Network Self-Organization in the Ontogenesis of the Mammalian Visual System*

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1 General Introduction

This chapter discusses the process of network self-organization, which is fundamental to the organization of the brain. The process takes place on several temporal scales: the ontogenetic/learning time scale of hours, days, and years; and probably also the functional time scale of fractions of a second to minutes. Several concepts and tools of network self-organization are introduced here. I start with a discussion of self-organization in general and subsequently demonstrate the essential mechanisms, with the help of examples taken from the ontogenesis of the visual system. Although a particular mathematical formulation has been chosen for this discussion, I do not intend to put it forward as a general basis for network self-organization. A canonical mathematical formulation of self-organization has yet to be developed.

1.1 Self-Organization

One often speaks of some structural trait of an organism as being "genetically determined." This seems to imply that the genes contain a blueprint describing the organism in full detail. However, all the stages of brain organization (not just evolution) more or less strongly involve 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 size, one can hardly imagine how ontogeny could select the correct wiring diagram out of all of the 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, that is, of general rules to generate neural structure and of principles of error correction. Above

all, ontogenesis can only produce structures with a high degree of regularity, for example, homogeneity, repetitivity, or continuity. Knowing the mechanism of ontogeny is of extreme importance: one cannot understand the function of the brain without knowing its structure, and one cannot know the structure of the brain without knowing the principles of its ontogenesis.

1.2 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 and temporal chemical patterns, e.g., in the Zhabotinski-Belusov reaction), and star and galaxy formation. I will attempt to give here a general description of the basic mechanisms of organization by using the important example of convective pattern formation, the so-called Bénard problem.

Organization takes place in systems consisting of a large number of interacting elements, such as atoms in a liquid or crystal or small subvolumes of liquid in convection currents, in a reaction-diffusion system or in an evolving star system, or, in the application that is of interest here, synapses in nerve networks. Initially, self-organizing systems are in a relatively undifferentiated state: atoms move randomly 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; for example, some convective fluid motion sets in. To stress the random nature of typical small deviations, they are called *fluctuations*.

In the prime example, 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 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 reproduction in Darwinian evolution. In the Bénard system, fluctuations are created by thermal motion. If a small column of liquid moves upward, more warm liquid is drawn in from the bottom, the column becomes less dense, and its upward movement is accelerated. Downward movement accelerates analogously.

2. *Limitation of resources leads to competition among fluctuations and to the selection of the most vigorously growing (the "fittest") at the expense of the others.* In the Bénard system, upward movement in one place requires downward movement in other places. The columns with the 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 with features of a concrete system is sometimes ambiguous. In the Bénard system, competition in terms of upward movement might also be seen as cooperation between upward movement occurring in one place and downward movement occurring in another place. Whole coherent patterns of movement, again, compete as long as there is local contradiction between them: liquid cannot move up and down at the same place.

A fundamental and very important observation about organizing systems is the fact that global order can arise from local interactions. Many originally random local fluctuations can coalesce into a globally ordered pattern of deviations from the original state. 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 one of extreme importance to the brain, in which local interactions between neighboring cellular elements create states of global order, ultimately leading to coherent behavior.

The stage for the organization of a pattern is set by 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. Because 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 topologically arranged; 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. However, in the concrete cases considered here, ordinary space will still play a dominant 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 another valid pattern. One of these has to be spontaneously selected during pattern formation, a process that is called *spontaneous symmetry breaking*. When the boundary or initial conditions are slightly deformed, so that the original symmetry is destroyed, one organized pattern is favored. In general, self-organizing systems react very sensitively to symmetry-breaking influences.

2 General Neural Network Organization

Two types of variables are relevant to network organization: signals and interconnections. Signals are the action potentials that are propagated down the axonal trees of neurons. Connections control neural interactions and are characterized by weight variables. These measure the size of the effect exerted on the postsynaptic membrane by arriving nervous impulses. Correspondingly, organization takes place on two levels: activity and connectivity.

On the ontogenetic time scale, one is interested mainly in network self-organization, which has the following general form. Assume that previous processes have already set up a primitive network. This network, together with input signals, creates activity patterns, and these activity patterns in turn modify connections by synaptic plasticity. The feedback loop between changes in synaptic strengths and changes in activity patterns must be positive, so that coherent deviations from the undifferentiated state self-amplify, conforming to the first of the principles previously formulated. 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 signals, the postsynaptic signal, and possibly modulatory signals that 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 which, in turn, increase the strength of the synapse. 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.

This rule is referred to as "Hebbian plasticity." The corresponding rule for inhibitory synapses would have a synapse strengthened if it was successful in inhibiting the postsynaptic element. At present, however, most authors consider inhibition as a rigid service system that does not take part in network self-organization.

Hebb's rule corresponds to the "self-reproduction" of the general scheme of organization. To stabilize the system, some competition for limited "resources" 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. (Although this rule leads to certain functional deficits and is probably not realistic, I employ it here for its technical convenience.) Synaptic plasticity, constrained by competition, implements organizing principles 1 and 2.

One synapse on its own cannot efficiently produce favorable events. For that it needs the cooperation of other synapses that converge onto the same postsynaptic neuron and that carry coincident signals. This implements the third organizing principle. 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 result from excitatory links between presynaptic neurons. They may, however, also be caused by simultaneous stimulation of sensory cells, in which 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 context with the emergence of global convection patterns in the Bénard phenomenon. The term *global order* is used for configurations that bring the local rules into a state of optimal mutual consistency with each other. The fact that the external world takes part in the game leads to the adaptation of the nervous system to it.

The rules for the adjustment of synaptic weights that have been introduced 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 controls are necessary: (1) genetic control of boundary conditions and interaction rules to favor certain useful connection patterns; and (2) control by central structures that 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. That state is thereby stabilized, and the likelihood for its future appearance is increased.

Central control as the *only* criterion for growth or decay of synapses is not sufficient. 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 that can be created by rules of local cooperation and competition under predetermined constraints.

Having briefly introduced relevant principles, I now present 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 decades.

3 Establishment of Topological Maps

3.1 Biological Background

At some stage in the development of the vertebrate embryo, the fibers of retinal ganglion cells grow out through the eye stalk toward the brain and establish retinotopic connections there. Neighboring cells in retina contact neighboring positions in the target structure. The most intensively studied case is that of retino-tectal connections in amphibia and fish. The interesting question is how fibers find their correct target positions. This problem of retinotopy has long been recognized as an important paradigm of ontogenetic brain organization in general. There are many topological fiber projections between thalamic nuclei and cortical areas and also between and within cortical areas. Retinotopy is one of those few biological phenomena studied with enough experimental intensity to allow their theoretical issues to be settled.

For a long time, the most puzzling aspect of the retinotopy problem was a mixture of rigid genetic determination on the one hand and plasticity on the other. The orientation of the projection is reliably prespecified, for instance, nasal retina reliably connecting to caudal tectum. On the other hand, magnification and position of the map are adjusted with flexibility so that all of the existing retinal tissue maps to all of the existing tectum, even if the sizes of these structures vary under some physiological conditions or after experimental manipulation. This property is called *systems matching*. For instance, because growth in retina and in tectum are disparate — retina grows in a concentric fashion, tectum (in some species) from front to back — the already existing fiber projections shift in an ordered fashion to achieve systems matching. The picture is further complicated by evidence that fibers are able to follow tectal tissue that 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 by, 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 that 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 retino-tectal system (for review, see Schmidt & Tiemann, 1985).

In spite of many ongoing controversies within the retino-tectal community, the preceding 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, I concentrate on the fiber-sorting mechanism C, because it deals with activity-dependent network organization and can be generalized to other interesting cases, in particular to processes in the cerebral cortex.

Basic to the fiber-sorting mechanism is the fact that the spontaneous activity of neighboring retinal ganglion cells is correlated because of excitatory connections in retina (Mastronarde, 1983; Meister, Wong, Baylor, & Shatz 1991). 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. Because of excitatory links within tectum, activity in neighboring tectal cells is correlated, just as in retina. Retino-tectal 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"). If all goes well, only fibers that have a maximal number of neighboring fibers (neighboring in the sense of tectum and retina) survive the competition. Moreover, there are no retinal spots that project to more than one spot of tectum, and there are no tectal spots that receive fibers from more than one spot of retina. This is a fully retinotopic mapping, which is distinguished by maximally conforming to the preceding constraints.

3.2 Formal Description

I concentrate here mainly on the sorting mechanism C, which illustrates network organization best. The temporal development of retino-tectal connections are described by a differential equation of the type:

$$\dot{W}_i = W_i F_i - W_i \sum_j W_j F_j / N \tag{1}$$

Here, W_i is the strength of synapse i, $\dot{W}_i$ is its rate of change, F_i is a rate coefficient, and N is the total number of synapses competing with each other. Assume that $\sum_i W_i/N = 1$ (otherwise it would quickly converge to 1). The quantity $\bar{F} = \sum_j W_j F_j / N$ can then be interpreted as the weighted mean of the coefficients F_i. Accordingly, Equation (1) can be written

$$\dot{W}_i = W_i (F_i - \bar{F}) \tag{2}$$

making it evident that the synapses that will grow are those with a growth coefficient above average, whereas the others diminish. As a consequence, the weighted average $\bar{F}$ grows, and more and more synapses fall below threshold, the system finally settling into the state in which only the synapses with maximal $F_i = \bar{F}$ survive.

According to Equation (1) or (2), nonexistent synapses ($W_i = 0$) cannot grow. To represent the formation of new synapses, a constant rate α of synapse formation is added to the growth term $W_i F_i$ and its average in the competitive term, turning the set of differential equations into

$$\dot{W}_i = \alpha + W_i F_i - W_i \sum_j (\alpha + W_j F_j)/N \tag{3}$$

or, equivalently,

$$\dot{W}_i = \alpha(1 - W_i) + W_i(F_i - \bar{F}) \tag{4}$$

In this differential equation, α acts as a convenient control parameter. The α-dependent term pulls the synaptic strengths toward the value 1, whereas the other term destabilizes that value. With positive α, more than just the synapses with maximal F_i can survive.

Retino-tectal connections have to be labeled by two indices, ρ and τ, for a retinal and a tectal cell, respectively, replacing W_i by $W_{\tau\rho}$. Conservation of axonal and dendritic arbor is implemented in the differential equation by a tendency for the averaged weights for all of the presynaptic and postsynaptic competitors of a given synapse $(\tau\rho)$ to converge to 1. This average is

$$B_{\tau\rho}(X) = (\sum_{\tau'} X_{\tau'\rho} + \sum_{\rho'} X_{\tau\rho'})/(2N) \tag{5}$$

where X stands for any array and N is the number of neurons both in retina and in tectum. With these changes, one arrives at the set of differential equations that are used for describing the self-organization of retino-tectal connections:

$$\dot{W}_{\tau\rho} = \alpha + W_{\tau\rho} F_{\tau\rho} - W_{\tau\rho} B_{\tau\rho}(\alpha + WF) \tag{6}$$

For the growth coefficients $F_{\tau\rho}$, see Equation (13). The first two terms on the right-hand side describe growth of synapse $(\tau\rho)$, the third term describes its competition with all synapses to the same tectal cell τ and from the same retinal cell ρ, B being the average over the growth terms of all of those other synapses (for a more thorough explanation, see Häussler and von der Malsburg 1983). In analogy to Equation (4), this equation can be rewritten as

$$\dot{W}_{\tau\rho} = \alpha(1 - W_{\tau\rho}) + W_{\tau\rho}(F_{\tau\rho} - B_{\tau\rho}(WF)) \tag{7}$$

The parameter α regulates the rate of formation of new synapses, arriving at the tectum by virtue of mechanism A. Positioning mechanism B is easily implemented here by starting the calculation with a more or less precisely ordered retinotopic mapping as the initial condition for $W_{\tau\rho}$.

Before Equation (6) or (7) can be used, the dependency of $F_{\tau\rho}$ on cellular signals and the dependency of signals on network structure have to be defined. The general Hebbian idea is that $F_{\tau\rho}$ is proportional to an appropriate measure of correlation between signals in retinal cell ρ and tectal cell τ. Activity arises spontaneously in retina and is propagated through W to the tectum. Suppose $f^r(t)$ is the normalized deviation of spontaneous activity in ganglion cell r from its temporal average, the only thing that needs to be known about f^r is that its correlation for different cells is

$$\langle f^r(t) f^{r'}(t) \rangle = \delta_{rr'} \tag{8}$$

The total activity in retinal cell ρ is

$$c^R_\rho(t) = \sum_r D^R_{\rho r} f^r(t) \tag{9}$$

Here, $D^R_{\rho r}$ describes the propagation of activity from cell r to cell ρ in retina. It is assumed to be a smooth and monotonically falling function of the distance $|\rho - r|$ (the latter tacitly implying periodic boundary conditions). Linear signal propagation is assumed for simplicity. For the interpretation of Equation (9), it is immaterial whether $D^R_{\rho r}$ describes forward propagation of activity from an earlier generation of cells, or whether it describes feed-back propagation within the same layer of cells. In the latter case, Equation (9) would be the result of some rapid iteration of signal exchange. In either case, the important property of $c^R_\rho(t)$ is the form of its autocorrelation function $\langle c^R_{\rho'} c^R_\rho \rangle$. Given Equations (8) and (9), this has the form

$$\langle c^R_{\rho'} c^R_\rho \rangle = \sum_{r r'} D^R_{\rho' r'} D^R_{\rho r} \langle f^{r'}(t) f^r(t) \rangle = \sum_r D^R_{\rho' r} D^R_{\rho r} = \bar{D}^R_{\rho' \rho} \tag{10}$$

The last equality sign defines a function $\bar{D}$ that again depends only on $|\rho' - \rho|$ and which is just a bit broader than $D^R_{|\rho - r|}$.

The total input signal afferent to tectal cell τ is

$$I_\tau(t) = \sum_{\rho'} W_{\tau \rho'} c^R_{\rho'}(t) \tag{11}$$

After propagation within tectum with the propagation kernel D^T, tectal activity is

$$c^T_\tau(t) = \sum_{\tau' \rho'} D^T_{\tau \tau'} W_{\tau' \rho'} c^R_{\rho'} \tag{12}$$

Now it is time to calculate the covariance of the signals on the presynaptic and post-synaptic sides of synapse $(\tau\rho)$, which will serve as a growth coefficient in Equation (6) or (7):

$$F_{\tau\rho} = \langle c^T_\tau(t) c^R_\rho(t) \rangle = \sum_{\tau' \rho'} D^T_{\tau \tau'} W_{\tau' \rho'} \langle c^R_{\rho'} c^R_\rho \rangle = \sum_{\tau' \rho'} D^T_{\tau \tau'} W_{\tau' \rho'} \bar{D}^R_{\rho' \rho} \tag{13}$$

With the previous assumptions about the retinal signal propagator and with similar assumptions about the tectal one, this is just a low-pass filtered version of the connectivity matrix W. For a given synapse $(\tau\rho)$, the growth coefficient $F_{\tau\rho}$ is a weighted sum of the strengths of neighboring synapses, that is, the strengths of connection from points neighboring ρ in retina to points neighboring τ in tectum.

The differential Equation (6) together with Equation (13) implements the features of the sorting mechanism C as described in the previous section. A simulation is shown in Figure 1. Like all self-organizing systems, the fiber-sorting mechanism described here has the capability of creating global order from local interactions. All such systems, however, are in danger of getting caught in local minima, which are of less-than-perfect global order. In the case given here, such minima are mappings that are only piecewise retinotopic —

disorganized mapping is created, it is impossible for fibers near the borders of domains to collect all their retinotopic neighbors, because some of them would have to tunnel through foreign territory. The danger of getting trapped in local minima is reduced by the positioning mechanism B, which already creates some retinotopic order in the initial state of the sorting mechanism. However, because the positioning mechanism (if properly discussed) has the same problem of avoiding local minima, and because this is a problem of general importance for self-organizing systems, I will discuss here some of the factors that are important to avoid local minima.

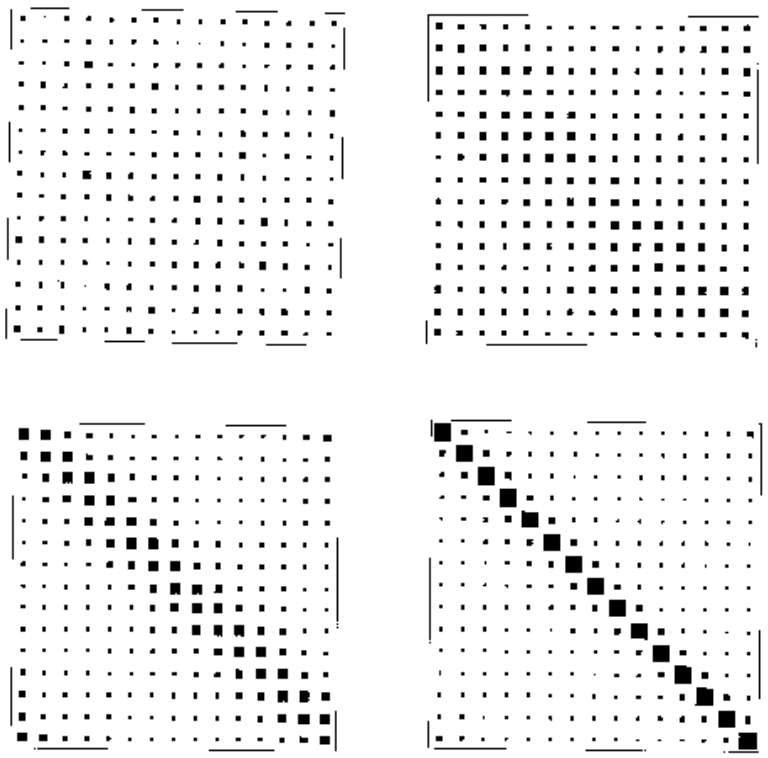

Figure 1: Development of a retinotopic mapping: Simulation of Equation (6), one-dimensional retina and tectum with wraparound boundary conditions. The retinal coordinate runs horizontally, the tectal vertically. The area of the small squares indicates the strengths $W_{\tau\rho}$ of synapses. The temporal sequence is left to right, top to bottom. In the initial state, the symmetry between the two orientations of the mapping is slightly broken to speed up the process. During the simulation, the control parameter α is slowly reduced.

The issue is conveniently studied with the help of stability analysis. This has been carried through for the case of one-dimensional retina and one-dimensional tectum in Häussler & von der Malsburg (1983), of which a qualitative outline is given here. (The two-dimensional case will be treated in a forthcoming paper with W. Wagner.) Equation (6) has a stationary homogeneous solution $W_{\tau\rho} = W_o = 1$. Consider the equivalent form

of Equation (7). It has two terms. The first of them stabilizes W_o, with a strength that is proportional to α, whereas the second term is destabilizing, having the general form of (1). Stability analysis now proceeds by rewriting Equation (7) in terms of the deviation $V_{\tau\rho} = W_{\tau\rho} - W_o$ from the stationary state and linearizing the equation in $V_{\tau\rho}$, striking out all terms of higher order (there are actually terms up to order 3). This approximation is accurate for small $V_{\tau\rho}$.

The resulting set of N^2 linear equations (N being the number of cells in retina and in tectum) has N^2 independent solutions, which I will call *modes*. Each mode grows or decays exponentially with its own characteristic rate constant, called its *eigenvalue*. The modes have a simple form if wraparound boundary conditions are used for retina and tectum. In that case, they are harmonic waves, that is, a product of a sinusoidal function of ρ and a sinusoidal function of τ. Modes differ in spatial frequency along each of the two coordinates, starting from zero frequency (corresponding to a constant function).

It is now important to know the spectrum of eigenvalues of the modes. In this case, it turns out that the spectrum contains $-\alpha$ as an additive constant common to all eigenvalues. Thus, α is a very convenient control parameter with which the spectrum can be shifted up and down. It further turns out that the smallest of all eigenvalues is that of the constant mode ($V = 1$), followed by all modes that are constant along either ρ or τ. This is due to the damping effect of the B-operator in Equation (7). The shape of the spectrum of all the other modes, which vary along both ρ and τ, is strongly determined by the shape of the low-pass filter $F_{\tau\rho}$, Equation (13). The higher the spatial frequency of a mode, the stronger the damping effect exerted by that filter, and the lower the eigenvalue of that mode. Hence, the modes with the highest eigenvalue are those with the lowest nonzero spatial frequency, corresponding to just one cycle and both along retina and tectum. There are two such modes (not counting versions shifted along retina or tectum), which correspond to two broad diagonals of different orientation in the (ρ, τ) matrix V. By appropriate choice of α, the spectrum can be shifted such that only the eigenvalues of these two diagonals are positive and all other modes have negative eigenvalues. Some further analysis (Häussler & von der Malsburg, 1983) shows that the nonlinear interactions between the two diagonal modes are of a competitive nature, such that one of them will eventually win and the other will die out. This amounts to spontaneous symmetry breaking between the two possible orientations of the retino-tectal mapping.

Once one of the globally ordered diagonal modes has won, one can safely lower α to permit modes with higher frequency to grow. Due to nonlinear interactions, the broad diagonal will excite those higher modes that are parallel to it and which have the same phase. All these modes conspire to sharpen the retino-tectal mapping, until, with $\alpha = 0$, a very precise and globally ordered retinotopic mapping is established. For a simulation see Figure 1.

The original proposal of a sorting mechanism based on signal correlations, together with simulations of the two-dimensional case is in Willshaw and von der Malsburg (1976). A version based on chemical marker induction instead of on electrical signals, together with a didactic analogy ("tea trade model") is contained in von der Malsburg and Willshaw (1977). A version with more biological detail in the rules for the making and breaking of

connections and with extensive simulations of experimental results is given in Willshaw and von der Malsburg (1979). A critical comparison with other theories is given in von der Malsburg and Willshaw (1981). An algorithmic caricature of the mechanism is known as Kohonen learning (Kohonen, 1982). The formulation given here, using linear signal propagation, is not an efficient basis for simulations. According to it, the postsynaptic signals c_τ^T are a very undifferentiated and flat function of position τ, being the result of repeated low-pass filtering of the original retinal spontaneous activity $f^r(t)$; see Equations (9) and (12). Much faster convergence is achieved by employing nonlinear sigmoid input-output functions in retina and tectum, creating broad localized blobs of strong activity on a silent background.

4 Ocularity Domains

There are several cases in which fiber systems originating in the two eyes innervate common target structures, for example, lateral geniculate body, optic tectum, or layer IV of visual cortex. This is the case in animals with binocular vision (and in frogs after certain experimental manipulations; Constantine-Paton & Law 1978). Both fiber systems are organized in a retinotopic fashion and overlap so that corresponding points in the two eyes innervate the same small region of the target structure. Ocularity domains are formed as a small local deviation from this pattern by the segregation of the two types of fibers over a small distance. These domains can have the form of patches, tufts, stripes, or layers.

It has first been shown in von der Malsburg (1979) that the fiber sorting mechanism described earlier can account for the formation of ocularity stripes if the system has two input sheets and if the fibers coming from the two sheets can be distinguished on the basis of their signals (Figure 2). Although the treatment in von der Malsburg (1979) makes explicit use of signals, the description here will go as far as possible on the basis of just their pair correlations. A straightforward generalization of the Hebbian correlation Equation (13) for the case with two retinae is

$$F_{\tau\rho}^{\gamma} = \langle c_\tau^T(t) c_\rho^\gamma(t) \rangle = \sum_{\tau'\rho'\gamma'} D_{\tau\tau'}^T W_{\tau'\rho'}^{\gamma'} \langle c_{\rho'}^{\gamma'} c_\rho^\gamma \rangle \tag{14}$$

where $\gamma \in \{l, r\}$ labels the two retinae of ocularity l and r. This is to be inserted in Equation (7). It is natural to assume that for signals from the same retina correlations are as discussed before, whereas for signals from different retinae correlations are zero or even negative. This correlation is to be inserted into Equation (7). The B-operator generalizes to

$$B_{\tau\rho}^{\gamma}(X) = (\sum_{\tau'} X_{\tau'\rho}^{\gamma} + \frac{1}{2} \sum_{\rho'\gamma'} X_{\tau\rho'}^{\gamma'})/(2N) \tag{15}$$

If Equations (14) and (15) where just inserted into Equation (7) and the simulation started with a near to homogeneous (all-to-all) mapping and large control parameter α, a bad instability would result. The two retinae would just carve up the postsynaptic

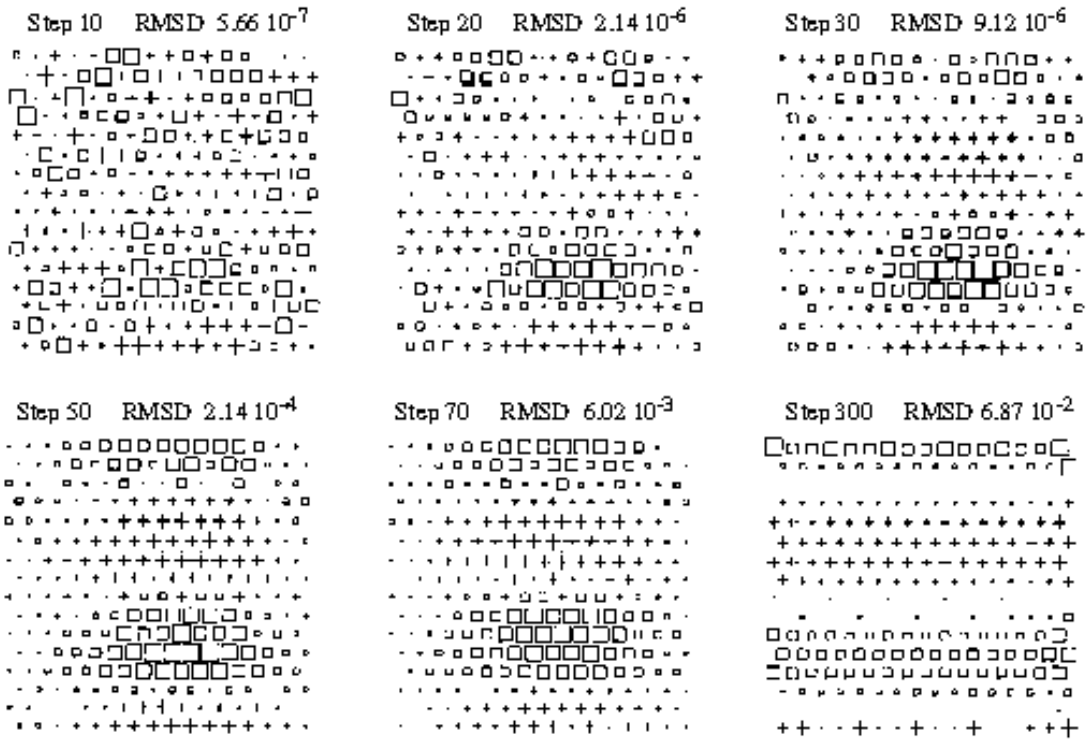

Figure 2: Development of Ocularity Domains. This figure is taken from von der Malsburg (1976). A two-dimensional patch of cortex receives input from two corresponding patches of retina. Relative size and sign of the left-right difference of innervation strength is represented by crosses and squares, indicating preponderance of one ocularity or the other. Within each figure, the size of symbols is normalized to the same maximal size. The root mean square of the left-right difference in innervation strength is given above each figure.

mappings within those chunks. Some measure has to be taken to limit the spatial scale over which the fibers of different ocularity actually segregate from each other to account for the observation that the two projections form a common retinotopic mapping that is only locally broken up into ocularity domains. Ocularity domain formation is actually a process that takes place very late in ontogeny, long after the establishment of retinotopic mappings (and also very long after the establishment of orientation columns; see next section). One way to model this is to use the following assumption. Early in ontogenesis, the fiber systems of the two eyes conspire to form a single retinotopic mapping. Only after this has been set up does segregation start. One possible way to model this sequence of events is to assume that the interocular correlation $\langle c^l_\rho c^r_{\rho'} \rangle$ is (for small $|\rho - \rho'|$) positive at first, and that it diminishes to small or negative values only after a fairly precise retinotopic mapping has formed. (Positive correlations for fibers of different ocularity afferent to cortex could be set up by mutual excitation within the lateral geniculate body.) By that time the formation of new fibers has ceased ($\alpha = 0$) and the appropriate version of Equation (7) now is

$$\dot{W}^\gamma_{\tau\rho} = W^\gamma_{\tau\rho}(F^\gamma_{\tau\rho} - B^\gamma_{\tau\rho}(WF)). \tag{16}$$

Now, growth of fibers is restricted to nonzero connections and all changes must take place within the small projection areas of retinal fibers that have developed in the early stage. It is necessary to assume that the term $D^T_{\tau\tau'}$ has shrunk to a range comparable to the size of the ocularity domains in this stage of development. (This is a natural assumption if that term is actually not mediated by the postsynaptic cells but rather as a consequence of axonal sprouting behavior.)

Equations of the type (14) through (16) have first been formulated in Miller, Keller & Stryker (1989), where the formation of ocularity stripes is also demonstrated in simulations. Their formulation deviates from the one here in two details. Their version of Equation (15) contains only the sum running over ρ and γ, and they freeze the explicit W terms on the right-hand side of Equation (16) to a constant receptive field $A_{\tau\rho}$.

5 Orientation Domains

This review of network self-organization so far has concentrated on cases where synaptic growth can be conditioned on merely binary correlations and where these correlations can be expressed as a simple function of synaptic strengths, as in Equation (13). In many cases, however, the underlying phenomenon by its very nature comprises higher order correlations and the nonlinear dependence of signals on synaptic strengths is essential. A case in point is the ontogenetic development of orientation sensitivity in vertebrate visual cortex. In this section, I describe a model that accounts for the following experimental data, derived from cat or primate (similar facts hold for many other species):

1. Most neurons in visual cortex are orientation sensitive. They best respond to the presence of light bars or edges within their receptive fields when these stimuli are

oriented within a restricted range around an optimal orientation.

2. Orientation selectivity is distributed over the cortical surface in a continuous fashion, with occasional interruptions. Iso-orientation domains, comprising cells selective for one orientation, are arranged in the form of irregular ripples.

3. Going from neuron to neuron in cortex, the position of receptive fields are subject to a large positional scatter. Similarity of orientation in two neurons is not contingent on overlap between their receptive fields (Hubel & Wiesel, 1974a,b).

4. This organization is already present, although in immature form, when the animal first opens its eyes, so that visual experience cannot be held responsible for its formation (Hubel & Wiesel, 1974c).

Before setting out to formulate a model for these facts, it is necessary to discuss in slightly more formal terms the adult structure that is to be developed ontogenetically. I will focus on one point of retina (or the geniculate body) and the extended patch of cortex that is innervated by it. Of interest are the points in time when a barlike stimulus hits the point in retina. These stimuli are classified according to their orientation in retinal coordinates. They form a one-parameter family, the parameter being the orientation θ of the stimulus (counted cyclically from 0 to 180 deg). In response to a stimulus, a subset of (somewhat less than one half of) the neurons in the cortical patch is excited to fire. This subset, being part of an "orientation domain," is spatially organized, as evidenced with the help of the deoxyglucose method (Singer, 1981; Hubel, Wiesel & Stryker, 1977; Humphrey, Skeen & Norton, 1980) or with the help of optical recording (Blasdel & Salama, 1986). Orientation domains have the general appearance of ripples of sand in flowing water, and they are more or less ordered, depending on the species studied. There has been much discussion as to whether orientation domains are to be idealized as ringlike or spokelike centered on nonoriented spots, or as waves. For the present purposes, this discussion is of minor importance, but to have something simple in mind, domains may be idealized as regular plane waves, perhaps best exemplified in the tree shrew (Humphrey et al., 1980) . When the orientation θ of the retinal stimulus is continuously rotated, the orientation domains in cortex shift or deform continuously too. By the time the retinal stimulus has turned through 180°, cortical activity again takes the shape of the first pattern encountered. Thus, the activity patterns in cortex also form a one-parameter family which can be labeled by the parameter θ counted cyclically from 0 to 180 deg.

When an extended oriented visual stimulus is applied to the retina, a larger cortical patch is activated, which expresses the shape of the stimulus by its shape, and which expresses the orientation of the stimulus locally by the ripple pattern of the orientation domains within the patch. When the stimulus moves without changing its orientation, the envelope shifts around, making the same member of the orientation pattern family visible in different parts of cortex. On the other hand, when the orientation of the stimulus is rotated, the cortical orientation domains shift through the different members of the family.

What is the detailed neurophysiological mechanism by which a cortical neuron decides whether to fire or not in response to an afferent stimulus? In this discussion, I distinguish three mechanisms that correspond to three sets of fibers. The first is the afferent receptive field aRF (or "classical receptive field"), the second is the intracortical receptive field iRF (or "nonclassical receptive field"), and the third is the formation of activity patterns in cortex by local activity feedback. The relative importance of these three mechanisms is difficult to determine experimentally, although it is a main point of discussion in the theoretical literature.

When discussing the ontogeny of orientation domains, two periods need to be distinguished — early ontogenesis, taking place before eye opening, and late ontogenesis, which has the benefit of patterned vision. The assumption underlying most models for the ontogenesis of orientation specificity is that the dominant mechanism is the aRF, cortical pattern formation playing a modulating influence. Let me refer to these models as aRF-based models. I will argue that they are difficult to reconcile with experimental fact. The model presented here, in contrast, places the main burden of orientation specificity in the immature cortex on cortical pattern formation, the iRF exerting a weak but important modulating influence. I will refer to this model as iRF-based.

In aRF models, the orientation specificity of a cortical neuron is the consequence of a spatial arrangement of retinal sensitivity within the confines of the afferent receptive field. An arrangement of excitatory subfields elongated along a certain orientation predisposes the neuron to respond preferentially to stimuli of that orientation. In aRF models, this arrangement is created during early ontogenesis. Linsker (1986) first proposed an ontogenetic mechanism based on signals of the afferent fibers having an isotropic correlation function, analogous to $\langle c^R_{\rho'} c^R_{\rho} \rangle$. This correlation is supposed to be positive over short distance and negative over longer distance, both fitting within the confines of the aRF. Coupled with a nonlinearity in the synaptic plasticity rule, these correlations lead to spontaneous breaking of the circular symmetry of the receptive field and thus create orientation specificity. Miller (1994) has simplified Linsker's formulation, giving it a form very similar to the one I have used for the formation of retinotopy and ocularity domains presented earlier. The formation of elongated ON and OFF regions within the receptive field of a cortical neuron, according to Miller's model, is analogous to the formation of ocularity stripes. The great attraction of Linsker's idea lies in the fact that it does not need any oriented stimulus within retina to produce oriented aRFs. However, for the Linsker mechanism to work, the profile of the correlation function has to fit the size of the receptive field within close tolerance. This is difficult to accommodate if cortical cells vary in receptive field size, which is actually the case (for cat, aRF size varies according to Albus, 1975a, by a factor of 7–9 at all excentricities; for monkey, it varies according to Schiller, Finlay & Volman, 1975, by factors of 3–4).

In the Linsker model, both in his version and in Miller's, orientation domains are formed in the following way. Two neighboring cortical cells have overlapping receptive fields and have excitatory coupling. Because of the coupling, the cells are simultaneously active with high probability, and because of the receptive field overlap, they see virtually the same symmetry breaking noise patterns. Thus they develop the same or similar

orientation preference. Miller has shown in simulations (Miller, 1994) that, given a regular array of receptive field positions (each one retinotopically shifted by a small fraction of receptive field diameter with respect to its neighbors), orientation specificity is indeed organized continuously (around occasional point defects, just as observed in many species).

Unfortunately, the Linsker model for early ontogenesis cannot deal with the experimental fact, listed earlier, that the receptive fields of cortical cells have a large retinotopic scatter that nevertheless does not disturb the very regular progression of orientation sensitivity. There are many cases in which neighboring neurons have completely nonoverlapping receptive fields and yet have very similar optimal orientation.

I am now going to propose a new model for the early ontogenesis of orientation specificity. It is of the iRF type and relies on the existence of running waves of spontaneous activity in retina, such as those that have been found experimentally (Meister et al., 1991). These waves are projected to cortex by the retinotopic mapping from retina via the lateral geniculate body. Within the cortical region activated by the wave, a rapid process of self-organization takes place by which the plexus of local connections creates one of the patterns of a one-parameter family of ripple patterns. Cortical neurons (or at least a subset of them) are assumed to receive input connections from other cortical neurons within an area that is large compared with the (projection of the) scatter in receptive field positions. Such connections have been described at least for the adult (Gilbert, Hirsch & Wiesel, 1990). These connections form the iRF of those neurons. The model supposes that the connections of the iRF are plastic in the Hebbian sense.

Consider a particular patch of cortex (see Figure 3). For the sake of the present discussion, call the ripple patterns within the patch "micropatterns," and use the term "macropattern" for the grosser activity pattern in the cortical region surrounding the patch at the time the patch is swept by a retinal wave. The micropatterns form a one-parameter family, the parameter having the topology of the circle. (Again, the simplest ideal version of the micropatterns is straight waves, the parameter being the phase of the wave.) The macropatterns are straight swaths of activity that run through the cortical patch. Also the macropatterns form a circular one-parameter family, the parameter being the orientation of the wave.

All the reorganization that is required during early ontogenesis of orientation specificity is the establishment of a reliable mapping between the two families of patterns. According to the model, this happens simply in the following way. When the projection of a retinal wave crosses the particular cortical patch, one of the micropatterns is activated (this choice is initially random). The neurons active in the micropattern (or at least some of them) receive intracortical signals that come from the macropattern corresponding to the orientation of the retinal wave. The synapses of these active fibers are strengthened in a Hebbian fashion, giving some of the neurons active in the micropattern an elongated iRF. The next time a wave of similar orientation crosses the patch, the same micropattern will be selected, some of its neurons being preactivated through their iRF. Overlapping macropatterns will activate overlapping micropatterns, these have similar compound iRFs because of the many neurons that are common to them. The developing mapping from the macropatterns to the micropatterns will therefore be continuous. If one could now record

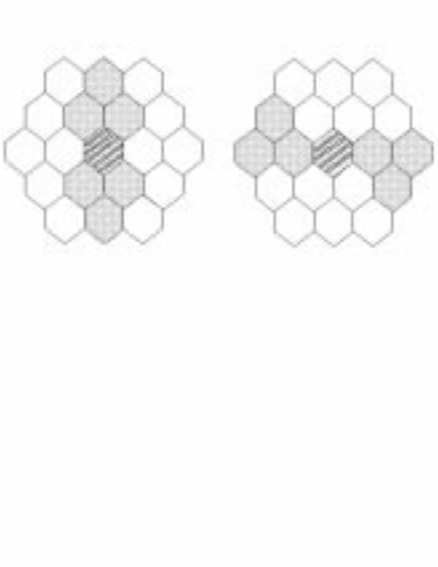

Figure 3: Model for the development of orientation domains. Both the macropatch (a patch of layer A, large hexagon composed of smaller hexagons) and the corresponding micropatch (patch of layer I, central hexagon) are shown. Each of the two versions shows the network when a retinal wave (indicated by shading) just passes over the center of the macropatch, producing a micropattern within the micropatch (rows of circles). Waves of different orientation produce micropatterns of different phase.

from individual cells in cortex, one would find that they responded selectively to retinal waves within a small range of orientations. This corresponds to orientation specificity of the iRF type.

Although cortical cells are now orientation specific, there is still nothing in their own aRF that corresponds to that specificity. However, as soon as the eyes open cells receive precisely patterned input constellations that have been produced by bars or edges of light passing over their receptive fields. Moreover, because of their iRFs, cells only respond to a narrow range of orientations. With the help of Hebbian plasticity in the afferent synapses, the oriented patterns of activity can now be turned into precisely structured aRFs that are, for instance, elongated along the orientation of the stimulus. This structuring of aRFs cannot be done in the early ontogenetic period because the retinal activity waves are much too broad for this purpose.

Now to formulate the model in mathematical terms. Group the neurons of cortex into two layers and designate their activity as $c^A(t)$ and $c^I(t)$. The A-layer corresponds best to layer IV of cortex and is controlled directly by the afferent input from retina via the geniculate body. The I-layer corresponds best to layers above and below layer IV. Consider a large patch ("macropatch") of the A-layer, sampled at a low spatial density, designating individual points in it by the index a (which refers to a two-dimensional coordinate). In the I-layer, consider a small patch ("micropatch") centered on the macropatch and sampled at a much higher density to allow the description of micropatterns. A possible sample scheme is indicated in Figure 3. The activity in the A-layer is dominated by retinal input. Assume for it the form of straight waves of activity. Of interest are the moments when a wave just crosses the central micropatch. These bars form a family of macropatterns. The synaptic connection strengths between a sample a within the A-layer and a sample i within the I-layer is given by W_{ia}. When an activity wave passes over the retinal region projecting to the cortical micropatch, its cells receive an input I_i through their direct receptive fields. Simultaneously, they receive intracortical input from a bar-shaped region in the macropatch. The dynamics of activity within the micropatch is described by

$$\dot{c}_i^I = -\alpha c_i^I + (K * S(c^I))_i + \sum_a W_{ia} S(c_a^A) + I_i. \tag{17}$$

Here, α is a decay constant (not to be confused with the control parameter used previously), the star designates a convolution, and S is the sigmoid input-output function

$$S(c) = \frac{1}{1 - \mathrm{e}^{-\beta(c-c_\circ)}} \tag{18}$$

with steepness parameter β and threshold $c_\circ$. $K_{i-i'}$ is a convolution kernel describing the fiber plexus within the I-layer. It has the general form

$$K(x,y) = qG^{\xi\eta}(x,y) - pG^{\xi'\eta'}(x,y), \tag{19}$$

where x is one component of the distance vector $i - i'$, y the other, p and q are constants, and the Gaussian G has the form

$$G^{\xi\eta}(x,y) = \mathrm{e}^{-\frac{x^2}{2\xi^2} - \frac{y^2}{2\eta^2}}. \tag{20}$$

2, and that ξ and η differ slightly to model a natural local anisotropy in the local fiber plexus (which may, of course, vary in orientation from region to region in cortex).

The activity of the micropatch, described by Equation (17), is zero when there is no input activity. However, when a wave is passing over its retinal projection region, both the direct input I_i and the indirect intracortical input $\sum_a W_{ia} S(c_a^A)$ spring to life and push c^I to positive values. Now, assume first that the iRFs W_{ia} are unstructured and that they give a flat though slightly noisy intracortical input signal, independently of the spatial profile of c_a^A. When the activity c^I in the micropatch reaches a point with critical steepness $S'(c^I)$, the activity pattern c^I branches away from homogeneity and a micropattern is created. When this critical steepness is reached just near the inflection point of S, then the growing pattern will be a standing wave (rather than a set of blobs). The orientation of that wave is determined by the orientation of the anisotropy in the kernel Equation (19), and its phase is selected by the noise in the input.

At this point, when both c^I and c^A are positive, the iRFs W_{ia} are modified by Hebbian plasticity:

$$\dot{W}_{ia} = hS(c_i^I)\{S(c_a^A) - W_{ia} \sum_{a'} S(c_{a'}^A)\}, \tag{21}$$

where h is a time constant. The first term corresponds to Hebbian growth in response to coincident activity on the presynaptic and postsynaptic sides of the connection ia, whereas the second term makes sure that $\sum_{a'} W_{ia'}$, the sum of synaptic strengths converging on a position i, is kept constant at 1. Due to Equation (21), simultaneously occurring macropatterns and micropatterns will be associated with each other. More specifically, an A-wave of a particular *orientation* will become associated with an I-wave of a particular *phase*. When a wave with the same orientation traverses the projection area of the micropatch again, it will create a wave in A and a patterned input into I that will select the micropattern with the same phase as before. In this way, a reliable association between macropatterns and micropatterns is developed. Overlapping macropatterns, that is, waves with similar orientation, will associate with overlapping micropatterns, that is, with waves of similar phase. Correspondingly, optimal orientation will vary smoothly within the I-layer: it will be constant along the wave crests of the micropatterns in I and will progress linearly in the direction at a right angle to the crests. It is not necessary that the iRFs of subregions within layer I be strongly modified. In fact, it would suffice if only a small minority of neurons had appropriate intracortical connections at all. It is only necessary that a wave crossing the macropatch create enough modulation in the input pattern to the micropatch reliably to break the symmetry between micropatterns.

A system very similar to the one described in Equations (17) through (21) has been simulated in Malsburg, (1973) ; the difference between the two models lies mainly in the interpretation of the two layers. The A-layer was then regarded as a patch of retina, and only the present I-layer was modeled for cortex. The simulations of Malsburg, (1973) showed that the form of receptive fields is adapted to the stimuli and that neighboring cells are likely to specialize to neighboring orientations, validating the preceding claims.

The model proposed here accounts for the early ontogenesis of orientation specificity in the presence of large random scatter in the retinotopic arrangement of afferent fibers. In cat (Albus, 1975) and in monkey (Hubel & Wiesel, 1974a) this scatter is at least as large as the average diameter of receptive fields. This makes it impossible for aRF theories of early ontogenesis to account for the regular progression of optimal orientation that is actually observed. The aRFs are simply too small to be structured by the crude waves of retinal spontaneous activity. The difference is made here by employing the iRFs of cortical cells, which are much larger in terms of retinal coordinates.

The formulation of network self-organization given in Equations (17) through (21) differs in a significant way from the earlier formulations that were employed as models for the establishment of retinotopy and of ocularity domains. Both retinotopy and ocularity are phenomena that can be expressed in terms of pair correlations of signals. These in turn can be expressed linearly in terms of the plastic synapses. The signal variables could in this way be eliminated from the equation for synaptic plasticity. Orientation, on the other hand, cannot be expressed in terms of pair correlations (these would be isotropic for an ensemble of patterns of all orientations). Consequently, one would have to work with correlations of higher order, which, with linear signal dynamics, would contain higher order products of the connectivity variables. Autonomous differential equations for synaptic weights would accordingly become rather unwieldy. This is why I take here the more general approach of using activity variables directly for describing the ontogenesis of orientation domains.

Acknowledgments

This work was supported by grants from the Human Frontier Science Program, the Bundesministerium Für Forschung und Technologie (413-5839-01 IN 101 B/9) and AFOSR (F 49620-93-1-0109). I thank J.-M. Fellous for critical reading of the manuscript and for his help with the preparation of my figures.

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