint processing (9). Studies based on lesions and on selective manipulations of early experience have identified tangential intrareal connections (22), interhemispheric callosal connections (14, 15), and feedback connections (15, 23) as substrates of these synchronization phenomena.

Experience-Dependent Plasticity of Feedforward Connections

The basic architecture of the feedforward connections to V1 seems to require no experience for its expression. For example, many neurons develop their characteristic selectivity for elementary features before birth in monkeys and before eye opening in other mammals (24); the same is true for the columnar arrangement of response properties and the layout of maps. The specification of these architectures is thus the result of evolutionary selection. Still, the expression of some of these properties does depend on activity. The blockade of spontaneous retinal discharges prevents the segregation of the afferents from the two eyes into ocular dominance columns (25); this finding suggests that spontaneous activity may promote axon sorting. Ganglion cells in the developing retina engage in coherent oscillatory activity (26), which enables the use of synchronous activity as a means of identifying the origin and neighborhood relations of afferents. However, a substantial fraction of neurons in V1—especially those in layers remote from thalamic input—develop feature-specific responses only if visual experience is available. RF properties and maps in these layers can be modified by manipulating visual experience during a critical period of early postnatal development (27). Thus, there is room for epigenetic shaping of RF-generating feedforward architectures.

This activity-dependent refinement of connections is based on a Hebbian correlation analysis. Synapses are strengthened if the probability is high that they are active in temporal contiguity with the postsynaptic target cell, and they destabilize if they are inactive while their target is driven by other inputs (28). Neurons wire together if they fire together. Such a selection mechanism is ideally suited for generating architectures that are capable of extracting consistent, frequently occurring relations. Of the many afferents that converge onto a particular target cell, only those that are frequently coactivated become consolidated. As a consequence, the cell becomes tuned to the stimulus configuration that produced this coherent input pattern. Accordingly, selective exposure to particular patterns increases the percentage of cortical cells tuned to these patterns, albeit within the limits of the genetically predetermined architecture. Thus, cells in V1 can be made to prefer certain orientations (29) or directions of motion (30) more than others, but they cannot be instructed to develop preferences for patterns to which they would not normally respond.

The extent to which preferences for more complex constellations of features are subject to experience-dependent specification at higher processing stages is largely unknown. Cells tuned to feature constellations that are characteristic of faces have been found in the inferotemporal cortex of baby monkeys (31), which suggests that even complex relations are extracted and represented by genetically determined feedforward architectures. It is not known whether this is also true for patterns that are less stereotyped and meaningful than faces.

Synaptic Mechanisms for the Selection of Feedforward Connections

The selection process appears to be initiated by signals generated in the postsynaptic neurons, which evaluate synchrony in the activity of converging afferents (28); morphological changes in axonal and dendritic arborizations are the end result (32). *N*-methyl-D-aspartate (NMDA) receptors have been assigned an important role in experience-dependent circuit selection. The activation of NMDA receptors helps to prevent the destabilization of inputs that fire in conjunction with the postsynaptic cell, promotes heterosynaptic repression of other inactive inputs, and is a necessary prerequisite for the reconnection of previously weakened connections (33). These findings support the hypothesis that NMDA receptors evaluate the coincidence between pre- and postsynaptic activation and that Ca^{2+} entry through the NMDA receptor serves as an early signal in the synapse stabilization cascade (34). Synapses weaken if they are inactive while the postsynaptic cell is discharging, and it has been proposed that such synapses cannot activate their NMDA receptors (33). Synapses can also weaken if they are active while the postsynaptic cell is prevented from responding (35)—another condition in which the activation of NMDA receptors is unlikely.

These conditions are strikingly similar to those required for the induction of synaptic gain changes in the adult, such as homosynaptic long-term potentiation (LTP), heterosynaptic depression, and homosynaptic long-term depression (LTD). These phenomena are all rapidly inducible and long-lasting changes of synaptic efficacy (Fig. 2), and they were first discovered in the hippocampus. Experimental results support the suggestion that these use-dependent changes in synaptic gain could also serve as a first step in experience-dependent circuit selection. In vitro studies of visual cortex slices demonstrated LTP (36) and LTD (37), revealed a dependence of plasticity on NMDA receptor activation similar to that seen in developmental changes (38), and, most important, showed an age-dependent decline in susceptibility to LTP induction that paralleled the time course of the critical period (39, 40) for experience-dependent modifications. This decline is associated with a reduced contribution of NMDA receptor–mediated synaptic responses (39, 40), which seems to involve three factors: a reduction in the number of NMDA receptors (41), an increase of postsynaptic inhibition that prevents lifting of the Mg^{2+} block (39), and a developmental change in the gating characteristics of the NMDA receptor (42). Rearing animals in

darkness, which prolongs the critical period, also retards the decline in LTP susceptibility (*43*). Furthermore, there is evidence that manipulations that facilitate LTP induction, such as addition of the neuromodulators acetylcholine and norepinephrine (*44*) or direct depolarization of postsynaptic cells, also favor the induction of experience-dependent modifications of RF properties (*45*). Although these analogies are attractive, there is still no direct proof that LTP and LTD serve as the first steps in developmental circuit selection.

It is of particular interest that the experience-dependent selection of feedforward connections is not determined solely by local correlations of activity, but is supervised by attentional mechanisms. Sensory signals induce circuit changes only when animals attend to these signals and use them for the control of behavior (*46*). Experience-dependent modifications also fail to occur when the noradrenergic, cholinergic, or serotoninergic projections to the visual cortex are inactivated; the permissive effects of these modulatory projections are mediated by β, M1, and S2 receptors, respectively (*47*). These results suggest that the developing brain can shape its own architecture not only as a function of frequently occurring input constellations, but also as a function of their behavioral relevance.

A large number of cellular mechanisms have been identified that change during early development in parallel with the decline of use-dependent plasticity. This suggests that numerous processes cooperate in the maintenance of use-dependent plasticity during the critical period (*48*). Recently, neurotrophins such as nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) have also been shown to play a role in the experience-dependent selection of feedforward connections, but the results are still inconclusive (*49*). Thus, although the rules that govern activity-dependent circuit selection are reasonably well understood, its underlying molecular mechanisms remain unclear.

Use-Dependent Plasticity of Assembly-Forming Connections

Few data are available on the developmental specification of feedback projections and reciprocal intra-areal and interareal cortico-cortical connections. Most of these path-

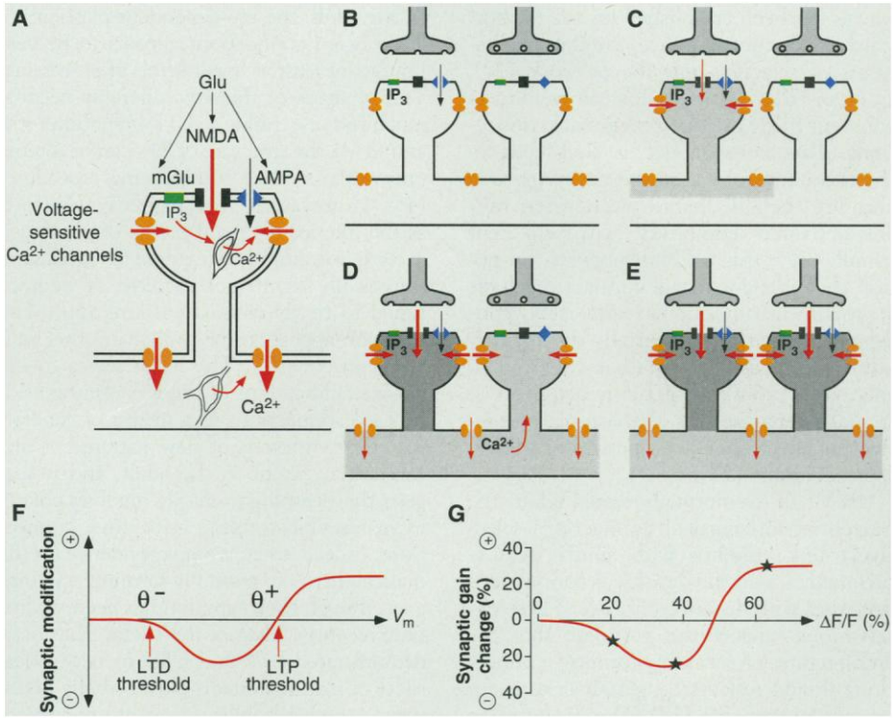

Fig. 2. Putative synaptic processes likely to mediate the induction of experience-dependent circuit selection during development and of long-lasting synaptic gain changes in the adult. Here, only glutamatergic synapses are considered. (**A**) Summary of ligand-gated and voltage-gated mechanisms that contribute to depolarization and modulate the concentration of Ca^{2+} ions $[Ca^{2+}]_i$ in the postsynaptic dendritic compartment. Glu, glutamate; IP_3, inositol trisphosphate; green, mGlu (metabotropic glutamate) receptor; black, NMDA receptor; blue, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor. (**B** through **E**) Homosynaptic and heterosynaptic modifications of synaptic transmission for two inputs terminating on spines of the same dendritic segment. Mechanisms influencing $[Ca^{2+}]_i$ are indicated by the same symbols as in (A). Red arrows indicate Ca^{2+} movements, and their thickness indicates the amplitude of the flux. The density of the shading reflects both the expected amount of depolarization and the increase in $[Ca^{2+}]_i$. In (B) through (D) only the input on the left is active, whereas in (E) both inputs are simultaneously active. The four conditions differ in the amplitude of the depolarizing responses of the postsynaptic dendrite. It is assumed that this amplitude is determined both by the activity of the modifiable synapses and by the state of other excitatory, inhibitory, and modulatory inputs to the same dendritic compartment (not shown). In (B), the left input fiber discharges at low frequency. Only AMPA and mGlu receptors are activated; voltage-gated Ca^{2+} conductances are inactive. There is no substantial rise in $[Ca^{2+}]_i$ and no lasting modification of synaptic transmission at the active synapse. In (C), the left input fiber discharges at higher frequency. Now both NMDA receptor–gated and voltage-gated Ca^{2+} channels are moderately activated. $[Ca^{2+}]_i$ rises to an intermediate level and leads to LTD of the active synapse. There is only a small spread of depolarization to other spines. In (D), the depolarizing response is assumed to be stronger than in (C), either because the left input fiber discharges at higher frequency or because it is active in conjunction with other excitatory inputs. Accordingly, the NMDA receptor–gated and voltage-gated Ca^{2+} conductances are also more activated. The massive increase of $[Ca^{2+}]_i$ in the activated spine leads to LTP. Moreover, depolarization spreads to other compartments of the cell and is thought to trigger action potentials. This spread of depolarization, aided perhaps by back-propagating Na^+ spikes (*63*), activates voltage-gated conductances. This is assumed to lead to an intermediate rise in $[Ca^{2+}]_i$ at the postsynaptic side of the inactive synapse, which as a result undergoes heterosynaptic depression. In (E), conditions are as in (D) except that the second input is now also active; this facilitates the recruitment of ligand-gated Ca^{2+} sources at the synapses of the second input and raises $[Ca^{2+}]_i$ above the LTP threshold, so that the second input is no longer depressed but undergoes LTP. Because the first input already causes substantial depolarization of the dendritic compartment, the second input can undergo LTP at amounts of activation well below those that would be required if the first input had not been activated. Most of the experience-dependent developmental circuit changes can be accounted for by this scenario if LTP and LTD are equated with consolidation and disruption of synaptic connections, respectively. (**F**) Illustration of the dependence of the polarity of synaptic gain changes on the depolarization level of the dendritic compartment. The ordinate is the direction of gain change; the abscissa is the membrane potential (V_m), displaying the depolarization achieved during activation; and θ^- and θ^+ are thresholds for the induction of LTD and LTP, respectively. (**G**) Experimentally determined (*65*) increases of dendritic Ca^{2+} concentration, expressed as fluorescence change (ΔF/F) of the Ca^{2+} indicator Fura-2 (abscissa) after activation protocols leading to weak LTD (first star), strong LTD (second star), and strong LTP (third star). The ordinate is the average amplitude of synaptic gain changes induced with the three stimulation protocols. As predicted by Lisman (*66*), there is a close correlation between changes in membrane potential (V_m), the increase of $[Ca^{2+}]_i$, and the polarity and magnitude of synaptic gain changes. [Parts (A) through (E) adapted from (*64*)]

ways attain their final selectivity only during postnatal life, and their architecture is highly susceptible to activity-dependent modifications. In cat V1 the tangential intracortical connections already exhibit a crude periodic patterning before eye opening, which suggests some experience-independent selectivity in the organization of these connections (*50*), but it is not known whether this selectivity is related to the columnar pattern of feature-specific cells that emerges at almost the same time. As the tangential axons continue to grow beyond the time of eye opening, they combine extension with refinement toward the highly selective mature pattern (*51*, but see *50*). Depriving kittens of vision delays this refinement (*52*), and data from strabismic kittens indicate that the vision-dependent selection of these intracortical connections follows a correlation rule in much the same way as has been established for the feedforward connections; hence, similar mechanisms of selection may be at work (*22*). Columns that exhibit a low probability of coherent firing lose their reciprocal connections. One consequence is that cells in these columns also lose the ability to synchronize their discharges even when they are activated conjointly with coherent stimuli (*19*); this finding supports the notion that corticocortical connections have a synchronizing action. Conversely, contiguous activation of spatially distant columns increases their mutual coupling to the extent that cells actually acquire two spatially separate RFs, the ectopic one reflecting the response properties of the remote columns (*53*).

In V1 of the normally reared adult, the tangential intracortical connections selectively link columns with similar feature preferences, and the density of connections decreases with distance (*11*, *54*). These observations support the postulate that the architecture of assembly-forming connections should reflect the gestalt criteria for perceptual grouping (*18*). The organization of the tangential connections in V1 seems appropriate for the grouping of responses according to the criteria of vicinity and similarity (Fig. 1). Because tangential connections are selected by experience according to a correlation rule, their mature architecture should reflect to some extent the joint probabilities with which particular features co-occurred during early development. Such acquisition of knowledge about typical feature constellations by changes in architecture would be ideally suited to support figure-ground distinctions and perceptual grouping. Responses to feature constellations that are characteristic for perceptual objects would become grouped preferentially and routed together through feedforward connections for further joint processing.

No data are yet available on the genetic constraints that limit the epigenetic modifiability of these tangential cortical connections, nor is it known whether their use-dependent selection is gated by modulatory systems. Data are also lacking on the development and epigenetic modifiability of reciprocal corticocortical long-range connections. Except for the callosal connections of cat area 17, which seem to exhibit a dependence on experience similar to that of the intrinsic tangential connections (*55*), virtually nothing is known about the role of experience in the development of interareal and feedback projections. However, it is unlikely that they would be less susceptible to epigenetic selection than are the intra-areal connections.

Plasticity in the Mature Cortex

In the adult, the use-dependent plasticity of feedforward connections appears to be very limited, at least at lower levels of processing. The synapses of thalamic afferents become much less susceptible to LTP induction (*40*), and in V1 the structure of RFs can be altered only with invasive conditioning procedures (*45*). However, even at higher levels (such as the inferior temporal cortex of primates), extensive training is required to produce a statistically significant increase of neurons tuned to newly learned patterns (*56*). The situation appears to be similar in other sensory cortices (*57*). This view seems to exclude modifications of the RF-forming feedforward connections as a means of generating representations of new patterns to any substantial extent in the adult, and it suggests that learning primarily involves changes in assembly-forming associative connections. Indeed, there is ample evidence for the malleability of assembly-forming circuits, even though their function has been studied only recently. Most of the studies that have demonstrated LTP and LTD in neocortical slices of mature animals have actually investigated the malleability of reciprocal corticocortical connections, although this is rarely made explicit. Recordings typically are obtained from neurons in the supragranular layers, and responses are investigated that are elicited from white matter, from layer IV, or from adjacent regions within the supragranular layers. If these responses are monosynaptic as claimed, they are mainly, if not exclusively, the result of either intra-areal (tangential or ascending) connections or of long-range corticocortical projections. Thus, it is safe to conclude that corticocortical connections in the adult can undergo LTP and LTD and hence are highly susceptible to use-dependent long-term modifications of their efficacy.

Evidence for use-dependent changes in the coupling strength of corticocortical connections is also available from in vivo recordings. Repeated coactivation of neuron pairs in the auditory cortex of monkeys led to enhanced synchronization of their discharges, and this effect occurred only when the monkeys paid attention to the tone used for activation (*58*). This finding is best explained by the enhanced efficacy of connections that do not contribute to the RF proper but have synchronizing effects, as is typical of tangential intracortical connections (*14*, *19*). Several studies have demonstrated striking rearrangements of retinotopic and somatotopic maps after prolonged stimulation of afferent pathways as well as after denervation (*57*, *59*). Because these modifications occurred over large distances, they could not be accounted for by adaptive changes at the level of feedforward connections and thus were attributed to enhanced efficacy of tangential intracortical connections. It appears that under the extreme condition of deafferentation, the intracortical association connections can increase their efficacy to the extent that they can actually drive cells in remote columns and hence generate RFs. Recent evidence suggests that this increase in efficacy is associated with sprouting and the formation of new synaptic contacts (*60*).

Long-term changes in the efficacy of the ensemble-forming association connections at one level of processing are expected to alter the activity patterns conveyed by feedforward connections to the next level. Hence, the response properties of neurons at the next level should change, which would seem to be inconsistent with the relative stability of RFs in the adult. One explanation is that the expected modifications may be revealed only if the effect of grouping operations, rather than the structure of classical RFs, is studied; such studies will require the application of more complex stimuli and the analysis of context-dependent response modifications (*61*).

Conclusions

Although data on the use-dependent development of cortical circuits are still sparse, the following conclusions appear to be warranted:

1) During early postnatal development, both the feedforward RF-generating connections and the reciprocal assembly-forming connections are susceptible to experience-dependent modifications, and these use-dependent changes appear to obey a correlation rule that emphasizes the role of coherent activity in circuit selection. Converging inputs that convey consistent messages (where the consistency criterion is repeated, correlated activation) become consolidated. Despite its substantial malleability, the architecture of the feedforward connections appears to be more constrained

by genetic predisposition than that of the assembly-forming connections, but more data are needed to substantiate this point.

2) After the end of morphogenesis, the architectures of both connection systems crystallize. In sensory cortices, most of the RF-forming pathways also seem to lose the ability to undergo use-dependent gain changes, whereas this ability is retained by the assembly-forming connections.

3) This persistent functional malleability of assembly-forming connections is the likely basis for the generation of new representations, because it allows for the rapid and flexible association of feature-representing neurons into new constellations. It also seems to be responsible for the short- and long-term changes observed in cortical maps after extensive stimulation or denervation.

4) The rules and induction mechanisms that underlie use-dependent gain changes of assembly-forming connections in the adult are similar to those that support circuit selection during development. It is therefore tempting to assume that LTP or LTD serve as an initial step in both processes. Because LTP and LTD are phenomena that can be rapidly reversed, they alone cannot suffice to generate new representations, that is, durable associations of feature-specific cells. They may, however, play an important role in the rapid and context-dependent association of neurons, and hence in the flexible selection and routing of activity across subsequent processing stages. Permanent associations could form if synapses that often undergo LTP, or whose potentiation is not rapidly reset, were to eventually strengthen irreversibly. Adult plasticity could thus be construed as the continuation of developmental processes; in such a model, they would only differ in that adult plasticity no longer leads to modifications of the blueprint of the architecture and operates mainly by regulating the efficacy of assembly-forming connections.

REFERENCES AND NOTES

1. J. Szentágothai, in *The Neurosciences 4th Study Program*, F. D. Schmitt and F. G. Worden, Eds. (MIT Press, Cambridge, MA, 1979), pp. 399–415; R. J. Douglas, K. A. C. Martin, D. Whitteridge, *Neural Comput.* **1**, 480 (1989).
2. D. H. Hubel and T. N. Wiesel, *J. Physiol. (London)* **160**, 106 (1962); D. H. Hubel, in *Sensory Physiology and Behavior*, R. Galun, P. Hillman, I. Parnas, R. Werman, Eds. (Plenum, New York, 1975), pp. 21–24.
3. B. Chapman, K. R. Zahs, M. P. Stryker, *J. Neurosci.* **11**, 1347 (1991); B. Jagadeesh, H. S. Wheat, D. Ferster, *Science* **262**, 1901 (1993).
4. J. H. R. Maunsell, *Science* **270**, 764 (1995).
5. D. O. Hebb, *The Organization of Behavior* (Wiley, New York, 1949); V. Braitenberg, in *Lecture Notes in Biomathematics 21, Theoretical Approaches in Complex Systems*, R. Heim and G. Palm, Eds. (Springer, Berlin, 1978), pp. 171–188; S. Grossberg, *Psychol. Rev.* **87**, 1 (1980); C. von der Malsburg, *Ber. Bunsenges. Phys. Chem.* **89**, 703 (1985); W. Singer, in *Models of the Visual Cortex*, D. Rose and V. G. Dobson, Eds. (Wiley, Chichester, UK, 1985), pp. 123–136; G. M. Edelman, *Neural Darwinism: The Theory of Neuronal Group Selection* (Basic, New York, 1987); *The Remembered Present* (Basic, New York, 1989); G. Palm, *Concepts Neurosci.* **1**, 133 (1990); M. Abeles, *Corticonics* (Cambridge University, Cambridge, 1991); G. L. Gerstein and P. M. Gochin, in *Information Processing in the Cortex, Experiments and Theory*, A. Aertsen and V. Braitenberg, Eds. (Springer, Berlin, 1992), pp. 139–173; M. P. Young and S. Yamane, *Science* **256**, 1327 (1992).
6. J. I. Nelson, in *Models of the Visual Cortex*, D. Rose and V. G. Dobson, Eds. (Wiley, Chichester, UK, 1985), pp. 108–122; C. Morrone, D. C. Burr, L. Maffei, *Proc. R. Soc. London Ser. B* **216**, 335 (1982); C. Blakemore and E. A. Tobin, *Exp. Brain Res.* **15**, 439 (1972); C. D. Gilbert and T. N. Wiesel, *Nature* **356**, 150 (1992).
7. V. A. F. Lamme, B. W. van Dijk, H. Spekreijse, *Nature* **363**, 541 (1993); V. A. F. Lamme, *J. Neurosci.* **15**, 1605 (1995).
8. Selective attention is considered a candidate mechanism for dynamic selection and flexible routing of responses [R. H. Wurtz, M. E. Goldberg, D. L. Robinson, *Prog. Psychobiol. Physiol. Psychol.* **9**, 43 (1980); J. Moran and R. Desimone, *Science* **229**, 782 (1985)].
9. For reviews see W. Singer, *Annu. Rev. Physiol.* **55**, 349 (1993); ———, in *Large-Scale Neuronal Theories of the Brain*, C. Koch and J. L. Davis, Eds. (MIT Press, Cambridge, MA, 1994), pp. 201–237; W. Singer and C. M. Gray, *Annu. Rev. Neurosci.* **18**, 555 (1995). The analysis of correlated firing among simultaneously recorded neurons was initially used as a tool to investigate neuronal connectivity. Hence, early cross-correlation studies did not consider stimulus- or context-dependent variations in correlation probability. Still, numerous studies revealed correlated firing among spatially distributed cortical neurons (*10, 11*) [K. Toyama, M. Kimura, K. Tanaka, *J. Neurophysiol.* **46**, 191 (1981); *ibid.*, p. 202; A. Michalski, G. L. Gerstein, J. Czarkowska, R. Tarnecki, *Exp. Brain Res.* **51**, 97 (1983); F. Aiple and J. Krüger, *ibid.* **72**, 141 (1988); Y. Hata, T. Tsumoto, H. Sato, K. Hagihara, H. Tamura, *Nature* **335**, 815 (1988); Y. Hata, T. Tsumoto, H. Sato, H. Tamura, *J. Physiol. (London)* **441**, 593 (1991); P. M. Gochin, E. K. Miller, C. G. Gross, G. L. Gerstein, *Exp. Brain Res.* **84**, 505 (1991); C. Schwarz and J. Bolz, *J. Neurosci.* **11**, 2995 (1991); A. W. Roe and D. Y. Ts'o, *Soc. Neurosci. Abstr.* **18**, 11.4 (1992)]. Later investigations focused on stimulus-induced correlated firing and emphasized the dynamic aspect and context dependence of synchronization phenomena. Stimulation-dependent synchronization always occurs with near-zero phase lag and is often associated with oscillatory firing patterns; it is not time-locked to the stimulus, which indicates that synchrony is generated by neuronal interactions. Such dynamic synchronization has been found between neurons distributed within the same cortical area (*12*), between neurons distributed across different areas within the same hemisphere (*13*), between neurons located in different hemispheres (*14, 15*), between visual areas and the multimodal association cortex (*16*), and between the somatosensory and motor cortices (*17*).
10. D. Ts'o, C. Gilbert, T. N. Wiesel, *J. Neurosci.* **6**, 1160 (1986).
11. D. Ts'o and C. Gilbert, *ibid.* **8**, 1712 (1988).
12. C. M. Gray and W. Singer, *Proc. Natl. Acad. Sci. U.S.A.* **86**, 1698 (1989); A. K. Engel, P. König, C. M. Gray, W. Singer, *Eur. J. Neurosci.* **2**, 588 (1990); M. S. Livingstone, *Soc. Neurosci. Abstr.* **17**, 73.3 (1991); R. Eckhorn, T. Schanze, M. Brosch, W. Salem, R. Bauer, in *Induced Rhythms in the Brain*, E. Basar and T. H. Bullock, Eds. (Birkhäuser, Boston, 1992), pp. 47–82; C. M. Gray and G. Viana Di Prisco, *Soc. Neurosci. Abstr.* **19**, 359.8 (1993); R. Eckhorn, A. Frien, R. Bauer, T. Woelbern, H. Kehr, *Neuroreport* **4**, 243 (1993) [but see T. J. Gawne and B. J. Richmond, *J. Neurosci.* **13**, 2758 (1993) for a differing interpretation].
13. R. Eckhorn *et al., Biol. Cybern.* **60**, 121 (1988); A. K. Engel, A. K. Kreiter, P. König, W. Singer, *Proc. Natl. Acad. Sci. U.S.A.* **88**, 6048 (1991); J. Bullier, M. H. J. Munk, L. G. Nowak, *Soc. Neurosci. Abstr.* **18**, 11.7 (1992); L. G. Nowak, M. H. J. Munk, N. Chounlamountri, J. Bullier, *Oscillatory Event-Related Brain Dynamics*, C. Pantev *et al.*, Eds. (Plenum, New York, 1994), pp. 85–98.
14. A. K. Engel, P. König, A. K. Kreiter, W. Singer, *Science* **252**, 1177 (1991).
15. J. I. Nelson, L. G. Nowak, G. Chouvet, M. H. J. Munk, J. Bullier, *Soc. Neurosci. Abstr.* **18**, 11.8 (1992).
16. S. L. Bressler, R. Coppola, R. Nakamura, *Nature* **366**, 153 (1993); P. R. Roelfsema, P. König, A. K. Engel, W. Singer, *Eur. J. Neurosci.* **7** (suppl.), 13.04 (1994).
17. V. N. Murthy and E. E. Fetz, *Proc. Natl. Acad. Sci. U.S.A.* **89**, 5670 (1992).
18. C. M. Gray, P. König, A. K. Engel, W. Singer, *Nature* **338**, 334 (1989); A. K. Engel, P. König, W. Singer, *Proc. Natl. Acad. Sci. U.S.A.* **88**, 9136 (1991).
19. P. König, A. K. Engel, S. Löwel, W. Singer, *Eur. J. Neurosci.* **5**, 501 (1993).
20. P. R. Roelfsema, P. König, A. K. Engel, R. Sireteanu, W. Singer, *ibid.* **6**, 1645 (1994).
21. M. Abeles, H. Bergman, E. Margalit, E. Vaadia, *J. Neurophysiol.* **70**, 1629 (1993); E. Vaadia *et al.*, *Nature* **373**, 515 (1995).
22. S. Löwel and W. Singer, *Science* **255**, 209 (1992).
23. A. M. Sillito, H. E. Jones, G. L. Gerstein, D. C. West, *Nature* **369**, 479 (1994).
24. D. H. Hubel and T. N. Wiesel, *J. Neurophysiol.* **26**, 994 (1963); T. N. Wiesel and D. H. Hubel, *J. Comp. Neurol.* **158**, 307 (1974).
25. M. P. Stryker and W. A. Harris, *J. Neurosci.* **6**, 2117 (1986).
26. L. Galli and L. Maffei, *Science* **242**, 90 (1988); M. Meister, R. O. L. Wong, D. A. Baylor, C. J. Shatz, *ibid.* **252**, 939 (1991).
27. C. Blakemore, R. C. van Sluyters, J. A. Movshon, in *Cold Spring Harbor Symposia on Quantitative Biology XL*, 601 (1976); Y. Frégnac and M. Imbert, *Physiol. Rev.* **64**, 325 (1984); M. P. Stryker, in *Development of the Visual System*, D. M.-K. Lau and C. J. Shatz, Eds. (MIT Press, Cambridge, MA, 1991), pp. 267–287; J. P. Rauschecker, *Physiol. Rev.* **71**, 587 (1991); C. S. Goodman and C. J. Shatz, *Neuron* **10** (suppl.), 77 (1993).
28. J. P. Rauschecker and W. Singer, *Nature* **280**, 58 (1979); K. D. Miller, J. B. Keller, M. P. Stryker, *Science* **245**, 605 (1989).
29. C. Blakemore and G. F. Cooper, *Nature* **228**, 477 (1970); H. V. B. Hirsch and D. N. Spinelli, *Science* **168**, 869 (1970); J. P. Rauschecker and W. Singer, *J. Physiol. (London)* **310**, 215 (1981).
30. F. Tretter, M. Cynader, W. Singer, *Brain Res.* **84**, 143 (1975).
31. H. R. Rodman, S. P. O'Scalaidhe, C. G. Gross, *J. Neurophysiol.* **70**, 1115 (1993).
32. M. J. Friedländer, K. A. C. Martin, D. Wassenhove-McCarthy, *J. Neurosci.* **11**, 3268 (1991); A. Antonini and M. P. Stryker, *ibid.* **13**, 3549 (1993); A. Kossel, S. Löwel, J. Bolz, *ibid.* **15**, 3913 (1995).
33. A. Kleinschmidt, M. F. Bear, W. Singer, *Science* **238**, 355 (1987); Q. Gu, M. F. Bear, W. Singer, *Dev. Brain Res.* **47**, 281 (1989); M. F. Bear, A. Kleinschmidt, Q. Gu, W. Singer, *J. Neurosci.* **10**, 909 (1990).
34. M. F. Bear, L. N. Cooper, F. F. Ebner, *Science* **237**, 42 (1987); K. Fox and N. W. Daw, *Trends Neurosci.* **16**, 116 (1993).
35. H. O. Reiter and M. P. Stryker, *Proc. Natl. Acad. Sci. U.S.A.* **85**, 3623 (1988).
36. A. Artola and W. Singer, *Nature* **330**, 649 (1987); T. Tsumoto, *Prog. Neurobiol.* **39**, 209 (1992); J. Hirsch and C. Gilbert, *J. Physiol. (London)* **461**, 247 (1993); A. Kirkwood, S. M. Dudek, J. T. Gold, C. D. Aizenman, M. F. Bear, *Science* **260**, 1518 (1993).
37. A. Artola, S. Bröcher, W. Singer, *Nature* **347**, 69 (1990); T. Tsumoto, *Neurosci. Res.* **16**, 263 (1993); A. Kirkwood and M. F. Bear, *J. Neurosci.* **14**, 1634 (1994); *ibid.*, p. 3404.
38. W. Singer and A. Artola, in *Excitatory Amino Acids and Synaptic Function*, A. Thomson, Ed. (Academic Press, London, ed. 2, in press).
39. N. Kato, A. Artola, W. Singer, *Dev. Brain Res.* **60**, 43 (1991); N. Kato, M. S. Braun, A. Artola, W. Singer, *Exp. Brain Res. Ser.* 20, 81 (1991).
40. M. C. Crair and R. C. Malenka, *Nature* **375**, 325 (1995).

41. T. Tsumoto, K. Hagihara, H. Sato, Y. Hata, *ibid.* **327**, 513 (1987); K. Bode-Greuel and W. Singer, *Dev. Brain Res.* **46**, 197 (1989); K. Fox, H. Sato, N. Daw, *J. Neurosci.* **9**, 2443 (1989); K. Fox, N. Daw, H. Sato, D. Czepita, *ibid.* **12**, 2672 (1992).
42. S. Hestrin, *Nature* **357**, 686 (1992).
43. A. Kirkwood, H.-K. Lee, M. F. Bear, *ibid.* **375**, 328 (1995).
44. S. Bröcher, A. Artola, W. Singer, *Brain Res.* **573**, 27 (1992).
45. Y. Frégnac, D. Shulz, S. Thorpe, E. Bienenstock, *Nature* **333**, 367 (1988); J. M. Greuel, H. J. Luhmann, W. Singer, *Science* **242**, 74 (1988).
46. Visual stimulation does not induce changes in ocular dominance and orientation selectivity of cortical neurons when applied during anesthesia. Likewise, monocular deprivation fails to induce circuit changes in awake animals when the signals conveyed by the open eye are inappropriate for visuomotor coordination. Conversely, even under anesthesia, passive visual stimulation produces changes in feedforward connections when paired with electrical activation of central core projections. For a review of literature on central gating of developmental plasticity, see W. Singer, *J. Exp. Biol.* **153**, 177 (1990).
47. T. Kasamatsu and J. D. Pettigrew, *J. Comp. Neurol.* **185**, 139 (1979); M. F. Bear and W. Singer, *Nature* **320**, 172 (1986); Q. Gu and W. Singer, *Eur. J. Neurosci.* **5**, 475 (1993); *ibid.* **7**, 1146 (1995). No data are yet available on a putative gating function of the dopaminergic system.
48. Modifications have been described for surface recognition molecules at synaptic locations, for distributions of a variety of neurotransmitter receptors and voltage-gated Ca^{2+} channels, for the gating characteristics of NMDA receptors, for the laminar distribution of modulatory afferents, and for a large number of second messenger systems (*46*) [C. Shaw, M. C. Needler, M. Wilkinson, C. Aoki, M. Cynader, *Prog. Neuro-Psychopharmacol. Biol. Psychiatry* **8**, 627 (1984)].
49. The effects of adding NGF were found to be compatible with the hypothesis that input selection could be based on competition for neurotrophins released by the postsynaptic target in an activity-dependent way [L. Maffei, N. Berardi, L. Domenici, V. Parisi, T. Pizzorusso, *J. Neurosci.* **12**, 4651 (1992); G. Carmignoto, R. Canella, P. Candeo, M. C. Comelli, L. Maffei, *J. Physiol. (London)* **464**, 343 (1993); N. Berardi *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **91**, 684 (1994); L. Domenici, A. Cellerino, N. Berardi, A. Lattaneo, L. Maffei, *Neuroreport* **5**, 2041 (1994)]. Application of BDNF but not of NGF was found to prevent sorting of thalamic afferents into ocular dominance columns [R. J. Cabelli, A. Hohn, C. J. Shatz, *Science* **267**, 1662 (1995)], and intracortical infusion of BDNF but not of NGF in monocularly deprived kittens unexpectedly promoted the disconnection of nondeprived inputs and thus reversed the polarity of the selection mechanism [R. A. W. Galuske, D. S. Kim, E. Castren, W. Singer, *Soc. Neurosci. Abstr.* **20**, 136.9 (1994)].
50. J. Lübke and K. Albus [*Eur. J. Neurosci.* **4**, 189 (1992)] concluded that the patchy pattern of intrinsic connections at the time of eye opening closely resembles the pattern seen in adults and requires no further developmental refinement.
51. D. J. Price and C. Blakemore, *Nature* **316**, 721 (1985); H. J. Luhmann, W. Singer, L. Martinez-Millan, *Eur. J. Neurosci.* **2**, 344 (1990); E. M. Callaway and L. C. Katz, *J. Neurosci.* **10**, 1134 (1990); R. A. W. Galuske and W. Singer, *Cereb. Cortex*, in press.
52. E. M. Callaway and L. C. Katz, *Proc. Natl. Acad. Sci. U.S.A.* **88**, 745 (1991).
53. W. Singer and F. Tretter, *Exp. Brain Res.* **26**, 171 (1976).
54. C. D. Gilbert and T. N. Wiesel, *ibid.* **9**, 2432 (1989); R. Malach, Y. Amir, M. Harel, A. Grinvald, *Proc. Natl. Acad. Sci. U.S.A.* **90**, 10469 (1993).
55. G. M. Innocenti and D. O. Frost, *Nature* **280**, 231 (1979); K. E. Schmidt, D.-S. Kim, W. Singer, T. Bonhoeffer, S. Löwel, *Proceedings of the 22nd Neurobiology Conference, Göttingen* (Thieme, Stuttgart, Germany, 1994), vol. 2, p. 502.
56. Y. Miyashita, *ibid.* **335**, 817 (1988); K. Sakai and Y. Miyashita, *ibid.* **354**, 152 (1991).
57. Although modifications of response properties have been described after conditioning and extensive stimulation in the auditory cortex [N. M. Weinberger, *Curr. Opin. Neurobiol.* **3**, 570 (1993); G. H. Recanzone, C. E. Schreiner, M. M. Merzenich, *J. Neurosci.* **13**, 87 (1993)] and in the somatosensory cortex [M. M. Merzenich and K. Sameshima, *Curr. Opin. Neurobiol.* **3**, 187 (1993); J. H. Kaas, in *The Cognitive Neurosciences*, M. S. Gazzaniga, Ed. (MIT Press, Cambridge, MA, 1995), pp. 51–71; M. M. Merzenich and C. de Charms, in *Mind and the Brain*, P. Churchland and R. Llinas, Eds. (MIT Press, Boston, in press)], the changes in RF properties were confined to modifications of tuning width and size and to minor changes in preferred features. Drastic alterations in the response properties of neurons can be observed in higher sensory areas and in motor centers as a function of changes in attention or of the behavioral task. Because these modifications occur at a fast time scale, they are probably caused by dynamic context-dependent rerouting of input signals rather than by synaptic modifications of feedforward connections.
58. E. Ahissar *et al.*, *Science* **257**, 1412 (1992).
59. Y. M. Chino, E. L. Smith, J. H. Kaas, Y. Sasaki, H. Cheng, *ibid.* **15**, 2417 (1995); L. M. Schmid, M. G. P. Rosa, M. B. Calford, *Neuroreport* **6**, 1349 (1995); A. Das and C. D. Gilbert, *Nature* **375**, 780 (1995).
60. C. Darian-Smith and C. D. Gilbert, *J. Neurosci.* **15**, 1631 (1995).
61. Context-dependent modifications of RFs have been shown in V1. Responses to stimuli presented in the classical RF are modulated by concomitant stimulation of neighboring regions in the visual field (*6*) but also following intensive and repeated activation of these regions [M. W. Pettet and C. D. Gilbert, *Proc. Natl. Acad. Sci. U.S.A.* **89**, 8366 (1992)].
62. Intrinsic connections span larger distances along trajectories corresponding to the location of orientation columns that respond to collinear contours [K. E. Schmidt, S. Löwel, R. Goebel, W. Singer, in preparation; D. Fitzpatrick, Y. Zhang, B. R. Schofield, E. C. Muly, *Soc. Neurosci. Abstr.* **19**, 179.2 (1993)].
63. G. J. Stuart and B. Sakmann, *Nature* **367**, 69 (1994); R. Yuste and W. Denk, *ibid.* **375**, 682 (1995).
64. A. Artola and W. Singer, *Trends Neurosci.* **16**, 480 (1993).
65. C. Hansel, A. Artola, W. Singer, *Eur. J. Neurosci.* (suppl. 7), 46.09 (1994).
66. J. Lisman, *Proc. Natl. Acad. Sci. U.S.A.* **86**, 9574 (1989).
67. I thank A. Kreiter, P. König, and P. Roelfsema for valuable comments on the manuscript; R. Goebel for composing the pattern in Fig. 1C; R. Ruhl for preparing the figures; and I. Pipacs for editing the text.

The Brain's Visual World: Representation of Visual Targets in Cerebral Cortex

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Microelectrode recordings from behaving monkeys have shown that neuronal responses in the visual cerebral cortex can depend greatly on which aspect of the scene is the target of the animal's attention. Accumulating evidence suggests that while the early stages of the visual pathway provide a faithful representation of the retinal image, later stages of processing in the visual cortex hold representations that emphasize the viewer's current interest. By filtering out irrelevant signals and adding information about objects whose presence is remembered or inferred, the cortex creates an edited representation of the visual world that is dynamically modified to suit the immediate goals of the viewer.

Research over the last three decades has yielded a wealth of information about the neural mechanisms underlying vision. Dozens of cortical visual areas have been characterized (Fig. 1), and the visual information encoded by neurons has been shown to differ greatly between areas (*1*). Whereas neurons in the primary visual area V1 (striate cortex) respond well to edges or bars of light, those at later stages of processing represent increasingly complex aspects of the retinal image (*2*). Neurons in later stages of the visual cortex can be extremely selective, responding only to specific, complex forms or patterns of motion (*3*). Thus, vision is supported by levels of cortical processing that collectively cover a range of stimulus attributes, from simple to complex. A widely held view is that the primary reason for these multiple levels is to generate this range of sensory representations.

Creating representations of the retinal image is, however, just one component of vision. Vision is an active process that selects a limited part of the visual image for concentrated attention. Although unselected portions of the image are not lost to perception, at any moment we can give full attention only to a severely limited amount of visual information (*4*). Once this subset of signals has been selected, it must then be interpreted. Thus, the events leading to visual awareness include a substantial editing process that de-emphasizes irrelevant information and adds interpretations and inferences about the meaning of the targeted information.

Studies of macaque monkeys have shown that this editing of visual signals begins in relatively early stages of processing in the cerebral cortex. What the observer is trying to see and what that observer knows about

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