

Principles of Cortical Network Organization

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GENERAL INTRODUCTION

Self-organization and Pattern Formation

The word “organization” can mean two things—the structure of a system, or the process by which the structure is brought into existence. We concentrate here on the process. Even then there are two interpretations of the word “organization.” It could refer to the realization of a preexisting plan, in which case one would speak of “assembly.” We here use the word “organization” exclusively to refer to the genesis of structures which arise through cooperative mechanisms as optimal equilibria of the participating forces. (To make the distinction, the term “self-organization” will also be used).

One often speaks of some structural trait of an organism as being “genetically programmed.” This seems to imply that the genes contained a blueprint describing the organism in full detail. However, all the stages of brain organization (not just evolution) involve, more or less strongly, an element of self-organization: an element of creativity. It has often been emphasized that the genes cannot, in any naive sense, contain the full information necessary to describe the brain. Cerebral cortex alone contains

on the order of 10^{14} synapses. Forgetting considerations of genome size¹, one can hardly imagine how ontogeny could select the correct wiring diagram out of all alternatives if all were equally likely. Besides, judging from the variability of the vertebrate brain structure, the precision of the ontogenetic process is not sufficient to specify individual connections.

The conclusion one must draw is that ontogeny makes use of self-organization: of general rules and of principles of error correction. Above all, ontogenesis can produce only structures with a high degree of regularity, e.g., homogeneity, repetitivity, or continuity. This conclusion is of course fundamental to the venture of doing research on cortical structure; scientific results can only arise from regularity. Knowing the mechanism of ontogeny is of extreme importance: one cannot understand the function of cortex without knowing its structure, and one cannot know the structure of cortex without knowing the principles of its ontogeny.

Abstract Scheme of Organization

There are well-studied paradigms of pattern formation, especially in physics, physical chemistry, and astronomy: convection, crystallization (or more generally, phase transitions), reaction-diffusion systems (the emergence of spatial chemical patterns, e.g., in the Zhabotinski-Belusov reaction), and star and galaxy formation. We will attempt to give here a general description of the mechanism of organization. It must be formulated in words rather than symbols since there is as of yet no canonical mathematical description of organization.

Organization takes place in systems consisting of a large number of microscopic elements: atoms in a liquid or crystal, small subvolumes of liquid in convection, a reaction-diffusion system or an evolving star system or, in the application interesting us here, synapses in a nervous network. Initially, self-organizing systems are in a relatively undifferentiated state: atoms are in random motion, and all subvolumes of the liquid are in the same state of motion or have the same chemical composition. Then some small, typically random deviations from that state arise; e.g., some convective fluid motion sets in. To stress the random nature of typical small deviations they are called fluctuations.

To make things more concrete, let us take as an example convective pattern formation—the Bénard phenomenon. A flat vessel is filled with liquid and its bottom is homogeneously heated. As long as the temperature gradient is below a certain threshold, heat is conducted from the lower to

¹ To specify one out of 10^{10} cells one needs about 33 bits. For the specification of 10^{14} synapses one therefore needs a trifle more than 33×10^{14} bits. Vertebrate phylogeny has taken less than 10^9 years. Counting a year for each generation, and assuming an accumulation of a few bits of genetic information in each generation, genetic information is only a few billion bits.

the upper surface without bulk movement of the liquid. However, above that threshold the warmer, lighter liquid near the bottom rises and cooler liquid from the top flows down. Under homogeneous conditions this flow pattern is very regular and has the form of hexagons or rolls.

From this and many other organizing systems the following three principles may be abstracted:

- 1) *Fluctuations self-amplify.* This self-amplification is analogous to the reproduction in Darwinian evolution. In the Bénard system, fluctuations are created by thermal motion. If the movement in a small column of liquid is upward, more warm liquid is drawn in from the bottom, and the column becomes less dense and is accelerated upward. Downward movement accelerates analogously.
- 2) *Limitation of some resource leads to competition among fluctuations and to the selection of the most vigorously growing (the "fittest") at the expense of others.* In the Bénard system, upward movement in one place requires downward movement in other places. The columns with least density will win and rise.
- 3) *Fluctuations cooperate. The presence of a fluctuation can enhance the fitness of some of the others, in spite of the overall competition in the field. (In many systems the "fitness" of a fluctuation is identical with the degree of cooperation with other fluctuations.)* The liquid near a column of rising liquid is dragged up by viscosity.

The identification of these three principles in a concrete system is sometimes ambiguous. In the Bénard system competition in terms of upward movement might also be called cooperation between upward movement in one place and downward movement in another. Whole coherent patterns of movement, again, compete as far as there is local contradiction between them: liquid cannot move up and down in the same place.

A fundamental and very important observation on organizing systems is the fact that global order can arise from local interactions. The intermolecular forces acting within a volume of liquid are of extremely short range, yet the patterns of convective movement they give rise to may be coherent and ordered on a large scale. This fact will be of extreme importance to the brain in which local interactions between neighboring cellular elements are to create states of global order, ultimately leading to coherent behavior.

The stage for the organization of a pattern is set by the nature of the forces between elements and by initial and boundary conditions. In the Bénard system, these forces are the hydrodynamic interactions, gravity, thermal conduction, and expansion. Boundary conditions are set by temperatures at

the upper and lower boundary and by the form of the vessel. In the nervous system, the stage for the generation of connection patterns is ultimately set by prespecified rules for the interaction of cellular processes and signals and by the environment. Since nerve cells are connected by long axons, there is an important and exciting difference between the nervous system and most other examples studied so far. Neural interactions are not necessarily topographic in form; connected cells are “neighbors” although they may be located at different ends of the brain. This gives rise to genuinely new phenomena. Some of the ordered structures within the nervous system may not “look” ordered to our eye, which relies essentially on spatial continuity. In most of the concrete cases considered below, however, ordinary space still plays a dominating role.

An organizing system may contain a symmetry such that there are several equivalent organized patterns. These compete with each other during organization. In the Bénard system, if set up in a circular pan, any organized pattern could be rotated around the center of the pan by an arbitrary angle to obtain an equivalent pattern. One of these has to be spontaneously selected during pattern formation, a process which is called “spontaneous symmetry breaking.” This usually is a very slow process. However, the boundary or initial conditions may be slightly deformed to destroy the original symmetry so that one organized pattern is favored. Organization is then much quicker. In general, self-organizing systems react very sensitively to symmetry-breaking influences.

Neural Network Organization in General

Two types of variables are relevant to network organization: signals and interconnections. Signals are action potentials propagated along axons. Connections are characterized by a weight variable, which measures the size of the effect exerted by a nervous impulse arriving at a nerve terminal on the postsynaptic element. Correspondingly, organization takes place on two levels: activity and connectivity.

On the ontogenetic time scale one is interested mainly in network organization. This organization has the following general form: A given network creates certain activity patterns, which are determined by the structure of the network and by input activity. Due to synaptic plasticity, connections are modified in strength in response to cellular signals in the activity patterns. Modifications in synaptic strengths in turn lead to modified activity patterns. In order to obtain reorganization (instead of stabilization) of a network, the feed-back loop between changes in synaptic strengths and changes in activity patterns must be positive, so that coherent deviations from an undifferentiated state self-amplify (according to the first of the

principles formulated above). The process is constrained by the requirement that modifications in a synaptic connection have to be based on locally available signals. These are the presynaptic signal, the postsynaptic signal, and possibly modulatory signals which are broadcast by central structures. The postsynaptic signal could be a local dendritic signal or the outgoing axonal signal.

The requirements of self-reinforcement and locality suffice to specify the mechanism of synaptic plasticity in excitatory synapses: A strong synapse leads to coincidences of pre- and postsynaptic signals; in turn, the synapse is increased in strength by such coincidences (the transmission delay is neglected in this argument). Donald Hebb (1949) gave this formulation:

“When an axon of cell A is near enough to excite cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A’s efficiency, as one of the cells firing B, is increased.”

One refers to this rule as to “Hebbian plasticity.” The corresponding rule for inhibitory synapses would have a synapse strengthened which was successful in inhibiting the postsynaptic element. At present, however, most authors consider inhibition a rigid service system not itself taking part in network reorganization.

Hebb’s rule corresponds to the “self-reproduction” of the general scheme of organization. In order to stabilize the system, some competition for a limited “resource” has to be introduced. Most likely, there is a mechanism of isostasy, by which each cell keeps the temporal average of its activity (taken over the span of some hours) constant. As a consequence the increase in strength in some synapses must be compensated for by a decrease in others. Only the more successful synapses can grow; the less successful ones weaken, and eventually disappear. For technical reasons, some models discuss a simpler competition rule for synapses, in which the sum of the synaptic weights of all synapses converging on a cell is kept constant. This rule leads to functional deficits and is probably not realistic. Synaptic plasticity, constrained by competition, implements the principles 2 and 3 of organizing systems as listed above.

One synapse on its own cannot efficiently produce favorable events. Only sets of synapses which converge on a postsynaptic neuron and carry coincident signals can effectively activate that neuron and can thereby cooperate in creating favorable events. In order for such coincidences to occur consistently there must be a causal connection between presynaptic cells. Synaptic plasticity is the means by which the nervous system detects such causal connections. Coincidences may be due to excitatory links between presynaptic neurons. They may, however, also be due to

simultaneous stimulation of sensory cells. In this case they point to the existence of causal connections in the external world.

The rules of cooperation and competition act on a local scale. The phenomenon of self-organization is the emergence of globally ordered states, as discussed in the example of global convection patterns in the Bénard phenomenon. These states are ordered in terms of optimal mutual consistency of all local rules with each other. The fact that the external world takes part in the game leads to adaptation of the nervous system to it.

The rules for adjustment of synaptic weights we have introduced so far are able to produce ordered connection patterns. However, they do not necessarily organize the nervous system for optimal biological utility. For this, two types of control are necessary: (a) genetic control of boundary conditions and interaction rules in order to favor certain useful connection patterns; and (b) control by central structures which are able to evaluate the degree of biological desirability of activity states. If a state proves to be useful, a gating signal is sent to all of the brain or to an appropriate part of it to authorize synaptic plasticity, which then stabilizes the state just reached or contributes to the likelihood of it happening again.

Central control as the *only* criterion for growth or decay of synapses is not sufficient: Let us assume our nervous system evaluates the usefulness of its state once per second. It then could create less than 3×10^9 bits of information in our lifetime, for that is about the maximum number of seconds given to us. This certainly is not sufficient to regulate the strengths of all of the 10^{14} synapses of our cerebral cortex. On the other hand, this amount of information may be sufficient to select from among the relatively small universe of ordered connectivity patterns which can be created by rules of local cooperation and competition under predetermined constraints.

Having briefly introduced relevant principles, we now enter a more detailed discussion of a few paradigmatic cases of network organization, stressing the application to the visual system. Retinotopy, ocularity, and orientation specificity are important examples which have been studied intensively both theoretically and experimentally over several years or decades.

Establishment of Topological Maps

At some stage in the development of the vertebrate embryo, the fibers of retinal ganglion cells grow out through the eye stalk towards the brain and establish retinotopic connections there: neighboring cells in retina connect to neighboring positions in the target structure. The most intensively studied case is that of retinotectal connections in amphibia and fish. The interesting question is this: How do fibers find their correct target position? This problem has long been recognized as an important paradigm case for the

general problem of organization of structured networks. There are many topological fiber projections between thalamic nuclei and cortical areas and also between and within cortical areas. Retinotopy is one of the few biological model problems experimentally addressed with enough intensity that theoretical issues can be decided.

For a long time the puzzling aspect of the retinotopy system was a mixture of rigid genetic determination on one hand and plasticity on the other. The orientation of the projection, e.g., nasal retina projecting to caudal tectum, is reliably prespecified. On the other hand, the magnification and the position of the map are flexibly adjusted, so that all of the existing retina maps to all of the existing tectum, both after experimental manipulation and in physiological conditions (for review see Fraser 1985), a property called "systems matching." For instance, since growth in retina and in tectum are disparate—retina grows in a concentric fashion, tectum from front to back—the already existing fiber projection shifts in an ordered fashion to attain systems matching. The picture is further complicated by evidence that fibers are able to follow tectal tissue which has been grafted to a new position within tectum (for a review of various experiments see Fraser 1985), seemingly proving the existence of rigid addresses in tectal cells.

The apparent contradictions are resolved, and all types of experiments are consistent with the assumption of the following three mechanisms:

- A) There is a mechanism to guide fibers to tectum.
- B) There is a mechanism to position fiber terminals within tectum. This mechanism is responsible for rigid constraints on the mapping. The nature of the mechanism is not yet known, but there is the widespread conviction that it is based on chemical marker gradients in retina and tectum.
- C) There is a fiber-sorting mechanism which improves the precision of the mapping over that attained by mechanism B alone and which is activity-dependent (Harris 1980). This mechanism is able to account for systems matching in the retinotectal system (for review see Schmidt and Tieman 1985).

In spite of many ongoing controversies within the retinotectal community, the above statements have gained wide acceptance. The division of labor between mechanisms B and C and the nature of C were first formulated by Willshaw and von der Malsburg (1976). In the present context we concentrate on the fiber-sorting mechanism C, since it deals with activity-dependent network organization and can be generalized to other interesting cases, in particular to neocortex.

Basic to the fiber-sorting mechanism is the fact that the spontaneous activity of neighboring retinal ganglion cells is correlated due to excitatory

connections in retina (Mastrorarde 1983). These correlations carry complete information about neighborhood relationships within retina, without coding for retinal position directly. They are used for fiber-sorting in the following way: Retinal fibers establish tentative contacts on tectum. Through these contacts they impress their activity patterns on tectal cells. Due to excitatory links within tectum, which play a role analogous to that of connections within retina, activity in neighboring tectal cells is correlated. Retinotectal contacts undergo a selective growth process, in which successful contacts grow in strength and less successful ones decay. Success is measured by the degree to which a contact is able to induce correlations between pre- and postsynaptic signals, and it depends on the number and strength of other fibers linking the same retinal and tectal locations. Competition among contacts is introduced by the inability of a tectal cell to receive more than a certain number of contacts and by the inability of retinal fibers to support more than a given number of contacts ("conservation of axonal arbor").

According to the rules just formulated for selective stabilization or elimination of contacts, the total pattern of retinotectal contacts evolves and changes while always favoring local configurations of fibers coming from neighboring positions in retina and going to neighboring positions in tectum. Under appropriate conditions, the projection system reaches and stabilizes in a global optimum throughout which this situation prevails; accordingly, this constitutes a retinotopic mapping. This has been shown in several sets of computer simulations and by mathematical analysis (Häussler and von der Malsburg 1983). There is, however, the danger that the system ends in a state of local optimum in which there are several part-maps of retina onto tectum which are incompatible. This can best be avoided by starting the sorting process in a configuration already containing some global order. This starting configuration also fixes the orientation of the final mapping. For these reasons it is necessary to postulate the positioning mechanism B.

The activity-dependent sorting mechanism has the systems matching property. If an actual fiber projection does not match all of retina to all of tectum, as it occurs after some surgical manipulation or in the physiological case of disparately growing retina and tectum, the sorting mechanism is able to coherently move fibers over the tectal surface until systems matching is achieved. The positioning mechanism B is important for getting the process started, but then the fiber sorting mechanism C takes over and dominates. If the optic nerve is crushed, a tectal graft of sufficient size is transposed onto another position in the tectum and the projection is allowed to regenerate; the positioning mechanism enables the graft to receive many of its original fibers although it now resides in a new position. This creates a local optimum which cannot be repaired by the sorting mechanism because it is limited to coherent modifications of an existing map. The observation that plastic map transformations are limited to coherent, i.e., neighborhood-

preserving, changes has also been made in the somatosensory system (see Merzenich, this volume).

Discussion of Retinotopy

How does our abstract scheme of organization apply to retinotopy? The undifferentiated state of the abstract scheme would correspond here to a fiber projection which connects all points in retina to all points in tectum with homogeneous density of innervation. The positioning mechanism B sets up “fluctuations” in the form of deviations of contact density from homogeneity, concentrating fibers from retinal positions to the corresponding tectal target positions. These fluctuations self-amplify according to the fiber-sorting mechanism, by setting up retinotectal signal correlations which in turn help the fluctuations grow. This rule directly corresponds to Hebbian plasticity. The example demonstrates the central importance of cooperation between fluctuations, in this case between “parallel” fibers.

One of the initially most surprising aspects of the fiber-sorting mechanism is its ability to create global order from local rules of interaction without having to hunt through the huge combinatorial space of all possible permuted projections. However, this ability cannot be taken for granted. It must be developed from proper control of structural parameters. The general rule is that the self-amplification of fluctuations must be so weak that only globally ordered systems of cooperating fluctuations are able to grow. This means that the system must be operated just above its plasticity threshold. The consequence of this is that growth is slow: the price to be paid for global order is the amount of time necessary for it to be established. The process is particularly time-consuming if there are several equivalent globally ordered configurations competing with each other, usually due to a symmetry. In the retinotectal case this is realized by ordered projections rotated with respect to each other. It is therefore highly advantageous to break the symmetry by the establishment, through an independent positioning mechanism B, of an already partially ordered initial mapping. Of course, B has the same problem, but it may use mechanisms which have an inherently larger physical interaction length, e.g., reaction-diffusion.

Rather little genetic information is needed to set the stage for retinotectal fiber-sorting. The ensuing organization process then creates a huge mass of information in the form of detailed cell-cell contacts. There is no violation of a “law of conservation of information” because by varying the genetic information one cannot create *any* connection pattern; rather, one can only select from a narrow universe of regular patterns.

The two logical steps of retinotopical network organization are the creation of a signal ensemble in retina and tectum which express the structure of the network and the plastic reaction of the network to the correlations in this

signal ensemble. Very little organization is necessary to establish local correlations in retina and in tectum and between regions in retina and tectum which happen to be strongly coupled by the tentative contacts.

Different interpretations of this process suggest various ways to apply the retinotectal model to other situations. From the point of view of a retinotectal synapse, the occurrence of correlations between signals on the fiber and on the tectal target cell indicates the presence of a causal connection. In this system this is due to loops of intraretinal, retinotectal, and intratectal connections. In other cases there may be causal connections in the external world. When positively reacting to these correlations, our individual contact tends to "model" the indirect causal connection by a direct link.

From the point of view of a tectal cell responding to retinal afferents, recurring patterns of correlated activity appear which are buried in the otherwise random signals on the afferents. When selectively strengthening those contacts which carry the patterns, the tectal cell starts to turn into a selective detector for those patterns. In the retinotectal system these patterns correspond to local clusters of retinal cells. When there are several separate pattern-carrying subsets of afferent fibers (here, sets of fibers coming from different loci in retina) our cell must decide among them due to the competitive aspect of contact growth. In this way tectal cells develop restricted receptive fields, which are shaped by retinal patterns of signal correlation and by competition among afferent fibers. Afferent patterns may also be created by interactions external to the nervous system. After eye opening, retinal activity patterns are strongly influenced by light patterns, which may, if there is still sufficient plasticity, influence the shape of receptive fields (see the section on orientation specificity and the refinement of binocular maps).

In this process of development of pattern selectivity different tectal cells compete with each other for retinal patterns. (This competition is due to conservation of axonal arbor by afferent fibers). The system therefore tends to distribute the representation of the afferent patterns evenly among the available tectal cells, such that, in this particular case, different retinal loci finally are represented by different tectal cells. In other contexts, this important aspect of the mechanism is called "competitive learning."

Different tectal cells which excite each other tend to respond at the same time and therefore tend to specialize to the same afferent pattern. This aspect of the mechanism is, of course, of paramount importance for establishing retinotopy. In other cases it serves to establish a continuous representation of patterns which is able to interpolate between those patterns which actually occurred (see the section on orientation specificity and Kohonen 1982).

The final aspect of the retinotopy mechanism which we would like to discuss is that of homeomorphic graph matching. The initial network consists

of the retinal and the tectal subnetworks (which, mathematically speaking, are graphs), plus a diffuse system of connections between them. The two subnetworks have a similar structure: two-dimensional sheets of cells with local connections. They may be loosely termed homeomorphic (or isomorphic if they are the same size). The fiber-sorting mechanism is able to “detect” the homeomorphism between the graphs and to represent it by selectively connecting corresponding nodes in the two graphs. This process is called “graph matching” by mathematicians, and may play an important role for cortical organization by “discovering” structural relationships between different objects represented in the brain, or between an external object and a structure within the brain.

Ocularity Domains

In many vertebrates the visual fields of the two eyes overlap. In these animals we find structures in the brain which receive overlapping retinotopic projections from the two eyes. There seems to be a general tendency for these projections to align such that corresponding points in the two retinæ project to the same point centrally. (This alignment presumably is the result of a retinotopic mechanism of type B). For the fiber-sorting mechanism C this situation presents a conflict which, if strong enough, leads to segregation of fibers into ocularity domains. To discuss this process let us again emphasize the essential postulates inherent in the fiber-sorting mechanism of retinotopy. They are that: (a) neighboring retinal cells are correlated; (b) neighboring target cells are connected; (c) correlated pathways converging on a target cell cooperate; (d) uncorrelated pathways converging on a target cell compete; and (e) afferent fibers tend to conserve their total axonal arbor. A cell in the target structure receives two sets of fibers from two retinal spots. Fibers within one set are correlated in their signals, but there are no correlations between signals of the two sets. Consequently, the two sets of fibers compete with each other (according to (d)), and one of them is disconnected. Thus, target cells decide upon one ocularity. Two sets of fibers from a small region in one eye which connect to two neighboring cells in the target structure cooperate with each other, because they are correlated (according to (a)), and because one of the sets connects indirectly to the target cell of the other set (according to (b)); this indirect connection helps the direct one to grow (according to (c)). This cooperation leads to the formation of coherent ocularity domains. The size of these is limited due to postulate (e): the disconnection of fibers of one ocularity from a given position locally reduces their axonal arbor, and these fibers must therefore increase their innervation strength in another place. If one assumes that afferent fibers do not sprout or move over larger distances, the size of ocularity domains is regulated by the size of afferent axonal arbors.

The form of ocularity domains is a considerably more complicated issue. Let us draw the analogy to the Bénard problem. There, the role of ocularity is taken by upward or downward convection of liquid. The interaction between the two types of movement has a shape very similar to ocularity interactions. Two kinds of ordered domains are possible in the Bénard system: "rolls" and "hexagons". Rolls would correspond to ocularity stripes, hexagons to a patchy distribution. The decision depends, in a complex way, on the form of interactions. It has been shown in simulations that a system set up to produce two overlapping retinotopic mappings is able to generate ocularity domains in the form of stripes (von der Malsburg 1979). Ocularity stripes have been observed in visual cortex (LeVay et al. 1975), and in the experimentally manipulated frog (Constantine-Paton and Law 1978). The latter observation is particularly interesting, since in this experiment the overlap between two projections was produced artificially, making it highly unlikely that there is a specific genetic program for ocularity stripes. The formation of ocularity domains has been shown to be abolished by intraocular injection of TTX (Meyer 1982; Stryker and Harris 1986), supporting the activity-dependence of the mechanism.

What determines the orientation of ocularity stripes within the target structure? If the relevant fiber interactions are isotropic in their spatial shape and range, stripe orientation must be decided by chance. However, if there is the slightest systematic anisotropy in those interactions, stripe orientation is determined by them. If, for instance, the local magnification factor of the retinotopic projection is larger along the x-coordinate than along the y-coordinate, the stripes most likely will be oriented parallel to the y-axis. It would be interesting to test this prediction experimentally.

The above considerations apply to the case in which innervation by both eyes is balanced. If the number of fibers from one eye exceeds those from the other, or if one eye is shut off from visual stimulation, the extent of territory of the dominant eye in the target sheet is increased at the expense of the other eye. Domains are then reduced to islands of minority territory in a sea of the other ocularity (LeVay 1977). This behavior has also been shown in simulations (von der Malsburg 1979).

Orientation Specificity

Three problems which have been the subject of much theoretical and experimental work are addressed here: What is the mechanism which gives neurons in primary visual cortex orientation sensitivity; what induces orientation sensitivity to be distributed continuously over the cortical surface; and how does this organization arise ontogenetically?

As to the mechanism of orientation sensitivity, the simplest theoretical possibility would be an arrangement of afferent fibers which gives individual

cells elongated receptive fields. Unfortunately it has not been possible, in spite of extensive experimental efforts, to demonstrate the existence of this receptive field organization. A second problem with the idea is that it gives no explanation for the orderly distribution of orientation sensitivity.

We know that the majority of fibers impinging on a cortical cell are of intracortical origin. Moreover, the response times of cortical cells to afferent stimulation are long enough for many rounds of exchange of intracortical excitation and inhibition. The response characteristics of cortical neurons are therefore in all likelihood determined largely by intracortical and not so much by afferent organization. These notions are the basis for the cooperative mechanism of orientation selectivity, which has been proposed by von der Malsburg (1973), Creutzfeldt et al. (1974), and Finette et al. (1978). According to the cooperative mechanism several groups of neurons compete for response to a visual stimulation. The groups are integrated by excitatory connections and inhibit each other. One group corresponds to each possible orientation, groups for neighboring orientations being partially identical. In the cooperative model, individual neurons need very little orientation specificity in their direct afferents; indeed, so little that it may be undetectable by itself. When, however, a cortical region is stimulated with an oriented retinal stimulus, the different groups of cells collectively add up the amount of afferent stimulation received by them and compete with each other in terms of this sum. Afferent excitation to the winning group may exceed that for the best competitor by only 1%, but after repeated exchange of excitation and inhibition this lead rapidly improves and finally, after a few dozen milliseconds, the winning group succeeds in silencing its competitors and gives a strong selective response.

With the cooperative mechanism, the problem of ontogenesis of orientation specificity is greatly reduced. It is no longer necessary to explain specific complicated connection patterns. What is left to establish is a reliable association between stimulus orientations and cortical activity patterns. For this it is simply necessary to slightly modify synaptic strengths in the afferent fibers. Let us first assume that this process takes place in the presence of actual visual stimulation, i.e., after birth. The necessary synaptic modifications are then easily accounted for on the basis of the principles discussed in connection with the ontogenesis of retinotopic projections (von der Malsburg 1973). The only difference here is that activity patterns in retina and in the postsynaptic sheet are somewhat more complicated.

Let us assume that intracortical interactions consist of short-range excitation and longer-range inhibition. Let us further make the very natural assumption that these interactions have a very slight but consistent anisotropy caused, for instance, by slightly anisotropic growth of the cortical sheet. Patterns of activity in cortex—the groups of our previous discussion—will then locally look like parallel bands, oriented along one of the axes of

anisotropy. Like with many natural phenomena—ripples of particles on the surface of a tea cup or of sand on a beach under the unisotropic influence of current or wind—the degree of long-range order will be low, just as in the deoxyglucose pictures of Löwel, Freeman et al. (1987). At different times, waves of different phase or position will be active, all having the same general orientation. All of these wave patterns in a small cortical region form a family which can be labeled by one parameter, ranging from 0° to 180° and corresponding to the phase of the activity wave. Now take the position of a cortical region just large enough to contain a family of patterns, say 1 mm in diameter. It receives afferent fibers from a local patch of retina (via the CGI). On these fibers appear patterns of activity which correspond to bars and edges of light. Also, these patterns form a family which can be labeled by the numbers from 0 – 180° , now corresponding to stimulus orientation. In this situation, synaptic plasticity will pair retinal activity patterns with cortical activity patterns in a reliable one-to-one fashion, such that neighboring retinal patterns connect to neighboring cortical patterns: Let cortical pattern A fire in response to retinal pattern a . All connections from cells active in a to cells active in A are strengthened. For an individual cortical cell this means that its receptive field, which initially may have been circular, is deformed to resemble retinal pattern a . This happens to all cells in cortical pattern A simultaneously. In this way, A is reliably linked to a , i.e., to a specific stimulus orientation. Groups which inhibit each other specialize to different orientations. The system will soon fall into an equilibrium in which different retinal orientations map to different cortical patterns such that neighboring orientations map to neighboring cortical patterns. With other words, when recording from cortical cells along an electrode track whose trajectory is orthogonal to the local activity waves, one will find a regularly progressing sequence of optimal orientations.

If it is true, as is suggested by experiments (Hubel and Wiesel 1974), that the association between oriented visual stimuli and cortical activity patterns is already fixed at birth, then the ontogenetic situation is somewhat less clear, but there is no principal difficulty. There could be waves of activity created spontaneously in the retinae of the embryo and which take on the role of oriented stimuli in the mechanism just outlined. Even without any patterned stimulation, cooperation and competition between the synapses afferent to a cortical cell may produce oriented receptive fields (Linsker 1986). Alternatively, there could be a small minority of retinal cells which are connected such as to be orientation specific and which establish patterned connections to cortex prior to eye opening (von der Malsburg and Cowan 1982).

How do orientation domains—the “groups” or “activity patterns” of our discussion—interact with ocularity domains? So far, we have assumed in

our discussion that formation of domains (ocularity domains or activity patterns) started from a homogeneous, though noisy, initial distribution. Domain formation then takes the form of a race of different self-amplifying patterns of imbalance. If there is no disturbing force, the race is won by that pattern which has the most internal cooperativity and the least competition. If, however, there are small but systematic forces which are able to influence the growing pattern, these forces get their way and determine its form. (In our analogy, an extremely weak temperature variation on the floor of the Bénard vessel determines the convection pattern). Now assume that ocularity domains had already formed and that you observed the development of an activity pattern under the influence of afferent excitation which happened to be dominated slightly by one eye. Afferent excitation would then be consistently stronger in the regions of the corresponding ocularity domains. Consequently, the developing activity pattern should be a replica of the ocular dominance pattern. The apparent independence of ocular dominance domains and orientation domains creates the problem of explaining how the two processes can take place independently. One possibility would be a fixation of orientation columns before segregation of ocularities. If ocularity development is slow, it is influenced only by the average of many cortical activity patterns. This average is likely to be homogeneous in its statistical properties and thus unlikely to disturb the precise form of ocularity domains. It would be interesting to learn from experiments whether this is indeed the sequence of events.

Experience-dependent Self-organization of the Visual Cortex

In the following discussion we wish to examine the extent to which the axioms and predictions of our theoretical considerations on self-organization match experimental data on the development of the mammalian visual cortex. Most of the evidence on activity-dependent reorganization of cortical connectivity during development comes from experiments on ocular dominance plasticity and, to a lesser extent, from experiments on the development of orientation selectivity (for review, see Frégnac and Imbert 1984 and Singer 1987). These data provide strong support for the hypothesis that visual cortex can be understood as a self-organizing system.

It is now well established that the representation of the two eyes in a regular pattern of slab-like ocularity domains is guided by self-generated activity. Under experimental conditions, fibers segregate into distinct ocularity clusters only if the two eyes are active and if their respective activity is not synchronous (Stryker and Harris 1986). Evidence is also available that under natural conditions and in the absence of any light

stimuli the two eyes are capable of generating, independently of each other, periodic bursts of activity that are highly synchronous in one eye (Rodieck and Smith 1966). Cross-correlation studies have further revealed that the activity of neighboring ganglion cells is correlated (Mastronarde 1983). Thus, as far as the patterns of self-generated activity are concerned, the prerequisites for activity-dependent self-organization of ocular dominance columns in the striate cortex are fulfilled. Data on the molecular mechanisms mediating axonal segregation are, however, still lacking.

More data are available on the activity-dependent pruning of connections that serve the formation of binocular receptive fields — the basis of binocular visual functions. To generate binocular fields, the segregated ocularity domains must be mapped through converging pathways onto common second order cells. During a later, postnatal phase of development, called the “critical period,” these second order connections undergo activity-dependent modifications. In this developmental phase, however, the relevant activity patterns are already dominated by visual input. Correspondingly, the connections subserving binocularity can be modified by manipulating visual experience. This activity-dependent shaping follows rules similar to those postulated by Hebb for adaptive neuronal connections in learning nerve nets. Connections are selected as a function of the statistical correlation between pre- and postsynaptic activation (Rauschecker and Singer 1979, 1981). Pathways having a high probability of being active at the same time as the postsynaptic target cell become stabilized, while those tending to be inactive while the postsynaptic target is driven by other inputs weaken and eventually disconnect. These rules have the effect of stabilizing selectively those subsets of converging afferents conveying correlated activity and capable of driving the postsynaptic target; they lead to competition between afferents conveying noncorrelated activity. In the latter case, one subset of afferents consolidates at the expense of the other.

There are further indications that the activation of the postsynaptic target must trespass a critical threshold before modifications can occur. This “plasticity threshold” appears to be different from the threshold of sodium-dependent action potentials, and is most likely related to the activation threshold of dendritic calcium conductances (Geiger and Singer 1986). A possible molecular mechanism for the implementation of this threshold process is the NMDA receptor, since selective blockade of this receptor system prevents use-dependent changes in binocularity (Kleinschmidt et al. 1987). This mechanism is ideally suited for evaluating the contingency of pre- and postsynaptic activation and for activating Ca^{2+} -conductances when a critical level of cooperativity is reached. The ionophore coupled to the NMDA receptor opens only and then becomes Ca^{2+} -permeable when the receptor is occupied by its endogenous ligand, and also when the postsynaptic

membrane is sufficiently depolarized (Dingledine et al. 1986; Thomson 1986; Watkins and Evans 1981).

Thus, the use-dependent modifications of binocular connections differ from the classical Hebbian postulates in at least two important aspects: First, there is a threshold for modifications. This implies that modifications occur only if a minimal number of parallel pathways are coactivated. This agrees with our postulate that input selection requires sufficient cooperativity between converging inputs. The modification rules as a whole agree with the decisive postulate that the selection process favors selective stabilization of coherently active groups of afferents and is self-amplifying. As connections start to strengthen at the expense of others, the probability that they will strengthen further increases.

The second difference from the classical Hebbian notion is that the postsynaptic signal relevant for contingency matching appears to be a local dendritic event rather than the global output signal of the neuron. This has three important consequences: First, several selection processes can occur rather independently at different sites of a neuron. Second, compared to action potentials, dendritic responses are relatively long-lasting. Thus, the temporal window for contingency matching may be considerably longer than the duration of single action potentials. Data on cooperative interactions in hippocampal long-term potentiation, as well as data from ocular dominance plasticity, suggest that the duration of this interval can be as long as several 100 ms (see Altmann et al. 1987; Andersen 1987; Levey and Steward 1983). Third, since the duration and the spatial spread of dendritic responses are modified by synaptic interference, the duration of the integration interval and the spatial extent over which activity in converging afferents is matched are adjustable. Synaptic events such as IPSPs which shorten dendritic time and length constants can be expected to raise the criterion for temporal and spatial contiguity in these Hebbian matching processes, and the reverse is true for modulatory inputs which increase membrane resistance. As the self-organizing process proceeds and generates increasingly selective connections and response properties, the criteria necessary for afferent activity to induce further changes are likely to become more specific. Hence, the self-organizing process is bound to converge toward states of high selectivity. The implication that the demands on the specificity of change-inducing activity increase with increasing selectivity of the system would easily account for the evidence that, early in development, rather global self-generated patterns of activity suffice to induce modifications; while later only highly structured activity patterns are able to support use-dependent selection of circuits.

It has been proposed that the pruning of interocular connections serves to select, among the many possible combinations of afferents, those subsets originating from corresponding loci in the two retinae. When the animal

fixates an object with both eyes, corresponding loci in the two eyes are exposed to similar luminance distributions. Hence, the activity patterns in afferents coming from corresponding retinal loci are likely to be correlated. The two retinotopic maps can thus be matched by evaluating contingencies using patterns in the outside world to close the loop.

It has also been postulated that this selection process must not depend solely on locally available retinal signals, but also needs to be controlled by more globally organized gating systems if it were to be successful (Singer et al. 1982). Obviously, selection may occur only when the two eyes are actually fixating a common target, and it must not occur when the eyes are moving or not aligned properly. In the latter case activity patterns from both eyes would be uncorrelated, and this would lead to a disruption of binocular connections. The same would be the case if the spontaneously produced bursts of activity that occur, e.g., in the geniculate afferents during certain sleep stages, were capable of inducing changes in circuitry. Moreover, to assure a sufficient degree of overlap of the images in the two eyes, some evaluation of the best match between the coarsely prespecified retinotopic representations ought to be made prior to selection. This requires preprocessing and control of eye movements, and hence an aroused and attentive brain.

In agreement with these postulates, it was found that proprioceptive signals from extraocular muscles which convey information about eye position and motility serve a gating function in ocular dominance plasticity (Buisseret and Singer 1983; Freeman and Bonds 1979). Thereafter, it was shown that central core projection systems whose activation is related to reticular arousal also have a permissive function in ocular dominance plasticity (Singer 1982; Singer and Rauschecker 1982). The initial proposal that this function is subserved by the noradrenergic projection alone (Kasamatsu and Pettigrew 1979; Kasamatsu et al. 1979) has now been extended by the finding that both the noradrenergic and the cholinergic projections to striate cortex cooperate in this gating function (Bear and Singer 1986).

Vision-dependent changes in circuitry can be induced only when these modulatory systems are sufficiently active, or when the corresponding neurotransmitters ACh and NE are substituted locally. This may account for the evidence that modifications occur under natural conditions only when the animals are alert and attentive to visual stimuli.

Thus, mechanisms are implemented which allow gating of local changes as a function of global states of the brain. As argued above, this is indispensable in this particular case of map matching, where two mobile sensory surfaces must be related to each other. It is also indispensable

whenever local self-organizing processes are to develop functions which are embedded in a more global context.

The Development of Orientation Domains

The developmental mechanisms by which neurons acquire their orientation selectivity and aggregate in columns and slabs are less well investigated than those regulating the expression of binocular receptive fields. However, there are numerous indications suggesting that the two processes are based on similar mechanisms and differ only because they occur at different levels of cortical processing.

In most neurons of the cat and monkey visual cortex, the expression of mature orientation selectivity requires experience with oriented contours (Buisseret and Imbert 1976, and for review, see Fregnac and Imbert 1984). Accordingly, restriction of experience to contours of a single orientation leads to a massively biased distribution of orientation preferences (Blakemore and Cooper 1970; Hirsch and Spinelli 1970), and functional columns encoding nonexperienced orientations remain confined essentially to layer IV (Singer et al. 1981).

Self-organizing processes of the type discussed above are capable of accounting for the development of an orderly pattern of equally spaced iso-orientation slabs that extend throughout all cortical layers if two prerequisites are fulfilled. First, there need to be units in layer IV with prespecified orientation selectivity; second, connections from these units to cells in the other layers must initially be exuberant, and then be pruned under the influence of visual experience according to the same rules that applied for the shaping of interocular connections. First order neurons which share the same orientation preference and possess adjacent receptive fields are activated coherently by contours of corresponding orientation. At the level of second order neurons, this will lead to selective stabilization of converging inputs which originate from first order cells sharing the same orientation preference. The main trajectories of intracortical excitatory connections are perpendicular to the laminations, suggesting that coupling is tighter along the vertical than along the tangential axis, an assumption supported by correlation analysis (for review see Toyama, this volume). If activity-dependent pruning, as predicted by the theory and substantiated in the case of ocular dominance plasticity, is self-amplifying and facilitated by cooperativity, vertical connections have a competitive advantage over oblique or horizontal connections. The consequence is that units within a vertical column are forced to assume the same orientation preference. This is invariably the case in all species investigated to date. Just as the reciprocal

excitatory interactions between adjacent target cells in the simulated tectum provided the basis for a common specialization of adjacent tectal cells for adjacent ganglion cells, the preferential vertical coupling between cortical cells provides a basis for their common specialization for input from first order cells sharing the same orientation preference and having adjacent receptive fields.

It is easy to see that such a matching process promotes the development of a connectivity pattern by which clusters of first order cells sharing some coherent properties become permanently associated with selected clusters of second order cells. This mechanism correctly predicts the expansions and contractions of orientation domains observed in kitten visual cortex after selective exposure to a single orientation (Singer et al. 1981). In normal development it could serve to generate second order cells with large, orientation selective receptive fields whose subunits consist of appropriately aligned smaller receptive fields of first order neurons (for a more explicit discussion of this process, see Singer 1985). Recently, it has been found that blockade of the NMDA receptor system also prevents the experience-dependent development of orientation selective receptive fields (Kleinschmidt et al. 1987). This may be taken as further support for the hypothesis that not only the general principles, but also the molecular mechanisms underlying the development of orientation selectivity, are similar to those mediating selective interocular interactions.

A good test for the validity of a global theory is to examine whether it is also capable of correctly predicting minor details. One of these detailed predictions is that ocular dominance and iso-orientation slabs should have trajectories orthogonal to area boundaries. The theory predicts further that, if there is anisotropy in the magnification factor of the cortical map, the slab trajectories should be orthogonal to the long axis of the anisotropic map. As recently reviewed by LeVay et al. (1985) and Löwel et al. (1987), this seems to be the case whenever domains with similar functions become organized in slabs or bands. Another prediction is that columnar systems should be particularly regular and form long continuous bands if interference with other columnar systems is minimal and if they can develop in areas where area boundaries are parallel to each other. The latter is truly the case in the cat visual cortex where the regularity of iso-orientation bands is maximal in the medial bank and minimal close to the occipital pole.

The theoretical considerations predict that the regularity of columnar systems should reflect the extent to which they are able to develop independently of each other. This in turn depends on the timing of their expression and on the interactions between the neuron populations within which they develop. In Tupaia, in which the ocularity domains are mapped into different layers, one expects very little interference with the development of orientation columns. In agreement with the theory, the system of

orientation columns is particularly regular in this species (Humphrey et al. 1980). In the monkey, ocular dominance domains are segregated in columns and develop prenatally and in a matrix of neurons lacking orientation selectivity (Rakic 1981). Also in agreement with theoretical expectations, ocular dominance columns in the monkey are particularly regular. Orientation columns, by contrast, are especially patchy in the monkey (Blasdel and Salama 1986; Hubel et al. 1978). The theory would attribute this to multiple anisotropies created by the well-expressed system of ocular dominance columns and by the additional system of blobs which appears to represent a superimposed map for color (Livingstone and Hubel 1984).

Such interference between interdigitating maps should lead to a correlation between the course of ocular dominance bands and discontinuities in the mapping of iso-orientation. The recent data of Blasdel and Salama (1986) suggest the existence of such a correlation in the monkey. Discontinuities in the mapping of orientation appears to be particularly frequent where iso-orientation slabs cross ocular dominance bands. In the cat little is known about the time course of the development of ocular dominance and orientation columns. However, both assume their mature pattern only postnatally (Mower et al. 1985; Stryker and Harris 1986; Swindale and Cynader 1986), and the ocular dominance columns develop within a substrate containing orientation selective units. That predicts that neither the ocular dominance nor the orientation columns should be as regular as the former in the monkey or the latter in the Tupaia. This is what the data show. However, comparison of the two columnar systems in double-labeling experiments revealed different space constants of columnar periodicity, supporting the notion that the respective substrate interactions occur in different neuron populations whose lateral interactions have different space constants (Löwel, Freeman et al. 1987; Löwel, Bischof et al. 1987).

Another and rather strong prediction derived from the theoretical considerations is that neurons within an iso-orientation domain ought to be tightly coupled with each other through reciprocal excitatory connections. This in turn should lead to cooperative interactions and reverberation if the pattern of afferent activity matches the resonance property of the respective column. The relative contribution of the subcortical input to the activation of the column will therefore be small in comparison to the excitation provided by intrinsic connections. A consequence of this is that afferent activation patterns not matching the resonance properties of the column should produce only very little excitatory *and* inhibitory synaptic activity. This seems to be in accordance with the results from intracellular recordings (Creutzfeldt et al. 1974; Ferster 1986). These authors agree that, despite the fact that the subcortical afferents do not differentiate between stimuli of different orientation, nonoptimally oriented stimuli produce much less synaptic activity, both excitatory and inhibitory, than optimally oriented stimuli.

The prediction that orientation selectivity is essentially a property of a resonant ensemble of selectively coupled neuron clusters could also account for a number of other puzzling experimental findings. Response latencies of orientation selective neurons in the cat visual cortex are often much longer than one would expect from adding up conduction times, synaptic delays, and summation intervals of postsynaptic potentials (Dinse and Best 1984). Long and, in particular, variable response latencies are to be expected if responses require some degree of cooperativity between reciprocally coupled units. Similarly, attempts to extrapolate from responses to small nonoriented stimuli to the structure of the "real receptive field" as it presents itself in responses to oriented stimuli have remained remarkably unsuccessful, suggesting that the oriented receptive field of most cortical neurons is probably the result of nonlinear dynamic interactions rather than of linear summation of activity in topologically ordered circuitry. The observation that, in dark-reared animals, a few hours of visual experience suffice to imprint virtually normal orientation selectivity into a previously entirely despecified cortex points in the same direction (Buisseret et al. 1978). While it is difficult to see how the topology of intracortical connections could be changed so rapidly, it is easy to see how small changes in synaptic gain can dramatically change the resonance properties of cooperatively coupled neuron ensembles.

Finally, there is now direct experimental evidence for reverberation in a resonant oscillator circuit that is tuned to orientation. If activated by an appropriately oriented stimulus, neurons within that particular orientation column engage in a resonant state characterized by periodic firing of neuron clusters, the resonance frequency being in the range of 40 to 60 Hz (Gray and Singer 1987). Such resonant states are associated with large amplitude oscillations of the local field potential whose phase is tightly locked to the activity of individual neurons. Statistical analysis of these oscillations reveal that they are chaotic, with the attractor having a relatively low dimensionality (Schuster, personal communication). This indicates that the oscillator is nonlinear. Also consistent with this nonlinearity is the finding that the transitions from inactive to active states and back are characterized by hysteresis. It has been demonstrated previously for responses to oriented but stationary flashed stimuli that cortical cells have the tendency to generate sustained responses once activated beyond a critical threshold (Singer 1979).

Consequences of Self-organization in the Network of Tangential Connections

So far we have dealt with self-organization processes that essentially serve to generate ordered topographic maps in which clusters of adjacent neurons

assume similar response properties. We shall now take this approach one step further and investigate the consequences of self-organization in the feature space in which "conceptual" rather than topological vicinity is the relevant selection criterion. It has been known for a long time that one of the prominent features of cortical organization is the presence of an extremely dense network of far-reaching connections which are tangential to the cortical lamination. However, it is only during the last few years that this important feature of cortical organization has received the attention of experimentalists. It is now known that these connections consist mainly of axon collaterals of pyramidal cells, are excitatory, and preferentially contact the apical dendrites of other pyramidal cells (Gilbert and Wiesel 1979, 1983; Kisvárdy et al. 1986). These pathways are thus capable of mediating reciprocal excitatory interactions between cortical neurons that are nonadjacent and located in different columns.

There are indications that these connections are organized in a selective way, linking neuron clusters that tend to be spaced periodically (Rockland and Lund 1982, 1983) and that they share the same orientation preference and/or the same eye dominance (T'so et al. 1986; but see Matsubara et al. 1985). Developmental studies in the cat have shown that these tangential connections essentially appear postnatally (Price and Blakemore 1985b), go through a phase of exuberant proliferation during which they are extremely numerous and far-reaching, and subsequently become pruned under the influence of visual experience. If visual experience is unrestricted, subpopulations of these pathways are stabilized; if visual experience is not available, only a rudimentary network of horizontal connections is maintained (Luhmann et al. 1986).

This intrinsic tangential network thus develops in much the same way as the long-range connections between the eyes and their target structures (see above) and as the association projections between different cortical areas (Innocenti et al. 1985; Price and Blakemore 1985a, b; Blakemore and Price 1987). The latter is not surprising since many of the corticocortical association fibers are actually collaterals of the intrinsic tangential projections, or vice versa. We propose, therefore, that the system of horizontal connections self-organizes according to the same principles as the retinotectal, the thalamocortical, and the intracolumnar intracortical connections. We assume that, out of the initial exuberant *Anlage*, only those connections spanning between neuron clusters whose activation patterns show some statistical correlation are stabilized by coherency matching. For neuron clusters too remote from each other to share a common input from retinocortical afferents, the degree of correlated activation no longer depends upon particular neighborhood relations, but will be determined essentially by coherencies between particular features of the visual scene. An elongated contour leads to coherent activation of clusters of neurons which share the

appropriate orientation preference. Because of the columnar organization, these clusters are distributed discontinuously along trajectories within striate cortex whose orientation on the retinotopic map depends on the position and the orientation of the contour border in visual space. Likewise, a slowly moving object coherently activates distributed clusters of neurons whose directional preference matches the object's direction of movement.

Selective stabilization of tangential intrinsic connections could thus generate a nontopographically organized map matching the coherent properties of "feature constellations" in physical reality rather than topographic coherencies. Just as tectal cells become "detectors" of coherency within retinal clusters; as binocular cells become "detectors" of coherency between pairs of corresponding retinal ganglion cells in the two eyes; and as orientation columns become "detectors" of coherencies within elongated arrays of retinal ganglion cells, the selectively coupled distributed clusters of feature detectors together become detectors of coherencies within elementary constellations of features.

As in the formation of topographic maps, there will be competition between many possible constellations of features which all show some coherency, and only the most consistent and most frequently occurring constellations will win. Those which best match the already established connectivity pattern will have a competitive advantage. This leads to the development of a map which represents not only coherent relations in particular feature constellations, but also the statistical probability with which these constellations occur in the physical world. Furthermore, it is likely that the selection process at this level of cortical organization is also dependent on the activity of central gating systems, as this is already the case for selection processes at lower levels. This would provide the additional option to override the probability functions inherent in the structure of the physical world and to preferentially represent constellations relevant to the system in a behavioral context.

Thus, by simple reiteration of the very same processes of self-organization which, at peripheral levels of the visual system, lead to the establishment of maps encoding for topographic neighborhood relations, it is possible to generate nontopographic maps which represent dimensional neighborhood relations in feature space. All that is needed is an architecture of connections allowing for interactions between clusters of feature-specific neurons. Once such maps are established, they will serve as detectors of coherencies in visual scenes. This, in turn, is the basis for any preattentive segmentation of scenes into "figures" and a necessary prerequisite for any subsequent identification of patterns. If such a cooperating cluster of neurons is presented with a pattern containing the appropriate coherent property, the detector ensemble enters a resonant state and the corresponding neurons distinguish themselves as members of a resonant ensemble because of coherent

reverberation. The condition is thus very similar to the processes occurring in an orientation column when it is stimulated by an appropriately oriented contour. The only difference is that now the detector is not a single column but a coupled cluster of columns. Just as an inappropriate stimulus fails to reveal the dynamic properties of an orientation column, any nonoptimal constellation of features will fail to reveal the dynamic properties of the corresponding detector ensembles in the map of feature space. This may be one reason why we have not yet seen them in action.

We wish to emphasize that this map of “neighborhood” or “conceptual” relations in feature space actually coexists in the same cortical area as the retinotopically organized maps which represent the topological relations between features. It is thus not required to sacrifice retinotopy in order to decode coherencies between parts of a figure which are non-neighbors on the topographic map. As discussed more explicitly elsewhere (von der Malsburg and Schneider 1986; Singer 1985), such a network would be ideally suited to perform many of the segmentation processes required at the level of preattentive vision. Scenes must first be subdivided into what is most likely to be coherent figures and noncoherent noise. The identification process itself can only start thereafter. However, during this preattentive process the topographic relation of the features identified as belonging to the figure must preserve their topological relation. Otherwise, the identification would not be possible. Hence, the mechanism which detects coherencies in the feature space must actually be implemented at a level of processing where topological relations are strictly preserved. The above-proposed organization of striate cortex therefore appears to be well adapted to perform segmentation of scenes while preserving retinotopy.

Thus, one of the basic principles of cortical organization appears to be allowing for parallel computation of both local and global correlations within the same representation. The genetically predetermined blueprint of afferent connections specifies the nature of the data base upon which these correlations are to be performed. In animals with binocular vision, the afferents from the two eyes are allowed to grow into the same cortical sheet, and both sets of afferents apparently rely on the same positional markers for the establishment of coarse retinotopy. This leads to the juxtaposition of roughly corresponding inputs from the two eyes. Because of this particular input arrangement, local correlations are not confined to evaluating coherencies in the activation of topographically neighboring ganglion cells in one retina, but can also evaluate coherencies between the activity in two different receptor surfaces. The input arrangement therefore determines, by virtue of creating particular topological vicinities, which activities are to be subjected to local correlations. In the striate cortex this allows extraction of orientation and direction from intraretinal correlations and disparity from interretinal correlations. Thus, the nature of features extractable by local

correlation depends critically and exclusively on the neighborhood relations established by input mapping. It remains to be determined to what extent the often very complex and massively interleaved input projections to higher cortical areas reflect the need to generate particular neighborhood relations between afferents from different sources. These local correlations could, in principle, be used also to evaluate coherencies at a more global scale if input connectivity provided the appropriate neighborhood relations. This, however, would require sacrificing retinotopy and would in addition necessitate extensive recombination of different sets of afferents. Thus, it appears well adapted for applying a different strategy for the evaluation of global coherency and for realizing this function with the superimposed network of tangential connections.

One of the conclusions we would like to draw from the considerations in this chapter is that it is crucial at the present stage to experimentally identify the functional properties of clusters in feature space that are likely to result from self-organizing horizontal interactions in striate cortex. Since the basic principles of cortical processing can be expected to be similar in all cortical areas, it will become a fascinating challenge to both theoreticians and experimentalists to examine the functional properties that emerge if these processes of self-organization are iterated beyond primary sensory areas and applied to architectonics in which "dimensional" or "conceptual" vicinity is ever more emphasized at the expense of topographical vicinity.

Finally, we wish to draw attention to the possibility that the ontogenetic self-organizing processes discussed in this chapter may more than only formally resemble the reorganization processes in the adult cortex, discussed by Merzenich in this volume. First, there is evidence that experience-dependent long-term changes of neuronal response properties can also occur in the striate cortex of adult cats (Singer et al. 1982). Both weakening of previously functional connections and selective strengthening of inactivated connections have been observed. However, as also reported by Merzenich, these changes in the adult occurred only when the distortions of sensory input were massive and forced the animal to readjust its behavioral response. Second, as Merzenich points out, the modifications in the adult appear to be based on selective strengthening of connections between coherently activated groups of neurons. Thus, contingency matching seems to also be the basic algorithm in adult plasticity. This suggests the possibility that some of the neuronal mechanisms which subservise ontogenetic self-organization actually persist into adulthood and then serve to mediate adaptive changes such as learning and memory. Most of the prerequisites postulated for learning mechanisms would be fulfilled: The modifications of the coupling strength of neuronal connections are activity-dependent; the modification rules are based on local contingency matching and hence have the ability to associate events contiguous in time and space; the occurrence of

modifications is gated by central core systems and hence can, in principle, be made dependent upon global states such as arousal, attention, and motivation; and finally, modifications are long-lasting and thus can serve to establish permanent representations. The essential features of learning—the evaluation of relations between events by selective correlations and the internalization of these interactions between the neuronal representation of the events—are thus shared by developmental self-organization.

The equivalence of experience-dependent self-organization and learning is made explicit in recent computer simulation experiments. Multilayer systems with the above-described properties self-organize and express maps and columnar organizations (Linsker 1986; von der Malsburg 1973, 1979). These very same systems, if exposed to patterns such as, e.g., the letters of the alphabet, establish representations of these patterns. After termination of the learning process, these representations can be used for classification and recognition of the learned patterns (Edelman and Reeke 1982; Frohn et al. 1987). In conclusion, it appears as if a rather restricted set of self-organizing principles is sufficient to account not only for the development, but also for the maintenance of a variety of the characteristic structural and functional features of cortical organization. The main differences between the developmental and the mature state appear to concern the turnover of connections rather than the processing and modification algorithms. During development, growth processes continuously supply new connections and therefore maintain a large repertoire for use-dependent selection. Moreover, during development, connections not selected for consolidation are physically removed. Once growth processes are terminated, the effects of developmental pruning become irreversible. In adulthood, by contrast, the repertoire of modifiable connections is much more restricted and probably fixed. However, when connections become weakened they do not seem to disappear physically and hence may remain able to be reactivated. What seems to change during the transition from the developmental to the mature state are the constraints of self-organization rather than the basic principles.

REFERENCES

- Altmann, L.; Luhmann, H.J.; Greuel, J.M.; and Singer, W. 1987. Functional and neuronal binocularity in kittens raised with rapidly alternating monocular occlusion. *J. Neurophysiol.*, in press.
- Andersen, P. 1987. Long-term potentiation — outstanding problems. In: *The Neural and Molecular Bases of Learning*, eds. J.-P. Changeux and M. Konishi, pp. 239–262. Dahlem Konferenzen. Chichester: John Wiley & Sons Ltd.
- Bear, M.F., and Singer, W. 1986. Modulation of visual cortical plasticity by acetylcholine and noradrenaline. *Nature* **320**: 172–176.
- Blakemore, C., and Cooper, G.F. 1970. Development of the brain depends on the visual environment. *Nature* **228**: 477–478.

- Blakemore, C., and Price, D.J. 1987. The organization and post-natal development of area 18 of the cat's visual cortex. *J. Physiol.* **384**: 263–292.
- Blasdel, G.G., and Salama, G. 1986. Voltage-sensitive dyes reveal a modular organization in monkey striate cortex. *Nature* **321**: 579–585.
- Buisseret, P., and Imbert, M. 1976. Visual cortical cells: their developmental properties in normal and dark reared kittens. *J. Physiol.* **255**: 511–525.
- Buisseret, P.; Gary-Bobo, E.; and Imbert, M. 1978. Ocular motility and recovery of orientational properties of visual cortical neurons in dark-reared kittens. *Nature* **272**: 816–817.
- Buisseret, P., and Singer, W. 1983. Proprioceptive signals from extraocular muscles gate experience-dependent modifications of receptive fields in the kitten visual cortex. *Exp. Brain Res.* **51**: 443–450.
- Constantine-Paton, M., and Law, M.I. 1978. Eye specific termination bands in tecta of three-eyed frogs. *Science* **202**: 639–641.
- Creutzfeldt, O.D.; Kuhnt, U.W.; and Benevento, L.A. 1974. An intracellular analysis of visual cortical neurones to moving stimuli; responses in a cooperative neuronal network. *Exp. Brain Res.* **21**: 251–274.
- Dingledine, R.; Hynes, M.A.; and King, G.L. 1986. Involvement of N-methyl-D-aspartate receptors in epileptiform bursting in the rat hippocampal slice. *J. Physiol.* **380**: 175–189.
- Dinse, H., and Best, J. 1984. Receptive field organization of the cat's visual cortex exhibit strong spatio-temporal interaction. *Neurosci. Lett.* **S18**: 75.
- Edelman, G.M., and Reeke, G.N., Jr. 1982. Selective networks capable of representative transformations, limited generalizations, and associative memory. *Proc. Natl. Acad. Sci. USA* **79**: 2091–2095.
- Ferster, D. 1986. Orientation selectivity of synaptic potentials in neurons of cat primary visual cortex. *J. Neurosci.* **6**: 1284–1301.
- Finette, S.; Harth, F.; and Csermely, T.J. 1978. Anisotropic connectivity and cooperative phenomena as a basis for orientation sensitivity in the visual cortex. *Biol. Cybern.* **30**: 231–240.
- Fraser, S.E. 1985. Cell interactions involved in neuronal patterning: an experimental and theoretical approach. In: *Molecular Bases of Neural Development*, eds. G.M. Edelman, W.E. Gall and W.M. Cowan, Neurosciences Research Foundation.
- Freeman, R.D., and Bonds, A.B. 1979. Cortical plasticity in monocularly deprived immobilized kittens depends on eye movement. *Science* **206**: 1093–1095.
- Frégnac, Y., and Imbert, M. 1984. Development of neuronal selectivity in primary visual cortex of cat. *Physiol. Rev.* **64**: 325–434.
- Frohn, H.; Geiger, H.; and Singer, W. 1987. A self-organizing neural network sharing features of the mammalian visual system. *Biol. Cybern.* **55**: 333–343.
- Geiger, H., and Singer, W. 1986. A possible role of calcium currents in developmental plasticity. *Exp. Brain Res. Ser.* **14**: 256–270.
- Gilbert, C.D., and Wiesel, T.N. 1979. Morphology and intracortical projections of functionally characterized neurons in the cat visual cortex. *Nature* **280**: 120–125.
- Gilbert, C.D., and Wiesel, T.N. 1983. Clustered intrinsic connections in cat visual cortex. *J. Neurosci.* **3**: 1116–1133.
- Gray, C.M., and Singer, W. 1987. Stimulus-specific neuronal oscillations in the cat visual cortex: a cortical functional unit. *Soc. Neurosci. Abst.*, in press.
- Harris, W.A. 1980. The effects of eliminating impulse activity on the development of the retinotectal projection in salamanders. *J. Comp. Neurol.* **194**: 303–317.
- Häussler, A.F., and von der Malsburg, C. 1983. Development of retinotopic projections — an analytical treatment. *J. Theor. Neurobiol.* **2**: 47–73.
- Hebb, D.O. 1949. *The Organization of Behaviour*. New York: Wiley.

- Hirsch, H.V.B., and Spinelli, D.N. 1970. Visual experience modifies distribution of horizontally and vertically oriented receptive fields in cats. *Science* **168**: 869–871.
- Hubel, D.H., and Wiesel, T.N. 1974. Ordered arrangement of orientation columns in monkeys lacking visual experience. *J. Comp. Neurol.* **158**: 307–318.
- Hubel, D.H.; Wiesel, T.N.; and Stryker, M.P. 1978. Anatomical demonstration of orientation columns in macaque monkey. *J. Comp. Neurol.* **177**: 361–380.
- Humphrey, A.L.; Skenn, L.C.; and Norton, T.T. 1980. Topographic organization of the orientation column system in the striate cortex of the tree shrew (*Tupaia glis*). II. Deoxyglucose mapping. *J. Comp. Neurol.* **192**: 549–566.
- Innocenti, G.M.; Frost, D.O.; and Illes, J. 1985. Maturation of visual callosal connections in visually deprived kittens: a challenging critical period. *J. Neurosci.* **5**: 255–267.
- Kasamatsu, T., and Pettigrew, J.D. 1979. Preservation of binocularity after monocular deprivation in the striate cortex of kittens treated with 6-hydroxydopamine. *J. Comp. Neurol.* **185**: 139–161.
- Kasamatsu, T.; Pettigrew, J.D.; and Ary, M.-L. 1979. Restoration of visual cortical plasticity by local microperfusion of norepinephrine. *J. Comp. Neurol.* **185**: 163–182.
- Kisvárdy, Z.F.; Martin, K.A.C.; Freund, T.F.; Maglóczy, Z.; Whitteridge, D.; and Somogyi, P. 1986. Synaptic targets of HRP-filled layer III pyramidal cells in the cat striate cortex. *Exp. Brain Res.* **64**: 541–552.
- Kleinschmidt, A.; Bear, M.F.; and Singer, W. 1987. Blockade of N-methyl-D-aspartate receptors disrupt experience dependent plasticity of kitten striate cortex. *Science* **238**: 355–358.
- Kohonen, T. 1982. Clustering, taxonomy, and topological maps of patterns. *Proc. 6th Internat. Conf. on Pattern Recognition*, Munich, pp. 114–128.
- LeVay, S.; Connolly, M.; Houde, J.; and van Essen, D.C. 1985. The complete pattern of ocular dominance stripes in the striate cortex and visual field of the macaque monkey. *J. Neurosci.* **5**: 486–501.
- LeVay, S., Hubel, D.H.; and Wiesel, T.N. 1975. The pattern of ocular dominance columns in macaque visual cortex revealed by a reduced silver stain. *J. Comp. Neurol.* **159**: 559–576.
- LeVay, S.; Hubel, D.H.; and Wiesel, T.N. 1977. Plasticity of ocular dominance columns in monkey striate cortex. *Phil. Trans. R. Soc. Lond. B.* **278**: 377–409.
- Levey, W.B., and Steward, O. 1983. Temporal contiguity requirements for long-term associative potentiation/depression in the hippocampus. *Neurosci.* **8**: 791–797.
- Linsker, R. 1986. From basic network principles to neural architecture: emergence of orientation selective cells. *Proc. Natl. Acad. Sci. USA* **83**: 8390–8394.
- Livingstone, M.S., and Hubel, D.H. 1984. Anatomy and physiology of a color system in the primate visual cortex. *J. Neurosci.* **4**: 309–356.
- Löwel, S.; Freeman, B.; and Singer, W. 1987. Topographic organization of the orientation column system in large flat-mounts of the cat visual cortex. A 2-deoxyglucose study. *J. Comp. Neurol.* **255**: 401–415.
- Löwel, S.; Bischof, H.-J.; Leutenecker, B.; and Singer, W. 1987. Topographic relations between ocular dominance and orientation columns in the cat striate cortex. *Exp. Brain Res.*, in press.
- Luhmann, H.J.; Martinez Millán, L.; and Singer, W. 1986. Development of horizontal intrinsic connections in cat striate cortex. *Exp. Brain Res.* **63**: 443–448.
- Mastrorarde, D.N. 1983. Correlated firing of cat retinal ganglion cells. I. Spontaneously active inputs to X- and Y-cells. *J. Neurophysiol.* **49**: 303–324.
- Matsubara, J.; Cynader, M.; Swindale, N.V.; and Stryker, M.P. 1985. Intrinsic projections within visual cortex: evidence for orientation-specific local connections.

- Proc. Natl. Acad. Sci. USA* **82**: 935–939.
- Meyer, R.L. 1982. Tetrodotoxin blocks the formation of ocular dominance columns in goldfish. *Science* **218**: 589–591.
- Mower, G.D.; Caplan, C.J.; Christen, W.G.; and Duffy, F.H. 1985. Dark rearing prolongs physiological but not anatomical plasticity of the cat visual cortex. *J. Comp. Neurol.* **236**: 448–466.
- Price, D.J., and Blakemore, C. 1985a. Regressive events in the postnatal development of association projections in the visual cortex. *Nature* **316**: 721–724.
- Price, D.J., and Blakemore, C. 1985b. The postnatal development of the association projection from visual cortical area 17 to area 18 in the cat. *J. Neurosci.* **5**: 2443–2452.
- Rakić, P. 1981. Development of visual centers in the primate brain depends on binocular competition before birth. *Science* **214**: 928–931.
- Rauschecker, J.P., and Singer, W. 1979. Changes in circuitry of the kitten's visual cortex are gated by postsynaptic activity. *Nature* **280**: 58–60.
- Rauschecker, J.P., and Singer, W. 1981. The effects of early visual experience on the cat's visual cortex and their possible explanation by Hebb synapses. *J. Physiol.* **310**: 215–239.
- Rockland, K.S., and Lund, J.S. 1982. Widespread periodic intrinsic connections in the tree shrew visual cortex. *Science* **215**: 1532–1534.
- Rockland, K.S., and Lund, J.S. 1983. Intrinsic laminar lattice connections in primate visual cortex. *J. Comp. Neurol.* **216**: 303–318.
- Rodieck, R.W., and Smith, P.S. 1966. Slow dark discharge rhythms of cat retinal ganglion cells. *J. Neurophysiol.* **29**: 942–953.
- Schmidt, J.T., and Tieman, S.B. 1985. Eye-specific segregation of optic afferents in mammals, fish, and frogs: the role of activity. *Cell. Mol. Neurobiol.* **5**: 5–34.
- Singer, W. 1979. Central core control of visual cortex functions. In: *The Neurosciences Fourth Study Program*, eds. F.O. Schmitt and F.G. Worden, pp. 1093–1109. Cambridge, MA: MIT Press.
- Singer, W. 1982. Central core control of developmental plasticity in the kitten visual cortex: I. Diencephalic lesions. *Exp. Brain Res.* **47**: 209–222.
- Singer, W. 1985. Activity-dependent self-organization of the mammalian visual cortex. In: *Models of the Visual Cortex*, eds. D. Rose and G. Dobson, pp. 123–136. Chichester: John Wiley & Sons, Ltd.
- Singer, W. 1987. Activity-dependent self-organization of synaptic connections as a substrate of learning. In: *The Neural and Molecular Bases of Learning*, eds. J.-P. Changeux and M. Konishi, pp. 301–336. Dahlem Konferenzen. Chichester: John Wiley & Sons, Ltd.
- Singer, W., and Rauschecker, J.P. 1982. Central core control of developmental plasticity in the kitten visual cortex. II. Electrical activation of mesencephalic and diencephalic projections. *Exp. Brain Res.* **41**: 199–215.
- Singer, W.; Freeman, B.; and Rauschecker, J.P. 1981. Restriction of visual experience to a single orientation affects the organization or orientation columns in cat visual cortex: a study with deoxyglucose. *Exp. Brain Res.* **41**: 199–215.
- Singer, W.; Treutter, F.; and Yinon, U. 1982. Central gating of developmental plasticity in kitten visual cortex. *J. Physiol.* **324**: 221–237.
- Stryker, M.P., and Harris, W.A. 1986. Binocular impulse blockade prevents the formation of ocular dominance columns in cat visual cortex. *J. Neurosci.* **6**: 2117–2133.
- Swindale, N.V., and Cynader, M.S. 1986. Physiological segregation of geniculocortical afferents in the visual cortex of dark-reared cats. *Brain Res.* **362**: 281–286.

- Thomson, A.M. 1986. A magnesium-sensitive post-synaptic potential in rat cerebral cortex resembles neuronal responses to N-methylaspartate. *J. Physiol.* **370**: 531–549.
- T'so, D.Y.; Gilbert, C.D.; and Wiesel, T.N. 1986. Relationship between horizontal interactions and functional architecture in cat striate cortex as revealed by cross-correlation analysis. *J. Neurosci.* **6**: 1160–1170.
- von der Malsburg, C. 1973. Self-organization of orientation sensitive cells in the striate cortex. *Kybernetik* **14**: 8–100.
- von der Malsburg, C. 1979. Development of ocularity domains and growth behaviour of axon terminals. *Biol. Cybern.* **32**: 49–62.
- von der Malsburg, C., and Cowan, J.D. 1982. Outline of a theory for the ontogenesis of iso-orientation domains in visual cortex. *Biol. Cybern.* **45**: 49–56.
- von der Malsburg, C., and Schneider, W. 1986. A neural cocktail-party processor. *Biol. Cybern.* **54**: 29–40.
- Watkins, J.C., and Evans, R.H. 1981. Excitatory amino acid transmitters. *Ann. Rev. Pharm. Tox.* **21**: 165–204.
- Willshaw, D.J., and von der Malsburg, C. 1976. How patterned neural connections can be set up by self-organization. *Proc. R. Soc. Lond. B* **194**: 431–445.

