Development of Ocular Dominance Stripes, Orientation Selectivity, and Orientation Columns

12

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Neurons in the somatosensory and visual cortices respond to spatially localized and specific kinds of stimuli. For example, neurons have a preference for stimulation through one of the two eyes (ocular dominance) and for stimuli of a particular orientation (orientation selectivity). This chapter reviews the variety of models that have been proposed to explain the development of ocular dominance and orientation selectivity in the mammalian visual cortex.

12.1 Introduction

12.1.1 Columnar Organization and Maps in the Adult Visual Cortex

The response properties of neurons in the somatosensory and visual cortices tend to remain unchanged with position perpendicular to the cortical surface (Mountcastle, 1957; Hubel and Wiesel, 1962). This property, termed columnar organization, means that for many purposes the cortex can be treated as a two-dimensional sheet. The term "column" is generally used (somewhat loosely) to define a set of cells having boundaries perpendicular to the cortical surface and spanning all the cortical layers and that possess some property in common, such as eye preference or selectivity for a particular orientation.

In contrast to columnar invariance, response properties often change systematically with sideways (tangential) movement through the cortex; these forms of variation are called mappings (see also chapter 11). The properties that have ordered mappings include (1) the spatial receptive field, i.e., the specific region of visual space within which a stimulus must be present in order for a cell to respond (see chapter 11); (2) ocular dominance, i.e., a preference for stimulation through one of the two eyes; and (3) orientation selectivity, i.e., a preference for a bar or an edge of a particular orientation. Ordered maps of other receptive field properties, such as preference for spatial frequency or for a particular direction of stimulus motion, have also been demonstrated. Additional maps may exist, although most of the possibilities are speculative (Swindale, 2000).

12.1.2 The Cortex as a Dimension-Reducing Map

In this section, a general framework for thinking about maps is presented. Each cell in the visual cortex can be thought of as representing (when maximally active) the presence in the image of a specific combination of stimulus features, e.g., the presence of an edge of a particular orientation moving in a particular direction across a specific small region of visual space in a particular eye. This set of properties defines a point $\mathbf{w}$ in an N-dimensional stimulus space $\mathbf{S}^N$ whose axes are the stimulus parameters of interest (figure 12.1). There is thus a mapping between an N-dimensional stimulus space and the two-dimensional sheet of the cortex. This type of mapping has been termed a dimension-reducing mapping (Durbin and Mitchison, 1990).

While one typically thinks of a map in terms of the way in which some property varies across a surface, it

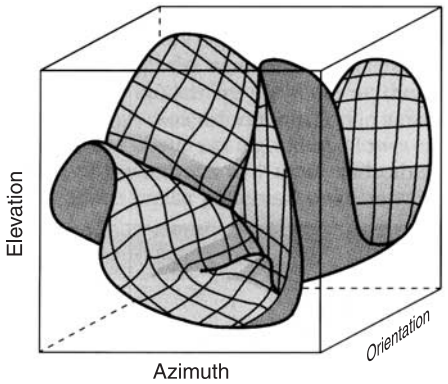

Figure 12.1
A stimulus space, **S**. The folded sheet represents the visual cortex; points on the grid represent position in cortical coordinates. The receptive field properties of each point in the cortex determine the position of the corresponding point of the sheet in **S**. A 3-D space is shown here, with the dimensions representing the receptive field position (elevation and azimuth) and preferred orientation.

is often useful to consider the mapping in the inverse direction, i.e., to consider the map as a projection of a 2-D surface into **S**. The complex foldings of the 2-D cortical sheet within **S** are thought to be subject to two constraints: a continuity constraint and a completeness constraint, which act in opposition. The continuity constraint means that the mapping should be locally smooth—neighboring points in the cortex have similar receptive fields (i.e., map to neighboring points in **S**)—while the completeness constraint means that the cortex should fill functionally important regions of **S** as completely as possible. Since for $N > 2$, not all points in **S** can be mapped to the cortex in a neighborhood-preserving way, the mapping must necessarily be incomplete. One might require, however, that some part of cortex come within some minimum distance of every functionally important point in **S**.

Alternatively, because receptive fields are not infinitely narrow, one can think of them as occupying small regions of stimulus space. More generally, one can think of the cortex as filling **S** with neural activity, and one interpretation of completeness is that the density of activity should be as uniform as possible (Swindale, 1991). The implications of this particular approach will be returned to later on. First, some specific mappings are described in more detail.

12.1.3 The Retinotopic Map

Each visual cortex (i.e., on the left and the right side of the brain) contains a topographic map of the contralateral visual field (see also chapter 11). This mapping exists because there is a topographically precise mapping from the retina to the layers of the lateral geniculate nucleus (LGN) and because there is a similarly precise mapping from each of these layers to layer IV of the visual cortex. To a first approximation, equal areas of the visual cortex are innervated, via the LGN, by equal numbers of retinal ganglion cells. Because ganglion cell density is highest in the central region of the retina, the visual world is not linearly scaled onto the cortex, but is distorted so that the magnification factor (square millimeter of cortex per square degree of visual angle) is greatest in the central visual field and least in the peripheral field. Although it is an important detail for modelers, relatively little is known about the local precision of the topography. The most precise mapping possible would have LGN axons connecting to cells in layer IV in a pattern that matched the locations of the ganglion cells driving the LGN axons. It is possible that the retinotopic map approaches this precision in layer IVCβ of the macaque monkey (Blasdel and Lund, 1983; Hubel et al., 1974; Blasdel and Fitzpatrick, 1984), where receptive fields are small and circularly symmetrical and the ret-

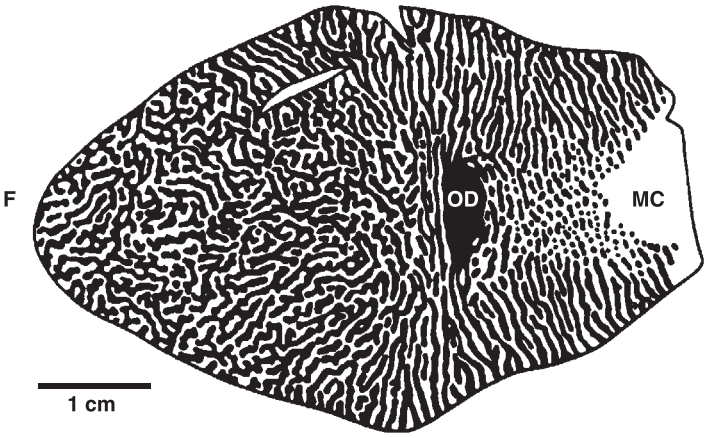

Figure 12.2
The complete pattern of ocular dominance stripes in the flattened visual cortex of a macaque monkey. A complete retinotopic map of the contralateral visual field is represented within the area of cortex shown. F, the region corresponding to the fovea; OD, the region corresponding to the optic disk; MC, the monocular segment. (From Florence and Kaas, 1992.)

inotopic map shows little disorder. In subprimate species, such as cats and ferrets, the degree of precision is probably much less than this (Albus, 1975).

12.1.4 Ocular Dominance Stripes

Eye dominance or ocular dominance columns form a pattern of periodic branching stripes with a width of about 0.5 mm, interdigitated with regions of the same width that prefer stimulation through the other eye (figure 12.2). The pattern reflects the fact that the inputs from the left and right eyes, relayed through separate layers of the LGN, terminate in nonoverlapping stripes in layer IV of the cortex. The similarity between ocular dominance stripes and other patterns such as fingerprints and the striped and spotted patterns found on the body surfaces of fish, frogs, and zebras has often been commented on and suggests the possibility that their development might be understood in terms similar to those postulated to explain pattern formation in these other systems (Murray, 1989).

12.1.5 Orientation Domains

In addition to a preference for stimulation via one or the other eye, most visual cortex neurons respond to bars or edges flashed or moved across the receptive field at specific orientations. One of the causes of this selectivity in those cells that receive inputs directly from the LGN is a receptive field organization in which one or more regions of ON responsiveness alternate with regions of OFF responsiveness (Hubel and Wiesel, 1962). The preferred orientation of these cells, which are called simple cells, can be predicted from the orientation of the line (or lines) that best separates the ON and OFF regions.

The overall layout of orientation preference is continuous and periodic (Hubel and Wiesel, 1974; Swindale et al., 1987; Bonhoeffer and Grinvald, 1991;

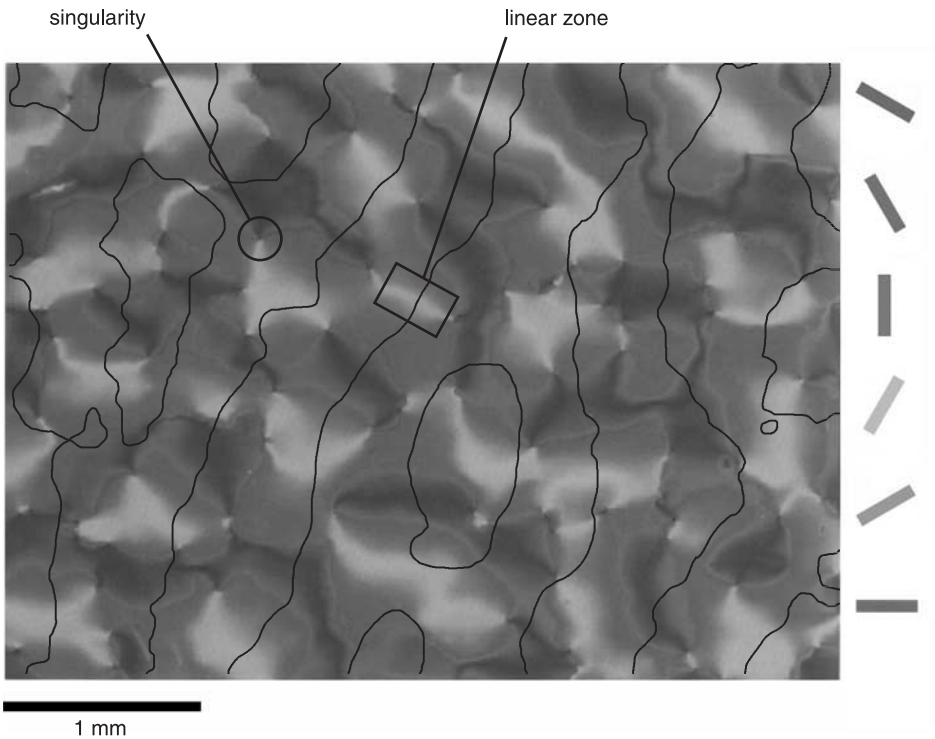

Figure 12.3
A map of orientation preference in the macaque monkey. Each gray level represents a unique orientation preference, as shown by the key on the right. A similar though not identical gray scale is used to represent orientation preference in figures 12.5b and 12.6. A singularity (circle) and a linear zone (rectangle) are indicated. Black lines mark the boundaries between ocular dominance columns. (Reproduced and redrawn from data in Blasdel, 1992, and Obermayer and Blasdel, 1993.)

Blasdel, 1992). Iso-orientation domains—regions of the map where orientation preference lies within a defined range—have a well-defined periodicity of about 1 mm in the cat and about 0.6 mm in the monkey (figure 12.3). The maps also include singular points where a single complete 180 degree set of domains meet. Because of their appearance in color-coded images, the singularities and the regions immediately surrounding them are often called pinwheels. They are characterized as positive if the orientation rotates in a clockwise direction when a clockwise circuit is made around the singularity, and as negative if it rotates in a counterclockwise direction. Areas of cortex between the singularity and pinwheel regions often contain iso-orientation domains that run in a roughly parallel direction; these are called linear zones.

12.1.6 Relationships between Different Visual Maps

Structural relationships between the different maps have been demonstrated in a number of instances,

although they are often weak. As mentioned earlier, there is a precise retinotopic map in layer IVC of the monkey, and cells have small, circularly symmetrical receptive fields. The retinotopic map interacts with the map of eye dominance in the following way: As layer IVC is traversed in a tangential direction, receptive field positions in the corresponding eye shift in a constant direction. As the boundary between neighboring ocular dominance stripes is crossed, the receptive field shifts into the other eye, to a location corresponding to that mapped to the center of the adjacent stripe (Hubel et al., 1974; Blasdel and Fitzpatrick, 1984). This type of z-folding is one way of ensuring that the entire visual field of each eye gets represented in the half of the cortex area that constitutes one set of eye dominance stripes.

A relationship between the retinotopic and orientation maps in area 17 of the cat was reported by Das and Gilbert (1997). They found fractures across which there were simultaneous jumps in both preferred orientation and receptive field position; in general, the retinotopic gradient and the orientation gradient were strongly correlated. It remains to be seen whether such correlations are a general feature of visual cortex maps; there is evidence from the tree shrew that they may not be (Bosking et al., 1997).

Combined maps of eye dominance and orientation (Bartfeld and Grinvald, 1992; Hübener et al., 1997) show a tendency for singularities to be located in the centers of eye dominance stripes and for iso-orientation domains to run across the boundaries of eye dominance columns at right angles (figure 12.3). A possible explanation for these orthogonal gradient relationships is that they maximize coverage uniformity (Swindale et al., 2000), i.e., the uniform representation of all combinations of the parameters represented in the map.

12.2 Development of Visual Cortex Maps—Neurobiological Background

An important issue is the extent to which environmentally driven patterns of neural activity determine the map structures. One possibility is that many aspects of visual cortex map organization (e.g., ocular dominance and orientation specificity) might be entirely the result of postnatal visual experience. At one point this seemed a realistic possibility, particularly when it was reported that stimulus specificity was absent in the visual cortex of very young kittens (Barlow and Pettigrew, 1971) and that rearing kittens in an environment with lines of a single orientation resulted in a visual cortex containing neurons whose orientation selectivities all matched the orientation experienced (Blakemore and Cooper, 1970; Hirsch and Spinelli, 1970). This view was probably strengthened by the fact that the earliest computational models of visual cortex development were able to show that environmentally driven patterns of neural activity could account for the development of orientation selectivity (Von der Malsburg, 1973), ocular dominance stripes (Von der Malsburg and Willshaw, 1976), and retinotopic maps (Willshaw and Von der Malsburg, 1976; see also chapter 11).

Subsequent work has not confirmed this extreme environmentalist viewpoint. It is now clear that many forms of stimulus selectivity, and their columnar organization, are either present at birth or can be shown to be present in animals reared in the dark from the time of eye opening. For example, in macaque monkeys (whose eyes are open at birth), orientation selectivity (Wiesel and Hubel, 1974), orientation columns (Blasdel et al., 1995), and ocular dominance columns (Horton and Hocking, 1996) are present at birth. In kittens (whose eyes open at 7–10 days after birth), orientation-selective neurons can be recorded

at 6–8 days of age (Albus and Wolf, 1984; Braastad and Heggelund, 1985), while orientation and ocular dominance columns are present in rudimentary form in normal or visually inexperienced kittens at 15 days of age (Crair et al., 1998).

Given these observations, attention has been devoted to roles that spontaneously occurring patterns of neural activity might play in the initial formation of ocular dominance and orientation maps (Katz and Shatz, 1996). These experiments generally suggest that spontaneous activity plays a crucial role (however, see Crowley and Katz, 2000, and section 12.5). For example, in kittens, silencing retinal activity by intraocular injections of tetrodotoxin abolishes ocular dominance columns (Stryker and Harris, 1986). Blocking activity in retinal ON-center ganglion cells by intraocular injection of DL-2-amino-4-phosphonobutyric acid (APB) prevents the development of orientation selectivity (Chapman and Gödecke, 2000).

Given the probable importance of spontaneous neural activity in the earliest stages of map development, it is not surprising that a disturbance of visual experience early in life can affect the later stages of map development in many different ways. Closing one eye during the first 2–6 weeks of age in kittens, or before 3 months of age in macaque monkeys, causes the ocular dominance stripes representing the closed eye to shrink in area, while the stripes representing the open eye expand and take over the territory vacated by the closed eye (Hubel et al., 1977; Shatz and Stryker, 1978). The interpretation of the analogous experiment in which animals are reared in an environment where lines of a single orientationpredominate has been less straightforward. However, a recent study in the cat using optical recording, which avoids many of the problems inherent in earlier studies, showed that iso-orientation domains corresponding to the orientation experienced do increase in size (Sengpiel et al., 1999). This confirms that neurons can change their orientation preference in response to environmentally driven patterns of stimulation.

Overall, these experiments support a restricted environmentalist viewpoint in which visually driven patterns of activity do not play a role in initially setting up the map, but can sculpt and modify a preexisting map by causing local shrinkage or expansion of columns. Whether early visually driven activity can go beyond this and change more global details, such as column periodicity, remains controversial (see section 12.4.2).

12.2.1 Role of Spontaneous Retinal Activity

Since many aspects of visual cortex map formation occur either in utero (as in primates) or postnatally in the absence of visual experience (as in cats and ferrets), visually driven activity cannot be the primary factor that establishes receptive field structure and columnar organization. Attention therefore has to be focused on patterns of spontaneous neural activity that occur before the eyes open. At a very early stage, before many synaptic connections have been made, cortical neurons are coupled by gap junctions, and small domains of cells exhibit coordinated transient elevations in Ca^{2+} levels (Kandler and Katz, 1998). These events could play a role in establishing common feature selectivity in the earliest stages of map formation.

Another form of spontaneous activity occurs in the embryonic retina, where ganglion cells fire in irregular bursts (Galli and Maffei, 1988). These bursts are correlated in neighboring ganglion cells and form waves that spread across the retina (Wong, 1999). Models for this behavior have been presented (Burgi and Grzywacz, 1994; Feller et al., 1997). While retinal waves are a likely candidate for a mechanism to refine topography and enforce laminar segregation of retinal

inputs in the LGN, they end a few days before the emergence of ocular dominance and orientation maps in ferrets, so their role in these aspects of map formation is uncertain. It is not known whether retinal waves occur in kitten or primate retinas, so their role in map formation in these species is also uncertain.

Spontaneous bursting has been demonstrated in ferret LGN (Weliky and Katz, 1999). This shows positive interocular correlations that are dependent on feedback from the visual cortex. Much more remains to be discovered about this phenomenon, particularly with respect to its spatiotemporal patterning, its persistence beyond the period of eye opening, and the role of cortical feedback and patterning in the cortex itself. These details are likely to be critical for future models.

12.2.2 Factors Affecting the Development of Ocular Dominance Columns

A brief summary of some experimental results pertinent to models of the formation of ocular dominance columns is given here

- Monocular deprivation during the critical period causes the ocular dominance stripes for the closed eye to shrink and those for the open eye to expand (Hubel et al., 1977; Shatz and Stryker, 1978; LeVay et al., 1980); this can occur after segregation is complete.
- Stripes shrunken by monocular deprivation can reexpand if the deprived eye is opened and the normal eye closed (reverse suturing) (LeVay et al., 1980; Swindale et al., 1981).
- Silencing retinal activity abolishes segregation (Stryker and Harris, 1986).
- The effects of monocular deprivation can be blocked by infusing the cortex with *N*-methyl-D-aspartate (NMDA) receptor antagonists (Bear and Rittenhouse, 1999).
- Infusion of the γ-aminobutyric acid (GABA) agonist muscimol into the cortex of monocularly deprived kittens (which will cause cortical neurons to hyperpolarize, so that their inputs will fail to evoke action potentials) causes strengthening of the inputs from the deprived eye and a weakening of the inputs from the normal eye (Reiter and Stryker, 1988).
- Infusion of neurotrophins (NT-4/5 or brain-derived neurotrophic factor) into kitten visual cortex blocks the formation of ocular dominance columns (Cabelli et al., 1995).
- Monocular deprivation by lid suture produces a bigger ocular dominance shift than monocular TTX injection (Rittenhouse et al., 1999).

12.2.3 Factors Affecting the Development of Orientation Columns

Observations that any model of orientation column development ought to be able to explain are the following:

- Orientation preferences should vary smoothly over most parts of the map, except in singularities and (possibly) short fracture regions.
- The power spectrum of the orientation vectors should have a strong nonzero peak.
- The map should contain half-rotation (i.e., 180-degree) singularities of positive and negative sign, with an irregular spacing and a density in the range of 2.0–3.5 per λ^2, where λ is the dominant wavelength as determined by Fourier spectral analysis.
- Singularities should be grouped so that approximately 70–80 percent of nearest-neighbor pairs are of opposite sign (Obermayer and Blasdel, 1997).

• There should be no statistical relationship between orientation and orientation gradient angle.

• Spatial segregation on ON and OFF center inputs within cortical receptive fields should be a primary determinant of orientation selectivity, since blocking activity in the ON pathway during development abolishes orientation selectivity (Chapman and Gödecke, 2000).

12.3 An Overview of Models of Visual Cortex Map Formation

The history of modeling of visual cortex maps begins with the demonstration by Von der Malsburg (1973) that oriented patterns of activity in a retina, connected initially at random by Hebbian synapses to a cortex with lateral short-range excitatory and long-range inhibitory connections, could give rise to neurons that are selective for specific orientations laid out in a spatially organized map. The components and assumptions of most models have changed very little since then (figure 12.4). In the following sections we describe these components and how they have typically been used.

12.3.1 Retinal Inputs

Inputs to the model cortex are typically represented in terms of static activation levels in one or more two-dimensional arrays that are assumed to correspond to sheets of cells in the retina or the LGN. These values are assumed to represent firing rates averaged over a period of time that is brief compared with the time scale of synaptic weight change. Models of ocular dominance column formation of course use two such arrays, one for the left and one for the right eye. Additional layers may be used to represent the activities of ON and OFF ganglion cell types; for example, four

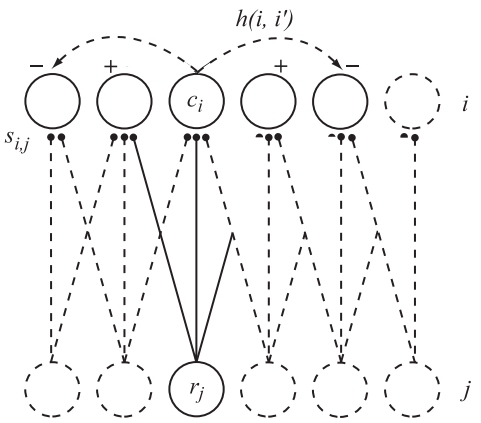

Figure 12.4
Generic structure of visual cortex map models. Units in an input layer (the LGN or retina) with activities r_j make connections with strengths $s_{i,j}$ to units in an output layer (the cortex) that have activities c_i. Local interactions between the cortical units are described by an interaction function $h(i, i')$, which is typically positive for short distances and negative for intermediate distances between points i and i'.

sheets of cells, corresponding to the ON and OFF layers in the two eyes, were used by Erwin and Miller (1998). Most, if not all, models assume that the input layers project directly to the cortex. Thus, either the LGN is assumed to pass on retinal activity without changing it, or activity is assumed to arise directly within the LGN.

Very simple patterns of activity have typically been assumed, including randomly oriented lines, randomly positioned circular or elongated blobs, and noise into which local correlations have been introduced. For models of ocular dominance column formation, one technique is to assign random values to the points in each array, smooth them with a Gaussian kernel, and then add a fraction of the values in each eye to those in the other. This creates a stimulus with defined local and intereye correlations. Very few simulations have used natural images, which is probably

justified given the ability of cortical maps to develop in the dark, nor have there been many attempts to use statistics based on the known spontaneous firing patterns of retinal or LGN neurons (Elliott and Shadbolt, 1999, is an exception).

12.3.2 The Cortex

In most, if not all, models, the cortex is represented by a single sheet of cells receiving connections from the input layers. In many cases, a fixed "Mexican hat" pattern of short-range excitatory and intermediate-range inhibitory connections between cortical points has been assumed (although without much in the way of empirical justification). Very few modelers have assumed the presence of more cortical layers, or of feedback from the cortex to the input layer(s).

For a given pattern of activity in the input layers, activity in each cortical unit is generally assumed to be determined by the sum of the input activities times the relevant weights plus a contribution from the activities of surrounding cortical units via the lateral interaction function. A threshold, or other response nonlinearity, may be applied to the outputs of the cortical units. Because the activity pattern in the cortical sheet cannot be determined simply—it may take many iterations before a stable cortical response to a particular input is generated—most models have found ways of sidestepping or simplifying this step. The ways in which this has been done are discussed in section 12.4.

12.3.3 Learning Rules

Many models (e.g., Von der Malsburg, 1973; Miller et al., 1989; Goodhill, 1993) are based on the simplest form of Hebbian learning, in which synaptic weights are increased by an amount proportional to the product of pre- and postsynaptic activation levels. Because these values cannot be negative, this means that weights cannot decrease. Without an additional regulatory mechanism, competition—the process in which an increase in the strength of some connections leads to the weakening of others—cannot occur. In these models, competition is typically implemented by ensuring that the sum of the synaptic strengths onto individual neurons (i.e., each point in the cortical array) remains a constant at each learning step, a procedure termed normalization. Normalization can be implemented by division or by subtraction. The choice is not trivial because it can significantly affect the way development proceeds (Miller and MacKay, 1994; Goodhill and Barrow, 1994; Wiskott and Sejnowski, 1998; see also chapter 10). In some models, alternative ways of implementing competition and avoiding normalization have been explored (see sections 12.4.5 and 12.4.6).

12.3.4 Initial Conditions

Many models assume some degree of topographic order in the initial set of connections between the input and cortical layers. In some models, connections from the input layer are assumed to be made initially within a small region of the cortical layer, described by an arbor function, which is in exact topographic correspondence with the input layer. The arbor function is fixed in size and position, so that a given afferent can only make or modify its connections with a fixed cortical region. Other models allow for a less rigid retinotopy and consequently permit less rigid initial conditions and more varied retinotopic outcomes. Initial connection strengths are generally assumed to be random. Periodic boundary conditions are often assumed for convenience; i.e., distances over the input and output arrays are calculated as though left and right edges, and the top and bottom edges, are contiguous.

12.4 The Models

While this general framework for modeling is about as simple as it could be, it can still prove unwieldy and slow when implemented on a computer. As a result, many modelers have found ways of further simplifying the calculations. This has had worthwhile consequences because it has resulted in a variety of related simpler models whose behaviors are easier to understand. Some of the ways in which simplification has been achieved are the following:

- *Linear Hebbian models.* In these models it is assumed that learning can be averaged over input patterns. This means that the quantities that are explicitly represented in the calculations are time-averaged spatial correlation functions present in each of the input layers, rather than explicit patterns of neuronal activity.
- *Competitive Hebbian models.* In these models the calculation of cortical activity following a stimulus is simplified by assuming that synaptic modification occurs only in the most active cortical unit and its nearest neighbors.
- *Lateral interaction models.* Here all the interactions are lumped into a single lateral interaction function. This leads to models that are computationally simple and that bring out similarities with more general theories of pattern formation.
- *Feature-based or dimension-reduction models.* In these, the description of the input space is simplified by representing stimuli as points in a feature space (section 12.1.2). This leads to very abstract models whose construction seems far removed from biology, yet which have been remarkably successful in explaining the phenomenology of visual cortex maps.
- *Models that avoid explicit normalization rules.* These include models based on competition for neurotrophins (section 12.4.5) and the BCM learning rule (section 12.4.6).

These classes of model are described in more detail in the following sections.

12.4.1 Linear Hebbian Models

Linear Hebbian models avoid the explicit representation of activity patterns in the input and output layers; instead, they assume that changes in synaptic strength are determined by time- and space-averaged patterns of correlation in the input layers. This simplification follows if the responses of the units in a layer are linearly related to the activities in the input layer and if the change in weights following each activity pattern is small. In this case, the learning rule can be expressed simply in terms of the time-averaged spatial correlations in the input patterns.

The Ocular Dominance Column Model of Miller et al.

The model of Miller et al. (1989) assumes two input layers, L and R, with four corresponding correlation functions, C^{LL}, C^{RR}, C^{LR}, and C^{RL}, specifying how the correlations in neural firing rates vary with lateral separation in the LGN layers. Inputs from a location j in the LGN are assumed to make contact with a retinotopically corresponding cortical neuron centered on a location i in the cortex and spread over a surrounding region described by a fixed arborization function $A(i-j)$. (It is assumed that any position j in the LGN maps directly to an equal position i in the cortex, so that LGN and cortical coordinates are interchangeable.) The arborization function is 1 over a small square region and zero elsewhere. The strengths of the connections at time t are given by the functions $s^{\mathrm{L}}(i,j,t)$ and $s^{\mathrm{R}}(i,j,t)$. Lateral cortical interactions are described by a Mexican hat function h, which is

a radially symmetrical difference of Gaussians with a fixed width. The contribution of a synapse $s(k, l)$ to the correlation value associated with a second synapse $s(i, j)$ is assumed to be proportional to the product of the correlation value associated with the separation between the cells of origin in the LGN [i.e., $C(j - l)$], the strength of the synapse itself [i.e., $s(k, l, t)$], and the value of the lateral interaction function for separation of the synapses in the cortex [i.e., $h(i - k)$]. This gives the following learning rule

$$s^{\mathrm{L}}(i, j, t + 1) = s^{\mathrm{L}}(i, j, t) + \varepsilon A(i - j) \sum_{k,l} h(i - k) \times [C^{\mathrm{LL}}(j - l)s^{\mathrm{L}}(k, l, t) + C^{\mathrm{LR}}(j - l)s^{\mathrm{R}}(k, l, t)], \qquad (12.1)$$

where ε is a constant determining the overall growth rate. The corresponding equation for s^{R} is obtained by interchanging L and R. Initial connection strengths are random within a small range. At each time step, after updating the connection strengths, a subtractive normalization procedure is carried out. Separate limits are also put on the maximum and minimum synaptic strengths.

For the model to work, it is sufficient that the within-eye correlations C^{LL} and C^{RR} are positive Gaussian functions, while the between-eye correlations C^{LR} and C^{RL} are either zero or negative. Under these conditions, cortical receptive fields, which are initially binocular and equal in size to the arbor function, gradually become smaller and monocular, while individual afferent arbors become smaller and often break up into patches confined to neighboring ocular dominance stripes. As a result of these changes, a striped pattern of ocular dominance develops. When the cortical interaction function contains both short-range excitatory and long-range inhibitory components, the spacing of the stripes is determined by the position of the peak in the Fourier transform of the cortical interaction function $h(x)$. Narrower within-eye correlation functions result in more binocular cells at the borders of the stripes and smaller receptive field sizes. When $h(x)$ is purely excitatory, segregation occurs, provided a constraint maintaining the total strength of individual axonal arbors is applied.

Further Applications of Correlation-Based Models

The conceptual framework offered by Eq. (12.1) can be extended to explain the development of orientation columns (Miyashita and Tanaka, 1992; Miller, 1994) and the joint development of orientation and ocular dominance columns (Erwin and Miller, 1998).

For orientation selectivity, cortical inputs are again represented by two sheets of cells, but in this case they represent ON-center and OFF-center LGN cells. The model now has to produce a segregation of inputs within individual receptive fields, rather than receptive fields that are entirely dominated by one or the other layer. This will happen if (1) a difference of Gaussians is used to describe the correlations, an upright 1 (positive near the origin) for ON-ON and OFF-OFF correlations, and an inverted 1 for ON-OFF and OFF-ON interactions; and (2) the functions change sign in a distance less than the width of the arbor function. This causes the development of receptive fields that are divided into two (or, occasionally, more) regions of ON and OFF responsiveness, from which an orientation preference can be calculated. This changes continuously over the surface of the cortex; singularities are present; and individual iso-orientation domains are morphologically similar to those observed in the monkey and cat. The overall orientation pattern, however, lacks a well-defined periodicity. Periodicity is a prominent characteristic of real orientation maps, and this suggests that the model needs modification.

However, the model's basic premise—that interactions between ON- and OFF-center afferents establish the initial map of orientation preference—is supported by experimental results showing that inactivation of ON-center pathways during early development blocks the emergence of orientation selectivity (Chapman and Gödecke, 2000).

To explain the joint development of orientation selectivity and ocular dominance, the model has four input layers: L-ON, L-OFF, R-ON, and R-OFF, with a corresponding 4×4 matrix of correlation functions. Erwin and Miller (1998) discuss the conditions that must be satisfied in order for the model to produce ocular dominance segregation as well as correlated orientation maps in the two eyes. Although these conditions can be satisfied, the model, like the simpler ON-OFF model, fails to generate periodic orientation columns. It is also unable to reproduce the tendency toward orthogonal intersection of ocular dominance column boundaries and iso-orientation domains, as observed in cats and monkeys. However, a weak tendency for orientation singularities to lie in the centers of the ocular dominance stripes can be produced by a two-stage model in which the correlation functions change over time in such a way that ON-OFF segregation occurs in advance of L-R segregation.

Linear correlation-based models would appear to be limited in terms of how well they can describe the appearance of cortical feature maps. As implemented by Miller and his colleagues, the arbor function has the undesirable effect of imposing a fixed retinotopy, while the normalization rules that are integral to the way the models work are complex and not derivable from known cellular mechanisms. In spite of this, the models are important because of the simplicity of the underlying assumption, namely, that Hebbian changes in synaptic strength build up slowly over time in ways that reflect time-averaged correlations in the patterns of input activity. It is important to see how far such simple assumptions can go in explaining cortical development.

12.4.2 Competitive Hebbian Models

When a stimulus is presented to a sheet of cells connected by a Mexican hat pattern of lateral connections, the activity patterns that develop tend to consist of isolated patches of high activity with a size that matches the extent of the lateral excitation in the network. This suggests the following way of simplifying the computationally time-consuming calculation of activity patterns in response to a stimulus: For any particular stimulus, find the cortical point that gives the largest initial response (ignoring lateral interactions); assume nearby cells will likewise be active (because of the lateral connections); and then modify the connections by a Hebbian rule. This will have the effect of making the ''winning'' cortical point, and its neighbors, more responsive to the stimulus in question. The application of a neighborhood rule enforces continuity in the mapping; i.e., it ensures that nearby cortical locations will develop similar receptive field profiles. The competitive element has the opposite effect and ensures that the map represents diverse features. Thus, even if a stimulus evokes only a very weak response in the cortex initially, that response will still evoke a modification that will strengthen the response, and if the stimulus is presented sufficiently often, it will gain a representation in the map.

This method was first proposed by Kohonen (1982) and is often termed the self-organizing feature map algorithm. It can be expressed mathematically as follows: First, compute the response c_i of each cortical point i to the stimulus r—i.e., $c_i = \sum_j s_{i,j} r_j$, where the summation is over all points, indexed by j, in the input—and find the winning cortical point i^* for which c is a maximum. Then change the connection strengths according to the following rule:

$$s_{i,j}(t+1) = \alpha(t)[s_{i,j}(t) + \varepsilon h(i,i^*)r_j], \quad (12.2)$$

where $\alpha(t)$ is a normalization factor chosen to keep the sum of the synaptic strengths at each cortical point (or the sum of their squares) a constant; and h is a neighborhood function, which is typically a Gaussian function of the distance between cortical points i and i^*. Input patterns r are chosen according to the mapping problem being studied. For example, when Obermayer et al. (1990) modeled the formation of orientation columns and the retinotopic map, points r_j were randomly positioned in a single 2-D input layer and the activity patterns were elliptical Gaussian blobs of varying position and orientation. Goodhill (1993) modeled the formation of ocular dominance columns and the retinotopic map, assuming short-range within-eye correlations and positive between-eye correlations. This was done to study the effects of changing the interocular correlation, given that this is likely to be changed by visual experience or by manipulations such as strabismus (a condition in which the two eyes point in different directions). Both models produce realistic patterns of orientation preference, or ocular dominance stripes, in which there are interesting accompanying variations in the retinotopic map. For the orientation column model, periodic fluctuations in retinal magnification factor develop, and these can be shown to correlate with the orientation gradient, i.e., the rate at which preferred orientation changes with distance in the map. Specifically, there was a negative gradient correlation, so that in regions where orientation changed rapidly with position, the retinal positions changed slowly, and vice versa. This negative gradient correlation has been observed in other models (see section 12.4.4) that implement related developmental principles. In the model of ocular dominance column formation, z-folds developed in the retinotopic map. These would appear to be a realistic feature given the evidence for this type of folding in the macaque monkey (see section 12.1.6).

Periodicity in this model appears to be determined by a variety of factors, including the size of the cortical neighborhood function and, in the case of ocular dominance, by the amount of interocular correlation. Goodhill (1993) showed that if this correlation is low or absent, then the stripes have a larger spacing than if the correlation is high. Since strabismus can be expected to reduce or abolish interocular correlations, Goodhill made the experimentally testable prediction that animals made artificially strabismic during the period when ocular dominance columns are developing should have larger than normal ocular dominance columns. Although initial tests in cats appeared to confirm this (Löwel, 1994; Tieman and Tumosa, 1997), more recent studies have not replicated the effect in cats (Sengpiel et al., 1998) or been able to demonstrate it in monkeys (Crawford, 1998; Murphy et al., 1998). A possible reason for this is that the periodicity of ocular dominance columns becomes established too early for strabismus to change it. Better tests of the prediction are likely to involve manipulations that can alter the correlations present in spontaneously occurring, prenatal patterns of activity.

The learning rule used in Eq. (12.2) differs from that used in the linear correlation models described in the section on the model of Miller et al. Here, learning is not strictly Hebbian, because although the rate of change is proportional to the level of presynaptic activity r_j, it is conditional on the synapse in question being close to a region of cortex that is responding strongly to the stimulus, rather than simply being the product of pre- and postsynaptic activities. Some physiological evidence points toward mechanisms similar to this. In rat visual cortex, it has been observed that when a connection between an afferent and a neuron is strengthened by the correlated stimulation of both cells, the connections from a nearby

but unstimulated afferent become strengthened as well (Kossel et al., 1990). This suggests that synaptic potentiation is accompanied by a signal that travels through tissue and potentiates nearby synapses. This mechanism has been termed volume learning (Montague and Sejnowski, 1994). Possible mechanisms for the spread include glial involvement and release of nitric oxide, arachidonic acid, carbon monoxide, hydrogen peroxide, and neurotrophins (Thoenen, 1995).

12.4.3 Lateral Interaction Models

Most, if not all, models describe the emergence of pattern in the cortical map as the result of processes that involve lateral interactions. The origins of these interactions are varied in the models, just as they are likely to be in the real brain. They include spatial correlations in the inputs, lateral intracortical interactions, the release of diffusible substances, and factors generally subsumed under the ambit of normalization—regulatory mechanisms exerted within individual axons, and mechanisms regulating the total number and strength of connections each cell receives.

A considerable simplification can be achieved by making the following assumptions: (1) all of the effects occur on a time scale that is short compared with the time scale of map development; (2) the effects add linearly; and (3) they are translationally invariant; i.e., the net effect of each type of interaction is a function of the distance between points and does not vary with absolute location in the cortex. It is then possible to lump all the interactions together and write down an equation for growth (e.g., of one type of connection) in terms of convolution with kernels that describe the lateral interactions within and between the pattern elements (Swindale, 1980, 1982). For left and right eye synapses, whose densities are, respectively, given by n_L and n_R as functions of position on the cortical surface, we can write

$$\frac{dn_L}{dt} = (n_L^* w_{LL} + n_R^* w_{RL}) f(n_L)$$
$$\frac{dn_R}{dt} = (n_R^* w_{RR} + n_L^* w_{LR}) f(n_R), \tag{12.3}$$

where w_{LL} and w_{RR} describe within-eye interactions; w_{RL} and w_{LR} describe, respectively, the effects of right-eye on left-eye, and left-eye on right-eye connections; and the asterisk denotes convolution.

The function $f(n)$ is used to terminate growth as it reaches some upper or lower limiting density; a suitable form is $f(n) = n(N - n)$, where N is the upper limiting density and the lower limit is assumed to be zero. If the within-eye interactions are described by an upright Mexican hat function, and the between-eye interactions by an inverted Mexican hat function, then an initial state in which left and right eye synapses have random densities > 0 and $< N$ evolves into a branching periodic pattern of stripes with the morphological features of ocular dominance columns (figure 12.5a).

A comparison can be made between this type of model and reaction-diffusion models of pattern formation, which were initially developed by Turing (1952) and later applied by others to various aspects of pattern formation, particularly animal coat patterns (Meinhardt, 1982; Murray, 1989; see also chapters 1, 2, and 3). As pointed out earlier, these often bear an interesting resemblance to ocular dominance stripe patterns. In Turing's formulation, substances called morphogens react with each other and diffuse laterally through the substrate (usually assumed to be two-dimensional). For two substances with linear first-order reaction kinetics, the concentrations evolve according to the following differential equations:

a

b

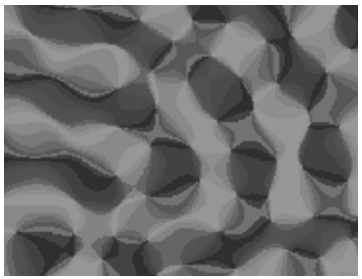

Figure 12.5
(*a*) Simulated pattern of ocular dominance stripes produced by a lateral interaction model [Eq. (12.3)]. (Reproduced from Swindale, 1980.) (*b*) Orientation preference map simulated using Eq. (12.5). For gray scale, see figure 12.3.

$$\frac{\partial X}{\partial t} = aX + bY + D_1 \frac{\partial^2 X}{\partial r^2}$$
$$\frac{\partial Y}{\partial t} = cX + dY + D_2 \frac{\partial^2 Y}{\partial r^2}, \qquad (12.4)$$

where X and Y are the morphogen concentrations; a, b, c, and d are rate constants; r is spatial position; and D_1 and D_2 are diffusion coefficients. Turing showed that with suitably chosen rate constants, initially nearly uniform concentrations of X and Y would develop into spatially periodic patterns. He supposed that these patterns, or prepatterns, would then trigger the differentiation of tissues into the observed pattern. Simulations of these, or related, systems of equations show that periodic spots or stripes of morphogen concentration are produced, although stripes are generally formed on narrow cylinders (Bard, 1981; Murray, 1981; Lyons and Harrison, 1991). A comparison of Eq. (12.3) with Eq. (12.4) makes the differences between the two mechanisms clear. Turing assumed that the actions of X and Y on themselves and each other were strictly local, which is appropriate for chemical reactions, while Eq. (12.3) assumes "action at a distance" as subsumed by the lateral interaction terms. Lateral interactions in the Turing model are mediated by the actual movement, via diffusion, of X and Y through the tissue, whereas in Eq. (12.3) lateral movement of synapses does not occur.

The lateral interaction model can also be implemented as a cellular automaton. This is a class of model in which pattern elements have discrete states at discrete times and simple neighborhood rules are used to determine state transitions at each time step (Wolfram, 1984). The stripe-forming behavior of Eq. (12.3) can be adequately approximated by the following procedure: Let n take only values of $+1$ or -1 on a discrete 2-D lattice indexed by (i, j). At each time step, calculate $a_{i,j} = \sum_{k,l} n_{i+k,j+l} w_{k,l}$, where w is also Mexican hat in form (e.g., $w_{k,l} = 1$ for $0 \leq |k, l| \leq d_E$; $w_{k,l} = -1$ for $d_E < |k, l| \leq d_I$, where the distances d_E and d_I define the spread of excitation and inhibition, respectively). The values of $n_{i,j}$ are then updated according to the sign of $a_{i,j}$. That is, if $a_{i,j} > 0$, $n_{i,j}$ is set to 1; if $a_{i,j} < 0$, $n_{i,j}$ is set to -1. It may also be noted that this system is isomorphic with a suitably connected Hopfield net (Hopfield, 1982). Thus ocular dominance stripe patterns are stable (ground) states of a Hopfield net with short-range excitatory and long-range inhibitory connections.

Orientation Columns

The approach of the previous section can be extended to orientation columns (Swindale, 1982). Here we assume that the quantity that is emerging in the map is an orientation, represented by a vector $\mathbf{z} = (a, b)$. In order to ensure that angles differing by 180 degrees are equivalent, we adopt the convention that the orientation represented by $\mathbf{z}$ is $\theta = 0.5\ \text{atan}(b/a)$. It is intuitive to regard $|\mathbf{z}|$ as a measure of the strength of orientation tuning; i.e., regions of cortex with narrow orientation tuning will have large values of $|\mathbf{z}|$, while regions of weak or disorganized selectivity will have small values of $|\mathbf{z}|$. As before, the change in $\mathbf{z}$ is assumed to be determined by many different processes, the net outcome of which is to make nearby regions develop similar preferences and to make regions further away develop dissimilar preferences. Thus, we write

$$\frac{d\mathbf{z}}{dt} = \mathbf{z}^* w_{\mathbf{z}} f(\mathbf{z}), \tag{12.5}$$

where $w_{\mathbf{z}}$ is a Mexican hat function describing the lateral interactions and $f(\mathbf{z})$ is used to keep $\mathbf{z}$ within bounds, e.g., $f(\mathbf{z}) = (1 - \mathbf{z})$. Solutions to Eq. (12.5), with values of $\mathbf{z}$ initially small and randomly distributed, are a good match to real orientation column patterns with respect to periodicity and singularity distribution (figure 12.5b).

A combined model for ocular dominance and orientation columns has been proposed (Swindale, 1992) based on the idea of competition for feature selectivity. It is supposed that development of one feature might be slowed down in regions where the other is emerging most rapidly and vice versa. The resulting model is able to reproduce the orthogonal pattern of the intersection of orientation domains with ocular dominance column borders as well as the tendency of singularities to lie in the centers of ocular dominance stripes (Erwin et al., 1995; Swindale, 1996).

12.4.4 Low-Dimensional Feature Map Models

In this section, we retain the simplifying idea of formulating a model in terms of low-level features, rather than the patterns of neural activity that correspond to them, and we return to the framework of the competitive Hebbian models discussed in section 12.4.2. We assume that the input to the cortex is a feature vector $\mathbf{v}$, which is a point in a feature space $\mathbf{S}^N$, as discussed in section 12.1.2. For a combined map of retinotopy, ocular dominance, and orientation, we might let $\mathbf{v} = \{x, y, n, a, b\}$, where x and y represent position in retinal space, n represents ocular dominance, and a and b represent the two components of the orientation vector (using the conventions described in the section on orientation columns). The cortex is represented by a 2-D sheet of points indexed by i, and $\mathbf{w}_i$ represents the feature vector currently mapped to point i. We can picture the sheet as folded inside $\mathbf{S}$ in the manner suggested by figure 12.1. Remember that the Kohonen algorithm (see section 12.4.2) worked by taking a stimulus, finding the most responsive cortical point, and then modifying its connections and those of its neighbors in such a way as to make it more responsive to the stimulus in question. The low-dimensional version of the Kohonen algorithm works in the same way if we assume that the closer $\mathbf{w}_i$ is to $\mathbf{v}$, the stronger is the response of point i to $\mathbf{v}$. As before, i^* denotes the most responsive point, which is given by $\min|\mathbf{w}_i - \mathbf{v}|\ \forall i$. Points in the cortex are then moved toward $\mathbf{v}$ by an amount given by

$$\mathbf{w}_i(t+1) = \mathbf{w}_i(t) + \varepsilon[\mathbf{v} - \mathbf{w}_i(t)]h(i^*, i). \tag{12.6}$$

As before, ε is a growth rate and $h(i^*, i)$ is a neighborhood function that equals 1 for $i = i^*$ and that falls smoothly to zero with increasing distance between i and i^*. Initial values of $\mathbf{w}(t = 0)$ are typically assumed to be small and random, with the exception of retinotopic space, where a linear mapping with some

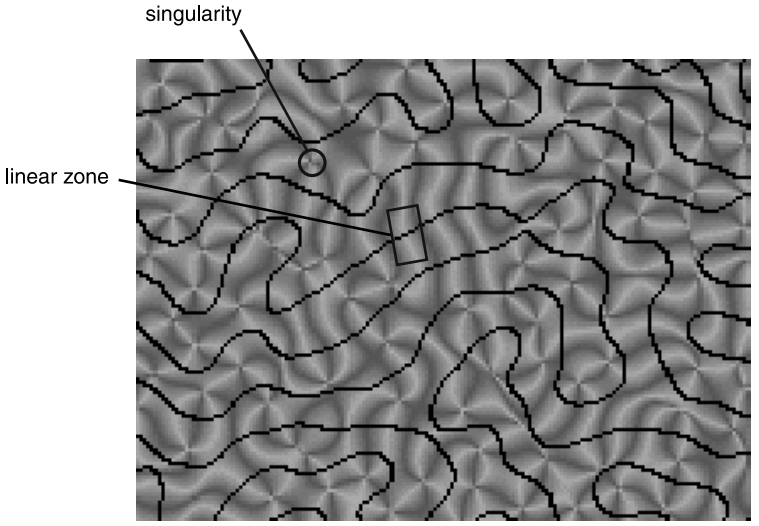

Figure 12.6
Combined feature map of orientation and ocular dominance produced by the low-dimensional Kohonen algorithm [Eq. (12.6)]. Dark lines mark the boundaries of the ocular dominance columns. Each gray level represents a unique orientation preference (for gray scale, see figure 12.3). An example of a singularity (circle) and a linear zone are shown (rectangle). Note the resemblance to the biological map shown in figure 12.3. (Figure provided by K. Obermayer; simulation details are given in Blasdel and Obermayer, 1994.)

specified amount of random scatter is usually assumed. At each time step, a new stimulus, typically chosen at random from a defined manifold within **S**, is presented and the procedure repeated until a stable, or nearly stable, mapping has been obtained.

Obermayer et al. (1991, 1992) used this algorithm as a model for visual cortex map formation. Despite the simplification involved, and the need to define a suitable scaling and metric for determining distances between points in **S**, the types of mappings obtained in the low- and high-dimensional instances are similar. For the complete case of retinotopy, ocular dominance, and orientation, the resulting maps capture the main features observed in the monkey, including periodic ocular dominance stripes, periodic iso-orientation domains, orientation singularities in the centers of ocular dominance stripes, and orthogonal crossings of iso-orientation domains and ocular dominance stripe borders (figure 12.6). The low-dimensional Kohonen algorithm has been applied to maps of direction preference (Swindale and Bauer, 1998). Mitchison and Swindale (1999) have studied the effects of making the learning rule in Eq. (12.6) more strictly Hebbian by making modification contingent on the receptive field of any cortical unit (not just the winning one) being sufficiently close to **v**.

It can be seen that the mappings produced by the Kohonen algorithm will tend to satisfy the continuity and completeness constraints discussed in section 12.1.2. That is, neighboring cortical points will tend to be close together in **S**, maximizing continuity, while for each **v** that is presented, there will generally

be a $\mathbf{w}_i$ that is close to $\mathbf{v}$, satisfying the completeness (or coverage) requirement. (This is really an empirical observation because there is no analytical proof that the Kohonen algorithm maximizes any combination of these properties.) If the set of stimuli that is used is finite and less than the number of cortical points, then of course a solution to the mapping can always be found where there is a matching point i for every $\mathbf{v}$, i.e., for which $|\mathbf{w}_i - \mathbf{v}| = 0$. Note that finding the solution that minimizes the distances in $\mathbf{S}$ between adjacent cortical points (i.e., that maximizes continuity in the mapping) is the same as solving the traveling salesman problem. In this problem, a route must be found in which neighboring points on the route (cities) are close together, minimizing the total distance traveled, and the route must pass through every city. The only difference is that solutions to the conventional traveling salesman problem are mappings from a 1-D route to a 2-D surface, whereas in the cortex the mapping is from a 2-D surface to an N-dimensional space. This means that any algorithm that can be shown to produce good solutions to the traveling salesman problem can be applied to the problem of cortical map formation, although of course not all algorithms may be equally suitable and the interpretation of the algorithms' behavior in biological terms may be difficult.

One such algorithm, the elastic net algorithm (Durbin and Willshaw, 1987; see also chapter 11), does have a plausible biological basis (Willshaw and Von der Malsburg, 1979) and has been applied successfully to cortical map formation (Durbin and Mitchison, 1990; Goodhill and Willshaw, 1990; Erwin et al., 1995; Goodhill and Cimponeriu, 2000). In this model (figure 12.7), a finite number of stimuli $\mathbf{v}_j$ $(j = 1 \ldots M)$ exert attractive "forces" and pull nearby cortical receptive fields $\mathbf{w}_i$ toward them. This part of the model can be considered to be Hebbian, inasmuch as Hebbian rules have the effect of making

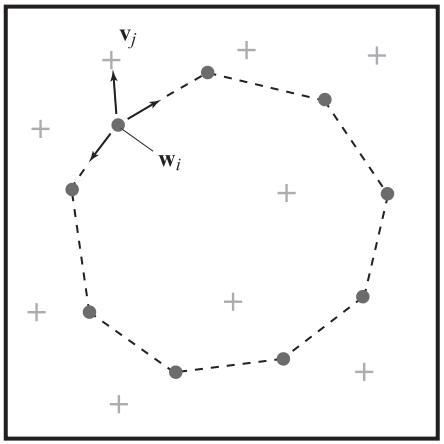

Figure 12.7
Illustration of how the elastic net algorithm works. For simplicity, a 1-D cortex (circles) is showed mapping to a 2-D stimulus space. The diagram shows the "forces" acting on one cortical point $\mathbf{w}_i$. Stimuli (crosses) exert attractive forces whose effects fall off as a Gaussian function of distance. The stimulus that has the strongest effect on the movement of $\mathbf{w}_i$ is thus the one closest to it, $\mathbf{v}_j$; other, more distant stimuli exert weaker attractive forces. Elastic forces are proportional to the distance between neighboring cortical points; in this case, they oppose the motion of $\mathbf{w}_i$ toward $\mathbf{v}_j$.

the receptive fields of cells change so that they are more responsive to those input patterns to which they are already most responsive. Units that are neighbors in the cortex are also connected by "elastic" and are thereby subjected to forces that tend to enforce continuity in the mapping. The learning rule is

$$\mathbf{w}_i(t+1) = \mathbf{w}_i(t) + \alpha \sum_j F_{i,j}(\mathbf{v}_j - \mathbf{w}_i) + \beta K \sum_{k \in N_i} (\mathbf{w}_k - \mathbf{w}_i), \tag{12.7}$$

where α and β are constants scaling the Hebbian and elastic forces, respectively, and the summation in the second term is over the nearest neighbors k of point

i. The "force" $F_{i,j}$ exerted by stimulus j on cortical point i is a Gaussian function of the distance between $\mathbf{w}_i$ and $\mathbf{v}_j$ (i.e., the response, assuming Gaussian receptive fields) normalized by the sum of the responses from all other cortical units, i.e.,

$$F_{i,j} = \frac{\exp(-|\mathbf{v}_j - \mathbf{w}_i|^2/2K^2)}{\sum_p \exp(-|\mathbf{v}_j - \mathbf{w}_p|^2/2K^2)}. \tag{12.8}$$

Normalization ensures that stimuli that are far away from any cortical point do not get ignored and exert forces that are as large as those exerted by stimuli that are closer to cortical units. The parameter K scales the receptive field sizes, i.e., the distance in $\mathbf{S}$ over which stimuli exert attractive forces. This distance may be large initially, and it is typically reduced in size (annealing) in order to make individual cortical points approach specific stimuli.

This algorithm provides good solutions to the traveling salesman problem (Durbin and Willshaw, 1987) and, like the low-dimensional Kohonen algorithm, produces realistic maps of orientation and ocular dominance columns.

To sum up this section, the advantages of feature-based algorithms are that they start with very general principles (continuity and completeness) and show how these lead to detailed predictions about the layout of cortical maps. They are computationally simple, which means that large areas of cortex can be modeled and that it is easy to run many simulations. Finally, the models work well, judged by results. The disadvantages are that it is difficult to reformulate the algorithms in terms of nuts-and-bolts models of neural development, which makes it hard to extend them by incorporating new biological details. Nor, arguably, do the models give insights into the significance of many of the biological mechanisms known to be involved. Setting up the models requires the definition of a suitable stimulus manifold, which generally has to be done in an ad hoc way. In addition, lateral interactions, such as the cortical neighborhood function, cannot be justified by reference to known biological interactions.

12.4.5 Models Based on Sprouting and Neurotrophic Interactions

Many models impose rigid constraints on the types of growth that afferent connections can exhibit. Growth may be restricted to within a predetermined arbor function; synapses may not be allowed to reappear once a connection strength has gone to zero in any area; and connections are generally assumed to be formed in response to scalar (i.e., the local concentration of a trophic molecule) rather than gradient (i.e., movement of a growth cone up or down a concentration gradient) growth cues. Real axons, of course, behave in more complex ways, with new connections formed by sprouting, often in response to chemical gradient cues, and by neurotrophic factors released by target neurons. Competition for neurotrophic support is thought to be one of the main mechanisms governing the selective elimination of connections during development in many parts of the nervous system (Purves, 1988; Van Ooyen and Willshaw, 1999; Van Ooyen, 2001; see also chapter 10), and there is evidence that this is true in the visual cortex as well. It is obviously of interest to explore models that explicitly represent such features. Elliott et al. (1996) have incorporated sprouting and retraction in a model of ocular dominance column formation with the specific intention of avoiding normalization rules. They do this by first assuming that two sheets of LGN neurons project to a cortex, with every LGN cell making connections within a retinotopically defined square region of cortex. Denoting the activity of the ith or jth LGN connection by σ_i or $\sigma_j \in \{1, -1\}$, the following energy function is defined:

$$E = -\frac{1}{2}\sum_{i,j} \sigma_i \sigma_j h(i, j), \tag{12.9}$$

where $h(i, j)$ is a coupling, or cortical neighborhood, function that has the value 1 when connections i and j are on the same cortical cell or are on nearest-neighbor cells, and that is zero otherwise. The LGN activity patterns are assumed to be randomly positioned circles of activity confined to one or the other sheet. Connections are assumed to either exist, in which case they have a nominal strength of 1, or to not exist, which is signaled by a strength value of zero and their absence from the summation in Eq. (12.9). They can appear or disappear from within an arbor region, with changes that decrease the value of E generally being favored over changes that increase it. Elliott et al. tested a ''relocation'' model in which fixed upper and lower limits were imposed on the number of connections per cell, and a connection was allowed to move to a new location within its parent arbor, provided the number of connections per cell remained within the limits. An ''interchange'' model was also tested; this required that each cell received a fixed number of connections and that a pair of axons was allowed to exchange connections provided they were within each other's arbor regions. In both types of model, change is accepted with a probability $1/(1 + e^{\Delta E/T})$, where T is a temperature, and updates are repeated many times for many different LGN activation patterns. Examples in which $T = 0$, and in which T was slowly reduced during development, were studied.

The advantage of this model is that it is formally simple and has obvious links with physical systems such as spin glasses (Elliott and Shadbolt, 1998a). An interpretation is possible in which the contribution of a pair of connections to E is inversely related to the level of neurotrophic support (low E means high neurotrophin levels and vice versa), while the neighborhood function h represents, in a crude way, the release and diffusion of neurotrophin molecules by postsynaptic cells through the tissue.

More complex models, which explicitly model activity-dependent release of neurotrophins, have recently been proposed (Harris et al., 1997; Elliott and Shadbolt, 1998b, 1999). These models avoid the use of synaptic weight normalization rules, are able to explain the effects of neurotrophin injections (section 12.2.2), and can explain segregation in the presence of positive interocular correlations. In the model by Elliott and Shadbolt (1998b, 1999), the general anatomical framework is similar to that just described. Neurotrophins are released by postsynaptic neurons in amounts proportional to their activity, diffuse through the tissue, and are taken up by afferent axons in amounts that are proportional to their activity and the number of synapses present in their arbor. Afferents are able to make or lose connections in proportion to a recent time average of the neurotrophin uptake. The LGN activity patterns are either correlated random noise (section 12.3.1) (Elliott and Shadbolt, 1998b) or simulated retinal waves (Elliott and Shadbolt, 1999). Like Goodhill (1993), Elliott and Shadbolt predict that a decrease in interocular correlations should increase column spacing (although, as discussed in section 12.4.2, the evidence for this effect is ambiguous). In addition, the model predicts that changes in the spatial extent of within-eye correlations should affect periodicity. This prediction may be testable by pharmacologically manipulating retinal activity at early stages of development in ferrets.

12.4.6 The BCM Modification Rule

Many of the models discussed in this chapter use a simple Hebbian rule for strengthening connections, while weakening occurs in a nonspecific way as a result of normalizing synaptic strengths onto neurons.

Nevertheless, it has been realized for a long time that there is a logical complement to Hebb's principle, namely, that when a presynaptic axon is active but fails to cause the postsynaptic cell to fire, its connection strength is weakened (Stent, 1973). Such behavior has been demonstrated physiologically and is known as long-term depression. Bienenstock, Cooper, and Munro (1982) developed this idea mathematically into what is now generally known as the BCM rule for synaptic modification. Considering only the inputs to a single cell, the learning rule for the jth connection carrying an input v_j to a cortical cell with an activity c is

$$s_j(t+1) = (1-\varepsilon)s_j(t) + \varphi[c(t)]v_j, \tag{12.10}$$

where $\varphi(c)$ is a function that is negative when the postsynaptic response c is below a modification threshold θ_M and positive when it is greater than θ_M. The small constant ε produces a constant decay in synaptic strength in the absence of any input or output activity; its effects can be ignored in the present context. In the absence of any kind of normalization, this rule has the undesirable feature that there can easily be situations in which all the inputs either increase or decrease without limit, leading to a loss of any kind of feature selectivity. This problem can be avoided by the use of a sliding modification threshold in which θ_M varies as a function of the recent average activity of the cell, $\bar{c}$. The time period over which this average is taken is not critical. The dependence of θ_M on $\bar{c}$ is important, however, and it can be shown that for stable feature selectivity to be guaranteed, θ_M must increase and decrease more rapidly, relative to a fixed value c_0, than does $\bar{c}$. This is achieved if

$$\theta_M(\bar{c}) = (\bar{c}/c_0)^p \bar{c}, \tag{12.11}$$

where $p > 1$ is an integer. With this rule, emergence of feature selectivity, for example, to oriented patterns of activity in a 2-D array of inputs, is guaranteed whatever the initial values of s_j.

Although a simulation of the development of a 1-D layout of orientation selectivity was presented by Bienenstock et al. (1982), the BCM rule does not appear to have been incorporated into any 2-D model of visual cortex map formation. This is a pity because it has the clear advantage of avoiding the complex normalization rules employed in many models. There is also a significant body of evidence supporting the idea of a synaptic modification threshold (Bear and Rittenhouse, 1999). For example, the finding that monocular deprivation produced by lid suture produces a bigger shift in ocular dominance than does silencing one eye's inputs by TTX injections (Rittenhouse et al., 1999) can be explained by a BCM mechanism (Blais et al., 1999).

12.5 Discussion

This chapter has given an overview of a variety of models of visual cortex development (additional coverage of many of the topics discussed here can be found in Erwin et al., 1995; Miller, 1995; Swindale, 1996). Almost all of these models assume as a framework a two-layer (LGN + cortex) feedforward net, spatially correlated patterns of activity in the input layer, and Hebbian modification. Lateral cortical interactions, mediated either by neural connections or by diffusion of plasticity-modifying substances, are universally assumed. Competition among inputs is enforced more variably, e.g., by the use of subtractive or divisive normalization rules, by competition for trophic support, or by the use of learning rules that allow for synaptic weakening as well as strengthening to occur (this is implicit in the low-dimensional Kohonen and elastic net models and explicit in the BCM learning rule).

Some of the models include retinotopic refinement as part of the mechanism, although in others a rigid retinotopy is built in. All of the ocular dominance column models are able to explain the formation of the basic striped pattern of ocular dominance, while individual models are able to account for the effects of experimental manipulations such as monocular deprivation, silencing of retinal inputs, and neurotrophin injections. Of the models for orientation columns, and those for the joint formation of ocular dominance and orientation columns, feature-based and competitive Hebbian models appear to perform better than linear correlation-based models. Despite these undoubted successes, there is probably no single model that is able to account for all of the phenomena listed in sections 12.2.2 and 12.2.3.

Future Modeling Studies

Piepenbrock and Obermayer (2000) have introduced a model that is a blend of linear Hebbian learning (see the section on the model of Miller et al.) and the nonlinear Kohonen mechanism (section 12.4.2). This is done by normalizing the net response of the cortex to each stimulus and by introducing a nonlinearity (parameterized by a constant β) in the cortical response. Low values of β approximate the linear case, where development is driven by the second-order statistics of the input patterns (i.e., the correlation functions C^{LL} etc.), while large values approximate the competitive case, where only a single small region of cortex responds to any stimulus. In this case, learning is essentially feature based, i.e., driven by higher-order statistics in the input patterns.

Several new experimental findings seem relevant to the further development of new models. Studies in the hippocampus (Bi and Poo, 1998) and cortex (Markram et al., 1997) show that the relative timing of pre- and postsynaptic spikes is a critical factor controlling connection strengths. If an action potential follows a synaptic input within about 20 ms, the input is potentiated; if the action potential precedes the presynaptic input by up to 20 ms, the input is weakened. The implications of this finding from a modeling perspective have only just begun to be explored. For example, timing, since it allows for weakening, can be used in place of normalization to mediate competition among inputs (Song et al., 2000) and stabilize postsynaptic firing rates (Kempter et al., 2001). Future models of visual cortex development will probably have to take into account the possibility that two inputs may be positively correlated at one temporal interval but negatively correlated at another. Feedback connections from cortex to LGN may alter this correlation structure (Weliky and Katz, 1999) and therefore may need to be incorporated.

It is possible that models of the formation of ocular dominance columns may need even more radical revision, since recent work has shown that segregation will occur in the ferret even after removal of both retinas (Crowley and Katz, 1999) and is present almost as soon as thalamic afferents have grown into layer IV (Crowley and Katz, 2000) (see also chapter 10). While it is possible that spontaneous activity in deafferented LGN layers might drive segregation, it is conceivable that it might be driven instead by eye-specific chemical labels (perhaps through mechanisms of the type discussed in section 12.4.3). While it is hard to see how chemical diffusion mechanisms might be extended to account for the formation of more complex properties such as orientation selectivity, different kinds of mechanisms might be involved in the formation of the two types of column.

Future Experimental Studies

Although the problems being addressed here are developmental, much remains to be learned about the

organization of visual cortical maps in adult animals, and these details are likely to be crucial in constraining developmental models. Current techniques (e.g., optical imaging and functional magnetic resonance imaging) average the signals from large numbers of neurons and across different layers, and it would be useful to have much more detailed information, at the single neuron level, about what receptive field properties are mapped, how they are mapped, and in which layers. Simultaneous extracellular recording of single-cell receptive field properties in groups of neurons whose spatial locations are precisely known (micromapping), relative to each other and to a coarser-scale map determined by optical imaging from the same region of tissue, may be the best approach to this problem. Knowing what happens at the very earliest, prenatal, stages of development is also likely to be crucial. The lack of knowledge about the spatiotemporal patterns of neural activity in the retina, LGN, and cortex during the periods when ocular dominance and orientation columns are forming is probably the weakest component of all models. Finally, little is known about the fine-scale structure of the retinotopic map in the adult visual cortex, or about the mechanisms that establish and refine retinotopy in young animals. Answers to these questions would be of great value to modelers.

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